Return on Investment in Vaccine Demand Interventions

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UNC ESHELMAN SCHOOL OF PHARMACY

Global Health Economics *for* Pharmacy

Value of Vaccination

By Sachiko Ozawa, Meghan L. Stack, David M. Bishai, Andrew Mirelman, Ingrid K. Friberg, Louis Niessen, Damian G. Walker, and Orin S. Levine

During The 'Decade Of Vaccines,' The Lives Of 6.4 Million Children Valued At $231 Billion Could Be Saved

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HEALTH AFFAIRS 30, NO. 6 (2011): –

ABSTRACT Governments constantly face the challenge of determining how much they should spend to prevent premature deaths and suffering in their populations. In this article we explore the benefits of expanding the delivery of life-saving vaccines in seventy-two low- and middle-income countries, which we estimate would prevent the deaths of 6.4 million children between 2011 and 2020. We present the economic benefits of vaccines by using a "value of statistical life" approach, which is based on individuals' perceptions regarding the trade-off between income and increased risk of mortality. Our analysis shows that the vaccine expansion described above corresponds to $231 billion (uncertainty range: $116–$614 billion) in the value of statistical lives saved. This analysis complements results from analyses based on other techniques and is the first of its kind for immunizations in the world's poorest countries. It highlights the major economic benefits made possible by improving vaccine coverage.

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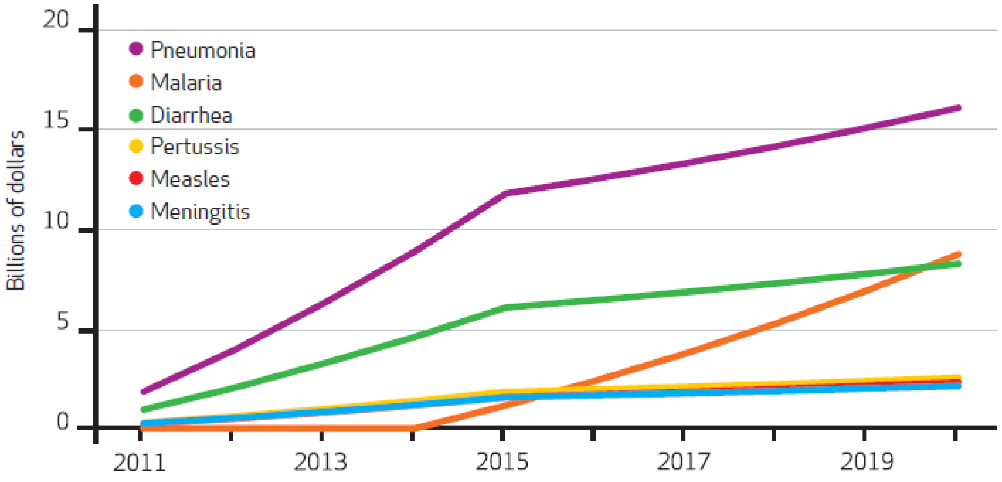
EXHIBIT 1

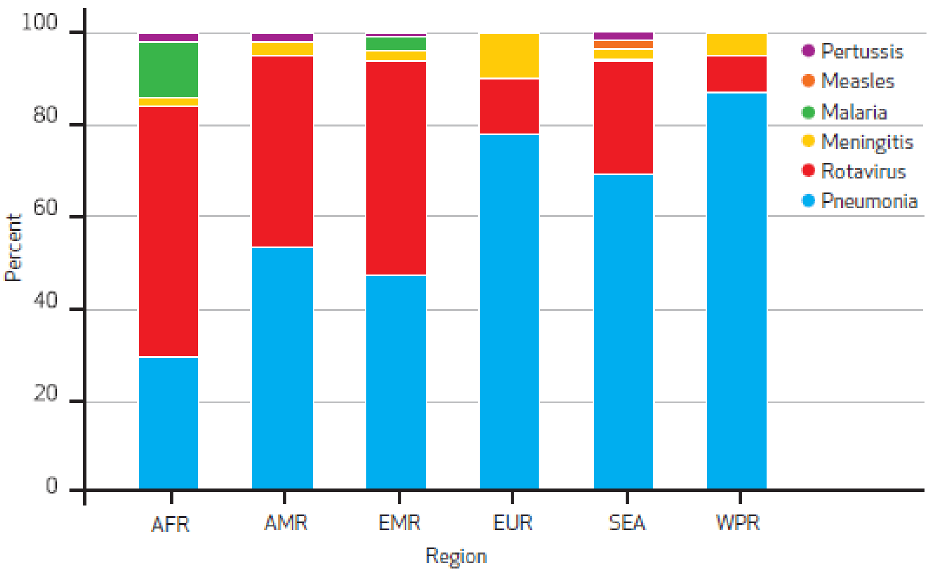
Annual Value-Of-Statistical-Life Savings, By Vaccine-Preventable Disease, 2011–20



SOURCE Authors' analysis.

EXHIBIT 3

Distribution Of Vaccine-Preventable Disease Treatment Costs Averted, By Region



SOURCE Authors' analysis. **NOTE** World Health Organization regional classifications are used: AFR, Africa; AMR, Americas; EMR, Eastern Mediterranean; EUR, Europe; SEA, South and East Asia; WPR, Western Pacific region.

THE PRICELESS PAYOFF

By Meghan L. Stack, Sachiko Ozawa, David M. Bishai, Andrew Mirelman, Yvonne Tam, Louis Niessen, Damian G. Walker, and Orin S. Levine

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Estimated Economic Benefits During The 'Decade Of Vaccines' Include Treatment Savings, Gains In Labor Productivity

ABSTRACT **In 2010 the Bill & Melinda Gates Foundation announced a $10 billion commitment over the next ten years to increase access to childhood vaccines in the world's poorest countries. The effort was labeled the "Decade of Vaccines." This study estimates both the short- and long-term economic benefits from the introduction and increased use of six vaccines in seventy-two of the world's poorest countries from 2011 to 2020. Increased rates of vaccination against pneumococcal and *Haemophilus influenzae* type b pneumonia and meningitis, rotavirus, pertussis, measles, and malaria over the next ten years would save 6.4 million lives and avert 426 million cases of illness, $6.2 billion in treatment costs, and $145 billion in productivity losses. Monetary estimates based on this type of analysis can be used to determine the return on investment in immunization from both the international community and local governments, and they should be considered in policy making.**

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Cost-effectiveness and economic benefits of vaccines in low- and middle-income countries: A systematic review

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ABSTRACT

Background: Public health interventions that prevent mortality and morbidity have greatly increased over the past decade. Immunization is one of these preventive interventions, with a potential to bring economic benefits beyond just health benefits. While vaccines are considered to be a cost-effective public health intervention, implementation has become increasingly challenging. As vaccine costs rise and competing priorities increase, economic evidence is likely to play an increasingly important role in vaccination decisions.

Methods: To assist policy decisions today and potential investments in the future, we provide a systematic review of the literature on the cost-effectiveness and economic benefits of vaccines in low- and middle-income countries from 2000 to 2010. The review identified 108 relevant articles from 51 countries spanning 23 vaccines from three major electronic databases (Pubmed, Embase and Econlit).

Results: Among the 44 articles that reported costs per disability-adjusted life year (DALY) averted, vaccines cost less than or equal to $100 per DALY averted in 23 articles (52%). Vaccines cost less than $500 per DALY averted in 34 articles (77%), and less than $1000 per DALY averted in 38 articles (86%) in one of the scenarios. 24 articles (22%) examined broad level economic benefits of vaccines such as greater future wage-earning capacity and cost savings from averting disease outbreaks. 60 articles (56%) gathered data from a primary source. There were little data on long-term and societal economic benefits such as morbidity-related productivity gains, averting catastrophic health expenditures, growth in gross domestic product (GDP), and economic implications of demographic changes resulting from vaccination.

Conclusions: This review documents the available evidence and shows that vaccination in low- and middle-income countries brings important economic benefits. The cost-effectiveness studies reviewed suggest to policy makers that vaccines are an efficient investment. This review further highlights key gaps in the available literature that would benefit from additional research, especially in the area of evaluating the broader economic benefits of vaccination in the developing world.

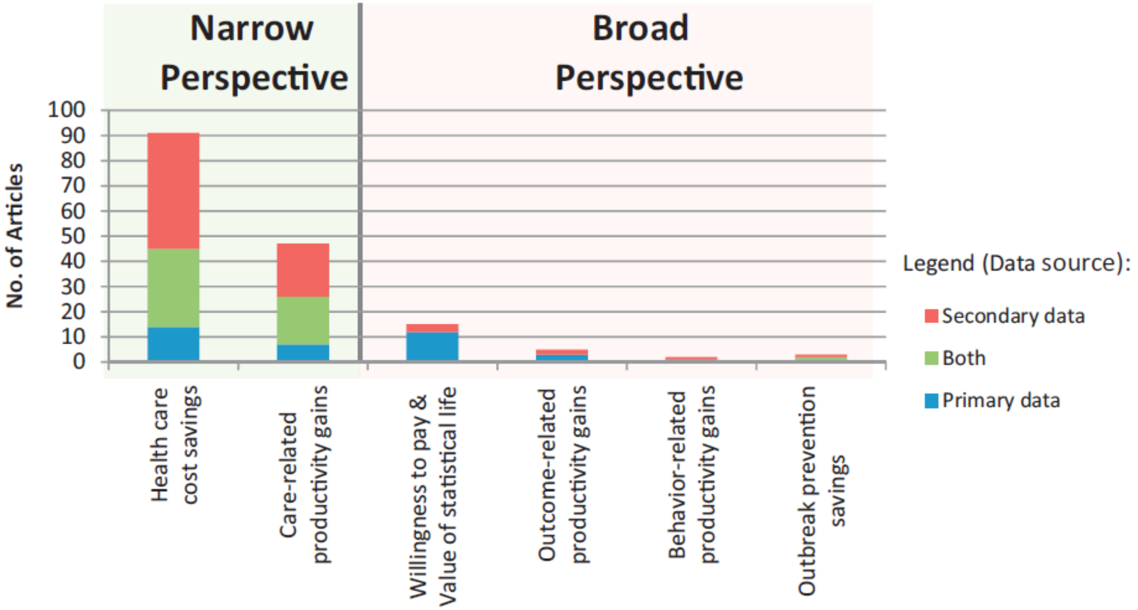

Fig. 3. Type of economic benefit by data source.

The economic and social benefits of childhood vaccinations in BRICS

Andrew J Mirelman,[a] Sachiko Ozawa[a] & Simrun Grewal[a]

Table 2. **Estimated annual economic and social benefits from increased *Haemophilus influenzae* type b, pneumococcal conjugate vaccine and rotavirus vaccine coverage, Brazil, the Russian Federation, India, China and South Africa (BRICS)**

Country	GDP per capita 2012 (US$)[15]	Life expectancy at birth (years)[16]	Estimated annual no. of averted deaths				Estimated annual economic and social benefits (US$)
			Hib	SP	RV	Total	
Brazil	11 359	73.8	0	25	10	35	18 162 707
Russian Federation	14 302	67.9	373	474	31	878	559 713 873
India	1 501	66.3	52 709	54 499	29 612	136 820	9 083 890 821
China	6 071	75.2	9 538	10 079	1 170	20 787	5 796 798 644
South Africa	7 525	57.1	856	319	85	1 260	398 019 961

GDP: gross domestic product; Hib: *Haemophilus influenzae* type b; RV: rotavirus; SP: Streptococcus pneumonia; US$: United States dollars.

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Costs of vaccine programs across 94 low- and middle-income countries

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ABSTRACT

While new mechanisms such as advance market commitments and co-financing policies of the GAVI Alliance are allowing low- and middle-income countries to gain access to vaccines faster than ever, understanding the full scope of vaccine program costs is essential to ensure adequate resource mobilization. This costing analysis examines the vaccine costs, supply chain costs, and service delivery costs of immunization programs for routine immunization and for supplemental immunization activities (SIAs) for vaccines related to 18 antigens in 94 countries across the decade, 2011–2020. Vaccine costs were calculated using GAVI price forecasts for GAVI-eligible countries, and assumptions from the PAHO Revolving Fund and UNICEF for middle-income countries not supported by the GAVI Alliance. Vaccine introductions and coverage levels were projected primarily based on GAVI's Adjusted Demand Forecast. Supply chain costs including costs of transportation, storage, and labor were estimated by developing a mechanistic model using data generated by the HERMES discrete event simulation models. Service delivery costs were abstracted from comprehensive multi-year plans for the majority of GAVI-eligible countries and regression analysis was conducted to extrapolate costs to additional countries.

