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A demographic framework for the evaluation of the impact of imported infectious diseases

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A demographic framework for the evaluation of the impact of imported infectious diseases: HBV as an example

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Abstract

This paper provides a basic framework for the the evaluation of the impact of "imported" infectious diseases. By combining some standard epidemiological formulations with the so called stable model with immigrations we try to answer the question of the role played by several demo-epidemiological profiles of the immigrants on the long term endemic profile of a given population.

1 Introduction

A quite relevant problem of the recent italian demographic evolution has been constituted by the continuous immigrations inflow from developing countries, such as Senegal, Nigeria or the North Mediterranean Africa, to which it superimposed in more recent years the stream from Eastern Europe, in particular from the former Jugoslavia and Albania. Despite the still very low level levels of social integration of immigrants in the population of destination, it is widely recognized at present, especially at the level of official policy, that the so called "migratory solution" appears at present perhaps the only available solution to both the problems of aging and decaying of the italian population. This aspect is common to other developed countries, many of which are experiencing levels of fertility well below replacement, but is especially relevant in Italy, which is characterized at present by the lowest TFR of the world.

The almost official existence of a "migratory solution" which could be pursued in the near future by many developed countries as the main policy against aging, engenders, as a central public health issue, that of monitoring and evaluate the impact of the "imported" infectious diseases.

For instance, with regards to the problem of control of diseases such as HBV (HBV control constituted the main motivation for the present study, but this could be repeated, mutatis mutandis, for many other infectious diseases: HIV and tuberculosis could constitute other relevant problems) it is to be remarked that all countries of origin of migration streams directed toward Italy are characterised by average or very often high levels of endemic HBV. Hence, an important question regards the possible impact of immigrations of carriers of HBV on the transmission dynamics of the disease in the "arrival" population. This is especially relevant if we consider that these flows have had a central role in the recruitment of new cohorts of internal prostitution (for instance a large part of the nigerian, albanese and former Jugoslavia women) which could reveal particularly effective for what concerns the diffusion of STD, since very often accepts unprotected sex.

In what follows we explicitly develop a basic demographic framework for evaluating the impact of external migrations on the dynamics of some typical endemic infectious disease, such as HBV, experienced at endemic levels by a given "host"[1] population which is subject to below-replacement fertility. In this preliminary investigation we will make the very simple assumption, typical of demographic analysis, by which immigrated individuals imediately subsume the demo-epidemiological patters of the host population. The emphasis of the paper will hence be on typically demographical problems. The demographic apparatus that we will consider and enlarge to deal with the dynamics of infectious diseases, is based on the so called stable population models with immigrations (Arthur et al. 1982, 1988, Mitra 1987, 1990). This model, initially developed to study the effects of immigrations on populations subjected to below replacement fertility, predicts that "if fertility persist at some level below replacement, a constant flow of permanent immigrants will generate a stationary population" (Arthur and Espenshade 1988, 316). The model enables one to answer, under the basic assumption of total adoption by the immigrants of the demographic patterns of the host population, specific

[1] A terminology clarification is needed: in the usual epidemiological jargon by host population we mean the population which is actually experiencing a disease. In this paper we sometimes use "host" population to refer to the population which hosts the migration stream.

questions such as: which will be the ultimate size and age structure of the long term stationary population corresponding to a prescribed immigration profile? What's the role of the age structure of immigrants? The complex metabolism of age structure permits to evidence a dramatic dependence of the ultimate size of the long term population on the immigrants age stucture: it's by no means the same thing if immigrants are young inviduals at beginning of their fertile period rather than old individuals. Due to the complex nonlinear underpinnning which result when we try to combine demographic and epidemiological factors, it becomes particularly of interest to answer questions such as: what's the impact on the long term endemic equilibrium of different migrations streams on the basis of the age of immigrants and their epidemiological statuses? Clearly, if we consider a migrant who is carrier of HBV, we expect completely different outcome if such a migrant is a young prostitute 20 years old rather than an old person near to retirement.

The present paper is organised as follows: in the second section we recall the properties of the basic age structured model with immigrations, in particular of the model of constant immigrations in a population with below replacement fertility following the basic work by Arthur et al. 1982. In section three a brief review is made of mathematical models for the geographical spread of infectious diseases. In the fourth section a simple aggregate (i.e.: without age structure) demo-epidemiological framework is developed by superimposing a typical SIR epidemic mechanism to a population experiencing below replacement fertility. The main difference with respect to traditional epidemiological formulations is the possibility of immigration of subjects of all possible epidemiological statuses. A more general model recognising age structure as well is developed in section five, in which a SIR model with age structure is superimposed to the full model of Arthur et al. Its equilibrium features are developed in section six, whereas in section seven some explicit formula aimed to define the impact of several age profiles of immigrants on the endemic profile of the host population are developed.A more general model recognizing the age of infection as well is briefly introduced in section eight: this model appears to remedy to a drawback implicitly introduced in the more simple formulations. A model for the evaluation of immigration profiles on the endemic structure of a disease as HBV is presented in section nine. Critical points of the approach and directions for future research are indicated in the last section.

2 Immigrations in populations with below replacement fertility

Even though the asymptotic outcome of the interaction through migrations of several populations experiencing their own internal metabolism, was already clarified since the beginning of the seventies, thanks to the development, by Rogers and coworkers (see for instance the classical Rogers 1975), of the so called multiregional and subsequently multistate schemes, the development of theoretical results for the assessment of the impact of several age structure of migrants on a given host stable population, is quite more recent. Arthur et al. (1982) have studied the long term consequences of a constant migration stream, characterized by a stationary structure of entries by age, on a below replacement population. Their analysis, limited to the standard demographic assumption of "imediate adoption" by the immigrants of the "host" population demographic behaviour, gives a simple "renewal model" based proof of the convergence to stationarity of such a population and supplies the basic formulas for the assessment of its asymptotic behaviour. In a subsequent paper Arthur and Espenshade (1988) have studied the long term behaviours which are implied by different assumptions on the age structure of immigrants. Mitra (1987 and 1990) has studied more in detail some asymptotic properties of populations subjected to migrations. Cerone (1987) has provided a more rigorous renewal analysis for the stable population model with immigrations. Schmertmann (1992) has considered more in detail the possible "rejuvenating" role played by the immigration streams in populations characterized by below replacement fertility. General theoretical results for multiregional-multistate extensions of the basic model are developed in a series of papers by Inaba (1988a,1988b,1993).

In what follows we recall the basic features and results for the stable population model with immigrations (SPI) with reference to the more relevant case of below replacement fertility.

