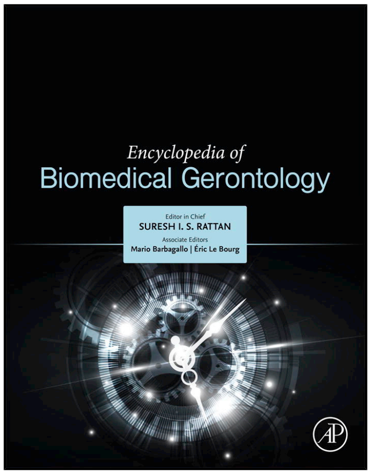

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Trade-Offs

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A General Introduction to Trade-Offs in Evolutionary Biology

The process of natural selection leads to favor traits that increase Darwinian fitness (i.e., the propensity of an individual to contribute to the gene pool of next generations). Therefore, natural selection should logically promote the evolution of organisms that reproduce asexually at increasing frequency and number during an infinite lifespan. Obviously, these organisms, often called "Darwinian demons" (Law, 1979) are not observed on earth. The existence of constraints explains this discrepancy between life histories currently observed in extant organisms and the expected outcome of natural selection. Two broad types of constraints have been identified: energy limitation and time constraints.

The most intensively studied type of constraint is energy limitation caused by resource restriction. In the living world, resources available to a given organism are limited, which influences the amount of energy this organism can allocate to competing biological functions such as growth, reproduction and survival-insurance mechanisms. Based on that empirical consideration, Cody launched the *Principle of Allocation* (Cody, 1966) stating that a given organism cannot maximize allocation to all biological functions simultaneously, and that increasing allocation to one function should lead to decrease allocation to another function. For instance, a substantial allocation of resources to a given reproductive event would lead to jeopardize survival to the next reproductive event. The concept of trade-off is thus closely related to that of constraints in life sciences, but also in other disciplines (e.g. Campbell and Kelly, 1994 in economics).

Under the assumption of inevitable trade-offs, one can reframe the process of natural selection as the selection for allocation strategies that maximize fitness (Stearns, 1992). Moreover, it could be reasonably expected that negative relationships among fitness components associated with different biological functions consistently show up. Decades of empirical studies have demonstrated that the reality is much more complex. Indeed, allocation strategies described in the literature strongly depend on the level of biological organization (e.g., species, population or individual).

When looking at relationships between allocation to competing biological functions across species either within or among taxa, negative relationships always occur. In most taxa studied so far, including both plants and animals, a high reproductive output generated by a combination between early reproduction and high fecundity is consistently associated with a short lifespan and vice versa (Gaillard et al., 2016). On the contrary, when looking at relationships between reproduction and lifespan among individuals within a given population or among populations within a given species, the outcome is highly variable and can include negative and null associations, or even positive associations between the different biological traits of interest (**Table 1**). In 1986, van Noordwijk and de Jong proposed a simple model (the so-called Y model) to account for this observed diversity of outcomes (Van Noordwijk and de Jong, 1986), which is based on the observed variation in allocation relative to the observed variation in resource acquisition. Thus, when resource allocation among individuals or populations varies at a larger extent than resource acquisition, trade-offs should occur (**Fig. 1**A). On the other hand, a higher variation in resource acquisition than in resource allocation prevents the detection of trade-offs (**Fig. 1**B). In that later case, individuals or populations facing with resource restriction will have both lower reproductive output and shorter lifespan than those facing with abundant resources. Note that when variation in resource allocation and variation in acquisition are equal, no relationship occurs between reproduction and survival.

At first sight, the Y model suggests that resource limitation does not play a key role in shaping trade-offs. Indeed, according to this model, we expect strong trade-offs in populations in which all individuals face with either consistently abundant or consistently scarce resources and in taxa in which species-specific fitness components are measured either under consistently abundant or consistently scarce resources. What matters is the variation in acquisition relative to the variation in allocation. This uncoupling between intensity of resource limitation and intensity of trade-off demonstrates that other constraints shape the existence of trade-offs.

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Table 1 Summary of the 14 studies published since 2015 testing for the presence of an early- vs. late-life trade-off.

