Polio Eradicators Use Integrated Analytical Models to Make Better Decisions

Kimberly M. Thompson, Radboud J. Duintjer Tebbens, Mark A. Pallansch, Steven G.F. Wassilak, and Stephen L. Cochi

2014 Edelman Award

March 31, 2014

Department of Health and Human Services
Centers for Disease Control and Prevention

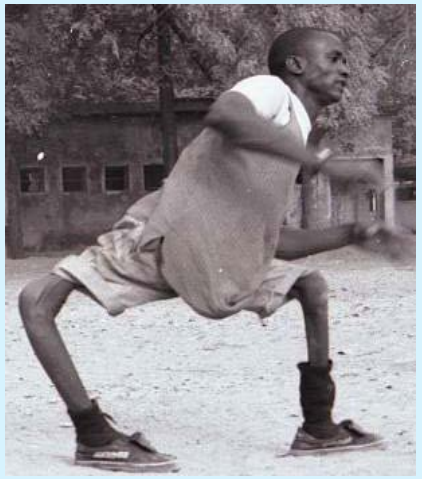
ORGANIZATIONAL OVERVIEW

Dr. Steven G. F. Wassilak
CDC Team Lead for Science, Innovation and Research for the Polio Response, Emergency Operations Center

Poliovirus

- 3 serotypes (types 1, 2, and 3)
- Approximately 1/200 infections lead to paralysis

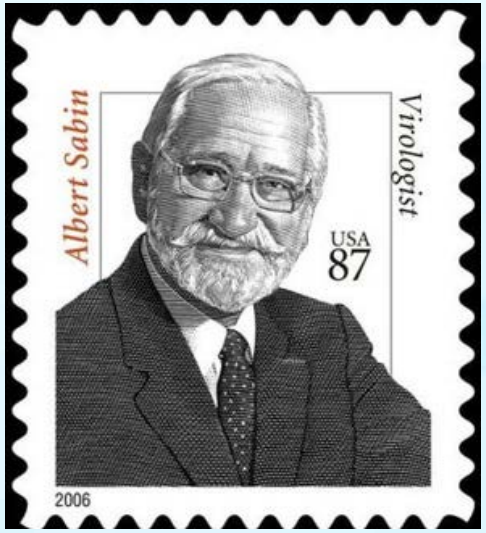
Polio: A paralyzing disease for life



Rancho Los Amigos Rehabilitation Hospital, California
Iron lungs, 1953 (prior to vaccine introduction)