In broad terms a population model with immigrations is described by the following McKendrick-Von Foerster type PDE (Langhaar 1972):

$$\left(\frac{\partial}{\partial} + \frac{\partial}{\partial}\right) n(a,t) = I(a,t) - \mu(a,t)n(a,t) \tag{1}$$

subjected to the following boundary and initial conditions:

$$\begin{aligned} n(0,t) &= B(t) = \int_0^\infty n(a,t)m(a,t)da \\ n(a,0) &= n_0(a) \end{aligned} \tag{2}$$

where $n(a,t)$ is the age structure of the population, $I(a,t)$ the age-structured immigration stream at time t, $B(t)$ the birth density per unit time, $m(a,t)$ and $\mu(a,t)$ the time invariant age dependent fertility and mortality rates. The previous models thereby embodies the critical demographic assumption that the immigrants, once entered, imediately subsume the demographic behaviours of the host population as stated by their mortality and fertility rates. Some general results concerning model (1) are available since the paper by Langhaar (1972) (some note is reported in the appendix).

It is to be noticed that, by correctly reinterpreting the several quantities involved (vectors and matrices in place of scalar functions), the formalism (1) can be extended to treat much more general population processes, such as general multiregional-multistate age dependent population dynamics subjected to immigrations from the rest of the world. In such case we would have for the i-th local population of a given multiregional system the following PDE:

$$\left(\frac{\partial}{\partial} + \frac{\partial}{\partial}\right) n_i(a,t) = -\left[\mu_i(a,t) + q_i(a)\right] n_i(a,t) + \sum_j q_{ji}(a,t) n_j(a,t) + I_i(a,t)$$

where q_{ji} are the "internal" migration rates from region j to region i, and:

$$q_i(a,t) = \sum_j q_{ij}(a,t)$$

is the total emigration rate from the i-th population. Moreover n_i are the population densities in the m regions, and finally I_i are the exogenous migrations from the rest of the world.

The last expression can be rewritten in compact form as:

$$\left(\frac{\partial}{\partial} + \frac{\partial}{\partial}\right) \underline{n}\,(a,t) = Q(a,t)\,\underline{n}\,(a,t) + \underline{I}\,(a,t) \tag{3}$$

where $\underline{n}, \underline{I}$ denote respectively the population vector of the n geographic areas involved and the vector of immigration from the rest of the world toward

such populations, and Q is a generalised survival (or attrition) matrix which captures the overall age dependent attrition process.

For what concerns dynamical properties of the model (3), a rigorous analysis is of given in Inaba 1988, who presents both a "traditional type" solution, by showing that the problem can be put in a standard renewal form and thereby analysed by means of standard demographic tools, and a modern semigroup approach.

In what follows we will, coherently with our main interest, rather be interested in the more specific and simpler models considered in the more recent demographic literature involving a constant over time migration stream toward a stable population with below replacement fertility. Let us then consider, following Arthur et al. (1982), a stably (ie characterized by time invariant age dependent mortality and fertility schedules) decaying "host" population due to a basic reproduction rate (R_0) less than one:

$$R_0 = \int_0^\infty m(a)\Phi(a)da < 1$$

where Φ is the survival function, which is exposed to a constant over time migration stream I(a). Under the given assumptions, equation 1 reduces to:

$$\left(\frac{\partial}{\partial} + \frac{\partial}{\partial}\right) n(a,t) = I(a) - \mu(a)n(a,t) \tag{4}$$

Under the assumption of below replacement fertility, the constant immigration model admits a unique stationary solution which is also GAS. Such equilibrium solution is found from the time independent ODE associated to (4):

$$\frac{dn(a)}{da} = I(a) - \mu(a)n(a) \tag{5}$$

Equation (5) gives:

$$n(a) = n(0)\Phi(a) + \int_0^a I(s)\frac{\Phi(a)}{\Phi(s)}ds = n_N(a) + n_I(a) \tag{6}$$

where:

$$\Phi(a) = e^{-\int_0^a \mu(s)ds}$$

is the survival function,and $n_N(a) + n_I(a)$ are, respectively the native and the immigrated components of the total population. By substituting (6) within the boundary condition (2) we get:

$$\begin{aligned} B(t) &= B = \int_0^\infty n(a,t)m(a)da = \\ &= \int_0^\infty \left[n(0)\Phi(a) + \int_0^a I(s)\frac{\Phi(a)}{\Phi(s)}ds \right] m(a)da = \\ &= n(0)\int_0^\infty \Phi(a)m(a)da + \int_0^\infty \int_0^a I(s)\frac{\Phi(a)}{\Phi(s)}m(a)dsda = \\ &= BR_0 + B_I \end{aligned} \tag{7}$$

where the first term is the internal components of births, while B_I are the births from immigrated individuals once entered the host population. We so easily get the equilibrium solution for total births:

$$B = \frac{B_I}{1 - R_0} \tag{8}$$

From (8) the equilibrium age structureof the total population follows by substituting (7) into (6):

$$\begin{aligned} n(a) &= n(0)\Phi(a) + \int_0^a I(s)\frac{\Phi(a)}{\Phi(s)}ds = B\Phi(a) + \int_0^a I(s)\frac{\Phi(a)}{\Phi(s)}ds = \\ &= \frac{B_I}{1 - R_0}\Phi(a) + n_I(a) \end{aligned}$$

Hence the total population at equilibrium is:

$$n = Be_0 + n_I \tag{9}$$

For what concerns dynamical properties of the basic model (4), a rigorous proof of the GA stability of the equilibrium solution has been given by Cerone (1987) (but see also the already quoted Inaba 1988) by showing that the problem can be put in a standard renewal form and thereby analysed by means of standard demographic tools. A heuristic justification only valid for the below replacement fertility case with constant immigrations, can be given (as done in Arthur et al. 1982), by constructing the long term renewal

equation of model (4). This is obtained by substituting the long term solution ($t > a$) of (4):

$$n(a,t) = B(t-a)p(a) + \int_0^a I(x)\frac{p(a)}{p(x)}dx = B(t-a)p(a) + n_I(a) \qquad (10)$$

into the birth equation. We so get:

$$B(t) = \int_0^\infty \left[B(t-a)p(a) + n_I(a)\right] m(a)da = \int_0^\infty B(t-a)\varphi(a)da + B_I \quad (11)$$

where B are the births from immigrants:

$$B_I = \int_0^\infty \int_0^a I(x)\frac{p(a)}{p(x)}m(a)dxda$$

The equation 11 is a renewal equation with a constant forcing term and can be easily solved by means of Laplace transform approach. Its asymptotic behaviour is obtained, by means of the tauberian theorems on Laplace transforms, the application of which is always valid under the assumption of $R_0 < 1$, as:

$$\lim_{t\to\infty} B(t) = \lim_{s\to 0} sB^*(s) = \lim_{s\to 0} \frac{B_I}{1-\varphi^*(s)} = \frac{B_I}{1-R_0}$$

which is exactly (8).

