Received: 25 February 2019 | Accepted: 25 August 2019

DOI: 10.1111/1365-2435.13444

Functional Ecology | BRITISH ECOLOGICAL SOCIETY

Are trade-offs really the key drivers of ageing and life span?

Alan A. Cohen[1] | **Christophe F. D. Coste**[2,3] | **Xiang-Yi Li**[4,5] | **Salomé Bourg**[6] | **Samuel Pavard**[3]

[1]Groupe de recherche PRIMUS, Department of Family Medicine, University of Sherbrooke, Sherbrooke, QC, Canada; [2]Center for Biodiversity Dynamics, Norwegian University of Science and Technology, Trondheim, Norway; [3]Unité Eco-anthropologie (EA), Muséum National d'Histoire Naturelle, CNRS 7206, Université Paris Diderot, Paris, France; [4]Institute of Biology, University of Neuchâtel, Neuchâtel, Switzerland; [5]Department of Evolutionary Biology and Environmental Studies, University of Zurich, Zurich, Switzerland and [6]CNRS, Laboratoire de Biométrie et Biologie Évolutive, UMR5558, Université Lyon 1, Villeurbanne, France

Correspondence
Alan A. Cohen
Email: Alan.Cohen@USherbrooke.ca

Funding information
Natural Sciences and Engineering Research Council of Canada, Grant/Award Number: RGPIN-2018-06096; Schweizerischer Nationalfonds zur Förderung der Wissenschaftlichen Forschung, Grant/Award Number: 163374 and 180145

Handling Editor: Jean-Michel Gaillard

Abstract

1. Current thinking in life-history theory and the biology of ageing suggests that ageing rates, and consequently life spans, evolve largely as a function of trade-offs with reproduction. While various evolutionary constraints are generally acknowledged to exist, their potential role in determining ageing rates is rarely considered.
2. This review integrates three types of information to assess the relative importance of constraints and trade-offs in shaping ageing rates: (a) empirical work on the presence of intraspecific trade-offs; (b) theoretical work on factors limiting the force of trade-offs; and (c) consideration of the biological mechanisms of ageing, as currently understood.
3. At the empirical level, evidence for intraspecific trade-offs is mixed, including some surprising failures to observe a trade-off in model organisms. At the theoretical level, the presence of multiple currencies and nonlinearity can weaken the strength and/or generality of trade-offs. Additionally, trade-offs among lower-level functions, such as between sources of mortality, can create constraints at higher organizational levels, for example such that reductions in reproduction are unable to produce decreases in ageing rate. In terms of ageing mechanisms, some mechanisms, such as the regulation of IGF-1 and related pathways, seem to agree quite well with trade-offs as a driving force; however, other mechanisms, such as dysregulation of the vertebrate stress response and stem cell exhaustion, seem more likely to impose constraints than to mediate trade-offs.
4. Taken together, these findings suggest that trade-offs alone are insufficient to understand how ageing rates evolve; instead, both trade-offs and constraints likely play important roles in shaping evolutionary patterns, with their relative importance varying across taxa. Accordingly, it is time to revisit the broad assumption that survival–reproduction trade-offs are the key force structuring much of life-history variation and the evolution of ageing rates.

KEYWORDS
ageing, constraint, cost of reproduction, disposable soma, life history, physiology, senescence, trade-off

1 | INTRODUCTION

Current thinking at the crossroads of life-history theory and ageing biology is that trade-offs between early and late life or between survival and reproduction structure how ageing rates evolve (Kirkwood, 2005; Lemaitre et al., 2015; Rodrigues & Flatt, 2016). Such trade-offs underlie both the antagonistic pleiotropy and the disposable soma theories of ageing (Kirkwood & Holliday, 1979; Williams, 1957) and have formed a cornerstone of our understanding of variation in life-history traits. Several nuances to these general statements are well recognized. For example, trade-offs may appear only under certain severe environmental conditions (Tavecchia et al., 2005), and mutation accumulation unrelated to trade-offs may also contribute to ageing (Everman & Morgan, 2018; Hughes, Alipaz, Drnevich, & Reynolds, 2002). Nonetheless, this overarching framework has continued to be broadly accepted.

Trade-off-based theories of ageing do not suggest a mechanism by which the trade-offs can be escaped. This is problematic in the light of recent work showing that a wide variety of species from across the tree of life, including those with distinct somas, appear not to age (Jones et al., 2014). Empirical work on trade-offs, recent theoretical advances and an increasing understanding of the mechanisms of ageing provide additional reasons to question the traditional framework. The goal of this review was thus to assess the evidence that trade-offs are in fact the primary evolutionary force shaping ageing rates. We use this discussion to propose new empirical and theoretical avenues for the study of how trade-offs shape ageing and life span.

1.1 | Definitions and scope

We consider a **trade-off** to be present when *an increase in fitness or a specific aspect of functioning via one component mechanism/trait inevitably results in a decrement to the fitness/functioning through another component mechanism/trait, producing a limit on the total fitness/function achievable*. We contrast trade-offs, which may be modulated via organismal or evolutionary processes to adjust the balance between the mechanisms/traits in question, with **constraints**, which are *limits on fitness or functioning that are not subject to important modulation*. For example, to the best of our knowledge, rates of wing wear in insects cannot be substantially changed via increased resource allocation; they thus represent a constraint rather than a trade-off. The relationship between trade-offs and constraints is nuanced. For example, trade-offs between mortality components (i.e. causes of death, such as cancer and metabolic dysfunction), discussed in detail below, may create a higher order constraint on the evolution of longer life span. Likewise, some low level of DNA damage accumulation may represent a constraint, but higher levels are likely preventable with sufficient resource allocation and thus reflect trade-offs. Despite these nuances, the distinction between trade-offs (modulable along an axis) and constraints (largely fixed and inescapable at short evolutionary time-scales) will be central to our argument. We also note that our definition of trade-offs is more mechanistic than some in the literature (e.g. 'costs paid in the currency of fitness when a beneficial change in one trait is linked to a detrimental change in another', Stearns, 1989). Our emphasis on mechanism rather than pattern is crucial because our core question is to what extent trade-offs drive the evolution of ageing mechanisms leading to variation in ageing rates.

To understand how life span and ageing evolve requires us to understand how trade-offs shape variance in life span and ageing rate between individuals within a species, currently poorly understood. From this perspective, it is useful to segregate trade-offs into genetic and individual variance components. The **genetic component** is caused by allelic polymorphism in genes related to strategies along the trade-off axis (here mainly the slow-fast continuum of life histories, Gaillard, Lemaitre, Berger, Bonenfant, & Devillard, 2016). The **individual component** is caused by individual stochasticity; in other words it is concerned with the outcomes of constraints (mostly physiological) at the individual level that generate the variety of possible realizations of each such strategy (life-history trajectories). Indeed, for a given genetic strategy, an individual's life history may show very different outcomes or trajectories because of individual costs and stochasticity, even in a constant environment.

At the level of individual life courses, the genetic component plays no role beyond defining the range and implications of plastic responses. In contrast, in interspecific (comparative) studies the individual component, though significant evolutionarily (Coste, & Pavard, in press), is statistically overwhelmed by its genetic counterpart (see how this improves drastically the detectability of trade-offs from the intra- to the interspecific level in Bernardo, 1996; Christians, 2000). In between, that is at the population/species level – the workplace of evolution – both components combine to generate a variety of life-history trajectories. At that level, the aggregated effects of these two components can even seemingly offset one another. This is not, however, the main hindrance to the phenotypic emergence of trade-offs, mainly caused by co-occurring non-iso-fitness genetic strategies and by individual stochasticity in resource acquisition. In the first case, the coexistence in a population of different acquisition strategies or of different qualities will generate bias preventing the statistical emergence of a potential genetic trade-off (Houle, 1991). In the second case, the capacity of an individual to acquire more resources (because of a localized and temporary beneficial microenvironment, for instance), than another, will also hinder the detection of the underlying allocation trade-off as famously proved by van Noordwijk and de Jong (1986).

We limit the scope of our discussion in several ways. First, we only consider animal literature, since it is in that kingdom that the trade-off framework in question has mostly been applied to understand ageing (but see Salguero-Gomez et al., 2016). Second, our interest in linking trade-offs to ageing implies that we consider ageing as a *physiological process of inexorable functional decline*, with at least some mechanisms that may be broadly shared across species. We are acutely aware that demographic ageing does not always map perfectly with physiological ageing (Vaupel, Baudisch,

Dolling, Roach, & Gampe, 2004; Wensink, Wrycza, & Baudisch, 2014); nonetheless, we make the simplifying assumption that demographic ageing is a reasonable proxy for physiological ageing. Third, most consideration of trade-offs in the context of ageing has revolved around resource allocation trade-offs, particularly between reproduction and survival functions, which is at the core of the disposable soma theory (Kirkwood, 1977, 2005; Kirkwood & Holliday, 1979). For this reason, our discussion tends to emphasize resource allocation trade-offs, though obviously many other kinds of trade-offs are also possible.

Fourth, our focus is largely on intraspecific trade-offs. There is now substantial evidence for the existence of a fast-slow life-history axis at the interspecific level in many taxa (Gaillard et al., 2016; Lemaitre et al., 2015; Salguero-Gomez et al., 2016), with important implications for how we understand trait structures at macroevolutionary scales. However, these broad patterns are hard to relate back to the mechanistic questions we are asking. For example, population growth rates are normally relatively close to stationary (e.g. between −0.5 and 1.5 across 389 diverse plant species, Salguero-Gomez et al., 2016), implying that if either reproduction or longevity increases, the other trait will decrease due to density dependence, independent of what physiological mechanisms may be involved. Furthermore, intraspecific variation represents the workplace of evolution, and it is here that we observe many of the exciting recent phenomena reshaping our understanding of trade-offs: context dependence, condition dependence, nonlinearity, etc. It is at the intraspecific level that a complex interplay of biology, genetics, allocation, environment, strategic choices and phenotypic plasticity waits to be elucidated.

