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Letter

Density Dependence, Senescence, and Williams' Hypothesis

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In 1957, George Williams [1] argued that higher, age-independent, adult mortality should be correlated with more rapid senescence. Charlesworth [2] and most subsequent studies have added the adjective 'extrinsic' to mean that the age-independent mortality was due to sources 'external' to the organism. We now know that neither age- nor condition-independent increases in extrinsic mortality are necessary for more rapid senescence to evolve, and analyses have also shown that higher mortality can lead to the evolution of slower senescence [3,4]. Indeed, there are empirical examples where an added source of mortality seems to have extended lifespan [5]. Nevertheless, Williams' hypothesis remains popular [6].

Recently Moorad *et al*. [7] (henceforth MPS) reviewed Williams' hypothesis and they made the strong claim (in at least ten different places throughout their paper) that Williams' hypothesis is wrong, flawed, and/or contains a conceptual error. They then claim to show that the hypothesis is wrong because, for an extrinsic source of mortality to affect senescence, it must act in an age-dependent fashion (and Williams' hypothesis involves age-independent mortality). This latter claim is also reiterated throughout their paper, where they say that '…formal theory shows that only mortality that is age-specific can influence the evolution of senescence…' and that 'mortality that is truly independent of condition…' cannot affect selection on senescence. This is further emphasized in an entire section of their paper titled 'Models that redefine extrinsic to mean something else', where they say that extrinsic mortality can affect selection only if '…one changes the meaning of "extrinsic" to mean age dependent'. There they also review Abrams [3] and Williams and Day [4], stating that these papers either support their view or, when they don't, it is because of differences in opinion ([7], p. 6).

The purpose of this letter is to point out that these conclusions are incorrect. Both Abrams ([3], p.882) and Williams and Day ([4], p.1482) have independently demonstrated that extrinsic mortality need not be age-dependent to drive the evolution of more rapid senescence. MPS mischaracterize [3] by incorrectly claiming that with '…age-independent density effects, Abrams' models found that the addition of extrinsic mortality had no effect…'. He did not. Likewise, [4] is mischaracterized by incorrectly claiming that any discrepancy between results comes from differences in opinion about how to measure fitness and that perhaps '…we need to examine whether [a] redefinition of fitness is justified'. In fact, these discrepancies are not a matter of opinion. In an online appendix (see supplemental material online), we provide a detailed analysis that illustrates this fact and we present a two-age model as a simple counterexample to MPS's claim that extrinsic mortality must be age-dependent in order to affect selection on senescence. This simple counterexample is nothing more than a special case of the general analysis already published in [3] and [4], but the restriction to two age-classes makes the analysis simpler.

One way to understand why density dependence is important in the evolution of senescence is to note that, roughly speaking, when a population is growing exponentially (i.e., no density dependence), the fitness consequence of a change in vital rates at age x is discounted by the probability of survival to age x and by the population growth rate (because offspring produced earlier can, themselves, reap the rewards of exponential growth). When age-independent extrinsic mortality increases, the discounting through survival gets stronger (i.e., there is a smaller probability of reaching age x), while the discounting through population growth gets weaker (i.e., the exponential growth potential is reduced), such that these two effects exactly cancel and Williams' hypothesis does not hold. But when a population is regulated by density dependence (and so on average is not growing) the latter effect need not exactly cancel the former, even when all density and mortality effects act in an age-independent way.

Indeed, the predictions made by existing theory are completely unambiguous and worth reiterating. If a population is growing exponentially, then a change in age-independent mortality will not affect selection on senescence (i.e., Williams hypothesis is not valid). For populations subject to density dependence things are more complicated for two reasons. First, depending on the form of density dependence, population size might continually change over time in complex ways. At present, little theory speaks to this interesting case (see Appendix in the supplemental material online for further discussion). Second, a change in mortality might affect population density, which then feeds back to affect vital rates in other ways. Nevertheless, if density dependence leads to a constant equilibrium population size then predictions are still completely unambiguous. If all mortality and density effects are age-independent, then Williams' hypothesis is correct when density dependence acts solely through fertility and it is incorrect when density dependence acts solely through mortality. It is a fact, not an opinion, that age-dependency of external mortality is not required for Williams' hypothesis to be valid.

Some previous studies have made the same claim as MPS, suggesting that Williams' hypothesis is wrong irrespective

of whether there is density dependence [8,9]. However, these studies have focused only on the case where density dependence acts solely through mortality and so their conclusions are actually in complete agreement with the above summary (see Appendix in the supplemental material online for further discussion).

Williams' hypothesis continues to occupy the attention of evolutionary biologists [6,10]. It is true that for organisms with high evolutionarily unavoidable mortality, investment in repair and maintenance for ages that are seldom reached does not make sense. Likewise, organisms that require a long time to mature must not deteriorate so rapidly that they never reproduce. Thus, we might expect a positive correlation between mean mortality rate and most measures of senescence in a diverse set of species. However, such a correlation is not very informative regarding the effect of mortality on the evolution of senescence in any particular lineage. The evolution of senescent traits in response to a new mortality source is influenced by many factors, including density dependence in all demographic rates, age-dependent effects of both altered density and the new mortality on existing mortality and fertility, and interactions between the mortality source and physiological changes caused by senescence [3,4]. In addition, senescence involves age-related changes in traits other than mortality, a fact that is often neglected. These changes in birth and growth rates are also likely to cause differential effects on the abundances of different age classes, further complicating evolutionary predictions about senescence. For example, when density dependence in fertilities is characterized by larger effects in more senescent individuals, Williams' hypothesis could again fail to hold.

