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Impact and cost-effectiveness of rotavirus vaccination in Palestine: examining a change from ROTARIX to ROTAVAC vaccines

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Context

- 14 out of 22 countries in the WHO Eastern Mediterranean Region (EMRO) have introduced rotavirus vaccine.
- Palestine is the first country to use ROTAVAC in routine immunization outside of India:

2016 Start of the program with support from RVF, introduced ROTARIX

2017 97% coverage after a year of implementation

2018 Switch to ROTAVAC

2019 Transfer of procurement's financial responsibility

- Switch provides an opportunity for empiric assessment of different rotavirus vaccine programmatic characteristics.

Product characteristics

ROTARIX

2 doses
1-dose plastic tube
Shelf-life 24 months at 2 to 8°C

Dose quantity 1.5 ml
Cold chain volume 17.1 cm^3 per dose
or 34.2 cm^3 per FIC

ROTAVAC

3 doses
5-dose vial and dropper
Shelf-life 60 months at -20°C /
6 months at 2 to 8°C post thaw
Dose quantity 0.5 ml
Cold chain volume 4.2 cm^3 per dose
or 12.6 cm^3 per FIC

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Objective of the analysis

To assess impact and cost-effectiveness of rotavirus vaccination in Palestine, specifically evaluating the economic implications of the change from ROTARIX to ROTAVAC.

Analysis overview

Study population: children < 5 years of age

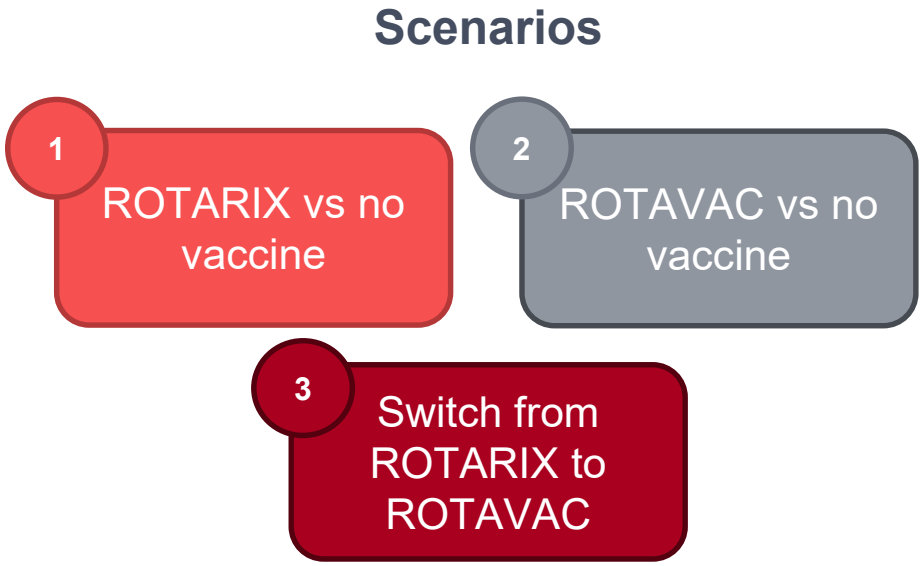
10 cohorts, from 2016 to 2025

Health system and societal perspectives

Results reported in 2018 US$

Discount rate 3%

3 scenarios evaluated



Model Outputs

Health impact (averted cases, visits, hospitalizations, deaths and DALYs)

Averted healthcare costs

Costs of vaccination program

Incremental cost-effectiveness ratio

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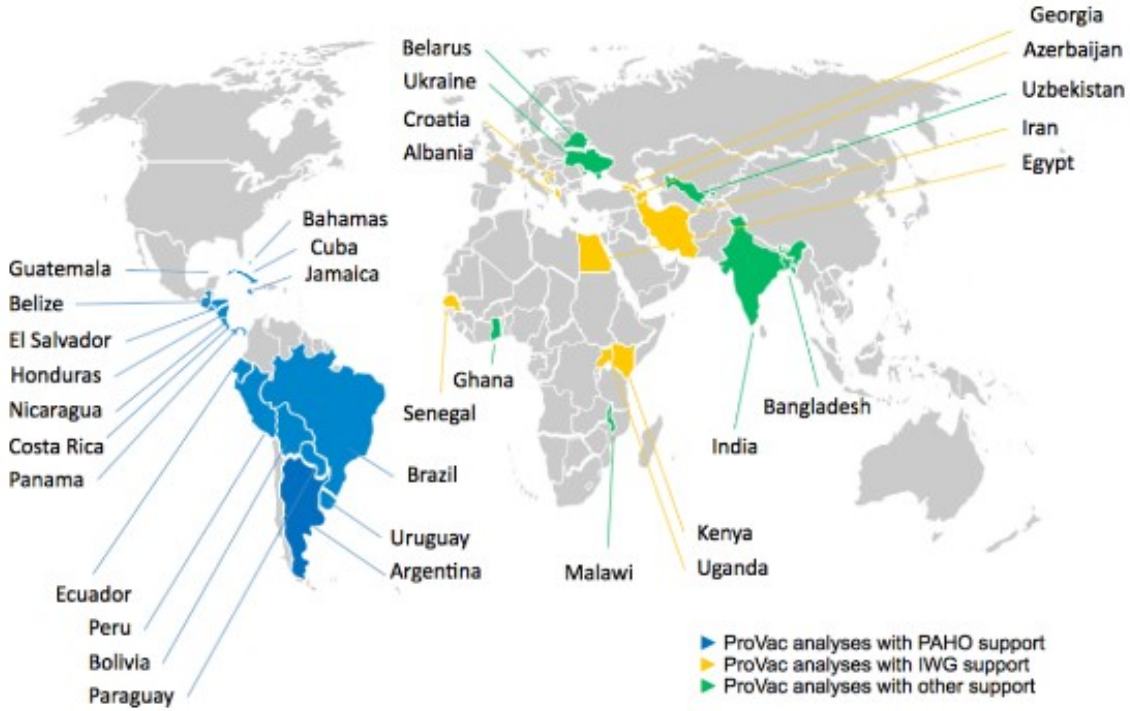
UNIVAC model