2 | EMPIRICAL EVIDENCE FOR INTRASPECIFIC TRADE-OFFS

2.1 | Trade-offs in experimental evolution of model organisms

A number of model organisms have been used to study trade-offs, with mixed results. In the fruit fly *Drosophila melanogaster*, classic selection studies gave contrasting results regarding a decrease in reproductive rate following selection for longer life span (but see Luckinbill, Arking, Clare, Cirocco, & Buck, 1984; Rose, 1984). Other selection experiments have shown trade-offs (e.g. Fabian et al., 2018). Recent work on *D. melanogaster* has also failed to confirm key predictions of life-history and the disposable soma theory. Flies on calorically restricted diets showed evolution of both fecundity and survival, but not in the negatively correlated way predicted by theory, and in ways that differed between the sexes (Zajitschek et al., 2018, 2016). Some *D. melanogaster* alleles appear to produce longer life span with earlier costs (Tatar et al., 2001; Yamamoto, Bai, Dolezal, Amdam, & Tatar, 2013), consistent with antagonistic pleiotropy, whereas others produce life span extension without costs that have been detected (Rogina, Reenan, Nilsen, & Helfand, 2000; Wang, Bohmann, & Jasper, 2003). An open question is thus the extent to which genetic variation related to antagonistic pleiotropy is the genetic variation shaped by selection to produce variation in life span. Additionally, gene-by-environment interactions may make this question even more challenging – and interesting – to explore.

More broadly, a large number of selection experiments have detected 'positive pleiotropy', positive genetic covariation between early- and late-life fitness or condition (Maklakov, Rowe, & Friberg, 2015). This has led to the proposal of a modified version of the mutation accumulation theory of ageing, in which the deleterious effects of mutations are present throughout life, but increase in magnitude with age (Maklakov et al., 2015). Interestingly, this idea is concordant with recent thinking on the evolution of cancer (DeGregori, 2011), as well as with complex systems explanations of ageing as a breakdown in homeostasis (Cohen, 2012, 2016): physiological regulatory networks are highly buffered and redundant, and loss of homeostasis in a given subnetwork thus is most likely to be expressed in the presence of other problems in the same or connected subnetworks (Nijhout, Sadre-Marandi, Best, & Reed, 2017). Early in life, buffering is likely to better mask the effects of mutations than later on when increasing dysregulation exposes the consequences of the mutation.

The positive pleiotropy/modified mutation accumulation theory implies that the declining force of selection with age is still important, but that the trade-offs in the antagonistic pleiotropy theory (between early- and late-life fitness), or in the disposable soma theory (between survival and reproduction) may not be major drivers of the evolution of ageing and life span. In support of such a model, high random mortality in the nematode *Caenorhabditis remanei* induces selection for shorter life span as predicted under classical theories, but high condition-dependent mortality induces selection for longer life span (Chen & Maklakov, 2012). Life span selection in nematodes is, more generally, highly conditional, with sex-specific effects reversible by selecting on complex traits such as learning ability and mate searching proficiency (Ancell & Pires-daSilva, 2017).

Evidence from experimental evolution in model organisms is thus mixed in its support a role for resource allocation trade-offs in determining life spans. While a number of genes in multiple species support antagonistic pleiotropy (Austad & Hoffman, 2018), other genes appear capable of extending life span without particular costs. Selection experiments also produce varied and confusing results. While the experimental approaches generally used with model organisms are considered by many to be a gold standard scientific technique, they do have some drawbacks as well (Austad & Podlutsky, 2005). First, experimental results may not be valid under different conditions, so the generalizability of the conclusions is not necessarily clear. This is particularly relevant in the context of laboratory evolution, where the laboratory environment is far removed from a heterogeneous natural environment. Second, selection experiments are difficult and can be biased by genetic background, breeding protocols and a number of other factors. Third, the organisms that are used in such studies are usually particularly short-lived

even within their clades; it is not clear to what extent this may bias the findings more generally.

2.2 | Trade-offs in the wild: Condition dependence and implications for genetic trade-offs

There is now an extensive literature showing that costs of reproduction (CoR) vary markedly in both presence and strength according to a number of factors. Here, we highlight some key findings relating to survival CoR. We note that this literature needs to be interpreted with some caution, given the substantial differences in a species' measured life span depending on conditions. For example, the Labord's chameleon (*Furcifer labordi*), which normally lives only 4–5 months in the wild and is the record holder for shortest life span among tetrapods, was shown to live up to 16 months if kept under ambient conditions; its life span also varies greatly across habitats and environmental conditions (Eckhardt, Kappeler, & Kraus, 2017).

2.2.1 | Poor environmental conditions can reveal otherwise hidden costs

There is evidence that survival CoR depends on environmental conditions and may be detectable only when resources are limited during specific years and/or for specific sites. For instance, in Soay sheep, survival CoR is only present during severe environmental conditions (wet and stormy winters occurring when population density was high; Tavecchia et al., 2005). A remarkable example in the seed beetle *Callosobruchus maculatus* has shown that environmental conditions (i.e. food availability) can not only change the mean fecundity and life span between environments, but also reverse the signs of phenotypic and genetic correlations from positive to negative under conditions when food is present or absent, respectively (Messina & Fry, 2003). In Alpine Ibex, there was no survival CoR either before or after an epizootic event (pneumonia), but the cost was high during it (Garnier, Gaillard, Gauthier, & Besnard, 2016). By contrast, studies on captive populations, where resources (at least food and water) can be considered as non-limiting, failed to detect any CoR in 18 mammal and 12 bird species kept in zoos (Ricklefs & Cadena, 2007), in Rottweiler pet dogs (Kengeri, Maras, Suckow, Chiang, & Waters, 2013), in laboratory mice (Tarin, Gomez-Piquer, Garcia-Palomares, Garcia-Perez, & Cano, 2014) and captive *Microcebus murinus* (Landes, Henry, Hardy, Perret, & Pavard, 2019). However, dependence of survival CoR on resource abundance is not universal: reproduction was not more costly under unfavourable or favourable environmental conditions in American red squirrels (Descamps, Boutin, McAdam, Berteaux, & Gaillard, 2009).

The condition dependence of CoR means some individuals may appear to escape trade-offs, having both higher reproduction and greater survival. Moreover, variation in acquisition is not independent from variation in allocation as assumed in van Noordwijk and de Jong (1986), which would have implicitly assumed an identical slope of the relationship between survival and reproduction across environment and individual quality (Descamps, Gaillard, Hamel, & Yoccoz, 2016; depicted in Figure 1).

2.2.2 | Is condition dependence detectable at a physiological scale?

Many of the studies examining survival–reproduction trade-offs in the wild are based on short-term survival, which is substantially easier to quantify than impact on ageing rate. Even though ageing is demographically detectable in the wild, for example as increases in mortality rates with age, (Nussey, Coulson, Festa-Bianchet, & Gaillard, 2008; Ricklefs, 1998), the percentage of individuals subject to ageing-related mortality is highly variable but usually low enough to present a measurement challenge. Accordingly, attempts to link CoR to ageing rate have often relied on physiological proxies for ageing, which can be measured short-term and which are not obscured by non-ageing-related mortality (but see Boonekamp, Salomons, Bouwhuis, Dijkstra, & Verhulst, 2014).

The most common proxies have been oxidative stress and telomere attrition (Costantini, 2014; Monaghan & Haussmann, 2006), though the justification for these choices based on the ageing biology literature is now doubtful (Belsky et al., 2018; Hekimi, Lapointe, &

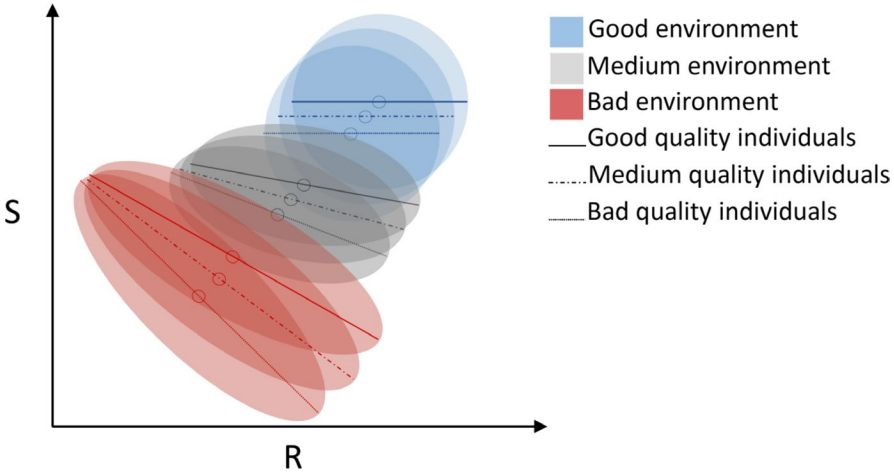

FIGURE 1 Period-individual survival as a function of reproduction (e.g. assuming that survival probability could be measured at the individual level, for instance with a biological marker) depicted in the case where the magnitude of the survival CoR depends on the interaction between environmental condition and individual quality

Wen, 2011; Young, 2018). Furthermore, reproduction is not straightforwardly associated with increased oxidative damage (Metcalfe & Monaghan, 2013; Monaghan, Metcalfe, & Torres, 2009; Selman, Blount, Nussey, & Speakman, 2012). While several studies show that reproduction decreases resistance to oxidative stress (e.g. Christe, Glaizot, Strepparava, Devevey, & Fumagalli, 2012), reproduction was found to have no effect on free-ranging female Soay sheep oxidative damage levels (Nussey, Pemberton, Pilkington, & Blount, 2009) and little effect in eastern chipmunks (Bergeron et al., 2011). In birds, several experimental studies demonstrate that reproduction does decrease oxidative resistance (Alonso-Alvarez et al., 2004; Wiersma, Selman, Speakman, & Verhulst, 2004) in a condition-dependent way (Noguera, 2017), leading to short-term mortality rather than a long-term change in longevity prospects (Alonso-Alvarez et al., 2006). This emphasizes the difficulty arising when trying to relate apparent CoR with the disposable soma theory (Monaghan et al., 2009).

2.2.3 | Importance and implications

The integration of all these factors implies that trade-offs are subject to strong stochastic influences caused by multiple driving forces, transforming detectability of survival CoR into a statistical challenge (Descamps et al., 2016) and the evolutionary demography modelling of trade-offs into a population-structured jigsaw (Coste, Austerlitz, & Pavard, 2017). Overall, there is clear evidence for CoR in some species under some conditions, but there is also clearly evidence that CoR is in fact highly contingent on a number of factors.