Species	*Early trait*	*Late trait*	*Sex*	*Relationship*	*Early-late life trade-off detected*	*References*
Birds						
Common tern (*Sterna hirundo*)	Age at first reproduction	Survival	M/F	0	No	(a)
	Age at first reproduction	Lifetime reproductive success	M/F	−	No	
Barn swallows (*Hirundo rustica*)	Reproductive effort (1–2 years)	Age at last reproduction	M/F	0	No	(b)
Black grouse (*Lyrurus tetrix*)	Mating success	Lifespan	M	0	No	(c)
	Age at first reproduction	Lifespan	M	+	Yes	
Song sparrows (*Melospiza melodia*)	Reproductive effort (1–2 years)	Lifespan	F	−	Yes	(d)
Egyptian vulture (*Neophron percnopterus*)	Age at first reproduction	Age at last reproduction	M/F	+	No	(e)
Southern fulmar (*Fulmarus glacialoides*)	Age at first reproduction	Reproductive lifespan	M/F	+	Yes	(f)
	Age at first reproduction	Survival	M/F	+	Yes	
Common blackbirds (*Turdus merula*)	Reproductive effort (2–3 years)	Reproductive success (>4 years)	M/F	0/−	Yes	(g)
	Reproductive effort (2–3 years)	Lifespan	M/F	0	No	
Mammals						
Svalbard reindeer (*Rangifer tarandus platyrhynchus*)	Reproductive success (2–6 years)	Reproductive success (≥7 years)	F	+	No	(h)
African elephant (*Loxodonta africana*)	Age at first reproduction	Reproductive rate	F	−	No	(i)
	Age at first reproduction	Lifespan	F	0	No	
Mountain goats (*Oreamnos americanus*)	Age at first reproduction	Reproductive success (≥7 years)	F	0 (−)	No	(j)
	Reproductive success (3–6 years)	Reproductive success (≥7 years)	F	0 (+)	No	
	Age at first reproduction	Lifespan	F	0	No	
	Reproductive success (3–6 years)	Lifespan	F	0	No	
Red squirrels (*Tamiasciurus hudsonicus*)	Age at first reproduction	Lifetime reproductive success	F	−	No	(k)
	Maximum annual number of offspring produced	Survival	F	−	Yes	
	Maximum annual number of offspring produced	Lifetime reproductive success	F	+	No	
Moose (*Alces alces*)	Age at first reproduction	Lifetime reproductive success	F	−	No	(l)
Soay sheep (*Ovis aries*)	Reproductive effort (number of sons, 1–6 years)	Lifespan	F	0 (+)	No	(m)
Bighorn sheep (*Ovis canadensis*)	Reproductive effort (number of sons, 2–7 years)	Lifespan	F	0 (+)	No	
Red deer (*Cervus elaphus*)	Reproductive effort (number of sons, 3–9 years)	Lifespan	F	0 (+)	No	
Mountain goat (*Oreamnos americanus*)	Reproductive effort (number of sons, 3–9 years)	Lifespan	F	0 (−)	No	
Insects						
Field cricket (*Gryllus campestris*)	Reproductive effort (<15 days)	Survival	M	+	No	(n)

The species, the early and late traits analyzed, the sex (F: female, M: male), the overall conclusion about the support for each study (yes/no) and the references are provided. For the column "relationship," the sign ("−," "+" or "0") represents the direction of the relationship. However, when the sign of the non-significant relationship was provided in the study, this information was added in brackets, next to the "0.". References: (a) Zhang et al., 2015, *J. Anim. Ecol.*, 84 (1), 199–207; (b) Balbontín & Møller, 2015, *Ecology*, 96 (4), 948–959; (c) Kervinen et al., 2016, *J. Anim. Ecol.*, 85 (3), 715–725; (d) Tarwater & Arcese, 2017, *Ecology*, 98(9), 2248–2254; (e) Sanz-Aguilar et al., 2017, *Sci. Rep.*, 7, 40,204; (f) Jenouvrier et al., 2018, *J. Anim. Ecol.*, 87 (1), 212–222; (g) Jankowiak et al., 2018, *Ibis*, 160 (1), 130–144; (h) Douhard et al., 2016 *Proc. R. Soc. B Biol. Sci.*, 283(1841), 20,161,760; (i) Lee et al., 2016, *Behav. Ecol. Sociobiol.*, 70 (3), 337–345; (j) Panagakis et al., 2017, *Am. Nat.*, 189 (6), 667–683; (k) Hämäläinen et al., 2017, *Sci. Rep.*, 7 (1), 9335; (l) Markussen et al., 2018, *Oecologia*, 186 (2), 447–458; (m) Douhard et al., 2019, *Proc. R. Soc. B Biol.* 286(1896), 20181968; (n) Rodríguez-Muñoz et al., 2019, *Evolution*, 73 (2), 317–328.

Among them, time constraints have a key role. At high levels of biological organization, the consistent occurrence of trade-offs among fitness components is mostly explained by time constraints. Within most taxonomic groups studied so far, species rank over a slow-fast continuum opposing short-lived species with early reproduction and high reproductive output to long-lived species with late reproduction and low reproductive output (Gaillard et al., 2016), leading a trade-off between reproductive effort

