



# Aging as a consequence of selection to reduce the environmental risk of dying

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**Each animal in the Darwinian theater is exposed to a number of abiotic and biotic risk factors causing mortality. Several of these risk factors are intimately associated with the act of energy acquisition as such and with the amount of reserve the organism has available from this acquisition for overcoming temporary distress. Because a considerable fraction of an individual's lifetime energy acquisition is spent on somatic maintenance, there is a close link between energy expenditure on somatic maintenance and mortality risk. Here, we show, by simple life-history theory reasoning backed up by empirical cohort survivorship data, how reduction of mortality risk might be achieved by restraining allocation to somatic maintenance, which enhances lifetime fitness but results in aging. Our results predict the ubiquitous presence of senescent individuals in a highly diverse group of natural animal populations, which may display constant, increasing, or decreasing mortality with age. This suggests that allocation to somatic maintenance is primarily tuned to expected life span by stabilizing selection and is not necessarily traded against reproductive effort or other traits. Due to this ubiquitous strategy of modulating the somatic maintenance budget so as to increase fitness under natural conditions, it follows that individuals kept in protected environments with very low environmental mortality risk will have their expected life span primarily defined by somatic damage accumulation mechanisms laid down by natural selection in the wild.**

aging | senescence | life-history modeling | mortality risk | evolution

There is substantial empirical support for the notion that animals on average live far longer in a properly designed protected environment than in their natural environment (1–4). This implies that ecological risk factors are major determinants of life expectancy in the wild (5, 6), irrespective of variation in mortality risk with age (7) and of variation in the degree of senescence in wild animals (8–12). Regardless of intraspecies genetic and phenotypic variation and the huge interspecies variability in the repertoires of abiotic and biotic risk factors causing mortality in the wild, all individuals are faced with the destiny that one day, they will draw the fatal ticket in the Darwinian lottery. This raises the question of whether there exists a ubiquitous life-history strategy response to this ominous fact that is favored by natural selection.

The hypothesis we will examine is that there exists such a life-history strategy, independent of temporal mortality risk profiles, which is materialized through a universal physiological principle of tuning the allocation to somatic maintenance to expected life span so that lifetime fitness is enhanced. The rationale for this is that an intimate link exists between the energy acquisition needs of an individual and mortality risk. Because somatic maintenance accounts for a substantial part of the lifetime need of acquired energy (13), restraining allocation to somatic maintenance from early on might reduce mortality risk because it allows either reduced energy acquisition activity or alternative use of the freed energy. Restraining the allocation to somatic maintenance incurs costs in terms of increasing somatic damage. However, as long as the accrued somatic damage is controlled in such a way that the costs do not materialize until rather late in life, when an individual

would most probably already be dead, the penalty in terms of fitness may be more than compensated for by increased earlier survival (14). A life-history analysis assessing the evolutionary relevance of this hypothesis by elucidating the link between energy acquisition, risk reduction, and somatic maintenance, which is also firmly linked to empirical data, has apparently not yet been articulated.

Our assessment of the above hypothesis is based on a simple life-history model illustrated using cohort survivorship data from the same species, obtained both in a natural ecological setting and also in a properly designed protective environment. This allows comparison of different somatic maintenance strategies with regard to female lifetime reproductive success and the intrinsic rate of natural increase, without invoking complex and specific population dynamics models that would narrow the empirical reach of predictions in terms of range of life-history regimes. The life-history model predicts that natural selection will, independent of temporal mortality risk profiles, favor restrained allocation to maintenance, despite causing accumulation of somatic damage in later life.

After we present our model and results illustrating its relevance for three real-life case studies, we will examine its implications and relationships with the main current theories of evolution of aging (mutation accumulation, antagonistic pleiotropy, and disposable soma theory) (14). Our hypothesis is conceptually closest to the disposable soma theory. In essence, the disposable soma theory proposes that natural selection should favor allocation to somatic maintenance only as much as is necessary to keep the organism in good functional condition for as long as it has a reasonable chance still to be alive, subject to the prevailing level of risk. Within this viewpoint, it is commonly suggested to be optimal to allocate surplus resources in other activities that enhance fitness,

## Significance

**A fresh perspective on the evolution of aging is developed, which focuses on optimizing an individual's exposure to mortality risk across the life course. A significant source of risk is associated with the act of acquiring the energy necessary for all functions of life. In particular, a considerable fraction of lifetime energy acquisition is used for somatic maintenance. We show how reduction of mortality risk through restrained allocation to somatic maintenance may enhance lifetime fitness but result in aging. Our results are discussed in relation to current theories of the evolution of aging, where we anticipate it will help to illuminate the debate about the mechanisms underlying aging in the wild and the nature and roles of trade-offs.**

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thereby predicting trade-offs between, for example, longevity and reproduction. In our model, however, the emphasis is specifically on how restraining the allocation to maintenance increases fitness in early and middle life by lessening the mortality risk as such, without being traded against any other trait before late in life. If the predicted intimate link between risk reduction and somatic maintenance can be established through further theoretical and experimental work, we anticipate that it will advance our understanding of the evolutionary basis of aging and of the nature of any trade-offs that might arise. We also expect that enhanced understanding of why aging occurs may contribute fresh insights to guide research on physiological causes of and possible interventions to improve the aging process, a matter of high biomedical importance.

### Life-History Model

**Cohort Survivorship Model.** The basis for all calculations to follow is a simple model (in the following called the cohort model) that generates a cohort survivorship curve in the wild as well as in a protected environment as a function of the hazard rate  $h(t)$  by a discrete time stochastic process on state space  $S = \{0,1\}$  with one-step transition probabilities:

$$\forall X_t^i, i \in 1, \dots, N_0, \forall t \in 0, \dots, t_m - 1: \Pr[X_{t+1}^i = 1 | X_t^i = 1] = 1 - h(t), \\ \Pr[X_{t+1}^i = 0 | X_t^i = 1] = h(t), \quad \Pr[X_{t+1}^i = 1 | X_t^i = 0] = 0, \quad \text{and} \quad \Pr[X_{t+1}^i = 0 | X_t^i = 0] = 1,$$

where the initial cohort size is  $N_0$  and the maximum life span is  $t_m$ . Using the survivorship curve as a scaffold for developing the model makes it possible to cover a wide range of life-history regimes and patterns of population dynamics, without needing to be mathematically specific about these regimes and patterns. The survivorship curve can of course be generated by closed form equations and associated calculus, but we have chosen to use a discrete stochastic process model mainly because 1) it allows the life-history model to be formulated with a minimum of mathematics such that the work can also be followed by those that are not well versed in the mathematical machinery of theoretical life-history biology, 2) it provides a high degree of biological realism, 3) it allows easy implementation of a whole range of various hazard rate functions  $h(t)$ , and 4) it allows very easy computation of variational bounds. Moreover, it is straightforward to let  $h(t)$  become a stochastic variable, which we have not pursued in this paper.

