



Review

Enabling implementation of the Global Vaccine Action Plan: Developing investment cases to achieve targets for measles and rubella prevention

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ABSTRACT

Global prevention and control of infectious diseases requires significant investment of financial and human resources and well-functioning leadership and management structures. The reality of competing demands for limited resources leads to trade-offs and questions about the relative value of specific investments. Developing investment cases can help to provide stakeholders with information about the benefits, costs, and risks associated with available options, including examination of social, political, governance, and ethical issues. We describe the process of developing investment cases for globally coordinated management of action plans for measles and rubella as tools for enabling the implementation of the Global Vaccine Action Plan (GVAP). We focus on considerations related to the timing of efforts to achieve measles and rubella goals independently and within the context of ongoing polio eradication efforts, other immunization priorities, and other efforts to control communicable diseases or child survival initiatives. Our analysis suggests that the interactions between the availability and sustainability of financial support, sufficient supplies of vaccines, capacity of vaccine delivery systems, and commitments at all levels will impact the feasibility and timing of achieving national, regional, and global goals. The timing of investments and achievements will determine the net financial and health benefits obtained. The methodology, framing, and assumptions used to characterize net benefits and uncertainties in the investment cases will impact estimates and perceptions about the value of prevention achieved overall by the GVAP. We suggest that appropriately valuing the benefits of investments of measles and rubella prevention will require the use of integrated dynamic disease, economic, risk, and decision analytic models in combination with consideration of qualitative factors, and that synthesizing information in the form of investment cases may help stakeholders manage expectations as they chart the course ahead and navigate the decade of vaccines.

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Contents

1. Introduction	B150
2. Development of integrated models	B150
3. Population immunity model	B151
4. Cost and valuation model components	B152
5. Discussion	B154
Acknowledgements	B155
Conflict of interest statement	B155
References	B155

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1. Introduction

Recognizing the significant health and financial benefits provided by vaccines [1–7], the Global Vaccine Action Plan (GVAP) aspires to create a world “in which all individuals and communities enjoy lives free from vaccine-preventable diseases” by extending the full benefits of immunization to all people by 2020 and beyond [8]. The GVAP represents one of the largest and most ambitious public health projects ever initiated, and it includes achievement of the existing disease eradication and elimination goals for polio, neonatal tetanus, measles, and rubella by 2020 [8]. Translating the vision into reality will require significant investments, and the GVAP suggests that as countries deal with difficult decisions related to competing health priorities “[e]xpenditures must be linked to outputs and impacts, showing a clear investment case for immunization” (Ref. [8, p. 5, point 19]).

Although the GAVI Alliance develops and relies on investment cases to support its decisions [9–11], the concept of investment cases for globally managing infectious diseases is relatively new [12–14]. Developing investment cases can help to provide stakeholders with information about the benefits, costs, and risks associated with the options, including examination of social, political, governance, and ethical issues, but the process of developing investment cases requires making choices related to framing the analyses and defining issues as inside or outside of the scope. Framing choices (e.g., perspective, options considered, time horizon, baseline, etc.) and other assumptions (e.g., discount rate, input values, etc.) influence the results of economic analyses, and confusion can arise when multiple analyses yield different results [14–16]. Efforts to standardize methods help, but analysts still make choices, which they must make transparent when presenting results, and analyses related to the same topic may ask different underlying questions, which analysts must also make clear.

Guidelines for economic analysis emphasize consideration of incremental impacts of one or more alternatives compared to the current baseline or *status quo* [16]. In the context of managing the prevention of infectious diseases, incremental economic indicators, including the incremental net benefits (INB) and incremental cost-effectiveness ratios (ICERs) may change over time, because new interventions become available, disease risks change, and/or intervention cost or valuation inputs change [16–18]. For example, a retrospective analysis of investments made by the United States to manage the risks of polio demonstrated significant historical changes, large net benefits associated with current and past investments, and uncertainty about forecasting the future path [18]. Economic analyses related to prospective global risk management for polio prevention demonstrate the need to consider forecasts for different scenarios that account for potential options, and they show the importance of framing assumptions related to the time horizon for the analysis [3,4,19,20]. While incremental analyses can provide the only information needed in static situations and when the baseline reflects a minimalistic approach (e.g., doing nothing), in dynamic situations and when the baseline requires substantial sustained commitments (e.g., high control) decision makers may also need context about the absolute benefits and costs of the current baseline expected path.

