The Measles and Rubella Investment Case

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(21 measles and rubella related publications)

Kid Risk, Inc.

Doing our best for children

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Research on globally-coordinated investments in measles and rubella management

In 2011, Kid Risk, Inc. began the developing models to support risk management efforts to reduce the burdens of measles, rubella, and congenital rubella syndrome (CRS), including the options of eradicating measles and/or rubella virus(es). We thank contributors to our measles and rubella modeling efforts, which includes peer-reviewed publications related to the following topics (publication dates):

- **NEW** - Editorial: what will it take to end human suffering from measles (2017)
- modeling and managing the risks of measles and rubella, part II (2017)
- development and application of a dynamic transmission model for measles and rubella to support risk and policy analyses (2017, published on-line May 31)
- primer on measles (2016)
- modeling and managing the risks of measles and rubella, part I (2016)
- evolution and use of dynamic transmission models for measles and rubella risk and policy analyses (2016, published on-line June 9)
- review of measles and rubella immunization and exposure histories (2016, published on-line August 2015)
- costs and valuation of health impacts of measles and rubella risk management policies (2016, published on-line August 2015)
- impact of outbreak response activities for the 2014 Ohio Amish measles outbreak (2016, published on-line June 2015)
- systematic review of measles and rubella serology studies (2016, published on-line June 2015)
- characterization of heterogeneity in childhood immunization coverage in Central Florida (2016, published on-line June 2015)
- review of measles and rubella health economics analyses (2016, published on-line December 2014)
- optimal global vaccine stockpile design for vaccine-preventable diseases with application to measles and cholera (2016, published on-line August 2014)
- characterization of disability-adjusted life years (DALYs) for infants born with congenital rubella syndrome (CRS) (2016, published on-line August 2014)
- characterization of adverse outcomes following rubella infection in pregnancy (2016, published on-line August 2014)
- valuing the efforts required to achieve the measles and rubella goals of the Global Vaccine Action Plan (2013)
- characterization of national and global decision options for managing measles and rubella population immunity (2012)
- measles and rubella research priorities (2012)
- valuing prevention in global health by managing population immunity for vaccine-preventable diseases (2012)
- results of a stakeholder engagement process to identify the desired content for investment cases to support globally-coordinated disease management activities (2012)
- development of the concept of an eradication investment case (2011)
- characterizing the challenges associated with evaluating the economics of disease elimination and eradication efforts (2011)

You can also learn some basics about measles, rubella, and CRS and read the Measles and Rubella Strategic Plan, 2012-2020.

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Topics

- Context
- Integrated dynamic disease and economic model for measles and rubella
- Comparison of 2 scenarios
- Discussion

http://www.wpro.who.int/vietnam/topics/immunization/measles_rubella/measles_rubella_big.png?ua=1

Motivation

- Multiple regional and global control or elimination targets established over the last several decades
- 2010 WHO SAGE
  - “SAGE concluded that measles can and should be eradicated. A goal for measles eradication should be established with a proposed target date based on measurable progress made towards existing goals and targets.”
- 2012 WHO GVAP
  - 2015 and 2020 regional elimination targets for measles and rubella
  - Making progress, but off-track
- 2017 M&RI Mid-term review
  - By 2020, determine whether a formal global goal for measles eradication should be set with timeframes for achievement
  - Need to begin preparations to support future deliberations

Economic studies of measles and rubella vaccination

- Large literature demonstrates measles and rubella immunization highly cost-effective and net beneficial
  - National control (i.e., paying costs for vaccines to prevent cases) began in 1963 for measles and 1969 for rubella in 1969 in US
  - Global control for measles due to EPI by 1988, still 40 countries yet to introduce rubella vaccine
- Measles vaccine gives highest returns on investment in relatively lower income countries
  - “Immunizations will yield a net return about 16 times greater than costs”
  - “The highest returns were associated with averting measles, at 58 times the cost (uncertainty range: 28-105) through two routine immunization doses and outreach campaigns” (94 countries)