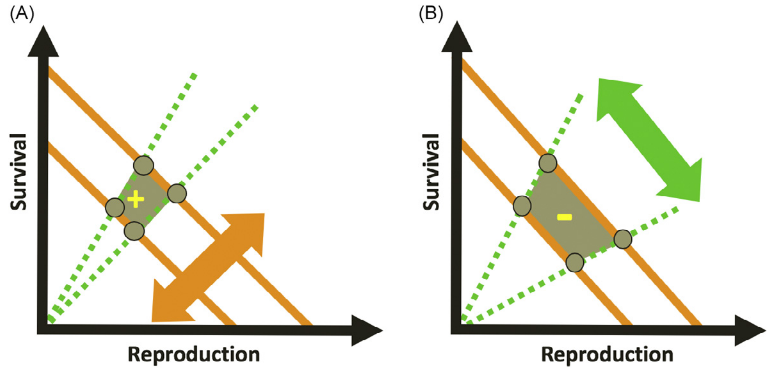


Fig. 1 Illustration of the Y-model proposed by Van Noordwijk and de Jong (1986). Depending on the relative variation in resource acquisition and resource allocation, two broad types of situations can be recognized: (A) the variation in resource allocation among individuals measured as the among-individual variance in intercepts of the relationships linking survival and reproduction within individuals (full *orange line*, two individuals displayed) is larger than the variation in resource allocation among individuals measured as the variance in among-individual slopes of the relationships linking survival and reproduction within individuals (dotted *green line*, two individuals displayed). In that case, the relationship between survival and reproduction across individuals is positive, which leads the existing trade-off at the individual level to be masked. (B) When the variation in resource allocation is larger than the variation in resource allocation among individuals, the trade-off existing at the individual level shows up at the population level.

and lifespan to occur. Pianka was the first to state explicitly that this trade-off is strongly associated with species size, with short-lived species being typically smaller than long-lived species (Pianka, 1970). As size provides the tempo of any organism's life cycle (Calder, 1984), organisms from large species live on the slow lane and spread their biological events over a long lifespan, whereas organisms from small species live on the fast lane and concentrate their biological events over a short lifespan. For instance, the number of heart beats during the entire life is similar between a mouse and an elephant, but the beat frequency is much higher in the mouse. Likewise, growing a large body takes time. As a result, gestation time of elephants is one order of magnitude longer than gestation time of mice. At the interspecific level, it is thus clear that time constraints shape the observed trade-offs between traits positively related to average individual fitness. At the intra-specific level, the pattern is far less clear. If resource limitation is linked to increased variance in resource acquisition (see Lomnicki, 1978), the Y model predicts that trade-offs should be more frequently detected when resource acquisition is low rather than high. Despite its high heuristic value, the Y model is based on strong assumptions. For instance, the key assumption that energy allocation to a trait should be independent of resource acquisition is a key assumption that is unlikely to hold in nature. When relaxed, a diversity of selection pressures occurs and both the intensity and sign of the relationship linking allocation to two traits might change substantially depending of the species time scale (Descamps et al., 2016).

The following contribution will be solely focused on intra-specific trade-offs. Among individuals, multiple trade-offs have been identified (Stearns, 1992). It is beyond the scope of this article to discuss all types of trade-offs occurring within organisms. Instead, we will focus on a trade-off constituting a cornerstone in aging research namely the trade-off between allocation to growth/reproduction early in life versus lifespan and health in late life. We will first describe the theoretical foundations of this trade-off. Then, using a compilation of studies performed on wild populations of animals and humans, we will evaluate the current level of support for this specific trade-off. Finally, we will review the problems of detecting trade-offs in both humans and vertebrate populations in the wild. Using simple life history simulations (see **Box 1**), we will illustrate the pitfalls of simply plotting measures of energy allocation to two competing traits positively correlated to individual fitness.

The Central Place of Trade-Offs in Aging Research

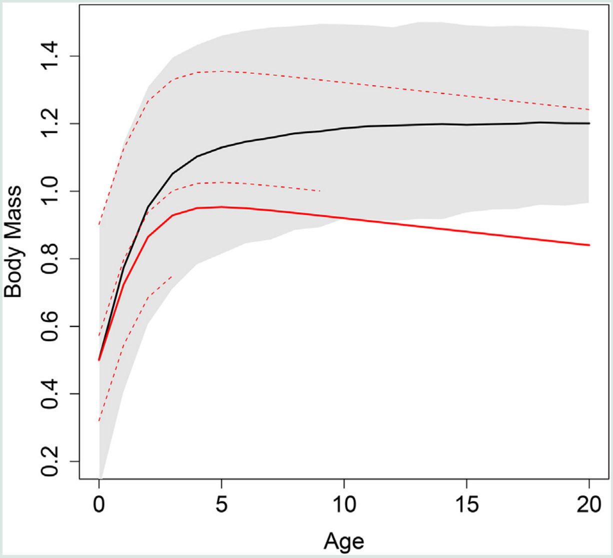
The importance of the trade-off concept is particularly pronounced in aging research, as the resource-based allocation trade-off between reproduction and survival insurance mechanisms constitutes the core of our current understanding of the evolution of aging (see Kirkwood (2017) and below). So far, empirical studies investigating how trade-offs shape "individual performance" (i.e., health, physiological traits, age-specific reproductive and survival rates) at old ages have been mainly performed in two main theoretical frameworks showing relatively porous frontiers: the *antagonistic pleiotropy* (Williams, 1957) and the *disposable soma* (Kirkwood, 1977) theories of aging.