**Wild-Type and Mutant Strategies.** Our starting point is a population of sexually reproducing individuals in their natural environment who spend enough energy on somatic repair to prevent accumulation of somatic damage from adversely affecting their survival and reproduction. In the following, we will call this population the hypothetical wild type as the leading hypothesis in this paper implies that it does not exist, and we use it only as a contrast to assess the evolutionary relevance of our hypothesis. The survivorship curve for a cohort of hypothetical wild-type individuals will be defined by a hazard rate function  $h_{wt}(t)$  that is solely determined by the biotic and abiotic environment. Assume the appearance of a mutant in the same natural environment, which after reaching maturity, starts to reduce its somatic maintenance budget by a certain fraction, reducing its hazard rate  $h_{mut}(t)$  below that of the wild type  $h_{wt}(t)$  due to reduced risk exposure. This incurs a penalty later via increased accumulation of somatic damage negatively affecting performance traits associated with survival (i.e., aging), which causes  $h_{mut}(t) > h_{wt}(t)$  at higher ages. This implies that  $h_{mut}(t)$  becomes a function  $\phi(t)$  of somatic damage  $D(t)$ , which can be expressed as  $h_{mut}(t, \phi(D(t)))$ . We assume that this function, describing how somatic damage accentuates the background mortality in the wild, is approximated by an additive relationship between the

mortality risks stemming from ecological factors and damage accumulation. This gives us

$$h_{mut}(t) = (1 - \varepsilon)h_{wt}(t) + \phi(D(t)), \quad [1]$$

where  $\varepsilon$  is the fractional reduction of early-life mortality risk due to reducing the somatic maintenance budget. Simplifying further, we let  $\phi$  be a linear function of  $D$ , such that  $\phi(t) = \alpha D(t)$ , where  $\alpha$  is a scaling constant. In the time interval  $(t - 1, t]$ , we assume that the accumulation of somatic damage in the mutant is

$$\psi(t) = \psi_0 + \kappa D(t - 1), \quad [2]$$

where  $\psi_0$  describes the generation of new damage (independent of accumulated damage),  $\kappa$  is a constant, and  $\kappa D(t - 1)$  describes new damage resulting from the already accumulated damage by a positive feedback process. The accumulated somatic damage at time  $t$  is thus

$$D(t) = \psi(t) + D(t - 1). \quad [3]$$

Letting  $D_0 = \psi_0$ , the closed form expression of Eq. 3 is

$$D(t) = \left(\frac{\psi_0}{\kappa}\right)[(1 + \kappa)^{t+1} - 1]. \quad [4]$$

As we can set  $\psi_0 = \kappa$  without loss of generality, the hazard rate function for a mutant individual may, therefore, be expressed as

$$h_{mut}(t) = (1 - \varepsilon)h_{wt}(t) + \alpha[(1 + \kappa)^{t+1} - 1]. \quad [5]$$

**Fitness Calculations.** Given fecundity as a function of age, the net reproductive rate or lifetime reproductive success ( $R_0$ ) and the intrinsic rate of natural increase ( $r$ ) associated with the mutant and the hypothetical wild-type females can be calculated from the predicted survivorship curves.  $R_0$  is given by

$$R_0 = \sum_{t=0}^{\rho} l(t)m(t), \quad [6]$$

where  $\rho$  is the average age at last reproduction,  $l(t)$  is the probability of being alive at age  $t$ , and  $m(t)$  is the average number of female offspring produced by an individual at age  $t$ .  $r$  follows from numerically solving the Euler–Lotka equation

$$\sum_{t=0}^{\rho} l(t)m(t)e^{-rt} = 1. \quad [7]$$

In both cases, we assume that at  $t = 0$ , the average age of the individuals in the initial cohort corresponds to the average age at which the individuals become sexually mature. This assumption causes overestimation of both fitness measures as the cohort model assumes  $l(t) = 1$  when  $t = 0$ , implying no juvenile mortality. However, as we are only interested in the difference between the mutant and the wild type, this is not a concern. We chose to use both  $R_0$  and  $r$  as fitness measures as their appropriateness is conditional on the life-history context (15), and applying both measures, therefore, provides a better foundation for making sound assessments of observed fitness differences across the slow–fast continuum of life histories (16).

### Results

We make use of three real-life case studies to assess the evolutionary relevance of our hypothesis by use of the above life-history model. They cover the three main types of hazard rate functions (temporal mortality risk) by addressing situations where the function

is apparently constant, increasing, or decreasing with age. In each case, calculations are based on the cohort model presented above and the associated hazard rate functions. Depending on context, the number of replicate runs of the cohort model to get averages and variational bounds ranged from 100 to 1,000. As we have no empirical information about the relationship between  $\varepsilon$  and the degree of somatic damage accumulation, we focus on how large  $\varepsilon$  has to be in order for the mutant strategy to have a higher fitness than the hypothetical wild type (as it is defined above). The smaller this  $\varepsilon$  threshold is, the stronger is the support for our hypothesis that without assuming any associated cost or trade-off in early and middle life, fitness can be enhanced by restraining the allocation to somatic maintenance.

