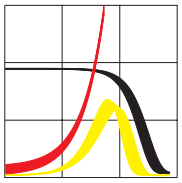

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Senescence can play an essential role in modelling and estimation of vector based epidemiological indicators: demographical approach

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ABSTRACT

In the paper we calculate basic epidemiological indicators, produced by an aging population of vectors. In calculations we follow two lines: calculations for demographically structured population and individual life-history approach. We discuss the advantages and limitations of these approaches and compare the results of our calculations with epidemiological indicators obtained for non-aging population of vectors.

INTRODUCTION

At the eve of the third millennium vector-based epidemics remain one of the most essential reasons of deaths on Earth. Various approaches with different success are applied to their investigation. Between vector-based infections, malaria is one of the well mathematically studied diseases. Mathematical modelling of malaria began in 1912 with R. Ross [1] and was continued by G. Macdonald [2]. Now hundreds of malaria models examine the circulation of parasites between human and *Anopheles* population, analyse quantitative epidemiological indicators and simulate the processes of malaria transmission [3]. Models provide concise and exact description of complicated non-linear phenomena and open a perspective for relating the process of infection in individuals to the incidence of infection in a population over time. Biology-based models are of direct use in comprehensive and sustainable intervention programs like onchocerciasias control and in developing optimal treatment regimes for various drugs [4 - 7]. Malaria is among the wide circle of diseases which are effectively analysed with mathematical models.

Classical models of malaria operate with such indicators as the basic reproductive number R_0, vectorial capacity C and entomological inoculation rate. The basic reproductive number R_0 is generally defined as the expected number of hosts who would be infected after one generation of the parasite by a single infectious person who had been introduced into the otherwise naïve population [8]. Vectorial capacity C stands for the number of infectious bites on humans that arise from all the mosquitoes that are infected by a single person on a single day [9]. EIR is defined as the expected number of infectious bites received by a host per day [10].

In all the models the assumption that mosquitoes do not senesce has been used to assess their role in pathogen transmission. Only in 2007 Styer et al. [11] show that mosquitoes *Ae. aegipti*, the vector transmitting malaria and dengue pathogens, senesce both in laboratory populations and in wild. It was shown that logistic or logistic-Makeham models provide the best fit of

mortality data in the mosquitoes. Departure from the paradigm of constant mortality allows viewing of vector-based epidemic as complex dynamic systems that must be studied more intensively and exactly than static age-independent one. Thus existing methods to study mosquito populations are no longer adequate [11].

The increase of mortality in a vector organism with age can influence important characteristics, concerned with the statics and dynamics of malaria epidemic. Proper adjustment of these characteristics to the aging vector population gives more reliable estimates for the rate of infection spread in human population. It indicates the most effective ways to control the vector-based epidemic. In the paper we compare basic epidemiological indicators, produced by an aging population of vectors with those without aging.

Presented consideration is valid not only in case of epidemic of malaria but also in other cases of vector-borne epidemics, for example, dengue fever.

RESULTS

1. Vectorial capacity in stable population

Following Styer et al. [11] consider the mean number of potentially infective bites, which a mosquito will produce till the rest of its life under the condition that the first biting an infectious host was made at age x

$$C_x = ma^2 S(x+n \mid x) e_{x+n},$$

where m is the vectors/hosts proportion, a is the number of bites per day, n is the duration of extrinsic incubation period, $S(x+n|x)$ is the probability to survive till age $x+n$ under the condition of surviving till the age x, e_{x+n} is remaining life expectancy at age $x+n$. The vectorial capacity of a population with a given fraction Ω_x of mosquitoes which made the first biting an infectious host at age x is given by the equation

$$C = \sum_{x=\sigma}^{\omega} C_x \Omega_x$$

with σ and ω denoting the minimal age of biting and the maximal life span respectively.

