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Dynamics and control of Ebola virus transmission in Montserrado, Liberia: a mathematical modeling analysis

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Abstract

Background—A substantial scale-up in public health response is needed to control the unprecedented Ebola virus disease (EVD) epidemic in West Africa. Current international commitments seek to expand intervention capacity in three areas: new EVD Treatment Centers (ETCs); case ascertainment through contact tracing; and household protective kit allocation.

Methods—We developed a transmission model of Ebola virus that we fitted to reported EVD cases and deaths in Montserrado County, Liberia. We used this model to evaluate effectiveness of

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LB: Data collection, data interpretation
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All authors declare no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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expanding ETCs, improving case ascertainment, and allocating protective kits for controlling the outbreak in Montserrado.

Findings—We estimated the basic reproductive number for EVD in Montserrado to be 2·49 [2·38–2·60]. We expect that allocating 4,800 additional ETC beds and increasing case ascertainment fivefold in November can avert 77312 [68400–85870] cases relative to the status quo by 15 December. Complementing these measures with protective kit allocation increases the expectation as high as 97940 [90096–105606] cases. If deployed by 15 October, equivalent interventions would have been expected to avert 137432 [129736–145874] cases. If delayed to 15 November, we expect the interventions will at best avert 53957 [49963–60490] cases.

Interpretation—The number of ETC beds needed to effectively control EVD in Montserrado substantially exceeds the total pledged by the United States to West Africa. Accelerated case ascertainment is required to maximize effectiveness of expanding ETC capacity. Distributing protective kits can further augment EVD prevention. Our findings highlight the rapidly closing window of opportunity for controlling the outbreak and averting a catastrophic toll of EVD cases and deaths.

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Keywords

Medical Subject (MeSH) Headings: Ebola; Ebola treatment centers; household protective kits; Mathematical modeling

INTRODUCTION

The scale of the Ebola virus disease (EVD) epidemic currently affecting West Africa is unprecedented.[1] As of 8 October, 2014, the World Health Organization (WHO) reported 4,656 cases EVD, with the majority occurring in Liberia,[2] where the epidemic is increasing most rapidly and is exacerbated by extraordinary socioeconomic disadvantage and health system inadequacies. While West African countries are among the least-developed globally, the gross domestic product in Liberia is especially low at $454 (US) per capita, compared to $809 in Sierra Leone and $3010 in Nigeria.[3] Prior to the epidemic, Liberia had only 2·8 healthcare workers per 10,000 persons and 51 medical doctors serving its 4·29 million population.[4,5]

Since Ebola virus (EBOV) spreads through bodily fluid contact from infected persons, overcrowded urban areas may present exceptionally high risk for disease transmission.[6] Over one million individuals and more than 90% of Montserrado County residents live in Monrovia, the nation's capital. Reducing transmission is particularly challenging in Monrovia's West Point slum where over 75,000 people live without running water, making it impossible to implement WHO-recommended hand-washing when caring for sick household members.[7] The current outbreak poses a mounting threat internationally as witnessed by infected individuals traveling from Monrovia to the United States and to Nigeria, causing an outbreak of at least 19 cases in the latter.[8,9]

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Containment of previous EVD epidemics in more remote areas has relied on identifying and monitoring contacts of EVD patients for symptoms, and performing hygienic burials to prevent family and community members from being exposed during funerals.[10,11] So far, these approaches have not been successful in curtailing the current epidemic in cities such as Monrovia. Responses including *cordons sanitaires,* border closures and international flight cancellations, curfews, and bans on public gatherings have resulted in overwhelming losses for impoverished national economies[11,12] and civil unrest.[13]

The WHO has urgently appealed to the international community to commit resources toward combating the epidemic.[10,14] On 16 September, the United States announced the largest and most comprehensive response to date, which includes constructing 17 new EVD Treatment Centers (ETCs) to isolate and treat 1,700 patients.[15,16] However, the pace of epidemic growth brings into question whether the extent and timing of commitments will be sufficient to curtail the epidemic. Following recommendations and provisions from the US Centers for Disease Control and Prevention (CDC), the Liberian Ministry of Health and Social Welfare has additionally begun distributing home-based protective kits and instructional programs to facilitate household-based isolation of infected individuals for whom beds are unavailable. To probabilistically assess the impact these various intervention strategies may have on controlling EBOV in Montserrado, we developed a mathematical model for EBOV transmission fitted to epidemiologic data of reported cases and deaths.[7] We used the model to evaluate the potential impact in Montserrado of expanding ETCs, improving case ascertainment, and allocating protective kits. We showed that substantially more ETCs than have been pledged will be needed to meaningfully avert cases and deaths. We also showed that the effectiveness of new ETCs can be maximized by concurrently improving case ascertainment, and that allocating protective kits further augments control probability. We found that equivalent interventions would have had substantially greater impact if initiated two weeks earlier, and that further delaying interventions will greatly limit their effectiveness.

