

The impact of reactive mass vaccination campaigns on measles outbreaks in the Katanga region, Democratic Republic of Congo

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1 Abstract

2 The Katanga region in the Democratic Republic of Congo (DRC) has been struck by
3 repeated epidemics of measles, with large outbreaks occurring in 2010–13 and 2015.
4 In many of the affected health zones, reactive mass vaccination campaigns were
5 conducted in response to the outbreaks. Here, we attempted to determine how ef-
6 fective the vaccination campaigns in 2015 were in curtailing the ongoing outbreak.
7 We further sought to establish whether the risk of large measles outbreaks in differ-
8 ent health zones could have been determined in advance to help prioritise areas for
9 vaccination campaign and speed up the response. In doing so, we first attempted to
10 identify factors that could have been used in 2015 to predict in which health zones
11 the greatest outbreaks would occur. Administrative vaccination coverage was not
12 a good predictor of the size of outbreaks in different health zones. Vaccination cov-
13 erage derived from surveys, on the other hand, appeared to give more reliable es-
14 timates of health zones of low vaccination coverage and, consequently, large out-
15 breaks. On a coarser geographical scale, the provinces most affected in 2015 could
16 be predicted from the outbreak sizes in 2010–13. This, combined with the fact that
17 the vast majority of reported cases were in under-5 year olds, would suggest that
18 there are systematic issues of undervaccination. If this was to continue, outbreaks
19 would be expected to continue to occur in the affected health zones at regular inter-
20 vals, mostly concentrated in under-5 year olds. We further used a model of measles
21 transmission to estimate the impact of the vaccination campaigns, by first fitting a
22 model to the data including the campaigns and then re-running this without vacci-

23 nation. We estimated the reactive campaigns to have reduced the size of the overall
24 outbreak by approximately 21,000 (IQR: 16,000–27,000; 95% CI: 8300–38,000) cases.
25 There was considerable heterogeneity in the impact of campaigns, with campaigns
26 started earlier after the start of an outbreak being more impactful. Taken together,
27 these findings suggest that while a strong routine vaccination regime remains the
28 most effective means of measles control, it might be possible to improve the effec-
29 tiveness of reactive campaigns by considering predictive factors to trigger a more
30 targeted vaccination response.

31 **Introduction**

32 There have been repeated outbreaks of measles in the Democratic Republic of
33 Congo (DRC). The Katanga region (formerly known as Katanga province) is in the
34 southeast of the country bordering Zambia and comprises the provinces of Haut-
35 Katanga, Haut-Lomami, Lualaba and Tanganyika. It has experienced large periodic
36 measles outbreaks, such as in 2006–07, 2010–13 (Grout et al., 2013; Mancini et al.,
37 2014). In response to these, reactive mass vaccination campaigns have been con-
38 ducted to protect those assumed to be at risk both within the outbreak area and
39 beyond.

40 Standard measles epidemic responses include reinforcing measles surveillance
41 in affected areas, providing free care to reduce measles mortality, and reactive vac-
42 cination campaigns in order to control measles transmission. In collaboration with
43 the World Health Organization (WHO) Regional Office for Africa (AFRO) and the
44 United Nations Children’s Fund (UNICEF), Médecins Sans Frontières (MSF) sup-
45 ported the Ministry of Health to respond to various measles outbreaks including
46 two major measles outbreaks in the Katanga region. Firstly, in 2010–13, a measles
47 epidemic was reported with over 96,000 suspected cases reported, 77% of which oc-
48 curred in children under 5 years of age, and more than 1400 deaths (Mancini et al.,
49 2014). In 2011, in response to the ongoing epidemic, MSF vaccinated more than 1.8
50 million children 26 of the 68 health zones in the Katanga region (Grout et al., 2013).
51 Secondly, in February 2015, a new measles epidemic started in Katanga, DRC, last-
52 ing the whole year and resulting in over 40,000 cases and more than 400 deaths
53 in 2015 (UN Children’s Fund, 2015). MSF responded with the standard epidemic
54 responses including a reactive vaccination campaign in order to stop measles trans-
55 mission during epidemics, targeting more than 25 health zones.

56 The time interval between the outbreak starting in different parts of Katanga
57 and the vaccination response implemented varied. Previously, modelling studies
58 in Niger have demonstrated that even late vaccination intervention in response to
59 an outbreak could prevent a large number of cases, though early intervention will
60 always have a larger impact (Ferrari et al., 2008; Grais et al., 2008; Dubray et al.,
61 2006; Grais et al., 2006). However, this may be context-specific and vary with local
62 epidemiology and outbreak patterns. The response to the Katanga outbreak pro-
63 vides an opportunity to retrospectively study the effectiveness of the campaigns
64 conducted in mitigating excess morbidity. More generally, important lessons could
65 be learned about the relationship between response times and effectiveness of cam-

66 paigns, and how campaign targets could be selected in the future to ensure greatest
67 impact.

68 We studied the 2015 measles outbreak and responsive mass vaccination cam-
69 paigns conducted as part of the standard epidemic response to assess whether the
70 most-affected areas could have been predicted from information on previous out-
71 breaks and administrative or otherwise estimated vaccination coverage. We further
72 investigated the outbreak in several health zones using a mathematical model of
73 measles transmission, to quantify the impact of vaccination campaigns that were
74 conducted in those areas.

