Vaccination of health care workers to control Ebola virus disease

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Abstract

Background

Health care workers (HCW) are known to be at risk of infection during Ebola virus disease outbreaks, particularly during the early phase when the disease may not have been confirmed or protective measures are not yet implemented. Therefore, vaccination of HCW is currently being considered as a public health intervention, both for personal protection, and to limit outbreak spread. There have not yet been mathematical modelling studies of such interventions, which can integrate both the direct and indirect effects of vaccination to fully quantify their effect.

Methods

We studied the dynamics of HCW infections during the 1995 Kikwit outbreak in the Democratic Republic of Congo, and during the 2013-16 West Africa outbreak. We generated a mathematical model that includes different rates of transmission for community and HCW, and the effect of control measures and behavioural change during the outbreak. We generalised the model to explore an higher transmission regime that more closely resembles the patterns seen in the West African outbreak, and assessed the impact of vaccination strategies targeting key groups.

Findings

We found that vaccination of health care workers ahead-of-time can greatly diminish the size and duration of outbreaks, but the benefit is dependent on the degree of community transmission. When within-community transmission is sustained, vaccination of the community is required to shorten the outbreak, and decrease the number of cases.

Interpretation

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 HCW.

Research in context

Evidence before this study

There are still no licensed vaccines for use against EVD. However, the results of the Guinea ring vaccination trial raises the possibility that vaccines can be used to control future outbreaks. Although health care workers (HCW) are known to be at risk during Ebola virus disease (EVD) outbreaks, there is no direct evidence of the effect of vaccinating HCW to mitigate outbreaks.

Added value of this study

Mathematical models can be useful tools to help draw together evidence and project the likely impact of different interventions. We developed a model of community and HCW transmission and fitted it to the best available outbreak data. We assessed the impact of vaccination strategies targeting HCW and community members, to quantify the impact of vaccination.

Implications of all the available evidence

We found that vaccination of HCW ahead-of-time can diminish the size and duration of outbreaks, as well as protecting the HCW themselves. The overall effect is dependent on the degree of within-community transmission. Reactive vaccination in response to an outbreak is likely to be much less effective at protecting HCW.

Introduction

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]. Several studies reported that the incidence of EVD among health care workers (HCW) was higher than in the general population [2][3][4][5], as in other outbreaks [6]. Since HCW are frequently in contact with patients, they are 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 their patients [7] or others in the community. For instance, in the outbreaks from the Democratic Republic of Congo (DRC) where the occupation of cases was reported, between 17 and 27% were HCW [8].

Mathematical models can be used to gain insight into the key drivers of outbreaks, 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], [12][13] [14][15]. Few mathematical models have studied HCW, despite strong evidence that these individuals are at high risk during EVD outbreaks [2] [3][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 decisions can be made once an EVD vaccine is available.

Methods

To determine the role that HCW play in transmission of EVD it is necessary to have - as a minimum - data on the occupation of each case. Such data are not available for many previous outbreaks [6]. The detailed dataset collected during the 1995 Kikwit outbreak in DRC does, however, provide an opportunity to quantify the role of HCW in the spread of that epidemic. To help generalise the results to other settings, we also developed a scenario that is informed by the transmission pattern in Guinea during the 2013-16 West African outbreak, where a lower fraction of cases were HCW and there was evidence of greater community transmission (Figure 1). The development of these scenarios is described below.

Kikwit outbreak data

Between January and July 1995, an outbreak of EVD occurred in Kikwit, DRC (Figure 1a)[6]. From January to April, there were infrequent cases in rural areas surrounding the city before introduction to Kikwit General Hospital on April 7th (Supplementary Section S1). Haemorrhagic fever was diagnosed on May 2nd, and on May 10th international assistance was initialised. Confirmation of EVD occurred on May 8th, and further control measures started on May 12th. The final case died on July 16th, giving 317 cases reported, 248 deaths, and a case-fatality ratio of 78% [18].

We used the following data available from a line list of EVD cases: their occupation (either HCW, or non-HCW, which we called "community"); the occupation of their likely infector (obtained by real-time epidemiological investigation); their date of onset, and date of recovery or death. There was some missing data in each field (Supplementary Section S1). We censored cases with symptom onset before April 7th, when the first case was admitted to Kikwit General Hospital, which results in 284 cases, of whom 73 were HCW (26%). For 191 cases, a likely named infecting individual and their occupation was available. We therefore computed eight daily time series: 6 time series of symptom onset date stratified by case and infector occupation, and two time series of deaths stratified by case occupation. We assumed the probability of recording onset date did not depend on time, location or occupation.

