IMMUNIZATION COSTING ACTION NETWORK

Supported by the Bill & Melinda Gates Foundation

The cost of delivering vaccines in low-and middle-income countries: Methods, findings and demonstration

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IHEA – BASEL, JULY 2019

PRESENTATION OUTLINE

- **Systematic Review**
  - Methods
  - Findings
- **Using the Immunization Delivery Cost Catalogue (IDCC)**
  - Web and Excel demonstrations
  - User feedback
  - The importance of comparable data
  - Real world example
  - Immunization delivery cost ranges
- **Questions, Discussion and Other Feedback**

Systematic Review: Methods

SYSTEMATIC REVIEW METHODS (1/2)

- **Systematic review to answer the question:**
  - What are the unit costs of delivering vaccines across different LMICs and through a variety of delivery strategies?

Health facility
Outreach/Mobile
Child health day/week
School
Campaign
Multiple Strategies

- **ICAN definition of delivery costs:**
  - Costs associated with delivering immunizations to target populations, exclusive of vaccine costs.
  - May include any or all of the following cost categories:

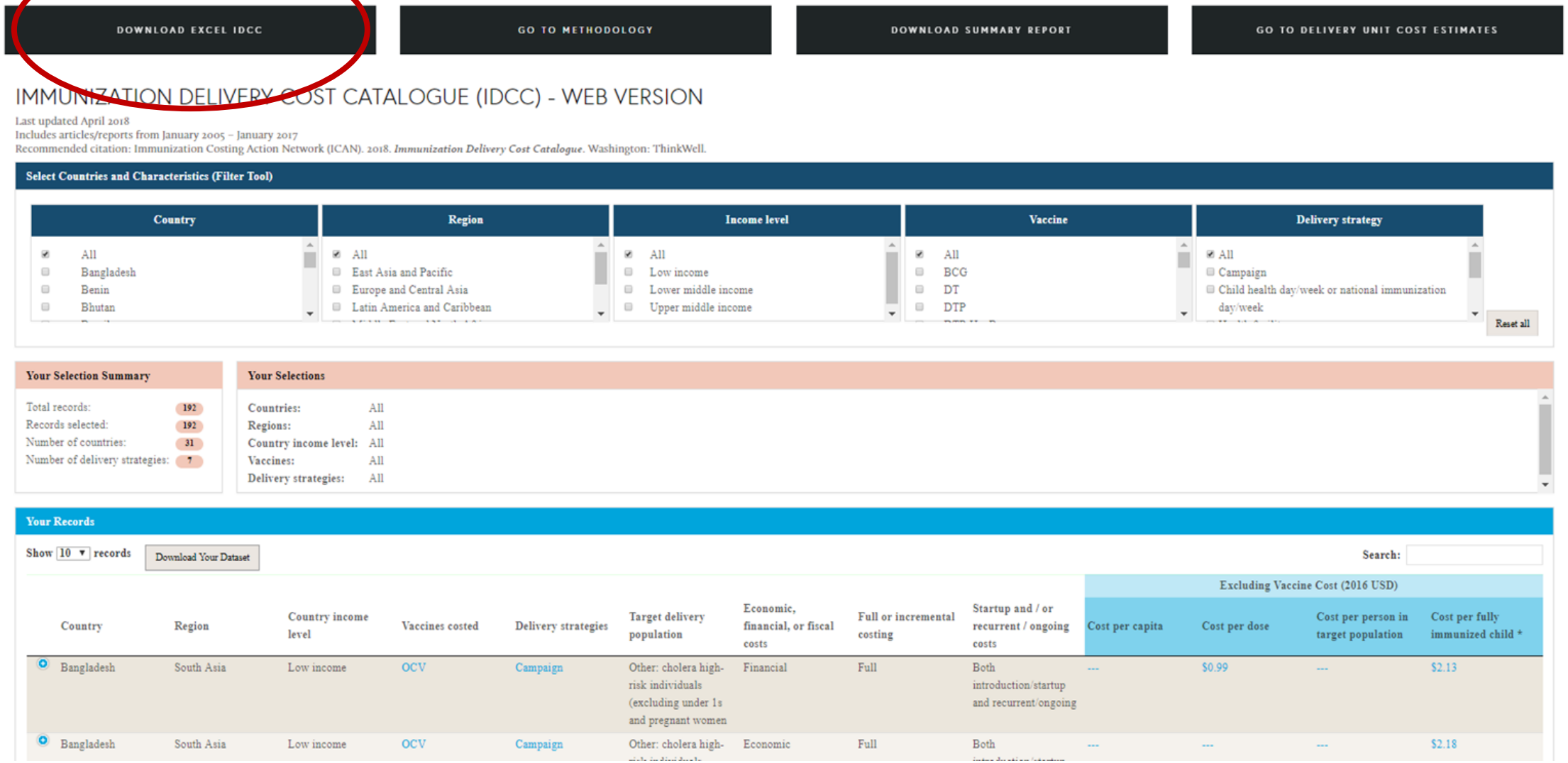
Paid and volunteer resources
Per diem and travel allowances
Cold chain equipment and overheads
Program management
Training and capacity building
Social mobilization and advocacy

SYSTEMATIC REVIEW METHODS (2/2)

- **Peer-reviewed articles/reports and grey literature:**
  - Over 15,000 articles/reports published between January 2005 and April 2018 considered, with 61 extracted
  - Over 400 immunization delivery unit costs – cost per dose, per capita, per full immunization of a vaccine, per fully immunized child, per person in the target population
- **Descriptive analysis and development of Immunization Delivery Cost Catalogue (IDCC):**
  - Standard presentation of existing unit cost data in 2016 USD, along with study methods, costing results, quality assessment, other contextual information
  - Quality assessment criteria in 3 categories: methodological rigor and reporting standards (8 items), uncertainty of results (3 items), and risk of bias and limitations (3 items)
  - Reclassification of author-reported costs into standard set of 14 cost categories
  - No interpolation
- **Initial release in April 2018, followed by refreshes in April 2019 and Sept 2019**

IMMUNIZATION DELIVERY COST CATALOGUE (IDCC)