Quite a remarkable problem is the evaluation of the impact on the long term equilibrium size of the population of several age profiles of the immigration schedule. Let us then consider the equilibrium size of the total population:

$$n = Be_0 + n_I = \frac{B_I}{1-R_0}e_0 + n_I \qquad (12)$$

which can be rewritten as:

$$\begin{aligned} n &= \frac{e_0}{1-R_0}\int_0^\infty \int_0^a I(s)\frac{\Phi(a)}{\Phi(s)}m(a)dsda + \int_0^\infty n_I(a)da = \qquad (13) \\ &= \frac{e_0}{1-R_0}\int_0^\infty \left(\int_0^a I(s)\frac{\Phi(a)}{\Phi(s)}m(a)\right)dsda + \int_0^\infty \left(\int_0^a I(s)\frac{\Phi(a)}{\Phi(s)}ds\right)da \end{aligned}$$

Let us now interchange the order of integration in both expressions We get, by writing as ω (rather than ∞) the upper bound of the possible ages (the domains changes from: $0 \leq a \leq \omega; 0 \leq s \leq a$; to $0 \leq s \leq \omega; s \leq a \leq \omega;$).

$$\begin{aligned} n &= \frac{e_0}{1-R_0}\int_0^{\infty}\left(\int_0^a I(s)\frac{\Phi(a)}{\Phi(s)}m(a)ds\right)da + \int_0^{\infty}\left(\int_0^a I(s)\frac{\Phi(a)}{\Phi(s)}ds\right)da = \\ &= \frac{e_0}{1-R_0}\int_0^{\omega} I(s)\cdot\left[\frac{1}{\Phi(s)}\left(\int_s^{\omega}\Phi(a)m(a)da\right)\right]ds + \int_0^{\omega} I(s)\left(\int_s^{\omega}\frac{\Phi(a)}{\Phi(s)}da\right)ds \quad (14) \\ &= \frac{e_0}{1-R_0}\int_0^{\omega} I(s)\cdot U(s)ds + \int_0^{\omega} I(s)e(s)ds \end{aligned}$$

where:

$$U(s) = \frac{1}{\Phi(s)}\left(\int_s^{\omega}\Phi(a)m(a)da\right) \quad (15)$$

The U(s) quantity represents the conditional (conditionally on being still alive at age s) expected number of of daughters remaining to be born since ages s per a single woman aged s. Definitively (14) expresses the final size at any moment of time as the sum of two components both related to the immigration flows: a)the future population of native-borns descendants of immigrants; b)the number of past immigrants who are still alive at that time. We can write:

$$n = \frac{Ve_0}{1-R_0} + \int_0^{\omega} I(s)e(s)ds \quad (16)$$

where:

$$V = \int_0^{\omega} I(s)\cdot U(s)ds \quad (17)$$

where V is the actual content of "birth potential" contained in the immigration profile. In particular if we assume that the migration flow is concentrated at only one age x, (ie: I(x) migrants aged exactly x) we can write:

$$n = \frac{e_0}{1-R_0}I(x)v(x) + I(x)e(x) \quad (18)$$

which has a quite easy interpretation.

3 Immigrations in demo-epidemiological models

There exists at present an extensive body of literature on the specific role of "demography" in epidemiological models. For what concerns the role of vital dynamics several efforts have been made in recent time to systematically remove the classical assumption of a constant population, typical of the simplest epidemic models. Among these, mostly stimulated by the need to understand the dynamics of long term epidemics, such as HIV, we recall Anderson, May and McLean (1988), Busenberg and VanDenDriessche (1991), Jacquez et al. 1988, Mena-Lorca and Hethcote (1992), Gao and Hethcote (1992), Mena-Lorca, Gao and Hethcote (1995), Thieme (1992 and 1994)

For what concerns more specifically the problem of migrations of pathogens among a system of local populations several research directions have been developed. A first one, quite popular among theoreticians, derives from the ideas of classical physical diffusion theory and is based on the superimposition of several epidemic mechanisms on a population which spreads spatially following a suitable diffusion PDE (some references in the classical Bailey 1975). Although such an approach can result quite useful for biological populations, its assumptions are very unrealistic for human populations and it will not furtherly mentioned here. More closely to the traditional demographic tool-box, Bailey (1975) introduces a simplified version of the classical "russian" model for influenza, in which epidemic spreads in a system of local subpopulations which interact among them on the basis of a classical markov migration model Remarkably, already at that time Bailey was noticing how sharply the introduction of geographical heterogeneity puts in crisis the classical homogeneous mixing apparatus based on bilinear mass action incidences: if we consider two cities which differ only in the amplitude of their populations, the respective localised FOI's would be different just because, under bilinear mass action assumptions, they directly reflect the relative size of their populations.

Specifically motivated by this last fact, i.e. that usually, since individuals are distributed in space, this implies, as a rule, non random mixing between individuals of different groups, Sattenspiel (1987) has modelled the spread of a disease as a consequence of the natural interaction among individuals of a population due to the need for the attendance of common social functions. She explicitly considers a population consisting of several interacting

subpopulation. Two different types of interactions between individuals are considered: interaction (essentially at random) between individuals within each subpopulations because of "geographic" (latu sensu) proximity, and interactions between individual of the same or different subpopulations because of the attendance of common social functions. The main results of the model are in Sattenspiel (1987) and Sattenspiel and Simon (1988).

Sattenspiel and Powell (1993) have studied the measles epidemic in Dominica in 1984 by connecting the geographic distribution of incidence of measles essentially to the observed mobility pattern. Motivated by such problems Sattenspiel (1994) and Sattenspiel and Dietz (1995) have considered in broad terms the problem of mobility by developing a basic mover-stayer type model which is quite well suited for the study of temporary mobility, ie simple patterns of mobility such as daily commuting, which involve a start from the residence place with a visit to another region and than coming back to the originary region (without multiple visits to other regions). Their model is based, given n interacting subpopulations, on a system of n^2 equations, describing the dynamics of both N_{ij} ("movers": those residents at region "i" who are in region "j" at time t) and N_{ii} type individuals. A merit of the scheme by Sattenspiel and Dietz is that of being a quite flexible tool in that practically all types of mobility behaviour can be represented as its special cases.

Sattenspiel and Dietz (1995) also show how to apply the model to study the geographical spread of diseases in subpopulations which are characterised among them by such mobility behaviours.

Despite the relevance of the aforementioned contributions, they just constitute examples of the role played by population mouvements in determining the actual transmission dynamics of a disease in a given population. As quoted in the introduction, the broad immigrations streams experienced by some developed countries such as Italy in the very last period, have a different nature compared with the problems those previously considered: they constitute in many cases definitive migrations which could contribute to shape in a new way the host population. In this case, even from the point of view of public health authorities, the more relevant questions do not regard, as in the Sattenspiel and Dietz model, the shape of the mobility process and the way in which this shape influences the dynamics of a a given infectous diseases, but essentially the features (age, epidemiological status, etc) of the entering population and how these features impact on the dynamics of the infectious diseases experienced by the host population. From this point of

view the natural tool-box appears to be the demographic theory exposed in the section two. It is therefore the aim of the present paper to develop a demoepidemic framework which tries to assess the role of immigrants profile in determining the shape of endemic profile of a population. Although very simple this type of models appears to be the natural tools by which to deal with the present problem. In what follows we will only be concerned with the case of a below-replacement fertility population since this latter was the motivation of the present work, but there are no difficulties in treating other cases.