UNIVAC is a single, universal vaccine impact and cost-effectiveness decision support model developed in a standardized, accessible Excel-based interface.

Developed as a follow-on to PAHO's TRIVAC model, which has been used in many studies worldwide.

Allows economic evaluation of:

- Rotavirus vaccine
- PCV vaccine
- Hib vaccine
- HPV vaccine
- Men ACYW vaccine
- Others



ProVac Tools for evidence-based decisions on new vaccines

Pan American Health Organization
Regional Office of the World Health Organization

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

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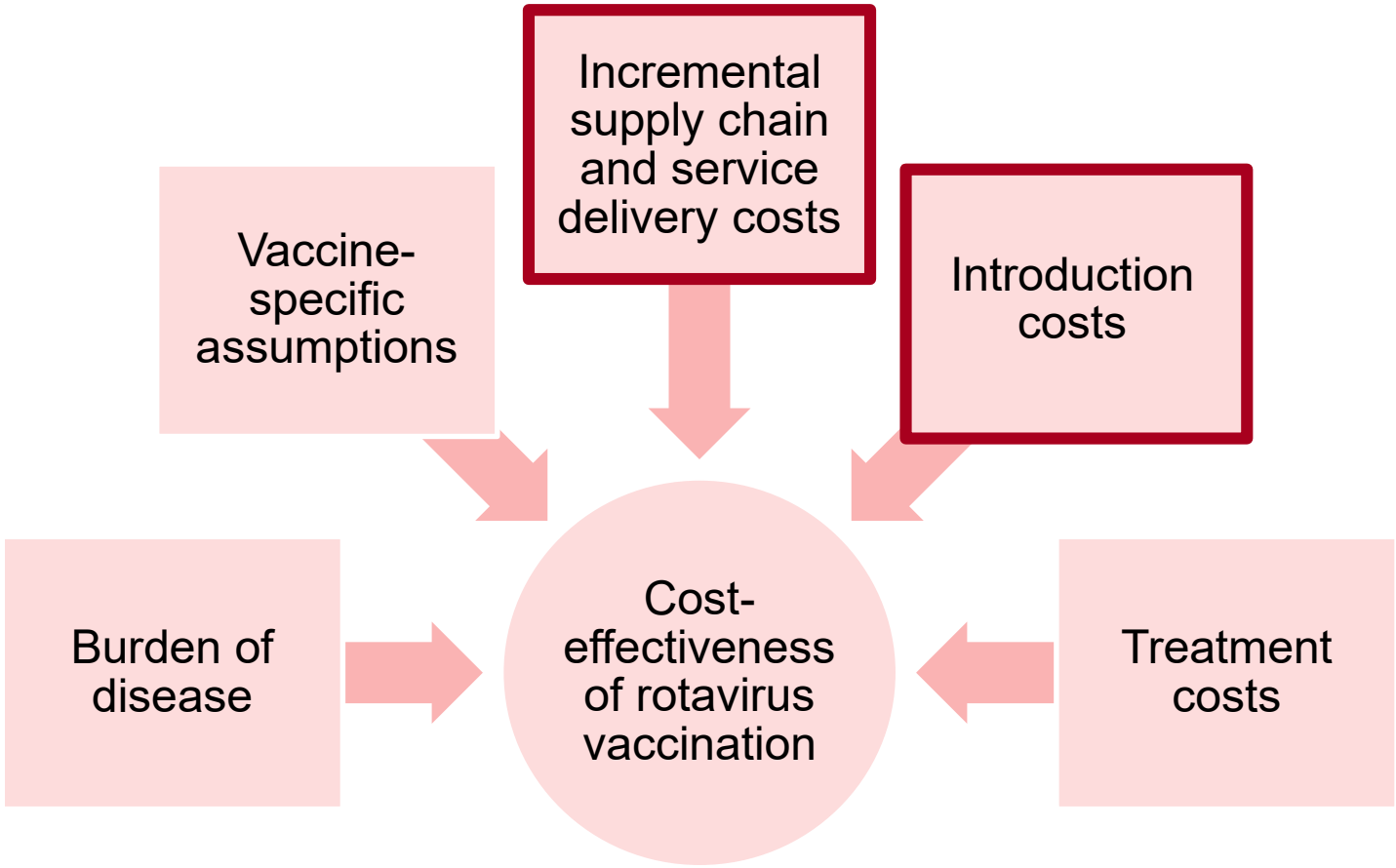
Data inputs


