

A DIFFERENTIAL EQUATIONS MODEL OF EAST COAST FEVER TRANSMISSION DYNAMICS

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Abstract

In this study a differential equation model of the transmission dynamics of East Cost Fever caused by *Theileria parva* transmitted by *Rhipicephalus appendiculatus* was developed. In this model cattle were assigned to four categories: susceptible, *T. parva* incubating, infectious (clinically infected) and recovered cattle population having immunity and still infect ticks but at a lower rate. Ticks were also categorized into various stages: eggs, larvae, susceptible nymphs, infected nymphs, susceptible adult ticks and infected adult ticks. The parameters of the model were obtained from literature assumed or calculated. Simulations with R software were run with and without seasonal questing activity of adult ticks. The results of the simulation model explained the seasonal differences of *R. appendiculatus* activity and transmission of *T. parva* between tropical eastern and central Africa and sub – tropical southern Africa. Besides, it showed that nymphs are the stage of *R. appendiculatus* that play important role in transmission of *T. parva* in southern Africa while both nymphs and adults transmit in eastern and central Africa. Future developments and data required to further develop the model were proposed.

Keywords: A model, Differential equations, *Rhipicephalus appendiculatus*, *Theirelia parva*

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Introduction

East Coast Fever (ECF) is an infectious disease of cattle caused by *Theileria parva* and transmitted by the main field vector, *Rhipicephalus appendiculatus* (Bazarusanga *et al.*, 2007). The occurrence of ECF in African cattle has been evident for more than a century in eastern, central and southern African countries (Norval *et al.*, 1991). The parasite is transmitted trans-stadially by *R. appendiculatus*, which have dropped from infected cattle during the preceding stage of the life cycle. To a lesser extent *T. parva* is transmitted by *R. zambeziensis* and *R. duttoni*, which play only a limited role in the epidemiology of ECF (Fandamu *et al.*, 2005). East Coast Fever is one of the principal disease problems hindering cattle development in affected African countries. However, its occurrence and the consequent outcomes, appear to vary between eastern and southern African regions. The occurrence ECF has been considered endemic in eastern Africa with relatively lower mortalities. For instance, Gitau *et al.* (1999) reported the incidence of ECF in smallholder dairy calves in Kenya to vary from 27 – 58% with mortality of 7.4%. In the same country Maloo *et al.*, (2001) reported incidence of ECF within the range of 20 – 39% in calves from different farming systems. The results of similar studies in Tanzania showed that the incidence of mortality due to ECF in dairy calves was 42% (Msami, 2001) while Swai *et al.* (2009) later reported a 37.5% mortality due to ECF. The evidence of infection was about 62.9% in Rwandan cattle (Bazarusanga *et al.*, 2007).

On the contrary, high incidence of mortalities have been associated with ECF outbreaks in southern African countries, which was in general greater than 90% (Norval *et al.*, 1992). Higher case-fatality rates were also observed in southern African regions. For instance Billiouw *et al.* (2002) reported case fatality of 60% in eastern Zambian cattle but a lower incidence of mortality (8.3% - 30.2%) was observed in one outbreak in the Southern province of the same country (Minjaw *et al.*, 1998). The transmission of *T. parva* to cattle has been known to depend on the abundance of the vector, the proportion of infected ticks and the presence of carrier or clinically infected cattle. For instance, it has been demonstrated that in eastern African countries the vectors are widely distributed and abundant throughout most of the year. In these areas the transmission of *T. parva* has been thought to be continuous and the disease is considered to attain endemic stability. In contrast in southern African countries where the availability of suitable environment for the vectors is limited both spatially and temporally, the transmission of *T. parva* has been thought to be seasonal and hence the disease did not attain endemic

stability (Norval *et al.*, 1991). However, the exact role of vector and cattle population dynamics on the epidemiological pattern of ECF has not been fully elucidated. Countries such as Zambia where both diapausing and non-diapausing vectors are thought to be found would benefit from an in-depth understanding of the epidemiology of ECF in order to devise appropriate control measures.