The analysis shows that the delivery of the full vaccination program across 94 countries would cost a total of $62 billion (95% uncertainty range: $43–$87 billion) over the decade, including $51 billion ($34–$73 billion) for routine immunization and $11 billion ($7–$17 billion) for SIAs. More than half of these costs stem from service delivery at $34 billion ($21–$51 billion)—with an additional $24 billion ($13–$41 billion) in vaccine costs and $4 billion ($3–$5 billion) in supply chain costs.

The findings present the global costs to attain the goals envisioned during the Decade of Vaccines to prevent millions of deaths by 2020 through more equitable access to existing vaccines for people in all communities. By projecting the full costs of immunization programs, our findings may aid to garner greater country and donor commitments toward adequate resource mobilization and efficient allocation. As service delivery costs have increasingly become the main driver of vaccination program costs, it is essential to pay additional consideration to health systems strengthening.

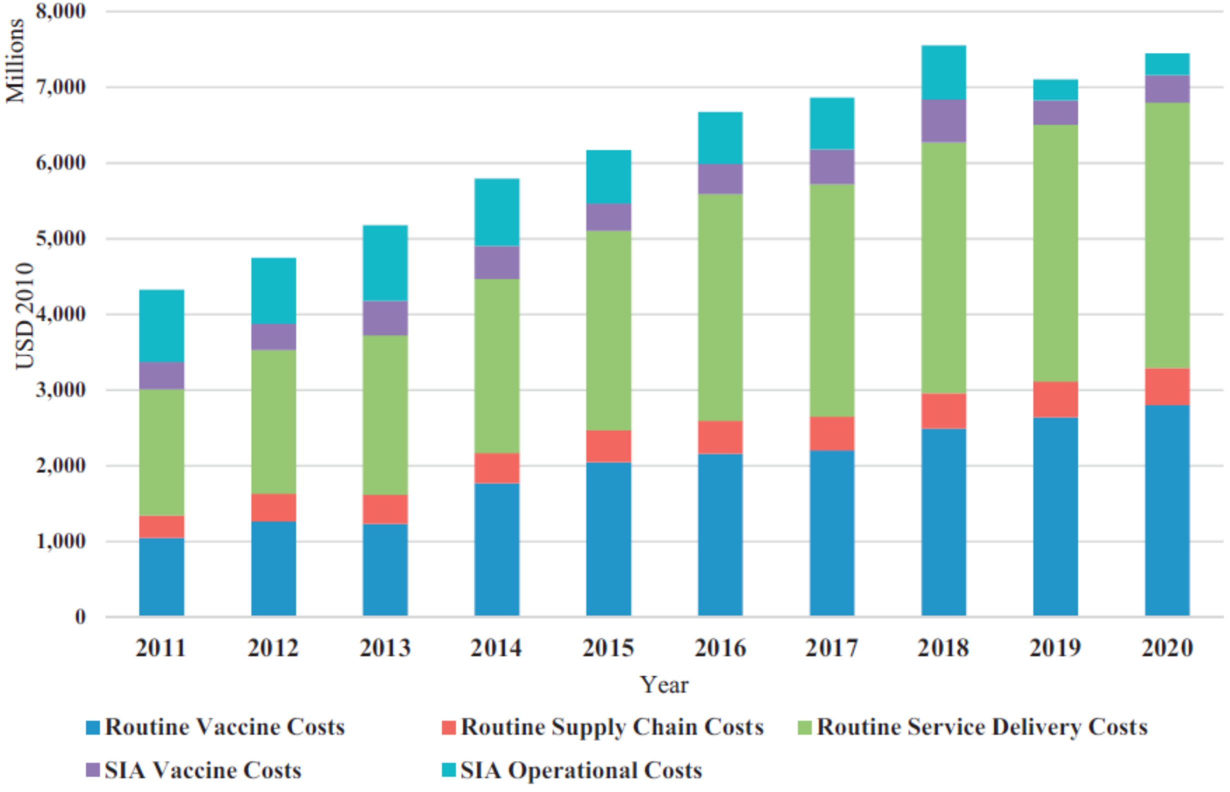

Fig. 2. Total immunization program costs by component and by routine vs. SIA, 2011–2020.

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Funding gap for immunization across 94 low- and middle-income countries

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ABSTRACT

Novel vaccine development and production has given rise to a growing number of vaccines that can prevent disease and save lives. In order to realize these health benefits, it is essential to ensure adequate immunization financing to enable equitable access to vaccines for people in all communities. This analysis estimates the full immunization program costs, projected available financing, and resulting funding gap for 94 low- and middle-income countries over five years (2016–2020). Vaccine program financing by country governments, Gavi, and other development partners was forecasted for vaccine, supply chain, and service delivery, based on an analysis of comprehensive multi-year plans together with a series of scenario and sensitivity analyses.

Findings indicate that delivery of full vaccination programs across 94 countries would result in a total funding gap of $7.6 billion (95% uncertainty range: $4.6–$11.8 billion) over 2016–2020, with the bulk (98%) of the resources required for routine immunization programs. More than half (65%) of the resources to meet this funding gap are required for service delivery at $5.0 billion ($2.7–$8.4 billion) with an additional $1.1 billion ($0.9–$2.7 billion) needed for vaccines and $1.5 billion ($1.1–$2.0 billion) for supply chain. When viewed as a percentage of total projected costs, the funding gap represents 66% of projected supply chain costs, 30% of service delivery costs, and 9% of vaccine costs. On average, this funding gap corresponds to 0.2% of general government expenditures and 2.3% of government health expenditures.

These results suggest greater need for country and donor resource mobilization and funding allocation for immunizations. Both service delivery and supply chain are important areas for further resource mobilization. Further research on the impact of advances in service delivery technology and reductions in vaccine prices beyond this decade would be important for efficient investment decisions for immunization.

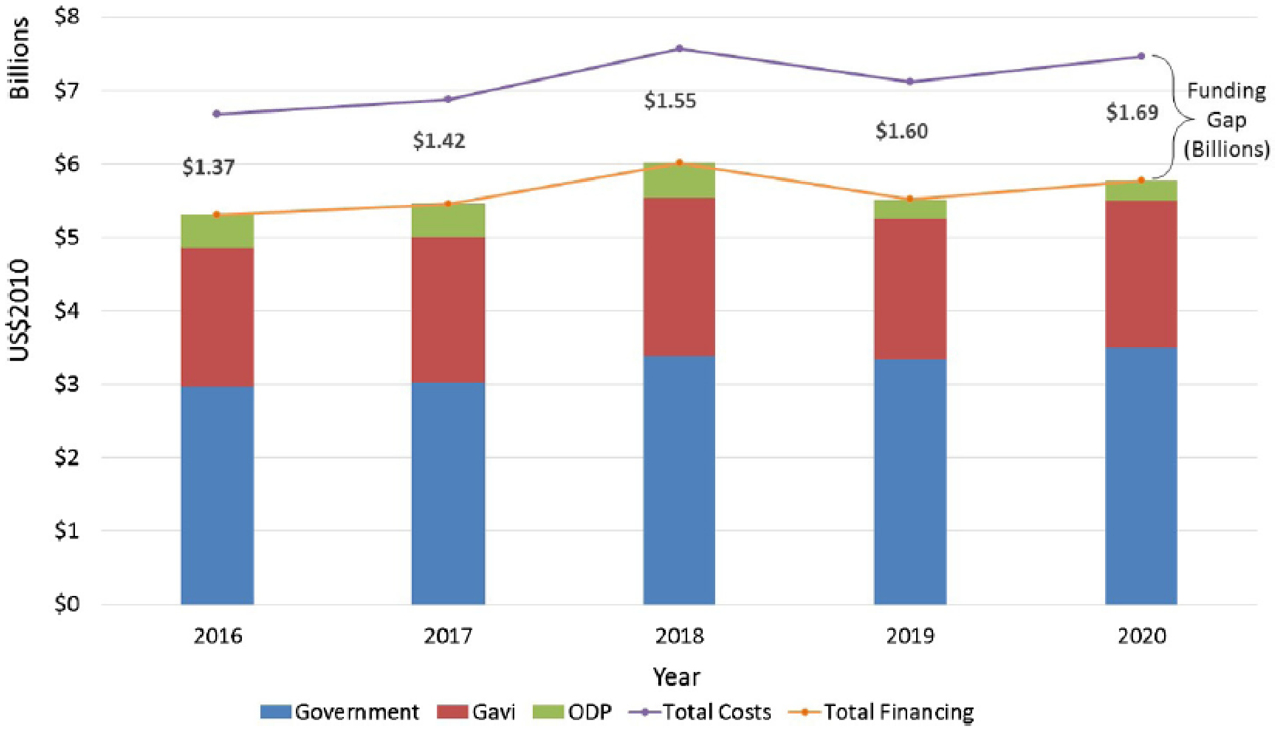
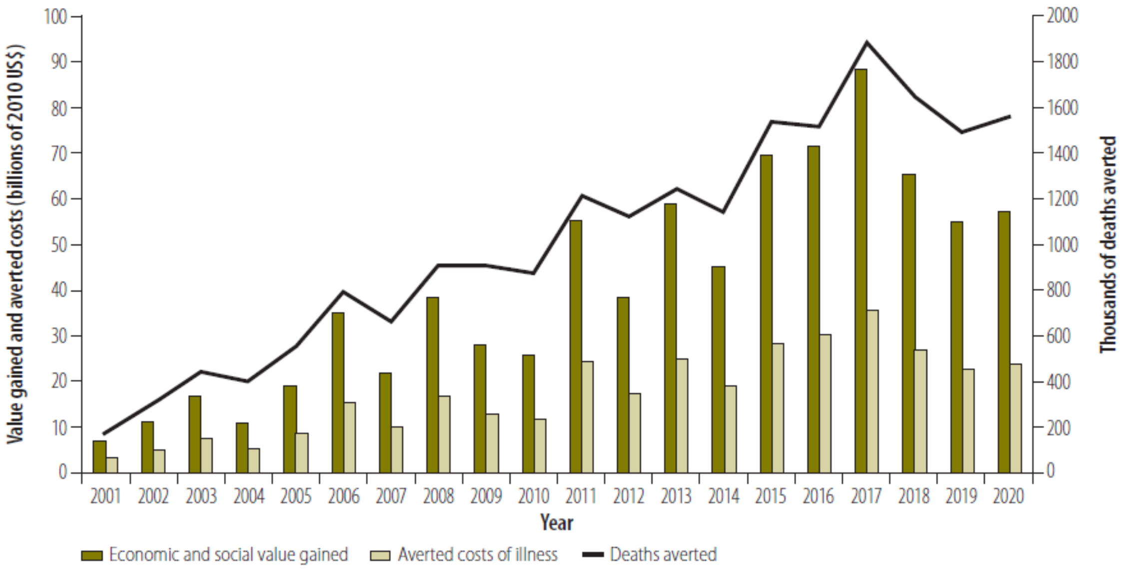


Fig. 1. Projected available costs, financing and funding gap by funding source by year.

Fig. 2. **Economic and social value gained, averted costs of illness and deaths averted annually, as the result of vaccinations against 10 diseases, 73 Gavi-supported low- and middle-income countries, 2001–2020**



Estimated economic impact of vaccinations in 73 low- and middle-income countries, 2001–2020

Sachiko Ozawa,[a] Samantha Clark,[b] Allison Portnoy,[c] Simrun Grewal,[d] Meghan L Stack,[e] Anushua Sinha,[f] Andrew Mirelman,[g] Heather Franklin,[f] Ingrid K Friberg,[h] Yvonne Tam,[b] Neff Walker,[b] Andrew Clark,[i] Matthew Ferrari,[j] Chutima Suraratdecha,[k] Steven Sweet,[l] Sue J Goldie,[l] Tini Garske,[m] Michelle Li,[n] Peter M Hansen,[o] Hope L Johnson[n] & Damian Walker[p]

Objective To estimate the economic impact likely to be achieved by efforts to vaccinate against 10 vaccine-preventable diseases between 2001 and 2020 in 73 low- and middle-income countries largely supported by Gavi, the Vaccine Alliance.

