Agent-Based Modeling and Simulation of Nosocomial Infection among Healthcare Workers during Ebola Virus Disease Outbreak in Sierra Leone

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Healthcare workers (HCWs) are often exposed to nosocomial infection when caring for patients with Ebola Virus Disease (EVD). During the 2014-2016 EVD outbreak in West Africa, more than 200 HCWs died of EVD in Sierra Leone. To determine the factors that are important for preventing infection among HCWs during EVD outbreak, we used agent-based modeling and simulation (ABMS) by focusing on education, training and performance of HCWs. Here, we assumed 1, 000 HCWs as "agents" to analyze their behavior within a given condition and selected four parameters (P1-P4) that are important in the prevention of infection: "initially educated HCWs (P1)", "initially educated trained (P2)", "probability of seeking training (P3)" and "probability of appropriate care procedure (P4)." After varying each parameter from 0% to 100%, P3 and P4 showed a greater effect on reducing the number of HCWs infected during EVD outbreak. compared with the other two parameters. The numbers of infected HCWs were decreased from 897 to 26 and from 1,000 to 59, respectively, when P3 or P4 was increased from 0% to 100%. When P2 was increased from 0% to 100%, the number of HCWs infected was decreased from 166 to 44. Paradoxically, the number of HCWs infected was increased from 56 to 109, when P1 was increased, indicating that initial education alone cannot prevent nosocomial infection. Our results indicate that effective training and appropriate care procedure play an important role in preventing infection. The present model is useful to manage nosocomial infection among HCWs during EVD outbreak.

Keywords: agent-based modeling and simulation; Ebola virus disease; healthcare workers; nosocomial infection; Sierra Leone

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Introduction

Ebola virus disease (EVD), formerly known as Ebola hemorrhagic fever, causes an acute severe illness which can be fatal if not treated. EVD first occurred in 1976 in 2 simultaneous outbreaks. According to a report by World Health Organization (WHO), one was in what is now, Nzara, South Sudan, and the other in Yambuku, Democratic Republic of Congo in a village near the Ebola River from which the disease takes its name (WHO, World Health Organization 2018). The 2014-2016 outbreak in West Africa was the largest and most complex Ebola outbreak since the virus was first discovered in 1976 and there were more cases and deaths in this outbreak than all others combined (WHO 2018). It also spread between countries, starting in Guinea then moving across land borders to Sierra Leone and Liberia. Scientists believe that the Ebola virus is animal-borne with bats being the most likely source and there is a spillover into the human population through close contact with the blood, secretions, organs or other bodily fluids of infected animals. Ebola virus then spreads from person to person by direct contact (through an injured skin or mucous membranes) with the blood, secretions, organs or other bodily fluids of infected people, and with surfaces and materials (e.g., bedding, clothing) contaminated with these fluids.

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Healthcare workers (HCWs) are usually exposed to different kinds of infectious diseases when carrying out their roles as the profession demands them to and the reason for this is yet to be understood. "Why are healthcare workers falling victims of the virus they have set out to defeat?" is a question which we intend to answer from this research. In this paper the term HCW refers to clinical staff only. HCWs bore the brunt of the 2014-2016 West Africa Ebola outbreak by working tirelessly to treat the sick and risking their lives whenever they go to work. They were frequently infected when caring for patients who were suspected as well as confirmed cases of EVD and this occurred as a result of close contact with patients without appropriate infection prevention and control (WHO 2018). According to WHO, HCWs are between 21 and 32 times more likely to be infected with Ebola than people in the general population (WHO 2015a). In Sierra Leone, the first Ebola case was recorded in May 2014 and since then, unto November 7, 2015, a total number of 221 HCWs were reported dead of EVD (WHO 2017). HCWs should always carry out standard precautions when caring for a patient irrespective of the suspect or confirmed infection status of the patient in order to protect themselves and prevent transmission of infections to their patients. Standard precautions include hand hygiene, use of personal protective equipment, needle safety, respiratory hygiene (cough etiquette), safe handling of contaminated equipment or surfaces in patient environment and proper disposal of sharps, body fluids and other clinical wastes (Punia et al. 2014.). Due to the fact that EVD is a deadly disease, HCWs caring for patients who are suspected or confirmed EVD patients should be diligent in carrying out infection control measures so as to prevent contact with the patient's blood or bodily fluids and contaminated surfaces or materials such as clothing and beddings.

