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Interim Report **IR-13-053**

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June 2015

Epidemic dynamics of a vector-borne disease on a villages-and-city star network with commuters

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Keywords: Epidemiology; Vector-borne disease; Frequency-dependent transmission; Star network; Basic reproductive number.

Abstract

We develop a star-network of connections between a central city and peripheral villages and analyze the epidemic dynamics of a vector-borne disease as influenced by daily commuters. We obtain an analytical solution for the global basic reproductive number R_0 and investigate its dependence on key parameters for disease control. We find that in a star-network topology the central hub is not always the best place to focus disease intervention strategies. Disease control decision is sensitive to the number of commuters from villages to the city as well as the relative densities of mosquitoes between villages and city. With more commuters it becomes important to focus on the surrounding villages. Commuting to the city paradoxically reduces the disease burden even when the bulk of infections are in the city because of the resulting diluting effects of transmissions with more commuters. This effect decreases with heterogeneity in host and vector population sizes in the villages due to the formation of peripheral epicenters of infection. We suggest that to ensure effective control of vector-borne diseases in star networks of village and cities it is also important to focus on the commuters and where they come from.

1. Introduction

The role of host mobility in the epidemic dynamics of vector-borne diseases was not taken into consideration during the malaria eradication programs of the 1950s and 1960s. This was cited as one of the reasons for failure of that program (Bruce-Chwatt, 1968; Prothero, 1977). Since then there has been a substantial increase in the human population size, revolutions in transportation technologies and a sharp rise in urbanization. Poor levels of hygiene in most tropical cities has led to a rise in incidence of vector-borne diseases such as malaria and dengue (Knudsen and Slooff, 1992; Robert et al., 2003; Sharma, 1996).

Concentration of most economic and social activities in cities has led to formation of mobility patterns of hosts between these central hubs and the surrounding villages. When hosts move between the central city and peripheral villages they form a network structure of contact between themselves and the vector populations of the two spatial places. Since malarial vectors have short maximum flight distances, such as about 691 metres per life time for *Anopheles funestus* and *Anopheles gambiae* (Midega

et al., 2007), it is effectively the host movements and their contact with stationary vectors that determine epidemic dynamics between two spatially separate localities.

Commuters move back and forth between two subpopulations forming a connecting link that couples the epidemic dynamics of those subpopulations (Barrat et al., 2008; Colizza and Vespignani, 2008). This coupling forms a system of populations with semi-independent local dynamics, called meta-populations (Adams and Kapan, 2009). An infection event at one spatial point could trigger a full-blown outbreak at another spatial point in this meta-population structure making the study of the role of connectivity important for disease control (Hanski and Gaggiotti, 2004; Hanski et al., 1997; Keeling et al., 2004).

Theoretical studies on vector-borne disease dynamics in interconnected populations have produced several useful results. For example, in meta-populations mobility leads to disease occurrence among connected patches and speeds up the time for disease to reach equilibrium in the system (Cosner et al., 2009; Hsieh et al., 2007; Torres-Sorando and Rodri'guez, 1997). Besides, for heterogeneous vector densities among patches the disease burden is determined by the patch with the largest vector

63 subpopulation and decreased with greater degree of mixing of host hosts (Adams and
64 Kapan, 2009). While most studies do not elicit a specific network structure, we believe
65 that geographical relationships between villages and cities are approximately structured,
66 such as a star-like formation in most tropical cities (Briggs and Mwamfupe, 2000) and
67 that host commute patterns are not random (Gonzalez et al., 2008). We construct a
68 simple star-network in which daily commuters connect an arbitrary number of villages
69 to a central city, and incorporate a vector-borne disease transmission epidemic model to
70 understand the influence of meta-population parameters on the epidemic dynamics. .
71 The most important parameter in epidemiology is the basic reproductive
72 number, defined as the total number of infections resulting from a single infectious
73 agent after its introduction into a totally susceptible population throughout the agent's
74 infectious period (Anderson and May, 1992; Arino and Van Den Driessche, 2003;
75 Diekmann et al., 1990; Dietz, 1993; Shao, 1999). Because of the importance of the basic
76 reproductive number in understanding infectious diseases epidemiology and guiding
77 their public health interventions (Ferguson et al., 2006; Ferguson et al., 2003; Ferguson

et al., 2005), we derive this quantity explicitly and investigate how it can inform disease control decisions and about behavior of the epidemic.

2. Model

2.1. Epidemiological dynamics in homogeneous star network

Network structure of host population assumed here is a star with daily commuters between the central node (city) and each of m peripheral nodes (or villages) (Figure 1).

For mathematical simplicity we assume that all peripheral populations have identical numbers of residents, mosquitoes and commuters to the city. This assumption is relaxed later. We also assume that infection dynamics of all peripheral populations are synchronized. The rate of movement of hosts is not affected by their disease statuses.