The role of age structure in vectorial capacity can be investigated by demographic methods. In mathematical demography the notion of stable population stands for a population in which the fertility, mortality and age structure do not depend on time and is widely used [12]. Distribution by age in such population is given by the formula

$$q(x) = \frac{S(x)e^{-rx}}{\int_0^{\infty} S(t)e^{-rt}dt}$$

where *r* is the intrinsic growth rate, which is defined by fertility function $f(x)$ and survival function $S(x)$ as solution of the Lotka equation

$$\int_0^\infty e^{-rx} S(x) f(x) dx = 1 .$$

Relationship between vectorial capacity and age structure is easy to obtain in the artificial situation when the first biting an infectious host is made at the same moment by all mosquitoes. In this case the distribution of age of the first biting an infectious host equals exactly to the age distribution in population. The vectorial capacity of stable population in this case equals

$$C = \int_\sigma^\infty C_x q(x) dx$$

$$= \frac{ma^2}{\int_0^\infty S(t) e^{-rt} dt} \int_\sigma^\infty S(x) S(x+n \mid x) e^{-rx} \int_{x+n}^\infty S(t \mid x+n) dt dx$$

$$= \frac{ma^2}{\int_0^\infty S(t) e^{-rt} dt} \int_\sigma^\infty e^{-rx} \int_{x+n}^\infty S(t) dt dx$$

In the case of non-aging population one obtains

$$C = \frac{ma^2}{g} \frac{\int_\sigma^\infty e^{-rx} e^{-g(x+n)} dx}{\int_0^\infty e^{-(r+g)x} dx} = \frac{ma^2}{g} e^{-gn-(r+g)\sigma} . \qquad (1)$$

In this case vectorial capacity decreases with increase of the intrinsic growth rate *r*. This is reasonable because the larger the *r* value in a stable population, the more young ages prevail the old ages.

Figure 1 presents the graphics of vectorial capacity in two aging populations as function of *r*. The same figure gives the vectorial capacity in a non-aging population. It is seen that both curves *C*(*r*) for aging population has maxima, which were not observed previously. Its presence can be explained by the fact that in aging population ($r<0$) the proportion of infected mosquitoes diminishes whereas in a juvenescent one ($r>0$) the greater part of mosquitoes are younger 3 days, when they still do not bite a host. We will discuss this issue later on (see Fig. 2 below).

It is noteworthy to stress that Styer et al. have drawn exhaustive experimental data to analyze the aging process in the mosquitoes which allowed them finding of the specific experimental value of $r=0.152$. Nonetheless the estimates by Spyer et al. proved to be twice as high as ours.

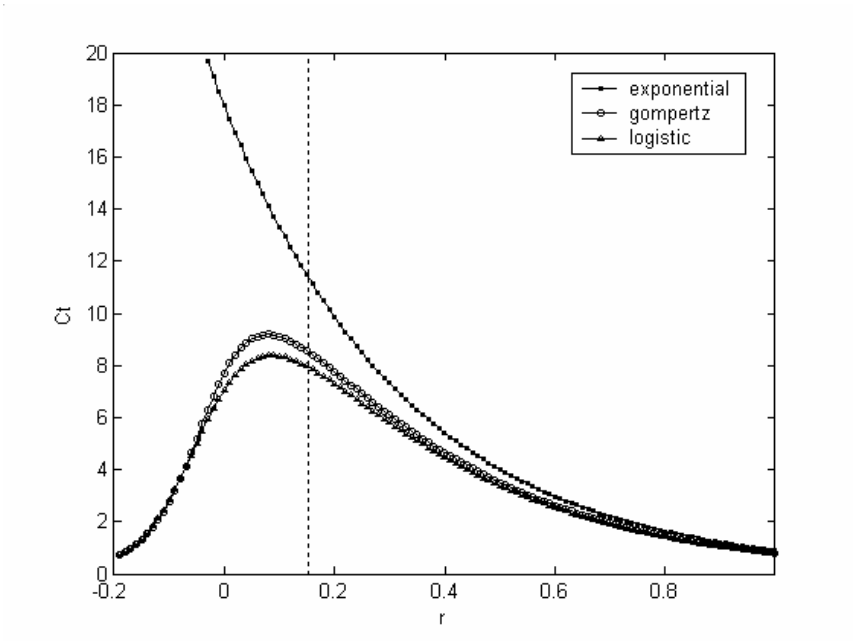

Figure 1. Vectorial capacity in stable populations,
calculated for different intrinsic growth rate *r* values for three mortality models.