AVAILABLE AT **IMMUNIZATIONECONOMICS.ORG/ICAN**



COMPANION PRODUCTS

AVAILABLE AT **IMMUNIZATIONECONOMICS.ORG/ICAN**

★★★★★★★★★★
★ Updated Versions to Be ★
★ Released in Fall 2019 ★
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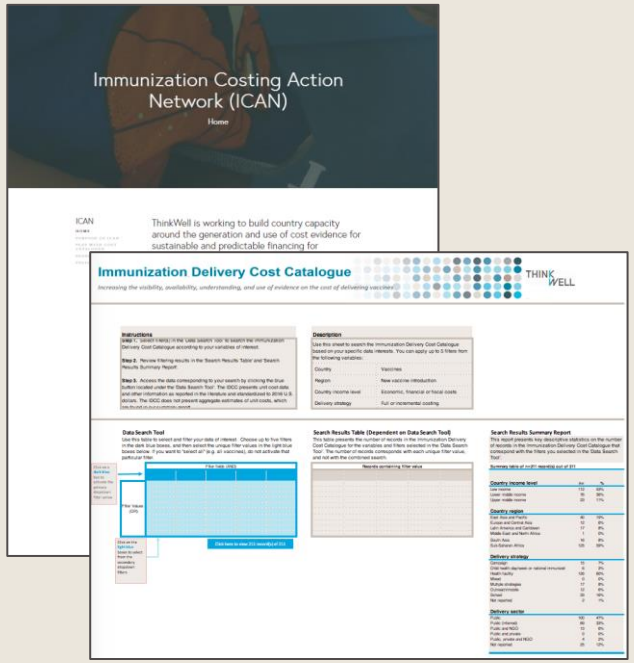
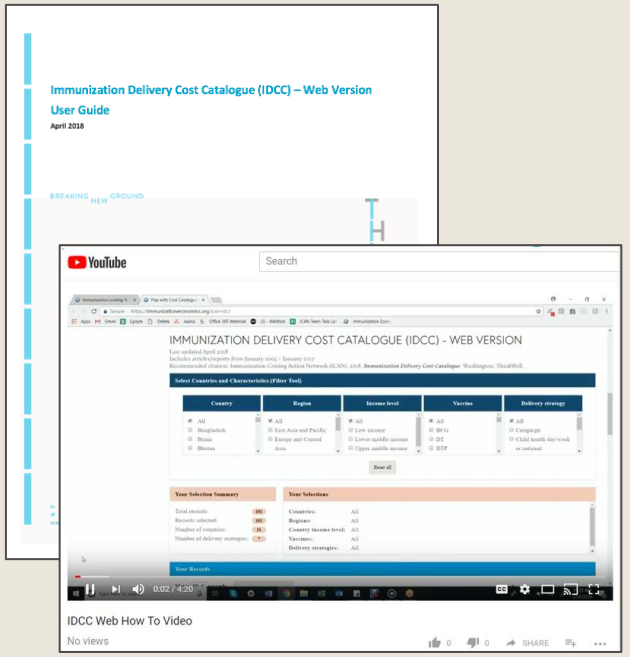
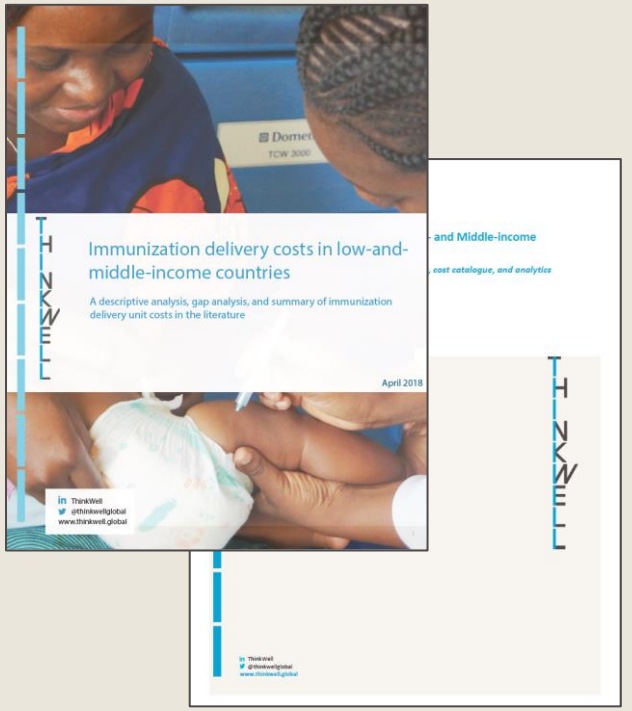
IDCC (web- and Excel tools)



User guides and how-to videos



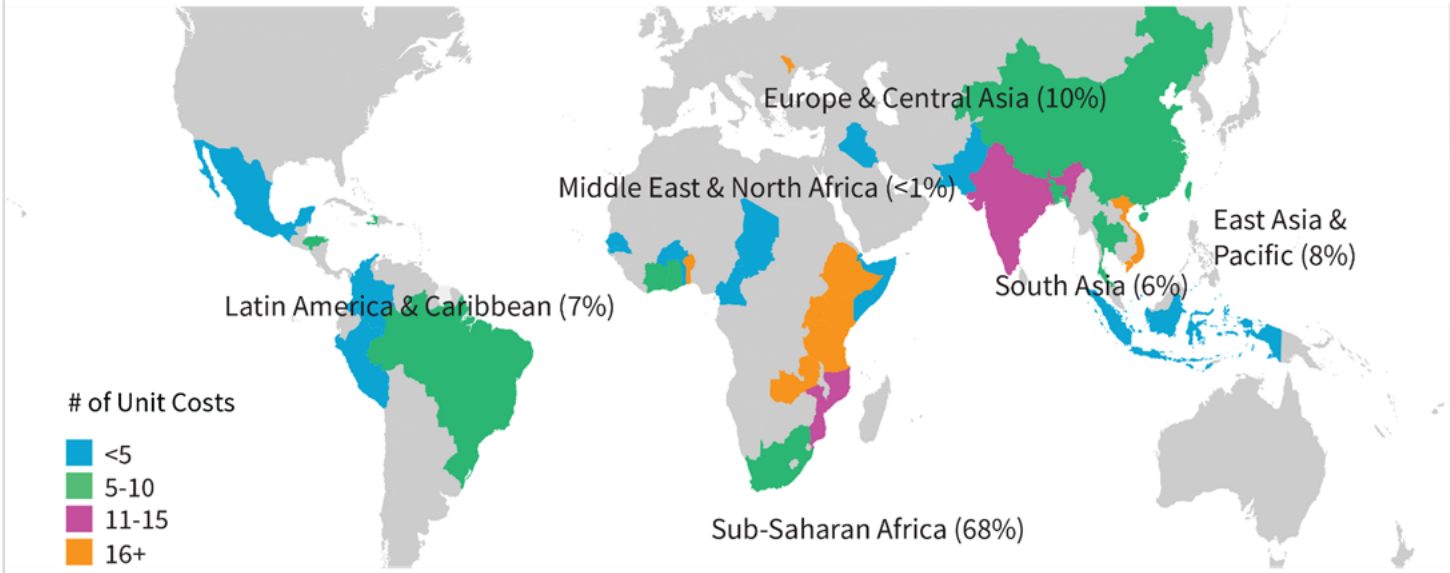
Analytic report and methodology note



Systematic Review:
Select findings

SYSTEMATIC REVIEW: MAJOR FINDINGS (1/5)