We adopt frequency-dependent transmission in a susceptible-infectious-susceptible (SIS) epidemic model for hosts (Anderson and May, 1992; Macdonald, 1956; Ross, 1911) and a susceptible-infectious (SI) epidemic model for mosquito vectors because once infected they do not recover from infection. There is no vertical

94 transmission within the mosquito population; that is, newborns do not acquire infection
95 from their parents. Susceptible mosquitoes are supplied by newborns. In this
96 construction an infection of a susceptible host occurs through a bite by an infected
97 mosquito, and an infection of a susceptible mosquito occurs through its bite of an
98 infected host. There is no direct transmission between hosts or between mosquitoes.
99 The variables describing epidemic dynamics of the SIS model among hosts and
100 the SI model among mosquitoes are as follows (see also Table 1). The number of
101 susceptible and infected mosquitoes is denoted respectively by x_u and y_u *in the central*
102 *city* (or urban area, and hence the subscript *u*), and by x_r and y_r *in a peripheral village*
103 (or rural area, and hence the subscript *r*). On the other hand, the number of susceptible
104 and infected hosts is denoted respectively by X_u and Y_u *in the central city*; by X_c and
105 Y_c in those hosts commuting (and hence the subscript *c*) from a peripheral village to the
106 central city every day and staying in the city only during daytime; and by X_r and Y_r for
107 resident hosts who stay in a *peripheral village* for the whole day.
108 During daytime in the city, there are $X_u + mX_c$ susceptible hosts and $Y_u + mY_c$
109 infected hosts (where m stands for the number of peripheral villages as noted before),

and x_u susceptible mosquitoes and y_u infected mosquitoes. During nighttime, $m(X_c + Y_c)$ people go back to their own villages, leaving only $X_u + Y_u$ in the city.

In a frequency-dependent transmission we assume that mosquitoes bite hosts at a constant rate. Transmission is therefore sensitive to the number of hosts available to receive the bites. Infection dynamics are separated into daytime and nighttime dynamics. The people who commute to the city can be infected when being bitten by an infected mosquito in the city during daytime and when being bitten by an infected mosquito in the village during nighttime. Writing only dynamics for infected components (see Electronic Supplementary Material (ESM) for full ODEs) we have the following expressions for dynamics at any arbitrary point in daytime (time is measured in units of days) $k \le t < k + 0.5$ $(k = 0,1,2...)$:

$$\frac{dY_u}{dt} = \frac{b_d \tau X_u}{N_u + mN_c} y_u - \gamma Y_u, \tag{1}$$

$$\frac{dy_u}{dt} = \frac{b_d \tau' (Y_u + mY_c)}{N_u + mN_c} x_u - D y_u, \tag{2}$$

$$\frac{dY_c}{dt} = \frac{b_d \tau X_c}{N_u + mN_c} y_u - \gamma Y_c, \tag{3}$$

$$\frac{dy_r}{dt} = \frac{b_d \tau' Y_r}{N_r} x_r - D y_r, \tag{4}$$

$$\frac{dY_r}{dt} = \frac{b_d \tau X_r}{N_r} y_r - \gamma Y_r, \quad (5)$$

where b_d is the rate at which a mosquito bites a host in daytime, τ is the per bite probability that the disease is transmitted from an infected mosquito to a susceptible host and τ' is the per bite probability that the disease is transmitted from an infected host to a susceptible mosquito. γ is the rate at which an infected host recovers (and becomes susceptible again) and D is the mortality rate of adult mosquitoes. Also, N_u, N_c and N_r are the respective numbers of host residents in the city, commuters from a village and daytime village residents. M_u and M_r are the respective numbers of mosquitoes in the city and in a single village. Therefore $X_u(t) = N_u - Y_u(t)$, $X_c(t) = N_c - Y_c(t)$, $X_r(t) = N_r - Y_r(t)$, $x_u(t) = M_u - y_u(t)$ and $x_r(t) = M_r - y_r(t)$ are the numbers of susceptible hosts and mosquitoes in each compartment. The rate at which a particular host is bitten by a particular mosquito during the day in the city is $b_d/(N_u + mN_c)$ and is b_d/N_r in one village.

Nighttime epidemiological dynamics are derived similarly for any time point $k + 0.5 \le t < k + 1$ $(k = 0,1,2,....)$ as

$$\frac{dY_u}{dt} = \frac{b_n \tau X_u}{N_u} y_u - \gamma Y_u \quad (6)$$

141 $$\frac{dy_u}{dt} = \frac{b_n \tau' Y_u}{N_u} x_u - D y_u \quad (7)$$

142 $$\frac{dY_c}{dt} = \frac{b_n \tau X_c}{N_r + N_c} y_r - \gamma Y_c \quad (8)$$

143 $$\frac{dy_r}{dt} = \frac{b_n \tau' (Y_r + Y_c)}{N_r + N_c} x_r - D y_r \quad (9)$$

144 $$\frac{dY_r}{dt} = \frac{b_n \tau X_r}{N_r + N_c} y_r - \gamma Y_r \quad (10)$$

145 where b_n is the mosquito biting rate at night.

146 In the following sections we derive analytical solution for the global basic

147 reproductive number R_0 of the star network and investigate its sensitivity to key

148 population and networks parameters relevant to disease control.

149

150 # 3. Results

151 ## 3.1. Basic reproductive number R_0 for the meta-population

152 Linearization of epidemic dynamics (1)-(10) by assuming that infected densities

153 are small near the disease-free equilibrium results into a system;

154 $$\frac{d\mathbf{y}}{dt} = \begin{cases} A_d \mathbf{y}(t), & \text{for } t \text{ at daytime } (k \le t < k + 0.5; \quad k = 0,1,2,\cdots), \\ A_n \mathbf{y}(t), & \text{for } t \text{ at nighttime } (k + 0.5 \le t < k + 1; \quad k = 0,1,2,\cdots), \end{cases} \quad (13)$$

where $\mathbf{y} = (Y_u, y_u, Y_c, y_r, Y_r)^T$ with T denoting vector transform, and

$$A_d = \begin{pmatrix} -\gamma & \beta_1 \tau N_u & 0 & 0 & 0 \\ \beta_1 \tau' M_u & -D & \beta_1 \tau' M_u m & 0 & 0 \\ 0 & \beta_1 \tau N_c & -\gamma & 0 & 0 \\ 0 & 0 & 0 & -D & \beta_2 \tau' M_r \\ 0 & 0 & 0 & \beta_2 \tau N_r & -\gamma \end{pmatrix}, \tag{14a}$$

