Received: 3 May 2021 | Revised: 10 December 2021 | Accepted: 13 January 2022

DOI: 10.1111/mec.16370

INVITED REVIEW

MOLECULAR ECOLOGY WILEY

Telomeres and anthropogenic disturbances in wildlife: A systematic review and meta-analysis

Pablo Salmón[1,2] | Pablo Burraco[1]

[1]Institute of Biodiversity, Animal Health and Comparative Medicine, University of Glasgow, Glasgow, UK

[2]Department of Plant Biology and Ecology, Faculty of Science and Technology, University of the Basque Country (UPV/EHU), Leioa, Spain

Correspondence
Pablo Salmón, Institute of Biodiversity, Animal Health and Comparative Medicine, University of Glasgow, Glasgow, UK.
Email: pablo.salmon@glasgow.ac.uk; pablo.salmon.saro@gmail.com

Funding information
Basque Government Postdoctoral Fellowship, Grant/Award Number: POS-2020-1-0007; FP7 People: Marie-Curie Actions, Grant/Award Number: 797879-METAGE

Abstract

Human-driven environmental changes are affecting wildlife across the globe. These challenges do not influence species or populations to the same extent and therefore a comprehensive evaluation of organismal health is needed to determine their ultimate impact. Evidence suggests that telomeres (the terminal chromosomal regions) are sensitive to environmental conditions and have been posited as a surrogate for animal health and fitness. Evaluation of their use in an applied ecological context is still scarce. Here, using information from molecular and occupational biomedical studies, we aim to provide ecologists and evolutionary biologists with an accessible synthesis of the links between human disturbances and telomere length. In addition, we perform a systematic review and meta-analysis on studies measuring telomere length in wild/wild-derived animals facing anthropogenic disturbances. Despite the relatively small number of studies to date, our meta-analysis revealed a significant small negative association between disturbances and telomere length (−0.092 [−0.153, −0.031]; $n = 28$; $k = 159$). Yet, our systematic review suggests that the use of telomeres as a biomarker to understand the anthropogenic impact on wildlife is limited. We propose some research avenues that will help to broadly evaluate their suitability: (i) further causal studies on the link between human disturbances and telomeres; (ii) investigating the organismal implications, in terms of fitness and performance, of a given telomere length in anthropogenically disturbed scenarios; and (iii) better understanding of the underlying mechanisms of telomere dynamics. Future studies in these facets will help to ultimately determine their role as markers of health and fitness in wildlife facing anthropogenic disturbances.

KEYWORDS
ageing, environmental stress, oxidative stress, physiological stress, pollution, telomerase, telomere dynamics

Pablo Salmón and Pablo Burraco contributed equally.

1 | INTRODUCTION

There is ample evidence that human population growth and its increasing ecological footprint are driving dramatic environmental changes for wildlife worldwide (Ceballos et al., 2020; Diffenbaugh & Field, 2013). Human-driven environmental changes often take place at a faster pace than historical environmental shifts, which can constrain the development of adaptive responses, and thus reduce individual performance and population resilience (Hendry et al., 2017; Saaristo et al., 2018). Evaluating how organisms cope with anthropogenic disturbance is therefore crucial to devise appropriate conservation plans (Brooks et al., 2006; Brum et al., 2017). To that aim, a broad number of molecular markers have been used across taxa and within different fields (e.g., ecotoxicology: Chapman, 2002; conservation physiology: Wikelski & Cooke, 2006), and some of them have arisen as surrogates of an individual's condition and fitness, hereafter called "biomarkers." The use of biomarkers has its origin in human toxicology, and when applied to wildlife management or assessment, it aims to evaluate whether organisms have been, or currently are being, exposed to human-derived disturbances or stressors, and whether this exposure has a negative impact on the individuals' health and future performance. Ideally, a given biomarker should not only provide information about the stress-induced homeostatic response, which may be adaptive, but it also should provide an inference of a measure of impairment, i.e., a link with health or fitness (Calow & Forbes, 1998). This deterministic approach can be challenging in natural populations, as differences in life-history trajectories between individuals, but also population-specific evolutionary processes, can make it difficult to delineate the response to a specific human disturbance (e.g., Whitehead et al., 2017).

The quantification of parameters linked to endocrine pathways, immune response or cellular damage, such as oxidative stress, have largely been used to evaluate the impact of human activities on natural populations (e.g., Beaulieu & Costantini, 2014; Burger et al., 2007; Huggett, 2018; Madliger et al., 2015, 2018; Ohmer et al., 2021; Figure 1). In addition to the use of these biomarkers, the estimation of the length of telomeres (the terminal chromosomal regions) has recently been suggested as a tool for assessing the link between environmental disturbance, physiology and fitness (Beaulieu & Costantini, 2014; Gormally & Romero, 2020; Madliger et al., 2018). However, despite the increase in the number of studies measuring telomeres in wildlife, our knowledge is still far behind the endocrine, immunological or oxidative stress metrics (Figure 1), among other markers. Recent reviews have highlighted the relevance of telomeres in toxicology (Shoeb et al., 2020), and specifically in environmental toxicology (Louzon et al., 2019); and several studies have started to include telomere estimates to understand the impacts of other global threats to biodiversity such as urbanization. A comprehensive evaluation of the link, or the lack thereof, between the exposure to anthropogenic disturbances and telomere dynamics will help to determine whether telomeres can be considered a biomarker in this context.

Here, we synthesize and evaluate the use of telomeres in studies addressing the impact of human disturbances on wild and wild-derived animals, hereafter wildlife. First, we provide a brief overview of the implications of telomeres at the organismal level (for previous and more extensive reviews on the topic see, e.g., Giraudeau et al., 2019; Young, 2018), followed by a synthesis of their methodological and theoretical advantages in comparison with relatively well-established physiological biomarkers. We then introduce the mechanistic link between the most common pollutants derived from human disturbances, such as metallic elements or organic compounds, and telomere dysfunction, drawing on knowledge from molecular and human occupational and environmental medicinal studies. We follow up with a systematic review and meta-analysis of the available publications investigating whether human disturbances alter wildlife telomeres, i.e., from specific chemical pollutants to the effect of urbanization, as an exemplification of broad human interventions. Finally, we discuss the possible limitations and future perspective on the use of telomeres in ecotoxicological and human-disturbance studies.

2 | BENEFITS OF MEASURING TELOMERE LENGTH IN WILDLIFE FACING HUMAN DISTURBANCES

Telomeres shorten with age as the result of the normal process of DNA replication, and therefore are often regarded as a metric of an individual's ageing rate (Epel et al., 2004), which is an idea initially

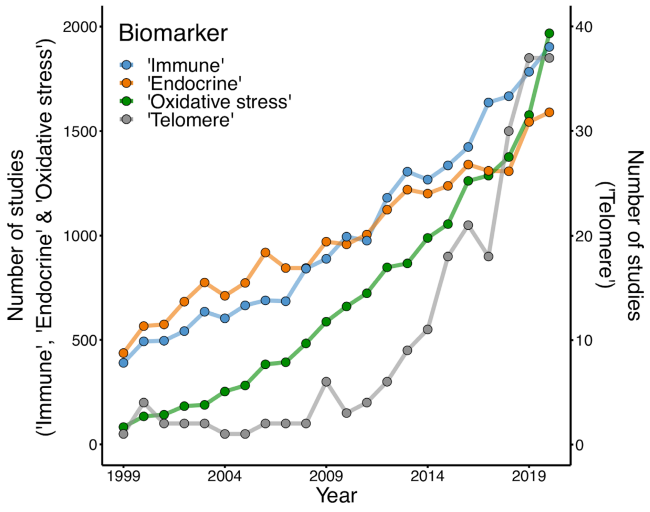

FIGURE 1 Number of publications per year (from 1999 to 2020) measuring either immune (blue), endocrine (orange) or oxidative stress (green) parameters in the left *y*-axis, or telomere length (grey) in the right *y*-axis, in wild animal populations coping with anthropogenic-origin disturbances. The search was done in March 2021 in Web of Knowledge and using the following string: ("biomarker"; i.e., "immune," "endocrine," oxidative stress" or "telomere," respectively) AND (pollut* OR disturb* OR anthrop* OR pestic* OR contam* OR biotic* OR abiotic*) NOT (human* OR domestic* OR captiv* OR plant* OR aquacultur*)