Kikwit had an approximate population of 200,000 in 1995 [19], and 429 HCW were employed at Kikwit General Hospital [20], which was the largest of its two hospitals. By 2003, 1047 HCW were employed in these two hospitals [21]. There was no information on the total number of HCW in other health care facilities surrounding Kikwit, therefore, based on this evidence we estimated there were 900 HCW in Kikwit in total in 1995. Our findings were not sensitive to this assumption (Supplementary Section S4.9).

Transmission Model

We developed a deterministic compartmental model of EVD transmission stratified by occupation, where the population is either HCW (h) or community (c) (Figure 2). On infection, cases leave the susceptible compartment, S, and enter an incubation period that follows an Erlang distribution with shape 2 and mean ϵ^{-1}, which is a more biologically realistic distribution than an exponential distribution [27]. 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 while in the I compartment. Finally, for each population (HCW and community) 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 equations of the model are displayed in Supplementary Section S3.2.

To account for the effect of control measures such as the arrival of new protective equipment for HCWs, the opening of isolation wards, population awareness of the disease, and the communication campaign in the population, we used flexible occupation-specific time-dependent decreasing functions for $\beta_{t,ij}$, modelled by a sigmoid function:

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

where $k = h$ if either i or j is h, and $k = c$ otherwise, and t is measured in days. The force of infection $\lambda_{t,ij} = \beta_{t,ij}\left(I_i/N_j\right)$. Where N_j is the total population size of HCW (900) or community members (200,000).

Parameter inference

We used a Bayesian framework to fit the model to the eight time series, using Metropolis-Hastings Markov chain Monte Carlo, and a negative binomial likelihood [28] [29](Supplementary section S3.2). We fixed the CFR, and the fraction of onset and death dates recorded for each occupation class to the observed values, and estimated their overdispersion parameters. There was no significant difference between occupations in completeness of dates, so we used the same fractions and CFR for HCW and community infections. The mean times from onset to recovery or death were fixed using estimates from the data (Table 1). We used flat priors for the transmission rates, overdispersion and 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 for each route of infection (R_{ij}), and the net reproduction number (R_n) using the next generation matrix (Supplementary section S3.1).

Transmission regimes in other outbreaks

The outbreak in Kikwit was brief in comparison with the 2013-16 West Africa epidemic. In the recent outbreak, outside of large cities the typical transmission pattern was for

overlapping outbreaks on the order of months occurring in many geographic regions (Supplementary section S2). Daily case incidence from three exemplar regions, one in Guinea (Figure 1c), Sierra Leone (Figure 1b), and Liberia (Figure 1d), show a similar pattern to that seen in Kikwit, namely a fairly short outbreak, with a high proportion of HCW infected early in the outbreak (Supplementary section S2). However, the Guinea time-series show sustained transmission in the community, which is not observed in Kikwit. In Liberia, the epidemics more closely resemble the Kikwit outbreak. In Sierra Leone, the longer outbreak in Kenema has a high fraction of HCW infected, especially early, although the percentage is not as high as the other examples. In all three settings, although data is available on occupation of cases, the records are less complete than in Kikwit, and do not provide infector-infectee pairs.

Since data from West Africa did not provide the same detailed information on transmission routes as in Kikwit, it was not possible to use the same modelling framework to study both epidemics. Therefore, we modified the model, so that it was applicable to a broader transmission regime that was not amplified by HCW-mediated transmission. We removed time dependencies in transmission changes inferred from Kikwit, and because there was better evidence of sustained community transmission in West African outbreaks, this regime has a within-community reproduction number with mean = 1.5, similar to values inferred in other studies [13][30][31]. We altered the between-occupation reproduction numbers to prevent HCW-mediated transmission from driving the epidemic. This allowed us to quantify the role of HCW vaccination under broad, but justifiable, modes of transmission in the population. We used the uncertainty in estimates inferred from the Kikwit data in the higher transmission scenario. To allow close comparison, we simulated this “prolonged-transmission” scenario in the same population size as the Kikwit simulations.

