

MODELING THE POTENTIAL IMPACT OF COMMUNITY HEALTH VOLUNTEERS IN THE DIAGNOSIS AND TREATMENT OF BURULI ULCER

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ABSTRACT

Buruli ulcer (BU) is a debilitating disease affecting the skin, soft tissue, and bone. It is the third most common mycobacterial disease in humans. The mode of transmission is not fully understood, posing challenges in prevention, and delayed diagnosis. One effective approach to promote early diagnosis and treatment is the utilization of community health volunteers (CHVs) for active case-finding. In this study, we developed an agent-based model to investigate the impact of CHVs in referring BU patients for treatment. We compared the effects of two strategies: offering self-referral alone versus self-referral combined with CHVs, on the early diagnosis and treatment of BU. Our findings confirm previous knowledge that integrating CHVs in active case-finding leads to earlier detection of BU cases, decreasing the number of individuals recovering with major disabilities.

1 INTRODUCTION

Buruli ulcer (BU) is a neglected tropical disease caused by infection with the *Mycobacterium ulcerans* bacterium (WHO 2023). Although BU has been reported in 33 countries globally, its prevalence is highest in west and central Africa, Australia, and Japan (Yotsu et al. 2015). However, the actual number of cases may be under-reported, as many countries likely to have cases do not report to the World Health Organization (WHO).

BU manifests as a painless itchy nodule, plaque, or oedematous lesion that eventually ulcerates within weeks with undermined edges (WHO 2023). WHO categorizes the disease based on the size and severity of the lesions, with category I appearing as one tiny lesion (32%), category II appearing in non-ulcerative and ulcerative plaque and oedematous forms (35%), and category III involving disseminated and mixed forms where ulcers spread to the bones and joints (33%) (WHO 2012).

In spite of the fact that BU does not directly result in death, if not treated early, it can lead to functional limitations, severe permanent disabilities, and social stigmatization (Stienstra et al. 2002; Ellen et al. 2003; Johnson et al. 2005). Early diagnosis and antibiotic treatment before ulceration are the quickest remedies for the disease, as late treatment can prove challenging, requiring extensive surgical debridement of the infected skin and neighboring damaged tissue, sometimes including skin grafting.

Implementing public health strategies, such as community involvement and training health workers to educate the general public, has proven effective in encouraging early diagnosis and treatment. One such intervention is the introduction of community health volunteers (CHV) to refer BU patients, which has improved the number of reported BU cases (Vouking et al. 2013; Barogui et al. 2014; Vouking et al. 2014). For example, in a high-endemic district in Ghana, using CHVs in active case-finding resulted in

a 70% increase in detected category 1 BU cases (Abass et al. 2015). Similarly, in the Ngoantet region of Cameroon, CHVs referred 95% of BU cases, and 91.5% of those suspected cases were confirmed by health personnel (Vouking et al. 2014). The effectiveness of CHV programs in controlling BU was further supported by Vouking et al. (2013), and Barogui et al. (2014) emphasized the essential role of CHVs in managing BU in Benin.

Although the literature demonstrates the impact of CHVs on BU case referral, no previous studies have explicitly analysed the contributions of self-referral (SR), CHVs, or their combined effects on early diagnosis and treatment using agent-based models (ABMs).

Using an agent-based model (ABM) for disease modeling, such as in the case of Buruli ulcers, provides several advantages over clinical trials. ABMs capture individual interactions and behaviors, offering a realistic portrayal of disease transmission dynamics over time. Unlike the trial-based studies by (Vouking et al. 2013; Barogui et al. 2014; Vouking et al. 2014), ABMs allow for a more detailed evaluation of intervention strategies, e.g., the varying impact of employing different numbers of CHVs. In the example we consider here, the prime reason for the use of an ABM is to give us more control over the details of the intervention. Moving beyond our initial model, an ABM could also enable us to account for population heterogeneity, considering factors like age, individual movements and behavior, as well as incorporating spatial and temporal dimensions. Their flexibility enables parameter modification and scenario testing, aiding in identifying effective disease control strategies (Hackl and Dubernet 2019; Macal 2016; Macal and North 2005; Smith et al. 2018).

In this study, we aim to quantify the impact of CHVs on BU referral using an ABM. Our model will capture the proportions of the population infected, in treatment, and recovered within each WHO category. Specifically, we will investigate how the implementation of CHVs: (i) influences the referral of BU patients for early diagnosis and treatment in the early categories of BU disease, and (ii) reduces the number of BU patients who recover with disabilities. No previous work has modeled BU using the WHO severity classification to describe disease progression.

To achieve this, we propose an ABM simulation as the most suitable tool for studying the dynamics of BU and the interactions between individuals. Our ABM focuses on the interactions between BU patients and CHVs, enabling us to assess the impact of different referral strategies on early diagnosis and treatment of BU. By investigating the specific contributions of CHVs through an ABM, this study aims to provide valuable insights into the effectiveness of CHV programs in BU control and management. These findings can inform policymakers and healthcare authorities on implementing CHVs as a proactive strategy for improving early detection and treatment, ultimately reducing the burden of BU-related disabilities.

