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Developing an Agent-based Model for Evaluating the Effectiveness of Malaria Interventions in Nanyumbu and Masasi Districts, Tanzania

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Abstract

Objective : Agent-based models and simulation (ABMS) can be utilized to understand the dynamism of transmission and the effect of interventions. We evaluated using ABMS, the efficacy of insecticide-treated bednets (ITNs) at different coverage levels and quality of houses for control of malaria in Masasi and Nanyumbu districts, Tanzania. **Methods:** The model was developed and simulated in Anylogic software with mosquitoes, humans, and the environment along with their attributes as agents. Using field data, buildings of different qualities were created to be human environment, and ITN use was assigned to respective human agents. Shapefiles were imported into the built-in global imaging system map in Anylogic for better placement of buildings using their coordinates, and coordinates of streams extracted from the study area map were used to allocate the aquatic environment of the mosquito agents. ITNs coverage scenarios of 16%, 40%, 64%, and 80% were simulated. The model was simulated for 90-day period and a model time-step was set to a day. The primary outcome was the prevalence of human agents with malaria infection at the end of the 90-day simulation period. **Results:** At the end of the 90-day simulation period and initial ITNs coverage of 16% (257/1607), the prevalence of malaria infection was 15.4% (248/1607). When the coverage was increased to 40%, 64%, and 80% malaria prevalence declined to 15.1% (242/1607), 14.1% (227/1607), and 13.9% (223/1607), respectively. ABMS clearly indicated that an increase in ITNs coverage was associated with a decline in the prevalence of infected humans and mosquito population in consistency with the field data. **Novelty:** This work is unique in a sense that it incorporated the data on house quality which has direct impact in malaria transmission.

Keywords: Agent based model; Anylogic; ITN coverage; Malaria control; Public health

1 Introduction

Malaria poses a persistent threat to the global public health, particularly among the under-five children in endemic regions in sub-Saharan African countries⁽¹⁾. Tanzania is among 10 countries with the highest prevalence of malaria globally, and in 2023 it accounted for 4% of the malaria cases and 5% of the global malaria-related deaths⁽¹⁾. Ninety five percent of the malaria infections in Tanzania are caused by *P. falciparum*, and *An. gambiae* complex is a major vector^(2,3). Major malaria control tools include vector control using insecticide-treated bed nets (ITNs) and indoor residual spraying (IRS), treatment of malaria cases using artemisinin-based combination therapy (ACT), and the use of chemoprophylaxis in pregnant women⁽¹⁾. Effective clinical trials are a major method used to assess the effectiveness of malaria control tools under real field conditions⁽⁴⁻⁶⁾. However, clinical trials are relatively expensive as they are labor intensive, and need a lot of resources⁽⁶⁾. Therefore, research methods such as modeling are used to complement clinical trials, and can be used to inform policymakers on the effectiveness of the control tools before they are introduced in the field⁽⁷⁾.

Agent-based modeling and simulation (ABMS) are among computational tools that have been used to study the epidemiology of infectious diseases such as dengue, zika, influenza, chikungunya and malaria, and the effect of their interventions⁽⁸⁻¹⁰⁾. An agent can be defined as an object that is introduced into the environment and senses several parameters needed for making a decision according to its goal⁽¹¹⁾. The agent can be a human, mosquito, an organization, a truck, or system depending on the purpose of the model. In malaria epidemiology simulation, ABMS provides a dynamic platform that can simulate the interaction between humans and mosquitoes and with their environment, hence providing the understanding of the malaria infection dynamics^(9,12,13). The ABMS also incorporates individual heterogeneities such as infection status, immunity level and adherence to interventions⁽¹⁴⁾. The ABMS algorithmic representation of the behavior of each agent makes it possible to foresee how each agent behaves and responds at an individual level, leading to a greater state of complexity and the emergence of new behaviors in relation to disease transmission^(7,11). This in turn are used to design targeted interventions and measure their efficacy⁽¹⁴⁾. Furthermore, the flexibility and adaptability nature of the ABMS makes it easier for researchers to implement different scenarios and explore diverse “what-if” scenarios and hence select the most appropriate for a specific geographical location^(10,14,15). The ability of ABMS to incorporate geographical data and physical space to capture the spatial movement of infections and climate data to get the temporal nature of epidemics also aids in resource allocation and targeted public health measures^(7,14).