derived from human studies (Mather et al., 2011; Wang et al., 2018). In the field of ecology and evolutionary biology, telomeres were initially considered as a potential marker of organismal chronological age and lifespan (e.g., Haussmann & Vleck, 2002; Nakagawa et al., 2004), with applications for wildlife conservation management (Nakagawa et al., 2004). However, almost two decades after these pioneering studies, the view of telomeres as a chronological age marker has been disregarded and, instead, telomeres are considered as a proximate cause of life history and physiological trade-offs (see, e.g., Young, 2018). In addition, evidence from wildlife populations is accumulating on the importance of environmental cues in the observed within-species variation in telomere length (e.g., Angelier et al., 2018; Burraco et al., 2021; Debes et al., 2016; Dupoué et al., 2017), together with apparent fitness-related benefits of maintaining longer telomeres across an individual's lifetime (Barrett et al., 2013; Bauch et al., 2014; Eastwood et al., 2019; Sudyka et al., 2014). Moreover, recent laboratory studies have evidenced their causative role in ageing and health links; for example, in modified laboratory mice, longer telomeres are associated with less DNA damage or low cholesterol, together with longer survival (e.g., Muñoz-Lorente et al., 2019). Therefore, the measurement of telomere length is gaining attention in ecological and environmental studies as a potential molecular marker on the overall health status of wild organisms.

In contrast to other molecular markers such as endocrine, immune or oxidative stress parameters, telomeres are predicted to be less sensitive to immediate disturbances, such as handling or circadian cycles, and, therefore, they could provide information about wildlife exposure to medium- or long-term disturbances (Gormally & Romero, 2020). Moreover, the measurement of telomere length in minimally invasive tissues such as blood, buccal swabs or tissue punches (e.g., ear and patagium, or feathers) has been shown to be a reliable metric of the telomere length in other tissues at the organismal level (e.g., Asghar et al., 2016; Debes et al., 2016; Kärkkäinen et al., 2020; Kesäniemi et al., 2019; Power et al., 2021; Reichert et al., 2013; Rollings et al., 2019; Turbill et al., 2013). This makes telomeres an attractive metric for wildlife studies where access to certain tissues is limited in natural populations.

3 | INFLUENCE OF ANTHROPOGENIC DISTURBANCES ON TELOMERE STRUCTURE AND ITS MAINTENANCE MECHANISMS

Occupational and environmental medicine research has presented telomeres as a chromosomal region sensitive to human-derived stressors in a broad sense, and in particular to chemical pollutants. Despite potential limitations of these studies, they provide interesting insights into the mechanisms behind anthropogenic disturbances and telomere dysfunction. In Box 1, we synthesize the biology of telomeres, introducing the molecular structures and mechanisms of maintenance that are more likely to be affected by human activity. In this section, we aim to provide ecologists, and environmental and evolutionary biologists with an accessible overview of how exposure to pollutants of concern links to those molecular pathways and structures described in Box 1, for natural populations. This mechanistic overview aims to aid the interpretation of telomere dynamics in wildlife exposed to anthropogenic disturbances, but also to encourage the study of new pathways in future research within the field.

3.1 | Chemical pollution (organic and inorganic)

Environmental pollution, via a plethora of inorganic and organic compounds such as metals, POPs (persistent organic compounds), or pesticides and pharmaceuticals, represents one of the main human-driven threats for wildlife. Some chemical pollutants, such as metals, are naturally found in the environment, but because of human activities, their concentration can reach much higher levels and become toxic. Furthermore, organisms cannot metabolize most of these substances into less toxic compounds, therefore facilitating their bioaccumulation (mostly in adipocytes, de Wit, 2002), which, together with their long residence times in air, water or soils, could increase the hazard and risk of toxicity (e.g., Arnold et al., 2014; Lv et al., 2019).

3.1.1 | Metallic/metalloid trace elements (MTE)

The exposure to metals can induce reactive oxygen species (ROS) production, induce genotoxicity and inhibit DNA repair mechanisms (Figure 2). Hence, these compounds could affect telomere length or its dynamics either acting in isolation or via interaction with other xenobiotics (e.g., Vriens et al., 2019). For example, in humans, chronic exposure to arsenic can result in carcinogenic manifestations and involve telomere elongations; this is partially attributed to an increase in telomerase activity (Jimenez Villarreal et al., 2018; Zhang et al., 2003) but also to ALT (alanine transaminase) pathways or epigenetic modifications (Bhattacharjee et al., 2020; Figure 2). Nonetheless, high exposure to arsenic has also been linked to telomere shortening via increased oxidative stress (Zhang et al., 2003). In contrast, lead and cadmium have been systematically associated with shorter telomeres because of their ability to cause oxidative damage (DNA, proteins and lipids) or to impair the DNA repair machinery (Hartwig, 2010; Figure 2). Moreover, MTEs could increase telomere shortening directly and indirectly, namely via mitochondrial impairment and dysfunction (Meyer et al., 2013). It remains controversial whether mitochondrial ROS are able to diffuse across the cytoplasm (Cleaver et al., 2014; Hoffmann et al., 2004; Zhang & Wong, 2021), but it has recently been shown that ROS derived from mitochondria could indeed be responsible for telomere dysfunction (Qian et al., 2019). Furthermore, it is plausible that mitochondrial dysfunction alone, in response to environmental pollutants, could trigger cellular senescence i.e, MiDAS (mitochondrial dysfunction-associated senescence) (Wiley et al., 2016; Figure 2), increasing cellular turnover and telomere shortening.

BOX 1 What are telomeres and how does their regulatory machinery work?

Our understanding of telomere structure and the pathways involved in the regulation of its length is key to interpret an individual's telomere length in relation to anthropogenic disturbances (see Section 3). Telomeres constitute a highly conserved system involved in the maintenance of genome stability and replication (Blackburn, 1991). In vertebrates, telomeres are noncoding regions that consist of double-stranded G-rich DNA repeats ending in a single-stranded 3′ overhang. These repeats are bound to the shelterin/telosome complex, which is composed of six proteins in most vertebrates (TRF1, TRF2, RAP1, TIN2, TPP1 and POT1; Figure 2). This protein complex helps to stabilize the telomere structure and prevents chromosome ends from being identified as a DNA double-strand break (Griffith et al., 1999; de Lange, 2005). Nonetheless, telomeres shorten during each cell division as a result of the normal process of DNA replication, the so-called "end replication problem" (Harley et al., 1990). This replicative shortening eventually destabilizes the shelterin/telosome complex, thus exposing the chromosome end and triggering the cellular replicative senescence signal. This process is characterized by activation of pathways related to the DNA damage response (e.g., p53 and p16; Figure 2) and can finally lead to cellular ageing (Jacobs & de Lange, 2004). Adjacent to the telomere structure are the subtelomeric regions, which, in contrast to telomeres, contain a low density of genes. Among other functions, genes contained in the subtelomeric regions are involved in the transcription of long noncoding RNA, named TERRA, playing a significant role in the regulation of telomere length, telomerase activity and telomeric heterochromatin (Luke & Lingner, 2009). Similar to telomeres, subtelomeres are rich in epigenetic marks such as DNA methylation or histone modifications (Figure 2), and therefore altered methylation/demethylation patterns in subtelomeric promoters can modify transcription levels and induce telomere length variation and dysfunction (Blasco, 2007).

Eukaryotes have developed strategies to counteract telomere shortening after each cell division, and the most common way is through the action of the enzyme telomerase. Telomerase is a reverse transcriptase formed by two main components (the catalytic domain TERT, and a noncoding RNA, TER; Figure 2), which elongates telomeres by synthesizing telomeric DNA repeats (Greider & Blackburn, 1989). Although telomerase activity may be a key component in attaining cellular immortality, in humans this enzyme is often repressed in somatic cells, whereas it is mostly expressed in highly proliferative ones such as germ cells, embryonic stem cells and haematopoietic cells (Blackburn et al., 2015). The inactivation of telomerase in post-embryonic stages may be a mechanism to avoid cancer development, as upregulated telomerase activity is associated with the development of a high number of tumours (Shay, 2016). Oncogenic studies have also observed that a proportion of tumour cells can maintain their chromosome-end integrity in the absence of telomerase (Cesare & Reddel, 2010). These cells can use one or more mechanisms that involve DNA recombination events to maintain their telomere length, referred to as alternative lengthening of telomere pathways or ALT (Bryan et al., 1997).