An important caveat here is that failure to detect CoR is not equivalent to their absence, according to our mechanistic definitions of trade-offs, constraints and CoR. Many studies in the wild have relatively small sample size, and this leads to two contradictory problems: (a) many underpowered studies may fail to detect an effect that is present, and (b) studies that find effects will tend to systematically overestimate them because only studies overestimating effects will be statistically significant (Gelman & Carlin, 2014). As a result, it is hard to know how to interpret the patchwork of evidence presented above: What are the relative roles for statistical artefacts, condition dependence in detection, and contingency in the presence of trade-offs? Likely all play a role, but the overall portrait will require substantial further work.

3 | THEORETICAL REASONS TO EXPECT WEAKER TRADE-OFFS

3.1 | Nonlinearity of trade-offs

Most empirical studies focusing on trade-offs deal with detection at the population level. The main goal for authors is generally to test for a negative relationship between two traits, often survival and reproduction (Charnov & Ernest, 2006; Levitan, 2000; Roff, Mostowy, & Fairbairn, 2002; Vøllestad & Quinn, 2003; Walker, Gurven, Burger, & Hamilton, 2008). In this context, the slope estimated through a classic linear regression gives an apparent answer, but without considering other potential shapes for the trade-off. Levins (1968) showed theoretically that the trade-off shape is an essential parameter for the expected result of evolution. For example, in portions of trait ranges where trade-offs are very steep or very shallow, the trade-off essentially seems to disappear (i.e. optimization is occurring on one trait at a time within those ranges). Despite such considerations, few studies have investigated the question of the trade-off shape (Jessup & Bohannan, 2008; Maharjan et al., 2013). The principal challenge to evaluate the linearity of trade-offs is to collect enough quality data, so theoretical studies are especially useful.

Bourg, Jacob, Menu, and Rajon (2019) studied the evolution of trade-off shape in a large population. They used an evolutionary resource allocation-based model with mutations on the endocrine system involved and demonstrated that trade-offs are not necessarily linear. Depending on the environmental context, the trade-off's shape tends to be shorter and more concave. They revealed that the trade-off shape depends directly on a rarely considered parameter: the cost of resource storage (Figure 2). Thus, depending on the acquired resource and its storage cost, individuals from a single population could evolve along different trade-off shapes. Furthermore, the whole population was able to reach a new trade-off shape only by improving their ability to use the energy thanks to the combined action of mutations and selection. The possibility of escape from a trade-off by mutation or by a diet modification should lead to a decrease of the trade-off's impact. Another interesting implication: for the many resources that cannot be stored, trade-offs should be highly concave and thus should only be strong for narrow ranges of traits.

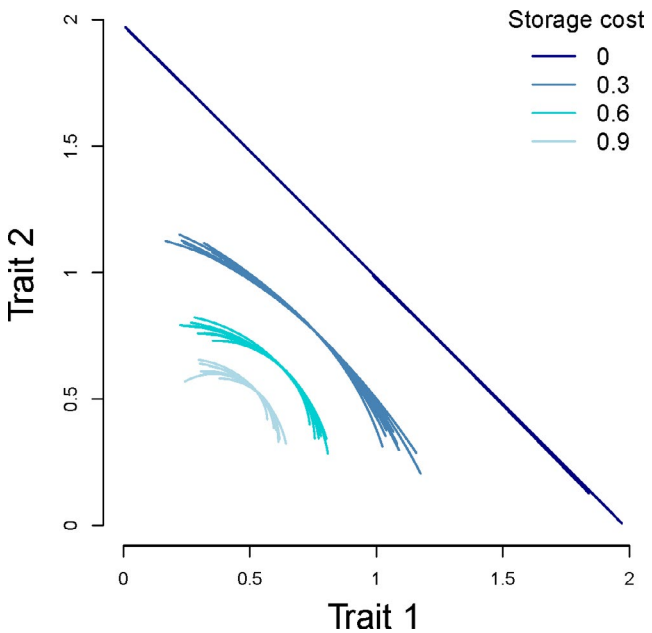

FIGURE 2 Shapes of trade-offs are different depending on the storage cost applied in simulations. Ten representative simulations per storage cost value are illustrated. The higher the storage cost, the more trade-offs are curved and short. Simulations originate from Bourg et al. (2019)

3.2 | The effect of social and sexual interactions

Social interactions within the same sex and/or between sexes can also affect the cost–benefit balances of somatic maintenance and reproduction, often leading to the weakening of trade-offs. For example, cooperation by food transferral from adults to their descendants can promote the evolution of longer life span in populations of overlapping generations (Gurven, Stieglitz, Hooper, Gomes, & Kaplan, 2012; Lee, 2003; Pavard & Branger, 2012); long life and post-reproductive life span can in turn promote the evolution of cooperation (Ross, Rychtar, & Rueppell, 2015) and suppress conflict (Port & Cant, 2013). As soon as the wheels of the positive feedback start to turn, the cost of somatic maintenance can be reduced quickly so that slowed ageing/increased life span does not necessarily cause detrimental effects on reproduction. Interactions between males and females can also strongly influence life span. For example, sexual conflict over mating can directly affect the life span and ageing rate of individuals, often causing reduced life span or even immediate death of females (reviewed in Adler & Bonduriansky, 2014). In social insects, however, mating can be a form of sexual cooperation. For example, mating alone (either with a fertile or a sterilized male) can substantially increase the life span of queens of the ant *Cardiocondyla obscurior*; queens that received viable sperm also have increased fecundity (Schrempf, Heinze, & Cremer, 2005). As we can see, under either sexual conflict or sexual cooperation, fecundity and life span can be shifted in the same direction, weakening/restricting trade-offs between reproduction and maintenance.

Moreover, social and sexual interactions can happen at the same time throughout different life stages of an individual in synergistic or antagonistic ways, further lightening the influence of trade-offs as a determinant of life span. For example, Berger, Lemaitre, Allaine, Gaillard, and Cohas (2018) showed recently that in cooperative breeding Alpine marmots, the presence of helpers (subordinate males) on the one hand improves the survival of male pups via thermoregulation during hibernation, but on the other hand can impose strong intrasexual competition pressure on these pups. The opposing influences from social and sexual interactions produced a nonlinear effect of the presence of helpers on the life span of male dominants. For the dominant males who have helpers in adulthood, they lived the longest (max 14 years) when having no helper at all, shortest (max 8 years) when having a single helper, and intermediate (max 11 years) when having two or more helpers at birth (Berger et al., 2018).

3.3 | Multiple resources

A third theoretical argument against the role of trade-offs in determining ageing rate was recently proposed by Cohen, Isaksson, and Salguero-Gomez (2017). They modelled lifetime reproductive success in a hypothetical species where resource allocation decisions were made simultaneously across multiple 'currencies' (i.e. resources that can be differentially allocated to survival or reproduction). Much of the literature primarily discusses energy budgets and energy allocation, but there is increasing evidence that energy alone does not fully capture the resources that may be allocated. Micronutrients such as carotenoids may be allocated to sexual selection or antioxidant function in some species (Isaksson, Sheldon, & Uller, 2011). Specific dietary nutrients such as proteins might also have differential roles, particularly if reproduction requires certain nutrients more than others (Cotter, Simpson, Raubenheimer, & Wilson, 2011; Raubenheimer, Simpson, Couteur, Solon-Biet, & Coogan, 2016). Non-physical resources such as time and risk may also be differentially allocated (Ketterson, Nolan, Wolf, & Ziegenfus, 1992). There is thus good reason to believe that multiple currencies do operate simultaneously to mediate any trade-offs that may exist; this model explored the evolutionary consequence of these multiple currencies.

In some runs, the currencies were allowed to have differential 'buying power' for survival and reproduction. For example, one currency might allow a gain of one unit of reproduction for a loss of one unit of survival, but another currency might allow a gain of two units of reproduction for one unit of survival. As long as the buying power differed across currencies, the model found that the trade-off was substantially weakened (i.e. higher lifetime reproductive success could evolve) relative to a single-currency model. Even when buying power was equal (probably unrealistic under real conditions), the evolution of the underlying physiological traits showed substantial stochasticity due to the presence of multiple optima in the state space. These findings imply that, under realistic scenarios of multiple currencies with differential buying power for survival and reproduction, trade-offs are likely to be substantially weaker than generally thought. They do not, however, imply that the trade-offs are completely absent.

3.4 | Trade-offs between mortality components

In the sixth prediction of his seminal article on the evolution of senescence (Williams, 1957), Williams anticipated that *'senescence should always be a generalized deterioration, and never due largely to changes in a single system*'. This idea was later reframed and formalized by Maynard Smith (1962): a synchrony of physiologically independent ageing processes is expected because natural selection will favour any genetic change that makes the physiological system that ages the fastest more durable while it would select less against mutations affecting systems that age more slowly (see Box 1 for an illustration of this principle). Moreover, it has been argued that covariation between risk of different causes of death at the individual level may hinder the effects of selection on mortality components at an evolutionary scale (see Box 1). The idea is that a primary defect of one system has consecutive effects in other systems, leading to inferential difficulties in characterizing causes of death. This has led researchers to envision senescence as the accelerated accumulation of health deficits resulting from deterioration of several physiological functions and leading ultimately to death (Kulminski et al., 2007; Yashin et al., 2007).

These hypotheses have been recently discussed in the light of new empirical evidence (reviewed in Gaillard & Lemaître, 2017) demonstrating that demographic, phenotypic and functional senescence are not synchronous (e.g. in Soay sheep in Hayward et al. (2015) or in

BOX 1 Trade-off between mortality components may explain non-synchronicity of senescence by causes of deaths

Let us assume a theoretical organism, absent of extrinsic mortality, whose adult mortality hazard $\mu(t)$ is shaped by three independent additive Gompertz-shaped (i.e. $\mu(t)=ae^{bt-\alpha}$) causes of death c_1, c_2 and c_3, such that $\mu(t)=\mu_1(t)+\mu_2(t)+\mu_3(t)$, with $t>\alpha$, and α the age at maturity. For simplicity, let us further assume that parameter a is constant (all causes have the same level of morbidity at first adult age α) and that cause-specific morbidity differs in the rate b_c at which mortality increases with age (with subscript c standing for causes of death 1, 2 or 3).

