Title: Effect of vaccinating health care workers to control Ebola virus disease: a modelling analysis of outbreak data

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Keywords: Ebola, vaccination, health care workers, outbreak control, public health

Abstract

Background

Health care workers (HCW) are known to be at risk of infection during Ebola virus disease outbreaks, particularly during the early phase before disease confirmation or protective measures. Therefore, HCW-targeted vaccination is being considered as a public health intervention: for individual protection, and to limit spread. There is an urgent need to quantify the effect of these vaccination strategies, including both direct and indirect effects of protection.

Methods

Using the timing, number, and ratio of HCW and community infections during twelve recent Ebola virus disease outbreaks, we defined two general types: 1: outbreaks where HCW amplified transmission; 2: outbreaks that do not show HCW amplification, but have higher community transmission. We generated a dynamic transmission model stratified into HCW and community members to explore the relative contribution of each group to transmission. We fitted the model to a type 1 outbreak, and calibrated the model to the type 2 pattern, and assessed the impact of HCW and community vaccination strategies in both.

Results

We found that in type 1 outbreaks, HCW have high transmission within HCW and to the community. Vaccination of HCW before the outbreak therefore has an outsize benefit on outbreak size, and requires few doses. Reactive-only vaccination strategies had little effect in the type 1 scenario, because of the rapid time course of these outbreaks. In contrast, in type 2 outbreaks, reactive community vaccination decreased the total number of cases, with or without HCW vaccination before the outbreak, although these strategies require many doses.

Conclusions

Vaccination of HCW ahead-of-time can be a useful strategy for combating Ebola virus disease outbreaks, especially when coupled with other interventions. Vaccination of HCW after an outbreak has started is likely to have little effect on overall transmission, but may help protect individual HCW.

Background

Since 1976, sub-Saharan Africa has been affected by more than 25 Ebola virus disease (EVD) outbreaks. The largest of these, the 2013-16 West African outbreak, resulted in more than 28,000 reported cases in Liberia, Sierra Leone and Guinea [1]. In this and in many other EVD outbreaks the incidence among health care workers (HCW) was higher than in the general population [2–6]. HCW are frequently in contact with patients, and are therefore at high risk of infection, especially before personal protective equipment is in use [7]. Furthermore, due to high rates of contacts within care facilities, and high-risk medical activities, HCW may transmit infection to co-workers, their patients [7] or others in the community. HCW are therefore a clear target for protection with vaccines, should those be licensed.

Mathematical models can be used to gain insight into key epidemiological drivers and to anticipate the consequences of potential control measures [9,10]. Numerous mathematical modelling studies of EVD have provided critical insight into transmission dynamics and interventions [9,11–15]. Few mathematical models have studied the role of HCW in EVD outbreaks, despite strong evidence that these individuals are at high risk during outbreaks [2–4,16]. The successful conclusion of the Guinea Phase III ring vaccine trial [17] raises the possibility that vaccines will be used to help mitigate future EVD outbreaks. Understanding the role of HCW in EVD transmission is crucial to properly assess the potential benefit of vaccination of HCW, so that appropriate policy decisions can be made once an EVD vaccine is available.

By generating a mechanistic transmission model that captures transmission within and between occupation groups, we are able to separately assess the effect of vaccination of HCW or the community, either before a simulated outbreak, or after the outbreak had started, with a single dose or prime-boost vaccine. We calibrated this model to observed patterns of infections from prior EVD outbreaks, which we determined fell into two general outbreak types. These types relate to the dynamics of HCW and community infections during each outbreak, and our model can generate outbreaks of both types. Our analysis therefore provides insight into the relative impact of different vaccination strategies, across the range of transmission scenarios observed in prior outbreaks.

Methods

Ebola Data

To determine the importance of HCW in transmission the occupation of each case is needed. However this information is rarely available for EVD outbreaks [8]. We used data for the twelve outbreaks where occupation of cases was recorded (Supplementary Section 1), and show the six most complete time series in the main text as examples: Bong County, Liberia (2014), Kenema district, Sierra Leone (2014), Kikwit, DRC (1995), Conakry (2014-15), Macenta (2014), and Gueckedou (2013-14) prefectures in Guinea (Figure 1).

Classification of EVD outbreaks into two types

We used the characteristics of the HCW infection dynamics to classify these twelve outbreaks into types. These were: i) the proportion of HCW infected through time; ii) the shape and timing of the cumulative distribution of HCW infections; iii) the weekly proportion of HCW infected, and iv) the total size of the outbreak (Figure 2) (Supplementary section S5). These four characteristics naturally separated the epidemics into two types, where in both, HCW were at high risk of infection due to their contact with EVD-infected patients. However, in type 1 outbreaks there was an early rapid increase in HCW incidence and in the cumulative proportion of HCW infected. In contrast, type 2 outbreaks exhibited a lower overall proportion of HCW infected, and a less obvious time period of high HCW incidence. The Kikwit outbreak is an exemplar of type 1 outbreaks, and therefore we explicitly fitted a transmission model to these data. Because the other datasets were not detailed enough to fit using the same modelling framework, we altered the parameters such that simulations of the calibrated model correspond to characteristics of type 2 outbreaks (Figure 2).