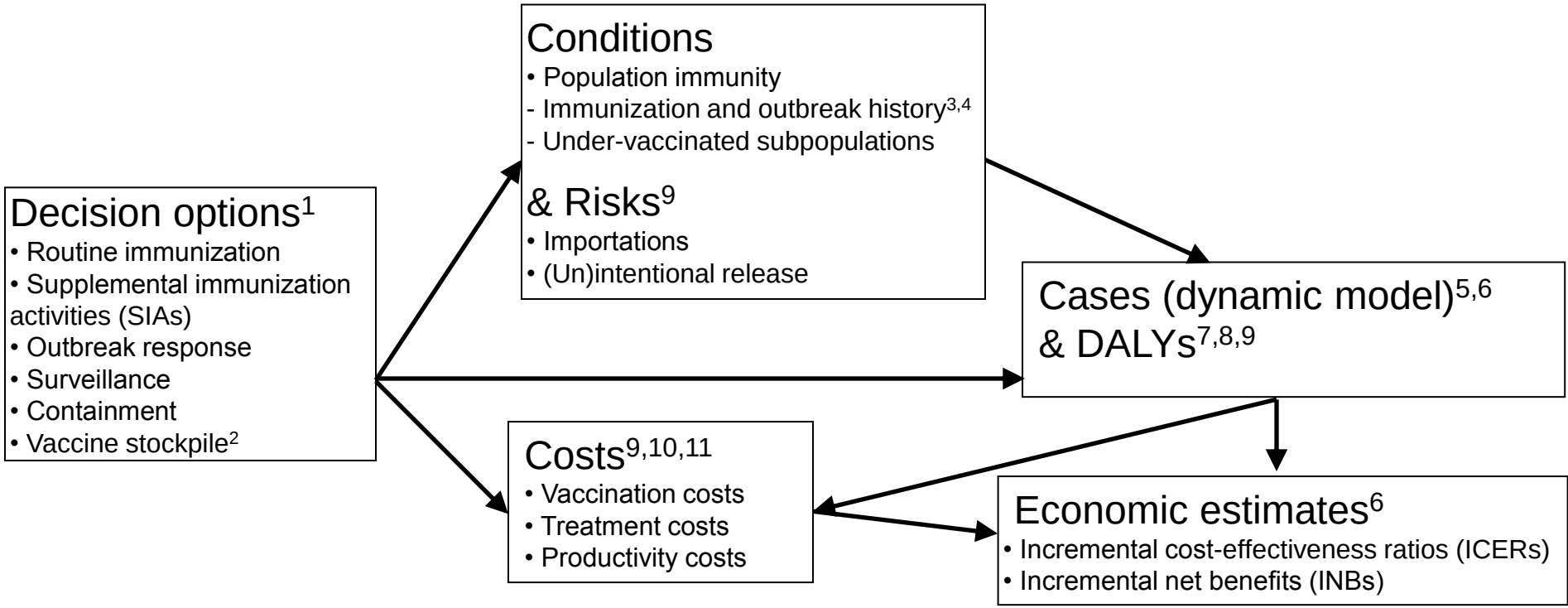
Economic perspective

- Economic literature demonstrates “high control” is not optimal if eradication is feasible
- International Taskforce for Disease Eradication (2015)

  “both measles and rubella eradication are technically feasible, but the very high contagiousness of measles is the biggest challenge to success, and measles and rubella eradication would require a sustained global commitment and a clear accountability framework such as exists for the GPEI.”
- Eradication generally requires paying large short-term costs to get long-term benefits
- World currently pursuing “high control” for measles and heading toward “high control” for rubella (as global equity improves), significant variability exists between countries and regions