One underutilized approach to addressing problems in healthcare quality and value is the use of computer simulation modeling. Computer simulation is a method used to build dynamic models and provides a platform to guide decision making prior to implementation in the real world (Laker et al. 2018). In order to improve quality and efficacy, computer simulation models are used in many industries (manufacturing, logistics, and air transportation). Over time, computer simulation has demonstrated benefits for visualizing complex interactions in dynamic systems, providing results much faster than would be possible in real time, and allowing "what if" analysis when changes to an actual system are difficult to implement, costly, or impractical (Laker et al. 2018). Modeling is a way to solve real-life problems when we cannot experiment with real objects to get the right answer due to the fact that experiments can be expensive or dangerous (Grigoryev 2014). Thus, we chose agent-based modeling and simulation to represent the real situation of HCWs in EVD outbreak.

Agent-based modeling and simulation (ABMS) is a relatively new approach composed of autonomous, interact-

ing "agents." It is a way to model the dynamics of complex systems and complex adaptive systems. ABMS also includes models of behavior (human or otherwise) and are used to observe the collective effects of "agent" behaviors and interactions (Macal and North 2010). The advances in computation have made possible a growing number of agent-based applications across a variety of domains and disciplines (Macal and North 2010). ABMS is used to model the actions and interactions of "agents" in order to assess their effects on a system as a whole. ABMS enables a modeler to see the system from different perspectives without knowing how the system behaves.

ABMS is composed of three main components: "agents" which are characterized in terms of their attributes (e.g., static or dynamic variables) and behaviors (e.g., conditional or unconditional actions), the environment in which the agents exist, and interactions which define the relationship between agents and their environment. Although there is no universally accepted definition of an "agent," this term is typically defined as an autonomous, discrete entity that has its own behaviors and goals, with a capability to adapt and modify its behaviors (Macal and North 2006). The actions and reactions of an "agent" depend on the state in which the "agent" is. Thus, the behavior of an "agent" is defined by using statecharts. "Agents" are broad concept and may represent different things such as people in different roles, equipment, vehicles, non-material things and organizations (Grigoryev 2014). In this study, however, we simply assumed HCWs as "agents" to analyze their behavior within a given condition. Our objective was to determine the factors which are important for the prevention of infection among HCWs during EVD outbreak using ABMS.

Methods

Description of model

This study was conducted using Anylogic 8 software (Anylogic North America, Oakbrook, IL, U.S.A.) to develop and experiment an agent-based model. We assumed a representative population of 1,000 HCWs during an Ebola outbreak for a period of 365 days. Each HCW changes his or her state in a statechart according to the rules of transition. In the statechart (Fig. 1), the rectangular boxes represent the states of HCWs and the arrows represent the transitions according to the rules. The diamond shape represents the decision making branch, from which the solid arrow represents transition under a certain condition (ex. "Yes"), and the dashed arrow represents the default (ex. "No"). We placed several parameters (P1 to P4) to define the ratio of HCWs to choose "Yes" to a given condition.

States and transitions

A statechart was developed, starting with a division of HCWs into two categories of "working" HCWs (initial assumption 70%) and "not working" HCWs (initial assumption 30%) within the employed HCWs after the start of the EVD outbreak (Fig. 1). The "not working" HCWs stopped working because of fear of the disease. In both categories, we assumed that 10% of "working" or "not working" HCWs had knowledge of EVD before the outbreak (parameter "initially educated HCWs (P1)"). HCWs who had knowledge of EVD

