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# The Economic Dynamics of Antibiotic Efficacy under Open Access

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**Abstract**

We analyze the exploitation of an antibiotic in a market subject to open access on the part of antibiotic producers to the common pool of antibiotic efficacy and compare it to the social optimum. Demand for the antibiotic is derived under the assumption that individuals differ with respect to their valuation of being in good health. The dynamics of the antibiotic efficacy is based on an epidemiological model which describes the dynamic interaction between the level of efficacy of the antibiotic and the level of infection in the population, including the fact that antibiotic consumption tends to deplete the efficacy of the antibiotic in combating bacterial infections as the bacteria develop resistance to the antibiotic. The antibiotic producers care only about the variables that affect the instantaneous demand for the drug, namely the current stock of infected population and the current level of efficacy of the antibiotic, and enter the market until price is driven down to average cost. The social optimum, on the other hand, takes into account the welfare of the entire population, including that portion of the population which is in good health and that which is infected but chooses not to consume the antibiotic, as well as the effect of the current treatment rate on the future efficacy of the treatment and the future stock of infected population. We show that depending on the parameters of the model, in particular the cost of production and the improvement in the recovery rate that results from treatment, the positive steady-state level of antibiotic efficacy to which the system tends under open access can be lower or higher than the level which should prevail in the socially optimal steady state. In fact there are parameter configurations for which the steady states can be exactly the same. But no matter how the steady states compare, the socially optimal and the open-access paths to steady state will differ and involve different paths for the treatment rates.

**Keywords:** economics of antibiotic resistance, antibiotic efficacy, renewable resource, open-access equilibrium, social optimum.

**Résumé**

Nous analysons l'exploitation de l'efficacité d'un antibiotique dans un marché où les producteurs de cet antibiotique ont libre accès au stock commun d'efficacité de l'antibiotique et nous comparons l'équilibre qui en résulte à l'optimum social. La fonction de demande pour l'antibiotique est dérivée sous l'hypothèse que les individus diffèrent par rapport à leur valorisation d'être en bonne santé. L'efficacité de l'antibiotique est modélisée comme une ressource naturelle renouvelable exploitée en accès libre. La dynamique de l'efficacité de l'antibiotique est basée sur un modèle épidémiologique, qui décrit l'interaction dynamique entre le niveau d'efficacité et la population infectée. Il tient compte du fait que la consommation d'antibiotique dans l'objectif de combattre les infections tend à décroître l'efficacité de l'antibiotique en raison de la sélection naturelle de bactéries résistantes. Dans ce contexte, les producteurs d'antibiotiques ne s'intéressent qu'au stock courant de la population infectée, ce qui détermine la taille de leur marché, et au niveau courant de l'efficacité de l'antibiotique, ce qui détermine la volonté à payer pour le médicament de la part de la population malade. Ces producteurs entrent sur le marché jusqu'à ce que l'égalité du prix et du coût moyen soit atteinte. Quant à l'optimum social, la fonction d'objectif à maximiser tient compte du bien-être de la population totale, incluant la portion qui est en bonne santé ainsi que celle qui est infectée et qui ne consomme pas l'antibiotique. Cette maximisation tient aussi explicitement compte de l'effet de la population actuelle traitée sur les niveaux futurs d'efficacité et de population infectée. Nos résultats montrent qu'en fonction des paramètres du modèle, plus particulièrement le coût de production et l'accroissement du taux de guérison dû au traitement d'antibiotique, que le niveau positif d'efficacité de l'antibiotique atteint à l'état stationnaire en accès libre peut être plus élevé ou plus faible que celui atteint en optimum social. Il existe même des configurations de paramètres pour lesquels les états stationnaires coïncident. Cependant, dans tous les cas, les sentiers menant vers ces états stationnaires en accès libre ainsi qu'en optimum social vont différer quant à la proportion de la population infectée qui reçoit un traitement.

**Mots clés** : économie de la résistance aux antibiotiques, ressources renouvelables, équilibre de libre accès, optimum social.

## 1 Introduction

It is a well established fact that antibiotic consumption tends to deplete the efficacy of many antibiotics in combating bacterial infections, as the bacteria develop resistance to the antibiotic.[1] The resulting reduction in the efficacy of antibiotic treatment of many diseases is a matter of growing concern, since it has serious consequences for public health and is the source of important economic costs to society.[2] The problem is complicated by the fact that individual decision makers, acting in their own best interest, do not take into account the effect of their current decisions on the future efficacy of the antibiotic. To realize the social optimum in such a context would require cooperative decision making. Thus the market outcome is unlikely to be socially optimal.

A useful way to approach this problem from an economic perspective is to think of the efficacy of the antibiotic as a common pool resource, much like fisheries for instance. That is the approach we take in this paper. More precisely, we analyze the exploitation of antibiotic efficacy in a market subject to open access on the part of the antibiotic producers to the common pool of efficacy and compare it to the social optimum.

An early contribution to the analysis of the market outcome in a context where the efficacy of a drug is declining in its use can be found in Tisdell (1982). In a highly stylized two-period model, he finds that the market outcome under perfect competition leads to lower efficacy of the drug than would be socially optimal. Our model differs considerably from that of Tisdell in a number of ways. First, we explicitly derive the demand function for the antibiotic under the assumption that individuals differ with respect to their valuation of being in good health. Second, we treat antibiotic efficacy as a common pool renewable resource. Third, we explicitly take into account the dynamic interaction between the level of efficacy of the antibiotic and the level of infection in the population. The underlying

[1] For a general overview of the problem of antibiotic resistance see Levy (2002). See also Levy and Marshall (2004) for a recent review of the biological and epidemiological literature on the subject.

[2] See for instance Holmberg, Solomon and Blake (1987), Phelps (1989), US Congress, Office of Technology Assessment (1995), Elbasha (2003) and Laxminarayan (2003).

dynamic system that describes the evolution of the two state variables, namely the level of antibiotic efficacy and the stock of infected population, is based on an epidemiological model (the SIS-model) borrowed from the biology literature. Fourth, the determination of the social optimum takes into account not only the surplus accruing to the consumers of the antibiotic, but also that of the infected individuals who choose not to buy it and that of the individuals in good health, in addition to the surplus derived by the producers of the antibiotic.

The antibiotic producers care only about the current stock of the infected population, which determines market size, and the current level of antibiotic efficacy, which affects the willingness to pay of the sick population. They ignore the dynamic effects of their decisions. We find that in the open-access equilibrium, the level of antibiotic efficacy tends to a positive steady-state level in which the efficacy renews itself so as to maintain the steady state. It turns out, interestingly, that this steady-state level of antibiotic efficacy can be lower or higher than the level which should prevail in the socially optimal steady state. This will depend on the set of parameters of the model, such as the cost of production and the improvement in the recovery rate that results from treatment, but also the natural recovery rates when infected with a resistant or a susceptible bacterial strain, the rate of transmission of the disease and the discount rate. The paths to steady state will also be different under open access and the social optimum and will involve different treatment rates.

Our approach owes a lot to the papers of Laxminarayan and Brown (2001), Wilen and Msangi (2003) and Rowthorn and Brown (2003).[3] We make use of the same epidemiological model to describe the dynamics of the antibiotic efficacy and of the infected population and their interaction. However they do not model demand and do not study the market outcome, but concentrate their analysis on the determination of the socially optimal treatment rates. Their objective function is also less general, since it does not take into account the welfare

[3]We should mention also the early contribution of Brown and Layton (1996), who model antibiotic resistance as a dynamic externality. More recently, Gersovitz and Hammer (2004) build on an epidemiological model that is related to the one used here (a form of the so-called SIR-model) to study the economic control of infectious diseases.

of all the population, whether ill or not and whether being treated or not, as we do here.

The rest of our paper is structured as follows. In section 2, we present the epidemiological model that serves as the basis for the biological dynamics that underlie both the open-access equilibrium and the social optimum. In section 3, we derive the demand function for the antibiotic. We characterize the open-access equilibrium in section 4 and the social optimum in section 5. In section 6, we compare the open-access outcome to the social optimum. We conclude in section 7.

## 2 The epidemiological constraints

In this section we present the basic SIS epidemiological model that describes the population dynamics underlying both the open-access equilibrium and the social optimum. This model assumes that the total population at time $t$, $N(t)$, can be compartmentalized into the population that is in good health but susceptible to the infection, $S(t)$, and that which is infected, $I(t)$. The infected population is further partitioned into those individuals infected with a drug-susceptible strain, $I_w(t)$, and those infected with a drug-resistant strain, $I_r(t)$. Hence, at any time $t$, $N(t) = S(t) + I(t) = S(t) + I_w(t) + I_r(t)$.[4]

Some of the uninfected hosts will become infected through contact with the infected population. The SIS-model assumes that the rate of addition to the infected population in this way is given by $\beta S(t)I(t)$, where $\beta$ denotes the rate of transmission of the infection between the healthy and the infected population. Some of the infected will recover. In the absence of treatment the natural rates of recovery are $r_r$ for those infected with the drug-resistant strain and $r_w$ for those infected with the drug-susceptible strain. If all the infected are treated with the antibiotic, the rate of recovery of those infected with the drug-resistant strain remains unchanged, while the rate of recovery of those infected with the

[4]The SIS-model is used to describe the dynamics of the population in the case of diseases where once an infected individual recovers he becomes susceptible again, as opposed to diseases where once an individual recovers he becomes immune (the SIR-model). These types of models were first developed by Ross (1911) and Kermack and McKendrick (1927) to study the spread of diseases in populations. We closely follow the formulation of the SIS-model used by Bonhoeffer, Lipsitch and Levin (1997) and by Wilen and Msangi (2003).

drug-susceptible strain increases to $r_w + r_f$. If a fraction $f \in [0,1]$ of the infected population is being treated with the antibiotic, the rate of recovery of those infected with the drug-susceptible strain will be $r_w + fr_f$. Hence the total infected population decreases at the rate $r_r I_r(t) + (r_w + fr_w) I_w(t)$.[5]

Then, if $E(t)$ is the new entries into the population (the births) and if the death rates of the healthy and the infected are respectively $n$ and $m$, the population dynamics can be described by:

$$\dot{S} = E - nS - \beta S(I_w + I_r) + r_w I_w + r_r I_r + f I_w r_f \quad (1)$$

$$\dot{I}_w = (\beta S - m - r_w - f r_f) I_w \quad (2)$$

$$\dot{I}_r = (\beta S - m - r_r) I_r. \quad (3)$$

We will henceforth assume $E = n = m = 0$, thus taking the total population to be constant. With a constant population, $\dot{S} = -\dot{I}$ and equation (1) becomes redundant, being simply the sum of equations (2) and (3). Furthermore, we can use the fact that $I_r = I - I_w$ to eliminate $I_r$, leaving two differential equations in $I$ and $I_w$. Now define $w(t) = I_w(t)/I(t)$ as a measure of the efficacy of the antibiotic, as in Laxminarayan and Brown (2001) and Wilen and Msangi (2003). The population dynamics can then be rewritten in terms of the two state variables $w$ and $I_w$ to give:

$$\dot{w} = w(1-w)(\Delta r - r_f f) \quad (4)$$

$$\dot{I} = (\beta(N - I) - r_r) I + wI(\Delta r - r_f f) \quad (5)$$

where $\Delta r \equiv r_r - r_w$ measures what is called in the epidemiological literature the fitness cost of resistance. The expression "fitness cost" refers here to the fact that although resistance procures the advantage of being able to survive the antibiotic treatment, this advantage comes at a *biological cost* for the resistant strain when $\Delta r > 0$. This is because, with

[5]This type of models implicitly assumes that it is not possible to control whether the patient is infected with the resistant or with the susceptible bacteria. This is not an unrealistic assumption when the cost of controlling for the type of bacteria before deciding on the treatment is very high and/or the delays it imposes are long. This seems to be very often the case in practice.