Incremental supply chain and service delivery costs
Vaccine-specific assumptions
Introduction costs
Burden of disease
Cost-effectiveness of rotavirus vaccination
Treatment costs

Vaccine assumptions

Dosing schedule based on Pentavalent vaccine

Price per dose: $4

Wastage: 0.3%

International delivery charges: $0.026 per dose

In-country delivery charges from airport to the Central Store: $0.029 per dose

Price per dose: $1 ($0.85 - $1.5)

Wastage: 4.7%

International delivery charges: $0.025 per dose

In-country delivery charges from airport to the Central Store: $0.017 per dose

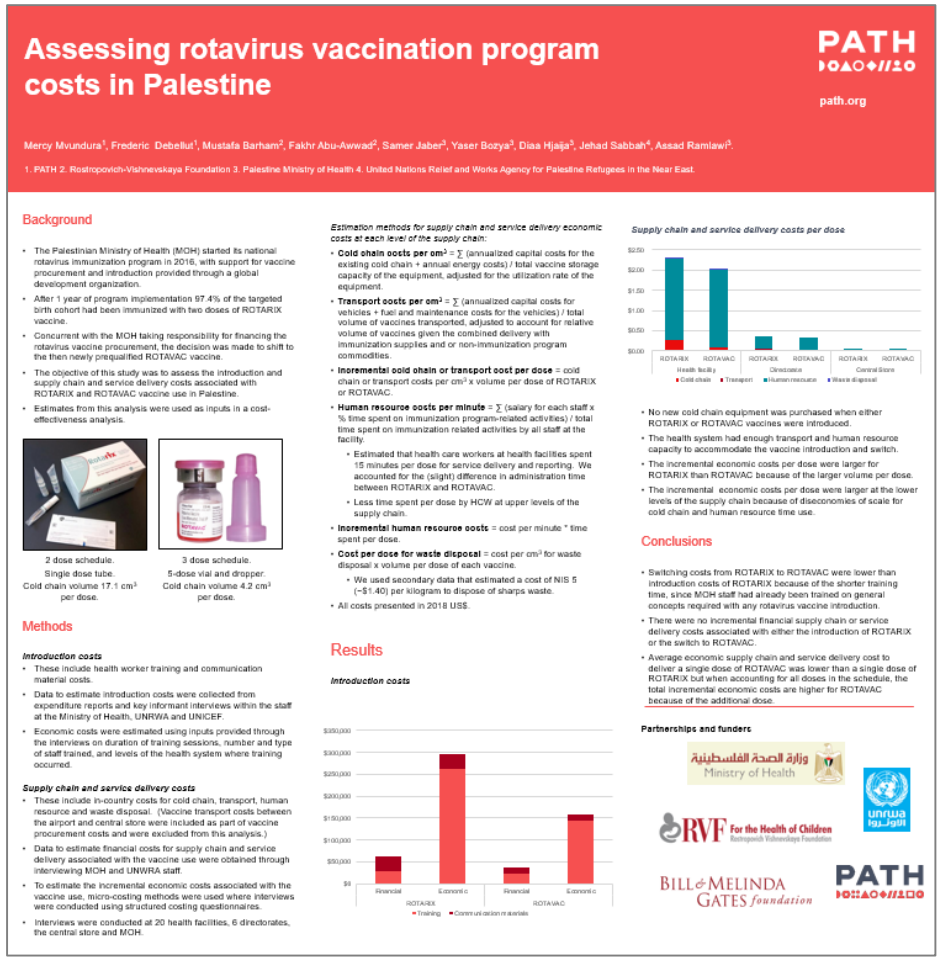
Vaccine program costs

Introduction costs were collected for both vaccines but initial intro costs with ROTARIX were applied to both vaccines in the analysis to allow for a fair comparison.

Total economic intro costs were close to $300,000

Supply chain and service delivery cost data were collected in 20 health facilities, 6 districts and at the central store

Overall the supply chain and service delivery costs per dose are $0.33 cheaper with ROTAVAC



Assessing rotavirus vaccination program costs in Palestine

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Mercy Mvundura[1], Frederic Debellut[1], Mustafa Barham[2], Fakhr Abu-Awwad[2], Samer Jaber[3], Yaser Bozya[3], Diaa Hjaija[3], Jehad Sabbah[4], Assad Ramlawi[3].

1. PATH 2. Rostropovich-Vishnevskaya Foundation 3. Palestine Ministry of Health 4. United Nations Relief and Works Agency for Palestine Refugees in the Near East.

