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Review Article
Computational and Mathematical Modelling: Applicability to Infectious Disease Control in Africa

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Abstract

Computational and mathematical models play important roles in proffering solutions to infectious diseases. Economic development and human health in Africa continues to decline as a result of the menace of infectious diseases. No doubt, Africa can be a haven of economic stability with a healthy population but not until this challenge is overcome. The significance of computational and mathematical modelling to the control of diseases cannot be overemphasized. Hence, an extensive study on the impact of computational and mathematical modelling to the control of infectious diseases in Africa is a timely study. Specifically, the scope of our study focused on four life-threatening infectious diseases common in Africa namely: The ebola virus disease, HIV/AIDs, typhoid fever and malaria. It discuss the modelling as applied to these infectious diseases, the results obtained and the future potential of each modelling technique. The severity and devastating effect of these diseases on both economic and human health in Africa informed our decision of this study. Despite the limitations inherent in existing models, strikingly revealed was the evidence that a combination of several control strategies yielded a better result than the use of a single control strategy. In conclusion, the knowledge of computational and mathematical modelling has improved the approach in managing and combating the transmission of infectious diseases. It has also helped in predicting risks of major outbreaks in Africa.

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INTRODUCTION

Pathogens are the causative agents of infectious diseases. These diseases can be transmitted by contact from persons to persons. The modes of transmissions vary from bites by insects or animals, to the usage of infected equipments or the consumption of contaminated food and water[1]. Presently, the negative impact of infectious diseases (IFDs, henceforth) in Africa cannot be ignored as the economic development and public health of citizens in Africa continues to be on the decline[2].

Africa has the opportunity of achieving a stable economy, strong, healthy and vibrant population if effective solutions are proffered to the menace of IFDs. The aim of this study is to identify and discuss the significance and applicability of computational and mathematical models to controlling infectious diseases in Africa.

According to a 2012 World Health Organization (WHO) Regional committee report for Africa, 63% of mortality in the African region was due to incidences of IFDs. The HIV/AIDS, malaria, tuberculosis, diarrhoea and other forms of child related diseases accounted for 88% of these deaths. Other IFDs such as ebola, cholera, meningitis, poliomyelitis and viral haemorrhagic fevers have also topped the list of contributors to the loss of lives in the African region[1].

In various attempts to overcome the health challenges and unstable economy currently affecting some countries within the African region, many prevention and control programmes have been adopted.

These programmes range from emergency intervention programmes, regional surveillance, timely vaccination and the adoption of disease prevention guidelines to vector control strategies and the application of mathematical and computational modelling techniques. These programmes are still being implemented as measures for preventing the emergence, resurgence and transmission of IFDs in Africa[3].

In this study, it present an extensive study of different mathematical and computational models and a comparative study of the impact of these models to the control of IFDs transmission in the African region with particular emphasis and focus on killer IFDs such as Ebola Virus Disease (EVD, hence forth), HIV/AIDS, malaria and tuberculosis. The criteria used for assessing the quality of each model reviewed in this study are the generalizability criteria for model evaluation. This criterion depicts a model to be good and effective where the model satisfies its original aim alongside, offering good predictors of future trends and observations[4].

MATERIALS AND METHODS

Mathematical and computational models: A mathematical model adopts mathematical concepts and descriptions to represent the behaviour of a system or real world situation. A computational model on the other hand, describes a system through algorithms and simulations. A computational model is applied in computational science where the need for large computational resources is required for the study of the characteristics of complex systems by simulation. Previous studies conducted by McKenzie *et al.*[5], Day *et al.*[6], Moghadas *et al.*[7], Grassly and Fraser[8] and Arino *et al.*[9] have revealed the role of computational and mathematical models in combating the spread of IFDs. It has also highlighted the initiation of control interventions and other interventions capable of truncating further recurrences of IFDs and thus preserving a healthy populace from the adverse effects of such IFDs.

The study of Chowell and Nishiura[10] revealed how mathematical modelling was applied at estimating the risk of a major outbreak of Ebola Virus Disease (EVD) and an evaluation of the effect of basic control measures on the spread of the disease. In their study Chowell and Nishiura[10], the new number of ebola cases for the 2014 ebola outbreak was modelled mathematically using Eq. 1 and 2, while the basic reproduction number R_0 was given as shown in Eq. 3-5.

The number of new cases (i) at calendar t is modelled as follows:

$$i(t) = k \exp(rt) \qquad (1)$$

where, k is a constant, as the observed data are cumulative I(t), the above Eq. 1 is integrated from the start time of exponential growth to the latest time t. This results into Eq. 2:

$$I(t) = \frac{k}{r}\left[\exp(rt) - \exp(rt_0)\right] \qquad (2)$$

$$R_0 = \frac{\beta_0}{\gamma} \qquad (3)$$

$$R_0 = \beta_0\left[1/(\gamma_{a0} + \gamma_I) + l_0\left(1/\gamma_r\right)\left(\gamma_{a0}/(\gamma_{a0} + \gamma I)\right)\right] \qquad (4)$$

$$R_0 = R_{comm} + R_{hosp} \qquad (5)$$

where, $R_{comm} = \gamma_0/(\gamma_{a0} + \gamma_I)$ and $R_{hosp} = \gamma_0 l_0 \left(1/\gamma_r\right)\left(\gamma_{a0}/\gamma_{a0} + \gamma_I\right)$.

In addition, from a mathematical point of view, Nishiura and Chowell[11] defined the force of infection of Ebola Virus Disease (EVD) as $\lambda(t)$ depicted in Eq. 6:

$$\lambda(t) = \int_{0}^{\infty} \beta(s)\Gamma(s)i(t-s)ds \qquad (6)$$

This finally yielded a measure of the risk of infection in a susceptible population. Nishiura and Chowell[11] also provided a comparative analysis of ebola virus disease, influenza and measles with respect to their rate of infectiousness per generation of cases. Ebola virus disease was found to be almost similar in terms of rate of transmission to influenza. Though infections per unit time of ebola virus disease was found to be lesser than that of influenza. The aim of their study was to compare infectiousness among different infectious diseases in order to describe different infectiousness concepts. The applicability of their study can help forecast the transmission rate of ebola, thus providing a suitable platform for timely intervention, towards the control of the infectious disease.

In the study conducted by Lessler *et al.*[12] they provided seven challenges associated with using infectious diseases models to inform data collection. According to their study[12], the challenges are inherent in the synergy between using infectious disease models to inform data collation. It was noted, however, that if such challenges are overcome, it will provide new insight and also help tremendously improve on how infectious disease threats are dealt with.

In another study, Weitz and Dushoff[13] applied the mathematical epidemiology toolkit to analyze the effects and consequences of post-death transmissions of ebola on individuals who are still alive. In their study, the identifiability problem was revealed as the reason for the lack of confidence with inferring underlying disease parameters from early-stage incidence data. From a control standpoint, they showed how a reduction in post-death transmissions can ultimately lead to a reduction in the overall spread of the ebola epidemic. They also stated that when significant attention is concentrated on the proportion of post-death transmissions it can help evaluate a cocktail of control strategies and forecast or estimate the trend of the epidemic.

Role and applications of computational and mathematical models in IFD transmission and control in Africa
Ebola virus disease: In 1976, the emergence of EVD was simultaneously observed in Sudan and the Democratic Republic of Congo (DRC)[14]. The name ebola was traced back

and coined from the location of its first occurrence in Yambuku village, very close to the ebola river in DRC[14]. Since, 1976 until year 2013, in Africa, report has it that a total of 2,316 human cases have been in occurrence of which, 1,595 deaths have been confirmed[15].