The models for age related mortality were used as described in Styer *et al.* [11]. The Gompertz model gives relationship between mortality and age in form

$$g(x) = ae^{bx}$$

while Logistic model uses the other form

$$g(x) = \frac{ae^{bx}}{1+\frac{as}{b}\left(e^{bx}-1\right)}.$$

It is worth mentioning that the Gompertz model leads to the Logistic model if a population of mosquitoes is heterogeneous with variance of heterogeneity equal to *s* [13]. We used for plotting the parameters values which are published by Styer *et al.* [11] and presented in table 1.

Table 1. Parameters for three mortality models as in [11]

	a	b	s
Exponential	0.0313	---	---
Gompertz	0.00662	0.06234	---
Logistic	0.00182	0.1416	1.073

The vectorial capacity values in a stable population, calculated for non-aging and aging models at some specific values of the intrinsic growth rate *r* are presented in Table 2. The followinf values of *r* are shown: *r*=0 (stationary population); *r**=0.152 as in Styer *et al.*[11], and values for *r***, which correspond to the maximum value of vectorial capacity in each model.

Table 2. Vectorial capacity values in stable population

	Stationary	R^*	r^{**}
exponential	18	11.4	19.7
gompertz	7.7	8.5	9.2
logistic	7.1	7.9	8.4

The patterns of age distribution in a stable population under different values of intrinsic growth rate *r* are given in figure 2.

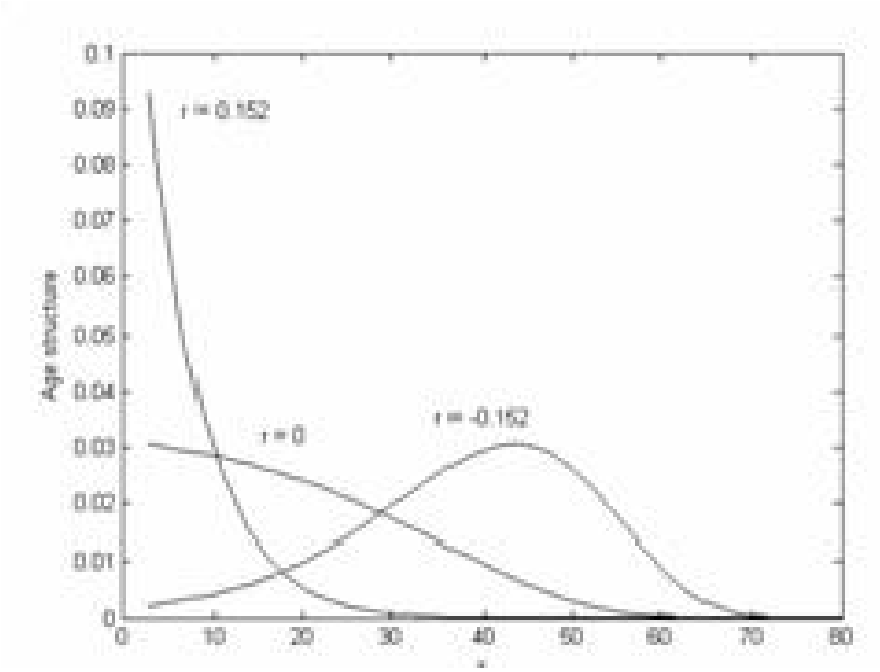

Figure 2. Age structure in a stable population for different values of intrinsic growth rate *r*.

One can see from figure 2 that in a growing stable population ($r>0$) the young ages prevail over the old ages while in a decreasing stable population ($r<0$) the old ages are presented in higher proportion. This explains non-monotonic behaviour of vectorial capacity in aging population as function of *r*, which is shown above in the figure 1. In the presence of senescence the maximal value for vectorial capacity is attained for a specific value of an intrinsic growth rate, which is defined by the choice of the mortality model. For lower *r* value vectorial capacity is not high because of a small life expectancy. For higher *r* values the population is "too young" to accumulate a high proportion of potentially infected bites.

