

Benefits of Vaccines

September 12, 2018
National Vaccine Advisory Committee

Sachiko Ozawa, MHS, PhD
Associate Professor
Eshelman School of Pharmacy
University of North Carolina at Chapel Hill
ozawa@unc.edu





Rising to the challenge

GAVI Alliance Partners' Forum
5-7 December 2012, Dar es Salaam, Tanzania

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

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.

At the start of the decade 2011-20, declared the Decade of Vaccines, the global health community committed itself to accelerating the introduction of new vaccines and increasing coverage of existing vaccines to save lives and avert illness in the world's poorest countries. Endorsed by all 194 member states of the World Health Organization (WHO) in May 2012, the Global Vaccine Action Plan identified vaccination as an essential public health tool for improving global health and advancing economic development. Despite increased global attention to immunization, comprehensive evidence on its value remains limited. For key stakeholders, including funders and multilateral organizations, estimating the global return on investment (ROI) associated with immunization can play an integral role in advocating for expanded investment during the decade.

The return on investment quantifies the net benefits gained from every dollar invested on an aggregate level. It can serve as a useful policy-making tool with advantages beyond estimates of costs or benefits alone because it provides an assessment of the returns in relation to their costs. Unlike cost-effectiveness analysis, which employs various health metrics such as disability-adjusted life-years or quality-adjusted life-years to measure benefits, return on investment measures benefits in monetary units, thus providing more comparability and easier comprehension. In addition, ROI analyses typically incorporate productivity losses and societal costs that go beyond the economic benefits captured in cost-effectiveness analyses. This versatility is particularly important for policy makers who require evidence to make financial decisions across sectors. Unfortunately, ROI estimates for health care interventions are rare, which lim-

DOI: 10.1377/hlthaff.2015.1086
HEALTH AFFAIRS 35,
NO. 2 (2016): 199-207
©2016 Project HOPE—
The People-to-People Health
Foundation, Inc.

Sachiko Ozawa (ozowad@jhu.edu) is an assistant scientist in the Department of International Health at the Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland.

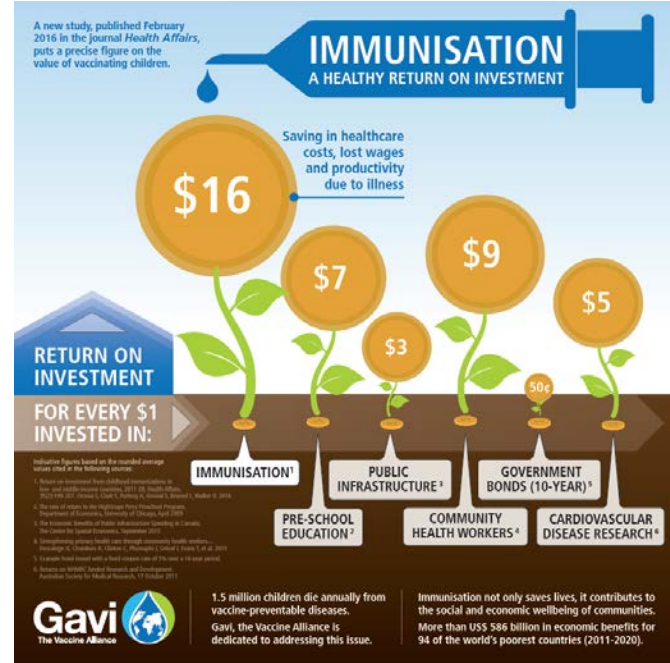
Samantha Clark is a research associate in the Department of International Health at the Johns Hopkins Bloomberg School of Public Health.

Allison Portnoy is an SD candidate in the Department of Global Health and Population, Harvard TH Chan School of Public Health, in Boston, Massachusetts.

Simrun Grewal is a PhD candidate in the Pharmaceutical Outcomes Research and Policy Program, University of Washington, in Seattle.

Logan Brenzel is a senior program officer for cost-effectiveness in vaccine delivery at the Bill & Melinda Gates Foundation in Washington, D.C.


Damian G. Walker is a deputy director for data and analytics in global development at the Bill & Melinda Gates Foundation in Seattle.





#AddisVxDec endorsement shows #Africa's leaders are ready 2 deliver on promise of #immunization 4 all. bit.ly/ADI_#28thAUs Summit

Every \$1 spent on childhood immunizations in Africa returns \$44 in economic benefits.



Immunization builds healthier:

- Children
- Communities
- Economies

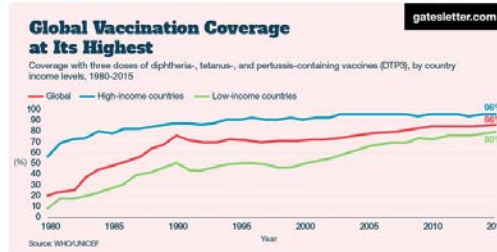
ADDIS DECLARATION ON IMMUNIZATION



Bill Gates
@BillGates

Following

For every \$1 spent on childhood vaccines, you get \$44 in benefits. You can't beat that deal: b-gat.es/2ltQaJ7



RETWEETS 5,431 LIKES 11,091

7:54 AM - 18 Feb 2017

308 5.4K 11K

"For every dollar spent on childhood immunizations, you get \$44 in economic benefits." gatesnotes.com/2017-annual-le... via @billgates



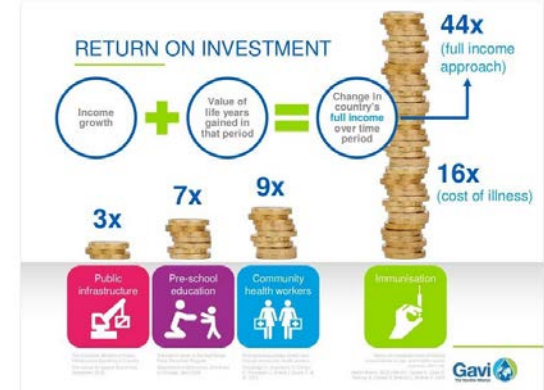
Warren Buffett's Best Investment
Read Bill and Melinda Gates's 2017 Annual Letter gatesnotes.com



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



Benefits of Vaccines



- Health



- Education



- Economics



- Equity



- Health Systems



- Global Healthy Security

<https://immunizationevidence.org>



Health Benefits

Growth, Development, & Nutrition

- Vaccinations positively predicted children's height, weight, and haemoglobin level in India (Bhargava et al. 2011; Anekwe & Kumar 2012)
- Immunization was protective against stunting in Kenya (Gewa & Yandell 2011)
- Vaccination associated with better child growth in Indonesia (Paknawin-Mock et al. 2000)
- Maternal immunization reduced likelihoods of prematurity and small-for-gestational-age births in US (Omer et al. 2011)

Long-term Disability

- Significant *sequelae* due to bacterial meningitis in Africa (Ramakrishnan et al. 2009)

Herd Effects

- Herd immunity from Rotavirus vaccine estimated in Australia, Belgium, Brazil, El Salvador, Mexico, Nicaragua, Panama, Rwanda, United States (Pollard 2015; Patel 2012; Ngabo 2016)
- Herd effect of pneumococcal conjugate vaccine estimated in US (Ray et al. 2006)

Evidence Gaps

How does maternal immunization benefit neonatal health?

What is the value of vaccination derived from herd effects?