Kikwit outbreak data

In Kikwit (DRC, 1995) there were infrequent cases in rural areas around the city before introduction to Kikwit General Hospital on April 7th (Figure 1a) [6]. Haemorrhagic fever was diagnosed on May 2nd, EVD on May 8th, international assistance was initialised on May 10th, and further control measures started on May 12th (Supplementary Section S2). The final case died on July 16th, giving 317 cases reported, 248 deaths, and a case-fatality ratio of 78% [18].

For each case, there was occupation (either HCW, or non-HCW, which we called "community"); the occupation of their likely infector (obtained by real-time epidemiological investigation); date of onset, and date of recovery or death. There were some missing data in each field (Supplementary Section S2). We censored cases with date of onset before April 7th, when the first case was admitted to Kikwit General Hospital, which resulted in 284 cases, of

whom 73 were HCW (26%). For 191 cases, a likely infector was available. We computed 8 daily time series: six time series of onset dates stratified by case and infector occupation, and two time series of deaths stratified by case occupation. There was no significant difference in the probability of recording onset date by time, location or occupation (Supplementary section S2).

Transmission Model

We developed a deterministic compartmental model of EVD transmission stratified by occupation, where individuals were either HCW (h) or community (c) (Figure 3). On infection, cases leave the susceptible compartment (S), and enter the latently infected compartment (E), with duration in E drawn from an Erlang distribution with shape 2 and mean ϵ^{-1} [19]. Following the latent period, individuals become infectious and symptomatic (I), and recover (R) or die (D). We did not have specific information about funeral transmission in Kikwit, and thus we considered that all transmission events occurred from the I compartment (Supplementary Section S3). For each occupation we tracked the source of infection and so we defined four time-dependent transmission rates: $\beta_{t,ij}$, where infectious, i, and susceptible, j, are c or h. The model considers each outbreak as independent of other areas, i.e. no introduction of cases during the outbreak, and no movement into or out of the population.

To account for the effect of control measures such as: the arrival of protective equipment for HCWs, the opening of isolation wards, and population awareness of EVD, we used flexible time-dependent decreasing sigmoid functions for the transmissibility, $\beta_{t,ij}$:

$$\beta_{t,ij} = \beta_{t_o,ij}\left(1 - {}^{\delta_k}/_{1 + e^{-\alpha_k(t-T_k)}}\right)$$

where δ is the reduction in the transmission rate, α is the shape of the change in the transmission rate, $k = h$ if either i or j is h, and $k = c$ otherwise, t is time and is measured in days, and T is the midpoint of the time of change for each occupation group. The force of infection is $\lambda_{t,ij} = \beta_{t,ij}(I_i/N_j)$, where N_j is the population size of HCW (900) or community members (200,000) in Kikwit (Supplementary Section S2).

Parameter inference for type 1 outbreaks

We used a Bayesian framework to fit the model to the Kikwit data, using Metropolis-Hastings Markov chain Monte Carlo, and a negative binomial likelihood (Supplementary section S3.2) [20,21]. We fixed the case fatality ratio (CFR), and the fraction of onset and death dates recorded, to the observed values, and estimated the parameters for overdispersion of those fractions (Supplementary Table 1). We fixed the mean times from onset to recovery or death to values from Kikwit. We used non-informative priors for transmission rates, overdispersion,

sigmoid function parameters, and the number of exposed and infected individuals at the start of the study period (Supplementary section S4.2). Using the posterior distribution of the transmission parameters through time, we calculated the reproduction number by occupation of infector and infectee (R_{ij}), and the net reproduction number (R_n) using the next generation matrix (Supplementary section S3.1).

Calibration of type 2 outbreak scenario

Data from available type 2 outbreaks were too incomplete to fit the model. Therefore, we calibrated the transmission parameters of the model to reproduce the dynamics of type 2 outbreaks. These are characterised by a longer time period of HCW infections, and the epidemics are longer and larger in both occupation groups (Figure 2). This suggests sustained transmission, unlike in type 1 outbreaks. Therefore, we added sustained transmission between community members, between HCW, and from HCW to community members, and we used the uncertainty generated from fitting to Kikwit data to give credible intervals (CI) (R_{cc}=R_{hc}=R_{hh}=1.5 (1.33-1.75)). To match characteristics of longer and larger epidemics, we decreased the transmission parameters later and less abruptly than in the type 1 scenario (T_h=130, α_c=0.05). We maintained the time difference between the decrease in HCW-related and within-community transmission parameters as in the type 1 scenario, and therefore T_c=155 (148-163) days (Table 1).

Simulation of vaccination

We extended the model to include vaccination strategies for HCW and community and compared the impact of different vaccination strategies using stochastic simulations (Table 2). We used the uncertainty in estimates inferred from the Kikwit data in simulations of both type 1 and type 2 outbreaks. To allow close comparison, we simulated both in the same population size of 200,000 (similar to Kikwit in 1995).

We selected values of coverage for ahead-of-time strategies (50%, 30%, 10%) based on evidence o f high turnover of HCW in recently affected countries [22,23], and the possibility that protection could wane. For single-dose vaccine, efficacy was 90% (ν_p=0.9) and protection was reached after one week; for prime-boost vaccine, efficacy was 90% (ν_b=0.9), where 80% was reached one week after prime (ν_p=0.8), and boost was given 28 days after prime. Vaccination reduced susceptibility by (1-ν_p) or (1-ν_b) compared with unvaccinated individuals. Speed of reactive mass vaccination was 1500 people per day, which is an operational maximum supplied by field teams. Reactive vaccination continued until all HCW and 70% of community members were vaccinated, at the same rate for single dose and prime-boost vaccination.