Therefore, the telomere length of an individual represents an equilibrium between the loss of terminal telomeric repeats with each DNA replication, the integrity of the shelterin/telosome complex and the addition of telomeric repeats by telomerase. However, not all the telomere loss is attributable to the "end replication problem." *In vitro* studies suggest that oxidative stress plays a major role in the remaining loss at the cellular level (Richter & Zglinicki, 2007; Von Zglinicki, 2002). Reactive oxygen species (ROS) seem to induce single strand breaks and lead to telomere loss (Figure 2), either directly at the telomeric regions or as intermediates in lesion repair (Von Zglinicki, 2002). This can be partially explained by the nucleotide composition of the telomeric repeats. Telomeres are rich in guanine (G-rich strand, Figure 2), which is the most easily oxidized of the natural bases (converted to 8-oxoG) and a preferred site for iron binding and iron-mediated Fenton reactions—a source of ROS (e.g., Oikawa et al., 2001). Cells are relatively efficient in repairing the DNA damage produced by daily cellular insults, but this process seems to be less efficient in telomeres (e.g., Kruk et al., 1995). Externally induced mild-oxidative stress might promote the accumulation of telomeric single-strand breaks (SSBs, Figure 2), which will eventually accelerate telomere shortening and lead to premature cellular senescence (Barnes et al., 2019; Correia-Melo et al., 2014). Also, acute oxidative stress or genotoxic agents could induce double-strand breaks (DSBs, Figure 2), which are more difficult to repair and can trigger a persistent DNA damage response in the cell, inducing a replicative senescence independently of telomere length (e.g., Fumagalli et al., 2012; reviewed in Victorelli & Passos, 2017). However, it is important to note that, at the organismal level (i.e., *in vivo*), the causal role of oxidative stress in telomere loss is far from being established. Current studies on this only partially support this hypothesis (e.g., Boonekamp et al., 2017; reviewed in Reichert & Stier, 2017), although a recent meta-analysis in nonhuman vertebrates suggests a link between the mechanisms to minimize the oxidative damage inflicted by ROS and telomere loss (Chatelain et al., 2020). Further mechanistic experiments are needed to fully understand the relationship between telomere loss and oxidative stress at the organismal level.

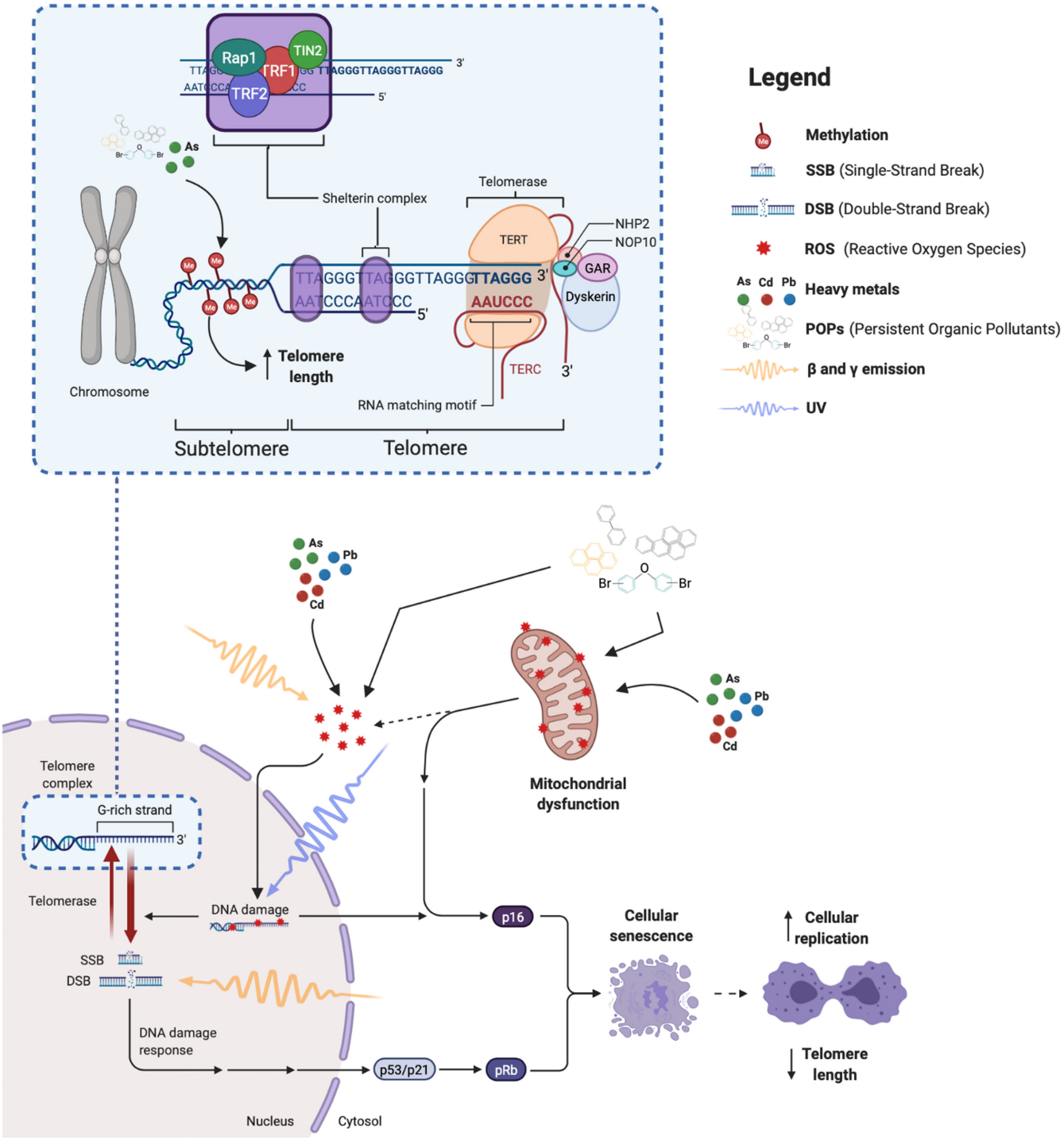

FIGURE 2 Overview of telomere structure, maintenance mechanisms and the main mechanisms of action of some common environmental disturbances on them, with particular emphasis on those derived from the anthropogenic activities. Figure created with BioRender.com

3.1.2 | Persistent organic pollutants (POPs)

In light of the available epidemiological studies, exposure to POPs is generally associated with shorter telomeres (reviewed by Liu et al., 2021), although this may depend on the particular compound or exposure intensity (e.g., Callahan et al., 2017; Shin et al., 2010; Vriens et al., 2019). Metabolism of POPs can induce oxidative stress via the production of ROS as by-products, and can also alter the mitochondrial redox status and function, such as via oxidative damage (Liu et al., 2020; Figure 2). Moreover, telomere dysfunction due to exposure to POPs may also be driven by reduced telomerase activity (e.g., Senthilkumar et al., 2011) or by the upregulation of TERRA (Yuan et al., 2018). Nonetheless, exposure to certain POPs, such as polychlorinated biphenyls (PCBs) or poly- and perfluoroalkyl substances

(PFAS), is suggested to upregulate telomerase activity, via decreasing TERT inhibition, and ultimately leading to longer telomeres (Huang et al., 2019; Figure 2). However, the observed telomere lengthening (or lack of change) in organisms coping with POP exposure can be a hormetic response to pollutant concentration, as observed in response to PCBs (Shin et al., 2010) or to arsenic (Zhang et al., 2003).