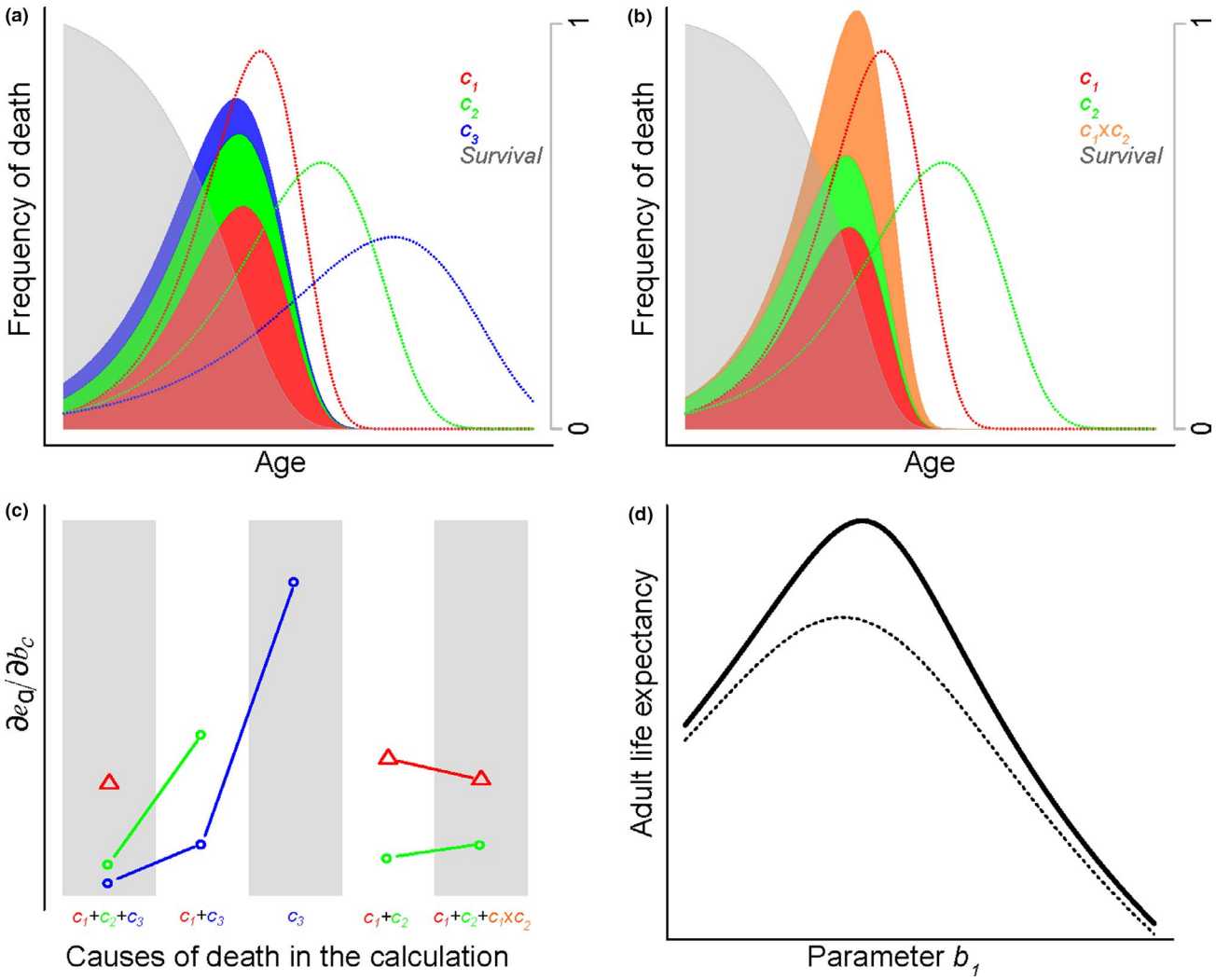

Figure 3a shows the staked distributions of deaths $f_c(t)=S_1(t)S_2(t)S_3(t)\mu_c(t)$ for the three causes of death c_1, c_2 and c_3, the corresponding survival $S(t)=S_1(t)S_2(t)S_3(t)$. It also shows the distribution of death from each cause $f_c(t)=S_c(t)\mu_c(t)$ in the case where individuals die only from this cause (lines). Density of deaths from c_1 is much larger than those from c_2 and c_3 because few individuals survive to ages where c_2 and c_3 are most likely (with a = 0.0015, b_1 = 0.1, b_2 = 0.07 and b_3 = 0.05).

Now let us assume a stationary population of a species whose fertility rates are constant over age. In this case, remaining life expectancy e_α is an adequate measure of adult fitness. Thus, sensitivity of e_α with respect to cause-specific parameter b_c, $\partial e_\alpha/\partial b_c$, is a proxy of the strength of natural selection on deleterious alleles increasing the pace at which mortality from cause c increases with age. Figure 3c shows these estimates in three scenarios (on the three left panels) where (i) the three causes c_1, c_2 and c_3 compete in the population, (ii) only c_2 and c_3 compete, and (iii) individuals die only from cause c_3. These results show that selection pressure on an allele increasing susceptibility to a specific cause of death depends on the age-specific amount of other deaths in the population. For example, removing c_1 from the population drastically increases the strength of negative selection on c_2 and only a little on c_3. More generally, gradient of selection occurs not only through age but also through causes of death. For example, assume that alleles for susceptibility to c_2 are at

BOX 1 (Continued)

the mutation–selection balance, with selection just above the threshold at which selection overcomes genetic drift into the population. Negative selection is weak but will eventually purge deleterious mutations. Everything else being equal, alleles for susceptibility to c_1 will be more intensely negatively selected. Purifying selection will decrease the number and the frequency of these alleles, eventually decreasing the amount of deaths from c_1. By contrast, susceptibility mutations to c_3 are neutral and mutations will accumulate, eventually increasing the amount of death from c_3. Natural selection will therefore tend to homogenize the rate at which cause-specific mortality increases with age. This was the idea developed by Maynard Smith (1962) and Williams (1957).

But then, do we expect that all primordial functions senesce at the same pace and therefore share the same *b* parameter? We do not think so, for several reasons. First, cause-specific genetic architecture (i.e. mainly the number, length and expression of genes) may differ between functions, leading to different cause-specific deleterious mutations rates. Second, biological function differs at many molecular and physiological levels. In the case of diseases for example, this leads to disease-specific constraints on its epidemiology (i.e. mainly its age-onset pattern and its penetrance) leading to different levels of selection (Pavard & Metcalf, 2007). We therefore do not expect cause-specific mutation–selection balances to equilibrate at the same allelic spectrum.

Now let us consider that causes of death are not independent and that cause c_3 is now the product, for instance, of a multiplicative interaction $c_1 \times c_2$, between c_1 and c_2, such that $\mu_{1\times2}(t) = za^2 e^{(b_1+b_2)(t-\alpha)}$ (where z is the coefficient of this interaction). This models, within an individual life, the fact that factors increasing c_1 may also be prone to increasing c_2 and *vice versa*. Figure 3b shows the distribution of deaths in this case (taking $z = 40$ such that $c_1 \times c_2$ is accounting for more than 25% of observed deaths). Figure 3c (two right panels) shows the $\partial e_\alpha / \partial b_c$ for c_1 and c_2 in this case. Adding interaction between causes of death tends to decrease selection on c_1 and increase selection on c_2. However, even with a strong interaction these changes are of small magnitude relative to the difference in elasticity between causes of deaths.

Finally, let us assume now a linear negative covariation between b_1 and b_2. This models a trade-off between causes of death at an evolutionary scale. Figure 3d shows e_α for a range of parameter b_1 (which corresponds here to $b_2 = -7b_1 + 0.14$; plain line). An optimum is then found corresponding to a unique couple but potentially different (b_1, b_2); their respective values depend on the magnitude of their covariation ($b_1 = 0.068$ and $b_2 = 0.092$ in this example). Adding positive interaction ($c_1 \times c_2$) to the model tends to flatten the optimum (dotted line), making it less stable, but still evolutionarily relevant.

reptiles in Massot et al. (2011)). Such asynchrony could be due to the relative rates of the decline for different fitness components in relation to their age-specific impacts on fitness (Cohen, 2004). It could also be due to constraint-based mechanisms of ageing (see below), which are not necessarily subject to simple adjustment through selection and may therefore not be easily 'synchronizable'. In particular, trade-offs between mortality components may provide part of the answer. Life-history theory – heavily influenced by the synchronicity theory – has indeed little envisioned the possible importance of trade-offs between mortality components, nor how they might lead to variation in optimal rates of senescence related to specific causes of death (see Box 1 for an illustration of such trade-offs).

In conclusion, trade-offs between mortality components may be an important and underexplored driver of the evolution of ageing. Finding evidence for such trade-offs at a population scale is, however, challenging because individuals die only once and gathering information on the proximal and distal reasons for individual death is difficult in captivity and generally impossible in nature. Investigations of such trade-offs will therefore mostly rely on experimentation or very detailed longitudinal studies, requiring (a) grouping individuals according to factors (genetic or environmental) expected to shape cause-specific mortality outcomes, (b) measuring biomarkers linked to cause-specific mortality or (c) empirically manipulating, over the course of an individual's life, the functions at the source of the mortality component trade-off. It is likely that mortality component trade-offs are also condition- or environment-dependent; for example, we would predict that the frequency of *APOE*-ε4 would decrease in sunnier environments as the trade-off between vitamin D absorption and neurodegeneration weakened (Oriá et al. 2007).

4 | WHAT AGEING MECHANISMS CAN TELL US ABOUT THE ROLE OF TRADE-OFFS

Most discussion of the role of trade-offs is divorced from what is known about the mechanisms of ageing. To some extent, this gap is bridged in the literature searching for specific genes and genetic patterns that might underlie antagonistic pleiotropy or mutation accumulation (Austad & Hoffman, 2018; Hughes et al., 2002); nonetheless, the individual genes are not the mechanisms, and there are insights to be gained from asking how known mechanisms could be modulated by trade-offs. A thorough review of ageing mechanisms is beyond the scope of this article; accordingly, we choose

several illustrative examples from the well-known framework of the Hallmarks of Aging (Lopez-Otin, Blasco, Partridge, Serrano, & Kroemer, 2013), as well as a few other mechanisms which were not included in that framework but which are broadly accepted (dysregulation after psychological stress; McEwen, 1998, structural damage; Rueppell, 2009 and age-related clonal hematopoiesis; Shlush, 2018).