2. Individual life-history approach

A supposition that mosquitoes in different age groups bite an infection host simultaneously, which was applied in calculation of vectorial capacity for a population, is very

artificial. Still it was studied as an interesting example. The other possible way to present vectorial capacity of a mosquito population is to consider a mosquito life history.

Let $\alpha(x)$ denote the intensity of host biting by mosquitoes of age *x*, *X* denote the prevalence of infectious hosts and *c* denote probability of the infection transmission from a host to mosquito. Let $f(x)dx$ be probability for a mosquito first time to be infected from a host at a small age interval $[x, x+dx]$. It is the product of probability to survive till age *x*, probability not being infected till this age and probability to become infected at this interval

$$\begin{aligned} f(x)dx &= \alpha(x)cXe^{-cX\int_{\sigma}^{x}\alpha(\tau)d\tau}e^{-\int_{0}^{x}g(u)du}dx \\ &= \alpha(x)cXS_{\alpha}(x)S(x)dx \end{aligned}$$

where $g(x)$ is the age-specific mosquito mortality, $S_{\alpha}(x)$ and $S(x)$ are probabilities not to be infected till age *x* and the survival function respectively. Mosquitoes, which survived an incubation period of duration *n*, continue to bite hosts with intensity $\alpha(x)$ and transmit the infection with probability *b*. The mean number of hosts infected by these mosquitoes till the rest of the mosquito life is

$$\begin{aligned} \Psi(x)dx &= f(x)S(x+n\,|\,x)\left(\int_{x+n}^{\infty} b\alpha(\tau)S(\tau\,|\,x+n)d\tau\right)dx \\ &= \alpha(x)cbXS_{\alpha}(x)\left(\int_{x+n}^{\infty}\alpha(\tau)S(\tau)d\tau\right)dx \end{aligned}.$$

Integral of the last expression by possible age of byting starting from σ gives expression for *lifetime transmission potential* – mean number of people infected by a mosquito during its life

$$\beta = \int_{\sigma}^{\infty}\Psi(x)dx = cbX\int_{\sigma}^{\infty}\alpha(x)S_{\alpha}(x)\left(\int_{x+n}^{\infty}\alpha(\tau)S(\tau)d\tau\right)dx\,. \qquad (2)$$

This formula presents lifetime transmission potential as in case of aging mosquito so in case of changing biting rate with age. More compact formulas correspond to specific cases. For constant biting rate one obtains

$$\begin{aligned} \beta &= \alpha^2 cbX\int_{\sigma}^{\infty}e^{-cX\alpha(x-\sigma)}\left(\int_{x+n}^{\infty}S(\tau)d\tau\right)dx \\ &= \alpha^2 cbX\int_{\sigma}^{\infty}e^{-cX\alpha(x-\sigma)}S(x+n)e_{x+n}dx \end{aligned}.$$

If additionally there is no aging, then

$$\beta = \alpha^2 cbX \int_{\sigma}^{\infty} e^{-cX\alpha(x-\sigma)-g(x+n)} \frac{1}{g} dx$$
$$= \frac{\alpha^2 cbX}{g(g+cX\alpha)} e^{-g(n+\sigma)}$$

For $\sigma = 0$ one obtains the formula, which is equivalent to that in [10].

3. Entomological inoculation rate and vectorial capacity of a birth cohort

Lifetime transmission potential can be used in calculation of entomological inoculation rate (EIR) defined as mean number of infectious bites received per day by a host [10]. Denote ε the constant rate of mosquito emergence per host per day. The number of mosquitoes per host equals $m = \varepsilon \times e_0$, thus one can write

$$EIR = \varepsilon\beta = \frac{m}{e_0}\beta = mcbX \int_{\sigma}^{\infty} \alpha(x) S_{\alpha}(x) \left(\frac{\int_{x+n}^{\infty} \alpha(\tau) S(\tau) d\tau}{\int_{0}^{\infty} S(\tau) d\tau} \right) dx .$$

Here we have used the equation (2). For a constant biting rate

$$EIR = mcb\alpha^2 X \int_{\sigma}^{\infty} e^{-cX\alpha(x-\sigma)} \left(\frac{\int_{x+n}^{\infty} S(\tau) d\tau}{\int_{0}^{\infty} S(\tau) d\tau} \right) dx .$$

Expression for EIR takes simple form in the absence of aging:

$$EIR = \frac{ma^2 cbX}{g + cX\alpha} e^{-g(n+\sigma)} .$$

For $\sigma = 0$ we obtain the formula, which is equivalent to that in [10].