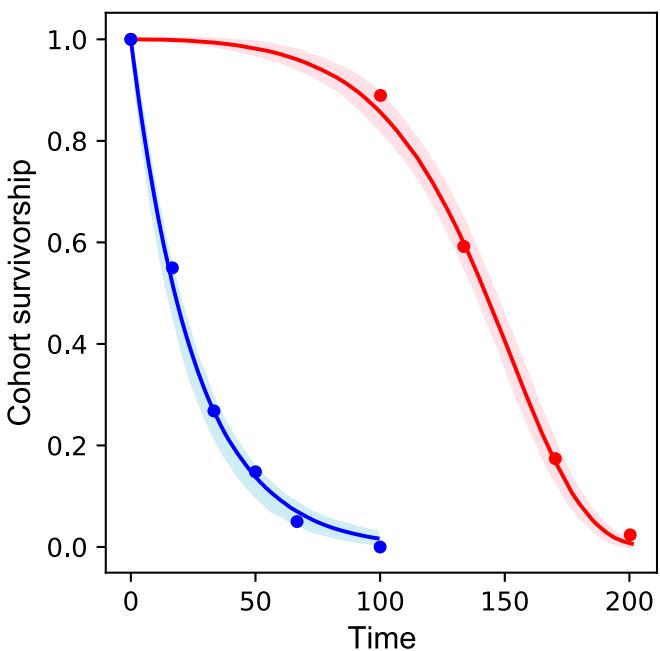
**Case Study 1: Constant Mortality Risk.** The survivorship of the bowl and doily spider (*Frontinella pyramitela*) in a wild as well as in a protected environment under a slightly calorie-restricted feeding regime (3) provides an excellent test set. The survivorship data in the wild were interpreted by the original author to indicate constant (and thus, nonsenescent) mortality. We used the survivorship data from the protected environment to estimate the parameters ( $\alpha, \kappa$ ) defining somatic damage accumulation in Eq. 5 by embedding the equation

$$h_{mut}(t) = \alpha[(1 + \kappa)^{t+1} - 1] \quad [\text{i.e., Eq. 5 where } h_{wt}(t) = 0] \quad [8]$$

in the cohort model and making use of a simple least squares method to fit the calculated survivorship curve to the observed curve (Fig. 1). Using Eq. 5 in the cohort model with the obtained estimates of  $\alpha$  and  $\kappa$  allowed us then to estimate the constant term  $(1 - \varepsilon)h_{wt}$ . In order to avoid confounding effects of possible somatic damage on mortality risk, we performed a least squares fitting of the calculated survivorship curve to only the second, third, and fourth empirical survivorship data points in the wild. Thus, the fit between the calculated survivorship curve and the fifth and sixth data points can be considered to be model predictions (Fig. 1, blue line). In order to keep things simple, the model assumes that the mortality risk for a given somatic damage level is the same in the wild and in captivity. The moderate discrepancy between the survivorship curve and the two last experimental data points (Fig. 1, blue line and dots) can be attributed to this conservative assumption. The blue survivorship curve in Fig. 1 does not assume any specific value of  $\varepsilon$  and  $h_{wt}$ . However, conditional on the assumption that the wild spider data reflect the mutant strategy, the predicted survivorship curve for the hypothetical wild type obtained by letting  $h(t) = h_{wt}$  in the cohort model will be a function of  $\varepsilon$ , due to the fitting term  $(1 - \varepsilon)h_{wt}$ . The shaded blue area in Fig. 1 describes the  $\pm 3$  SD variation of the hypothetical wild type's mean survivorship for  $\varepsilon = 0.04$ . Accounting for measurement noise associated with field data, we see that the survivorship curve of the mutant is predicted to be practically indistinguishable from the hypothetical wild-type curve.

In order to study the survival of the mutant relative to the wild type as a function of the risk reduction level ( $\varepsilon$ ), we calculated the difference in number of wild-type and mutant individuals as a function of time for the above four risk reduction levels (Fig. 2). We see that except for  $\varepsilon = 0.01$ , the mutant cohort is clearly larger than the wild-type cohort across the entire time span. The variability is substantial, but a pairwise comparison of the areas under 1,000 cohort survivorship curves showed that the area is largest for the mutant in 56.4, 99.2, 100, and 100% of cases for  $\varepsilon = 0.01, 0.02, 0.03$ , and  $0.04$ , respectively.

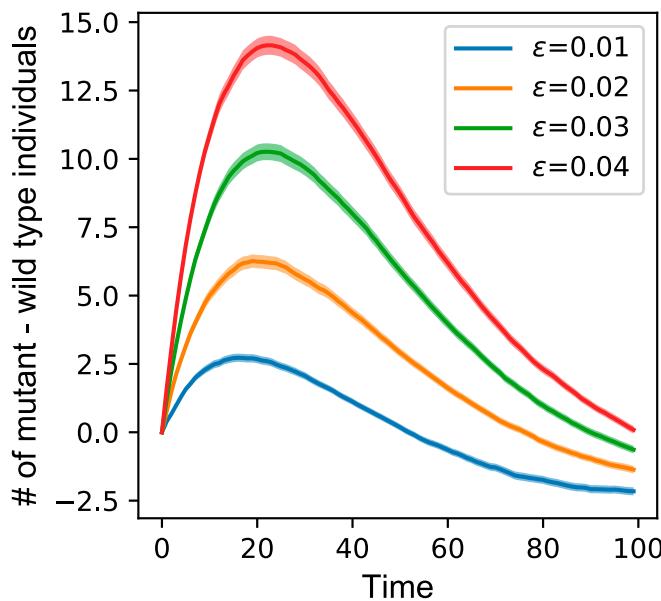
In bowl and doily spiders, first egg deposition occurs 8 to 14 d after mating, and assuming a 50:50 sex ratio, the first egg clutch contains about 24 female eggs (3). One can reasonably assume that there will be no effect of accumulated somatic damage in this first round (17, 18), so egg clutch size for the hypothetical



**Fig. 1.** Survivorship curves for newly matured female bowl and doily spider *F. pyramitela*. The red and blue solid circles describe measured survivorship in a protected environment under a slightly calorie-restricted feeding regime and in the wild, respectively. The data were extracted from ref. 3 and rescaled such that  $t = 100$  corresponds to 30 d. The red line is the mean survivorship curve in a protected environment obtained by Eq. 8 (100 replicates of the cohort model) and ordinary least squares curve fitting, giving  $\alpha = 2.22 \cdot 10^{-4}$  and  $\kappa = 0.033$  (shaded red area:  $\pm 3$  SD). The blue line is the mean survivorship curve in the wild obtained by Eq. 5 (100 replicates of the cohort model) and using ordinary least squares curve fitting to the empirical data (blue dots; numbers 2, 3, and 4 from the left), giving  $(1 - \varepsilon)h_{wt} = 0.03855$ . The shaded blue area describes the  $\pm 3$  SD variation of the hypothetical wild type's mean survivorship when  $\varepsilon = 0.04$ . Initial cohort size  $N_0 = 1,000$ . Note that the blue line from the fourth blue data point is a prediction and not a curve-fitting result.