At a relatively macro level, the role of insulin-like growth factor (IGF)-1 and related pathways supports the role of trade-offs in determining ageing rate. Within vertebrates, increased IGF-1 levels are broadly associated with increases in both somatic growth and reproduction, but also with decreases in life span and accelerated ageing (Dantzer & Swanson, 2012). Crucially, IGF-1 may explain life-history variation at both the intra-individual and interspecific levels: it responds to environmental changes to mediate intra-individual trade-offs, but also appears to explain lineage-specific differences in growth and ageing, such as in dog breeds (Greer, Hughes, & Masternak, 2011). Furthermore, the IGF-1 receptor gene is a canonical example of a conserved genetic mechanism by which life span can be extended in organisms ranging from yeast to mammals (Tatar, Bartke, & Antebi, 2003). IGF-1 would thus appear to be the ideal mechanistic candidate to explain life-history trade-offs in vertebrates, although more work needs to be done to fully confirm this (Swanson & Dantzer, 2014). One attractive hypothesis is that IGF-1 and related pathways are a 'public' mechanism by which multiple other 'private', or species-specific, mechanisms are regulated (Partridge & Gems, 2002).

Many of the downstream processes likely controlled by IGF-1 and related pathways also lend themselves relatively easily to a trade-off-based understanding of ageing. For example, DNA damage accumulation can likely be modulated, at least to some extent, by investing in mechanisms such as antioxidant protection and repair, which may be resource intensive. Loss of proteostasis as well would seem to be modulable by allocation of resources to clearance of proteins, an ATP-dependent process (Kaushik & Cuervo, 2015). On the other hand, other ageing mechanisms appear to be more strongly associated with various biological and physiological constraints that would not be subject to modulation via greater allocation of resources. In particular, many known ageing mechanisms are essentially cancer protection mechanisms, notably telomere attrition, cellular senescence and the inflammatory cascades that can result (Schosserer, Grillari, & Breitenbach, 2017; Shay & Wright, 2011). This is a canonical example of the above-mentioned mortality source trade-offs, where a trade-off between ageing and cancer creates a higher-order constraint. Direct allocation of resources (energetic or otherwise) would be unlikely to reduce cellular senescence, since a decrease in cellular senescence would imply an increase in cancer risk, and presumably selection has optimized the balance between the two.

A second example of a constraint-based mechanism is the dysregulatory effects of chronic psychological stress in vertebrates. Organisms appear unable to fully return to a baseline physiological state after prolonged stress (McEwen, 1998), creating a long-term dysregulation which can accelerate other ageing mechanisms through positive feedback loops (Tomiyama et al., 2012). This mechanism is, as far as we know, completely independent of resource allocation strategies or other trade-offs, and reflects an inherent weakness in the structure of the underlying regulatory networks, a constraint.

The distinction between trade-off-based and constraint-based mechanisms is not always clear. For example, while the level of DNA damage might be adjustable via resource allocation, some minimal level is probably unavoidable and might be considered a constraint. Likewise, rates of DNA damage might have impacts on the rates of cellular senescence (d'Adda di Fagagna, 2008), such that even if the mechanism itself represents a constraint, upstream changes in resource allocation could modulate rates of accumulation of senescent cells. Despite these nuances, however, it is clear that many ageing mechanisms are not subject to much modulation by resource allocation or trade-offs. Perhaps the clearest examples are the impacts of chronic stress and structural damage such as wing wear in insects. Another example is age-related clonal hematopoiesis, a process by which natural selection among different clonal stem cell lineages can produce decreases in diversity, with impacts on ageing (Shlush, 2018). This loss of diversity does not appear to be in any way resource related, as far as we know.

Broadly, then, it is useful to consider to what extent ageing mechanisms can be modulated via trade-offs, versus to what extent they are inherent in the physiological nature of the species in question (constraints). The mortality source trade-offs noted above are an interesting case: they are trade-offs at a lower level of organization that produce constraints at a higher level.

5 | DISCUSSION

There can be no doubt that trade-offs are often present in multiple evolutionary contexts, including those structuring ageing rates. Indeed, a wide variety of studies reviewed here confirms this in different contexts: in the lab, in the wild, and based on the known mechanisms of ageing. Nonetheless, there is also now sufficient evidence to say that the trade-off paradigm, while important, is incomplete as a way to understand how ageing rates and life span evolve. Numerous studies both in the laboratory and in the wild have failed to confirm basic predictions, enough to imply that trade-offs are variable in their importance and strength depending on a wide variety of factors. Recent work on hyperfunction theory (Lind et al., 2019), which posits that ageing arises from hyperfunction of reproduction-related genes late in life, also complements our review by suggesting alternative mechanisms for the evolution of ageing beyond trade-offs.

Specifically, we argue that many ageing mechanisms reflect physiological constraints that are largely isolated from modulation by trade-offs, whereas others are subject, more or less directly, to such modulation. The importance of the various ageing mechanisms may depend on both the species/taxon and on environmental conditions, implying that the role of trade-offs is

also likely to vary. Considering numerous other mitigating factors (condition and environment dependence of trade-offs, nonlinear trade-off shapes, social and sex-specific factors, multiple resource currencies, etc.), trade-offs should sometimes but not always be a crucial force in structuring life histories generally and ageing rates specifically. Seen another way, an exciting current challenge is to elucidate (a) the variance decomposition of ageing based on covariance with other traits (including links to other mortality components); (b) the variance decomposition of the part of this covariance that is genetic; and finally (c) their translation into variance in fitness in a potentially structured population (e.g. through heterogeneity or sociality) whose vital rates and their covariances fluctuate in time.

To summarize, we are proposing a model of the evolution of ageing in which there are numerous ageing mechanisms, some broadly shared across species, others highly specific to certain taxa (Cohen, 2018). Some of these mechanisms emerge from constraints related to the particular physiology and environment of the species; others reflect trade-offs that are modulable via mechanisms such as resource allocation. The various mechanisms can then interact with each other via feedback effects. The importance of trade-offs in determining the ageing rate of a given species thus depends on the particular combination of mechanisms and their susceptibility to trade-offs. It also depends on a host of factors that influence the strength of trade-offs more generally than in the context of ageing: the functional form of the trade-off and whether the trait values are in a range with a strong negative slope; the number of currencies involved in the trade-off; social and sexual modulating factors; and contingency of the trade-off on environment and condition. Accordingly, we predict that a substantial portion of the variance in ageing rates across species is attributable not only to coherent adjustment via trade-off-based mechanisms, but also to the species-specific set of mechanistic constraints, with the trade-off portion of the variance highly dependent on the various potential mitigating factors listed above. For example, the variance attributable to trade-offs could be substantially weakened in a species where the trade-offs are strong only under highly restricted conditions that do not represent the norm for the species. This theoretical model appears to be supported by the diversity of evidence for trade-offs in the laboratory and in the wild: apparently contradictory studies may be reflecting this complex underlying reality, as much as being the product of methodological and measurement challenges. This is strongly parallel to the recent theoretical work of Baudisch, Vaupel, Wensink and colleagues showing that the classic work on ageing demography by Hamilton (1966) is but a special case, with broader patterns substantially more varied and complex than Hamilton had predicted (Baudisch, 2005; Vaupel et al., 2004; Wensink, Caswell, & Baudisch, 2017). Just as Hamilton's exponential increases in mortality are a special (though important) case rather than a universal phenomenon, trade-offs as key drivers of ageing are also likely a special but important case.

Some readers may find this model unsurprising: Is it not well known that there are both trade-offs and constraints, for example? We would argue that (a) while the general existence of constraints is acknowledged, they are rarely discussed or incorporated into our paradigmatic way of thinking; and (b) while nuances related to trade-offs are acknowledged, their primacy as a driving force is not generally thought to be called into question, as we are proposing occurs under many circumstances. This current way of thinking has several limits. First, researchers who are not experts in trade-offs and life-history theory are unlikely to consider the presence of constraints in this context, and are likely to overestimate the role of trade-offs. Second, even for those more expert in the field, consideration of a major role for constraints should lead us to ask different questions. For example, research on empirical support for mutation accumulation versus antagonistic pleiotropy has generally supposed that there is a relatively general answer to this question; consideration of the multiplicity of ageing mechanisms, and the constraint- versus trade-off-based nature of these mechanisms, explicitly predicts that there is no universal answer to this question. Third, our model provides a useful framework to understand the heterogeneity of ageing patterns across the tree of life. Some taxa may share physiological traits (and thus ageing mechanisms) that make trade-offs relatively universal within the taxon; others may escape trade-offs to varying degrees for the same reason. Fourth, our model implies that the classical evolutionary theories of ageing (mutation accumulation, antagonistic pleiotropy and the disposable soma) are insufficient to explain the evolution of ageing: ageing can, and probably does, emerge in some taxa largely due to constraint-based mechanisms unrelated to mechanistic trade-offs; in other taxa, all mechanisms may be weak enough for the species to largely escape ageing.

Accordingly, our model also raises a series of new questions/predictions that should be pursued:

1. We predict that there should be taxa in which mechanistic trade-offs play a minimal role in structuring life span. Teleost fishes are a good candidate, with many species ageing very quickly and others very slowly or not at all. Contrasting patterns are clear in well-known examples such as semelparous salmon, killifish, guppies and rockfish.
2. How strongly do mechanistic trade-offs structure interspecific patterns in life-history variation in various taxa? Pattern-level trade-offs are well described in some taxa, and we predict that this will be paralleled by mechanistic trade-offs in some but not all cases. This could be tested, for example, by identification of mechanisms structuring trade-offs (e.g. potentially IGF-1 in mammals), or by finding taxa where no trade-off pattern is apparent.
3. Does the presence of IGF-1 as an upstream control mechanism in mammals imply that trade-offs are universally important in mammals? If so, could we nonetheless detect variation in the strength of trade-offs as a driving force within mammals (e.g. some taxa in which the trade-offs are present but weaker)?
4. What are the relative roles, synergies and antagonisms between genetic and individual trade-offs, and how do these impact the role of trade-offs in determining ageing rates?

5. What is the relationship between constraints and trade-offs in species with negligible/negative senescence? Do these species escape both constraints and trade-offs, and if so in equal measure?
6. How do constraint-based and trade-off-based mechanisms interact with each other? For example, in feedback loops among mechanisms, is the trade-off aspect amplified, or is the constraint aspect amplified, or does it depend?
7. We have focused on ageing as a potential product of trade-offs. Beyond ageing, how important are trade-offs in generating observed evolutionary patterns? Obviously, this is an age-old question, but one that takes on a new light given the various limitations to trade-offs discussed here.