In the type 1 scenario, simulated reactive strategies began on day 20 (April 27th), which is when health authorities were alerted to an outbreak of bloody diarrhoea in Kikwit [18]. This was earlier than detection of EVD, but we assumed that surveillance systems have been enhanced since 1995, and that EVD would be confirmed more quickly. For type 2 simulations, early transmission was much slower and had wide credible intervals. We therefore started reactive vaccination when the mean number of cases was similar to the type 1 outbreak on day 20, which was day 40 (median = 53 cases in type 1, 38 in type 2). At 40 days, no simulation of the type 2 scenario had more than 100 cases.

In ahead-of-time vaccination strategies of type 1 outbreaks the number of exposed and infected HCW at the start of the epidemic simulation were drawn from independent Poisson distributions with means equal to $(1-\nu_p)E_{0ch}(T_0)$, $(1-\nu_p)E_{0hh}(T_0)$ and $(1-\nu_p)I_h(T_0)$, and values drawn from the joint posterior distribution. For type 2 outbreaks, epidemics were seeded with 5 infected and 5 exposed community members.

We sampled 600 parameter sets from the joint posterior distribution and for each set generated 15 stochastic simulations. We compared the distribution of the number of cases in the set of simulations, and the time to extinction (0 individuals in *E* or *I*). We reported median and 95% CI for the difference between the baseline scenario without vaccination, and each vaccination scenario.

Results

Classification of outbreak types

Using four key characteristics of the transmission dynamics we classified twelve localised EVD outbreaks into two types (Figure 2 and Supplement S5). Kikwit, DRC (1995) and Bong County, Liberia (2014) are exemplar type 1 outbreaks, characterised by rapid infection of HCW, a higher proportion of HCW infected in total, shorter duration of HCW infections, and a smaller overall outbreak size. The outbreaks in Kenema district, Sierra Leone (2014), Conakry (2014-15), Macenta (2014), and Gueckedou (2013-14) prefectures in Guinea are examples of type 2 outbreaks. These showed HCW infections over a longer time period, a lower overall proportion of HCW infected, and larger total epidemic size. By classifying outbreaks under these broad types, we can determine the effect of HCW-targeted vaccination strategies under the range of observed transmission regimes.

Fit of model to outbreak data

Our fitted model captured the dynamics of EVD in Kikwit for each route of transmission (Supplementary section S4.1). We found that the initial reproduction numbers from HCW were high (median R_{hh}=2.68, R_{hc}=3.99) (Table 1 and Figure 4). In contrast, the within-community reproduction number was less than one, and therefore transmission was not sustainable. Although there was a low per capita rate of transmission from the community to HCW (median R_{ch}=0.16), this represents a considerable risk to HCW: on average, each eight community cases caused one HCW infection. Overall, the net reproduction number at the start of the study period was 2.98 (2.11-4.36), with a major contribution from HCW, despite their low number. The timing and shape of the decrease in transmission rate depended on the occupation of the case (Figure 4 and Table 1). We inferred an early and rapid decrease in HCW-related transmission however we find that within-community transmission changed several weeks later. The net reproduction number fell below one after 30 (27-35) days (Figure 4c). Stochastic simulations of the type 1 scenario resulted in 288 (180-406) cases (observed value = 284), and the final case was reported on day 115 (93-155) (Figure 5).

Simulations from type 1 and the type 2 parameter regimes generated outbreaks with similar features to observed outbreaks, matching patterns of cumulative proportion of HCW infected either through time or in total, as well as characteristics of number infected at each stage of the outbreak (Figure 2, Supplement S5.1). In the type 2 scenario the outbreak was larger than in type 1 (677 cases (133-3179)) and the epidemic lasted longer (203 (168-232) days). In the baseline simulation, 70 (41-105) HCW were infected in the type 1 scenario (observed value = 73), whereas 77 (5-431) HCW were infected in the type 2 scenario (Figure 5).

Comparison of vaccination strategies

Ahead-of-time vaccination strategies had greater effect in type 1 outbreaks, whereas reactive and combined strategies had greater effect in type 2 scenarios (Figure 5).

Ahead-of-time vaccination decreased the median number of cases in both scenarios, but the effect was much more pronounced in type 1 outbreaks, and depended on the coverage achieved: 50% coverage of HCW decreased the total number of cases (type 1: 121 (50-243), type 2: 468 (73-1808)). This strategy did not markedly shorten the outbreaks, and in type 2 scenarios, even at 50% coverage, there was a substantial probability of long and large outbreaks, where 46% of simulated outbreaks had more than 500 cases. At lower coverage, there was less impact on total cases or duration, but there was a decrease in the number of cases in HCW.

Reactive mass vaccination with single or prime-boost vaccine was of limited benefit either to the entire population (Figure 5a) or to HCW (Figure 5b) in type 1 outbreaks. In contrast, in the type 2 scenario, vaccination substantially decreased the total number of cases, and there were 385 (17-2455) fewer cases in the entire population. Of those, 63 (3-389) fewer cases were in HCW. Very few type 2 outbreaks generated large outbreaks with reactive mass vaccination (14% of simulations resulted in more than 500 cases). In both type 1 and 2 scenarios, the single dose vaccine resulted in fewer cases than prime-boost, because of the delay until the boost dose, although the difference was small: 3 (-26-35) cases in type 1, and 4 (0-22) in the type 2 regime.