The rest of the paper is structured as follows. Section 2 presents the literature review. Section 3 provides a description of the model, and some of the key assumptions we have made. In Section 4, we present numerical simulations of the model, and Section 5 contains our conclusions based on these simulations.

2 LITERATURE REVIEW

Mathematical and epidemiological models have contributed significantly to disease research, providing insights into controlling and managing diseases (Hollingsworth 2009). These models are often used alongside experimental studies to help policymakers in deciding on preventive and treatment measures. Currie et al. (2020) provided insights on how simulation modeling can be used to support decision-makers in reducing the impact of COVID-19, but its conclusions are also relevant to other diseases. ABMs are well-suited for situations where individual interactions and behaviors are crucial. In the context of COVID-19, ABMs were effective for capturing the dynamics of transmission, considering heterogeneity, and studying interventions that rely on personal choices and behaviors within a population (Currie et al. 2020). In the past, simulation modeling has also been used in modeling the spread of cancer (Preziosi 2003), HIV (Wilensky 1997), and malaria (Smith et al. 2018) among others. We briefly discuss two key selected studies particularly relevant to our work below.

Modu et al. (2020) used a hybrid methodology that combines a mathematical model and an ABM to model and analyze malaria transmission for heterogeneous populations. The mathematical model describes the spread of malaria based on mosquito and human populations using a compartmental transmission model, while the ABM includes humans, mosquitoes, pathogens, and environmental agents. They validated the models against reported malaria cases in three cities and found that the ABM was robust in predicting the season of malaria and possible fluctuations. Their methodology provides a useful reference for developing similar ABMs.

Yang and Wilensky (2011) developed a simulation tool called *Epidemiology: Understanding Disease Dynamics and Emergence through Modeling (epiDEM)*, which models the spread of an infectious disease in a closed population. The model is based on the Kermack-McKendrick model and uses agents to represent individuals interacting in the environment according to pre-set rules. Each agent in the model has direct neighbors and surroundings, and there is a chance for an infected person to recover after reaching the estimated recovery time. The epiDEM model is built in *NetLogo* (Wilensky 1999), which allows the user to set the initial population, probability of contracting infection, and average recovery time. The interface allows monitoring of infection and recovery rates and changes in the reproductive number and recovered population per tick. On the *NetLogo* interface, colors can represent an individual's health status, and sliders can enable the setting of parameter values.

ABMs are ideal for modeling BU due to their incorporation of BU patient-CHV interactions. ABMs simulate agents with predefined rules, effectively capturing stochasticity, individuality, and spatial variation. They represent individuals, enabling a granular view of the population. ABMs emphasize emergent behavior and offer a micro-scale perspective, distinguishing them from other simulation techniques. The stochastic nature of ABMs accurately mimics BU transmission.

Our model is based on worked examples in *NetLogo*, particularly *epiDEM* (Yang and Wilensky 2011), and builds on the concepts from introductory sample models (Wilensky 1999).

3 MODEL DESCRIPTION

The model description follows the ODD (Overview, Design concepts, Details) protocol for describing ABM (Grimm et al. 2006; Grimm et al. 2020).

To investigate how the two modes of referral affect the numbers of recovered individuals with disabilities, we use an ABM as that allows us to model the impact of the CHVs who find new cases via random interactions with the population. An individual starts treatment either following an interaction with a CHV or via self-referral.

The transmission mechanism of BU into the skin is still unknown but it is assumed to be transmitted through interaction with the environment where the bacterium resides. As a result, we model transmission by assuming a person who is in a particular area has a probability of contracting BU (as described in Section 3.3). There is no chance of transmission outside of that area.

3.1 Entities, state variables and scales

The model contains two types of agents: (a) people in the general population and (b) CHVs. We classify the general population as susceptible (*S*), infected (*I*), treated (*T*) or recovered (*R*), and the *I*, *T* and *R* populations are each grouped into 3 categories as described in Table 1.

We represent the area occupied by the total population using a 17×17 grid of square cells representing the spatial distribution of agents. CHVs move around seeking for BU infected people. If an individual and a CHV occupy the same patch, they are considered to be in the same place and in contact with each other. Only when this occurs will the CHV refer the infected individual for treatment.

Our model allows CHVs to exhibit random movement due to the difficulty in accurately predicting their precise movement patterns within the community, primarily due to limited data, including geographical information. Employing a random movement approach simplifies the model while effectively capturing

the dynamic behavior of CHVs. Furthermore, the random movement paradigm adeptly accounts for the serendipitous encounters CHVs have with infected BU patients during their routine daily activities.

The model is two-dimensional and an agent's location is defined by which cell it is in. We assume a time step of one week, and simulations run for 400 weeks.

Table 1: Description of the agent population and their state variables.