Methods We used health impact models to estimate the economic impact of achieving forecasted coverages for vaccination against *Haemophilus influenzae* type b, hepatitis B, human papillomavirus, Japanese encephalitis, measles, *Neisseria meningitidis* serogroup A, rotavirus, rubella, *Streptococcus pneumoniae* and yellow fever. In comparison with no vaccination, we modelled the costs – expressed in 2010 United States dollars (US$) – of averted treatment, transportation costs, productivity losses of caregivers and productivity losses due to disability and death. We used the value-of-a-life-year method to estimate the broader economic and social value of living longer, in better health, as a result of immunization.

Findings We estimated that, in the 73 countries, vaccinations given between 2001 and 2020 will avert over 20 million deaths and save US$ 350 billion in cost of illness. The deaths and disability prevented by vaccinations given during the two decades will result in estimated lifelong productivity gains totalling US$ 330 billion and US$ 9 billion, respectively. Over the lifetimes of the vaccinated cohorts, the same vaccinations will save an estimated US$ 5 billion in treatment costs. The broader economic and social value of these vaccinations is estimated at US$ 820 billion.

Conclusion By preventing significant costs and potentially increasing economic productivity among some of the world's poorest countries, the impact of immunization goes well beyond health.

Abstracts in عربي, 中文, Français, Русский and Español at the end of each article.

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VALUE OF VACCINES

By Sachiko Ozawa, Samantha Clark, Allison Portnoy, Simrun Grewal, Logan Brenzel, and Damian G. Walker

Return On Investment From Childhood Immunization In Low- And Middle-Income Countries, 2011–20

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ABSTRACT An analysis of return on investment can help policy makers support, optimize, and advocate for the expansion of immunization programs in the world's poorest countries. We assessed the return on investment associated with achieving projected coverage levels for vaccinations to prevent diseases related to ten antigens in ninety-four low- and middle-income countries during 2011–20, the Decade of Vaccines. We derived these estimates by using costs of vaccines, supply chains, and service delivery and their associated economic benefits. Based on the costs of illnesses averted, we estimated that projected immunizations will yield a net return about 16 times greater than costs over the decade (uncertainty range: 10–25). Using a full-income approach, which quantifies the value that people place on living longer and healthier lives, we found that net returns amounted to 44 times the costs (uncertainty range: 27–67). Across all antigens, net returns were greater than costs. But to realize the substantial positive return on investment from immunization programs, it is essential that governments and donors provide the requisite investments.

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Seth Berkley @GaviSeth — Following

Investing $1 in vaccines can get a return of up to $44. Here's the @Health_Affairs research behind it: ow.ly/5MSO309hDHL #vaccineswork

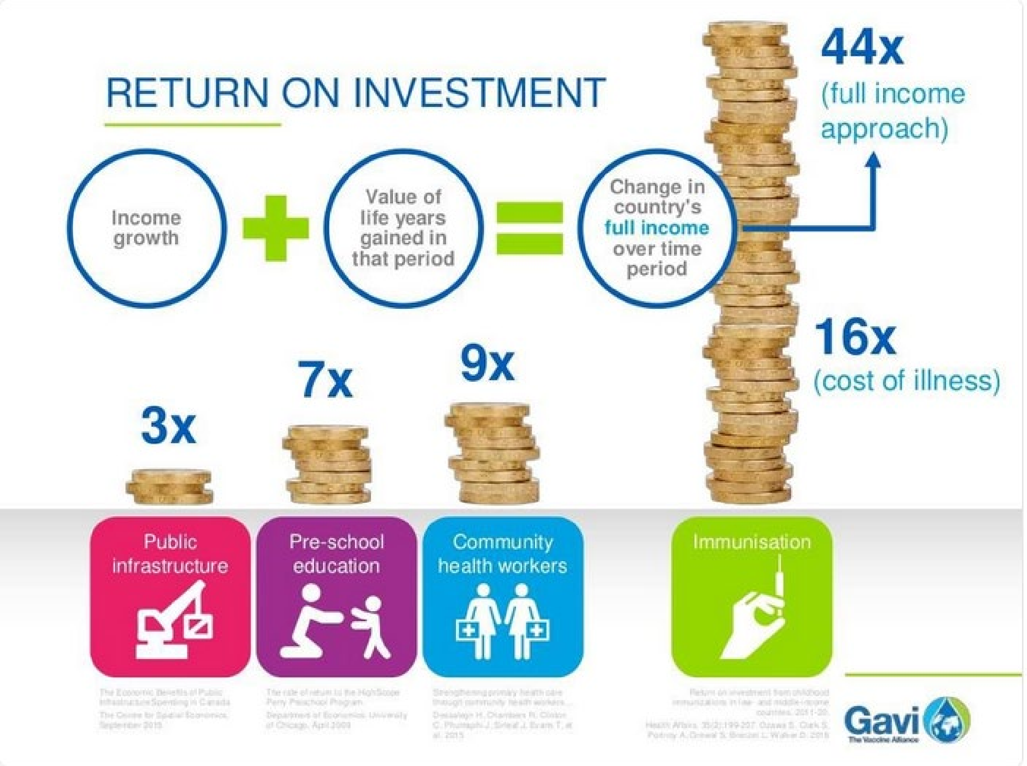
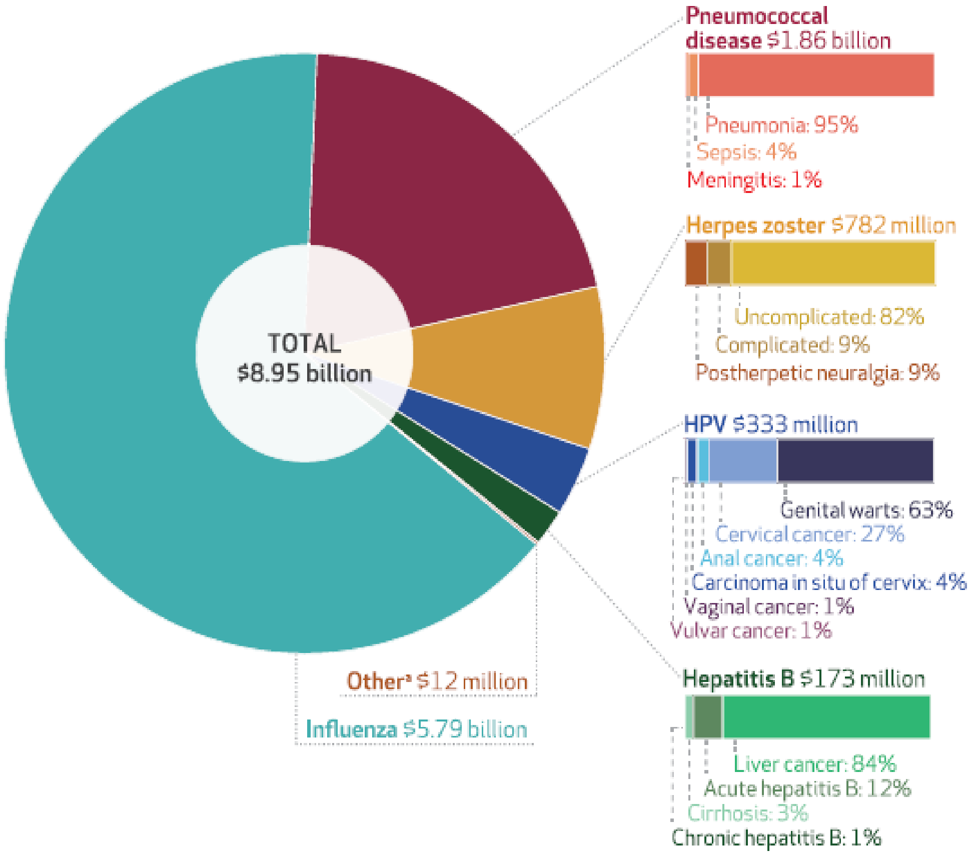


EXHIBIT 3

Annual economic burden of vaccine-preventable diseases, by pathogen, 2015



SOURCE Authors' analysis. **NOTES** All dollar amounts are for all US adults relevant to each vaccine-preventable disease (which target different age groups). The breakdown of results by age is presented in the online Appendix (see Note 7 in text). HPV is human papillomavirus. [a]Includes economic burden attributable to diphtheria, hepatitis A, measles, meningococcal disease, mumps, pertussis, rubella, tetanus, and varicella.

WEB FIRST

By Sachiko Ozawa, Allison Portnoy, Hiwote Getaneh, Samantha Clark, Maria Knoll, David Bishai, H. Keri Yang, and Pallavi D. Patwardhan

Modeling The Economic Burden Of Adult Vaccine-Preventable Diseases In The United States

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ABSTRACT Vaccines save thousands of lives in the United States every year, but many adults remain unvaccinated. Low rates of vaccine uptake lead to costs to individuals and society in terms of deaths and disabilities, which are avoidable, and they create economic losses from doctor visits, hospitalizations, and lost income. To identify the magnitude of this problem, we calculated the current economic burden that is attributable to vaccine-preventable diseases among US adults. We estimated the total remaining economic burden at approximately $9 billion (plausibility range: $4.7–$15.2 billion) in a single year, 2015, from vaccine-preventable diseases related to ten vaccines recommended for adults ages nineteen and older. Unvaccinated individuals are responsible for almost 80 percent, or $7.1 billion, of the financial burden. These results not only indicate the potential economic benefit of increasing adult immunization uptake but also highlight the value of vaccines. Policies should focus on minimizing the negative externalities or spillover effects from the choice not to be vaccinated, while preserving patient autonomy.

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Incremental Value of Vaccination

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Systematic review of the incremental costs of interventions that increase immunization coverage

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ABSTRACT

Achieving and maintaining high vaccination coverage requires investments, but the costs and effectiveness of interventions to increase coverage remain poorly characterized. We conducted a systematic review of the literature to identify peer-reviewed studies published in English that reported interventions aimed at increasing immunization coverage and the associated costs and effectiveness of the interventions. We found limited information in the literature, with many studies reporting effectiveness estimates, but not providing cost information. Using the available data, we developed a cost function to support future programmatic decisions about investments in interventions to increase immunization coverage for relatively low and high-income countries. The cost function estimates the non-vaccine cost per dose of interventions to increase absolute immunization coverage by one percent, through either campaigns or routine immunization. The cost per dose per percent increase in absolute coverage increased with higher baseline coverage, demonstrating increasing incremental costs required to reach higher coverage levels. Future studies should evaluate the performance of the cost function and add to the database of available evidence to better characterize heterogeneity in costs and generalizability of the cost function.