Vaccination strategies

We extended the model to include vaccination of HCW and community populations and compared the impact of different vaccination strategies using stochastic simulations. We considered the following strategies: i) reactive mass vaccination of the population, prioritising HCW, with a prime-boost vaccine (strategy a), or a single dose vaccine (strategy b); ii) ahead-of-time vaccination of HCW, with three levels of coverage: 10% (strategy c), 30% (strategy d), or 50% (strategy e); iii) combined strategies of ahead-of-time vaccination of HCW at three levels of coverage plus reactive mass vaccination of

203 remaining HCW and the community (strategies f, g, and h). We selected values of
204 coverage that were realistic given high HCW turnover in recently affected countries [32]
205 [33], and the possibility of waning of protection.
206
207 For single-dose vaccine, efficacy was 90% (ν_p=0.9) and protection is reached after one
208 week; for prime-boost vaccine the efficacy was 90% (ν_b=0.9), where 50% was reached
209 one week after prime (ν_p=0.5), and boost is given two weeks after prime. Vaccination
210 reduces susceptibility by (1- ν_p) or (1- ν_b) compared with unvaccinated individuals. The
211 rate of mass vaccination, τ, was equivalent to vaccination of 15,000 people per day,
212 which is an operational value supplied by field teams. Vaccination proceeded until the
213 whole population was vaccinated, and was the same rate for single dose and prime-
214 boost vaccination.
215

216 ## Stochastic simulation of vaccination

217 We sampled 600 parameter sets from the joint posterior distribution and for each set
218 we generated 15 stochastic simulations. We compared the distribution of the number of
219 cases generated in the set of simulations, and the time to extinction (no individual left
220 infected or exposed). We assessed the effect of different vaccination strategies by
221 comparing to the baseline simulation, and reported median and 95% credible intervals
222 (CI) for these distributions.
223
224 All simulated reactive mass vaccination scenarios began vaccination on day 20 (April
225 27th), which is when health authorities were first alerted to an outbreak of bloody
226 diarrhoea [18]. This was earlier than detection of EVD in Kikwit, but to ensure that our
227 results are relevant to the current context, we assumed that surveillance systems have
228 been enhanced since 1995, and therefore EVD would be detected more quickly. In
229 ahead-of-time vaccination schemes the number of exposed and infected HCW at the
230 start of the epidemic simulation were drawn from independent Poisson distributions
231 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
232 from the joint posterior distribution.
233

Results

Transmission parameters

Our model captured the dynamics of EVD in Kikwit for each route of transmission (Figure 3 and Supplementary section S6). We found that the initial reproduction numbers involving HCW as index case were high (Table 2). 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, this represents a considerable risk to HCW: on average, each eight community cases caused one HCW infection. Overall, the reproduction number at the start of the study 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 3 and Table 2). We inferred an early and rapid decrease in HCW-related transmission. This estimate is consistent with epidemiological reports of this outbreak: clinical diagnosis of viral haemorrhagic fever was established in early May. In contrast, we find the within-community parameters change several weeks later. The overall reproduction number fell below one after 30 (27-35) days (Figure 3d), and so the epidemic began to decrease.

At the start of the study we estimated that there were 23 (14-36) community and 10 (5-18) HCW exposed or infectious across all simulations. These results suggest EVD was present in Kikwit before 7th April (day 0).

Simulations without vaccination

Stochastic simulations in the Kikwit scenario resulted in 288 (180-406) cases (observed value = 284), and the final case was reported on day 115 (93-155) (Figure 4). As described, we defined the prolonged-transmission scenario with sustained community transmission, and a later change in behaviour (Table 2). In the prolonged-transmission scenario the outbreak was larger (900 cases (430-1306)) and the epidemic lasted longer (137 (115-181) days).

In the baseline simulation, 70 (41-105) HCW are infected in the Kikwit transmission regime (observed value = 73), whereas 267 (125-548) HCW are infected in the

prolonged-transmission regime (Figure 5). This represents 30% (14-61%) of all HCW in the simulation.

Ahead-of-time vaccination of health care workers

In both transmission regimes, the effect of ahead-of-time HCW vaccination on total number of cases depended on the coverage achieved, where coverage is either due to staff turnover since vaccination, or waning of protection (Figure 5). 50% coverage of HCW decreased the total number of cases (Kikwit: 121 (50-240), prolonged-transmission: 277 (130-528)) but did not markedly shorten the outbreaks. However, the total number of HCW infected was much higher in the prolonged-transmission regime (42 (10-118) compared with 17 (3-39) in the Kikwit scenario) (Figure 5).

At lower coverage of HCW, there is less impact on the total number of cases or duration, but this intervention decreases the number of cases in HCW (Figure 5). In strategies with 10% or 30% coverage, there was a small decrease in the time to extinction and total number of cases. Simulated outbreaks resulted in 244 (101-427) in and 174 (69-327) cases respectively in the Kikwit scenario, and a similar incremental percentage of cases was averted in the high transmission scenario (Supplementary section S4.5).