METHODS

Model description

We developed a mathematical model that tracks susceptible, latently infected, infectious, and recovered individuals as well as infectious deceased victims. We assumed that infected individuals become ascertained via presentation to ETCs or through active contact-tracing. We further assumed that hospitalized and other ascertained individuals who die receive sanitary burials, preventing transmission after death. By contrast, EVD patients who are not ascertained contribute to transmission until they are buried.

Calibration

We derived EVD parameters from epidemiologic data on the current epidemic.[1] We propagated uncertainty in epidemiological parameters onto the model predictions by performing Bayesian Markov Chain Monte Carlo sampling for model calibration. We calibrated the model to reproduce cases and deaths reported in Montserrado for the period from 14 June (when the first cases were reported) to 23 September.[7] The Web Appendix

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provides a detailed description of the model equations and calibration. Our model predictions under the status quo are based on the assumption of no change in the 23 September population behavior and mixing patterns by 15 December.

Interventions

We compared outcomes individually and in combination of accelerating case ascertainment, ETC expansion, and distributing protective kits to households of ascertained patients for whom ETC beds are unavailable (Table 1). Given empirical uncertainty in the efficacy of protective kits in reducing household transmission, we varied the efficacy from 10% to 50%. We also compared intervention initiation on 15 October, 31 October and 15 November. The status quo intervention was defined in terms of 23 September case ascertainment and ETC capacity, and all behavior and contact patterns relevant to transmission as they were occurring at that time.

Our primary outcome measure was the expected number of cases averted by 15 December, around which we computed 95% credible intervals via bootstrap resampling. As a secondary outcome measure, we computed deaths averted by 15 December, presented in the web appendix.

Role of the funding sources

The sponsors of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

RESULTS

Transmission dynamics and status-quo forecasts

For Montserrado, we estimated a basic reproductive number (R_0) of 2·49 [95% CI 2·38–2·60]. This value defines the expected number of cases caused by an infected person in an otherwise susceptible population in the absence of any public health or clinical interventions. We estimated that as of 5 October, 7,260 total cases [5,132–11,560] and 2,941 total deaths [4,070–6,140] had occurred, of which we predicted 1,975 [1,390–3,100] and 1,315 [959–1,984] would be reported, respectively. The Liberian Ministry of Health and Social Welfare data reports 1,635 cumulative cases and 1,081 cumulative deaths as of that time. Without expanded control effort beyond levels of 23 September, our model projects 170,996 total cases [81,909–361,793] and 90,122 total deaths [44,734–194,801] by 15 December. Of these, we estimate 42,669 cases [20,471–94,143] and 27,175 deaths [13,498–59,791] will have been reported.

Comparing effects of ETC construction and protective kits

We found that the impact of expanding ETC capacity depends upon concomitantly accelerating case ascertainment, reducing household and community transmission before hospitalization (Figure 2). For example, we estimate that for status-quo case ascertainment, the addition of 4,800 beds over four weeks would be expected to avert 49,553 [41,720–

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58,152] cases. Providing 2,400 beds over two weeks while concurrently accelerating case ascertainment fivefold would be expected to avert 62,220 [53,556–70,654] cases.

Protective kits may reduce transmission under scenarios where ETC capacity is exceeded. At status-quo case ascertainment and hospital capacity, distributing kits to households of ascertained cases for whom there are no beds available can be expected to avert 4,497 [−5,153–13,524] to 30,557 [22,535–38,663] cases, corresponding to intervention efficacy ranging from 10% to 50% (Figure 3). Expected averted cases can be increased to within the range of 26,746 [19,003–35,127] to 75,065 [67,330–82,994] if case ascertainment is increased fivefold.

