

ESTIMATION OF PARAMETERS IN A CLOSED PYGMY POPULATION IN CAMEROON^{*†}

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Abstract

Inspired by Kouakep [16], we consider in this note a wellposed model with differential susceptibility and infectivity adding continuous age structure to an ODE model for a “Baka” pygmy group in the East of Cameroon (Africa). Assuming a very low contribution of carriers to infection compared to acute infection, we estimate a probability $p(a)$ (to develop symptomatic Hepatitis B state at age a) and acute carriers’ transmission rate. The value $R_0 = 2.67 > 1$ of the basic reproduction number estimated from data in the east of Cameroon confirms that HBV is endemic in the Baka pygmy group.

Keywords Hepatitis B; parameters estimation; Baka pygmy group; Cameroon

2000 Mathematics Subject Classification 35Q92; 92D30; 92D25

1 Introduction

Hepatitis B is endemic in Africa [23]. There are few data updated on epidemiology of Hepatitis B in Africa, especially in Cameroon [17, 21, 25]. But common measures and surveys on clinical cases show that average prevalence in Cameroon is almost 10% and the average of prevalence for the three pygmy groups (the Baka, the Bakola and the Bedzan.) studied by Foupouapouognigni et al. [12] is around 11%. Since 20,000 years, the Pygmies have lived in a forest environment in Cameroon prominently as hunter-gatherers (Verdu et al. [20]).

HBV (Hepatitis B Virus) epidemiology in Cameroon social context briefly presented:

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- 1) Professor Njoya Oudou, a specialist of Hepatitis diseases in [25] argues that 10 percent [3,17,25] of Cameroonians suffer from hepatitis B and need around USD 800 per month [5] for the treatment, even vaccination costs USD 50 per vaccinated individual [5]. Total population of Cameroon is around 22 millions [21,24].
- 2) The relative importance of mother-child transmission of HBV (Hepatitis B virus) in Cameroon is not well known [17].
- 3) Treatments available for chronic hepatitis (not the acute one which is incurable) such as Interferon-alpha, Lamivudine, Adefovir or Entecavir [18] are expensive. Vaccine since 1981 [3,18] GenHevac B protects 98% at least 10 years.
- 4) The rate of superinfection with other diseases such as hepatitis D is 25% [17,18]. World Hepatitis day is held every year in July.
- 5) The maximal life span (years) is 51 years [21] and the birth rate is 32.49 per 1000 [15] in Cameroon.

Our main result is to practically estimate HBV prevalences, the probability $p(a)$ (to develop symptomatic Hepatitis B state at age a) and acute carriers' transmission rate β_i . According to WHO [23] and Bonzi et al. [3], chronic carriers (most of time asymptomatic) have a low infectious rate. As a consequence in this work we assume that $\beta_e \approx 0$ compared with β_i . The work is organized as follows. In Section 2, we present the model and estimate the parameters with least squares. Here we perform numerical simulations. Later in Section 3 we present results through evaluated prevalences and graphics. Finally we give a discussion in Section 4.

2 Model, Parameters Estimations and Numerical Simulations

2.1 Presentation of Cameroonian pygmy groups useful for our simulations

We now consider the tree pygmies seen as almost globally closed populations with 44700 to 56000 individuals studied in Foupouapouognigni Y. et al. [12], that is, the Baka group is the largest one (40,000 to 45,000 individuals), and its distribution overlaps the two administrative regions of the south and the east of Cameroon; the Bakola pygmies are the next most populous group (4,000 to 5,000 individuals), mostly located in the western part of the southern region in the Atlantic Ocean division; the Bedzan group is the smallest one (700 to 1,000 individuals) and is located in the northern part of the central region. According to Foupouapouognigni [12], HBV surface antigen (HBsAg) was screened by a third-generation EIA (Monolisa AgHBs

Plus; Bio-Rad). Of the samples tested, there are 11.8%, 95% CI, 9.2 to 14.9% were positive for the three pygmy populations surveyed.