$r_r > r_w$, the resistant strain clears at a faster rate than the susceptible strain in the absence of treatment and hence the susceptible strain naturally ends up dominating the bacteria population in the long-run.

When the fitness cost is zero it can be seen from equation (4) that the level of efficacy of the antibiotic can never be replenished, since $f \geq 0$. In that sense the efficacy of the antibiotic can then be considered a nonrenewable resource. On the other hand, if the fitness cost is positive, the level of efficacy can be replenished by setting $f < \Delta r/r_f$ and the efficacy of the antibiotic can be considered a renewable resource. Thus the fitness cost is an important element in the analysis of antibiotic resistance. We will assume the fitness cost to be positive, although it will be fairly straightforward to derive the results for a zero fitness cost as a special case of the more general results.

There exist three steady state configurations to the population dynamics described by (4) and (5). Let $w^{SS}$ and $I^{SS}$ denote the steady-state values of $w$ and $I$ respectively.

For any $f \neq \Delta r/r_f$, we have $\dot{w} = 0$ for $w = 0$ or $w = 1$ and there are two distinct steady states, given by:

$$(I^{SS}, w^{SS}) = \left(\frac{\beta N - r_r}{\beta}, 0\right) \tag{6}$$

and

$$(I^{SS}, w^{SS}) = \left(\frac{\beta N - r_w - r_f f}{\beta}, 1\right). \tag{7}$$

For $f = \Delta r/r_f$, we have $\dot{w} = 0$ for any value of $w$ and hence all

$$(I^{SS}, w^{SS}) = \left(\frac{\beta N - r_r}{\beta}, w \in [0, 1]\right) \tag{8}$$

constitute steady states. We will assume throughout $\beta N - r_r > 0$ and $\beta N - r_w - r_f > 0$, thus guaranteing the existence of positively valued steady states for $I$.

Clearly, the dynamic system described by (4) and (5) depends in an important way on the proportion $f$ of the population being treated. In particular, if an optimal policy happened to require $f$ to vary over time, then the differential equation system would be non stationary.

Before introducing economic and policy considerations, it is useful to characterize in more detail in $(I, w)$-space the dynamic behavior of the system for all possible values of $f$. From (5) we verify that

$$\left.\frac{dw}{dI}\right|_{\dot{I}=0} = \frac{\beta}{\Delta r - r_f\ f}\ , \tag{9}$$

which is the slope of the isocline for $I$ in $(I, w)$-space. This isocline must go through the point $(I, w) = ((\beta N - r_r)/\beta, 0)$. It is easily verified from equation (5) that $I$ is increasing anywhere to the left of the isocline and it is decreasing anywhere to the right.

Consider first the case of $f \in [0, \Delta r/r_f)$. In that case the isocline for $I$ is a positively sloped straight line through $(I, w) = ((\beta N - r_r)/\beta, 0)$ and $w$ is increasing for any $w \in (0, 1)$, as can be seen from equation (4). This is illustrated in Figure 1a, where the arrows indicate the direction of the forces driving $(I, w)$ over time. From any initial state the system converges to the steady state $((\beta N - r_w - r_f f)/\beta, 1)$. Thus, with a relatively low and constant treatment rate the drug-susceptible bacteria will dominate the bacterial population and the efficacy of the antibiotic will be fully replenished in the long-run. This case includes the case where there is absence of treatment ($f = 0$) and can serve to illustrate the concept of fitness cost. Indeed, it is now immediate that if $f = 0$, then $\Delta r = r_r - r_w > 0$ implies that the susceptible strain will dominate in the long-run.

Figure 1b illustrates the position of the $\dot{I} = 0$ isocline for two different values of $f < \Delta r/r_f$. As $f$ is increased from $f_1$ to $f_2 > f_1$, the $\dot{I} = 0$ isocline pivots to the left through the point $(I, w) = ((\beta N - r_r)/\beta, 0)$. As a consequence the long-run equilibrium will feature a lower steady-state level of infection when a higher (constant) fraction of the infected population is treated.

Consider now the case of $f \in (\Delta r/r_f, 1]$, which is illustrated in Figure 2. In this case the isocline for $\dot{I} = 0$ is a negatively sloped straight line through $(I, w) = ((\beta N - r_r)/\beta, 0)$ and $w$ is decreasing for any $w \in (0, 1)$, as indicated by the direction of the arrows in Figure 2. Therefore from any initial state the system converges to the steady state $((\beta N - r_r)/\beta, 0)$

and the resistant strain ends up dominating the bacterial population in the long-run.[6]

There remains the case of $f = \Delta r/r_f$. In that case, the $\dot{I} = 0$ isocline is the vertical line going through $(I, w) = ((\beta N - r_r)/\beta, 0)$, as illustrated in Figure 3. Any point on this vertical line is then a steady state, since the rate of treatment exactly compensates the fitness cost effect so as to keep the efficacy of the antibiotic stationary, no matter what its level. Hence if the treatment rate is fixed at $\Delta r/r_f$, the system will move horizontally to a stationary point on the $I$ isocline which will depend strictly on the initial level of efficacy of the antibiotic.

Thus far our analysis has been purely descriptive, in the sense that we have limited our attention to the purely biological aspects of the population dynamics, without considering how the treatment rate is determined. We now turn to the introduction of economic factors, beginning with the demand for antibiotics, which will allow us to characterize both the open-access equilibrium and the socially optimum uses of the antibiotic, subject to the biological constraints just described.

## 3 The demand for antibiotics

Let $\theta$ represent an individual's valuation of being in good health, with $\theta$ being distributed over the total population $N$ with distribution function $F(\theta)$. When infected, this individual can choose whether or not to buy the antibiotic at price $p$.[7] It is assumed that the individual knows whether he is infected or not but, when infected, cannot tell whether he is infected with the drug-resistant or the drug-susceptible strain of the bacteria.

When an individual is infected, the probability of being infected with a drug-resistant strain is given by $\frac{I_r}{I} = 1 - w$, in which case the recovery rate is $r_r$ whether he takes the

[6] As in the case of $f \in [0, \Delta r/r_f)$, the $\dot{I} = 0$ isocline will pivot to the left through the point $(I, w) = ((\beta N - r_r)/\beta, 0)$ if $f$ is increased. In this case however the long-run steady state is independent of $f$ since only the resistant strain remains in equilibrium and the level of efficacy of the antibiotic is driven to zero.

[7] Our approach to the derivation of demand begs the important question of the doctor-patient relationship, which is beyond the scope of this paper. Actually, it is the doctor who prescribes the antibiotic to the patient. The patient then decides whether to purchase the antibiotic or not. So the demand function for the antibiotic should probably take into account the doctor's decision rule as to whether or not to prescribe the antibiotic as well as the patient's decision process. Introducing the doctor's decision rule would make it possible to address the issue of the doctor's awareness of the dynamic effects of antibiotic consumption on the efficacy of antibiotic and its social welfare implications.

antibiotic or not. On the other hand, there is a probability $\frac{I_w}{I} = w$ of being infected with the drug-susceptible strain, in which case he can expect to recover at the rate $r_w$. Therefore the expected recovery rate without treatment is:

$$\pi(w) = wr_w + (1-w)r_r.$$

If the infected individual buys the antibiotic, he increases his chances of recovery only if the bacterial strain he is suffering from is susceptible to treatment. His expected recovery rate is then increased only by $r_f w$ when he buys the antibiotic, since there is a $1-w$ chance that the bacteria is resistant. The utility derived from health considerations by the individual of type $\theta$ will therefore be given by:

$$u(\theta) = \begin{cases} \theta & \text{if in good health} \\ \pi(w)\theta & \text{if infected and not taking the antibiotic} \\ \pi(w) + r_f w]\theta & \text{if infected and taking the antibiotic.} \end{cases}$$

Denote by $\tilde{\theta}$ the individual type who is indifferent between buying the antibiotic or not when infected. The value of $\tilde{\theta}$ is determined by:

$$\pi(w)\tilde{\theta} = [\pi(w) + r_f w]\tilde{\theta} - p$$

which means that

$$\tilde{\theta} = \frac{p}{r_f w}. \tag{10}$$

Individuals with $\theta \geq \tilde{\theta}$ will thus buy the antibiotic and those with $\theta < \tilde{\theta}$ will not. If the whole population $N$ were infected, the proportion of individuals willing to buy the antibiotic would be $[1 - F(\tilde{\theta})]$. But this is not the case: uninfected individuals will not buy the antibiotic. We will assume that the infection spreads equally over the population $N$, so that being infected and having a certain valuation $\theta$ are independent events. Then the fraction of the infected population willing to buy the antibiotic is given by $\frac{I}{N}\left[1 - F\left(\tilde{\theta}\right)\right]$ and, since individuals

have a unitary demand, total demand will be:[8]

$$\begin{aligned} Q &= N\frac{I}{N}\left[1-F\left(\tilde{\theta}\right)\right] \\ &= I\left[1-F\left(\frac{p}{r_f w}\right)\right]. \end{aligned}$$

Therefore the inverse demand function is:

$$P\left(\frac{Q}{I},w\right) = r_f w F^{-1}\left(1-\frac{Q}{I}\right). \tag{11}$$

For simplicity, let us assume that $\theta$ is distributed uniformly over the population, with supports $[0,1]$. The inverse demand function then becomes:

$$P\left(\frac{Q}{I},w\right) = r_f w\left(1-\frac{Q}{I}\right). \tag{12}$$

Notice that the intercept of the inverse demand function is $r_f w$ and its slope is $r_f w/I$. The variable $w$ can be viewed as an (endogenous) index of the quality of the drug, which can vary between zero and one. For $w = 0$, demand is identically zero. For a given size of the infected population, $I$, the inverse demand curve pivots upwards through the point $(Q,p) = (I,0)$ as the quality of the antibiotic increases from zero to one and demand is at its highest when $w = 1$.

Because of unitary demand, $Q/I$ represents the fraction of the infected population treated and is thus equal to the parameter $f$ in the dynamic constraints (4) and (5). The inverse demand function can therefore be rewritten as a function of the fraction of the infected population being treated and the efficacy of the antibiotic to give:

$$P\left(f,w\right) = r_f w\left(1-f\right). \tag{13}$$

## 4 Open-access equilibrium

In a regime where there is open access to the stock of antibiotic efficacy, antibiotic producers will enter until, at equilibrium, price equals average production costs, thus dissipating any

[8]Define the joint probability of an individual $i$ being infected and having a valuation of good health higher than $\tilde{\theta}$ as $\Pr(i = \text{infected}, \theta_i \geq \tilde{\theta})$. Then, by independence, we have $\Pr(i = \text{infected}, \theta_i \geq \tilde{\theta}) = \Pr(i = \text{infected})\Pr(\theta_i \geq \tilde{\theta}) = \frac{I}{N}\left[1-F\left(\frac{p}{r_f w}\right)\right]$.

rent that might be had on the common pool of antibiotic efficacy. We will assume that the antibiotic producers are identical, each having a constant unit cost of production of $c > 0$. If $Q(t)$ is the total industry production and sales of the antibiotic under open access, then the open-access equilibrium is characterized by:

$$P\left(\frac{Q(t)}{I}, w\right) = c. \tag{14}$$

Substituting for the inverse demand function (12) derived above and assuming $w \neq 0$, we find that:

$$Q(t) = I(t)\left(1 - \frac{c}{r_f w(t)}\right), \tag{15}$$

or:

$$f(t) = \frac{Q(t)}{I(t)} = 1 - \frac{c}{r_f w(t)}. \tag{16}$$

Hence, under open access, antibiotic production is economically viable and the fraction of the infected population treated will be positive at any date $t$ if and only if $r_f w(t) > c$. Note that since $w(t) \leq 1$, this requires $r_f > c$.