Integrated model

System dynamics + decision, risk, and economic analyses



1. Thompson et al. National and global options for managing the risks of measles and rubella. *Journal of Vaccines and Vaccination* 2012; 3:165, doi: 10.4172/2157-7560.1000165.
2. Thompson and Duintjer Tebbens. Framework for optimal global vaccine stockpile design for vaccine-preventable diseases: Application to measles and cholera vaccines as contrasting examples. *Risk Analysis* 2016; 36(7):1487-1509.
3. Thompson et al. Synthesis of evidence to characterize national historical measles and rubella immunization and exposure histories. *Risk Analysis* 2016; 36(7):1427-1458.
4. Thompson and Odahowski. Systematic review of measles and rubella serology studies. *Risk Analysis* 2016; 36(7):1459-1486.
5. Thompson. Evolution and use of dynamic transmission models for measles and rubella risk and policy analysis. *Risk Analysis* 2016; 36(7):1383-1403.
6. Thompson and Badizadegan. Modeling the transmission of measles and rubella to support global management policy analyses and eradication investment cases. *Risk Analysis* 2017; 37(6): 1009-1131.
7. Thompson et al. Characterization of the risks of adverse outcomes following rubella infection in pregnancy. *Risk Analysis* 2016; 36(7):1315-1331.
8. Simons et al. Systematic review of the manifestations of Congenital Rubella Syndrome in infants and characterization of disability-adjusted life years (DALYs). *Risk Analysis* 2016; 36(7):1332-1356.
9. Thompson and Odahowski. The costs and valuation of health impacts of measles and rubella risk management policies. *Risk Analysis* 2016; 36(7):1357-1382.
10. Thompson et al. Enabling implementation of the Global Vaccine Action Plan: Developing investment cases for globally managing measles and rubella. *Vaccine* 2013; 31S:B149-B156.
11. Ozawa S, Yemeke T, Thompson KM. Systematic review of the incremental costs of interventions that increase immunization coverage. Submitted. 2018.

