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Systematic review of the incremental costs of interventions that increase immunization coverage

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ABSTRACT

Achieving and maintaining high vaccination coverage requires investments, but the costs and effectiveness of interventions to increase coverage remain poorly characterized. We conducted a systematic review of the literature to identify peer-reviewed studies published in English that reported interventions aimed at increasing immunization coverage and the associated costs and effectiveness of the interventions. We found limited information in the literature, with many studies reporting effectiveness estimates, but not providing cost information. Using the available data, we developed a cost function to support future programmatic decisions about investments in interventions to increase immunization coverage for relatively low and high-income countries. The cost function estimates the non-vaccine cost per dose of interventions to increase absolute immunization coverage by one percent, through either campaigns or routine immunization. The cost per dose per percent increase in absolute coverage increased with higher baseline coverage, demonstrating increasing incremental costs required to reach higher coverage levels. Future studies should evaluate the performance of the cost function and add to the database of available evidence to better characterize heterogeneity in costs and generalizability of the cost function.

1. Introduction

Vaccines represent some of the most cost-effective and cost-beneficial public health interventions [1,2]. Immunization prevents an estimated 2 to 3 million cases of vaccine preventable diseases annually [3]. Estimates suggest that between 2001 and 2020, immunization will prevent over 20 million deaths and save an estimated $350 billion in cost-of-illness across 73 low- and middle-income countries [4]. Spurred by initiatives such as the World Health Organization (WHO) Expanded Program on Immunization (EPI) introduced in 1974, Gavi, the Vaccine Alliance, launched in 2000 [5], and the 2012 Global Vaccine Action Plan [6], global immunization coverage continues to improve [7,8]. The global proportion of children receiving 3 doses of diphtheria-tetanus-pertussis (DTP3) vaccine increased from 5% in 1974 to 86% in 2015, albeit with intermittent periods of stagnation and decline [3,9]. Despite the remarkable progress, many countries remain off track with respect to achieving the global goals of 90% immunization coverage nationally and 80% in each district [3,10,11]. An estimated 19.4 million children do not receive basic vaccines, and the WHO reports that increased immunization coverage could avert an additional 1.5 million premature global deaths annually [3].

Recent concerted efforts to improve immunization coverage strive to strengthen national routine immunization programs [12]. Increased use of health economic analyses in decision-making motivated recent studies that characterized the costs of immunization programs in order to inform programming and policy decisions [13–15]. Comprehensive multi-year plans (cMYPs) [16,17] and aggregations of primary data collected from health facilities [18] provide some estimates of the costs of routine immunization programs at the national level and explore some determinants that explain cost variability within and between countries [15]. Such national level costs of immunization programs can support decisions about introducing new vaccines and expanding immunization programs [19,20]. However, little is known of the costs of interventions to improve immunization coverage, which represents an important consideration for policy makers. Given the importance of improving coverage particularly to reach

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harder-to-reach subpopulations, we sought to estimate the non-vaccine costs of interventions to increase absolute immunization coverage.

Prior published reviews evaluated many interventions aimed at increasing immunization coverage [12,21–26]. A review of the grey literature reported costs per dose of mass immunization campaigns in Cameroon, Senegal, and Turkey ranging from $0.91 to $1.24 (in US$1985–1987, i.e., $1.99 - $2.72 in US$2016) and reported the cost per fully vaccinated child ranging from $18.93 to $27.38 (i.e., $41.45–$59.96 in US$2016) [21]. A systematic review identified 10 studies with immunization costs across low- and middle-income countries and found similar average costs per dose delivered for campaigns (range $1–20 in US$2001, i.e., $1.36–$27.10 in US$2016) and for routine services (range $0.5–16 in US$2001, $0.68–$21.68 in US$2016), and reported that the costs per fully vaccinated child ranged widely from $0.9 to $245 (in US$2001, i.e., $1.22–$332.02 in US$2016) [22]. One review reported increasing costs at higher levels of baseline coverage [26]. Other existing primary literature on the costs of attaining higher immunization coverage relied largely on global level modeling [27] or national data [28]. Although economies of scale may exist in interventions to increase immunization coverage [26,28], reaching the last remaining pockets of un- and under-vaccinated individuals may require special efforts and relatively higher costs per vaccine-recipient reached [22]. Translating effective interventions into sustained increased immunization coverage, with the associated health and economic benefits [2], requires political and financial commitment [29,30].

