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The effect of immunization on measles incidence in the Democratic Republic of Congo: Results from a model of surveillance data

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ABSTRACT

Background: Measles continues to be a leading cause of vaccine-preventable disease mortality among children under five despite a safe and efficacious vaccine being readily available. While global vaccination coverage has improved tremendously, measles outbreaks persist throughout sub-Saharan Africa. Since 2010, the Democratic Republic of Congo (DRC) has seen a resurgence of measles outbreaks affecting all 11 provinces. These outbreaks are mainly attributed to gaps in routine immunization (RI) coverage compounded with missed supplementary immunization activities (SIAs). We utilized national passive surveillance data from DRC's Integrated Disease Surveillance and Response (IDSR) system to estimate the effect of immunization on measles incidence in DRC.
Methods: We investigated the decline in measles incidence post-immunization with one dose of measles containing vaccine (MCV1) with and without the addition of supplementary immunization activities (SIAs) and outbreak response immunization (ORI) campaigns. Measles case counts by health zone were obtained from the IDSR system between January 1, 2010 and December 31, 2013. The impact of measles immunization was modeled using a random effects multi-level model for count data with RI coverage levels and mass campaign activities from one year prior.
Results: The presence of an SIA (aIRR [95% CI] 0.86 [0.60–1.25]) and ORI (0.28 [0.20–0.39]) in the year prior were both associated with a decrease in measles incidence. When interaction terms were included, our results suggested that the high levels of MCV1 reported in the year prior and the presence of either mass campaign was associated with a decrease in measles incidence.
Conclusions: Our results highlight the importance of a two-dose measles vaccine schedule and the need for a strong routine immunization program coupled with frequent SIAs. Repeated occurrences of large-scale outbreaks in DRC suggest that vaccination coverage rates are grossly overestimated and signify the importance of the evaluation and modification of measles prevention and control strategies.

1. Introduction

Measles is a highly contagious viral respiratory infection that can lead to deadly complications. It continues to be among the largest causes of vaccine-preventable disease mortality among children under five, despite the availability of a safe and efficacious vaccine [1]. While measles vaccine induces immunity that is effectively life-long, vaccine efficacy is expected to be 85% at 9–11 months of age and increases to 95% at ≥12 months [2–4]. Prior to vaccine licensure, measles caused an estimated two million deaths and more than

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15,000 cases of blindness worldwide each year [5]. While global immunization has improved tremendously, an estimated 158,000 people died from measles-associated complications in 2011 [5]. More than 95% of measles-related deaths occur in resource-limited countries, where health infrastructure is weak and vaccine coverage is low [5].

Between 2001 and 2008, measles mortality in the World Health Organization African Region (WHO-AFRO) was reduced by >90% due to improvements in routine immunization (RI) and implementation of Supplementary immunization activities (SIAs) [6]. While measles RI coverage increased from 54% in 2000 to 73% in 2010, the African region saw a resurgence of measles in 2010, with 28 countries reporting outbreaks and case-fatality rates as high as 5–10% [6–9]. Overall incidence in the region increased from 40 cases per million in 2009 to 165 cases per million in 2010 [10]. Regional investigations indicated that the main cause was the accumulation of susceptibles due to gaps in providing children with two doses of measles-containing vaccine (MCV) [11,12].

In the Democratic Republic of Congo (DRC), reported MCV1 coverage increased from 46% in 2000 to 72% in 2012, but still remained below the recommended 95% necessary for measles elimination [10,13]. DRC's Expanded Programme on Immunization (EPI) strategic plan includes one dose of MCV1 at 9–11 months of age, followed by the second dose administered through rolling "follow-up" campaigns targeting children 6–59 months every three years, providing a second opportunity for first vaccination or a second dose for children unable to access routine immunization services[14–16]. SIAs were carried out in 2002–2004 and again in 2006–2007; suspected measles cases counts reached a historic low in 2009 [17].