We can now first characterize the different steady states under open-access equilibrium, before turning to the analysis of the transition to a steady state from different possible initial conditions.

### 4.1 The steady states under open access

Consider first the epidemiological steady state given by (6). Since the efficacy of the treatment is driven down to zero in this steady state ($w = 0$), so is demand. Any positive production would lead to losses, so that the equilibrium output of the antibiotic will be zero ($Q^{SS} = 0$) and nobody gets treated. This steady state would therefore be characterized in open access by:

$$(f^{SS}, I^{SS}, w^{SS}) = \left(0, \frac{\beta N - r_r}{\beta}, 0\right). \tag{17}$$

However, from (13) we know that with $w = 0$, $P(f, w) = 0$. Therefore, since $c > 0$, the equilibrium condition (14) cannot hold and such a steady state is ruled out in open access.

In the epidemiological steady state given by (7), the quality of the drug is maximal ($w = 1$). Therefore, from (16), $f = 1 - c/r_f$ and this steady state will be characterized in open access by:

$$(f^{SS}, I^{SS}, w^{SS}) = \left(1 - \frac{c}{r_f}, \frac{\beta N - r_w - r_f + c}{\beta}, 1\right). \tag{18}$$

The steady-state antibiotic production will in this case be

$$Q^{SS} = \left(1 - \frac{c}{r_f}\right)\left(\frac{\beta N - r_w - r_f + c}{\beta}\right).$$

Finally, steady states which satisfy (8) occur only when $f = \Delta r/r_f$ and are compatible with any value of $w \in [0, 1]$ in the epidemiological model. But, from (16), we see that $f = \Delta r/r_f$ can be the open-access equilibrium treatment rate only if

$$\frac{\Delta r}{r_f} = 1 - \frac{c}{r_f w(t)}. \tag{19}$$

This means that $w$ must take on the unique value that satisfies (19) in order for the system to be in such a steady state under open access. Hence there is a unique steady state of this type in open access, given by:

$$(f^{SS}, I^{SS}, w^{SS}) = \left(\frac{\Delta r}{r_f}, \frac{\beta N - r_r}{\beta}, \frac{c}{r_f - \Delta r}\right). \tag{20}$$

In this steady state the aggregate antibiotic production will be

$$Q^{SS} = \frac{\beta N - r_r}{\beta}\left(1 - \frac{r_f - \Delta r}{r_f}\right).$$

Notice that the steady-state configurations (18) and (20) are mutually exclusive. Which one is relevant will depend on the values of the parameters. To be more precise, if $c = r_f - \Delta r$, they are indistinguishable and $w^{SS} = 1$. If $c < r_f - \Delta r$, then (20) must be the relevant steady-state configuration, since this is incompatible with (16) when evaluated at $w^{SS} = 1$. If $c > r_f - \Delta r$ then (18) must be the relevant steady-state configuration, since it must then be the case that $w^{SS} = 1$ and $f^{SS} = 1 - c/r_f < \Delta r/r_f$.

Notice also that if $c = r_f - \Delta r$ then $c < r_f$ and therefore $f^{SS} > 0$. Furthermore, if $c \geq r_f$, then $c > r_f - \Delta r$, which means that $w^{SS} = 1$ and hence $f^{SS} = 0$.

### 4.2 The transition to steady state under open access

At time $t = 0$, a stock of infected population $I(0) = I_0 \in (0, N]$ and a stock of efficacy $w(0) = w_0 \in (0, 1)$ are inherited. The initial state is therefore interior, except for possibly $I = N$.[9] As long as $w > c/r_f$, the antibiotic production is economically viable and the firms will enter and produce a positive amount of the antibiotic.

Consider first the case where $c \leq r_f - \Delta r$. From the initial state $(I_0, w_0)$ the open-access equilibrium will then converge asymptotically to the steady state defined in (20). To see this, distinguish between four types of states, according as to whether $I$ lies in $(I, w)$-space to the left or to the right of the $\dot{I} = 0$ isocline and $w$ is greater or smaller than $w^{SS}$. Let I and II denote states for which $w > w^{SS}$ and III and IV denote states for which $w < w^{SS}$, with states of type I and III lying to the left of the $\dot{I} = 0$ isocline and those of type II and IV to its right. We know from the open-access equilibrium condition (16) that $f = 1 - c/r_f w$ and that in the steady state given by (20), $w^{SS} = c/(r_f - \Delta r)$. Therefore $w \gtreqless w^{SS}$ is equivalent to $f \gtreqless \Delta r/r_f$ in equilibrium.

We have seen in Section 2 that for states of types I and II the $\dot{I} = 0$ isoclines will be negatively sloped and that $w$ will be decreasing over time. As for the stock of infected population, $I$, it will be increasing over time when to the left of the isocline and decreasing when to the right. We are therefore in a situation such as the one depicted in Figure 2 for a fixed $f > \Delta r/r_f$. However, in open access, as the equilibrium quality of the antibiotic decreases so will the demand for it and, consequently, the fraction of the infected population treated. But since the $\dot{I} = 0$ isocline is not independent of $f$, this means that the system is non stationary: the $\dot{I} = 0$ isocline will pivot over time towards the right through the point

[9] We explicitly ignore the trivial case of $I_0 = 0$, in which case the population remains healthy forever according to equation (5). We thereby implicitly assume that some exogenous event occurs initially which causes a portion of the population to become infected by the bacteria. We also assume that a portion of the initially infected population suffers from the resistant strain and a portion suffers from the susceptible strain, so that $I_w(0)$ and $I_r(0)$ are both strictly positive. It then follows that $w_0 (= I_w(0)/I(0))$ is strictly between zero and one. If we had $w_0 = 0$ (everyone is initially infected with the resistant strain) or $w_0 = 1$ (no one is initially infected with the resistant strain), then $w$ remains constant (see equation (4)) and the system would converge to either the steady state defined in (17) if $w_0 = 0$ or in (18) if $w_0 = 1$.

$((\beta N - r_r)/\beta, 0)$, as can be seen from equation (9).

Consider then an initial state $(I_0, w_0)$ with an infected population that is relatively low and an antibiotic efficacy relatively high, so that it belongs to type I. Then the dynamics will be as depicted in Figure 4a. Over time, $w$ decreases and $I$ increases, while the $\dot{I} = 0$ isocline continuously pivots toward the vertical line through $((\beta N - r_r)/\beta, 0)$. At the time at which the $(I(t), w(t))$-path crosses the isocline corresponding to $f(0) = c/r_f w_0$, say at $t = t_1 > 0$, the isocline corresponding to $f(t_1) = c/r_f w(t_1)$ will be further to the right of the initial isocline, as is illustrated in Figure 4a. The state therefore remains of type I and the path is still decreasing over time. The state will in this way converge asymptotically to the steady state defined in (20), as $f(t)$ converges to $\Delta r/r_f$ and the isocline converges to the vertical line through $((\beta N - r_r)/\beta, 0)$.

The situation is different when the initial state is characterized by sufficiently high values of both the efficacy of the antibiotic and the stock of infected population, so as to be of type II, with, as for type I, $f(t) > \Delta r/r_f$. Then, at first, both $I$ and $w$ will be decreasing as will be $f$. As for type I the isocline is negatively sloped and it is pivoting towards the right as $f$ falls. But this means that at some time, say $t = t_1$, the $(I(t), w(t))$-path will hit the isocline corresponding to $f(t_1)$. At that date, the system switches to the regime in which the state is of type I and $I(t)$ goes from decreasing to increasing. The state again converges in the same way to the steady state defined in (20). Such a case is illustrated in Figure 4b.

A pattern that is in some way similar will occur if the initial state happens to be of type III, with still a relatively high stock of infected population, but now a relatively low level of efficacy of the antibiotic. This is illustrated in Figure 5a. In this case, since $f(t) < \Delta r/r_f$, $w$ is increasing (see (4)) and the $\dot{I} = 0$ isocline is positively sloped and pivoting towards the left as $f$ increases with $w$ (see (9)). For any state of this type, both $I$ and $w$ will be increasing along the equilibrium path. But since the isocline is pivoting towards the left, this means that the state trajectory must, at say $t = t_1$, hit the isocline corresponding to $f(t_1)$. When this occurs, it must be the case that $I(t_1) > I^{SS}$, since the isocline is positively

sloped. At that point, there is a switch to a regime in which the state is of type IV, as the stock of infected population goes from increasing to decreasing, and the isocline continues to pivot towards the vertical line through $((\beta N - r_r)/\beta, 0)$.

For any initial state of type IV, the dynamic forces will be pushing $w$ up and $I$ down and $f$ will be increasing with $w$. The state converges in this way to the steady state defined in (20), as the isocline simultaneously converges to the vertical line through $((\beta N - r_r)/\beta, 0)$. This is the case illustrated in Figure 5b.

Figure 6 summarizes these long-run outcomes for the four types of initial states. In all cases, there is convergence to the same steady state, with $f^{SS} = \Delta r/r_f$, $I^{SS} = (\beta N - r_r)/\beta$ and $w^{SS} = c/(r_f - \Delta r)$. When beginning from initial states of type I and IV, the state converges directly to this steady state. When beginning from initial states of type II or III, there is a form of overshooting, in the sense that the stock of infected population moves beyond its steady-state level before, at some point, reversing its direction to converge to that steady state. For an initial state of type II, $I$ is initially higher than $I^{SS}$, then falls below it before eventually beginning to increase in order to reach $I^{SS}$ again in the long-run. For a type IV initial state, $I$ is initially lower than its steady-state level, moves beyond it and, at some point, begins to decrease towards it in order reach it in the long-run.

To see why the overshooting occurs when the initial state is characterized by either relatively high antibiotic efficacy and high stock of infected population (type II) or relatively low antibiotic efficacy and low stock of infected population (type III), divide both sides of (4) by $1 - w$ and both sides of (5) by $I$, and subtract one from the other to get:

$$\frac{\dot{I}}{I} - \frac{\dot{w}}{1-w} = \beta[I^{SS} - I], \tag{21}$$

where $I^{SS} = (\beta N - r_r)/\beta$, the long-run stationary stock of infected population.

We immediately see that if the initial state is of either type I or type IV, both sides of this equation are of the same sign, since $I$ and $w$ are initially moving in opposite directions. This will remain so until the steady-state is reached, at which point we have $\dot{I} = \dot{w} = 0$ and $I = I^{SS}$. There can be no overshooting in those cases.

On the other hand, if the initial states are of either type II or type III, then $I$ and $w$ are initially moving in the same direction, with $\left[\frac{\dot{I}}{I} - \frac{\dot{w}}{1-w}\right]$ being initially negative if of type II and positive if of type III and, in both cases, tending to zero over time as $I$ tends to $I^{SS}$. The left-hand side will go through zero and change sign when $I$ first reaches $I^{SS}$, with $\frac{\dot{I}}{I} = \frac{\dot{w}}{1-w}$. At that point, $I$ and $w$ will both still be moving in the same direction. But the isocline is pivoting in the direction opposite to the movement of $I$. Therefore $I$ will eventually have to change direction, since it must at some point cross the $\dot{I}$ isocline.

Consider for example the case of an initial state of type II. Since the antibiotic is very effective and the stock of infected population is high, demand for the antibiotic is high and a large fraction of the infected population gets treated. As a result, both $I$ and $w$ will be decreasing initially. At some point $I$ will reach $I^{SS}$, but with still $w > w^{SS}$. At that time, $I$ and $w$ are still decreasing, the state still being of type II since the $\dot{I}$-isocline is negatively sloped.[10] But the isocline is pivoting towards the right as the treatment rate decreases and $I$ will eventually have to hit it, after which point $I$ begins to increase, the state having become of type I. We will from that point on have $I$ increasing and $w$ decreasing, until the steady state is reached. While all this is occurring, the treatment rate has been continuously decreasing (see (16)), until it also reaches its steady state value of $f^{SS} = \Delta r/r_f$. The same type of reasoning applies when the initial state is of type III.