Geographic spread of data



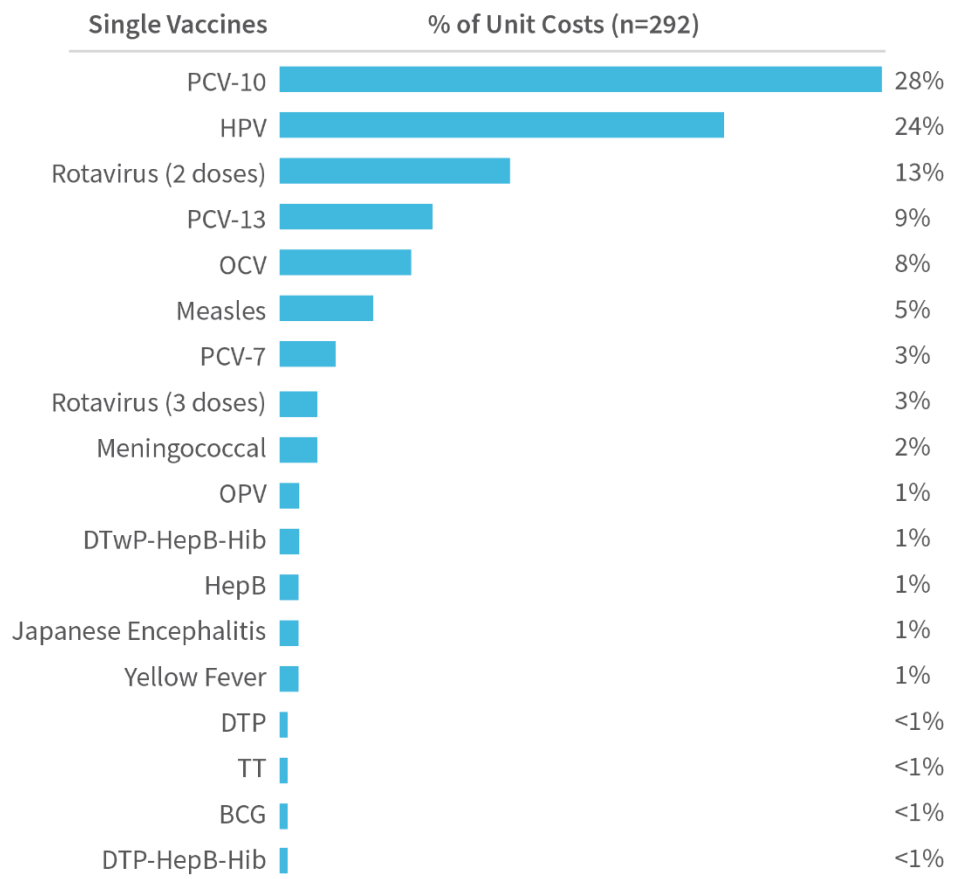
Country	Unit Costs (n)	Country	Unit Costs (n)
Uganda	89	China	6
Benin	42	Brazil	5
Moldova	42	Bhutan	5
Tanzania	35	Kenya	5
Rwanda	24	Cameroon	4
Zambia	23	Colombia	4
Vietnam	19	The Gambia	4
Ethiopia	14	Peru	4
India	14	Burkina Faso	2
Mozambique	11	Chad	2
Ghana	8	Indonesia	2
Cote d'Ivoire	7	Iraq	2
Honduras	7	Mexico	2
South Africa	6	Togo	2
Bangladesh	6	Pakistan	1
Haiti	6	Senegal	1
Thailand	6		

Distribution by Country Income Level

Low income (56%) | Lower middle income (36%) | Upper middle income (7%)

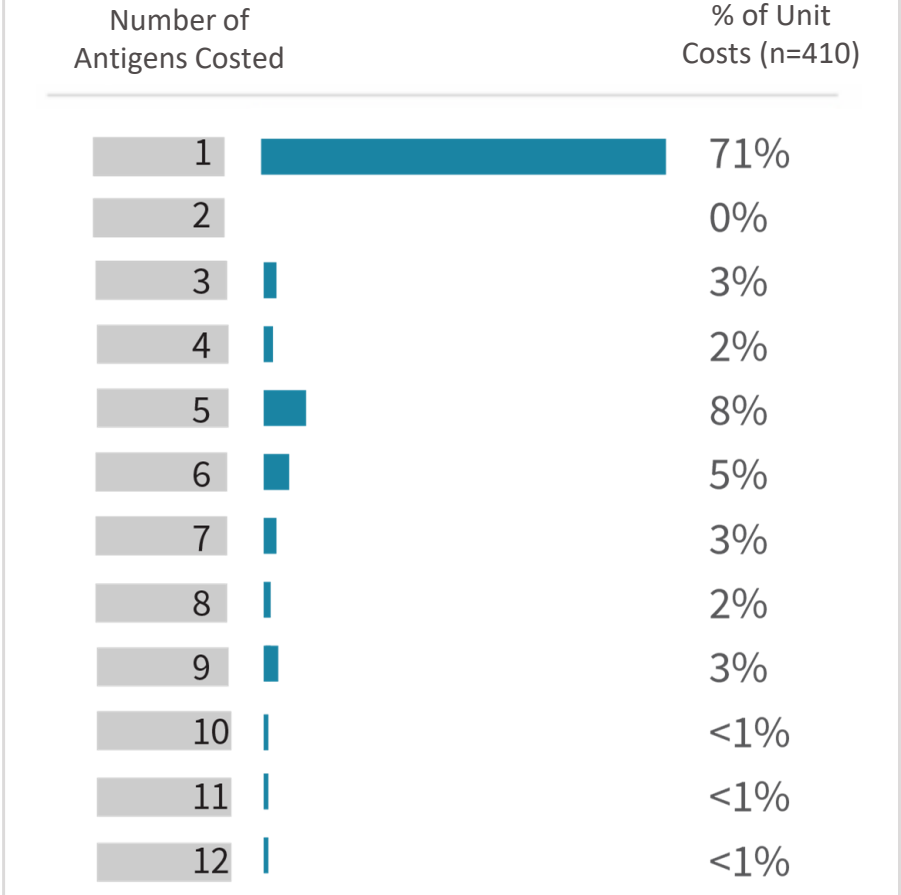
SYSTEMATIC REVIEW: MAJOR FINDINGS (2/5)

Vaccines represented



Note: Percentages do not sum to 100% due to rounding.

Multiple vaccines and vaccine schedules



SYSTEMATIC REVIEW: MAJOR FINDINGS (3/5)

New vaccine introductions

Nearly two-thirds of the unit costs relates to new vaccine introduction.

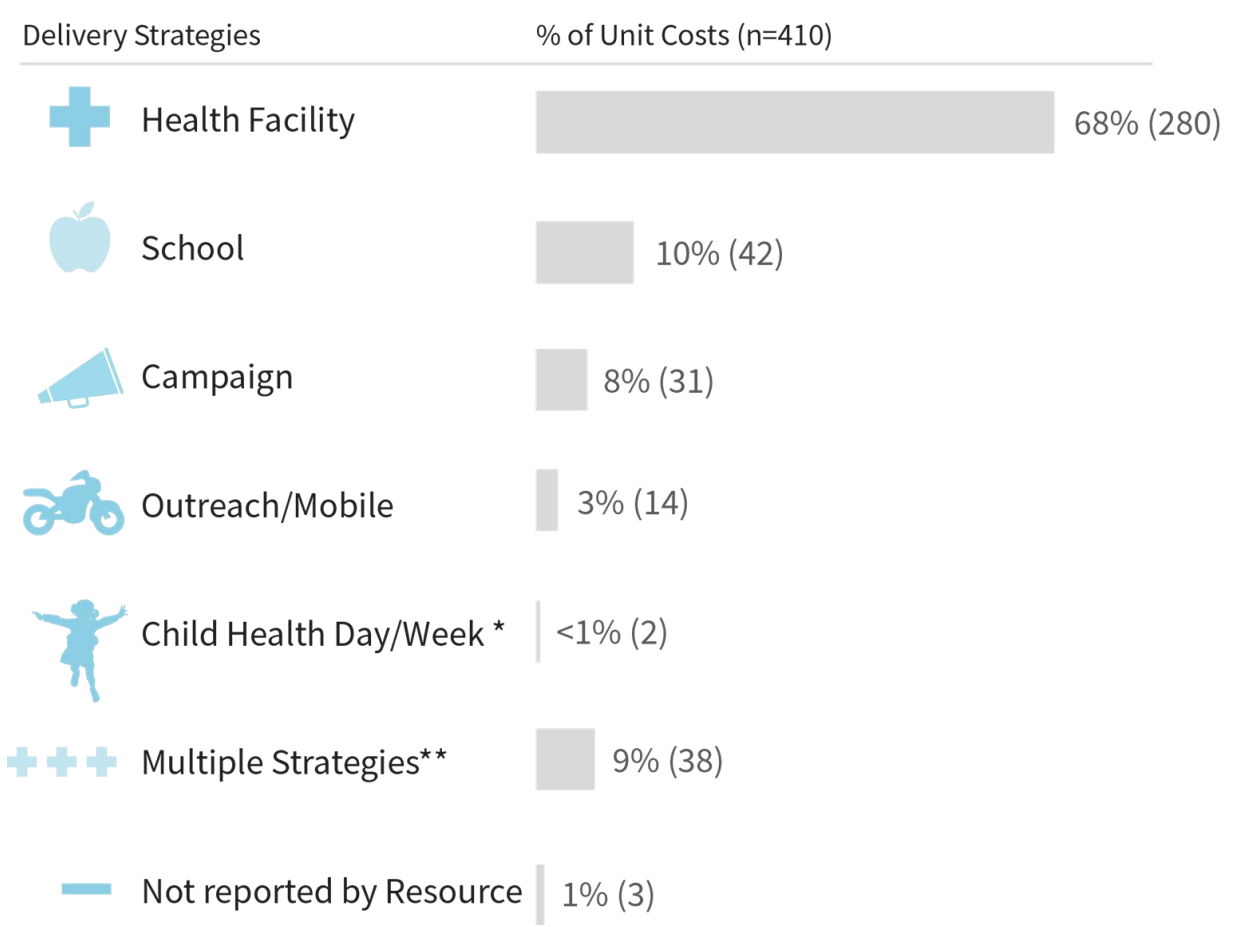
86% of unit costs on new vaccine introductions represent vaccines costed incrementally.

