



# Commentary: Oxidative stress as a cost of reproduction: beyond the simplistic trade-off model

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A commentary on

**Oxidative stress as a cost of reproduction: beyond the simplistic trade-off model**

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Current theory proposes that life history traits cannot be simultaneously maximized because there are costs paid in the currency of fitness when a change in one trait, for example increased reproduction, results in a detrimental change in another, for example decreased survival. The underlying reasoning is that resources (e.g., nutrients, energy, time) are finite and this gives rise to trade-offs in their allocation among traits, activities, or processes that compete for the same resource. Therefore, allocation of a resource to one trait means that less can be invested to other traits. This simple concept, referred to as a trade-off, has had a prominent role in our understanding of how life history variation arises.

We currently know very little about how these costs of reproduction are actually incurred, since the majority of studies have focussed on the outcomes rather than the mechanisms. In the last decade, there has been substantial interest in the role of oxidative stress as a mechanism underlying the cost of reproduction and other life-history trade-offs. Oxidative stress is a complex multifaceted biochemical condition of the organism that occurs when generation of oxidative molecular damage increases (Costantini, 2008, 2014; Metcalfe and Alonso-Alvarez, 2010; Isaksson et al., 2011). Several recent studies have, however, found weak or no support that reproductive effort increases oxidative damage (Costantini, 2014). In a recent article, Metcalfe and Monaghan (2013) have pointed out that several of these studies testing the role of oxidative stress as a cost of reproduction did not include data on non-breeding controls, making it hard to exclude seasonal or ontogenetic causes of changes in oxidative stress. They also highlighted, however, that females may tailor their own level of reproduction to avoid oxidative damage, hence it would be also important to manipulate the reproductive effort. In another article, Speakman and Garratt (2014) reinforced the idea of testing the oxidative cost of reproduction by randomly assigning animals to two groups, one of which is forced to reproduce and another one that is prevented from doing so. This is because even if individuals can choose their level of reproduction, what they cannot avoid, is an increase in metabolic rate, relative to a non-reproductive control animal. Recent experimental (Costantini et al., 2014) and meta-analytic (Blount et al., 2015) work has, however, found that oxidative damage is lower in reproducing than in non-reproducing individuals, providing again little support for the oxidative cost of reproduction hypothesis.

An important question then is whether non-reproducing individuals are truly appropriate controls. The answer does not seem to be so straightforward. Non-reproducing individuals may differ from reproducing individuals in several characteristics, which might make them incomparable. Many animal species exhibit seasonal changes in life-history stages, and some of these life-history transitions, such as that from a non-reproductive to a reproductive status, are

accompanied by dramatic changes in hormonal profile and behavior (Norris and Lopez, 2011). To mention a few examples, the diet composition of non-reproducing Wilson's storm petrels (*Oceanites oceanicus*) significantly differed from that of reproducing individuals (Quillfeldt, 2002). Glucocorticoid concentration was found to be lower (Riou et al., 2010; Selva et al., 2011; Novikov et al., 2015) or higher (Fischer et al., 1995) in reproducing than in non-reproducing individuals. Factors like diet and glucocorticoids have been shown to influence the regulation of the oxidative balance. For example, depending on the amount and exposure time, glucocorticoids can either decrease or boost antioxidant defenses with consequences for the generation of oxidative damage that might not be easy to predict (Costantini, 2014). These findings imply that any differences in oxidative status between reproducing and non-reproducing individuals (e.g., due to different metabolic rate) might be strengthened/offset/masked by differences in these other traits. Although some of the factors (e.g., diet quality) may be controlled to some extent in captivity experiments, other important issues may arise. For example, granivorous songbird individuals may select seeds richer in antioxidants when facing challenging conditions (Beaulieu et al., 2014). Moreover, it is often forgotten that preventing individuals from reproducing is not a natural condition nor is it a free choice of the individual. These protocols that do not allow animals to breed ignore the lessons learned from earlier studies on animal behavior and welfare showing that animals may undergo measurable detrimental physiological changes when they are prevented from carrying out particular kinds of behaviors, including social interactions with a mate and generation of offspring (Palmer, 2010).

Finally, some of these potential issues might be exacerbated in field experiments, where the oxidative status of non-reproducing individuals is compared to that of reproducing individuals. In cooperative breeders, a comparison of oxidative status between breeders and non-breeders appears to be appropriate because it is known that there are individuals that do not actively reproduce but help in providing care to offspring of other individuals. In other species, however, the reason of why an individual is not reproducing is often unknown and standardization is hard to achieve. For example, in many seabirds, sabbatical

intermittent non-breeding years (the so called "sabbatical years") are common. It is thought that birds skip reproduction (and so take sabbaticals) when they are in poor condition, hence the costs of reproduction would be too high to sustain (Giudici et al., 2010). Hence, it might happen that oxidative stress is higher in non-reproducing than in reproducing individuals. An experimenter would interpret this result as evidence against the oxidative cost of reproduction. An alternative and more plausible interpretation would be that non-reproducing individuals suffer higher oxidative stress because they are in poor health.

In conclusion, as pointed out by Metcalfe and Monaghan (2013) and Speakman and Garratt (2014), it is certainly interesting to compare oxidative status metrics between non-reproducing and reproducing individuals because this comparison would enable to assess how the individual oxidative status changes through the transition from a non-reproductive to a reproductive status. However, there may be a number of potential caveats in the use of non-reproducing individuals as controls to infer about the oxidative cost of reproduction that, if not being carefully considered, might lead to erroneous interpretations and conclusions. We should recognize that natural selection does not favor individuals that do not reproduce. Hence, individuals that choose their own level of reproduction appear to be more appropriate controls in experimental investigations of the oxidative cost of reproduction hypothesis. Finally, we should not forget that prior work looked at the short-term changes in oxidative status, while looking at seasonal dynamics of oxidative balance and how this relates to reproduction appears a better approach to assess whether oxidative stress is one cost of reproduction.

## AUTHOR CONTRIBUTIONS

The author confirms being the sole contributor of this work and approved it for publication.

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**Conflict of Interest Statement:** The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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