Notice that if $c = r_f - \Delta r$, then the initial states are necessarily either of type III or type IV. The dynamics is as described above for initial states of those types, with the particularity that the steady state is characterized by $w^{SS} = 1$. As already noted in the previous section, if $c = r_f - \Delta r$ then $c < r_f$ and therefore $f^{SS} > 0$.

If the endogenous quality of the drug was initially lower than the economically viable level, that is if $w < c/r_f$, then no antibiotic is produced and the fraction treated is initially zero. But with $f = 0$, $w$ will be increasing. As for $I$, it will be increasing if of type III (the case illustrated in Figure 6) and decreasing if of type IV. Therefore in both cases the state

[10]This can be seen by setting $\dot{I} = 0$ in (5) and remembering that $f > \Delta r/r_f$ when the state is either of type II or type I.

will eventually reach a point where production becomes profitable and producers enter.

We have so far been considering the case where $c \leq r_f - \Delta r$, so that the steady state is as defined in (20). Consider now the case where $c > r_f - \Delta r$. Production cost is then relatively high and, as was the case for $c = r_f - \Delta r$, $f < \Delta r / r_f$, so that initial states are necessarily of either type III or type IV. The corresponding dynamics will be as described above for those types of states, except for the fact that the level of antibiotic efficacy will now attain $w = 1$ before the stock of infected population can reach the level $I = (\beta N - r_r)/\beta$. The relevant steady state configuration is then that given by (18), with $w^{SS} = 1$ and $I^{SS} = (\beta N - r_w - r_f + c)/\beta > (\beta N - r_r)/\beta$. Because of the relatively high cost, the treatment rate will be relatively low. In particular, if $c \geq r_f$, which implies $c > r_f - \Delta r$, the open-access steady state will be of this type, but with $f^{SS} = 0$, as well as $f = 0$ all along the path leading to it.

## 5 The social optimum

The instantaneous social welfare is given by the sum of the surplus of all consumers, whether or not they are infected and, when infected, whether or not they buy the antibiotic, and the surplus of the antibiotic producers. It can be written as:

$$\begin{aligned} & W(f, w, I) \\ &= N \int_0^1 u(\theta) d\theta - cfI \\ &= (N - I) \int_0^1 \theta d\theta + I \int_0^{\tilde{\theta}(p)} \pi(w) \theta \; d\theta + I \int_{\tilde{\theta}(p)}^1 \{[\pi(w) + r_f w]\theta - p\} \; d\theta + [p - c] fI \\ &= \frac{1}{2}(N - I) + \frac{1}{2}\pi(w) I + \frac{1}{2} r_f w I f^2 + [r_f w (1 - f) - c] fI, \end{aligned} \tag{22}$$

where $p = P(f, w) = r_f w (1 - f)$ is the price of the antibiotic and, exactly as in (10), $\tilde{\theta}(p) = \frac{P(f(t), w)}{r_f w} = (1 - f)$ defines the consumer who is indifferent between buying or not buying the antibiotic.

The first of those four terms is the surplus derived by that portion of the population which is in good health, $\theta = 1/2$ being the mean valuation of good health. The second term

is the surplus accruing to that portion of the infected population which values good health at less than $\tilde{\theta}(p)$ and hence chooses not to buy the antibiotic. They recover at the natural recovery rate $\pi(w)$. The third term is the surplus that accrues to those who choose to buy the treatment at price $p$, since they have a valuation of good health higher than $\tilde{\theta}(p)$. They recover at the augmented rate $\pi(w) + r_f w$. The last term is the surplus of the producers of the antibiotic.

Determining the social optimum means choosing the path of $f(t)$ so as to maximize:

$$\int_0^\infty e^{-\rho t} W(f(t), w(t), I(t)) dt \tag{23}$$

subject to the differential equations (4) and (5), which determine the evolution of the state variables $w(t)$ and $I(t)$, and to $0 \leq f \leq 1$. The given initial conditions are $w(0) = w_0$ and $I(0) = I_0$ where, by assumption, $w_0 \in (0, 1)$ and $I_0 \in (0, N]$ (see footnote 9).[11]

The current value Hamiltonian for this problem is given by:

$$\begin{aligned} H(f, w, I, \mu, \lambda) &= \frac{1}{2}(N - I) + \frac{1}{2}\pi(w)I + r_f w f I - \frac{1}{2} r_f w I f^2 - cfI \\ &\quad + \mu w(1 - w)(\Delta r - r_f f) + \lambda I[(\beta(N - I) - r_r + w(\Delta r - r_f f)] \end{aligned} \tag{24}$$

and its derivative with respect to the control variable $f$ is:

$$\frac{\partial H}{\partial f} = \left[r_f w(1 - f^*) - c\right] I - r_f w \left[\mu(1 - w) + \lambda I\right], \tag{25}$$

where $\mu$ and $\lambda$ are the shadow values associated to the level of antibiotic efficacy and to the stock of infected population respectively.

The following conditions, as well as (4) and (5), are necessary for an optimum:

$$\frac{\partial H}{\partial f} \leq 0, \quad \frac{\partial H}{\partial f} f = 0, \quad f \geq 0 \qquad \text{or} \qquad \frac{\partial H}{\partial f} \geq 0, \quad \frac{\partial H}{\partial f}(1 - f) = 0, \quad f \leq 1 \tag{26}$$

[11] The state variables are also constrained, since we must have $w(t) \in [0, 1]$ and $I(t) \in [0, N]$. We neglect those constraints, since, if $w(t)$ reaches either 1 or 0, it will stay there forever. As for $I(t)$, for any interior value to the left of the $\dot{I} = 0$ isocline, the dynamic forces always push it away from 0, and, for any value to the right of the $\dot{I} = 0$ isocline, including $I = N$, those forces always push it away from $N$. See the discussion of the epidemiological dynamics of Section 2.

$$\rho\mu - \dot{\mu} = r_f f I - \frac{1}{2} r_f f^2 I - \frac{1}{2}\Delta r I + (\Delta r - r_f f)[\mu(1-2w) + \lambda I] \tag{27}$$

$$\begin{aligned}\rho\lambda - \dot{\lambda} &= r_f w f - \frac{1}{2} r_f w f^2 - cf - \frac{1}{2}(1-\pi(w)) \\ &\quad + \lambda[\beta(N-2I) - r_r + w(\Delta r - r_f f)].\end{aligned} \tag{28}$$

Condition (26) is the first-order condition for the maximization of the Hamiltonian with respect to $f(t)$ at each $t$. Conditions (27) and (28) are the arbitrage equations that determine the evolution of $\mu(t)$ and $\lambda(t)$.

In the case of an interior solution for $f$, condition (26) can be written:

$$r_f w(1-f) = c + \frac{r_f w}{I}\left[\mu(1-w) + \lambda I\right]. \tag{29}$$

The left-hand side of this equation is the price of the antibiotic. The condition says that the price of the antibiotic must be equal to the full marginal cost of treatment, which is the sum of the marginal cost of producing the antibiotic, $c$, and the marginal opportunity cost — through its effect on both the quality of the antibiotic, $w$, and the stock of infected population, $I$, — of using it to treat a fraction $f$ of the infected population.

The variable $\mu$ measures the marginal shadow price of antibiotic efficacy. The variable $w(= I_w/I)$ being the level of antibiotic efficacy, its complement, $1-w(= I_r/I)$, measures the level of antibiotic resistance. Hence $\mu(1-w)$ evaluates the level of antibiotic resistance at the marginal shadow price $\mu$. The variable $\lambda$ measures the marginal shadow cost of infection.[12] Hence $\lambda I$ is the implicit (negative) value of the stock of infected population, evaluated at $\lambda$. The sum of those two terms, $[\mu(1-w) + \lambda I]$, can be either positive or negative and can possibly change sign over time. When positive (negative), the overall net opportunity cost — in excess of the marginal cost of production $c$ —, of marginally increasing the fraction of the infected population treated is positive (negative). The socially optimal price of the antibiotic at that date will then be higher (lower) than the marginal cost of production.

Contrary to the competitive producers in an open-access regime, the socially optimal solution takes into account the fact that the current treatment decision affects both the

[12]Numerical simulations indicate that $\lambda$ is indeed negative, as expected, whereas $\mu$ is positive.

future level of efficacy of the antibiotic and the future stock of infected population. This is reflected in the expression $[\mu(1-w)+\lambda I]$ and its sign. In open access the producers act myopically and enter until price is driven to average cost. As shown in Section 4, this means that $f = 1 - c/r_f w$ in equilibrium.[13] If we now denote by an asterisk the socially optimal values of the variables, then, using (29), we can write, for any $t$:

$$f(t) - f^*(t) = \left(\frac{w(t) - w^*(t)}{r_f w(t) w^*(t)}\right) c + \frac{1}{I^*(t)} \left[\mu^*(t)(1 - w^*(t)) + \lambda^*(t) I^*(t)\right]. \tag{30}$$

We see that for identical levels of antibiotic efficacy — for instance at $t = 0$ —, the fraction treated under open access will be greater than is socially optimal if $[\mu(1-w) > -\lambda I]$, since the full social cost of treatment then exceeds the cost of producing the antibiotic. The reverse is true if $[\mu(1-w) < -\lambda I]$.

### 5.1 The steady states in the social optimum

Setting $\dot{w} = \dot{I} = \dot{\mu} = \dot{\lambda} = 0$ generates a socially optimal steady state. Consider first the epidemiological steady state given by (6). The antibiotic is completely inefficient in this steady state ($w = 0$). Therefore no socially valuable production can take place and the steady state of this type at the social optimum is:

$$(f^{SS^*}, I^{SS^*}, w^{SS^*}) = \left(0, \frac{\beta N - r_r}{\beta}, 0\right). \tag{31}$$

This steady state turns out to be unstable so that, when starting from an initial state $(I_0, w_0)$ which is interior, the system will move away from it.[14] We can therefore ignore it in what follows.

In the epidemiological steady state given by (7), antibiotic efficacy is at its maximum level ($w = 1$). Setting $w = 1$ in (26), in (5) with $\dot{I} = 0$ and in (28) with $\dot{\lambda} = 0$ yields three equations in $I$, $\lambda$ and $f$ whose solution for those three variables will depend strictly on

[13] Marginal cost is what matters for the determination of the social optimal price, whereas average cost is what matters in the determination of the open-access equilibrium price. Because of our assumption that the unit cost of production is constant, we have marginal cost equal to average cost.

[14] Linearizing the system of differential equations (4), (5), (27) and (28) with $f$ satisfying (26), it is verified that the trace of the matrix of the linearized system is positive when evaluated at this steady state.

the parameters of the problem. This is shown in the Appendix, where it is also shown that any $f \in [0,1]$ can be part of the solution to those equations given appropriate values of the parameters. The socially optimal fraction of the sick population treated at this steady state will therefore depend on the parameters of the model and can take on any value from zero to one. This means that when this is the relevant steady state configuration, we will have:

$$(f^{SS^*}, I^{SS^*}, w^{SS^*}) = \left( f \in [0,1], \frac{\beta N - r_w - r_f f}{\beta}, 1 \right) \tag{32}$$

Finally, the relevant description of the steady state can be of the type characterized by (8). This steady state is shown in the Appendix to be given by:

$$(f^{SS^*}, I^{SS^*}, w^{SS^*}) = \left( \frac{\Delta r}{r_f}, \frac{\beta N - r_r}{\beta}, -\frac{J}{2H} + \sqrt{\left(\frac{J}{2H}\right)^2 - \frac{K}{H}} \right) \tag{33}$$

where

$$\begin{aligned} H &= (r_f - \Delta r)\frac{\Delta r(r_r - \beta N)}{2\rho} \\ J &= (r_f - \Delta r)(\rho + \beta N - r_r)\left(\frac{\Delta r}{2\rho} - 1\right) + \frac{r_f}{2}(r_r - 1) - c\Delta r \\ K &= c(\rho + \beta N - r_r). \end{aligned}$$

The steady state configurations (33) and (32) are mutually exclusive. In fact, when $w^{SS^*} = 1$ in (33) they are indistinguishable. This will occur when (see the Appendix):

$$c = \tilde{c}(r_f) = \frac{\Delta r \left[\frac{\Delta r}{2} - (\beta N - r_r + \rho)\right]}{\beta N - r_r + \rho - \Delta r} + \left( \frac{\beta N - r_r + \rho + \frac{1}{2} - \frac{1}{2}(\Delta r + r_r)}{\beta N - r_r + \rho - \Delta r} \right) r_f. \tag{34}$$

For $c \leq \tilde{c}(r_f)$, the socially optimal steady state will be as defined in (33). For $c > \tilde{c}(r_f)$, it will be as defined in (32).