In summary, to understand the effect of an environmentally imposed change in mortality (or fertility) on the evolution of senescence at least three types of measurements are needed: (i) the direct age-specificity of the change in demographic rates, where 'direct' means age-differences due to age-related factors other than senescence (a point also made by MPS); (ii) the interaction of existing senescence with the environmental factor (e.g., are there greater effects of the factor on individuals with greater senescent decline?); (iii) the density-dependent feedbacks from the environmental change on all life history parameters, including the interactions mentioned in point (ii). Future work should also reassess how to compare rates of senescence, because the trajectories of mortality (or other fitness parameters) versus age are not characterized by a single simple function [11,12]. In addition, it should expand theory to consider variable environments, where results are likely to differ from those of the equilibrium conditions assumed in this and most previous work.

Supplemental Information

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Density Dependence, Senescence, and Williams' Hypothesis (Appendix)

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1 Introduction

In this appendix we make precise our objections through a detailed analysis of a simple two-age model. We focus on the specific claim made in Moorad et al. [1] that 'mortality that is truly independent of condition...' cannot affect selection on senescence, and that extrinsic mortality can affect selection only if '...one changes the meaning of extrinsic to mean age dependent.' This is an unambiguous statement and the message it conveys is reiterated several times throughout their paper. It also forms the basis for Moorad et al.'s [1] central claim that Williams' hypothesis is flawed/wrong (since, if extrinsic mortality must be age-dependent to affect the evolution of senescence as Moorad et al. claim, then Williams' must be wrong because his hypothesis is about age-*independent* extrinsic mortality). As we explain in our letter, however, both Abrams ([2], p.882) and Williams and Day ([3], p.1482) independently demonstrate that Moorad et al.'s claim that extrinsic mortality must be age-dependent is simply not true. Below we will provide a simpler analysis that is a special case of the analyses published in Abrams [2] and Williams and Day [3] to demonstrate this fact.

For simplicity, throughout we make the assumption that the organism in question is asexual in order to put aside any complications of sexual reproduction. We also assume that mutations are relatively rare, an assumption that is implicit in using optimization techniques. Finally, we work in discrete time since many people often find this setting easier to think about. Therefore, the growth *rate* r of Moorad et al. [1] is equivalent to what we will call the growth *factor*, λ, below with the condition that $r > 0$ is equivalent to $\lambda > 1$, $r < 0$ is equivalent to $\lambda < 1$, and $r = 0$ is equivalent to $\lambda = 1$. Although not all of these assumptions are explicitly mentioned in Moorad et al. [1], many of them are implicit in their analysis. In any event, our principle point of disagreement is not affected by focusing on this simple case.

We agree with Moorad et al. [1] that the word 'extrinsic' can be vague and can mean different things to different people, and therefore we will give it a precise definition here. We choose a definition that is both in keeping with how most of the previous theoretical literature on senescence has used the term and one that is also aligned with the above quote from Moorad et al. [1]. Specifically, we refer to a source of mortality as being 'extrinsic' if the following two conditions hold: (i) the mortality is independent of other sources of mortality (in the probabilistic sense of the word) including those that might be thought of as being intrinsic to the organism, like mortality related to condition or senescence itself, and (ii) the mortality is independent of age (i.e., the mortality rate imposed by the external factor is the same for all age classes).

The above two conditions constitute our definition of extrinsic mortality but things can become subtly more complicated when there is density dependence. For example, an increase in the extrinsic mortality rate (as defined above) will usually decrease population density, and if the effect of such a change in density on vital rates is different for different age classes, then even though the extrinsic mortality itself acts in an age-independent way (by our definition) it might still induce an age-specific change in vital rates (like mortality or fertility) as a result of such demographic feedbacks. In this sense, even extrinsic mortality as defined above might ultimately not be truly independent of age because of an age-dependent demographic feedback [2]. Therefore, to be completely unambiguous, when considering density dependence we will only consider forms of density dependence that are also independent of age. In other words, if there is ever a demographic feedback that occurs through density dependence, we will assume that it too affects all age classes in an identical fashion. As a result, whenever we consider in change in extrinsic mortality, there is no sense in which it can result in any age-dependent effects on the vital rates. Of course this is clearly a highly unrealistic case and one that is probably never realized in any real biological population. The point of focusing on this case though is to illustrate that the way of thinking about Williams' hypothesis that is advocated by Moorad et al. [1] is

incorrect. Namely, they claim (as in the above quote) that if extrinsic mortality ever has an effect on the evolution of senescence, then it is because somehow this mortality ultimately results in an age-dependent effect on vital rates. We will show that this is not true. It *is* the case that, for enhanced extrinsic mortality to cause an evolutionary change in senescence the enhanced mortality must result in age-dependent differences in *selection* (by definition) but it is not true that it must result in age-dependent affects on the vital rates.

Although some of the analysis below is quite general we will also attempt to highlight the general issues throughout with a running example. For simplicity (and so one can obtain explicit expressions for all quantities of interest) we consider a species with two age classes that lives is a seasonal environment. We census the population at the start of spring. Both age 1 and age 2 individuals produce offspring during the summer, with fecundity m_1 and m_2. The offspring then survive the winter with probability s_0, and age 1 individuals survive the winter with probability s_1. All age 2 individuals die at the end of the breeding season. Thus, the number of age 1 and age 2 individuals at the start of spring next year (denoted by $n_1(t+1)$ and $n_2(t+1)$ respectively) can be computed from the number of these kinds of individuals at the start of spring this year (denoted by $n_1(t)$ and $n_2(t)$) as

$$n_1(t+1) = n_1(t)m_1s_0 + n_2(t)m_2s_0 \quad (1)$$

$$n_2(t+1) = n_1(t)s_1 \quad (2)$$

or in matrix notation

$$n(t+1) = Ln(t) \quad (3)$$

where n is a vector whose components are the numbers of individuals in the different age classes and L is the Leslie matrix

$$L = \begin{bmatrix} m_1 s_0 & m_2 s_0 \\ s_1 & 0 \end{bmatrix} \tag{4}$$

In what follows we first consider the density independent case since this will serve as a useful benchmark. We then consider how things are altered under density dependence.