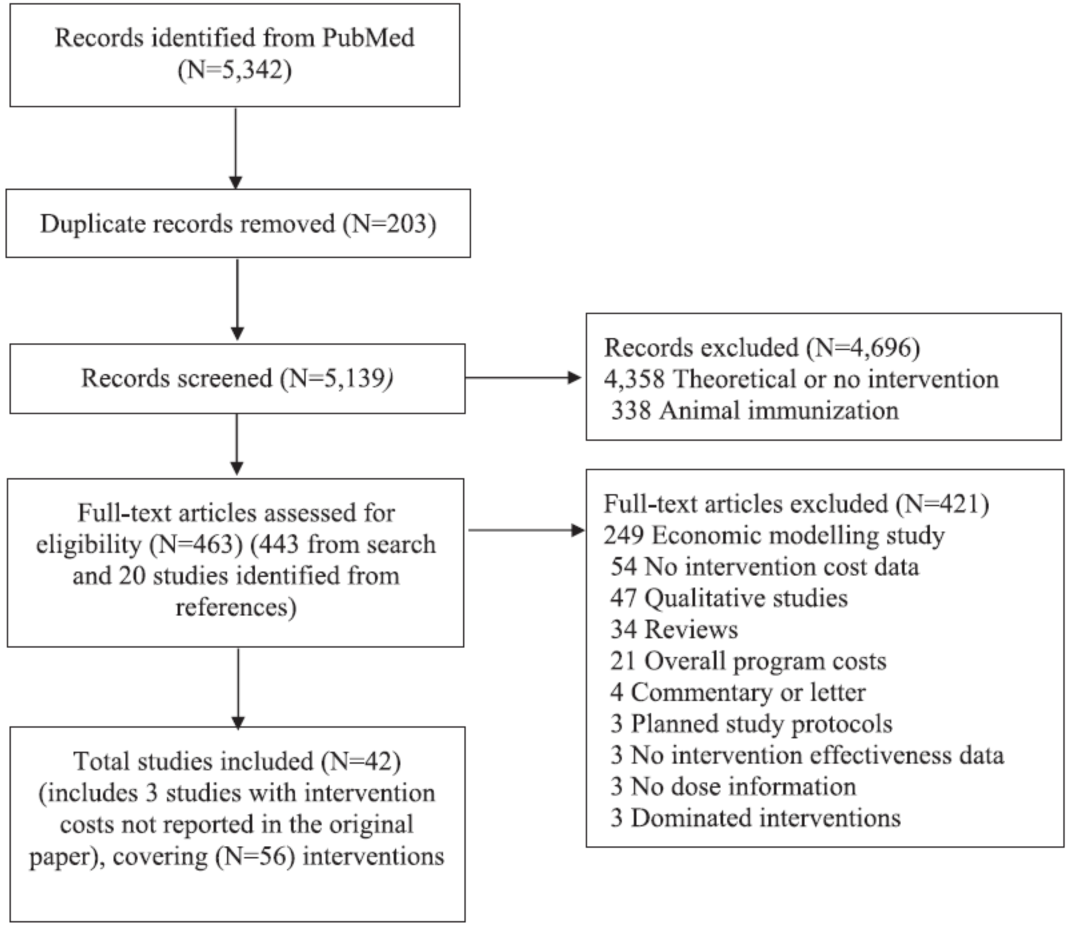

Fig. 1. Literature search process.

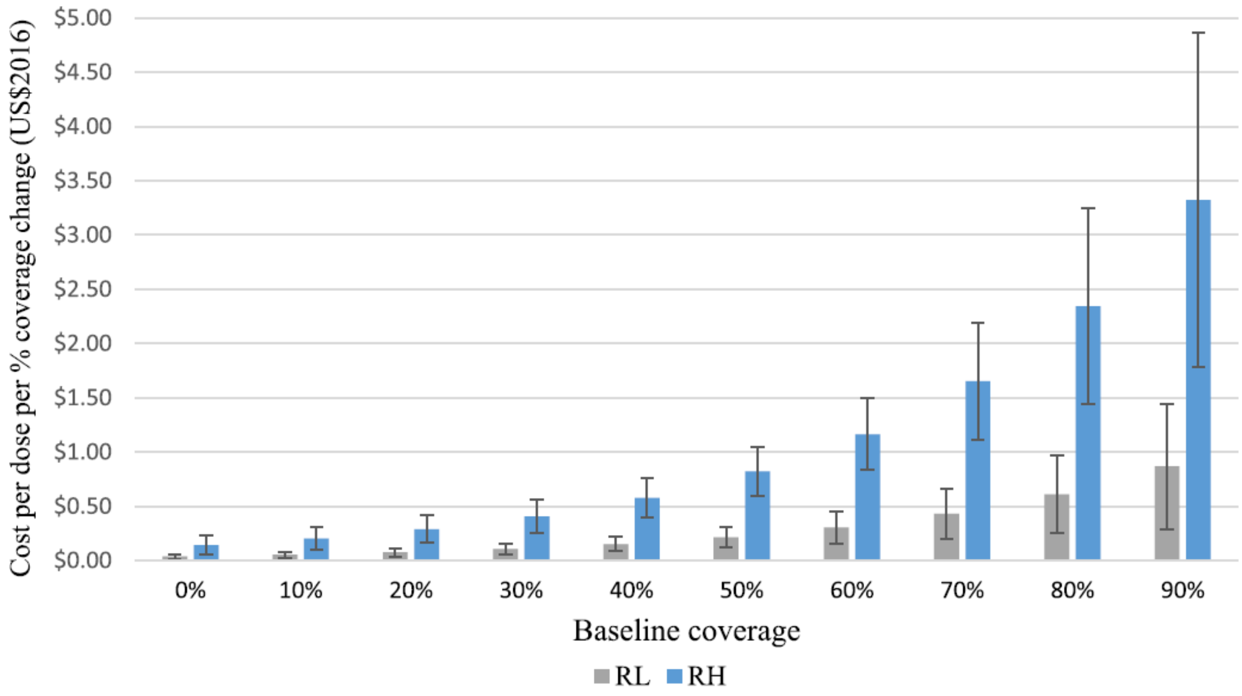

Fig 2. Intervention cost per dose per percent coverage change by baseline coverage.

RH: relatively high-income (high-income or upper middle-income)
RL: relatively low-income (low-income or lower middle-income)

Table 3
Intervention cost per dose per percent absolute coverage change by relative income* and baseline coverage.

		Routine baseline coverage (%)								
Relative income**	0	10	20	30	40	50	60	70	80	90
RL	$0.04	$0.05	$0.08	$0.11	$0.15	$0.21	$0.30	$0.43	$0.61	$0.87
RH	$0.14	$0.20	$0.29	$0.41	$0.58	$0.82	$1.16	$1.65	$2.34	$3.32
Relative income, delivery***	0	10	20	30	40	50	60	70	80	90
RL, RI	$0.03	$0.04	$0.06	$0.09	$0.12	$0.18	$0.25	$0.36	$0.52	$0.74
RL, SIA	$0.04	$0.06	$0.09	$0.13	$0.18	$0.26	$0.38	$0.54	$0.77	$1.10
RH, RI	$0.13	$0.19	$0.27	$0.39	$0.56	$0.79	$1.14	$1.62	$2.32	$3.32
RH, SIA	$0.20	$0.28	$0.41	$0.58	$0.83	$1.19	$1.70	$2.42	$3.47	$4.95

* RH: relatively high-income (i.e., high-income or upper middle-income); RI: routine immunization; RL: relatively low-income (i.e., low-income or lower middle-income); SIA: campaign or supplementary immunization activity.
** Cost per dose per unit absolute coverage change = exp (0.0349 * Routine baseline coverage + 1.3432 * (0 if RL, 1 if RH) – 3.2882).
*** Delivery not statistically significant, but statistical model provided for context: Cost per dose per unit absolute coverage change = exp (0.0357 * Routine baseline coverage + 1.504 * (0 if RL, 1 if RH) + 0.4014 * (0 if RI, 1 if SIA) – 3.5201).

Table 1
Costs and key characteristics of interventions to increase immunization coverage.

Country, year [Ref]	Relative income *	Intervention category **	Vaccine no. & types ***	Intervention description	Cost per dose (US$2016) ‡	Baseline coverage, absolute coverage change §
Bangladesh, 2014 [65]	RL	Both RI: Hs (a)	5 (B, D, E, M, P)	Extended clinic hours, vaccinator training, active surveillance, and community participation targeting children living in urban slums	$ 2.69	69, 56 m
USA, 2014 [66]	RH	Dem RI: Re (c)	1 (F)	Text message reminder for urban, low income pregnant women	$ 11.31	47, 2.7 n
Thailand, 2015 [67]	RH	Sup RI: SR (c)	4 (B, D, E, P)	Phone-to-phone information sharing application for identification of children needing vaccination among Highland minority and stateless populations along Thailand border	$ 54.45 f,g	91.7, 2.7 m
Somalia, 2015 [68]	RL	Sup SIA (a,b,d)	2 (M, P)	Integrated human and animal vaccination outreach campaign targeting nomadic pastoralist populations	$ 3.35 e	69, 31 k,p
USA, 2015 [69]	RH	Dem RI: Re (c)	7 (D, E, H, M, P, Q, V)	Collaborative centralized reminder/recall notifications for children behind in immunization schedule in urban and rural counties	$ 1.72	53.9, 12.8 k,p
USA, 2015 [69]	RH	Dem RI: Re (c)	7 (D, E, H, M, P, Q, V)	Practice based reminder/recall notifications	$ 0.22	53.9, 9.3 k,p
USA, 2015 [70]	RH	Dem RI: Re (c)	4 (N, S, U, V)	Text message reminders for adolescents at private pediatric and safety net practices	$ 2.64	46.5 r, 13.32 n
USA, 2015 [70]	RH	Dem RI: Re (c)	4 (N, S, U, V)	Postcard reminders for parents of adolescents missing vaccine doses in an urban area	$ 1.94	46.5 r, 11.04 n
USA, 2015 [70]	RH	Dem RI: Re (c)	4 (N, S, U, V)	Email reminders for parents of adolescents missing vaccine doses in an urban area	$ 1.26	46.5 r, 22.34 n
USA, 2015 [71]	RH	Dem RI: Re (c)	3 (N, S, U)	Text message reminders for parents of adolescents missing vaccine doses in an urban area	$ 4.33	92.9 r, 3.1 n
USA, 2015 [72]	RH	Sup SIA (b,c)	1 (F)	School based immunization for elementary school children in 2009–2010 flu season	$ 51.02	58.6, 11.2 n
USA, 2015 [72]	RH	Sup SIA (b,c)	1 (F)	School based immunization for elementary school children in 2010–2011 flu season	$ 50.66	58.6, 12 n
USA, 2016 [73]	RH	Dem RI: Re (c,d)	7 (D, E, H, M, P, Q, V)†	Text messaging reminders for Patients over 65 years or with chronic conditions in general practices	$ 10.86	88 r, 16.3 n
UK, 2016 [74]	RH	Dem RI: Re (c)	1 (F)	Cellphone and text messaging follow up of first time mothers by nurse practitioners	$ 2.88	49.9, 1.7 n
Bangladesh, 2016 [75]	RL	Dem RI: Re (a)	6 (B, D, E, F, H, M)	Mobile phone application to electronically register births and send reminders targeting children living in hard to reach rural areas and urban streets	$ 76.21 f,g	49.8, 17.65 h,q
China, 2016 [76]	RH	Both RI: Hs (c)	5 (B, D, E, M, P)	Advocacy to increase EPI awareness and funding among local leaders, EPI standard setting, training of health staff, targeted communications, immunization supporting equipment, collaboration between sectors and communities	$ 1.76 g	64.7, 21.1 m

* RH: relatively high-income (i.e., high-income or upper middle-income); RL: relatively low-income (i.e., low-income or lower middle-income).
** Both: supply and demand; Dem: demand; Sup: supply; SIA: supplemental immunization activities; RI: routine immunization; Subcategories of RI: Ed: education; Hs: health system strengthening; Re: reminder; SR: screening and referral; Ir: introduction of routine immunization; a: targets unreached population; b: involves vaccine delivery; c: targets people covered by routine immunization; d: includes non-immunization components.
*** B: Bacillus Calmette–Guérin (BCG); D: diphtheria tetanus pertussis (DTP); M: measles (includes measles conjugate vaccine (MCV), measles (M), measles rubella (MR), measles mumps rubella (MMR) vaccines); T: tetanus, F: Influenza/flu; H: Haemophilus influenzae type b (Hib); E: hepatitis B; P: polio (OPV/IPV); S: smallpox; V: varicella; Q: pneumococcal (PCV); C: cholera; N: meningococcal (MCV4); S: human papillomavirus (HPV), U: tetanus diphtheria pertussis (Tdap).
† Antigens targeted were inferred from official immunization schedules.
‡ e: costs includes or possibly includes cost of vaccines; f: intervention cost estimates provided by study authors; g: implementation costs incurred by other entity not included in intervention cost.
§ h: coverage change calculated as average of changes in coverage across multiple antigens or intervention groups; k: assumes baseline coverage is zero; m: coverage change calculated as final intervention coverage minus baseline intervention coverage; n: coverage change calculated as final intervention coverage minus final control coverage; p: coverage change calculated as final proportion vaccinated from a previously unvaccinated baseline population; q: baseline coverage as average of baseline coverages across multiple antigens; r: baseline immunization coverage in the target population and area extracted from historic state and local immunization registries or other sources other than reported in paper.

