Antecedent causes of a measles resurgence in the Democratic Republic of the Congo

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Abstract

Introduction: Despite accelerated measles control efforts, a massive measles resurgence occurred in the Democratic Republic of the Congo (DRC) starting in mid-2010, prompting an investigation into likely causes. Methods: We conducted a descriptive epidemiological analysis using measles immunization and surveillance data to understand the causes of the measles resurgence and to develop recommendations for elimination efforts in DRC. Results: During 2004-2012, performance indicator targets for case-based surveillance and routine measles vaccination were not met. Estimated coverage with the routine first dose of measles-containing vaccine (MCV1) increased from 57% to 73%. Phased supplementary immunization activities (SIAs) were conducted starting in 2002, in some cases with sub-optimal coverage (≤95%). In 2010, SIAs in five of 11 provinces were not implemented as planned, resulting in a prolonged interval between SIAs, and a missed birth cohort in one province. During July 1, 2010-December 30, 2012, high measles attack rates (>100 cases per 100,000 population) occurred in provinces that had estimated MCV1 coverage lower than the national estimate and did not implement planned 2010 SIAs. The majority of confirmed case-patients were aged <10 years (87%) and unvaccinated or with unknown vaccination status (75%). Surveillance detected two genotype B3 and one genotype B2 measles virus strains that were previously identified in the region. Conclusion: The resurgence was likely caused by an accumulation of unvaccinated, measles-susceptible children due to low MCV1 coverage and suboptimal SIA implementation. To achieve the regional goal of measles elimination by 2020, efforts are needed in DRC to improve case-based surveillance and increase two-dose measles vaccination coverage through routine services and SIAs.

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Introduction

Measles is a highly-infectious and potentially fatal viral disease characterized by fever and rash. In 2012, measles caused an estimated 122,000 vaccine-preventable deaths worldwide [1]. Estimated measles vaccine effectiveness (VE) is 84% when administered at 9-11 months of age, and 93% when given at ≥12 months of age [2]. Because >93%-95% population immunity is necessary to prevent measles epidemics, the World Health Organization (WHO) recommends all children receive two doses of measles vaccine [2, 3]. In 2008, countries in the WHO African Region (AFR) adopted a measles-pre-elimination goal to be achieved by the end of 2012 with the following targets: 1) >98% reduction in estimated regional measles mortality compared with 2000; 2) national measles incidence of <5 cases per 1,000,000 population per year; 3) >90% national coverage with the first dose of measles-containing vaccine (MCV1) and >80% MCV1 coverage in all districts; and 4) >95% coverage in all districts for MCV supplementary immunization activities (SIAs). Also included were surveillance performance targets of: 1) ≥2 cases of non-measles febrile rash illness per 100,000 population; 2) ≥1 suspected measles case investigated with blood specimens in ≥80% of districts [4].

In the Democratic Republic of the Congo (DRC), MCV1 given at 9 months of age was introduced into the Expanded Programme on Immunization in 1977 [5]. The Reaching Every District (RED) approach to strengthening RI services was implemented beginning in 2003 [6]. To provide a second opportunity for measles vaccination, nationwide measles SIAs started in 2002, using a phased approach intended to cover the country every 3 years [7]. Integrated Disease Surveillance and Response (IDS) was established in 2000 with aggregate reporting of 18 infectious diseases, including measles. Case-based surveillance with laboratory confirmation of suspected measles cases was established in 2003.

In 2011, AFR countries adopted a goal for measles elimination by 2020 [8]. However, starting in 2010 and continuing through 2014, DRC experienced the largest nationwide measles outbreak in AFR since the start of accelerated measles control efforts [9-12]. DRC is a key country for regional elimination efforts because of its large population, central location with nine international borders, and persistent reservoir of circulating measles viruses [9, 13]. We conducted a descriptive epidemiological analysis using immunization and surveillance data to understand the likely causes of the measles resurgence and develop recommendations for elimination efforts.

Methods

Study setting

In 2012, DRC had an estimated population of 78.1 million persons, 3.1 million live births, and 14.7 million children aged <5 years [14]. The DRC health system has 513 zones de santé (health districts) in 11 provinces. Challenges for vaccination include a large target population, poorly accessible areas, complex logistics, a lack of government funding, weak health systems, civil unrest, and displaced persons [15-17]. The number of displaced persons peaked in 2013, with 2.9 million internally displaced persons (IDPs) in the eastern and northern provinces of DRC and 438,869 Congolese in other African countries [18-21]. The last population census was conducted in 1981 making estimation of the vaccination target population challenging.

Measles immunization, 2002-2012

To assess measles vaccination coverage in comparison with AFR indicator targets, we calculated MCV1 administrative coverage for 2004-2012 at the national, provincial, and district levels by dividing the reported number of MCV1 doses administered by the number of targeted children aged <12 months, according to the DRC Ministry of Public Health (MOPH), multiplied by 100 (national target: >90%; district target: >80%). The number of districts reporting >80% MCV1 coverage was divided by the number of districts expected to report and multiplied by 100 (target: 100%) [22]. We reviewed WHO-United Nations Children's Fund (UNICEF) annual estimates of national MCV1 coverage among children aged <12 months, and population-based survey estimates of national and provincial MCV1 coverage among children aged 12-23 months during 2004-2012 [23-27]. We reviewed implementation dates, administrative coverage, and survey results from SIAs and outbreak response immunization (ORI) during 2002-2012; the AFR target of >95% SIA coverage in all districts could not be assessed due to unavailable data [22].

Measles surveillance, 2004-2012

Through IDS, aggregate numbers of suspected measles cases and deaths were reported weekly from districts to the national level [28]. Through measles case-based surveillance, suspected measles cases were investigated using a case investigation form and laboratory testing of a blood specimen at the National Institute for Biomedical Research in Kinshasa [29]. Specimens were tested using standard enzyme-linked immunosorbent assays for measles-specific immunoglobulin M (IgM) antibodies; specimens with a negative or indeterminate result were tested for rubella-specific IgM (Enzygnost ELISA™, Siemens Healthcare Diagnostics Products, Marburg, Germany). A suspected measles case was defined as an illness with maculopapular rash and fever and one or more symptoms of cough, coryza, or conjunctivitis, or where a clinician suspects measles. A laboratory-confirmed measles case was defined as a suspected measles case with a positive laboratory test result for measles-specific IgM in the absence of measles vaccination within 30 days of specimen collection. An epidemiologically-linked case was defined as a suspected measles case having contact (or living in the same district) with a laboratory-confirmed measles case whose rash onset was within the preceding 30 days. A clinically-compatible case was defined as a suspected measles case without a laboratory test result or established epidemiological link. We classified all laboratory-confirmed, epidemiologically-linked, and clinically-compatible measles cases as confirmed measles cases.