Health Benefits

Demographic Transition

- Immunization associated with reduced child mortality in India (Kumar 2009)
- By reducing child mortality, immunization may reduce birth rates, family size (Barnighausen et al. 2008)

Indirect Health Benefits

- Non-specific effect of measles vaccination on overall child mortality in India (Kabir et al. 2003)
- High coverage of HepB, Polio and Hib vaccines were protective against acute lymphoblastic leukemia in US (Pagaoa et al. 2011)

Maternal Health

- Maternal immunization improves maternal and child health (Steedman et al. 2016)

Evidence Gaps

What is the value of vaccination in triggering a fertility decline?

What is the anticipated value of prospective vaccines?



Education Benefits

Cognition

- Childhood vaccination correlates with increased cognitive test scores in the Philippines (Bloom et al. 2010)
- Early childhood diarrhea associated with cognitive function in Brazil (Niehaus et al. 2002)
- Pneumococcal meningitis frequently correlates with cognitive impairment (Goetghebuer 2000; Ramakrishnan 2009)
- Pneumococcal otitis media associated with lower scores on cognitive ability, speech, language, and school performance in United States (Teele et al. 1990)

Educational Attainment

- Measles vaccination associated with increased educational attainment in South Africa (Tobenna et al. 2015; Anekwe et al. 2015)
- Maternal tetanus immunization associated with increased educational attainment among children in Bangladesh (Canning et al. 2011)
- Diarrhea associated with poor school performance in Brazil (Lorntz et al. 2006)

Evidence Gaps

What is the value of vaccination in promoting cognitive development, school attendance, & educational attainment?



Economic Benefits

Cost-Effectiveness

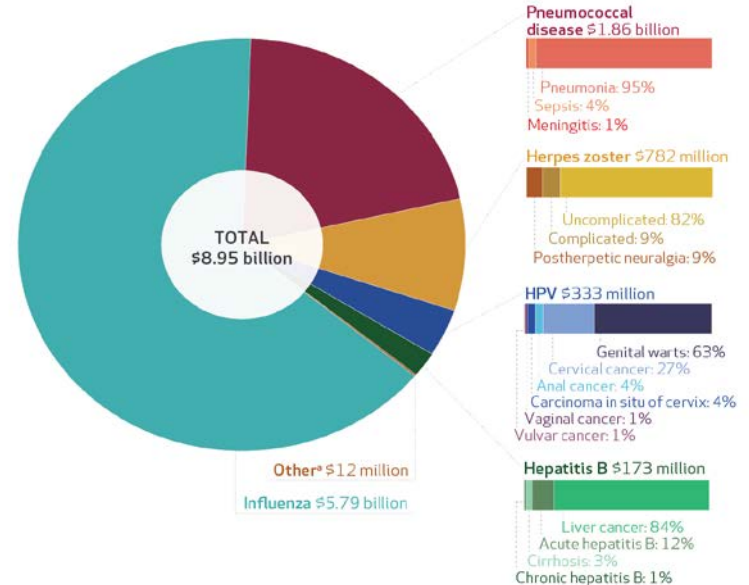
- Vaccines are an efficient, cost-effective investment (Ozawa et al. 2012 [LMICs]; Boujaoude et al. 2018 [Rotavirus]; Ng et al. 2018 [HPV]; Pasquini-Descomps 2017 [H1N1]; Saokaew et al. 2016 [Pneumococcal]; Szucs & Pfeil 2013 [Zoster]; Thompson & Odahowski 2014 [MR])

Cost of Treating Illness

- Vaccines can avert significant costs of preventable illness globally (Ozawa et al. 2017; Stack et al. 2011; Ozawa et al. 2011)
- Economic burden of vaccine-preventable diseases in United States (Ozawa et al. 2016; McLaughlin et al. 2015)

Estimated burden of \$9 billion (\$4.7–\$15.2 billion) for 2015, from VPDs related to 10 vaccines recommended for US adults

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



Sachiko Ozawa et al. Health Aff 2016;35: published online

©2016 by Project HOPE - The People-to-People Health Foundation, Inc.

HealthAffairs



Economic Benefits

Poverty

- Vaccine-preventable diseases can cause borrowing and loss of assets (Alamgir et al. 2010 [pneumonia]; Van Damme et al. 2004 [dengue]; Hendrix et al. 2017 [diarrhea])
- Vaccines can prevent millions of cases of medical impoverishment in 41 LMICs (Chang et al. 2018; Verguet et al. 2016)
- Immunization can offset the impact of poverty on child survival (Bawah et al. 2009)

Outbreak Costs

- Economic impact of epidemics (Suarez & Bradford 1993 [cholera]; Kirigia et al. 2009 [cholera]; Smith et al. 2009 [pandemic flu])

Return on Investment

- ROI \$16-44 for every \$1 invested in childhood vaccination (Ozawa et al. 2016)
- ROI €4 for every €1 spent to vaccinate healthcare workers against pertussis in the Netherlands (Tariq et al. 2015)
- 21% rate of return for childhood vaccination in the Philippines (Bloom et al. 2005)

Evidence Gaps

What is the value of vaccination in promoting labor force participation, hours worked & earnings?

What are the costs and benefits of reaching hard-to-reach populations?



Equity Benefits

Gender Inequity

- Girls benefited from greater reductions in child mortality from measles vaccination (Koenig et al. 2001)

Wealth Inequity

- Vaccination has greatest benefit amongst the poor (Chang et al. 2018; Bawah et al. 2010; Johannsen et al. 2015 [pneumococcal]; Rheingans et al. 2012 [rotavirus]; Bishai et al. 2003 [measles])
- Immunization was the most equitably distributed child health service across wealth quintiles in 54 countries (Boerma et al. 2008)

Health Inequity

- Vaccines are critical for immunocompromised children (Shigayeva et al. 2016 [pneumococcal]; Madhi et al. 2005 [pneumococcal]; Ramakrishnan et al. 2010 [Hib])

Evidence Gaps

What is the value of vaccination in reducing social and economic inequities?



Health systems benefits

Vaccines Alleviate Health Systems Pressure

- Vaccine introduction reduced hospital admissions (Burnett et al. 2017; Ngabo et al. 2016)

Health Systems Strengthening

- Polio eradication efforts delivered other health benefits, strengthened health systems (Cochi et al. 2016)
- Polio and measles/rubella program infrastructures leveraged during pandemic H1N1, Ebola outbreaks (Andrus et al. 2016; Shuaib et al. 2014)

Synergies With Other Health Services

- Vaccinations in early infancy provides an opportunity for developmental screening (Olusanya 2009)
- Introduction of HPV vaccine in Rwanda provided additional health services to all school-children (Torres-Rueda et al. 2016)

Evidence Gaps

What is the value of vaccination in strengthening health systems?

What is the value of vaccination in improving access to health services?



Global health security benefits

Health Security

- Global immunization controls emerging disease outbreaks and spread of disease across national borders (Andrus et al. 2010)

Antibiotic Resistance

- Vaccination reduced the rate of antibiotic and multi-drug resistant strains of pneumococcal disease in South Africa (Von Gottberg et al. 2014)
- Vaccines reduced antibiotic use in Israel and the United States (Fireman et al. 2003; Degan et al. 2001)

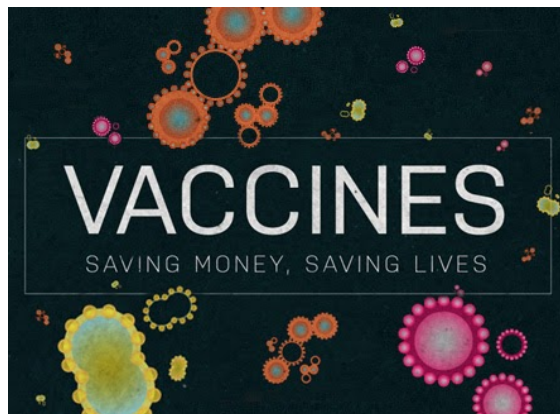
Evidence Gaps

What is the value of vaccination in controlling the development of antimicrobial resistance?