In 1957, the evolutionary biologist George C. Williams proposed that an allele increasing fitness during early life will be selected even if it reduces fitness in late life (Williams, 1957). In other words, if an allele increases the efficiency of an individual to transmit early in life its genes to the next generation it will be selected and thus increase in frequency in the population (but if the population is declining) even if this same allele reduces reproductive performance, health and survival prospects much later in life (Williams, 1957; Gaillard and Lemaître, 2017). Basically, the range of action of such antagonistic pleiotropic (AP) alleles could thus be particularly broad. In males, they could potentially be involved in the growth of secondary sexual traits or in the spermatogenesis process

Box 1 Detecting trade-offs in the wild: the ruses of individual heterogeneity.

Individual heterogeneity often leads to hide trade-offs, as first nicely demonstrated by Vaupel and Yashin (1985). We illustrate this point with the specific case of detecting senescence in body mass (i.e., the age-specific decrease in body mass with increasing age). We simulated a population in which individuals share all the same senescence pattern in body mass, die at very different ages (i.e., a large variation across individuals in the age range at which body mass was measured), and were subjected to a high selective disappearance (i.e., heavy individuals at birth lived much longer than light ones). When looking at individual trajectories of body mass (red curves on the figure), they are parallel and display the expected senescence in mass. When simply looking at average age-specific body mass, a totally different outcome is found. Senescence in body mass does not occur anymore and, on the contrary, body mass consistently increases with age, although at very slow rate at old ages (black curve on the figure). This is because only the heaviest individuals are alive at old ages and can thus be measured. Light individuals do not live long and do not provide any body mass measurements at old ages.

When marked, individual heterogeneity at the population level is thus likely to hide any evidence of senescence that exists at the individual level. This problem strongly limits our current assessment of the existence of senescence across traits in the wild. In particular, species-specific body mass trajectories are generally built from transversal data (i.e., individuals are only measured once) from which age is estimated (e.g., from tooth wear or tooth sectioning in mammals). From these data, it is not possible to account for individual heterogeneity, leading our current assessment on the commonness of this biological process to be markedly underestimated.



In *black solid line*, the average value of body mass in function of age in the simulated population associated with the 95% quantile of body mass distribution (in *gray*). In *red solid line*, the average value of body mass in function of age when accounting for the confounding effect of selective disappearance. Some individual trajectories are represented in red dashed lines. We simulated body mass (BM) trajectories over age (*t*) using the following equation:

$$BM(t) = \frac{1}{(1 + e^{-t})} - 0.008t$$

The first term of the equation describes the growth during the juvenile stage and the second term describes the senescence of body mass throughout the adult stage. To mimic the heterogeneity in quality among individuals in the simulated population, we associate to each individual a value of condition (i.e., residuals of the relationship between body mass and age), which was sampled on a normal distribution of mean 0 and standard deviation 0.2. This condition value is kept constant through the lifetime of the individual. We then considered that individual survival is highly impacted by condition values using the following logistic equation:

$$s(condition) = \frac{1}{(1 - e^{-0.7 - 3.85 \times condition})}$$

Individuals with higher condition are thus much less likely to die than those with lower condition. For each individual at each age, if the individual is still considered alive, total individual body mass is computed by adding the value of the body mass with age to the condition value.

while in females, they could influence various aspects of the female reproductive cycle. The deleterious late-life effects of such alleles can be equally broad and affect multiple physiological pathways associated with fitness and thus be involved in many age-specific diseases. This theoretical framework proposed by Williams has stimulated a consequent body of research in biogerontology and numerous AP alleles have been identified in laboratory organisms (see Austad and Hoffman (2018) for a recent review). For instance, in *Caenorhabditis elegans*, daf-2 mutants show a reproductive rate reduced of 20% but live twice as long compared to non-mutants (Jenkins et al., 2004). So far, most AP alleles have been logically identified in laboratory organisms and the rare supports from the antagonistic pleiotropy theory of aging in populations of wild animals rely on the use of quantitative genetic approaches (see Charmantier et al. (2014) for a review).

The second theoretical framework giving a central place to the trade-off between reproduction and survival prospects is the disposable soma theory of aging (Kirkwood, 1977). This theory takes its origin in the inaccuracy of the macromolecular synthesis and on the assumption that physiological mechanisms that have evolved to maintain the integrity of the soma (e.g., protein clearance mechanisms) are energetically costly (Kirkwood, 2017). Individuals thus face a trade-off between the allocation to reproduction and somatic maintenance. An increase in the allocation of resources to reproduction (e.g., heavier offspring) impairs the efficiency of the somatic maintenance mechanisms, which lead to the progressive accumulation of damages, and on the long run, impair health and survival prospects (i.e., a trade-off also coined "early-late life trade-off," see Lemaître et al. (2015)). While the principle of allocation was not explicitly mentioned in the first work introducing the disposable soma theory (Kirkwood, 1977; Kirkwood and Holliday, 1979), the tight conceptual links between these two frameworks have become evident in the past recent years (Kirkwood, 2017; Lemaître et al., 2015) and the trade-off between allocation to reproduction during early life and lifespan is currently one of the most studied.