We finally briefly mention another possible useful development, which is our aim to consider in a foregoing work. It still lacks, at least to my knowledge, in epidemiological theory an explicit consideration of infection processes within systems of subpopulations interacting among them through the typical demographic mechanism of the multiregional model (a.4). The multiregional model is obtained by superimposing the typical markov model for population redistribution to classical population theory à la Lotka-Leslie (Rogers 1975). The direct consideration of whatever epidemiological mechanism, for instance a classical SIR scheme, within the frame of the demographic multiregional scheme briefly introduced in section two, gives rise the following multiregional multistate model:

$$\begin{aligned}
\left(\frac{\partial}{\partial} + \frac{\partial}{\partial}\right) X_i(a,t) &= -\left[\mu_i(a,t) + q_i^X(a) + \lambda_i(a,t)\right] X_i(a,t) + \\
&\quad + \sum q_{ji}^X(a,t) X_j(a,t) + I_i^X(a,t) \\
\left(\frac{\partial}{\partial} + \frac{\partial}{\partial}\right) Y_i(a,t) &= \lambda_i(a,t) X_i(a,t) - \left[\mu_i(a,t) + \upsilon_i(a) + q_i^Y(a)\right] Y_i(a,t) \\
&\quad + \sum q_{ji}^Y(a,t) Y_j(a,t) + I_i^Y(a,t) \\
\left(\frac{\partial}{\partial} + \frac{\partial}{\partial}\right) Z_i(a,t) &= \upsilon_i(a) Y_i(a,t) - \left[\mu_i(a,t) + q_i^Z(a)\right] Z_i(a,t) + \\
&\quad + \sum q_{ji}^Z(a,t) Z_j(a,t) + I_i^Z(a,t)
\end{aligned} \tag{19}$$

The previous model, which assumes migration rates differentiated on the basis of the epidemiological statuses of migrants,despite the trick of writing the incidence of the disease as a linear term, is a genuine nonlinear multistate-multiregional model for the geographical diffusion of epidemics.

A simplified version without age of the previous model takes the form:

$$\begin{aligned}
\dot{X}_i(t) &= \Lambda_i - [\mu_i + q_i + \lambda_i(t)] X_i(t) + \sum q_{ji}(t) X_j(t) + I_i^X(t) \\
\dot{Y}_i(t) &= \lambda_i(t) X_i(t) - [\mu_i + v_i + q_i] Y_i(t) + \sum q_{ji} Y_j(t) + I_i^Y(t) \\
\dot{Z}_i(t) &= v_i Y_i(t) - [\mu_i + q_i] Z_i(t) + \sum q_{ji} Z_j(t) + I_i^Z(t)
\end{aligned} \tag{20}$$

which adds vital dynamics as well to the basic markov scheme used by Bailey 1975. A simplified version of model (20) was considered for instance in Scalia Tomba (1991) to deal with the problem of migrations of individuals from high risk groups to lower risk groups as a consequence of the social alarm induced by HIV/AIDS.

4 A basic SIR model with constant immigrations spread in all the epidemiological classes

In thus chapter we start our investigation of the demographic problem of evaluating the consequences of a definitive immigration stream with its epidemiological load toward a given host population.To do this we will cast the study of the transmission dynamics of a typical SIR disease within the demographic frame of "stable through immigrations" populations.

Let us to begin start from the following basic SIR model characterized by a stationary demography obtained through a below replacement fertility plus constant immigrations in all epidemiological classes.

$$\begin{aligned}
\dot{X} &= I_X + bN - (\mu + \lambda) X \\
\dot{Y} &= I_Y + \lambda X - (\mu + v) Y \quad \lambda = \beta Y \\
\dot{Z} &= vY + I_Z - \mu Z
\end{aligned} \tag{21}$$

The previous model differs from the classical SIR epidemiological model in that the recruitment takes place in all the distinct epidemiological classes and not only in the susceptible one.

By adding the three state equations we get:

$$\dot{N} = \dot{X} + \dot{Y} + \dot{Z} = I + bN - \mu(X + Y + Z) \tag{22}$$

ie:

$$\dot{N} = I + (b - \mu)N \tag{23}$$

where: $I = I_X + I_Y + I_z$,which, under the below replacement fertility assumption, gives rise to a long term stationary population at the level I/r $(r = b - \mu)$. This is formally analogous to the assumption, quite frequent in standard epidemiological modelling, of a constant recruitment in the susceptible class plus mortality at a constant rate (sometimes called CID, "constant immigration demography". For what concerns the specific role of the CID assumption the reader may refer for instance to Bailey 1975, Jacquez et al. 1988, Capasso 1992, Mena-Lorca and Hethcote 1993. All these models assume that, as usual in standard epidemiological theory, all the recruitment flow is concentrated within the susceptible class.

The most peculiar feature of epidemic models with immigrations not limited to the sole susceptible class but spread over all the epidemiological classes is the imediate lost of the existence of the DFE, a fact which implies the lost of the threshold character typical of the classical epidemiological models. This fact was pointed out by Bailey (1975) an in his basic model for susceptible and carriers dynamics, with recruitment at constant rate in both classes. Bailey's model is described by the equations:

$$\begin{aligned} \dot{X} &= I_X - \beta XY \\ \dot{Y} &= I_Y - vY \end{aligned}$$

Having always in mind the role of carriers in a basic SIR model, in his nowadays classical paper (1976), Hethcote noticed that the presence of a constant number of carriers in the host population prevents the existence of the disease free equilibrium equilibrium, thereby eliminating the thresholds character of the model. This is quite obvious to realize: a constant inflow of infectious individuals from year to year implies that eradication is definitively a not reachable target, a fact observed many times in real populations. This fact raises the need to redefine the target of the possible immunization policies, usually aimed to eradication in classical epidemiological models. We will discuss these aspects more fully elsewhere.