ABMS has been used in different countries to evaluate the effect of malaria interventions^(8,12,14). Whereas there are studies that have evaluated using ABMS the effect of ITNs on malaria control, there is limited information on the studies that have incorporated in the model the effect of the quality of house eaves i.e., open eaves, partial-closed eaves, or closed eaves on the effectiveness of ITNs. An eave is a space between the walls and the roof or ceiling. The predominant mode of malaria transmission is through indoor mosquito biting, and open or partially closed eaves are a major entry point for mosquitoes in the houses, thus significantly impacting malaria transmission^(16,17). Incorporating in this model the quality of eaves from houses in the study area was expected to show how the quality of eaves can influence the effect of ITNs in malaria transmission and intervention. Therefore, the focus of this study was to evaluate using the ABMS the effect of the coverage of ITNs in relation to the house quality on the dynamics of malaria transmission.

Table 1. Summary of the human and mosquito agents' input parameters

Agents	Parameters	Value/range of value	Notes/ References
Humans	The incubation period of <i>P. falciparum</i>	9-14 days	(3)
	Transmission probability of infection from infectious mosquito to susceptible human	0.04	
	The probability of a human agent being recovered (treatment probability)	0.95-1	(19)
	ITNs use	Yes/No	This study
	House category	Closed-eaves, open-eaves and Partially	This study
	Coordinates	Longitude and latitudes	
	Infection status	Positive or negative	
	Development time from egg to adult	$1/(-0.0094T^2+0.049T-0.522)$	(20)
	Number of eggs per reproduction	50–200 eggs	
	Extrinsic incubation period of <i>P. falciparum</i>	$111/(T-16)$ (Days)	(21)
Anopheles mosquitoes	Duration of the adult stage	2 weeks in colder climate and up to 1 month warm climate	(3)
	The maximum number of eggs laid by an Anopheles mosquito in her lifespan	500	
	Blood meal digestion and eggs development in Anopheles mosquitoes' body	$-1.23T+77$ (hr)	(15,22)
	Aquatic mortality rate	0.2	(22)
	Adult mortality rate	-	(15)
		$\log(0.000828T^2+0.0036T+0.522)$	
	Probability of successfully bite	0.3–1	0.3 when the human agent is sleeping under bed-net and 1 when the human agent is not protected

T, temperature in °C

Table 2. Input dataset

Dataset	Data	Source
Spatial data	Raster	
	Mean air temperature	
	Mean relative humidity	TMA
	Vector	
	Point	Villages and wards
	Polyline	Rivers
	Polygon	Boundary of region and district
Human data	Point	House coordinate
	Human demographic and malaria status	

2.3 Human sub-model

Human agents were assumed to be static, and placed in the house agent according to the field data. This is because the Anopheles mosquito biting starts at dusk and ends at dawn and the focus was on under five children who are expected to be in the house during that time. The use of ITN was implemented in individual human agents based on the field data. In the initialization of the model, the human population was initialized as either susceptible or infected. The heterogeneity of humans was implemented by inputting the demographic details of the human agents. The interaction of host and vector was implemented using connected links⁽²³⁾, whereby the host could be connected with multiple vectors and communicate, thus acquiring infection or passing on the infection.

2.4 Mosquito sub-model

The Anopheles mosquitoes were modeled by considering its life cycle which consists of four stages: egg, larva, pupa and adult. The first three stages, egg, larva and pupa were modeled as one stage termed aquatic, which lasted for 10-14 days⁽³⁾. The mosquito agent was initialized in any of the two stages with 30% aquatic and 70% adult (50% male and 50% female). At adult stage, female mosquitoes started to move around as malaria vectors. Male mosquitoes do not take a blood meal, and thus do not transmit malaria infection; therefore, their movements were not modeled and they exited the model through the death state⁽²⁴⁾. Female mosquitoes need blood for egg maturation, thus their movements for searching for blood meal, resting, and oviposition were modeled.