2 Density independence (DI)

By density-independence we mean that all vital rates are independent of density. Thus, under DI the population size will change exponentially. In this case all life history strategies that have an intrinsic growth factor larger than 1 will persist (we will use the terms 'growth factor' and 'growth rate' interchangeably). However, over time the strategy with the largest growth rate will come to make up the greatest *fraction* of the population. Therefore, over a long (evolutionary) time frame, after many mutations have occurred, we expect the population to be dominated by the life history strategy that has the largest growth rate. Thus, we can predict which life history strategy will dominate by predicting the life history strategy that maximizes growth rate.

For and exponentially growing population, the growth rate, λ, of any strategy is defined implicitly by the Euler-Lotka equation

$$\sum_i \lambda^{-i} l_i m_i = 1 \tag{5}$$

where l_i is the probability of surviving to age i and m_i is the fecundity of individuals of age i. To find the strategy that maximizes λ we first need to delineate the strategies that are of interest. For example, in the case of antagonistic pleiotropy we are interested in the trade-off between early and late-life fitness components. At the optimal life history the effect on λ of any change in one component of fitness must be exactly balanced by the effect on λ of the resulting change (due to pleiotropy) in the other component of fitness (if this wasn't true then it would be possible to increase λ). And we can use the results of Hamilton [4] to compute the effect on λ of a change in any life history component of interest.

Running Example - For our running example the Euler-Lotka equation is

$$\lambda^{-2} s_0 s_1 m_2 + \lambda^{-1} s_0 m_1 = 1 \tag{6}$$

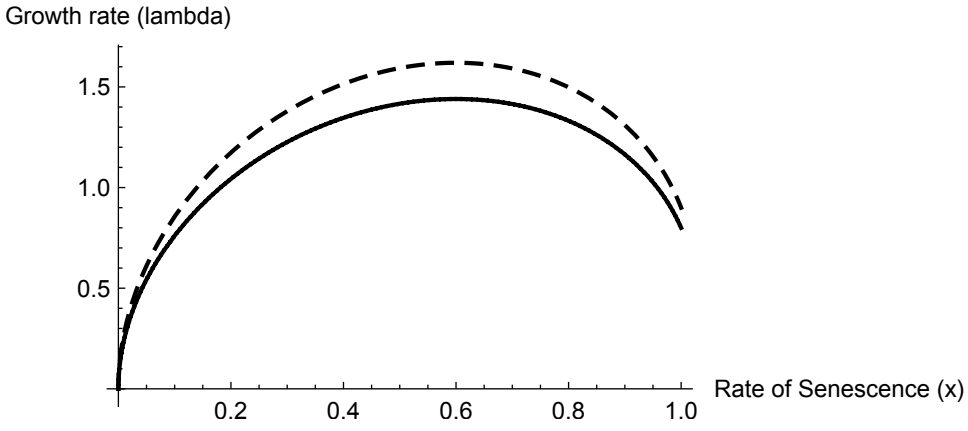
(note that $l_2 = s_0 s_1$ and $l_1 = s_0$). In fact, although the Euler-Lotka equation typically defines λ implicitly as a function of the life history parameters, this model is simple enough that we can write down λ as an *explicit* function of these fitness parameters:

$$\lambda = \frac{1}{2}\left(m_1 s_0 + \sqrt{m_1^2 s_0^2 + 4 m_2 s_0 s_1}\right) \tag{7}$$

In other words, equations (6) and (7) are simply two different but equivalent ways of expressing how the dominant eigenvalue of L is a function of the vital rates.

Let's now consider a case of antagonistic pleiotropy in which there is a trade-off between the age-specific survival probabilities s_0 and s_1. To make things concrete, let's use x to denote the intrinsic survival probability of a newborn reaching age 1, and $1 - x$ to be the intrinsic survival probability of an age 1 individual reaching age 2. In this case we can

think of x as a measure of the rate of senescence. Large values of x mean that early-life survival is high and late-late survival is low, and so the drop in survival with age is large (i.e., a large rate of senescence). Further, let's use p to denote an age-independent survival probability related to sources of mortality external to the organism (i.e., extrinsic mortality). From our definition of 'extrinsic' we have $s_0 = px$ and $s_1 = p(1-x)$. In this context, Williams' hypothesis is about how changes in p affect senescence (here defined by x). And again we stress that there is no age-dependence in this external source of mortality and that it acts in way that is independent of the 'intrinsic' survival rate at each age, x and $1-x$. The figure below plots the growth rate λ as a function of x for two different values of p (and with $m_0 = 1$ and $m_1 = 9$). The top (dashed) curve corresponds to $p = 0.9$ and the bottom (solid) curve corresponds to $p = 0.8$.