4.0.1 Equilibrium calculations

Since DFE are no more possible, the system only possesses an endemic equilibrium of which it is quite easy to conjecture the global stability. We get:

$$\begin{array}{lll} \dot{X}=0 & \rightarrow & X^* = \frac{I_X+bN}{\mu+\lambda} \\ \dot{Y}=0 & \rightarrow & Y^* = \frac{I_Y+\lambda^* X^*}{\mu+v} = \frac{I_Y}{\mu+v} + \frac{\lambda^*}{\mu+v} X^* = \frac{I_Y}{\mu+v} + \frac{\lambda^*}{\mu+v}\frac{I_X+bN}{\mu+\lambda^*} \\ \dot{Z}=0 & \rightarrow & Z^* = N - (X^* + Y^*) \end{array}$$

and so, suppressing the * for short:

$$\begin{array}{l} X = \frac{I_X+bN}{\mu+\lambda} \\ Y = \left(\frac{I_Y}{\mu+v} + \frac{\lambda}{\mu+v}\frac{I_X}{\mu+\lambda}\right) + \frac{\lambda}{\mu+v}\frac{bN}{\mu+\lambda} \\ \lambda = \beta Y = \beta\left[\left(\frac{I_Y}{\mu+v} + \frac{I_X}{\mu+v}\frac{\lambda}{\mu+\lambda}\right) + \frac{\lambda}{\mu+v}\frac{bN}{\mu+\lambda}\right] \end{array} \tag{24}$$

Notice that in the last equilibrium expressions we have separated the old term inherited from the basic SIR model without immigrations from the new one due to migrations.

a)by assuming that the equilibrium FOI is much larger than the death rate, we get the approximate evaluation for the equilibrium FOI itself:

$$\lambda = \beta Y = \beta\left[\left(\frac{I_Y}{\mu+v} + \frac{I_X}{\mu+v}\right) + \frac{bN}{\mu+v}\right] = \frac{\beta}{\mu+v}\left[(I_X + I_Y) + bN\right] \tag{25}$$

The last expression, apart the neglection of the death rate is quite similar to the equilibrium FOI of the basic SIR model:

$$\lambda = \mu\left[\frac{\beta N}{\mu+v} - 1\right] = \frac{\beta\mu N}{\mu+v} - \mu \tag{26}$$

with the difference due to the explicit appearance of the two migrations terms. Anyway this last notation suggests a useful interpretation of the equilibrium FOI of the basic SIR model. The equilibrium FOI is the percentage rate at which new infections appear, at equilibrium. In the last expression this rate is defined as the difference between the product and the death rate.

b)More precisely, let us work on the general:

$$\lambda = \frac{\beta}{\mu+v}\left[\left(I_Y + I_X\frac{\lambda}{\mu+\lambda}\right) + \frac{\lambda bN}{\mu+\lambda}\right] = \frac{\beta}{\mu+v}\left[\frac{(\mu+\lambda)I_Y + \lambda(I_X+bN)}{\mu+\lambda}\right]$$

from which we get:

$$\lambda(\mu+\lambda) = \frac{\beta}{\mu+v}\left[\mu I_Y + \lambda(I_X + I_Y + bN)\right]$$

so obtaining the quadratic equation in λ:

$$\lambda^2 - (A - \mu)\lambda - B = 0 \tag{27}$$

where:

$$A = \frac{\beta}{\mu+v}(I_X + I_Y + bN) \quad B = \frac{\beta}{\mu+v}\mu I_Y \tag{28}$$

It's easy to check that equation (3.9) always has two real solutions, only one of which is positive, the greater one namely, and so adequate to the representation of the equilibrium FOI. In fact:

$$\lambda = \frac{1}{2}\left(A - \mu \pm \sqrt{(A-\mu)^2 + 4B}\right)$$

which shows that, independently on the fact that A is greater or lesser than μ, one and only solution is always epidemiologically meaningful.

Finally, the susceptible fraction at equilibrium is given by:

$$s = \frac{X}{N} = \frac{I_X + bN}{N(\mu + \lambda)}$$

4.0.2 The effects of vaccination

Let us now introduce vaccination into the basic system, by assuming that: i)a fraction p_1 of the native newborn population is vaccinated at birth, ii)there exist a screening on immigrants, which is of course uneffective on recovered and infective individuals, but is able to immunize a fraction p_2 of the susceptibles. The basic system of the previous section will consequently modify to:

$$\begin{aligned} \dot{X} &= (1-p_2)I_X + (1-p_1)bN - (\mu+\lambda)X \\ \dot{Y} &= I_Y + \lambda X - (\mu+v)Y \qquad\qquad \lambda = \beta Y \\ \dot{Z} &= p_1 bN + p_2 I_X + vY + I_Z - \mu Z \end{aligned} \tag{29}$$

Since our system has no threshold character we can not have a goal of eradication unless we assume the imported infections can be driven to zero. Rather it is expected that the role of vaccination can be that of minimizing the number of infections due to the internal metabolism of the disease.

We get:

$$
\begin{aligned}
X^* &= \frac{(1-p_2)I_X + (1-p_1)bN}{\mu+\lambda} \\
Y^* &= \frac{I_Y + \lambda X^*}{\mu+v} = \frac{I_Y}{\mu+v} + \frac{\lambda}{\mu+v}\frac{(1-p_2)I_X + (1-p_1)bN}{\mu+\lambda} \\
\lambda^* &= \beta Y^* = \beta\left[\frac{I_Y}{\mu+v} + \frac{\lambda^*}{\mu+v}\frac{(1-p_2)I_X + (1-p_1)bN}{\mu+\lambda^*}\right]
\end{aligned}
\tag{30}
$$

In particular, if the vaccination of immigrant susceptibles is not possible at the moment of entry but must be delayed ($p_2 = 0$) the last expressions simplify to:

$$
\begin{aligned}
X^* &= \tfrac{I_X+(1-p_1)bN}{\mu+\lambda^*} \\
Y^* &= \tfrac{I_Y+\lambda^* X^*}{\mu+v} = \tfrac{I_Y}{\mu+v} + \tfrac{\lambda^*}{\mu+v}\tfrac{I_X+(1-p_1)bN}{\mu+\lambda^*} \\
\lambda^* &= \beta Y^* = \beta\left[\tfrac{I_Y}{\mu+v} + \tfrac{\lambda^*}{\mu+v}\tfrac{I_X+(1-p_1)bN}{\mu+\lambda^*}\right]
\end{aligned}
\tag{31}
$$

Determination of the equilibrium FOI is analogous to the previous case; suppressing again * for short, we get:

$$
\lambda = \beta\left[\frac{I_Y}{\mu+v} + \frac{\lambda}{\mu+v}\frac{(1-p_2)I_X + (1-p_1)bN}{\mu+\lambda}\right] \tag{32}
$$

from which follows:

$$
\lambda(\mu+\lambda) = \frac{\beta}{\mu+v}\left[I_Y(\mu+\lambda) + \lambda\left((1-p_2)I_X + (1-p_1)bN\right)\right] \tag{33}
$$

i.e.:

$$
\lambda(\mu+\lambda) = \frac{\beta}{\mu+v}\left[\mu I_Y + \lambda\left(I_Y + (1-p_2)I_X + (1-p_1)bN\right)\right] \tag{34}
$$

giving the quadratic equation in λ:

$$
\lambda^2 - (A_V - \mu)\lambda - B_V = 0 \tag{35}
$$

In particular:

$$
A_V = \tfrac{\beta}{\mu+v}(I_Y + (1-p_2)I_X + (1-p_1)bN) \quad B_V = \tfrac{\mu\beta}{\mu+v}I_Y \tag{36}
$$

and:

$$B_V = B \quad \frac{B}{\mu} < A_V < A \tag{37}$$

As for its counterpart without vaccination (3.6), equation (4.6) has one and only one epidemiologically meaningful solution.

