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# A Note on Proportionate Mixing Assumption Revisited for a Model with Vertical Transmission

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***Abstract*—We conditionally extend formulas of (Dietz and Schenzle, J. Math. Biol. 22: 117-120, 1995) for the "transmission potential" of an immunizing infection with pre-infection possible before birth and vertical transmission admitted. We look for minimum proportion to be covered to reduce basic reproduction rate below 1 by acting through vaccination. We present also a new criterion allowing the selection of an immunizing vaccination strategy by bringing the reproduction number below 1. We find that reduce vertical transmission, adds chances to eradicate disease. Moreover reduce age of vaccination reduces the minimum vaccination coverage inducing global immunization against disease by bringing down the basic reproduction number.**

***Keywords*-Transmission potential, minimum proportion for vaccination immunization, endemic disease, pre-infection. AMS Classification: 35K55, 92D30, 49J20, 92D25.**

## I. Introduction: Motivation and Formulation of the Model

### A. Motivation

We study an immunizing infection in a closed population where, as [5, (Dietz and Schenzle 1985)], susceptible newborns are added according to the constant positive rate $\Lambda$, infective newborns at constant positive rate $\Lambda'$ of total infective at the same index $c \geq 0$ (seen e.g. as the infection time of infected population or any other biological structure with dc/dt=1), and susceptible individuals die according to the rate $\mu(a)$, where $a$ denotes the chronological age of an individual. We use proportionate mixing that is more accurate for an age strutured model describing a closed population (of size $n(t,a)$ at time $t$ and chronological age $a$) that is not big. Vertical transmission is introduced here (contrary to [5, (Dietz and Schenzle 1985)] and according to [1, (Busenberg and Cooke 1993)] due to its importance. As main results, we find that reduce vertical transmission, adds chances to eradicate disease. Moreover reduce age $V$ of vaccination reduces the minimum vaccination coverage inducing global immunization against disease by bringing down the basic reproduction number.

### *B. Formulation of the models and equilibria*

*1) The model and its aggregated form with perfect vaccine and vertical transmission:* In equilibrium, we assume that the size $N$ of the population is:

$$N = \Lambda \int_0^\infty e^{-M(a)} da = \Lambda L$$

where $M(a) = \int_0^a \mu(s)ds$, $n(t,a) \overset{t \to +\infty}{\to} n^\infty(a) = \Lambda e^{-M(a)}$ and $L$ denotes the life expectancy of newborn. We analyse the basic reproduction rate [4, (Dietz 1975)] or infectious contact number [7, (Hethcote 1976)] $R_0$ without vaccination (resp. $R_0(\Psi)$ with vaccination rate $\Psi$) estimated from equilibrium force of infection $\lambda_0$ (resp. $\lambda_\Psi$).

As [5, (Dietz and Schenzle 1985)] in most cases, we defined (or assume):

- $K(\Psi, \lambda_\Psi)$ as the smallest contact rate above wich a positive endemic level is possible for the vaccination rate or strategy $\Psi$ [5];
- $\gamma(a)$ as the age-specific per capita contact or activity rate; it takes also into account the age specific (average) probability of becoming infected through a contact with infectious individual;
- $\lim\limits_{a \to +\infty} \left[ a p_\infty(a) e^{-M(a)} \right] = 0$ because we assume also that the function $a \overset{J}{\to} a p_\infty(a) e^{-M(a)}$ belongs to $L^1(0, +\infty)$;
- $x(t,a)$ as the density of susceptibles at time $t$ and age $a$;
- $y(t,a,c)$ as the density of infectives at time $t$ , chronological age $a$ and level $c$;
- $d_1(a,c)$ is the additional death rate due to disease to be added to the rate of healing or immunization (we later simplify it into the form $d_1(a,c) \equiv \overline{d}_1(a)$);
- we see then that dynamic of the compartment of retired individuals is decoupled from the model studied for our immunizing infection;
- $c$ could be greater than $a$ (notion of "pre-infection" included: infection before birth possible);
- a consequence is this modified version of the force of infection (compare to [5, (Dietz and Schenzle 1985, p. 118)]):

$$\lambda(t) = \frac{f}{N} \int_0^\infty \int_0^\infty p(t,a') y(t,a',c) dc da'$$