27% of unit costs on new vaccine introduction costed the introduction of HPV vaccine.

Vaccines	# of unit costs (Incremental)
HPV	69
PCV-10	80
Rotavirus (2 doses)	38
PCV-13	27
PCV-7	9
Rotavirus (3 doses)	8
Measles	5
Other vaccines with fewer than 5 unit costs	24
Total	**260**

SYSTEMATIC REVIEW: MAJOR FINDINGS (4/5)

Delivery strategies costed



* Includes child health days/weeks or national immunization days/weeks
** Refers to two or more delivery strategies in combination

SYSTEMATIC REVIEW: MAJOR FINDINGS (5/5)

Type of Costing	Type of Unit Costs Included				Total # of Unit Costs
	Economic	Financial	Fiscal	Not reported/ unclear	
Full costing	87 (21%)	29 (7%)	0 (0%)	18 (4%)	140 (34%)
Incremental costing	108 (26%)	84 (20%)	46 (11%)	8 (2%)	246 (60%)
Not reported	4 (1%)	20 (5%)	0 (0%)	0 (0%)	24 (6%)
Total Unit Costs	199 (49%)	133 (32%)	46 (11%)	26 (6%)	410 (100%)

Note: Percentages do not sum to 100% due to rounding.

Using the IDCC:
Web and Excel demonstrations

IMMUNIZATION DELIVERY COST CATALOGUE (IDCC)

Web demonstration
http://immunizationeconomics.org/ican

What are the delivery costs of HPV in Sub-Saharan Africa using non-facility-based delivery strategies?

IMMUNIZATION DELIVERY COST CATALOGUE (IDCC)

Excel demonstration

http://immunizationeconomics.org/ican

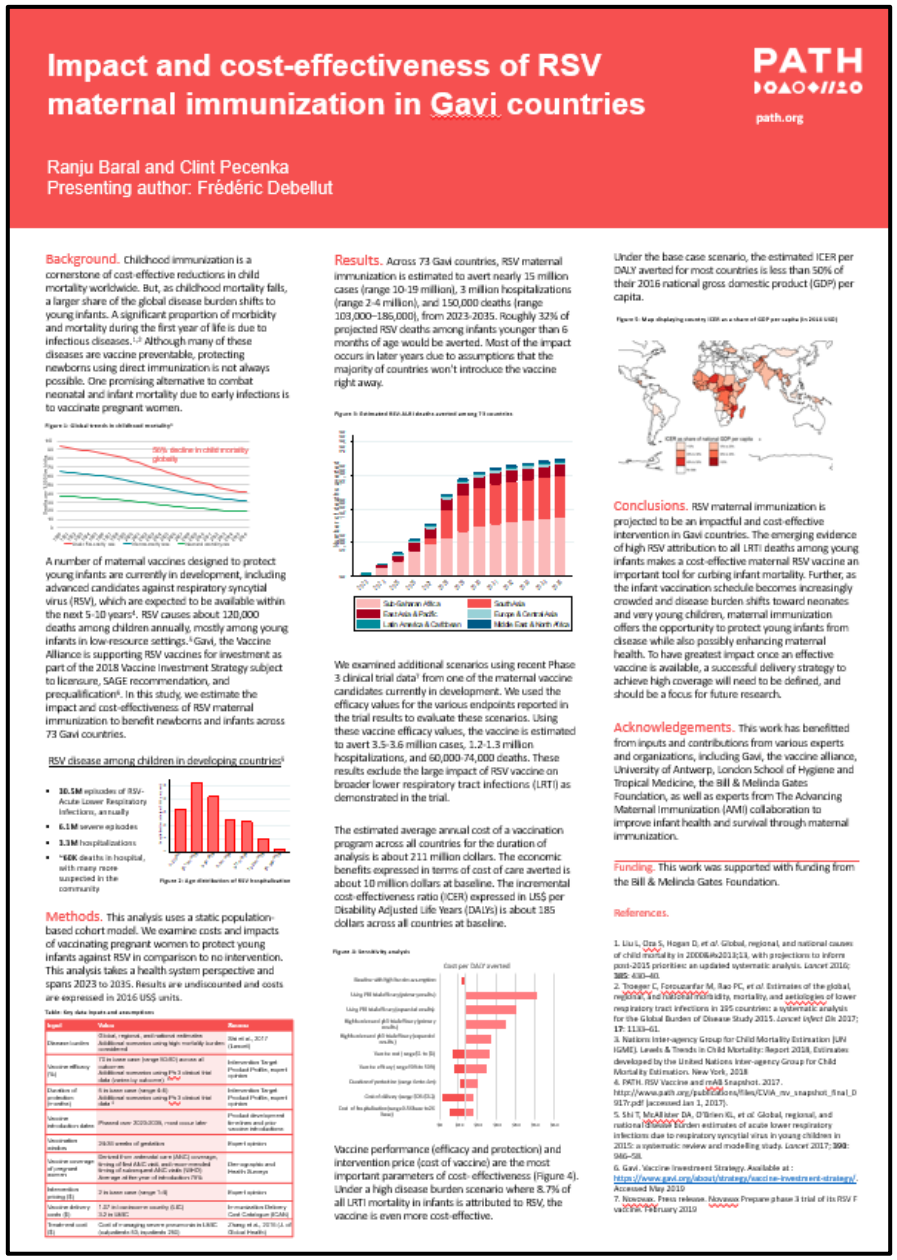
What are the delivery costs of outreach/ mobile delivery in East Asia and the Pacific?

User perspective: PATH's Center of Vaccine Innovation and Access

Lessons learned working with the IDCC

USER PERSPECTIVE

- **PATH's Health Economics and Outcomes Research team:**
  - Within the Center for Vaccine Innovation and Access
  - Conducts impact and cost effectiveness modelling, cost of illness and cost of delivery studies across a range of vaccines and vaccine-preventable diseases
- **Uses to-date:**
  - Inform cost-effectiveness analyses of rotavirus and RSV vaccination across LMICs
  - Inform multiple country-specific studies
  - Provide information from the literature to country-level decision-makers



Impact and cost-effectiveness of RSV maternal immunization in Gavi countries

PATH
path.org

Ranju Baral and Clint Pecenka
Presenting author: Frédéric Debellut

Background. Childhood immunization is a cornerstone of cost-effective reductions in child mortality worldwide. But, as childhood mortality falls, a larger share of the global disease burden shifts to young infants. A significant proportion of morbidity and mortality during the first year of life is due to infectious diseases.[1,2] Although many of these diseases are vaccine preventable, protecting newborns using direct immunization is not always possible. One promising alternative to combat neonatal and infant mortality due to early infections is to vaccinate pregnant women.