Models of vector population dynamics in combination with epidemiological processes were recommended to be basic components in the understanding and management of vector-borne diseases (Gettinby, 1989; Gilioli *et al.*, 2009; Sutton *et al.*, 2012). In this regard, mathematical models have been shown to play role in providing quantitative evidence for understanding the epidemiology of infectious diseases (MacDonald, 1961). Previously few models have been developed to describe different aspects of ECF. One of such models was developed by Medley *et al.* (1993). The authors quantified the rate at which cattle become infected with *T. parva* in endemic areas and clearly showed the role of carrier animals in the transmission of the parasite. They have also quantified the role of control measures using acaricide and immunization by infection and treatment method on the transmission dynamics of *T. parva*. Randolph and Rogers (1997) have developed a model that describes the vector population and were able to predict the seasonality and dynamics in the number of all stages of *R. appendiculatus*.

The possibility of satellite driven *R. appendiculatus* population model using climatic data was suggested by Randolph and Rogers (1997). Similarly, Berkvens (1994) suggested the possibility of accurately modelling the population dynamics of *R. appendiculatus* being driven by temperature and duration of development period. A more comprehensive model was developed by Gilioli *et al.* (2009). This model described both the vector and host aspects of ECF. It captured important aspects of the tick/cattle/ECF systems in the epidemiology of ECF. Other important and relevant factors such as questing activity of adult ticks, host-pathogen-vector interactions and their impact on the transmission dynamics of *T. parva* has not been quantified. The inclusion of these parameters in the model and quantification of their effect on the *T. parva* infection process will add to the body of knowledge and could provide reliable quantitative evidence on the epidemiology of ECF. In this regard, we developed a differential equations model which describes the role of *R. appendiculatus* abundance and host attributes on the transmission dynamics of *T. parva*.

Methodology
Populations Dynamics

The transmission dynamics and the epidemiology of ECF involved the modeling of two interacting populations both the *R. appendiculatus* (equation 7) and cattle populations (equation 1). For this purpose, cattle population was categorized into four compartments depending upon their infection status. These are: Susceptible (*S*): these are cattle which have not been infected and are fully susceptible (irrespective of their age) to *T. Parva* infection (equation 2). Those hosts in the susceptible state upon acquiring the *T. parva* infection can move into exposed state. Exposed (*E*): these are cattle which are infected with *T. parva* and incubating the parasites but not infectious to the tick vectors (equation 3). From the exposed state the hosts, which become clinically infected move into the infectious state and a proportion with low parasitaemia will move into recovered. Infectious (*I*): clinically sick cattle that are sources of infection for the tick vectors (equation 4). Hosts that survive the initial infection remain carrier and enter state of recovered. Recovered (*R*): cattle that are recovered from initial infections and remain carriers of *T. Parva* (equation 5). Note that animals in this class can still infect ticks, but at lower rate (Norval *et al.*, 1992).

For ticks, we described all stages of *R. appendiculatus* populations. The eggs (*E_g*) were modelled as one compartment with hatchability rate of η (see equation 8). The larvae (*L*) consist of non-infected population that can acquire *T. parva* from cattle if they attach to infected cattle (see equation 9). The nymphs comprise infected (*I_N*) and non-infected sub-populations (*S_N*) (equation 10 & 11). The nymphs are the immature stage of *R. appendiculatus* that can transmit *T. parva* if the preceding larvae acquire the infections. The adult *R. appendiculatus* (equation 13 & 14) are also divided into infected (*I_A*) and non-infected sub-populations (*S_A*). The adults are considered the most efficient vectors of *T. parva*. (Berkvens, 1992; Walker, 2003; Gilioli *et al.*, 2009). Different compartments of Cattle and Tick population and their interaction considered are depicted in figure 1 and the parameterization of each of the components was described

as shown in Table 1.