Beginning July 2010, reported measles cases increased in DRC [15,16]. South Kivu and Katanga reported elevated cumulative measles attack rates and 14 health zones had confirmed outbreaks (defined as ≥3 laboratory-confirmed cases occurring in a health zone in one month [12,18]). Katanga, Kasai Oriental, South Kivu, and Maniema provinces were the most heavily affected, reporting the highest cumulative attack rates [7,12,14,16]. In 2011, measles outbreaks were confirmed in all 11 provinces in more than 108 health zones [12]. High numbers of measles cases continued to be reported in 2012, with the highest reported cumulative attack rates from Orientale and Equateur provinces [12]. Gaps in measles RI coverage, particularly in children > 5 years, compounded with postponed SIAs, largely due to limited finances and delays in resource mobilization, likely led to the accumulation of susceptibles and outbreaks throughout the country.

While measles cases reported through surveillance systems typically represent only a small fraction of the true number of cases, surveillance data can be used to assess measles incidence trends over time [19]. Therefore, we utilized national passive surveillance data from DRC's Ministry of Health (MOH) Integrated Disease Surveillance and Response (IDSR) system to estimate the effect of measles immunization on measles incidence in DRC between 2010 and 2013.

2. Data and methods

2.1. Suspected measles case counts

Measles is one of 13 reportable diseases in DRC's passive surveillance system[15]. Suspected measles cases are identified at the health facility level and reported to the corresponding health zone. In DRC, there are 516 health zones. Data are then forwarded to the antennes,[2] provinces, and eventually complied at the national level in the IDSR surveillance system [16,20]. The standard WHO case definition is used, with a suspected measles case defined as any person with fever and maculopapular rash, in addition to cough or coryza or conjunctivitis; or a person in whom a clinician suspects measles [18].

Suspected measles case counts, by health zone, for children 12–59 months were obtained from the IDSR system during the period January 1, 2010 to December 31, 2013. Human Subjects Protection boards at both the Kinshasa School of Public Health and UCLA approved the study protocol.

2.2. Vaccine coverage

We used health zone-level administrative measles RI coverage estimated by the DRC-EPI from 2009 to 2013. These rates were calculated by dividing the reported number of measles vaccine doses administered to the target age group (<12 months) by the estimated target population [12,13]. Fourteen (0.6%) health zones had missing RI coverage, therefore we imputed the WHO/UNICEF 2012 estimated national MCV1 coverage of 73%. All SIA data, including catch-up or follow-up campaigns were also collected and complied by EPI. Additionally, Medecins San Frontieres (MSF) regularly conducts outbreak response immunization (ORI) campaigns to reduce transmission from outbreak zones to neighboring areas [15,16]. Data on ORI activities were obtained directly through EPI, MSF, and a literature review.

2.3. Data compilation

Each individual observation represented an aggregate of the total suspected case counts in children aged 12–59 months in a given year in a given health zone; the final dataset included 2047 observations. An indicator variable was used to represent the presence of a SIA in a given health zone in that year. A second indicator variable was used to represent the presence of an ORI in a given health zone in that year. Routine MCV1 coverage was grouped into four categories (0–79%, 80–89%, and 90–100%, 100%+). The lowest coverage category was based on the standard WHO recommendation of 80% coverage in every health zone [10].

2.4. Statistical methods

All statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, NC); maps were created using arcGIS Desktop (ESRI 2011). Measles case counts and estimated incidence rates were calculated. Corresponding 95% confidence intervals (CI) were estimated by province yearly using generalized linear models [21]. Estimated incidence rates were defined as the total number of suspected measles cases among children 12–59 months per year per province divided by the total population of children 12–59 months per year per province.

To assess the relationship between measles incidence and vaccine coverage, we modeled incidence using a random effects multi-level model for count data, with a negative binomial distribution to account for overdispersion [22]. To account for measles case clustering, we included a random intercept at both the antenne and provincial levels. Our outcome was total suspected cases in a given year in a given health zone, with the health zone's population of children aged 12–59 months as an exposure offset variable. Routine immunization is a continuous event that occurs throughout the entire year, and we predicted that effects might not be seen immediately. Thus, we modeled measles incidence using vaccine coverage, the presence of an SIA, and the presence of an ORI data from the year prior. Incidence rate ratios (IRRs) and corresponding 95% confidence intervals were estimated using a model fit to four predictor variables: year, vaccine coverage (lagged one year),

[2] Antenne is a level situated between the health zone (district) and provincial levels.

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