75 **Methods**

76 **Data sources and cleaning**

77 Suspected measles cases (WHO definition) from 2010–16 were collated from the in-
78 tegrated disease surveillance (IDS) system, described in Mancini et al. (2014). These
79 data are split into age groups 1-4 years and 5 years and over, at the level of health
80 zones. The database did not contain any information on cases under the age of 1
81 year.

82 Administrative coverage data from 2009-16 collected by the Ministry of Health
83 was available as the number of doses administered per week was collected at the
84 level of health zones, separated into age groups 9-11 months and 12-23 months.

85 Population denominators were extracted from the coverage data. Since the last
86 census in DRC prior to this study had been done in 1981, these numbers are subject
87 to considerable uncertainty.

88 We further used vaccination coverage estimates from a previous study by Taka-
89 hashi et al. (2017). These used data collected as part of the Demographic and Health
90 Survey (DHS) in 2013–14, extrapolated from geo-located information on children’s
91 vaccination status from vaccine cards and parental recall. We averaged the esti-
92 mates by month of age to arrive at the proportion of under-5 year olds that were
93 unvaccinated, that is had received no dose of measles-containing vaccine.

94 Information on reactive mass vaccination campaigns conducted in 2015 was ex-
95 tracted from MSF reports. The total number of vaccine doses administered was
96 collated at the level of health zones, and at various temporal resolutions from days
97 to a single number of doses delivered for a whole campaign.

98 **Factors that could predict outbreak size**

99 We tested the predictability of outbreaks from demographic factors and outbreak
100 and vaccination history in a negative binomial Generalized Linear Model with log-
101 arithmic link. Robust standard errors and p-values were calculated using the *sand-*
102 *wich R* package (Zeileis, 2004; Zeileis, 2006). The number of suspected cases re-

103 ported during the 2015 outbreak at the health zone level was modelled as a function
104 of health zone population size, the number of cases in the 2010–13 outbreak, MoH
105 administrative and estimated vaccination coverage.

106 **Modelling measles with mass vaccination campaigns**

107 We modelled measles transmission at the level of health zones using a stochastic
108 transmission model with a fixed time step of 2 weeks, corresponding to the gen-
109 eration time of measles (Bjørnstad et al., 2002). At each time step t , the number of
110 new infections in health zone i , I_{it} was drawn from a negative binomial distribution
111 with mean $\lambda_{it}S_{i(t-1)}$ and shape m , allowing for overdispersion of transmission, or
112 superspreading (Lloyd-Smith et al., 2005):

$$I_{it} \sim \text{NB}(\lambda_{it}S_{i(t-1)}, m)$$

113 where $S_{i(t-1)}$ and $I_{i(t-1)}$ are the number of people susceptible and infected, re-
114 spectively, at time $t - 1$, and λ_{it} is the force of infection experienced by susceptibles
115 in health zone i at time t :

$$\lambda_{it} = R_0 \frac{I_{i(t-1)}}{N_i}$$

116 where N_i is the population size of health zone i , R_0 is the basic reproduction
117 number.

118 When a mass vaccination campaign was conducted, the number of susceptible
119 people immunised was calculated by multiplying the number of doses adminis-
120 tered with the proportion of the population still susceptible S_{it}/N_i , and a campaign
121 efficiency factor e_i , estimated as part of the inference procedure described below.
122 This factor comprises both vaccine efficacy and the efficiency in targeting suscep-
123 tible children, which were not identifiable separately. With a perfect vaccine and
124 random distribution, this would take a value of 1. If vaccines were preferentially
125 given to susceptibles, it would take values of greater than 1 (subject to vaccine ef-
126 ficacy). If vaccines were preferentially given to already immune children, it would
127 take values of less than 1.

128 During a two-week span, half of vaccinations were modelled to be administered
129 before transmission occurred and half afterwards. While the measles vaccine takes
130 2 weeks to come into effect, it provides potentially high level of protection from 72
131 hours after administration (Barrabeig et al., 2011; Kutty et al., 2013; National Health
132 Service, 2017). We therefore assumed that vaccination starts to fully immunise a
133 child instantaneously.

134 For the counterfactual scenarios of how the outbreaks would have evolved with-
135 out a reactive mass vaccination, we simulated the model from the time of the mass
136 vaccination campaigns, but without reducing the number of susceptibles as a con-
137 sequence of vaccination. We then drew samples from the joint distribution of tra-
138 jectories and observations, to obtain alternative trajectories of observed cases. To

139 evaluate the impact of the campaigns, we calculated the reduction in the number of
140 cases observed in each of the trajectories. If this yielded a negative difference (i.e., if
141 random sampling yielded alternative trajectories with more cases than the observed
142 ones), we treated the impact as 0 (i.e., same number of cases in both scenarios).

143 **Selection of health zones for fitting and estimating populations**

144 The health zones selected for the dynamic model were ones that reported more
145 than 10 cases in at least one week in 2015 and had a reactive mass vaccination cam-
146 paign with the number of doses delivered and results from a follow-up coverage
147 survey available. A total of eight health zones were modelled, including the one
148 that saw most cases (Malemba-Nkulu, 8856 reported cases) and 7 of the 13 health
149 zones with most cases in 2015: Ankoro (3910), Kinkondja (2773), Mukanga (2723),
150 Bukama (2632), Songa (928) and Kabalo (904).