Significant uncertainty exists about the actual path that the world will follow with respect to pursuit of the GVAP, even as it relates to the existing goals for measles and rubella. The GVAP explicitly includes the goal of achieving measles elimination in four WHO regions and rubella elimination in two WHO regions by 2015, and elimination of both measles and rubella in at least five WHO regions by 2020 [8, p. 6, footnote 1]. The Pan American Health Organization (PAHO), which represents the WHO region of the Americas, pursued a 1994 goal to eliminate endemic measles by 2000 and a 2003 goal to eliminate endemic rubella by 2010

(regional certification currently pending). Beginning in 2001, the Measles and Rubella Initiative aggressively developed and supported global mortality reduction goals for measles, and it added rubella formally to its focus in 2012 [21]. Efforts aimed at mortality reduction and regional elimination produced the current *status quo* and led to the expected current path [22]. Specifically, current regional goals include elimination (i.e., stopping endemic transmission) of measles in four other regions (Eastern Mediterranean by 2015, European by 2015, Western Pacific by 2012, and African by 2020), reducing measles mortality by 95% compared with 2000 levels by 2015 in the South-East Asia Region, stopping rubella in the European region by 2015, and pursuing accelerated rubella control with a CRS prevention goal in the Western Pacific region by 2015. Countries currently choose from a wide range of strategies as they manage and seek to optimize population immunity for measles and rubella [22]. Aggregating the activities of individual nations to the regional level and then data from the regions to the global level for measles and rubella presents numerous challenges. Achieving the GVAP goals will require coordination and cooperation [23] and sustained, significant commitment of resources [24].

Allocating scarce resources without appreciation of the dynamics of infectious diseases can yield non-optimal outcomes [25,26]. Unfortunately, experience with current disease elimination and eradication efforts and global efforts reveal chronic funding gaps [24,27,28], so unless something changes, scarce resources will present a real challenge to implementing the GVAP. However, cost-sharing opportunities may exist and the GVAP implicitly seeks to ensure sufficient resources to manage all vaccine-preventable diseases (VPDs), which may mean that sufficient resources will become available. The question remains: How will the world get from where it is now to the one envisioned by the GVAP? We discuss the path and issues associated with answering this question in the context of developing an investment case for the implementation of the GVAP for measles and rubella.

2. Development of integrated models

We reviewed the existing economic analyses for measles and rubella. We searched PubMed and the Science Citation Index for peer-reviewed articles published in English between January 1, 1963 and November 1, 2012 using the terms “(measles or rubella) AND (economic analysis OR (cost and (benefit or effectiveness or eradication or elimination)))”. Our search revealed over 300 papers, 80 of which included quantitative cost-effectiveness and/or benefit–cost results. Only a small number of studies demonstrate the economic benefits of eliminating measles nationally (e.g., for the USA [29,30], Canada and western European countries [31,32], and Uganda [33]) and regionally (e.g., Latin America and the Caribbean [34], western Europe [31]), and only two studies characterize the economic benefits of global eradication [35,36]. No existing peer-reviewed economic analyses characterize the cost-effectiveness or benefits and costs of rubella elimination or eradication. Appropriately valuing the benefits of investments of measles and rubella prevention will require the use of integrated dynamic disease, economic, risk, and decision analytic models in combination with consideration of qualitative factors.

The numbers of measles and/or rubella cases will depend on the dynamics of the diseases and national, regional, and global vaccination policy choices made, and estimating these requires using dynamic transmission models. We assume the use of appropriate infection transmission models to characterize population immunity and the incidence of adverse health outcomes as a function of historical, current, and future policies, and we highlight the dynamic complexities that will impact health and financial

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