Reactive mass vaccination

In the Kikwit scenario, reactive mass vaccination was of limited benefit either to the entire population (Figure 5a) or to HCW (Figure 5b). The single dose reactive mass vaccination strategy resulted in 63 (25-110) fewer cases. Since the decrease in HCW transmission inferred in the model (T_h) occurred early, reactive vaccination - even when HCW were prioritised - did not reduce the number of HCW infected.

In contrast, in the prolonged-transmission scenario, vaccination substantially decreased the total number of cases. There were 487 (246-989) fewer cases in the entire population, as well as 193 (69-434) fewer cases in HCW. This difference was driven by prioritisation of HCW for vaccination, and because rapid mass vaccination quickly decreased within-community transmission.

In both scenarios, the single dose vaccine resulted in fewer cases than prime-boost, due to the two-week delay until the boost dose, although the difference was fairly small: 19 (3-43) cases in Kikwit, and 96 (41-184) in the prolonged-transmission regime.

Combined vaccination strategies

In combination strategies we found a decreased number of cases in both HCW and the population as a whole, and an earlier time of epidemic extinction for all values of coverage in both transmission regimes (Figure 5).

In Kikwit, greater than 30% coverage in HCW resulted in the 95% CI of simulated values excluding the median number of the baseline simulation, and the outbreak was shorter than the baseline (extinction on day 96 (72-135)). There is little additional benefit to HCW of combined strategies, compared with ahead-of-time HCW vaccination, because the reactive campaign begins too late to protect unvaccinated HCW.

In the prolonged-transmission scenario, for all values of HCW coverage the 95% CI excluded the baseline median (900 cases), and baseline lower CI (430 cases). The time-to-extinction is reduced for all levels of coverage, but the 95% CI do not exclude the median of the baseline. In contrast to the Kikwit scenario, the combination strategies provide extra protection to HCW directly, because reactive campaigns prioritise HCW, and thus reduce transmission between HCW.

These results suggest combined strategies can decrease the number of cases, even at low HCW coverage, especially in prolonged-transmission scenarios, when coupled with the change in transmission rate in the model.

Discussion

Using a model of EVD transmission stratified by occupation and route of transmission, we have investigated the likely impact of HCW vaccination strategies during outbreaks.

In transmission regimes that resemble the outbreak in Kikwit – where the community reproduction number was below 1 throughout the epidemic and HCW appeared to have catalysed transmission into the community – ahead-of-time vaccination of HCW can

have an outsize impact on the number of cases. Direct protection of HCW may prevent their infection by hospitalised cases, and decrease their role in further spread. In these scenarios, where spread 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 prolonged-transmission scenario, within-community transmission is above the epidemic threshold, and HCW act in a similar manner to community members, with no early decrease in HCW-related transmission rate. In transmission regimes like this, ahead-of-time vaccination of HCW can still provide individual protection to HCW and have a modest impact on overall transmission. However, reactive community vaccination is more effective under these circumstances as this helps to reduce the within-community reproduction number to less than one. It is of note that the total number of HCW infected in the prolonged-transmission scenario is vastly higher than in the Kikwit scenario because HCW remain at high risk of infection, even if they are not catalysing the outbreak, because of the much larger within-community epidemic. In prolonged-transmission scenarios, combined strategies give the largest reduction in cases.

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

The data from Kikwit are the best available for analysis of HCW transmission, because the occupation, plus the likely source of infection are given for most cases, and dates of symptom onset and death or recovery are by day. However, there are some missing data, and the suggested routes of infection may not be complete. We do not consider transmission after death, which could affect the estimates of transmission rate. Our methods assumed that individuals mix randomly within occupation groups, and there is

no heterogeneity within groups. Despite these limitations, the general conclusions are robust to the precise value of the number of HCW, and the transmission values used in vaccination simulations. No such detailed data are available from the West African outbreak. Instead, we had to construct a scenario that approximated the epidemiological situation in which HCW played a less significant role in transmission, and community transmission was higher. The observed patterns seen in West Africa lie between these two scenarios, where HCW are at high risk of infection, but there is evidence of longer sustained transmission in the community, although on a local level are somewhat more similar to the Kikwit transmission regime. Therefore these scenarios can be viewed as the range of expected effects of health care worker vaccination. Collecting and publishing more detailed information on the route of transmission in future EVD outbreaks would greatly improve our understanding of the epidemiology of this disease and the potential benefits that might accrue from control measures targeted at different transmission routes.