Combined ETC and protective kit interventions

Given our projection that incidence in Montserrado is likely to soon exceed ETC capacity under current international commitments, protective kits may supplement hospital-based case isolation (Figure 3). For instance, if kits halve transmission, we expect that allocating kits while increasing case ascertainment would avert 46,123 [37,897–54,295] to 78,623 [71,304–86,442] cases if 600 new beds are concurrently allocated over the span of two weeks. With 4,800 new beds delivered by mid-November, the averted cases increase to the range of 65,228 [57,385–72,705] to 97,940 [90,096–105,606], compared to 58,529 [50,557–67,738] to 77,312 [68,400–85,870] without kits.

Impact of intervention pace and timing

For scenarios where households of ascertained cases receive protective kits, rollout of programs increasing case ascertainment within two weeks avert more cases than slower rollout alternatives (Figure 3). It is less clear whether the timing for rolling out ascertainment influences effectiveness of ETC expansion when protective kits are not allocated (Figure 2). However, rates at which ETCs are constructed substantially affect the expected cases averted. For instance, we estimate the averted cases increase from 39,314 [29,664–48,414] to 62,222 [53,556–70,654] when 2,400 new beds are constructed over the span of four weeks versus two weeks, even when both scenarios are complemented with fivefold acceleration of case ascertainment (Figure 3).

Had more timely interventions been implemented, the expected cases and deaths averted would have been much higher under all intervention scenarios (Figure 2, Figure 3, Web Appendix). Without protective kits, concurrent deployment of the maximal ETC and ascertainment interventions initiated 31 October is expected to avert 77,312 [68,400–85,870] cases. Augmenting these interventions with kits can increase averted cases to between 81,627 [73,536–89,790] and 97,940 [90,096–105,606], depending on kit efficacy. Initiating all three interventions on 15 October would have averted up to 137,432 [129,736–145,874] cases. In the latter scenario, kit allocation does not impact outcomes significantly, reflecting the lesser importance of the kits when adequate ETCs are available. If initiated 15 November, our projections suggest that these interventions will avert between 31,690 [24,506–39,680] and 53,957 [46,963–60,490] cases. Our model predicted a cumulative 27,378 [17,671–75,717] cases and 18,606 [12,108–49,373] deaths under this best-case scenario for timely intervention initiated 15 October, compared to 65,367 [28,991–204,523]

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cases and 41,754 [19,327–122,955] deaths, and 112,960 [50,589–291,771] cases and 66,820 [31,556–171,299] deaths for 31 October and 15 November start dates, respectively.

DISCUSSION

Our analysis suggests that the ETC capacity needed to reduce the severity of the current outbreak tremendously exceeds current international commitments. ETC expansion can be maximally effective if case ascertainment is concurrently accelerated, and we expect providing protective kits to further reduces cases and deaths. While the window of opportunity for timely control of the EVD outbreak has passed, the risk for catastrophic devastation both in West Africa and beyond may have only just begun. Further delays in providing effective interventions will continue undermining the likelihood for averting cases and deaths, suggesting the need to scale interventions to the continuously increasing need more expeditiously despite potential costs.

Rapid epidemic growth exacerbated by the inadequate and delayed international response has left many people with no other option but to care for sick relatives within their home. As a stop-gap measure, protective kits have begun to be provided to households of infected individuals for whom hospital beds are not available in an attempt to reduce household transmission.[14,16,17] Although the kits do not facilitate treatment *per se*, they do include soap and bleach along with personal protective equipment such as gloves and masks, and sanitary containers for disposing contaminated materials. A previous model suggesting that these measures may be effective stand-alone interventions assumed that they achieve a 90% reduction in household transmission.[18] However, there is considerable uncertainty in efficacy of these kits, as evidenced by estimates from previous outbreaks in the Democratic Republic of the Congo and Uganda, where their efficacy was 12% [0%–78%] and 88% [1%–92%], respectively.[18] Considering a range in efficacy from 10% to 50%, our predictions suggest that while these protective kits can complement improvements in ETC capacity and case isolation, they would alone remain insufficient to reverse the EVD outbreak in Montserrado.

Analyzing outbreaks at localized geographical resolutions complements recent models of the current West African EVD epidemic that have predominantly sought to replicate national-scale transmission dynamics.[1,9,17,19–21] Although the epidemic is unfolding across several countries, interventions must ultimately be implemented and scaled to specific community needs.[10,12] Additionally, epidemic dynamics and reporting vary geographically due to inherent differences in health system capacity, timing of index cases, and unique local conditions that may exacerbate transmission.[17] Focusing on Montserrado, where transmission rates appear highest,[7] allows us to evaluate timing and scale of interventions required in this most challenging of settings. Predicted intervention requirements in Montserrado are likely applicable yet conservative relative to those necessary in regions where transmission rates are lower.