4.0.3 Stability analysis

It is quite natural to conjecture that, since the system does not possess any DFE equilibrium, the unique endemic equilibrium of the system (3.1) be always GAS. The actual proof can be done for instance by adopting Beretta and Capasso (Capasso 1993) representation which uses as main ingredients the existence of a unique endemic equilibrium plus bilinearity of the FOI (see the appendix for the actual proof). Another simple strategy is to observe that the total population decouples and always goes to its equilibrium. This permits to study the long term behaviour of the full system as the behaviour of an asymptotic two-dimensional system, of which it is easy to prove the global stability. For details see Manfredi and Salinelli (1997).

5 The fully age structured SIR problem with immigrations

By explicitly introducing age-structure within the basic SIR problem of the previous section, we have the following system of Ross-McKendrick-VonFoerster PDE's:

$$\begin{aligned} \Delta X(a,t) &= I_X(a,t) - (\mu(a) + \lambda(t))X(a,t) \\ \Delta Y(a,t) &= I_Y(a,t) + \lambda(t)X(a,t) - (\mu(a) + v)Y(a,t) \\ \Delta Z(a,t) &= I_Z(a,t) + vY(a,t) - \mu(a)Z(a,t) \end{aligned} \tag{38}$$

where:

$$\Delta = \frac{\partial}{\partial a} + \frac{\partial}{\partial t}$$

is the McKendrick-VonFoerster aging operator, and $\mu(a)$ is the age dependent force of mortality. As a starting point we will choose the simplest assumption for the FOI $\lambda(t)$, ie of course the traditional homogeneous mixing assumption:

$$\lambda(t) = \beta \int_0^\infty Y(a,t)da = \beta Y(t) \tag{39}$$

System (1) has to be completed by suitable BC. Assuming no vertical transmission of the disease (all births susceptibles):

$$X(0,t) = B(t) \quad Y(0,t) = 0 \quad Z(0,t) = 0 \tag{40}$$

where B(t) are the births per unit time. Finally we need a set of prescribed initial distributions:

$$X(a,0) = X_0(a) \quad Y(a,0) = Y_0(a) \quad Z(a,0) = Z_0(a) \tag{41}$$

By adding the three equation (1), we obtain the total population PDE:

$$\Delta n(a,t) = I(a,t) - \mu(a)n(a,t) \tag{42}$$

where I(a,t) is the total immigration rate of age a at time t:

$$I(a,t) = I_X(a,t) + I_Y(a,t) + I_Z(a,t)$$

The PDE (5.4) inherits the following boundary and initial conditions:

$$BC: \; n(0,t) = B(t) \quad n(a,0) = n_0(a) = X_0(a) + Y_0(a) + Z_0(a)$$

If we explicitly assume that the total immigrations take place at a constant rate and with a time invariant age-structure, we get:

$$\Delta n(a,t) = I(a) - \mu(a)n(a,t) \tag{43}$$

which is the basic PDE of the so called "constant immigrations" extension of the stable population model encountered in the second section. Notice that in the event of constant births and deaths rates we can recover, by integrating both members of (40) over all the age span, the ODE (23). The integration gives:

$$\dot{N}(t) = \int_0^\infty I(a)da + \int_0^\infty b(a)n(a,t)da - \int_0^\infty \mu(a)n(a,t)da = \tag{44}$$

$$= \tag{45}$$

from which (23) follows by assuming age independent birth and death rates:

$$\dot{N} = I + (b - \mu)N$$

For more detailed considerations on the mathematical properties of the system (38) see Manfredi and Salinelli (1997).

6 Characteristics of the endemic equilibrium corresponding to the stable long term population

The equilibrium system associated to system (5.1) is given by the following ODE system:

$$\begin{array}{l} \frac{dX(a)}{da} = I_X(a) - (\mu(a) + \lambda)X(a) \\ \frac{dY(a)}{da} = I_Y(a) + \lambda X(a) - (\mu(a) + v)Y(a) \quad \lambda = \beta Y \\ \frac{dZ(a)}{da} = I_Z(a) + vY(a) - \mu(a)Z(a) \end{array} \tag{46}$$

where λ is the constant FOI of equilibrium. The inherited initial conditions at age zero are:

$$\begin{aligned} X(a &= 0) = B \\ Y(a &= 0) = 0 = Z(a = 0) \end{aligned}$$

Of course:

$$\frac{dn(a)}{da} = I(a) - \mu(a)n(a)$$

which is the equilibrium equation of the underlying demography.
System (46) is a linear forced system of the form:

$$\frac{dU(a)}{da} = B(a)U(a) + I(a) \tag{47}$$

where:

$$B(a) = \begin{pmatrix} -(\mu(a) + \lambda) & 0 & 0 \\ \lambda & -(\mu(a) + v) & 0 \\ 0 & v & -\mu(a) \end{pmatrix}; I(a) = \begin{matrix} I_X(a) \\ I_Y(a) \\ I_Z(a) \end{matrix} \tag{48}$$

Under usual assumptions system (46) has one and only one solution, so guaranteeing that the endemic state solution is always well defined. The explicit solution of the equilibrium system should provide also an expression for the equilibrium FOI of the model.

Explicit calculations give us:

$$\begin{aligned} n(a) &= n(0)e^{-\int_0^a \mu(s)ds} + \int_0^a e^{-\int_s^a \mu(x)dx} I(s)ds \\ X(a) &= X(0)e^{-\int_0^a (\mu(s)+\lambda)ds} + \int_0^a e^{-\int_s^a (\mu(x)+\lambda)dx} I_X(s)ds \\ Y(a) &= Y(0)e^{-\int_0^a (\mu(s)+v)ds} + \int_0^a e^{-\int_s^a (\mu(x)+v)dx} \left[I_Y(s) + \lambda X(s)\right] ds \\ Z(a) &= n(a) - X(a) - Y(a) \end{aligned} \tag{49}$$

By remembering that $Y(0) = 0$, $n(0) = X(0) = B$, and introducing the following quantities:

$$\begin{aligned} \Phi(a) &= e^{-\int_0^a \mu(s)ds} \\ \Lambda(a) &= e^{-\lambda a} \\ V(a) &= e^{-va} \end{aligned}$$

we can write (49) in a more interpretable form:

$$\begin{aligned} n(a) &= B\Phi(a) + \int_0^a I(s)\tfrac{\Phi(a)}{\Phi(s)}ds \\ X(a) &= B\Phi(a)\Lambda(a) + \int_0^a I_X(s)\tfrac{\Phi(a)}{\Phi(s)}\tfrac{\Lambda(a)}{\Lambda(s)}ds \\ Y(a) &= \int_0^a I_Y(s)\tfrac{\Phi(a)}{\Phi(s)}\tfrac{V(a)}{V(s)}ds + \int_0^a \lambda X(s)\tfrac{\Phi(a)}{\Phi(s)}\tfrac{V(a)}{V(s)}ds \\ Z(a) &= n(a) - X(a) - Y(a) \end{aligned} \tag{50}$$

