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Evaluating large-scale blood transfusion therapy for the current Ebola epidemic in Liberia

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ABSTRACT

Background. To combat the 2014-2015 Ebola epidemic in West Africa, the World Health Organization urged the rapid evaluation of convalescent whole blood (CWB) and plasma (CP) transfusion therapy. However, the feasibility and likely impacts of broad implementation of transfusions are yet unknown.

Methods. We extended an Ebola transmission model published by the US Centers for Disease Control and Prevention to include hospital-based convalescent donations and transfusions. Using recent epidemiological estimates for Ebola in Liberia and assuming that convalescent transfusions reduce the case-fatality rate to 12.5% (Range: 7.5-17.5%), we projected the impacts of a country-wide ramp up of transfusion therapy.

Results. Under the 10% case hospitalization rate estimated for Liberia in September 2014, large-scale CP therapy is expected to save 3586 lives by October 2015 (3.1% mortality reduction, 95% CI: 0.52%-4.5%). Under a higher 30% hospitalization rate, CP transfusions are expected to save 151 lives (0.9% of the total, 95% CI: 0.21%-11%).

Conclusion. Transfusion therapy for Ebola is a low cost measure that can potentially save many lives in West Africa, but will not measurably impact prevalence. Under all scenarios considered, CP transfusions are predicted to achieve greater reductions in mortality than CWB.

INTRODUCTION

The ongoing Ebola virus disease (EVD) epidemic in West Africa is the largest ever recorded, and has overwhelmed the healthcare systems in Sierra Leone, Liberia and Guinea [1]–[4]. There are several promising vaccines and therapeutics under accelerated testing and production [3], [5], but are not expected to become widely available for many months [6]. One of the only therapeutic methods immediately available and prioritized for evaluation by the World Health Organization (WHO) [7], [8] is blood transfusions from EVD survivors [9]–[12]. Convalescent patients have EVD-specific antibodies in their serum that potentially facilitate recovery in acutely ill patients. This form of passive polyclonal antibody therapy has been applied successfully to treat other infectious diseases [13], including cytomegalovirus, hepatitis B, rabies, respiratory syncytial virus, vaccinia, and varicella-zoster viruses [14].

Convalescent transfusions are relatively simple, low cost, and scalable in low-income countries [7]. The evidence for their efficacy is limited but positive, including an eight-patient human study during a 1995 Ebola outbreak in Democratic Republic of Congo [9] that reported a case fatality rate of 12.5% under transfusion therapy and supportive care, and multiple animal studies [15]. Even minimally equipped medical settings can perform whole blood transfusions, which require blood collection, blood grouping, testing for EVD and several transfusion-transmittable diseases (HIV, Hepatitis B, and Hepatitis C), and administration to critically acute patients [16]. Convalescent patients can donate blood starting 28 days following recovery as either convalescent plasma (CP) or convalescent whole blood (CWB) [16]. While CWB requires minimal equipment, CWB donation is more physiologically demanding and donors must wait 12-16 weeks between consecutive donations [16]. CP donation requires medical facilities that can separate the plasma and return the red blood cells [8] but the wait between CP donations is just two weeks, which increases the availability of treatments [16]. These facilities are not yet

common in Africa [17], but international efforts are underway to bring the technology to hospitals in the affected countries.

The WHO has advocated convalescent transfusions as the most promising of the available treatments for the ongoing West African epidemic [8], [16], [18]. Although mathematical models have been used extensively to investigate and design intervention measures for Ebola [2], [19]–[25], none have addressed the challenges and impact of broad use of transfusion therapy. Here, we extend an established mathematical modeling framework [2] to assess scalability of transfusions and likely impacts on Ebola incidence and mortality. Both the supply (convalescent survivors) and demand (hospitalized patients) are limited by Ebola hospitalization rates, which are perilously low in some regions and have become a major focus of international public health efforts.

METHODS

We extended a dynamic model of Ebola transmission [2] recently used by the CDC to project the current epidemic in West Africa [2] to include hospital-based collection and transfusion of convalescent blood and plasma. It is a deterministic compartmental susceptible-exposed-infectious-recovered (SEIR) model that tracks the numbers of susceptible individuals, exposed and incubating cases, symptomatic and infectious patients, convalescent Ebola survivors, and Ebola fatalities. Infectious Ebola patients are segregated into one of four groups: hospitalized in Ebola Treatment Units but not receiving transfusions, hospitalized and receiving transfusion therapy, non-hospitalized but isolated and quarantined in Community Care Centers, and the remainder who are non-hospitalized and non-isolated. Based on data from Liberia, we assumed that isolation rates steadily increased from 8% of all Ebola cases in September 1, 2014 [2] to an average of 40% by December 1, 2014. However, unlike the isolation rate, the hospitalization rate remained low throughout this period, due to shortages of local staff and other logistical

challenges in scaling up Ebola treatment units. Our baseline scenario assumes that 10% of cases were hospitalized. We also model a United Nations/World Health Organization target where the isolation and hospitalization rate steadily increase to total 70% by December 1, 2014, of which 30% are assumed hospitalized and an additional 40% are isolated and quarantined [26].