Pygmy populations (living in bush or mostly in forests) are relatively “closed” or isolated, and small, which can be a good example for our application [12].

2.2 Data and numerical simulations: Application to the largest pygmy group in Cameroon when $R_0 > 1$

We recall again that simulating data coming from [12] is interesting because pygmy groups are almost small and closed populations living in deep forests with good properties for mass action law in respect of their way of life.

With these data of Foupouapouognigni Y. et al. [12] on the Baka pygmy population, we observe simulations on a maximum of time $t_{\max} = 150$ years with a maximal life span $A = 60$ years. We recall the assumption that Cameroon is in an endemic situation for HBV [12, 17, 23].

1a) We consider the following (chronological) age-structured and wellposed model inspired by a manuscript of kouakep [16] (through semigroup theory [2, 11]) with differential susceptibility and infectivity:

$$\begin{aligned}(\partial_t + \partial_a + \mu) s(t, a) &= -\lambda(t, a)s(t, a), \\(\partial_t + \partial_a + (\mu_I + \mu)) i(t, a) &= \lambda(t, a)p(a)s(t, a), \\(\partial_t + \partial_a + \nu_E) e(t, a) &= \lambda(t, a)q(a)s(t, a), \\(\partial_t + \partial_a + \mu) r(t, a) &= \mu_I i(t, a),\end{aligned}\tag{2.1}$$

$$\lambda(t, a) = \beta_i \int_0^\infty i(t, a') da' + \beta_e \int_0^\infty e(t, a') da',$$

for $t > 0$ and $a > 0$. Here $s(t, a)$ denotes the age-specific density of susceptible, $e(t, a)$ and $i(t, a)$ denote respectively the the age-specific density of chronic carriers and acute infected individuals (that can be symptomatic or asymptomatic) while $r(t, a)$ denotes the recovered individuals from acute infection. In addition $p \in L_+^\infty(0, \infty)$ is a given function such that $0 \leq p(a) \leq 1$ *a.e.* while $q(a) \equiv 1 - p(a)$. Function q represents the age-specific probability to become a (asymptomatic) chronic carrier when becoming infected at age a . Function p denotes the probability to develop an acute (symptomatic) infection when getting the infection at age a . We refer to Edmunds et al. [7] for more explanation on the age-dependence susceptibility to the infection. In order to take into account this age-specific susceptibility dependence we will use in this work a simplest prototypical shape curve of the form

$$p(a) = 1 - \kappa e^{-ra},\tag{2.2}$$

for some $\kappa \in [0, 1]$ and $r > 0$ estimated with least squares from data in [12]. This differential susceptibility is a particularly important point for HBV infection. Recall that according to CDC¹ about 90% of children will remain chronically infected with HBV while 95% of adults will develop acute infection and will completely recover from HBV infection.

Parameter $\mu > 0$ denotes the natural death rate, $\nu_I := (\mu_I + \mu) > 0$ and ν_E denote the exit rates associated to each infected class. The term ν_I gathers recovery rate μ_I due to acute infection and natural death rate while ν_E corresponds to the additional death rate due to chronic infection and its consequences. Here we neglect possible recovery from chronic disease. The term $\lambda(t, a)$ corresponds to the age-specific force of infection and follows the usual bilinear law of mass-action, that is

$$\lambda(t, a) = \int_0^\infty [\beta_i(a, a')i(t, a') + \beta_e(a, a')e(t, a')] da'.$$

Here $\beta_i(a, a')$ and $\beta_e(a, a')$ respectively denote the contact transmission rates of acute infected individual and asymptomatic carriers of age a' with susceptible of age a . We shall later assume that the contact between individuals is homogeneous so that

$$\beta_i(a, a') \equiv \beta_i > 0 \quad \text{and} \quad \beta_e(a, a') \equiv \beta_e \geq 0.$$