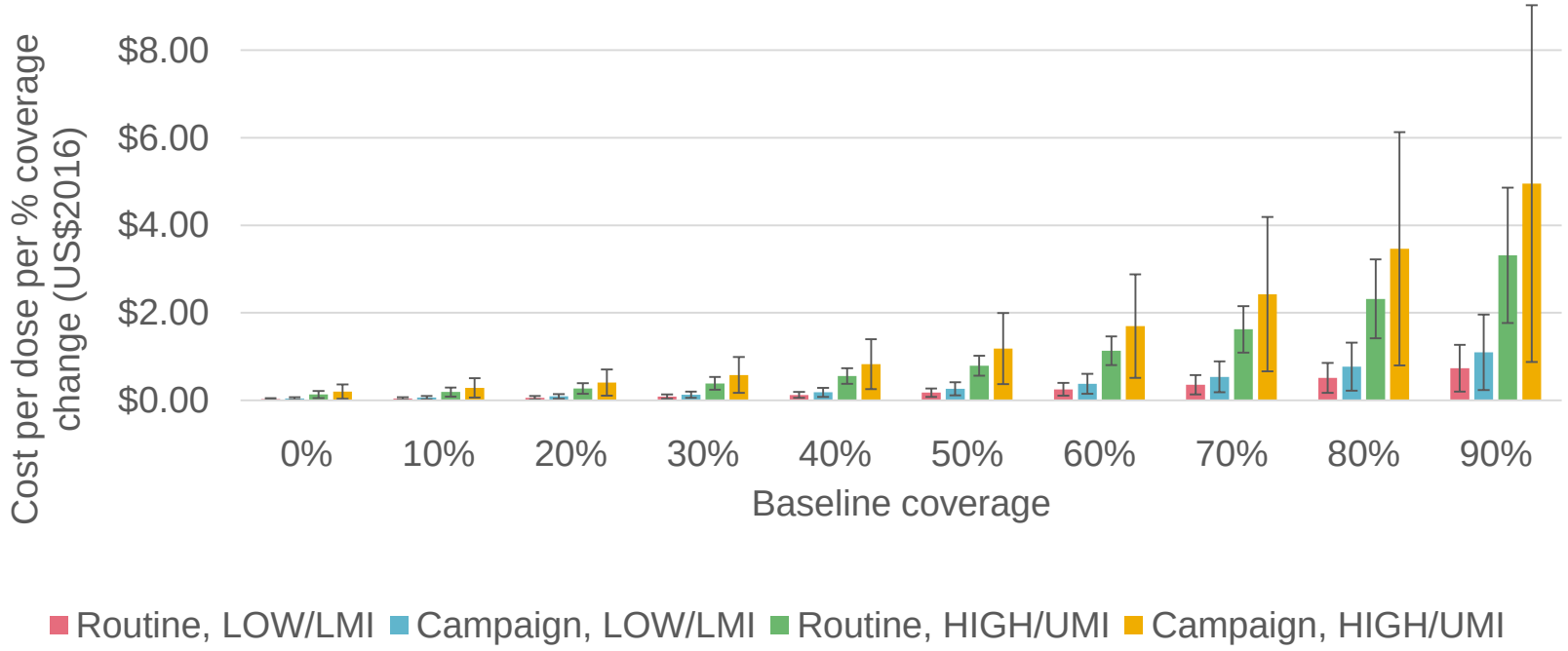
Bounding future scenarios

- Status Quo:
  - maintain 2016 vaccine schedule and coverage 2017 through 2055, continued periodic SIAs
  - no new introductions of rubella vaccine
- Eradicate ASAP:
  - increase immunization coverage (bounded by historical performance to some degree)
  - introduce rubella vaccine in all countries by 2023