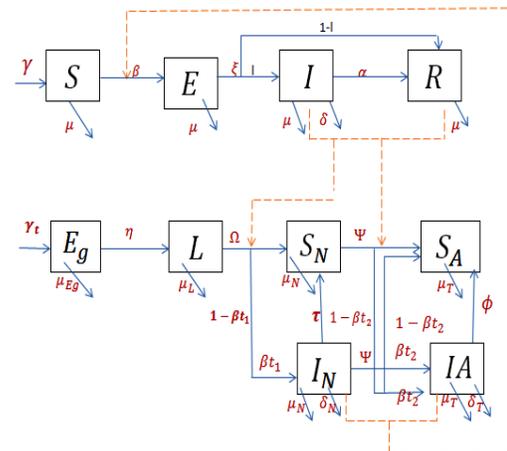


Figure 1: Diagram showing cattle – *R. appendiculatus* interaction dynamics

Dynamics of infection in ticks

The vector population is stratified as infected or non-infected. The vectors themselves acquire *T. parva* infection during the preceding stages if they attach and feed on clinically sick or carrier hosts. This approach of infection dynamics is based on previous descriptions by Norval *et al.* (1992); Medley *et al.* (1993); O’Callaghan *et al.* (1998) and Gilioli *et al.* (2009). The larvae are the first stage, which will become infected from cattle with a rate βt_1 (equation 12). This will depend on the infectious bovine infection rate vis-à-vis larvae βt_1 and the recovered bovine infection vis-à-vis larvae βt_2 . The infected nymphs will transmit *P. parva* when feeding on cattle and become susceptible to re-infection. It was assumed that both infected and non-infected nymphs have the same rate of acquiring infection βt_2 (equation 15). This will depend on the infectious bovine infection rate vis-à-vis nymphs βt_3 and the recovered bovine infection vis-à-vis nymphs βt_3 .

Estimation of the force of infection in cattle

The force of infection β (equation 6) or *T. parva* infection rate in cattle population is the measure of the rate at which susceptible cattle become infected. This rate was calculated on the basis of binomial probability law. The infection rate depends on the attachment rate of infected nymphs and adult ticks on susceptible cattle. Suppose that the probability that an attached and feeding-infected adult tick transmit the infection is p_1 then the probability that adult ticks do not transmit is $(1 - p_1)$. The probability that an infected attached and feeding nymph transmits *T. parva* to

susceptible cattle is p_2 and the probability that they do not transmit the infection is $(1 - p_2)$. The probability that attached and feeding infected nymphs and attached and feeding adult ticks on susceptible cattle do not transmit *T. parva* is:

$$(1 - p_1)^{\text{attachedandfeedinginfectednymphs}} \times (1 - p_2)^{\text{attachedandfeedinginfectedadultticks}}$$

And the probability that they transmit *T. parva* is:

$$1 - ((1 - p_1)^{\text{attachedandfeedinginfectednymphs}} \times (1 - p_2)^{\text{attachedandfeedinginfectedadultticks}})$$

By the logarithmic transformation: $\gamma = -\ln(1 - \Pi)$, where γ is a rate and Π a probability

So

$$\beta = -\ln(1 - 1 + ((1 - p_1)^{\text{attachedandfeedinginfectednymphs}} \times (1 - p_2)^{\text{attachedandfeedinginfectedadultticks}}))$$

$$\beta = -\ln((1 - p_1)^{\text{attachedandfeedinginfectednymphs}} \times (1 - p_2)^{\text{attachedandfeedinginfectedadultticks}})$$

In our model we assumed that tick attachment rate is constant and depends on the number of ticks pick-up and the lack of resistance of cattle to ticks Medley *et al.* (1993).

Seasonality in questing activity of adult ticks

Questing activity of adult ticks plays a central role in the occurrence and epidemiology of ECF in Africa. In the equatorial regions and eastern Africa adult ticks are active and questing throughout the year. In these regions it has been assumed that ECF tend to reach endemic stability. In southern Africa, a strict seasonal adult activity is observed(Madder and Berkvens, 1997). They are questing during the rainy season while the unfed adult ticks often go into diapause and remain inactive for several months. In our computer simulation 2 scenarios were considered to explain the questing activity of adult ticks (qaa):

Scenario 1: Seasonal questing activity of adult ticks

The sinusoidal function was used for seasonal questing activity of adult ticks. This was described as: $qaa = 0.5 * (1 + \sin((\text{times} + 90) * \pi / 180))$

Scenario 2: Non seasonal questing activity of adult ticks

It was assumed that about 50% of adult ticks are questing. This was described as: $qaa = 0.50$

Description of parameters for the vector and host population models

The parameters used in this model were estimated, assumed or taken from published sources. These parameters were

utilized to simulate the cattle and tick populations and their interactions. The force of infection and the infection in ticks were calculated after the simulations.