According to WHO [22, 23], Edmunds et al [9] and Bonzi et al [3] chronic carriers (most of time asymptomatic) have a low infectious rate. As a consequence throughout of this work we assume that

$$0 \leq \beta_e \ll \beta_i. \quad (2.3)$$

This problem is supplemented together with the boundary conditions:

$$\begin{aligned} s(t, 0) &= \Lambda, \quad (\text{constant influx}), \\ i(t, 0) &= e(t, 0) = 0, \quad (\text{no vertical transmission [7, 8]}), \\ r(t, 0) &= 0, \quad (\text{no immunity at birth}), \end{aligned} \quad (2.4)$$

and initial data

$$s(0, a) = s_0(a), \quad i(0, a) = i_0(a), \quad (2.5)$$

with

$$e(0, a) = e_0(a), \quad r(0, a) = r_0(a). \quad (2.6)$$

Note that the r -components of the system decouples from the other and have therefore no impact upon the long time behaviour of the system. It will be omitted in

¹Centers for Disease Control and Prevention, USA: www.cdc.gov

the sequel. Here we recall that the boundary conditions $i(t, 0) = e(t, 0) = 0$ correspond to no vertical transmission, that is also assumed in the sequel. Hence, as in the work of Edmunds et al. [7, 8], we shall focus, in this work, on horizontal transmission taking into account age-specific susceptibility. This age-structured model (2.1)-(2.6) generalizes a discrete age one presented by Bonzy et al. [3, Fig.3, page 62]. We introduce the threshold parameter R_0 known as basic reproduction number (Dietz [4] 1975) defined by [16] as

$$R_0 := \Lambda \left[\frac{\beta_i}{\nu_I} \int_0^\infty p(a) e^{-\mu a} da + \frac{\beta_e}{\nu_E} \int_0^\infty q(a) e^{-\mu a} da \right]. \quad (2.7)$$

We set

$$I_e^\infty = \int_0^{+\infty} i_e(a') da'$$

and

$$E_e^\infty = \int_0^{+\infty} e_e(a') da'.$$

1b) It is easy to see that at endemic steady state (s_e, i_e, e_e, r_e) we get

$$\lambda(t, a) \equiv \lambda_e(a) \equiv \lambda_e = \beta_i I_e^\infty + \beta_e E_e^\infty,$$

which is obviously positive and unique as solution of a decreasing function goes to 0 since $R_0 > 1$. And we obtain the following system of ordinary differential equations satisfied by the unique endemic equilibrium (s_e, i_e, e_e, r_e) :

$$\begin{aligned} (\partial_a + \mu) s_e(a) &= -\lambda_e s_e(a), \\ (\partial_a + (\mu_I + \mu)) i_e(a) &= \lambda_e p(a) s_e(a), \\ (\partial_a + \nu_E) e_e(a) &= \lambda_e q(a) s_e(a), \\ (\partial_a + \mu) r_e(a) &= \mu_I i_e(a), \end{aligned} \quad (2.8)$$

This problem is supplemented together with the boundary conditions:

$$\begin{aligned} s_e(0) &= \Lambda, \text{ (constant external influx),} \\ i_e(0) &= e_e(0) = 0, \text{ (no vertical transmission),} \\ r_e(0) &= 0, \text{ (no immunity at birth).} \end{aligned} \quad (2.9)$$

The model (2.1)-(2.6) could be rewritten as an abstract Cauchy problem

$$\begin{aligned} u'(t) &= Au(t) + F(u(t)), \quad t > 0, \\ u(0) &= u_0. \end{aligned} \quad (2.10)$$

This can be seen as a Lipschitz perturbation F of a nondensely defined Hille-Yosida operator A and then prove its well posedness on suitable L^1 -like positive

cones with the integrated semigroup approach (see explanations in Kouakep [16] or Djidjou et al. [5,6]). Then standard methodologies [5] apply to provide the existence and uniqueness of mild solution for system (2.1)-(2.6).

2.3 Method of least squares for parameters' evaluation

1) Our aim is to compare the specific class prevalence (p'_i) statistically adjusted from data [12] and estimated prevalence (p_i) from model (2.1)-(2.6) for the seven classes in the Table 1.