The model tracks the number of courses of treatment available from convalescent blood and plasma donations from EVD survivors and dispenses them immediately to treat hospitalized patients. Convalescent patients are recruited for donation when they are discharged from hospitals. We assume no compensation for donations, and that only 50% enter the donation system and less than 70% return for repeat donation, based on empirical observations [16]. An estimated 43% of patients are eligible to donate whole blood, with the remainder disqualified because of transfusion-transmittable infections, blood type mismatches, and low hemoglobin, while 86% of patients are eligible for plasma donation (see Supplemental Information). Following WHO guidelines [16], donations can be made one month following discharge, and repeated multiple times after a delay (two weeks for CP and approximately 14 weeks for CWB). The per-treatment cost is $75, including supplies for both donation and transfusion [27]–[29], spot testing for transfusion-transmittable diseases (HIV, Malaria and others) [9], and blood group typing, but not including supportive care, training of staff, and equipment for preparation of plasma.

In the absence of transfusions, our model correctly predicts cases and fatalities (Supplementary Figure S2). The Supplementary Information provides the model equations, parameter ranges, and a validation of model projections from data. We ran the model on 120 parameter combinations, selected by Latin Hypercube Sampling [30] and report the 95% confidence intervals (CI) across the 120 analyses. This study uses published aggregated

anonymized data, and thus meets legal and institutional requirements for protection of human subjects.

RESULTS

Assuming that the case hospitalization rate remains at 10% and convalescent transfusion therapy is maximally scaled up in Liberia starting December 1, 2014, we estimate that the whole blood (CWB) and plasma (CP) based interventions will avert a total of 851 (0.73%, 95% CI: 0.19%-1.1%) and 3586 (3.1%, 95% CI: 0.52%-4.5%) EVD fatalities, respectively, but neither will measurably impact overall incidence (Figure 1). However, the available data is consistent with hospitalization rate of 30% in early December 2014. The model suggests that a 30% hospitalization rate should significantly mitigate the course of the epidemic to the extent that the epidemic in Liberia would be controlled by January 2015, consistent with the recent leveling of EVD incidence in Liberia reported by WHO [31]. In this scenario, CWB and CP are estimated to reduce the number of deaths by 65 (0.37%, 95% CI: 0.07%-2.6%) and 151 (0.9%, 95% CI: 0.21%-11%), respectively.

Under the dire scenario of a 10% hospitalization rate, the model predicts that mass CWB-based transfusions starting in December 2014 would result in 1594 out of 14883 total hospitalized cases receiving transfusion therapy (Figure 2). Among the cases hospitalized after the intervention roll-out, 14% would be treated (95% CI: 8.6%-23%). With CP transfusions, the

model predicts a larger supply, resulting in 6683 patients treated (60% of those hospitalized after the roll-out; 95% CI: 33%-70%). At a cost of $75 per transfusion, the total costs of the intervention are estimated to be $0.120M and $0.503 for CWB and CP, respectively, excluding transfusion infrastructure and labor.

The epidemiological impact of a large-scale transfusion therapy intervention is limited by several factors. While CWB and CP transfusions lower case fatality rates in treated patients, they have only a minimal effect on transmission, primarily through prevention of postmortem exposure during traditional burials. Since transfusions are undertaken only in the hospital setting, the number of treated patients is constrained by the hospitalization rate. If we denote the hospitalization rate as p_H and the difference in case fatality rates for untreated and treated hospital patients as $\delta_H - \delta_T$, then the relative reduction in mortality is at most $p_H(\delta_H - \delta_T)$. Thus, at hospitalization rates of 10% and 30% and case fatality rates of $\delta_H = 67\%$ for patients hospitalized without transfusion treatment [1] and $\delta_T = 12.5\%$ for those treated [9], transfusion therapy can at most reduce overall mortality by 5.4% and 16% during the intervention period, respectively. When hospitalized patients receive supportive intravenous fluids, case fatality rate is estimated to decrease to 43% [32]. In this case, transfusion therapy is expected to reduce overall mortality by 3.1% and 9.2%, under 10% and 30% hospitalization, respectively. The supply of CWB and CP donations is expected to further limit the number of transfusions until late in the epidemic (Figure 2), when supply starts to exceed the number of treatable patients. Consequently, the estimated reduction in mortality is lower than these theoretical upper bounds during the intervention period.