Usually, female Anopheles mosquitoes are expected to start biting at dusk and end at dawn, thus in the model search for blood meal was triggered by the event “bite” and the time of the day was checked by the function “is Night”^(3,9). If it was night then the female mosquitoes would start searching for humans to obtain a blood meal. Since humans are modeled inside the house, then mosquito has to go into the house to get blood meal. In the model, houses were modeled to be in one of the three categories in relation to the presence of open eaves, partially closed eaves and closed eaves. The probability of mosquitoes entering the house was controlled by the type of eaves, which were assumed to be 0.55, 0.38 and 0.14 for open eaves, partially closed eaves and closed eaves, respectively^(16,17). Once the mosquito gets in the house it would search for humans for blood meal. After successfully feeding, female mosquitoes would rest for 2-3 days depending on the environmental temperature for blood to be digested and the eggs to be developed^(3,15,25) and thereafter, they would search for water bodies to lay eggs and then move back to search for a human to obtain the next blood meal. In this model, it was considered that blood meal search and resting would take place in the same location (house) and on the same night⁽¹⁰⁾. The repetitive process of searching for blood meal, resting, and oviposition is known as the gonotrophic cycle, and normally the female mosquito goes up to three cycles in its life time. The gonotrophic cycle was included in this model since it is central to malaria transmission dynamics^(22,26). In each subsequent gonotrophic cycle, the capacity of a female mosquito to lay eggs was reduced by 20% compared to the previous cycle⁽²²⁾. The implementation of the gonotrophic cycle is explained in the oviposition algorithm in Figure 2.

```

Algorithm 2: Mosquito ovipositioning
Input: reproduction number, cycle counter
Output: number of mosquito
1 Begin
2   reprNumber ← uniform (50, 200)
3   counter ← 0
4   if counter = 1 then
5     reprNumber ← reprNumber - (reprNumber * 0.2)
6   end if
7   else
8     reprNumber ← reprNumber - (reprNumber * 0.2)
9   end else
10  for i ← 0 to reprNumber n do
11    Mosq most ← main.add_mosq (i)
12    most.set_isBaby(true)
13  end for
14  counter ++
15 End
    
```

Fig 2. Mosquito oviposition algorithm

2.5 Transmission sub-model

Malaria is transmitted from human to mosquito and from mosquito to human, and it has a significant incubation period. Susceptible-exposed-infected-recovered (SEIR) model was chosen to represent malaria infection transmission as it takes into consideration the incubation period which is represented as an exposed state⁽⁹⁾. An agent (host or vector) at any time point was exactly in one of the states. The human agents have four states Susceptible-Exposed-Infected-Recovered (SEIR), and mosquito agents have three states Susceptible-Exposed-Infected (SEI) as displayed in Figure 3. Susceptible was referred to as a state in which an agent was not infected but not immune to the infection. Exposed referred to a state where the agent had acquired infection but had not yet been infectious and thus couldn't infect other agents. Infected state refers to the state in which an agent could transmit the infection to another susceptible agent once they come into contact. In recovered state, the human agent had been cured and the drug continued to provide a prophylactic effect for nearly four weeks, protecting the human agents against new infections. Thereafter, the human agent would shift back to susceptible state^(14,19). During the blood meal stage of the mosquito, the infectivity status of the vector and host was determined by checking in which of the SEI states the vector was at that particular time. If the mosquito agent was in the infectious state and the human agent in the susceptible state, the mosquito would transmit the infection to the human agent through the message passing "infect" and led to the human agent to transit from the susceptible to the exposed state with the probability of 0.04^(9,19). If the mosquito agent was in a susceptible state and the human agent was in an infectious state, then mosquito agent would acquire the infection from the human agent through message passing "get infected" and then transit to the exposed state with the probability of 0.02⁽³⁾. Otherwise, it would just send a "bite" message without transmitting or acquiring infection. The mosquito agent in the exposed state would complete the incubation period of 9-11 days and transit to the infectious state and remain infected throughout its life^(3,9).