We analyzed de-duplicated IDS and measles case-based surveillance data from 2004-2012. To assess case-based surveillance performance in comparison with AFR targets, we calculated two indicators as follows: 1) the number of districts annually reporting ≥1 suspected measles case with a collected blood specimen divided by the number of districts expected to report (target: ≥60%); and 2) the number of suspected measles cases reported annually and "discarded" as non-measles because of a negative test result divided by the estimated population from DRC MOPH, multiplied by 100,000 (target: ≥2.0). Estimated annual measles incidence was calculated by dividing the number of suspected cases reported through IDS by the estimated annual population from DRC MOPH, multiplied by 1,000,000 (target: <5) [22].
Epidemiological description of the measles resurgence

We conducted an epidemiological analysis of the resurgence period, defined as starting in the first month with a confirmed measles outbreak in 2010 and continuing through the end of 2012, using IDSR and case-based surveillance data from July 1, 2010-December 31, 2012. A confirmed measles outbreak was defined as ≥3 laboratory-confirmed cases occurring in a district in one month. We analyzed suspected measles cases and deaths reported through IDSR by date of rash onset, province, and district. Confirmed measles cases reported through case-based surveillance were analyzed by date of rash onset, age, vaccination status, province, and district. Cumulative measles attack rates were calculated by dividing the number of suspected cases reported through IDSR during the resurgence period, or a 6-month subset of the resurgence period, by the estimated 2012 population from DRC MOPH and multiplying by 100,000. Cumulative measles attack rates and confirmed measles outbreaks by district for 6-month periods were mapped. Analyses were conducted using Excel (Microsoft Corporation), SAS version 9.3 (SAS Institute), and ArcGIS (ESRI).

To identify circulating measles virus strains, nasopharyngeal swabs were collected and tested at the National Institute for Communicable Diseases in South Africa. Ribonucleic acid (RNA) was extracted using the QIAamp® viral RNA mini kit (QIAGEN®) and amplified by reverse-transcriptase polymerase chain reaction. Amplicons were sequenced and analyzed using Sequencher software (Gene Codes Corporation 4.1.4, Ann Arbor, MI). Phylogenetic analysis of the viral nucleoprotein (N) gene relative to WHO measles reference strains was performed using the maximum likelihood algorithm of MEGA version 5.1 software with bootstrap test of phylogeny [30].

Results

Measles immunization, 2002-2012

National MCV1 administrative coverage among children aged <12 months increased from 64% to 89%, and WHO-UNICEF estimates of MCV1 coverage increased from 57% to 73% during 2004-2012. National MCV1 coverage among children aged 12-23 months estimated from surveys was 63% in 2007, 67% in 2010, and 75% in 2012. MCV1 coverage survey estimates were lower than reported administrative coverage for comparable years. In all years, MCV1 administrative coverage varied substantially by province and was below the target of >90% at the national level and >80% in all districts (Table 1).

A phased catch-up SIA targeting children aged 6 months-14 years was implemented during 2002-2006 (median reported administrative coverage: 96%; range: 73%-102%), and a phased follow-up SIA targeting children aged 6-59 months was completed during 2006-2010 (median reported administrative coverage: 99%; range: 92%-113%). A 4-year gap between these SIAs occurred in three provinces (Nord Kivu, Kasai Oriental, and Bandundu). In 2009, another phased follow-up SIA was initiated in Nord Kivu (reported administrative coverage: 112%); however, the phase planned for 2010 was not implemented, leading to a 4-5 year gap between SIAs in five provinces (Kasai Oriental, Kasai Occidental, Katanga, Maniema, and Sud Kivu) and a missed cohort of children born in 2006 in Kasai Oriental (Figure 1 and Table 2). After the start of the 2010 outbreaks, the entire country was covered by a combination of subnational measles follow-up SIAs and ORIs targeting children aged 6-59 months or 6 months-14 years during 2011-2012 (median reported administrative coverage: 101%; range: 93%-112%) (Figure 1 and Table 3).

During 2002-2012, ≤95% administrative coverage was reported from ≥1 measles SIA in eight of 11 provinces (Figure 1). Availability of SIA coverage estimates from surveys during this period was limited. Coverage survey estimates for SIAs implemented in 2006, 2007 and 2011 were >95% in Kinshasa, Bandundu, Nord Kivu, and Maniema, and 94% in Kasai Occidental, Katanga, and Maniema (Table 2, Table 3). Coverage survey estimates for ORIs implemented during 2010-2012 were >95% in Equateur, 92%-95% in Kasai Occidental and two ORIs in Maniema, and 68% in Katanga (Table 3). In general, SIA and ORI coverage survey estimates were lower than reported administrative coverage (Table 2, Table 3).

Measles surveillance, 2004-2012

Measles case-based surveillance did not meet both annual performance indicator targets during 2004-2012. The number of suspected measles cases reported through case-based surveillance (16,789) was 3.6% of the total reported to IDSR (459,326); the number of suspected measles deaths reported through case-based surveillance (52) was 0.6% of the total reported to IDSR (8,400). Suspected measles incidence reported through IDSR did not meet the target of <5 per 1,000,000 population during 2004-2012. During 2006-2009, incidence decreased 96%, from 1,164 to 47 per 1,000,000. During 2010-2011, incidence increased from 73 to 1,769 per 1,000,000, and was 935 per 1,000,000 in 2012 (Table 4).