Background

- The Palestinian Ministry of Health (MOH) started its national rotavirus immunization program in 2016, with support for vaccine procurement and introduction provided through a global development organization.
- After 1 year of program implementation 97.4% of the targeted birth cohort had been immunized with two doses of ROTARIX vaccine.
- Concurrent with the MOH taking responsibility for financing the rotavirus vaccine procurement, the decision was made to shift to the then newly prequalified ROTAVAC vaccine.
- The objective of this study was to assess the introduction and supply chain and service delivery costs associated with ROTARIX and ROTAVAC vaccine use in Palestine.
- Estimates from this analysis were used as inputs in a cost-effectiveness analysis.

2 dose schedule.
Single dose tube.
Cold chain volume 17.1 cm^3 per dose.

3 dose schedule.
5-dose vial and dropper.
Cold chain volume 4.2 cm^3 per dose.

Methods

Introduction costs

- These include health worker training and communication material costs.
- Data to estimate introduction costs were collected from expenditure reports and key informant interviews within the staff at the Ministry of Health, UNRWA and UNICEF.
- Economic costs were estimated using inputs provided through the interviews on duration of training sessions, number and type of staff trained, and levels of the health system where training occurred.

Supply chain and service delivery costs

- These include in-country costs for cold chain, transport, human resource and waste disposal. (Vaccine transport costs between the airport and central store were included as part of vaccine procurement costs and were excluded from this analysis.)
- Data to estimate financial costs for supply chain and service delivery associated with the vaccine use were obtained through interviewing MOH and UNWRA staff.
- To estimate the incremental economic costs associated with the vaccine use, micro-costing methods were used where interviews were conducted using structured costing questionnaires.
- Interviews were conducted at 20 health facilities, 6 directorates, the central store and MOH.

Estimation methods for supply chain and service delivery economic costs at each level of the supply chain:

- **Cold chain costs per cm^3** = ∑ (annualized capital costs for the existing cold chain + annual energy costs) / total vaccine storage capacity of the equipment, adjusted for the utilization rate of the equipment.
- **Transport costs per cm^3** = ∑ (annualized capital costs for vehicles + fuel and maintenance costs for the vehicles) / total volume of vaccines transported, adjusted to account for relative volume of vaccines given the combined delivery with immunization supplies and or non-immunization program commodities.
- **Incremental cold chain or transport cost per dose** = cold chain or transport costs per cm^3 x volume per dose of ROTARIX or ROTAVAC.
- **Human resource costs per minute** = ∑ (salary for each staff x % time spent on immunization program-related activities) / total time spent on immunization related activities by all staff at the facility.
  - Estimated that health care workers at health facilities spent 15 minutes per dose for service delivery and reporting. We accounted for the (slight) difference in administration time between ROTARIX and ROTAVAC.
  - Less time spent per dose by HCW at upper levels of the supply chain.
- **Incremental human resource costs** = cost per minute * time spent per dose.
- **Cost per dose for waste disposal** = cost per cm^3 for waste disposal x volume per dose of each vaccine.
  - We used secondary data that estimated a cost of NIS 5 (~$1.40) per kilogram to dispose of sharps waste.
- All costs presented in 2018 US$.

Results

Introduction costs

Supply chain and service delivery costs per dose

- No new cold chain equipment was purchased when either ROTARIX or ROTAVAC vaccines were introduced.
- The health system had enough transport and human resource capacity to accommodate the vaccine introduction and switch.
- The incremental economic costs per dose were larger for ROTARIX than ROTAVAC because of the larger volume per dose.
- The incremental economic costs per dose were larger at the lower levels of the supply chain because of diseconomies of scale for cold chain and human resource time use.

Conclusions

- Switching costs from ROTARIX to ROTAVAC were lower than introduction costs of ROTARIX because of the shorter training time, since MOH staff had already been trained on general concepts required with any rotavirus vaccine introduction.
- There were no incremental financial supply chain or service delivery costs associated with either the introduction of ROTARIX or the switch to ROTAVAC.
- Average economic supply chain and service delivery cost to deliver a single dose of ROTAVAC was lower than a single dose of ROTARIX but when accounting for all doses in the schedule, the total incremental economic costs are higher for ROTAVAC because of the additional dose.