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 mass vaccination strategies may be required to control the outbreak when within-community transmission is intense.

Contribution of authors

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.

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415 Declaration of Interests

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420
421

422 Figure Legends

423
424 Figure 1. A) Daily incidence time series of EVD onset during the 1995 EVD outbreak in Kikwit
425 (population≈200,000), stratified by occupation. The red line marks the start date of the study. B)
426 Weekly incidence time series of reported EVD onset in Kenema, Sierra Leone in 2014-15 (population-
427 609,873 [22], C) Daily incidence time series of EVD onset in Macenta prefecture, Guinea in 2014-15
428 (population=278,456 [23]), D) daily incidence time series of EVD onset in Bong County, Liberia in 2014
429 (population=328,919 [24]). All are stratified by occupation, and inset shows cumulative proportion of
430 HCW infected during the outbreak. Data from Sierra Leone are from [25], from Guinea are from the
431 Guinean Ministry of Health patient database, and from Liberia from a curated database of public
432 reports [26].
433
434
435 Figure 2. Schematic of the model structure. The population is stratified by occupation, so *i* and *j* are
436 HCW (*h*) or community members (*c*). Individuals begin susceptible to infection (S_i), and on infection
437 they enter an exposed class (E_i) split by the route of infection (E_{ii}, E_{ji}). There are 2 sequential *E*
438 compartments so that the duration of the latent period is Erlang-distributed (see Methods). After the
439 E_2 compartments, individuals enter the infectious compartment (I_i), and then die (D_i) or recover (R_i).
440 The force of infection, λ, depends on the route of transmission. When vaccination campaigns are
441 implemented, susceptible individuals can enter the prime ($V_{p,i}$) and boost ($V_{b,i}$) compartments, and
442 are then subject to a lower force of infection equal to 1-vaccine efficacy (v_p or v_b).

443
444 Figure 3. Posterior model fit for daily community onset (A) and HCW onset (B), showing observed data
445 from Kikwit (black), posterior mean (solid), median (dashed), 50% CI (dark) and 95% CI (light). Note
446 that model is fitted to 8 time series (Supplementary Section S4.1), but aggregated incidence plots are
447 given here for clarity. Model-inferred posterior reproduction number trajectories where community
448 members are infected (C) and HCW are infected (D). In C) the HCW-to-community reproduction
449 number (dark) and community-to-community (light) are given with mean and 50% and 95% CI. D) In

D) the HCW-to-HCW reproduction number (dark) and community-to-HCW reproduction number (light) decrease at the same time, T_h. The horizontal dashed line indicates the epidemic threshold, when R=1. The overall reproduction number combines all four reproduction number trajectories (E). Inset figures on C, D, and E show the corresponding trajectories for the prolonged-transmission regime. This scenario used the uncertainty and correlation structure of the relatively low-transmission Kikwit scenario, but had higher values of community-to-community transmission, and did not feature HCW as "catalysers" of the epidemic.

Figure 4. Simulated epidemics under the baseline scenario without vaccination (grey), and with three vaccination scenarios (colours). A and B show incidence and cumulative number of cases in the Kikwit scenario, for HCW and community members combined. C and D show under the prolonged-transmission regime. Note different y-axis.

Figure 5. Summary statistics of the stochastic simulations generated for each scenario. Number of cases in the entire population (A), number of cases in the 900 simulated HCW (B), and time to extinction (C) in the Kikwit 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 prolonged-transmission scenario. 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%. Note different y-axes.