Similar to the observations that have been made in laboratory studies testing the antagonistic pleiotropy of aging (Austad and Hoffman, 2018), the negative fitness consequences of an early allocation to reproduction are not limited to a shortened lifespan per se but can affect a wide range of traits underlying reproductive performance (Lemaître et al., 2015). While negative relationships between reproductive effort in early life and fitness-related traits in late life have been detected in the lab (see Hunt et al. (2004) for a case-study in field crickets, *Teleogryllus commodus*), field studies testing predictions of the disposable soma theory have become increasingly popular during the last three decades (Lemaître et al., 2015). This can be explained by (i) the accumulation of evidence that aging is the rule rather than the exception among animal populations in the wild, which has thus broadened the scope of model organisms to study both the causes and consequences of the aging process (Nussey et al., 2013) and (ii) the fact that, contrary to the antagonistic pleiotropy theory of aging, genetic data are not mandatory to valid or invalid the presence of trade-off between allocation to reproduction in early life and fitness-related traits in late-life. By compiling studies performed in vertebrates in the wild, Lemaître and colleagues found in 2015 a general support for a trade-off between allocation to reproduction during early life and a various set of fitness-related traits in late life (e.g., lifespan, rate of reproductive senescence) (Lemaître et al., 2015). In the next section, we take advantage of the flourishing literature in this research area to provide an update of Lemaître et al.'s review.

Revisited Evidence for Early-Late Life Trade-Off in the Wild

In their review published in 2015, Lemaître and colleagues identified 26 studies (published between 1990 and 2014) testing for the presence of early-late life trade-offs in wild vertebrate populations. Using the exact same protocol, we retrieved 14 new studies (see **Table 1** for a full list), which emphasize the importance of trade-offs in the current aging research. Among these studies, five supported the existence of a trade-off between at least one reproductive trait measured during early life and one trait measuring reproductive or survival performance much later in life. For instance, in song sparrows (*Melospiza melodia*), females allocating the most to reproduction (i.e., highest product between the total number of days when females cared for offspring and the number of offspring within the clutch) had a reduced lifespan (Tarwater and Arcese, 2017). Recently accumulated knowledge thus reveals that the picture might be more complex than previously thought, maybe because of less publication bias nowadays than years ago when fewer studies addressed that topic.

Similar to the first synthesis (Lemaître et al., 2015), results reported within a same study often revealed contrasting results with respect to potential trade-offs, as in common blackbirds (*Turdus merula*) where females allocating the most to reproduction during the 2nd and 3rd year of life had a reduced reproductive success from the 4th year of life onwards, but not a reduced lifespan (Jankowiak et al., 2018). This is in accordance with the idea that patterns of aging are asynchronous among traits within individuals, and that a high allocation in reproduction in early life to one trait may have negative influence on only some but not all traits at old ages. In the context of inevitable trade-offs among competing physiological functions, this suggests that natural selection should limit the accumulation of somatic damages in tissues or organs that are the most tightly linked to fitness (see Gaillard and Lemaître (2017) for a discussion). Such hypothesis could explain why, for a given population, the propensity to detect a trade-off differs according to what traits are studied during both early and late life while at the same time shed a new light of the evolutionary origins of the asynchrony in senescence patterns among phenotypic traits (Gaillard and Lemaître, 2017).

Half of recent studies (7 out of 14) have been published on birds while ca. 43% (6 out of 14) have been performed on mammals, which confirms that our current knowledge on the role of trade-offs in shaping aging patterns principally relies on these two vertebrate classes. However, while we were not aware of studies testing for early-late life trade-offs in wild insects when performing the first synthesis (Lemaître et al., 2015), such work has been recently performed in field crickets (*Gryllus campestris*) and failed to detect any early-late life trade-offs (Rodríguez-Muñoz et al., 2019). More studies in a larger range of taxa are now needed to evaluate whether invertebrates escape early vs. late-life trade-offs.

The first synthesis performed by Lemaître and colleagues highlighted a clear lack of studies on males (Lemaître et al., 2015). Interestingly, our update reveals that lots of efforts have been made to fill this gap. About 50% of the new compiled studies investigated the existence of early-late life trade-offs in both sexes. These studies, mostly performed on birds, reveal that the presence of an early vs. late-life trade-off is equally supported between males and females (**Table 1**). Elevated reproductive expenditure in males during early life (e.g., through an early entrance in reproduction) is associated with elevated fitness costs later in life (see **Table 1**) and studies investigating how much reproductive expenditure differ between females and males might shed new light on the evolution of sex differences in mortality patterns across the tree of life (Marais et al., 2018). It would now be particularly important to