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Economic value of vaccinating geographically hard-to-reach populations with measles vaccine: A modeling application in Kenya

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ABSTRACT

Background: Since special efforts are necessary to vaccinate people living far from fixed vaccination posts, decision makers are interested in knowing the economic value of such efforts.
Methods: Using our immunization geospatial information system platform and a measles compartment model, we quantified the health and economic value of a 2-dose measles immunization outreach strategy for children <24 months of age in Kenya who are geographically hard-to-reach (i.e., those living outside a specified catchment radius from fixed vaccination posts, which served as a proxy for access to services).
Findings: When geographically hard-to-reach children were not vaccinated, there were 1427 total measles cases from 2016 to 2020, resulting in $9.5 million ($3.1–$18.1 million) in direct medical costs and productivity losses and 7504 (3338–12,903) disability-adjusted life years (DALYs). The outreach strategy cost $76 ($23–$142)/DALY averted (compared to no outreach) when 25% of geographically hard-to-reach children received MCV1, $122 ($40-$226)/DALY averted when 50% received MCV1, and $274 ($123-$478)/DALY averted when 100% received MCV1.
Conclusion: Outreach vaccination among geographically hard-to-reach populations was highly cost-effective in a wide variety of scenarios, offering support for investment in an effective outreach vaccination strategy.

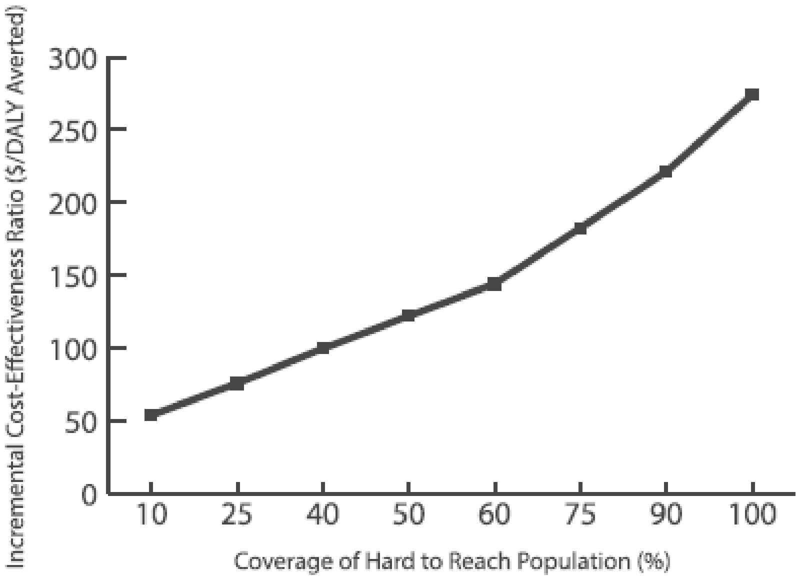

Fig. 3. Incremental cost-effectiveness ratio (ICER) for vaccinating the geographically hard-to-reach target populations with measles 1st and 2nd dose vaccines through proposed outreach vaccination sessions in Kenya. Note: Results assume fixed vaccination post catchment radius of 5 km (km), outreach vaccination post catchment radius of 10 km, measles second dose vaccination coverage among individuals who receive a first measles vaccine dose of 50%, and logistics costs assuming a child is immunized every 15 min. The target population refers to children under 24 months of age.

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Review

Defining hard-to-reach populations for vaccination

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ABSTRACT

Extending the benefits of vaccination to everyone who is eligible requires an understanding of which populations current vaccination efforts have struggled to reach. A clear definition of "hard-to-reach" populations – also known as high-risk or marginalized populations, or reaching the last mile – is essential for estimating the size of target groups, sharing lessons learned based on consistent definitions, and allocating resources appropriately. A literature review was conducted to determine what formal definitions of hard-to-reach populations exist and how they are being used, and to propose definitions to consider for future use. Overall, we found that (1) there is a need to distinguish populations that are hard to reach versus hard to vaccinate, and (2) the existing literature poorly defined these populations and clear criteria or thresholds for classifying them were missing. Based on this review, we propose that hard-to-reach populations be defined as those facing supply-side barriers to vaccination due to geography by distance or terrain, transient or nomadic movement, healthcare provider discrimination, lack of healthcare provider recommendations, inadequate vaccination systems, war and conflict, home births or other homebound mobility limitations, or legal restrictions. Although multiple mechanisms may apply to the same population, supply-side barriers should be distinguished from demand-side barriers. Hard-to-vaccinate populations are defined as those who are reachable but difficult to vaccinate due to distrust, religious beliefs, lack of awareness of vaccine benefits and recommendations, poverty or low socioeconomic status, lack of time to access available vaccination services, or gender-based discrimination. Further work is needed to better define hard-to-reach populations and delineate them from populations that may be hard to vaccinate due to complex refusal reasons, improve measurement of the size and importance of their impact, and examine interventions related to overcoming barriers for each mechanism. This will enable policy makers, governments, donors, and the vaccine community to better plan interventions and allocate necessary resources to remove existing barriers to vaccination.

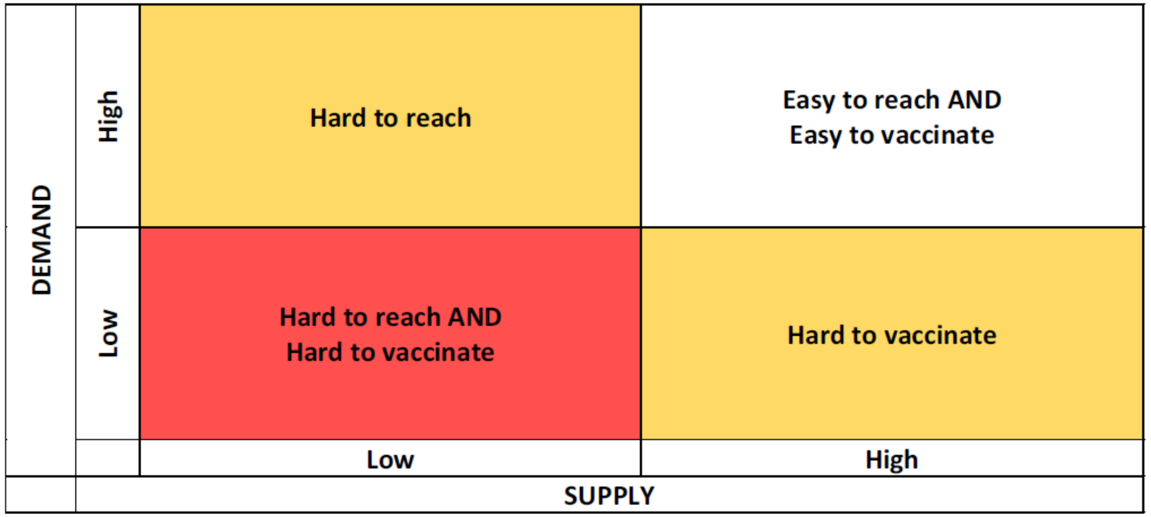

Fig. 1. Conceptual framework of hard-to-reach and hard-to-vaccinate populations.

Table 1
Defining hard-to-reach populations for vaccination, based on current literature.

	Hard-to-reach populations	
	Mechanisms	**Descriptions**
1	Geography by distance	Long distances from health facilities prevent individuals from accessing vaccination services and health providers from reaching individuals during outreach activities.
2	Geography by terrain	Inaccessible and difficult to traverse terrain, such as mountainous areas, wetlands, and islands, prevents individuals from accessing vaccination services and outreach teams from accessing populations.
3	Transient or nomadic movement	Movement by transient or nomadic populations, such as migrants, reduces their access to regular health care and complicates tracking of vaccination status, resulting in missed opportunities for vaccination.
4	Healthcare provider discrimination	Discriminated individuals may be denied services or face ill-treatment, which prevents them from receiving health services and vaccination.
5	Lack of healthcare provider recommendations	Healthcare providers not recommending or endorsing vaccines results in missed vaccination opportunities.
6	Inadequate vaccination systems	Inadequate vaccination infrastructure, human resources, and supply chain disruptions can make people living in catchment areas served by these systems hard to reach for vaccination.
7	War and conflict	In conflict settings, lack of security and destruction of health infrastructure can reduce access to health services and thwart immunization outreach activities.
8	Home births or other home-bound mobility limitations	Homebound individuals and mothers delivering at home may lack mobility to access vaccination services at health facilities.
9	Legal restrictions	Onerous paperwork and registration requirements by health facilities can prevent undocumented or migrant populations from accessing health services. In some instances, care is restricted to those with legal status.

Table 2
Defining hard-to-vaccinate populations, based on current literature.

	Hard-to-vaccinate populations	
	Mechanisms	**Descriptions**
1	Distrust	Lack of trust in vaccines or health institutions, compounded by misinformation, can lead individuals to refuse vaccination.
2	Religious beliefs	Religious populations can object to immunizations based on religious beliefs, such as prohibitions against taking life, dietary laws, or interference with the natural order.
3	Lack of awareness	Lack of awareness of vaccine benefits and recommendations can lead to lower vaccination uptake.
4	Poverty or low socioeconomic status	Low socioeconomic status can preclude individuals from receiving vaccines. Even when vaccines are offered for free, individuals can face other financial barriers.
5	Lack of time	Inflexible scheduling and long wait times can thwart vaccination, especially among individuals with time constraints.
6	Gender-based discrimination	Discriminatory norms in the community, such as gender-based discrimination, lead to lack of agency and access to resources, resulting in fewer vaccinations for women and girls.

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A systems map of the economic considerations for vaccination: Application to hard-to-reach populations

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ABSTRACT

Background: Understanding the economics of vaccination is essential to developing immunization strategies that can be employed successfully with limited resources, especially when vaccinating populations that are hard-to-reach.

Methods: Based on the input from interviews with 24 global experts on immunization economics, we developed a systems map of the mechanisms (i.e., necessary steps or components) involved in vaccination, and associated costs and benefits, focused at the service delivery level. We used this to identify the mechanisms that may be different for hard-to-reach populations.

Results: The systems map shows different mechanisms that determine whether a person may or may not get vaccinated and the potential health and economic impacts of doing so. The map is divided into two parts: 1) the costs of vaccination, representing each of the mechanisms involved in getting vaccinated (n = 23 vaccination mechanisms), their associated direct vaccination costs (n = 18 vaccination costs), and opportunity costs (n = 5 opportunity costs), 2) the impact of vaccination, representing mechanisms after vaccine delivery (n = 13 impact mechanisms), their associated health effects (n = 10 health effects for beneficiary and others), and economic benefits (n = 13 immediate and secondary economic benefits and costs). Mechanisms that, when interrupted or delayed, can result in populations becoming hard-to-reach include getting vaccines and key stakeholders (e.g., beneficiaries/caregivers, vaccinators) to a vaccination site, as well as vaccine administration at the site.

Conclusion: Decision-makers can use this systems map to understand where steps in the vaccination process may be interrupted or weak and identify where gaps exist in the understanding of the economics of vaccination. With improved understanding of system-wide effects, this map can help decision-makers inform targeted interventions and policies to increase vaccination coverage in hard-to-reach populations.

Table 1
Description and example components of costs, health effects, and benefits of vaccination used in the systems map.