Vectorial capacity *C* in a birth cohort is connected with *EIR* by equation

$$C = \frac{1}{bc} \frac{d}{dX} EIR\,|_{X=0} .$$

By substitution one obtains a vectorial capacity in aging population in form

$$C = m \int_{\sigma}^{\infty} \alpha(x) \left(\frac{\int_{x+n}^{\infty} \alpha(\tau) S(\tau) d\tau}{\int_{0}^{\infty} S(\tau) d\tau} \right) \frac{d}{dX} \left(X S_{\alpha}(x) \right)|_{X=0}\, dx$$
$$= m \int_{\sigma}^{\infty} \alpha(x) \left(\frac{\int_{x+n}^{\infty} \alpha(\tau) S(\tau) d\tau}{\int_{0}^{\infty} S(\tau) d\tau} \right) dx$$

For a constant biting rate

$$C = \frac{m\alpha^2}{\int_0^\infty S(\tau)d\tau} \int_\sigma^\infty \left(\int_{x+n}^\infty S(\tau)d\tau \right) dx . \qquad (3)$$

This expression is equivalent to the expression for a total vectorial capacity in stationary population, given by the formula (1) for the intrinsic growth rate r=0.

If in addition there is no senescence, then vectorial capacity equals

$$C = m\alpha^2 \int_\sigma^\infty e^{-g(x+n)}dx = \frac{m\alpha^2}{g} e^{-g(\sigma+n)} .$$

The above formulas for EIR and for vectorial capacity C were first derived in [10] for non-aging populations. Now we have expanded the area of their adequacy for ageing populations. The results of such broadening (for r=0) can be seen in Fig. 1.

4. The dynamics of malaria infection in the presence of senescence

The dynamics of malaria infection is determined by epidemic in mosquitoes and in human populations. These two populations intersect, thus the equations for dynamics of malaria infection can be used to determine the conditions for the human epidemic growth or elimination. To derive the equations consider the probability density function $f(t)$ for age t of the first byte, which made the mosquito, born in year y, to be infected

$$f_y(t)dt = c\alpha(t)X(y+t)e^{-c\int_\sigma^t \alpha(\tau)X(y+\tau)d\tau} S(t)dt ,$$

where $X(y)$ is the proportion of infected people in the population in year y. We suppose that mortality and biting rate of mosquitoes are constant in time but depend on age. The probability $p(x)$ that a mosquito of age x born in year y is infectious equals

$$p_y(x) = \int_\sigma^{x-n} f_y(t)S(t+n \mid t)S(x \mid t+n)dt$$

$$= cS(x) \int_\sigma^{x-n} \alpha(t)X(y+t)e^{-c\int_\sigma^t \alpha(\tau)X(y+\tau)d\tau} dt .$$

Denote $Y(T)$ the proportion of the infected mosquitoes and $N(T)$ the number of all mosquitoes at time T. To calculate $Y(T)$ one is to take into account all cohorts of mosquitoes living at time T. Let $\varepsilon(t)dt$ be the number of mosquitoes emerged at time interval $(t, t+dt]$. Then

$$Y(T) = \frac{1}{N(T)} \int_{\sigma+n}^{\infty} \varepsilon(T-x) p_{T-x}(x)dx$$
$$= \frac{1}{N(T)} c \int_{\sigma+n}^{\infty} \varepsilon(T-x) S(x) \int_{\sigma}^{x-n} \alpha(t) X(T-x+t) e^{-c\int_{\sigma}^{t} \alpha(\tau) X(T-x+\tau)d\tau} dtdx \quad . \tag{4}$$