Conclusions

- A large and growing literature demonstrates the significant and multiple types of health and economic benefits associated with vaccines
- **Significant additional work remains** to further characterize and communicate the value of vaccines
- Research demonstrating the benefits of vaccines can be a **powerful tool to influence policies**

Thank You!



Ozawa et al. Vaccines Work Infographic (2012).
<https://www.trendhunter.com/trends/vaccines-work-infographic>

Sachiko Ozawa, MHS, PhD
University of North Carolina at Chapel Hill
ozawa@unc.edu



The Role of Vaccines in the Prevention of Antimicrobial Resistance

Kent E. Kester, M.D.

Disclosure Statements

- Vice President and Head, Translational Science & Biomarkers, Sanofi Pasteur
- Member of the DHHS Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria (PACCARB)
- All comments reflect personal opinion and should not be construed to represent the official positions of either Sanofi Pasteur or the PACCARB

Antimicrobial Resistance (AMR): A Global Healthcare Emergency

- **Resistance to antibiotics**

- Resistant bacteria/fungi account for >2 million infections and >23,000 deaths/year in the United States (CDC 2013)
- A predictable biologic process (example of *Staph. aureus*—originally sensitive to penicillin and now commonly resistant to β -lactam antibiotics)
- Some bacteria are intrinsically resistant to many antibiotics (e.g., *Acinetobacter*); use of broad-spectrum antibiotics (in ICUs) selects for these bacteria contributing to healthcare-associated infections
- Continued emerging resistance by *Klebsiella*, *E. coli*, *Pseudomonas*, and *N. gonorrhoeae*

- **Highlighted by limited pipeline of novel antibiotics**

- AMR crisis often simplistically reduced to a lack of antibiotics
- Key factors: Cost of new antibiotic development, risk of inducing resistance, challenging clinical trial requirements, label indications (organism vs. syndrome), antibiotic stewardship, market, etc.
- Pew Antibiotic Pipeline Study: <http://www.pewtrusts.org/en/research-and-analysis/issue-briefs/2014/03/12/tracking-the-pipeline-of-antibiotics-in-development>

CONTINUED CONCERNS ABOUT ANTIBIOTIC RESISTANT GONORRHEA



Gonorrhea
is expected to
eventually wear down
our last highly
effective antibiotic



Lab tests show a small
but growing fraction of
gonorrhea samples have
**signs of emerging
antibiotic resistance**



CDC recommends a
two-drug combination
to preserve our **last
highly effective
antibiotic**

For more information, visit
cdc.gov/nchstp/newsroom



U.S. Department of
Health and Human Services
Centers for Disease
Control and Prevention

AMR Priority Pathogen Lists

CDC Priority Pathogens

- Urgent Threats
 - *C. difficile*
 - Carbapenem-resistant enterobacteriaceae (CRE)
 - *N. gonorrhoeae*
- Serious Threats
 - *A. baumannii*
 - Resistant campylobacter
 - Fluconazole-resistant *Candida*
 - Extended spectrum β - lactamase (ESBL) GNRs
 - Vancomycin-resistant enterococcus (VRE)
 - Resistant typhoidal/non-typhoidal salmonellae
 - Resistant *Shigella*
 - MRSA
 - Resistant pneumococcus
 - Resistant TB (MDR TB/XDR TB)
- Concerning Threats
 - Vancomycin-resistant *Staph. Aureus*
 - Erythromycin-resistant Group A streptococci
 - Clindamycin-resistant Group B streptococci

WHO Priority Pathogens



WHO PRIORITY PATHOGENS LIST FOR R&D OF NEW ANTIBIOTICS

Priority 1: CRITICAL[#]

Acinetobacter baumannii, carbapenem-resistant
Pseudomonas aeruginosa, carbapenem-resistant
*Enterobacteriaceae**, carbapenem-resistant, 3rd generation
cephalosporin-resistant

Priority 2: HIGH

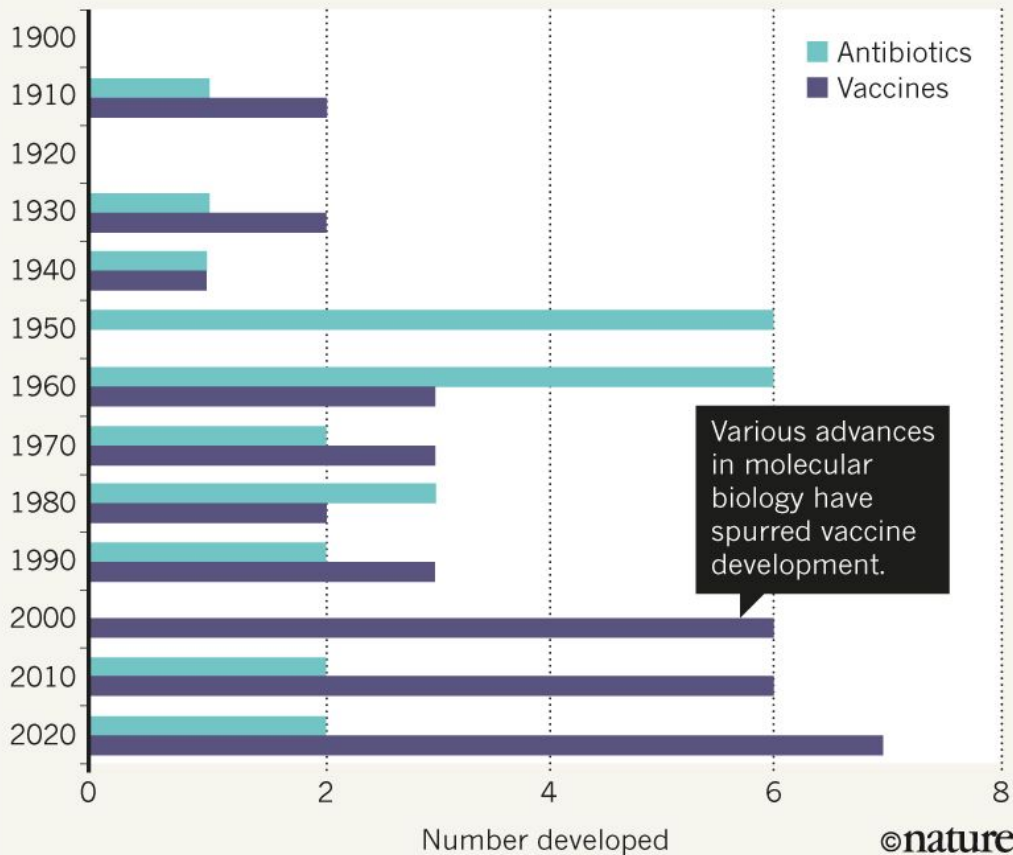
Enterococcus faecium, vancomycin-resistant
Staphylococcus aureus, methicillin-resistant, vancomycin
intermediate and resistant
Helicobacter pylori, clarithromycin-resistant
Campylobacter, fluoroquinolone-resistant
Salmonella spp., fluoroquinolone-resistant
Neisseria gonorrhoeae, 3rd generation cephalosporin-resistant,
fluoroquinolone-resistant

Priority 3: MEDIUM

Streptococcus pneumoniae, penicillin-non-susceptible
Haemophilus influenzae, ampicillin-resistant
Shigella spp., fluoroquinolone-resistant

VACCINES IN THE LEAD

Since the 1980s, 22 vaccines have been deployed in the clinic, but no truly new class of antibiotics has been discovered or engineered.