We can see that, although decreasing p (i.e., increasing age-independent mortality) reduces the growth rate for any fixed value of x (as expected) it does not alter where the growth rate reaches a maximum as a function of x. In fact, for this simple model we can find the value of x that maximizes λ directly by differentiating (7), setting the result to zero, and solving for x. We get

$$x^* = \frac{\sqrt{m_2}}{2\sqrt{m_2} - m_1} \tag{8}$$

We can see that, as illustrated in Figure 1, the optimal rate of senescence does not depend on the extrinsic source of mortality p, meaning that Williams' hypothesis does not hold in this case.

Before moving to the density-dependent case it is worth laying out how Hamilton's [4] approach relates to the above result in this simple model. As we have already mentioned, this example is simple enough that we can write the growth rate λ explicitly as a function of the life history parameters and so, to find the optimal life history, we can directly differentiate this function. More generally, Hamilton [4] differentiated λ *implicitly* using the Euler-Lotka equation. To do so in this simple example we differentiate λ in equation (6) implicitly with respect to the life history parameters s_0 and s_1. We get

$$\begin{aligned} \frac{\partial \lambda}{\partial s_0} &\propto m_1 + s_1 m_2 \lambda^{-1} \\ \frac{\partial \lambda}{\partial s_1} &\propto s_0 m_2 \lambda^{-1} \end{aligned} \tag{9}$$

where the constant of proportionality in both is the same and is equal to $1/T$, where T is a measure of generation time given by $T = s_0 m_1 \lambda^{-1} + 2 s_0 s_1 m_2 \lambda^{-2}$. Equations (9) are exactly Hamilton's [4] fitness sensitivity expressions in the context of this simple example. To complete the picture, recall that both s_0 and s_1 are functions of x in our example, and so the optimal life history occurs when the fitness effects through expressions (9) exactly balance one another. In other words, the optimal value of x must satisfy

$$\frac{\partial \lambda}{\partial s_0}\frac{ds_0}{dx} + \frac{\partial \lambda}{\partial s_1}\frac{ds_1}{dx} = 0 \tag{10}$$

or, using Hamilton's [4] expressions (9) and noting that $s_0 = px$ and $s_1 = p(1-x)$ and so

$ds_0/dx = -ds_1/dx$, we get

$$m_1 + s_1 m_2 \lambda^{-1} - s_0 m_2 \lambda^{-1} = 0 \tag{11}$$

It is important to note that in equation (11) λ is not arbitrary, but rather it is defined by the Euler-Lotka equation (i.e., either by 6 or equivalently by 7). Thus, if we substitute this definition into (11) we can then solve for the optimal value of x and we get (8) as before (as we must since both calculations are simply different ways of computing the same thing). And as we already mentioned, extrinsic mortality has no effect on the optimal rate of senescence. In fact, we can see directly from Hamilton's [4] expressions (9) that extrinsic mortality will have no effect because they do not depend on p. To see this it is critical to note that λ *does* depend on p (it can be seen to be proportional to p from equation (7)) but the s'*s* are proportional to p as well and because every s is multiplied by a λ^{-1} in Hamilton's [4] expressions (9) the p'*s* cancel.

3 Density dependence (DD)

So far our conclusions agree with the claims of Moorad et al [1]. We now turn the the case of density-dependence. We take the existence of DD to mean that at least some of the vital rates dependent on population density. Usually, however, people mean a bit more than this when invoking density dependence. In particular, since a population might still grow in an unbounded way even if the vital rates depend on density (e.g., if DD is weak), people usually take DD to mean that population size is regulated in some way. Consequently, we define DD as a situation in which at least some of the vital rates depend on density, and they do so in a way that prevents unbounded population growth.

How do we incorporate DD? In general this can be complicated because, under DD the long-term population size can reach a steady state, it can display periodic behaviour, or it can even display chaotic behaviour. How we model evolution (and the predictions that can be made about evolution) therefore typically depends on what sorts of long-term population dynamics we want to consider. Although it is perhaps not very realistic, the majority of theory on the evolution of senescence and Williams' hypothesis involving density dependence (including Moorad et al. [1]) either implicitly or explicitly assumes that, in the long term, the population size reaches a steady state. Therefore we make this assumption here as well.

What above evolution? How do we predict the evolutionary outcome under DD? Presumably, if during the process of evolution the population is to eventually settle down to an 'optimal' strategy, then this means that evolutionary change would essentially stop. In turn this means that the 'optimal' strategy must be 'uninvadable'. In other words, once most individuals in the population are using this strategy, it must be the case that any mutant strategy that appears will have a lower fitness (i.e., a lower growth rate, λ). Otherwise, the population would continue to evolve.

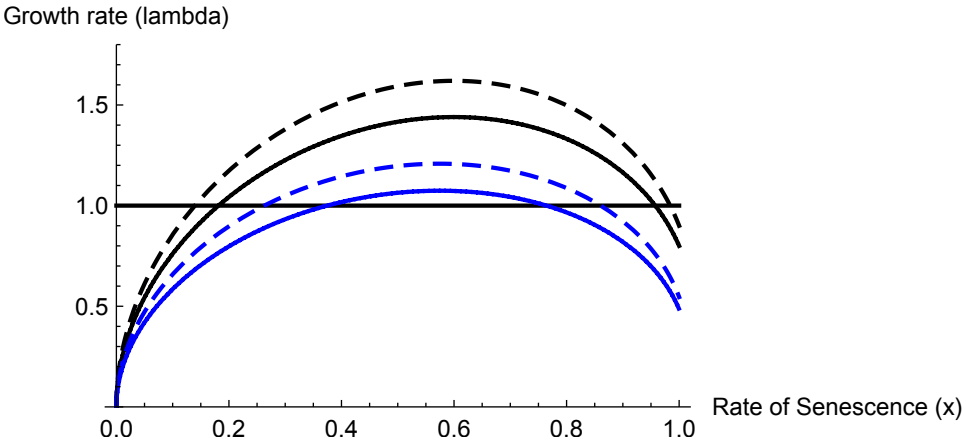
Given the above, there are therefore two conditions that must be used to characterize the predicted evolutionary outcome. Namely, once the population has reached demographic and evolutionary equilibrium we require that: (1) the population is not changing in size and thus $\lambda = 1$, and (2) the growth rate λ must be maximized as a function of the life history strategy of interest. The key difference from the DI case is therefore that some of the life history parameters now depend on density (which we denote by N) and λ must therefore be maximized *subject to the constraint that, at this maximum, the density N is such that we also have $\lambda = 1$.*