151 Since a large proportion of cases was found in children (77% in 1-to-5 year olds,
152 with no further age-breakdown available), and none of the vaccination campaigns
153 targeted over-15 year olds, we modelled measles transmission to be occurring ex-
154 clusively in under-5 year olds. The relevant population sizes were estimated as the
155 number of doses administered in the vaccination campaigns divided by the cover-
156 age estimated from concurrent vaccination surveys. Where vaccination campaigns
157 were limited to under-5 or under-10 year olds, we estimated the total population
158 size under 15 as 2.72 or 1.39 times the estimated population size, respectively, based
159 on multipliers used for estimating the sizes of age groups in the administrative cov-
160 erage data provided.

161 **Model fitting and counterfactual scenarios**

162 The model was fitted simultaneously to the eight selected health zones. The likeli-
163 hood of observing bi-weekly incidence D_{it} in health zone i at time t was taken to
164 follow a negative binomial distribution with fixed overdispersion ϕ .

$$D_{it} \sim \text{NB}(\rho I_{it} + \mu, \phi)$$

165 where ρ is the proportion of cases that is reported, μ is the rate of background
166 reporting of measles, either due to cases that were not part of the epidemic or mis-
167 classification, for example of rubella cases, and ϕ is the reporting overdispersion.

168 The value of the basic reproduction number R_0 , the efficacy of mass vaccination
169 e_i , mean reporting rate ρ , background reporting rate m , observation overdispers-
170 ions, the proportion immune r_{i0} in health zone I and the mean number of individ-
171 uals infectious I_{i0} at the first data point with at least 10 cases in health zone i (taken
172 to be the start of the time series), were all estimated as part of the inference proce-
173 dure, as well as likely trajectories of the state variables. The reporting rate ρ_i and
174 initial number infectious I_{i0} was allowed to vary between health zones. The prior
175 distribution on the mean reporting rate was weakly informed by a coverage survey

176 that was conducted in Kabalo. The initial proportion immune r_{i0} was estimated
 177 with a mean and lower bound given by the vaccination coverage per health zone
 178 v_i estimated in (Takahashi et al., 2017). Informed or regularising prior distributions
 179 of the parameters to be estimated are shown in Table 1.

Table 1: *Prior distributions of parameters used in the transmission model. The distribution of the basic reproduction number was truncated at a lower bound of 0. The proportion initially immune was truncated to be between v_i and 1. The mean and actual proportions reported were truncated to be between 0 and 1. The number initially infectious were truncated at a lower bound of 0.*

Parameter	Symbol	Prior distribution	Source
Basic reproduction number	R_0	Gaussian(15, 5)	Anderson and May (1991)
Overdispersion of transmission	m	Gamma(1, 0.1)	n/a
Efficacy of campaigns	e_i	Gaussian(1, 1)	n/a
Background reporting	μ	Gamma(1,1)	n/a
Proportion initially immune	r_{0i}	Gaussian(v_i , 1)	Takahashi et al. (2017)
Mean proportion reported	ρ	Gaussian(0.059, 0.009)	Médecins Sans Frontières (2015)
Proportion reported	ρ_i	Gaussian(ρ , 0.1)	n/a
Mean initially infectious	I_0	Gamma(2, 5)	n/a
Number initially infectious	I_{0i}	Gamma($\frac{I_0}{r_{0i}}$, $\sqrt{\frac{I_0}{r_{0i}}}$)	n/a
Overdispersion of reporting	ϕ	Gamma(1, 0.1)	n/a

180 The model was fitted to the data using a particle filter in combination with
 181 Metropolis-Hastings Markov chain Monte Carlo (pMCMC) with the *libbi* software
 182 library (Murray, 2013) as implemented in the *RBi* package using the statistical soft-
 183 ware *R* (Jacob and Funk, 2019; R Core Team, 2017). The number of particles and
 184 proposal distribution was adapted using the *RBi.helpers* package (Funk, 2019), be-
 185 fore the pMCMC sampler was run to generate 4096 samples after thinning, with
 186 262,144 particles. The inference pipeline was run on an Nvidia Tesla P100 16GB
 187 NVLink GPU.

188 Results

189 Outbreak size

190 In total, 40,562 cases and 485 deaths were reported in the Katanga region over
 191 the course of the year (case-fatality ratio: 1.2%). The majority of cases were re-
 192 ported from Haut-Lomami (23,984, 59%) and Tanganyika (12,110, 30%) provinces,
 193 with the outbreak in Tanganyika peaking significantly later than the one in Haut-
 194 Lomami (Fig. 2). Of the 68 health zones, 16 reported over 90% of cases (Fig. 1).