State variable	Description
susceptible?	Is the person susceptible?
infection-length	The total duration an individual has spent with BU from initial infection to category one.
infection-lengthTwo	The duration an individual has spent with category two BU.
infected?	Is the person infected in BU category one?
infectedTwo?	Is the person infected in BU category two?
infectedThree?	Is the person infected in BU category three?
hospitaltwo?	Is the infected BU patient on antibiotic and minor surgery treatment?
hospitalthree?	Is the infected BU patient on antibiotic and major surgery treatment?
antibiotics?	Is the infected BU patient on antibiotic treatment?
antibiotic-time	The duration an infected BU patient has been on antibiotics treatment
hospital-time-two	The duration an infected BU patient has been on antibiotic and minor surgery treatment
hospital-time-three	The duration an infected BU patient has been on antibiotic and major surgery treatment
noDisability?	Does the BU patient recover with no disability?
minorDisability?	Does the BU patient recover with minor disability?
majorDisability?	Does the BU patient recover with major disability?
CHV	Community Health Volunteers

3.2 Process Overview and Scheduling

Figure 1 presents an outline of the sequence of processes and the schedule of interactions between agents at each time step.

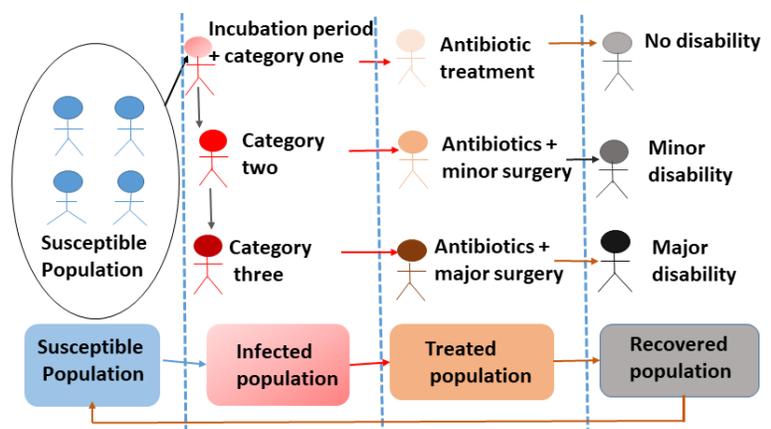


Figure 1: Illustration of different states of the model to simulate the progress of BU in a population.

At each time step, the time counter, the unit values of chosen input parameters and the infection history are updated. Next, we let agents move randomly across space. If they are uninfected and move into the patch representing initial infection (the habitat of *M. ulcerans*), they become infected and move to category 1. If they are already infected and enter the same patch as a CHV agent, the CHV will refer them to treatment. Infected individuals who are not in treatment move through the categories of infection. The infected BU patients can also start treatment through SR. Infected individuals proceed to commence treatment and can recover with either no disability or different forms of disability dependent on their infection category prior to treatment. Finally, model outputs are updated. The graphical interface outputs are re-drawn, and updated population information is written to an output file.

3.3 Design Concepts

The basic principle of this model is to illustrate how interactions between CHV and BU patients influence treatment referral. The CHV interactions mimic the search for infected people in the population. When the CHV occupies the same grid square as a BU patient, we observe both agents as being on the same patch. This implies that the two agents interacted, leading to the referral of an infected BU individual. The alternative route to treatment is via SR. In SR, BU patients seek treatment without the involvement of a CHV.

We observe two key elements of stochasticity used in initializing the model and during the simulation. These include: (a) randomness on how populations move within the grid squares, and (b) the time spent in each infection category. Threshold time (the time it takes to transition from category one to category two infection (equal to BU-symptoms plus Threshold-timeone)) and the agent's time to recovery, both of which influence disease progression periods, are generated from an exponential distribution for each infected person.

3.4 Initialization

At the start, we choose the ratio of CHVs to the total population in the simulation, using 100 : 1000 as the base level. These initial values were chosen to provide a sufficient sample size while allowing a suitable simulation time. At each simulation run, we use the parameters in Table 2.

3.4.1 Submodels

The clock process keeps track of time in the model and is represented in weeks. Agents move forward one step at a time and turn at random angles between 0° and 360° in the move process.

The infection process follows three procedures: infect-start, infect-two, and infect-three. During infect-start, the population interacts with the habitat of *M. ulcerans*, and an uninfected individual has a chance of contracting BU. Infected agents transition to category two infection when their infection length exceeds the threshold time in infect-two. In infect-three, agents with category two BU infection transition to category three when their infection-lengthTwo exceeds the threshold timeTwo.

The treatment process is initiated through SR or meeting a CHV, and the infected individuals receive antibiotic and surgical treatments depending on their BU infection category. In SR, agents receive treatments after being infected for a period called BU-symptoms. In Meet-chvs, infected individuals meet a CHV, who refers them for treatment. Once in treatment, agents are no longer counted as infected, and their infection length parameter(s) are reset to zero.

In the recovery process, a person in treatment will recover after reaching their recovery time. Each individual's recovery time is generated from an exponential distribution with a mean equal to the average recovery time. If antibiotic-time exceeds the recovery timeone, hospital-time-two exceeds the recovery timetwo, or hospital-time-three exceeds the recovery timethree, BU patients recover with no disability, minor disability or major disability, respectively.

Finally, the update global variables process considers the weekly progress of the population and updates agent locations and states accordingly.

3.4.2 Model parameter values

Some parameter values have been obtained from experimental data available in literature and also estimated based on the assumptions about BU disease. Other parameters are difficult to specify accurately so we have estimated them based on similar observations cited in previous studies. Reasons for choosing particular parameter values are given below.