Vaccines

- Introduction in the 1950s and 1960s
- Opportunity to manage risks



Polio eradication

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

World Health Organization

ROTARY INTERNATIONAL

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

unicef

Role of CDC in the GPEI

- Primary technical partner
- Funding support

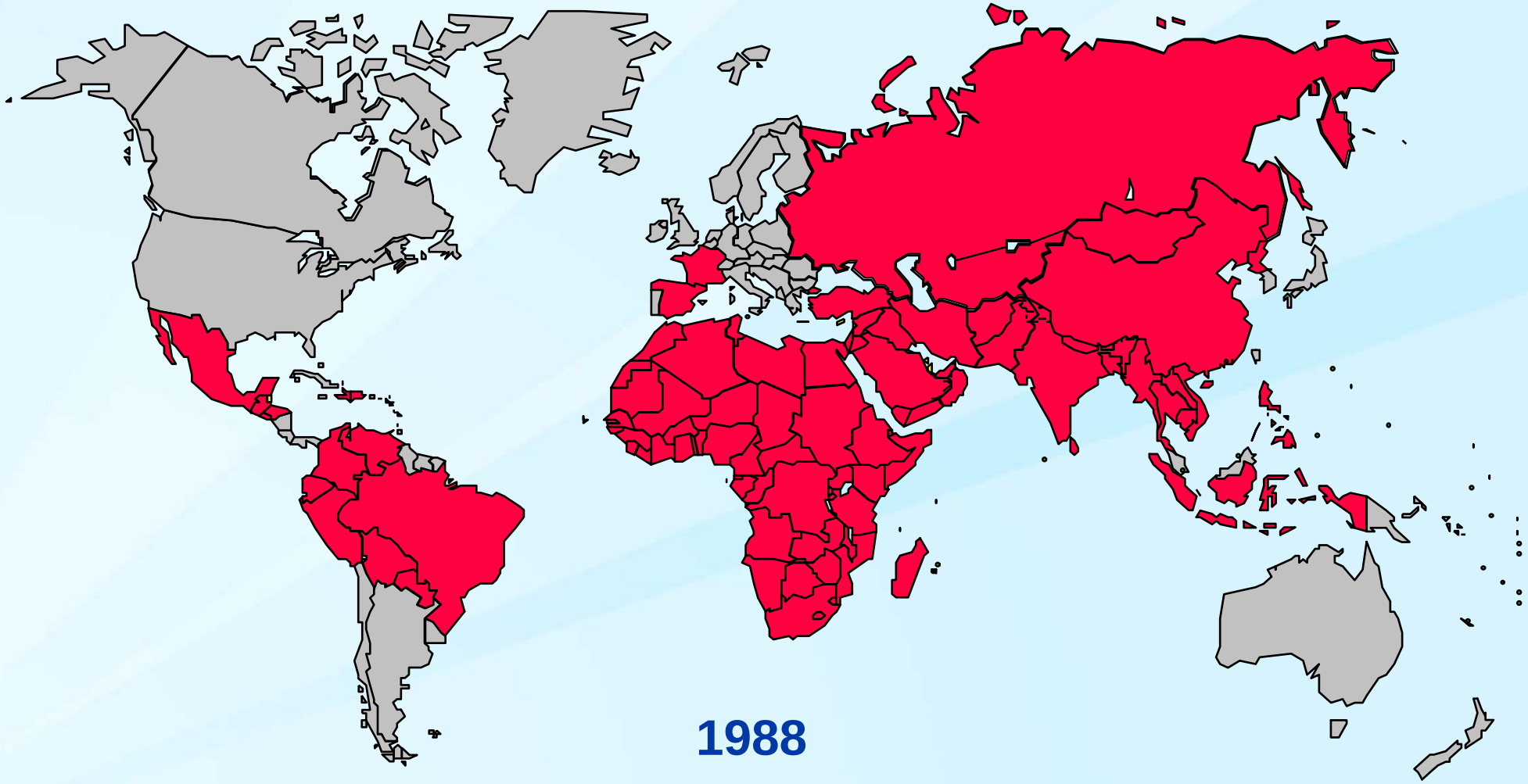
GPEI key operational strategies

1. Routine Immunization

2. Supplemental Immunization Activities (SIAs or mass campaigns)

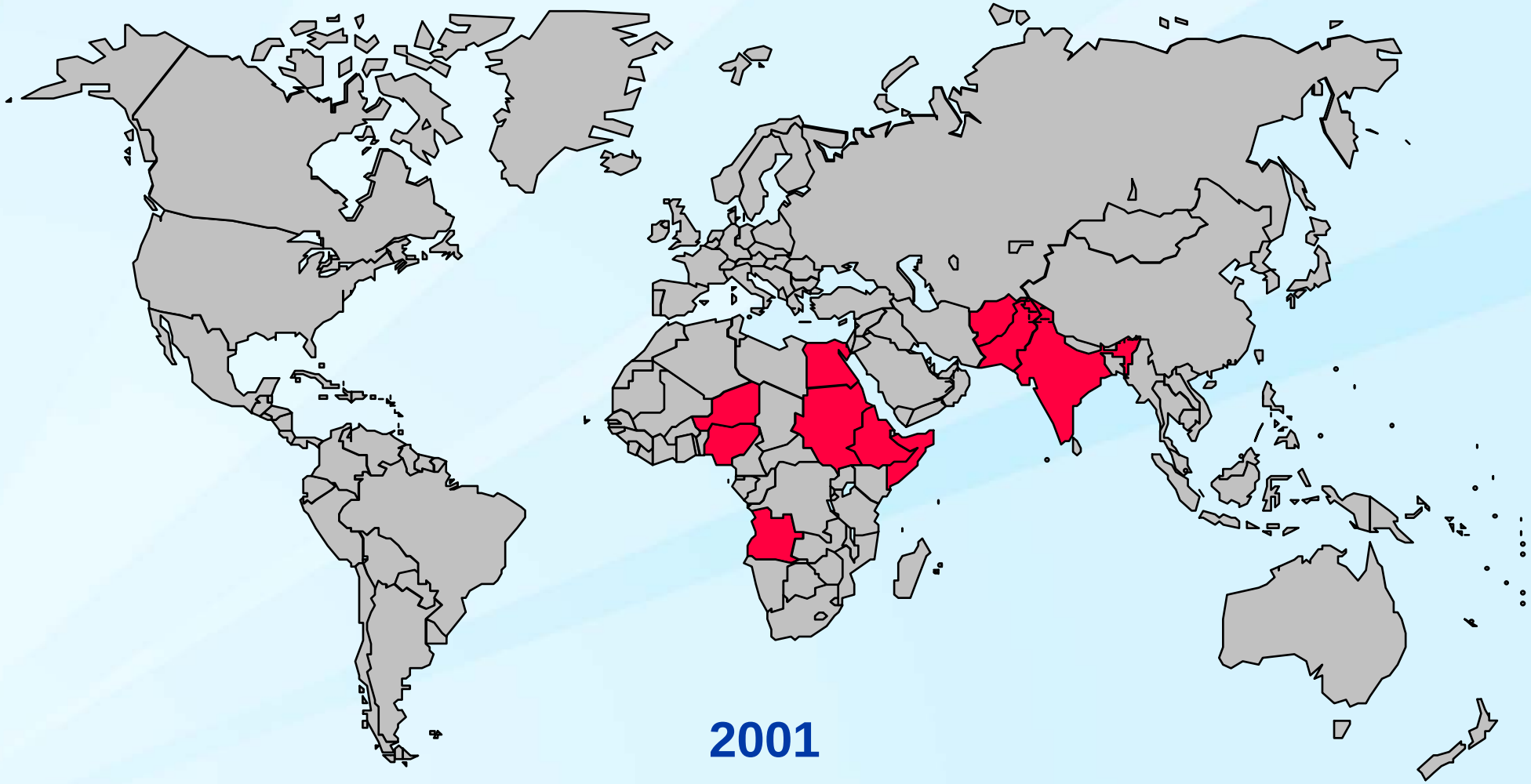
3. Surveillance

GPEI launch: >125 polio-affected countries



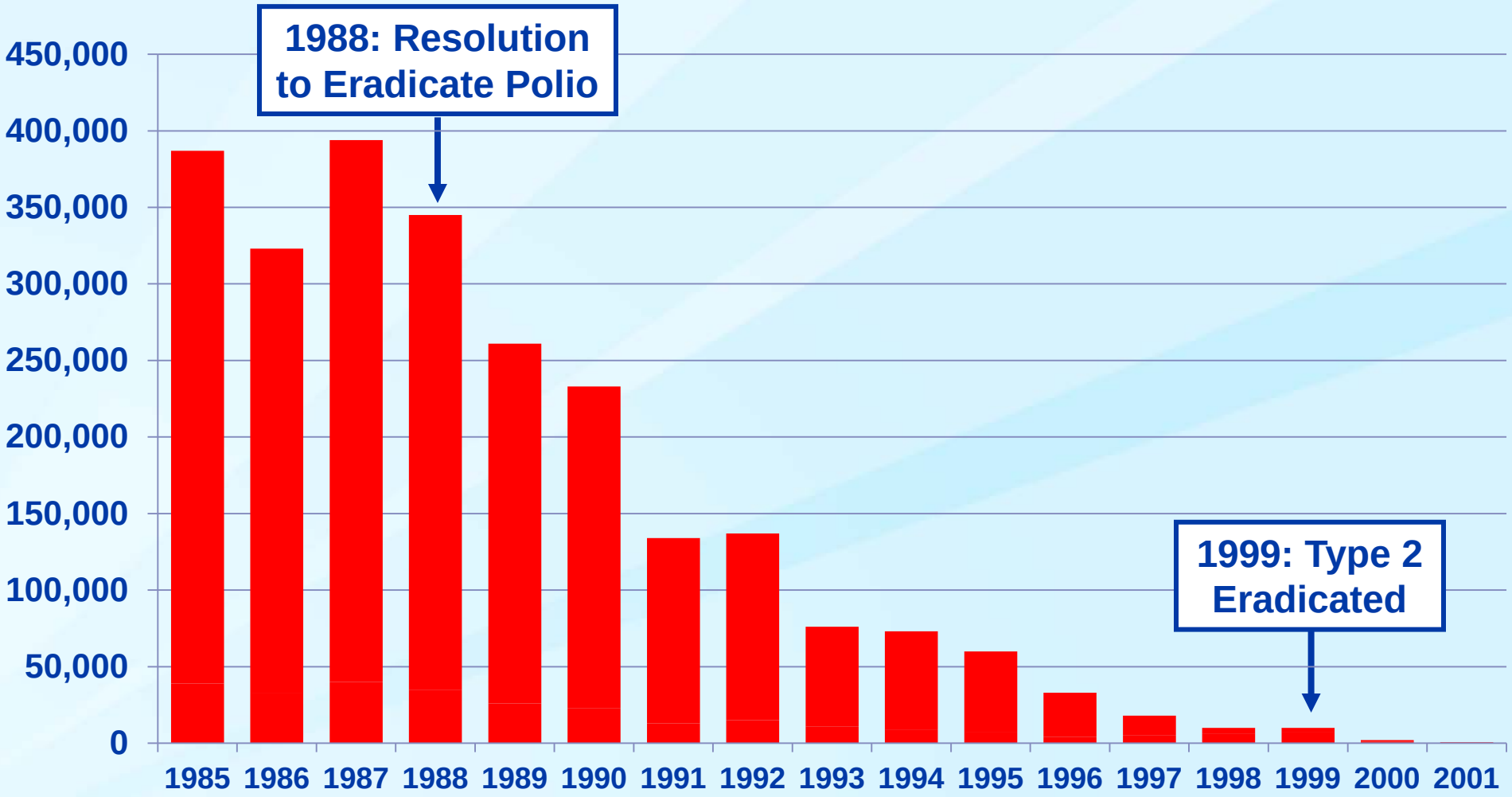
1988

Original target date: 10 polio-affected countries



2001

Estimated polio cases: 1988-2001



Source: WHO/Polio database, data as of March 2014 for 193 WHO Member States

Collaboration

- **CDC and Kid Risk, Inc. collaboration started in late 2001**
  - Combine CDC expertise with operations research and management science (OR/MS) tools
  - Model poliovirus transmission and assess the health and economic impacts of policies
- **Goal: Improve evidence-based decision making**
  - Peer-reviewed technical publications
  - Broad and effective communication with stakeholders

www.kidrisk.org (over 35 publications)

Kid Risk, Inc.

Doing our best for children

Better Decisions

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Kimberly M. Thompson, Sc.D.

Research on risk management strategies for polioviruses

Even though polio no longer causes widespread fear, 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. Over a decade later, this research collaboration continues to thrive and expand, and we thank many contributors. In addition to many presentations, our polio research led to peer-reviewed publications related to:

- the decision options that national and international health leaders will face after eradicating wild polioviruses
- dynamically modeling poliovirus transmission and outbreaks
- the health and financial benefits of historical poliovirus vaccination in the United States
- risk management in a polio-free world
- characterization of the risks of future options
- characterization of the costs of future options
- trade-offs associated with outbreak response options
- consideration of the costs and value of global poliovirus surveillance
- lessons learned during this collaborative project (as of December 2006)
- the choice of eradication vs. control (this paper won the 2008 Jay Wright Forrester Award from the System Dynamics Society)
- the risks, costs, and benefits of global policies for managing polio after eradication
- uncertainty and sensitivity analyses of our results related to global post-eradication policies
- the need for global cooperation on a vaccine stockpile and coordinated OPV cessation
- the role of system dynamics in our research
- the consequences of priority shifting when seeking to eradicate multiple diseases
- a framework for optimizing the future use of vaccines from the global polio vaccine stockpile
- building an "individual-based" or "agent-based" model to explore and optimize post wild poliovirus eradication outbreak response strategies
- the economic and health benefits of the Global Polio Eradication Initiative
- trends in the risk of U.S. polio outbreaks and poliovirus vaccine availability for outbreak response
- the role of risk analysis in polio eradication
- the probability of undetected wild poliovirus circulation after apparent global interruption of transmission
- current polio global eradication and control policy options, including perspectives from modeling and prerequisites for oral poliovirus vaccine cessation
- prevention as the new paradigm in global health
- modeling poliovirus risks and the legacy of polio eradication
- pre-eradication national vaccine decision options
- expert review of the literature on poliovirus immunity and transmission
- poliovirus immunity and transmission quantitative synthesis of expert assessments of the evidence
- modeling population immunity
- cVDPV risks and characterization of OPV evolution
- characterizing poliovirus transmission and evolution using a model applied to diverse situations
- IPV costs and individual and population immunity considerations for national immunization policy makers evaluating the adoption of IPV
- supplemental immunization activities (SIAs) and the role of expanded age groups

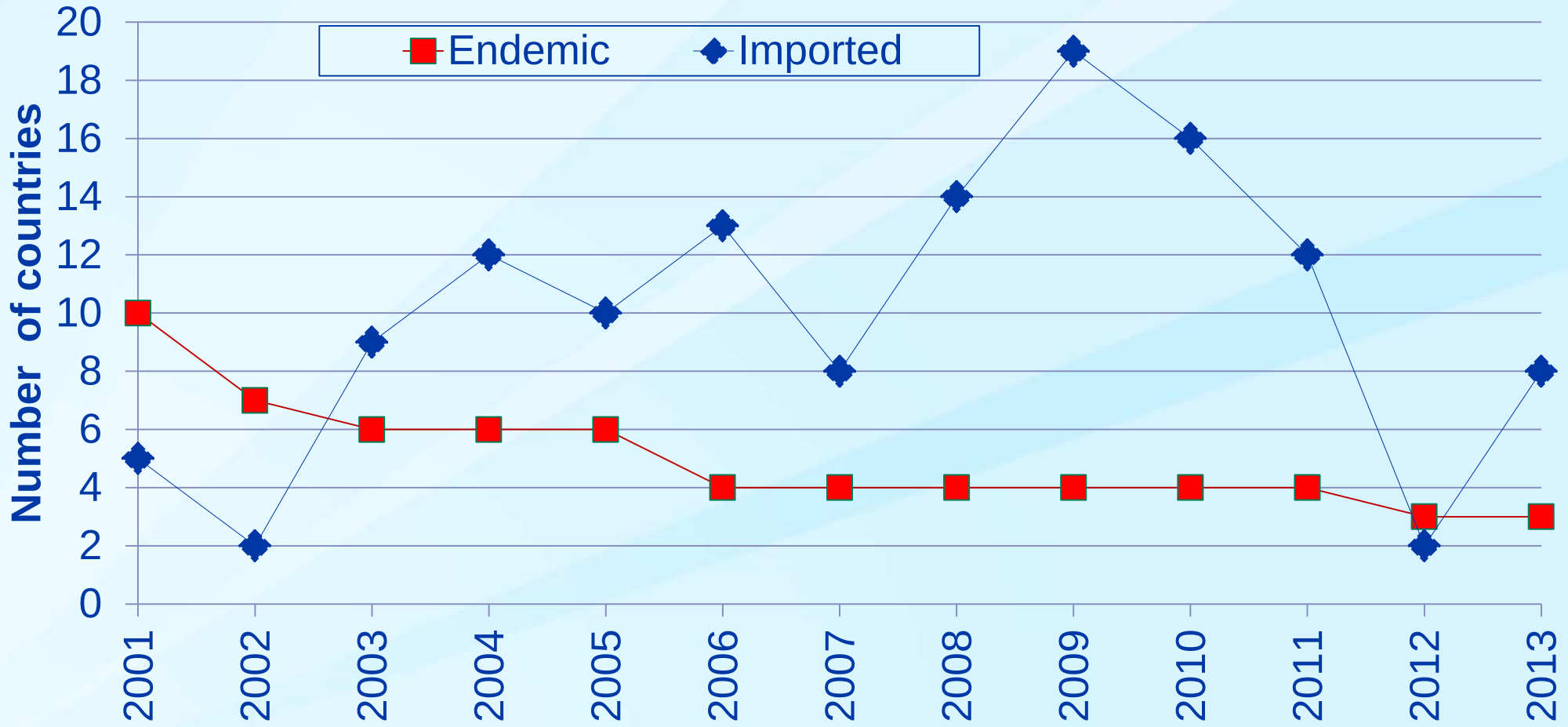
Dr. Bruce Aylward, World Health Organization, Assistant Director-General of Polio, Emergencies, and Country Collaboration

"…This work has been fundamental to so much of what's happened in the eradication program over the last few years, and it's helped to support many of our decisions over the last decade and to bring the world much, much closer to one where future generations will never know the terror of this disease."

PROBLEMS AND CHALLENGES

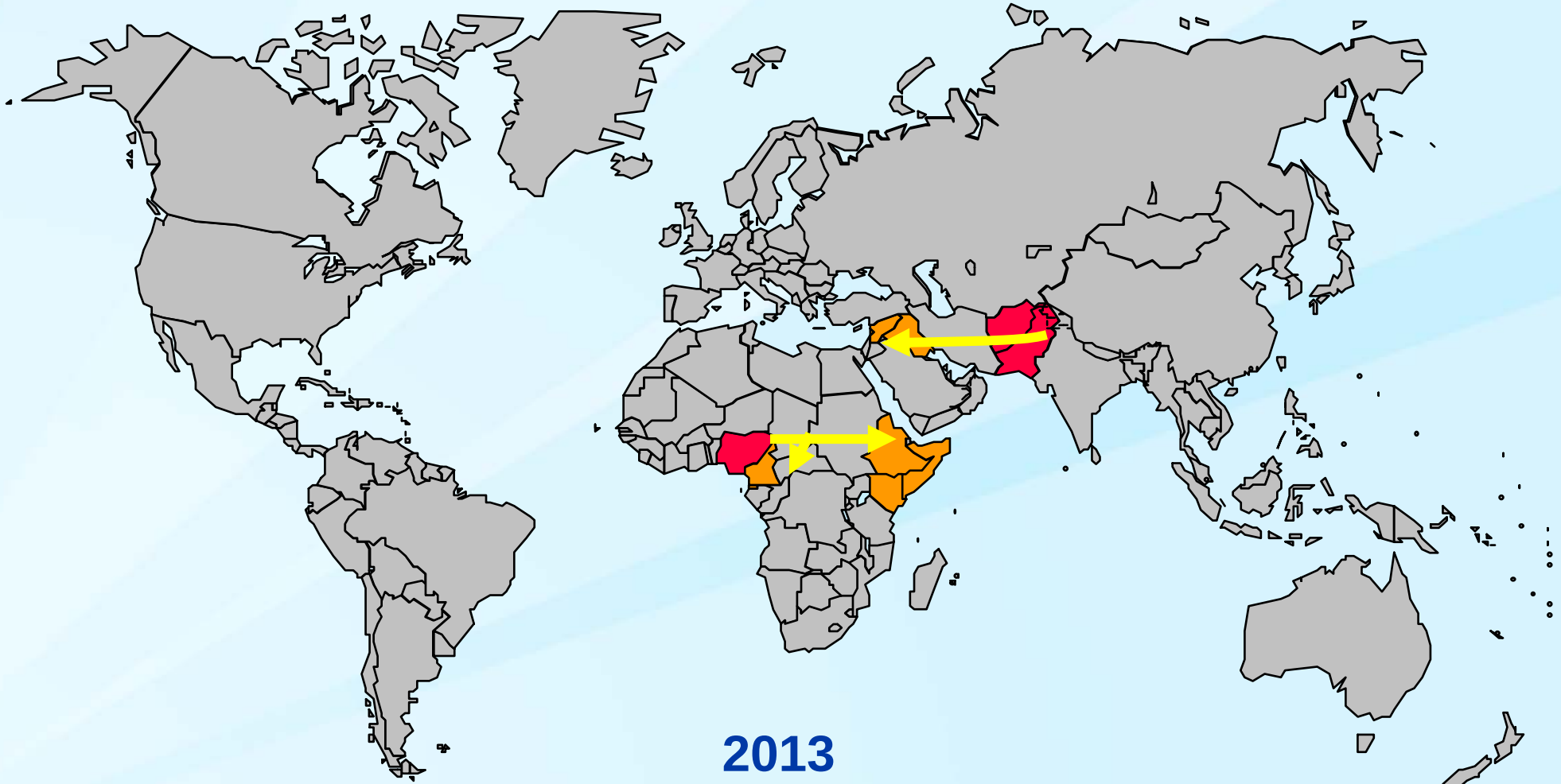
Dr. Mark A. Pallansch
CDC Director of the Division of Viral Diseases