Table1: Parameters used to simulate the models and their values as obtained from different sources

Parameters	Value	Sources
Cattle		
γ	Reproduction rate of cattle/day	0.0009772 Gilioli <i>et al.</i> (2009)
β	Force of infection (scenario 1)	0.012032 Calculated
β	Force of infection (scenario 2)	0.01842936 Calculated
$1/\xi$	Rate of incubation of <i>T.parva</i> /day	1/7-1/15 Medley <i>et al.</i> (1993); Fandamu <i>et al.</i> (2006); Konnai <i>et al.</i> (2007)
$1/\alpha$	Rate of recovery/day	1/18 Medley <i>et al.</i> (1993)
l	Proportion of animal with develop clinical signs	0.50 Assumed
μ	Natural mortality rate of cattle/day	0.000788 Gilioli <i>et al.</i> (2009)
δ	Mortality rate due to ECF/day	0.05*1/18-0.46*1/18 Medley <i>et al.</i> (1993) ; Kirvaria <i>et al.</i> (2004); Latif <i>et al.</i> (2001a)
Ticks		
γ_t	Number of eggs/female/day	100-300 (Walker <i>et al.</i> , 2003) Branagan(1973)
η	Ecdysis rate/day	1/30-1/85 Branagan (1973)
μE_g	Mortality rate of eggs/day	1/30 Branagan (1973)
μ_L	Natural mortality rate of larvae/day	175 Newson <i>et al.</i> (1984)
μ_N	Natural mortality rate of nymphs/day	360 Newson <i>et al.</i> (1984)
μ_A	Natural mortality rate of adult ticks/day	420 Newson <i>et al.</i> (1984)
δ_N	Extra mortality of nymphs due to ECF/day	0.00009 assumed
δ_A	Extra mortality of adult ticks due to ECF/day	0.00009 assumed
qaa	Questing activity of Adult ticks	0.5 assumed
Ω	Moulting rate of engorged larvae /day	1/8-1/53 Branagan (1973)
Ψ	Moulting rate of engorged nymphs /day	1/12-1/86 Branagan (1973)
τ	<i>T.parva</i> survival time in nymph / days	1/2*1/182-1/2*1/350 Ochianda <i>et al.</i> (2003)
ϕ	<i>T.parva</i> survival in adult ticks / days	1/2*1/439-1/2*600 Young <i>et al.</i> (1983); Newson <i>et al.</i> (1984) Madder(2003) ; Young <i>et al.</i> (1987); Ochianda (2006)
att_{LL}	Attachment rate of larvae	0.799 Medley <i>et al.</i> (1993)
aat_{NN}	Attachment rate of nymphs	0.799 Medley <i>et al.</i> (1993)
aat_{AA}	Attachment rate of adult ticks	0.799 Medley <i>et al.</i> (1993)
β_{t1}	Bovine infection rate vis-à-vis larvae (Scenario1)	0.00162 Calculated
β_{t1}	Bovine infection rate vis-à-vis larvae (Scenario 2)	0.00165 Calculated
β_{t2}	Bovine infection rate vis-à-vis nymphs (Scenario 1)	0.0162 Calculated
β_{t2}	Bovine infection rate vis-à-vis nymphs (Scenario 2)	0.0165 Calculated
p_1	Probability that infected adult tick transmit <i>T. parva</i>	0.9 Medley <i>et al.</i> (1993)
p_2	Probability that infected nymphs transmit <i>T.parva</i>	0.9 Medley <i>et al.</i> (1993)
p_{t1}	Infectious bovine infection rate vis-à-vis larvae	0.07-0.0708 assumed
p_{t2}	Recovered bovine infection rate vis-à-vis larvae	0.000935 assumed
p_{t3}	Infectious bovine infection rate vis-à-vis nymphs	0.708-0.75 Ogeden <i>et al.</i> (2003) ; Konnai <i>et al.</i> (2007)
p_{t4}	Recovered bovine infection rate vis-à-vis nymphs	0.009035 Medley <i>et al.</i> (1993)

Results and Discussion

In this paper, a differential equations model, which explains the transmission dynamics of East Coast Fever, was developed. The simulations using R Software were based on the parameter values presented in Table 1 and on two scenarios (Scenario 1: Seasonal questing activity of adult; Scenario 2: non seasonal questing activity of adult ticks). The initial conditions to run the Model were: S= 100; E= 0; I= 0; R= 0; EG= 5000; L= 2500; SN=1200; IN=4; SA=600, IA=2 and the time was 1500 days.