Table 1: HBV data for Baka pygmy group [12] adjusted for 50000 individuals

Age (yrs)	$m = i_e + e_e$	s_e	Specific prevalence
≤ 10	549	2335	$p'_1 = \mathbf{0.23}$
11-20	1236	9478	$p'_2 = \mathbf{0.13}$
21-30	1373	12225	$p'_3 = \mathbf{0.11}$
31-40	824	10989	$p'_4 = \mathbf{0.07}$
41-50	550	6730	$p'_5 = \mathbf{0.08}$
> 50	550	8243	$p'_6 = \mathbf{0.07}$
Total	5082	50.000	$p'_7 = \mathbf{0.10}$

2) Knowing that $q(a) = ue^{-va} \equiv 0.643e^{-0.156a}$ and $p(a) = 1 - q(a)$, we get:

$$\begin{aligned}
 s_e(a) &= \Lambda e^{-(\mu+\lambda_e)a}, \\
 i_e(a) &= \Lambda e^{-(\mu+\mu_I)a} \lambda_e \int_0^a e^{(\mu_I-\lambda_e)\tau} p(\tau) d\tau, \\
 e_e(a) &= \Lambda e^{-\nu_e a} \lambda_e \int_0^a e^{(\nu_e-\mu-\lambda_e)\tau} q(\tau) d\tau, \\
 r_e(a) &= \mu_I e^{-\mu a} \int_0^a e^{\mu\tau} i_e(\tau) d\tau.
 \end{aligned} \tag{2.11}$$

3) We obtain for the i -th age class $[a_1(i); a_2(i)]$ in Table 1, the evaluation of the estimated prevalence as

$$p_i := \frac{\int_{a_1(i)}^{a_2(i)} [i_e(\tau) + e_e(\tau)] d\tau}{\int_{a_1(i)}^{a_2(i)} [s_e(\tau) + i_e(\tau) + e_e(\tau) + r_e(\tau)] d\tau} \tag{2.12}$$

4) We set

$$\begin{aligned}
 S_e(i) &:= \int_{a_1(i)}^{a_2(i)} s_e(\tau) d\tau, & I_e(i) &:= \int_{a_1(i)}^{a_2(i)} i_e(\tau) d\tau, \\
 E_e(i) &:= \int_{a_1(i)}^{a_2(i)} e_e(\tau) d\tau, & R_e(i) &:= \int_{a_1(i)}^{a_2(i)} r_e(\tau) d\tau.
 \end{aligned} \tag{2.13}$$

5) We present then the Baka HBV acute prevalences in Table 1. But it is difficult to obtain with formula of the endemic equilibrium, for $\Delta_{i_e, e_e} = (i_e(a_1) - i_e(a_2)) + (e_e(a_1) - e_e(a_2))$ the form

$$\Delta_{i_e, e_e} = (i_e(a_1) + e_e(a_1)) - (i_e(a_2) + e_e(a_2)) = m(a_1) - m(a_2). \quad (2.14)$$

According to [14], it is possible to define e_e in respect to i_e (with $m(a) := (i_e(a) + e_e(a))$):

$$\begin{aligned} e_e(a) &= 0.05i_e(a) = \frac{m(a)}{21}, \quad \text{if } a > 10\text{yrs}, \\ e_e(a) &= d(a)i_e(a) = \frac{d(a)}{1 + d(a)}m(a), \quad \text{if } a \leq 10\text{yrs}. \end{aligned} \quad (2.15)$$

with $d(a) \in [0.3; 0.9]$ or simply $d(a) = d^* = 0.6$ (see also Goyal et al. [13]).

6) One can theoretically solve the six (resp. seven) nonlinear equations

$$\frac{E_e(i) + I_e(i)}{S_e(i) + E_e(i) + I_e(i) + R(i)} = p'_i$$

in order to find $\beta_i, \beta_e, \Lambda, \lambda_e, \mu_I, \nu_e$ (resp. with μ for $i = 7$).

7) But practically, we can approximate p'_i with Table 1 provided by [12] and these coefficients numerically with the likelihood maxima or (as in this work) the **least squares** methods.

