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Review

Bridging the gap: Need for a data repository to support vaccine prioritization efforts☆

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ABSTRACT

As the mechanisms for discovery, development, and delivery of new vaccines become increasingly complex, strategic planning and priority setting have become ever more crucial. Traditional single value metrics such as disease burden or cost-effectiveness no longer suffice to rank vaccine candidates for development. The Institute of Medicine—in collaboration with the National Academy of Engineering—has developed a novel software system to support vaccine prioritization efforts. The Strategic Multi-Attribute Ranking Tool for Vaccines—SMART Vaccines—allows decision makers to specify their own value structure, selecting from among 28 pre-defined and up to 7 user-defined attributes relevant to the ranking of vaccine candidates. Widespread use of SMART Vaccines will require compilation of a comprehensive data repository for numerous relevant populations—including their demographics, disease burdens and associated treatment costs, as well as characterizing performance features of potential or existing vaccines that might be created, improved, or deployed. While the software contains preloaded data for a modest number of populations, a large gap exists between the existing data and a comprehensive data repository necessary to make full use of SMART Vaccines. While some of these data exist in disparate sources and forms, constructing a data repository will require much new coordination and focus. Finding strategies to bridge the gap to a comprehensive data repository remains the most important task in bringing SMART Vaccines to full fruition, and to support strategic vaccine prioritization efforts in general.

1. Introduction

Development of new vaccines—irrespective of a country's income level—often falls prey to competing demands, shrinking budgets and lengthening development timelines [1]. The tradeoffs inherent to new vaccine discovery, development, and delivery are shaped by public health needs, and such factors as technical feasibility, financial yields, affordability, regulation, and also public opinions concerning the diseases. These dynamics create a complex maze of choices with limited data to support and coordinate vaccine development efforts. Information deficiency also challenges strategic and transparent decision making in vaccine prioritization efforts. In a broad sense, decision making processes employed by various stakeholders remain opaque.

Consider the case of tuberculosis. An estimated 8.6 million new incident cases and 1.3 million deaths were reported worldwide in 2012 [2]. Although a vaccine is currently available and still used to vaccinate newborns, Bacille Calmette–Guérin (BCG) does not confer consistent protection against the infection in adults [3,4]. Drug-resistant strains of tuberculosis further challenge effectiveness in adults. A comprehensive analysis toward an improved vaccine for tuberculosis would ideally involve an understanding of—among other factors—how BCG imparts immunity, and why its effectiveness varies widely among infants, children and adults. In addition, the financial implications to develop a new vaccine, public awareness, and vaccine adoption are some of the many factors needed to evaluate a vaccine for development. In South Africa, for example, where the tuberculosis epidemic causes significant health and economic burden [2], this information is largely fragmented

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or inconsistent, but remains integral to the vaccine development process. The paucity and quality of data pose a significant challenge especially in the context of developing countries.

There is an enormous gap in estimating disease burden and vaccine candidate characteristics required to support effective vaccine development decisions. Consider a simple alternative for potential new vaccines to enhance protection against pneumococcal infection. Existing vaccines have used two approaches—either a multivalent polysaccharide vaccine or a protein conjugate vaccine. The 23-valent pneumococcal polysaccharide (PPS23) is recommended in the United States for at risk children over age two and adults over age 64, using a single dose primary vaccination followed by a booster shot at five years for persons at high risk. Three conjugate vaccines are currently marketed, the broadest spectrum having 13 serotypes (PCV13), with three doses recommended in the United Kingdom and a four-dose sequence in the United States [5].

The disparate effectiveness rates and immunization schedules—with the associated costs of vaccine purchase and administration—raise obvious questions about desirable directions for further vaccine development. Should we seek to reduce dosage frequency, or expand the number of serotypes involved? How does the rising risk of antibiotic-resistant bacterial populations influence these choices? Can we develop one vaccine appropriate both for infants and older children as well as senior adults, or is it best to rely on a combination of these strategies? And with each of these choices come concerns about the risk of scientific failure, potential risks of adverse effects, and the potential for prevention of pandemic outbreaks. All of these issues represent tradeoffs that can be considered, but they also indicate the need for comprehensive data that could be used in a formal systems-based approach for priority setting.