Epidemiological description of the measles resurgence

During July 1, 2010-December 31, 2012, 211,236 suspected measles cases were reported through IDSR and 8,142 were reported through case-based surveillance. Of those reported through case-based surveillance, 4,252 (52%) were confirmed as measles (2,465 by laboratory testing and 1,787 by epidemiological link) and 866 (11%) were laboratory-confirmed as rubella (Figure 2 and Table 3). Of the 4,250 confirmed measles cases with age information, 2,839 (67%) were among children aged <5 years, and 879 (21%) were among children aged 5-9 years; 1,036 (24%) were among unvaccinated persons, and 2,168 (51%) were among persons with missing or unknown vaccination status (Table 5).

The first confirmed measles outbreaks of 2010 were reported in three geographic foci: 1) Lemera district bordering Burundi in Sud Kivu province in July 2010; 2) Sakania district bordering Zambia in Katanga province in August 2010; and 3) Dikolo district bordering Angola in Katanga province in September 2010. During July-December 2010, Sud Kivu and Katanga reported elevated cumulative measles attack rates and had 14 districts with confirmed outbreaks. In 2011, the epidemic peaked with confirmed measles outbreaks reported from 108 districts in all 11 provinces and the highest cumulative attack rates reported in Sud Kivu, Katanga, Maniema, and Kasai Oriental provinces. In 2012, a second epidemic peak occurred with confirmed outbreaks reported from 126 districts in all 11 provinces and the highest cumulative attack rates reported from Province Orientale and Equateur (Figure 2, Figure 3 and Figure 4). Measles virus genotype results were available from 47 confirmed measles cases in 13 (6%) of 218 districts that had a confirmed outbreak and 8 (73%) of 11 provinces. Three genetic groups of measles virus strains were detected each, associated with one of the three initial outbreak foci and thereafter clustered geographically. Of 47 measles viruses, 13 (28%) were from a group of B3.1 genotypic strains (B3-RwaAng) related to measles virus.
previously detected in Rwanda and Angola; these strains were first detected in a Sud Kivu district bordering Burundi and localized to northeastern DRC during the outbreak. Another 20 (43%) were from a group of B3 genotypic strains (B3-ZamZimSA) related or identical to measles viruses detected during 2009-2011 in Zambia, Zimbabwe and South Africa [31, 32]; these strains were first detected in a Katanga district bordering Zambia and localized to southern and central DRC. Finally, 13 (28%) were from a group of B2 genotypic strains (B2-AngNamDRC) related to those previously detected in Angola, Namibia, and DRC [13]; these strains were first detected in a Katanga district bordering Angola and localized to southern DRC (Figure 3 B, and Figure 4). One district in Bas-Congo province reported both B3-ZamZimSA and B2-AngNamDRC strains in the third-quarter of 2011 (Figure 3 B).

During the resurgence period, the national cumulative attack rate based on IDSR reporting was 272 cases per 100,000 population. The provinces with high cumulative attack rates (>100 cases per 100,000 population) were Katanga, Maniema, Kasai Oriental, Province Orientale, Equateur, and Sud Kivu. Among these six provinces, estimated MCV1 coverage in the 2010 survey ranged from 46% to 66% (median: 54%), and four provinces had planned SIAs in 2010 that were not implemented. By contrast, estimated MCV1 coverage in the 2010 survey among the five provinces without high cumulative attack rates ranged from 49% to 91% (median 80%), and one province had a planned SIA in 2010 that was not implemented (Table 1 and Figure 1).

Discussion

Following accelerated measles control efforts and dramatic decrease in measles incidence, a massive measles resurgence occurred in DRC. The results of this study suggest the resurgence was likely caused by an accumulation of measles-susceptible children not vaccinated due to low RI coverage and suboptimal SIA implementation. Furthermore, detailed epidemiological analyses necessary for guiding timely outbreak response were limited by under-performing case-based surveillance. Despite implementation of the RED strategy and increasing MCV1 coverage in DRC during 2004-2012, coverage remained far below WHO-recommended targets for monitoring progress toward measles elimination [9, 33]. Results from coverage surveys indicated challenges with the reliability of administrative coverage and highlighted the need to conduct surveys to monitor coverage. In countries where only a single routine dose of measles vaccine is provided, achieving high coverage through both RI and SIAs is necessary to reduce measles incidence [22].

After implementation of the initial measles catch-up SIA during 2002-2006, measles incidence in DRC decreased dramatically. However, the catch-up SIA and follow-up SIAs were implemented in a phased manner to accommodate logistical challenges and resource limitations. This phased approach to implementation left a gap of 4-5 years between SIAs in some provinces, as well as a missed birth cohort in one province, which likely allowed for missed birth cohort in one province, which likely allowed for sustained measles virus transmission, similar to what has recently occurred in other large AFR countries [9, 34-36].

In DRC, widespread measles outbreaks continued during 2013-2014 among children who were targeted by SIAs and ORIs during 2011-2012. During 2013, 88,382 suspected and 1,321 confirmed cases were reported nationally, mostly from Province Orientale, Equateur and Kasai Occidental; during 2014, 35,835 suspected and 1,643 confirmed cases were reported nationally (DRC MOPH and WHO-DRC unpublished data). Although administrative coverage from the 2011-2012 campaigns was generally high (>92%), suboptimal coverage was estimated by surveys conducted after the 2012 ORI in Katanga (68%), and in districts with outbreaks after the 2011 SIAs in Equateur and Province Orientale (<50%) [11, 17]. Additionally, some SIAs and ORIs were delayed because of the amount of time it took to secure and disburse funds, and to complete the extensive planning and logistics needed to reach poorly-accessible areas.

Although measles case-based surveillance with laboratory testing has been functional in DRC since 2003, performance indicators were unmet during 2004-2012, and challenges occurred with missing data (e.g. vaccination status). Surveillance guidelines specify that all suspected measles cases should be reported through measles case-based surveillance; however, the number of suspected measles cases reported through case-based surveillance was <4% of IDSR-reported cases [28]. This disparity was partly caused by the underutilization of measles case-based guidelines for the use of “line-lists” and the “epidemiologically-linked” case classification during confirmed outbreaks. These guidelines ensure that key epidemiological data, including age, vaccination status, and date of rash onset are collected for all cases, without requiring blood specimen collection and testing of all outbreak cases that might overburden the laboratory [29]. Case-based measles surveillance is a cornerstone of the measles elimination strategy; rapid case detection and laboratory confirmation is essential for rapid response, including effectively defining the target geographical area and age-group for SIAs and ORIs [37].