In particular by substituting the expression for the number susceptibles in the infectious equation we get:

$$\begin{aligned} Y(a) &= \int_0^a I_Y(s)\frac{\Phi(a)}{\Phi(s)}\frac{V(a)}{V(s)}ds + \int_0^a \lambda X(s)\frac{\Phi(a)}{\Phi(s)}\frac{V(a)}{V(s)}ds = \\ &= Y_1(a) + \lambda\int_0^a \left[B\Phi(s)\Lambda(s) + \int_0^s I_X(u)\frac{\Phi(s)}{\Phi(u)}\frac{\Lambda(s)}{\Lambda(u)}du\right]\frac{\Phi(a)}{\Phi(s)}\frac{V(a)}{V(s)}ds \\ &= Y_1(a) + \lambda\left[BQ_1(a) + Q_2(a)\right] \end{aligned} \tag{51}$$

where:

$$
\begin{aligned}
Q_1(a) &= \int_0^a \Phi(s)\Lambda(s)\frac{\Phi(a)}{\Phi(s)}\frac{V(a)}{V(s)}ds = \Phi(a)V(a)\int_0^a \frac{\Lambda(s)}{V(s)}ds = \\
Q_2(a) &= \int_0^a \int_0^s I_X(u)\frac{\Phi(s)}{\Phi(u)}\frac{\Lambda(s)}{\Lambda(u)}\frac{\Phi(a)}{\Phi(s)}\frac{V(a)}{V(s)}duds
\end{aligned}
$$

The last of (51) decomposes the total number of infectives individuals aged a at equilibrium into two main components: a first component composed by immigrated infectives (i.e. infected abroad) survived to death and recovery, and a second component composed by individuals who were infected within the population. This last can be furtherly decomposed into two parts: native susceptibles and immigrated susceptibles.

From the last relations it's easy to determine the equilibrium FOI:

$$\lambda = \beta \int_0^\infty Y(a)da = \beta Y \tag{52}$$

We have:

$$
\begin{aligned}
Y &= \int_0^\infty Y(a)da = \int_0^\infty \left[Y_1(a) + \lambda\left(BQ_1(a) + Q_2(a)\right)\right]da = \\
&= Y_1 + \lambda\left(BQ_1 + Q_2\right)
\end{aligned} \tag{53}
$$

where:

$$Q_1 = \int_0^\infty Q_1(a)da \quad Q_2 = \int_0^\infty Q_2(a)da \tag{54}$$

Hence:

$$\lambda = \beta\left[Y_1 + \lambda\left(BQ_1 + Q_2\right)\right]$$

and finally:

$$\lambda = \frac{\beta Y_1}{1 - \beta\left(BQ_1 + Q_2\right)} \tag{55}$$

The last relationship implies that to have an epidemiologically meaningful (i.e. positive) equilibrium FOI we have to show that:

$$\left(BQ_1 + Q_2\right)\beta < 1 \tag{56}$$

For more details see Manfredi and Salinelli (1997).

7 Effects of the immigrants profile on the endemic equilibrium

By simple manipulations of the equilibrium age structure it is possible to put in evidence the role of the immigrants profile on the long term equilibrium of the population. Let us then generalise formulas such as (18) to all the epidemiological classes. We get for the total number of susceptibles at equilibrium:

$$\begin{aligned} X &= \int_0^\infty X(a)da = \int_0^\infty \left[B\Phi(a)\Lambda(a) + \int_0^a I_X(s)\frac{\Phi(a)}{\Phi(s)}\frac{\Lambda(a)}{\Lambda(s)}ds \right] da = \\ &= B\int_0^\infty \Phi(a)\Lambda(a)da + \int_0^\infty \left(\int_0^a I_X(s)\frac{\Phi(a)}{\Phi(s)}\frac{\Lambda(a)}{\Lambda(s)}ds \right) da = \\ &= Be_0^X + \int_0^\infty I_X(s) \left(\int_s^\infty \frac{\Phi(a)}{\Phi(s)}\frac{\Lambda(a)}{\Lambda(s)}da \right) ds = \\ &= Be_0^X + \int_0^\infty I_X(s)e_s^X ds \end{aligned} \tag{57}$$

Formula (57) is analogous to (18), and its interpretation is straightforward. The quantity e_0^X is the expectation of life in the susceptible state for newborn individuals. Hence (57) says that the total number of susceptible at equilibrium is the sum of two components: a)a traditional one, given by the product of the number of births per unit time times the expectation of life in the susceptible state (s state); b)a second one due to immigration of susceptibles, which is the sum of the several generation of entries of susceptible individuals of the various ages times their expectation of life in s state state at the age of entrance.The susceptible fraction at equilibrium may then be expressed as:

$$S = \frac{Be_0^X + \int_0^\infty I_X(s)e_s^X ds}{Be_0 + \int_0^\omega I(s)e(s)ds} \tag{58}$$

Formula (57) can be furtherly developed by introducing the definition of B at equilibrium, hence deriving the complete role of immigrations on the equilibrium schedules of the population.

Perhaps the most simple and interesting application of the framework developed so far is the evaluation of the impact of several age profiles of the

immigrants on the susceptible fraction at equilibrium, via their impact on the FOI: this can be easily accomplished numerically via formulas as (58).

Similar manipulations can be done on the other relevany quantities.For the total number infectives at equilibrium we have:

$$\begin{aligned} Y &= \int_0^\infty Y(a) = \int_0^\infty \left[\int_0^a I_Y(s) \frac{\Phi(a)}{\Phi(s)} \frac{V(a)}{V(s)} ds + \int_0^a \lambda X(s) \frac{\Phi(a)}{\Phi(s)} \frac{V(a)}{V(s)} ds \right] da = \\ &= \int_0^\infty \int_0^a I_Y(s) \frac{\Phi(a)}{\Phi(s)} \frac{V(a)}{V(s)} ds da + \int_0^\infty \int_0^a \lambda X(s) \frac{\Phi(a)}{\Phi(s)} \frac{V(a)}{V(s)} ds da = \\ &= \int_0^\infty I_Y(s) \left(\int_s^\infty \frac{\Phi(a)}{\Phi(s)} \frac{V(a)}{V(s)} da \right) ds + \lambda Q \end{aligned} \tag{59}$$

where:

$$Q = \int_0^\infty \int_0^a X(s) \frac{\Phi(a)}{\Phi(s)} \frac{V(a)}{V(s)} ds da = \int_0^\infty X(s) \left(\int_s^\infty \frac{\Phi(a)}{\Phi(s)} \frac{V(a)}{V(s)} da \right) ds \tag{60}$$

Hence similar interpretations to those previously used for the susceptibles are possible; in particular an expression for the FOI can be derived.