2001-2013: 50 countries reporting polio cases,



Thompson et al., Risk Analysis, 2013

Poliovirus spread 2013-4
3 polio-endemic countries, 7 countries affected by outbreaks



2013

Difficult to see poliovirus transmission

- Many asymptomatic infections
- The global surveillance system only detects paralytic polio
- Fewer cases to see

The Global Polio Laboratory Network

Managing immunity with poliovirus vaccines

- Countries determine their own immunization strategies as they manage population immunity

- Two poliovirus vaccines with very different costs, risks, and protection from infection

Oral poliovirus vaccine (OPV)

- **Benefits**
  - Relatively cheap and easy to administer
  - Causes infection that can spread to contacts
  - Good protection from re-infection
- **Risks**
  - Very rare cases of vaccine associated paralytic polio (VAPP) in approximately 1 per 1,000,000 infections
  - Can evolve to cause circulating vaccine-derived polioviruses (cVDPVs) in populations with low coverage

Inactivated poliovirus vaccine (IPV)

- **Benefits**
  - No VAPP
  - No cVDPVs

- **Costs**
  - Relatively expensive to make and administer (injection)
  - Essentially no protection from live poliovirus infection
  - High coverage required to prevent transmission

Endgame

- Complicated post-eradication choices
- Funding gaps represent a real threat
- High stakes

Dr. Stephen L. Cochi
CDC Senior Advisor to the Director of the Global Immunization Division

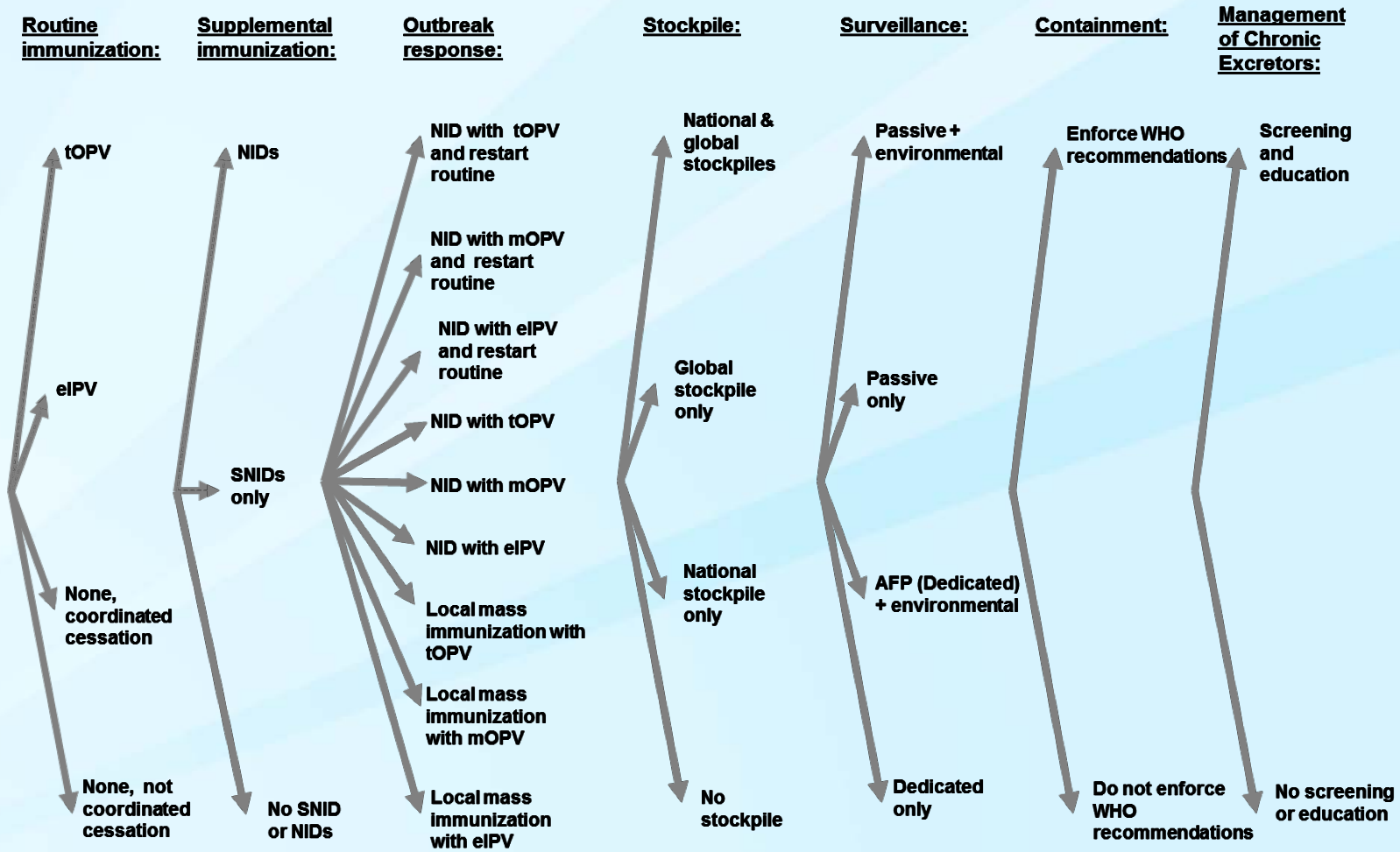
"… Here in India I am happy to report that these strategies have yielded tremendous "real world" results, and as of today it has been officially certified that another nearly 2 billion people live in a now polio-free region of the world"

APPROACHES AND METHODOLOGY

Dr. Radboud J. Duintjer Tebbens
Kid Risk, Inc., Vice President

Decision options (post-eradication)

Major decision options for countries using routine tOPV



Sangrujee et al., Medscape General Medicine, 2003

Objective

- **Overall decision options *i***
  - Minimize incremental costs per disability-adjusted life year (DALY) saved (Incremental Cost-Effectiveness Ratio)

$$\min_i \frac{C_i - C_{SQ}}{(P_{SQ} - P_i)D}$$

  - Maximize difference between economic value of prevented polio cases and incremental costs (Incremental Net Benefits)

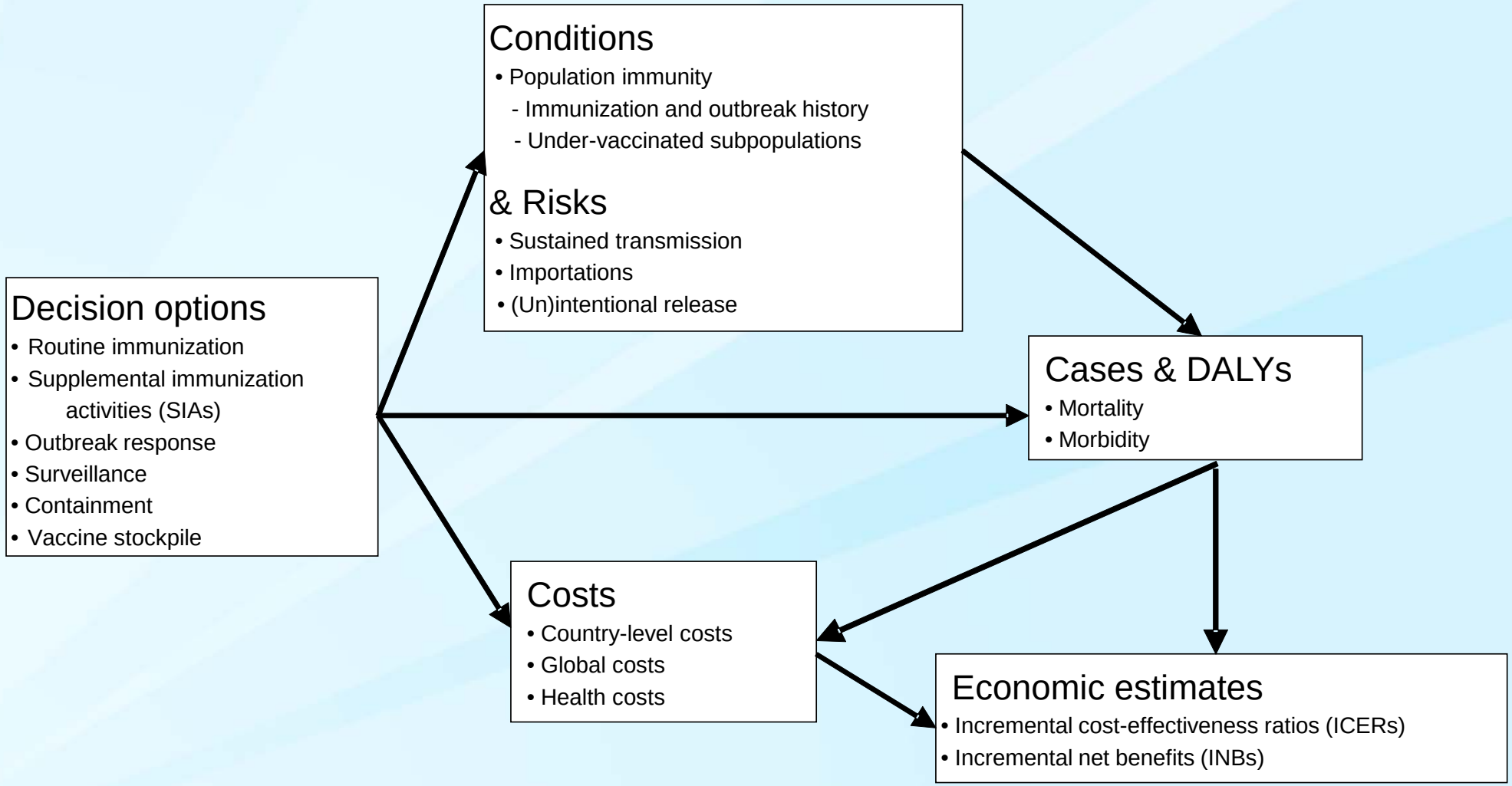
$$\max_i (P_{SQ} - P_i)H - (C_i - C_{SQ})$$

C_i = discounted cumulative costs for option *i*
C_{SQ} = discounted cumulative costs for *status quo*
P_i = discounted cumulative paralytic polio cases for option *i*
P_{SQ} = discounted cumulative paralytic polio cases for *status quo*
D = DALY per paralytic polio case
H = economic value of a prevented paralytic polio case