During 2009-2010, the African region experienced a measles resurgence with 28 of 46 AFR countries reporting laboratory-confirmed measles outbreaks, including large outbreaks in Burkina Faso, DRC, Ethiopia, Malawi, Nigeria, South Africa, Zambia, and Zimbabwe [9, 31, 32, 38, 39]. The regional resurgence was generally characterized by outbreaks with cases occurring among older children and young adults as a result of long-standing gaps in vaccination, combined with reduced risk of measles virus exposure due to decreased incidence since 2000 [9]. By contrast, 87% of measles cases during the resurgence in DRC occurred among children <10 years old, indicating persistent low population immunity among young children and on-going measles virus transmission. Virologic surveillance detected concurrent transmission of three separate measles virus strains in DRC; these strains were previously identified in neighboring countries, including a B3 strain detected in outbreaks throughout southern Africa during 2009-2011 [32].

During July 1, 2010-December 30, 2012, high measles attack rates occurred in provinces (Katanga, Maniema, Kasai Oriental, Province Orientale, Equateur, and Sud Kivu) that had estimated MCV1 coverage in the 2010 survey lower than the national estimate (67%) and did not implement planned 2010 SIAs. Kasai Occidental province had a relatively low attack rate (68 cases per 100,000 population) during 2010-2012 despite having 49% estimated MCV1 coverage in the 2010 survey and not implementing a planned 2010 SIA. The lower reported attack rate in Kasai Occidental might have reflected underreporting from poor surveillance quality or a relative delay in the progression of the outbreak due to the northwest geographic spread of the outbreak over time from the initial foci in the south and east; in 2013, the measles attack rate in Kasai Occidental increased to >100 cases per 100,000 population (DRC MOPH and WHO-DRC unpublished data). An additional factor that may have impacted relative attack rates among provinces during the measles outbreak was the increase in number of IDPs and refugees, as well as affected areas, during 2010-2013 [18-21]. There was some overlap between the provinces with high measles attack rates and those with large numbers of displaced persons; however, a
The study analyses had limitations. First, reported administrative coverage was likely overestimated due to unreliable denominators, as indicated by coverage >100% and lower coverage estimates by survey. Second, analysis of campaign quality was limited in part by the small number of coverage surveys conducted and lack of detailed post-campaign reports available. Not all available coverage surveys were performed using probability-based sampling methods, so representativeness of the estimates could not be determined. Third, under-reporting through case-based surveillance and the number of districts that were silent for IDS reporting suggest measles incidence was likely underestimated. Fourth, because suspected measles cases reported through IDS were not confirmed, some illnesses attributable to other causes of febrile rash, including rubella, were likely misclassified in IDS as suspected measles.

Conclusion

To achieve measles elimination in DRC, we recommended specific efforts to improve case-based surveillance and increase two-dose measles vaccination coverage. Realistic plans need to be developed to fully implement case-based surveillance, including adequate costing and resource mobilization for blood collection supplies, testing, and specimen transport. Periodic refresher trainings should be provided to ensure the implementation of measles case-based surveillance according to WHO guidelines [22, 29]. Additionally, WHO-recommended measles case-based surveillance performance indicators should be calculated monthly in a surveillance bulletin provided to all districts and used as a tool for supervision, management, and surveillance strengthening [29]. Measures to strengthen RI services are needed, including increased supportive supervision, human resources, and training, as well as improved micro-planning, vaccine management, and logistics. Because of suboptimal MCV1 coverage, periodic high-quality, nationwide SIAs should be implemented, ideally without phases and covering the entire country during a 4-7 day period; however, if a limitation in resources necessitates a phased approach, then the number of phases and the time needed to cover the entire country should be minimized [40]. SIA frequency and target age groups should be based on epidemiological analyses, and adequate resources made available to ensure optimal implementation [41]. According to WHO guidelines, SIA planning should start at least 6-8 months in advance, with close supervision and monitoring during implementation, and a post-campaign coverage survey [40]. To ensure timely outbreak response, a national measles outbreak preparedness plan is needed [37].

During September 2013-August 2014, with funding and support from Gavi the Vaccine Alliance, WHO, UNICEF, and the Measles & Rubella Initiative, the DRC MOPH conducted a phased nationwide measles SIAs targeting children aged 6 months-9 years, incorporating SIA best practices identified during a workshop in Kinshasa in April 2013, and post-campaign coverage surveys were completed in four provinces. The country will need to conduct the next follow-up SIA in 2016 and should begin the planning process in early 2015. To achieve measles elimination in AFR by 2020, additional commitments and resources will be needed to implement strategies for increasing two-dose vaccination coverage and improving surveillance in DRC.

Competing interests

The authors declare no competing interests

Authors’ contributions

HMS, KK, MA, BGM and JLG designed the study. BIK, AM, CS, JM1T, ES, and SBS participated in data collection. HMS, TC, RO, SBS, KK, MA, BGM, RTP, and JLG participated in data analysis and interpretation. HMS, SBS, KK, MA, RTP, and JLG wrote the report. All authors reviewed and approved the final report.