  - continue vaccination throughout the time horizon (cost savings from potential reductions in vaccination not considered)

Cost premium (incremental costs) for increasing coverage

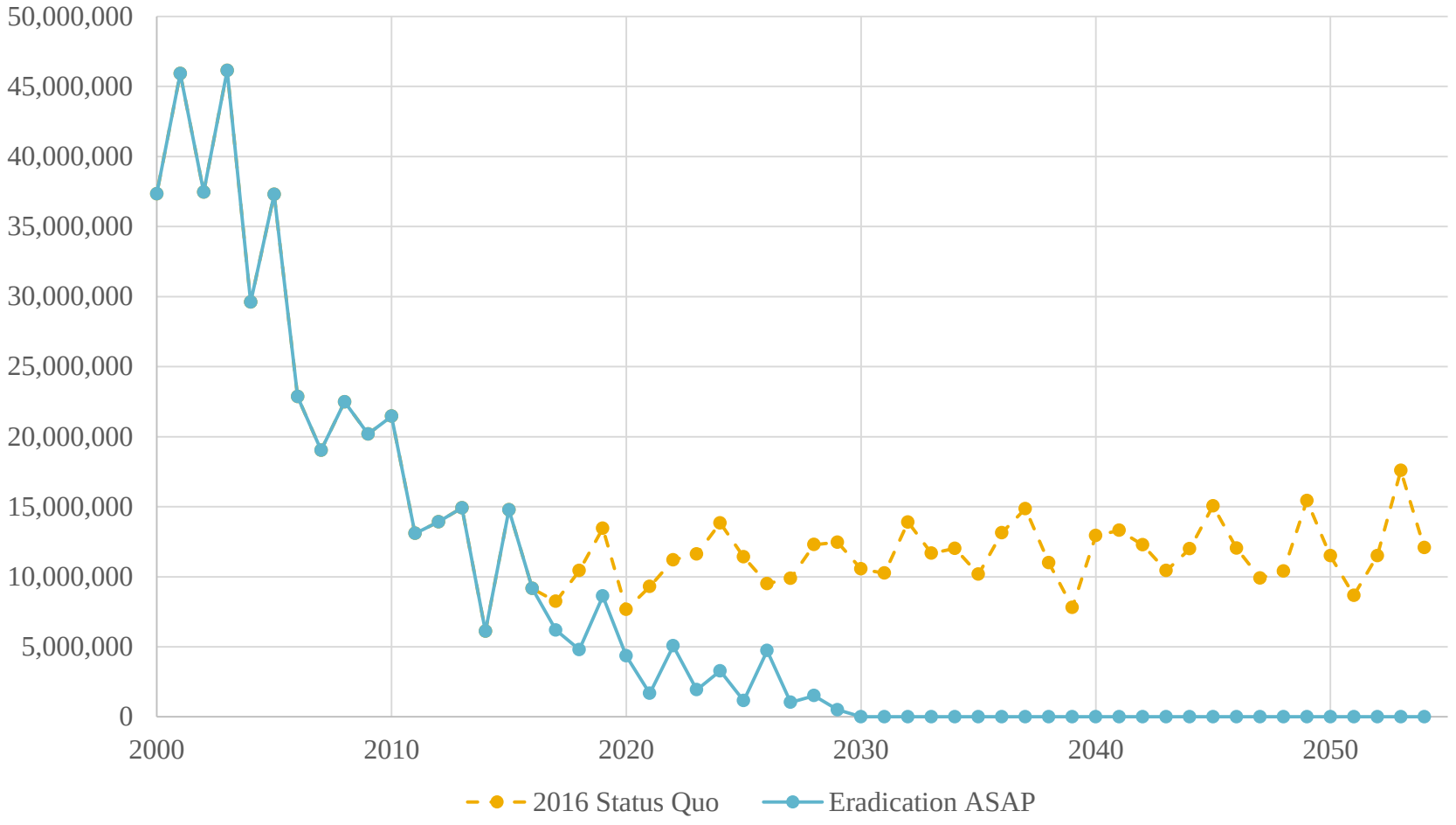
Ozawa S, Yemeke T, Thompson KM. Systematic review of the incremental costs of interventions that increase immunization coverage. Submitted. 2018.