Formula (4) gives a relationship between numbers of infectious people and infectious mosquitoes. A classical differential equation for proportion of infected people [10] is

$$\frac{d}{dT} X(T) = mb\alpha(T) Y(T)(1 - X(T)) - \rho X(T), \tag{5}$$

where ρ is the duration of human infection. Equations (4) and (5) completely describe dynamics of the vector borne epidemic in the presence of vector senescence. In literature investigation of malaria epidemic development is limited by the asymptotic behaviour of function (4) and the solution of equation (5) in time [14 - 18]. In the absence of aging and constant rate of biting the condition that the epidemic persists is formulated in form of inequality for the basic reproductive number

$$R_0 = \frac{m\alpha^2 bc}{\rho} \times \frac{\exp(-gn)}{g} > 1. \tag{6}$$

Below we show how this condition changes in presence of mosquitoes aging and indicate the conditions when ignoring of aging gives too pessimistic prognoses for the epidemic development. In the present consideration we restrict ourselves with a constant rate of biting $\alpha(t) = \alpha$, which corresponds to the classical approach.

5. Stationary and stable populations of mosquitoes

Consider first the case of stationary population when the new generations of mosquitoes emerge at the constant rate ε. The size of the stationary population equals $N = \varepsilon \int_0^{\infty} S(\tau)d\tau$.

Substituting this to (4) one obtains a proportion of infected mosquitoes at time T in form

$$Y(T) = \frac{\alpha c \int_{\sigma+n}^{\infty} S(x) \int_{\sigma}^{x-n} X(T-x+t) e^{-\alpha c\int_{\sigma}^{t} X(T-x+\tau)d\tau} dtdx}{\int_0^{\infty} S(\tau)d\tau}.$$

Function $Y(T)$ and solution of equation (5) $X(T)$ tend in time either to zero (if no epidemic begins), or to certain values $\widetilde{Y}$ and $\widetilde{X}$. In the last case the epidemic persists. To find out a condition of the epidemic endurance one expresses the value $\widetilde{Y}$ in form

$$\widetilde{Y} = \frac{\alpha c \int_{\sigma+n}^{\infty} S(x) \int_{\sigma}^{x-n} \widetilde{X} e^{-\alpha c \widetilde{X}(t-\sigma)} dt dx}{\int_0^{\infty} S(\tau) d\tau} = \frac{\alpha c \widetilde{X} \int_{\sigma+n}^{\infty} S(x) \int_0^{x-n-\sigma} e^{-\alpha c \widetilde{X} t} dt dx}{\int_0^{\infty} S(\tau) d\tau}.$$

On the other hand from the condition $\frac{d}{dT}\widetilde{X}(T) = 0$ it holds that

$$mb\alpha\widetilde{Y}(1-\widetilde{X}) - \rho\widetilde{X} = 0$$

and

$$\widetilde{Y} = \frac{\rho\widetilde{X}}{m\alpha b(1-\widetilde{X})}.$$

Finally one obtains the equation for the stationary value $\widetilde{X}$ in form

$$\frac{\rho\widetilde{X}}{m\alpha b(1-\widetilde{X})} = \frac{\alpha c \widetilde{X} \int_{\sigma+n}^{\infty} S(x) \int_0^{x-n-\sigma} e^{-\alpha c \widetilde{X} t} dt dx}{\int_0^{\infty} S(\tau) d\tau} = \frac{\alpha c \widetilde{X} \int_0^{\infty} S(x+n+\sigma) \int_0^{x} e^{-\alpha c \widetilde{X} t} dt dx}{\int_0^{\infty} S(\tau) d\tau}.$$

Introduce a function $f(t) = \int_t^{\infty} S(x+n+\sigma) dx$ and a value $R_0^s = \frac{m\alpha^2 bc}{\rho} \times \frac{\int_0^{\infty} f(t) dt}{\int_0^{\infty} S(x) dx}$. Rewrite the equation in form

$$\frac{\rho\widetilde{X}}{m\alpha b(1-\widetilde{X})} = \frac{\alpha c \widetilde{X} \int_0^{\infty} e^{-\alpha c \widetilde{X} t} \int_t^{\infty} S(x+n+\sigma) dx dt}{\int_0^{\infty} S(\tau) d\tau} = \frac{\alpha c \widetilde{X} \int_0^{\infty} e^{-\alpha c \widetilde{X} t} f(t) dt}{\int_0^{\infty} S(\tau) d\tau},$$

from which it follows that

$$\frac{\widetilde{X}}{R_0^s} = \widetilde{X}(1-\widetilde{X}) \frac{\int_0^{\infty} e^{-\alpha c \widetilde{X} t} f(t) dt}{\int_0^{\infty} f(\tau) d\tau}. \qquad (7)$$