wild type and the mutant will be identical. As spiders bred in captivity have a 24% reduction in egg number in the second batch, we assumed that the [unlikely (3)] second egg clutch of the hypothetical wild type and the mutant contains 24 and 18 eggs, respectively. Using these figures and Eqs. 6 and 7 and assuming that the first and second egg depositions occurred 12 and 24 d after mating, respectively, we then calculated the expected female lifetime reproductive success ( $R_0$ ) and the intrinsic rate of natural increase ( $r$ ) of the mutant and the hypothetical wild-type female spider populations as a function of  $\varepsilon$  (Fig. 3). We see that as long as the risk reduction is somewhat above 3%, the mutant will have a higher fitness than the hypothetical wild type for both fitness measures. At a risk reduction level of 4%, the model predicts that the mutant increases  $R_0$  and  $r$  by 1.4 and 2.7%, respectively, which arguably gives natural selection ample scope to operate.

The predictions in Figs. 2 and 3 for the bowl and doily spider are likely to be quite generic for species having 1) an approximate constant mortality risk in the wild, 2) about two times longer average life span in a protected environment than in the wild, and 3) a survivorship curve in a protected environment resembling that in Fig. 1. The reason for this is that the number of mutant individuals is likely to be generally higher than the number of hypothetical wild-type individuals at any time point, and as long as the accumulated somatic damage starts to negatively affect the mutant fecundity at a late-life stage, we would get similar results irrespective of the number of reproductive



**Fig. 2.** Predicted temporal difference between the hypothetical wild type and mutant survivorship in *F. pyramitela* females ( $\pm 3$  SEM). The parameter values are identical with those used in Fig. 1, but in this case, the relationship  $(1 - \varepsilon)h_{wt} = 0.03855$  was used to calculate a distinct  $h_{wt}$  value for each  $\varepsilon$  value. Each curve is based on 1,000 replicates of the cohort model.

events and associated variation in reproductive output with age that is not linked to somatic damage.

**Case Study 2: Increasing Mortality Risk with Age.** Kawasaki et al. (4) investigated life span and aging in the dipteran *Telostylinus angusticollis* in the wild while simultaneously estimating these parameters under a range of conditions in a laboratory stock that was established from the same wild population. In this organism, male mortality rates in the wild showed a clear increase with age. Interestingly, such an increase was not apparent for females in the wild. As the survivorship curves of the two sexes in the wild differed markedly, while the survivorship curves in captivity were quite similar, this provides an opportunity not only to examine the case of increasing wild-type mortality but also, to test our hypothesis against distinct cohort survivorship scenarios within the same species.

Repeating the procedure we used for the bowl and doily spider data, we find that Eq. 8 once more captures the survivorship data for females and males in a protected environment very well (Fig. 4). Again, the survivorship curve for females (Eq. 5) accords very well with the empirical data (Fig. 4). However, Eq. 5 was far from able to recapitulate the wild male data. Kawasaki et al. (4) reported that wild males spent much of their time walking through aggregation sites on tree trunks, fighting rivals, and attempting to copulate with females. As several predatory skinks (*Eulamprus tenuis*) were typically seen hunting for *T. angusticollis* on each tree where flies aggregated, the authors suggested that these visual predators targeted males disproportionately, due to their greater activity. The data (Fig. 4) suggest, however, that the mortality risk is actually slightly lower in males compared with females at ages up to about one-third of the maximal life span. This indicates that the mortality risk increases substantially more with age in males compared with females. Kawasaki et al. (4) hypothesized that the harsh environment experienced by wild males, due to their more demanding reproductive strategy, enhances the somatic effects of aging on predation risk and other risk factors. In line with this reasoning,

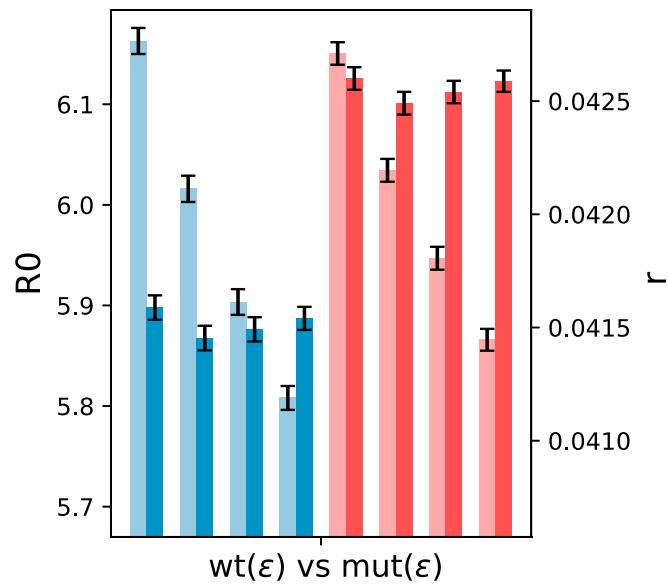
we added the simple phenomenological term  $\omega t^\tau$ , where  $\omega$  and  $\tau$  are constants, to the right-hand side of Eq. 5, such that

$$h_{mut}(t) = (1 - \varepsilon)h_{wt} + \alpha[(1 + \kappa)^{t+1} - 1] + \omega t^\tau. \quad [9]$$

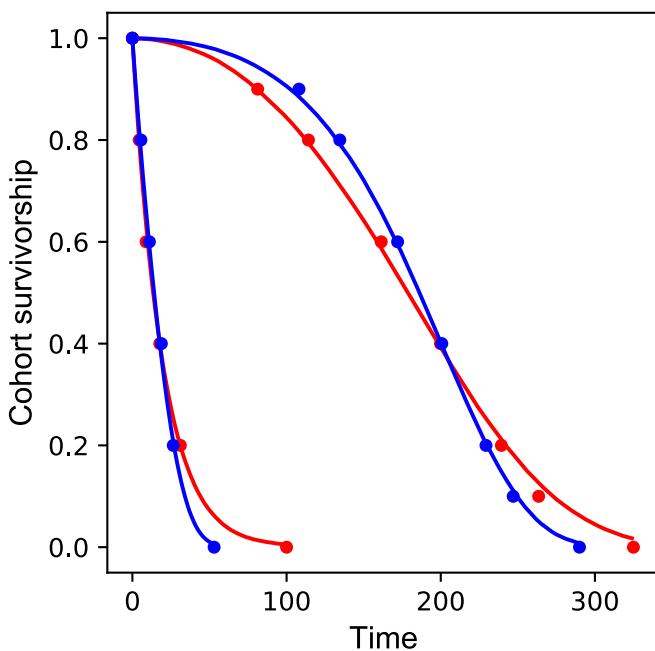
Eq. 9 recapitulates the survivorship data for wild males very well (Fig. 4), but it should be noted that the added term also incorporates possible age-related effects independent of somatic damage, as increasing physical exhaustion in itself would likely enhance the vulnerability to predation and other risk factors.