- $f$ as the probability of infectiousness (depending on $c$ in [5, (Dietz and Schenzle 1985)] but constant here as an average since several health public policy ignore probability variations at first approximation);
- probability that an individual of age $a$ has contact with an individual of age $a'$given that it has a contact with a member of the population

$$p(t,a,a') \equiv p(t,a') = \frac{\gamma(a') n(t,a')}{\int_0^\infty \gamma(u) n(t,u) du}$$

with

$$p(t,a') \overset{t \to +\infty}{\to} p_\infty(a') = \frac{\gamma(a') n^\infty(a')}{\int_0^\infty \gamma(u) n^\infty(u) du}$$

- transmission potential

$$R_0(\Psi) = \frac{K(\Psi, \lambda_\Psi)}{K(\Psi, 0)}$$

We formulate, with the notation $\partial_z := \frac{\partial}{\partial z}$, a model with vertical transmission by combining approach of [3, (Castillo-Chavez and Feng 1998)] and [5, (Dietz and Schenzle 1985)]:

$$\begin{cases} (\partial_t + \partial_a)\, x = -\left(\lambda(t) + \Psi(a) + \mu(a)\right) x \\ (\partial_t + \partial_a + \partial_c) y(t,a,c) = \\ \qquad -\left(d_1(a,c) + \mu(a)\right) y(t,a) \\ x(t,0) = \Lambda \geq 0 \\ x(0,a) = x_0(a) \geq 0 \\ y(0,a,c) = y_0(a,c) \geq 0 \\ y(t,a,0) = \lambda(t) x(t,a) \\ y(t,0,c) = \Lambda' \int_0^\infty p(t,a') y(t,a',c) da' \end{cases} \tag{1}$$

*Remark 1:* In fact there are certain probability for the infected population $y(t,a',c)$ giving a birth to a health newborn, this indicates that there are some input of newborns in to the formulation of $x(t,0)$ from $y(t,a',c)$. However, this could be neglected since we assume that infected population is very small compared to healthy one: it justfies also our constant influx of health newborns $\Lambda$. We will focus later on $\Lambda'$ since we want to sketch in priority the impact of vertical transmission on basic reproduction rate.

For sake of simplicity, we select the special case: $d_1(a,c) \equiv \overline{d}_1(a)$ and use the new variable

$$\mathbf{y}(t,a) = \int_0^\infty y(t,a,c) dc$$

Then the wellposed system (1) rewrites as

$$\begin{cases} (\partial_t + \partial_a)\, x = -(\lambda(t) + \Psi(a) + \mu(a)) x(t,a) \\ (\partial_t + \partial_a)\, \mathbf{y}(t,a) = -\left(\overline{d}_1(a) + \mu(a)\right) \mathbf{y}(t,a) \\ \qquad + \lambda(t) x(t,a) \\ x(t,0) = \Lambda \geq 0 \\ x(0,a) = x_0(a) \geq 0 \\ \mathbf{y}(0,a) = \mathbf{y}_0(a) \geq 0 \\ \mathbf{y}(t,0) = \Lambda' \int_0^\infty p(t,a') \mathbf{y}(t,a') da' \\ \lambda(t) = \frac{f}{N} \int_0^\infty p(t,a') \mathbf{y}(t,a') da' \end{cases} \tag{2}$$

*2) Cauchy problem and integrated solutions in brief:* The system (2) can be re-written under the form of a Cauchy problem:

$$\begin{cases} \frac{dw(t)}{dt} = Aw(t) + F(t,w(t)) := G(t,w(t)) \\ w(0) = w_0 \in D(A) \end{cases} \tag{3}$$

with

$$w(t) \equiv \begin{pmatrix} 0 \\ 0 \\ x(t,.) \\ \mathbf{y}(t,.) \end{pmatrix}$$

and

$$D(A) = \{0\} \times \{0\} \times \left(W^{11}(0;+\infty)\right)^2$$

Consider $v \equiv \begin{pmatrix} \alpha \\ \beta \\ \widehat{x} \\ \widehat{y} \end{pmatrix}$ and the Banach space

$$X = \mathbb{R} \times \mathbb{R} \times \left(L^1(0;+\infty)\right)^2$$

endowed with the usual norm

$$\|v\|_X = |\alpha| + |\beta| + \int_0^\infty \left[|\widehat{x}(a)| + |\widehat{\mathbf{y}}(a)|\right] da$$