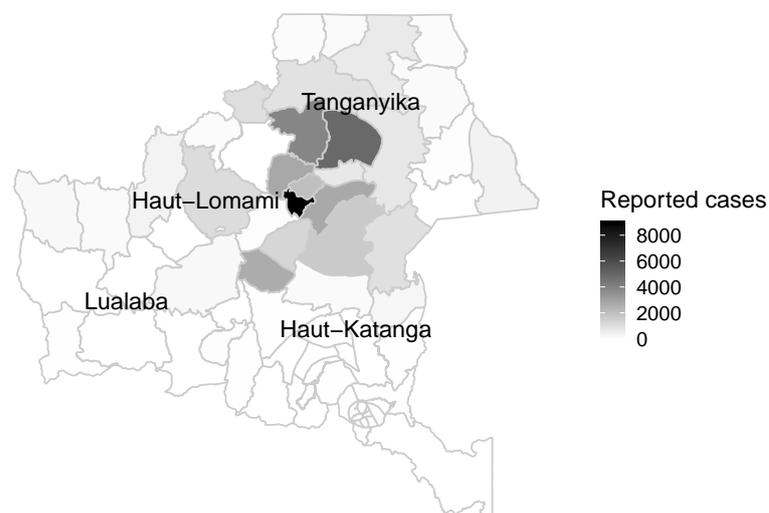


Figure 1: Number of cases by health zone in the Katanga region, 2015.

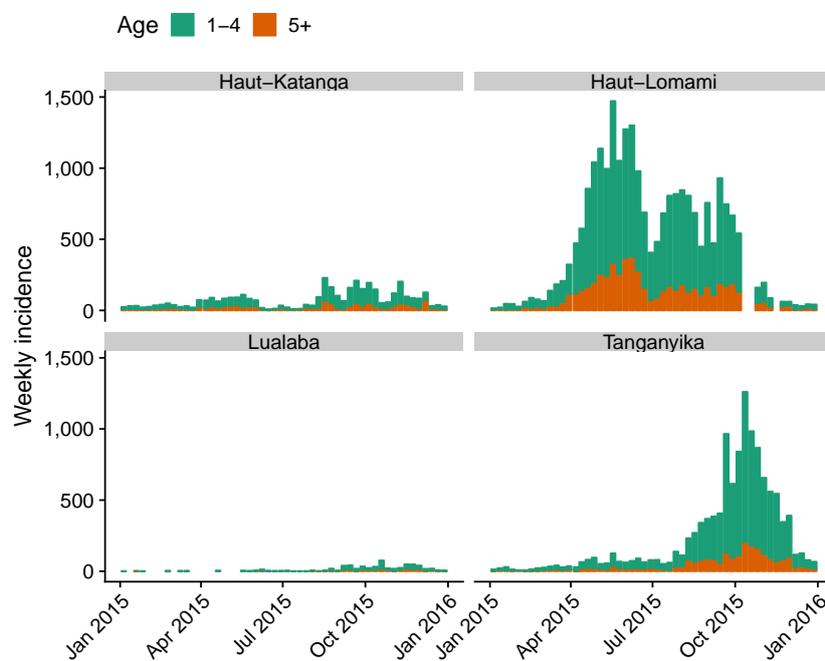


Figure 2: Number of cases by age group and province in Katanga, 2015.

195 **Predictability of outbreak size**

196 There was a positive correlation between reported incidence in the 2010–13 out-
197 break and the 2015 outbreak (Pearson’s $r=0.31$, $p=0.01$, Fig. 3). All the health zones
198 with more than 10 cases per 1000 in 2015 (Malemba-Nkulu, Kinkondja, Manono,
199 Ankoro, Lwamba, Mitwaba, Mukanga, Bukama) had also reported more than 5
200 cases per 1000 in 2010–13.

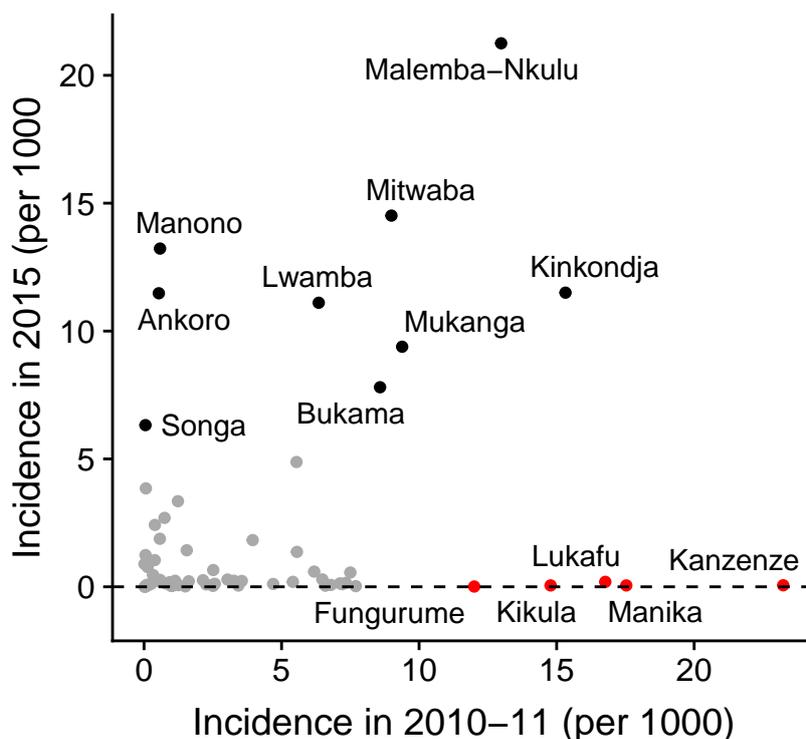


Figure 3: Incidence (number of cases divided by estimated population size) in 2010–13 vs 2015. Health zones with more than 5 cases per 1000 in 2015 are indicated in black, and other health zones with more than 10 cases per 1000 in 2010–13 in red.