Running Example - To make our point we will assume that density dependence acts solely through fecundity and in an age-independent manner. Specifically, we assume that m_1 and

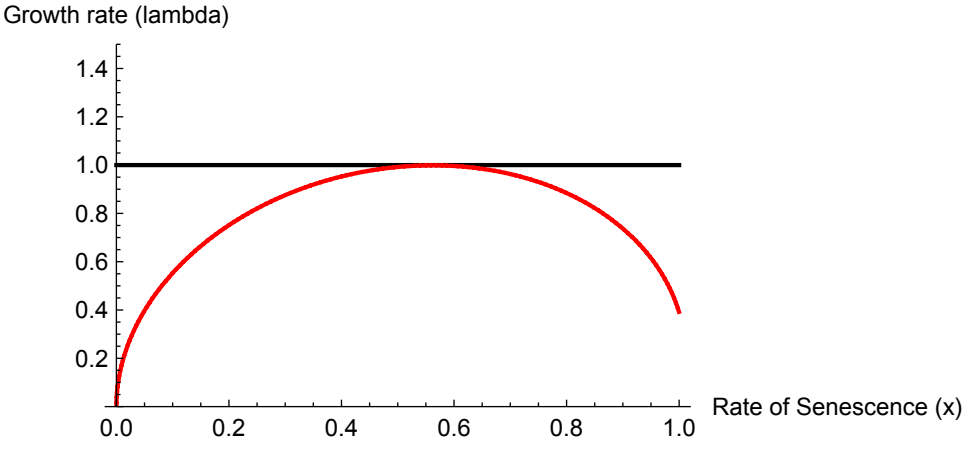
m_2 can be written as $m_i = f(N)b_i$ where b_i is the fecundity of an age i individual when population density is low, and $f(N)$ is a decreasing function of population density N (with $f(0) = 1$) that captures the age-independent density dependence. All other assumptions about the model structure remain the same as the DI case (including the assumption that extrinsic mortality acts in an age-independent way). This is a situation in which Moorad et al. ([1]; p. 525) claim Williams' hypothesis is still not valid (just as it wasn't in the DI case above) because, as Moorad et al. [1] claim, 'density dependent population regulation cannot, by itself, cause changes in selection'. As our example will illustrate, this is not true. The mere addition of density-dependence on fertility (in a completely age-independent way) does indeed cause changes in selection on senescence. It is difficult to tell where the error in this part of Moorad et al.'s [1] analysis lies because many key components of their analysis are not clearly stated or defined. For example, what they mean by extrinsic mortality being age-dependent is never explicitly defined despite this forming the backbone of their entire argument (we also could not obtain a clear answer in our correspondence). Their text, however, suggests that they consider extrinsic mortality to be age-dependent if it results in a change in the stable age distribution. For example, when explaining what they claim is a flaw in Williams' model they say 'It has long been known that the addition of age-independent mortality can have, by definition, no effect on age-distributions. It follows that mortality that is truly independent of condition will not affect within- or among age distributions of phenotypes' ([1], p. 520). But this is both incorrect (with density dependence, the stable age distribution can indeed change as a result of a change in age-independent mortality - our simple model below provides an example) and irrelevant (a change in the age distribution is neither necessary nor sufficient for a change in age-specific selection on senescence).

Returning to our example, equations (6) and (7) continue to hold under DD but now the m's are functions of population density N. Thus, to construct a plot analogous to that of Figure 1 we now must also specify the population density N. Figure 2 illustrates this for

the same two values of p used in Figure 1 (again dashed and solid) but now for two different values of population density as well (black vs blue). We have chosen $f(N) = e^{-N}$ for simplicity, and the black plot corresponds to $N = 0$ and so is identical to that of Figure 1 while the blue plot corresponds to $N = 0.5$. We have also plotted the $\lambda = 1$ line.



We can see that in general λ is larger in low density populations for any given value of x (as we would expect). Now as we have stressed, at eco-evolutionary steady state not only must λ be maximized but the population density must also have reached a value such that $\lambda = 1$. Graphically, this means that the population density must be such that the graph of λ as a function of the life history strategy (here rate of senescence x) must be tangent to the $\lambda = 1$ line when it reaches its maximum. The plot must therefore look like that shown in Figure 3 at eco-evolutionary equilibrium.