BU-symptoms: how long a person is infected before symptoms show (incubation period). According to (Group 1971), the incubation period for BU was found to be under 3 months. In this model, we choose to use 3 months which is ≈ 13 weeks for the simulation.

Threshold-timeone: the time it takes from the development of symptoms to the transition to a category one infection. The average threshold-timeone was estimated to be approximately 4 weeks or longer ((WHO 2023)) and 6 weeks in pigs (Bolz et al. 2016). We assume a value of 6 weeks.

Threshold-time: the time it takes to transition from development of symptoms to category two infection and is calculated as BU-symptoms plus threshold-timeone.

Threshold-timeTwo: the time it takes from developing a category two infection to the transition to category three infection. According to (WHO 2023; Portaels et al. 2001), the average threshold-timetwo was estimated to be approximately 4 weeks.

SR probabilities: the probabilities that individuals with BU in categories 1, 2 and 3 will self-refer for treatment, respectively. (WHO 2023) reported that 70% of all BU cases were diagnosed after ulceration (category 3). To mimic this, we set the SR probabilities for BU patients in categories 1, 2 and 3 be 10%, 20% and 70%, respectively.

Recovery-timeone: the period it takes for an individual who has been on antibiotic treatment to recover fully. According to (Nienhuis et al. 2010; Johnson 2020), the average recovery time for treatment was 8 weeks. In this model, we use the same value in our simulations.

Recovery-time-two: the period it takes for an individual who has been on antibiotic treatment and minor surgeries to recover fully. BU patients who start treatment when the ulcers are deep (WHO category 2) have a median healing time of 30 weeks (95% CI 26 – 34 weeks) (Nienhuis et al. 2010). Hence, we use a value of 30 weeks as the recovery-time-two in our simulations.

Recovery-time-three: This is the period it takes for an individual who has been on antibiotic treatment and major surgeries to recover fully. This treatment was estimated to take an average of 1 year which is equivalent to 52 weeks (WHO 2023).

We generate the values for the threshold-timeone, threshold-timeTwo, recovery-time-two and recovery-time-three from an exponential distribution with mean equal to their respective averages.

Table 2: State constants and population initialization parameters used in the model.

Name	Baseline value	Probability distribution
BU-symptoms	13.0 weeks	-
Threshold-timeone	6.0 weeks	Exponential
Threshold-timeTwo	4.0 weeks	Exponential
Self-refer-prob-category1	10%	-
Self-refer-prob-category2	20%	-
Self-refer-prob-category3	70%	-
Recovery-timeone	8 weeks	Exponential
Recovery-timetwo	30 weeks	Exponential
Recovery-timethree	52 weeks	Exponential

4 SIMULATION RESULTS

The model was implemented in NetLogo version 6.2.2 (Wilensky 1999) which is freely available. We design a procedure where agent behaviors and interactions imitate the transitions of BU patients from infection to treatment. Using NetLogo, we created CHV and population agents and depicted them as person shapes. During the simulation, the agents are initialized in terms of their spatial positions in the environment and follow predefined processes of movement, infection, seeking treatment, and recovery as explained in Section 3.4.1.

In all simulations, we initialize the total population as 1000, and the area of simulation is a 17×17 square grid. We used 10 simulation runs in generating experimental results, balancing computational efficiency and obtaining meaningful insights. Using 10 runs appears to provide a reasonable approximation of the model's behavior while capturing the desired variation and insights.

We describe the performance of the model in different scenarios in Sections 4.1 and 4.2. In Figures 2 and 3, we illustrate the trend in the number of agents who are susceptible (a), infected in category one (b), infected in category two (c), infected in category three (d). We include the populations on antibiotics and in-hospital treatment (e-g), populations with no disability, minor disability and major disability (h-j).

4.1 ABM with SR only (SR1)

In this scenario, we let BU patients start treatment through SR only and keep track of the progression of the population within the infected, treated and recovered states.

In Figure 2, the number of BU patients progressing from infected category 1 to category 2 drops from a maximum of approximately 50 to 15. On average, there are approximately 3 category 3 patients.

In the first 50 weeks, the number of BU patients starting antibiotic treatment increases rapidly from 0 to 30, followed by a decrease with regular fluctuations. We observe a similar pattern for BU patients in hospital two. The number of people in treatment at hospital three is increasing.

In Figure 2, we observe the highest number of disability were those with major disabilities. This could be because BU patients start treatment late (hospital three) and hence develop a major disability.

After 400 weeks, there are approximately 200 people with no disability. Cumulatively, around 250 to 400 people are suffering from either a minor or a major disability.

4.2 Self-referral and CHV for active case-finding

In this scenario, we let CHV only refer infected people who show symptoms (thus excluding those in the incubation period). We let BU patients start treatment through both SR and CHV (SR1CHV1 and SR4CHV4) and compare with SR alone (SR1). We initialize the simulation with 100 CHV and 80 CHV and observe the number of cumulative infected and in-treatment populations over time.

In Figure 3, specifically for (SR1CHV1), the transition of BU patients from infected category 1 to category 2 shows a significant decrease, dropping from a peak of approximately 60 to just 2 cases. Category 3 patients are notably scarce on average.