It has also been revealed that in, 2014 alone, a total of 24,788 human cases leading to 10,251 deaths have been reported[15]. Not surprising that in August, 2014, WHO declared ebola a public health emergency of international concern[14]. There is no known cure for ebola and no licensed ebola vaccine is in existence yet. There exist package of interventions such as surveillance, good laboratory services, safe burials, case management and social mobilization to help control the outbreak and spread of the disease[14].

Studies on modelling have played significant roles in sensitizing the public of the dangers associated with an epidemic. It has also provided insights into the impact of present and future control measures. Lewnard *et al.*[16], developed a transmission model to assess and ascertain the impact of non-pharmaceutical interventions from the international community through contact tracing, provision of new EVD treatment and management centres and the provision of household protective kits. The knowledge of how these interventions can be applied individually or collectively to prevent future EVD outbreaks and deaths in Liberia was also presented.

The model developed by Lewnard *et al.*[16] predicted 1,975 EVD cases and 1,315 resulting deaths as against the figures from the Liberian Ministry of Health and Social Welfare which reported 1,635 EVD cases and 1,081 deaths[16].

Discussing individually and as a group the 3 intervention strategies earlier mentioned the model revealed the relationship between EVD treatment centres and case ascertainment. Here, the impact of introducing new EVD treatment centres depended on an acceleration of case ascertainment. Protective kits alone however, could not guarantee maximum protection from EVD but might be able to reduce the spread of the disease under conditions where the capacity of EVD treatment centres had been exceeded. The model showed further that augmenting EVD treatment centres and case ascertainment with protective kits between October 31, 2014-December 15, 2014 had the potential to increase the number of EVD cases prevented from 81,627-97,940 based on kit quality[16]. Even though the model had the following limitations (i) Status quo ascertainment was unknown, (ii) The notion that all persons infected with ebola (both dead and alive) contributed equally to the rate of transmission, (iii) That EVD cases indentified in Montserrado from June-October 2014 were acquired within Montserrado

and (iv) Ebola was not transmitted during sanitary burials, findings showed that the number of proposed EVD centres from international commitments was insufficient in dealing with the number of expected cases and deaths. Clearly, this transmission model's findings reflect the purpose for its design and uncertainty errors were accounted for using a Bayesian framework, thus it can say the model passes the generalizability criteria.

Atangana and Goufo[17] developed a model describing the transmission of ebola for a given West African country first by using the classical derivative which talks about the rate of change as an approximation of the real velocity of the object under consideration.

According to Atangana and Goufo[17], the rate of change of susceptible population was given as a mathematical differential equation depicted as:

$$\frac{dS(t)}{dt} = -iS(t)I(t) + sR(t) - \alpha N \qquad (7)$$

while the rate of change of infected group was given as:

$$\frac{dI(t)}{dt} = -iS(t)I(t) - dI(t) - rI(t) \qquad (8)$$

The rate of recovery was described with an ordinary mathematical differential equation represented by:

$$\frac{dR(t)}{dt} = rI(t) - sR(t) \qquad (9)$$

and finally, the rate of change in death was given by:

$$\frac{dD(t)}{dt} = dI(t) + \alpha N \qquad (10)$$

The classical derivative was then modified to account for time scale and fractional order, this was called the beta derivative. In the formulation of the model, the rate of death caused by ebola the infected, the susceptible and the rate of recovery were accounted for. The model was solved numerically via an iteration method with simulations carried out in terms of data and time for different values of beta. The model as a function of the order of the derivative showed a more realistic result for all beta values less than 0.5. In conclusion, the model revealed that in the absence of any form of adequate prevention and control, regardless of the number of infected, the entire nation could be wiped out within the speed of light[17].

Fasina *et al.*[18] applied a dynamic transmission model to study the impact of forceful interventions in swiftly preventing an EVD outbreak in Nigeria. Fasina *et al.*[18] conducted a stochastic EVD outbreak simulations based on an earlier simplified model developed by legrand[19].

In their model design, a transmission tree was analyzed to estimate the case fatality rate, the number of infected healthcare workers and the average number of secondary cases by generation of the disease. With the use of two compartments, infectious individuals in the community were separated from those who had been selected and placed in isolation in hospital. With the use of epidemic models, they projected the size of the outbreak in Nigeria in a situation where control interventions had been carried out at different dates, thereby estimating the number of cases averted by an early start of interventions[18]. Legrand *et al.*[19] developed a stochastic EVD simulations. They modelled a population by placing the population into five groups namely (i) Susceptible individuals, (ii) Exposed individuals, (iii) Infectious individuals, (iv) Hospitalized individuals and (v) Individuals removed from isolation after recovery or disease-induced death. Stochastic simulations of the transmission model were implemented in an attempt to predict and project the size of the outbreak in Nigeria especially in a situation where interventions had been initiated at different dates. It is also to estimate the number of cases prevented by an early start of these interventions. Based on EVD epidemiology, certain parameters were set such as incubation period of 6-12 days, infectious period of 5-7 days and a case fatality of 35-50%. Furthermore, the average time from when symptom starts to diagnosis was put at 5 days prior to the implementation of interventions. The basic reproductive number was determined by adjusting the baseline transmission rate for an effective population size of 10 million (10,000,000). At the beginning of interventions, the average time from symptom onset to diagnosis was adjusted to 1 day while the infectiousness of hospitalized individuals was adjusted by 80% to show the tightening of infection control routines in hospital environment relating to levels before the occurrence of the index case. Starting with the introduction of the index case, followed by 12 local individuals exposed by the index case, 200 stochastic simulations were performed. The timing of start of interventions for the simulated outbreak was put at 3 days in line with the Nigerian outbreak response and then 10, 20, 30, 40 and 50 days. The model concluded with the following: (i) That the size of the simulation outbreak agreed with the Nigerian outbreak when

interventions were rapidly instituted on day 3 of the outbreak and (ii) The outcome of delayed interventions in the simulation outbreak indicated the need for quick and forceful control measures. This model clearly revealed the impact of forceful implementation of control interventions in reducing the spread of EVD in Nigeria. Since this agreed with the initial aim of the model, it can be inferred that the model met the generalizability criterion.

Fisman *et al.*[20] applied an Exponential Adjustment model to the study of ebola virus disease. They integrated incidence decay into the Exponential Adjustment model (IDEA)[21] to formulate a mathematical model that is a useful prognostic tool for epidemic processes especially in situations when data is not sufficient. Fisman *et al.*[21] applied this model to the ebola epidemic in order to observe mathematically trends of epidemic growth, evaluate the degree to which control interventions were likely to influence epidemic size and duration.

The model was represented by some mathematical difference equations with discrete time steps as depicted in Eq. 11-13.

$$S_{t+1} = S_t - Re_t\, I_t \tag{11}$$

$$I_{t+1} = Re_t\, I_t \tag{12}$$

$$R_{t+1} = R_t + I_t \tag{13}$$

The model proved to be ideal for studies with limited ebola epidemiological data. The model had a good fitting to data. In conclusion, the model showed that in a case where there was inadequate effective control measures, epidemic increased to tens and maybe hundreds, of thousands of people which was obviously similar to the case in Liberia as at the time of writing. The model satisfied the generalizability criterion for a good model.