$$A_n = \begin{pmatrix} -\gamma & \beta_3 \tau N_u & 0 & 0 & 0 \\ \beta_3 \tau' M_u & -D & 0 & 0 & 0 \\ 0 & 0 & -\gamma & \beta_4 \tau N_c & 0 \\ 0 & 0 & \beta_4 \tau' N_r & -D & \beta_4 \tau' M_r \\ 0 & 0 & 0 & \beta_4 \tau N_r & -\gamma \end{pmatrix}, \tag{14b}$$

where

$$\beta_1 = \frac{b_d}{N_u + mN_c},\ \beta_2 = \frac{b_d}{N_r},\ \beta_3 = \frac{b_n}{N_u},\ \text{and}\ \beta_4 = \frac{b_n}{N_r + N_c}\ . \tag{15}$$

The solution to equation (13) for $t = k$ is given by $\boldsymbol{y}(k) = \boldsymbol{y}(0) e^{\frac{k}{2}(A_d + A_n)} = \boldsymbol{y}(0)^{k\bar{A}}$, where

$$\bar{A} = \frac{A_d + A_n}{2}. \tag{16}$$

In the ESM an equation for non-integer time point ($t \neq k$) is shown, which is a bit more complicated but it does not affect the subsequent calculations of the basic reproductive number by assuming that infection starts at $t = 0$, as in the next generation matrix method we count the cumulative number of secondary infections toward $t \to \infty$.

166 Equation (16) is the averaged matrix for daytime dynamics and nighttime

167 dynamics, which is possible because of linearization around the disease-free

168 equilibrium. In the ESM the basic reproductive number is calculated using the method

169 of next-generation matrix (Diekmann et al., 1990; Diekmann et al., 2010; Diekmann et

170 al., 2012; Heesterbeek, 2000; Heesterbeek, 2002), which after rearrangement gives the

171 expression for the basic reproductive number R_0 for the whole system as

172
$$R_0 = \sqrt{\frac{\rho_1+\rho_2+\rho_3+\rho_4}{2} + \sqrt{\frac{\left(\rho_1+\rho_2+\rho_3+\rho_4\right)^2}{4} - \left(\rho_1\rho_3+\rho_1\rho_4+\rho_2\rho_4\right)}}, \quad (17)$$

173 where

174
$$\begin{aligned}
\rho_1 &= \frac{1}{D\gamma}\left(\frac{\beta_1+\beta_3}{2}\right)^2 \tau\tau' N_u M_u = \frac{\tau\tau' N_u M_u}{4D\gamma}\left(\frac{b_d}{N_u+mN_c} + \frac{b_n}{N_u}\right)^2, \\
\rho_2 &= \frac{1}{D\gamma}\left(\frac{\beta_1}{2}\right)^2 \tau\tau' mN_c M_u = \frac{\tau\tau' mN_c M_u}{4D\gamma}\left(\frac{b_d}{N_u+mN_c}\right)^2, \\
\rho_3 &= \frac{1}{D\gamma}\left(\frac{\beta_4}{2}\right)^2 \tau\tau' N_c M_r = \frac{\tau\tau' N_c M_r}{4D\gamma}\left(\frac{b_n}{N_r+N_c}\right)^2, \\
\rho_4 &= \frac{1}{D\gamma}\left(\frac{\beta_3+\beta_4}{2}\right)^2 \tau\tau' N_r M_r = \frac{\tau\tau' N_r M_r}{4D\gamma}\left(\frac{b_d}{N_r} + \frac{b_n}{N_r+N_c}\right)^2,
\end{aligned} \quad (18)$$

175 are the basic reproductive numbers of infection cycles for: city residents and city

176 mosquitoes (ρ_1), daytime commuters and city mosquitoes (ρ_2), returning nighttime

177 commuters and village mosquitoes (ρ_3), and non-commuting village residents and

178 village mosquitoes (ρ_4) (see Figure 2). See ESM for the derivation of (17)-(18). More

179 important applications of the explicit formula (17) for whole system basic reproductive

180 number is seen in sensitivity analyses discussed in the next sections.

181

182 **3.2. Sensitivity analysis of parameters to system basic reproductive number**

183 ***Where should mosquito control be focused between the city and surrounding***

184 ***villages?***

185 In this section we show how the analytical results for the basic reproductive

186 number obtained in the last section (equation 17) can be used to design the control

187 strategy. This is based on the derivation of the dependence of the global basic

188 reproductive number R_0 on a given epidemiological or network parameters shown in

189 details in the ESM. Here we choose the number of mosquitoes in a village and the city,

190 M_r and M_u respectively as the target parameters for control of the vector-borne

191 disease. We consider the relative impact on R_0 of proportional changes in the mosquito

192 populations of city or villages. Since R_0 also estimates the effort required to control a

193 disease (Smith et al., 2007), we are hereby answering the question of where to focus

194 control effort for a certain predetermined fractional reduction in R_0 given a distribution

195 of mosquitoes between the city and villages.(see ESM for full derivation). We obtain

196 conditions when intervening in city will lead to more prevention of disease as

197 $$\frac{\partial R_0}{\partial(\log M_u)} > \frac{\partial R_0}{\partial(\log M_r)} \Leftrightarrow \frac{\rho_1+\rho_2}{\rho_3+\rho_4} > 1. \qquad (20)$$

198 From equation (20) we see that focusing control efforts in the city is more effective

199 when $\rho_1+\rho_2 > \rho_3+\rho_4$. But if it becomes such that $\rho_3+\rho_4 > \rho_1+\rho_2$ then focusing