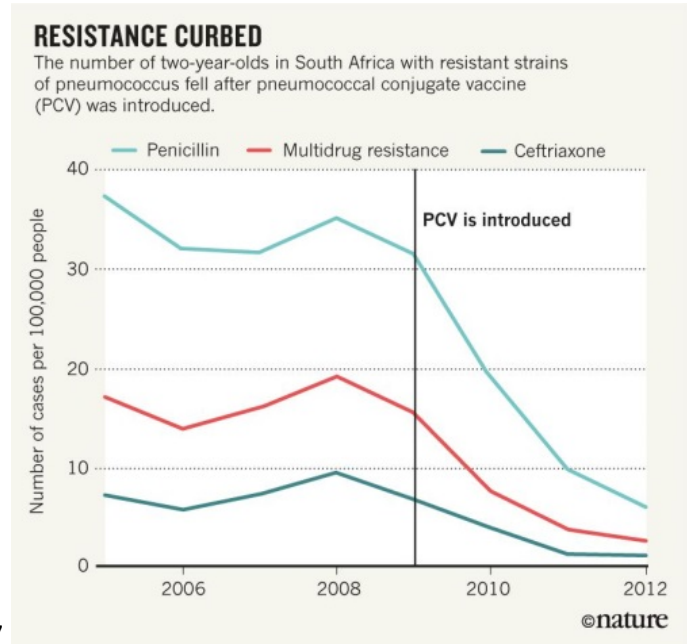
What role can vaccines play to reduce/prevent AMR?

- **Direct effect**

- Vaccines that specifically target pathogens associated with AMR (e.g., MRSA, *Pseudomonas*, *Klebsiella*, etc.)
- Challenge: Very specific targets gives limited market

- **Indirect effects**

- Prevention of bacterial/viral diseases that cause clinical syndromes for which antibiotics are frequently prescribed (e.g., influenza, pneumococcus, *Haemophilus*, etc.)



DHHS PACCARB: Vaccines as a key element in the response against AMR

2017 top recommendations for incentivizing the development of vaccines against AMR:

- Additional funding for vaccines that prevent viral/bacterial infections that drive antibiotic use
- Optimize regulatory interactions (FDA, CDC/ACIP, etc.)
- Incentivize vaccine update (e.g., education, reimbursement strategies, etc.)

Other recommendations:

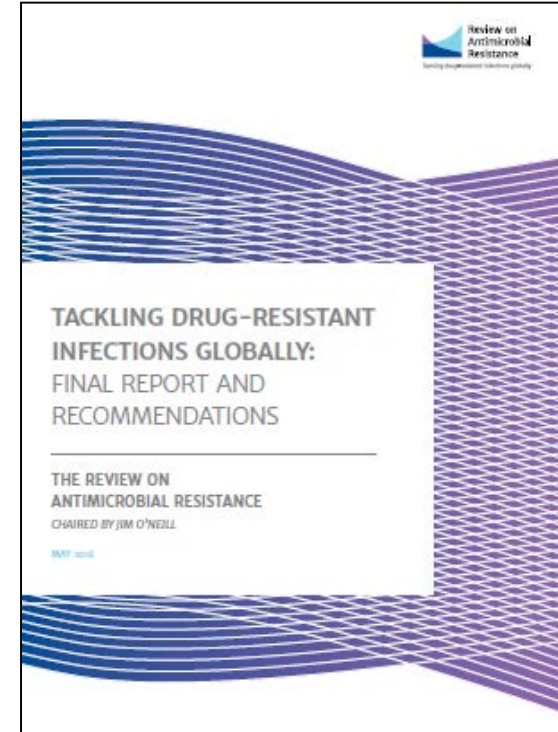
- Analysis of cost/societal impacts associated with new vaccine development (generate value evidence)
- Enhanced surveillance to measure antibiotic use for vaccine-preventable diseases (generate value evidence)
- Financial incentives to encourage development of vaccine directed against pathogens with high rates of AMR (R&D)



European Responses



- Reduction of antibiotic use by preventing bacterial infections
 - Increased use of conjugate pneumococcal vaccines
- Reducing antibiotic misuse by preventing viral diseases
- Prevention of spread of AMR pathogens by vaccination (e.g., pertussis and Hib vaccines)
- Improved AMR surveillance
- Enhanced funding for early research in epidemiology and immunology of AMR pathogens and healthcare-associated infections



Mathematical Modeling to Assess Impact of Vaccines on Antibiotic Resistance

- Limited published data (Atkins KE, et al. Lancet Infect Dis 2018: e204-e213)
- Focus on *S. pneumoniae* and *S. aureus*
- Significant gaps in models
 - No consideration of reduction in co-infections (e.g., post-influenza bacterial pneumonia)
 - Limited international data (different societal healthcare factors)
 - Need to assess more pathogens in the context of existing or potential vaccines
 - No incorporation of economic outcomes
- This can be an important element in generating value evidence for vaccines and their role in preventing AMR

Other Initiatives

- CARB-X: BARDA/International partnership
 - Focus on development of antibiotics and vaccines for AMR
- Chatham House: Value of Vaccines in the Avoidance of AMR
 - Generation of value evidence
- BMGF: Childhood pneumonia prevention
 - Generation of value evidence; advocacy and communication
- Wellcome Trust: Evaluation of likelihood of development/deployment of vaccines on the WHO AMR list
 - Generation of value evidence
- WHO/UN Interagency Coordination Group: WHO AMR Global Action Plan
 - Communication and advocacy

Vaccines for AMR: What is Needed?

- Economics: Modeling the healthcare costs associated with AMR
 - How these costs would be reduced as a result of vaccine development and use
- Awareness: Better recognition that vaccines, along with the development of new antibiotics and antibiotic stewardship, are a key element in the fight against AMR
 - Data that shows the impact of existing vaccines on AMR (direct and indirect impacts)
 - Modeling of health/economic benefits of enhanced investment in vaccines with communication to policy-makers
- Research & Development
 - Challenging business case for AMR vaccines
 - Priority pathogens: Assess the ability to induce broader immune responses
 - Regulatory: How best to include impact on AMR in clinical development/clinical trial design?