These questions illustrate the ways that an understanding of the limits of trade-offs and the potential role of constraints can reorient our science. At the broadest level, evolutionary processes can be conceived of as a dance between trade-offs and constraints, with one or the other taking the lead at various points but with both always present. Until now, we have focused primarily on one partner, even while the presence of the other was acknowledged; it is time to focus on the interplay. In the context of ageing in particular, this understanding appears poised to lead us towards novel evolutionary theories of ageing with the potential to explain not only how ageing can evolve, but also why it varies as it does across the tree of life.

ACKNOWLEDGEMENTS

We thank Jean-Michel Gaillard and Jean-François Lemaitre for valuable comments and discussions. A.A.C. is supported by a CIHR New Investigator Salary Award and is a member of the FRQ-S funded *Centre de recherche du CHUS* and *Centre de recherche sur le vieillissement*. This work was funded by National Science and Engineering Research Council Discovery Grant # RGPIN-2018-06096 to A.A.C. X.Y.L. would like to thank Hanna Kokko for constructive discussions and career support, and the Swiss National Science Foundation for funding (project funding Nr. 163374 granted to Hanna Kokko and career funding Ambizione Nr. 180145 to X.Y.L.). A.A.C. declares a conflict of interest as founder and Chief Scientific Officer at Oken.

AUTHORS' CONTRIBUTIONS

A.A.C. proposed and led the collaboration. All authors wrote, edited, revised and extensively discussed the manuscript.

DATA AVAILABILITY STATEMENT

This article does not use data.

ORCID

Alan A. Cohen https://orcid.org/0000-0003-4113-3988
Xiang-Yi Li https://orcid.org/0000-0001-8662-0865

REFERENCES

Adler, M. I., & Bonduriansky, R. (2014). Sexual conflict, life span, and aging. *Cold Spring Harbor Perspectives in Biology*, *6*, a017566. https://doi.org/10.1101/cshperspect.a017566

Alonso-Alvarez, C., Bertrand, S., Devevey, G., Prost, J., Faivre, B., Chastel, O., & Sorci, G. (2006). An experimental manipulation of life-history trajectories and resistance to oxidative stress. *Evolution*, *60*, 1913–1924. https://doi.org/10.1111/j.0014-3820.2006.tb00534.x

Alonso-Alvarez, C., Bertrand, S., Devevey, G., Prost, J., Faivre, B., & Sorci, G. (2004). Increased susceptibility to oxidative stress as a proximate cost of reproduction. *Ecology Letters*, *7*, 363–368. https://doi.org/10.1111/j.1461-0248.2004.00594.x

Ancell, H., & Pires-daSilva, A. (2017). Sex-specific lifespan and its evolution in nematodes. *Seminars in Cell and Developmental Biology*, *70*, 122–129. https://doi.org/10.1016/j.semcdb.2017.05.012

Austad, S. N., & Hoffman, J. M. (2018). Is antagonistic pleiotropy ubiquitous in aging biology? *Evolution, Medicine, and Public Health*, *2018*, 287–294. https://doi.org/10.1093/emph/eoy033

Austad, S. N., & Podlutsky, A. (2005). A critical evaluation of nonmammalian models for aging research. *Handbook of the Biology of Aging* (Vol. *6*, pp. 449–467) . Academic Press,

Baudisch, A. (2005). Hamilton's indicators of the force of selection. *Proceedings of the National Academy of Sciences of the United States of America*, *102*, 8263–8268. https://doi.org/10.1073/pnas.0502155102

Belsky, D. W., Moffitt, T. E., Cohen, A. A., Corcoran, D. L., Levine, M. E., Prinz, J. A., … Caspi, A. (2018). Eleven telomere, epigenetic clock, and biomarker-composite quantifications of biological aging: Do they measure the same thing? *American Journal of Epidemiology*, *187*, 1220–1230. https://doi.org/10.1093/aje/kwx346

Berger, V., Lemaitre, J. F., Allaine, D., Gaillard, J. M., & Cohas, A. (2018). Early and adult social environments shape sex-specific actuarial senescence patterns in a cooperative breeder. *American Naturalist*, *192*, 525–536. https://doi.org/10.1086/699513

Bergeron, P., Careau, V., Humphries, M. M., Réale, D., Speakman, J. R., & Garant, D. (2011). The energetic and oxidative costs of reproduction in a free-ranging rodent. *Functional Ecology*, *25*, 1063–1071. https://doi.org/10.1111/j.1365-2435.2011.01868.x

Bernardo, J. (1996). The particular maternal effect of propagule size, especially egg size: Patterns, models, quality of evidence and interpretations. *American Zoologist*, *36*, 216–236. https://doi.org/10.1093/icb/36.2.216

Boonekamp, J. J., Salomons, M., Bouwhuis, S., Dijkstra, C., & Verhulst, S. (2014). Reproductive effort accelerates actuarial senescence in wild birds: An experimental study. *Ecology Letters*, *17*, 599–605. https://doi.org/10.1111/ele.12263

Bourg, S., Jacob, L., Menu, F., & Rajon, E. (2019). Hormonal pleiotropy and the evolution of allocation trade-offs. *Evolution*, *73*(4), 661–674. https://doi.org/10.1111/evo.13693

Charnov, E. L., & Ernest, S. K. (2006). The offspring-size/clutch-size trade-off in mammals. *American Naturalist*, *167*, 578–582. https://doi.org/10.1086/501141

Chen, H. Y., & Maklakov, A. A. (2012). Longer life span evolves under high rates of condition-dependent mortality. *Current Biology*, *22*, 2140–2143. https://doi.org/10.1016/j.cub.2012.09.021

Christe, P., Glaizot, O., Strepparava, N., Devevey, G., & Fumagalli, L. (2012). Twofold cost of reproduction: An increase in parental effort leads to higher malarial parasitaemia and to a decrease in resistance to oxidative stress. *Proceedings of the Royal Society B: Biological Sciences*, *279*, 1142–1149. https://doi.org/10.1098/rspb.2011.1546

Christians, J. K. (2000). Trade-offs between egg size and number in waterfowl: An interspecific test of the van Noordwijk and de Jong model.

Functional Ecology, *14*, 497–501. https://doi.org/10.1046/j.1365-2435.2000.00444.x

Cohen, A. A. (2004). Female post-reproductive lifespan: A general mammalian trait. *Biological Reviews*, *79*, 733–750. https://doi.org/10.1017/S1464793103006432

Cohen, A. A. (2016). Complex systems dynamics in aging: New evidence, continuing questions. *Biogerontology*, *17*, 205–220. https://doi.org/10.1007/s10522-015-9584-x

Cohen, A. A. (2018). Aging across the tree of life: The importance of a comparative perspective for the use of animal models in aging. *Biochimica Et Biophysica Acta (BBA) - Molecular Basis of Disease*, *1864*, 2680–2689. https://doi.org/10.1016/j.bbadis.2017.05.028

Cohen, A. A., Isaksson, C., & Salguero-Gomez, R. (2017). Co-existence of multiple trade-off currencies shapes evolutionary outcomes. *PLoS ONE*, *12*, e0189124. https://doi.org/10.1371/journal.pone.0189124

Cohen, A. A., Martin, L. B., Wingfield, J. C., McWilliams, S. R., & Dunne, J. A. (2012). Physiological regulatory networks: Ecological roles and evolutionary constraints. *Trends in Ecology and Evolution*, *27*, 428–435. https://doi.org/10.1016/j.tree.2012.04.008

Costantini, D. (2014). *Oxidative stress and hormesis in evolutionary ecology and physiology: A marriage between mechanistic and evolutionary approaches*. Berlin, Heidelberg: Springer-Verlag.

Coste, C. F. D., Austerlitz, F., & Pavard, S. (2017). Trait level analysis of multitrait population projection matrices. *Theoretical Population Biology*, *116*, 47–58. https://doi.org/10.1016/j.tpb.2017.07.002

Coste, C. F. D., & Pavard, S. (in press). Analysis of a multitrait population projection matrix reveals the evolutionary and demographic effects of a life history trade-off. *Ecological Modelling*.

Cotter, S. C., Simpson, S. J., Raubenheimer, D., & Wilson, K. (2011). Macronutrient balance mediates trade-offs between immune function and life history traits. *Functional Ecology*, *25*, 186–198. https://doi.org/10.1111/j.1365-2435.2010.01766.x

d'Adda di Fagagna, F. (2008). Living on a break: Cellular senescence as a DNA-damage response. *Nature Reviews Cancer*, *8*, 512–522. https://doi.org/10.1038/nrc2440

Dantzer, B., & Swanson, E. M. (2012). Mediation of vertebrate life histories via insulin-like growth factor-1. *Biological Reviews of the Cambridge Philosophical Society*, *87*, 414–429. https://doi.org/10.1111/j.1469-185X.2011.00204.x

DeGregori, J. (2011). Evolved tumor suppression: Why are we so good at not getting cancer? *Cancer Research*, *71*, 3739–3744. https://doi.org/10.1158/0008-5472.CAN-11-0342

Descamps, S., Boutin, S., McAdam, A. G., Berteaux, D., & Gaillard, J.-M. (2009). Survival costs of reproduction vary with age in North American red squirrels. *Proceedings of the Royal Society B: Biological Sciences*, *276*, 1129–1135. https://doi.org/10.1098/rspb.2008.1401

Descamps, S., Gaillard, J. M., Hamel, S., & Yoccoz, N. G. (2016). When relative allocation depends on total resource acquisition: Implication for the analysis of trade-offs. *Journal of Evolutionary Biology*, *29*, 1860–1866. https://doi.org/10.1111/jeb.12901

Eckhardt, F., Kappeler, P. M., & Kraus, C. (2017). Highly variable lifespan in an annual reptile, Labord's chameleon (*Furcifer labordi*). *Scientific Reports*, *7*, 11397. https://doi.org/10.1038/s41598-017-11701-3

Everman, E. R., & Morgan, T. J. (2018). Antagonistic pleiotropy and mutation accumulation contribute to age-related decline in stress response. *Evolution*, *72*, 303–317. https://doi.org/10.1111/evo.13408

Fabian, D. K., Garschall, K., Klepsatel, P., Santos-Matos, G., Sucena, E., Kapun, M., … Flatt, T. (2018). Evolution of longevity improves immunity in *Drosophila*. *Evolution Letters*, *2*, 567–579.