2. Approaches to new vaccine prioritization

Data-related challenges repeatedly surfaced during our work on an Institute of Medicine (IOM) project—pursued in collaboration with the National Academy of Engineering—that has resulted in a software product for prioritization called SMART Vaccines—short for Strategic Multi-Attribute Ranking Tool for Vaccines (available for free at www.nap.edu/smartvaccines).

Previous IOM efforts have relied on a single metric approach to produce a rank-ordered listing of vaccines. A set of publications issued in 1985 [6] and 1986 [7] used infant mortality equivalents as the sole benefit measure to rank new vaccines for development that are of interest to the United States and the developing countries, respectively. A subsequent report released in 2000 employed cost-effectiveness as an efficiency criterion to produce a priority list of vaccines for development [8]. Recent stakeholder feedback has indicated that both these approaches have been limited in their use because of the narrowness of employed measures to help prioritize vaccine candidates. To help create a broader evaluation mechanism that would go beyond the traditional health and economic measures, the IOM, in its recent multi-phase effort, has employed a multi-attribute utility theory based approach to rank vaccines.

The multi-attribute utility theory is a special class of multi-criteria decision analysis tools, whose previous applications have ranged from environmental engineering and academic program evaluation to energy and national security resource planning (see for example [9,10]). The application of this method represents a novel mechanism for prioritizing new vaccines, and by extension—with further work—potentially to strategic planning and allocation of public health resources and interventions.

Uniquely, SMART Vaccines allows specification of numerous programmatic, policy, intangible and other attributes—from the total of 28 built-in and up to seven user defined vaccine attributes—that are traditionally omitted from cost-effectiveness and similar analyses in the comparative evaluation of vaccines. SMART Vaccines then elicits the set of attributes the user wishes to include in the analysis, and leads the user to set weights on how much each of these attributes should matter in the final evaluation. Next, SMART Vaccines calculates a SMART Score for each vaccine candidate, displayed graphically, and then allows users to conduct dynamic sensitivity analysis to see how SMART Scores vary as attributes and weights are changed. The software structure, use, and interpretation of the SMART Scores among other details can be found in the *Ranking Vaccines* reports [11–13].

Over the course of laying the axiomatic groundwork using multi-attribute utility theory [11], and prototyping and testing of SMART Vaccines 1.0 [12] coupled with application evaluation with some user groups [13], the need for systematically collected datasets for comparing vaccine candidates became apparent. Data were sparse for disease burdens, associated treatment costs as well as careful characterization of potential new vaccine candidates that often need to be compared for go or no-go executive decisions for investment and development. The need for a coordinated and systematic way to expand vaccine data collection efforts, especially in developing countries, was evident.

3. Data demands

Published studies, reports, and publicly available datasets provided focused data for population cohorts used in SMART Vaccines. Extrapolation of findings to country-level populations with a wider range of demographics was challenging. Data for SMART Vaccines are entered by the user in a three step process that considers population, disease, and vaccine characteristics, shown as screenshots in Figs. 1–3. However, these data may be conceptually organized into four groups:

3.1. Demographic data

Common life table data describing age composition and life expectancy are needed entries for specifying populations of interest (Table 1). This first group of data may be obtained from publicly available sources such as the United Nations World Population Prospects and the World Health Organization (WHO) Global Health Observatory. This is supplemented with standard life expectancy as a constant benchmark (i.e., Japanese women with the greatest longevity). Hourly wage rates must also be estimated and input. For pre-loaded populations, these were available from the International Labor Organization. Average hourly earnings to all adults was applied—whether working at home, in the labor force, unemployed or some combination—using standard economic approaches that assign a value of productive time to all persons. Adult-like values of time to children were imputed on the premise that a sick child would demand the attention of an adult, hence costing the adult the opportunity cost of that time involved in child caring. Locating and compiling these demographic data may be cumbersome, but a necessary step in understanding a vaccines candidates potential within a population.

3.2. Disease burden

Information about the disease is specified into health burden—incidence, case fatality rate, and other complications due to the disease (Table 2). This second group of data relating to disease burden and mortality can be sourced from the following: WHO health statistics and information systems; the Institute for Health Metrics and Evaluation's Global Burden of Disease study [14]; and the National Vital Statistics Report and the Morbidity and Mortality