Combined strategies decreased the number of cases and shortened the outbreak for all values of coverage. In the type 1 scenario, combined strategies did not decrease number of HCW cases compared with ahead-of-time HCW vaccination, because reactive strategies began too late to protect additional HCW. In the type 2 scenario, for all values of HCW coverage, the 95% CI excluded the baseline median (677 cases), and time-to-extinction was reduced. In contrast to the type 1 scenario, the combination strategies provide extra protection to HCW directly, because reactive campaigns prioritize HCW, and thus reduce transmission between HCW.

Discussion

We used as much information on HCW-related transmission as possible to classify outbreaks into two broad types: the first, where the infection is catalysed by HCW and community transmission is low, was observed in Kikwit (1995) and some prefectures of Guinea and counties of Liberia (2013-16); and the second, where there is high risk to HCW, but the epidemic is not amplified by their transmission, was observed in other prefectures/districts/counties of Guinea, Sierra Leone, and Liberia (2013-16). We used this to quantify the likely effect of HCW-targeted vaccination strategies before and during EVD outbreaks of both types.

Using a mechanistic transmission model stratified by occupation and route of transmission, we found that in type 1 outbreaks, ahead-of-time vaccination of HCW can have an outsize impact on the number of cases. Direct protection prevented infection of HCW, but also decreased their role in further spread. In these scenarios, where transmission is more dependent on the health care setting and perhaps, therefore more amenable to rapid decreases in transmission, there are limited additional benefits of reactive mass vaccination, both in

number of cases averted, and the duration of the outbreak. Indeed, the model suggests that ahead-of-time vaccination of health care workers, even at modest coverage (30% immunised) is more effective than mass vaccination in response to such outbreaks. Ahead-of-time health care worker vaccination strategies require many fewer doses than mass vaccination strategies.

In the type 2 scenario, where within-community transmission is above the epidemic threshold, and there is no early decrease in HCW-related transmission rate, ahead-of-time vaccination of HCW could still provide individual protection to HCW and had a modest impact on overall transmission. However, reactive community vaccination (with or without ahead-of-time HCW vaccination) is more effective under these circumstances as this contributes to reducing the reproduction number below one.

In all modeled scenarios, ahead-of-time vaccination of HCW provided direct protection for HCW, and also decreased the number of cases in HCW due to indirect protection. In this model, we used the effective vaccine coverage, because we could not distinguish 30% protection of all HCW from 100% protection of 30% of the HCW. Further information on the likely protective effect of available vaccines would allow more specific examination of this distinction.

Data from Kikwit (1995) are the best to study HCW transmission, because detailed information on most cases was available, including the likely source of infection. However, there were some missing data, and the suggested routes of infection may not be accurate. We did not consider transmission after death, which could affect the estimates of transmission rate.

This model framework was not able to test other potential vaccination strategies, such as ring vaccination, because we do not track specific contacts that individuals make. Our model assumed that individuals mix randomly within occupation groups, and there is no heterogeneity within groups. Despite this limitation, the general conclusions are robust to the precise value of the number of HCW, and the transmission values used in vaccination simulations.

Achieving ahead-of-time coverage may be challenging, due to high rates of turnover of health care staff, the large geographic area at risk of outbreaks, and because the duration of protection offered by vaccines is currently unclear. However, strategies that target HCW in

towns or cities nearby to an emerging outbreak are a potential way of achieving ahead-of-time coverage, at the same time as implementing enhanced protective measures.

Not all EVD outbreaks are of these two types, since there are not always HCW infections [24]. In those cases, vaccination of HCW would not assist in control. Collecting and publishing more detailed information on occupation of cases and the route of transmission in future EVD outbreaks would greatly improve our understanding of the epidemiology of this disease and the potential benefits from control measures targeted at different transmission routes.

Conclusions

In conclusion, ahead-of-time HCW vaccination decreases the number of cases seen, by directly protecting vaccinated HCW, and indirectly protecting non-vaccinated HCW and the community. Reactive community vaccination strategies may be required to control the outbreak when within-community transmission is intense. This analysis quantifies the impact of realistic and feasible vaccination strategies which may be implemented in the event of a future EVD outbreak.

List of abbreviations

EVD: Ebola virus disease

HCW: Health care workers

DRC: Democratic Republic of Congo

Declarations

Funding

AR[1] is supported by the Norwegian Institute for Public Health "A randomised trial of ring vaccination to evaluate Ebola vaccine efficacy and Safety in Guinea, West Africa". AC is funded by the Medical Research Council (MR/J01432X/1). RME and WJE were supported by the Innovative Medicines Initiative 2 (IMI2) Joint Undertaking under grant agreement EBOVAC1 (grant 115854). The IMI2 is supported by the European Union Horizon 2020 Research and Innovation Programme and the European Federation of Pharmaceutical Industries and Associations. AR[2] was supported by the Fischer Family Trust and MB by the National Institute for Health Research Health Protection Research Unit in Immunisation at the London School of Hygiene & Tropical Medicine in partnership with Public Health England. The views expressed are those of the authors and not necessarily those of the funders. The funders had no role in study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the paper for publication.