Gaillard, J.-M., & Lemaître, J.-F. (2017). The Williams' legacy: A critical reappraisal of his nine predictions about the evolution of senescence. *Evolution*, *71*, 2768–2785. https://doi.org/10.1111/evo.13379

Gaillard, J.-M., Lemaitre, J.-F., Berger, V., Bonenfant, C., & Devillard, S. (2016). Axes of variation in life histories. In R. M. Kliman (Ed.), *The encyclopedia of evolutionary biology* (pp. 312–323). Cambridge, MA: Elsevier.

Garnier, A., Gaillard, J. M., Gauthier, D., & Besnard, A. (2016). What shapes fitness costs of reproduction in long-lived iteroparous species? A case study on the Alpine ibex. *Ecology*, *97*, 205–214. https://doi.org/10.1890/15-0014.1

Gelman, A., & Carlin, J. (2014). Beyond power calculations: Assessing Type S (Sign) and Type M (Magnitude) errors. *Perspectives on Psychological Science*, *9*, 641–651. https://doi.org/10.1177/1745691614551642

Greer, K. A., Hughes, L. M., & Masternak, M. M. (2011). Connecting serum IGF-1, body size, and age in the domestic dog. *AGE (Dordr)*, *33*, 475–483. https://doi.org/10.1007/s11357-010-9182-4

Gurven, M., Stieglitz, J., Hooper, P. L., Gomes, C., & Kaplan, H. (2012). From the womb to the tomb: The role of transfers in shaping the evolved human life history. *Experimental Gerontology*, *47*, 807–813. https://doi.org/10.1016/j.exger.2012.05.006

Hamilton, W. D. (1966). The moulding of senescence by natural selection. *Journal of Theoretical Biology*, *12*, 12–45. https://doi.org/10.1016/0022-5193(66)90184-6

Hayward, A. D., Moorad, J., Regan, C. E., Berenos, C., Pilkington, J. G., Pemberton, J. M., & Nussey, D. H. (2015). Asynchrony of senescence among phenotypic traits in a wild mammal population. *Experimental Gerontology*, *71*, 56–68. https://doi.org/10.1016/j.exger.2015.08.003

Hekimi, S., Lapointe, J., & Wen, Y. (2011). Taking a "good" look at free radicals in the aging process. *Trends in Cell Biology*, *21*, 569–576. https://doi.org/10.1016/j.tcb.2011.06.008

Houle, D. (1991). Genetic covariance of fitness correlates: what genetic correlations are made of and why it matters. *Evolution*, *45*, 630–648.

Hughes, K. A., Alipaz, J. A., Drnevich, J. M., & Reynolds, R. M. (2002). A test of evolutionary theories of aging. *Proceedings of the National Academy of Sciences of the United States of America*, *99*, 14286–14291. https://doi.org/10.1073/pnas.222326199

Isaksson, C., Sheldon, B. C., & Uller, T. (2011). The challenges of integrating oxidative stress into life-history biology. *BioScience*, *61*, 194–202. https://doi.org/10.1525/bio.2011.61.3.5

Jessup, C. M., & Bohannan, B. J. (2008). The shape of an ecological tradeoff varies with environment. *Ecology Letters*, *11*, 947–959. https://doi.org/10.1111/j.1461-0248.2008.01205.x

Jones, O. R., Scheuerlein, A., Salguero-Gomez, R., Camarda, C. G., Schaible, R., Casper, B. B., … Vaupel, J. W. (2014). Diversity of ageing across the tree of life. *Nature*, *505*, 169–173. https://doi.org/10.1038/nature12789

Kaushik, S., & Cuervo, A. M. (2015). Proteostasis and aging. *Nature Medicine*, *21*, 1406–1415. https://doi.org/10.1038/nm.4001

Kengeri, S. S., Maras, A. H., Suckow, C. L., Chiang, E. C., & Waters, D. J. (2013). Exceptional longevity in female Rottweiler dogs is not encumbered by investment in reproduction. *AGE (Dordr)*, *35*, 2503–2513. https://doi.org/10.1007/s11357-013-9529-8

Ketterson, E. D., Nolan, V. Jr, Wolf, L., & Ziegenfus, C. (1992). Testosterone and avian life histories: Effects of experimentally elevated testosterone on behavior and correlates of fitness in the dark-eyed junco (*Junco hyemalis*). *American Naturalist*, 980–999. https://doi.org/10.1086/285451

Kirkwood, T. B. (1977). Evolution of ageing. *Nature*, *270*, 301–304. https://doi.org/10.1038/270301a0

Kirkwood, T. B. L. (2005). Understanding the odd science of aging. *Cell*, *120*, 437–447. https://doi.org/10.1016/j.cell.2005.01.027

Kirkwood, T. B., & Holliday, R. (1979). The evolution of ageing and longevity. *Proceedings of the Royal Society of London. Series B: Biological Sciences*, *205*, 531–546.

Kulminski, A., Ukraintseva, S. V., Akushevich, I., Arbeev, K. G., Land, K., & Yashin, A. I. (2007). Accelerated accumulation of health deficits as a

characteristic of aging. *Experimental Gerontology*, *42*, 963–970. https://doi.org/10.1016/j.exger.2007.05.009

Landes, J., Henry, P. Y., Hardy, I., Perret, M., & Pavard, S. (2019). Female reproduction bears no survival cost in captivity for gray mouse lemurs. *Ecology and Evolution*, *9*, 6189–6198. https://doi.org/10.1002/ece3.5124

Lee, R. D. (2003). Rethinking the evolutionary theory of aging: Transfers, not births, shape senescence in social species. *Proceedings of the National Academy of Sciences of the United States of America*, *100*, 9637–9642. https://doi.org/10.1073/pnas.1530303100

Lemaitre, J. F., Berger, V., Bonenfant, C., Douhard, M., Gamelon, M., Plard, F., & Gaillard, J. M. (2015). Early-late life trade-offs and the evolution of ageing in the wild. *Proceedings of the Royal Society B: Biological Sciences*, *282*, 20150209. https://doi.org/10.1098/rspb.2015.0209

Levins, R. (1968). *Evolution in changing environments: Some theoretical explorations*. Princeton, NJ: Princeton University Press.

Levitan, D. R. (2000). Sperm velocity and longevity trade off each other and influence fertilization in the sea urchin *Lytechinus variegatus*. *Proceedings of the Royal Society B: Biological Sciences*, *267*, 531–534.

Lind, M. I., Ravindran, S., Sekajova, Z., Carlsson, H., Hinas, A., & Maklakov, A. A. (2019). Experimentally reduced insulin/IGF-1 signaling in adulthood extends lifespan of parents and improves Darwinian fitness of their offspring. *Evolution Letters*, *3*, 207–216. https://doi.org/10.1002/evl3.108

Lopez-Otin, C., Blasco, M. A., Partridge, L., Serrano, M., & Kroemer, G. (2013). The hallmarks of aging. *Cell*, *153*, 1194–1217. https://doi.org/10.1016/j.cell.2013.05.039

Luckinbill, L. S., Arking, R., Clare, M. J., Cirocco, W. C., & Buck, S. A. (1984). Selection for delayed senescence in drosophila melanogaster. *Evolution*, *38*, 996–1003.

Maharjan, R., Nilsson, S., Sung, J., Haynes, K., Beardmore, R. E., Hurst, L. D., … Gudelj, I. (2013). The form of a trade-off determines the response to competition. *Ecology Letters*, *16*, 1267–1276. https://doi.org/10.1111/ele.12159

Maklakov, A. A., Rowe, L., & Friberg, U. (2015). Why organisms age: Evolution of senescence under positive pleiotropy? *BioEssays*, *37*, 802–807. https://doi.org/10.1002/bies.201500025

Massot, M., Clobert, J., Montes-Poloni, L., Haussy, C., Cubo, J., & Meylan, S. (2011). An Integrative study of ageing in a wild population of common lizards. *Functional Ecology*, *25*, 848–858. https://doi.org/10.1111/j.1365-2435.2011.01837.x

Maynard Smith, J. (1962). Review lectures on senescence - I. The causes of ageing. *Proceedings of the Royal Society of London. Series B. Biological Sciences*, *157*, 115–127.

McEwen, B. S. (1998). Stress, adaptation, and disease. Allostasis and allostatic load. *Annals of the New York Academy of Sciences*, *840*, 33–44. https://doi.org/10.1111/j.1749-6632.1998.tb09546.x

Messina, F. J., & Fry, J. D. (2003). Environment-dependent reversal of a life history trade-off in the seed beetle *Callosobruchus maculatus*. *Journal of Evolutionary Biology*, *16*, 501–509. https://doi.org/10.1046/j.1420-9101.2003.00535.x

Metcalfe, N. B., & Monaghan, P. (2013). Does reproduction cause oxidative stress? An open question. *Trends in Ecology and Evolution*, *28*, 347–350. https://doi.org/10.1016/j.tree.2013.01.015

Monaghan, P., & Haussmann, M. F. (2006). Do telomere dynamics link lifestyle and lifespan? *Trends in Ecology and Evolution*, *21*, 47–53. https://doi.org/10.1016/j.tree.2005.11.007

Monaghan, P., Metcalfe, N. B., & Torres, R. (2009). Oxidative stress as a mediator of life history trade-offs: Mechanisms, measurements and interpretation. *Ecology Letters*, *12*, 75–92. https://doi.org/10.1111/j.1461-0248.2008.01258.x

Oriá, R. B., Patrick, P. D., Blackman, J. A., Lima, A. A. M. & Guerrant, R. L. (2007). Role of apolipoprotein E4 in protecting children against early childhood diarrhea outcomes and implications for later development. *Medical Hypotheses*, *68*(5), 1099-1107.

Nijhout, H. F., Sadre-Marandi, F., Best, J., & Reed, M. C. (2017). Systems biology of phenotypic robustness and plasticity. *Integrative and Comparative Biology*, *57*, 171–184. https://doi.org/10.1093/icb/icx076

Noguera, J. C. (2017). Interacting effects of early dietary conditions and reproductive effort on the oxidative costs of reproduction. *PeerJ*, *5*, e3094. https://doi.org/10.7717/peerj.3094

Nussey, D. H., Coulson, T., Festa-Bianchet, M., & Gaillard, J.-M. (2008). Measuring senescence in wild animal populations: Towards a longitudinal approach. *Functional Ecology*, *22*, 393–406. https://doi.org/10.1111/j.1365-2435.2008.01408.x

Nussey, D. H., Pemberton, J. M., Pilkington, J. G., & Blount, J. D. (2009). Life history correlates of oxidative damage in a free-living mammal population. *Functional Ecology*, *23*, 809–817. https://doi.org/10.1111/j.1365-2435.2009.01555.x

Partridge, L., & Gems, D. (2002). Mechanisms of ageing: Public or private? *Nature Reviews Genetics*, *3*, 165–175.