Integration of OR/MS tools

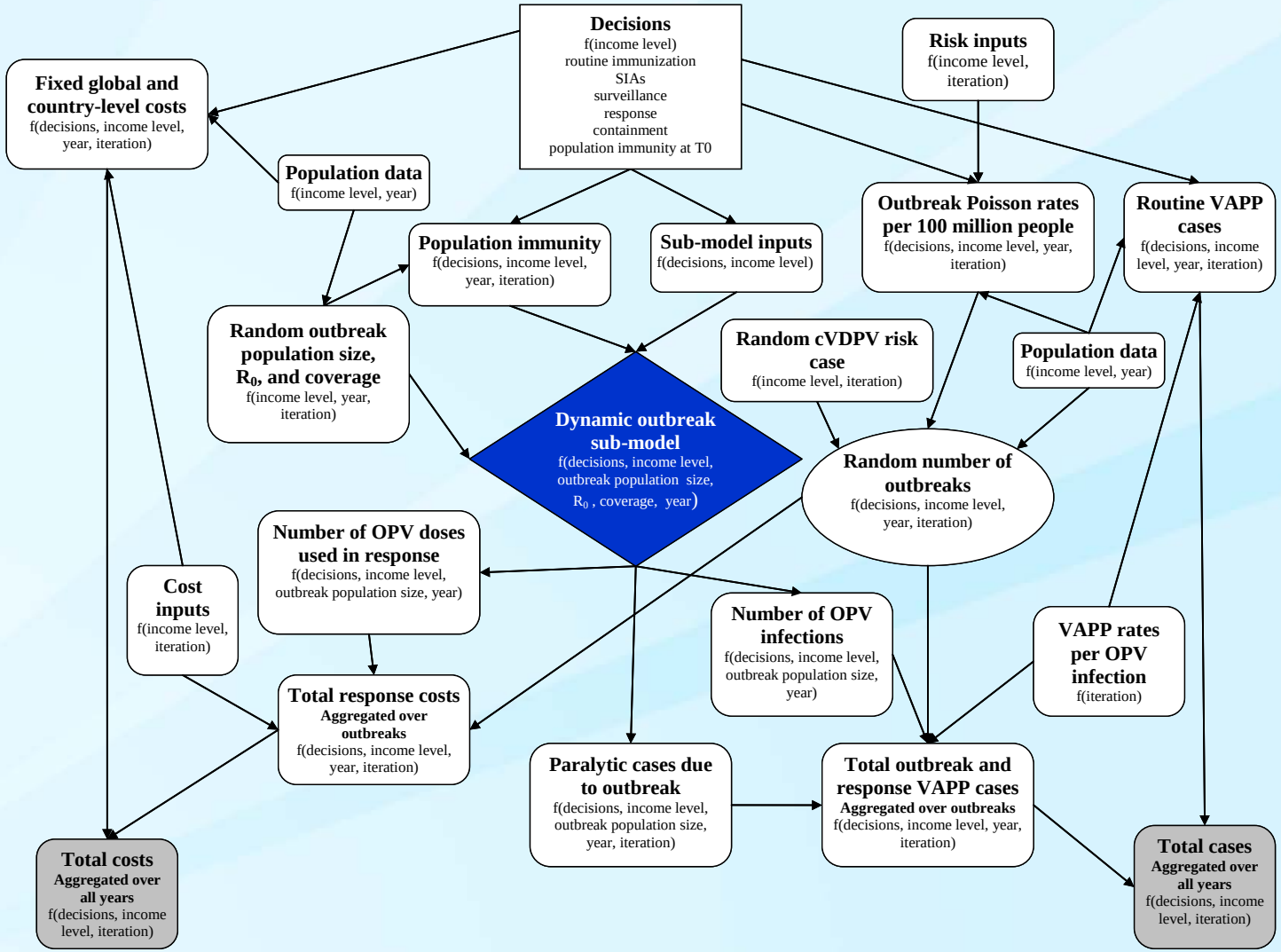
- **Frame overall problem in decision analytic context**
- **Probabilistic risk analysis modeling**
  - Time-varying risk of virus reintroduction f(decision option)
  - Uncertainty in model inputs
- **System dynamics modeling**
  - Population immunity f(decision options)
  - Expected polio cases if poliovirus reintroduced
  - Important feedbacks and time delays

Integrated model (high level influence diagram)



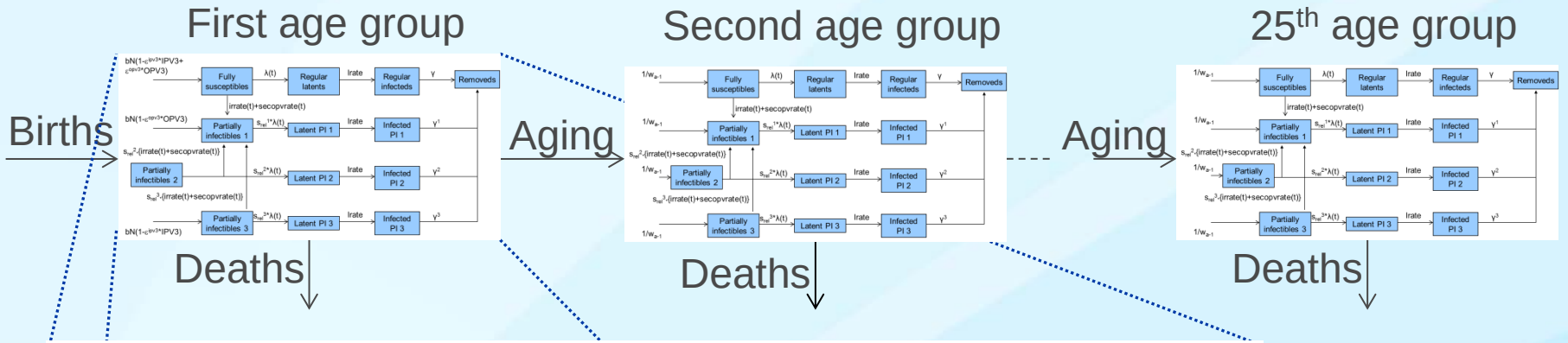
Thompson et al., American Journal of Public Health, 2008

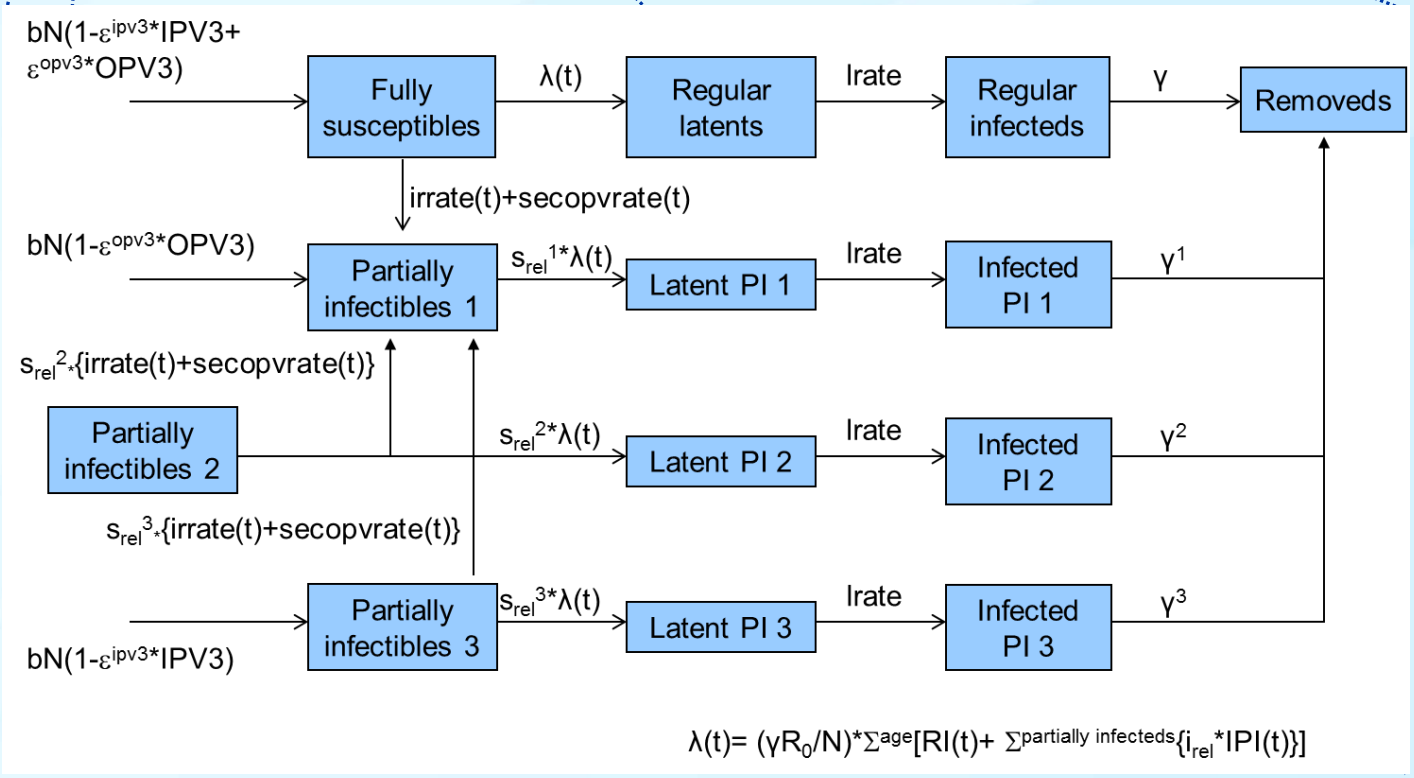
Integrated model (full influence diagram)