Authors' contributions

AR[1], RME, AC and WJE developed the analysis plan; JJMT, AR[2] and KS collected and cleaned data from 1995 Kikwit outbreak, and 2013-2016 Guinea outbreak; AR[1] implemented the analysis and ran the model, with contribution from AC; AR[1] and RME interpreted the results, wrote the first draft and the supplemental material. AC, WJE, MB, AR[2], JJMT, KS contributed to the manuscript. All authors approved the final version.

Acknowledgements

We acknowledge Sebastian Funk for technical support.

Availability of data and material

The datasets on Kikwit used and/or analysed during the current study are available from Dr Muyembe Tamfun on reasonable request. Data from Guinea are available from Dr Keïta on reasonable request. Datasets on other outbreaks are public data, and all sources are named in the text, and can be requested from the corresponding author.

Ethics approval

This study is a secondary analysis of previously collected data.

Consent for publication

Not applicable

Competing interests

RME and WJE were supported by the Innovative Medicines Initiative 2 (IMI2) Joint Undertaking under grant agreement EBOVAC1 (grant 115854). The IMI2 is supported by the European Union Horizon 2020 Research and Innovation Programme and the European Federation of Pharmaceutical Industries and Associations.

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Figure Legends

Figure 1. Incidence time series of EVD onset in five of the outbreaks used in the analysis. Daily incidence in Kikwit (DRC 1995, Panel A), Macenta (Guinea 2014, Panel B), Conakry (Guinea, 2014-2015, Panel D) and Gueckedou (Guinea, 2014, Panel E); Weekly incidence in Kenema (Sierra Leone, 2014, Panel C). Bong County, Liberia is not shown here because the data are infrequently reported making incidence estimation difficult. Cumulative statistics only are shown for Bong County.

Figure 2. Classification of EVD outbreaks into two types according to their dynamics. Dark grey marks the 95% CI in type 1 outbreak simulations, light grey areas correspond to 95% CI for type 2 outbreak simulations. A) Cumulative proportion of HCW among the total number of HCW infected through time. B) Weekly proportion of HCW among the total number of HCW infected in EVD outbreaks through time. C) Proportion of HCW infected through time. D) Distribution of the number of community cases, where vertical lines represent the number of community cases observed in each outbreak.

Figure 3. Schematic of the model structure. The population is stratified by occupation, so *i* and *j* are HCW (*h*) or community members (*c*). Individuals begin susceptible to infection (S_i), and on infection they enter an exposed class (E_i) split by the route of infection (E_{ii}, E_{ji}). There are 2 sequential *E* compartments so that the duration of the latent period is Erlang-distributed (see Methods). After the E_2 compartments, individuals enter the infectious compartment (I_i), and then die (D_i) or recover (R_i). The force of infection, λ, depends on the route of transmission. When vaccination campaigns are implemented, susceptible individuals can enter the prime ($V_{p,i}$) and boost ($V_{b,i}$) compartments, and are then subject to a lower force of infection equal to 1-vaccine efficacy (v_p or v_b).

Figure 4. Reproduction number trajectories used in simulation. A) HCW-to-community reproduction number (blue) and community-to-community (red) are given with mean and 50% and 95% CI.B) HCW-to-HCW reproduction number (blue) and community-to-HCW reproduction number (red) decrease at the same time, T_h. The horizontal line indicates R=1. C) The overall reproduction number trajectories combined all four trajectories (see Methods) in type 1 (dark grey) and type 2 (light grey) scenarios, with 50% and 95% CI.

Figure 5. Summary statistics of the stochastic simulations generated for each outbreak scenario. Upper panels show type 1 simulations, and lower show type 2. Number of cases in the entire population (A), number of cases in the 900 simulated HCW (B), and time to extinction (C) in the type 1 scenario; Number of cases in the entire population (D), number of cases in the 900 simulated HCW (E), and time to extinction (F) in the type 2 scenario. Rectangles show the 50% CI, with horizontal lines at the median, and arrows represent the 75% CI. Simulations without vaccination are shown in grey, and each colour represents a vaccination strategy: reactive mass vaccination with (a) prime-boost vaccine or (b) single dose vaccine; ahead-of-time HCW vaccination only, with coverage in HCW of (c) 10%, (d) 30% or (e) 50%; ahead-of-time HCW vaccination plus reactive mass vaccination, with coverage in HCW of (f) 10%, (g) 30% or (h) 50%. The 95% CI in each scenario are given in the Supplement (S6.5) Note different y-axes.