3.2 | Radiation

Radiation refers to the emission of energy in the form of particles or waves. The energy of radiation is often classified either as nonionizing (lower frequency and energy) or ionizing (higher frequency and energy), and defines its ability to penetrate solid matter, including biological structures. Overall, studies suggest telomeres are key elements in the process of radiation-induced carcinogenesis, either via direct damage to their structure (including shelterin proteins), or via its maintenance mechanisms. However, the mechanisms behind the effects of each type of radiation are yet not fully understood. Big data studies will help to infer how exposure to each radiation type has negative consequences both at the molecular and at the organismal level.

3.2.1 | Nonionizing radiation

Nonionizing radiation does not have sufficient energy to ionize atoms, but it can be biologically hazardous because it induces the excitation of biological molecules. This is the case of the ultraviolet (UV) radiation that is not absorbed by ozone. Telomeres are hypersensitive to damage following UV radiation (Figure 2) as they form cyclobutene pyrimidine dimers (CPDs), which are mutagenic and lethal (Cadet et al., 2005). The repair mechanisms of these photoproducts involve the excision of the damaged segments and opposite CPDs in proximity could mimic double-strand break, triggering a DNA damage response (Witkin, 1976). Therefore, cells might use a lesion-tolerance strategy rather than repair the CPDs in order to prevent double-strand breaks and continue proliferating without accelerating telomere shortening (Rochette & Brash, 2010).

3.2.2 | Ionizing radiation

Although rare, wildlife can be threatened by high levels of ionizing radiation after a nuclear accident or in scenarios where radioactive elements are naturally present. Ionizing radiation can directly damage DNA during or shortly after exposure to the radioactive particles (Figure 2). Even so, telomeres represent a small proportion of the nuclear DNA and therefore the probability that radioactive particles interact with the telomeres is rather low. In contrast, the radioactive particles can interact with other cellular components generating free radicals and ROS, and thus potentially inducing telomere dysfunction (Figure 2). Several studies have found altered telomere dynamics and telomerase expression in humans exposed to acute ionizing radiation (Lustig et al., 2016; Sishc et al., 2015; Yoshida et al., 2016). However, the cohort consequences of these effects are far from clear, as for example denoted by an overall lack, at the whole-genome level, of transgenerational effects of exposure to Chernobyl ionizing radiation (Yeager et al., 2021).

3.3 | Air pollution

Air pollution via particulate matter (PM) or nitrogen oxides (NO_x), but also via persistent organic compounds such as PCBs and others (see Section 3.1 for details), are among the most common sources of pollution in anthropogenic landscapes (e.g., Hochella et al., 2019; Moll et al., 2019). Their relationship with telomere dysfunction arises via oxidative stress and ROS formation. In particular, PM can induce an oxidative stress state either transporting ROS to the body via inhalation and/or through the catalytic generation of ROS (Bates et al., 2019). Both processes could eventually lead to DNA damage, increases in cell proliferation or apoptosis, and overall shorter telomeres (Gutiérrez-Castillo et al., 2006; Peixoto et al., 2017). Epidemiological studies on humans show that exposure to PM does not only alter telomere dynamics in those tissues directly exposed to the stressor such as lung or skin cells, but also in peripheral blood and in the placenta (Liu et al., 2021). In addition, increases in telomere length have been reported in peripheral blood in response to short-term PM exposure, and although the mechanisms are not fully understood, these seem to be independent of telomerase expression via methylation on its promoter (Dioni et al., 2011). Therefore, exposure to PM can include systemic effects and influence telomere dynamics in early life (Martens et al., 2017), although these effects can take place in a complex way, probably linked to the nature of the particles.

3.4 | Light and noise pollution

In contrast to the large number of studies on the effect of PM or chemical pollutants on telomeres, the consequences of artificial light at night (ALAN) or noise exposure on telomere length have been less explored. This is probably the result of being often an overlooked source of pollution in human populations, only regarded as a risk under certain circumstances (e.g., Münzel et al., 2021). Conversely, ALAN and noise exposure are a current concern with important implications for wildlife populations (e.g., Duquette et al., 2021; Sanders et al., 2021). Therefore, it is not surprising that empirical studies linking these two pollutants and telomere length are based on wildlife studies. Although the mechanisms behind the effects of ALAN and noise pollution on telomere dysfunction might not be straightforward, these might respond to indirect pathways linked to increases in oxidative stress and subsequent ROS production, for example due to altered circadian rhythms (e.g., Cai et al., 2020; Sardon Puig et al., 2018; Wilking et al., 2013). However, the studies currently available

(mostly in birds, see Table 1; e.g., Grunst et al., 2020; Grunst et al., 2019; Injaian et al., 2019) indicate that noise and light pollution only subtly affect telomere dynamics, although the combination of several stressors might magnify telomere dysfunction.

4 | SYSTEMATIC REVIEW AND META-ANALYSIS ON WILDLIFE TELOMERE LENGTH FACING ANTHROPOGENIC DISTURBANCES

4.1 | Literature search, data extraction and effect size calculation

To synthesize and assess research gaps and biases in current knowledge of wildlife telomere length in ecotoxicological and anthropogenic disturbance studies, on March 6, 2021, we systematically searched the peer-reviewed scientific literature using Web of Science and the following string: (telomere) AND (pollut* OR disturb* OR anthrop* OR pestic* OR contam* OR biotic* OR abiotic*). We restricted the search to those studies in nonhuman organisms and focused on those performed at the organismal level in wild or wild-derived populations, and cell culture-based studies were excluded in subsequent steps. We also excluded those studies in which telomere length was not reported. The initial search produced 1,239 studies that were screened for duplication, and those studies in nonrelevant disciplines or topically irrelevant based on reading titles and abstracts were filtered out ($n_{excluded}$ = 1,132; see Figure S1). After compiling the remaining results into a database, we screened 63 studies of which 35 were retained ($n_{excluded}$ =28; Figure S1). We excluded six of those studies as they did not directly measure telomere length or were conducted in study systems under strong artificial selection (mainly studies on laboratory rodents), and we identified, screened and included three records via other sources, resulting in a final 31 studies in the review in Table 1.

From the studies in Table 1, we extracted information regarding the study subject (taxonomic group, species and developmental stage of the individuals), study condition (field or laboratory) and design (wild or captive populations, use of the natural variation or experimental approaches, number of telomere measurements per individual, sampled tissue and method of telomere measurement) and anthropogenic disturbance information (type of disturbance in a broad sense). The complete list of moderators, its detailed description and levels are shown in Table S1. In addition, where possible, we extracted statistical information from each study to transform the association between an anthropogenic disturbance and telomere length using Fisher's transformation for among-study comparison (*Zr*, the effect size). This was achieved using the means, sample sizes and standard deviations, *t*-values, *F*-values or correlation coefficients and following standard equations (Koricheva et al., 2013; Nakagawa & Cuthill, 2007). Effect sizes assessing categorical predictor variables (e.g., those measuring telomere length in polluted and control habitat or condition) were first transformed into standardized mean differences (Cohen's *d*, Cohen, 2013) and then to Pearson's correlation coefficient (*r*) before applying Fisher's transformation (Nakagawa & Cuthill, 2007). Where a categorical predictor had multiple levels (e.g., a gradient of anthropogenic habitat), we used the two extremes of the environmental gradient for analysis. Where more than one effect size could be calculated from the same data due to reporting of multiple statistical outputs, we followed the order of preference: (i) mean telomere differences between anthropogenic and control or correlation coefficients between telomere and anthropogenic disturbance, (ii) coefficient of correlation and (iii) inferential statistics (e.g., *F*-value, *t*-value). Where necessary, data extraction was conducted from figures using WEBPLOTDIGITIZER (Rohatgi, 2021). From each study, we also extracted the direction of the relationship between telomeres and anthropogenic disturbance, either negative for a decrease or faster shortening, or positive for telomere length elongation or maintenance. When no information was available for the calculation of the effect sizes of interest, we contacted the corresponding authors and four authors provided us with the required data or information. Full or partial extraction of relevant data was possible from the published material of 28 studies (90% of all the studies included in Table 1) and we obtained a total of 159 effect sizes (*k*; see figure S1).

