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Assessing the cost-effectiveness of different measles vaccination strategies for children in the Democratic Republic of Congo

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A B S T R A C T

Introduction: One of the goals of the Global Measles and Rubella Strategic Plan is the reduction in global measles mortality, with high measles vaccination coverage as one of its core components. While measles mortality has been reduced more than 79%, the disease remains a major cause of childhood vaccine preventable disease burden globally. Measles immunization requires a two-dose schedule and only countries with strong, stable immunization programs can rely on routine services to deliver the second dose. In the Democratic Republic of Congo (DRC), weak health infrastructure and lack of provision of the second dose of measles vaccine necessitates the use of supplementary immunization activities (SIAs) to administer the second dose.

Methods: We modeled three vaccination strategies using an age-structured SIR (Susceptible-Infectious-Recovered) model to simulate natural measles dynamics along with the effect of immunization. We compared the cost-effectiveness of two different strategies for the second dose of Measles Containing Vaccine (MCV) to one dose of MCV through routine immunization services over a 15-year time period for a hypothetical birth cohort of 3 million children.

Results: Compared to strategy 1 (MCV1 only), strategy 2 (MCV2 by SIA) would prevent a total of 5,808,750 measles cases, 156,836 measles-related deaths and save U.S. $199 million. Compared to strategy 1, strategy 3 (MCV2 by RI) would prevent a total of 13,232,250 measles cases, 166,475 measles-related deaths and save U.S. $408 million.

Discussion: Vaccination recommendations should be tailored to each country, offering a framework where countries can adapt to local epidemiological and economical circumstances in the context of other health priorities. Our results reflect the synergistic effect of two doses of MCV and demonstrate that the most cost-effective approach to measles vaccination in DRC is to incorporate the second dose of MCV in the RI schedule provided that high enough coverage can be achieved.

1. Introduction

Measles is a highly infectious disease that can lead to severe illness, lifelong complications and death [1]. The disease remains one of the major causes of childhood vaccine preventable diseases globally, despite the fact that an effective and inexpensive vaccine exists. To meet measles mortality and morbidity reduction goals outlined in the Global Measles and Rubella Strategic Plan

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(2012–2020), WHO recommends high vaccination coverage with two doses of measles containing vaccines (MCV) [2]. Since 2000, vaccination has led to a 79% reduction in measles mortality [2]. 2015, there were still an estimated 132,200 measles-related deaths, the majority among children under the age of five [2]. More than 95% of these deaths occur in resource-limited countries with weakened public health infrastructures [2].

In Sub-Saharan Africa, measles remains a major public health problem, with an estimated 28,000 deaths still occurring yearly [3]. Measles deaths generally occur due to complications, with infants and malnourished children at highest risk of death [4]. Measles immunization requires a two-dose schedule due to vaccine efficacy and competing maternal antibodies at younger ages [2]. One dose of measles vaccine at 9 months of age confers only 85% protection and children require 2 doses for the vaccine to be >99% effective [2]. The first dose of MCV should be offered through Routine Immunization (RI) services and only countries with strong, stable immunization programs are able to rely on routine services to deliver the second vaccine dose. Countries unable to achieve high and homogenous vaccine coverage through their routine systems must deliver the second dose in the form of supplementary immunization activities (SIAs) [5]. In these countries, special efforts must be undertaken to ensure that children missed during routine services are immunized, especially in hard-to-reach, poor communities [5].

The Democratic Republic of Congo (DRC) is struggling to recover from a devastating multi-year conflict. Limited roads, electricity and water continue to leave a significant portion of the country inaccessible. Coupled with a lack of human resources, these challenges have led to limited improvements in health infrastructure and difficulty implementing routine immunization services effectively. In 2010, DRC saw a resurgence of measles with large scale outbreaks occurring throughout the country [6]. In 2013, national RI coverage was still estimated at 71.6%, well below the WHO recommended 95% [7,8], and in 2015, WHO/UNICEF estimates of MCV1 coverage was 77% [9], which is the value used in the model analyses.

The country's effort to reduce measles mortality currently consists of 3 strategies; (1) increase routine immunization coverage of MCV1, administered at 9 to 11 months of age, (2) implement SIAs to provide a second opportunity for MCV, and (3) expand epidemiologic surveillance [6,10]. In 2012, DRC's Expanded Program on Immunization (EPI) committed to measles elimination by 2020. This plan proposed a shift in the administration of MCV2 from SIAs to the RI schedule.

Whereas several studies have assessed the cost-effectiveness of measles elimination or eradication, few studies have addressed the cost-effectiveness of differing vaccination strategies. The diversity of both measles epidemiology and health system infrastructure across countries make analyses context specific. A comparison of the costs and benefits of providing the second doses of measles vaccine through RI services and SIAs can guide the selection of the most appropriate measles immunization strategy for DRC.