Large changes to the donation rates, mortality rates, and efficacy of transfusion have intuitive effects (Table 1). Under a CP intervention with 10% hospitalization, increasing the initial donation rate from 50% to 100% of previously hospitalized survivors is expected to increase the

number of donations by 21% and decrease overall fatalities by 0.6%; reducing the case fatality rates of hospitalized patients from 67% to 40% is expected to decrease the overall fatality rate by 2.1%, because more survivors means more potential convalescent donors. Delaying the implementation of transfusions until January 2015 increases the expected mortality by 0.5%, and an additional 30 day delay would increase it by 1%. CWB is expected to be in much shorter supply than CP, and thus its success is much more sensitive to donor recruitment and retention rates. For example, increasing the probability of a second donation from 70% to 90% would increase the number of courses by 60% under CWB, but only by 9.6% under CP. In theory, the CWB supply could be significantly augmented (331%) by donations from convalescent cases who were never hospitalized.

DISCUSSION

To our knowledge, this is the first quantitative assessment of a large-scale convalescent blood transfusion campaign for the current Ebola epidemic. In a best-case scenario, such an intervention may substantially reduce the number of fatalities but will not measurably impact incidence. Hospitalization improves EVD survival rates and is a prerequisite for becoming either a convalescent blood product donor or a transfusion therapy recipient. Thus, as public health efforts increase hospitalization rates, the overall burden of disease should decrease, and the availability of convalescent donors and patients would increase. However, even under a more optimistic scenario of a 30% hospitalization rate, CWB donations are expected to remain in short supply until very late in the epidemic. This could potentially be remedied by expanding the donors pool outside the hospital setting and recruiting known survivors of EVD. Plasma-based

therapy is considered safer and more efficient than CWB therapy and the waiting period between consecutive donations is shorter. However, plasma extraction requires expensive equipment that is not yet available in many Liberian health care facilities. Assuming that hospitalization rates remain low (10%), broad implementation of convalescent whole blood (CWB) therapy (but not plasma therapy) on December 1, 2014 is expected to prevent 851 deaths (0.73%) by October 2015. Convalescent Plasma (CP)-based therapy is expected to prevent many more deaths, exceeding CWB by a factor of 4.2 and 2.3, under the 10% and 30% hospitalization rates, respectively. Delaying the start of CP by two months is expected to increase the mortality by 1%, pointing to the need of timely implementation of any plasma transfusions. In the 30% hospitalization scenario where the epidemic is controlled, a nationwide convalescent plasma therapy intervention should still save an additional 151 lives (0.9% of the total) by October 2015. At a cost of $75 per CWB transfusion, excluding costs associated with labor, the overall cost of a transfusion campaign in Liberia is estimated be quite modest, costing less than one million US dollars. However, there may also be significant additional costs associated with training staff and treating infections detected in donor blood. A CP system would require additional infrastructure investments but would potentially quadruple the number of lives saved if hospitalization rates remain low.

There are numerous challenges to implementing a large-scale transfusion therapy campaign. In addition severe resource limitations, including lack of supplies, equipment, space and personnel for taking, testing and processing blood donations, the system will be fundamentally constrained by the ratio of convalescent donors to hospitalized patients requiring therapy. This ratio can be particularly low in the early stage of an epidemic, when new cases outpace recovered cases, and is exacerbated by Ebola's high fatality rate and low hospitalization rate in West Africa. Although transfusion therapy coupled with supportive care may have an efficacy as high as 90% [9], these practical challenges of implementation will likely persist throughout resource-limited regions of Africa, and severely limit the overall reduction in

fatalities. Despite these obstacles, ramping up convalescent whole blood and particularly convalescent plasma therapy can tangibly reduce mortality in the ongoing West African Ebola epidemic.

Limitations

Our analysis relies on a compartmental model that does not account for the complex social and geographic factors that impact Ebola transmission and health seeking behavior. We assume that human behavior, treatment efficacy, and disease transmission and progression rates are static, but account for the introduction of greater case isolation and increased hospitalization. Although our quantitative findings held up to sensitivity and uncertainty analysis, as well as to comparison with other models and epidemiological data, we place much more stock in our qualitative findings.

The use of blood transfusion therapy for Ebola is controversial. While it is supported by some small studies [9], [15], [16], indirectly supported by the positive findings with monoclonal therapies [33]–[36] and is biologically plausible [16], its efficacy has not been rigorously established through published randomized controlled trials [16] but such studies are now underway in West Africa [37], [38]. The beneficial effect was not successfully reproduced in all animal models [39]. Additionally, the possible risks of passive immunization for Ebola include antibody-dependent enhancement [10] and increased of accidental exposure among health care workers, which is difficult to estimate. The broad use of transfusion therapy to treat cases in developed countries reflects medical consensus in some beneficial effect of the therapy [40]. CWB and CP transfusion therapy may also indirectly improve outcomes, as they require a higher level of supportive care than commonly provided in Liberia, including intravenous rather than oral rehydration or no hydration therapy at all. The model accounted for the supportive care

given to all treated cases [9], [15] and considered the impacts of lower therapeutic efficacy in the sensitivity analysis.