Duintjer Tebbens et al., Risk Analysis, 2008

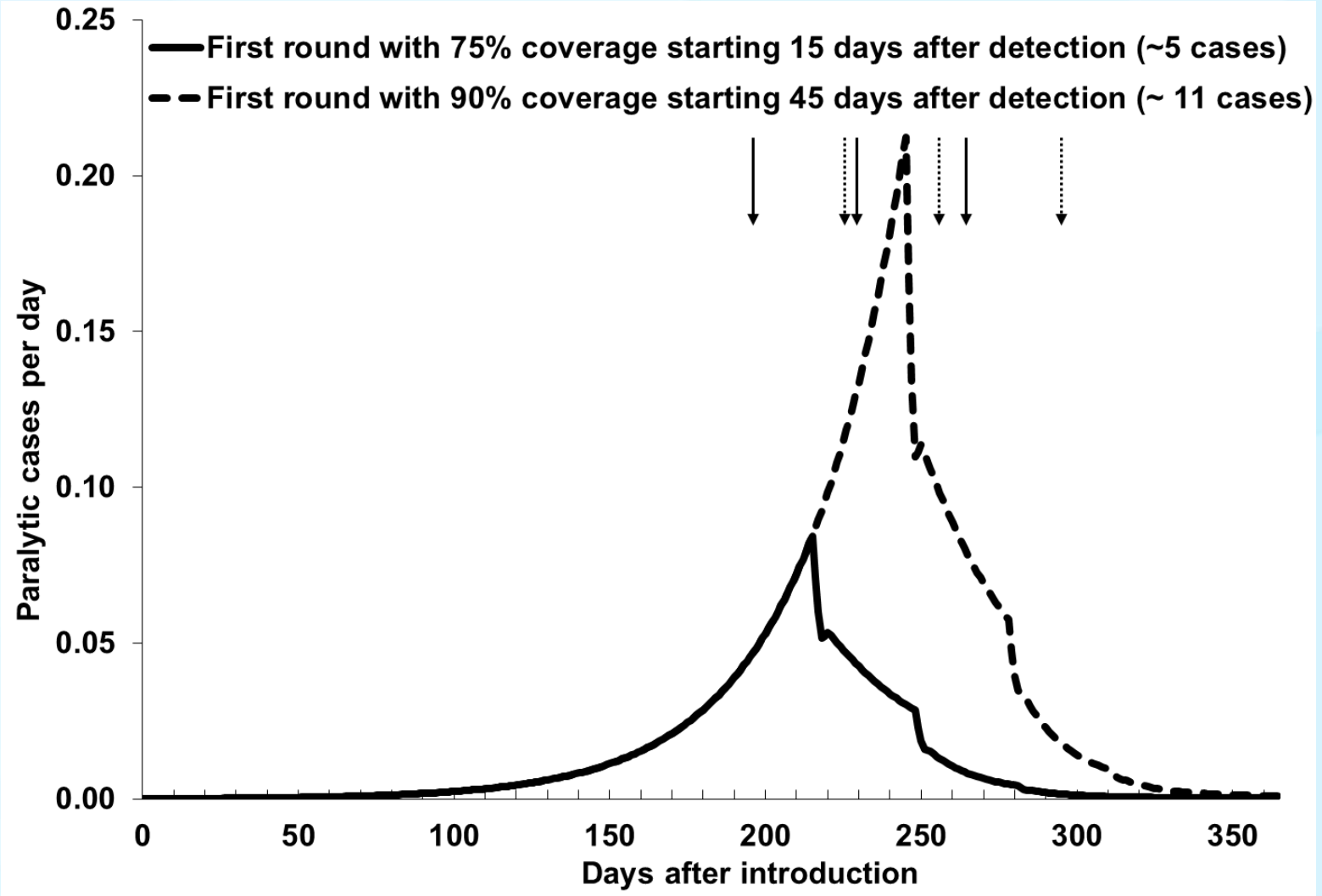
Dynamic transmission model





Total of 325 stocks to model population immunity and virus behavior

Outbreak response



Thompson, Risk Analysis, 2006

Outbreak response

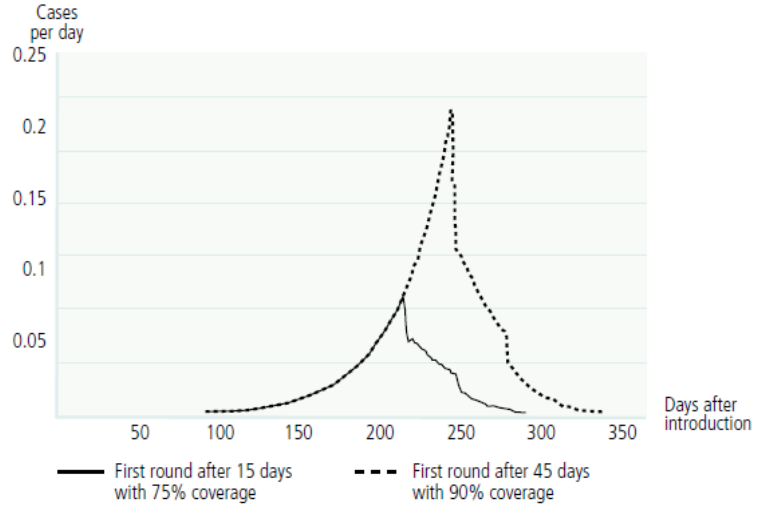
Polio outbreak response: the faster, the better…

In line with the standing recommendations for outbreak response by the Advisory Committee on Polio Eradication (ACPE) (see page 2), mathematical modelling predicts that a rapid, large-scale immunization response is preferable to a delayed response. Exploring the trade-offs between time and coverage, mathematical modelling suggests that an initial quick response with medium coverage (above 70%) is more beneficial in controlling an outbreak than a delayed activity with higher coverage, as long as the initial rapid response is followed by two, large-scale campaigns attaining high coverage (at least >90%).

See figure on right: in a hypothetical outbreak in a low income country of 10 million people, implementing a first round with 75% coverage 15 days after the onset of the first paralytic case leads to 5 cases, compared to 11 cases if the first round occurs 45 days after the onset of the first paralytic case, but attains 90% coverage.

Rapid response translates into a lower number of cases

Main assumptions: 10 million people, low-income country, no SIAs in the previous 5 years, 50% routine OPV3 coverage, R0=10, AFP surveillance, 2nd and 3rd rounds cover 90% of under fives, all rounds use mOPV



Adapted from Kim THompson and Radboud Duintjer Tebbens

Polio News, Issue 25, Autumn 2005

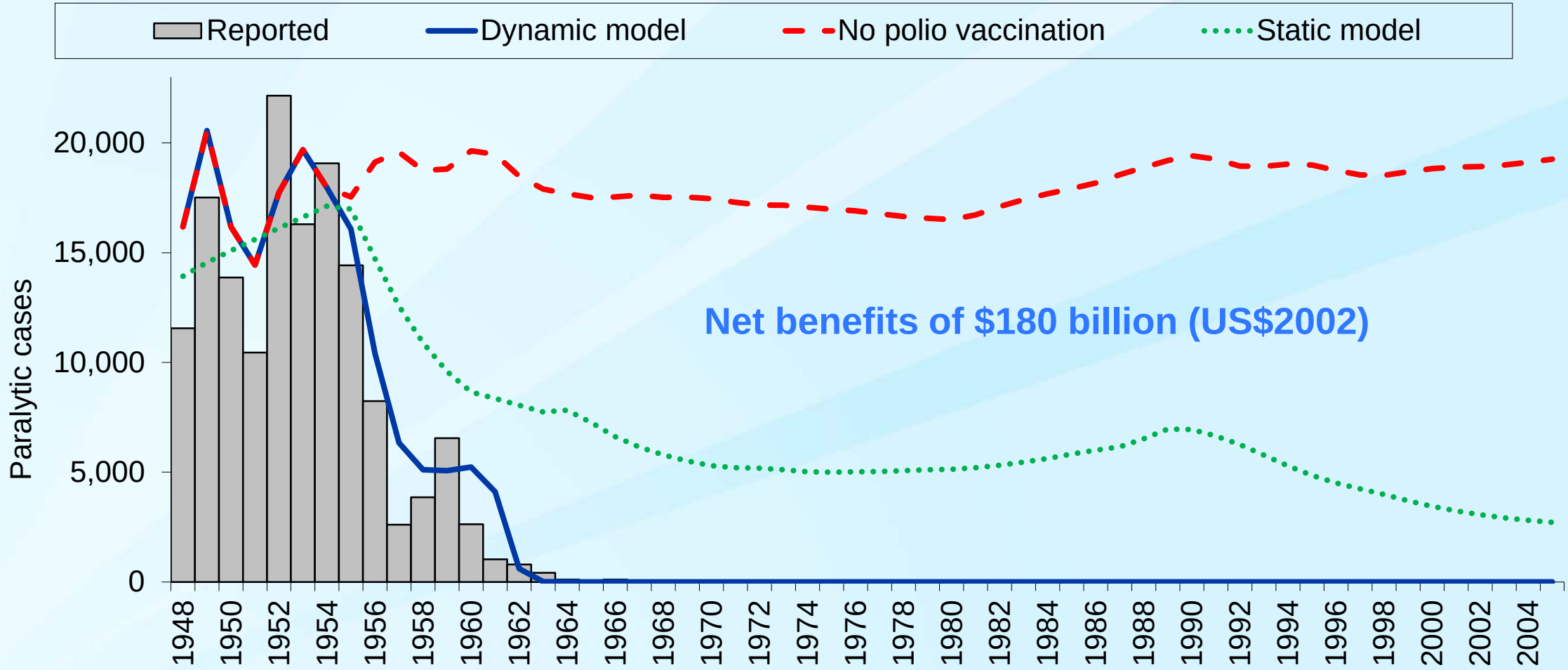
Dr. Bruce Aylward, World Health Organization, Assistant Director-General of Polio, Emergencies, and Country Collaboration

"…This work clearly demonstrated that speed trumps coverage at the beginning of an outbreak response and that was a fundamental shift in the way people were approaching polio outbreak response… most indicative of the depths of impact of this new understanding on our work is that it underpinned a World Health Assembly resolution"

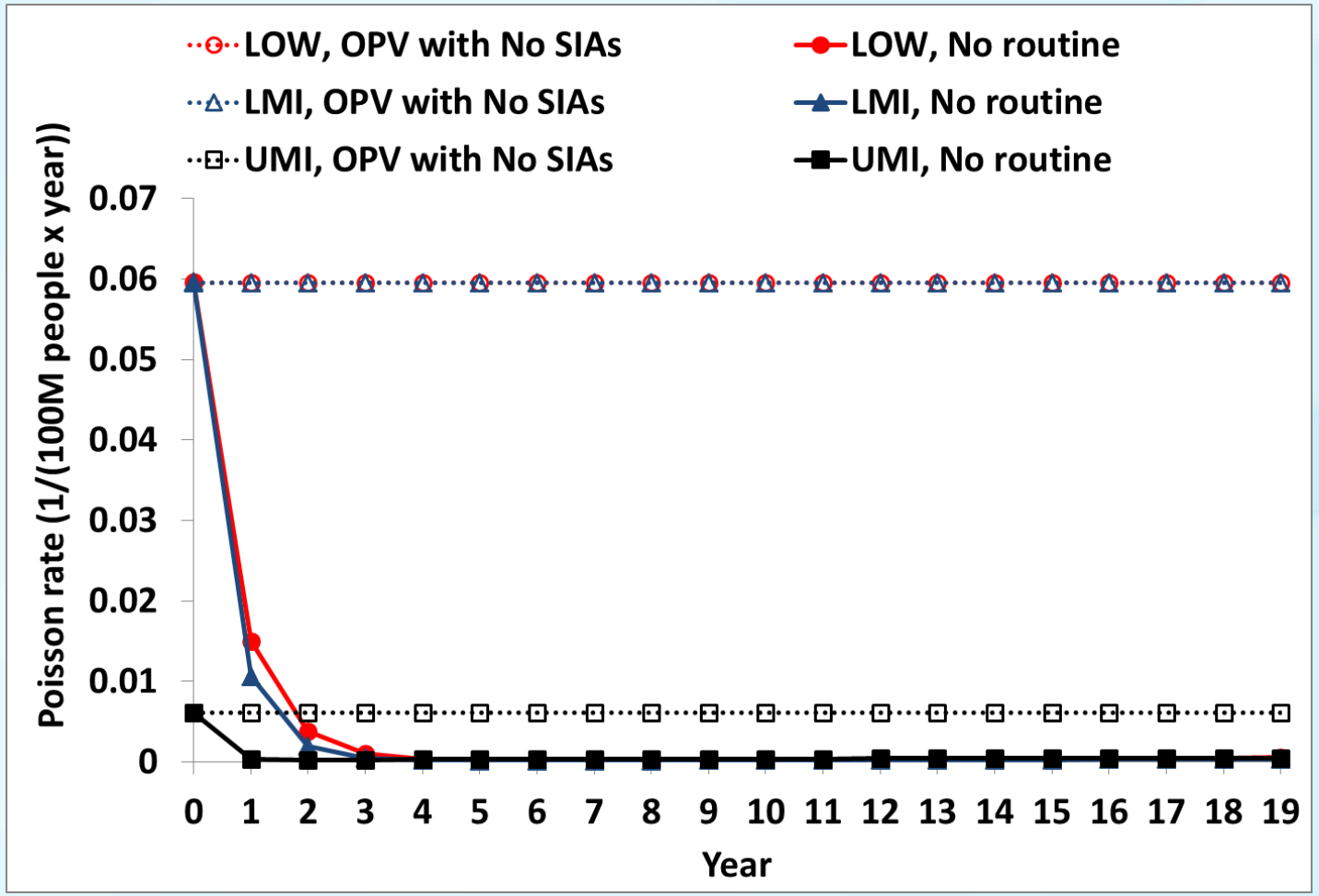
RESULTS, IMPACT, AND CONCLUSIONS

Dr. Kimberly M. Thompson
Kid Risk, Inc., President

Integrated analysis: The US experience



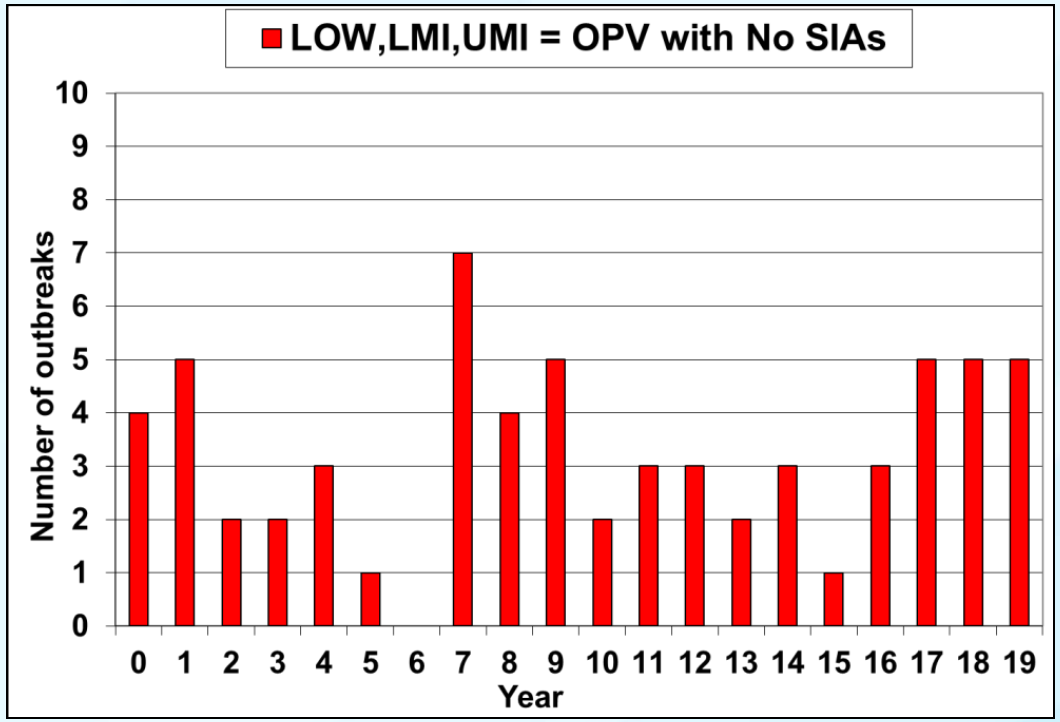
Characterization of post-eradication risks