200 control efforts in villages becomes more effective. Substituting equation (18) into

201 equation (20) results into an expression for a critical value, denoted hereby by θ_c which

202 is related to the ratio of mosquito densities in the city and villages as

203 $$\frac{\partial R_0}{\partial(\log M_u)} > \frac{\partial R_0}{\partial(\log M_r)} \text{ if and only if } \frac{M_u}{M_r} > \theta_c, \qquad (21)$$

204 where

205 $$\left(\frac{M_u}{M_r}\right)_c = \theta_c = \frac{N_c\left(\frac{b_n}{N_r+N_c}\right)^2 + N_r\left(\frac{b_d}{N_r}+\frac{b_n}{N_r+N_c}\right)^2}{N_u\left(\frac{b_d}{N_u+mN_c}+\frac{b_n}{N_u}\right)^2 + mN_c\left(\frac{b_d}{N_u+mN_c}\right)^2}. \qquad (22)$$

206 or, by defining the proportions of city residents, $p_u = N_u / N$, commuters,

207 $p_c = mN_c / N$, village residents, $p_r = mN_r / N$, of humans,

208
$$\left(\frac{M_u}{M_r}\right)_c = \theta_c = \frac{m\left(p_c\left(\frac{b_n}{p_r + p_c}\right)^2 + p_r\left(\frac{b_d}{p_r} + \frac{b_n}{p_r + p_c}\right)^2\right)}{p_u\left(\frac{b_d}{p_u + p_c} + \frac{b_n}{p_u}\right)^2 + p_c\left(\frac{b_d}{p_u + p_c}\right)^2}. \qquad (22)'$$

209 To see how the strength of connections between city and village through

210 commuting affects the optimum mosquito control in city and villages, we here fix the

211 proportion of city host population, p_u, and the number of villages, m in (22)', and

212 allow the proportion of commuters, p_c (and hence village hosts, $p_r = 1 - p_u - p_c$), to

213 vary so we can observe how θ_c varies with the proportion of commuters, p_c. Since θ_c is

214 a threshold value, it divides the region into two, each with different implications to the

215 focus of disease control as shown in Figure 3. In the region under the curve which

216 corresponds to $(M_u / M_r) < \theta_c$, focusing on the city is not effective in this case and

217 therefore control efforts should be targeted to the surrounding villages. The region

218 above the curve corresponds to $(M_u / M_r) > \theta_c$ when focusing on the central city is more

219 effective than focusing on the surrounding villages. From Figure 3 we observe that an

220 increase in commuters to the central city makes infections more likely to occur in the

surrounding villages making focus of mosquito control there more effective. This is because in frequency-dependent transmission the efficiency of transmission depends on the possibility of one person being bitten by a mosquito in succession; one to receive an infection and second to pass it on (Keeling and Rohani, 2011). When more commuters move to the city, they leave a smaller number of people in the villages making vector-borne disease transmissions more efficient than in the city. Since people in the city do not move, any increase in the number of hosts because of the incoming commuters serves to make the possibility of a mosquito biting a host in two successions less likely, lowering the infection risk.

3.3. Epidemic occurrence with intensity of village-to-city connections

3.3(a) Homogeneous case

The host and vector meta-population structure we assume in this paper is quite simple: a star network with the central city and m surrounding villages (Figure 1). However, we can ask several important questions about the effects of host population structure within this framework.

For subsequent analyses, we assume that the total nighttime populations of city residents, N_u, and the total nighttime villages residents, $m(N_c + N_r)$, are constant. Consequently, the total host population, denoted by $N = N_u + m(N_c + N_r)$, is also kept constant. The total mosquito population $M = M_u + mM_r$ is also kept constant. We assume, for simplicity, that the biting rates during day and night are the same: $(\text{i.e.}, b_d = b_n = b)$. The more general case of heterogeneous bite rates was also analyzed (see section 4 in ESM) and has similar results to the homogeneous case reported in this section. We introduce the fractions of city residents, p_u, commuters, p_c, and village residents, p_r in the whole host population as $p_u = N_u/N$, $p_c = mN_c/N$, $p_r = mN_r/N$ and those of city and village mosquitoes as $q_u = M_u/M$ and $q_r = mM_r/M$ respectively. For example, we can change the fraction of commuters by increasing the number N_c of daytime commuters while keeping the nighttime total population $m(N_c + N_r)$ constant, and ask how this changes the global basic reproductive number R_0.

We here examine whether or not increasing connectivity would increase R_0 when metapopulation is nearly isolated. This could be answered by looking at the partial derivative of R_0 with respect to p_c, $(\partial R_0 / \partial p_c)$, as $p_c \to 0$ while keeping

253 $p_c + p_r = 1 - p_u$ constant. We find a paradoxical case where increasing connectivity

254 (i.e., number of commuters) in the network decreases the basic reproductive number,

255 lowering the possibility of disease occurrence (see full derivation in the ESM). This

256 happens if the following condition is true,

257 $$\frac{q_u}{p_u} > \frac{q_r}{1 - p_u}, \tag{23}$$

258 or simply if $q_u > p_u$ (as $q_r = 1 - q_u$).

259 Equation (23) shows that a paradoxical region in which there is decreasing

260 possibility of disease occurrence with increasing connectivity exists when the ratio of

261 mosquitoes to hosts in the city exceeds the ratio of mosquitoes to hosts in the villages.