CONCLUSIONS

Large-scale convalescent blood or plasma transfusion therapy is likely to be a relatively inexpensive means to save lives but not reduce transmission in the ongoing West African Ebola epidemics. Broad expansion of hospital-based care should reduce the overall Ebola mortality and increase the fraction of cases that could potentially receive convalescent transfusion therapy. Investment in convalescent plasma transfusion facilities as an alternative to whole blood transfusions should substantially increase the blood supply and thereby increase the lifesaving impacts of a large-scale transfusion intervention in Liberia by a factor of two to four.

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FOOTNOTE PAGE

A conflict of interest statement

We declare no conflicts of interest.

A funding statement

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Any meeting(s) where the information has previously been presented

None

References

[1] WHO Ebola Response Team, “Ebola Virus Disease in West Africa - The First 9 Months of the Epidemic and Forward Projections,” *N. Engl. J. Med.*, vol. 371, no. 16, pp. 1481–1495, 2014.

[2] M. I. Meltzer, C. Y. Atkins, S. Santibanez, B. Knust, B. W. Petersen, E. D. Ervin, S. T. Nichol, I. K. Damon, and M. L. Washington, “Estimating the future number of cases in the Ebola epidemic - Liberia and Sierra Leone, 2014–2015,” *MMWR Surveill Summ*, vol. 63, no. suppl 3, pp. 1–14, 2014.

[3] A. P. Galvani, M. L. Ndeffo-Mbah, N. Wenzel, and J. E. Childs, “Ebola Vaccination: If Not Now, When?,” *Ann. Intern. Med.*, vol. 161, no. 10, 2014.

[4] A. Camacho, A. J. Kucharski, S. Funk, J. Breman, P. Piot, and W. J. Edmunds, “Potential for large outbreaks of Ebola virus disease,” *Epidemics*, no. 0, p. -, 2014.

[5] J. E. Ledgerwood, A. D. DeZure, D. A. Stanley, L. Novik, M. E. Enama, N. M. Berkowitz, Z. Hu, G. Joshi, A. Ploquin, S. Sitar, I. J. Gordon, S. A. Plummer, L. A. Holman, C. S. Hendel, G. Yamshchikov, F. Roman, A. Nicosia, S. Colloca, R. Cortese, R. T. Bailer, R. M. Schwartz, M. Roederer, J. R. Mascola, R. A. Koup, N. J. Sullivan, and B. S. Graham, “Chimpanzee Adenovirus Vector Ebola Vaccine — Preliminary Report,” *N. Engl. J. Med.*, vol. 0, no. 0, p. null, 0.

[6] S. Strauss, “Biotech drugs too little, too late for Ebola outbreak,” *Nat. Biotechnol.*, vol. 32, no. 9, pp. 849–850, 2014.

[7] “Statement on the WHO Consultation on potential Ebola therapies and vaccines,” World Health Organization, Sep. 2014.

[8] T. Burnouf, J. Emmanuel, D. Mbanya, M. El-Ekiaby, W. Murphy, S. Field, and J.-P. Allain, “Ebola: a call for blood transfusion strategy in sub-Saharan Africa,” *The Lancet*, vol. 384, no. 9951, pp. {1347–1348, 2014.

[9] K. Mupapa, M. Massamba, K. Kibadi, K. Kuvula, A. Bwaka, M. Kipasa, R. Colebunders, and J. Muyembe-Tamfum, “Treatment of Ebola hemorrhagic fever with blood transfusions from convalescent patients,” *J. Infect. Dis.*, vol. 179, no. Supplement 1, pp. S18–S23, 1999.

[10] A. Takada, “Do therapeutic antibodies hold the key to an effective treatment for Ebola hemorrhagic fever?,” *Immunotherapy*, vol. 5, no. 5, pp. 441–443, 2013.

[11] E. O. Saphire, “An update on the use of antibodies against the filoviruses,” *Immunotherapy*, vol. 5, no. 11, pp. 1221–1233, 2013.

[12] R. Emond, B. Evans, E. Bowen, and G. Lloyd, “A case of Ebola virus infection.,” *Br. Med. J.*, vol. 2, no. 6086, p. 541, 1977.

[13] A. Casadevall, E. Dadachova, and L. Pirofski, “Passive antibody therapy for infectious diseases,” *Nat. Rev. Microbiol.*, vol. 2, no. 9, pp. 695–703, 2004.