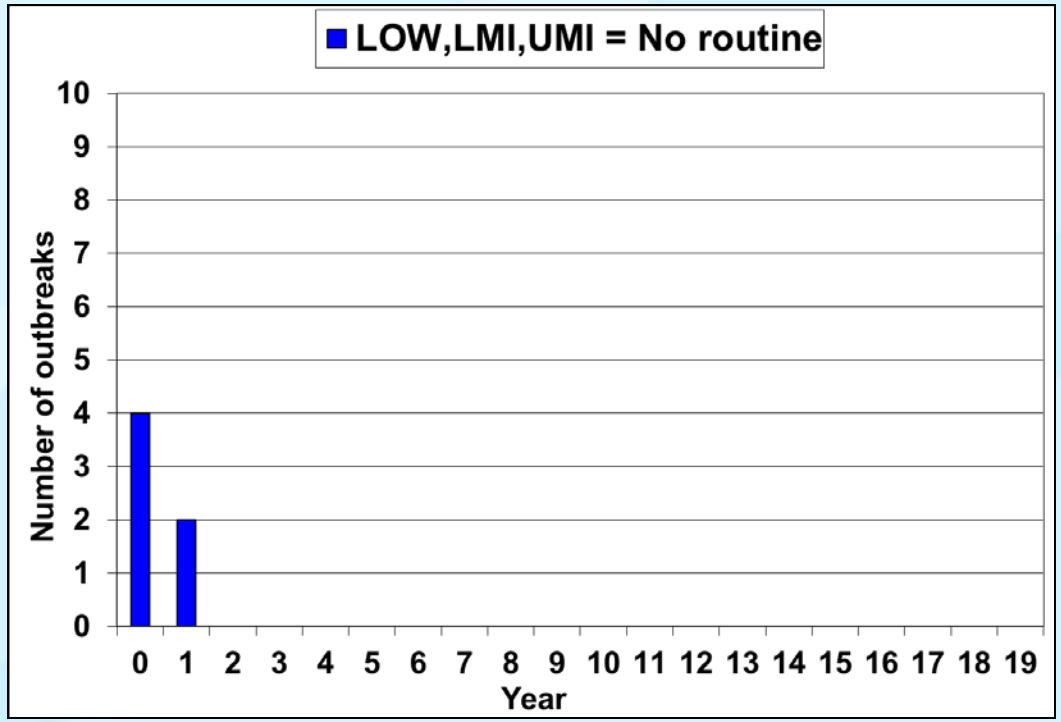


LMI=lower middle-income countries; Low=low-income countries; OPV = oral poliovirus vaccine; SIAs = supplemental immunization activities; UMI = upper-middle income countries

Based on Duintjer Tebbens et al., Risk Analysis, 2006; estimates for realistic population immunity at year 0, cVDPV risks based on confirmed cVDPVs only, and enforced containment

Stochastic simulation showing possible futures

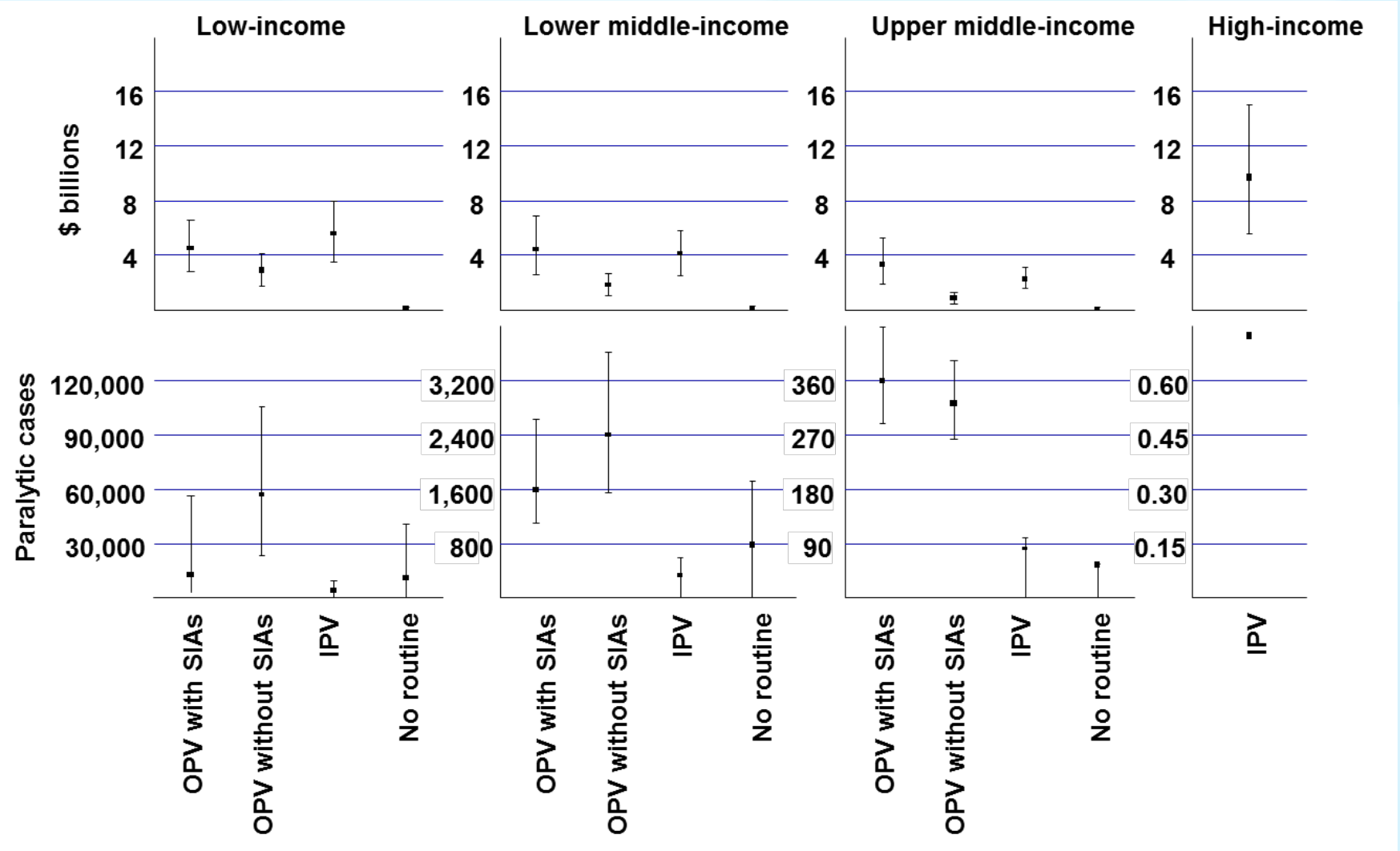




LMI=lower middle-income countries; Low=low-income countries; OPV = oral poliovirus vaccine; SIAs = supplemental immunization activities; UMI = upper-middle income countries