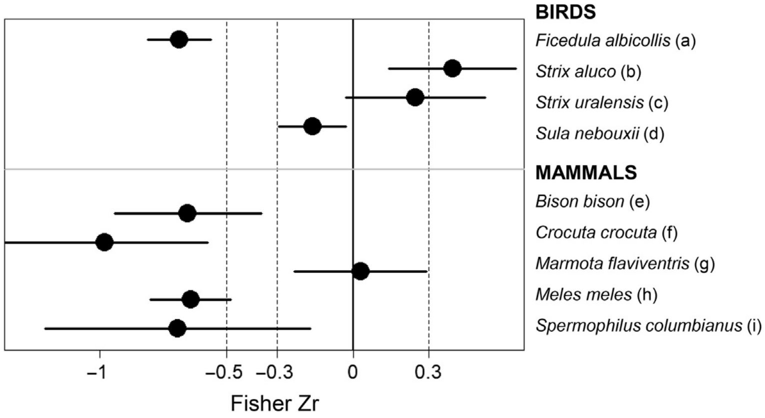


Fig. 2 The different effect size for the relationship linking age at first reproduction and lifetime reproductive success in females. All effect sizes are associated with their 95% confidence interval. (a) Gustafsson & Pärt, 1990, *Nature*, 347, 279; (b) Millon et al., 2010, *J. Anim. Ecol.*, 79, 426–435; (c) Brommer et al., 1998, *J. Anim. Ecol.*, 67, 359–369; (d) Kim et al., 2011, *Oecologia*, 166, 615–626; (e) Green & Rothstein, 1991, *Oecologia*, 86, 521–527; (f) Lewin et al., 2017, *Funct. Ecol.*, 31, 894–902; (g) Oli & Armitage, 2003, *Oecologia*, 136, 543–550; (h) Dugdale et al., 2010, *J. Evol. Biol.*, 23, 282–292; (i) Neuhaus, 2000, *Behav. Ecol. Sociobiol.*, 48, 75–83.

consider offspring sex when testing the relationship between early-life reproduction and fitness-related traits in late life as the energy intake during gestation is often higher when females are expecting a son rather than a daughter (e.g., 10% higher in humans (Tamimi et al., 2003)). A recent analysis of four free-ranging populations of large herbivores has revealed that females producing a high number of sons early in life do not suffer from an impaired survival (Douhard et al., 2019), but this trade-pff may manifest itself in terms of senescence. Finally, the lack of studies focusing on the long-term costs of growth, which was already highlighted in 2015, remains particularly pronounced. As the growth process is known to be particularly costly in terms of energetic expenditure (Metcalfe and Monaghan, 2003), such studies are now badly required.

As evidenced in both **Table 1** and Lemaître et al. (2015), studies that have tested for early-late life trade-offs have used a wide array of traits. Among traits used to depict reproductive allocation to reproduction during early life, the age at first reproduction is probably the most common (with the assumption that reproducing early is particularly resource demanding). We detected in the literature 25 studies that tested for an association between age at first reproduction and components of lifetime reproductive success. For nine vertebrate populations in the wild, we computed standardized effect size. For this, each correlation coefficient was converted into a Fisher Zr coefficient and the 95% confidence interval associated with each measurement was also computed based on the sample size (Lipsey and Wilson, 2001). All effect sizes are presented in **Fig. 2**. We found a substantial variation between the different effect sizes ranging from −0.754 for the spotted hyena (*Crocuta crocuta*) to 0.374 for tawny owl (*Strix aluco*). Five out of 9 effect sizes were lower than −0.5 indicating a strong negative correlation, which means that individuals with low age at first reproduction (i.e., high performance early in life) have higher lifetime reproductive success (i.e., high performance later in life). This result does not support the existence of a trade-off, at least at first glance. Indeed, we reported only the raw correlation coefficient between only two different traits and several confounding factors can potentially mask the presence of the trade-off. First, we chose for the sake of clarity to restrict our analysis to the most studied early- and late-life traits (i.e., age at first reproduction and lifetime reproductive success, respectively) but performance both at early and late ages cannot be simply described by only one trait and is rather the combination of multiple traits. This is thus not surprising that studies investigating early-late life trade-offs reported different relationships, leading sometimes to highly variable results (**Table 1** and Lemaître et al. (2015). Second, everything else being equal, an early age at first reproduction leads to an increased lifetime reproductive success. This makes the detection a trade-off more difficult. Even this trade-off occurs in some populations listed in **Fig. 2**, it might not always counter-balance the positive influence of an early reproduction on individual fitness. Third, we did not correct for the confounding effect of individual heterogeneity (van de Pol and Verhulst, 2006) with for instance high-quality individuals being consistently better in both early and late performance than other individuals (see also **Box 1**). The problem of individual variation in resource acquisition affects trade-off studies in both wild animals and humans.