[14] D. S. Dimitrov and J. D. Marks, “Therapeutic antibodies: current state and future trends–is a paradigm change coming soon?,” in *Therapeutic Antibodies*, Springer, 2009, pp. 1–27.

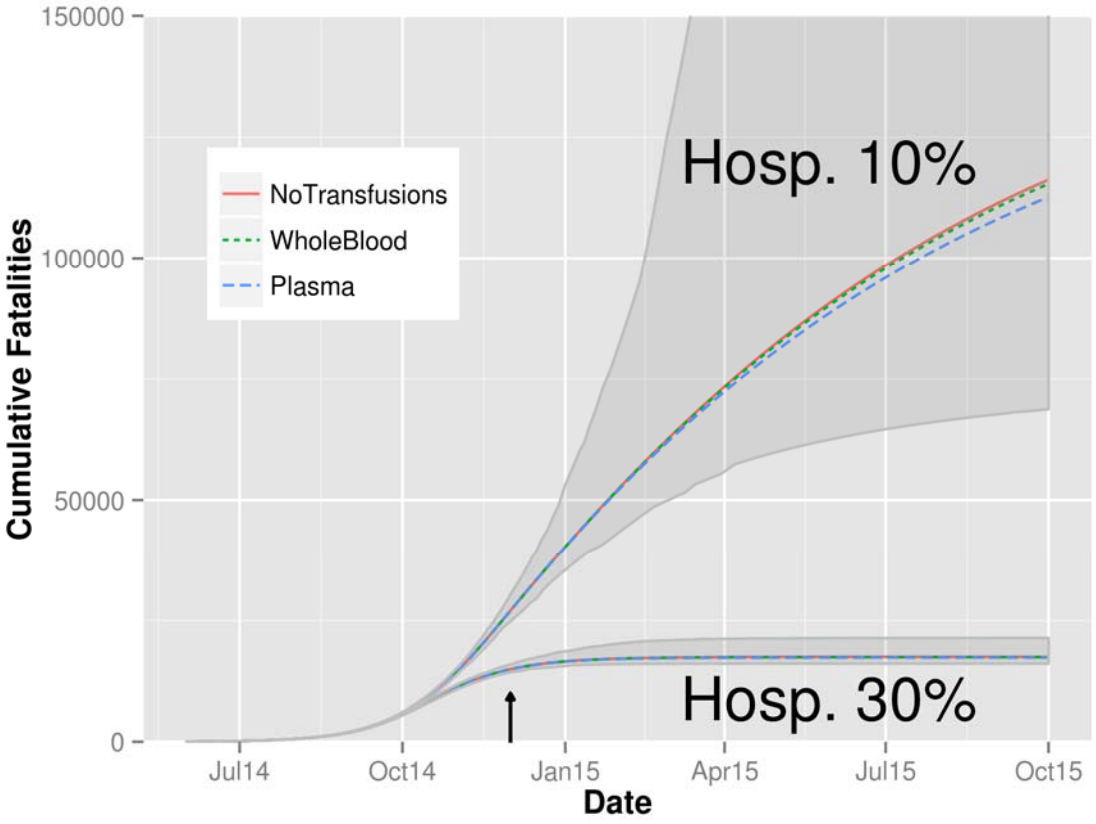
[15] J. M. Dye, A. S. Herbert, A. I. Kuehne, J. F. Barth, M. A. Muhammad, S. E. Zak, R. A. Ortiz, L. I. Prugar, and W. D. Pratt, “Postexposure antibody prophylaxis protects nonhuman primates from filovirus disease,” *Proc. Natl. Acad. Sci.*, vol. 109, no. 13, pp. 5034–5039, 2012.