OPV with low coverage is not a good epidemiological option

Integrated analysis: Post-eradication vaccination strategy optimization

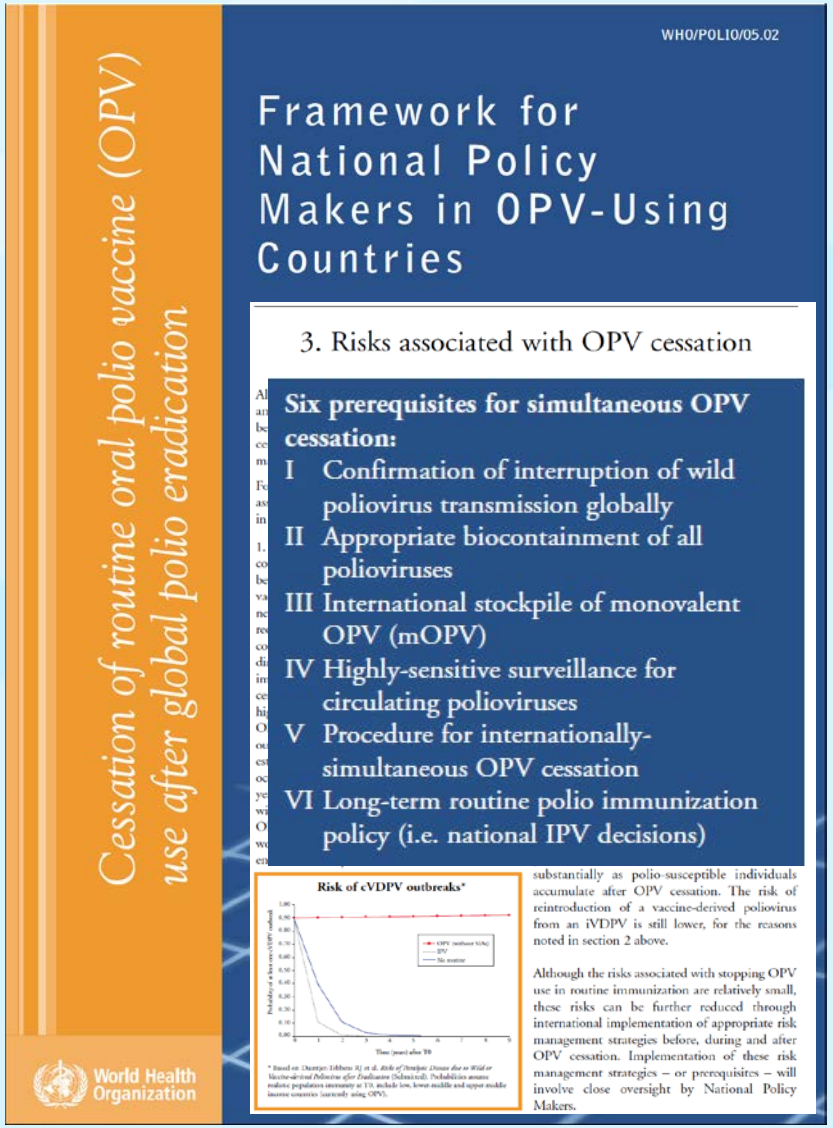


Continued OPV use after eradication is not a good economic or health option

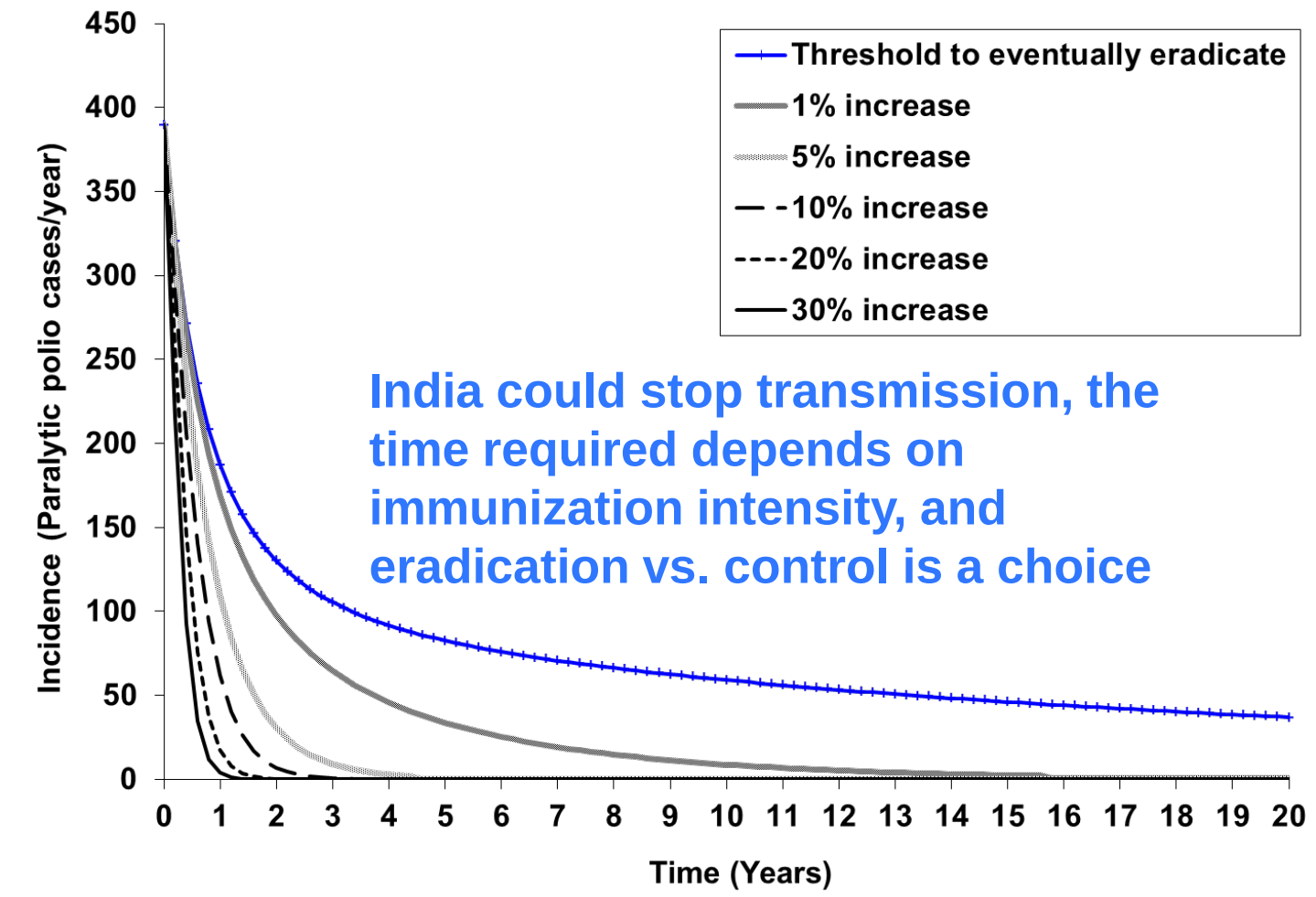
Thompson et al., American Journal of Public Health, 2008

Impact

- Agreement to coordinate OPV cessation
- 2008 WHA Resolution 61.1 asks the WHO Director-General “to set, if and when appropriate, a date for the eventual cessation of use of oral poliomyelitis vaccine use in routine immunization programmes”

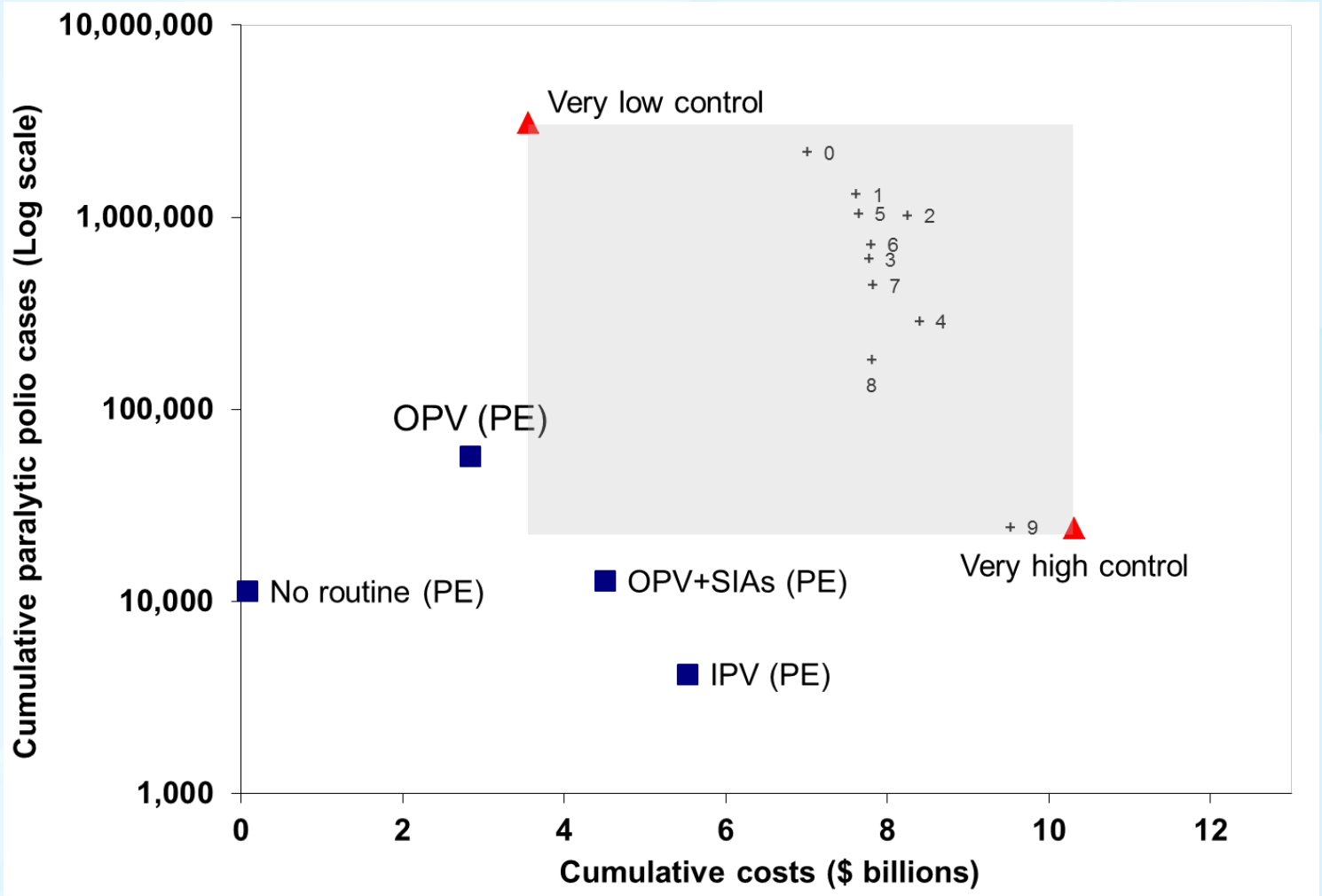


Integrated analysis: Control vs. eradication
Can we stop transmission in Northern India?



Thompson and Duintjer Tebbens, Lancet, 2007

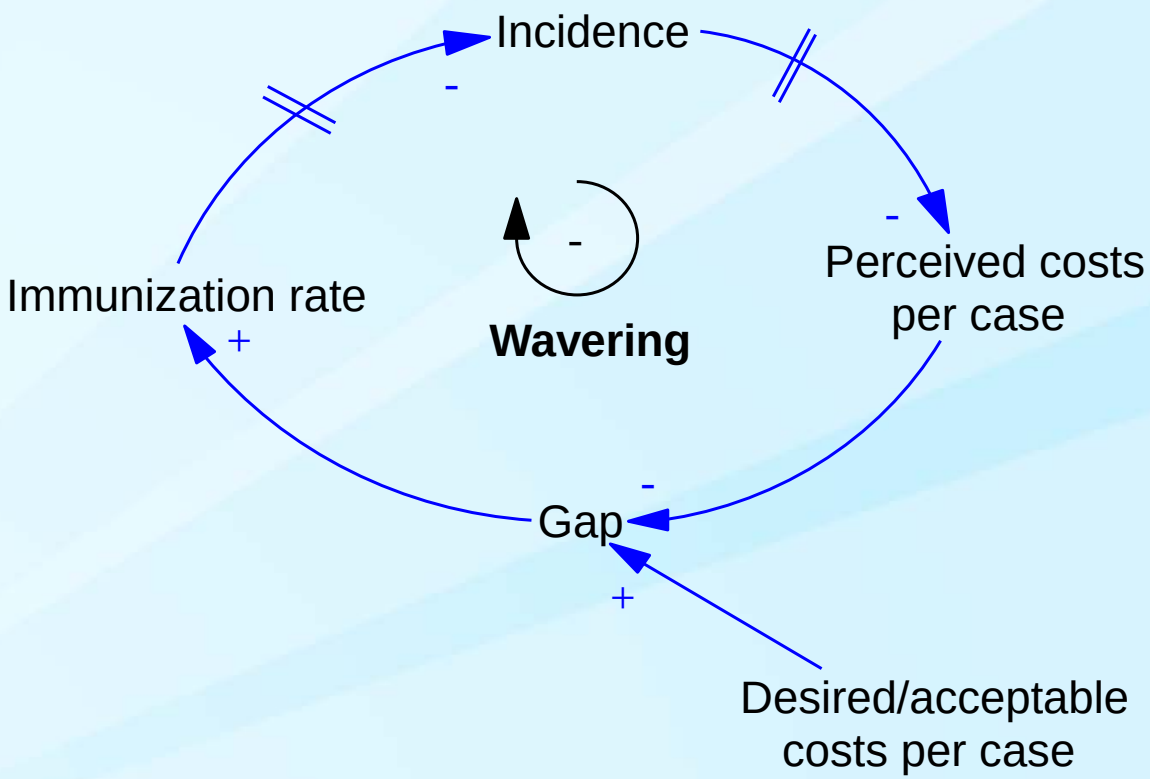
Integrated analysis: Control vs. eradication
What are the cost and case trade-offs?



Post-eradication (PE) options offer lower cases and costs than control

Thompson and Duintjer Tebbens, Lancet, 2007

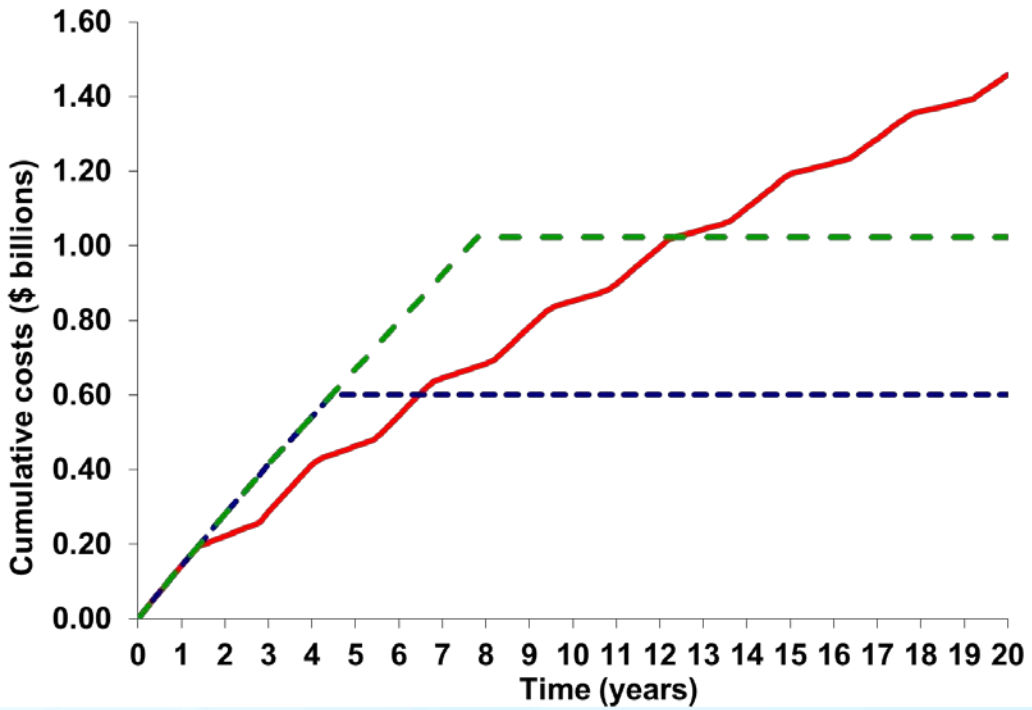
Integrated analysis: Control vs. eradication
What happens with a wavering commitment?