A number of maternal vaccines designed to protect young infants are currently in development, including advanced candidates against respiratory syncytial virus (RSV), which are expected to be available within the next 5-10 years[4]. RSV causes about 120,000 deaths among children annually, mostly among young infants in low-resource settings.[5] Gavi, the Vaccine Alliance is supporting RSV vaccines for investment as part of the 2018 Vaccine Investment Strategy subject to licensure, SAGE recommendation, and prequalification[6]. In this study, we estimate the impact and cost-effectiveness of RSV maternal immunization to benefit newborns and infants across 73 Gavi countries.

RSV disease among children in developing countries[5]

- **30.5M** episodes of RSV-Acute Lower Respiratory Infections, annually
- **6.1M** severe episodes
- **3.3M** hospitalizations
- **~60K** deaths in hospital, with many more suspected in the community

Methods. This analysis uses a static population-based cohort model. We examine costs and impacts of vaccinating pregnant women to protect young infants against RSV in comparison to no intervention. This analysis takes a health system perspective and spans 2023 to 2035. Results are undiscounted and costs are expressed in 2016 US$ units.

Results. Across 73 Gavi countries, RSV maternal immunization is estimated to avert nearly 15 million cases (range 10-19 million), 3 million hospitalizations (range 2-4 million), and 150,000 deaths (range 103,000–186,000), from 2023-2035. Roughly 32% of projected RSV deaths among infants younger than 6 months of age would be averted. Most of the impact occurs in later years due to assumptions that the majority of countries won't introduce the vaccine right away.

Sub-Saharan Africa · South Asia · East Asia & Pacific · Europe & Central Asia · Latin America & Caribbean · Middle East & North Africa

We examined additional scenarios using recent Phase 3 clinical trial data[7] from one of the maternal vaccine candidates currently in development. We used the efficacy values for the various endpoints reported in the trial results to evaluate these scenarios. Using these vaccine efficacy values, the vaccine is estimated to avert 3.5-3.6 million cases, 1.2-1.3 million hospitalizations, and 60,000-74,000 deaths. These results exclude the large impact of RSV vaccine on broader lower respiratory tract infections (LRTI) as demonstrated in the trial.

The estimated average annual cost of a vaccination program across all countries for the duration of analysis is about 211 million dollars. The economic benefits expressed in terms of cost of care averted is about 10 million dollars at baseline. The incremental cost-effectiveness ratio (ICER) expressed in US$ per Disability Adjusted Life Years (DALYs) is about 185 dollars across all countries at baseline.

Vaccine performance (efficacy and protection) and intervention price (cost of vaccine) are the most important parameters of cost- effectiveness (Figure 4). Under a high disease burden scenario where 8.7% of all LRTI mortality in infants is attributed to RSV, the vaccine is even more cost-effective.

Under the base case scenario, the estimated ICER per DALY averted for most countries is less than 50% of their 2016 national gross domestic product (GDP) per capita.

Conclusions. RSV maternal immunization is projected to be an impactful and cost-effective intervention in Gavi countries. The emerging evidence of high RSV attribution to all LRTI deaths among young infants makes a cost-effective maternal RSV vaccine an important tool for curbing infant mortality. Further, as the infant vaccination schedule becomes increasingly crowded and disease burden shifts toward neonates and very young children, maternal immunization offers the opportunity to protect young infants from disease while also possibly enhancing maternal health. To have greatest impact once an effective vaccine is available, a successful delivery strategy to achieve high coverage will need to be defined, and should be a focus for future research.

Acknowledgements. This work has benefitted from inputs and contributions from various experts and organizations, including Gavi, the vaccine alliance, University of Antwerp, London School of Hygiene and Tropical Medicine, the Bill & Melinda Gates Foundation, as well as experts from The Advancing Maternal Immunization (AMI) collaboration to improve infant health and survival through maternal immunization.

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References.

1. Liu L, Oza S, Hogan D, *et al.* Global, regional, and national causes of child mortality in 2000–13, with projections to inform post-2015 priorities: an updated systematic analysis. Lancet 2016; 385: 430–40.
2. Troeger C, Forouzanfar M, Rao PC, *et al.* Estimates of the global, regional, and national morbidity, mortality, and aetiologies of lower respiratory tract infections in 195 countries: a systematic analysis for the Global Burden of Disease Study 2015. Lancet Infect Dis 2017; 17: 1133–61.
3. Nations Inter-agency Group for Child Mortality Estimation [UN IGME]. Levels & Trends in Child Mortality: Report 2018, Estimates developed by the United Nations Inter-agency Group for Child Mortality Estimation. New York, 2018
4. PATH. RSV Vaccine and mAB Snapshot. 2017. http://www.path.org/publications/files/CVIA_rsv_snapshot_final_D917.pdf (accessed Jan 1, 2017).
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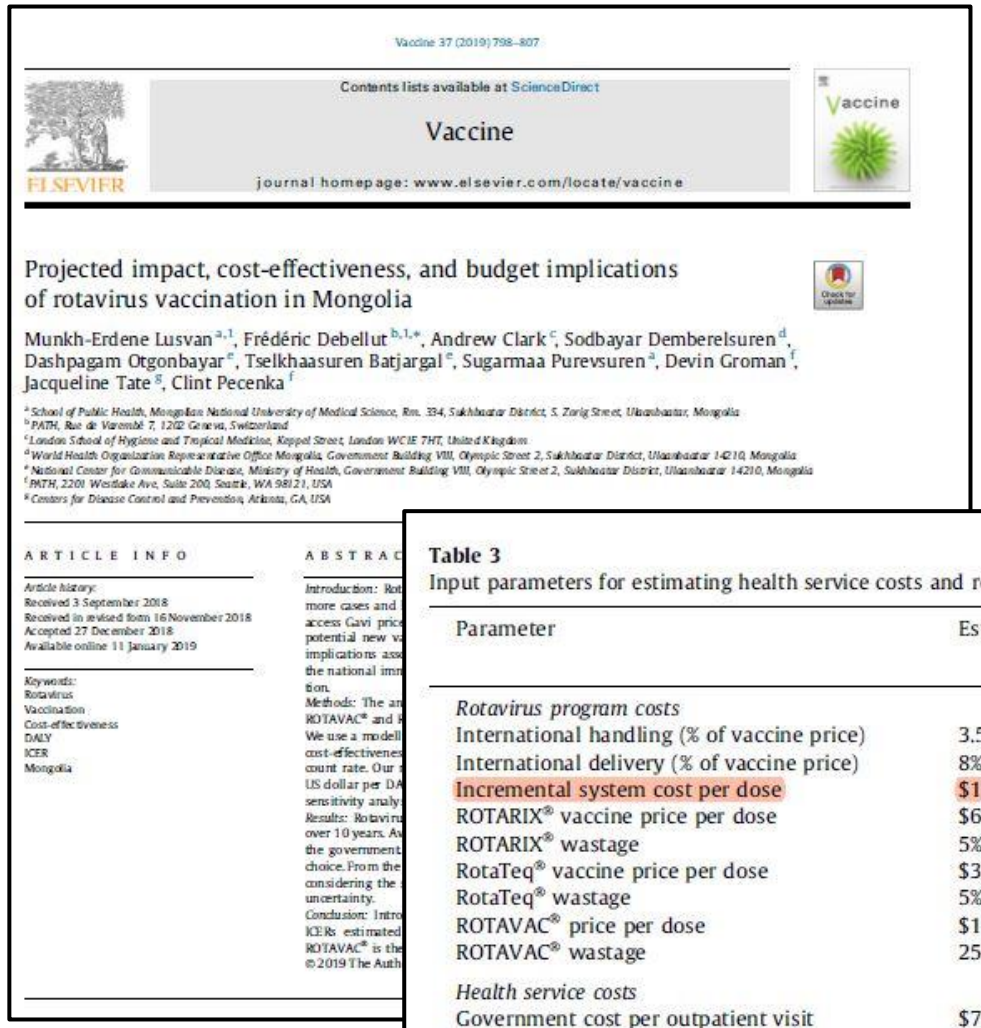
6. Gavi. Vaccine Investment Strategy. Available at : https://www.gavi.org/about/strategy/vaccine-investment-strategy/. Accessed May 2019
7. Novavax. Press release. Novavax Prepare phase 3 trial of its RSV F vaccine. February 2019