As a result of challenges encountered from previous studies[9,22,24], House[25] used a different technique by developing a model that focused on time between outbreaks, number of deaths and final number of cases, for all 24 ebola outbreaks as detailed by WHO[14]. The modelling process commenced with modelling the start of a new outbreak as a memory less poisson process with a rate λ. Next was the assumption that each new outbreak had a case fatality ratio derived from a beta distribution and lastly, the final size model was a function of two parts: (i) A geometrically distributed number of cases, A and (ii) A branching process model of human-to-human transmission[26,27]. All aforementioned models were fitted with Bayesian Markov Chain Monte Carlo with uninformative priors[28] and a simulation study was carried out to test identifiability. Augmenting the final size data by an outbreak of an unknown size caused the model to be refitted.

The likelihood function for the transmission model was represented by Eq. 14:

$$L(D|p,\, q) = \Pi_i\, Pr\,[K = K_i]|p,\, q] \tag{14}$$

The likelihood for the new outbreak model was presented by Eq. 15:

$$L(D\,|\,\lambda) = \frac{(\lambda T)^N e^{-\lambda T}}{N!} \tag{15}$$

The results from the model on ebola transmission dynamics showed that (1) Even though the rate of new epidemics and case fatality ratio were both high, there was a notable difference from outbreak to outbreak, (2) The effective basic reproductive ratio for individual-to-individual transmission was just less than 1 and (3) An extremely large variability in the final size of outbreaks was observed. The model showed a basic reproductive ratio <1, a fast rate of new outbreaks and a high case fatality ratio which it had set out to, thus satisfying the generalizability criterion.

After a critical analysis of the predictions by the model Lewnard *et al.*[16] developed and the observation of a pessimistic prediction of the growth rate of the epidemic as of October 2014.

Chowell *et al.*[22], improved upon the study of Lewnard *et al.*[16]. There was a calibration of the mechanistic model developed by Lewnard *et al.*[16] to an epidemiological data of cases and deaths. Applying data from constantly changing epidemic in Liberia, Chowell *et al.*[22] showed that an integration of simple logistic growth models with traditional mechanistic models can be used to evaluate predictions in situations where epidemiological data are insufficient. This forecast tallied with recent field reports from at least two counties in Liberia. The model also revealed the need for the total effective susceptible population size as being a dynamic variable instead of a fixed quantity due to changes in population behaviour and the effect of control interventions. Validation is a very important process that has to be conducted on models.

A further validity check was conducted on the model and saw the fitting of the model to data from Sierra Leone and Guinea which reveal a consistent reduction in the final size predictions for both countries with estimated effective reproduction numbers of 1.2 and 1.4, respectively.

Rivers *et al.*[29] conducted a study on the impact of interventions on the ebola epidemic in Sierra Leone and Liberia. They developed a compartmental model that described the natural history and epidemiology of ebola. The model was further transformed into a deterministic version and validated using least-squares optimization. Besides a mathematical description of the model, the model was transformed into a stochastic model by implementing the Gillespie's algorithm[30] with a tau-leaping approximation. The findings of this model were interesting.

The findings revealed that some form of coordinated intervention was important for the near term. The model also showed that the outbreak was at the point where it could least be controlled and this agreed with predictions by other models. Identifying infected ebola individuals via intensified contact tracing and placing them in isolation with dedicated care, proved to be the most effective combined control strategy. Also, the use of a hypothetical pharmaceutical intervention impacted on mortality. Even though these interventions reduced the number of ebola cases, they were not sufficient enough to stop the progress of the epidemic.

The focus of the study conducted by Althaus *et al.*[24] was on the quantification of the effects of early interventions in order to reduce the spread and transmission of ebola. It was also to determine the risk of a single undetected case leading to a new outbreak. The EVD transmission model was described with a set of ordinary mathematical differential equations as shown below in Eq. 16-20:

$$\frac{dS}{dt} = -\beta(t)SI \qquad (16)$$

$$\frac{dE}{dt} = \beta(t)SI - \sigma E \qquad (17)$$

$$\frac{dI}{dt} = \sigma E - \gamma I \qquad (18)$$

$$\frac{dR}{dt} = (1-f)\gamma I \qquad (19)$$

$$\frac{dD}{dt} = f\gamma I \qquad (20)$$

Comparing the risks of an outbreak emanating from a single undetected case in Nigeria with ongoing EVD transmission in other West African countries showed that Nigeria had a much higher risk of 89%. Even though the basic reproduction number of the model was quite high (that is, 9.10) because it was calculated for just the index case the net reproduction number was reduced below 15 days as a result of the swift implementation of control measures after the arrival of the index case. The model however, suffered from the following structural limitations: (i) By applying a deterministic model to an outbreak of just 20 cases, stochastic effects may have influenced the outcome of the epidemic, (ii) There was the assumption that EVD cases were equally infectious throughout the infectious period, (iii) There was no differentiation between transmission in health-care environments and in the community, (iv) All control interventions were considered together and their implementation were assumed to have contributed to the exponential drop in the transmission rate and (v) The transmission clusters in Lagos and Port Harcourt were taking as a single outbreak with the assumption that control measures had similar effect in both locations. In conclusion, the model revealed that the transmission potential of index cases can be quantified in the absence of the number of secondary cases. The model also described the time window for successful prevention of new EVD outbreaks caused through air travel.

In the study of the transmission dynamics of the ebola haemorrhagic fever, Legrand *et al.*[19] developed a stochastic compartmental model using epidemiological data obtained from two different outbreaks (a 1995 outbreak in DRC and 2000 outbreak in Uganda). The model took into consideration, the spread of EVD in different epidemiological terrains such as illness in the community, hospitalisation and traditional burial while estimating the basic reproduction number. This was estimated as 2.7 in both outbreaks. Being a stochastic model, individuals were thus grouped into the following classes: (i) Susceptible: Those infected with ebola due to contact with infectious case, (ii) Exposed: Infected individuals not showing symptoms yet, (iii) Symptomatic individuals in the community, (iv) Infectious individuals now hospitalised, (v) Dead cases with the potential to transmit the virus during burials and (vi) Those either cured, dead or buried, hence having no potential for further transmission. The impact of control measures was explored by simulating the model under different epidemic scenarios using the Gillespie's first reaction method[31]. Here, a key parameter considered was the immediate response to the use of control interventions. Just as the authors initially set out to understand and suggest where control interventions could be effective, the model concluded by showing that increased hospitalisation rate reduces the future epidemic size. This further satisfied the generalizability criterion.

A spatial-agent based model for incorporating both detailed geographical and demographic data from Liberia was developed by Merler *et al.*[32]. Amongst things that were modelled are; mobility of individuals not affected by EVD, those seeking for help in health care institutions, individuals caring for infected persons who have not been admitted into a hospital and the number of funeral attendees. These categories of individuals were classified into geographically chosen and randomly allocated households to match the population density projections on a grid of 3,157 cells covering Liberia. Calibration of the model was done using a Markov Chain Monte Carlo approach. This has enabled the estimation of transmission parameters and the investigation of the effectiveness of control measures such as the availability of treatment centres, practice of safe burial procedures and the use of household protection kits. The model showed that the decline in the number of new cases both at country and county levels was due largely to the increasing number of treatment centres, practice of safe burials and the effective distribution of household protection kits. The impact of the model is visible in the fact that it provided a means of evaluating the available control measures as well as providing insight into the role each control measure played in the reduction of incidence cases reported since September 7, 2014. The model can also offer predictions of future burden of the epidemic and the number of ebola virus cases. The model did show potential for being used for evaluating pharmaceutical interventions as well.