4.2 | Meta-analysis and publication bias

We used phylogenetic multilevel meta-analytic mixed-effect models for testing the overall effect of anthropogenic disturbances on telomere length, in addition to the effects of each of the seven *ad hoc* selected moderators (Table S1). For that aim, we used the package METAPHOR version 2.1.0 (Viechtbauer, 2010) in R version 3.5.2. (R Core Team, 2018). In each model, we used the effect size (*Zr*) as the dependent variable along with the sampling variance associated with each effect size, which is $(n - 3)^{-1}$. We first fitted an intercept-only model to estimate the overall effect (i.e., meta-analytic mean). We then subsequently built individual meta-analytic models to examine the effects of moderators of interest (Table S1), where levels had four or more studies and 12 effect sizes. In all models we included the *study ID* as a random factor, which encompasses effect sizes extracted from the same study, and *species ID*, as some species occurred in multiple studies. Residual variance was modelled by adding an *observation ID* as a random factor (Harrison, 2014). To minimize the nonindependence of the estimates, we included the species phylogeny in the models as a random effect, using a phylogenetic relatedness correlation matrix (e.g., Chamberlain et al., 2012; Sánchez-Tójar et al., 2020). To this aim, we built a phylogeny by retrieving the phylogenetic relationships from the Open Tree of Life (Hinchliff et al., 2015) using the package ROTL (Michonneau et al., 2016). We estimated branch lengths using Grafen's method (Grafen, 1989) using the function "*compute.brlen*" (APE R package Paradis & Schliep, 2019). We present estimates (i.e., means) with their 95% confidence intervals (CI) in square brackets throughout and the mean effect size is considered significantly different from zero if the

TABLE 1 Summary of the systematic review of studies linking telomere length and anthropogenic-origin disturbances, including direct or indirect actions, such as pollution, urbanization or habitat fragmentation, on nonhuman animals

Species	Field/lab.	Exp./corr.	Develop. stage	Type of Anthropogenic Disturbance	Summary of the relationship between telomere length (TL) and/or dynamics (TD) and the disturbance	Tissue	Reference
Amphibian *Nanorana parkeri*	Lab.	Exp.	Larval	Oxygen	TL: no differences	heart, liver, muscle	Han et al. (2018)
Aves *Cephus grylle mandtii*	Field	Corr.	Adult	Hg, PCBs, DDTs, HCH, HCB, PBDEs, PFAS	TL: negative with pesticides	RBCs	Eckbo et al. (2019)
Aves *Haliaeetus albicilla*	Field	Corr.	Nestling	POPs (several)	TL: no change	RBCs	Sletten et al. (2016)
Aves *Hydrobates pelagicus*	Field	Corr.	Nestling–adult	Human presence level	TL and TD: no differences/change	RBCs	Watson et al. (2015)
Aves *Larus hyperboreus*	Field	Corr.	Adult	PFAS	TL and TD: no differences with many organic pollutants. TD: slower shortening with PFTeDA	RBCs	Sebastiano et al. (2020)
Aves *Milvus milvus*	Field	Corr.	Nestling	Lead and mercury	TL: no differences	RBCs	Powolny et al. (2020)
Aves *Parus major*	Field	Corr.	Nestling	Urbanization	TL: no differences	RBCs	Biard et al. (2017)
Aves *Parus major*	Field	Exp.	Nestling	light	TL and TD: no differences/change	RBCs	Grunst et al. (2019)
Aves *Parus major*	Field	Corr.	Nestling	Road proximity, metals (Pb, Cd, As, Cu, Zn)	TL: no differences with proximity to road or with metal concentration. TD: negative with road proximity	RBCs	Grunst et al. (2020)
Aves *Parus major*	Field	Corr.	Nestling	Noise	TL: negative among small, but not large, brood members	RBCs	Grunst, Grunst, Pinxten, et al. (2020)
Aves *Parus major*	Field	Exp.	Nestling	Light	TD: no change	RBCs	Ouyang et al. (2017)
Aves *Parus major*	Field	Exp.	Nestling	Urbanization	TL: negative	RBCs	Salmón et al. (2016)
Aves *Parus major*	Field	Corr.	Juvenile-adult	Urbanization	TL: selective disappearance of birds with shorter telomeres in urban birds. TD: slower shortening in urban birds	RBCs	Salmón et al. (2017)
Aves *Parus major*	Field	Exp./corr.	Nestling	As, Cd, Ni, Pb, Cu	TL: no differences	RBCs	Sánchez-Virosta et al. (2020)
Aves *Parus major, Ficedula hypoleuca*	Field	Corr.	Nestling–adult	Metals (As, Pb, Cd, Cu, Ni), calcium, metallothioneins	Parus major TL: shorter in contaminated area. Ficedula hypoleuca TL: no differences	liver	Stauffer et al. (2017)

(Continues)

TABLE 1 (Continued)

Species	Field/lab.	Exp./corr.	Develop. stage	Type of Anthropogenic Disturbance	Summary of the relationship between telomere length (TL) and/or dynamics (TD) and the disturbance	Tissue	Reference
Aves *Passer domesticus*	Field	Exp.	Nestling	Noise pollution	TL: shorter with noise	RBCs	Meillère et al. (2015)
Aves *Rissa tridactyla*	Field	Corr.	Adult	POPs (organochlorine pesticides and polychlorobiphenyls)	TL: negative with oxychlordane (females), unchanged for other POPs	RBCs	Blévin et al. (2016)
Aves *Rissa tridactyla*	Field	Corr.	Adult	PFASs	TL: no differences. TD: elongation over 2 years	RBCs	Blévin et al. (2017)
Aves *Tachycineta bicolor*	Field	Exp.	Nestling	Traffic noise	TD: faster shortening with noise	RBCs	Injaian et al. (2019)
Aves *Tachycineta bicolor*	Field	Exp.	Adult	Aerial vehicles	TD: no change	RBCs	Scholten et al. (2020)
Aves *Taenopygia guttata*	Lab.	Exp.	Nestling–adult	Traffic noise	TL and TD: shorter and faster shortening, respectively, in juveniles	RBCs	Dorado-Correa et al. (2018)
Aves *Taenopygia guttata*	Lab.	Exp.	Adult	"Cocktail" of metals (Pb, Cr, As, Cu, Ni, Co, Cd)	TL: negative in feather	RBCs and feather	Saulnier et al. (2020)
Aves *Turdus merula*	Field	Corr.	Juvenile–adult	Urbanization	TL: negative	RBCs	Ibáñez-Álamo et al. (2018)
Aves *Zonotrichia capensis*	Lab.	Exp.	Adult	Drinking water salinity	TL: no change	RBCs	Sabat et al. (2019)
Fish *Coregonus peled*	Lab.	Exp.	Adult	Noise	TL: tissue and exposure-time dependent	brain, muscle, dorsal fin, gonads	Sapozhnikova et al. (2020)
Fish *Gobio occitaniae*	Field	Corr.	Adult	Combination of trace metals (Al, As, Co, Pb, Zn, Ni, Cd, Cr, Cu)	TL: no differences	pelvic fin	Petitjean et al. (2020)
Fish *Squalius cephalus*	Field	Corr.	Juvenile–adult	Urbanization, pollutants (PAHs, phthalate esters, pyrethroids, OCPs, PCBs, PBDEs)	TL: negative with Σphthalate	pelvic fin	Molbert, Angelier, et al. (2021)
Gastropoda *Cantareus aspersus*	Lab.	Exp.	Subadult	PAHs, Cd, Hg	TL: no differences	haemolymph	Louzon et al. (2020)
Mammal *Ctenomys Torquatus*	Field	Corr.	Juvenile, subadult and adult	Coal	TL: negative	liver, kidney, muscle, skin	Matzenbacher et al. (2019)
Mammal *Myodes glareolus*	Field	Corr.	Adult	Ionizing radiation	TL: negative in testis and liver, no relation in brain, heart, ovary	testis, liver, brain, heart, ovary	Kesäniemi et al. (2019)

TABLE 1 (Continued)

Species	Field/lab.	Exp./corr.	Develop. stage	Type of Anthropogenic Disturbance	Summary of the relationship between telomere length (TL) and/or dynamics (TD) and the disturbance	Tissue	Reference
Mammal *Ursus americanus*	Field	Corr.	Adult (2–24 years)	Urbanization	TD: faster shortening, mediated by changes in hibernation length	WBCs	Kirby et al. (2019)

Note: The search was done on 6 March, 2021 by using Web of Knowledge (see text for details). Field/lab. = study carried out in free-ranging animals (field) or under laboratory conditions (captive or derived) populations. Exp./corr. = study using an experimental manipulation of the anthropogenic-origin disturbance (exp.) or makes use of the species natural variation (corr.). Develop. stage = developmental stage nomenclature for the species.