Let's now use this fact to compute the predicted value of x. As before we will do so using Hamilton's [4] results. Equations (9) continue to hold, as do equations (10) and therefore (11) since they characterize the fact that when λ is maximized, early and late-life fitness effects must be balanced. But we must now also enforce the condition that at eco-evolutionary steady state the population size is unchanging (i.e., $\lambda = 1$). Substituting this into equation (11) gives the necessary condition

$$m_1 + s_1 m_2 - s_0 m_2 = 0 \tag{12}$$

or, more explicitly

$$b_1 f(\hat{N}) + s_1 b_2 f(\hat{N}) - s_0 b_2 f(\hat{N}) = 0 \tag{13}$$

where $\hat{N}$ is the population size at which $\lambda = 1$. We can cancel $f(\hat{N})$ from this equation to get

$$b_1 + s_1 b_2 - s_0 b_2 = 0 \tag{14}$$

which can then be solved for the optimal value of x to get

$$x^* = \frac{1}{2} + \frac{b_1}{2 b_2 p} \tag{15}$$

Notice that now the optimal rate of senescence *does* depend on p. In particular, as p goes down (i.e., as age-independent extrinsic mortality goes up) the optimal rate of senescence, x, goes up exactly in accordance with Williams' hypothesis [5].

Incidentally, we point out that equation (14) is exactly the necessary condition that we would get if we had instead simply maximized R_0 in this model in the absence of density dependence (i.e., assuming $N = 0$). Specifically, $R_0 = s_0 m_1 + s_0 s_1 m_2 = s_0 b_1 + s_0 s_1 b_2$ where the last equality holds when $N = 0$. If we then differentiate this with respect to x and set the result equal to zero we get exactly equation (14). This is no coincidence. A beautiful (and we believe underappreciated) paper by Mylius and Diekmann [6] proves that whenever density dependence acts in an age-independent way through feertility (as assumed here in our simple model) the optimal life history is always one that maximizes R_0. We have used Hamilton's [4] equations here rather than the results of Mylius and Diekmann [6] simply to better match the approach taken by Moorad et al. [1]. However, the techinques of Mylius and Diekmann [6] provide a much more general and simpler way to obtain the same prediction.

It is also worth noting that we can see directly from Hamilton's [4] expressions (9) that extrinsic mortality p will affect the predictions under this form of density dependence. Unlike in the DI case, the population density will always adjust in the long term so that $\lambda = 1$. Thus, as Hamilton [4] himself noted, expressions (9) become

$$\begin{aligned} \frac{\partial \lambda}{\partial s_0} &\propto m_1 + s_1 m_2 \\ \frac{\partial \lambda}{\partial s_1} &\propto s_0 m_2 \end{aligned} \tag{16}$$

or, under the form of DD considered here

$$\begin{aligned} \frac{\partial \lambda}{\partial s_0} &\propto b_1 + s_1 b_2 \\ \frac{\partial \lambda}{\partial s_1} &\propto s_0 b_2 \end{aligned} \tag{17}$$

(because both have the same density dependence factor $f(\hat{N})$). Now the p's that are part of the survival probabilities s_0 and s_1 no longer cancel as they did in the DI case.

As an aside, one might wonder if perhaps λ is not always equal to 1 in the density dependent case. For example, suppose a population has reached eco-evolutionary equilibrium. Now imagine increasing the age-independent extrinsic mortality by decreasing p. The first immediate effect will be that the population size decreases and so we have $\lambda < 1$ during this phase. Doesn't this contradict the assumption made above that we must have $\lambda = 1$? This appears to be part of the justification given in Moorad et al. [1] for their belief that there is no difference in predictions between DI and DD. For example, they state that Williams and Day's [3] defense of Williams' hypothesis 'begins with the condition that density regulation maintains stable population sizes with no time lag regardless of any mortality effects caused by changing density ([1], p.524)', and that 'even long-term stationary populations are not invariant. They are dynamically stable and must be in states of increase ...[$\lambda > 1$]... and decrease...[$\lambda < 1$]...for much of the time. ([1], p. 525)' Such transient effects on the population size certainly will occur, and are potentially very interesting, but these quotes suggest that Moorad et al. [1] have not appreciated an important aspect of the mathematical foundation of all optimization models based on the Euler-Lotka (EL) equation; namely, all mathematical analyses are valid only for the asymptotic state of the population. This means that such analyses (including those of Moorad et al. [1]) cannot speak to these transient effects. They apply only once the population has reached a stable age-distribution and is growing exponentially (the DI case) or once the population has reached stable age distribution and is stationary in size (the DD

case). This is simply a mathematical fact and it invalidates all of Moorad et al.s [1] arguments having to do with these transient effects.

Indeed, for similar reasons, most of the considerations of p. 525 of their paper are mathematically invalid. To reiterate, anytime one uses the Euler-Lotka equation in such models one is necessarily assuming that the population size is changing exponentially and that the dynamics have reached their asymptotic state (and so a stable age distribution has been reached). These assumptions form the very basis of how the Euler-Lotka equation is derived (e.g., see [7]). Thus, the EL equation can only be used in three situations: (i) the population is growing exponentially ($\lambda > 1$), (ii) the population is declining exponentially ($\lambda < 1$), or (iii) the population is constant is size (i.e., changing exponentially with a growth rate of $\lambda = 1$.). Therefore, if DD prevents unbounded population growth then, asymptotically, the population must either reach a constant size (i.e., $\lambda = 1$ and we can use the EL equation as we have above), or it will continue to fluctuate in size (in which case the population will not, typically, be changing exponentially and so we cannot use the EL equation). Thus, there is no actual mathematical basis to Moorad et al.'s [1] claim that setting $\lambda = 1$ in the analysis of DD is arbitrary and that, although '...it does make it slightly easier to develop models if one assumes that [λ] is constant over time [and equal to 1] models that permit [λ] to change in response to some ecological shift are not intractable (Box 3)'. Everything in their Box 3 is based on the EL and so necessarily excludes the very cases that they are attempting to explain. It is certainly interesting to ask about the validity of Williams' hypothesis in situations where DD results in continual fluctuations in population size but nothing in the analysis of Abrams [2], nor Williams and Day [3], nor Moorad et al. [1] speaks to this question. (Note that it is possible that the EL equation sometimes provides an *approximation* under other conditions, but whether this is true, and how accurate the approximation might be, typically must be determined on a case-by-case basis.).