201 Further, there was a positive correlation of reported incidence in 2015 and ad-
202 ministrative vaccination coverage, and a negative correlation with coverage as es-
203 timated from DHS data (Fig. 4).

204 Combining these factors and population size in a regression model confirms
205 these correlations, with coefficients corresponding to the number of cases in 2010–13
206 and vaccination coverage estimated by DHS as strongest predictors of the number
207 of cases that occurred in 2015 (Table 2). Population size and routine vaccination
208 coverage as measured by the EPI programme did not have a strong influence on the
209 number of cases in 2015. Correlation between model predictions and true number
210 of cases was 0.3 (95% CI 0.1-0.5, $p=0.01$, Fig. 5).

211 To further investigate the relationships underlying the results, we tested an ad-
212 ditional model variant, where we distinguished the four provinces comprising the
213 Katanga region in the model, to determine whether effects were being identified at

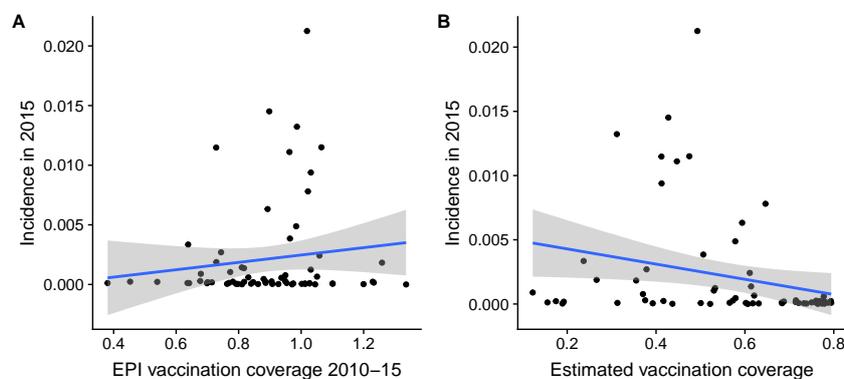


Figure 4: Vaccination coverage versus reported incidence (number of cases divided by estimated population size) in 2015. Linear trends are indicated by blue lines, with 95% confidence intervals indicated in grey. A) Mean vaccination coverage in 2010–15 as measured by the EPI programme. B) Vaccination coverage estimated from DHS data.

Table 2: Regression coefficients for model of case numbers in 2015, with lower and upper 95% confidence interval limits.

Coefficient	Estimate	p-value	Lower limit	Upper limit
(Intercept)	5.7	<0.001	5.4	6.1
Population size	0.1	0.8	-0.4	0.6
Number of cases 2010–13	0.8	<0.001	0.2	1.3
Mean EPI coverage 2010–15	0.3	0.09	-0.1	0.7
DHS coverage estimate	-1.3	<0.001	-1.8	-0.9

214 the fine level of the health zone or the coarser province level. In that case, province
215 as a categorical explanatory variable in the regression replaced some of the predic-
216 tive value both of the number of cases in 2010–13 (regression coefficient 0.4, $p=0.05$)
217 and the coverage estimate from DHS data (-1.1, $p<0.001$), but both retained predic-
218 tive value, the coverage estimate strongly so. This suggests that some predictive
219 value of case numbers in 2010–13, and strong predictive value of the coverage esti-
220 mate was retained at the lower level of the health zone.

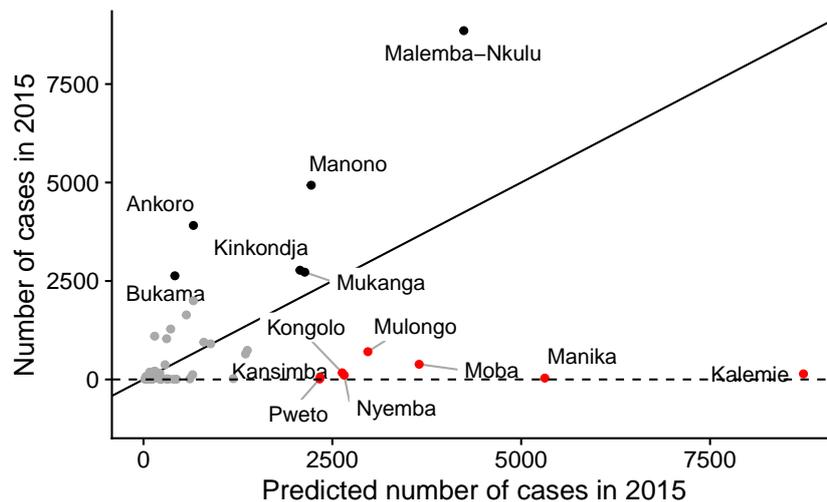


Figure 5: Predictions from the regression model vs. true number of cases. As in Fig. 3, health zones with more than 5 cases per 1000 in 2015 are indicated in black, and other health zones with more than 10 cases per 1000 in 2010–13 in red.