[16] "Use of Convalescent Whole Blood or Plasma Collected from Patients Recovered from Ebola Virus Disease for Transfusion, as an Empirical Treatment during Outbreaks," World Health Organization, 1.0, Sep. 2014.
[17] J. B. Tapko, B. Toure, and L. G. Sambo, "Status of Blood Safety in the WHO African Region: Report of the 2010 Survey," World Health Organization, 2014.
[18] "Experimental therapies: growing interest in the use of whole blood or plasma from recovered Ebola patients (convalescent therapies)," World Health Organization, Sep. 2014.
[19] A. Pandey, K. E. Atkins, J. Medlock, N. Wenzel, J. P. Townsend, J. E. Childs, T. G. Nyenswah, M. L. Ndeffo-Mbah, and A. P. Galvani, "Strategies for containing Ebola in West Africa," *Science*, 2014.
[20] C. M. Rivers, E. T. Lofgren, M. Marathe, S. Eubank, and B. L. Lewis, "Modeling the Impact of Interventions on an Epidemic of Ebola in Sierra Leone and Liberia," *PLOS Curr. Outbreaks*, vol. Nov, 2014.
[21] C. L. Althaus, "Estimating the reproduction number of Zaire ebolavirus (EBOV) during the 2014 outbreak in West Africa," *PLOS Curr. Outbreaks*, vol. Sep, Sep. 2014.
[22] G. Chowell, N. W. Hengartner, C. Castillo-Chavez, P. W. Fenimore, and J. M. Hyman, "The basic reproductive number of Ebola and the effects of public health measures: the cases of Congo and Uganda," *J. Theor. Biol.*, vol. 229, no. 1, pp. 119 – 126, 2004.
[23] H. Nishiura and G. Chowell, "Early transmission dynamics of Ebola virus disease (EVD), West Africa, March to August 2014," *Rapid Commun*, vol. 19, pp. 1–6, 2014.
[24] P. E. Lekone and B. F. Finkenstaedt, "Statistical Inference in a Stochastic Epidemic SEIR Model with Control Intervention: Ebola as a Case Study," *Biometrics*, vol. 62, no. 4, pp. 1170–1177, 2006.
[25] J. Legrand, R. Grais, P. Boelle, A. Valleron, and A. Flahault, "Understanding the dynamics of Ebola epidemics," *Epidemiol. Infect.*, vol. 135, no. 04, pp. 610–621, 2007.
[26] "Ebola Response Roadmap Situation Report for October 29, 2014," World Health Organization, 2014.
[27] M. van Hulst, C. T. S. Sibinga, and M. J. Postma, "Health economics of blood transfusion safety - focus on sub-Saharan Africa," *Biologicals*, vol. 38, no. 1, pp. 53 – 58, 2010.
[28] B. Jacobs and A. Mercer, "Feasibility of hospital-based blood banking: a Tanzanian case study," *Health Policy Plan.*, vol. 14, no. 4, pp. 354–362, 1999.
[29] R. Toner, L. Pizzi, B. Leas, S. Ballas, A. Quigley, and N. Goldfarb, "Costs to hospitals of acquiring and processing blood in the US," *Appl. Health Econ. Health Policy.*, vol. 9, no. 1, pp. 29–37, 2011.
[30] M. D. McKay, "Latin hypercube sampling as a tool in uncertainty analysis of computer models," in *Proceedings of the 24th conference on Winter simulation*, 1992, p. 564.
[31] "Ebola Response Roadmap Situation Report for January 7, 2015," World Health Organization, 2015.
[32] E. I. Bah, M.-C. Lamah, T. Fletcher, S. T. Jacob, D. M. Brett-Major, A. A. Sall, N. Shindo, W. A. Fischer, F. Lamontagne, S. M. Saliou, D. G. Bausch, B. Moumié, T. Jagatic, A. Sprecher, J. V. Lawler, T. Mayet, F. A. Jacquerioz, M. F. Méndez Baggi, C. Vallenas, C. Clement, S. Mardel, O. Faye, O. Faye, B. Soropogui, N. Magassouba, L. Koivogui, R. Pinto, and R. A. Fowler, "Clinical Presentation of Patients with Ebola Virus Disease in Conakry, Guinea," *N. Engl. J. Med.*, vol. 372, no. 1, pp. 40–47, 2015.

[33] X. Qiu, J. Audet, G. Wong, L. Fernando, A. Bello, S. Pillet, J. B. Alimonti, and G. P. Kobinger, “Sustained protection against Ebola virus infection following treatment of infected nonhuman primates with ZMAb,” *Sci. Rep.*, vol. 3, 2013.
[34] X. Qiu, G. Wong, J. Audet, A. Bello, L. Fernando, J. B. Alimonti, H. Fausther-Bovendo, H. Wei, J. Aviles, E. Hiatt, and others, “Reversion of advanced Ebola virus disease in nonhuman primates with ZMapp,” *Nature*, vol. 514, pp. 47–53, 2014.
[35] G. Wong, G. P. Kobinger, and X. Qiu, “Characterization of host immune responses in Ebola virus infections,” *Expert Rev. Clin. Immunol.*, vol. 10, no. 6, pp. 781–790, 2014.
[36] G. G. Olinger, J. Pettitt, D. Kim, C. Working, O. Bohorov, B. Bratcher, E. Hiatt, S. D. Hume, A. K. Johnson, J. Morton, M. Pauly, K. J. Whaley, C. M. Lear, J. E. Biggins, C. Scully, L. Hensley, and L. Zeitlin, “Delayed treatment of Ebola virus infection with plant-derived monoclonal antibodies provides protection in rhesus macaques,” *Proc. Natl. Acad. Sci.*, vol. 109, no. 44, pp. 18030–18035, 2012.
[37] “First trials for Ebola treatments to start at MSF sites in December,” Médecins Sans Frontières (MSF), Nov. 2014.
[38] D. Butler, “First trials of blood-based Ebola therapy kick off,” *Nature*, Dec. 2014.
[39] P. B. Jahrling, J. B. Geisbert, J. R. Swearengen, T. Larsen, and T. W. Geisbert, “Ebola hemorrhagic fever: evaluation of passive immunotherapy in nonhuman primates,” *J. Infect. Dis.*, vol. 196, no. Supplement 2, pp. S400–S403, 2007.
[40] H. Feldmann and T. W. Geisbert, “Ebola haemorrhagic fever,” *The Lancet*, vol. 377, no. 9768, pp. 849–862, 2011.