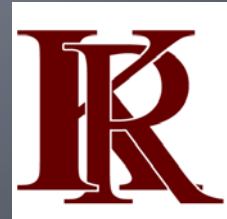
Summary

- There is a clear role for vaccines in the fight against AMR pathogens
- R&D Challenges: Investment, markets, impact data, regulatory, etc.
- Policy Challenges: Better utilization of existing vaccines, regulatory, direct/indirect impact on AMR, etc.
- Evolving convergence around many of these aspects
 - R&D efforts for novel vaccines are essential
 - Data generation and communication/advocacy for the role of vaccines in AMR is equally important

The Economics of Polio Eradication

Dr. Kimberly M. Thompson
NVAC Meeting, September 12, 2018

Kid Risk, Inc.
www.kidrisk.org



Collaboration

Co-authors

James Alexander, Emilia Anis, Bruce Aylward, Gregory Armstrong, Albert Barskey, Cara Burns, Victor Cáceres, Konstantin Chumakov, Stephen Cochi, Esther de Gourville, Ousmane Diop, Kathleen Gallagher, Howard Gary, Itamar Grotto, Neal Halsey, Lee Hampton, David Heymann, Tapani Hovi, Kun Hu, Hamid Jafari, Denise Johnson, Dominika Kalkowska, Olen Kew, Jong-Hoon Kim, Kasper Kisjes, Jennifer Linkins, Phil Minor, John Modlin, Steven Oberste, Mark Pallansch, Peter Patriarca, Hazhir Rahmandad, Nalinee Sangrujee, Lester Shulman, Philip Smith, Roland Sutter, Radboud Duintjer Tebbens, Linda Venczel, Gregory Wallace, Steven Wassilak, Margie Watkins, Peter Wright

Other contributors

Global Polio Laboratory Network, Emmanuel Abanida, Mohammed Ado, Yael Alfasy, Uttara Aggarwal, Lorraine Alexander, Katerina Alves, Abhijeet Anand, Larry Anderson, Jon Andrus, Humayun Ashgar, Ananda Bandyopadhyay, Sonali Bari, Lawrence Barker, Scott Barrett, Hyam Bashour, Carrie Beam, Thomas Bell, Zulfiqar Bhutta, Christopher Black, Ivana Boko, Francois Bompard, Lee Bookman, Arnold Bosman, Carla Boudreau, Louis Boviero, Shanda Boyle, Patrick Briand, Brenton Burkholder, Anthony Burton, Fred Caillette, Joel Calmet, Jason Cecil, Claire Chauvin, Qi Chen, Paul Chenoweth, Susan Chu, Nesia Cohen, Marc Collett, Roger Cooke, James Cosgrove, Alejandro Costa, Laurent Coudeville, Jagadish Desphande, Deepak Dhongde, Walter Dowdle, Philippe Duclos, John Edmunds, Ellie Ehrenfeld, Derek Ehrhardt, Martin Eichner, Concepción Estívariz, Andrew Etsano, Hans Everts, Noha Farag, Christine Fares, Christine Feig, Peter Figueroa, Paul Fine, William Foege, Jackie Fournier, Marta Gacic-Dobo, Michael Galway, Gian Gandhi, Edgar Garcia, Alex Gasasira, Evgeny Gavrilin, John Glasser, Yael Glazer, Jean-Marc Glinz, Tracey Goodman, Ruslan Gosinov, Varja Grabovac, Ulla Griffiths, Nicky Gumede-Moeletsi, Steve Hadler, Shanelle Hall, Lee Hampton, Karen Hennessey, Sid Hess, Musa Hindiyeh, Brian Hirten, Raymond Hutubessy, Maria Iakovenko, Jane Iber, Alan Janssen, Julie Jenks, Jacob John, Todd Jordan, Samuel Katz, Bob Keegan, Nino Khetsuriani, James Koopman, Fran Kopel, Donald Kraybill, Dorota Kurowicka, Scott Lambert, Mauricio Landaverde, John Lange, Laura Laughlin, Tracy Lieu, Asta Lim, Robb Linkins, Marc Lipsitch, Benjamin Lopman, Sara Lowther, Patrick Lydon, Michael Lynch, Ondrej Mach, Chris Maher, Melinda Mailhot, Naile Malakmadze, Apoorva Mallya, Yossi Manor, Rebecca Martin, Maureen Martinez, Javier Martin-Gonzalez, Eric Mast, Robert Matthews, Steve McLaughlin, Mark McKinlay, Ella Mendelson, Elizabeth Miller, Fred Modell, Vicki Modell, Linda Muller, Neal Nathanson, Van Hung Nguyen, Rosa Norman, Deo Nshimirimana, Patrick O'Connor, Hiromasa Okayasu, Jean Marie Okwo Bele, Paul Oostvogel, Walter Orenstein, Ann Ottosen, Fem Paladin, Carol Pandak, Sirima Pattamadilok, Muhammed Pate, Christina Pedreira, Pelin Pekgun, Stanley Plotkin, Sarah Poser, Becky Prevots, Nelson Repenning, Gloria Rey, Lance Rodewald, Oliver Rosenbauer, Jennifer Rubin, Hardeep Sandhu, Anne Schuchat, Robert Scott, Tika Ram Sedai, John Sever, Jing Shaw, Meredith Shirey, Simarjit Singh, Bryon Skinner, Jean Smith, Robert Snyder, Danit Sofer, Stephen Sosler, Thomas Sorensen, John Sterman, Jeanette St. Pierre, Peter Strebel, David Sugerman, Graham Tallis, Rudi Tangermann, Iris Tetford, Jean Gabriel Tezier, Kirk Thompson, Jos Vandelaer, Harrie van der Avoort, Anton van Loon, Rui Vaz, Everardo Vega, John Vertefeuille, Maya Vijayaraghavan, Arie Voorman, Michael Watson, Robert Weibel, Merav Weil, Jay Wenger, Bruce Weniger, Chris Wolff, Lara Wolfson, David Wood, Wenbo Xu, Michel Zaffran, Yan Zhang, Shuangli Zhu

Funding

Unrestricted gifts to Harvard Kids Risk Project and Kid Risk, Inc.

CDC: U50CCU300860, U01IP000029, U66IP000169, NVPON37(FY2005), 200-2010-M-33379, 200-2010-M-33679, 200-2010-M-35172, U66IP000519, 200-2015-M-61344, 200-2015-M-63078, U2RGH001913

Bill & Melinda Gates Foundation: 4533-17492, 4533-18487, 4533-21031, 4533-23446, 4533-25298, OPP1129391

WHO Polio Research Committee APW200179134; WHO APW201612899

Better Decisions



Contact information:

Address:
Kid Risk, Inc.
605 N. High St., #253
Columbus, OH 43215
Phone: 617-680-2836

Kid Risk, Inc. Officers:

Kimberly M. Thompson, Sc.D., President
Karen G. Tepichin, J.D., Secretary
Michele Courton Brown, Treasurer

Board Members:

Dennis M. Bier, M.D.
Walter R. Dowdle, Ph.D.
Rick Hackman
Marie C. McCormick, M.D., Sc.D.
Kimberly M. Thompson, Sc.D.