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Tables and figures

Table 1: coverage with the routine first dose of measles-containing vaccine by administrative reporting, survey, and WHO-UNICEF estimate during 2004-2012 and cumulative measles attack rates during July 1, 2010-December 31, 2012, Democratic Republic of the Congo

Table 2: coverage from measles supplementary immunization activities (SIA) by administrative reporting and post-campaign surveys, Democratic Republic of the Congo, 2002-2010

Table 3: coverage from measles supplementary immunization activities (SIA) during 2011-2012 and outbreak response immunization (ORI) during 2010-2012 by administrative reporting and post-campaign surveys, Democratic Republic of the Congo

Table 4: measles surveillance data reported through Integrated Disease Surveillance and Response and measles case-based surveillance, Democratic Republic of the Congo, 2004-2012

Table 5: confirmed measles cases+ reported through measles case-based surveillance by age group and measles vaccination status, Democratic Republic of the Congo, July 1, 2010-December 31, 2012

Figure 1: administrative measles vaccination coverage from supplementary immunization activities (SIA) and outbreak response immunization (ORI) by province and year during 2002-2012, and cumulative measles attack rates reported through Integrated Disease Surveillance and Response during July 1, 2010-December 31, 2012, Democratic Republic of the Congo

Figure 2: suspected measles cases reported through Integrated Disease Surveillance and Response and confirmed measles cases reported through case-based surveillance by week, Democratic Republic of the Congo, July 1, 2010-December 31, 2012 (+53 cases confirmed by epidemiologic-link and reported through outbreak line-lists were missing date of rash onset)

Figure 3: district maps of (A) cumulative measles attack rates reported through Integrated Disease Surveillance and Response and
(B) confirmed measles outbreaks and measles virus strains reported through case-based surveillance for 6-month periods, Democratic Republic of the Congo, July 1, 2010-December 31, 2012 (provinces: 1. Province Orientale, 2. Nord Kivu, 3. Sud Kivu, 4. Maniema, 5. Katanga, 6. Kasai Oriental, 7. Kasai Occidental, 8. Bandundu, 9. Bas-Congo, 10. Kinshasa, and 11. Equateur; districts with first confirmed outbreaks: a. Lemera, b. Sakania, and c. Dilolo; each dot represents 1-8 viruses with the same genotype in a district within a month)

**Figure 4**: phylogenetic analysis of the viral nucleoprotein gene of measles virus strains detected in the Democratic Republic of the Congo, July 1, 2010-February 28, 2012 (scale bar distance of 0.005=2 nucleotides substitutions in the 450 nucleotide sequenced region; sequence names contain information on the sequence source, district, country, epidemiologic week, year, and sequential case number; Genbank accession numbers indicated in brackets; abbreviations: MVi, measles virus sequenced from isolates; MVs, measles virus sequenced from clinical specimens; COD, Democratic Republic of the Congo; GAB, Gabon; NGA, Nigeria; CAE, Cameroon)

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### Table 1: coverage with the routine first dose of measles-containing vaccine by administrative reporting, survey, and WHO-UNICEF estimate during 2004–2012 and cumulative measles attack rates during July 1, 2010–December 31, 2012, Democratic Republic of the Congo

| Province             | MCV1 administrative coverage (%) | MCV1 coverage (%) by survey | Cumulative attack rate |
|----------------------|----------------------------------|-----------------------------|------------------------|
|                      | 2004  | 2005  | 2006  | 2007  | 2008  | 2009  | 2010  | 2011  | 2012  | DHS 2007 | MIC S 2010 | EPI 2012 |
| Katanga              | 66    | 76    | 79    | 74    | 83    | 88    | 91    | 89    | 91    | 52    | 66    | 72    | 774    |
| Maniema              | 48    | 81    | 69    | 85    | 82    | 87    | 92    | 96    | 97    | 45    | 46    | 67    | 543    |
| Kasai Oriental       | 63    | 65    | 68    | 75    | 73    | 85    | 86    | 88    | 89    | 59    | 52    | 62    | 504    |
| Province Orientale   | 45    | 50    | 53    | 70    | 71    | 73    | 78    | 70    | 75    | 50    | 60    | 62    | 366    |
| Equateur             | 51    | 56    | 74    | 83    | 74    | 86    | 80    | 83    | 84    | 42    | 51    | 74    | 112    |
| Sud Kivu             | 50    | 63    | 76    | 104   | 84    | 87    | 94    | 93    | 96    | 84    | 57    | 86    | 107    |
| Bandundu             | 75    | 73    | 77    | 89    | 71    | 88    | 90    | 88    | 91    | 79    | 91    | 88    | 95     |
| Kasai Occidental     | 65    | 73    | 73    | 71    | 82    | 94    | 93    | 80    | 104   | 45    | 49    | 54    | 68     |
| Bas-Congo            | 79    | 84    | 82    | 88    | 83    | 91    | 89    | 78    | 85    | 88    | 77    | 78    | 46     |
| Kinshasa             | 78    | 80    | 77    | 76    | 77    | 86    | 85    | 79    | 82    | 91    | 86    | 88    | 25     |
| Nord Kivu            | 86    | 95    | 81    | 80    | 78    | 91    | 93    | 98    | 94    | 86    | 80    | 88    | 13     |
| National             | 64    | 70    | 73    | 79    | 77    | 86    | 87    | 85    | 89    | 63    | 67    | 75    | 270    |
| National WHO-UNICEF estimates | 57 | 61 | 63 | 68 | 64 | 72 | 74 | 74 | 73 | - | - | - | - |
| % of districts with MCV1 >80% | 26 | 35 | 37 | 49 | 44 | 68 | 68 | 60 | 68 | - | - | - | - |

Abbreviations: MCV1 = first dose of measles-containing vaccine, DHS = Demographic Health Survey, MICS = Multiple Indicator Cluster Survey, EPI = Expanded Programme on Immunization, Democratic Republic of the Congo, WHO = World Health Organization, UNICEF = United Nations Children's Fund, IDSR = Integrated Disease Surveillance and Response, MOPH = Ministry of Public Health

a Calculated by dividing the number of MCV1 doses given by the targeted number of children <12 months of age and multiplying by 100; target >90%
b Estimates from coverage surveys conducted among children aged 12–23 months of age [24–26]c Calculated by dividing the number of suspected cases reported to IDSR during July 1, 2010 to December 31, 2012 by the estimated 2012 population from the MOPH and multiplying by 100; target >90%
d Annual estimates of national MCV1 coverage for children <12 months of age [23]
e Calculated by dividing the number of districts reporting >80% MCV1 coverage by the number of districts expected to report and multiplying by 100; target: 100%
Table 2: coverage from measles supplementary immunization activities by administrative reporting and post-campaign surveys, Democratic Republic of the Congo, 2002–2010