While the existing literature provides some limited insights, no prior studies characterized a cost function of the non-vaccine costs of interventions to increase immunization coverage (i.e., the incremental costs of increasing coverage). Estimates of the non-vaccine cost per dose of interventions could help decision makers understand the financial requirements for reaching immunization coverage goals. In the absence of prior studies, we reviewed and synthesized the available evidence and developed a cost function of the non-vaccine cost per dose of interventions as a function of baseline coverage for relatively low- and high-income countries for campaigns and routine immunization to provide context that may support expanded immunization efforts.

2. Methods

We searched PubMed on March 25, 2017 to find the titles and abstracts of papers published in English that included a combination of the following terms: "immuniz*" or "vaccine*" and "cost," "intervention," "campaign," "improv*," "increas*," "expand*," and "coverage." We screened the titles and abstracts to identify studies that describe specific interventions to improve immunization coverage for one or more vaccine preventable diseases that report both the costs and effectiveness of the interventions. We excluded studies that did not include interventions and studies that targeted animal immunizations. We reviewed the full text of articles for which we could not determine relevance based only on title and abstract. We contacted the authors of studies that reported intervention effectiveness only and requested estimates of the associated intervention costs. We excluded any studies lacking estimates of both costs and effectiveness. We also reviewed studies included in systematic reviews identified by the search, and relevant studies not captured in our PubMed search that we identified in the references of papers, but this did not lead to the inclusion of any additional studies.

All authors independently reviewed all of the literature assessed for eligibility and reached consensus on studies meeting inclusion criteria. The second author (TTY) conducted the initial extraction of the data from the included studies, while the first author (SO) and the last author (KMT) independently reproduced the extracted data. We resolved discrepancies in the interpretation of the extracted data through discussion. For each included study, we extracted information on the specific intervention, country setting, target population, vaccines targeted, intervention costs (excluding vaccine costs), and baseline and final immunization coverage. We categorized the interventions as either occurring in campaign settings (i.e., supplementary immunization activities or SIAs) or in routine immunization (RI) settings, the latter of which we further categorized as: introduction of routine immunization (Ir), education (Ed), reminders (Re), screening and referral (SR), or health system strengthening (Hs). We also categorized interventions as demand-side if they sought to increase the utilization of vaccines and/or adherence to immunization schedules, supply-side if they increased immunization supply or addressed health system barriers to immunization uptake, or both. We characterized countries as relatively low (RL) or relatively high (RH) income based on the World Bank Income Level at the time of the study for the countries in which the studies occurred (i.e., assigning low- and lower middle-income countries to RL, and high- and upper middle-income countries to RH) [31]. For studies that reported costs as an average cost per number of participants, we estimated the total intervention cost from the average cost and number of participants. We converted all intervention costs reported in a foreign currency to US$ using an online historical foreign currency exchange tool [32]. We converted all intervention costs to 2016 US dollars (US$2016 and henceforth simply $) using the consumer price index [33]. For studies with unclear information, including ambiguity about the potential inclusion of the costs for the vaccines in reported intervention costs, we contacted the study authors to request clarification or additional information.

For studies that reported final and baseline immunization coverage for an intervention, we calculated coverage change as the percent difference between the final and baseline values. For studies reporting only coverage differences between one or more intervention groups and a control group, we computed the percent difference between intervention coverage and the control coverage. For studies that reported coverage changes across multiple vaccines, we averaged the changes in coverage. For studies with an unvaccinated baseline population, we calculated coverage change as the final proportion of the population vaccinated after the intervention. Finally, for studies with more than one intervention and for which the authors reported intervention costs and coverage information separately, we reported the multiple interventions separately (see technical appendix).

We extracted the number of vaccine doses delivered in each intervention and the cost per dose reported in the studies when reported. For studies that did not report these, we estimated the number of doses and then estimated the cost per dose. We determined the number of doses according to the coverage outcome definition for each study and then used coverage change information to derive the number of doses delivered. For studies targeting multiple vaccines, we used the number of doses for all vaccines and the number of participants attaining full vaccination status (see technical appendix). We also extracted the baseline immunization coverage in the target population and area, above which the intervention sought improvement.

We used statistical models to examine the relationship between intervention cost per dose and changes in coverage as a function of baseline coverage, delivery (i.e., RI or SIA), and relative income level (RL or RH). We explored other factors, such as the inclusion of vaccine delivery activities or reported externalities. We examined outliers in the data to understand the study context and we excluded very poor and dominated interventions (i.e., studies with very high costs or very low or negative coverage improvements