The number of BU patients initiating antibiotic treatment experiences rapid growth from 0 to around 60 within the initial 50 weeks, followed by a slow decline. BU patients receiving treatment in hospitaltwo and hospitalthree gradually increase from 0 to approximately 100. The number of BU patients without disability totals approximately 250 within 400 weeks. Cumulatively, there are around 450 and 300 individuals with minor and major disabilities, respectively, in the same timeframe.

A comparison between SR1 and SR1CHV1 in Figure 3 reveals that SR alone has the highest numbers of infected individuals across all categories, more patients in hospitaltwo and hospitalthree treatment, and a higher count of people with major disabilities compared to SR&CHV. Moreover, SR alone has the lowest figures for individuals on antibiotic treatment, hospitaltwo, those with no disabilities, and those with minor disabilities.

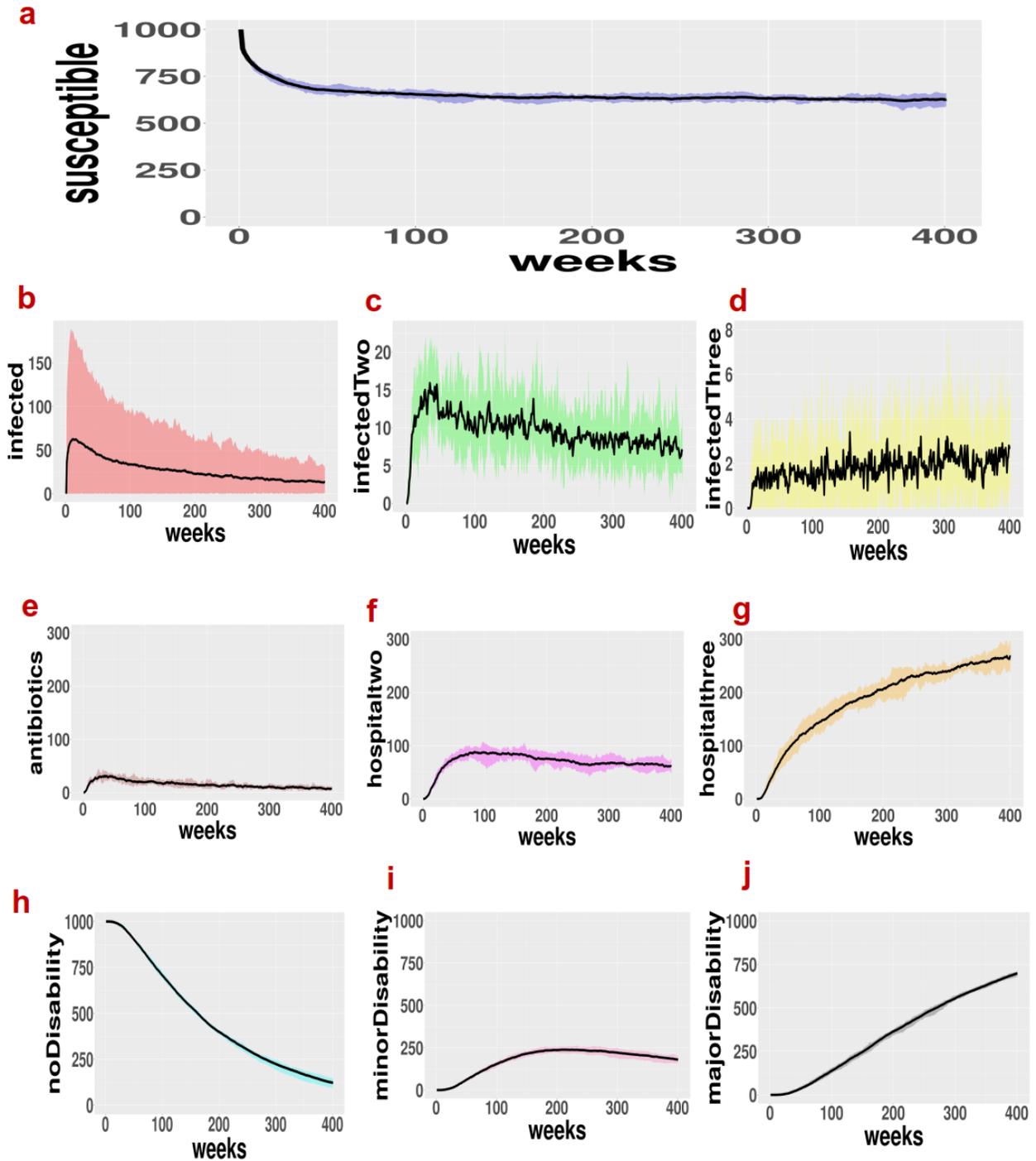


Figure 2: **SR only (SR1)**: We illustrate data as the mean (solid line) and minimum and maximum values (shading) of estimates of 10 simulations from 10 model runs of the ABM.