262 This condition is shown graphically for homogeneous assumptions in Figure 4 (dark

263 lines) which is for basic reproductive number R_0 dependency on the whole range of

264 proportion of commuters p_c, and not just for $p_c \to 0$. The paradoxical region is

265 observed in panels *b*-*d* (dark line). The reverse is true when the mosquitoes to hosts

266 ratio is higher in villages than in the city, that is $q_u / p_u < q_r / (1 - p_u)$. This condition

267 holds in panel *a* of Figure 4. In frequency-dependent transmissions where the mosquito

268 bite rate is assumed constant, the number of mosquitoes relative to that of hosts in a

given area is critical in determining whether infection will occur at all. In fact if there are more hosts than mosquitoes, as is the case in some temperate regions, the chances of an epidemic occurring are very slim indeed (Keeling and Rohani, 2011). However, whenever the mosquitoes to hosts ratio becomes larger than a critical level then an epidemic is will occur. The paradoxical region of decreasing basic reproductive number with increasing number of commuters to the city occurs because movement of hosts acts to reduce the efficiency of infection in the city by increasing the number of hosts relative to mosquitoes while at the same time the increased efficiency of transmissions in the villages not enough to compensate the decrease in the city. In the homogeneous case this paradoxical region becomes more pronounced with increasing mosquito density in the city (Figure 4d) because then more commuters are needed before the epidemic can start increasing again. The sharp rise in basic reproductive number at very high proportions of commuters is a direct artifact of frequency-dependency assumptions. That is when there are extremely small numbers of hosts left in the villages relative to the number of mosquitoes, making transmissions extremely efficient leading to the observed sharp rise in the values of the basic reproductive number.

285

286 ***3.3(b) Heterogeneous case***

287 Furthermore, we investigated the influence of heterogeneity in the number of
288 hosts and mosquitoes in the villages on the behavior of the paradoxical region. We fixed
289 the number of city hosts at 20% of the total population and assumed that all villages had
290 the same proportion of commuters to the city. Keeping total host and total vector
291 populations in villages constant, heterogeneity was introduced through random
292 assignments of host and vector population sizes among a fixed number of villages using
293 a uniform distribution in a simplex (see ESM section 5 for details). While in the
294 homogeneous case all villages had the same numbers of hosts and vector populations,
295 the randomization in the heterogeneous case produced villages with various sizes of
296 human and vector populations. Field evidence suggests a high degree of clustering in
297 mosquito populations among villages (Keating et al., 2005; Mbogo et al., 2003) and our
298 purpose here was to imitate this heterogeneity using a simple probability distribution.
299 Results are shown in Figure 4 with grey lines.

Firstly, we observe that depending on the ratio of mosquitoes to hosts, heterogeneity can increases the basic reproductive number even for lower values of the proportion of commuters as seen in Fig 4a and 4b. With more mosquitoes in the destination this increase only occurs for higher proportions of commuters as seen in Fig 4c and 4d. Random heterogeneity can result into some villages having higher numbers of mosquitoes than that of humans leading to a formation of peripheral epicenters with higher transmissions than in the homogeneous case. Also heterogeneity could result in some mosquito to host ratios becoming smaller in some villages than in the corresponding homogeneous case, but the existence of epicenters in villages with higher mosquito to host ratios outweighs in the net effect. This result has direct implications for surveillance systems, it is important to try to understand the demographic characteristics of surrounding villages both in terms of their host and mosquito densities.

Secondly we observe that heterogeneity tends to narrow the paradoxical region. The paradoxical region depends on the relative densities of hosts and mosquitoes in an area. In this case we fixed the city host densities, then from the conditions for the

316 occurrence of the paradoxical region, that is when $(q_u / p_u) > (q_r / 1 - p_u)$ only the
317 second part of the inequalities is varying. Some of these variations are likely to make
318 the second part of the inequality much closer to the first part in absolute size, or even
319 reverse the inequality, narrowing the paradoxical region. Heterogeneity among host and
320 vector populations in villages increases the importance of peripheral epicenters as
321 sources of infection, narrowing the paradoxical region.
322

323 ## 4. Discussion

324 We constructed a simple star network model of connections between a central
325 city and an arbitrary number of surrounding villages. Then we incorporated a classic
326 epidemic model for vector-borne diseases in order to understand the effects of
327 connectivity as effected by daily commuters on the epidemic dynamics and disease
328 control decisions.

329 Through the method of next generation matrix we obtained an explicit
330 expression for the basic reproductive number R_0 of the system. A basic reproductive
331 number is an important quantity in epidemiology because it has implications in planning

of public health interventions against infectious diseases by aiming to maintain its value below the threshold, which is unity (Anderson and May, 1992; Ferguson et al., 2006; Ferguson et al., 2003; Ferguson et al., 2005; Scherer and McLean, 2002). The behavior of the basic reproductive number can be more complicated at the threshold value; such as disease-free state being unstable even for $R_0 < 1$ (Hadeler and Van den Driessche, 1997; Van den Driessche and Watmough, 2000; Van den Driessche and Watmough, 2002) or the threshold vanishing altogether as in complex networks (Barrat et al., 2008). However, it provides a good theoretical approximation for most practical purposes of disease control (Anderson and May, 1992).

The primary goal of this research was to investigate explicitly the role that commuters play in affecting the behavior of an epidemic and the implications to disease control in a defined network structure. Based on the basic reproductive number, two questions were asked and answered; first one was on effects of commuters on the decision of where to direct disease control efforts between the city and villages when we aim to reduce a predetermined fraction of the basic reproductive number R_0 and the second one was on the effects of commuters on the overall behavior of the epidemic.