Partnerships and funders

وزارة الصحة الفلسطينية Ministry of Health

RVF For the Health of Children

UNRWA

BILL & MELINDA GATES foundation

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Estimated health outcomes

(10 cohorts vaccinated over 2016 – 2025)

	Without vaccine	With vaccine	Averted
RVGE Cases	782,660	213,380	569,280
RVGE Outpatient visits	414,027	112,879	301,148
RVGE Hospital admissions	111,209	30,320	80,889
RVGE Deaths	140	38	102
DALYs *(discounted)*	5,380	1,459	3,921

DALY = Disability Adjusted Life Years (sum of years of life lost to deaths and of years of life lost to disability)

Estimated costs

(10 cohorts vaccinated over 2016-2025)

	Without vaccine	With vaccine	Averted
RVGE Treatment costs **(Health system perspective)**	$19.4M	$5.3M	$14.1M
RVGE Households costs	$11M	$3M	$8M
RVGE Total costs **(Societal perspective)**	$30.4M	$8.2M	$22.2M

	With ROTARIX $4/dose	With ROTAVAC $0.85/dose	With ROTAVAC $1/dose (base case)	With ROTAVAC $1.5/dose
Vaccine program costs	$19M	$14.8M	$15.5M	$17.8M

All figures are discounted and expressed in million US$

Incremental cost-effectiveness ratio (ICER)

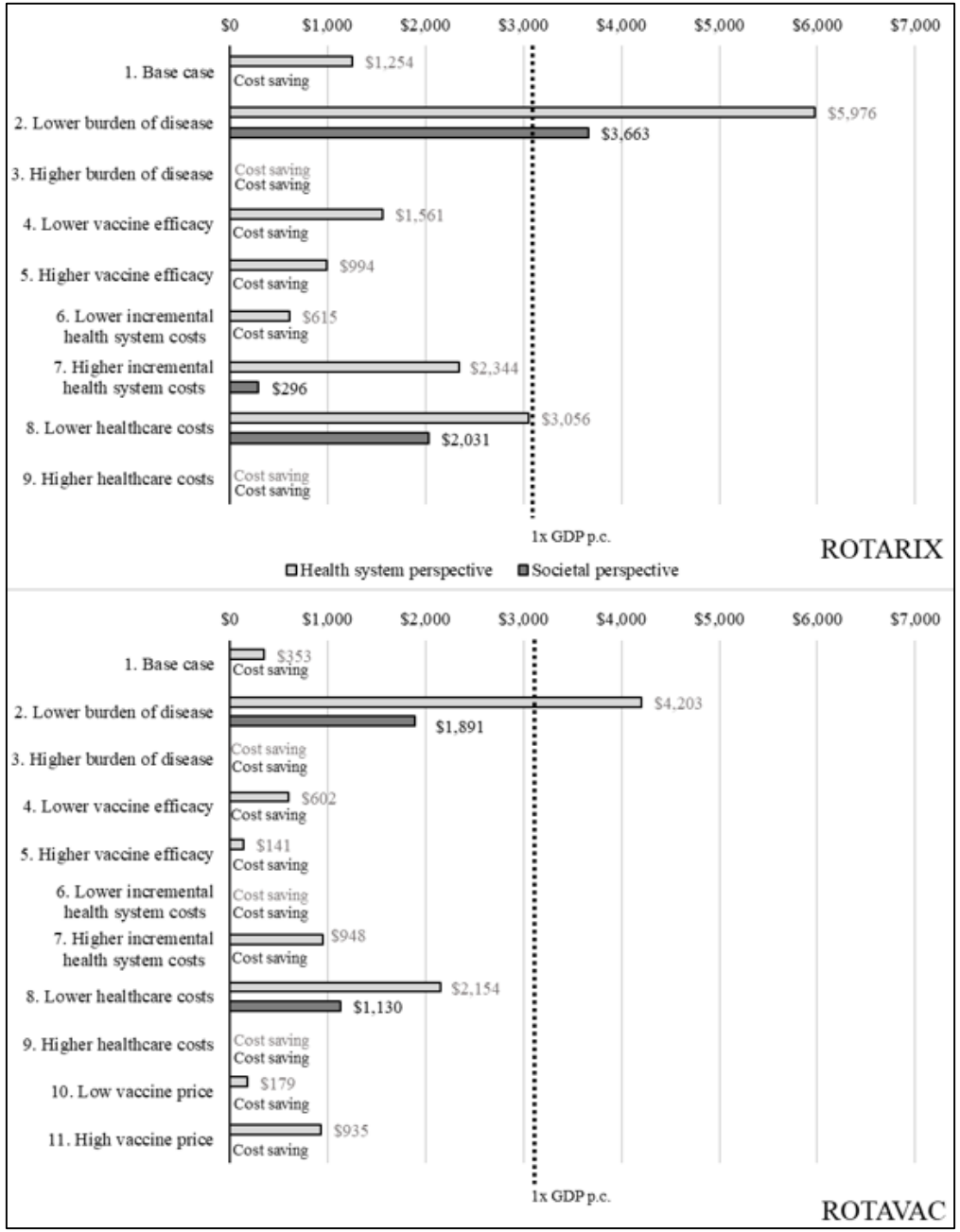
	Health system perspective	Societal perspective
ROTARIX vs. no vaccination	$1,254	Cost-saving
ROTAVAC* vs. no vaccination	$353	Cost-saving
ROTAVAC* vs. ROTARIX	Cost-saving	Cost-saving

* At $1 per dose

- ICERs are usually compared to a specific willingness-to-pay (WTP) threshold.
- In Palestine, the practice has been to use 1 times GDP per capita as a WTP threshold.
- Palestine's GDP per capita was $3,095 in 2017 US$ (World Bank).
- Both vaccines are likely cost-effective interventions under these criteria, with an economic advantage for ROTAVAC.