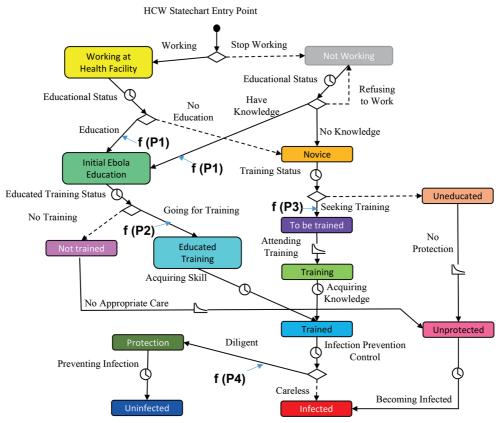


Fig. 1. Agent-based simulation model (Anylogic) of Healthcare workers during EVD Outbreak.
The statechart is an algorism of each HCW's behavior after the onset of EVD outbreak (working in a health facility or not working) to the point of being infected or uninfected.
rectangular boxes, states of HCWs; diamond, branch from which the solid arrow represents transition under a certain condition (ex. "Yes"), and the dashed arrow represents the default (ex. "No"); arrows, transitions; P1, parameter "initially educated HCWs"; P2, parameter "initially educated trained"; P3, parameter "probability of seeking training"; P4, parameter "probability of appropriate care procedure".

transited to "initial Ebola education" state.

The rest of the "working" HCWs were ignorant of EVD and thus belonged to the "novice" state. We assumed that 60% of "not working" HCWs moved to the "novice" state whilst the rest remained at the "not working" state. Those who were working and had preknowledge of EVD either went for the intensive training during the outbreak (parameter "initially educated trained (P2)") or decided not to attend for reasons such as confidence in the knowledge they already had, busy schedules or long distance to the training center. Those who did not attend the training were "unprotected" and eventually became "infected" through the time transition of 2 to 21 days (the incubation period of the Ebola virus) when carrying out duties in health facilities.

HCWs at the "novice" state attended the training during the EVD outbreak at a rate of 50 HCWs per 5 days in a week or moved to the state of "uneducated" depending on the parameter "probability of seeking training (P3)" at 95%. Those who attended the training moved to the "trained" state and thus carried out appropriate infection, prevention, and control depending on the parameter "probability of appropriate care procedure (P4)" during work. Carrying out appropriate care procedure during work lead to the state of being "protected" and then, the "uninfected" state. On the other hand, not carrying out appropriate care procedure during work lead to infection of HCWs. Also, untrained HCWs ("uneducated" state) were "unpro-

tected" which lead to the "infected" state (Fig. 1).

Parameters

Several parameters focusing on education, training and performance of HCWs were included in the development process to represent some characteristics of the model. These parameters include the following items, but we specifically designated the parameters that are related to the decision making process at the branch (diamond shapes in Fig. 1) as P1-P4.

- Total healthcare workers: the number of HCWs used as agents in the model (1,000 HCWs).
- Working fraction: The fraction of HCWs who continued working after the onset of the outbreak (initial assumption 70%).
- Not working uneducated: the percentage of HCWs who stopped working after the onset of the outbreak and did not have knowledge of EVD (initial assumption 60% of the HCWs who stopped working).
- Trainees per week: the number of HCWs trained in a week (50 HCWs). In Sierra Leone, a cumulative sum of 100 HCWs were trained per week at the two training venues (International Organization for Migration 2015).
- Training time: the time spent to complete intensive training of

HCWs who did not have pre-knowledge of EVD (5-days course in the academy (Jones-Konneh et al. 2017)).

- Initially educated HCWs (P1): the percentage of the total HCWs that had knowledge of EVD before the outbreak (initial assumption 10%).
- Initially educated trained (P2): the percentage of HCWs who had knowledge of EVD before the outbreak and attended intensive training during the outbreak (initial assumption 90%).
- Probability of seeking training (P3): the probability for HCWs without knowledge of EVD to attend intensive training during the outbreak (initial assumption 95%).
- Probability of appropriate care procedure (P4): the probability for HCWs to carry out their work diligently without being infected (initial assumption 99%).

Parameter variation and simulations

Several "what if?" scenarios were run after varying four parameters (P1-P4) that determine the behavioral choice of the HCWs at the branches in the statechart: the "Initially educated HCWs (P1)", "Initially educated trained (P2)", "probability of seeking training (P3)" and "probability of appropriate care procedure (P4)". Each parameter was varied one at a time from a minimum of 0% to a maximum of 100% at a step of 10%. The simulation was run 11 times for each parameter for a simulation period of 365 days to determine the number of HCWs that will be infected during each experiment. Also, we examined the variation of the working fraction but the outcome was the same on the 365th day (data not shown). The experiments were plotted in a 2D histogram for each parameter.