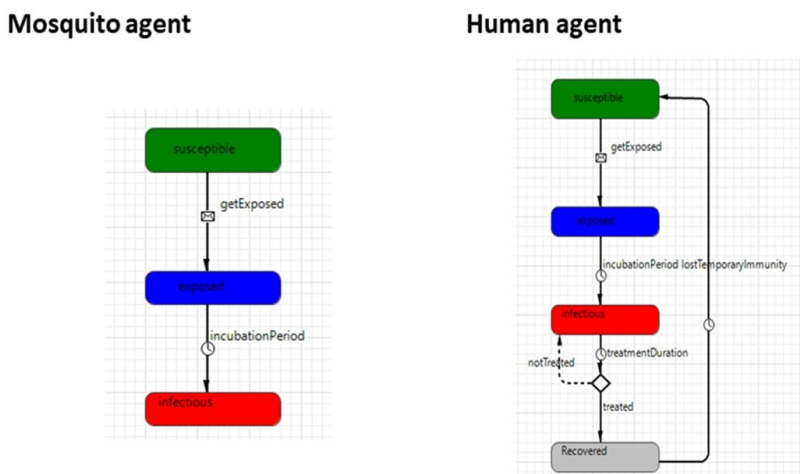


Fig 3. Agents states and transitions between states' in mosquito (left) and human (right) in the developed model

2.6 Malaria intervention

Transmission of malaria is highly dependent on the population of the mosquito, the infectivity of the mosquito and their access to the host. Any action that reduces any of the dependent variables of malaria transmission is considered to be an intervention. In this paper, ITN has been applied as the intervention which acts as the physical barrier by limiting the access of mosquitoes to humans and also the insecticides chemical in ITN can either kill or repel mosquitoes^(27–29). In modeling the impact of ITN on mosquitoes, the repellence and killing ability of the insecticide were considered. The killing ability is represented by the mortality rate which is the probability that a mosquito is killed after coming in to contact with insecticide-treated bed-nets. ITN mostly works on adult female mosquitoes when they are searching for blood meal. Thus, the mortality rate due to insecticide chemical was modeled for adult females only. When the mosquito was searching for a blood meal, the model checked if the human agent was under ITN or not. If the human agent was under ITN then one of the three actions would take place; the mosquito would be repelled by the probability of 0.6 and move on to find another human agent, or would be killed by the

probability of 0.3 and removed from the model, or would successfully bite by the probability of 0.1⁽²⁷⁾. If the human agent was not under ITN, then it was assumed that the biting would be successful⁽²²⁾. Figure 4 display the mosquito biting algorithm.

```

Algorithm 1: Biting
Input: Host, Vector
Output: Infectious status
1 Begin
2   if vector is infectious then
3     if host is susceptible then
4       infect host
5     end if
6   else if host is exposed then
7     bite host
8   end if
9   else if host is infectious then
10    bite host
11  end if
12 end if
13 if vector is susceptible then
14   if host is susceptible then
15     bite host
16   end if
17   else if host is exposed then
18     host bitten
19   end if
20   else if host is infectious then
21     mosquito infected
22   end if
23 end if
24 if vector is exposed then
25   if host is susceptible then
26     host bitten
27   end if
28   else if host is exposed then
29     host bitten
30   end if
31   else if host is infectious then
32     host bitten
33   end if
34 end if
35 End
    
```

Fig 4. Mosquitoes biting algorithm

2.7 Environmental

In the development of the environmental sub-model, houses were integrated as human host environment, and streams as mosquito environment. The spatial distribution of houses was also taken into consideration as it influences the human-mosquito interaction especially in relation to the proximity of human dwellings and potential mosquitoes’ breeding sites. Streams acting as breeding sites for mosquitoes contribute significantly to the vector population. The monthly temperature was also included in the model to incorporate its effect in the development rate of mosquito and their overall lifespan^(15,25). Several stages in mosquito life cycle are temperature dependent, such as the incubation period, egg development and mortality rate.