Notice also that in order to have $w^{SS^*} = 0$ in (33), it must be the case that $K = 0$. But this is not possible, since $c > 0$. Therefore the socially optimal level of antibiotic efficacy will be strictly positive.

As shown in the Appendix, when $w^{SS^*} = 1$, we must have:

$$f \quad \begin{cases} > 0 \quad \text{if} \quad c < \left(1 + \dfrac{1 - r_w}{2(\beta N - r_w + \rho)}\right) r_f \\ \\ = 0 \quad \text{if} \quad c > \left(1 + \dfrac{1 - r_w}{2(\beta N - r_w + \rho)}\right) r_f > r_f. \end{cases} \tag{35}$$

### 5.2 The transition to steady state in the social optimum

The social planner takes into account the full marginal cost of treatment, which reflects the shadow values attached to the efficacy of the drug and to the infected population in addition to the unit cost of production. Because of this it is not the case that $w \gtreqless w^{SS^*}$ corresponds to $f \gtreqless \Delta r/r_f$, as it was in the open-access equilibrium. The definitions of the four types of state introduced in Section 4.2 are still valid after replacing $w^{SS}$ by $w^{SS^*}$, but they cannot be expressed in terms of $f$ being greater or smaller than $\Delta r/r_f$ anymore. This means that the direction of movement of $w$ may change as $f$ goes from, say, $f > \Delta r/r_f$ to $f < \Delta r/r_f$ although the state remains of the same type. It therefore becomes much more complicated to fully describe analytically the dynamic forces within each type of state, which themselves depend on the parameters and on the initial state. For this reason, we rely on numerical simulations to explore the transition to steady state.[15] We report here, for illustrative purposes, simulations for a set of parameters such that $c < \tilde{c}(r_f)$, so that the steady state is as defined in (33). The simulations show that the system converges to this steady state when beginning from an initial state which satisfies $I \in (0, N]$ and $w \in (0, 1)$. Similar simulations have been carried out for the case of $c > \tilde{c}(r_f)$, with similar results. Recall that in this last case, the states can only be of either type III or type IV.

Figure 7 illustrates the evolution of $(I, w)$ beginning from the four possible types of initial states, each with the same properties as in the corresponding Figure 6 for the open-access equilibrium:[16] one with the initial state to the left of the $\dot{I} = 0$ isocline (type I) and one to its right (type II), both with $w_0 > w^{SS^*}$; one with the initial state to the left of the isocline

[15]For simulations purposes, the continuous time and continuous variables problem was approximated by a discrete time and a discrete variables problem. The numerical simulations were then performed by formulating the optimal control problem in a recursive way. We used the value function iteration procedure (see Judd (1998), pages 412–413) to determine the value function $V$ that satisfies the Bellman equation corresponding to the recursive formulation. The simulations were run with numerous parameter sets in order to verify the robustness of the results. We also verified that the steady-state results obtained numerically for the state, co-state and control variables correspond to those obtained analytically. In particular, we have made sure that the co-state variables $\mu$ and $\lambda$ satisfy $\mu = \partial V/\partial w$ and $\lambda = \partial V/\partial I$ at the steady state.

[16]The simulations represented in Figure 7 were run with the following parameter values: $\beta = 0.6, r_r = 0.25, r_w = 0.15, r_f = 0.3, N = 1, c = 0.1, \delta = 0.971$, where $\delta$ represents the time discrete discount factor.

(type III) and one to its right (type IV), both with $w_0 < w^{SS}$.[17]

As with the open-access equilibrium, the system tends in the long-run to a steady state in which the treatment rate is such that antibiotic efficacy renews itself in order to maintain its steady state level. The steady-state stock of infected population ($(\beta N - r_r)/\beta$) and the steady-state treatment rate ($\Delta r/r_f$) will be the same as in the open-access equilibrium. The steady-state quality of the antibiotic will in general be different, although it is conceivable that it be the same as well. But in all cases, the approach to the steady state will differ.

## 6 Comparing the socially optimal and the open-access steady states

Whether the steady-state level of antibiotic efficacy in the social optimum is higher or lower than in the open-access regime depends crucially on the values of the parameters. In what follows we concentrate on the parameters $r_f$ and $c$, which measure respectively the increase in the recovery rate resulting from treatment and the unit cost of production of the antibiotic.

Equating the steady-state values for $w$ in (20) and (33), we find that we will have $w^{SS^*} = w^{SS}$ for:

$$c = -\frac{\Delta r(\beta N - r_r + \rho)}{\beta N - r_r + 2\rho} + \left( \frac{\Delta r(\beta N - r_r + \rho) + \rho(r_r - 1)}{\Delta r(\beta N - r_r + 2\rho)} \right) r_f. \tag{36}$$

This is a straight line in $(r_f, c)$ space. Its intercept is negative and the sign of its slope depends on the sign of $\Delta r(\beta N - r_r + \rho) + \rho(r_r - 1)$.[18] For any point above that line, we will have $w^{SS^*} \leq w^{SS}$ (with strict inequality as long as $w^{SS^*} < 1$), while for any point below it we have $w^{SS^*} > w^{SS}$. Thus for any given value of $r_f$, if the cost of producing the antibiotic is sufficiently large, the open-access equilibrium will result in a higher steady-state level of antibiotic efficacy than is socially optimal. In fact, if the slope of this line is negative, this will always be the case. On the other hand, when the slope is positive, there will exist some

[17] The case where the initial state is of type III in Figure 7 illustrates a situation where $\dot{w}$ goes from negative to positive while the state $(I, w)$ remains of type III. This is because the optimal treatment rate is initially greater that $\Delta r/r_f$ but decreasing. When it reaches $\Delta r/r_f$ it continues to decrease for some time before beginning to increase again to reach $f = \Delta r/r_f$ at the steady state. But as $f$ goes from greater to smaller than $\Delta r/r_f$, $w$ goes from decreasing to increasing and moves over time towards its steady state level $w^{SS^*}$.

[18] Recall that $\beta N - r_r$ was assumed positive from the outset, in order to guarantee the existence of positive steady states.

values of $r_f$ such that for a low enough cost of production the social optimum will require a higher steady-state level of antibiotic efficacy than what would result in open-access. This is the case represented in Figure 8, where condition (36) is drawn as a solid line. Notice that the slope will be positive for $\rho$ sufficiently small and it will be positive for any $\rho$ if $\Delta r > 1 - r_r$.

From the analysis of the open-access steady state in section 4, we know that for $c \geq r_f - \Delta r$ we will have $w^{SS} = 1$. The condition $c = r_f - \Delta r$ is drawn as a dashed line in Figure 8. This line will always lie above the line representing $w^{SS^*} = w^{SS}$ in the positive quadrant. For points on it, the open-access steady-state configurations (18) and (20) are indistinguishable. For points above it, the open-access steady state is as defined in (18), with $w^{SS} = 1$ and $I^{SS} = (\beta N - r_w - r_f + c)/\beta > (\beta N - r_r)/\beta$. The open-access steady state has $f^{SS} > 0$ for points between the line $c = r_f - \Delta r$ and the forty-five degree line $c = r_f$, but $f^{SS} = 0$ for points above the line $c = r_f$.

Also depicted in Figure 8 is the straight line defined by $c = \tilde{c}(r_f)$. For points on it $w^{SS^*} = 1$ and the socially optimal steady-state configurations (33) and (32) are indistinguishable. For points above it, we have $w^{SS^*} = 1$ but with $I^{SS^*} = (\beta N - r_w - r_f f)/\beta > (\beta N - r_r)\beta$ as in the socially optimal steady-state configuration (32). As can be seen from (35), when $w^{SS^*} = 1$ and

$$r_f < c < \left(1 + \frac{1 - r_w}{2(\beta N - r_w + \rho)}\right) r_f,$$

the socially optimal rate of treatment will be positive, whereas the firms would find it unprofitable to produce the drug in open-access equilibrium and hence the treatment rate would be zero. This steady-state threshold level of social profitability is higher than is the threshold level of private profitability, since the socially optimal solution takes into account the welfare of the whole population and the epidemiological dynamics, contrary to the firms in open access.

For illustrative purposes, Figure 9a depicts numerical simulations that compare the transitions to steady state for a case where the initial state $(I_0, w_0)$ is of type II (see Figures 6

and 7) and the steady-state level of antibiotic efficacy is lower in the social optimum than in open access. The evolution of the state paths have in common the "overshooting" pattern in the level of infection, which is stronger in the social optimum than in open access. This means that although in both cases it will end up at the same steady-state level, for a good part of the socially optimal trajectory the stock of infected population will be maintained below the minimal level reached under open access. The level of antibiotic efficacy decreases in a monotone fashion in each case and it is always higher in open access than what it would be in the social optimum for the same stock of infected population, except for a single point where the two paths cross. This suggests that the socially optimal fraction of the infected population treated at each instant will be greater than under open access, except asymptotically as both tend to the same steady state value of $\Delta r/r_f$. This is indeed verified numerically, as shown in Figure 9b.

Similar numerical simulations with initial states of types I, III or IV and with $w^{SS^*}$ greater, smaller or equal to $w^{SS}$ yield, *mutate mutandis*, similar qualitative results.

## 7 Conclusion

We have modeled the level of efficacy of an antibiotic in treating a bacterial infection as a resource stock which is depleted by consumption of the antibiotic, as the bacteria become resistant, but which may be renewed if managed properly. This has served as the basis for analyzing the economic dynamics of the use of the antibiotic to treat a bacterial infection under two scenarios. One is the market equilibrium in which antibiotic producers have open access to the common pool of antibiotic efficacy and enter until price is driven down to average cost. They care only about their production cost and the determinants of current demand for their product, which are its quality, as measured by the current level of efficacy of the antibiotic, and the current stock of infected population, but they ignore their individual effects on the evolution of those state variables. The other is the social optimum, which takes into account, in addition to the surplus of the producers, the welfare of all the population,

whether healthy or infected and, when infected, whether treated with the antibiotic or not.

It turns out that the comparison of the steady-state level of antibiotic efficacy under the two scenarios is ambiguous. Consider a parameter configuration such that the steady state level of antibiotic efficacy is less than one in both the open access equilibrium and the social optimum. Then, whether the steady-state level of efficacy in open-access equilibrium is lower or higher than in the socially optimal steady-state will depend on the epidemiological and the economic parameters. For instance, for a given cost of production of the antibiotic, if the increase in the recovery rate that results from treating the infection is sufficiently high, then the socially optimal steady-state level of antibiotic efficacy can be higher than in the open-access equilibrium, but the reverse is true if the increase in the recovery rate is sufficiently low. In both cases, the steady-state stock of infected population and the steady-state treatment rate will be the same in the open-access equilibrium as in the social optimum. But the trajectories leading to those long-run steady-states will always differ considerably.