Positive cone of $X$ is

$$X_+ = [0;+\infty) \times [0;+\infty) \times \left(L^1_+(0;+\infty)\right)^2$$

We define also

$$X_0 = \{0\} \times \{0\} \times \left(L^1(0;+\infty)\right)^2$$

and its positive cone

$$X_{0+} = \{0\} \times \{0\} \times \left(L^1_+(0;+\infty)\right)^2.$$

We set $u \equiv \begin{pmatrix} 0 \\ 0 \\ \widehat{x} \\ \widehat{y} \end{pmatrix}$ and the linear and closed operator defined on $D(A)$ by:

$$\begin{array}{llll} A: & D(A) & \to & X \\ & u & \longmapsto & \begin{pmatrix} \widehat{x}(0) \\ \widehat{y}(0) \\ -\frac{d\widehat{x}}{da} - \left(\Psi(.) + \mu(.)\right) \widehat{x} \\ -\frac{d\widehat{y}}{da} - \left(\overline{d}_1(.) + \mu(.)\right) \widehat{y} \end{pmatrix} \end{array}$$

It always exists $\bar{\mu} \in [0;+\infty)$ such that: $\forall a \geq 0,\ \mu(a) \geq \bar{\mu}$. Then we have for each $\lambda > -\bar{\mu}$

$$(\lambda - A)^{-1} X_+ \subset X_{0+} \tag{4}$$

and $(-\bar{\mu}, \infty) \subset \rho(A)$ with

$$\|(\lambda - A)^{-1}\|_{\mathcal{L}(X)} \leq \frac{1}{\lambda + \bar{\mu}},\ \ \forall \lambda > -\bar{\mu}. \tag{5}$$

The part $A_0$ of $A$ defined by

$$\begin{array}{rcl} A_0 : D(A_0) \rightarrow & & X \\ u \longmapsto & & \begin{pmatrix} 0 \\ 0 \\ -\frac{d\widehat{x}}{da} - (\Psi(.) + \mu(.))\,\widehat{x} \\ -\frac{d\widehat{y}}{da} - \left(\overline{d}_1(.) + \mu(.)\right)\widehat{y} \end{pmatrix} \end{array}$$

with $D(A_0)$ defined by

$$\left\{ u \equiv \begin{pmatrix} 0 \\ 0 \\ \widehat{x} \\ \widehat{y} \end{pmatrix} \in D(A) :\ Au \in \overline{D(A)}, \right.$$

$$\left. \widehat{x}(0) = \widehat{y}(0) = 0 \right\}$$

$A_0$ verifies the Hille-Yosida property: It exists $\bar{\mu} \in [0;+\infty)$ such that $\forall a \geq 0,\ \mu(a) \geq \bar{\mu}$ and we have for each $\lambda > -\bar{\mu}$

$$\|(\lambda - A_0)^{-1}\|_{\mathcal{L}(X_0)} \leq \frac{1}{\lambda + \bar{\mu}},\ \ \forall \lambda > -\bar{\mu}. \tag{6}$$

and (by lemma 2.1 of [6, Ducrot et al. 2010]): $X_1 := \overline{D(A_0)}$. Assumption 2.2 of [6, Ducrot et al. 2010, p. 267] is satisfied. Then its lemma 2.3[6, Ducrot et al. 2010, p. 267] applies: $A_0$ is the infinitesimal generator of a $C_0$-semigroup $(T_{A_0}(t))_{t \geq 0}$ on $X_1$.

We define (with $\lambda(t) = \frac{f}{N}\int_0^\infty p(t,a')\widehat{y}(a')da'$) also the Frechet differentiable in the second variable $u$ ( and then "locally" Lipschitz in $u$) perturbation (for each $t \geq 0$):

$$\begin{array}{rcccl} F(t,.) : & X_0 & \rightarrow & & X \\ & u & \longmapsto & & G(t,u(.)) - Au \end{array}$$

with

$$F(t,u(.)) = \begin{pmatrix} -\Lambda \\ -\Lambda' \int_0^\infty p(t,a')\widehat{y}(a')da' \\ -\lambda(t)\widehat{x} \\ \lambda(t)\widehat{x} \end{pmatrix}$$

The model (3) is well posed with an integrated solution $w$ globally defined in time through a bounded dissipativity property[2], [6], [8], [10], [12], [13]. $w$ satisfies (in Bochner sense for integrals):

$$\int_0^t w(s)ds \in D(A)$$

and

$$w(t) = w_0 + A\int_0^t w(s)ds + \int_0^t F(s,w(s))ds$$

$$(t \geq 0)$$

*3) Stationary solution of (2):* A stationary solution $(\overline{x}_\Psi; \overline{\mathbf{y}}_\Psi)$ of (2) (with the force of infection at equilibrium $\lambda_\Psi$) satisfies:

$$\begin{cases} \overline{x}_\Psi(a) = \Lambda e^{-(\mathbf{\Lambda}_\Psi(a) + \Phi(a) + M(a))} \\ \overline{\mathbf{y}}_\Psi(a) = \Lambda' \displaystyle\int_0^\infty p_\infty(a')\overline{\mathbf{y}}_\Psi(a')da' e^{-(D_1(a)+M(a))} \\ \qquad + \displaystyle\int_0^a \lambda_\Psi \overline{x}_\Psi(s) e^{(\Phi(s)-\Phi(a)+M(s)-M(a))}ds \\ \lambda_\Psi := \dfrac{f}{N}\displaystyle\int_0^\infty p_\infty(a')\overline{\mathbf{y}}_\Psi(a')da' \end{cases} \tag{7}$$

with:

$$\mathbf{\Lambda}_\Psi(a) = \int_0^a \lambda_\Psi da' = \lambda_\Psi . a$$

$$\Phi(a) = \int_0^a \Psi(a')da'$$

and

$$D_1(a) = \int_0^a \overline{d}_1(a')da'$$

Then $\lambda_\Psi$ is a fixed point of the function

$$g(z) = \left(\Lambda' \int_0^\infty p_\infty(a')e^{-(D_1+M)(a')}da' \right.$$
$$\left. + \frac{f\Lambda}{N}\int_0^\infty p_\infty(a)\int_0^a e^{-(\Phi(a)+M(a)+s.\mathbf{z})}dsda\right).z$$

We defined then the non-increasing function

$$h(z) = \Lambda' \int_0^\infty p_\infty(a') e^{-(D_1(a')+M(a'))} da' + \frac{\Lambda f}{N} \int_0^\infty p_\infty(a) \int_0^a e^{-(\Phi(a)+M(a)+s.\mathbf{z})} dsda$$

and the treshold

$$K_0^\Psi := h(0)$$

Solution(s) of the equation $g(z) = z$ are $z = \lambda_\Psi^- = 0$ (Disease free equilibrium) and (if $K_0^\Psi \geq 1$) $z = \lambda_\Psi^+$ where $\lambda_\Psi^+$ is the only non zero solution of the equation: $h(z) = 1$ corresponding to the endemic equilibrium.

## II. Transmission potentials

As [5, (Dietz and Schenzle 1985)], we defined

$$K(\Psi, \lambda_\Psi) = (h(\lambda_\Psi))^{-1}$$

It is obvious that $K(\Psi, \lambda_\Psi) = K(0, \lambda_0)$ then the potential transmission is

$$R_0(\Psi) = \frac{K(\Psi, \lambda_\Psi)}{K(\Psi, 0)} = \frac{K(0, \lambda_0)}{K(\Psi, 0)} \quad (8)$$

Then if we set these two non-increasing functions:

$$A(\Phi) := \Lambda' \int_0^\infty p_\infty(a') e^{-(D_1(a')+M(a'))} da' + f\frac{\Lambda}{N} \int_0^\infty a p_\infty(a) e^{-(\Phi(a)+M(a))} da$$

and

$$B(\lambda_0) : = \Lambda' \int_0^\infty p_\infty(a') e^{-(D_1(a')+M(a'))} da' + f\frac{\Lambda}{N} \int_0^\infty p_\infty(a) \int_0^a e^{-(M(a)+s.\lambda_0)} dsda$$

$$R_0(\Psi) = \frac{A(\Phi)}{B(\lambda_0)} \quad (9)$$

$R_0^{\Lambda'=0}(\Psi)$ is the basic reproduction rate $R_0$ without vertical transmission and $R_0^{\Lambda'\neq 0}(\Psi)$ is the basic reproduction rate $R_0$ with vertical transmission. We set

$$U_1 := \int_0^\infty p_\infty(a) \int_0^a e^{-(M(a)+s.\lambda_0)} dsda$$

and

$$U_2 := \int_0^\infty a p_\infty(a) e^{-(\Phi(a)+M(a))} da$$

Two cases appear:

C1) If

$$U_1 \geq U_2$$

then

$$R_0^{\Lambda'=0}(\Psi) \leq R_0^{\Lambda'\neq 0}(\Psi)$$

C2) If

$$U_1 \leq U_2$$

then

$$R_0^{\Lambda'=0}(\Psi) \geq R_0^{\Lambda'\neq 0}(\Psi).$$

*Remark 2:* C2) is satisfied if

$$e^{-M(a)} \int_0^a e^{-s.\lambda_0} ds \leq a e^{-(\Phi(a)+M(a))}$$

that means

$$\frac{1 - e^{-\lambda_0 a}}{\lambda_0} \leq a e^{-\Phi(a)}$$

The approximation (for $\lambda_0$ very small compared to maximal reacheable human age or life expectancy/lifespan) provides the approximation

$$a \lesssim a e^{-\Phi(a)}$$

or

$$1 \lesssim e^{-\Phi(a)}$$

In that case, the second case C2) is probably less recurrent than obvious case C1)