Research on risk management strategies for polioviruses

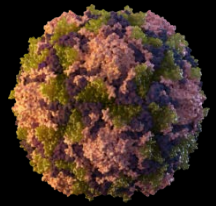
Even though polio no longer causes widespread fear, please take a couple of minutes to [learn more about polioviruses](#) and why you should still care about them. In 2001, we launched a collaboration with the U.S. Centers of Disease Control and Prevention (CDC) with support from the CDC-Harvard Joint Initiative in Vaccine Economics (JIVE) to create useful analytical modeling tools to help decision makers consider the implications of the various global immunization and risk management choices after eradicating wild polioviruses. We thank many [contributors](#) for support of our polio modeling efforts. The research led to many [presentations](#) and peer-reviewed publications related to the following topics (publication dates, see [overview](#) for brief context):

- **NEW** - the important role of system dynamics in [integrated poliovirus modeling](#) (2018)
- **NEW** - planning for [globally coordinated cessation of bivalent oral poliovirus vaccine](#) (2018)
- **NEW** - polio in [Pakistan and Afghanistan](#) (2018)
- lessons learned from [overcoming the failure to vaccinate and the role of subpopulations](#) in maintaining transmission (2017)
- lessons learned from [globally-coordinated cessation of serotype 2 oral poliovirus vaccine for other serotypes](#) (2017)
- systematic review of [poliovirus environmental surveillance studies published in English between 1975-2016](#) (2017)
- benefits of [temporary recommendations for travel immunization requirements](#) for serotype 1 wild polioviruses (2017)
- modeling [poliovirus vaccine supply and stockpile dynamics during the endgame](#) (2017)
- characterization of the costs and benefits of [using IPV in addition to OPV for outbreak response](#) (2017)
- remaining [prepared and managing the poliovirus endgame risks](#) (2017)
- the potential benefits of [new poliovirus vaccines](#) (2016)
- the [role of comprehensive screening and effective polio antiviral drugs](#) for long-term immunodeficiency-associated vaccine-derived poliovirus (iVDPV) excretors (2016)
- the [importance of maintaining and intensifying coverage with bivalent oral poliovirus vaccine \(bOPV\) prior to bOPV cessation](#) (2016)
- consideration of the implications of uncertainty in [cost assumptions on long-term poliovirus risk management](#) (2016)
- the [risks of inadvertent trivalent oral poliovirus vaccine use after coordinated global serotype 2 oral poliovirus vaccine \(OPV\) cessation](#) (2016)
- implementation of [coordinated global serotype 2 OPV cessation and the risks of potential non-synchronous cessation](#) (2016)
- characterization of [outbreak response options after OPV cessation and during the polio endgame](#) (2016)
- modeling the risks of [immunodeficiency-associated long-term vaccine derived-poliovirus excretors](#) and the potential role of poliovirus antiviral drugs (2015)
- [economic analysis of poliovirus risk management policy options for 2013-2052](#) (2015)
- [oral poliovirus vaccine needs](#) for managing the risks of circulating vaccine-derived polioviruses during the endgame (2015)
- the impact of different oral poliovirus vaccine formulations in managing population immunity and [the importance of vaccine choices](#) (2015)
- health and economic consequences of different options for [timing of globally-coordinated oral poliovirus vaccine cessation](#) (2015)
- good news about [IPV safety](#) (2015)
- trade-offs associated with different immunization activities in [northwest Nigeria](#) and their impact on population immunity to transmission (2015)
- characterization of heterogeneity in childhood immunization coverage in [Central Florida](#) (2015)
- managing population immunity to reduce the risks of [transmission of imported live poliovirus](#) (2015)
- poliovirus surveillance and the chances of [undetected circulation](#) in the absence of detected polio cases (2015)
- the use of [integrated analytical models](#) to support global polio eradication efforts (winner of the 2014 INFORMS Edelman Award for excellence in analytics and operations research)(2015)
- modeling polio in [Israel](#) (2015, published on-line December 2014)
- the role of [IPV in managing the risks of OPV cessation](#) (2014)
- modeling [OPV cessation dynamics](#) (2014)
- the potential for poliovirus transmission among the [North American Amish](#) (2014)
- modeling strategies to increase population immunity in [the high-risk area in northwest Nigeria](#) (2014)
- modeling strategies to increase population immunity in [2 high-risk areas in northern India](#) (2014)
- the need to focus on [performance](#) in managing population immunity to transmission (2014)
- supplemental immunization activities (SIAs) for polio vaccines and [the role of expanded age groups](#) (January 2014)
- IPV costs and individual and population immunity considerations for [national immunization policy makers](#) evaluating the adoption of IPV (2014, published online 2013)
- [characterizing poliovirus transmission and evolution](#) using a model applied to diverse situations (2013)

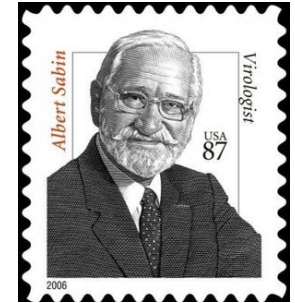
Topics

- Complexities associated with modeling polio vaccine benefits
- Control vs. eradication
- Economic benefit estimates
 - US investments in polio control and elimination
 - Global Polio Eradication Initiative
- Building economic cases for vaccination
 - Completion of polio eradication
 - Other vaccine-preventable diseases

Poliovirus complexities



- Positive stranded RNA virus
- Three serotypes (1, 2, 3)
- Live polioviruses (PV)
 - Wild (WPV)
 - Oral (OPV) vaccine (attenuated)
 - Vaccine-derived (VDPV), OPV-related
- Inactivated (IPV) vaccine
- Paralytic polio
 - Vaccine associated paralytic polio (VAPP) from OPV: approximately 1/1,000,000 infections
 - WPV: approximately 1/200 infections
 - Individuals with B-cell related immunodeficiencies at particular risk for prolonged infection (iVDPV)
- Complex immunity (reinfection)



Control vs. Eradication

- Economic literature demonstrates “high control” is not optimal if eradication is feasible

Geoffard P-Y, Philipson T. Disease eradication private versus public vaccination. *American Economic Review* 1997;87(1):222-230

Barrett S. Eradication versus control: the economics of global infectious disease policies. *Bulletin of the World Health Organization* 2004;82(9):683-688

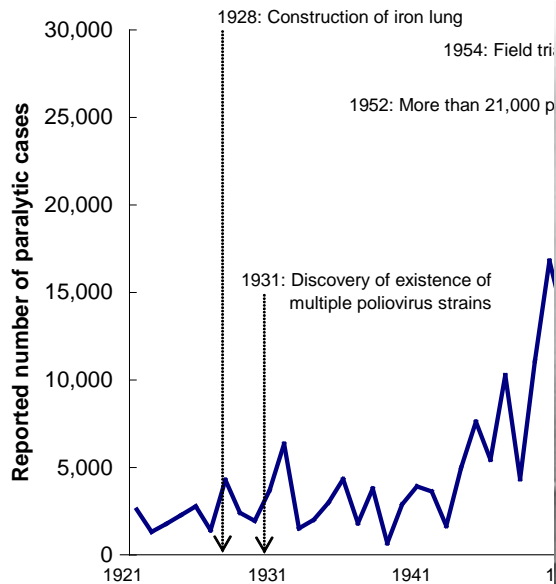
- Polio-specific, static economic analyses

Musgrove P. Is polio eradication in the Americas economically justified? *Bulletin of the Pan American Health Organization* 1988;22(1):1–16.

Bart K, Foulds J, Patriarca P. Global eradication of poliomyelitis: benefit-cost analysis. *Bulletin of the World Health Organization* 1996;74:35–45.

Kahn MM, Ehreth J. Costs and benefits of polio eradication: a long-run global perspective. *Vaccine* 2003;21:702–50

U.S. polio experience since 1921



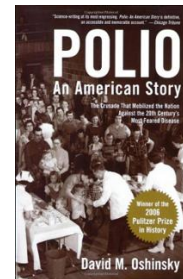
Thompson KM, Duintjer Tebbens RJ.
Retrospective cost-effectiveness analyses for
polio vaccination in the United States. Risk
Analysis 2006;26(6):1423-1440

Vaccination polic
in the Unites



Photograph courtesy of Children's Hospital Archives, Boston, MA.