There in fact exist some parameter configurations such that the steady state level of efficacy would be equal to one under open access while it would be less than one at the social optimum. This will involve a unit cost of production which is relatively high and hence a relatively low treatment rate under open access. Should the unit cost of production exceed the improvement in the recovery rate that results from treatment, the open access treatment rate would be zero in such an open-access steady state, since the firms would find it unprofitable to produce. The threshold cost level for social profitability of treatment is however higher than this, because, contrary to the firms under open access, the social optimum takes into account the welfare of all the population, whether healthy or not, as well as the epidemiological dynamics.

The open-access equilibrium and the social optimum are two benchmark cases. Pharmaceutical companies are usually given patent rights for the production of the drug they have discovered in order to encourage research and development, with the result that they benefit from a monopoly situation for a finite period of time. The open-access scenario can be viewed

as a good approximation of the situation which arises after the expiration of the patent. An obvious next step, which is the subject of ongoing research, is to analyze and compare to the social optimum a situation where a producer has monopoly rights for a finite period of time and becomes one of many producers in open access once those monopoly rights expire. The analyses and comparisons carried out in this paper provide useful inputs for further research in this direction. They should also have useful implications for the analysis of optimal policies towards antibiotic use in general, although, given the complicated dynamics involved and the ambiguities encountered in comparing the two benchmark scenario, one can expect the task to be arduous.

## Appendix

We first recall the full dynamic system, involving the state and co-state variables, which the socially optimal solution must satisfy. It is given by:

$$\dot{w} = w(1-w)(\Delta r - r_f f) \tag{A–1}$$

$$\dot{I} = I(\beta(N-I) - r_r + w(\Delta r - r_f f)) \tag{A–2}$$

$$\dot{\mu} = \rho\mu + \frac{1}{2}\Delta r I - r_f f I + \frac{1}{2} r_f f^2 I - (\Delta r - r_f f)[\mu(2w-1) - \lambda I] \tag{A–3}$$

$$\begin{aligned}\dot{\lambda} &= \rho\lambda + \frac{1}{2}(1-\pi(w)) - r_f w f + \frac{1}{2} r_f w f^2 + cf \\ &\quad -\lambda[\beta(N-2I) - r_r + w(\Delta r - r_f f)]\end{aligned} \tag{A–4}$$

In addition, the first-order condition (26) for the maximization of the Hamiltonian must be satisfied at every point in time, including at a steady state. A steady state solution is given by $\dot{w} = \dot{I} = \dot{\mu} = \dot{\lambda} = 0$.

## A The socially optimal steady state with $w^{SS^*} = 1$

Setting $w = 1$ in (A–1), we have $\dot{w} = 0$. Setting $\dot{I} = 0$, $\dot{\lambda} = 0$ and $w = 1$ in (A–2) and (A–4) gives:

$$I = \frac{\beta N - r_w - r_f f}{\beta} \tag{A–5}$$

$$\lambda = \frac{f(r_f - c) - \frac{1}{2} r_f f^2 - \frac{1}{2}(1 - r_w)}{\rho + \beta I} \tag{A–6}$$

For convenience, we rewrite the first-order condition (26) as:

$$r_f I(1 - \frac{c}{r_f} - f - \lambda) + \sigma_0 - \sigma_1 = 0 \tag{A–7}$$

where $\sigma_0$ and $\sigma_1$ are the Lagrange multipliers associated to the constraints $f \geq 0$ and $f \leq 1$ respectively and

$$\sigma_0 f = 0, \quad \sigma_1(1 - f) = 0, \quad \sigma_0 \geq 0, \quad \sigma_1 \geq 0.$$

Equation (A–5), (A–6) and (A–7) together determine $I^{SS^*}$, $\lambda^{SS^*}$ and $f^{SS^*}$.

Setting $f = 0$, we find:

$$\sigma_0 = -\frac{r_f(\beta N - r_w)}{\beta}\left(1 - \frac{c}{r_f} + \frac{1 - r_w}{2(\beta N - r_w + \rho)}\right).$$

This expression is negative if $c \leq r_f$. This means that if $c \leq r_f$ the treatment rate must be positive, since $\sigma_0$ must be non-negative. However if $c > r_f$, then for $c$ sufficiently high the expression in parentheses will be negative and $\sigma_0$ will be positive, which means that the optimal treatment rate is $f = 0$. In fact, we must have

$$f > 0 \quad \text{if} \quad c < \left(1 + \frac{1 - r_w}{2(\beta N - r_w + \rho)}\right) r_f$$

and

$$f = 0 \quad \text{if} \quad c > \left(1 + \frac{1 - r_w}{2(\beta N - r_w + \rho)}\right) r_f > r_f$$

.

Setting $f = 1$, we find:

$$\sigma_1 = -\frac{\beta N - r_w - r_f}{\beta}\left(c + \frac{\frac{1}{2} r_f - c - \frac{1}{2}(1 - r_w)}{\beta N - r_w - r_f + \rho} r_f\right) \tag{A–8}$$

Clearly there exist admissible values of the parameters for which $\sigma_1 \geq 0$ and $f = 1$ is a solution.

An interior solution for $f$ must satisfy (A–5), (A–6) and (A–7) with $\sigma_0 = \sigma_1 = 0$. It is easy to verify numerically that there exist values of the parameters for which the solution for $f$ is interior.

We therefore conclude that $f^{SS^*}$ can take any value from zero to one, with the exact value depending on the set of parameters.

## B The socially optimal steady state with $f^{SS^*} = \frac{\Delta r}{r_f}$

For an interior solution to the maximization of the Hamiltonian, $f$ must satisfy equation (29), in addition to (A–1)-(A–4). Setting $f = f^{SS^*} = \Delta r / r_f$, we have $\dot{w} = 0$, from (A–1), and from (A–2):

$$I^{SS^*} = \frac{\beta N - r_r}{\beta}. \tag{A–9}$$

Setting $\dot{\mu} = 0$ in (A–3) and substituting for $f^{SS^*}$ and $I^{SS^*}$, we get the steady-state solution for $\mu$:

$$\mu^{SS^*} = \frac{\Delta r}{2\rho}\left[1 - \frac{\Delta r}{r_f}\right]\left[\frac{\beta N - r_r}{\beta}\right]. \tag{A–10}$$

We still need to determine the steady-state levels of antibiotic efficacy, $w^{SS^*}$, and of the shadow cost of infection, $\lambda^{SS^*}$. Setting $\dot{\lambda} = 0$ in (A–4) and substituting for $f^{SS^*}$ and $I^{SS^*}$ we get:

$$\lambda = \frac{\frac{1}{2}(r_r - 1) - \frac{c}{r_f}}{\rho + \beta N - r_r} + \frac{\frac{1}{2}\Delta r\left[1 - \frac{\Delta r}{r_f}\right]}{\rho + \beta N - r_r} w \tag{A–11}$$

which is a positively-sloped straight line in $(w, \lambda)$ space.

Substituting for $f^{SS^*}$ and $I^{SS^*}$ into (29), we get:

$$\lambda = \left[1 - \frac{\Delta r}{r_f}\right]\left(1 - \frac{\Delta r}{2\rho}\right) - \frac{c}{r_f}\frac{1}{w} + \frac{\Delta r}{2\rho}\left[1 - \frac{\Delta r}{r_f}\right] w \tag{A–12}$$

which represents a hyperbola with a vertical asymptote at $w = 0$ and an oblique asymptote with a positive slope. These two curves will intersect to the right of the vertical asymptote, *i.e.* where $w > 0$. This is because the ratio of the slope of the oblique asymptote and the

slope of (A–11) is $(\rho + \beta N - r_r)/\rho > 1$ and the hyperbola (A–12) approaches its oblique asymptote from below. The point of intersection yields $w^{SS^*}$, which is given by:

$$w^{SS^*} = -\frac{J}{2H} + \sqrt{\left(\frac{J}{2H}\right)^2 - \frac{K}{H}} \tag{A–13}$$

where

$$\begin{aligned} H &= (r_f - \Delta r)\frac{\Delta r(r_r - \beta N)}{2\rho} \\ J &= (r_f - \Delta r)(\rho + \beta N - r_r)\left(\frac{\Delta r}{2\rho} - 1\right) + \frac{r_f}{2}(r_r - 1) - c\Delta r \\ K &= c(\rho + \beta N - r_r). \end{aligned}$$

Depending on the set of parameters we have $w^{SS^*} < 1$ or $w^{SS^*} = 1$. The analysis of the parameter space concentrates on the space $(r_f, c) \in (\Delta r, \beta N - r_w] \times (0, \infty)$. The lower bound on $r_f$ guarantees that $\Delta r/r_f < 1$, which implies that the level of antibiotic efficacy decreases if the whole infected population is treated. There exists an arbitrage between keeping the level of efficacy high and keeping that of infection low. The upper bound on $r_f$ guarantees that the level of infection is non-negative at $f = 1$ in the steady state defined by (7). The admissible interval for $c$ guarantees that the unit cost of production is positive, as assumed.

From (A–13) we find that $w^{SS^*} = 1$ implies:

$$c = \tilde{c}(r_f) = \frac{\Delta r\left[\frac{\Delta r}{2} - (\beta N - r_r + \rho)\right]}{\beta N - r_r + \rho - \Delta r} + \left(\frac{\beta N - r_r + \rho + \frac{1}{2} - \frac{1}{2}(\Delta r + r_r)}{\beta N - r_r + \rho - \Delta r}\right) r_f. \tag{A–14}$$

This equation represents a straight line that divides the $(r_f, c)$-space. Everything else equal, for a small enough fitness cost we have $\beta N - r_r + \rho - \Delta r > 0$ and this line is then positively-sloped and has a negative intercept. We then have $w^{SS^*} < 1$ below the line and $w^{SS^*} = 1$ above it.

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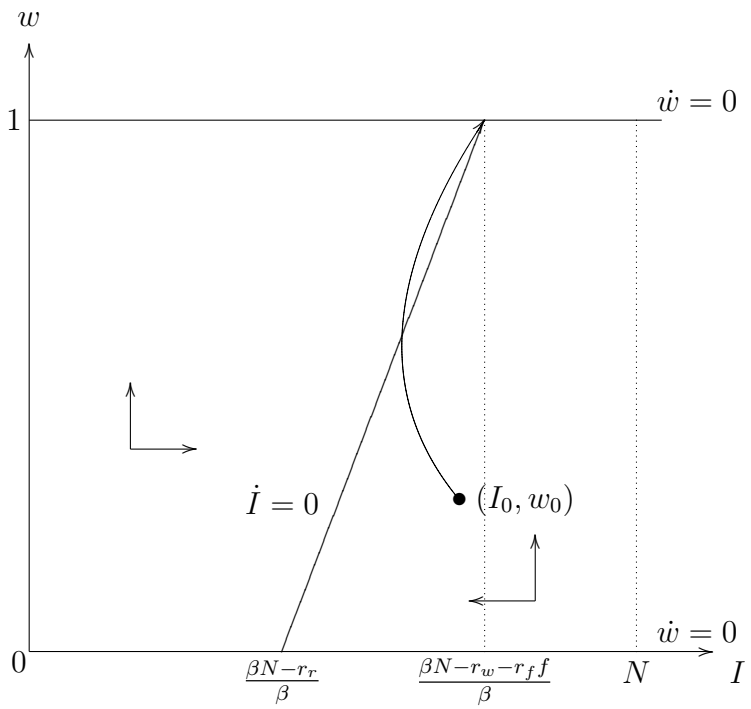


Figure 1a: Epidemiological dynamics with $f \in \left[0, \frac{\Delta r}{r_f}\right)$