Finally we wish to stress (as we said in our letter) that the form of DD really does dictate whether Williams' hypothesis holds. To highlight this fact we now show that if we simply change DD so that it acts in an age-independent way through survival then Williams' hypothesis no longer holds. Specifically we now treat the m's as density-independent but define $s_0 = pxf(N)$ and $s_1 = p(1-x)f(N)$. Again expressions (16) hold but now, under this form of DD, they simplify to

$$\begin{aligned} \frac{\partial \lambda}{\partial s_0} &\propto m_1 + p(1-x)f(\hat{N})m_2 \\ \frac{\partial \lambda}{\partial s_1} &\propto pxf(\hat{N})m_2 \end{aligned} \tag{18}$$

We cannot yet tell from these expressions what will happen because $f(\hat{N})$ will likely depend on p. In fact, from equation (7) we can see that

$$\lambda = \frac{1}{2}\left(m_1 x + \sqrt{m_1^2 x^2 + 4m_2 x(1-x)}\right) pf(N) \tag{19}$$

and since $\hat{N}$ is the population size for which $\lambda = 1$ we have

$$f(\hat{N}) = \frac{2}{p\left(m_1 x + \sqrt{m_1^2 x^2 + 4m_2 x(1-x)}\right)} \tag{20}$$

Thus, $f(\hat{N})$ is proportional to $1/p$ and so the p's in Hamilton's expressions cancel, meaning extrinsic mortality has no effect on the optimal life history. Thus, under this form of DD Williams' hypothesis is not valid. So the form of DD really does determine whether Williams' hypothesis is valid.

Incidentally, if we take equation (11) with $\lambda = 1$ and then substitute this form of DD we get

$$m_1 + p(1-x)f(\hat{N})m_2 - pxf(\hat{N})m_2 = 0 \tag{21}$$

and if we then also substitute in the expression for $f(\hat{N})$ we get the condition

$$2m_2 - 4m_2x + m_1^2x + m_1\sqrt{m_1^2x^2 + 4m_2x(1-x)} = 0 \tag{22}$$

Although perhaps not immediately obvious, this last condition is exactly the necessary condition we would get if we had instead simply maximized λ in this model in the absence of density dependence (i.e., assuming $N = 0$). Again this is no coincidence. The paper by Mylius and Diekmann [6] proves that whenever density dependence acts in an age-independent way through survival as assumed here, the optimal life history is always one that maximizes λ.

4 Conclusions

Moorad et al. [1] claim that Williams made a conceptual error in his 1957 paper and so his hypothesis is wrong/flawed etc. because 'mortality that is truly independent of condition...' cannot affect selection on senescence, and that extrinsic mortality can affect selection only if '...one changes the meaning of extrinsic to mean age dependent.' As we mentioned in our letter both Abrams ([2], p.882) and Williams and Day ([3], p.1482) independently demonstrate that this is not true. Here, with the above results, we have again demonstrated this fact.

Although the mathematical details are obviously important we feel that it is equally

important that some sort of intuition for the results be obtained from the mathematics. To this end let's again consider equation (11) from our simple two-age model, which is repeated here for easy reference:

$$m_1 + s_1 m_2 \lambda^{-1} - s_0 m_2 \lambda^{-1} = 0 \tag{23}$$

Recall that this equation specifies the balance that must occur between early and late-life fitness effects of a change in senescence at the optimal life history. The first two terms are the early-life effect (i.e., the effect of a change in survival to age 1) and the last term is the late-life effect (i.e., the effect of a change in survival from age 1 to age 2).

In all analyses (both DI and DD) a key ingredient in the evolution of senescence is the idea that the fitness consequence of a change in vital rates at age a must discounted by the probability of survival to age a (because only the surviving fraction of the population expresses the trait). This is captured by the s's in equation (23). Now in the DI case, because the population is growing exponentially, the fitness consequence of a change in vital rates at age a must also be discounted by the population growth rate (because offspring produced earlier can, themselves, reap the rewards of exponential growth). This is captured by the λ's in equation (23). As a result, when extrinsic mortality increases, the discounting through survival gets stronger (i.e., there is a smaller probability of reaching age a - the s's in equation (23) decrease) while the discounting through population growth gets weaker (i.e., the exponential growth potential is reduced and so λ^{-1} in equation (23) gets larger). You can see in equation (23) that these two effects exactly cancel, and Williams hypothesis therefore does not hold.

Under DD there is no longer any discounting due to population growth because at eco-evolutionary equilibrium the population is constant in size. In other words, equation (23) becomes

$$m_1 + s_1 m_2 - s_0 m_2 = 0 \tag{24}$$

Notice that the fitness consequence of a change in vital rates at age a are still discounted by the probability of survival to age a (through the s's). And because this gets stronger as extrinsic mortality increases, *all else equal* this will tend to make Williams' hypothesis valid. You can see this in equation (24) by the fact that early-life reproduction (the m_1 term) is not discounted as much as late-life reproduction. This is precisely the effect that Williams [5] identified in his 1957 paper and so, in a very important sense, Williams' intuition and reasoning was absolutely correct.