Vaccination Costs	**Health Effects for Individual**	**Immediate Economic Benefits**
Cost of transport for beneficiary/caregiver	Adverse events from vaccination	Cost of transport for beneficiary/caregiver averted
Cost of social mobilization	Beneficiary has longer lifespan	Treatment costs averted
Cost of communication materials	Beneficiary can develop adequate cognitive function	Hospitalization costs averted
Productivity losses	Beneficiary can absorb nutrition	Time away from productive work/chores/school averted
Cost of vaccination training	Death averted	Time of others caring for children/animals averted
Cost of vaccinator	Disability averted	Travel time of beneficiary/caregiver averted
Cost of provider incentives	Illness averted	**Secondary Economic Benefits**
Cost of transport for vaccinator	**Health Effects for Others**	Demographic dividend
Cost of cold boxes/carriers	Distress averted from family illness	Economic growth
Cost of vaccines	Control of antimicrobial resistance	Equity
Cost of transport for vaccines	Other people stay healthy	Poverty averted
Cost of transport for supplies	**Health Measures**	Costs of caring for disabled averted
Cost of supplies	QALYs gained	
Cost of vaccines waste disposal	DALYs averted	
Cost to beneficiary/caregiver of vaccination		
Cost of vaccination site		
Cost of beneficiary/caregiver incentives		
Cost of vaccination record-keeping		
Opportunity Costs		
Travel time of beneficiary/caregiver		
Time of others caring for children/animals		
Time away from productive work/chores/school		
Time of vaccinator to treat other patients		
Opportunity cost of outreach		

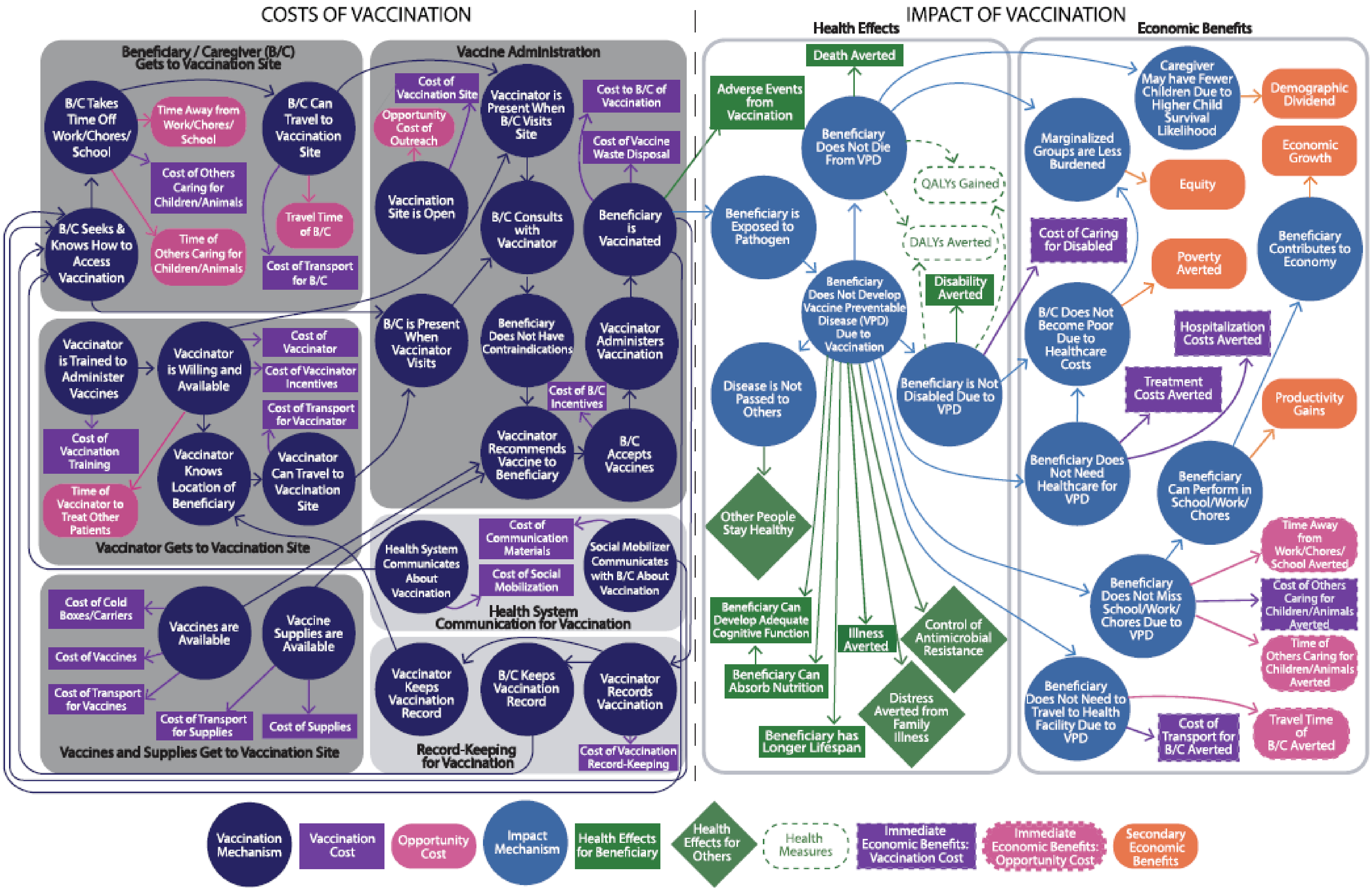

Fig. 1. Systems map of vaccination costs and economic impact.

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Review

Systematic review of the costs for vaccinators to reach vaccination sites: Incremental costs of reaching hard-to-reach populations

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A B S T R A C T

Introduction: Economic evidence on how much it may cost for vaccinators to reach populations is important to plan vaccination programs. Moreover, knowing the incremental costs to reach populations that have traditionally been undervaccinated, especially those hard-to-reach who are facing supply-side barriers to vaccination, is essential to expanding immunization coverage to these populations.

Methods: We conducted a systematic review to identify estimates of costs associated with getting vaccinators to all vaccination sites. We searched PubMed and the Immunization Delivery Cost Catalogue (IDCC) in 2019 for the following costs to vaccinators: (1) training costs; (2) labor costs, per diems, and incentives; (3) identification of vaccine beneficiary location; and (4) travel costs. We assessed if any of these costs were specific to populations that are hard-to-reach for vaccination, based on a framework for examining supply-side barriers to vaccination.

Results: We found 19 studies describing average vaccinator training costs at $0.67/person vaccinated or targeted (SD $0.94) and $0.10/dose delivered (SD $0.07). The average cost for vaccinator labor and incentive costs across 29 studies was $2.15/dose (SD $2.08). We identified 13 studies describing intervention costs for a vaccinator to know the location of a beneficiary, with an average cost of $19.69/person (SD $26.65), and six studies describing vaccinator travel costs, with an average cost of $0.07/dose (SD $0.03). Only eight of these studies described hard-to-reach populations for vaccination; two studies examined incremental costs per dose to reach hard-to-reach populations, which were 1.3–2 times higher than the regular costs. The incremental cost to train vaccinators was $0.02/dose, and incremental labor costs for targeting hard-to-reach populations were $0.16–$1.17/dose.

Conclusion: Additional comparative costing studies are needed to understand the potential differential costs for vaccinators reaching the vaccination sites that serve hard-to-reach populations. This will help immunization program planners and decision-makers better allocate resources to extend vaccination programs.

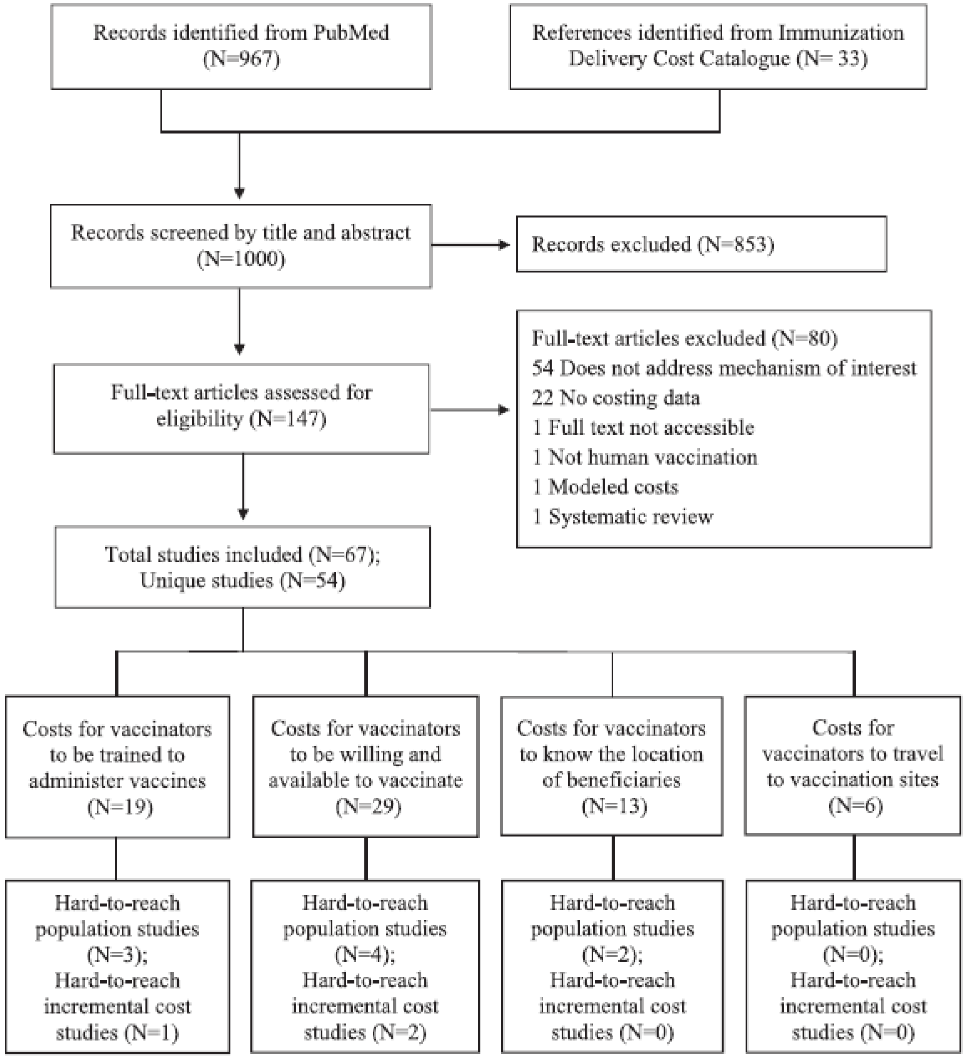

Fig. 1. Literature search process for systematic review of costs for vaccinators to reach vaccination sites, 2000–2019.

Category	Average Cost	Evidence
Vaccinator Training Costs	$0.67/person vaccinated or targeted (SD $0.94) $0.10/dose delivered (SD $0.07)	19 studies
Vaccinator Labor and Incentive Costs	$2.15/dose (SD $2.08)	29 studies
Costs for a Vaccinator to Know the Location of a Beneficiary	$19.69/person (SD $26.65)	13 studies
Vaccinator Travel Costs	$0.07/dose (SD $0.03)	6 studies
Incremental Costs to Reach Hard-to-Reach Populations	1.3-2 times higher	2 studies

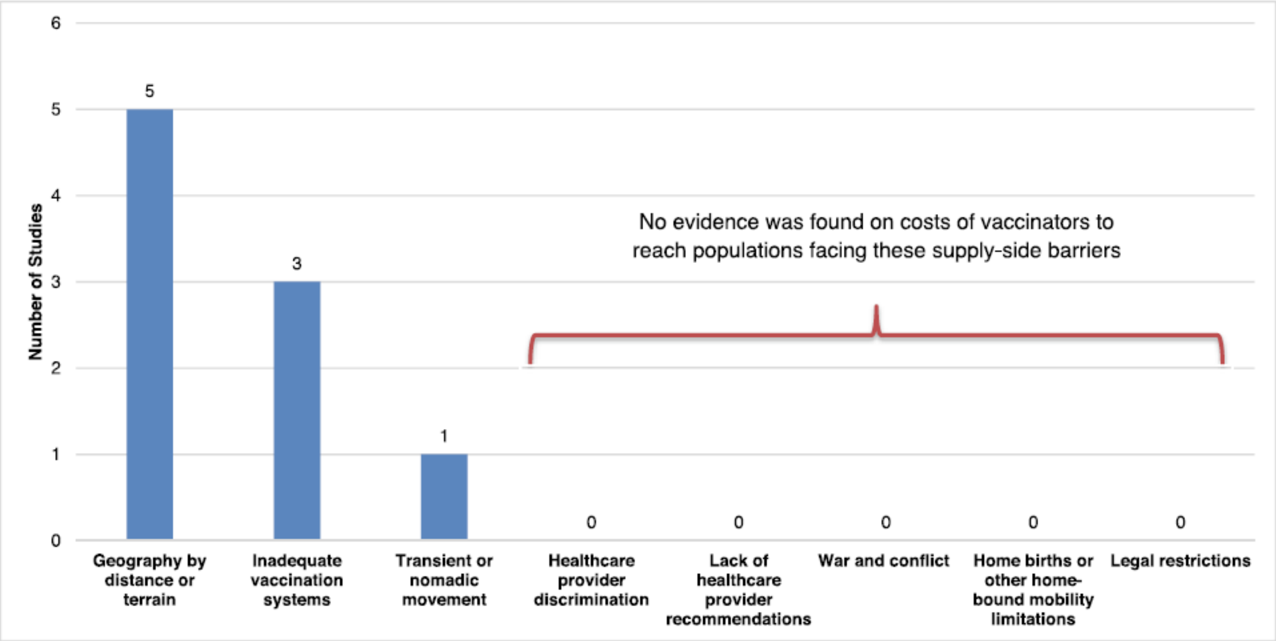

Fig. 2. Distribution of mechanisms that make a population hard-to-reach, across studies describing costs of vaccinators to reach hard-to-reach populations, systematic review, 2000–2019.