8 Recognising the age of infection as a remedy to a drawback of the previous formulation

The model developed in the last sections is based on quite restrictive assumptions, namely the fact that: a)the immigrant population, once entered, imediately subsume the demographic and epidemiological behaviours of the host population, b)the two subgroups imediately start mix homogeneously. A further assumption that was implicit in our previous reasoning was the absolute absence, in the immigrated population, of any "memory" of their past epidemiological experience. In other term, in the previous formulation, once an infectious immigrant aged a enter the host population, not only he subsumes the new epidemiological rules of his new homeland, but also chancels hist past experience, to become in any sense equal to a native aged a. A possible remedy to this problem could be the explicit introduction of the age

of infection. A more general model recognising both ages, the anagraphical age (a) and the age of infection (c), is the following:

$$\begin{aligned} \Delta X(a,t) &= I_X(a,t) - (\mu(a) + \lambda(t))X(a,t) \\ \Delta Y(a,c,t) &= I_Y(a,c,t) - (\mu(a) + v(c))Y(a,c,t) \\ \Delta Z(a,t) &= I_Z(a,t) + \int_0^\infty v(c)Y(a,c,t) - \mu(a)Z(a,t) \end{aligned} \tag{61}$$

where:

$$\Delta = \frac{\partial}{\partial a} + \frac{\partial}{\partial c} + \frac{\partial}{\partial t}$$

The new BC are:

$$X(0,t) = B(t) \quad Y(a,0,t) = \lambda(t)X(a,t) \quad Z(0,t) = 0 \tag{62}$$

9 SEICR and SICR aggregate models for HBV with immigrations

The problem of immigrations in all the epidemiological compartments, described in the previous pages for a basic SIR model with time invariant vital dynamics, is easily extended to whatever type of epidemiological model. Let us now, coherently with our main interest in HBV, consider the problem within the frame of the following basic SEICR model with carriers and constant immigrations:

$$\begin{aligned} \dot{X} &= I_X + bN - (\mu + \lambda)X \\ \dot{H} &= I_H + \lambda X - (\mu + \sigma)H \\ \dot{Y} &= I_Y + \sigma H - (\mu + v)Y \qquad \lambda = \beta_1 Y + \beta_2 C \\ \dot{C} &= qvY + I_C - (\mu + \vartheta)C \\ \dot{Z} &= (1-q)vY + \vartheta C + I_Z - \mu Z \end{aligned} \tag{63}$$

which, neglecting the exposed class gives rise to the following SICR model:

$$\begin{aligned} \dot{X} &= I_X + bN - (\mu + \lambda)X \\ \dot{Y} &= I_Y + \lambda X - (\mu + v)Y \\ \dot{C} &= qvY + I_Y - (\mu + \vartheta)C \\ \dot{Z} &= (1-q)vY + I_Z - \mu Z \end{aligned} \qquad \lambda = \beta_1 Y + \beta_2 C$$

This models, together with their age-structured counterparts, can be used to make evaluations, from the point of view of public health, of the impact of several age profiles of immigrants, in particular individuals carriers of HBV, on the endemic profile of the host population.

10 Removing the basic model assumptions: directions of inquiry

A first direction is the systematic development of formulas such as those presented in the seventh section to extract all useful information they convey. A useful development could be that of the possible analogon of the concept of reproductive value of demography in epidemiological context: for instance with the goal to trace the ultimate effect of a young sexually active 20 years old individual who migrates into a population in which the disease is endemic.

Furthermore the basic model is based on the two simplest among all possible assumptions on the demo-epidemiologic behaviours of locals and immigrated. On the demographic side it is assumed that the immigrants forget their old demographic behaviours to imediately subsume those of the host population. This is assumed also on the epidemiological side, but it seems quite unlikely due to different habits and levels of social integration of immigrants, possibly, genetic diversity and so on. In particular the assumption that the two populations, host and immigrated, mix homogeneously is very unlikely as well.

Of particular interest, from the applied point of view, seems the generalisation of the basic framework to treat the special situations faced in recent times by developed countries as Italy for selected diseases, such as HBV. For instance using core models to keep into account of the recruitment of prostitutes via immigration, and so on.

A further assumption that was implicit in our previous reasoning was the absolute absence, in the immigrated population, of any "memory" of their past epidemiological experience. This problem was briefly discussed in section eight, and it the first natural extension we aim to investigate.

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11 Appendix 1

11.1 Equilibrium calculations: some simple case

Type 2 mortality plus age-independent immigration Let us for simplicity assume that all the age-dependent immigration functions are constant and take place only on a given age interval (a_1, a_2) which could also be taken as the entire entire age span $(0, L)$. This amounts to define:

$$I_X(a) = \frac{I_X}{\Delta} = i_X \quad I_Y(a) = \frac{I_Y}{\Delta} = i_Y \quad I_Z(a) = \frac{I_Z}{\Delta} = i_Z$$

and:

$$I(a) = \frac{I}{\Delta} = i$$

By combining this assumption with that of age-independent mortality (type 2) the equilibrium system becomes the following non-homogeneous constant coefficients system:

$$\begin{array}{l} \frac{dX(a)}{da} = i_X - (\mu + \lambda)X(a) \\ \frac{dY(a)}{da} = i_Y + \lambda X(a) - (\mu + v)Y(a) \\ \frac{dZ(a)}{da} = i_Z + vY(a) - \mu Z(a) \\ \frac{dn(a)}{da} = i - \mu n(a) \end{array} \qquad \lambda = \beta Y \tag{64}$$

Explicit calculations (tedious but simple) give:

$$
\begin{array}{lll}
n(a) = & n(0)e^{-\mu a} & a \leq a_1 \\
& n(0)e^{-\mu a} + \frac{i}{\mu}\left[1 - e^{-\mu(a-a_1)}\right] & a_1 < a \leq a_2 \\
& n(0)e^{-\mu a} + \frac{i}{\mu}\left[e^{-\mu(a-a_2)} - e^{-\mu(a-a_1)}\right] & a_2 < a \\
X(a) = & n(0)e^{-(\mu+\lambda)a} & a \leq a_1 \\
& n(0)e^{-(\mu+\lambda)a} + \frac{iX}{\mu+\lambda}\left[1 - e^{-(\mu+\lambda)(a-a_1)}\right] & a_1 < a \leq a_2 \\
& n(0)e^{-(\mu+\lambda)a} + \frac{iX}{\mu+\lambda}\left[e^{-(\mu+\lambda)(a-a_2)} - e^{-(\mu+\lambda)(a-a_1)}\right] & a_2 < a
\end{array}
$$

and so on.

11.1.1 Type 1 mortality plus constant immigration rates

Let us assume that the survival function be of the so called type 1:

$$
\Phi(a) = \begin{array}{ll} 1 & a \leq L \\ 0 & a > L \end{array}
$$

Let us further assume that the immigration functions are constant on a given age interval (a_1, a_2) which could also be taken as the entire entire age span $(0, L)$. In this latter case this amounts to define:

$$
I_X(a) = \frac{I_X}{L} = i_X \quad I_Y(a) = \frac{I_Y}{L} = i_Y \quad I_Z(a) = \frac{I_Z}{L} = i_Z
$$

and:

$$
I(a) = \frac{I}{L} = i
$$