221 The impact of mass vaccination campaigns

222 To investigate the impact of the mass vaccination campaign in more detail, we fit-
223 ted a dynamic model to the case trajectories in 8 health zones (Fig. 6). We esti-
224 mated a basic reproduction number of 4.3 (mean; interquartile range, IQR: 4.0–4.5)
225 and an average reporting rate of 24% (IQR: 19%–29%), corresponding to a total of
226 77,000 (IQR: 73,000–81,000; 95% CI: 66,000–91,000) estimated cases from 19,079 re-
227 ported cases in the 8 health zones. On average, 55% (IQR: 49%–62%) of under-5 year
228 olds were estimated to have been immune before the outbreak. The estimated cam-
229 paign efficacy factor ranged from 0.21 (IQR: 0.09–0.31) in Kinkondja to 0.59 (IQR:
230 0.33–0.83) in Ankoro.

231 In total, we estimate that 21,000 (IQR: 16,000–27,000; 95% CI: 8300–38,000) cases
232 were averted by the vaccination campaigns in the seven health zones analysed, cor-
233 responding to relative reduction in case load of 21% (IQR: 17%–25%, 95% CI: 9.3%–
234 34%). Of the approximately 250,000 doses delivered to under-5 year olds in the
235 8 health zones, we estimated 22,000 (IQR: 17,000–26,000, 95% CI: 11,000–37,000) or
236 9.2% (IQR: 7.2%–11%, 95% CI: 4.5%–15%) of administered doses went to susceptible
237 children.