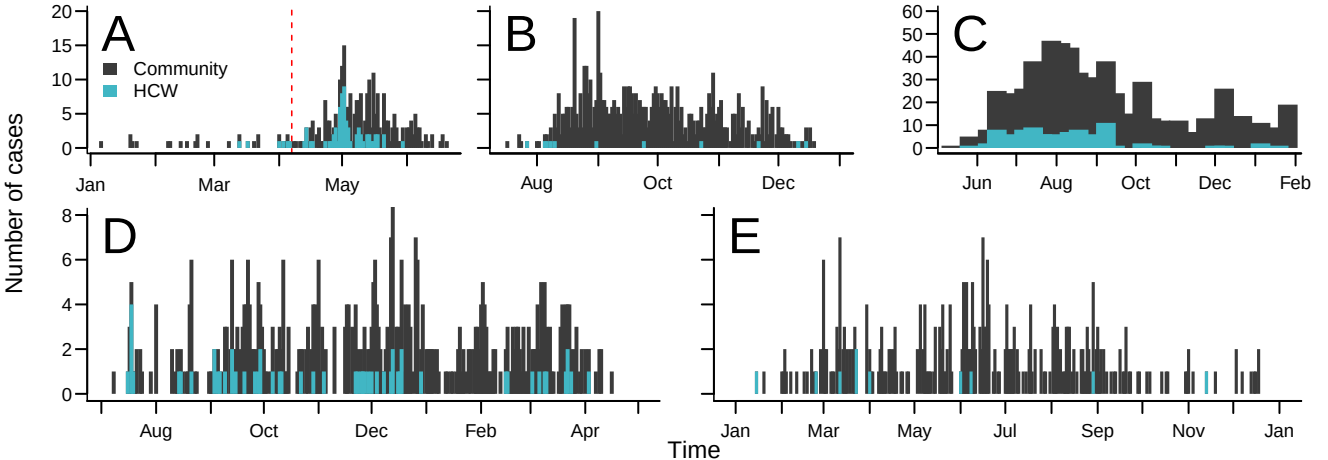
507 # Tables
508

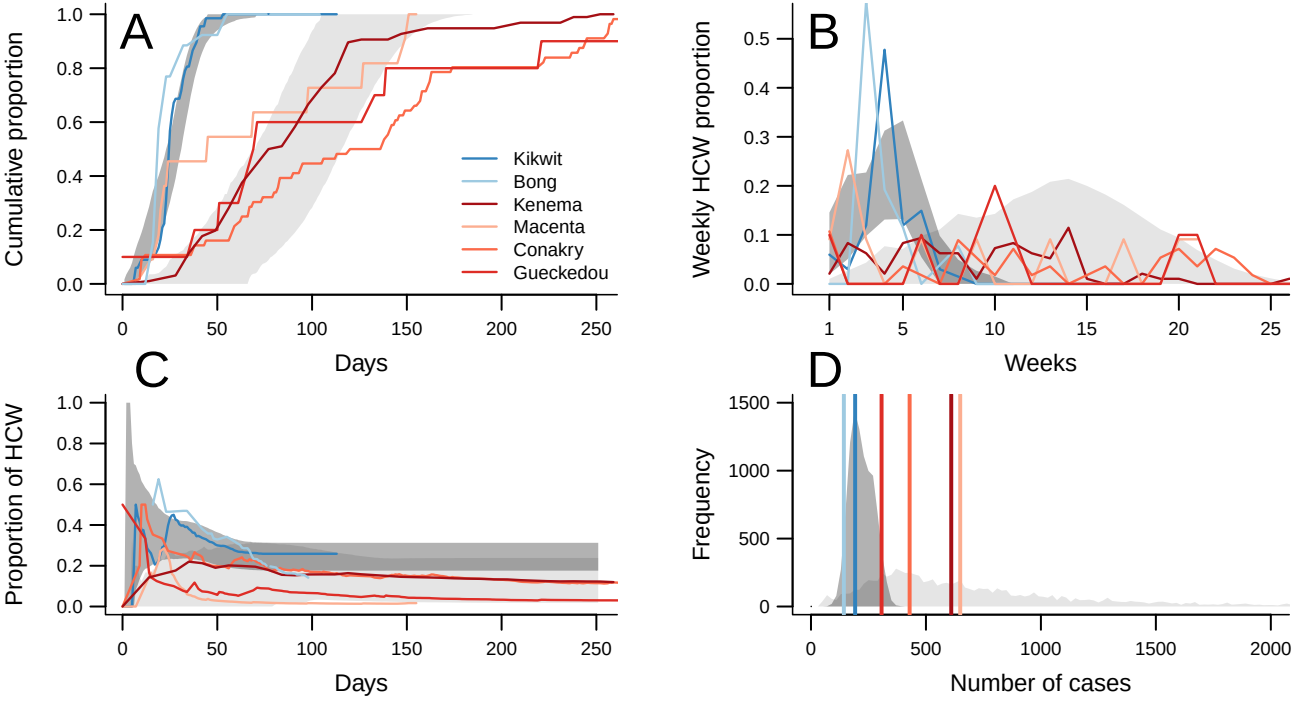
		hh	*ch*	*hc*	*cc*	**Overall**
Type 1 scenario	R_0	2.68 (1.83-4.01)	0.16 (0.05-0.37)	3.99 (2.47-6.29)	0.70 (0.53-0.95)	2.98 (2.11-4.36)
	T_{change} (days)	T_h = 30 (27-35)	T_h	T_h	T_c = 55 (50-62)	
	shape	α_h = 2.20 (0.23-4.83)	α_h	α_h	α_c = 2.49 (0.21-4.86)	
Type 2 scenario	R_0	1.50 (1.33-1.75)	0.16 (0.05-0.37)	1.50 (1.33-1.75)	1.50 (1.33-1.75)	1.99 (1.71-2.38)
	T_{change} (days)	T_h = 130	T_h	T_h	T_c = 155 (148-163)	
	shape	α_c = 0.05	α_c	α_c	α_c	