In a meta-population it is not always obvious where to focus disease control strategies because of the unknown influence of commuters as well as relative densities of mosquitoes to hosts. Besides, the disease control decision is normally a function of many factors such as economic, humanitarian, clinical and even political factors. Different points of view can give different prescriptions for disease control. For example, from an optimal control perspective some studies suggest focusing on subpopulations with the lowest number of infected hosts (Mbah and Gilligan, 2011; Rowthorn et al., 2009). Our study prescribes from the perspective of effectiveness of infections as influenced by commuters. We find that the decision of where to focus control efforts is sensitive to the proportion of commuters and the relative mosquito densities in the city and villages but an increase in the number of commuters from the villages to the city makes focusing on the surrounding villages more effective in vector-borne diseases. This is because when more and more people commute they make infections in the villages more effective thereby increasing chances of an epidemic in the whole meta-population.

We found that commuters can influence the epidemic dynamics by lowering the basic reproductive number in certain conditions. In frequency-dependent transmissions the effective ratio of mosquitoes to hosts is key in determining the occurrence of an epidemic. When this ratio is high in the city (and therefore higher basic reproductive number) any increase in the commuters to the city lowers the basic reproductive number leading to a paradoxical region. On the other hand, when this ratio becomes higher in the surrounding villages than in the city the paradoxical regions narrows down as commuting has weaker effect in this case. Particularly, for higher mosquito to host population ratios in the city heterogeneity in host and vector populations in villages increases the basic reproductive number and narrows the paradoxical region because of formation of peripheral epicenters with highly efficient transmissions. Therefore, understanding the demographic dynamics of villages in terms of its hosts and vectors is important for planning disease control.

Our two results can be combined to inform disease control strategies. The first result emphasizes focusing control in the surrounding villages after determining key parameters which are commuters and the mosquito densities in city and villages; the

second results emphasizes on the surveillance of the surrounding villages in order to capture those epicenters of infections. It is well known that rural tropical Africa has more vector borne disease transmissions than the urban Africa because of the presence of large vector populations and ubiquity of breeding sites in the former (Walker, 2002). Recent theoretical and empirical studies have shown that movements of hosts between two spatial points such as from villages to central cities is responsible for persistence of vector-borne diseases in cities despite control strategies (Adams and Kapan, 2009; Le Menach et al., 2011; Wesolowski et al., 2012). Our study has pinpointed one possible way of how such movements affect disease control decisions and the behavior of the epidemic dynamics of vector-borne diseases.

Acknowledgements

E.A.M. thanks the Japanese government Monbukagakusho (MEXT) scholarship through the Japanese Embassy in Tanzania for financial support. We also thank the Centre for Promotion of Integrated Sciences (CPIS) of The Graduate University for Advanced Studies (SOKENDAI) for a partial support of this study.

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509

Figure Legends

Figure 1. A star-network with a central city and m peripheral villages. Mobility patterns in the homogeneous assumption is such that daily commuters (shown by C in the figure) from surrounding villages connect the infection dynamics of all populations of villages with each other as well as with the city. Mosquitoes don't move between city and village or between villages.

Figure 2. Basic reproductive numbers for various infection cycles: In homogeneous assumption that m village populations in the star network are identical in their resident and commuter host and mosquito population sizes, we derive individual basic reproductive numbers (ρ_i's) for four infection cycles in the network as shown: city hosts and city mosquitoes infection cycle (ρ_1), daytime commuters and city mosquitoes infection cycles (ρ_2), nighttime commuters and village mosquitoes infection cycle (ρ_3), and village hosts and village mosquitoes infection cycle (ρ_4).

525 **Figure 3:** Ratio of city-to-villages mosquito densities (M_u / M_r) as a function of the

526 proportion of commuters, p_c from villages. When we change p_c, the total nighttime

527 populations are kept constant; the proportion of city residents $p_u = 0.2$ remains

528 unchanged while the proportion of village residents, p_r changes with $p_c$as

529 $p_r = 1 - p_u - p_c = 0.8 - p_c$. (Parameters: $\gamma = 1/30$, $D = 1/7$, $m = 5$, $b_d = b_n = 0.15$)

530

531 **Figure 4.** Dependence of basic reproductive number R_0 on the proportion of commuters

532 p_c that move to the city everyday in homogeneous assumption *(solid black curves)* and

533 heterogeneous assumption *(gray curves)*. The proportion of mosquitoes in villages q_r

534 differs for each panel such that in 4a, ($q_r = 0.85$); in 4*b*, ($q_r = 0.50$); in 4*c*,