Vaccination recommendations should be tailored to each country, offering a framework where countries can adapt to local epidemiological and economical circumstances in the context of other health priorities [11]. In DRC, interpretable data on what strategies are needed to effectively and efficiently control measles is critical. We utilized cost specific data from a DRC health care perspective to analyze and compare the costs and benefits of two different strategies for administering two doses of measles-containing vaccine (MCV) to one dose of MCV through routine immunization.

2. Methods

We modeled three vaccination strategies using an age-structured SIR (Susceptible-Infectious-Recovered) model to simulate natural measles dynamics along with the effect of immunization. Strategy 1 (baseline): One dose of measles vaccine delivered through the routine immunization services at 9 months of age at the most recent reported coverage rate.

Strategy 2: One dose of measles vaccine delivered through routine immunization services at 9 months of age with multiple opportunities for immunization through national SIAs up to the age of five years (SIAs doses are independent of the dose received through the routine system).

Strategy 3: Two doses of measles vaccine delivered through routine immunization services at 9 months and 18 months of age.

The population was divided into five age cohorts: 0–9 months, 9–18 months, 18 months-5 years, 5–15 years, and 15+ years. Aging from one cohort to the next happens at a rate inversely proportional to the age width of the cohort, and the birth rate into the first cohort is based on the 2014 estimates for annual births [12]. In addition to the aging from one cohort to the next, individuals are removed from each cohort at a cohort-specific rate so that the overall age structure matches the 2015 UN Population Division estimates.

Upon the transition from the first to the second age cohort, individuals have a chance of being immunized with a first RI dose, with coverage and vaccine efficacy specified. Similarly, upon transition from the second to the third age cohort, children have a chance of being immunized with a second RI dose, with coverage specified by second-dose RI coverage and the vaccine efficacy corresponding to the efficacy in those over 12 months of age. Children in the second and third age cohorts are eligible for SIA vaccination doses, which have the older-child efficacy and are distributed at a specified rate. The SIA coverage rate is the probability of receiving an SIA dose over a 4-year interval.

The system is initialized and allowed to burn-in for 40 years with the scenario-specific immunization rates, so that the population distribution and disease dynamics reach equilibrium. During the burn-in, a steady additional force of infection is applied to avoid disease fade-out. Then the system is simulated for 15 years with dynamics that approximate 2015 dynamics. The number of infections and immunizations over these 15 years are then normalized to get an annual value. The annual incidence across the population as a function of first-dose RI coverage can be seen in Fig. 1.

The equations for propagating the system are as follows:

$$F_{inf}(t_j) = (R_0/\tau_{inf})(\Sigma I_i/(\Sigma(S_i + I_i + R_i)) + \beta_{intro}(t_j < T_{burn} * 365)$$

$$S_1(t_{j+1}) = S_1(t_j) + \Delta t(B/365 - F_{inf}(t_j)S_1(t_j) - a_1 S_1(t_j) - d_1 S_1(t_j))$$

$$I_1(t_{j+1}) = I_1(t_j) + \Delta t(F_{inf}(t_j)S_1(t_j) - I_1(t_j)/\tau_{inf} - a_1(I_1(t_j) - d_1 I_1(t_j))$$

$$R_1(t_{j+1}) = R_1(t_j) + \Delta t(I_1(t_j)/\tau_{inf} - a_1 R_1(t_j) - d_1 R_1(t_j))$$

$$\begin{aligned} S_2(t_{j+1}) = {} & S_2(t_j) + \Delta t((1 - c_{RI1}k_{eff1})a_1 S_1(t_j) - r_{SIA}k_{eff2}S_2(t_j) \\ & - F_{inf}(t_j)S_2(t_j) - a_2 S_2(t_j) - d_2 S_2(t_j)) \end{aligned}$$

$$\begin{aligned} I_2(t_{j+1}) = {} & I_2(t_j) + \Delta t(a_1 I_1(t_j) + F_{inf}(t_j)S_2(t_j) - I_2(t_j)/\tau_{inf} \\ & - a_2(I_2(t_j) - d_2 I_2(t_j)) \end{aligned}$$

$$\begin{aligned} R_2(t_{j+1}) = {} & R_2(t_j) + \Delta t(c_{RI1}k_{eff1}a_1 S_1(t_j) + a_1 R_1(t_j) + r_{SIA}k_{eff2}S_2(t_j) \\ & + I_2(t_j)/\tau_{inf} - a_2 R_2(t_j) - d_2 R_2(t_j)) \end{aligned}$$