Results

Original scenario

The simulation was run with the parameters at the initial value assumption as mentioned above and the number of HCWs infected were 71 in 1,000 HCWs. Fig. 2 shows the time trend of this result. It also shows how the number of "not working" HCWs decreases with time.

Scenario 1

The "initially educated HCWs (P1)" parameter was varied from 0% to 100% at a step of 10% whilst the other parameters were kept constant. Paradoxically, increasing P1 resulted in an increase in the number of HCWs infected. At 0% when no HCW had pre-knowledge of EVD, 56 HCWs were infected, whereas at 100% when every HCW had pre-knowledge of EVD, 109 were infected (Fig. 3A).

Scenario 2

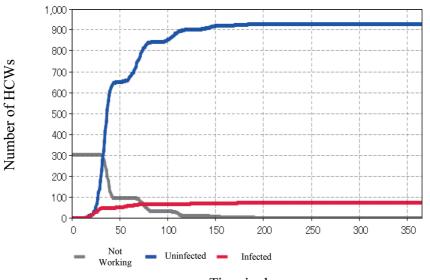
The "initially educated trained (P2)" parameter was varied from 0% to 100% at a step of 10% with all other parameters kept constant. At a value of 0% when no HCW with pre-knowledge of EVD attended the training, 166 HCWs were infected whilst at 100% when all HCWs with pre-knowledge of EVD attended the intensive 3-day training, 44 out of 1,000 HCWs were infected (Fig. 3B).

Scenario 3

The "probability of seeking training (P3)" was varied from 0% to 100% at a step of 10%. At 0% when no HCW attended the training 897 HCWs were infected whilst at 100% when all HCWs attended the training 26 were infected (Fig. 3C). There was a wide variation in the distribution of the number of HCWs infected by EVD.

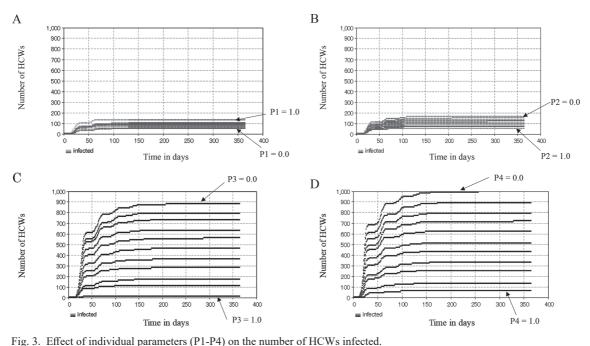
Scenario 4

The "probability of appropriate care procedure (P4)" was varied from 0% to 100% at a step of 10% with all other



Time in days

Fig. 2. Time trend of infection of HCWs in the original scenario. After the onset of the EVD outbreak, 30% of HCWs (which reduces with time when they start working at their various health facilities) stopped working. The HCWs working either got infected or remain uninfected within the 365 days period.



The parameters (P1-P4) were varied separately from 0% to 100% at a step of 10% according to the Scenarios 1-4. (A) P1 (initially educated HCWs) variation from 0% to 100% resulted in 56 to 109 HCWs infected, (B) P2 (initially educated trained) variation resulted in 166 to 44, (C) P3 (probability of seeking training) variation resulted in 897 to 26, and (D) P4 (probability of appropriate care procedure) variation resulted in 1,000 to 59 HCWs infected, respectively.

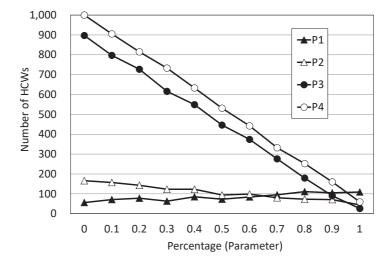


Fig. 4. Number of infected HCWs corresponding with varied parameters. P1, "initially educated HCWs" (closed triangle); P2, "initially educated trained" (open triangle); P3, "probability of seeking training" (closed circle); P4, "probability of appropriate care procedure" (open circle).

parameters kept constant. At 0% when no HCW carried out the appropriate care procedure, all of the HCWs were infected (1,000 HCWs) whereas at 100%, 59 HCWs were infected (Fig. 3D). This result also showed a wide variation in the distribution of the number of HCWs infected.