A pairwise comparison of the areas under 1,000 cohort survivorship curves showed that the female mutant wins in 40, 99.6, 100, and 100% of cases for  $\varepsilon = 0.01, 0.02, 0.03$ , and  $0.04$ , respectively. The male mutant wins in 100% of the cases for the last three  $\varepsilon$  values. Due to lack of fecundity data in ref. 4, we were unable to estimate  $R_0$  and  $r$ . However, the comparison results above suggest that a small  $\varepsilon$  value will also be sufficient to make the male and female mutant strategies superior for both fitness measures in this case. The above results for males are likely to apply to many organisms where male mortality risk increases with age due to a physically demanding and risk-prone reproductive strategy.

**Case Study 3: Decreasing Mortality Risk with Age.** Considerable attention has been given to organisms sporting reduced mortality and increased fecundity with age. This phenomenon is sometimes dubbed “negative senescence” (19, 20). However, reduced mortality and increased fecundity with age are frequently associated with indeterminate growers such as mollusks, crustaceans, reptiles, amphibians, and fish (18, 21). This suggests that the increase in size, rather than some reduction in damage, is the major reason for the observed pattern. Due to the paucity of experimental studies documenting that the age profiles of physiological senescence markers of such species do stand out, it cannot be ruled out that they experience some age-related accumulation of damage, which is confounded by the fitness gain associated with increased size. Guided by life-history data



**Fig. 3.** Pairwise comparison of predicted lifetime reproductive success ( $R_0$ ) (Eq. 6) and intrinsic rate of increase ( $r$ ) (Eq. 7) for the hypothetical wild type (wt; light color) and mutant (mut; full color) *F. pyramitela* females ( $\pm$ SEM) as a function of the assumed risk reduction level  $\varepsilon \in \{0.01, 0.02, 0.03, 0.04\}$  with ascending  $\varepsilon$  order. Note that the actual  $R_0$  and  $r$  values are unrealistically high as we assume no juvenile mortality due to a lack of data. The text has further explanation.



**Fig. 4.** Male (blue) and female (red) survivorship curves in the wild (left curve) and in captivity (right curve) for the dipteran *T. angusticollis*. The empirical data (solid circles) were extracted from ref. 4 and rescaled such that  $t = 100$  corresponds to 20 d. Eq. 8 was used to generate the two captivity survivorship curves. Eqs. 5 and 9 were used to generate the survivorship curves in the wild for females and males, respectively. Parameter values for females:  $\alpha = 0.00287$ ,  $\kappa = 0.00842$ , and  $(1 - \varepsilon)h_{wt} = 0.0503$ . Parameter values for males:  $\alpha = 0.00057$ ,  $\kappa = 0.0173$ ,  $(1 - \varepsilon)h_{wt} = 0.0435$ ,  $\omega = 0.0001$ , and  $\tau = 1.8$ . Initial cohort size:  $N_0 = 1,000$ . Each of the four curves displays the mean of 100 replicates of the cohort model. Note that as only the second, third, and fourth data points for females in the wild were used for curve fitting, the fit between the calculated line and the fifth and sixth data points is a prediction.

of the European lobster (*Homarus gammarus*) (22), which sports indeterminate growth over a period of several decades as well as a large increase in the number of fertilized eggs with age, we tested whether negative senescence would still favor a restrained allocation to somatic maintenance. We let the hypothetical wild-type mortality risk decrease directly proportional to increase in size with age,  $h_{wt}(t) = h_{wt}(0)(1 - \beta t/t_m)$ , where  $t_m = 100$  (corresponding to 50 y) and the constant  $\beta$  was scaled such that the hazard rate at  $t_m$  was 20% of the rate at  $t = 0$ . Analogously, the wild-type fecundity was allowed to increase in direct proportionality to the increase in size with age,  $m_{wt}(t) = \sigma(1 + \gamma t/t_m)$ , where  $\sigma = 1$  and  $\gamma = 4$ . We let  $\sigma = 1$  since we were only interested in the relative differences in fitness between the wild type and the mutant. Female European lobsters spawn every second year, so every fourth value of the fecundity function was used in the fitness calculation. Due to lack of data, we assumed the form of the survivorship curve in a protected environment to be identical with the one for the bowl and doily spider (Fig. 1) (i.e., we assume that female lobsters in a protected environment live about twice as long as in the wild). The fecundity of the mutant was assumed to be a function of somatic damage accumulation according to

$$m_{mut}(t) = m_{wt}(t)(1 - \mu \alpha[(1 + \kappa)^{t+1} - 1]), \quad [10]$$

where the term  $(1 - \mu \alpha[(1 + \kappa)^{t+1} - 1])$  describes the fractional decrease in fecundity relative to the wild type for a given time point  $t$ . We let  $\mu = 50$ , such that the fecundity of the mutant was about 70% of the hypothetical wild type at  $t = t_m$ . The analysis was done in the same way as for *Frontinella*, with the only distinction being that in this case, we could keep the same  $h_{wt}(0)$