A

Community
HCW

HCW Proportion

B

HCW Proportion

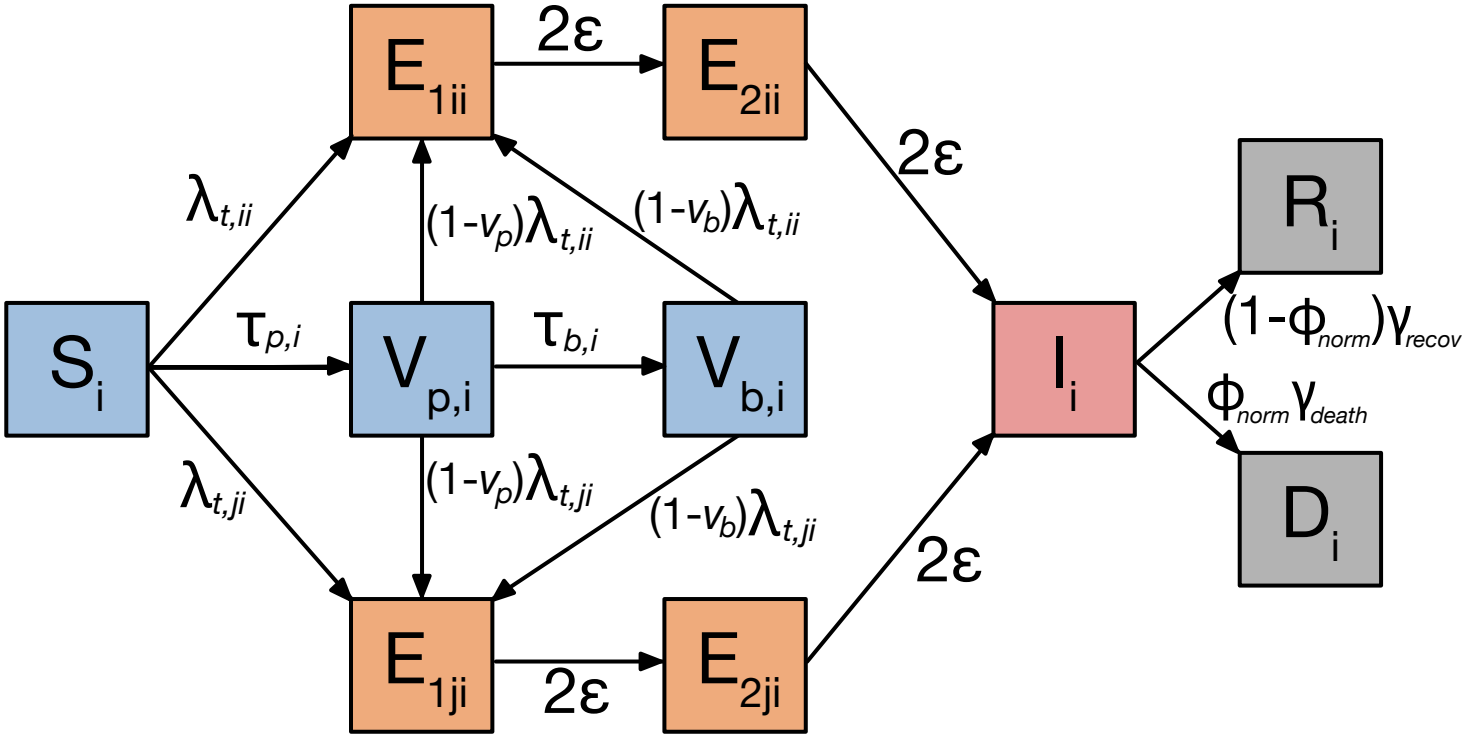
Number of cases per day or week

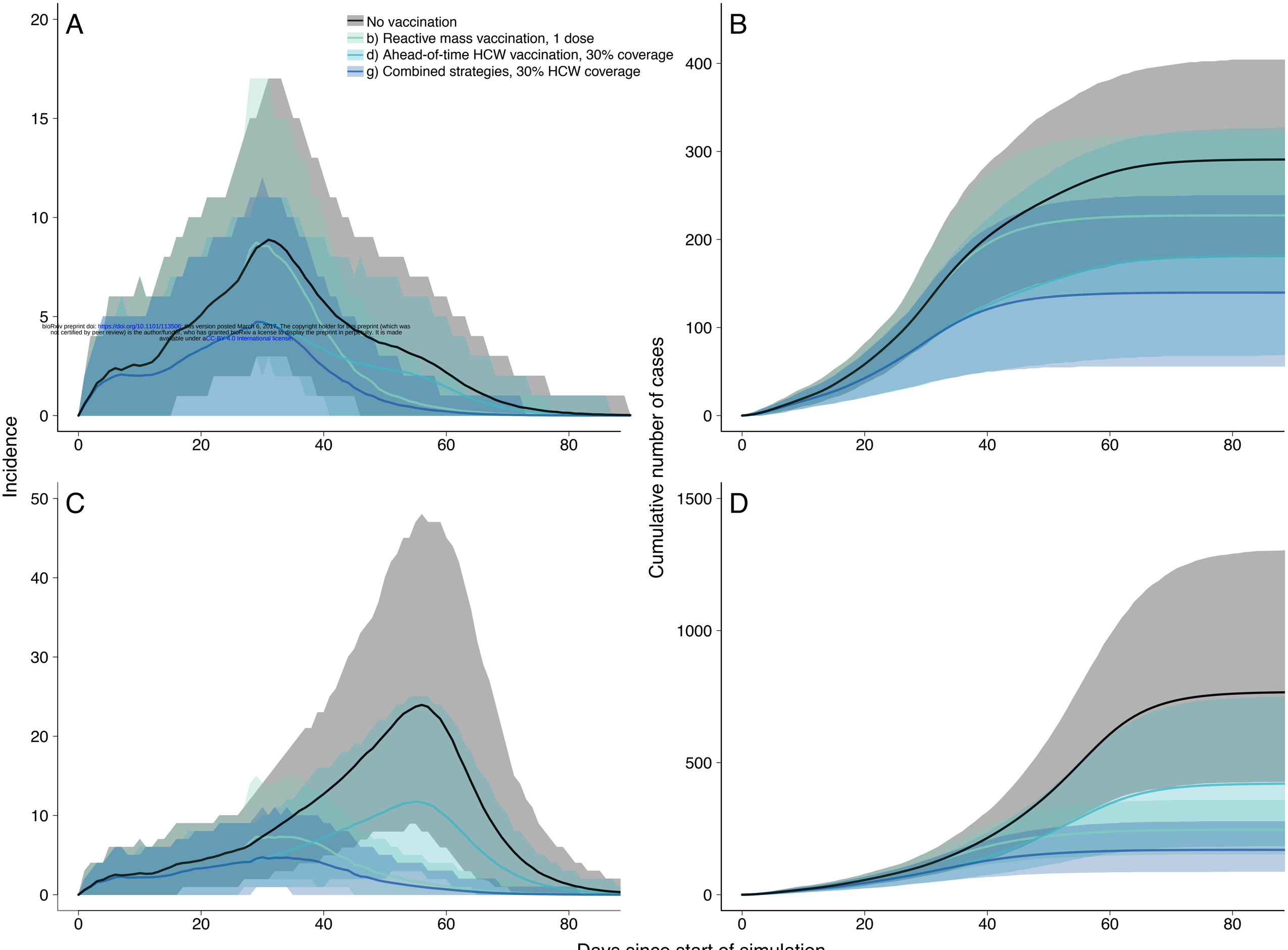
C

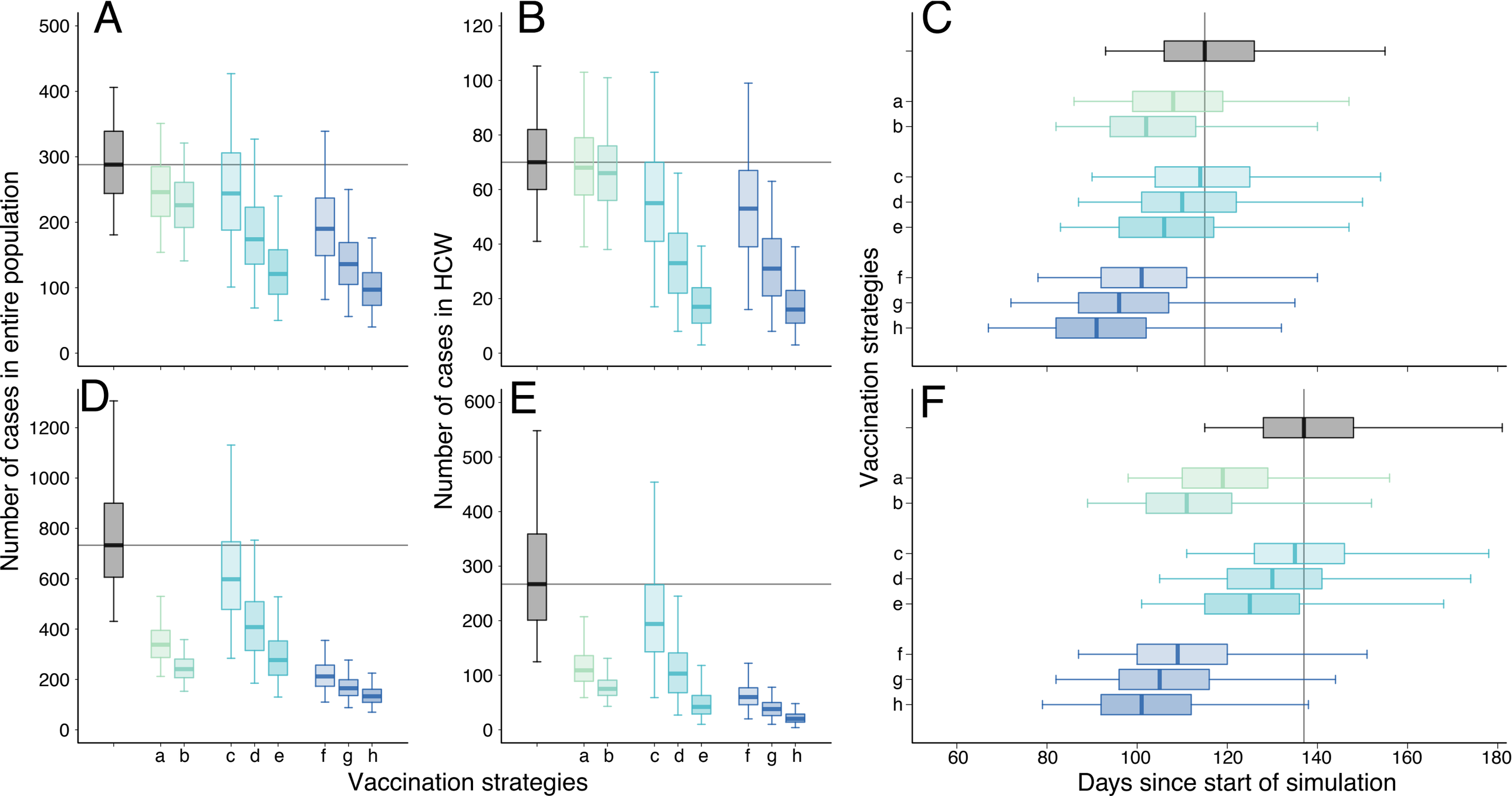
HCW Proportion

D

HCW Proportion


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




A
B
C
D
E
F
Number of cases in entire population
Number of cases in HCW
Vaccination strategies
Vaccination strategies
Days since start of simulation
a
b
c
d
e
f
g
h
0
100
200
300
400
500
0
20
40
60
80
100
120
0
200
400
600
800
1000
1200
0
100
200
300
400
500
600
60
80
100
120
140
160
180

Tables

Parameter	Description	Fixed value	Posterior median (95% CI)	Reference
$E_{1cc}(T_0)$	At T_0, the number of exposed *c* who were infected by *c*		13 (5—24)	
$E_{1hc}(T_0)$	At T_0, the number of exposed *c* who were infected by *h*		2 (0—7)	
$E_{1ch}(T_0)$	At T_0, the number of exposed *h* who were infected by *c*		4 (1—10)	