In summary, varying the "probability of seeking training (P3)" and the "probability of appropriate care procedure (P4)" had a greater effect on the number of HCWs infected than the other two parameters "initially educated HCWs (P1)" and "initially educated trained (P2)". Increasing P1 paradoxically increased the number of HCWs infected (Fig. 4).

Discussion

This is the first research with ABMS for the analysis of HCWs' behavior during EVD outbreak. Many HCWs were infected with EVD because they did not carry out or were not aware of basic infection, prevention and control measures like hand hygiene, wearing gloves or proper waste disposal (WHO 2015b). In this model, we examined four parameters that were hypothesized to be very important in the prevention of infection among HCWs: "initially educated HCWs (P1)", "initially educated trained (P2)", "probability of seeking training (P3)" and "probability of appropriate care procedure (P4)". The "probability of seeking training (P3)" and the "probability of appropriate care procedure (P4)" had a more significant effect on the number of HCWs infected. Thus, these two parameters are more important than "initially educated HCWs (P1)" and "initially educated trained (P2)" when considering the protection of HCWs during an EVD outbreak. Furthermore, increasing the parameter "initially educated HCWs (P1)" paradoxically increased the number of HCWs infected. The initial working fraction did not alter the final outcome of the HCWs infected during the outbreak (data not shown).

Some HCWs were infected or died of EVD and as a result, many abandoned their jobs (stayed away from work) for fear of the disease (Medecins Sans Frontieres 2014; Lupton 2015). Even though there was lack of knowledge and misconception about Ebola amongst HCWs, they grad-ually learned more about Ebola and how to protect themselves, and returned to their work (Raven et al. 2018).

Initially educated HCWs (P1)

Education of HCWs on EVD before an outbreak influenced the rate of infection of HCWs. However, the variation in the distribution of HCWs infected was narrow (Fig. 3A). Without initial education of HCWs, the number of HCWs infected was small (56 in 1,000 HCWs). Paradoxically, increasing the parameter "initially educated HCWs" lead to an increase in the number of HCWs infected (negative effect) due to the transition rule that not all of them attended the training during the outbreak (Fig. 4 Closed triangle). According to a study done in Lagos, Nigeria, a high proportion of HCWs had good knowledge of EVD which did not translate to good practice and a conclusion was drawn that training on EVD was crucial for good practices of standard health precautions and infection control (Oladimeji et al. 2015). Thus, initial education alone without training during the outbreak cannot prevent the infection of HCWs.

Initially educated trained (P2)

The training of HCWs with pre-knowledge of EVD also influenced the rate of HCWs' infection. The variation in the distribution of HCWs infected was narrow (Fig. 3B). At 0%, the HCWs infected were 166, the value of which was decreased as the percentage of trained HCWs increased. Thus, there was a positive effect (reduction in the number of HCWs infected) when they were trained. During training, realistic drills (simulations) are conducted and HCWs are offered both practical and honest feedback on their performance. Drills play a definite role when tasks are infrequent and complex, relatively new and evolving, and when consequences of sub-standard performance can be life-threatening (Agency for Healthcare Research and

Quality 2015).

Probability of seeking training (P3)

The number of HCWs who were trained during EVD outbreak determined the rate of infection of HCWs. If HCWs are not trained they will be exposed to the virus, and being ignorant of prevention and control measures will lead to infection. Increasing the number of HCWs being trained during an outbreak will thus reduce the infection rate among HCWs. Appropriate training of HCWs is critical, ensuring that they are equipped with the knowledge needed to work in the face of an epidemic (Annan et al. 2017). This calls for an intensive training, so that HCWs will be thoroughly equipped to fight this biological war. Training programs address weaknesses and improve the performance of HCWs. All HCWs should be trained even if they have knowledge of the virus, as the training will deal with practical, onsite issues and not merely the study of the virus and management. As mentioned earlier, increasing the parameter "initial educated HCWs (P1)" paradoxically increased the number of HCWs infected.