2.4 Simulations and evaluation of some coefficients in the case

$$R_0 > 1$$

Practically, while estimating $\beta_i, \beta_e, \Lambda, \lambda_e, \mu_I$ and ν_e :

1) We use the least squares method with $\frac{26}{3} \leq \mu_I \leq 26$, since the average time $\frac{1}{\mu_I}$ spending in the acute class/compartement belongs to $[2, 6]$ (in weeks).

2) The maximal life span A plays a great role on prevalence estimations. One can modify also the numerical codes to estimate $d(a) = d^*$. In fact, by varying the value of d^* between 0.3 and 0.9, we obtain similar observations as above.

3) Then with numerical constraint on μ_I , we can estimate the transmission coefficient of acute infectious β_i by assuming that $\beta_e \approx 0$ [3, 22] and

$$3.a) \text{ theoretically: } \beta_i \approx \frac{\lambda_e}{\int_0^{+\infty} i_e(\tau) d\tau};$$

$$3.b) \text{ practically: } \beta_i \approx \frac{\lambda_e}{\int_0^{60} i_e(\tau) d\tau} \text{ by considering maximum age at 60 years that is just beyond the maximal life span in Cameroon.}$$

We made simulations with the values in Table 2 (by using the software (c) Scilab). We denote in Table 2: “**p**” for people, “*yr*” for year and “ofs” for offspring or births.

Table 2: Values for $R_0 = 2.67 > 1$ estimated with (2.7)

Estimated:	$p(a)$		β_i	β_e
value/range:	$1 - 0.643.e^{-0.156a}$		183	≈ 0
Unit:	probability		$(\mathbf{p} * yr)^{-1}$	$(\mathbf{p} * yr)^{-1}$
Age	ν_I	ν_E	μ	Λ
[0;60]	8.68	8.5	0.028	5647
yr	yr^{-1}	yr^{-1}	yr^{-1}	ofs/yr

3 Results

A) Using Table 1, the least squares approximations provide the curve 1 of the function $q : a \rightarrow q(a) = 1 - p(a)$.

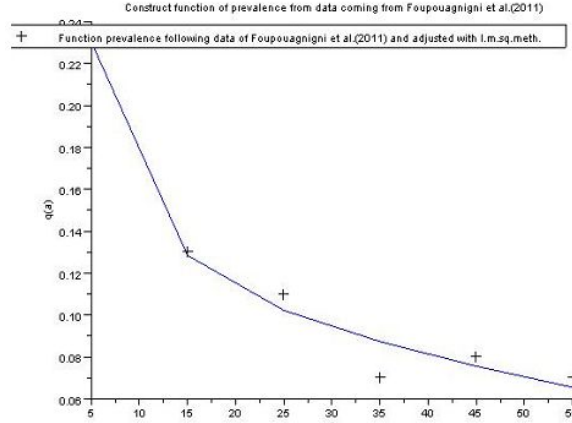


Figure 1: Function $q : a \rightarrow q(a) = 1 - p(a)$ adjusted from data of Foupouapouognigni et al. [12]

B) The estimated prevalences are provided in Table 3. We obtain then Figures 2 to 4 presented therein, which show the numerical stability of the endemic equilibrium for long time dynamics of the model.

Table 3: Baka data, estimated prevalence VS real specific prevalences for the Baka pygmy group following [12] adjusted to 50000 individuals $R_0 = 2.67 > 1$

Age (yrs)	Estimated prevalence p_i	Specific prevalence p'_i
≤ 10	$p_1 = 0.0379$	$p'_1 = \mathbf{0.23}$
11-20	$p_2 = 0.0846$	$p'_2 = \mathbf{0.13}$
21-30	$p_3 = 0.0875$	$p'_3 = \mathbf{0.11}$
31-40	$p_4 = 0.0760$	$p'_4 = \mathbf{0.07}$
41-50	$p_5 = 0.0632$	$p'_5 = \mathbf{0.08}$
> 50	$p_6 = 0.0520$	$p'_6 = \mathbf{0.07}$
Global	$p_7 = 0.07$	$p'_7 = \mathbf{0.10}$