| Province            | Year | Month | SIA type | Target age group | Children vaccinated | Administrative coverage (%)<sup>a</sup> | Coverage by survey (%)<sup>b</sup> |
|---------------------|------|-------|----------|------------------|---------------------|--------------------------------------|----------------------------------|
| Kasaï Oriental      | 2002 | Dec.  | Catch-up | 6m–14y           | 3,478,261           | 96                                   | -                                |
| Nord Kivu           | 2002 | Dec.  | Catch-up | 6m–14y           | 2,076,563           | 96                                   | -                                |
| Kasaï Occidental    | 2004 | Oct.–Nov. | Catch-up | 6m–14y            | 2,473,668           | 88                                   | -                                |
| Katanga             | 2004 | Oct.–Nov. | Catch-up | 6m–14y          | 3,784,714           | 87                                   | -                                |
| Maniema             | 2004 | Oct.–Nov. | Catch-up | 6m–14y          | 768,987             | 102                                  | -                                |
| Sud Kivu            | 2004 | Oct.–Nov. | Catch-up | 6m–14y          | 1,577,385           | 73                                   | -                                |
| Equateur            | 2005 | Oct.   | Catch-up | 6m–14y          | 3,268,004           | 87                                   | -                                |
| Province Orientale  | 2005 | Oct.   | Catch-up | 6m–14y          | 3,691,667           | 91                                   | -                                |
| Bas-Congo           | 2006 | Dec.   | Catch-up | 6m–14y          | 3,268,004           | 97                                   | -                                |
| Kinshasa            | 2006 | Nov.   | Catch-up | 6m–14y          | 900,330             | 103                                  | -                                |
| Bandundu            | 2006 | Nov.   | Catch-up | 6m–14y          | 3,064,629           | 97                                   | 98<sup>d</sup>                   |
| Nord Kivu           | 2006 | Oct.   | Follow-up | 6–59m       | 2,659,229           | 97                                   | -                                |
| Kasaï Oriental      | 2006 | May    | Follow-up | 6–59m       | 1,257,999           | 94                                   | -                                |
| Kasaï Occidental    | 2007 | Aug.–Sep. | Follow-up | 6–59m   | 1,068,950           | 100                                  | 94<sup>d</sup>                   |
| Katanga             | 2007 | Aug.–Sep. | Follow-up | 6–59m       | 1,624,002           | 99                                   | -                                |
| Maniema             | 2007 | Sep.   | Follow-up | 6–59m       | 290,803             | 97                                   | -                                |
| Sud-Kivu            | 2007 | Sep.   | Follow-up | 6–59m       | 821,937             | 113                                  | -                                |
| Equateur            | 2008 | Nov.   | Follow-up | 6–59m       | 1,449,659           | 103                                  | -                                |
| Province Orientale  | 2008 | Nov.   | Follow-up | 6–59m       | 1,361,433           | 94                                   | -                                |
| Bas-Congo           | 2009 | Nov.   | Follow-up | 6–59m       | 482,070             | 92                                   | -                                |
| Kinshasa            | 2009 | Nov.   | Follow-up | 6–59m       | 1,086,047           | 96                                   | -                                |
| Nord Kivu           | 2009 | Nov.   | Follow-up | 6–59m       | 1,073,437           | 112                                  | -                                |
| Bandundu            | 2010 | Jan.   | Follow-up | 6–59m       | 1,274,163           | 105                                  | -                                |

Abbreviations: m=month, y=year, SIA=Supplementary Immunization Activity

<sup>a</sup>“Catch-up” SIAs are one-time campaigns targeting a wide age range with the aim to quickly reduce measles susceptibility in the population. “Follow-up” SIAs are periodic campaigns targeting children born since the last SIA to reduce the accumulation of susceptible children

<sup>b</sup>Calculated by dividing the number of measles vaccine doses administered by the targeted number of children and multiplying by 100; target >95%

<sup>c</sup>Estimates from coverage surveys conducted among children in the age group targeted

<sup>d</sup>2006 and 2007 survey coverage estimates are overall estimates for the three campaigns indicated
### Table 3: coverage from measles supplementary immunization activities during 2011–2012 and outbreak response immunization during 2010–2012 by administrative reporting and post-campaign surveys, Democratic Republic of the Congo