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Review

Promoting, seeking, and reaching vaccination services: A systematic review of costs to immunization programs, beneficiaries, and caregivers

Tatenda T. Yemeke [a], Elizabeth Mitgang [b], Patrick T. Wedlock [b], Colleen Higgins [a], Hui-Han Chen [a], Sarah W. Pallas [c], Taiwo Abimbola [c], Aaron Wallace [c], Sarah M. Bartsch [b], Bruce Y Lee [b], Sachiko Ozawa [a,d,*]

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ABSTRACT

Introduction: Understanding the costs to increase vaccination demand among under-vaccinated populations, as well as costs incurred by beneficiaries and caregivers for reaching vaccination sites, is essential to improving vaccination coverage. However, there have not been systematic analyses documenting such costs for beneficiaries and caregivers seeking vaccination.

Methods: We searched PubMed, Scopus, and the Immunization Delivery Cost Catalogue (IDCC) in 2019 for the costs for beneficiaries and caregivers to 1) seek and know how to access vaccination (i.e., costs to immunization programs for social mobilization and interventions to increase vaccination demand), 2) take time off from work, chores, or school for vaccination (i.e., productivity costs), and 3) travel to vaccination sites. We assessed if these costs were specific to populations that faced other non-cost barriers, based on a framework for defining hard-to-reach and hard-to-vaccinate populations for vaccination.

Results: We found 57 studies describing information, education, and communication (IEC) costs, social mobilization costs, and the costs of interventions to increase vaccination demand, with mean costs per dose at \$0.41 (standard deviation (SD) \$0.83), \$18.86 (SD \$50.65) and \$28.23 (SD \$76.09) in low-, middle-, and high-income countries, respectively. Five studies described productivity losses incurred by beneficiaries and caregivers seeking vaccination (\$38.33 per person; SD \$14.72; n = 3). We identified six studies on travel costs incurred by beneficiaries and caregivers attending vaccination sites (\$11.25 per person; SD \$9.54; n = 4). Two studies reported social mobilization costs per dose specific to hard-to-reach populations, which were 2–3.5 times higher than costs for the general population. Eight studies described barriers to vaccination among hard-to-reach populations.

Conclusion: Social mobilization/IEC costs are well-characterized, but evidence is limited on costs incurred by beneficiaries and caregivers getting to vaccination sites. Understanding the potential incremental costs for populations facing barriers to reach vaccination sites is essential to improving vaccine program financing and planning.

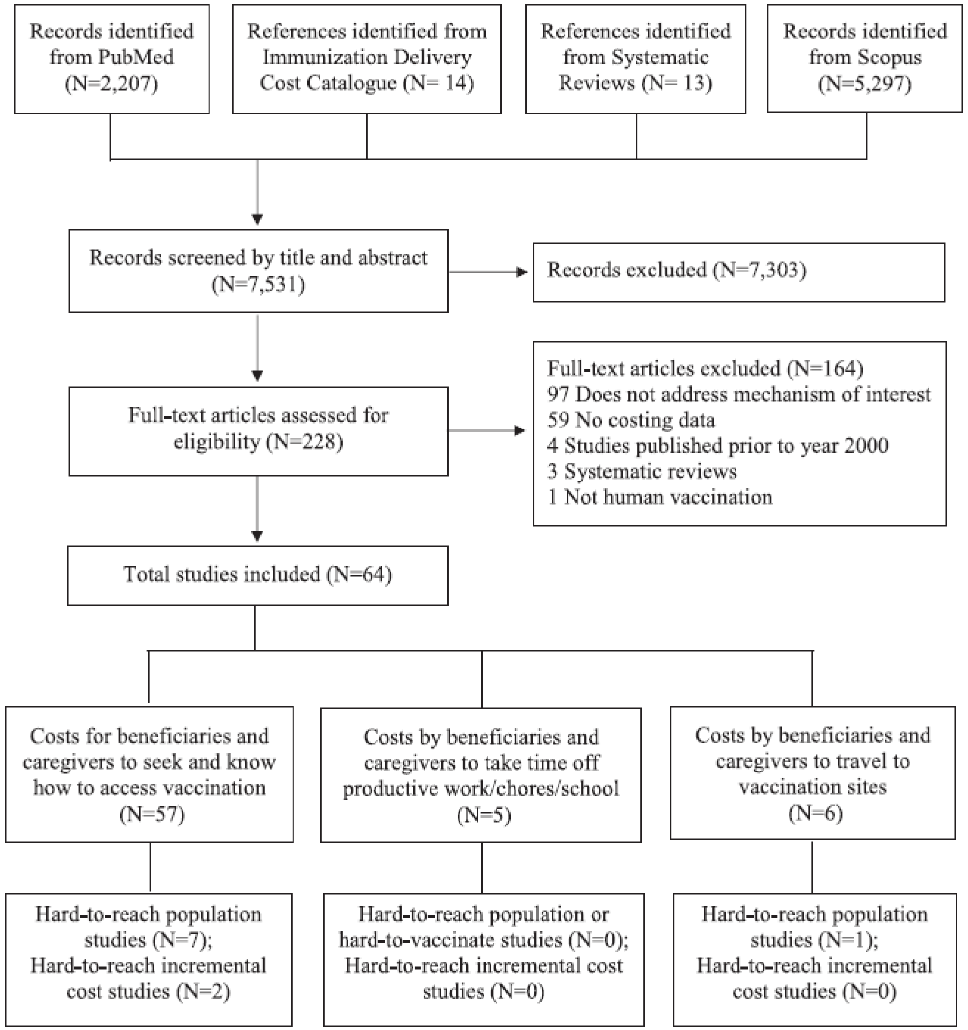

Fig. 1. Literature search process for systematic review of costs for beneficiaries and caregivers to seek and reach vaccination sites, 2000–2019.

Category	Average Cost	Evidence
Information, Education, and Communication (IEC) Costs, Social Mobilization Costs, Costs of Interventions to Increase Vaccination Demand	$0.41/dose (SD $0.83) in low-income country $18.86/dose (SD $50.65) in middle-income country $28.23/dose (SD $76.09) in high-income country	57 studies (11 low-, 11 middle-, 21 high-income with costs)
Education	$46.13/dose (SD$57.83) mostly high-income countries	6 studies
Reminders	$40.90/dose (SD$101.56) mostly high-income countries	12 studies
Immunization Information System	$2.20/dose (SD$1.48) in high-income countries	5 studies
Expand Routine Immunization Services	$0.55/dose (SD$0.93) in LMICs	8 studies
Campaigns/SIAs	$0.09/dose (SD$0.07) in LMICs	11 studies
Productivity Losses Incurred by Beneficiaries and Caregivers Seeking Vaccination	$38.33/person (SD $14.72)	5 studies (3 with costs)
Travel Costs Incurred by Beneficiaries and Caregivers Attending Vaccination Sites	$11.25/person (SD $9.54)	6 studies (4 with costs)
Social Mobilization Costs to Reach Hard-to-Reach Populations	2-3.5 times higher	2 studies

T.T. Yemeke, E. Mitgang, P.T. Wedlock et al. Vaccine 39 (2021) 4437–4449

Vaccination Demand Resilience (VDR) Framework

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How to increase and maintain high immunization coverage: Vaccination Demand Resilience (VDR) framework

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ABSTRACT

Background: Resilience in vaccination demand is ever more critical as the COVID-19 pandemic has increased our understanding of the importance of vaccines on health and well-being. Yet timid demand for COVID-19 vaccines where available and reduced uptake of routine immunizations globally further raise the urgent need to build vaccination resilience. We demonstrate the complexity of vaccination demand and resilience in a framework where relevant dimensions are intertwined, fluid, and contextual.
Methods: We developed the Vaccination Demand Resilience (VDR) framework based on a literature review on vaccination demand and expert consultation. The matrix framework builds on three main axes: 1) vaccination attitudes and beliefs; 2) vaccination seeking behavior; and 3) vaccination status. The matrix generated eight quadrants, which can help explain people's levels of vaccination demand and resilience. We selected four scenarios as examples to demonstrate different interventions that could move people across quadrants and build vaccination resilience.
Results: Incongruence between individuals' attitudes and beliefs, vaccination behavior, and vaccination status can arise. For example, an individual can be vaccinated due to mandates but reject vaccination benefits and otherwise avoid seeking vaccination. Such incongruence could be altered by interventions to build resilience in vaccination demand. These interventions include information, education and communication to change individuals' vaccination attitudes and beliefs, incentive programs and reminder-recalls to facilitate vaccination seeking, or by strengthening healthcare provider communications to reduce missed opportunities.
Conclusions: Vaccination decision-making is complex. Individuals can be vaccinated without necessarily accepting the benefits of vaccination or seeking vaccination, threatening resilience in vaccination demand. The VDR framework can provide a useful lens for program managers and policy makers considering interventions and policies to improve vaccination resilience. This would help build and sustain confidence and demand for vaccinations, and help to continue to prevent disease, disability, and death from vaccine-preventable diseases.