The Reproduction-Longevity Trade-Off in Humans

In humans, physiological and fitness costs of reproduction are widely assumed to be higher in women than men because of the high energy demands of pregnancy and lactation (Penn and Smith, 2007). If women "trade" a long lifespan for enhanced reproductive success, this cost of reproduction should be strongest in historical populations where both fertility and mortality are high (Doblhammer and Oeppen, 2003). Westendorp and Kirkwood provided the first support to this hypothesis by highlighting that aristocratic British women born before 1876, who gave birth at young ages and to a high number of children, died early (Westendorp and Kirkwood, 1998). Although controversial (see Le Bourg (2007) for an overview of the debate), this pioneer article had generated many subsequent studies. Some studies have found the predicted negative relationship between the number of children born and maternal longevity (e.g., Penn and Smith (2007)), while many others have reported a positive correlation or no association (e.g., Helle et al. (2002) and Sear (2007)). Overall, there appears to be a lack of support for the trade-off between parity and longevity in historical populations of humans (Le Bourg, 2007), although a meta-analysis would be useful to produce a more clear-cut conclusion.

There are several methodological issues that may explain some of the discrepancies between predictions and observations, including criteria used to build the dataset. Analyses of the potential trade-off between reproduction and longevity were often restricted to women who survived beyond the expected age of menopause (45–55 years) in studies using historical data. However, recent theoretical work suggests that excluding women dying during reproductive ages from the analysis underestimates the potential trade-off between reproduction and longevity (Helle, 2017). Although accounting for selection during the reproductive lifespan did not alter the results in several historical populations (Helle, 2019), future studies should ensure that the absence of trade-off is not due to a biased data selection.

Costs of reproduction can vary with the characteristics of both parents and children. For example, in the historical Swedish and German populations, a negative relationship between parity and post-menopausal longevity was restricted only to poor, landless women (e.g., Lycett et al. (2000)). Among other women, with higher socio-economic status (e.g., families of noble tenants, wealthy farmers), the relationship between the number of children and longevity was either positive or null (Lycett et al., 2000). Physiological costs of reproduction also change in relation to age of the children. The energetic demands of lactation are much larger than those of pregnancy in mammals (Jasienska, 2009), so that the number of offspring born gives only a rough approximation for the total cost of reproduction. Unfortunately, information about breast-feeding or socioeconomic status is often not available in studies relying on historical demographic data (Jasienska, 2009). Compared to other species, the importance of offspring sex on the outcome of the early- late-life trade-off has attracted lots of attention in humans. For instance, in a pre-industrial Finnish population, the lack of a trade-off between the number of children born and post-menopausal longevity is a consequence of the highly divergent effects of sons and daughters: longevity of women decreased by 0.65 (±0.29) years for each son born, while it increased by 0.44 (±0.29) years for each daughter (Helle et al., 2002). This gender bias may be due to a combination of biological and sociocultural processes because in this system, only daughters helped their mothers in their everyday tasks (Helle et al., 2002). However, this relationship between offspring sex and maternal longevity has not been confirmed by other studies in pre-industrial populations (Cesarini et al., 2009).

Studies of contemporary populations can help us to better understand the physiological mechanisms underlying the impact of reproduction on longevity, although such studies often examine mortality risk, not longevity, for women with relatively low number of children (Le Bourg, 2007). A U-shaped relationship between the number of children and risk of mortality is generally reported in contemporary populations: women with no children, and those with more than two to four children, die earlier than women with one or two children (Le Bourg, 2007). Cumulative costs of reproduction increase risk of cardiovascular diseases, diabetes and strokes (Jasienska, 2009). On the other hand, many studies reported protective effects of early reproduction and high parity against the risk of breast, uterine and ovarian cancers, especially when the mother is in good nutritional condition (Jasienska, 2009). These mechanisms are however not sufficient to explain all links between reproduction and longevity. For instance, they do not explain the relationships between the number of children and fathers' longevity/mortality risk reported in some studies (e.g., Westendorp and Kirkwood (1998)). More work is needed to assess the consequences of reproductive stress for both sexes.

Conclusion

This article highlights the relevance of the trade-off concept in the current research on aging. Here, we deliberately focus on the resource-based allocation trade-off between the allocation to reproduction during early-life and lifespan and/or rate of senescence in late-life but did not discuss in details the proposed physiological pathways underlying these trade-offs. Such physiological pathways are probably very diverse (e.g., oxidative stress, telomere loss) and most importantly, there are all controlled by trade-offs acting as the cellular and molecular levels. This is, for instance, the case of immunity (**Box 2**). For an organism, the ability to fight off infections is an important determinant of fitness and immunity is thus considered as one of the most important physiological function for individuals (Sheldon and Verhulst, 1996). However, immunity is a costly defense mechanism that entails subsequent energy costs. Consequently, limited resources allocated to the immune function are not available for other physiological or developmental processes. Multiple studies in eco-immunology have thus described the existence of trade-offs between immunity and other energetically costly functions, such as growth and reproduction. However, when looking within the immune function, it appears that trade-offs also occur at a finer scale, notably between the allocation of resources toward the adaptive and innate components of immunity (**Box 2**). This emphasizes the diversity of trade-offs occurring at very different scales (cell, physiological function, individual) among organisms and how trade-offs shape most biological features of organisms (and not only the aging phenotype).