Figure 1. Projected impact of large-scale transfusion therapy in Liberia beginning December 1 2014 on cumulative fatalities. Grey ribbon: 95% CI for expected fatalities assuming no transfusion intervention. Arrow: start of transfusion intervention. Under a 10% hospitalization rate, convalescent plasma transfusions are expected to reduce cumulative fatalities by 3.1% (95% CI: 0.52%-4.5%) by October 1, 2015. Increasing the hospitalization rate to 30% by December 1, 2014 is projected to contain the spread; in this case, convalescent plasma transfusion is expected to achieve a 0.9% reduction in cumulative fatalities (95% CI: 0.21% -11%). Given the more limited supply of whole blood transfusions, they are projected to lower expected cumulative fatalities by only 0.73% (95% CI: 0.19%-1.1%) and 0.37% (95% CI: 0.069%-2.6%), under 10% and 30% hospitalization rates, respectively.

Figure 2. Projected numbers of Ebola cases not hospitalized, hospitalized without transfusion therapy, and hospitalized with transfusion therapy assuming a 10% hospitalization in Liberia, using (a) convalescent-whole blood (CWB) transfusions, and (b) convalescent plasma (CP) transfusions. Even if equipment and staff are available, it would not be possible to treat all hospitalized patients due to shortages of convalescent donors. With a CWB-based intervention, we estimate that 14% of patients hospitalized after the December 2014 implementation would receive therapy; with CP, the estimated fraction treated increases to 60%.