- Increasing performance requires resources
  - Systematic literature review to characterize cost function, significant limitations in the literature

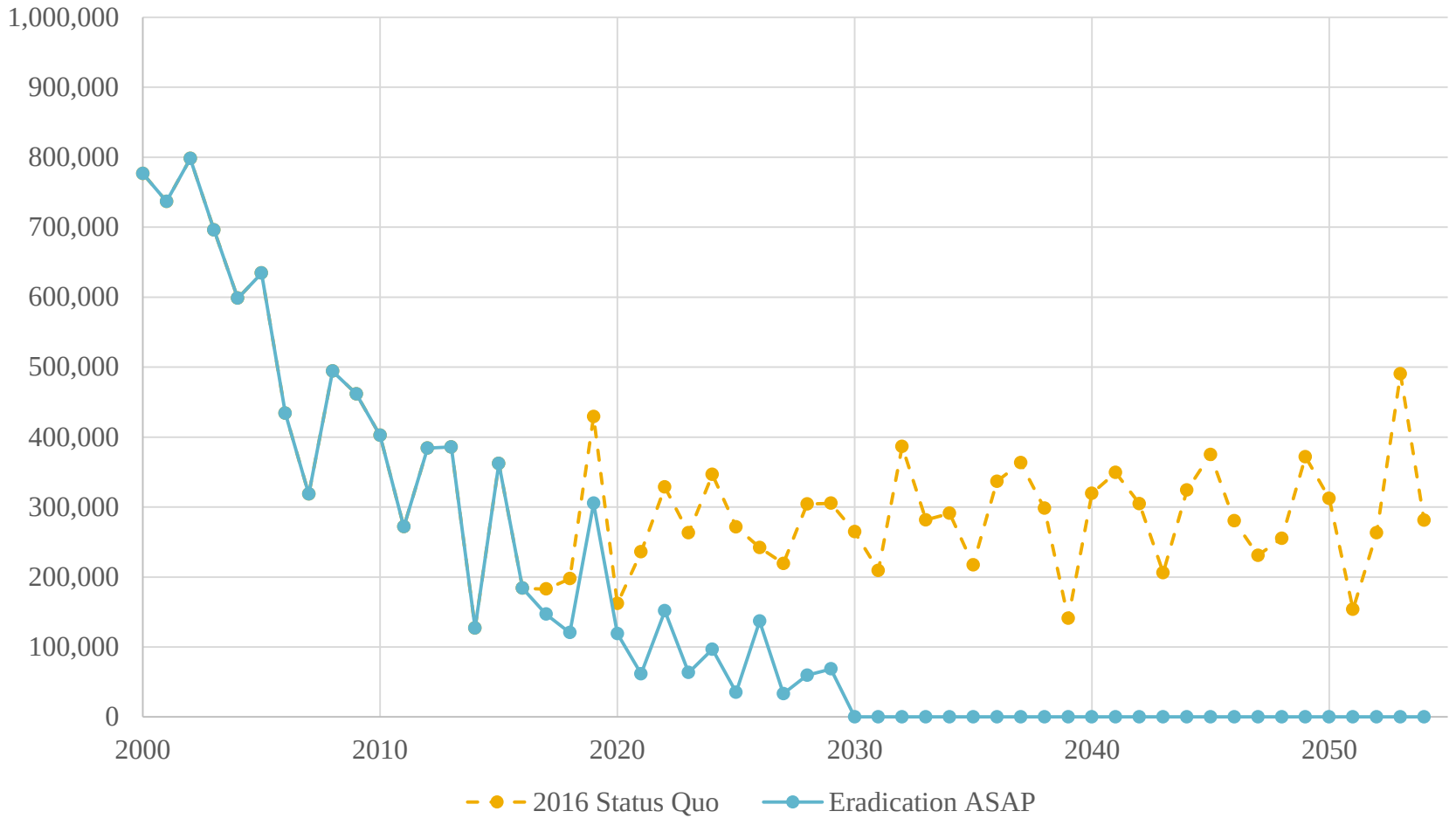


HIGH=high-income, LOW=Low-income, LMI=Lower middle-income, UMI=Upper middle-income countries