238 There was heterogeneity in impact between health zones. The greatest abso-

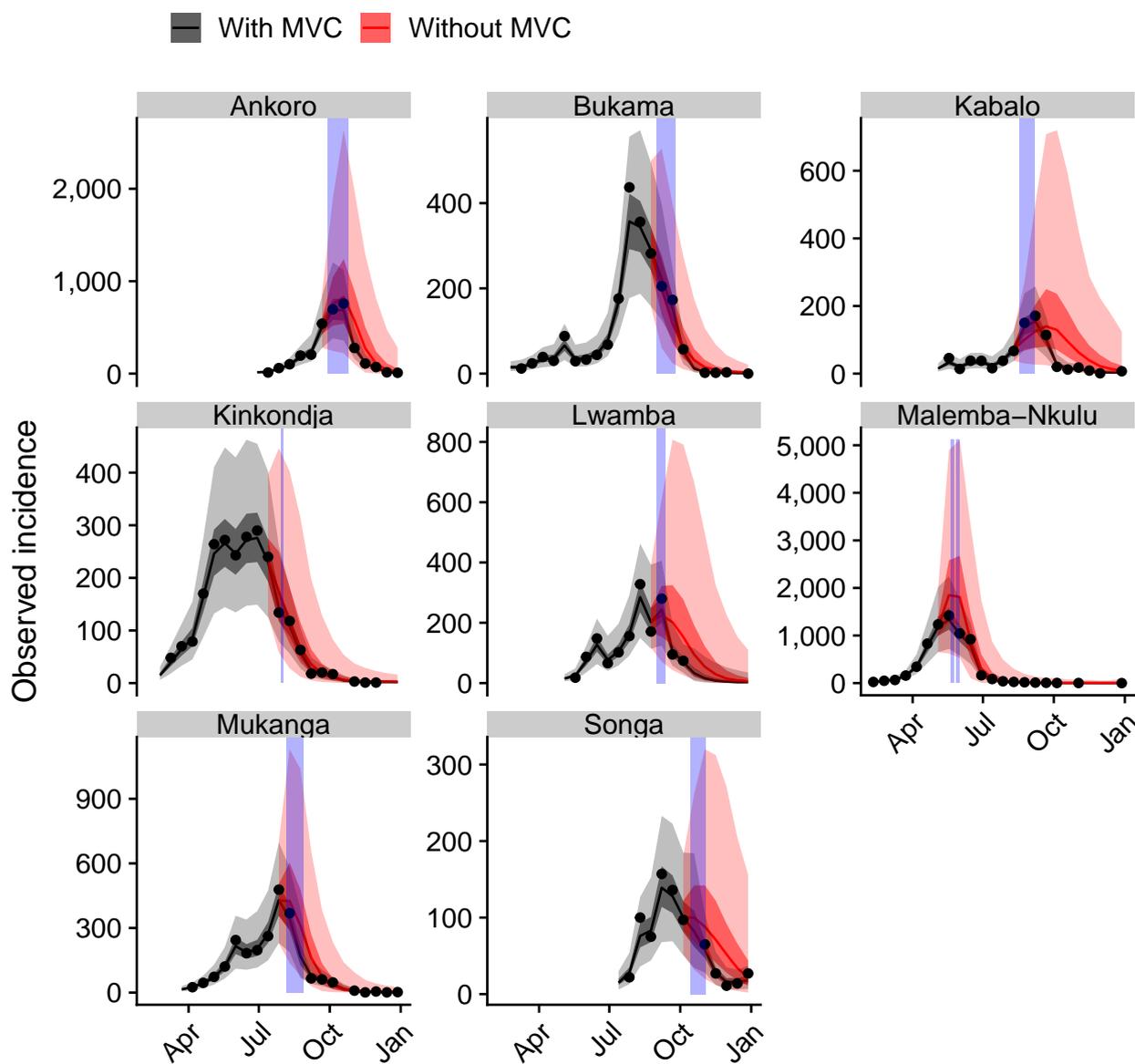


Figure 6: Model fits (black) to the 2015 data and counterfactual scenarios without mass vaccination campaigns (red). The data are shown as black dots, and periods of mass vaccination campaigns as blue vertical bars. Median fitted trajectories are shown as lines, 50% (dark grey) and 95% (light grey) credible intervals as shades.

Table 3: Summary of posterior estimates.

Parameter	Symbol	Posterior mean	(IQR)
Basic reproduction number	R_0	4.3	(4.0–4.5)
Overdispersion of transmission	m	0.17	(0.14–0.2)
Efficacy of campaigns (mean)	e_i	0.34	(0.14–0.48)
Background reporting	μ	1.4	(1.0–1.7)
Proportion initially immune (mean)	r_{0i}	0.55	(0.49–0.62)
Number initially infectious (mean)	I_{0i}	66	(46–78)
Proportion of cases reported (mean)	ρ_i	0.24	(0.19–0.29)
Overdispersion of reporting	ϕ	0.044	(0.022–0.061)

239 lute impact achieved by a mass vaccination campaign in the health zones investi-
 240 gated was in Malemba-Nkulu with 6800 (IQR: 4000–9100; 95% CI: 0–17,000) cases
 241 averted with 26,208 doses, while the greatest relative impact was in Kabalo with
 242 a 33% (IQR: 17%–54%; 95% CI: 0%–73%) reduction in case load from an estimated
 243 20,727 doses (Table 4). On the other hand, only 230 (IQR: 0–810; 95% CI: 0–2400) or
 244 2.4% (IQR: 0%–11%; 95% CI: 0%–29%) of cases were estimated to have been averted
 245 in Bukama from an estimate 31,400 doses. Speed of implementation of the mass
 246 vaccination campaign (or shorter delay to implementation) was highly correlated
 247 with a greater relative reduction of cases (Pearson’s $p = -0.85$, $p=0.008$).

Table 4: Absolute and relative impact of mass vaccination campaigns in different health zones. Estimates shown are posterior means. The delay shown in the last column is the number of weeks between the start of the outbreak (end of the first two-week period with more than 10 cases) and the beginning of the vaccination campaign.

Health zone	Doses (est.)	Cases averted	(IQR, 95% CI)	Relative reduction	(IQR, 95% CI)	Delay (weeks)
Ankoro	26,199	4800	(2200–7300, 0–12,000)	24%	(13%–37%, 0%–55%)	11
Bukama	34,100	230	(0–810, 0–2400)	2.4%	(0%–11%, 0%–29%)	25
Kabalo	20,727	3000	(1000–4700, 0–9100)	33%	(17%–54%, 0%–73%)	13
Kinkondja	20,792	510	(0–970, 0–2800)	5.5%	(0%–12%, 0%–29%)	20
Lwamba	44,148	3400	(870–5400, 0–12,000)	21%	(6.7%–35%, 0%–61%)	14
Malemba-Nkulu	46,330	6800	(4000–9100, 0–17,000)	23%	(16%–31%, 0%–47%)	14
Mukanga	30,133	2200	(670–3500, 0–6800)	15%	(5.7%–25%, 0%–44%)	17
Songa	19,660	970	(240–1500, 0–3300)	19%	(6.2%–32%, 0%–54%)	11

248 Discussion

249 In spite of repeated strategic and reactive vaccination campaigns, large measles out-
 250 breaks continue to occur in Katanga, DRC, causing significant morbidity and mor-
 251 tality. Strategies to mitigate the burden of measles are urgently needed. Here we
 252 conducted both predictive and retrospective modelling of the measles outbreaks in
 253 Katanga in 2015, with the aim to evaluate the impact of the vaccination response as
 254 well as potential for improvement.

255 The predictability of outbreaks is related to the quality of the available data. We
 256 found little relationship between reported administrative vaccination coverage and
 257 observed incidence. In fact, there was a small positive correlation, that is more cases

258 occur where vaccination uptake as indicated by the EPI programme is higher. This
259 could be because high routine vaccination rates might be an indicator of surveil-
260 lance quality and therefore case reporting. At the same time, Strategic Immunisa-
261 tion Activities were conducted across Katanga after the 2011 outbreak (Scobie et al.,
262 2015). We did not have access to any details of these campaigns, which may have
263 been targeted at areas with low reported vaccination rates, thus raising immunity in
264 those health zones. Not all of the suspected cases included in this study may have
265 been measles and instead have been misdiagnoses due to rubella or other causes of
266 rash (Graaf, 2015). While we included a parameter for misclassification in the mod-
267 elling analysis, this is difficult to identify and may be an underestimate. Lastly,
268 there is uncertainty around the population estimates used as denominator when
269 estimating coverage, as high rates of migration and urban growth make existing
270 data quickly outdated.