Equation (7) has a root $\widetilde{X} = 0$ and optionally the second one, satisfying the condition $0 < \widetilde{X} < 1$. To find out the condition of existing nonzero root, note that for any $0 < \widetilde{X} < 1$

$$0 < \left(1 - \widetilde{X}\right) \frac{\int_0^\infty e^{-\alpha c \widetilde{X} t} f(t) dt}{\int_0^\infty f(\tau) d\tau} < 1.$$

Then the equation

$$\frac{1}{R_0^s} = \left(1 - \widetilde{X}\right) \frac{\int_0^\infty e^{-\alpha c \widetilde{X} t} f(t) dt}{\int_0^\infty f(\tau) d\tau}$$

has a solution if and only if

$$R_0^s = \frac{m\alpha^2 bc}{\rho} \times \frac{\int_0^\infty f(t) dt}{\int_0^\infty S(x) dx} > 1. \qquad (8)$$

Value R_0^s can be presented using vectorial capacity in a stationary population (3) as $R_0^s = \frac{bc}{\rho} C$ and has the meaning of the basic reproductive number, which for non-aging population of mosquitoes equals $R_0 = \frac{m\alpha^2 bc}{\rho g} e^{-gn}$ [14]. For non-aging mosquitoes the expression (8) gives the value $R_0^s = \frac{m\alpha^2 bc}{\rho g} e^{-g(n+\sigma)}$, which differs from the classical expression by factor $e^{-g\sigma}$ because in the present consideration we suppose that mosquitoes start biting not earlier than at age σ. Condition (8) replaces the classical condition (6) in the presence of senescence in population of mosquitoes.

The stationary value for proportion of infectious people $\widetilde{X}$ can be calculated numerically as a nonzero solution of equation (5) or can be approximated analytically by expansion of the right part of expression

$$1 - \widetilde{X} = \frac{1}{R_0^s} \frac{\int_0^\infty f(t) dt}{\int_0^\infty e^{-\alpha c \widetilde{X} t} f(t) dt}$$

on $\widetilde{X}$ in the range of 0. The approximate formula is

$$\widetilde{X} \approx \left(R_0^s - 1\right) \Big/ \left(R_0^s + \frac{\alpha c \int_0^\infty t f(t) dt}{\int_0^\infty f(t) dt} \right),$$

which takes a classical form in the case of non-aging mosquitoes when $R_0^s = R_0$ [14]

$$\widetilde{X} = \frac{R_0 - 1}{R_0 + \frac{\alpha c}{g}}.$$

Figure 3 presents exact and approximate values for $\widetilde{X}$ versus R_0^s. It is seen that the approximation is good and it can represent the exact dependence $\widetilde{X}$ (R_0^s) in practical applications.

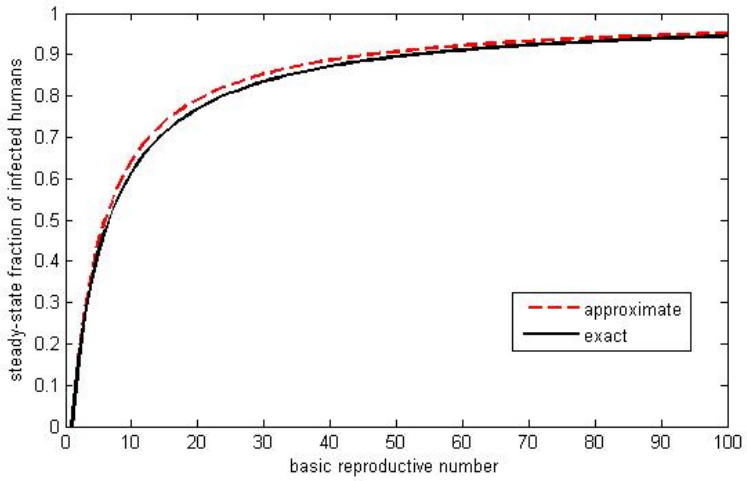

Figure 3. Exact and approximate values for stationary values of the proportion of infected humans as functions of basic reproductive number.