USER PERSPECTIVE: EXAMPLE MONGOLIA



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journal homepage: www.elsevier.com/locate/vaccine

Projected impact, cost-effectiveness, and budget implications of rotavirus vaccination in Mongolia

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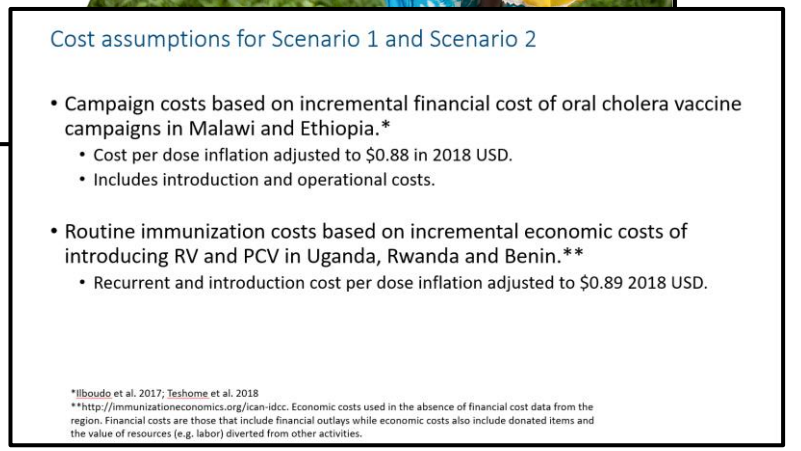
Mongolia

Table 3
Input parameters for estimating health service costs and rotavirus vaccine program costs (2017 US$).

Parameter	Estimate	Scenarios		Source/s
		Low	High	
Rotavirus program costs				
International handling (% of vaccine price)	3.5%	–	–	Assumption
International delivery (% of vaccine price)	8%	–	–	Assumption
Incremental system cost per dose	$1.91	$0.50	$2.50	[43], assumption for Low and High
ROTARIX® vaccine price per dose	$6.20	$2.02	$15.76	[38]
ROTARIX® wastage	5%	–	–	Assumption
RotaTeq® vaccine price per dose	$3.50	$3.20	$7	[11], assumption for Low and High
RotaTeq® wastage	5%	–	–	Assumption
ROTAVAC® price per dose	$1	$0.5	$2	[11], assumption for Low and High
ROTAVAC® wastage	25%	–	–	Assumption
Health service costs				
Government cost per outpatient visit	$7.29	$3.65	$14.58	Modelled using WHO-CHOICE, assumption for Low and High
Household cost per outpatient visit	$2.64	$1.32	$5.28	
Government cost per inpatient admission	$77.93	$38.97	$155.86	
Household cost per inpatient admission	$96.27	$48.13	$192.54	

USER PERSPECTIVE: OTHER EXAMPLES



USER PERSPECTIVE

- **Uses and benefits:**
  - Locate relevant delivery cost estimates
  - Categorize studies that might be relevant for different vaccines or delivery strategies
  - Easily understand study characteristics
  - Methodology description and how-to videos useful

- **Challenges:**
  - Many data gaps – must be careful in how data are used
  - Communicate caveats around use of limited data points to country decision-makers
  - Explore uncertainty through sensitivity analysis

Using the IDCC:
The importance of comparable unit costs

IDENTIFYING COMPARABLE UNIT COSTS

- **Data are highly heterogeneous:**
  - Many different vaccines, delivery strategies, country and study contexts
  - Undefined terms and conflicting definitions
  - Costs estimated using different methods
  - Widely variable classification of costs into cost categories and cost activities

- **Some data may not be comparable:**
  - Economic, incremental cost per dose for school-based delivery ≠ Financial, full cost per fully immunized child for health-facility based delivery

REAL WORLD EXAMPLE

- **Real world example of request for cost data:**
  - The EPI Manager approaches you, a local/international researcher, with a request for technical assistance. S/he wants to estimate the delivery cost to government to implement a measles-rubella campaign nationwide.
  - There are no known campaign costing studies done in the country. There are also no upcoming campaigns they could cost, nor do they have the budget or time for this.

- **What would you search for in the IDCC to find evidence to present to the EPI Manager?**

REAL WORLD EXAMPLE: CAN ALL THE RECORDS FROM YOUR SEARCH RESULTS BE USED IN YOUR ANALYSIS?

Select summary of the 20 records		
Section	**Variable**	**Results**
Background information	Country	13 different countries
	Country income level	Low income (16), lower middle income (2), upper middle income (2)
	Region	Latin America & Caribbean (5), South Asia (3), Sub-Saharan Africa (12)
	Geographic setting	Rural (4), urban (6), urban and rural (3), not reported (7)
Vaccines	Vaccines costed	Meningococcal (5), OCV (10), YF (1), Measles (2), OPV (2)
Vaccine delivery	Routine or SIA	SIA – campaign (12), SIA – campaign with mop-up (2), SIA – catch up (1), SIA – National Immunization Week (2), SIA – outbreak campaign (3)
	Delivery strategy	Campaign (15), NIW (2), health facility (2), outreach/mobile (1)
Study design & methodology	Economic, financial, fiscal costs	Economic (11), financial (7), not reported or unclear (2)
Cost categories included	Highest level of costs included	National (7), province/region/state (1), district (6), city (4), facility (2)
	Supply chain only?	No (16), Yes (4)
	No. cost categories included	Range of 4-13

REAL WORLD EXAMPLE

- What are your top 3 criteria/variables for determining whether a record can be used for this analysis?

- Vote for your top 3 criteria to determine whether a record can be used for this analysis at:

www.menti.com

Use code 919393

THE ART AND SCIENCE OF COMPARISON

Suggested key criteria for determining comparability of unit costs

Level	Variable
Must-have	• Economic, financial, or fiscal costs • Full or incremental costing • Startup and/or recurrent/ ongoing costs • Delivery platform (routine vs. SIA) • Supply chain only costs
Probably important to have	• Delivery scale (pilot/project or full) • Highest level of costs included

Level	Variable

Might be important to have	• Number of included cost categories
	• Inclusion of major cost categories:
	  • Paid human resources
	  • Cold chain equipment and their overheads
	  • Vehicles, transport and fuel
	  • Training and capacity building

Depends	• Vaccine • Country income level • Vaccine delivery strategy • Other criteria

REAL WORLD EXAMPLE

- **Once you have selected what you think are comparable unit costs, how would you present them to the EPI Manager?**
  - Show him/her all comparable unit costs as individual values and let him/her decide
  - Present the unit costs as a range (minimum unit cost – maximum unit cost)
  - Calculate the median of the comparable unit costs
  - Calculate the mean of the comparable unit costs
  - A combination of the above
  - Other