Abbreviations: RBCs, red blood cells; TD, telomere dynamics; TL, telomere length; WBCs, white blood cells.

95% CI did not overlap with it. We investigated inconsistency across studies by estimating the heterogeneity I^2_{total} and the equivalent for each random effect following Senior et al. (2016) and implemented in the function "*i2_ml*" (METAFOR R package, Viechtbauer, 2010). Heterogeneity refers to the unexplained variation among effect sizes after accounting for sampling variance, and I^2 values around 25%, 50% and 75% are considered as low, moderate and high levels of heterogeneity, respectively (Higgins et al., 2003). We also estimated the percentage of heterogeneity explained by the moderators in each model using $R^2_{marginal}$ (Nakagawa & Schielzeth, 2013). Results of the intercept-only model and moderators were graphically represented as orchard plots using the R package orchard version 0.0.0.9 (Nakagawa, Lagisz, Jennions, et al., 2021; Nakagawa, Lagisz, O'Dea, et al., 2021). To check for possible publication bias we performed two extra multilevel meta-regressions with the same random structure as above but using as moderator either (i) the square root of the inverse sampling variance (precision; a variant of an Egger's regression based on Nakagawa & Santos, 2012) to test for small-study bias (Nakagawa, Lagisz, Jennions, et al., 2021; Nakagawa, Lagisz, O'Dea, et al., 2021); or (ii) year of study publication mean-centred for time-lag bias (Koricheva & Kulinskaya, 2019).

4.3 | Results and discussion of the systematic review and meta-analysis

Due to conserved molecular structure and maintenance pathways, we may expect a similar outcome in wildlife (particularly in response to chemical pollution) as in the human literature, that is an overall negative effect on telomere length in response to anthropogenic disturbances, which could lead to premature ageing with subsequent negative consequences for individuals' performance and lifespan. Our systematic review indicates that more than a third of the studies provide equivocal support for a negative effect of anthropogenic disturbances on telomeres; that is, they find a few, from an array of analysed pollutants/disturbances, to be associated with telomeres, or they report developmental stage or sex-specific effects (11 out of 28 studies; Table 1, e.g., Blévin et al., 2016; Dorado-Correa et al., 2018; Stauffer et al., 2017). However, the meta-analytic mean for all the effect sizes (k = 159) revealed a significant negative association between anthropogenic disturbance and telomere length/change, although the effect was small and with an overall moderate heterogeneity (estimate: −0.092 [−0.153, −0.031]; I^2_{total} =53.3%; Figure 3a). This result concurs with a recent meta-analysis on stressors and telomere length across nonhuman vertebrates, where the stressor category "human disturbance" was also negatively associated with telomere length (18 studies; k = 55; estimate: −0.29 [−0.46, −0.12]; Chatelain et al., 2020).

Further analyses classifying the effect sizes in three broad anthropogenic disturbance categories indicated a negative effect on telomere length for organic pollutants (estimate: −0.104 [−0.208, −0.006]; Figure 3b) and those under the category "others" (including ALAN, noise and urbanization; estimate: −0.088 [−0.161, −0.015];

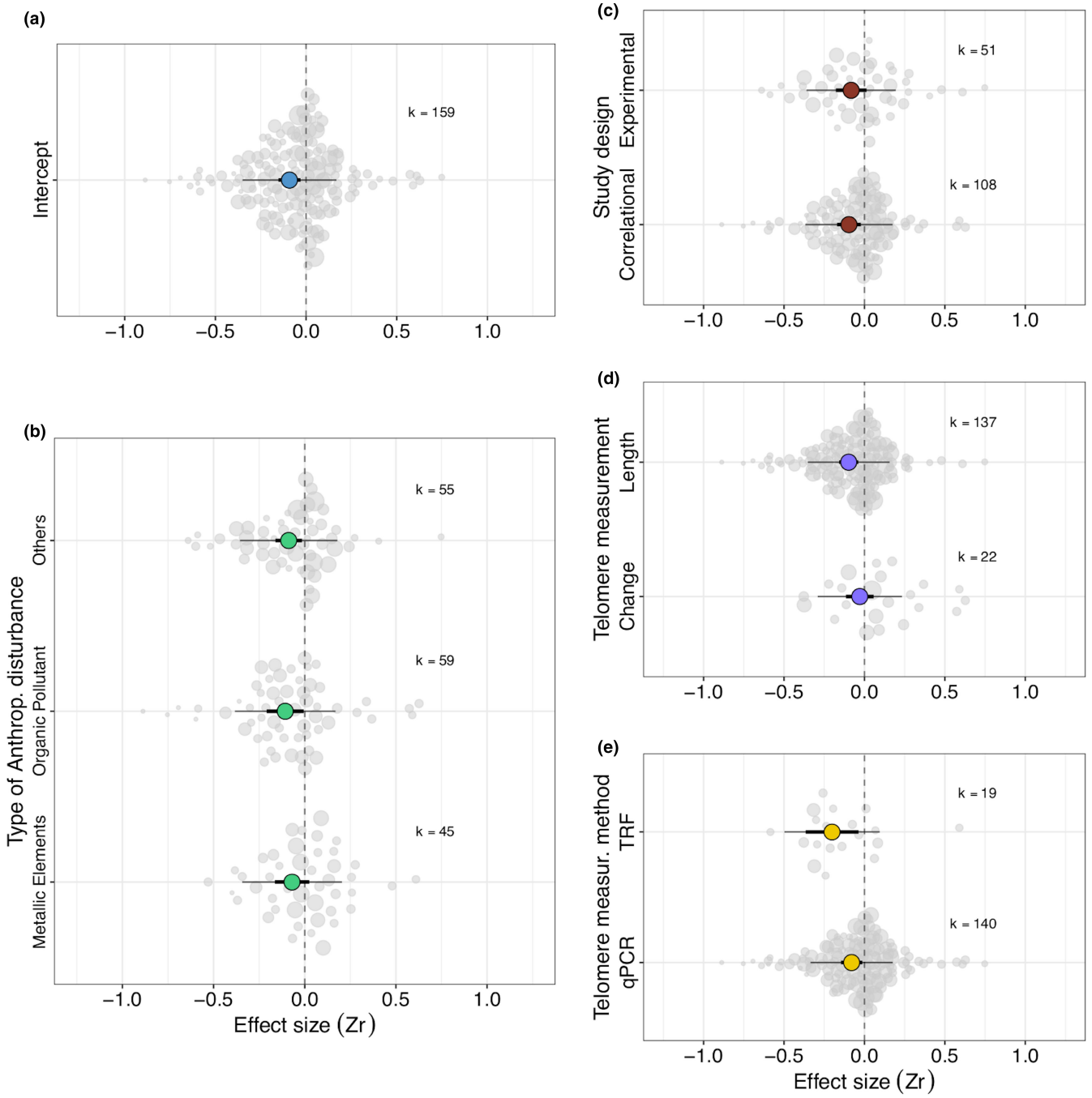

FIGURE 3 Orchard plots showing (a) meta-analytic mean; (b) type of anthropogenic disturbance; (c) experimental design; (d) number of telomere measurements per individual, one ("Length") or multiple ("Change"); and (e) method used to measure telomere length. See Table S1 for a detailed description of each moderator level. Plots show model means and 95% confidence interval (thick whisker), 95% precision interval (thin whisker) and individual effect sizes in the background (their size is scaled to illustrate the sample size from which they were estimated; e.g., the larger the point, the bigger the sample size). Negative values on the *x*-axis represent shorter telomere length or increase shortening (negative change), whereas positive values illustrate longer telomere length or elongation (positive change). Vertical dashed line drawn at an $x = 0$. "*k*" indicates the number of observations (effect sizes) per moderator

Figure 3b). However, for the category "Metallic Elements" (i.e., studies on the exposure to elements such as Zn, As or Cu), the estimate 95% CI overlapped zero (estimate: −0.070 [−0.164, 0.025]; Figure 3b). Post-hoc Wald tests revealed statistically significant differences between the categories ($p < .05$ in all cases), although the type of anthropogenic disturbance as a moderator only accounted for 1.3% of the heterogeneity (Table S2). Regarding the study characteristics, correlational or field studies show a significant negative effect on telomeres ("Correlational": −0.096 [−0.170, −0.023]; Figure 3c; "Field": −0.110 [−0.185, −0.034]; Figure S3a), which contrast with the observed pattern for experimental and studies under captive conditions ("Experimental": −0.083 [−0.178, 0.013];

Figure 3c; "Laboratory": −0.059 [−0.193, 0.075]; Figure S3a; Table S2). Both experimental and captive studies investigating the impact of anthropogenic disturbance on wildlife telomeres are scarce ($n = 13$ and 6 studies respectively; Table 1) and often looked at acute or subchronic effects, as opposed to correlational and field studies that are based on organisms with a medium to long history of exposure, and hence are more likely to detect an effect on telomeres (Table 1).