Pavard, S., & Branger, F. (2012). Effect of maternal and grandmaternal care on population dynamics and human life-history evolution: A matrix projection model. *Theoretical Population Biology*, *82*, 364–376. https://doi.org/10.1016/j.tpb.2012.01.007

Pavard, S., & Metcalf, C. J. (2007). Negative selection on BRCA1 susceptibility alleles sheds light on the population genetics of late-onset diseases and aging theory. *PLoS ONE*, *2*, e1206. https://doi.org/10.1371/journal.pone.0001206

Port, M., & Cant, M. A. (2013). Longevity suppresses conflict in animal societies. *Biology Letters*, *9*, 20130680. https://doi.org/10.1098/rsbl.2013.0680

Raubenheimer, D., Simpson, S. J., Le Couteur, D. G., Solon-Biet, S. M., & Coogan, S. C. (2016). Nutritional ecology and the evolution of aging. *Experimental Gerontology*, *86*, 50–61. https://doi.org/10.1016/j.exger.2016.04.007

Ricklefs, R. E. (1998). Evolutionary theories of aging: Confirmation of a fundamental prediction, with implications for the genetic basis and evolution of life span. *American Naturalist*, *152*, 24–44. https://doi.org/10.1086/286147

Ricklefs, R. E., & Cadena, C. D. (2007). Lifespan is unrelated to investment in reproduction in populations of mammals and birds in captivity. *Ecology Letters*, *10*, 867–872. https://doi.org/10.1111/j.1461-0248.2007.01085.x

Rodrigues, M. A., & Flatt, T. (2016). Endocrine uncoupling of the trade-off between reproduction and somatic maintenance in eusocial insects. *Current Opinion in Insect Science*, *16*, 1–8. https://doi.org/10.1016/j.cois.2016.04.013

Roff, D. A., Mostowy, S., & Fairbairn, D. J. (2002). The evolution of trade-offs: Testing predictions on response to selection and environmental variation. *Evolution*, *56*, 84–95. https://doi.org/10.1111/j.0014-3820.2002.tb00851.x

Rogina, B., Reenan, R. A., Nilsen, S. P., & Helfand, S. L. (2000). Extended life-span conferred by cotransporter gene mutations in Drosophila. *Science*, *290*, 2137–2140. https://doi.org/10.1126/science.290.5499.2137

Rose, M. R. (1984). Laboratory evolution of postponed senescence in drosophila melanogaster. *Evolution*, *38*, 1004–1010.

Ross, C., Rychtar, J., & Rueppell, O. (2015). A structured population model suggests that long life and post-reproductive lifespan promote the evolution of cooperation. *Journal of Theoretical Biology*, *369*, 85–94. https://doi.org/10.1016/j.jtbi.2015.01.020

Rueppell, O. (2009). Aging of social insects. In J. Gadau, & J. Fewell (Eds.), *Organization of insect societies: From genome to sociocomplexity* (pp. 51–73). Cambridge, UK: Harvard University Press.

Salguero-Gomez, R., Jones, O. R., Jongejans, E., Blomberg, S. P., Hodgson, D. J., Mbeau-Ache, C., … Buckley, Y. M. (2016). Fast-slow continuum and reproductive strategies structure plant life-history variation

worldwide. *Proceedings of the National Academy of Sciences of the United States of America*, *113*, 230–235. https://doi.org/10.1073/pnas.1506215112

Schosserer, M., Grillari, J., & Breitenbach, M. (2017). The dual role of cellular senescence in developing tumors and their response to cancer therapy. *Front Oncol*, *7*, 278. https://doi.org/10.3389/fonc.2017.00278

Schrempf, A., Heinze, J., & Cremer, S. (2005). Sexual cooperation: Mating increases longevity in ant queens. *Current Biology*, *15*, 267–270.

Selman, C., Blount, J. D., Nussey, D. H., & Speakman, J. R. (2012). Oxidative damage, ageing, and life-history evolution: Where now? *Trends in Ecology and Evolution*, *27*, 570–577. https://doi.org/10.1016/j.tree.2012.06.006

Shay, J. W., & Wright, W. E. (2011). Role of telomeres and telomerase in cancer. *Seminars in Cancer Biology*, *21*, 349–353. https://doi.org/10.1016/j.semcancer.2011.10.001

Shlush, L. I. (2018). Age-related clonal hematopoiesis. *Blood*, *131*, 496–504. https://doi.org/10.1182/blood-2017-07-746453

Stearns, S. C. (1989). Trade-offs in life-history evolution. *Functional Ecology*, *3*, 259–268. https://doi.org/10.2307/2389364

Swanson, E. M., & Dantzer, B. (2014). Insulin-like growth factor-1 is associated with life-history variation across Mammalia. *Proceedings of the Royal Society B: Biological Sciences*, *281*, 20132458. https://doi.org/10.1098/rspb.2013.2458

Tarin, J. J., Gomez-Piquer, V., Garcia-Palomares, S., Garcia-Perez, M. A., & Cano, A. (2014). Absence of long-term effects of reproduction on longevity in the mouse model. *Reproductive Biology and Endocrinology*, *12*, 84. https://doi.org/10.1186/1477-7827-12-84

Tatar, M., Bartke, A., & Antebi, A. (2003). The endocrine regulation of aging by insulin-like signals. *Science*, *299*, 1346–1351. https://doi.org/10.1126/science.1081447

Tatar, M., Kopelman, A., Epstein, D., Tu, M. P., Yin, C. M., & Garofalo, R. S. (2001). A mutant Drosophila insulin receptor homolog that extends life-span and impairs neuroendocrine function. *Science*, *292*, 107–110. https://doi.org/10.1126/science.1057987

Tavecchia, G., Coulson, T., Morgan, B. J. T., Pemberton, J. M., Pilkington, J. C., Gulland, F. M. D., & Clutton-Brock, T. H. (2005). Predictors of reproductive cost in female Soay sheep. *Journal of Animal Ecology*, *74*, 201–213. https://doi.org/10.1111/j.1365-2656.2005.00916.x

Tomiyama, A. J., O'Donovan, A., Lin, J., Puterman, E., Lazaro, A., Chan, J., … Epel, E. (2012). Does cellular aging relate to patterns of allostasis? An examination of basal and stress reactive HPA axis activity and telomere length. *Physiology and Behavior*, *106*, 40–45. https://doi.org/10.1016/j.physbeh.2011.11.016

van Noordwijk, A. J., & de Jong, G. (1986). Acquisition and allocation of resources: Their influence on variation in life history tactics. *The American Naturalist*, *128*, 137–142. https://doi.org/10.1086/284547

Vaupel, J. W., Baudisch, A., Dolling, M., Roach, D. A., & Gampe, J. (2004). The case for negative senescence. *Theoretical Population Biology*, *65*, 339–351. https://doi.org/10.1016/j.tpb.2003.12.003

Vøllestad, L. A., & Quinn, T. P. (2003). Trade-off between growth rate and aggression in juvenile coho salmon, *Oncorhynchus kisutch*. *Animal Behaviour*, *66*, 561–568. https://doi.org/10.1006/anbe.2003.2237

Walker, R. S., Gurven, M., Burger, O., & Hamilton, M. J. (2008). The trade-off between number and size of offspring in humans and other primates. *Proceedings of the Royal Society B: Biological Sciences*, *275*, 827–833. https://doi.org/10.1098/rspb.2007.1511

Wang, M. C., Bohmann, D., & Jasper, H. (2003). JNK signaling confers tolerance to oxidative stress and extends lifespan in Drosophila. *Developmental Cell*, *5*, 811–816. https://doi.org/10.1016/S1534-5807(03)00323-X

Wensink, M. J., Caswell, H., & Baudisch, A. (2017). The rarity of survival to old age does not drive the evolution of senescence. *Evolutionary Biology*, *44*, 5–10. https://doi.org/10.1007/s11692-016-9385-4

Wensink, M. J., Wrycza, T. F., & Baudisch, A. (2014). Interaction mortality: Senescence may have evolved because it increases lifespan. *PLoS ONE*, *9*, e109638. https://doi.org/10.1371/journal.pone.0109638

Wiersma, P., Selman, C., Speakman, J. R., & Verhulst, S. (2004) Birds sacrifice oxidative protection for reproduction. *Proceedings of the Royal Society of London. Series B: Biological Sciences*, *271*, S360–S363, https://doi.org/10.1098/rsbl.2004.0171

Williams, G. C. (1957). Pleiotropy, natural-selection, and the evolution of senescence. *Evolution*, *11*, 398–411. https://doi.org/10.1111/j.1558-5646.1957.tb02911.x

Yamamoto, R., Bai, H., Dolezal, A. G., Amdam, G., & Tatar, M. (2013). Juvenile hormone regulation of Drosophila aging. *BMC Biology*, *11*, 85. https://doi.org/10.1186/1741-7007-11-85

Yashin, A. I., Arbeev, K. G., Kulminski, A., Akushevich, I., Akushevich, L., & Ukraintseva, S. V. (2007). Health decline, aging and mortality: How are they related? *Biogerontology*, *8*, 291–302. https://doi.org/10.1007/s10522-006-9073-3

Young, A. J. (2018). The role of telomeres in the mechanisms and evolution of life-history trade-offs and ageing. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *373*, 20160452. https://doi.org/10.1098/rstb.2016.0452

Zajitschek, F., Georgolopoulos, G., Vourlou, A., Ericsson, M., Zajitschek, S. R. K., Friberg, U., & Maklakov, A. A. (2018). Evolution under dietary restriction decouples survival from fecundity in drosophila melanogaster females. *Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*. https://doi.org/10.1093/gerona/gly070

Zajitschek, F., Zajitschek, S. R., Canton, C., Georgolopoulos, G., Friberg, U., & Maklakov, A. A. (2016). Evolution under dietary restriction increases male reproductive performance without survival cost. *Proceedings of the Royal Society B: Biological Sciences*, *283*, 20152726. https://doi.org/10.1098/rspb.2015.2726

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

How to cite this article: Cohen AA, Coste CFD, Li X-Y, Bourg S, Pavard S. Are trade-offs really the key drivers of ageing and life span? *Funct Ecol*. 2020;34:153–166. https://doi.org/10.1111/1365-2435.13444