Scenario analysis

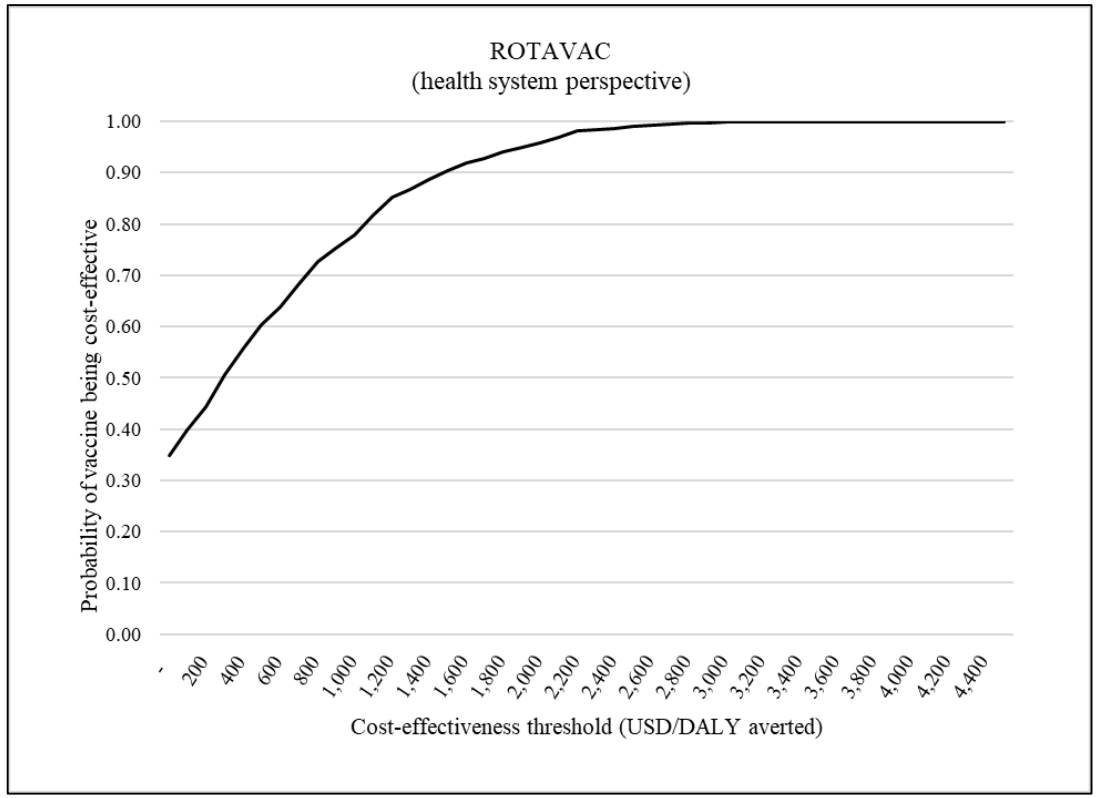
- Scenario analysis focused on disease burden, vaccine efficacy, health system costs, healthcare costs, and price for ROTAVAC.
- Most scenarios yield an ICER below the threshold.
- With ROTAVAC, results are above threshold only for the low-disease burden, health system perspective scenario.



Probabilistic sensitivity analysis

- 1,000 runs, ROTAVAC only
- ROTAVAC has 80% chance to be cost-effective at a WTP threshold of $1,100.
- ROTAVAC has 90% chance to be cost-effective at a WTP threshold of $1,500.

Cost-effectiveness acceptability curve



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Conclusion

- Rotavirus vaccination is a **cost-effective intervention in Palestine**, averting a share of the rotavirus burden and generating savings on healthcare costs, for the health system and for households.
- ROTAVAC presents an **economic advantage** over ROTARIX. Shifting from ROTARIX to ROTAVAC was a **cost-saving option** because of:
  - Lower vaccine price per dose.
  - Smaller cold chain volume and, hence, lower supply chain costs.
- Lower supply chain costs are driven by cold chain costs at the health facility level as well as in-country transportation costs.
- The assumed similar efficacy of both vaccines may be confirmed by the ongoing epidemiological surveillance.
- Countries should systematically assess the different products available and their characteristics as part of their decision-making process.

Study collaborators and funding source

Mercy Mvundura - PATH

Samer Jaber - Palestinian Ministry of Health

Yaser Bouzya - Palestinian Ministry of Health

Jehad Sabbah - United Nations Relief and Works Agency for Palestine Refugees in the Middle East

Mustafa Barham - Rostropovich-Vishnevskaya Foundation

Fakhr Abu-Awwad - Rostropovich-Vishnevskaya Foundation

Diaa Hjaija - Palestinian Ministry of Health

Assad Ramlawi - Palestinian Ministry of Health

Andy Clark - LSHTM

Clint Pecenka – PATH

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Thank you!