- **Vote for your preferred way of presenting comparable unit costs to the EPI Manager at:**

www.menti.com

Use code 919393

Using the IDCC:
Immunization Delivery Cost Ranges

IMMUNIZATION DELIVERY COST RANGES – METHODS

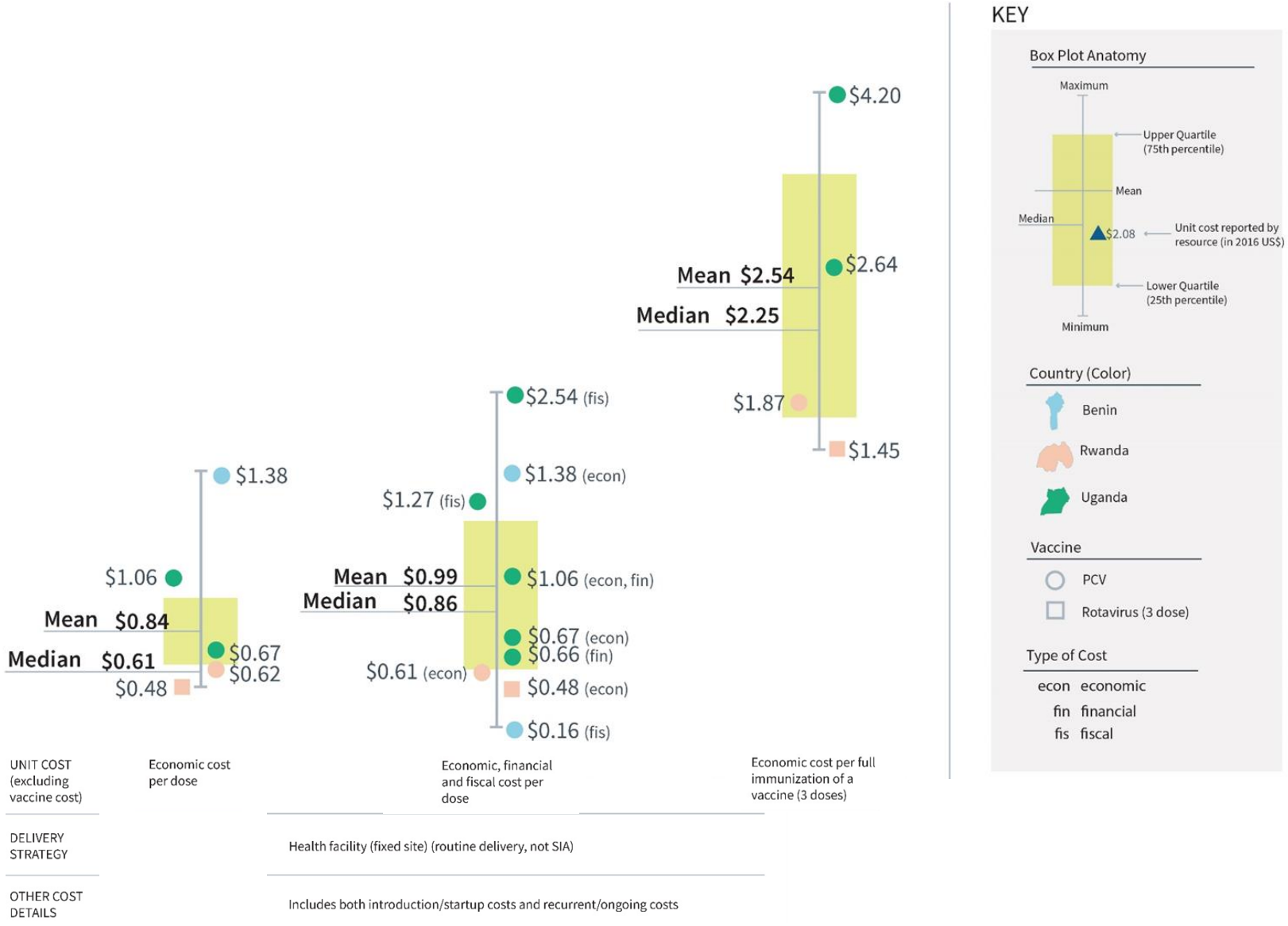
- **Explored 14,000+ combinations of unit costs to identify those that are comparable**

- **Cost ranges include four or more unit costs that match on a set of variables:**
  - Economic, financial, or fiscal costs
  - Full or incremental costing
  - Supply chain only costs
  - Delivery platform (routine vs. SIA)
  - Introduction/startup costs and/or recurrent/ongoing costs or both
  - Highest level of costs included
  - Delivery scale (pilot/project or full)

- **Additional variables were used to check validity of unit costs comprising a cost range:**
  - Vaccines costed
  - Vaccine delivery strategy
  - Number of antigens costed
  - Number of included cost categories
  - Inclusion of major cost categories
  - Etc.

IMMUNIZATION DELIVERY COST RANGES (1/3)

Incremental cost per dose for single, newly introduced vaccines, excluding vaccine cost (2016 USD)



IMMUNIZATION DELIVERY COST RANGES (1/3)

Incremental cost per dose for single, newly introduced vaccines, excluding vaccine cost (2016 USD)

Countries	Vaccines costed	Delivery strategy and platform	Delivery unit cost (excluding vaccine cost)	Other cost details	Individual immunization delivery unit costs from articles/reports (2016 USD)	Cost range (2016 USD)	Descriptive statistics (2016 USD)
Benin, Rwanda, Uganda (LICs, SSA region)	PCV 7/10/13 Rotavirus (3 dose)	Health facility (fixed site) (Routine, not SIA delivery)	Economic cost per dose	Full scale implementation Highest level of costs: national Unit costs include both introduction/ startup costs and recurrent/ ongoing costs	$0.48 (Rota, Rwanda) $0.62 (PCV, Rwanda) $0.67 (PCV, Uganda) $1.06 (PCV, Uganda) $1.38 (PCV, Benin)	$0.48 - $1.38	Mean: $0.84 25th percentile: $0.62 Median: $0.61 75th percentile: $1.06

Other interpretive notes:

All unit costs include 10-13 cost categories (of 15) with all 4 major categories included (Paid human resources; Cold chain equipment and overheads; Vehicles, transport and fuel; Training and capacity building)

The estimates from Rwanda are based on a sample of 3 facilities, while the other estimates had samples of 46-49 facilities

The individual unit costs come from articles/reports with a quality score of 2.1-2.7 (of 3)

References:

[1] Ngabo, F., Levin, A., Wang, S. A., Gatera, M., Rugambwa, C., Kayonga, C., … Hutubessy, R. (2015). A cost comparison of introducing and delivering pneumococcal, rotavirus and human papillomavirus vaccines in Rwanda. *Vaccine*, 33(51), 7357–7363. https://doi.org/10.1016/j.vaccine.2015.10.022