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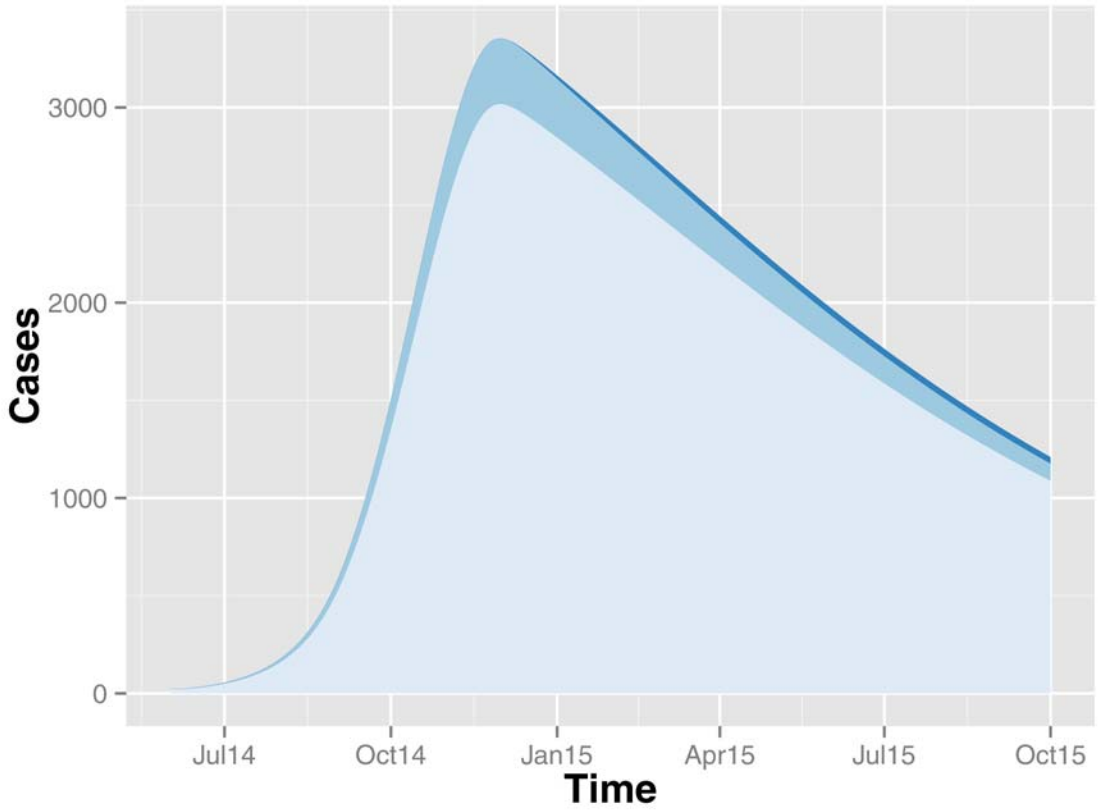
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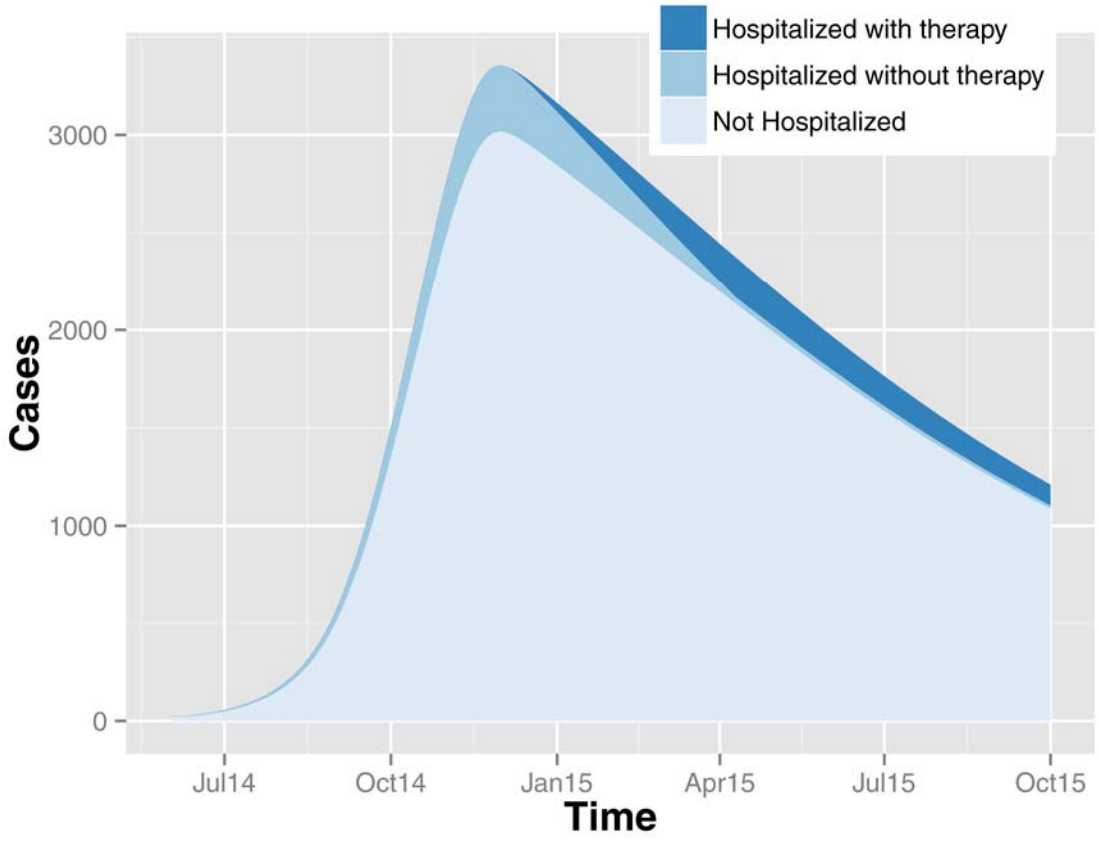
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Table 1. Projected impacts of large-scale convalescent plasma transfusion campaign under a range of scenarios. Percentages indicate relative change with respective to the baselines in the first two rows. This assumes a 10% hospitalization rate.

Scenario	Base value	Alt. value	Fatalities CWB	Fatalities CP	Treated CWB	Treated CP
No transfusions	-	-	116229		0	
Transfusion intervention	-	-	-0.73%	-3.1%	1594	6683
Higher donation rate	q_1=0.5	1.0	-1.8%	-3.7%	147%	20.8%
Higher donor retention	q_2=0.7	0.9	-1.2%	-3.4%	60.3%	9.6%
Community donations	σ_C= 0.0	0.3	-3.2%	-3.9%	331%	25.0%
Lower therapeutic efficacy	1- δ_T =0.875	0.7	-0.5%	-2.0%	-6.0%	-4.3%
Higher community mortality	δ_C = 0.80	0.9	9.4%	8.3%	0.0%	0.0%
Higher hospital mortality	δ_H = 0.67	0.9	2.3%	0.2%	-67.0%	-36.6%
Low hospital mortality	δ_H = 0.67	0.4	-3.7%	-5.2%	65.5%	14.2%
Delayed implementation (30 d)	2014-12-01	2014-12-31	-0.6%	-2.6%	-18.4%	-17.0%
Delayed implementation (60 d)	2014-12-01	2015-01-30	-0.5%	-2.1%	-35.0%	-32.6%