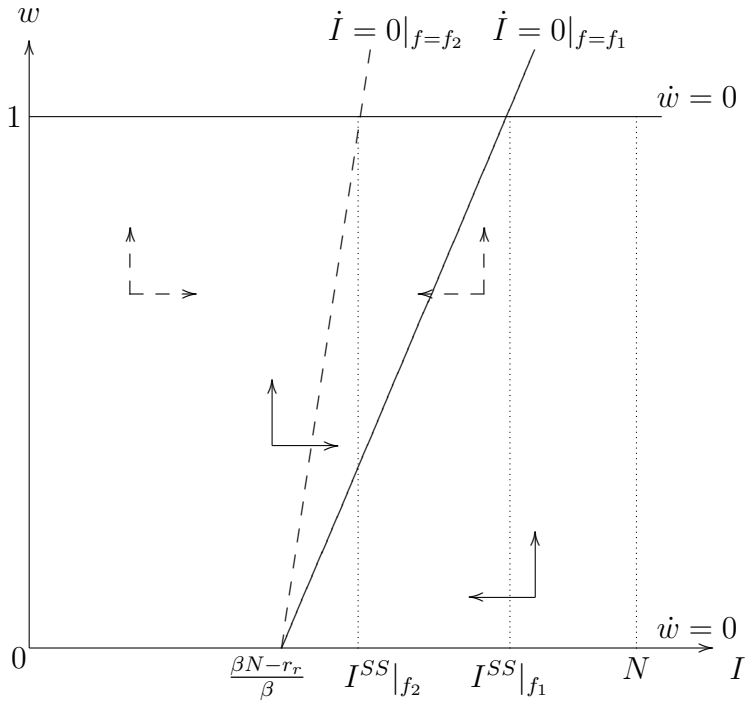


Figure 1b: Epidemiological dynamics with $f_1 < f_2 < \frac{\Delta r}{r_f}$

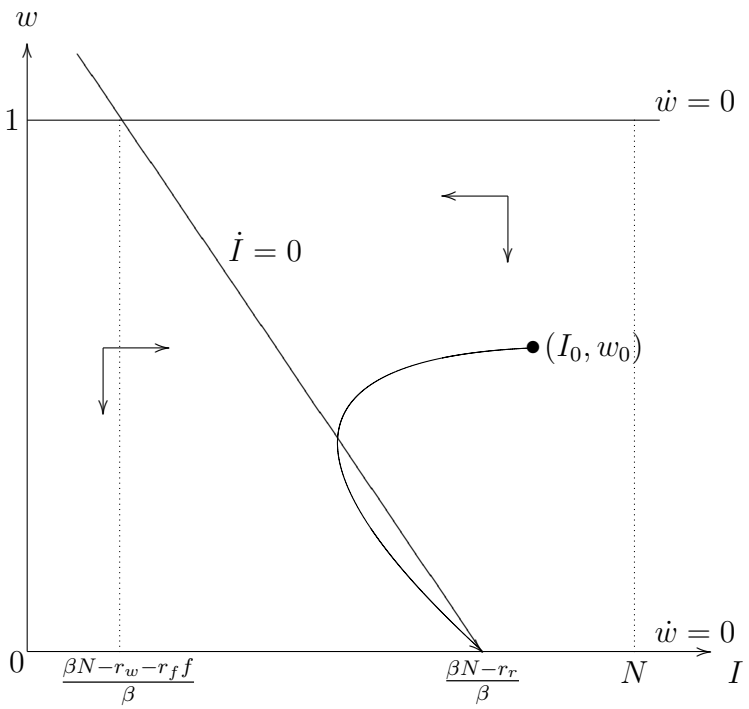


Figure 2: Epidemiological dynamics with $f \in \left(\frac{\Delta r}{r_f}, 1\right]$