Chowell *et al.*[33], applied a simple mathematical model to study the effects of the early detection of ebola. From their study, they highlighted that in situations where there were no vaccines or effective drugs for the disease, a useful way of controlling the spread of the disease was by identifying infected individuals early enough in order to truncate the transmission of the disease.

Chowell *et al.*[10] discovered that there was a strong correlation between the effect of early detection of pre-symptomatic infections and the effectiveness of isolation of infected individuals.

The result produced from their study has the potential to initiate effective control measures against the spread of EVD. Finally, the results obtained by Chowell *et al.*[10] suggested an integrative strategy that combines early diagnosis of high-risk individuals, health workers, care givers, at the pre-symptomatic stage with public health strategies to improve the speed and efficiency of isolation of infected patients as a guaranteed means of rapidly reducing the transmission of ebola. This model also satisfies the generalizability criterion.

Webb and Browne[34], conducted a study by applying a mathematical model to model the 2014-2015 ebola epidemic in Sierra Leone and Guinea. They incorporated the age of infection into their model to monitor the transmission of the infection. Mathematical model simulations indicated that successive removal of infected individuals resulted in a reduction of the severity of the epidemic. This model satisfies the generalizability criterion because it achieved positive results and it provided insight into reducing the ebola epidemic.

Camacho *et al.*[35], applied a mathematical model of EVD to estimate the variations in the extent of transmissions of ebola virus in the nine most affected district of Sierra Leone between the period 10th August, 2014 and 18th January, 2015. They used their mathematical model to study the patterns of transmission in different regions and to finally evaluate whether bed capacity was enough to meet up with future demands of ebola cases. With their mathematical model, they were able to estimate the number of ebola cases that would occur up till March, 2015 and made meaningful comparison with the expected number of beds and expected future capacity of ebola cases.

Agusto *et al.*[36], designed a mathematical model and applied the model to estimate the population-level impact of basic non-pharmaceutical measures against the outbreak of ebola. Some unique features of this particular model were the incorporation of the effects of traditional belief systems and customs, disease transmissions within healthcare settings and among ebola-deceased patients. They were able to perform sensitivity analysis in order to determine the parameter that had the most effect on disease transmission. The model was parameterized by using data from Guinea. The model concluded by showing that reduction in new ebola cases can be achieved by increasing health-worker's daily shifts from 8-24 h, restricting hospital visitation to 1 h and by sensitizing the populace to abandon detrimental traditional/cultural belief systems. One of the discovery by Agusto *et al.*[36] is the impact or the contribution of traditional/cultural beliefs to the spread of the (EVD). This model was able to produce good results.

Typhoid fever: Typhoid fever is caused by the bacterium *Salmonella typhi.* Its mode of transmission is through ingested contaminated food or drink. Such contaminations can be from the faeces or urine of infected individuals[37]. The disease can affect different organs of the human body and it can also lead to complications. In worst case scenario, it can lead to death[38].

Mushayabasa *et al.*[39] revealed through a mathematical model that in malaria affected regions, a typhoid epidemic has the tendency of causing higher cumulative cases of

dually-infected patients. These patients exhibit the clinical symptoms of both malaria and typhoid than singly-infected persons showing the clinical symptoms of either malaria or typhoid.

In course of developing the model, Mushayabasa *et al.*[39] performed separate studies on the transmission dynamics of malaria and typhoid. Using compartmental models for the studies, the typhoid model integrated both typhoid treatment and typhoid carriers. The total population was subdivided into: The susceptible S, the infectious I, the treated/recovered R and the chronic enteric carriers C. In the malaria aspect of the model, the model by Li[40] was adopted to reveal the transmission dynamics between humans and *Plasmodium falciparum.* In the final co-infection model the human population consists of the following mutually exclusive compartments: The susceptible, those exposed to malaria only, infectious persons infected only with malaria, infectious persons infected only with typhoid, singly-infected typhoid carriers, those infected with typhoid and exposed to malaria, dually-infected persons with malaria and typhoid and showing clinical symptoms of both diseases, typhoid carriers exposed to malaria, dually-infected typhoid carriers who show clinical symptoms of malaria only and the recovery population. From analysis, the typhoid model revealed the possession of globally stable states, whereas, the malaria model did reflect a backward bifurcation phenomenon.

In a related study, Mushayabasa[41] investigated the impact of vaccination on the long term transmission dynamics of typhoid fever. He applied a mathematical model to the study conducted in the Kassena-Nankana district of Upper East region of Ghana. The model (a derivative of the SIR model developed by Adetunde[42]) incorporated both a vaccinated class and the viral dynamics. The host population was subdivided into five different classes namely: Susceptible S (t), Vaccinated V(t), Infective I(t), Carriers C(t) and Recoveries R(t). The total population was presented as N = S+V+I+C+R. The model formulated by Mushayabasa took the form as depicted in Eq. 21-25:

$$S' = \Lambda - \alpha SI - (\varphi + \mu)S + \omega V \qquad (21)$$

$$V' = \varphi S - (\omega + \mu)V \qquad (22)$$

$$I' = \alpha SI - (\beta + b + \sigma + \mu)I \qquad (23)$$

$$C' = \beta I - (\gamma + \mu + d)C \qquad (24)$$

$$R' = \gamma C + bI - \mu R \qquad (25)$$

The model showed that the vaccine induced reproduction and the no-vaccine reproduction numbers, respectively gave threshold conditions that determined the occurrence of typhoid fever in the community. Knowledge of these threshold conditions had the potential of giving insights into the outcome of the use of vaccination as a measure of control. Finally, the model concluded with the view that vaccination was a necessary control strategy if the rate of cumulative new typhoid cases in the district was to reduce. Furthermore, the government and the public health sector were encouraged to carry out vaccination of susceptible individuals in order to minimise typhoid-induced mortality and prevalence.

In another study, Mushayabasa *et al.*[43] evaluated the effect of drug resistance on the transmission dynamics of typhoid fever by applying a mathematical model. In the design of the model, the host population was distributed into: Susceptible, sensitive strain non-symptomatic infectious persons, drug-resistant infectious carriers and drug-resistant symptomatic infectious carriers. The model worked on the assumption that infection could only result from direct contact with an infectious individual. Another assumption was that recruited individuals were supposed to be susceptible, though this might not always be the case. In the study, it was revealed that in the event of an outbreak with more drug-sensitive cases than drug-resistant cases, about 10-15 months would be required before symptomatic drug-resistant cases would outnumber all typhoid cases.

The model further showed that with the increase in drug-resistant typhoid cases, alongside the potential of it outnumbering drug-sensitive cases on the long run, there would be a high prevalence of typhoid in the community.