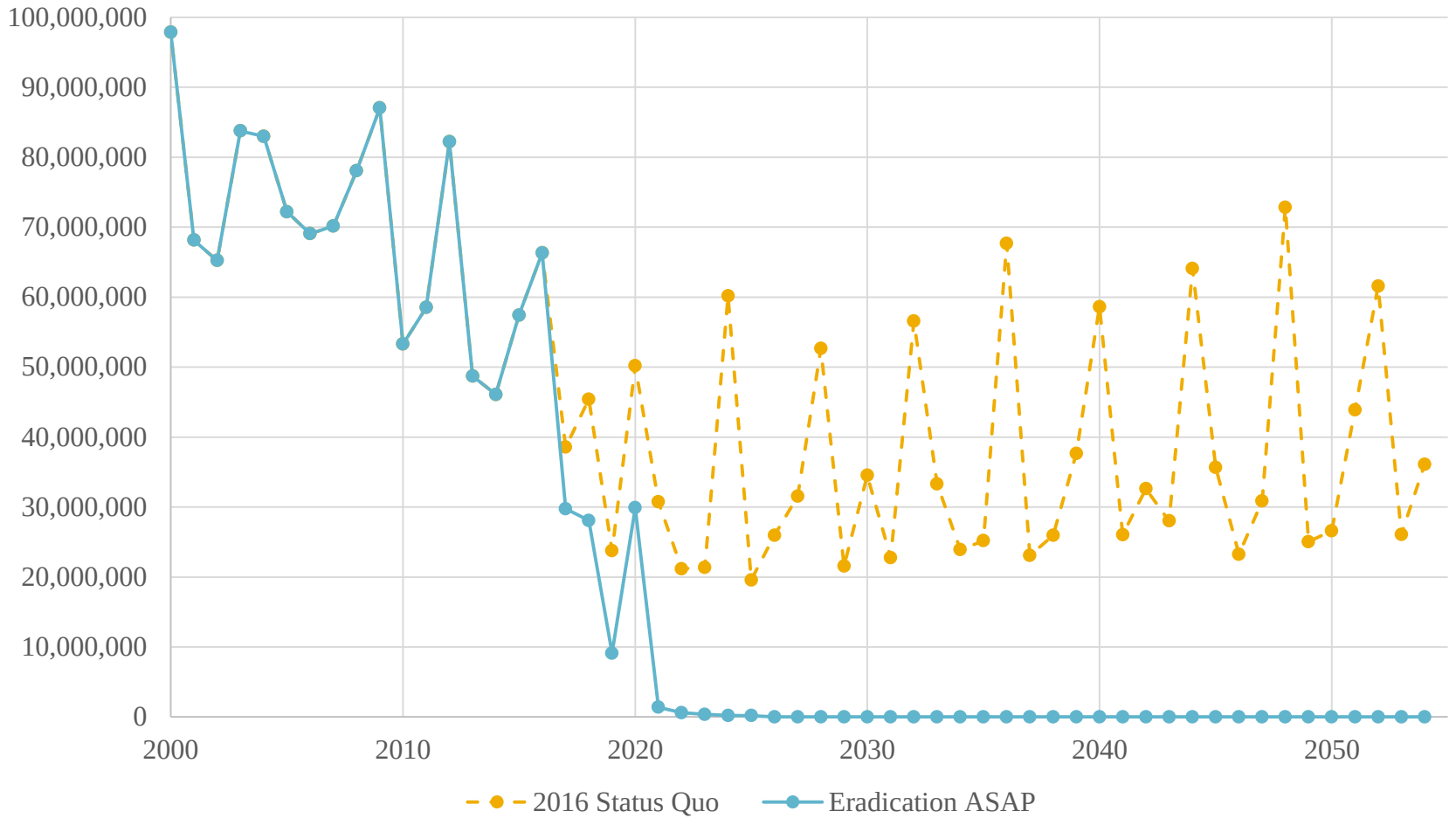
Measles incidence - Preliminary



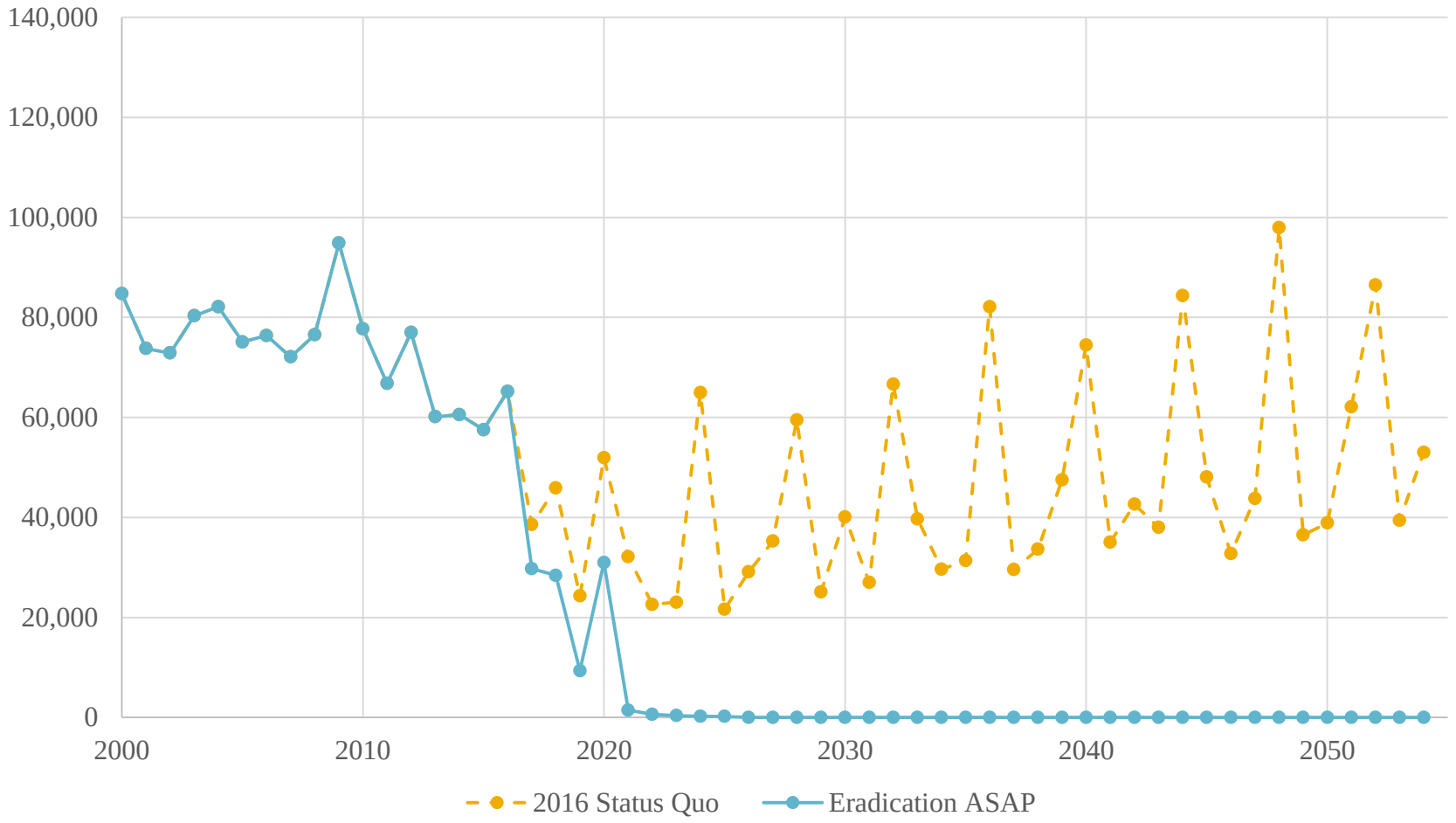
Measles mortality - Preliminary



Rubella incidence - Preliminary



CRS and rubella infections in pregnancy losses - Preliminary



Preliminary incremental cost analysis

- Discounted costs of immunization, treatment, and productivity over the time horizon of 2017-2055, assumes no differences in surveillance costs, technical support/coordination costs, other programmatic costs
- Incremental immunization costs of eradication ASAP compared to status quo: approximately $12 billion (US$2016)
- Incremental savings in expected treatment costs: $100 billion saved in treatment costs by eradication ASAP compared to the status quo
- Incremental total net benefits of avoided productivity losses of over $1.5 trillion

Perspectives on costs

- Analysis does not estimate total costs for eradication
  - Assumes similar programmatic costs over the time horizon for surveillance, coordination, technical support, etc., but would need to cost these out to characterize full costs of either scenario
  - Focuses on costs of increasing immunization required to eradicate
    - Countries that eliminated prior to 2017 pay on-going high costs for immunization to maintain their elimination + pay costs for responding to outbreaks from importations (after eradication, costs for outbreak response go away, for status quo they continue)
    - Countries yet to eliminate pay costs for immunization that maintain their current level of control for the status quo, for the eradication ASAP scenario they pay costs to improve their immunization and start paying outbreak response costs once they eliminate (until outbreak response costs go away)