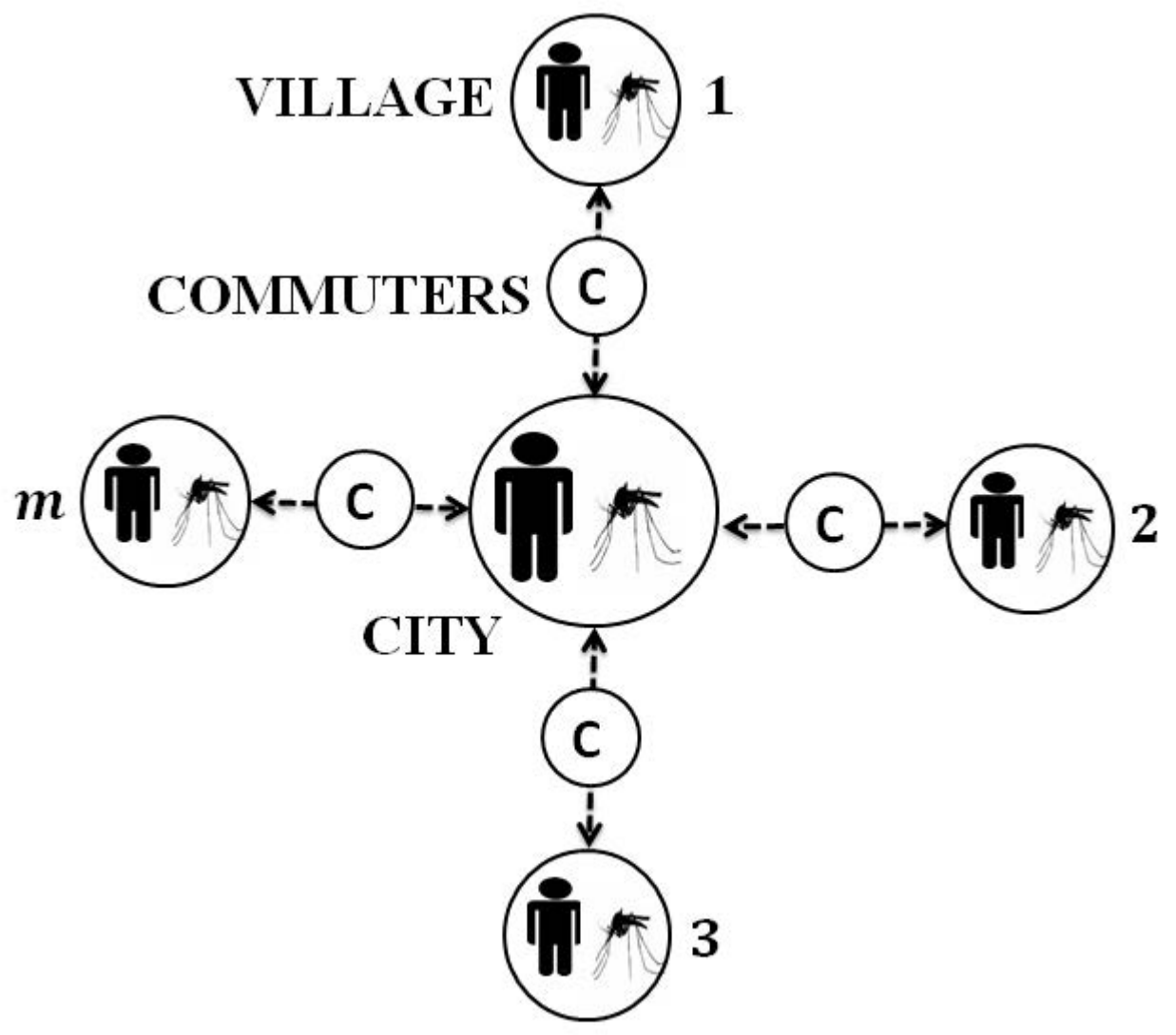
535 ($q_r = 0.40$); and in 4*d*, ($q_r = 0.20$). Corresponding city mosquito densities can be

536 obtained using the assumption that $q_r + q_u = 1$. The proportion of city residents is fixed

537 at $p_u = 0.2$ and the proportion of commuters, p_c, as well as that of village residents,

538 $p_r = 1 - p_u - p_c = 0.8 - p_c$, are changed simultaneously along the horizontal axis.