Mushayabasa developed a deterministic model to model the impact of optimal screening on the transmission dynamics of typhoid fever[44]. He focused his interest in a model with relevant biological detail, reflecting multiple control strategies and implementing an optimal control theory. In the process of formulating the model, the total population at time t, was subdivided into six mutually-exclusive compartments namely, susceptible, exposed, symptomatic infectious, chronic enteric carriers, screened typhoid patients and the recovered. In the final outcome of the model, it was evident that the implementation of optimal control strategies could effectively control and/or eliminate the spread of typhoid fever in the event of an epidemic in the community. The model further revealed the need for quarantining only symptomatic individuals in an event where an outbreak has spanned over 150 days. The model has its limitation of assuming that the

spread of the disease was only possible via human contact. Nevertheless, the model revealed that screening symptomatic and asymptomatic infectious patients was only ideal for the short term but in the long term, attention should be paid to only symptomatic infectious individuals, thereby reducing cost and managing the spread of the disease. In this regard, the model achieved the aim which it set out to during formulation, thus satisfying the generalizability criterion.

Further study was conducted by Mushayabasa[45] on the assessment of the impact of treatment and educational campaigns on the transmission dynamics of typhoid in Zimbabwe. This study birthed the development and analysis of a deterministic model for the control of typhoid outbreak. The model considered the saturated incidence rate of the disease during the modelling process. Categories of human population for this model are: The susceptible, latently infected individuals and the infectious individuals. The model revealed that early treatment drastically reduced the amount of new typhoid cases as compared to the treatment on the infected. With an over 40% consistency rate of effective educational campaign, the model predicted that typhoid could be controlled. Thus, educational campaigns are good indicators to controlling infectious diseases. The model had its own limitations. These include: (i) Assumption that transmission was via human contact only (ii) Assumption that recruited individuals are susceptible, which was not the case in all communities. The model revealed that an integrative approach of educational campaign and proper treatment can produce significant effect in combating typhoid fever.

Mushayabasa *et al.*[43] in 2013 analysed the impact of carriers, direct and indirect transmission on the prevalence of typhoid fever. They used a mathematical model to conduct the analysis. The model was useful in calculating the basic reproductive number, as well as investigated the global stability. Sensitivity analysis, on the other hand on the reproductive number, revealed that typhoid prevalence was significantly determined from indirect transmission as opposed to direct transmission. This model satisfied the generalizability criterion of a good model.

In another study, a novel mathematical model of typhoid-malaria co-infection dynamics was developed by Mutua *et al.*[46]. The model is a dual-purpose model. Through the mathematical analysis of the model, they were able to specifically identify unique features associated with each type of disease and their corresponding co-infections. The development of their model, provided them the opportunity to identify specific thresholds related to the global dynamics of each disease. The analysis conducted with their model

informed them of the possibility of applying concurrent interventions, thereby leading to the possible eradication of the diseases. The case study for their study was the Eastern Province of Kenya. Simultaneous management of both diseases hold great promises in dealing with co-epidemics. Their model also satisfied the generalizability criterion.

HIV/AIDS: Human Immunodeficiency Virus (HIV) is a virus that fights and weakens the immune system and weakens one's ability to combat infections and diseases[47]. The transmission of the virus is majorly through body fluids that affect specific cells of the immune system. It is commonly transmitted through unprotected sexual intercourse. It could also be transmitted through the sharing of needles or injections with an infected patient. During child conception, development, child birth and breastfeeding, HIV can also be transmitted from an infected mother to a child[47]. The HIV advances to Acquired Immunodeficiency Virus (AIDS) at an advanced stage.

Mathematical modelling has contributed immensely to the understanding of the dynamics of HIV infections and transmissions[48-55]. McCluskey[49] developed a mathematical model for HIV/AIDs staged progression and amelioration. The model developed by McCluskey had varying population sizes, admission into the susceptible class was proportional to the active population class. The model also made provision for people infected with the disease to undergo amelioration by translating from more advanced stages of the infection to less advanced stages of infection. Equations that depict these characteristics are as shown in the subsequent sections. The differential equation for the active population subgroups was given by Eq. 26:

$$
\begin{aligned}
S' &= bN - dS - \sum_{m-1}^{r} c\beta_m \frac{I_m}{N} S, \\
I_1' &= \sum_{m-1}^{r} c\beta_m \frac{I_m}{N} S - (k_1 + d)I_1 + g_2 I_2, \\
I_m' &= k_{m-1}I_{m-1} - (k_m + g_m + d)I_m + g_{m+1} + I_{m+1}, \\
&\text{from} = 2, ..., r-1 \\
I_r' &= k_{r-1}I_{r-1} - (k_r + g_r + d)I_r
\end{aligned}
\tag{26}
$$

where, b is the rate constant for new individuals entering into the susceptible state of the population under study. The rate constant for death not directly related to the disease is denoted by d (which was assumed non-negative). The average number of contacts made by a susceptible individual per time is c. For m = 1,........,r, β_m is the probability that a new infection

results from the interaction between a susceptible and an infective class. By applying proportional mixing, the force of infection is given by:

$$\sum_{m-1}^{r} c\beta_m \frac{I_m}{N} S$$

McCluskey[49] constructed a Lyapunov function in a bid to determine local stability of disease free equilibrium. He defined the tri-diagonal matrix.

Cassels *et al.*[50] developed a mathematical model for HIV transmission. The aim of their study was to predict population-level outcomes from individual-level inputs.

They provided an equation as shown in Eq. 27:

$$R_O = \beta cD \qquad (27)$$

where, R_O represents the expected number of secondary infections generated by the first individual. The R_O is a function of biological and behavioural factors. Thus, for a homogeneous population, it defined in Eq. 27.

Auvert *et al.*[56] developed a stochastic model: A modified form of the simulation model SimulAIDS[57-59] to study the significance of sexual behaviour and biological factors on the transmission dynamics of HIV in sub-Saharan Africa. The model incorporated several parameters that provided a detail description of sexual behaviour, thus allowing for easy identification of specific factors that most strongly influenced the HIV outbreak. The SimulAIDS: A Monte-Carlo simulation model was applied to select certain demographic and sexual behavioural characteristics. A generic Sexually Transmitted Disease (STD) was also included in the simulation model. In the study, sexual behaviour was discussed in the context of one of three types of heterosexual partnerships namely one-off, short-term and long-term. The results of the model revealed that the disparities in sexual behaviour was potentially responsible for the differences in HIV prevalence in sub-Saharan Africa. The results of the model also revealed that the number of men involved in non-spousal relationships, including meetings with commercial sex workers and having short term partners, was the major determinant amongst others in the spread of HIV. So far, the model realized its objectives of examining the significance of sexual behaviour and the role of biological factors in the spread of HIV in sub-Saharan Africa, thus meeting the requirements of the generalizability criterion.

Karrakchou *et al.*[51] utilised an existing mathematical model developed by Gumel *et al.*[60] to predict the number of cell-free HIV in the blood during typical course of HIV infection. In their study, the authors investigated the optimal strategy for administering anti-viral drug therapies in combating HIV infection. The authors focused on studying the basic role of chemotherapy treatment in managing the reproduction rate of the virus. In a bid to achieving this aim, Karrakchou *et al.*[51] conducted an analysis of the interactions of healthy CD4+T cells and infected CD4+T cells. The existence and uniqueness of an optimal control pair in administering drug therapies for the control of HIV infection was revealed through numerical simulations using Gauss-Seidel first order implicit finite difference method.