The patterns observed in Figure 3 suggest that when CHVs are introduced, fewer people will require referrals, resulting in outcomes that fall between those of SR1 and SR1CHV1. Additionally, when CHVs

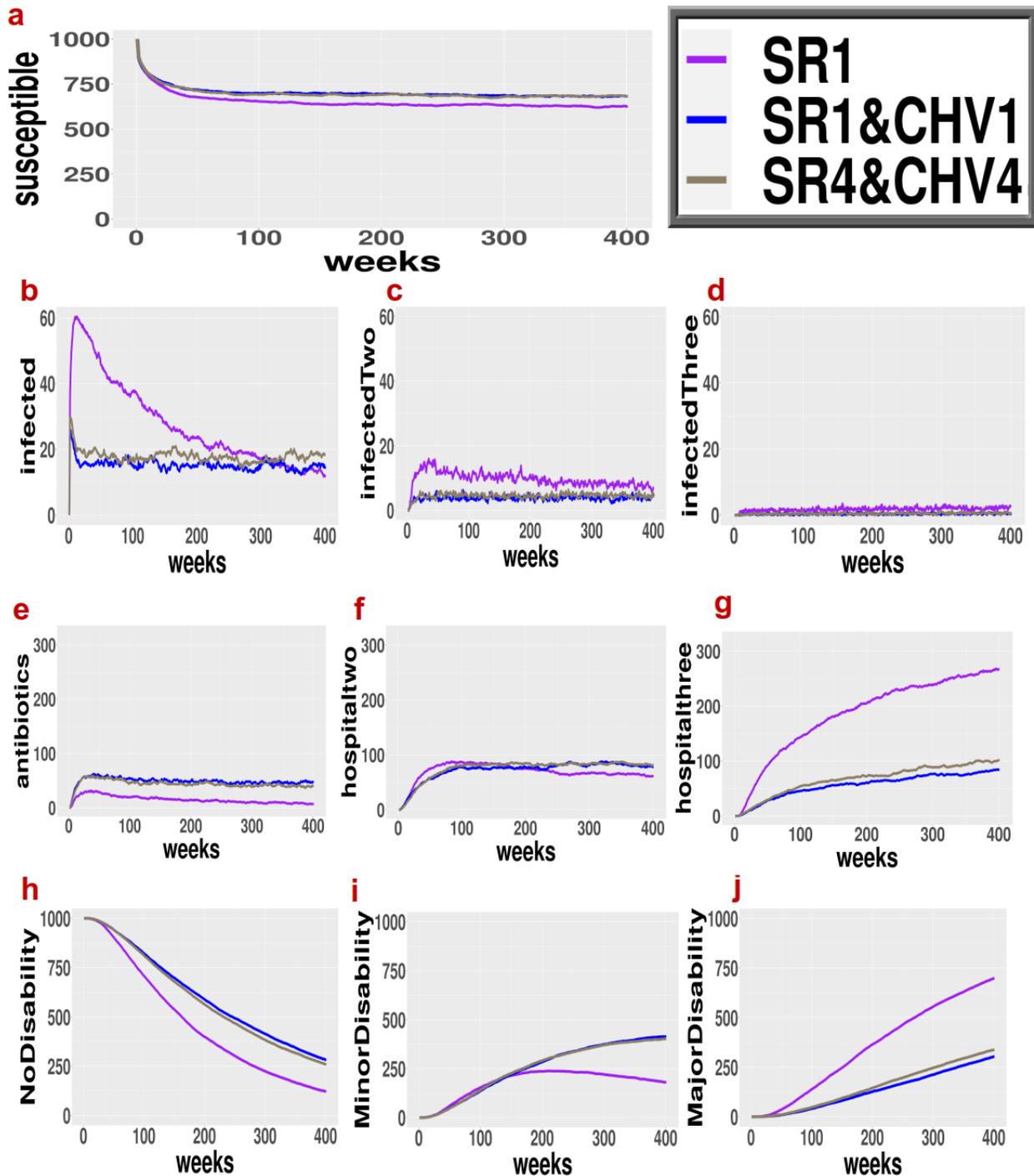


Figure 3: **SR and CHV refer infected people for treatment (SR1CHV1 and SR4CHV4)**: these plots illustrate the mean of estimates of 10 simulations from 10 model runs of the ABM for SR4CHV4 compared with the base case scenario (SR1).

were reduced to 80 as depicted in Figure 3, this led to a decrease in cases of individuals recovering with no disabilities, an increase in infected cases, hospital three admissions, and instances of major disabilities.

These findings imply that the incorporation of CHVs played a pivotal role in encouraging early treatment initiation among the BU-infected population, subsequently reducing the number of cases with disabilities.

4.3 Varying the number of CHV

In this scenario, we observe the effect of the number of CHVs on the number of people with no, minor and major disability.