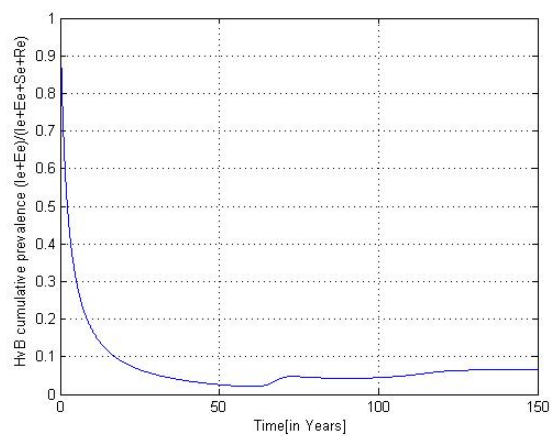


Figure 2: Prevalence estimated per time

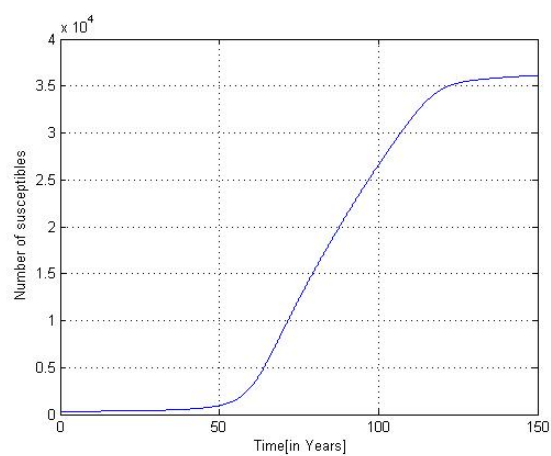


Figure 3: Function of susceptible' density per time

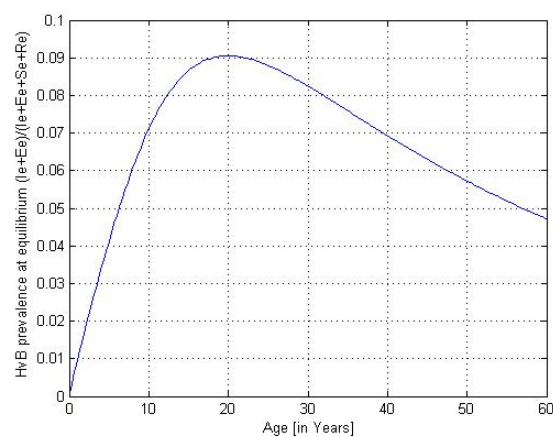


Figure 4: Estimated prevalence at equilibrium

4 Discussion

The above example with differential susceptibility and age structure shows that it is possible to estimate interesting parameters from biological data.

We estimate parameters in Table 2 from (Foupouapouognigni et al. [12], 2011) on Baka pygmy group in the East Cameroon region. The gap on Figure 4 for small ages is probably due to the fact that vertical transmission is neglected [5, 6, 19] in Cameroon [1] (See the first three lines of Table 3). Moreover the last line indicates a gap at age less than 10 years. We obtain similar results with the general function $q(a) = \exp(-0.645a^{0.455})$ stated in (Edmunds et al. [7] 1993). The value $R_0 = 2.67 > 1$ of the basic reproduction number estimated from data in [12] confirms that HBV is endemic in the Baka pygmy group.

We need to point out the fact that this model left out the vaccination since it is very expensive in Africa, especially in the population studied in Cameroon. Further investigations will be done to include a prospective campaign of mass vaccination for children and young adults in an extended version of (2.1)-(2.6) and estimate parameters. Studies including vertical transmission like those of (El-Doma [10] 2006) could be used in Chinese case as [5] if we modify them in order to add the hypothesis of differential mortality according to susceptible, acute or carrier classes as in model (2.1)-(2.6).

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