A brief description of the Gauss-Seidel method[61] reveals that it is an iterative technique that can help to solve a square system of n linear equations with unknown x. The following equations reveal how this method is implemented:

$$Ax = b \qquad (28)$$

Equation 28 is defined by this iteration:

$$L_x x^{(k+1)} = b - U x^{(k)} \qquad (29)$$

where, x^k is the kth approximation or iteration of x, x^{k+1} is the next or k+1 iteration of x and the matrix A is decomposed into a lower triangular component L_* and a strictly upper triangular component U[62]:

$$A = L^* + U$$

In details, writing out A, x and b, we have that:

$$A = \begin{bmatrix} a_{11} a_{12} a_{13} \ldots \ldots a_{1n} \\ a_{21} a_{22} a_{23} \ldots \ldots a_{2n} \\ \ldots \ldots \ldots \ldots \ldots \\ \ldots \ldots \ldots \ldots \\ \ldots \ldots \ldots \ldots \ldots \\ a_{n1} a_{n2} a_{n3} \ldots \ldots a_{nn} \end{bmatrix}, x = \begin{bmatrix} x_1 \\ x_2 \\ x_3 \\ . \\ . \\ . \\ x_n \end{bmatrix}, b = \begin{bmatrix} b_1 \\ b_2 \\ b_3 \\ . \\ . \\ . \\ b_n \end{bmatrix} \qquad (30)$$

The system of linear equations can be re-written as:

$$L_* x = b - Ux \qquad (31)$$

The Gauss-Seidel method now solves the left hand side of this expression for x, using previous value for x on the right hand side. This may be written analytically as:

$$x^{(k+1)} = L_*^{-1}(b - Ux^{(k)}) \qquad (32)$$

Taking advantage of the triangular form of L_*, the elements of $x^{(k+1)}$ can be sequentially computed by applying forward substitution to produce:

$$x_i^{(k+1)} = \frac{1}{a_{ii}}\left(b - \sum_{j=1}^{i-1} a_{i,j}x_j^{(k+1)} - \sum_{j=i+1}^{n} a_{i,j}x_j^{(k)}\right),$$
$$i, \, j = 1, 2, 3, \ldots\ldots\ldots n^{63} \qquad (33)$$

The procedure is generally continued until the changes made by an iteration are below some tolerance, such as a sufficiently small residual.

Comparing disease transmission prior and after chemotherapy treatment revealed the vital role chemotherapy played in suppressing viral reproduction, as well as improving the immune system. In conclusion, the application of the model showed that shortly after the commencement of treatment, the growth of uninfected T cells and the reduction in viral population becomes evident. This also satisfied the generalizability criterion.

In order to achieve a decline in HIV incidence, it is essential for the case reproduction to be kept below 1[64]. Granich *et al.*[65] used a hypothetical model to investigate the effect of a universal voluntary HIV testing and immediate intervention with antiretroviral therapy (ART) strategy on the case reproduction number and the long-term dynamics of the HIV outbreak. The model was developed under the assumption that all HIV transmission was heterosexual and data from a South African outbreak served as the source for the hypothetical test case of a generalised epidemic used. The model also studied what conditions were necessary for the elimination of HIV. The model revealed the potential for transitioning from the endemic phase to the elimination phase within 5 years of commencement of ART. Furthermore, the model showed that the case reproduction number and mortality could decline to less than 1 on full implementation of the strategy. The model however, was constrained by the lack of much better data to guarantee the acceptability and uptake of universal voluntary HIV testing, the infectiousness of those on ART, adherence, behavioural transformation upon commencement of ART and the degree of emergence of resistance. The ability of the model to satisfy its initial aim suggests its satisfaction of the generalizability criterion.

Hallett *et al.*[66] developed a mathematical model that provided a mechanistic description of the interactions between sexual behaviour and transmission through a population reflecting these natural epidemiological dynamics and the effects of ART. Utilizing a simulation model in a Bayesian framework in combination with HIV prevalence and sexual behaviour data, the aforementioned hypothesis was evaluated. This was done to establish the fact that decline in HIV prevalence has a strong link to changes in sexual behaviour.

The definition of the model was established by a set of ordinary differential equations and solved through numerical computations using a user-defined software. The model is specified by the following set of differential equations as obtained from the study of Hallett *et al.*[66]:

$$\frac{dS}{dt} = \pi - \sum_{i=1}^{3}\left(\lambda_i^I I_i + \lambda_i^A A_i + \lambda_i^R R_i\right)\frac{S}{N} - \mu S$$

$$\frac{dI_1}{dt} = \sum_{i=1}^{3}\left(\lambda_i^I I_i + \lambda_i^A A_i\right)\frac{S}{N} - \tau_1 I_1 + \phi A_1 - (\rho_1 + \mu)I_1$$

$$\frac{dI_2}{dt} = \rho_1 I_1 - \tau_2 I_2 + \phi A_2 - (\rho_2 + \mu)I_2$$

$$\frac{dI_3}{dt} = \rho_2 I_2 - \tau_3 I_3 + \phi A_3 - (\rho_3 + \mu)I_3$$

$$\frac{dA_1}{dt} = \tau_1 I_1 - (\tau^R + \phi + \sigma_1 + \mu)A_1$$

$$\frac{dA_2}{dt} = \tau_2 I_2 + \sigma_1 A_1 - (\tau^R + \phi + \sigma_2 + \mu)A_2 \qquad (34)$$

$$\frac{dA_3}{dt} = \tau_3 I_3 + \sigma_2 A_2 - (\tau^R + \phi + \sigma_3 + \mu)A_3$$

$$\frac{dR_1}{dt} = \sum_{i=1}^{3}\lambda_i^R R_i \frac{S}{N} + \tau^R A_1 - (\omega_1 + \mu)R_1$$

$$\frac{dR_2}{dt} = \tau^R A_2 + \omega_1 R_1 - (\omega_2 + \mu)R_2$$

$$\frac{dR_3}{dt} = \tau^R A_3 + \omega_2 R_2 - (\omega_3 + \mu)R_3$$

The model categorised people starting sex into one of three sexual behavioural groups namely: Those in spousal relationships, those in long-term casual relationships and those with multiple numbers of sexual partners. Furthermore, the parameters of the model indicated for separately each gender, the proportion of the population entering each group, the relative rates of partner change for each group and the average rate of partner change across all groups. Application of the model to data from Zimbabwe showed strong evidence for changes in risk behaviour impacting the course of HIV epidemics, thus altering the natural course of the HIV epidemic. The modelling analysis however is limited by the assumption of a model that adequately reflects HIV transmission in a population and a model set on identifying changes in risk behaviour that have occurred after the epidemic has peaked. The model having fulfilled its initial aim, satisfies the generalizability criterion.

Mushayabasa and Bhunu[67] studied the connection between HIV and cholera in a cholera-endemic population. The total human population for this study was categorised into the following: Susceptible individuals those infected with cholera only, those infected with HIV only and those infected with both cholera and HIV. With a deterministic compartmental model, the authors revealed that in a cholera-endemic environment, HIV infection is linked with the increased risk of cholera infection and *Vice-versa*. Further numerical analysis of the model showed that under different start up conditions, the number of cholera only cases outnumbered both HIV only cases and dual cases. The model met the criteria for a good model as it satisfied its aim.