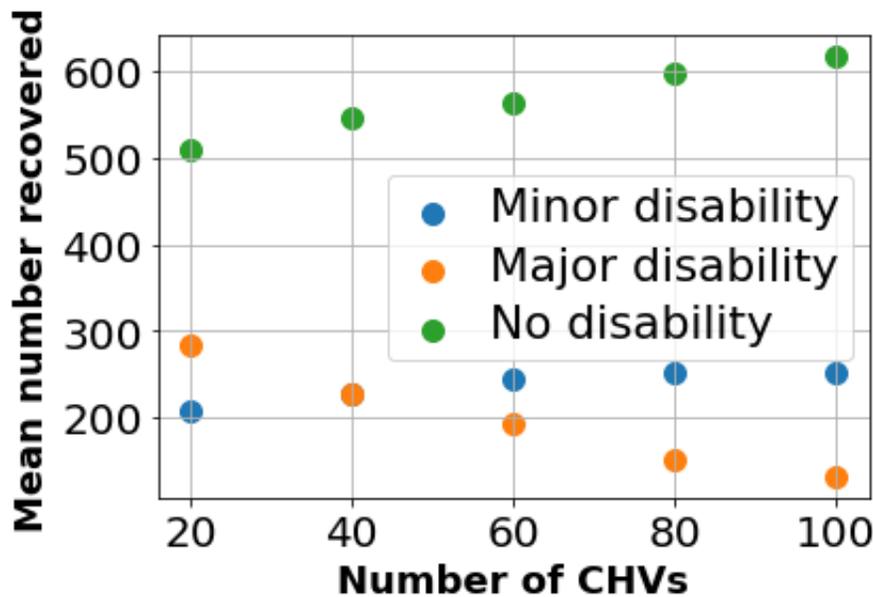


Figure 4: **Varying the number of CHV:** The mean number of people that recover with a major, minor and no disability between 300 and 400 weeks for different numbers of CHV.

Figure 4 shows that increasing the number of CHVs results in a significant decrease in the mean number of people with major disabilities.

This observation can be attributed to the early tracking and initiation of antibiotic treatment for infected individuals due to CHVs. Consequently, there is a reduction in the number of cases progressing to the late category of infection, resulting in fewer delayed treatment starts.

5 CONCLUSION

In this study, we presented an ABM that simulates the interactions between BU patients and CHV to investigate how CHV could improve early diagnosis and treatment of BU. We examined the impact of SR alone versus SR and CHV combined and the effects of varying the number of CHVs and having them only refer infected patients with symptoms. We also tracked the progression of BU within the infected and treated population over 400 weeks.

Our simulation results showed that the scenario with both SR and CHV had the highest number of patients on antibiotics treatment, leading to more people recovering with no disability and fewer individuals with minor and major disabilities. In contrast, using only SR resulted in an increasing number of late category cases, leading to delayed treatment and more people recovering with minor and major disabilities. The introduction of CHVs for active case finding results in treatment starting earlier, which coincides with our initial expectations.

Our model provides insights into the proportion of patients in each stage with or without CHV, which is crucial in predicting disease progression when there is insufficient data on BU cases. However, we

acknowledge some limitations in our study, including the lack of detailed information on CHV for BU and the absence of experimental data to validate the model. Additionally, our assumption that CHVs are 100% accurate at detecting BU immediately after encountering an infected patient may not always be realistic. We recommend collecting mobility data on agents within a community and updating the impact of CHV on BU.

Finally, this model could be customized to model the introduction of CHVs for detection of other neglected tropical diseases by adjusting features of the infection and the disease's treatment and recovery processes.