Differential Equations

Cattle

$$N = S + E + I + R$$

$$(1) \frac{dS}{dt} = \gamma N - (\mu + \beta)S$$

$$(2) \frac{dE}{dt} = \beta S - (\mu + \xi)E$$

(3)

$$\frac{dI}{dt} = \xi l E - (\mu + \delta + \alpha) I \quad (4)$$

$$\frac{dR}{dt} = E \xi (1 - l) + \alpha I - \mu R \quad (5)$$

$$\beta = -\log \left(\left((1 - p_1)^{(att_{AA} \times qaa \times I_{A/N})} \right) \times \left((1 - p_2)^{(att_{NN} \times I_{N/N})} \right) \right) \quad (6)$$

Ticks

$$Nt = Eg + L + S_N + I_N + S_A + I_A \quad (7)$$

$$\frac{dEg}{dt} = \gamma t att_{AA} qaa (S_A + I_A) - (\mu_{Eg} + \eta) Eg \quad (8)$$

$$\frac{dL}{dt} = \eta Eg - (att_{LL} + \mu_L) L \quad (9)$$

$$\frac{dS_N}{dt} = (1 - \beta t_1) att_{LL} \Omega L - (att_{NN} + \mu_N) S_N \quad (10)$$

$$\frac{dI_N}{dt} = \Omega \beta t_1 att_{LL} L - (\mu_N + \delta_N + att_{NN}) I_N \quad (11)$$

$$\beta t_1 = (pt_1 I + pt_2 R) / N \quad (12)$$

$$\frac{dS_I}{dt} = [(1 - \beta t_2) att_{NN} \Psi (S_N + I_N)] + \Phi I_A - (\mu_T + att_{AA} qaa) S_A \quad (13)$$

$$\frac{dI_A}{dt} = \beta t_2 att_{NN} \Psi (S_N + I_N) - (\mu + \delta_A + att_{AA} qaa + \Phi) I_A \quad (14)$$

$$\beta t_2 = (pt_3 I + pt_4 R) / N \quad (15)$$

T. parva transmission dynamics (scenario 1): Seasonal questing activity of adult

The *T. parva* transmission model is presented in Figure1. It was shown that the transmission of *T. parva* to cattle population reaches a peak at the beginning of the infection process and the peak coincides with the peak number of nymphal stages of the vector *i.e.*, the infection rate in cattle (Figure1: lower panel) varies with the number of nymphs of *R. appendiculatus* (Figure1: upper panel). This clearly shows that nymphs play more important role in the transmission of *T. parva* than adults. There was a periodic fluctuation in the infection rate in cattle that coincides with change in the number of nymphs.

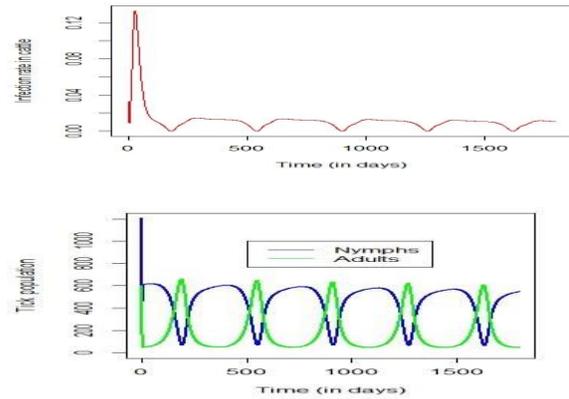


Figure1: Transmission dynamics of *T. Parva* with a seasonal questing activity of adult ticks

By scenario1 this simulation showed that nymphs are important in the transmission of *T. parva* to cattle. This could be due to the fact that adults that emerge from nymphs go to diapause and the *T. parva* infection they acquire during the preceding nymphal stage may die during the diapause period. Therefore, the force of infection is related to the abundance of nymphs. This contradicts the previous thoughts that nymphs play minor role in the transmission of *T. parva* (Madder and Berkvens, 1997). But our results are in agreement with the observations of Fandamu *et al.* (2006) in Southern Zambia who recorded high sero-prevalence of ECF in cattle during September which was probably a result of nymphal challenges during their abundance between May and August. The results of field survey by Latif *et al.* (2001a and b) in Zimbabwe also demonstrated occurrence of clinical ECF in cattle following their exposure to *R. appendiculatus* during nymphal activity. Similarly, the observations made by Mulumba *et al.* (2001) in southern Zambia showed that cases of ECF occurs following nymphal periods.