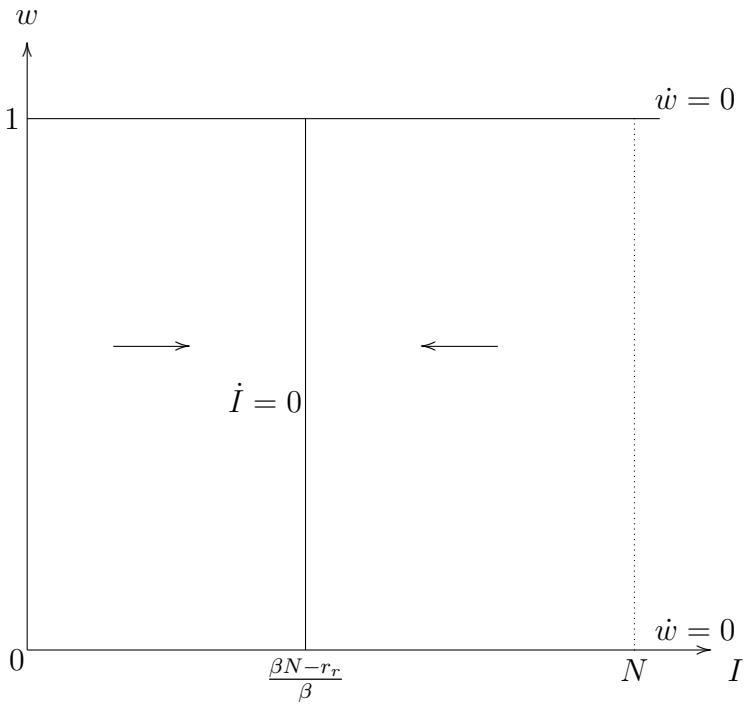


Figure 3: Epidemiological dynamics with $f = \frac{\Delta r}{r_f}$

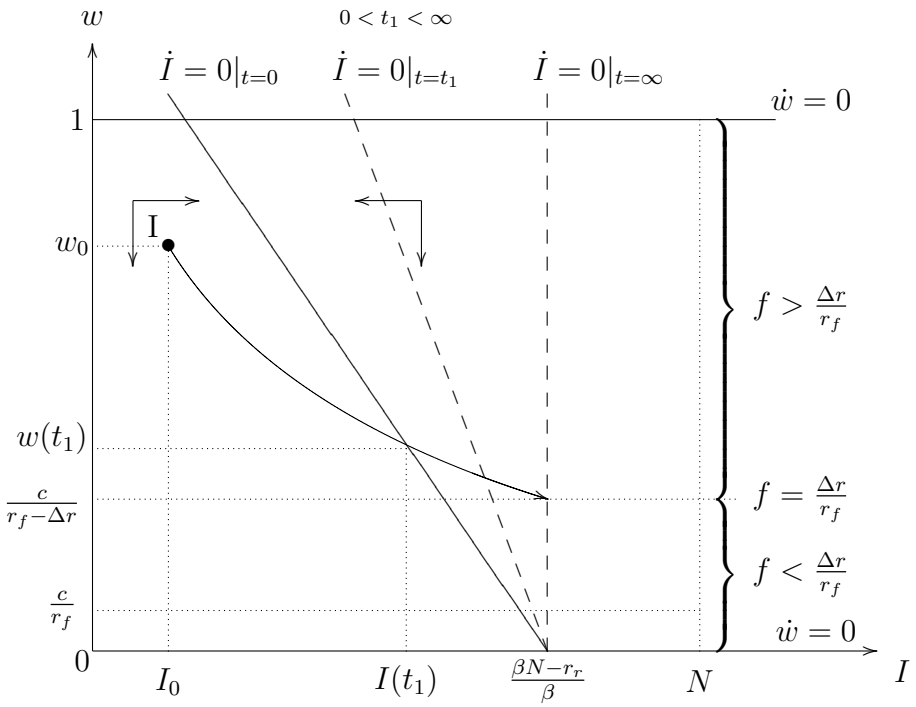


Figure 4a: Open-access dynamics with initial state of type I

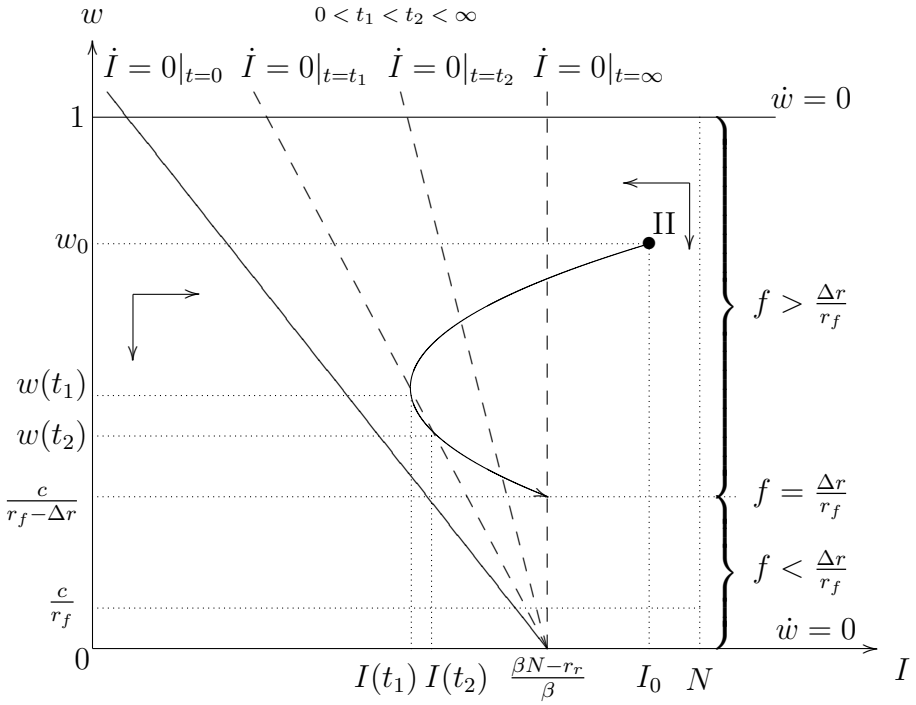


Figure 4b: Open-access dynamics with initial state of type II

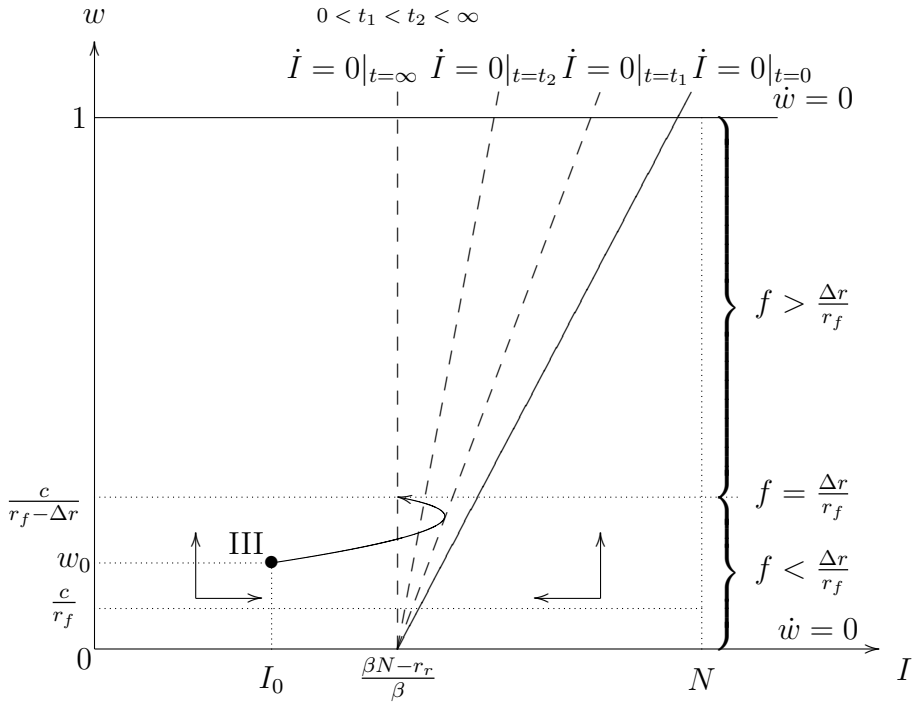


Figure 5a: Open-access dynamics with initial state of type III

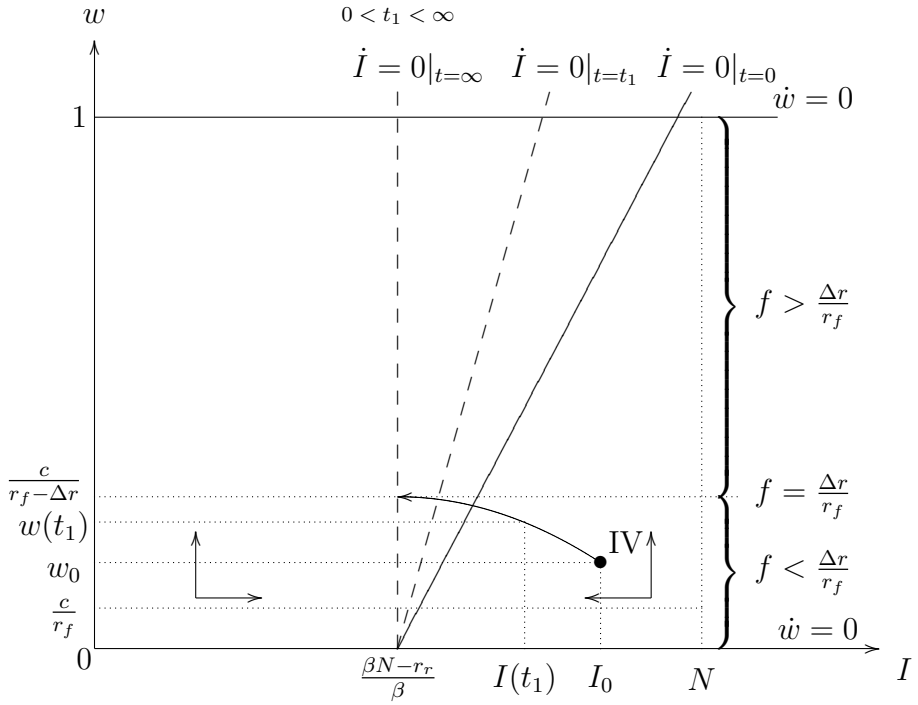


Figure 5b: Open-access dynamics with initial state of type IV

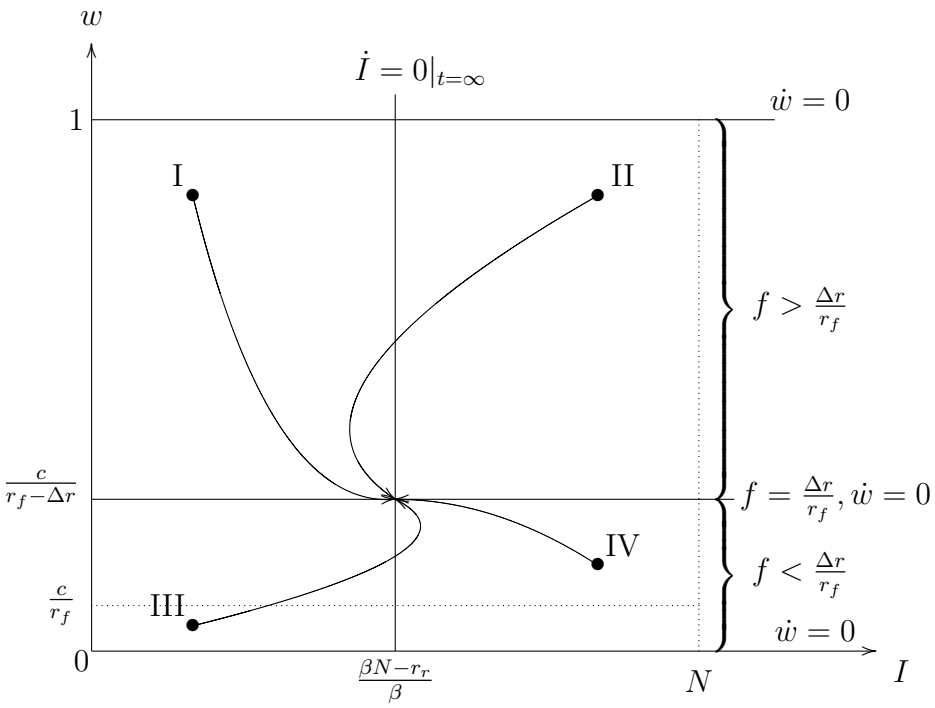


Figure 6: Convergence to steady state under open access

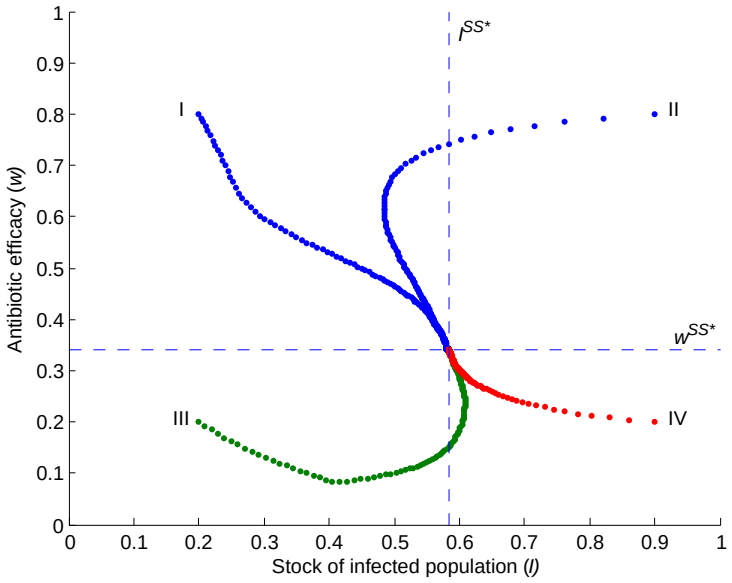


Figure 7: Convergence to steady state in the social optimum

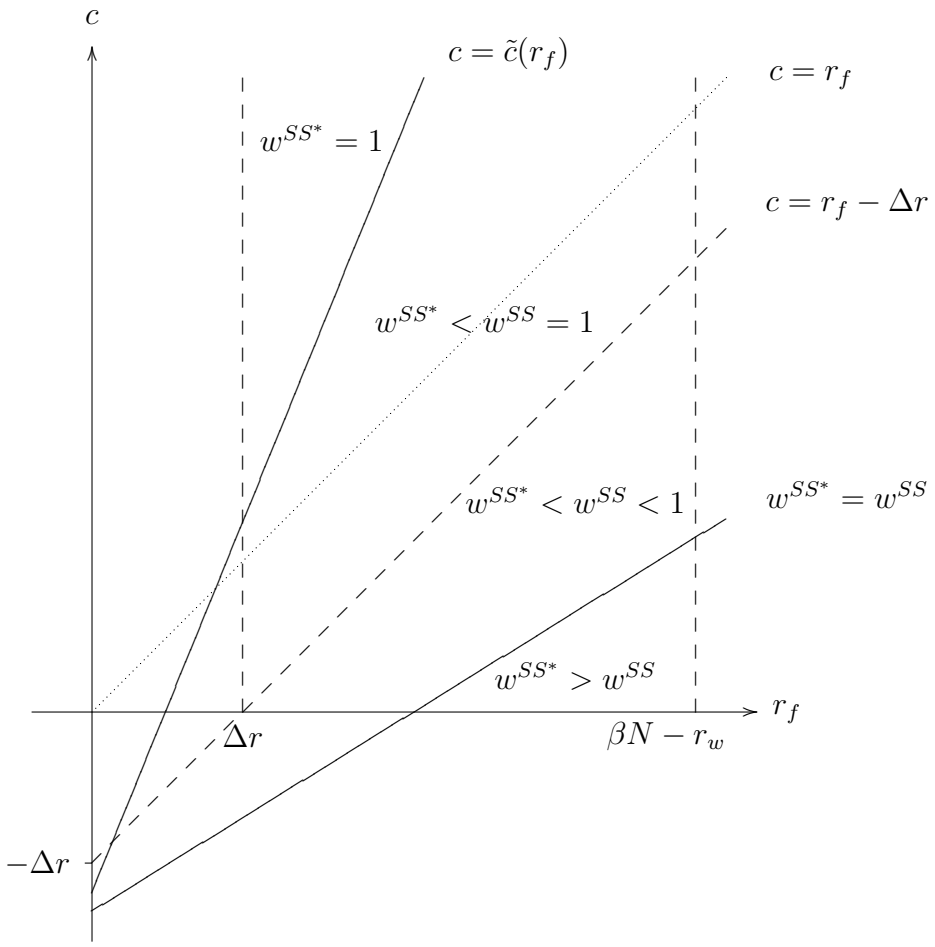


Figure 8: Comparison of the steady states

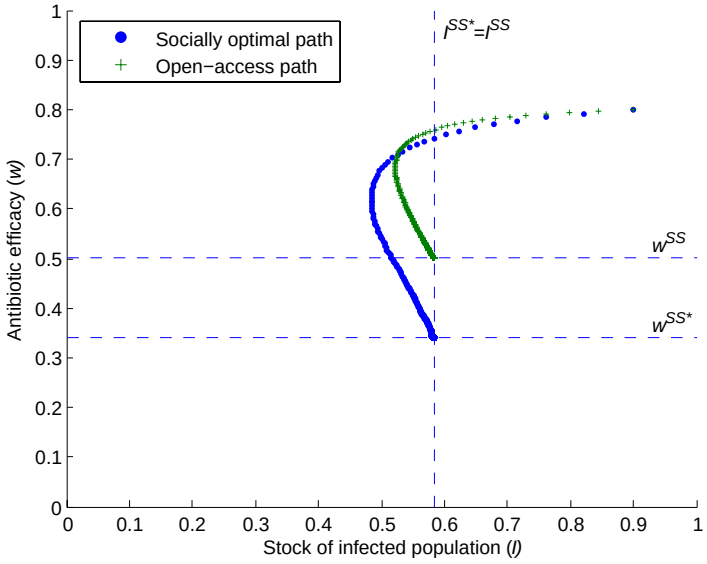


Figure 9a: Comparison of the socially optimal and open-access paths

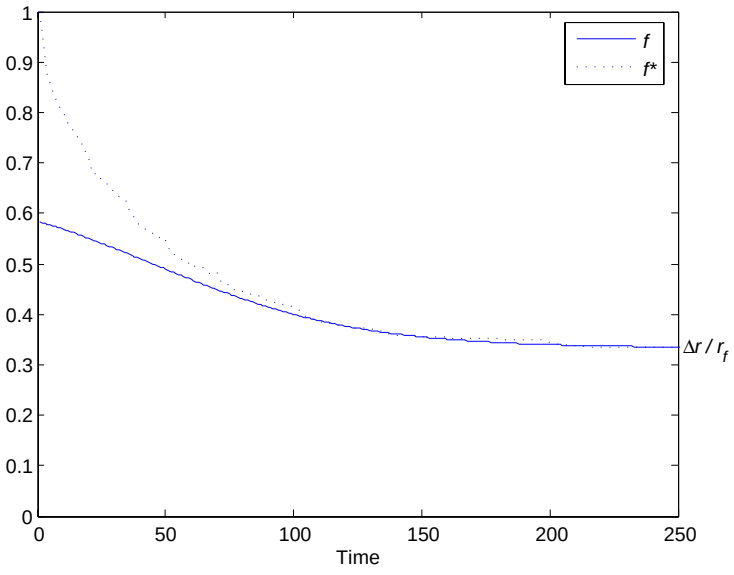


Figure 9b: Comparison of the socially optimal and open-access treatment rates