In a stable mosquito population the condition for the beginning of epidemic can be found using formula for vectorial capacity

$$R_0^s = \frac{bc}{\rho} C = \frac{ma^2 bc}{\rho \int_0^\infty S(t) e^{-rt} dt} \int_\sigma^\infty e^{-rx} \int_{x+n}^\infty S(t) dt dx$$

$$= \frac{ma^2 bc}{\rho} \times \frac{\int_0^\infty e^{-rt} f(t) dt}{\int_0^\infty e^{-rt} S(t) dt}.$$

Then the condition (6) transforms into

$$R_0^s = \frac{m\alpha^2 bc}{\rho} \times \frac{\int_0^\infty e^{-rt} f(t)dt}{\int_0^\infty e^{-rt} S(x)dx} > 1.$$

The second part of the expression reflects the role of aging in analysis of epidemic dynamics. When aging presents, the R_0 value may be less then in absence of aging. This means that in critical regimes the epidemic, which is predicted by a non-aging model, may not begin practically.

DISCUSSION

All the models of vector-borne diseases are usually based on the same simplifying assumptions, like constancy of vector mortality rate. What important factors have been omitted from these models? Which of them must be included? Without doubts, aging is one of factors to be adequately treated in analysis of malaria transmission.

The mosquito non-aging assumption was coined in 1950-years by McDonald [2, 19] who reasoned that predation and disease would kill mosquitoes well before they had an opportunity to die from senescence. Departure from the paradigm of constant mortality was undertaken only in 2007 by Styer et al. [11]. These authors demonstrated that the static age-independent models are too simple to describe mosquitoes and the diseases they transmit. They show that the existing methods of analysis of mosquito populations are no longer adequate. Age-dependent factors should be included in vector-based disease transmission models to describe and more accurately predict the dynamics of pathogen transmission.

We have analyzed a model in which the phenomenon of mosquito aging was included. We have derived new formulas for the basic reproductive number R_0, vectorial capacity C and entomological inoculation rate EIR. We show that the role of the vector population age structure in calculation of vectorial capacity is essential. Under all equal conditions the "old population" has the higher vectorial capacity than the "young population", composed mostly from the newly emerged mosquitoes.

In a growing stable population the young ages prevail over the old ages while in a decreasing one the old ages are presented in higher proportion. This results in non-monotonic behaviour of vectorial capacity in aging population as function of intrinsic growth rate r. The maximal value of vectorial capacity is attained for a specific value of the intrinsic growth rate. At low r values, vectorial capacity is low due to a small life expectancy whereas at higher r the population is "too young" to accumulate potentially infected bites.

The lifetime transmission potential was derived in the paper as in case of aging mosquito so in case of changing biting rate with age, and for specific cases compact formulas were found. The formulas for EIR and vectorial capacity *C,* derived by Smith and McKenzie, were expanded for ageing populations. Equations were given which completely describe dynamics of the vector borne epidemic in the presence of vector senescence.

Investigation of malaria epidemic development till now was limited by the asymptotic behaviour of the proportion of the infected mosquitoes and the solution of equation for the proportion of infected people in time. We demonstrated how epidemic changes in presence of mosquitoes aging and indicated the conditions when ignoring of aging gave too pessimistic prognosis for the epidemic development.

It is well known that epidemic begins only when $R_0>1$. In African populations its value ranges from near one to more than 3000 [14]. Our estimations help to compute these values more exactly thus making the estimations of the borders of malaria epidemic more correct.

At the dawn of the new century, infectious diseases are still causing huge mortality mostly in developing countries. Malaria, yellow fewer, Ebola, dengue and AIDS are the well known diseases, which can touch the countries of the developed world. For example, the epidemic effect of dengue reached Florida and southern Texas [17].

Our studies demonstrate that in critical regimes the epidemic, which is predicted by a non-aging model, may not begin practically.

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