Since the early 70s, the study of trade-offs occupies a central place in life sciences (Stearns, 1992). The interest in trade-offs has been reinforced in the last decade with the emergence of the "Evolutionary Medicine" field (see Stearns and Medzhitov (2016) for a recent synthesis). The general aims of evolutionary medicine is to study diseases through the lens of evolutionary biology in order to provide new insights on its ecological and biological origins and at the same time suggesting new therapeutic approaches. While this research field is already particularly vast, it is interesting to notice that the occurrence of many diseases can be revisited at the light of the numerous trade-offs acting among organisms (Stearns and Medzhitov, 2016). In this article, we have reviewed in details how substantial allocation to reproduction can have long-term deleterious consequences in terms of survival or reproductive

Box 2 Trade-offs among immunity components.

Immunity is a complex physiological function, composed of multiple effectors. The age-specific levels of basal immunity and the efficiency to mount an immune response are determined by resource-based allocation trade-offs.

In vertebrates, the immune system has two distinct but complementary components: the innate and the adaptive system. These components are themselves composed of both cellular and humoral effectors. Innate immunity is the oldest immune response in the evolutionary history of vertebrates. It is a rapid and non-specific response that includes anatomical barriers, anti-microbial soluble proteins (e.g., complement, lysozyme), natural killer cells, phagocytic cells and effectors of the inflammatory response. On the contrary, the adaptive (acquired) immunity is based on the ability to recognize and target specific antigens and is capable of producing long-lasting immunological protection against particular parasites as a result of immunological memory. This response is mediated by lymphocytes, composed principally of B and T cells. Trade-offs have been identified within a subset of T cells, the *helper T cells* (Th), which coordinate immune response to infection. Th cells are differentiated into several subtypes, most importantly Th1 and Th2, depending on their specific production of cytokines. Th1 cells produce messenger molecules (cytokines) that play a key role in amplifying immune effector mechanisms directed against intracellular microparasites (e.g., viruses, some bacteria and protozoa) while Th2 cells produce cytokines that promote mechanisms directed against macro-parasites (e.g., helminths). Th1 and Th2 cells are reciprocally downregulated: both classes of cytokines suppress production of the reciprocal type. Organism can favor one over the other, illustrating how trade-offs could occur among immune components (Ezenwa et al., 2010).

Immunity is an energetically costly function, but immune costs are also variable across subsystems of defense (i.e., innate or adaptive immune response; cellular or humoral component) and stages (i.e., development, maintenance or activation) (McDade et al., 2016). The developmental costs of innate immunity are quite low, whereas adaptive immunity —that requires diversification processes for lymphocyte development— is energetically costly to develop. Adaptive immunity thus involves higher up-front developmental costs. While innate immunity represents low developmental costs, it represents very high operating costs for the activation of acute phase proteins, cytokines or the proliferation of leukocytes (McDade et al., 2016). On the contrary, the activation costs of acquired immunity, once developed, are low (McDade et al., 2016). These distinct profiles of costs and effectiveness of adaptive and innate immunity have implications for trade-offs in the allocation of resources to the different components of immunity. Considering the substantial costs entailed by the immune function (including the immunopathology costs) and the negative cross-regulations among immune components (see above), the various components of immunity do not operate at their maximum all along the life course (Martin et al., 2007). There is thus a balance between the energy costs entailed by highly responsive immune system and the fitness benefits of preventing or neutralizing diseases or pathogens, in response to local environmental conditions. It is also allowed by the immune plasticity, in both its nature and its magnitude. Trade-offs between innate and immune response have thus been reported in several vertebrate studies. In particular, upregulation of the humoral response may be at the expense of cellular responses. A study in tree swallow (*Tachycineta bicolor*) nestlings that assessed multiple markers of innate and acquired immunity across habitats with low and high food quality provided some evidence for trade-offs between innate and acquired immune measures but only under certain conditions (Pigeon et al., 2013). This study highlights that trade-offs may be more complex than a simple trade-off when resources are limited. Although trade-offs may be present when resources are limiting, negative correlations may also be caused by preferential allocation to certain immune components according to the pathogenic environment. Overall, one predicts that high nutritional abundance, high pathogen exposure and low environmentally-driven mortality during sensitive periods of immune development should favor relatively higher levels of allocation to acquired immunity, whereas undernutrition, low pathogen exposure, and high environmentally-driven mortality should favor innate immune defenses (as explained in McDade et al. (2016)).

performance at late ages. Recent empirical studies suggest that such impaired fitness in the elderly might be explained by a greater susceptibility to certain diseases. As mentioned above, epidemiological studies have revealed that a higher number of pregnancies (i.e., a proxy of reproductive allocation) can increase the risk of suffering from diabetes and cardiovascular diseases in women (see Jasienska et al. (2017)). Similarly, specific alleles linked to an increase risk of contracting specific diseases while at the same time potentially increasing reproductive performance during early life (e.g., APO ε4 coding for a specific form of the apolipoprotein in human populations) have been identified, thus highlighting how evolutionary theory of aging (i.e., the "antagonistic pleiotropy" (Williams, 1957)) can be particularly relevant to understand the etiology of late-onset diseases (Gaillard and Lemaître, 2017).

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