*Remark 3:* Another remark for inequality

$$\frac{1 - e^{-\lambda_0 a}}{\lambda_0} \leq a e^{-\Phi(a)}$$

coming from case C2), is the fact that it corresponds to a "massive and agressive" campaign ($\Phi$ huge) of vaccination that reverse the effect of vertical transmission ($\lambda_0$ very small). C2) naturally traduces the supplementary infectious cases brought by vertical transmission reduced by vaccination, but not enough to be similar to the case $\Lambda' = 0$. Because of the term $e^{-\Phi(a)}$ at the numerator of $R_0(\Psi)$, we see that $R_0(\Psi) \leq R_0(0) := R_0$: vaccination reduces the basic reproduction rates (see also [9, (Kouakep and Houpa 2014)] for the case without vertical transmission).

## III. A criterion for "sufficient" vaccination strategies and minimal proportion for immunization of an almost closed population

We observe that if $R_0 \neq 0$

$$\frac{R_0(\Psi)}{R_0} = \left(1 - \frac{\frac{f\Lambda}{N}\int_0^\infty a p_\infty(a) e^{-M(a)}\left[1 - e^{-\Phi(a)}\right] da}{A(0)}\right) \tag{10}$$

*Theorem 4:* We assume that $R_0 > 1$. To reach a basic reproduction rate $R_0(\Psi)$ below 1, the following inequality schould be satisfied by the choosen vaccination rate $\Psi$:

$$\left(\frac{f\frac{\Lambda}{N}\int_0^\infty a p_\infty(a) e^{-M(a)}\left[1 - e^{-\Phi(a)}\right] da}{A(0)}\right) > 1 - \frac{1}{R_0} \tag{11}$$

A sufficient condition to reach $R_0(\Psi)$ below 1 is the condition (for a.e $a > 0$):

$$\left(\frac{\frac{f}{N}\left[1 - e^{-\Phi(a)}\right]}{\frac{\Lambda'}{\Lambda}\left[1 + \frac{e^{-D_1(a)}}{a}\right]}\right) > 1 - \frac{1}{R_0} \tag{12}$$

*Remark 5:* Inequality (12) induces a kind of control on age $a > 0$ (for a vertically transmited disease as hepatitis B) that could reduce globally the number of infected childs and infectives.

we define the non-increasing function:

$$\begin{aligned} G(b) :=& \Lambda' \int_b^\infty p_\infty(a') e^{-(D_1(a') + M(a'))} da' \\ &+ f\frac{\Lambda}{N}\int_b^\infty a p_\infty(a) e^{-M(a)} da \end{aligned}$$

Following [5, (Dietz and Schenzle 1985)], we propose in the next result a formula showing minimum proportion $p^*$ to be covered if vaccination takes place at age $V$:

*Theorem 6:* A formula showing minimum proportion $p^*$ to be covered if vaccination takes place at age $V$ is given by:

$$p^* = \left(1 - \frac{1}{R_0}\right)\frac{G(0)}{G(V)} \tag{13}$$

## IV. Discussion

Formula (11) suggests that a pressure is done by vertical transmission on the inequality to satisfy if we want to bring the transmission potential rate below 1, compared to the situation without vertical transmission. With (12) we see also that if size at equilibrium $N$ of population increases, then achieve global immunization through vaccination is more difficult.

We observe a similar situation for the minimal proportion for vaccination: reduce $\Lambda'$ (vertical transmission), adds chances to satisfy criterion (11) for disease eradication. A discussion is necessary around the formula (13). [11, (Sall et al. 2004)] said truth when they pointed out the fact that neglect vertical transmission in vaccinal strategies for sub-Saharan Africa is a mistake: we see by formula (13) that reduce age $V$ of vaccination (in biological ranges) reduces the minimum vaccination coverage $p^*$ inducing immunization.

A further work will consider an imperfect vaccine and differential infectivity as [3, (Castillo-Chavez and Feng 1998)] and [9, (Kouakep and Houpa 2014)] in a specific case as hepatitis B. Migrations could be also considered.

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