The house agent was created with an empty population and later on, using the function “add_house” the house agent was added and positioned in the study area according to the coordinates (latitude and longitude) and with the attributes h_id and h_category. A house had three categories: with closed eaves, partially closed eaves, and open eaves. It was necessary to incorporate the impact of eaves on controlling the entry of mosquitoes because biting was modeled to occur at night inside the house. Eaves are known to be the primary entrance of mosquitoes in the house, and eaves’ category is essential in determining the rate of malaria transmission^(16,17).

The mosquito environment in the study area was designed to replicate natural habitats conducive for breeding such as streams. The stream agent was instantiated with an empty population and later on using the function “add_stream” the stream agent was added and positioned in the study area GIS map according to the coordinates (latitude and longitude) and with the attribute stream area for integrating the district specific temperature to be used for the mosquito development cycle.

2.8 Simulation and scenarios tested

The model was simulated with 1607 humans, 1563 houses and the initial number of 1000 entire mosquito populations over a 90-day period with the goal of observing the impact of using ITN on the number of infected human and mosquito population

density. The increase of bed-net coverage is anticipated to reduce the number of infection to humans by limiting the contact between humans and mosquitoes, and consequently reducing the mosquito population. Thus, the model was tested with four scenarios of bed-nets coverage at 16%, 40%, 64%, and 80% to represent the minimum, moderate, maximum, and targeted coverage nationwide⁽³⁰⁾. In all four scenarios, the initial number of infected humans was based on the field data which was 217 out of 1607 (13.5%). Likewise, the initial percentage of infected female mosquitoes was 30 of the total female population for each scenario. Furthermore, the quality of eaves i.e., open, partial-closed, and closed was kept constant for all the scenarios of bed-nets coverage. Due to stochasticity in the initialization of the mosquitoes and some parameters, for each coverage scenario, the model was simulated 10 times over a 90-day period to reduce biasness, and the average result was taken for analysis.

Ethical consideration

Approval to conduct this study using secondary data was obtained from Kibong’oto Infectious Diseases Hospital- Nelson Mandela African Institution of Science and Technology- Centre for Educational Development in Health, Arusha with approval number KNCHREC00067/09/2022.

3 Results and Discussion

3.1 Relationship between ITNs coverage and mosquito population

The relationship between ITNs coverage and mosquito population at four different scenarios of ITNs coverage is presented in Figure 5. At the end of the 90-day simulation period, and the initial ITNs coverage of 16% it was observed that the mosquito population grew by 2400% from the initial of 1000 to 25,000 mosquitoes. With the increased ITNs coverage to 40%, 64%, and 80%, the mosquito population increased only by 100% to 2000, and then declined by 80% to 200, and 97% to 30 mosquitoes, respectively. On the other hand, at the end of 90-day simulation period the female mosquito population declined from 2,358 to 706, 36, and 13 at the ITNs coverage of 16%, 40%, 64%, and 80%, respectively. The increase of mosquito population by more than 20 folds at the end of the 90-day simulation and the ITNs coverage of 16% probably indicates that at a very low ITNs coverage mosquitoes are able to get into contact with a large proportion of unprotected humans and obtain a blood meal. Thus, at a very low ITNs coverage the effect of this intervention in protecting the whole population becomes almost negligible, allowing the mosquito population to thrive and more people to be infected. To the contrary, the observed trend of decline in the population of mosquitoes when the bed nets coverage was increased to 40%, 64% and 80% indicates that the increase in ITNs coverage means a large proportion of the population is protected by the intervention, therefore, denying the blood meal to a large proportion of mosquitoes. This in turn leads to a decline in the mosquito population as observed in the model. Female mosquitoes require a blood meal for the development and maturation of the fertilized eggs in their wombs⁽³⁾, and when their access to the blood meal is limited it leads to less or no reproduction. Therefore, when the ITNs coverage at the population level reaches 80%, much fewer mosquitoes are able to access the blood meal and reproduce, and also the whole population including those not using the bed nets is protected against the infection since there is an overall reduction in the mosquito population and hence reduction in malaria transmission^(24,28,29,31).