EVD cases are often identified and reported well after symptoms onset.[1] Thus, most cases reported each day likely became symptomatic days before, and may have transmitted in the intervening time. The assumption that daily reported cases accurately represent the number

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of individuals entering the infectious class without taking into account underreporting or the delay in reporting may lead to underestimation of the actual epidemic. We addressed this challenge by fitting our model to estimate the delay between the beginning of the infectious period and time of ascertainment. Caveats regarding our findings include the scarcity of empirical assessment of ascertainment rates and uncertainty in the population mixing patterns by which we assume EBOV can continue spreading within the remaining susceptible population. To address the limitation that status-quo ascertainment is unknown, we used a Bayesian framework to propagate uncertainty regarding this parameter onto our model predictions to ensure the robustness of our results. As it is unclear to what extent unquantified factors such as human behavior changes and population mixing may reduce transmission, the conventional homogeneous mixing assumptions here allow for worst-case estimates of the attack rate and thus inform conservative response strategies. Within the range of current reported epidemiologic observations, our projections may be slightly high given that the initiation of protective kit distribution in late September and early October, which may contribute to earlier deceleration of the epidemic than would be predicted under the status-quo (Figure 1, Figure 3).

Another limitation is the model assumption that EBOV-infected living and deceased individuals contribute to transmission at equal rates. Given that viral load levels of *Zaire ebolavirus* vary during the course of infection in non-human primates,[22,23] living and deceased persons may transmit differentially due to viremia differences and rates at which susceptible persons contact them.[24] As the interventions we considered primarily address isolating infected persons within ETCs or within their own homes, our outcomes are most useful for informing control of transmission from living EVD patients. Additionally, we assumed that cases occurring in Montserrado from 14 June onward were acquired within the county. Although this may not strictly be the case, the relative geographic isolation of the early epidemic foci in Montserrado and Lofa Counties suggest imported cases would not be an influential source for transmission in Montserrado. Last, we assumed that no transmission occurs during sanitary burials, as no data are available to parameterize the relative risk of infection during such events. In the absence of concurrent interventions the only effect offered by ascertainment is sanitary burial. We did not identify appreciable changes in cases or deaths averted from altering ascertainment rates when beds remain at their 23 September levels (Figure 2). Thus, allowing for risk of transmission during sanitary burials would likely have a small marginal impact on our results.

We do not consider the costs of intervention implementations. Although the costs of scaling-up construction of new ETCs, accelerating case ascertainment, and providing household protective kits are an important factor for measuring the feasibility of different intervention strategies, intervention needs and costs will increase if the outbreak continues expanding at its current rate. Further studies should integrate both speed and cost of intervention measures to evaluate the health and economic burdens of delaying scaling-up EVD control measures in West Africa.

In addition to non-pharmaceutical interventions, several potential medicinal treatments and vaccines for EVD control are currently being developed and tested.[25,26] Although these measures will likely not be available for large-scale distribution until much later in the

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epidemic, they have the potential to contribute significantly to reducing disease burden and saving lives. Further studies should investigate the potential impact of combining pharmaceutical and non-pharmaceutical interventions.

Continued spread of EBOV threatens affected West African nations and the rest of the world, making outbreak containment a global health priority. As vaccines to prevent EVD remain unavailable, our study urges a rapid and immediate scaling-up of currently-available non-pharmaceutical intervention strategies to minimize the occurrence of new cases and deaths. Perhaps most alarming is that while we may still be within the midst of what will ultimately be viewed as the early phase of the current EVD outbreak, the window of opportunity for averting calamitous repercussions from an initially delayed and insufficient response is rapidly diminishing. Our predictions indicate that current commitments are grossly inadequate to provide beds for all infected individuals even only considering near-term growth of the epidemic in Montserrado. Although transmission reduction afforded through provision of home protective kits could have a limited impact on mitigating temporary bed shortages, our results suggest EBOV transmission will not be curtailed without much greater commitment to improving all preventive measures that international aid is currently attempting to address.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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RESEARCH IN CONTEXT

Systematic review

We searched scientific literature listed in PubMed and Google Scholar, using various search terms: “Ebola transmission model”, “Ebola control”, “Ebola treatment centers”, and “Ebola household protective kit”. We restricted the search to documents in English and French. The last search was done on October 14, 2014. The search yielded no studies evaluating the speed of intervention measures needed to curtail the ongoing Ebola outbreak in West Africa.