█ Vaccine-associated
— Wild-type



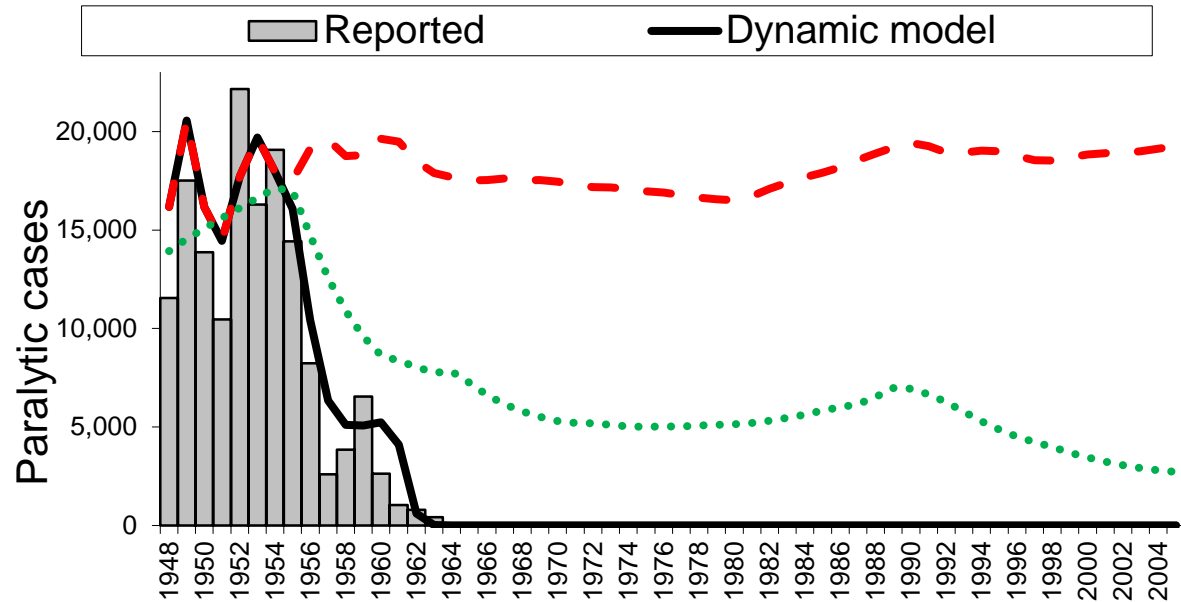
certified
polio-free

and then trivalent OPV

1997-'00:
transition to eIPV

Economic benefits estimates

- Retrospective and prospective analysis of US investments in polio control and elimination prevented over 1 million cases of paralytic polio, with saved treatment costs implying net economic benefits exceeding \$180 billion



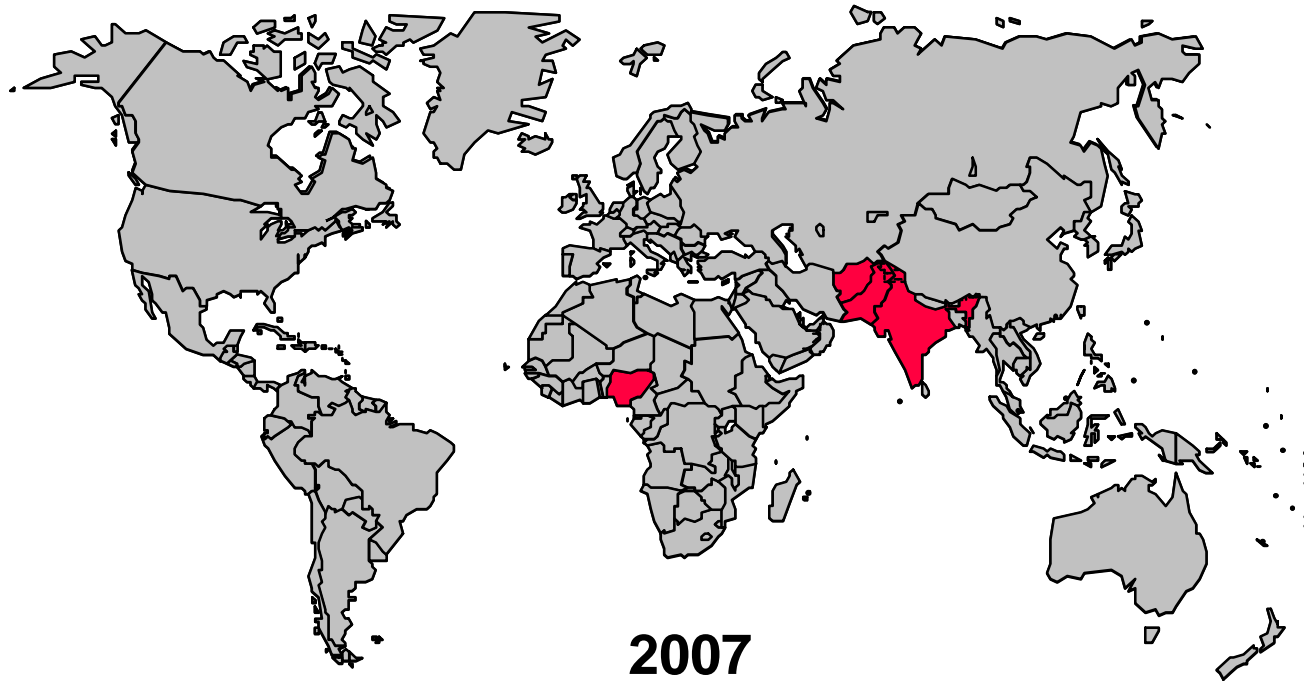
Thompson KM, Duintjer Tebbens RJ. Retrospective cost-effectiveness analyses for polio vaccination in the United States. Risk Analysis 2006;26(6):1423-1440