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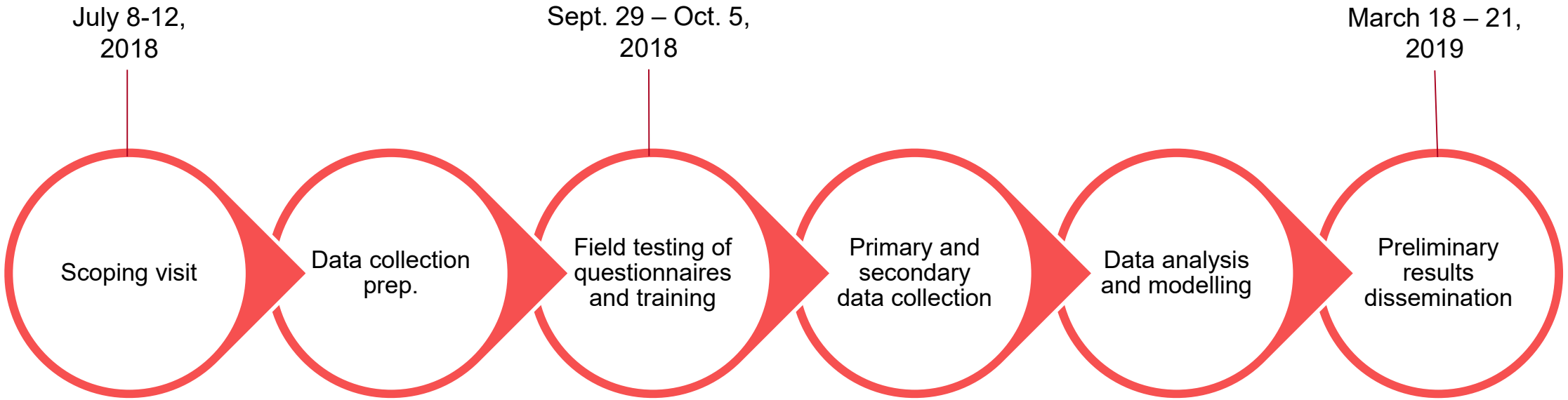
Process overview



- Stakeholder engagement
- Scope of the analysis
- Approach to modelling
- UNIVAC orientation

- Available local data
- Identification of data sources
- Development of questionnaires
- Secondary data collection

- Field testing and adaptation
- Training on questionnaires and data collection
- Modelling of treatment costs

- Supply chain and service delivery data collection in HF, HD, and CS
- Secondary data collection (introduction costs and vaccine procurement)
- Surveillance data

- Discussion on disease burden modelling
- Supply chain and service delivery cost data analysis
- Conducting cost effectiveness analysis
- Scenario analysis

- Presentation and discussion of results with the MoH (PMD, PHC, EPI)
- Deputy Ministry of Health
- UNRWA
- Local WHO
- RVF

HF = Health Facilities, HD = Health Directorate, CS = Central Store

Burden of disease

Annual incidence per 100,000 among U5 before vaccine introduction			
	Base	**Low**	**High**
Overall RVGE incidence[1]	10,000	7,000	14,000
RVGE non severe cases[2]	8,224	6,160	11,373
RVGE non severe visits[3]	4,350	3,259	6,016
RVGE severe cases[2]	1,776	839	2,627
RVGE severe visits[3]	939.5	444	1,390
RVGE severe hospitalizations[4]	1,421	555	2,102
Severe RVGE deaths[5]	2.03	0.84	4.88

1. Global RVGE incidence as reported by Bilcke et al in their systematic review and meta-analysis including 21 studies worldwide. Commonly use for RV disease burden modelling.

2. Non-severe and severe RVGE cases are differentiated using another systematic review and meta-analysis by Fisher Walker et al. which gives proportion of RV in severe diarrhea episodes per WHO region (using EMRO here)

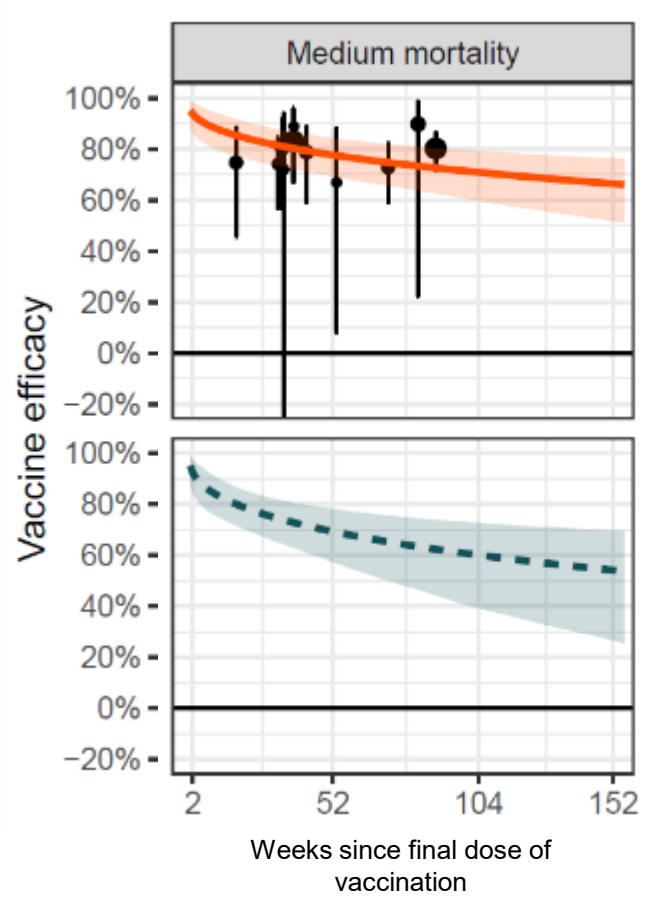
3. Using the Palestine MICS 2014: treatment seeking rate in case of diarrhea 52.9%