One third of the reviewed studies are based on measurements of telomere change, namely a longitudinal approach consisting of more than one telomere length estimate per individual over time ($n = 10$, e.g., Blévin et al., 2017; Dorado-Correa et al., 2018; Kirby et al., 2019). The meta-analytic estimate for longitudinal studies included zero ("Change" estimate: −0.029 [−0.115, 0.058]; Figure 3d), in contrast to those studies based on one telomere length measurement per individual that showed an overall negative effect of the anthropogenic disturbances ("Length" estimate: −0.098 [−0.158, −0.038]; Figure 3d). This pattern may be the result of the lower number of effect sizes for telomere change ($k = 22$ vs. 137 for telomere length), but it could also correspond to the short time between samples in most of the studies reporting telomere change (Ouyang et al., 2017; Scholten et al., 2020) or the reduced fraction of species lifespan covered, for example only the nestling period (e.g., Grunst et al., 2019). Alternatively, the selective disappearance of individuals with a certain telomere length in the studied populations could also explain the observed pattern (e.g., Salomons et al., 2009). Indeed, we lack longitudinal studies of wildlife that simultaneously evaluate telomeres across an organism's lifespan as well as address the impact of anthropogenic disturbances (e.g., Salmón et al., 2017).

Studies of humans and wildlife suggest that most of the telomere loss within an individual occurs during the early life stages (e.g., Asghar et al., 2015; Factor-Litvak & Susser, 2015; Heidinger et al., 2012; Louzon et al., 2020) and, therefore, we expected a stronger effect during that stage in response to anthropogenic disturbances. However, we did not find a significant effect of the developmental stage at which telomere length was measured ("Early" estimate: −0.050 [−0.133, 0.032]; "Juvenile" estimate: −0.135 [−0.278, 0.008]; "Adult" estimate: −0.065 [−0.141, 0.011]; Figure S3b), and there were no differences among the developmental stage levels (all p-values of post-hoc comparisons were >.090). It is possible that the small number of studies and the discrepancy across them regarding the analysed tissue and taxonomic groups or species-specific developmental differences might have masked effects in this respect.

Current knowledge suggests differences between the telomere biology (including the underlying maintenance and repair mechanisms) of endotherms and ectotherms (reviewed in Olsson et al., 2018). Contrary to endotherms, telomerase expression is not repressed in the somatic tissues of many ectothermic species, characterized by indeterminate growth (Gomes et al., 2010); thus, replicative senescence could theoretically be minimized in this group. Our meta-analysis indicates a negative effect of anthropogenic stressors on telomeres of endotherms but not ectotherms ("Endotherm" estimate: −0.106 [−0.180, −0.031]; "Ectotherm" estimate: −0.067 [−0.198, 0.064]; Figure S3c). This could be explained by the constitutive expression of the enzyme telomerase throughout ectotherms' lifetime and also by the upregulation of the mechanisms that may counteract or buffer the negative effects of anthropogenic disturbances on telomeres (e.g., telomerase, antioxidant activities, mitochondrial efficiency; Burraco et al., 2020). Nonetheless, our understanding of the telomere maintenance mechanisms in non-model species is limited and the number of studies conducted in ectotherms in response to anthropogenic disturbances remains very low to be able to obtain a clear conclusion ($n = 4$ in this review, all cross-sectional studies).

Regarding the effect of the telomere length measurement method, the association between telomeres and anthropogenic disturbance was negative regardless of the method ("qPCR" estimate: −0.080 [−0.146, −0.013]; "TRF" estimate: −0.201 [−0.366, −0.037]; Figure 3e), although the estimate for TRF was significantly more negative than for qPCR (QM_2 11.20, $p = .004$). Similar methodological differences have been reported previously (e.g., see Kärkkäinen et al., 2021; Wilbourn et al., 2018). We cannot disregard the differences between methods in the small number of studies and effect sizes using the TRF technique ($n = 4$ studies, $k = 24$), and more studies are needed to elucidate the observed pattern. Finally, we did not detect any publication bias for small studies (slope: −0.000 [−0.008, 0.007], $p = .945$; $R^2_{marginal} = 8.1 \times 10^{-5}$; Figure S4a) or time-lag (slope: 0.025 [−0.003, 0.054], $p = .077$; $R^2_{marginal} = .099$; Figure S4b).

5 | PERSPECTIVES ON TELOMERES AS BIOMARKERS OF THE EFFECTS OF ANTHROPOGENIC DISTURBANCES

Our systematic review and meta-analysis suggest that telomere length is proving itself to be an integrative marker to evaluate the overall effects of anthropogenic disturbances on wildlife. However, and importantly, this effect is small, and stressor- and taxon-dependent, which is in accordance with previous studies, for example on adversity and general stressors in humans and wildlife (Chatelain et al., 2020; Pepper et al., 2018). We cannot reach a conclusion about the adequacy of telomeres as a biomarker *sensu stricto*, that is as an indicator of the impact of experienced conditions on individual health and a predictor of future performance. So far, we lack key information on the causal relationship between specific disturbances and the organismal response in terms of telomeres. Moreover, we are in need of studies exploring the link between telomere length and individuals' fitness or performance in anthropogenically influenced scenarios, which has been done only recently in a handful of studies and with a mixed results (Kirby et al., 2019; Louzon et al., 2020; Salmón et al., 2017; Scholten et al., 2020; Sebastiano et al., 2020). Both are critical aspects for the broad implementation of telomeres in the estimation of ecological risk (Calow & Forbes, 1998; Forbes et al., 2006; Timbrell, 1998).

5.1 | Need for causality between disturbances and telomere length

The involvement of telomeres in health and fitness is frequently discussed in the literature, where telomeres are often suggested as a noncausal biomarker of cumulative damage in other biological structures (e.g., Young, 2018). This criticism responds to the difficulty in manipulating telomere length itself. Some experimental work has shown that the manipulation of telomere length is possible, for example via strains selected for telomere length (Muñoz-Lorente et al., 2019) or the direct manipulation of telomere length using certain drugs, often via telomerase activation (reviewed in Criscuolo et al., 2018). These manipulations are difficult in wild and wild-derived captive populations or not adequate in certain species with active telomerase expression across their life course (e.g., Au et al., 2009; Bousman et al., 2003; Kesäniemi et al., 2019). To fully understand the role of telomeres as a biomarker of anthropogenic disturbances we need, in addition to health and lifespan implications, to be able to predict the direction of the telomere dynamics (i.e., shortening or lengthening) in response to anthropogenic disturbances. This could be investigated by the manipulation of the disturbance instead, such as pollutant levels (see e.g., Parolini et al., 2016). Our literature synthesis evidences the lack of experimental studies in this respect and, despite our meta-analysis suggesting an overall small decrease in telomere length in response to disturbances (Figure 3a), the response in experimental studies is far from clear (Figure 3b,c). Some study systems present opportunities in this respect as the manipulation of anthropogenic disturbance levels can be done during early development. Moreover, when telomeres are measured in minimally invasive tissues, it could be possible to track the telomere length and performance of the experimental individuals, providing information on the long-term and fitness implications (Figure 4). Some recent studies have started to include telomere length measurements in experiments using realistic levels of organic pollutants in fish (Molbert, Agostini, et al., 2021), amphibian larvae (Cheron et al., 2022) and avian embryos (Parolini et al., 2021). Further implementation of telomere length measurements in this context, combined with longitudinal designs and fitness or performance metrics, will clearly help to evaluate the role of telomeres as a biomarker (see below and Section 5.2; Figure 4).