Blower and Wagner[68] incorporated realism into the existing HIV transmission model by Granich *et al.*[65] to study the impact on the HIV outbreak in South Africa (SA) of (i) A universal test and treat strategy and (ii) Realising universal access to treatment. The model in contrast to Granich *et al.*[65], predicted the possibility of HIV elimination in SA within 40 years at a cost of ~$12 billion more than realising universal access. It was clear that an under-estimation of the survival time on treatment and ignoring the risk of resistance contributed to the under-estimation of the control reproduction number. The model further showed that ~1.5 million people would need second-line regimens after 20 years under the realisation of universal access in contrast to an ~2 million under a universal test and treat strategy. As a result of the huge cost involved in implementing a universal test and treat strategy, the authors suggested the need for achieving universal access to treatment as quickly as possible, especially in resource constrained countries. Also, the universal access to treatment was shown to be a very effective 'treatment as prevention' strategy that could bring the HIV outbreak in SA close to elimination as well as reducing infection by ~4 million after 20 years and ~11 million after 40 years. The model also met the criteria of a good model having fulfilled its aim.

Boily *et al.*[69] applied a integrated mathematical modelling approach to study and evaluate a large-scale of HIV prevention interventions. Their mathematical model was embedded within a Bayesian framework. Empirical and behavioural data were sought from different subpopulations where the interventions were needed. The results obtained from their research showed that it could be applied in the design of large-scale future interventions and the results will be more beneficial to public health interventions.

Malaria: Malaria is a critical and life-threatening disease ravaging Africa and some other parts of the world. The disease is caused by *Plasmodium* parasites. The parasite is transmitted to an individual from a bite by an infected female anopheles mosquito. According to WHO, in 2013 alone, malaria caused about 584,000 deaths among African children[70]. Still, another 1.5-3 million deaths of non-immune individuals occur on a yearly basis. Despite the preventable and curable nature of the diseases, non-immune migrants still stand a high risk of infection upon indiscriminate exposure. Hence, the need for increased prevention and control strategies that would dramatically reduce the burden of the disease on the population.

Tumwiine *et al.*[71] developed a model that allowed for the recruitment of individuals through immigration of infective migrants. The design of the model assumed a population with a constant influx rate Λ occuring via birth or by immigration, with a fraction ø considered to be infective and the remaining 1-ø as susceptible. Also assumed by the model, is the fact that no immigrant entered the immune class. The rate at which the human hosts got infected by the infected mosquitoes and the rate at which the susceptible mosquitoes got infected by the human hosts were used to model the horizontal transmission of the disease. The model categorised the population sizes of the human hosts as being susceptible, infected or temporally immuned, while the female mosquito host was subclassed into the susceptible and the infected. In conclusion, the model revealed the important role migration played in the transmission dynamics of malaria with recommendation on the need to consider these roles in the formation of public health control policies. This model also satisfies the generalizability criterion.

Considering the role of temporal immunity on the transmission dynamics of malaria in a human host and the mosquito vector, Tumwiine *et al.*[72] yet developed another model with standard incidence for the transmission dynamics of malaria in a human host and the mosquito vectors whereby the pool of susceptible individuals were refilled by immunity loss to the disease and newborns. The total population of the model was categorised into the following: (a) The number of susceptible human hosts at time t, (b) The number of infected human hosts at time t, (c) The number of partially immune human hosts at time t, (d) The number of susceptible mosquito vectors at time t and (e) The number of infected mosquito vectors at time t. The model assumed the following: (a) A bite from the infectious female mosquito on the human host leads to the development of malaria, (b) A bite from an infected female mosquito on an infected human host is ignored, (c) Bites in human hosts is carried out randomly, (d) Immunity gained by recovered human hosts is only temporal and as such can be lost, thereby making them susceptible again to re-infection, (e) Susceptibility to infection for all newborns is possible, however, vertical transmission is absent,

(f) The lifecycle of mosquitoes end in death from infection and (g) There is variability in total human and mosquito populations overtime. The model also revealed that loss of immunity did not affect the basic reproduction number and that the disease is eliminated as long as the basic reproduction number stays ≤ 1. However, a basic reproduction number >1, causes instability in the disease-free equilibrium point with the endemic rising to a unique equilibrium point. At this stage, it becomes possible for a re-invasion as the disease is never eliminated. The model concluded with the recommendation that focus be placed more on treatment and reduction on the contact between mosquito vector and the human host in order to reduce the basic reproduction number. Thus, the need for more effective drugs, treated bed nets and insecticides to clamp down on the mosquito population. Model again satisfies the requirements of the generalizability criterion.

Ducrot *et al.*[73] in a bid to distinguish between susceptibility, the exposedness and the infectivity of the human host in the transmission dynamics of malaria, developed a deterministic mathematical model with two host types in the human population, with the ultimate goal of preventing malaria in areas of low, intermediary and high transmissions. The non-immune host was defined to be vulnerable as it could suffer and/or die of malaria, whereas, the semi-immune host was defined to have at one time or the other acquired immunity even if immunity lost along the way. Also, the semi-immune host type was considered to be non-vulnerable and above death from malaria but could still suffer from malaria. Immunity rather than the age of the individual formed the basis for the structuring of population based on the fact that both children and adult share same risk of malaria disease and infection depending their previous infection experiences[74,75]. The non-immune population was modelled as a susceptible-exposed-infectious-susceptible type until some non-immune becomes semi-immune and stays so for the rest of life, now taking on a susceptible-exposed-infectious-recovered-susceptible model type. On the other hand, the mosquito population was modelled as a susceptible-exposed-infectious type. The model worked under the assumptions that (a) Both human and mosquito populations were born susceptible, (b) The immigration of non-immune to a non-immune susceptible class at rate p and the immigration of semi-immune to a semi-immune susceptible class at rate 1-p and (c) The immigration of the exposed, infectious and immuned humans were ignored. Simulating the model using realistic parameter values compatible with malaria with a basic reproductive number close to one, the model showed backward bifurcation. Further evaluation of the model using parameters that correspond to

a stable area of transmission such as seen in most parts of Africa, the model showed a unique endemic state solution that was locally asymptotically stable. In other words, for the elimination of malaria, simultaneous target of control on the non-immune and semi-immune or mosquito population was required, as well as the continous elimination of 88.70% of susceptible mosquitoes at birth. In an area of low or intermediary transmission however, the model showed that it was possible to eliminate malaria through targeted control on a specific host type. Also, in an area of high transmission, targeted control on the non-immune group can eliminate malaria. The model further revealed the role of vaccines in controlling malaria in areas where malaria transmission varies year in year out. The model further suggests the elimination of mosquitoes where it is not possible to target control on either the non-immune or semi-immuned hosts. Because a small disturbance in the ecology of a given area could re-establish malaria in any of the three populations, the model recommends keeping the basic reproductive number within a domain such that the equilibrium point is asymptotically stable. The model is considered to be good model as it satisfied its initial aim.