REFERENCES

- Abass, K. M., T. S. Van Der Werf, R. O. Phillips, F. S. Sarfo, J. Abotsi, S. O. Mireku, W. N. Thompson, K. Asiedu, Y. Stienstra, and S.-A. Klis. 2015. "Buruli Ulcer Control in a Highly Endemic District in Ghana: Role of Community-Based Surveillance Volunteers". *The American Journal of Tropical Medicine and Hygiene* 92(1):115–117.
- Barogui, Y. T., G. E. Sopoh, R. C. Johnson, J. de Zeeuw, A. D. Dossou, J. G. Houezo, A. Chaaty, J. Aguiar, D. Agossadou, P. A. Etorh et al. 2014. "Contribution of the Community Health Volunteers in the Control of Buruli Ulcer in Bénin". *PLoS Neglected Tropical Diseases* 8(10):e3200.
- Bolz, M., N. Ruggli, N. Borel, G. Pluschke, and M.-T. Ruf. 2016. "Local Cellular Immune Responses and Pathogenesis of Buruli Ulcer Lesions in the Experimental Mycobacterium Ulcerans Pig Infection Model". *PLoS Neglected Tropical Diseases* 10(4):e0004678.
- Currie, C. S., J. W. Fowler, K. Kotiadis, T. Monks, B. S. Onggo, D. A. Robertson, and A. A. Tako. 2020. "How Simulation Modelling Can Help Reduce the Impact of COVID-19". *Journal of Simulation* 14(2):83–97.
- Ellen, D. E., Y. Stienstra, M. A. Teelken, P. U. Dijkstra, W. T. Van Der Graaf, and T. S. Van Der Werf. 2003. "Assessment of Functional Limitations Caused by Mycobacterium Ulcerans Infection: Towards a Buruli Ulcer Functional Limitation Score". *Tropical Medicine & International Health* 8(1):90–96.
- Grimm, V., U. Berger, F. Bastiansen, S. Eliassen, V. Ginot, J. Giske, J. Goss-Custard, T. Grand, S. K. Heinz, G. Huse et al. 2006. "A Standard Protocol for Describing Individual-Based and Agent-Based Models". *Ecological Modelling* 198(1-2):115–126.
- Grimm, V., S. F. Railsback, C. E. Vincenot, U. Berger, C. Gallagher, D. L. DeAngelis, B. Edmonds, J. Ge, J. Giske, J. Groeneveld et al. 2020. "The Odd Protocol for Describing Agent-Based and Other Simulation Models: A Second Update to Improve Clarity, Replication, and Structural Realism". *Journal of Artificial Societies and Social Simulation* 23(2):00.
- Group, U. B. 1971. "Epidemiology of Mycobacterium Ulcerans Infection (Buruli Ulcer) at Kinyara, Uganda". *Transactions of the Royal Society of Tropical Medicine and Hygiene* 65(6):763–775.
- Hackl, J., and T. Dubernet. 2019. "Epidemic Spreading in Urban Areas Using Agent-Based Transportation Models". *Future Internet* 11(4):92.
- Hollingsworth, T. D. 2009. "Controlling Infectious Disease Outbreaks: Lessons from Mathematical Modelling". *Journal of Public Health Policy* 30(3):328–341.
- Johnson, P. D. 2020. "Buruli Ulcer: Cured by 8 Weeks of Oral Antibiotics?". *The Lancet* 395(10232):1231–1232.
- Johnson, P. D., T. Stinear, L. Pamela, G. Pluschke, R. W. Merritt, F. Portaels, K. Huygen, J. A. Hayman, and K. Asiedu. 2005. "Buruli Ulcer (M. Ulcerans Infection): New Insights, New Hope for Disease Control". *PLoS Medicine* 2(4):e108.
- Macal, C. M. 2016. "Everything You Need to Know About Agent-Based Modelling and Simulation". *Journal of Simulation* 10(2):144–156.
- Macal, C. M., and M. J. North. 2005. "Tutorial on Agent-Based Modeling and Simulation". In *Proceedings of the Winter Simulation Conference*, edited by M. E. Kuhl, N. M. Steiger, F. B. Armstrong, and J. A. Joines, 14 pp.–. Orlando, FL, USA.
- Modu, B., N. Polovina, and S. Konur. 2020. "Agent-Based Modelling of Malaria Transmission Dynamics". *arXiv preprint arXiv:2004.06477*.
- Nienhuis, W. A., Y. Stienstra, W. A. Thompson, P. C. Awuah, K. M. Abass, W. Tuah, N. Y. Awua-Boateng, E. O. Ampadu, V. Siegmund, J. P. Schouten et al. 2010. "Antimicrobial Treatment for Early, Limited Mycobacterium Ulcerans Infection: A Randomised Controlled Trial". *The Lancet* 375(9715):664–672.
- Portaels, F., P. Johnson, W. M. Meyers, W. H. Organization, G. B. U. Initiative et al. 2001. "Buruli Ulcer: Diagnosis of Mycobacterium Ulcerans Disease: A Manual for Health Care Providers". Technical Report WHO/CDS/CPE/GBUI/2001.4, World Health Organization.
- Preziosi, L. 2003. *Cancer Modelling and Simulation*. Florida, United States: CRC Press.
- Smith, N. R., J. M. Trauer, M. Gambhir, J. S. Richards, R. J. Maude, J. M. Keith, and J. A. Flegg. 2018. "Agent-Based Models of Malaria Transmission: A Systematic Review". *Malaria Journal* 17(1):1–16.

- Stienstra, Y., W. T. van der Graaf, K. Asamoah, and T. S. van der Werf. 2002. "Beliefs and Attitudes Toward Buruli Ulcer in Ghana". *The American Journal of Tropical Medicine and Hygiene* 67(2):207–213.
- Vouking, M. Z., I. Takougang, L. M. Mbam, L. Mbuagbaw, C. N. Tadenfok, and C. V. Tamo. 2014. "The Contribution of Community Health Workers to the Control of Buruli Ulcer in the Ngoantet Area, Cameroon". *Pan African Medical Journal* 16(1):05.
- Vouking, M. Z., V. C. Tamo, and L. Mbuagbaw. 2013. "The Impact of Community Health Workers (CHWs) on Buruli Ulcer in Sub-Saharan Africa: A Systematic Review". *Pan African Medical Journal* 15(1):07.
- WHO 2012. "Treatment of Mycobacterium Ulcerans Disease (Buruli Ulcer): Guidance for Health Workers". <https://www.who.int/publications/i/item/9789241503402>. Last accessed: 11 October 2023.
- WHO 2023. "Buruli Ulcer (Mycobacterium Ulcerans Infection)". <https://www.afro.who.int/health-topics/buruli-ulcer>. Last accessed: 11 October 2023.
- Wilensky, Uri 1997. "Netlogo HIV Model: Center for Connected Learning and Computer-Based Modeling, Northwestern University. Evanston, IL".
- Wilensky, U. 1999. "NetLogo. Evanston, IL: Northwestern University". Center for Connected Learning and Computer-Based Modeling. Retrieved from <http://ccl.northwestern.edu/netlogo>.
- Yang, C., and U. Wilensky. 2011. "NetLogo Epidem Basic Model". Center for Connected Learning and Computer-Based Modeling Northwestern University Evanston IL, pages Evanston, IL.
- Yotsu, R. R., C. Murase, M. Sugawara, K. Suzuki, K. Nakanaga, N. Ishii, and K. Asiedu. 2015. "Revisiting Buruli Ulcer". *The Journal of Dermatology* 42(11):1033–1041.

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