The seasonal pattern of abundance of *R. appendiculatus* has previously been reported for subtropical southern Africa. Specifically our results agree with the findings of Pregram and Banda (1990) who have reported similar phenology of cattle ticks in Zambia. Similarly, Fandamu *et al.* (2005) observed that adult *R. appendiculatus* were active only during rainy season in Zambia; larvae emerged from them were active towards the end of the rainy season and nymphs are active during the cool dry season. The absence of overlapping activity of the different stages of *R. appendiculatus* was consistent with our research. Norval *et al.* (1991) also reported similar findings from Zimbabwe. This seasonal pattern of activities of different stages of *R. appendiculatus* has been shown to be set by newly molted

adult ticks, which undergo diapause in the southern Africa region (Berkvens *et al.*, 1995; Madder and Berkvens, 1997).

***T. parva* transmission from (scenario 2): non seasonal questing activity of adult ticks).**

There was no periodicity in the infection rate of *T. parva* in cattle in eastern Africa. The infection rate in cattle escalates with time and this increment was matched with increment in the number of nymphs and adult ticks. The number of active adult was lower. The rate of infection reaches a peak (Figure2, lower panel) when the number of nymphs reaches a peak (Figure2, upper panel). Nymphs were found to play an important role in the transmission of *T. parva*.

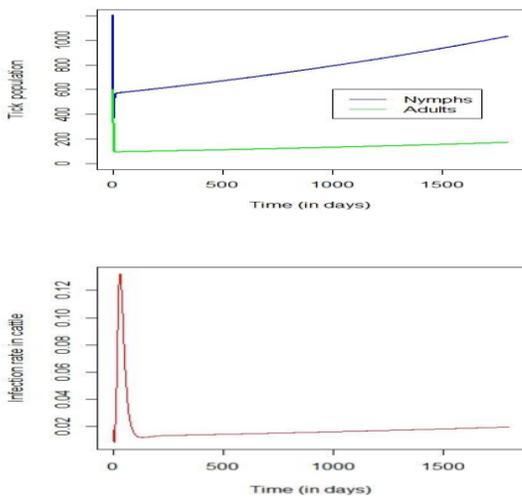


Figure2: Transmission dynamics of *T. parva* with a non-seasonal questing activity of adult ticks

By scenario 2, the model showed that all stages of *R. appendiculatus* are abundant year round. This supports the hypothesis that transmission of *T. parva* to cattle can occur throughout the year in eastern Africa. In support of our modeling Bazarusanga *et al.* (2007) observed similar situations in Rwanda. Similar situations were also observed by McCulloch *et al.* (1968) in Tanzania, Branagan (1973) and Kaiser *et al.* (1988) around Lake Victoria. The year round activities of all stages of *R. appendiculatus* near the equator have also been shown previously (Randolph and Rogers, 1997). This is in good consent with the previous observations that support the absence of diapause near equator and in eastern Africa (Branagan, 1973).

In both scenarios the situation showed that recovered carrier cattle play an important role in the transmission and the epidemiology of *T. parva*. Our results support the work of previous investigators. For instance, transmission can occur for both carrier and clinically infected cattle in eastern Africa where adult ticks and immature stages are active throughout the year (Norval *et al.*, 1991). Similarly,

Medley *et al.* (1993) showed the degree at which carrier cattle transmit *T. parva* to ticks and then susceptible cattle in eastern Africa. Latif *et al.* (2001 a&b) have also shown that carrier cattle often play important role in the transmission of *T. parva*.

Conclusion

In conclusion, our simulation explained the differences in the seasonality of *R. appendiculatus* activity and transmission of *T. parva* between tropical eastern and central Africa and sub-tropical southern Africa. It showed that nymphs are the stages of *R. appendiculatus* that vector *T. parva* in southern Africa while both nymphs and adults transmit in eastern and central Africa. Other laboratory studies need to be done to reevaluate the ability of nymphs and carrier cattle in the transmission of ECF in addition the next step will be to include other important parameters such management system and control measure in our model so that we can use it evaluate their effect on the ECF transmission dynamics.

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