Interpretation

This is the first study to evaluate the impact of the speed of implementing non-pharmaceutical interventions to curb the 2014 Ebola outbreak in Liberia. There is an urgent need for a much more substantial and prompt scaling up of interventions to avert catastrophic disease burden. As such, our findings underscore the inadequacy, both in timing and scale, of current US commitments to expand capacity of isolation and case ascertainment capacity.

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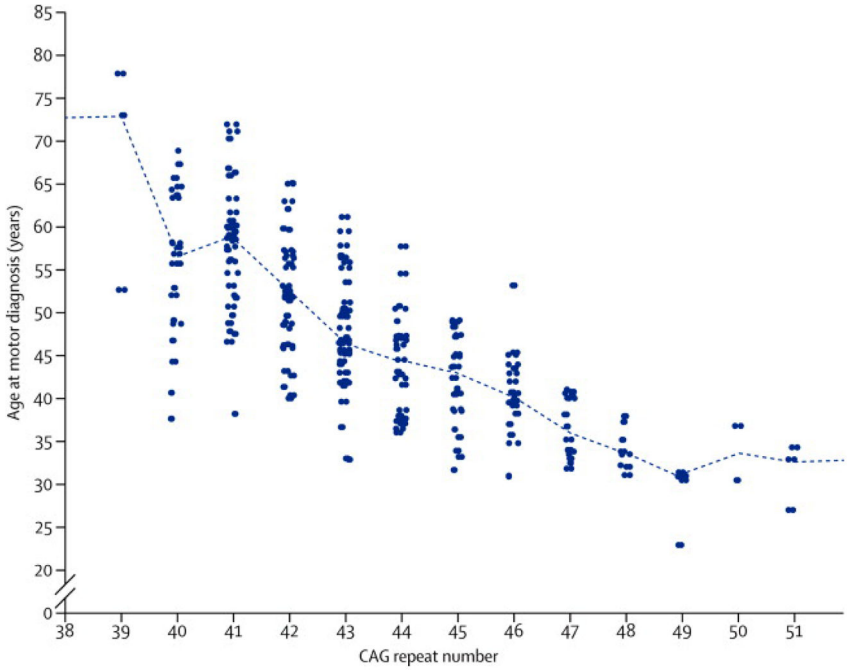

Figure 1. Model calibration

A: Reported and model-predicted cases, with black points showing observed data used in model calibration, blue points showing observations outside the fitting period, and shaded areas showing 95% credible intervals around model predictions; B: Reported deaths, as in (A). Credible intervals are computed based on 5,000 simulations. The superimposed line indicates median predicted cases and deaths.

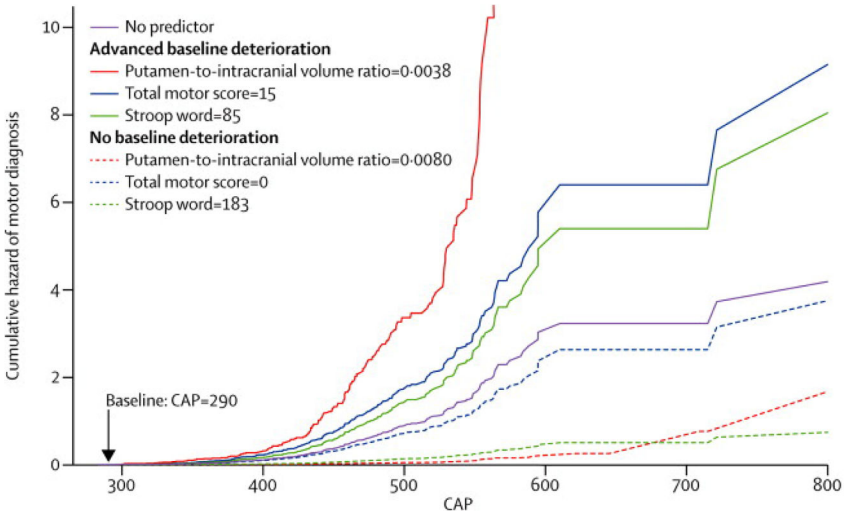

Figure 2. Impact of adding new Ebola treatment centers and increasing case ascertainment

Intervention effects for programs initiated 31 and 15 October, respectively, considering expansions in ETCs and case ascertainment. Roman numerals I, II, and III describe ETC construction at the rates of 3, 6, and 12 ETCs per week, respectively. Ascertainment labels are defined in Table 1. We expand the figure in the online supplemental materials to illustrate effects under all modeled ETC deployment schedules.