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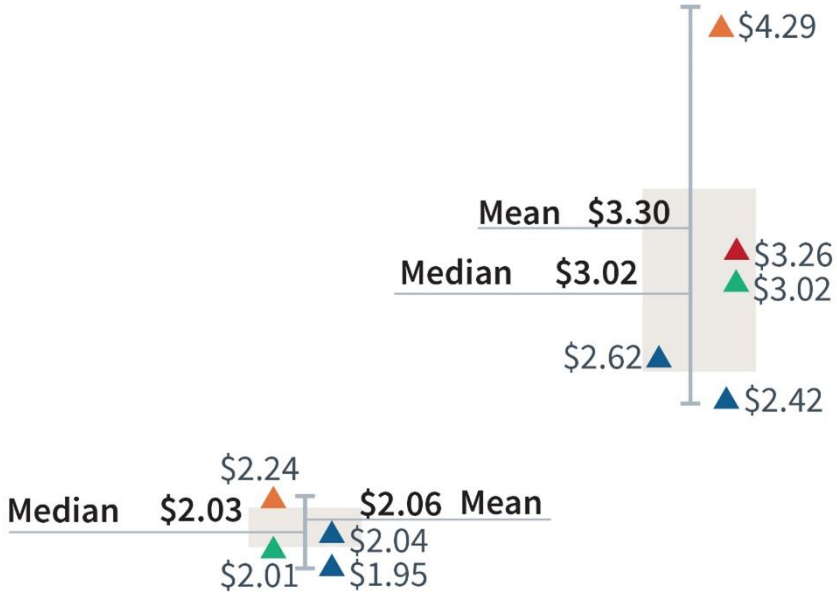
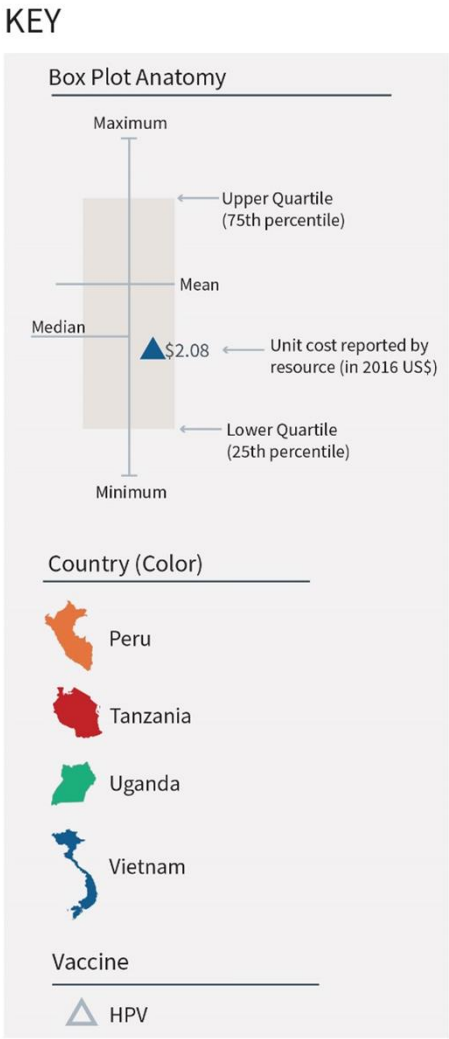
IMMUNIZATION DELIVERY COST RANGES (2/3)

Incremental cost of introducing HPV vaccine to an existing schedule, excluding vaccine cost (2016 USD)

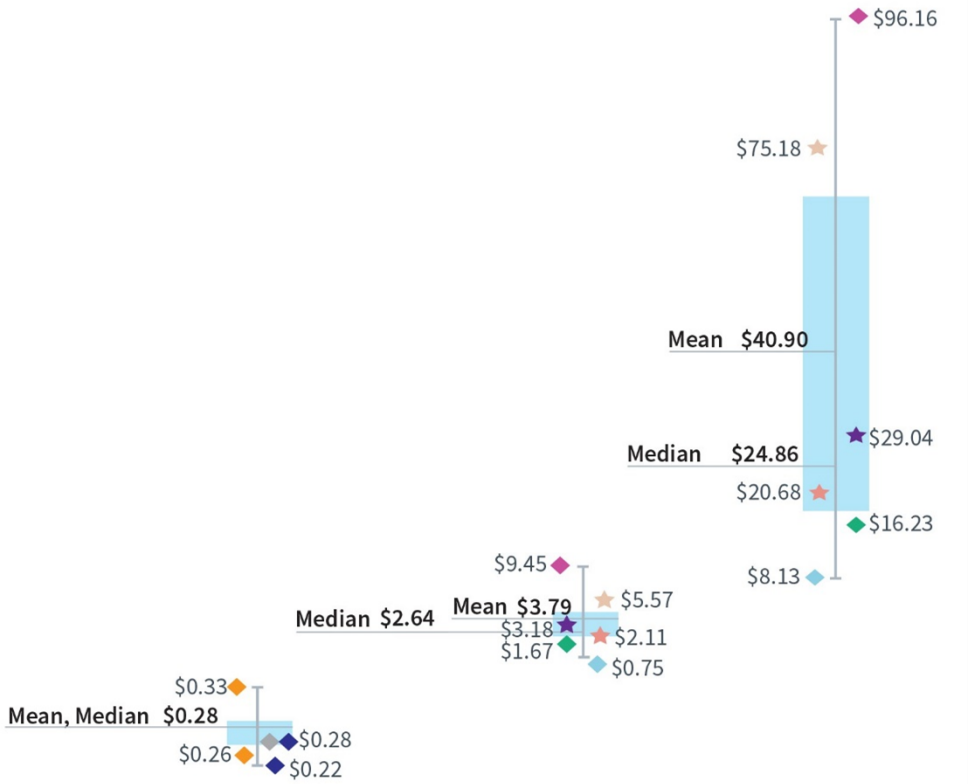


UNIT COST (excluding vaccine cost)	Financial cost per dose	Economic cost per dose
DELIVERY STRATEGY	School (routine delivery, not SIA) (costs are related to pilot/project delivery)	Health facility, school (routine delivery, not SIA) (costs are related to pilot/project delivery)
OTHER COST DETAILS	Includes both introduction/startup costs and recurrent/ongoing costs	



IMMUNIZATION DELIVERY COST RANGES (3/3)

Full delivery cost for a schedule of vaccines, excluding vaccine cost (2016 USD)



UNIT COST (excluding vaccine cost)	Economic cost per dose	Economic cost per dose	Economic cost per fully immunized child (defined as children who have received DTP3)
DELIVERY STRATEGY	Health facility (routine delivery, not SIA)	Health facility & multiple strategies (i.e., two or more delivery strategies) (routine delivery, not SIA)	Health facility & multiple strategies (i.e., two or more delivery strategies) (routine delivery, not SIA)
OTHER COST DETAILS	Supply chain only costs, Includes both introduction/startup costs and recurrent/ ongoing costs	All costs (i.e., not supply chain only), Includes both introduction/ startup costs and recurrent/ongoing costs	All costs (i.e., not supply chain only), Includes both introduction/startup costs and recurrent/ongoing costs

IMMUNIZATION DELIVERY COST RANGES – SUMMARY OF FINDINGS

- **Large variability in the data, even in comparable settings:**
  - Different vaccines, delivery strategies, country contexts
  - Wide cost ranges
  - Further work by EPIC 3 to create additional modeled estimates for countries where cost evidence does not exist

- **Cost ranges may be higher than current estimates used in many LMICs for budgeting:**
  - $0.16 to $2.54 incremental cost per dose (including economic, financial, and fiscal costs) for single, newly introduced vaccines
  - $1.95 to $4.29 incremental cost per dose (including economic and financial costs) for introducing HPV vaccine via school- and health facility-based delivery on a pilot/project basis
  - $0.75 to $9.45 full cost per dose (economic costs) for schedules of four to eight vaccines delivered to children under one; cost per FIC $8.13-$96.16
  - $0.22 to $0.33 full cost per dose (economic costs) for the supply chain-related costs of delivering vaccination schedules containing 6-7 antigens

DISCUSSION

1. How could the IDCC be useful for your country or countries that you work with?
2. How might the EPI or broader MoH use the data and findings?
3. How might researchers use the data and findings?
4. Are there any suggestions on how to improve the presentation of the data?

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THANK YOU