$E_{1hh}(T_0)$	At T_0, the number of exposed *h* who were infected by *h*		4 (0—12)	
$I_c(T_0)$	At T_0, the number of infectious *c*		9 (1—24)	
$I_h(T_0)$	At T_0, the number of infectious *h*		2 (0—7)	
ϵ^{-1}	Incubation period	9.5 days		[11], [34]
γ_{death}^{-1}	Duration from onset of symptoms to death	10 days		From data
γ_{recov}^{-1}	Duration from onset of symptoms to recovery	18 days		From data
ρ_{onset}	Proportion of reported cases with onset date	0.9		From data
ρ_{death}	Proportion of reported cases with death date	0.95		From data
ψ_{onset}	Overdispersion of reporting proportion of onset date		0.17 (0.03—0.41)	
ψ_{death}	Overdispersion of reporting proportion of death date		0.36 (0.13—0.73)	
τ_p or τ_b	Vaccination rate (prime or boost)	Equivalent to 15,000 doses per day		
ν_p or ν_b	Vaccine efficacy, prime or boost.	Single dose: ν_p=0.9; Prime-boost: ν_p=0.5, ν_b=0.9.		

Table 1. Key parameters relating to transmission, with fixed or estimated values. Details of all parameters are given in Supplementary Section S4.2.

		hh	*ch*	*hc*	*cc*	Overall
Kikwit 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)	
Prolonged-transmission scenario	R_0	2.68 (1.83-4.01)	0.16 (0.05-0.37)	1.50 (1.33-1.75)	1.50 (1.33-1.75)	2.87 (2.12-4.14)
	T_{change} (days)	T_c = 55 (50-62)	T_c	T_c	T_c	
	shape	α_h = 2.20 (0.23-4.83)	α_h	α_c = 2.49 (0.21-4.86)	α_c	

Table 2. Values of the reproduction number, time of change in transmission, and shape of the decrease in transmission. We give values inferred from the Kikwit data, and those used in simulations in the prolonged-transmission scenario described in Methods. Mean values and 95% CIs are given. Comparison of the R_0 trajectories is given in Figure 2.

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