| Province          | Districts in province | Districts covered | Year  | Month   | SIA type/ ORI | Target age group | Children vaccinated | Administrative coverage (%) | Coverage by survey (%) |
|-------------------|-----------------------|-------------------|-------|---------|---------------|------------------|---------------------|--------------------------|---------------------|
| Bandundu          | 52                    | 46                | 2012  | Jan.    | Follow-up     | 6–59m            | 1,239,803           | 99                       | -                    |
|                   | 6                     | 2012              | Jan.  | ORI     | 6–59m         | 129,000          | 96                  | 102                     | -                    |
|                   | 5                     | 2012              | Oct.–Nov. | ORI | 6m–14y     | 507,034          | 105                 | -                       | -                    |
| Bas-Congo         | 31                    | 5                 | 2011  | Jul.    | ORI          | 6–59m            | 65,657              | 99                       | -                    |
|                   | 18                    | 2012              | Jan.  | Follow-up | 6–59m      | 303,786          | 97                  | -                       | -                    |
|                   | 9                     | 2012              | Jan.  | ORI     | 6m–14y       | 530,149          | 100                 | -                       | -                    |
|                   | 1                     | 2012              | Oct.  | ORI     | 6m–14y       | 82,842           | 102                 | -                       | -                    |
| Equateur          | 69                    | 3                 | 2011  | Jul.    | ORI          | 6–59m            | 106,103             | 91                       | -                    |
|                   | 66                    | 2011              | Sep.  | Follow-up | 6–59m      | 1,419,411        | 94                  | -                       | -                    |
|                   | 1                     | 2012              | Apr.–May | ORI | 6m–14y     | 128,752          | 108                 | -                       | -                    |
|                   | 6                     | 2012              | Sep.  | ORI     | 6m–14y       | 477,066          | 94                  | 96                      | -                    |
| Kasai Occidental  | 44                    | 1                 | 2011  | Jan.–Feb. | ORI        | 6m–14y           | 123,045             | 93                       | -                    |
|                   | 3                     | 2011              | Mar.–Apr. | ORI | 6m–14y     | 430,571          | 104                 | -                       | -                    |
|                   | 9                     | 2011              | May   | ORI     | 6m–14y       | 792,389          | 111                 | -                       | -                    |
|                   | 4                     | 2011              | Jul.  | ORI     | 6–59m         | 125,109          | 106                 | -                       | -                    |
|                   | 29                    | 2011              | Jul.  | Follow-up | 6–59m      | 684,176          | 98                  | -                       | -                    |
|                   | 5                     | 2012              | Aug.  | ORI     | 6m–14y       | 348,176          | 104                 | 94                      | -                    |
| Kasai Oriental    | 51                    | 31                | 2011  | Jul.    | Follow-up   | 6–59m            | 729,336             | 103                     | -                    |
|                   | 4                     | 2011              | Mar.–Apr. | ORI | 6–59m     | 159,542          | 104                 | -                       | -                    |
|                   | 14                    | 2011              | Apr.  | ORI     | 6–59m        | 564,252          | 99                  | -                       | -                    |
|                   | 2                     | 2011              | Jun.  | ORI     | 6m–14y       | 268,586          | 99                  | -                       | -                    |
|                   | 8                     | 2012              | Mar.  | ORI     | 6m–14y       | 478,588          | 104                 | -                       | -                    |
|                   | 1                     | 2012              | Nov.  | ORI     | 6–59m        | 67,152           | 103                 | -                       | -                    |
| Katanga           | 68                    | 2                 | 2010  | Oct.–Dec. | ORI        | 6m–14y           | 144,071             | 90                       | -                    |
|                   | 27                    | 2011              | Jan.–Aug. | ORI | 6m–14y    | 1,847,096        | 102                 | -                       | -                    |
|                   | 24                    | 2011              | May   | ORI     | 6m–14y       | 1,917,060        | 103                 | -                       | -                    |
|                   | 17                    | 2011              | Jul.  | Follow-up | 6–59m      | 585,633          | 105                 | -                       | -                    |
|                   | 2                     | 2011              | Oct.–Dec. | ORI | 6m–14y     | 167,485          | 74                  | -                       | -                    |
|                   | 10                    | 2012              | Aug.  | ORI     | 6m–14y       | 941,879          | 97                  | 68                      | -                    |
| Kinshasa          | 35                    | 25                | 2011  | Dec.    | Follow-up   | 6–59m            | 1,089,048           | 101                     | -                    |
|                   | 10                    | 2011              | Dec.  | ORI     | 6m–14y       | 937,439          | 89                  | -                       | -                    |
| Maniema           | 18                    | 14                | 2011  | May     | ORI         | 6m–14y           | 833,512             | 101                     | 95                   |
|                   | 4                     | 2011              | Jul.  | Follow-up | 6–59m      | 58,202           | 103                 | 98                      | 94                   |
|                   | 2                     | 2012              | Aug.  | ORI     | 6m–14y       | 81,247           | 96                  | 94                      | -                    |
| Nord Kivu         | 28                    | 19                | 2012  | Jan.    | Follow-up   | 6–59m            | 948,237             | 112                     | -                    |
|                   | 5                     | 2012              | Jan.  | ORI     | 6–59m        | 284,592          | 107                 | -                       | -                    |
|                   | 1                     | 2012              | Aug.  | ORI     | 6m–14y       | 197,820          | 116                 | -                       | -                    |
| Province Orientale| 83                    | 7                 | 2011  | Jul.    | ORI         | 6–59m            | 119,586             | 93                       | -                    |
|                   | 1                     | 2011              | Sep.  | ORI     | 6m–14y       | 74,549           | 108                 | -                       | -                    |
|                   | 76                    | 2011              | Sep.  | Follow-up | 6–59m      | 1,456,498        | 96                  | -                       | -                    |
|                   | 2                     | 2012              | Aug.–Nov. | ORI | 6m–14y     | 97,332           | 99                  | -                       | -                    |
| Sud Kivu          | 34                    | 1                 | 2010  | Nov.–Dec. | ORI        | 6m–14y           | 88,853              | 100                     | -                    |
|                   | 4                     | 2011              | Feb.–Jun. | ORI | 6m–14y    | 250,877          | 81                  | -                       | -                    |
|                   | 25                    | 2011              | May   | ORI     | 6m–14y       | 1,826,722        | 102                 | -                       | -                    |
|                   | 4                     | 2011              | Jul.  | Follow-up | 6–59m      | 95,955           | 105                 | -                       | -                    |

Abbreviations: m=month, y=year, SIA=Supplementary Immunization Activity, ORI=Outbreak Response Immunization

- "Follow-up" SIA: periodic campaigns targeting children born since the last SIA to reduce the accumulation of susceptible children
- ORI: campaigns conducted in response to confirmed outbreaks, with target age and geographic area based on epidemiology and available resources

- Calculated by dividing the number of measles vaccine doses administered by the targeted number of children and multiplying by 100; target >95%
- Estimates from coverage surveys conducted among children in the age group targeted
- District-level coverage survey estimates available for campaigns conducted by MSF in 19 of 27 districts [12]
### Table 4: measles surveillance data reported through Integrated Disease Surveillance and Response and measles case-based surveillance, Democratic Republic of the Congo, 2004–2012

| Indicator | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | Total |
|-----------|------|------|------|------|------|------|------|------|------|-------|
| **IDSR** |      |      |      |      |      |      |      |      |      |       |
| No. suspected measles cases | 42,827 | 53,022 | 79,873 | 55,440 | 12,490 | 3,364 | 5,364 | 133,907 | 73,038 | 459,326 |
| No. suspected measles deaths | 1,097 | 595 | 1,181 | 1,463 | 247 | 73 | 82 | 1,650 | 2,012 | 8,400 |
| Suspected measles incidence per 1,000,000<sup>a</sup> | 640 | 782 | 1,164 | 823 | 180 | 73 | 73 | 1,769 | 935 | 6,412 |
| **Case-based surveillance** |      |      |      |      |      |      |      |      |      |       |
| No. suspected measles cases | 769 | 1,364 | 2,148 | 1,923 | 1,178 | 701 | 1,453 | 3,170 | 4,083 | 16,789 |
| No. confirmed measles cases | 387 | 429 | 780 | 543 | 219 | 44 | 190 | 1,824 | 2,248 | 6,664 |
| Lab-confirmed | 382 | 407 | 780 | 468 | 213 | 44 | 188 | 1,077 | 1,209 | 4,768 |
| Confirmed by epi-link | 2 | 10 | - | 73 | - | - | 1 | 747 | 1,039 | 1,872 |
| Clinically compatible | 3 | 12 | - | 2 | 6 | - | 1 | - | - | 24 |
| No. lab-confirmed rubella cases | 61 | 122 | 205 | 244 | 231 | 101 | 199 | 452 | 1,906 |
| Districts with ≥1 specimen (%)<sup>b</sup> | 20 | 43 | 56 | 48 | 41 | 46 | 57 | 65 | - |
| Non-measles febrile rash per 100,000<sup>c</sup> | 0.4 | 1.3 | 2.0 | 2.0 | 1.4 | 0.8 | 1.7 | 1.8 | 2.3 | - |