Probability of appropriate care procedure (P4)

Even though HCWs had been effectively trained, their attitude towards work was a vital factor towards their protection from the virus. Carrying out donning and doffing diligently will prevent exposure of body parts and contact with the virus. Hand hygiene being done, according to the five moments of hand hygiene by WHO (WHO 2009), with an appropriate care procedure is another important part of the prevention control measures. HCWs must be emotionally stable, being focused when carrying out duties in order to do their job well. Emotionally stable individuals are more likely to be effective workers and as a result, emotional stability can positively influence nursing care quality (Teng et al. 2009). Therefore, the informed consent of HCWs must be consulted before they are sent into the wards to ensure that they are in the right mood to carry out their job. Emotionally stable nurses can deal calmly with these crises or emergencies without letting negative personal emotions interfere with their rational decision-making (Teng et al. 2009). If HCWs are not in the right frame of mind (calm) when working in the treatment ward, they might carry out wrong procedures and the possibility of infection becomes higher.

In Sierra Leone, in addition to their official employment in governmental facilities, many HCWs work in private clinics, outpatient offices or in their communities (WHO 2015c). HCWs want to carry out their duties hurriedly in order to finish early and go work in another health facility. Working hurriedly can increase the possibility of making a mistake. Hence, during an EVD outbreak HCWs working especially at treatment centers must be given substantial incentives and restricted from working at another health facility.

Also, every HCW entering the ward must be accompa-

nied by a buddy to observe each other during work in order to reduce mistakes and fatigue. There is also the need for continuous training after the intensive five-day training of HCWs (Jones-Konneh et al. 2017). These periodical follow up training can be done at individual treatment centers or hospitals to remind HCWs of how to carry out their duties so as to prevent infection.

Benefits of ABMS

The use of agent-based modeling and simulation to carry out this experiment was of great advantage. Any experiment to verify the number of HCWs infected during EVD outbreak is not allowed in real life because it is too dangerous, costly and not ethical. The simulation showed the outcome of not being trained and wrong attitude towards work. HCWs are usually very busy and individuals have different personalities. ABMS can simulate such polyclonal population with a statistical and probabilistic analysis of individual HCW's behavior. Thus, ABMS is a very useful tool which must be used in the health sector to solve problems of real life. This model was created based on the experience in Sierra Leone, but the result can be widely applicable to any country in the fight against infection of HCWs during EVD or any other serious outbreak.

Limitations

This study did not disaggregate the details of HCWs' behavior such as appropriate care procedure. Infection of HCWs can occur at any moment and occasion, and the model itself is based on many assumptions without actual geographical, spatial and temporal distribution of HCWs. However, this work showed the HCWs behavioral framework and the factors affecting the outcome. Actual surveillance of HCWs who worked during the outbreak might supplement for the validation of our results, however ethical review board approval and informed consent of individual participants of the surveillance to access confidential data such as infection history for EVD is necessary.

It also did not include the delay in the political decisions including acceptance of international relief aids to establish a training academy for training of HCWs. In Sierra Leone, it took almost half-a-year after the onset of the EVD outbreak to start the intensive education in the academy (Jones-Konneh et al. 2017). Before that, the appropriate care was not taken and the patient outcome was miserable. The social environment can be added in future models.

This model only focused on the behavior of HCWs who were confronted with this biological crisis. Further modeling with patients, families, facilities and environmental factors will give us a further insight of community behavior.

Conclusion

The welfare of HCWs must be of utmost importance to all authorities concerned. If HCWs are infected during

an EVD outbreak then there will be no hope for the patients leading to massive deaths. In our model, the "Probability of seeking training (P3)" and "Probability of appropriate care procedure (P4)" had a more significant impact in the prevention of EVD infection among HCWs than the "Initially educated HCWs (P1)" and "Initially educated trained (P2)". When HCWs are trained (having the knowledge they need) and carry out their duties diligently, they will be protected from EVD infection. The relevance of this simulation model extends not only to the immediate Ebola response but beyond Ebola to other serious outbreaks threat to the lives of HCWs. Our results demonstrate the importance of effective training and the right attitude towards work to fight against infection among HCWs.

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Conflict of Interest

The authors declare no conflict of interest.

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