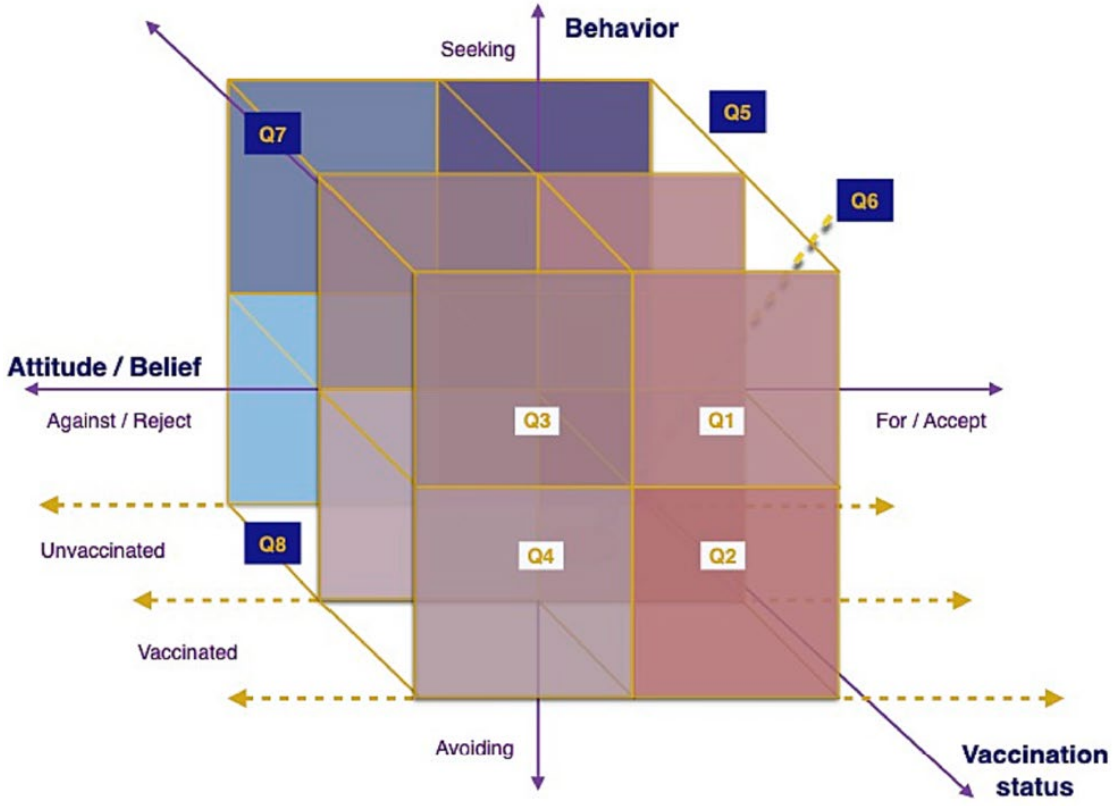


Fig 1. The Vaccine Demand Resilience (VDR) Framework

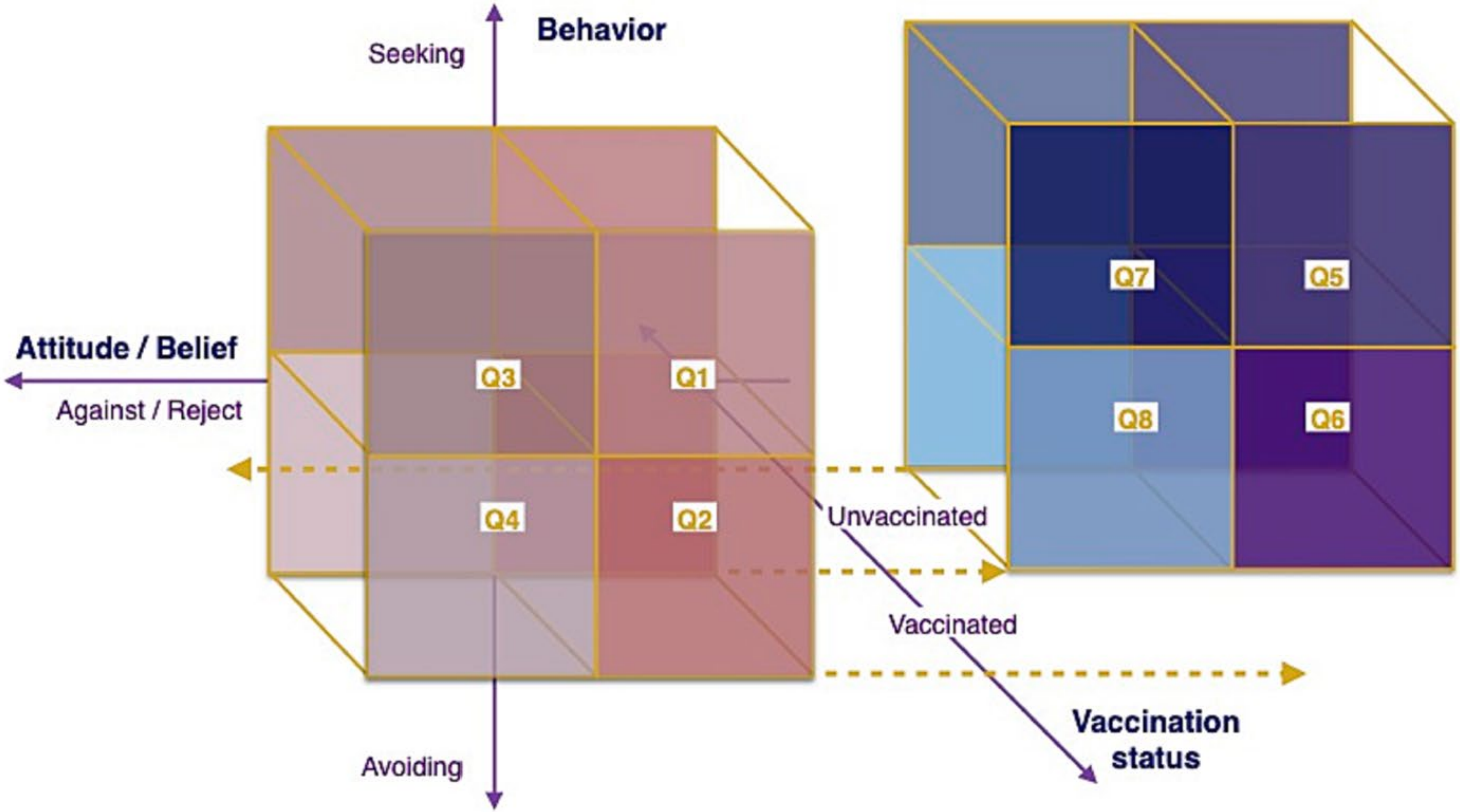


Fig. 2. Subdividing the Vaccine Demand Resilience (VDR) framework on attitudinal/belief and behavioral dynamics of vaccinated populations (left, in pink) and unvaccinated populations (right, in blue).

Table 1
The Vaccination Demand Resilience (VDR) framework components and relevant interventions.

Quadrant	Accepting*	Seeking*	Vaccinated*	Definition	Description	Relevant Interventions
Q1	+	+	+	Individual accepts the benefits of vaccination, seeks vaccination, and is vaccinated	Individuals who fully accept the benefits of vaccination and actively seek vaccination until they are vaccinated. Their demand for vaccination is resilient.	• Interventions to reinforce and maintain vaccine acceptance and seeking behavior, such as reminders
Q2	+	–	+	Individual accepts the benefits of vaccination, but avoids seeking vaccination, yet is vaccinated	Individuals who accept the benefits of vaccination and are vaccinated but face barriers that prevent them from fully seeking vaccination. These individuals are at risk of being unvaccinated, having partial compliance to immunization schedules, or not receiving all doses.	• Interventions to facilitate or induce seeking behavior, by increasing convenience and affordability, such as incentive programs and reminder-recall interventions
Q3	–	+	+	Individual rejects the benefits of vaccination, but seeks vaccination, and is vaccinated	Individuals who seek vaccination due to mandates or due to decision environments that default to vaccination, such as for schooling or employment, but do not accept the benefits of vaccination.	• Knowledge, education, and awareness interventions tailored to reasons for lack of acceptance of vaccination • Interventions to strengthen mandates/ sanctions for non-vaccination, such as narrowing exemptions
Q4	–	–	+	Individual rejects the benefits of vaccination, and avoids seeking vaccination, yet is vaccinated	Individuals who are vaccinated because of mandates or due to decision environments that default to vaccination, such as for schooling or employment, but do not accept the benefits of vaccination. Individual would not seek vaccination in the absence of mandate and may actively seek exemptions where possible.	• Knowledge, education, and awareness interventions tailored to reasons for lack of acceptance of vaccination • Interventions to strengthen mandates/ sanctions for non-vaccination, such as narrowing exemptions • Interventions to facilitate or induce seeking behavior, by increasing convenience and affordability, such as incentive programs and reminder-recall interventions

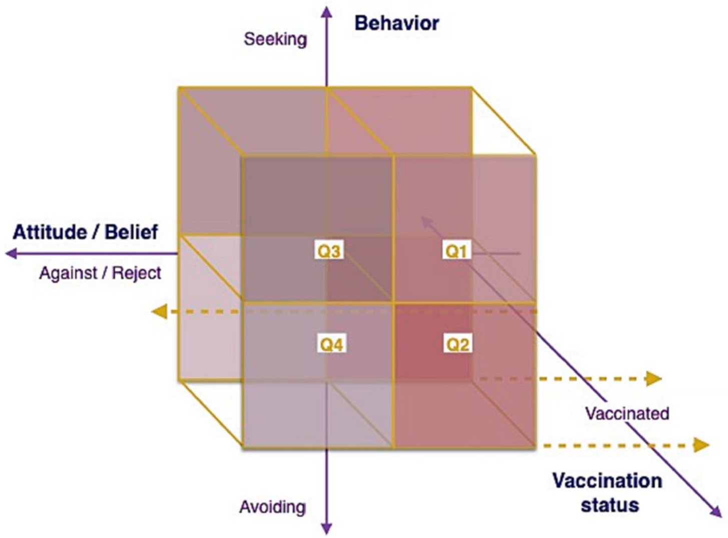
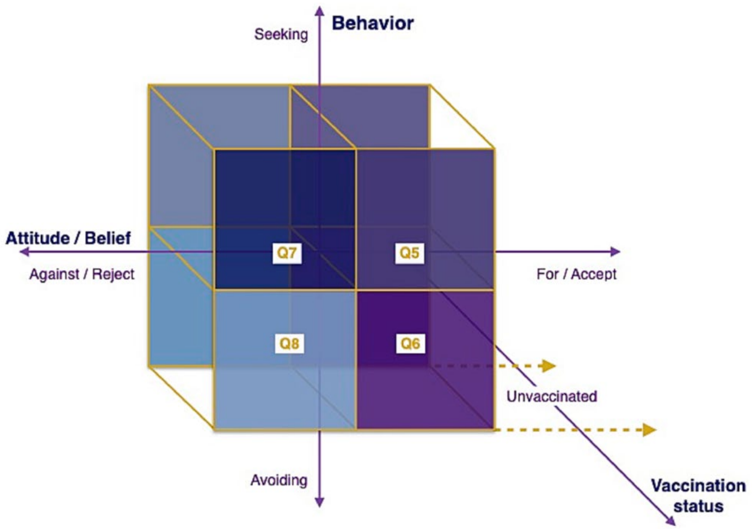


Table 1
The Vaccination Demand Resilience (VDR) framework components and relevant interventions.

Quadrant	Accepting*	Seeking*	Vaccinated*	Definition	Description	Relevant Interventions
Q5	+	+	–	Individual accepts the benefits of vaccination, and seeks vaccination, but is not vaccinated	Individuals who accept the benefits of vaccination and seek vaccination but are unvaccinated due to supply factors, such as vaccine unavailability or missed opportunities for vaccination.	• Interventions to improve vaccination supply • Interventions to strengthen patient provider communication • Intervention to reduce missed opportunities for vaccination at health facilities
Q6	+	–	–	Individual accepts the benefits of vaccination, but avoids seeking vaccination, and is not vaccinated	Individuals who accept the benefits of vaccination but avoid seeking vaccination and remain unvaccinated, due to factors such as inconvenience and time constraints.	• Interventions to facilitate or induce seeking behavior, by increasing convenience and affordability, such as incentive programs and reminder-recall interventions
Q7	–	+	–	Individual rejects the benefits of vaccination, but seeks vaccination, yet is not vaccinated	Individuals who seek vaccination because of mandates, even while rejecting the benefits of vaccination; however, they are unvaccinated because of supply factors or missed opportunities for vaccination.	• Knowledge, education, and awareness interventions tailored to reasons for lack of acceptance of vaccination • Interventions to improve vaccine availability, supply and ease of access, such as vaccine outreach programs
Q8	–	–	–	Individual rejects the enefits of vaccination, and voids seeking vaccination, nd is not vaccinated	Individuals who are anti-vaccination, rejecting the benefits of vaccination, actively avoiding seeking vaccination and remain unvaccinated. Individuals may have a strong ideological or belief systems for rejecting vaccinations.	• Knowledge, education, and awareness interventions tailored to reasons for lack of acceptance of vaccination • Interventions that engage religious leaders and social influencers and are contextualized to beliefs and ideologies driving vaccine hesitancy and rejection • Interventions to facilitate or induce seeking behavior, by increasing convenience and affordability, such as incentive programs and reminder-recall interventions • Interventions to strengthen mandates/ sanctions for non-vaccination, such as narrowing exemptions



Return on Investment in Vaccine Demand Interventions…?

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