Abbreviations: No.=number, IDSR=Integrated Disease Surveillance and Response, epi-link=epidemiological link, MOPH=Ministry of Public Health

<sup>a</sup> Calculated by dividing the number suspected measles cases reported annually by the estimated annual population from MOPH and multiplying by 1,000,000; target: <5 per 1,000,000

<sup>b</sup> Calculated by dividing the number of districts reporting ≥1 suspected measles case with a blood specimen collected in a year by the number of districts expected to report and multiplying by 100; target: ≥80%

<sup>c</sup> Calculated by dividing the number of suspected measles cases reported annually that were discarded as non-measles due to a negative measles IgM test result by the annual estimated population from MOPH and multiplying by 100,000; target: ≥2 per 100,000

### Table 5: confirmed measles cases+ reported through measles case-based surveillance by age group and measles vaccination status, Democratic Republic of the Congo, July 1, 2010–December 31, 2012

| Age group | Cases with ≥1 dose MCV No. | % | Cases not vaccinated No. | % | Cases with missing or unknown vaccination status No. | % | Total cases No. | % |
|-----------|-----------------------------|---|--------------------------|---|------------------------------------------|---|----------------|---|
| <9 months | 39 | 3.7 | 151 | 53.9 | 90 | 32.1 | 280 | 6.6 |
| 9–59 months | 706 | 27.6 | 642 | 25.1 | 1,211 | 47.3 | 2,559 | 60.2 |
| 5–9 years | 212 | 24.1 | 149 | 17.0 | 518 | 58.9 | 879 | 20.7 |
| 10–14 years | 53 | 22.2 | 37 | 15.5 | 149 | 62.3 | 239 | 5.6 |
| ≥15 years | 36 | 12.3 | 57 | 19.5 | 200 | 68.3 | 293 | 6.9 |
| Total | 1,046 | 24.6 | 1,036 | 24.4 | 2,168 | 51.0 | 4,250 | 100.0 |

Abbreviations: MCV=measles-containing vaccine, No.=number

+ Confirmed cases were defined as all laboratory-confirmed, epidemiologically-linked, and clinically-compatible measles cases.
Figure 1: administrative measles vaccination coverage from supplementary immunization activities (SIA) and outbreak response immunization (ORI) by province and year during 2002-2012, and cumulative measles attack rates reported through Integrated Disease Surveillance and Response during July 1, 2010-December 31, 2012, Democratic Republic of the Congo

| Province             | Administrative coverage (%) of measles campaigns by year | Cumulative attack rate |
|----------------------|---------------------------------------------------------|------------------------|
| Nord Kivu            | 96 103 112                                              | 112 13                 |
| Kasai Oriental       | 96 94 90 101 104                                       | 504                    |
| Katanga              | 90 97 90                                               | 774                    |
| Maniema              | 101 96                                                 | 543                    |
| Sud Kivu             | 73 101 99                                              | 107                    |
| Kasai Occidental     | 88 100 104                                             | 68                     |
| Equateur             | 87 103 93 97                                           | 122                    |
| Province Orientale   | 91 94 96 99                                             | 366                    |
| Kinshasa             | 97 96 95 99                                            | 25                     |
| Bas-Congo            | 97 92 99 99                                             | 46                     |
| Bandundu             | 101 105 101 95                                         | 95                     |

Catch-up SIA (target age group: 6 months to 14 years)
Follow-up SIA (target age group: 6 to 59 months)
2011-2012 follow-up SIA (target age group: 6 to 59 months) combined with ORIs (6 to 59 months or 14 years)
2010-2012 ORIs (target age group: 6 to 59 months or 14 years)
Planned 2010 SIA that was not implemented

Figure 2: suspected measles cases reported through Integrated Disease Surveillance and Response and confirmed measles cases reported through case-based surveillance by week, Democratic Republic of the Congo, July 1, 2010-December 31, 2012 (+53 cases confirmed by epidemiologic-link and reported through outbreak line-lists were missing date of rash onset)
Figure 3: district maps of (A) cumulative measles attack rates reported through Integrated Disease Surveillance and Response and (B) confirmed measles outbreaks and measles virus strains reported through case-based surveillance for 6-month periods, Democratic Republic of the Congo, July 1, 2010-December 31, 2012 (provinces: 1. Province Orientale, 2. Nord Kivu, 3. Sud Kivu, 4. Maniema, 5. Katanga, 6. Kasai Oriental, 7. Kasai Occidental, 8. Bandundu, 9. Bas Congo, 10. Kinshasa, and 11. Equateur; districts with first confirmed outbreaks: a. Lemera, b. Sakania, and c. Dilolo; each dot represents 1-8 viruses with the same genotype in a district within a month)
Figure 4: Phylogenetic analysis of the viral nucleoprotein gene of measles virus strains detected in the Democratic Republic of the Congo, July 1, 2010-February 28, 2012 (scale bar distance of 0.005=2 nucleotides substitutions in the 450 nucleotide sequenced region; sequence names contain information on the sequence source, district, country, epidemiologic week, year, and sequential case number; Genbank accession numbers indicated in brackets; abbreviations: MVi, measles virus sequenced from isolates; MVs, measles virus sequenced from clinical specimens; COD, Democratic Republic of the Congo; GAB, Gabon; NGA, Nigeria; CAE, Cameroon).