539 (Parameters are: $b_n = b_d = 0.15$, $m = 5$, $D = 1/7$, and $\gamma = 1/30$.)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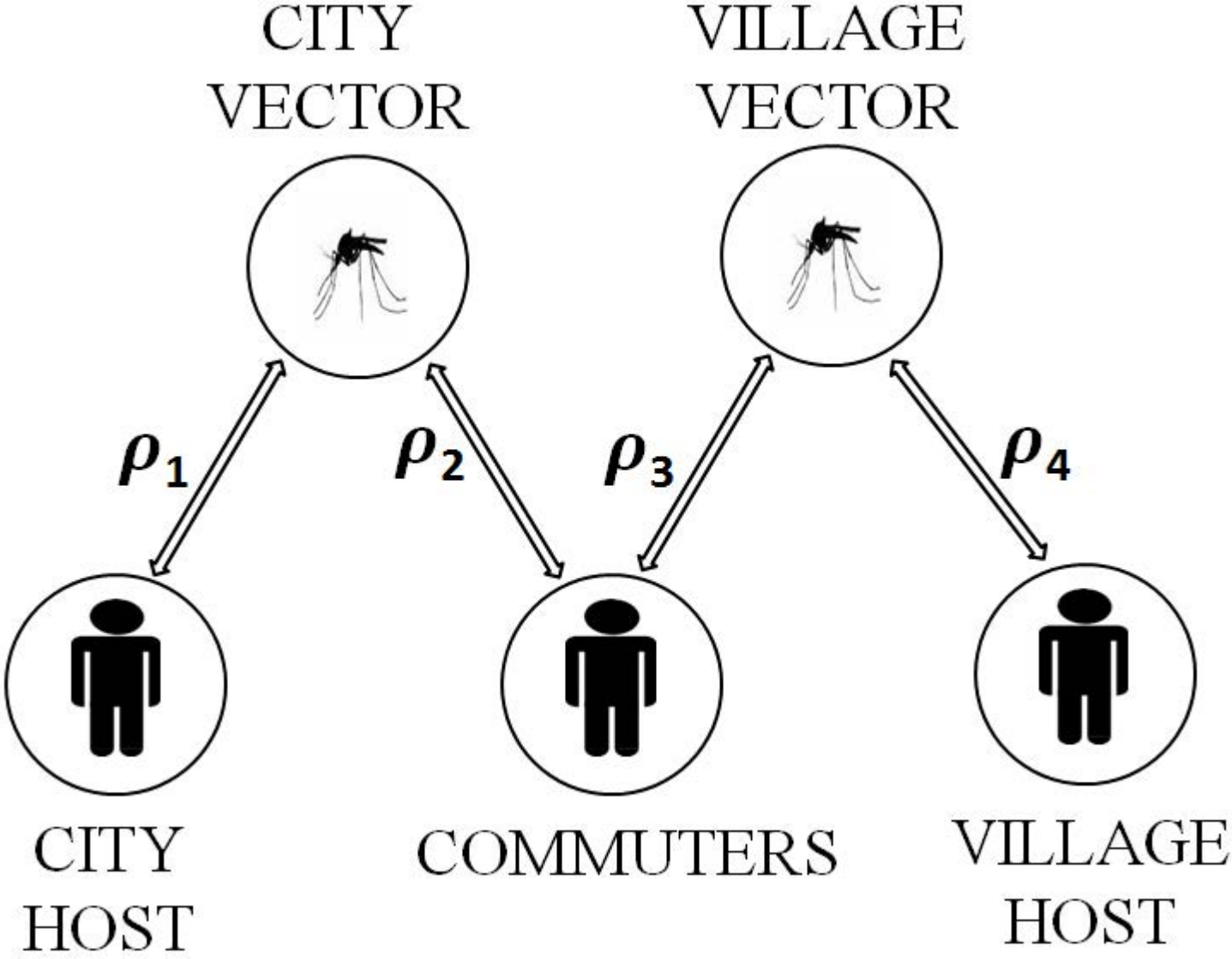
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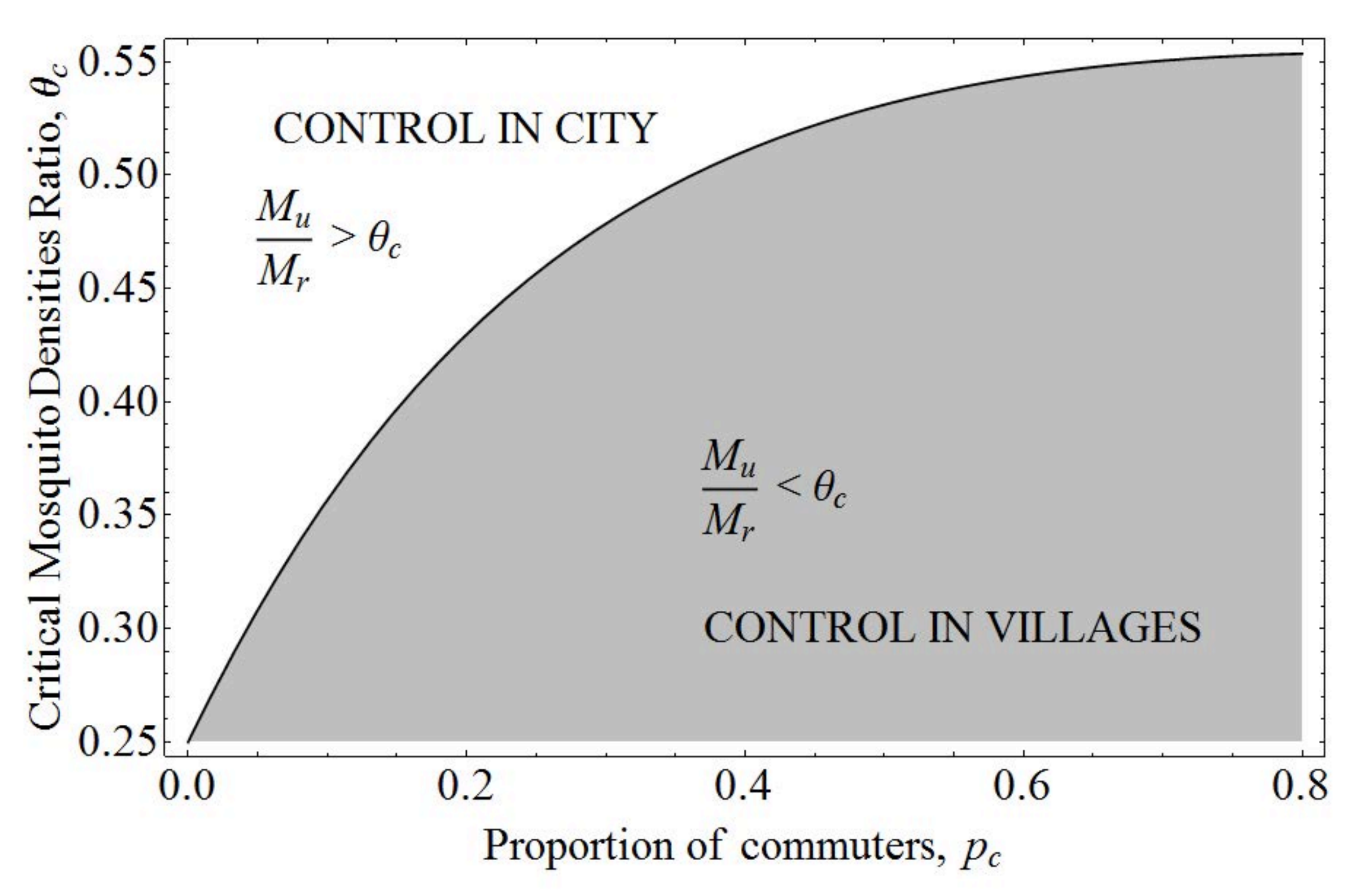
CONTROL IN CITY
$\frac{M_u}{M_r} > \theta_c$
$\frac{M_u}{M_r} < \theta_c$
CONTROL IN VILLAGES
Critical Mosquito Densities Ratio, θ_c
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.0
0.2
0.4
0.6
0.8
Proportion of commuters, p_c

a

b

c

d

R_0

230

180

130

70

50

0

0.5

0.9

Proportion of commuters, p_c