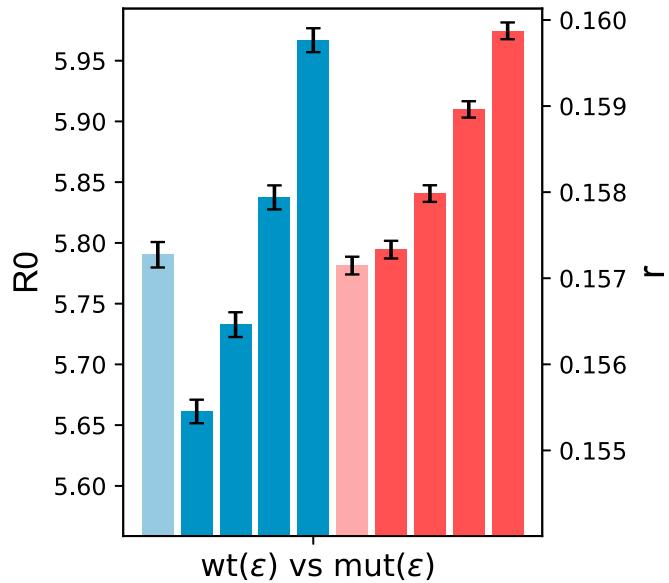
value for all the four  $\varepsilon$  cases because we did not have access to empirical survivorship data for parameter estimation demanding recalculation of the hypothetical wild-type mortality risk for each case. At a risk reduction level of 4%, the model predicts that the mutant increases  $R_0$  and  $r$  by 2.9 and 1.7%, respectively. The results (Fig. 5), therefore, suggest that natural selection will also force so-called negative senescent organisms with indeterminate growth to restrain their somatic maintenance budget, so as to increase their fitness by reducing mortality risk.

## Discussion

**Possible Shortcomings of the Life-History Model.** There can indeed be a nonlinear relation between risk reduction through restraint of somatic maintenance and the appearance of negative phenotypic effects affecting fitness due to some physiological threshold effect, where there is minimal phenotypic effect below this threshold due to some buffering or robustness mechanism (23, 24). We have not explicitly modeled this possibility due to lack of relevant empirical test data. Nevertheless, this possibility would only strengthen our conclusions.

We conjecture that our results apply to a phylogenetically widely distributed set of organisms. However, in illustrating the concept we have deliberately chosen examples of species where we can be reasonably confident that survival data in the wild are unlikely to have been influenced by modifications to the environment (e.g., from markedly reduced predation) (25). A large amount of the survival data from vertebrates (mammals, birds, fish, reptiles) is exposed to such concerns (ref. 26 and references therein), and we have not so far been able to find vertebrate test data of sufficient quality.

Although we refer to sexual populations within the model, we have not as yet attempted to incorporate sex genetically within



**Fig. 5.** Predicted lifetime reproductive success ( $R_0$ ) (Eq. 6) and intrinsic rate of increase ( $r$ ) (Eq. 7) for females with indeterminate growth and negative senescence not restraining (wt; light color) and restraining (mut; full color) somatic maintenance ( $\pm$ SEM). The increases in size and fecundity with age and reproduction frequency are based on life-history data of the European lobster. The four risk reduction levels are the same as in Fig. 3, and the corresponding  $R_0$  and  $r$  values for the mutant are displayed in ascending  $\varepsilon$  order in both cases. As  $h_{wt}$  in this case is not dependent on  $\varepsilon$ , a pairwise comparison between the wild type and the mutant for each  $\varepsilon$  value is not needed here. Note that the actual  $R_0$  and  $r$  values are unrealistically high due to zero juvenile mortality, even with  $\sigma = 1$  in the basic fecundity equation  $m_{wt}(t) = \sigma(1 + \gamma t/t_m)$ . The results are based on 1,000 replicates of the cohort model for each case. The text has further explanation.

the model. Ultimately, it would have to be shown how the mutant will spread in the population while interbreeding with the wild type across a range of different life-history cases. However, to do this would require use of different genetic models with explicit assumptions about a range of parameters due to lack of prior information on genetic architecture, and it would require the integration of these models with population dynamic models addressing a whole range of distinctly different life histories. Nevertheless, we think our framework provides a motivational starting point for such work by showing how natural selection might drive the establishment of a genetic program that leads to reduced allocation to somatic maintenance from an initial state where there is no such reduction.

Even though our two fitness measure calculations for case studies 1 and 3 gave similar results, we acknowledge the need to pursue more in-depth work with less restrictive assumptions to get a better understanding of how these two fitness measures for the mutant and hypothetical wild-type strategies will vary as a function of the life-history context. With reference to the paragraph above, a portfolio of species-specific models combining population genetics and dynamics would provide such insight, but such an undertaking is beyond the scope of this paper.

There may also be cases where the necessary assumptions of the life-history model do not apply: for example, for those organisms sporting asexual reproduction, modularity, lack of germline sequestration from the soma, and regenerative capacity (ref. 7 and references therein). Moreover, the model framework does not cover situations where somatic maintenance is a polyphenic trait (27). The dauer larval diapause and its associated adult phenotypes in the nematode (*Caenorhabditis elegans*), reproductive dormancy in the fruit fly (*Drosophila melanogaster*) and other insects, and the worker castes of the honeybee (*Apis mellifera*) are examples of polyphenic regulation of somatic maintenance and survival. That is, the same genotype can, depending upon its environment, express alternative sets of life-history phenotypes that differ markedly with respect to somatic maintenance, survival ability, and thus, life span. Such polyphenisms are likely caused by temporally and/or spatially varying, stressful environments that impose diversifying selection, thereby favoring the evolution of plasticity of somatic maintenance and survival under strong regulatory control (27). Thus, despite the fact that life-history models of these three cases demand another framework, they show that somatic damage accumulation can be under deliberate regulation, in line with the basic tenet of this paper. However, it should be noted that in honeybees, the temporal forager cast performing the most risky work is characterized by being in a controlled nutrient-deprived and immune-compromised physiological state mediated by pathways connected to regulation of aging (28). Foragers have a potential life span of only a few weeks, strongly suggesting that allocation to somatic maintenance is tuned to the environmental mortality risk. As this feature is likely to have evolved as an energy-saving mechanism to increase the reproductive output of honeybee colonies (28, 29), it represents a special case supporting the main hypothesis underlying this paper.

Available empirical data do not allow us to make an assessment of how a given risk reduction level  $\varepsilon$  translates into a percentage-wise reduction of the somatic maintenance energy budget. This is a concern. However, in the case of eutherians, the energy expenditure is 25% higher than the basal metabolic rate during pregnancy and 1.5 to 2.0 times higher during lactation (13). As the basal metabolic rate to a high degree reflects the amount of energy routed toward somatic maintenance, this suggests that in the case of eutherians at least, a predominant part of the lifetime acquisition of energy is dedicated to somatic maintenance. This in turn implies that a few percent reduction of the somatic maintenance budget will free a substantial amount of energy that either does not need to be acquired or can be used to alleviate risk by other means.