Of course all else might not always be equal because, when there is DD, some of the vital rates will be depressed at eco-evolutionary equilibrium owing to population density. Thus, we can think of this as another way in which the fitness consequences of change in vital rates at age a must be weighted. It appears that Williams' [5] reasoning implicitly assumed that such density effects apply equally across ages and so all else would be equal [3]. For example, if DD acts through fertility, then equation (24) becomes

$$b_1 f(\hat{N}) + s_1 b_2 f(\hat{N}) - s_0 b_2 f(\hat{N}) = 0 \tag{25}$$

Since all terms in this equation are depressed equally by the DD (because DD is acting uniformly through fertility in an age-independent way) this does not affect the *balance* of early versus late-life effects. In other words, all else is indeed equal and so the discounting that occurs through survival when extrinsic mortality increases does indeed select for greater senescence as Williams [5] argued.

On the other hand, sometimes all else will not be equal. For example, if DD acts uniformly through survival then equation (24) becomes

$$m_1 + s_1^* f(\hat{N}) m_2 - s_0^* f(\hat{N}) m_2 = 0 \tag{26}$$

where we have defined $s_i^* = s_i / f(\hat{N})$ for clarity of notation. Now, we can see that the depression of vital rates as a result of DD affects only some of the terms and so it has the potential to alter the balance. When extrinsic mortality increases, the discounting through survival gets stronger (i.e., there is a smaller probability of reaching age a) just as Williams [5] argued, and again the reduced population size that results means that DD gets weaker. Here, however, this weaker DD affects the mortality rates and this exactly counteracts the effect that Williams [5] identified. Put another way, with this form of DD, when extrinsic mortality is increased, the compensation that occurs through DD means that the overall probability of surviving to any given age is unchanged (and thus Williams' hypothesis does not hold).

Whether one chooses to view the above conclusions as meaning that Williams' [5] reasoning was wrong, conceptually flawed, etc. is a matter of opinion, but the above predictions themselves are facts not opinions.

So why all the confusion in the literature?

To finish we summarize exactly what previous theory tells us about Williams' hypothesis, with the aim of dispelling some of the confusion on the topic that seems to have crept into the literature. To do so we also comment upon three other papers on this topic that have been published and that are discussed in Moorad et al. [1].

We begin with the results of Abrams [2], that show three unambiguous facts about Williams' hypothesis:

1. If a population is growing exponentially, then a change in age-independent mortality will not affect selection on senescence (i.e., Williams hypothesis is not valid).

2. For populations subject to density dependence, and where this DD is age-independent and leads to a stable population size, Williams hypothesis is valid if the DD acts solely through fertility and it is invalid if the DD acts solely through mortality.

3. For populations subject to other forms density dependence the outcome can be more complex.

Thus, without question, it is a fact that age-dependency of external mortality (as defined here) is not required for Williams hypothesis to be valid (incidentally, [2] also shows that, when mortality is age- or condition-dependent, selection can be changed in either direction - a point on which Moorad et al [1] agree). In 1995 Mylius and Diekmann [6] then published a paper that provided a very general and simpler way to model life history evolution under density dependence. Williams and Day [3] then used the theoretical results in [6] to extend the analysis of [2] other ways, part of which involved independently re-deriving the above three facts.

With this as a backdrop, it is indeed confusing that at least three other theoretical studies published since then seem to contradict these facts and to contradict one another as well. First, Caswell [8] and Caswell and Shyu [9] make the very same point as Moorad et al.'s [1] main thesis; namely, that Williams hypothesis is *never* valid unless the extrinsic mortality is age-dependent. To make matters even more confusing, they come to their conclusion for entirely different reasons than those Moorad et al. [1]. So, taken at face value, their results seem to directly contradict fact (2) above. Then, in 2018, da Silva [10] also examined Williams' hypothesis and claimed exactly the opposite of Caswell et al. [8, 9]; namely, that under density dependence, Williams's hypothesis is *always* valid. Clearly these claims can't all be correct.

Unlike Moorad et al. [1], the discrepancy between the results of Caswell et al. [8, 9] and fact (2) above stem entirely from a difference in definitions. Caswell et al. [8, 9] (implicitly) define age-independent DD as DD that affects all entries of the Leslie matrix in the same way. In our simple example this is mathematically equivalent to assuming that DD acts solely on mortality in an age-independent way. As a result, the findings of Caswell et al. [8, 9] are actually in complete agreement with fact (2) - Williams' hypothesis does not hold when DD acts uniformly on mortality rates. However, from a biological standpoint, it seems reasonable to consider DD acting uniformly on fertility across all ages as being age-independent as well. This is the case we explored above where Williams' hypothesis *is* valid. In this case not all entries of the Leslie matrix are affected by DD in the same way (only the top row is affected) and so Caswell et al. [8, 9] simply excluded it from their analysis. Again, it is important to stress, however, that this simple difference in definition is *not* what underlies the discrepancy between Moorad et al. [1] and previous findings (as we have explained in detail in the bulk of this appendix).

In the case of da Silva [10], however, unfortunately the problem is simply that the analysis is incorrect. In particular, the analysis is mathematically inconsistent because, while it correctly notes that $\lambda = 1$ in the DD case ($r = 0$ in [10]), it does not actually incorporate the very DD in the vital rates that causes λ to equal 1. As a result, [10] simply recovers only part of the story; namely, the part that was identified by Williams [5] and that assumes all else is equal. As we have explained above, however, when DD is explicitly incorporated into the vital rates, all else need not be equal - it depends on how the DD operates, exactly as detailed in fact (2).

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