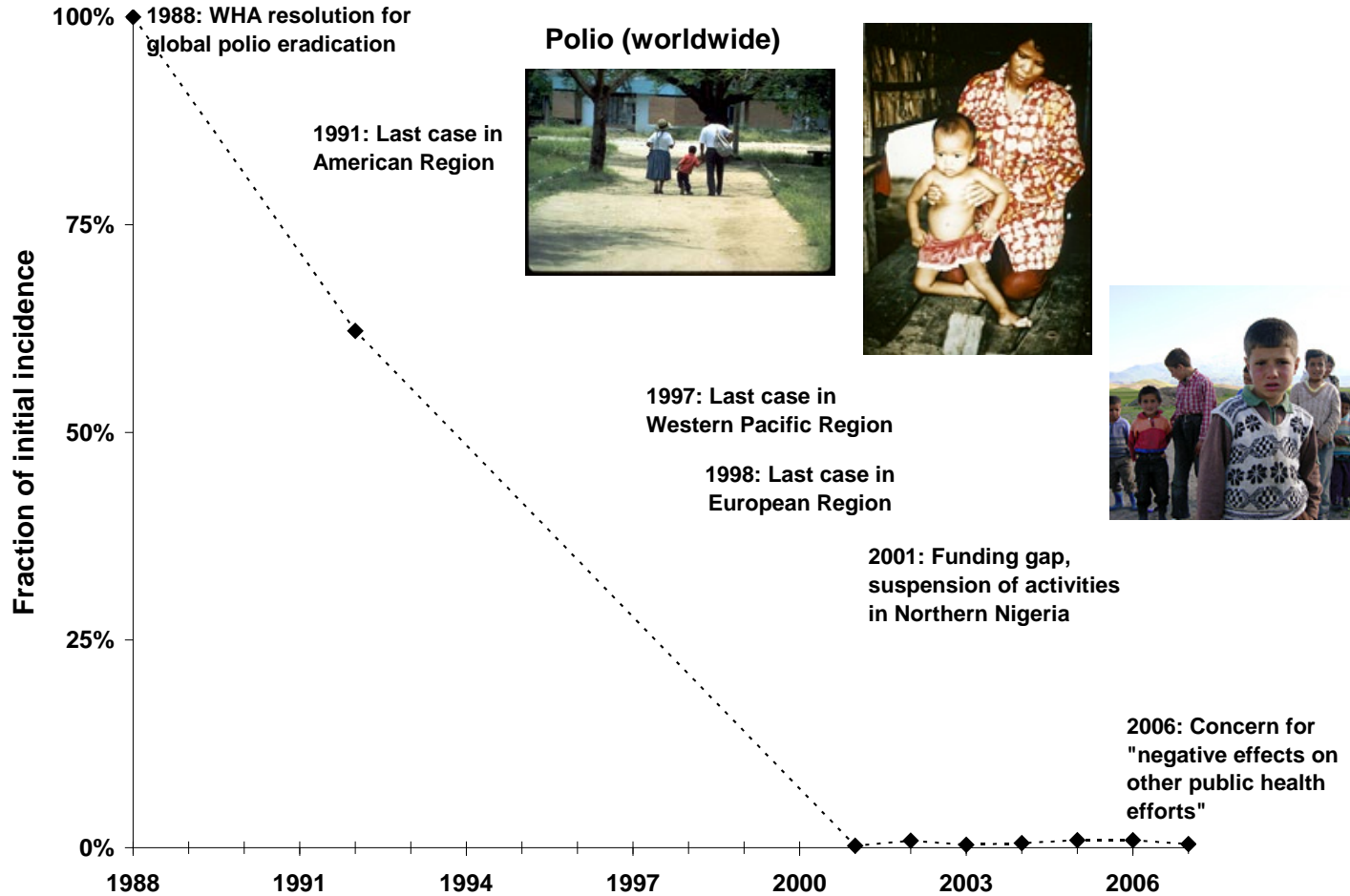
Global polio eradication

- Polio transmission in the US stopped in the mid-1970s
- The last polio case in the Americas (western hemisphere) occurred in 1991
- 1988 World Health Assembly resolved to eradicate wild polioviruses by the year 2000
- Global Polio Eradication Initiative (GPEI) launched



GPEI progress





Control vs. Eradication

■ Post-eradication immunization policies and eradication vs. control

Thompson KM, Duintjer Tebbens RJ. Eradication versus control for poliomyelitis: An economic analysis. *The Lancet* 2007;369(9570):1363-1371

Thompson KM, et al. The risks, costs, and benefits of future global policies for managing polioviruses. *AJPH* 2008;98(7):1322-1330

- Analysis of cumulative costs and cases for a 20-year period for low-income countries showed eradication options better than control
- Exploration of dynamic feedback in behavior showed higher cumulative costs and cases associated with a wavering commitment to eradication than with a strategy of intensively pursuing eradication until done
- India model showed the need to significantly intensify efforts to achieve eradication rapidly and emphasized that India could stop WPV transmission if it chose to do so
 - Success in India in 2011 followed intensive efforts to find every child and fill gaps in population immunity
 - Polio eradication efforts helped energize other immunization activities in India

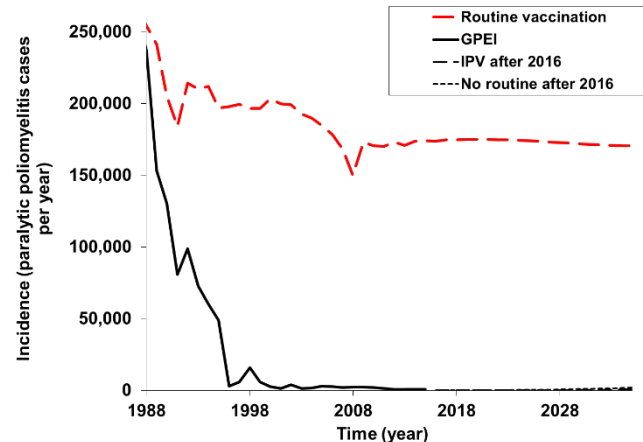
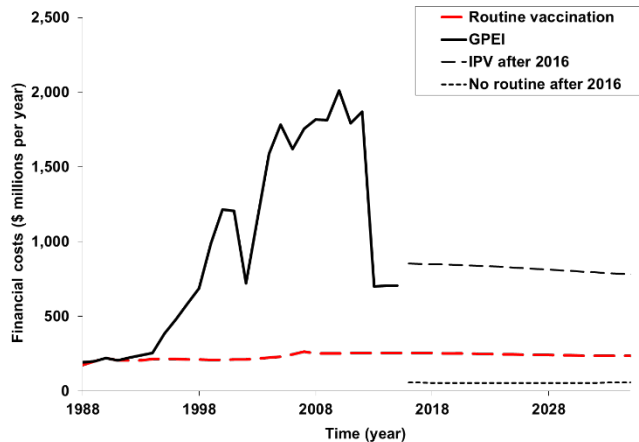


Economic benefits estimates

■ Retrospective and prospective analysis of GPEI benefits

Duintjer Tebbens RJ, Pallansch MA, Cochi SL, Wassilak SG, Linkins J, Sutter RW, et al. Economic analysis of the Global Polio Eradication Initiative. *Vaccine* 2011 December 16;29(2):334-43

- Analysis performed in 2011, assumed eradication of WPVs by 2012, considered the use of either IPV or no poliovirus vaccine after WPV eradication compared to on-going routine immunization with OPV
- Estimated net benefits of approximately \$40-50 billion for GPEI polio benefits alone, \$17-90 billion more if include Vitamin A benefits



Economic benefits estimates

- Prospective economic analysis published in 2015 to explore strategies related to GPEI 2013-2018 strategic plan

Duintjer Tebbens et al. An economic analysis of poliovirus risk management policy options for 2013-2052. BMC Infect Dis 2015;15:389

- Sophisticated global model that captures variability, uncertainty, and time
- Assumed eradication of WPV1 would occur in 2016, considered minimum routine immunization policy of either one dose of IPV or no poliovirus vaccine after WPV eradication compared to continued OPV use
- Finishing WPV eradication followed by OPV cessation and global IPV use promises an estimated approximately \$16-17 billion in incremental net benefits for OPV cessation compared to continuing OPV use
- Outcomes depend on making good choices to manage risks for the endgame (high quality surveillance and outbreak response, access to vaccine stockpiles, maintaining immunity prior to OPV cessation, etc.)

Building economic cases

- Need an updated polio eradication and endgame plan for 2019 on
 - Unfortunately, polio eradication still not completed
 - Each year of delay adds high costs and extends the polio endgame
 - Endgame resources (funds and vaccines) remain an issue
 - Need an updated economic analysis to support plan
- Overall economics of polio eradication still uncertain
 - Need to update GPEI economic analysis (from 2011) once polio eradication finished
 - Global introduction of IPV significantly increased GPEI costs
- Other vaccine-preventable diseases
 - Integrated economic and dynamic disease modeling also applicable to other vaccines
 - Characterizing the benefits of vaccines and valuing prevention

Thank you

For more details:

www.kidrisk.org