4. Assuming a larger proportion of severe cases would seek treatment or be referred to hospitals: 80%

5. Median value of 3 sources of data estimating RV related death per country (MCEE, IHME and WHO CDC)

Vaccine efficacy and waning

- Vaccine efficacy and waning based on data from 8 published randomized controlled trials in medium U5 mortality settings
  - 91% vaccine efficacy after 2 doses
  - 58% vaccine efficacy after 1 dose
  - Waning
- Assuming similar efficacy of ROTARIX and ROTAVAC
- With ROTAVAC, model assumes full protection after 2nd dose but 3rd dose is required



Introduction costs

ROTARIX introduction costs applied to both vaccines

	West Bank and Gaza
Financial costs	**$61,398**
Training	$27,511
Communication materials	$33,887
Economic costs	**$296,263**
Training	$262,376
Communication materials	$33,887

Treatment costs

- Direct medical costs were modelled using a study estimating unit costs of public hospitals and primary healthcare centers in Palestine[1] and local protocol and costs for laboratory tests and drugs.
- Non-medical (household) costs include meals, transportation for child and caregiver.
- Indirect cost corresponds to loss of productivity for caregiver.

	Health system perspective (Direct medical costs)	Direct non-medical cost	Indirect cost	Societal perspective (Direct med. costs + direct non-med. costs + indirect costs)
Treatment cost for RVGE inpatient care	$173.85	$28.04	$35.59	$237.48
Treatment cost for RVGE outpatient care	$7.63	$9.35	$4.45	$21.43

1. Younis M. Z. et al. Estimating the unit costs of public hospitals and primary healthcare centers. Int J Health Plann Mgmt (2012). https://doi.org/10.1002/hpm.2147

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Supply chain and service delivery costing

- Estimated the cost per dose for supply chain and service delivery for all vaccines used in the EPI program.
- Then used these data to estimate the incremental economic costs of adding rotavirus vaccine into the immunization schedule in Palestine.
- Costing data collection was done using structured costing questionnaires
- Data were collected from:
  - 10 health facilities in West Bank and 10 in Gaza
  - 5 directorates in West Bank and 1 in Gaza
  - The Central Store in Nablus

Incremental supply chain and service delivery economic cost estimates

	ROTARIX			ROTAVAC – 5 dose vials		
Cost category	Average	Min	Max	Average	Min	Max
Estimated incremental economic costs per dose at the health facility level						
Cold chain	$0.28	$0.04	$1.41	$0.07	$0.01	$0.34
Waste disposal		$0.02			$0.01	
Human resource	$2.01	$1.53	$2.32	$1.95	$1.47	$2.24
Total	$2.32	$1.59	$3.75	$2.02	$1.49	$2.59
Estimated incremental economic costs per dose at the directorate level						
Cold chain	$0.03	$0.0330	$0.05	$0.024	$0.006	$0.091
Transport	$0.022	$0.0138	$0.044	$0.005	$0.003	$0.011
Human resource	$0.30	$0.10	$0.50	$0.30	$0.10	$0.50
Total	$0.35	$0.15	$0.59	$0.33	$0.11	$0.60
Estimated incremental economic costs per dose at the central Store						
Cold chain	$0.0114	-	-	$0.012	-	-
Transport	$0.003	-	-	$0.003	-	-
Human resource	$0.01	-	-	$0.001	-	-
Total	$0.03	-	-	$0.016	-	-
Total incremental economic costs per dose costs at all levels of the supply chain						
Total	$2.695	$1.77	$4.37	$2.362	$1.62	$3.21

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Limitations

- Unable to use local data for disease burden modelling...
  - Incomplete set of data from HMIS for hospitals (year 2015)
  - Follow up of different age groups in Gaza between MoH (U3) and UNRWA (U5)
  - PHC visits for diarrhea in West bank were reported for all the population, except for 1 district
- …addressed through scenario analysis accounting for uncertainty around the data used
- Assumption around similar efficacy of ROTARIX and ROTAVAC may be confirmed or informed by the epidemiological study.
- Difficult to capture differences between West Bank and Gaza outside of supply chain and service delivery cost.
- Assumption that services are provided through the 10-year period without changes