271 Vaccination rates as estimated from cluster surveys as part of the DHS pro-
272 gramme, on the other hand, were well correlated with case data, with higher vac-
273 cination rates corresponding to lower case burden. These estimates encompass
274 all vaccination activities and not just routine immunisation, and they do not suf-
275 fer from denominator issues caused by uncertainty in the population sizes within
276 health zones.

277 Reconstructing the outbreak with a mathematical model of the case trajectories
278 suggested that reactive mass vaccination campaigns reduced the case load substan-
279 tially, and more so the earlier it was implemented. We estimated that tens of thou-
280 sands of susceptibles were immunised during those campaigns and, consequently,
281 tens of thousands of cases averted in under-5 year olds. While the estimated over-
282 all proportion of doses that went to susceptibles may appear low at approximately
283 10%, this must be seen in the context of conducting vaccination campaigns during
284 ongoing outbreaks, where part of the population may already have been infected
285 and thus naturally immunised. In all health zones, we estimated that vaccines were
286 preferentially given to immune children, who may have been immunised through
287 routine vaccination, been targeted in previous campaigns, or infected and acquired
288 natural immunity during the ongoing or previous outbreaks. At the same time, the
289 estimated 21,000 cases averted correspond to a reduction in burden of over 20%. In
290 the health zones modelled, the case-fatality ratio in the reported data was 1.2%, sug-
291 gesting that around a hundred infant lives were probably saved by the campaigns.

292 Our transmission model suffered from several limitations. We did not have ac-
293 cess to an age breakdown of cases older than 5 years, and information on under-1
294 year olds was missing completely. Because of this, we only modelled transmission
295 in under-5 year olds. At 77% of reported cases, it seems safe to assume that trans-
296 mission in under-5 year olds was driving the outbreaks. The estimated basic re-
297 production number of 4.3 (IQR: 4.0–4.5) is small in comparison with other settings,
298 possibly because transmission does not occur in school-like settings with close mix-
299 ing of large numbers of children, but rather households and communities affecting
300 children before they reach school age.

301 The estimated impact of the campaigns might have been greater if cases averted
302 in over 5-year olds had been taken into account. We further ignored any spatial

303 progression of the outbreak or connectivity between health zones and modelled
304 each area in isolation. In reality, mass vaccination campaigns that reduced cases in
305 one area may well have prevented subsequent cases in nearby areas in other health
306 zones. Lastly, we assumed constant reporting rates. If, on the other hand, reporting
307 quality changes between regions or over time, it would affect our fits which would
308 interpret these changes as changes in transmission rather than reporting.

309 In spite of enormous efforts, measles is proving difficult to control in Katanga.
310 On the 10th June 2019, the DRC Ministry of Health officially declared a new measles
311 outbreak in 23 out of the 26 provinces of DRC, with initial cases for this outbreak
312 reported in late 2018. This new measles outbreak coincided with an ongoing Ebola
313 outbreak in the North Kivu and Ituri provinces of DRC which had begun in August
314 2018. There have been suggestions that the diversion of resources and attention
315 towards the Ebola response may have reduced the healthcare capacity required to
316 respond to a surge in measles cases (Arie, 2019). Although at the time of writing,
317 the health zones most affected by the measles outbreak were outside the area where
318 Ebola was mostly concentrated, it has been shown during the 2013–16 outbreak in
319 West Africa that reduced vaccination services as a result of an Ebola outbreak can
320 have a severe impact on measles circulation (Takahashi et al., 2015; Colavita et al.,
321 2017; Wesseh et al., 2017).

322 The ability to partly predict the case load in 2015 from outbreaks in 2010–13 at
323 the province level suggests that there might be underlying problems in the provi-
324 sion of routine immunisation services that did not change in the intervening time.
325 At the end of outbreaks as big as the ones occurring in Katanga, not many children
326 are left susceptible, whether a mass vaccination campaign has been conducted or
327 not. The fact that another big outbreak could happen so soon after the last suggests
328 a rapid increase in susceptibles that have not been served by the routine vaccina-
329 tion programme, and strengthening this should be a priority. At the same time, it is
330 clear that the mass vaccination campaigns only prevent part of the observed cases,
331 partly because of unavoidable delays in confirming an outbreak and launching a
332 campaign. Preventive strategies based on predictive models have a potential to
333 have a much greater impact if they can prevent outbreaks altogether, but their use
334 is based on the predictive potential of the models used. We found that vaccination
335 estimates based on a spatial model applied previously to vaccination survey data
336 was a good predictor of outbreak size at the relatively fine level of health zones.
337 There is enormous promise in using such estimates to guide strategic immunisa-
338 tion activities and close any existing gaps in immunity. As has been proven many
339 times over, it is only through strong and comprehensive routine vaccination, sup-
340 plemented by strategic campaigns where necessary, that sustained measles control
341 and, ultimately, elimination can be achieved.

342 **Ethics**

343 This research fulfilled the exemption criteria set by the MSF Ethics Review
344 Board (ERB) for a posteriori analyses of routinely collected clinical data and thus
345 did not require MSF ERB review.

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