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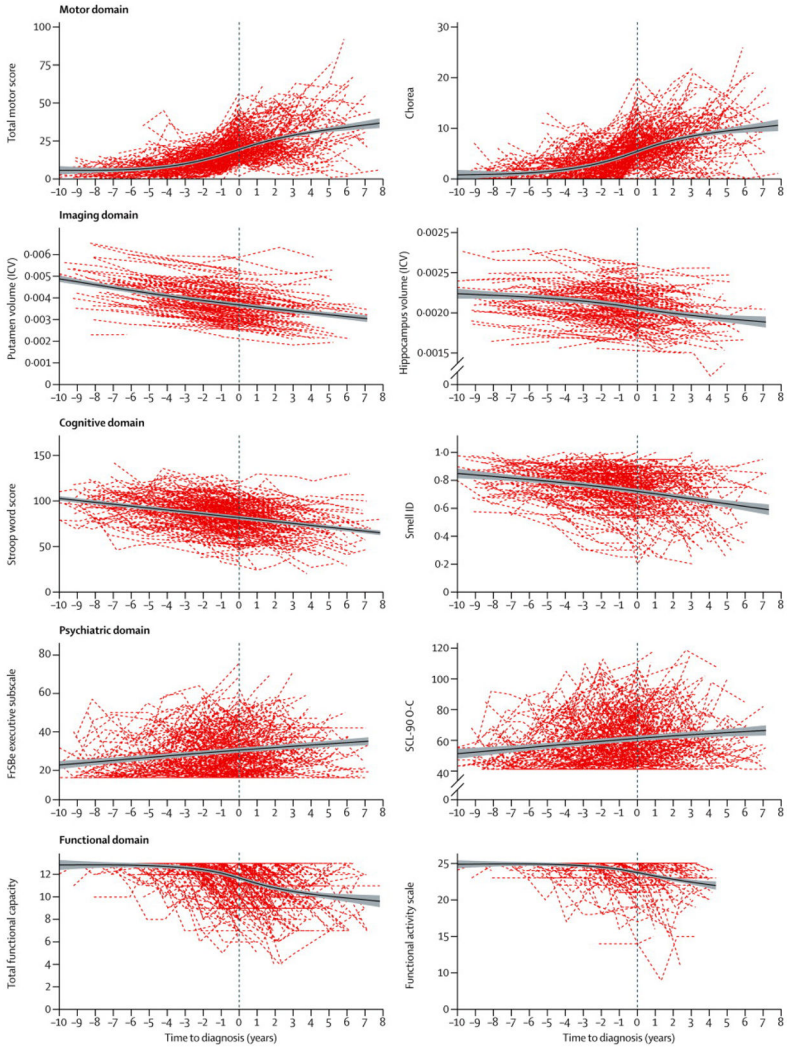

Figure 3. Impact of augmenting interventions with protective kit allocation

A: Effectiveness of programs beginning 31 October, considering all possible expansions in ETCs and case ascertainment, and varying efficacy levels for protective kits. Roman numerals II and III describe ETC construction at the rates of 6 and 12 ETCs per week, respectively. Ascertainment labels are defined in Table 1. We expand the figure in the online supplemental materials to illustrate effects under all modeled ETC deployment schedules. B: Effects of equivalent interventions initiated 15 October. C: Effects of equivalent interventions initiated 15 November.

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Table 1

	Model parameter affected	Total change	Deployment schedule
Improving surveillance	Ascertainment rate	0–400% increase	Remains at baseline (0); 12.5% per week over 4 weeks (1A); 25% per week over 2 weeks (1B); 25% per week over 4 weeks (2A); 50% per week over 2 weeks (2B); 50% per week over 4 weeks (3A); 100% per week over 2 weeks (3B); 100% per week over 4 weeks (4A); 200% per week over 2 weeks (4B)
Building ETCs	Number of beds	0–48 new ETCs (0–4800 new beds)	Three ETCs per week for 2 and 4 weeks (I); Six ETCs per week for 1, 2, and 4 weeks (II); 12 ETCs per week for 1, 2, 3, and 4 weeks (III)
Allocating household protective kits	Transmission rate for ascertained cases	10–50% reduction in transmission rate for ascertained cases that remain at home	N/A (implemented among all newly ascertained cases)