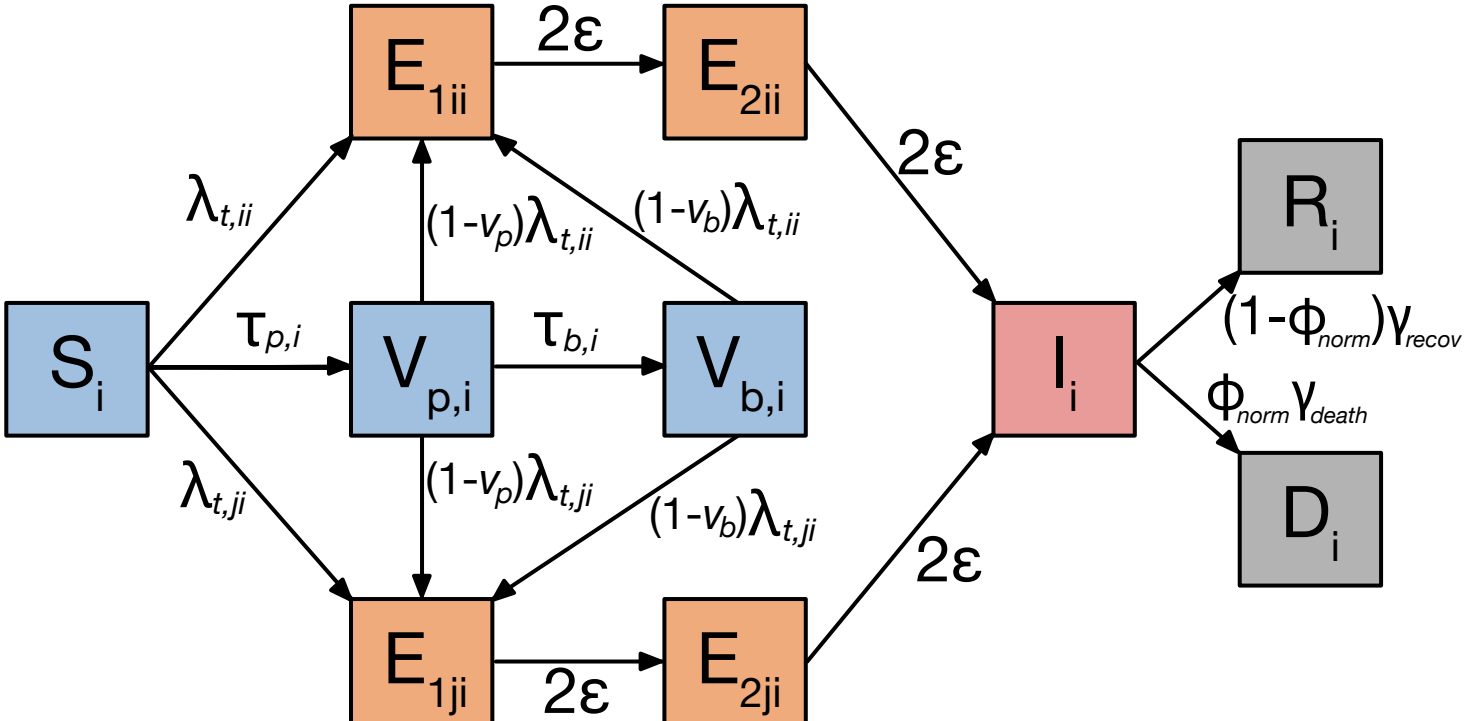
509 Table 1. Values of the reproduction number, time of change in transmission, and shape of the
510 decrease in transmission. Type 1 values are inferred from fitting the model to the Kikwit data. Type 2
511 values are used as described in Methods to simulate outbreaks. Mean values and 95% CIs are given.
512 Comparison of the R_0 trajectories is given in Supplementary Figure 5.2.
513
514

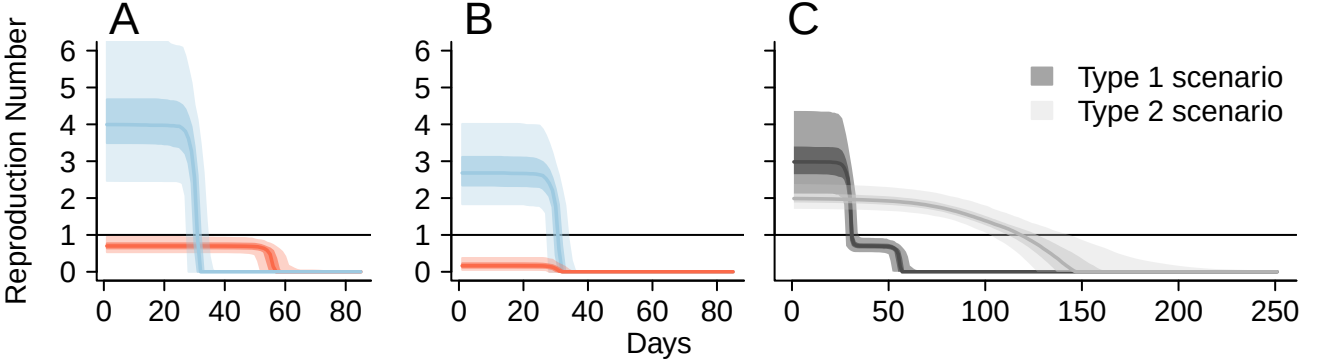
Strategy	**HCW ahead-of-time coverage**	**HCW reactive coverage**	**Community reactive coverage**	**Vaccine**
a	0%	100%	70%	Prime-boost
b		100%	70%	Single dose
c	10%			-
d	30%			-
e	50%			-
f	10%	100%	70%	Single dose
g	30%	100%	70%	Single dose
h	50%	100%	70%	Single dose