An issue that might be raised regarding the real-life data in wild and protected environments is that individuals in the wild might have a higher metabolic demand, forcing them to allocate less to somatic maintenance without there being a specific genetic program effecting this. Our hypothetical wild type, which we use as a contrast to the mutant strategy, is assumed to be able to allocate enough energy to somatic maintenance such that neither its fecundity nor any other fitness trait are negatively affected by accumulated somatic damage throughout its life span in the wild. Considering that the allocation to somatic maintenance represents a fraction of the total energy acquisition and that numerous caloric restriction experiments across a wide range of species show that the somatic maintenance is even enhanced when the energy supply is reduced, we think it is fair to claim that individuals in the wild are not normally forced to constrain their allocation to somatic maintenance due to a shortage in acquired energy. We have made use of survivorship data from protected environments for the sole purpose of getting at least a tentatively empirically justified estimate of the effect of somatic damage accumulation with age on mortality risk. This means that only the estimates of the parameters  $\alpha$  and  $\kappa$ , defining somatic damage accumulation in Eq. 5, will be affected by a possible difference in allocation to somatic maintenance between individuals in the wild and in a protected environment. Thus, negative phenotypic effects stemming from somatic damage will turn up earlier in the wild than what we have estimated. However, the close fit between predictions and empirical data (Figs. 1 and 3, wild cases) does not provide strong support for this possibility.

Predator-induced stress (predation risk or the fear of becoming prey) has been shown to have pronounced effects on prey species by inducing behavioral, morphological, and physiological responses (30–33). In two species of water fleas (*Daphnia longispina* and *Diaphanosoma brachyurum*) (34) and in parental spider mites (*Tetranychus urticae*) (35), it was recently shown that the physiological response to predator-induced stress mediated by predator cues caused pronounced effects on the aging pattern. Our life-history model does not incorporate such effects, as it implies that the rate of somatic damage accumulation may be under deliberate regulatory control driven by perceptual information and anticipatory inference (36). However, these data clearly support our main thesis, namely that there is an intimate positive link between mortality risk and allocation to somatic maintenance. This is further substantiated by the fact that the adaptive responses to perceived predation risk often come at the cost of limiting the quality and quantity of food available to the prey (35, 37). Thus, the costs of these adaptive responses to enhanced mortality risk are likely to be partly mitigated by a restrained allocation to somatic maintenance causing a reduced energy acquisition demand.

**Hazard Rate Function Considerations.** It should be noted that Eq. 5 can be written as  $h_{mut}(t) = \lambda + \hat{\alpha}e^{\beta t} - \alpha$ , where  $\lambda = (1 - \varepsilon)h_{wt}(t)$ ,  $\beta = \ln(1 + \kappa)$ , and  $\hat{\alpha} = \alpha(1 + \kappa)$ . Thus, except for the constant term  $-\alpha$ , Eq. 5 is identical with the Gompertz–Makeham hazard function, where  $\hat{\alpha}e^{\beta t}$  is the Gompertz hazard rate function (38). Strictly speaking, instead of representing an alternative way of deriving the Gompertz–Makeham hazard rate function from biological principles (39), the Gompertz–Makeham hazard rate function can be seen as an approximation conditional on the assumption that the biological premises underlying Eq. 5 are correct. It is worthwhile to notice that the term  $\beta = \ln(1 + \kappa)$  shows how the strength of the positive feedback loop between acquired damage and new damage alluded to above influences the exponent of the Gompertz hazard rate function. As the biological premises underlying Eq. 5 are quite naïve, we anticipate that their sophistication might lead to a more nuanced relationship between the Gompertz–Makeham hazard rate function and a biologically grounded derivation of  $h(t)$ . However, there is

no a priori reason for claiming that such a function will become equivalent to the Gompertz–Makeham function, as there is no biological justification for the latter other than that it describes a wide range of biological data very well. We did not pursue this issue further in this paper, as the removal of  $-\alpha$  causes maximally a few percent discrepancy between the survivorship curves.

**Trade-Off Considerations.** Much of the focus to date in the life-history literature on evolutionary theories of aging has been on the idea of metabolic or physiological trade-offs. Where the point at issue is how the organism's energy budget is optimally allocated between activities such as growth, reproduction, maintenance, and repair, it is logical to expect that such trade-offs should exist, and much evidence supports this. However, there is also evidence that expected trade-offs are sometimes either not seen or absent (40), raising important questions about why this should be the case (41). In the present analysis, we have considered an additional issue of life-history optimization, which may help to throw light on the debate. We suggest that restraining allocation to somatic maintenance from early on will reduce mortality risk. This reduction may be achieved by reducing risk-prone energy acquisition activities as such (see discussion in the previous section) or by channeling more energy into other physiological compartments affecting mortality risk, such as 1) energy storage to enhance the probability of surviving periods of starvation, heat, and cold stress; 2) enhanced immune system mobilization; and 3) enhanced capacity for detoxification. Channels like 2 and 3 might seem contradictory as they relate directly to somatic maintenance. However, the point is that they also demand energy reserve to be invoked, which means that all three channels are intimately connected to the additional energy storage that can be built up by restraining the overall somatic maintenance budget. It is premature to make strong claims about the regulatory machinery that could be responsible for controlling the allocation to somatic maintenance, but if we assume, for example, that this machinery regulates processes like mitochondrial heteroplasmy and protein turnover, then extra energy storage can clearly be built up while somatic maintenance is restrained.

In those cases where energy acquisition activity is not reduced, it may under some life-history regimes be advantageous to use the freed energy to enhance reproductive effort instead of, for example, building reserve to reduce mortality risk. Then, there will be a trade-off situation, but it will not involve somatic maintenance as such. In some cases, it may even be beneficial to further restrain somatic maintenance for enhanced reproduction, but then, this further restraint will come on top of the first one. As revealed, for example, by empirical studies of fitness costs of reproduction (42), the verification of trade-offs is challenging. The fresh possibilities suggested by our hypothesis will thus need careful examination.

**Genetic Considerations.** Mortality in a protected environment is arguably strongly associated with the physiological decline caused by somatic damage accumulation. The overall shape and monotonicity of cohort survivorship curves in protected environments suggest that this accumulation, in terms of effect on fitness trait performance, is a gradual and quite strongly bounded process for the greater part of the total life span. As available data clearly show that longevity is a heritable trait (43–50), the allocation to somatic maintenance in a wide range of organisms and the pace of physiological deterioration due to somatic damage accumulation are most likely under stabilizing natural selection in the wild.