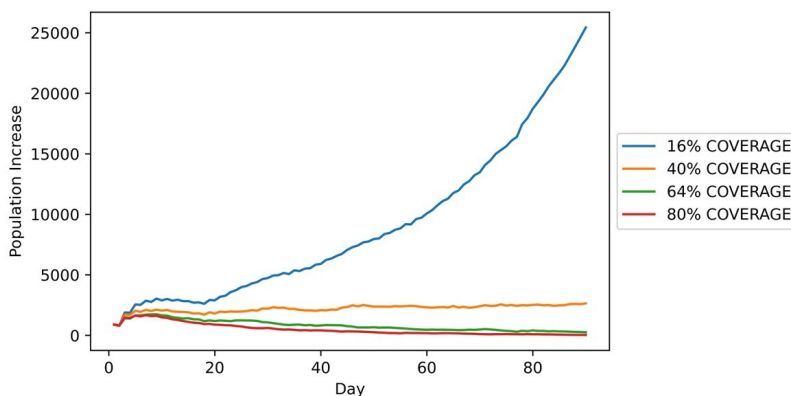


Fig 5. Impact of ITN coverage on mosquito population

3.2 Relationship between ITNs coverage and human infection

Before the simulation, 13.5% (217/1607) of the study population were infected with malaria. At the end of 90-day simulation period and bed-nets coverage of 16%, the prevalence of malaria infection increased to 15.4% (248/1607). When the bed-nets coverage was increased to 40%, 64%, and 80% the prevalence of malaria infection at the end of the 90-day simulation period declined to 15.1% (242/1607), 14.1% (227/1607), and 13.9% (223/1607), respectively, Figure 6 and Table 3. Furthermore, at the end of 90-day simulation period and ITNs coverage of 16% the malaria infection rate increased by 14.1% from 13.5% to 15.1%, and when the ITNs coverage was increased to 40%, 64%, and 80%, the infection rate increased only by 11.9%, 4.4%, and 2.9%, respectively. Thus, as the ITNs coverage was increasing the trend of prevalence of humans infected with malaria was declining. Furthermore, at 16% ITNs coverage malaria infection in the population grew by 14%, however, when the coverage of ITNs was increasing, the infection growth was declining, whereby at the coverage of 80% it grew only by 2.9%. This is consistent with the study by Gharakhanlou et al which showed the trend of decline in malaria infection with an increase in ITNs coverage⁽¹⁴⁾. In Iran Gharakhanlou et al., indicated that with the bed-nets coverage of 10%, 25% and 40% malaria prevalence declined by 18.9%, 42.9% and 90.2%, respectively⁽¹⁴⁾. The ABMS findings also showed that the prevalence of human infected with malaria at the ITNs coverage of 80% was 13.9%, and it was almost similar to the prevalence of 14.2% reported in a study conducted by Mwaiswelo et al., at the ITNs coverage of 82%⁽¹⁸⁾. On the other hand, the change of ITNs coverage from 16% to 40% reduced malaria transmission only by 1.9%, whereas the increase of ITNs coverage to 64% and 80% reduced the transmission by 8.4% and 9.7%, respectively.