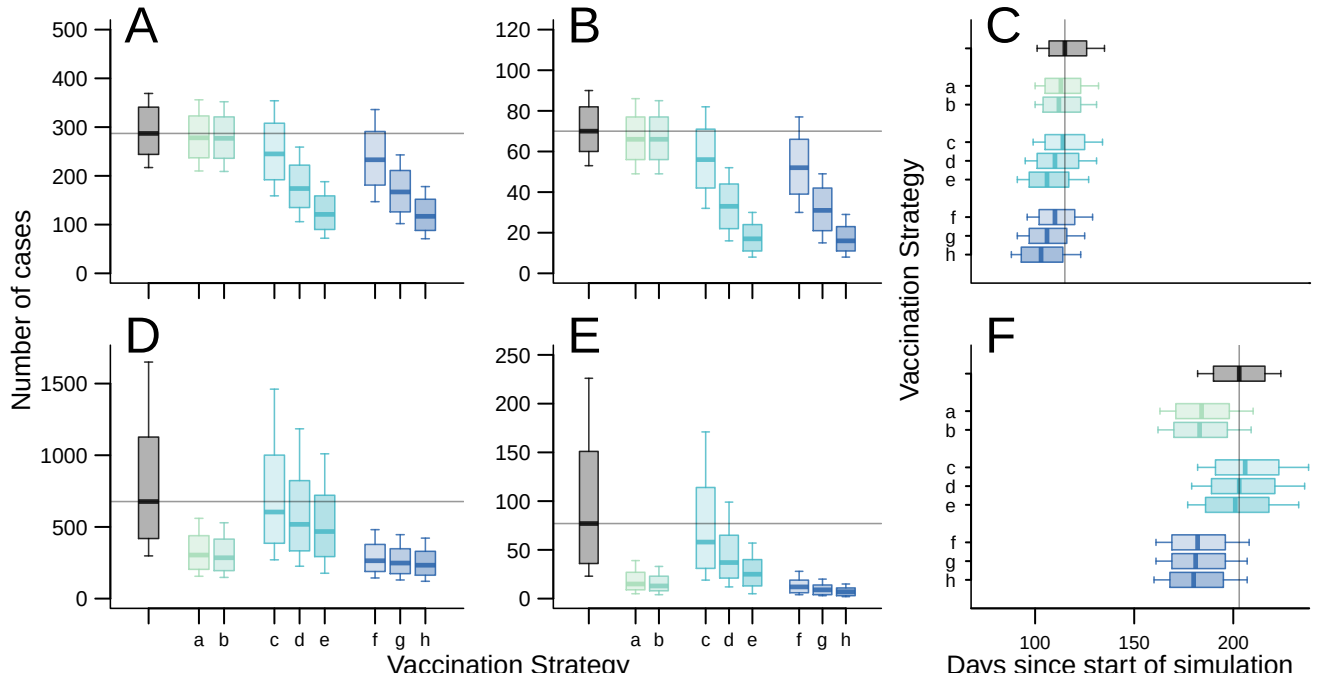
515
516 Table 2. Vaccination strategies tested in this analysis. We considered the following: i) reactive mass
517 vaccination of the population, prioritising HCW, with a prime-boost vaccine (strategy a), or a single
518 dose vaccine (strategy b); ii) ahead-of-time vaccination of HCW, with three levels of coverage: 10%
519 (strategy c), 30% (strategy d), or 50% (strategy e); iii) combined strategies of ahead-of-time
520 vaccination of HCW at three levels of coverage plus reactive mass vaccination of remaining HCW and
521 the community (strategies f, g, and h). We selected values of coverage that were realistic given high
522 HCW turnover in recently affected countries [22] [23], and the possibility of waning of protection.
523


A
B
C
D
E
Community
HCW
Number of cases
Time
Jan
Mar
May
Aug
Oct
Dec
Jun
Feb
Apr
Jul
Sep
Nov


A
Cumulative proportion
1.0
0.8
0.6
0.4
0.2
0.0
0
50
100
150
200
250
Days
Kikwit
Bong
Kenema
Macenta
Conakry
Gueckedou
B
Weekly HCW proportion
0.5
0.4
0.3
0.2
0.1
0.0
1
5
10
15
20
25
Weeks
C
Proportion of HCW
1.0
0.8
0.6
0.4
0.2
0.0
0
50
100
150
200
250
Days
D
Frequency
1500
1000
500
0
0
500
1000
1500
2000
Number of cases


S_i
E_{1ii}
E_{2ii}
$V_{p,i}$
$V_{b,i}$
E_{1ji}
E_{2ji}
I_i
R_i
D_i
2ε
$\lambda_{t,ii}$
$(1-v_p)\lambda_{t,ii}$
$(1-v_b)\lambda_{t,ii}$
$\tau_{p,i}$
$\tau_{b,i}$
$\lambda_{t,ji}$
$(1-v_p)\lambda_{t,ji}$
$(1-v_b)\lambda_{t,ji}$
$(1-\phi_{norm})\gamma_{recov}$
$\phi_{norm}\gamma_{death}$


A
B
C
Reproduction Number
Days
Type 1 scenario
Type 2 scenario
0
1
2
3
4
5
6
0
20
40
60
80
0
50
100
150
200
250


A
B
C
D
E
F
Number of cases
Vaccination Strategy
Days since start of simulation
a
b
c
d
e
f
g
h
100
150
200