The genetic basis responsible for causing the gradual development of physiological decline is likely to vary between species (i.e., there may be several genetic and thus, physiological realizations manifesting the restrained allocation to somatic maintenance). The observed smooth and monotonic decrease of cohort survivorship curves in protected environments suggests that the genes that collectively constitute a given genetic basis act in concert through

their associated physiological mechanisms in a highly controlled manner throughout an organism's life span in the wild as well as in a protected environment. This implies that for a gene or gene variant to become part of a given genetic basis, it is not enough that it provides a sufficiently high early-life fitness gain compared with late-life fitness loss. It will in addition need to be integrable with a regulatory architecture capable of optimizing the allocation to somatic maintenance across the whole life span.

The notion that the pace of somatic damage accumulation is under stabilizing selection and tuned by the mortality risk associated with a given biotic and abiotic environment does not resonate very well with the mutation accumulation theory of aging (51) (but see *Predictions*). At a superficial level, such selection may appear consistent with the antagonistic pleiotropy theory (52). However, as mortality risk can be considered a high-level phenotype, our hypothesis implies that the genetic structure underlying the physiological mechanisms causing reduction of mortality risk in early life through restrained allocation to somatic maintenance is also responsible for causing increased mortality risk in late life by the very same physiological mechanisms. Strictly speaking, antagonistic pleiotropy denotes per definition a situation where one gene controls more than one trait, where at least one of these traits is beneficial to the organism's fitness early on in life and at least one is detrimental to the organism's fitness later on. Thus, this genetically caused temporal change in mortality risk cannot be interpreted as the outcome of antagonistic pleiotropy unless one adopts a more general definition of what the theory encompasses than what is currently advocated. However, by opening up, the conceptual content of the term "antagonistic pleiotropy" will become confusingly broad. Also, the fact that fecundity, together with the performance of several other traits, may become reduced in late life does not change this conclusion, as the hypothesized underlying genetic structure is not supposed to cause an increase in early-life fecundity or improved performance of any other trait not directly impacting mortality risk.

Considering the disposable soma theory (53, 54), our hypothesis differs from the common explication of the theory by not involving any direct trade-off (i.e., somatic maintenance is not sacrificed on behalf of reproductive effort or some other purpose). However, as the disposable soma theory is an optimization theory, it suggests, consistent with how it was originally proposed (53), that stabilizing natural selection has shaped an underlying causative genetic architecture, reflecting that there is little or no benefit to be gained from allocating more to somatic maintenance than is needed for the organism to remain in sound condition through most of its expected survival time in the wild environment. Thus, as its central idea is consistent with our results as well as the associated genotype–phenotype map restrictions listed above, we consider our life-history model to be a first step toward a formal explication of this idea. However, a mature theory of aging in nature, characterized by a broad explanatory scope as well as a high-resolution predictive capacity, will have to firmly link physiology and genetics into a consistent explanatory whole. We anticipate that the establishment of such a theory will demand extensive use of "causally cohesive genotype–phenotype" modeling where low-level parameters in physiological models have an articulated relationship to the individual's genotype and where higher-level phenotypes emerge from the mathematical model describing the causal dynamic relationships between these lower-level processes (55). This way of modeling bridges the gap between standard population genetic models that simply assign phenotypic values directly to genotypes and mechanistic physiological models without an explicit genetic basis, and it enables a causally coherent depiction of the genotype-to-phenotype map that can easily be embedded in a population context (55).

**Predictions.** Based on the premises of the life-history model and the results, we can make the following predictions and inferences.

- 1) We predict that closer study of high-resolution markers of molecular senescence (56) as well as physiological performance will also reveal evidence of aging in cases where current data (12) appear to still support the conclusion that mortality risk in the wild is constant. Our results for females in the wild in case studies 1 and 2 show the marginal impact somatic damage accumulation might have on the hazard rate function. However, it should be noted that in the *Frontinella* case, the data (3) do indeed suggest that although the hazard rate is constant in the wild throughout the first half of the cohort survival span, it increases in the latter half, after the cohort size is reduced by about 90%.
- 2) In organisms showing decreasing mortality and increasing fecundity with age due to indeterminate growth, high-resolution molecular senescence data will reveal that they still age while they grow.
- 3) If predation pressure represents a major mortality risk in the unperturbed natural environment, reduction of this pressure due to habitat change will cause an increase in the fraction of senescent individuals and temporary directional selection for enhanced allocation to somatic maintenance.
- 4) There is not necessarily a positive association between decreased environmental mortality due to reduced predation pressure and delayed senescence when one compares the survivorship of contrasting populations in a laboratory environment (57). The reason is that the individuals exposed to the strongest predation pressure will arguably need to maintain high-level phenotypic performance in a number of traits of importance to predation risk [like swimming performance (57) and cognitive ability (58)]. This implies that the high-predation individuals will need to allocate more to somatic maintenance despite that they live shorter in the wild than the low-predation individuals. Thus, when one compares the temporal survivorship of two contrasting populations in a protected environment, the

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one being adapted to a high-predation pressure will start out from a higher somatic maintenance set point, therefore experiencing a reduction in phenotypic performance (including fecundity) and succumbing to somatic damage-driven mortality later (57). It should be emphasized that a higher food availability in the high-predation habitat, as was the case in the seminal guppy study (57) we alluded to, explains why the high-predation group could sport both enhanced somatic maintenance as well a higher reproductive output in the wild.

- 5) If a population has been under stabilizing selection with regard to allocation to somatic maintenance for a long time, this will make room for accumulation of mutations displaying purely late-life deleterious effects in a protected environment. However, according to our results, the presence of such mutations does not explain the existence of senescent individuals in the wild and thus, should not be interpreted as support for the mutation accumulation theory of aging (59).

**Concluding Remarks.** We acknowledge that further theoretical as well as experimental work will be needed before one can reach a firm conclusion on the explanatory scope of the hypothesis we propose in this paper. We anticipate that subjecting the hypothesis to such scrutiny will reveal valuable insights concerning the link between genetics, physiology, and senescence in the wild.

**Data Availability.** The numerical code used for analysis was written in Python in a JupyterLab environment. A refactored version is publicly available on GitHub at <https://github.com/stifwo/advantageous-aging> (60) and Zenodo (DOI: 10.5281/zenodo.4756831).

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