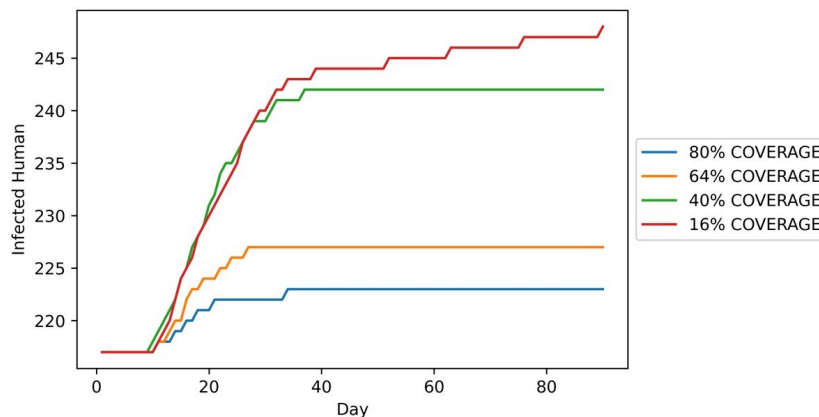


Fig 6. Infected human in different ITN coverage

Table 3. Infected human in different ITN coverage

Variable	16% Coverage	40% Coverage	64% Coverage	80% Coverage
Initial infection	13.5% (217/1607)	217/1607 (13.5%)	217/1607 (13.5%)	217/1607 (13.5%)
Final infection after 90 days	15.4% (248/1607)	242/1607 (15.1%)	227/1607 (14.1%)	223/1607 (13.9%)
Change of infection from the initial value	14.1% (1.9/13.5)	11.9% (1.6/13.5)	4.4% (0.6/13.5)	2.9 (0.4/13.5)
Infection reduction rate	0%	1.9%	8.4%	9.7%

Comparison between human agents who were using bed-net and those not using was performed at all four ITNs coverage scenarios, Table 4. At the end of 90-day simulation period and bed nets coverage of 16%, the new infection rate was 0.5% (1/217) among those using bed nets, and it was 13.8% (30/217) among those not using bed-net. When the ITNs coverage was increased to 40%, 64%, and 80% the new infection rate among those not using bed nets declined to 11.5% (24/217), 4.1% (9/217) and 1.9% (4/217), respectively. These findings indicate that the risk of malaria infection is lower to bed net users compared to those not using. Moreover, the reduced rate of infection to non-net users with increased coverage of bed-nets indicates the provision of indirect protection to non-user due to the community effect, which occurs when a significant number of people in the community sleep under the ITNs, resulting in the reduction of mosquito reproduction capacity and lifespan, thereby reducing

the transmission of malaria^(28,29,31). Our findings are in agreement with those from Malawi⁽³²⁾ and Kenya⁽³³⁾. In Malawi bed net use reduced malaria infection by 30% compared to non-net use⁽³²⁾, whereas in Kenya there was a reduction of malaria parasite carriage by 45% among net users⁽³³⁾. Similar findings have also been reported in Benin, Cameroon, India and Sudan⁽³⁴⁾.

Strength, limitation and future work

The strength of this study is in the incorporation in the model the quality of houses and air temperature, which have direct effect in malaria transmission and mosquito life cycle, respectively. On the other hand, the human agent was modeled as static, and this is a limitation since if the human was mobile would probably modulate the human agent - mosquito contact, and hence the malaria prevalence in the population. In the future work human mobility will be considered as well as the additional of other interventions such as drugs.

Table 4. Infected human with and without bed-net

Variable	16% Coverage		40% Coverage		64% Coverage		80% Coverage	
	Use bed-net	No bed-net	Use bed-net	No bed-net	Use bed-net	No bed-net	Use bed-net	No bed-net
Bed net usage, N=1607								
Initial	20 (1.2%)	197 (12.3%)	55 (3.4%)	162 (10.1%)	103 (6.4%)	114 (7.1%)	134 (8.3%)	83 (5.16%)
Final	21 (1.3%)	227 (14.1%)	56 (3.5%)	186 (11.6%)	104 (6.5%)	123 (7.7%)	136 (8.4%)	87 (5.5%)
New Infection, N=217	1 (0.5%)	30 (13.8%)	1 (0.5%)	24 (11.5%)	1 (0.5%)	9 (4.1%)	2 (0.9%)	4 (1.9%)

N, total number in a population per category

4 Conclusion

The ABMS clearly depicted an inverse relationship between ITNs on one hand and mosquito population growth and proportion of infected humans on the other hand, whereby an increase in ITNs coverage was associated with a decline in the prevalence of infected humans and mosquito population in consistency with the field data. Thus, ABMS using Anylogic offers a powerful platform for studying malaria transmission dynamics and assessing the impact of interventions.

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