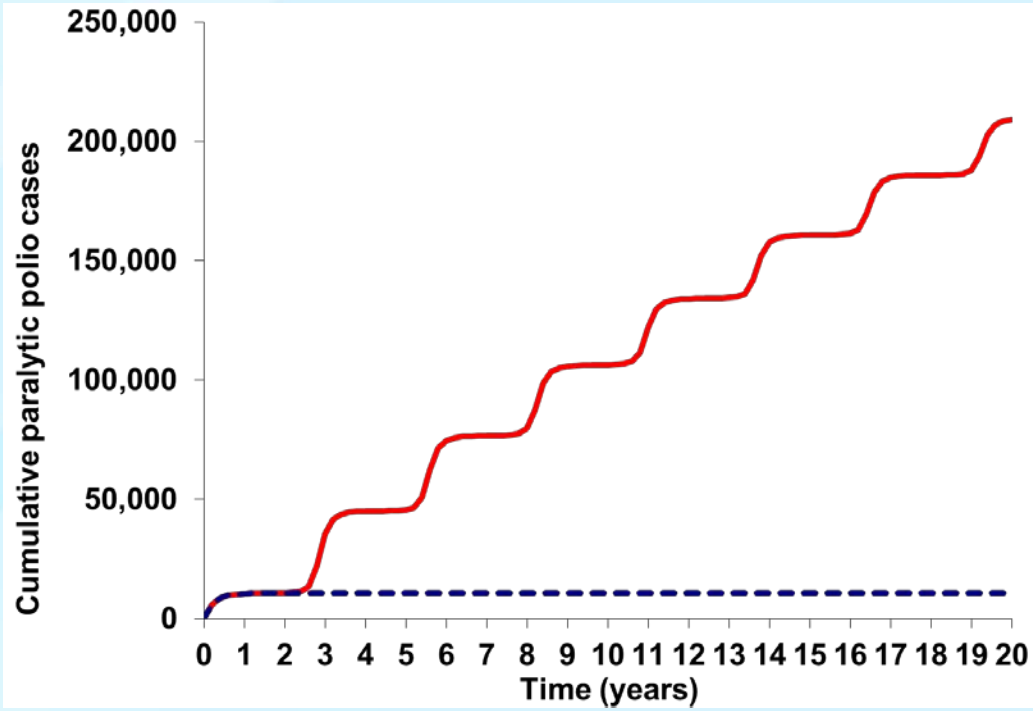


Integrated analysis: Control vs. eradication
What happens with a wavering commitment?

Vaccinate intensely until eradication (possibly longer - - - -)

Vaccinate intensely until things look good then waver





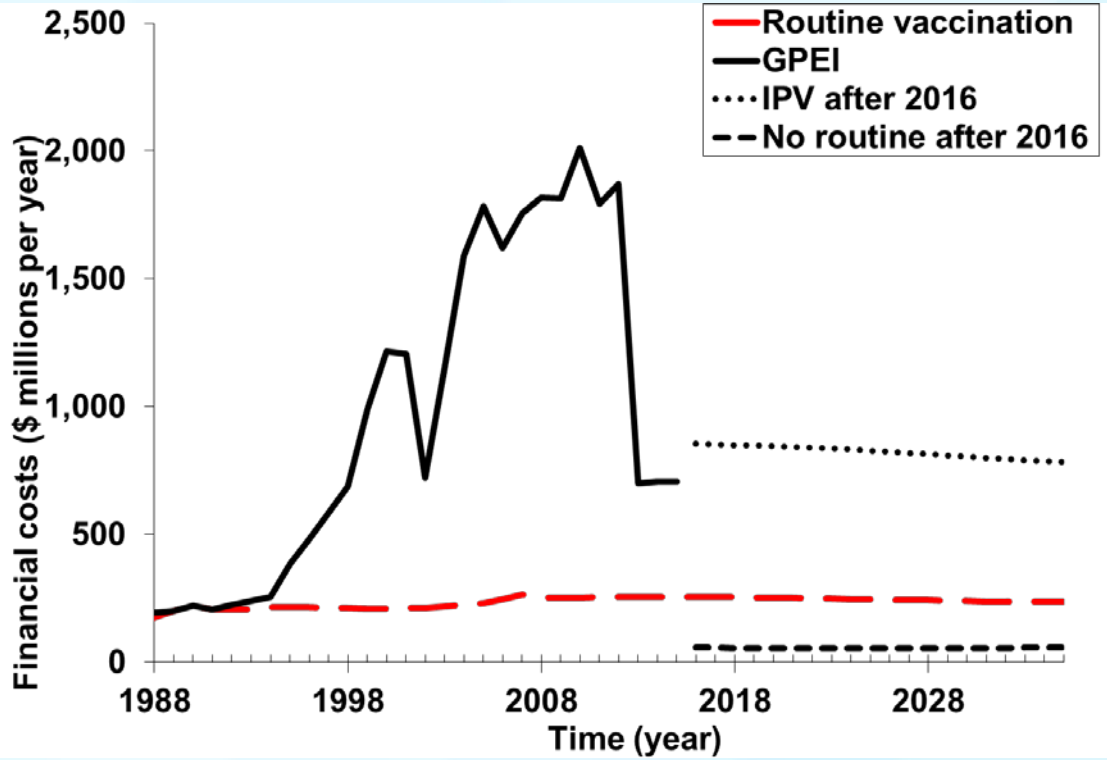
Wavering is more costly with respect to both costs and cases in the long run

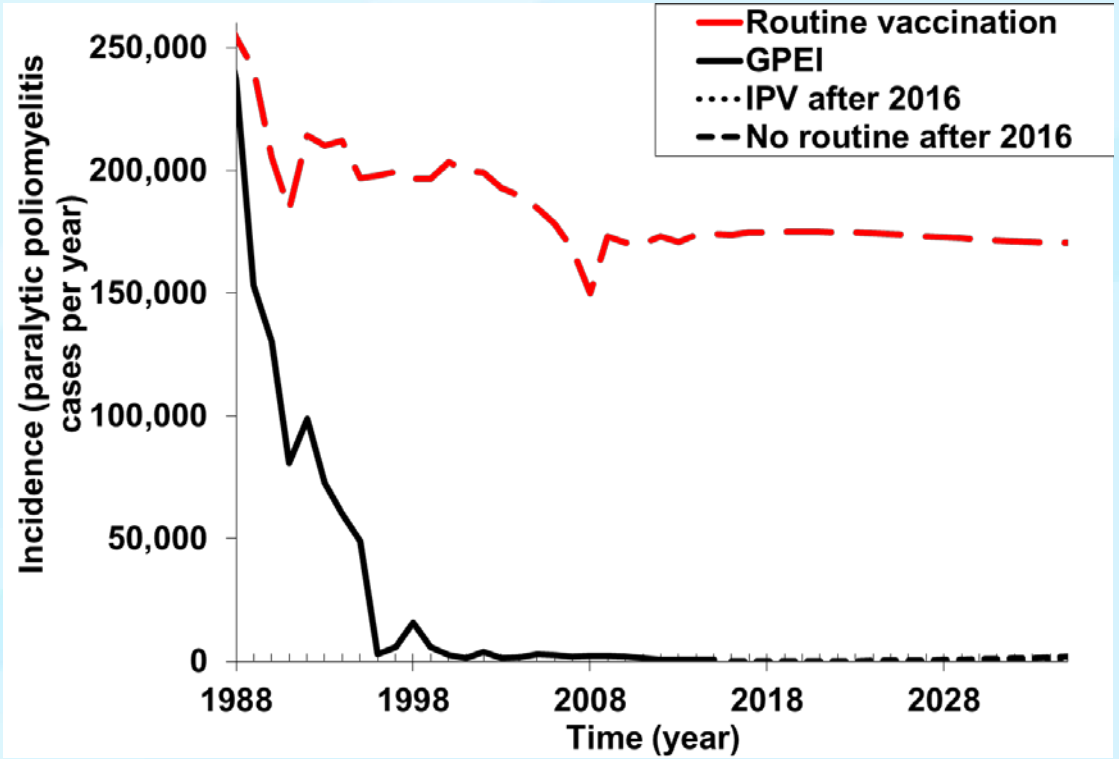
Thompson and Duintjer Tebbens, Lancet, 2007

February 2007 WHO stakeholder consultation

Dr. Margaret Chan, WHO Director-General, told the attendees that their "commitment must not waver" and they would be "seeing today new data that show why, over a 20-year period, every proposed option for controlling polio will cost more, in human suffering and dollars, than finishing eradication. In other words, getting the job done is your best buy."

Integrated analysis: Impacts of the GPEI





Expected net benefits of the GPEI exceed $40-50 billion (US$2010)

Duintjer Tebbens et al., Vaccine, 2011

Importance to stakeholders

Dr. Carol Pandak, Rotary International, Director of PolioPlus: “We regularly use the $40-50 billion estimate of net benefits of the GPEI as we raise funds to finish polio eradication both within and outside of Rotary. The modeling work made a compelling case for stable and sustained funding, and this helped all of us as we plan ahead.”

Impacts

Integrated analyses used to support the economic case to raise the funds needed to realize net benefits of $40-50 billion of the GPEI

April 2013: Global Vaccine Summit yields US$4 billion in funding commitments to polio endgame plan

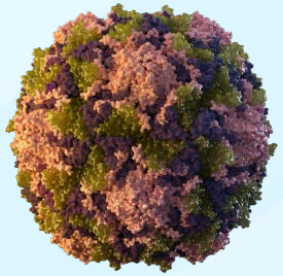
https://www.rotary.org/en/global-vaccine-summit-yields-us4-billion-funding-commitments-polio-endgame-plan

Dr. Bruce Aylward, World Health Organization, Assistant Director-General of Polio, Emergencies, and Country Collaboration

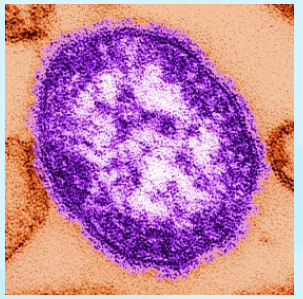
"…At a time when most people have forgotten polio, I cannot overstate how critical it was to have these numbers to illustrate the gains of completing polio eradication and the benefits of eradication over control."

Transportability

- Additional polio complexities



- Other vaccine-preventable diseases



- Complex systems that require consideration of variability, uncertainty, and time

Conclusions

- Insights
- Costs and lives saved

Acknowledgments for this presentation

- **Funding to Kid Risk, Inc. for first 2 authors from CDC Cooperative Agreement U66 IP000169**
- **Thank you**
  - Drs. Bruce Aylward, Carol Pandak, and Walter Orenstein for providing stakeholder perspectives
  - Katerina Alves, Sona Bari, Thomas Bell, Christopher Black, Ivana Boko, Lee Bookman, Louis Boviero, James Cosgrove, Christine Fares, Jean-Marc Glinz, Brian Hirten, Alan Janssen, Todd Jordan, Sarah Poser, Oliver Rosenbauer, Bryon Skinner, Jeanette St. Pierre
  - The GPEI partners for the images used in this presentation
  - Sid Hess, Pelin Pekgun, Carrie Beam, and the Edelman judges for comments

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"…mathematical modeling can give us an idea of the future and the potential costs and impact of our policy options …. As other teams create analytical models to support decision makers who manage complex systems, I can vouch for how transformational these are for strategic and program planning."

Thank you

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Trade-offs between objectives

- Trade-offs mainly between human health and money
- Economic results estimated with and without monetization of health outcomes
- Sensitivity analyses explored different values for health outcomes and discount rates

Streams of net benefits

- Ongoing prevention implies ongoing net savings, our work support the efforts to sustain the prevention (outbreak response)
- Economic benefits at any point in time depend on the assumptions made about time horizon, discount rate, and other factors
- Decision makers focused on making the biggest impact on human health as cost-effectively as possible