  - Many stakeholders and different answers to the question of how much will eradication cost (from their perspective), in addition to the issue that the actual pathway will likely differ from the ideal path

Insights

- Accelerated immunization and eradication will prevent significant disease burden and save costs, but will require greater vaccination costs (this could be offset by reducing vaccination after eradication)
- Failure to maintain or intensify MR vaccination will lead to sustained/increased burdens of disease at high costs
- Rubella eradication looks like “low hanging fruit,” but requires that all countries use rubella containing vaccines

Limitations

- Prospective analyses require judgment (assumptions about the future)
- Cost evidence limited, not all costs included
- Actual costs and benefits depend on real path
  - Baseline could get better (or worse) than modeled status quo
  - Actual path to eradication depends on commitment and availability of resources (insufficient amounts of either will add costs associated with delay)
  - Costs and benefits of eradication depend on when we actually resolve to eradicate

What assumptions matter?

- Rubella vaccine introduction
  - Timing of introduction in countries yet to start
  - High coverage and catch-ups
- Importations (containment)
- Weakest links
  - Must achieve and maintain very high population immunity everywhere (maintenance in countries that nationally eliminate critical)
  - Countries with poor performing systems will face challenges, timing of measles eradication depends on which countries take the longest

Next steps

- Finalize analyses and write up
- Respond to questions and comments
- Review by IVIR-AC and peer-reviewers

Thank you
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