Oluwagbemi *et al.*[76] developed AnoSpex: A stochastic, spatially-explicit computational model for the metapopulation dynamics of anopheles mosquitoes. The model is an integration of mathematical and computational methods. For instance, the cumulative physiological development CD_t for a given cohort of age n and time t, was given[76] as:

$$CD_t = \sum_{\tau = t-n}^{t} r(T_\tau) \tag{35}$$

Besides, the model helped to model anopheles mosquito movements by adapting knowledge from cellular automata and applying the Von Neumann neighbourhood algorithm. There exist a random selection of one of the possible four directions for any dispersing anopheles mosquito. A mathematical formula was adopted to estimate the distance between one residential property and another. The distance between one residential property and another is given[76] as d:

$$d = \sqrt{\left(p_j - p_i\right)^2 + \left(q_j - q_i\right)^2} \tag{36}$$

Where each residential property within a grid is represented by the coordinates is represented by (p_j, p_i) and (q_j, q_i). Besides, AnoSpEx[76] model adopted the enzyme kinetics equations[77-79] for the stepwise transition of immature stages of anopheles mosquitoes from one level to the other[77-79].

$$r(T) = \frac{\rho_{25C} \cdot \frac{T}{298} \cdot \exp\left[\frac{\Delta H_A^{\#}}{R}\left(\frac{1}{298} - \frac{1}{T}\right)\right]}{1 + \exp\left[\frac{\Delta H_L}{R} \cdot \left(\frac{1}{T_{\frac{1}{2}L}} - \frac{1}{T}\right)\right] + \exp\left[\frac{\Delta H_H}{R} \cdot \left(\frac{1}{T_{\frac{1}{2}H}} - \frac{1}{T}\right)\right]} \quad (37)$$

The model also consists of growth algorithms for each developmental stage of the malaria vector. The model was developed using C++ codes in a visual C++ integrated development environment. Majority of AnoSpEx codes were newly written and integrated with few Skeeter Buster [80] codes. The model is also rich and parameterized with field data. Weather data was obtained from Macha, Zambia. Data for three species of mosquitoes were collected namely: *Anopheles gambiae*, *Anopheles funestus* and *Anopheles arabiensis*. A preliminary validation of AnoSpEx with CDC

(Center for Disease Control) traps, HLC (Human Land captures), CBT (Cattle-baited traps) mosquito data revealed that AnoSpEx predicted similar trend with real-life female anopheles mosquito collection data, thus revealing that the model is good and a potential tool to further develop and implement additional control and novel eradication strategies for malaria.

RESULTS

The results section shows the model types that have been reviewed, the classification of infectious disease for each model type, the criterion applied, the references and remarks. These results are highlighted in Table 1-4. It should be noted that there are numerous articles in existence for each category of infectious disease, however, only able to review a selected number out of the existing articles on the modelling of ebola, typhoid fever, HIV/AIDS and malaria.

Table 1: Results showing some collections of reviewed modelling articles for EVD

Model types	IFDs	Criterion	Authors and references	Applicability to IFDs (remarks)
Mathematical models	Ebola	Generalizability	Nishiura and Chowell[10,11]	Good
Mathematical model	Ebola	Generalizability	Weitz and Dushoff[13]	Good
Mathematical model	Ebola	Generalizability	Lewnard et al.[16]	Good
Mathematical model	Ebola	Generalizability	Atangana and Goufo[17]	Good
Mathematical model	Ebola	Generalizability	Fasina et al.[18]	Good
Mathematical model	Ebola	Generalizability	Fisman et al.[21]	Good
Computational and mathematical model	Ebola	Generalizability	House[25]	Good
Computational and mathematical model	Ebola	Generalizability	Chowell et al.[22]	Good
Mathematical model	Ebola	Generalizability	Rivers[29]	Good
Mathematical model	Ebola	Generalizability	Althaus et al.[24]	Good
Computational model	Ebola	Generalizability	Merler et al.[32]	Good
Mathematical model	Ebola	Generalizability	Chowell et al.[33]	Good
Computational and mathematical model	Ebola	Generalizability	Webb and Browne[34]	Good
Computational and mathematical model	Ebola	Generalizability	Camacho et al.[35]	Good
Computational and mathematical model	Ebola	Generalizability	Agusto et al.[36]	Good

Table 2: Results showing some collections of reviewed modelling articles for typhoid fever

Model types	IFDs	Criterion	Authors and references	Applicability of IFDs (remarks)
Mathematical models	Typhoid fever	Generalizability	Mushayabasa et al.[39,41,43], Mushayabasa[44,45]	Good
Mathematical model	Typhoid fever	Generalizability	Adetunde[42]	Good
Mathematical model	Typhoid fever	Generalizability	Mutua et al.[46]	Good

Table 3: Results showing some collections of reviewed modelling articles for HIV/AIDS

Model types	IFDs	Criterion	Authors and references	Applicability to IFDs (remarks)
Mathematical models	HIV/AIDS	Generalizability	McCluskey[49]	Good
Mathematical model	HIV/AIDS	Generalizability	Cassels et al.[50]	Good
Computational model	HIV/AIDS	Generalizability	Tameru[52]	Good
Computational model	HIV/AIDS	Generalizability	Wang et al.[54]	Good
Mathematical model	HIV/AIDS	Generalizability	Eaton et al.[55]	Good
Computational model and simulation	HIV/AIDS	Generalizability	Auvert[56]	
Computational model and simulation	HIV/AIDS	Generalizability	Robinson et al.[57,58]	Good
Mathematical model	HIV/AIDS	Generalizability	Gumel et al.[60]	Good
Mathematical model	HIV/AIDS	Generalizability	Karrakchou et al.[51]	Good
Mathematical model	HIV/AIDS	Generalizability	Granich et al.[65]	Good
Mathematical model	HIV/AIDS	Generalizability	Hallett et al.[66]	Good
Mathematical model	HIV/AIDS	Generalizability	Mushayabasa and Bhunu[67]	Good
Mathematical model	HIV/AIDS	Generalizability	Blower and Wagner[68]	Good
Mathematical model	HIV/AIDS	Generalizability	Boily et al.[69]	Good

Table 4: Results showing some collections of reviewed modelling articles for malaria

Model types	IFDs	Criterion	Authors and references	Applicability to IFDs (remarks)
Mathematical models	Malaria	Generalizability	Tumwiine *et al.*[71,72]	Good
Mathematical model	Malaria	Generalizability	Ducrot *et al.*[73]	Good
Mathematical model	Malaria	Generalizability	Andersen *et al.*[74]	Good
Computational and mathematical model	Malaria	Generalizability	Oluwagbemi *et al.*[76]	Good

DISCUSSION

Our review of study manuscript covered some of the existing study on computational and mathematical modelling of infectious diseases such as malaria, ebola, HIV/AIDS and typhoid fever. From the results obtained in Table 1-4, it is evident that computational and mathematical modelling play very significant roles in proffering control measures to infectious diseases such as malaria, typhoid, ebola and HIV/AIDS. The models reviewed met the criteria for a good model as they all satisfied their aims and goals.

CONCLUSION

In conclusion, computational and mathematical modelling has influenced the management of IFDs in Africa. Prior to the introduction of prevention and control strategies for stemming the tide of IFDs in Africa, 63% of total deaths was attributed to IFDs with the economic and human health in Africa declining continuously. With the aid of computational and mathematical modelling as a preventive and control strategy, Africa today has improved in combating the spread of IFDs, thereby reducing the adverse effect of infectious diseases on the populace. The risk of a major outbreak of infectious disease can now be predicted, as well as estimate the trend of an epidemic and the consequence of standard control measures on the transmission of IFDs. Furthermore, modelling has shown the importance of timing of intervention, what type and the location where such interventions are needed.

SIGNIFICANT STATEMENT

This study is important in that, it provides health professionals and stake holders of Non-Governmental Health Organizations, proper understanding of the applicability of computational and mathematical modelling towards controlling the menace of infectious diseases in Africa. The study also revealed knowledge that provides a common collaborative platform for computer scientists and mathematicians to solve public health problem by proffering solutions to some of the most devastating infectious diseases. Finally, this study acts as a reference point that allows the

scientific community access to some of the study on the application of computational and mathematical modelling towards the control and management of infectious diseases.

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