In some cases, manipulation of the anthropogenic disturbance is not possible, either because the work is carried out in sensitive species/populations or because of disturbance complexity (e.g., urbanization intensity). In those cases, although correlative, a longitudinal measurement of telomere length could still provide a valuable approach to the within-individual trajectory of telomere length in response to a given disturbance (Figure 4). Longitudinal designs would allow differentiation of between- and within-individual effects of the anthropogenic disturbance on telomeres and simultaneously minimize the effects of environmental conditions or differential survival (e.g., McLennan et al., 2017; Salmón et al., 2017). This approach gains further relevance in light of the benefits that telomere change might have over telomere length as a predictor of survival (Boonekamp et al., 2014; Salomons et al., 2009; Wood & Young, 2019). Therefore, coupling information from multiple telomere measurements per individual over time, together with a corresponding estimate on the degree of disturbance, will be an advancement from the common single- (or two point) based correlational studies. Nonetheless, wild organisms are often exposed to a mixture of anthropogenic disturbances, for example regarding chemical pollution (Blévin et al., 2016; Dietz et al., 2019), and the specific contribution to telomere length of each disturbance may still need to be evaluated. Spatial and temporal replications may also help to understand the relative contribution of disturbances to the telomere dynamics of wild populations. In natural conditions, the allocation of resources to different life-history traits (e.g., growth or timing of reproduction) may also partially explain the within-individual variation in telomere length in response to anthropogenic disturbances, and hence they should ideally be considered. In addition, where possible, it is important to account for different stages that characterize the life cycle of many species, i.e., early-life, adulthood or senescence (Figure 4), in the sampling design. This is of particular interest in studies of long-lived organisms or those undergoing metamorphosis, but also if we consider that the fitness implications of telomeres may be age-dependent.

5.2 | Include performance or fitness proxies

As highlighted by our systematic review, the vast majority of studies do not have information on the fitness or performance consequences of telomere length differences as a result of exposure to anthropogenic disturbances (but see, e.g., Louzon et al., 2020; Salmón et al., 2017; Sebastiano et al., 2020). This is an important point as the power of biomarker use in wildlife lies in the reliability in making inferences, based on a given measurement, about an individual's past stress exposure or of the long-term consequences of stress. We acknowledge that the lack of information on the organismal implications of telomeres in ecotoxicological and environmental studies often resides in the complexity to get such estimates in natural or wild-derived populations. Indeed, this lack of information is not exclusive but a recurrent issue in the ecological literature on telomeres. Fortunately, studies are (slowly) adding information on the link between individual quality and telomere length (Angelier et al., 2019; Cheron et al., 2021; Le Vaillant et al., 2015). For a given species, evidence for the explanatory power of telomeres is therefore a prerequisite for integrating telomere length information within an ecological context, and to implement this knowledge in conservation strategy. Therefore, new studies exploring, in anthropogenic scenarios, how a given telomere length relates to individual performance, such as foraging efficiency or postnatal growth, or to individual fitness, via proxies such as reproductive output or mortality risk, will aid our understanding of the role of telomeres as a biomarker (Figure 4).

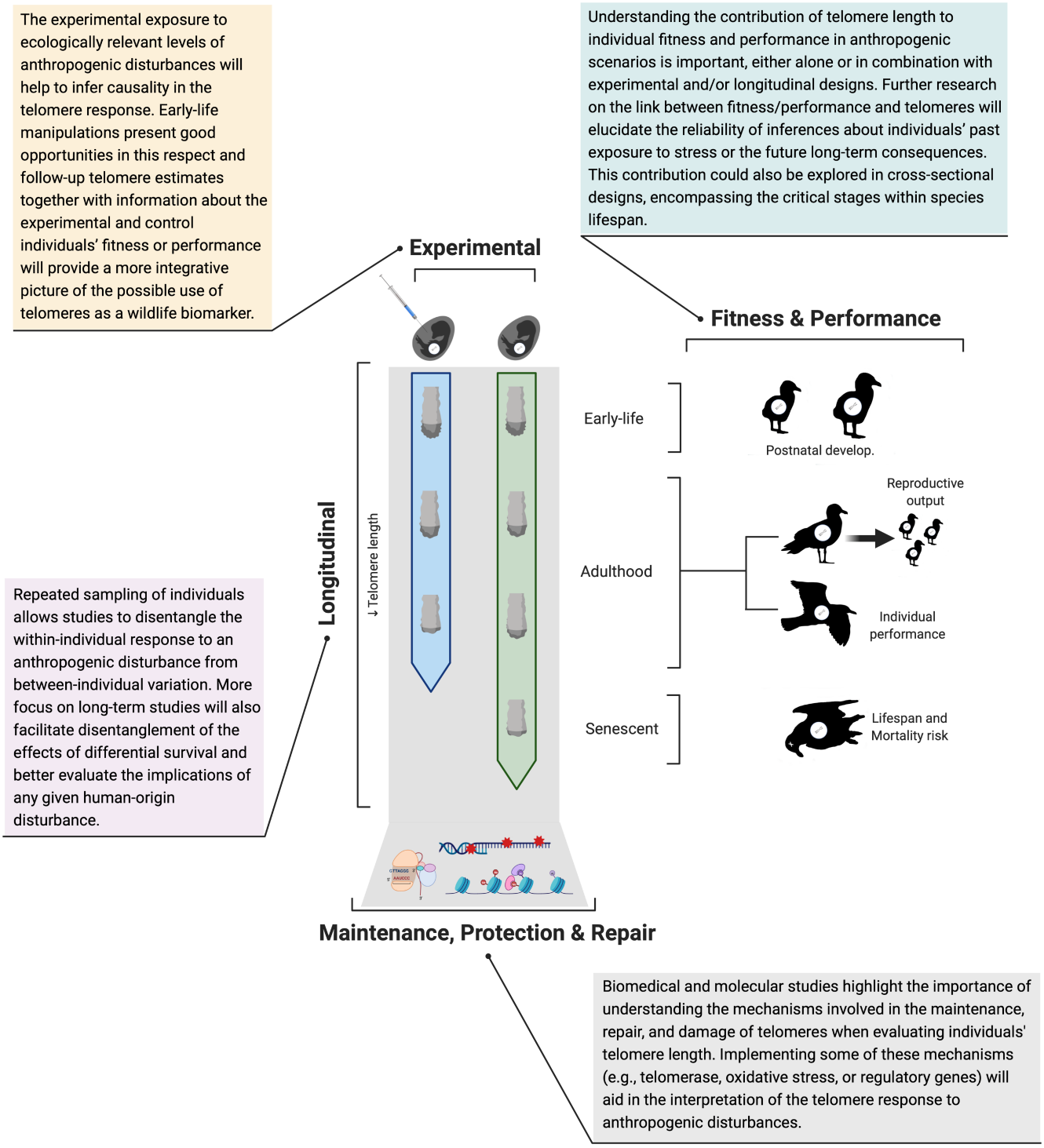

FIGURE 4 Conceptual synthesis of the key directions for future studies aiming to evaluate the telomere implications of anthropogenic disturbances on wildlife. Figure created with BioRender.com and silhouettes obtained from Phylopic

5.3 | Further considerations

Similar to other molecular markers, the use of telomeres has limitations when applied to wild organisms, such as storage of the biological material (i.e., to avoid DNA degradation, Eastwood et al., 2018; Reichert et al., 2017), or purely analytical factors (e.g., Morinha et al., 2020). Therefore, it is important to accurately validate the technique for telomere estimation in a given species (e.g., Aubert et al., 2012; Nussey et al., 2014). For instance, the telomeric motif (see Box 1 and Figure 2) can also be present within the chromosomes (i.e., interstitial telomeric sequences, ITSs), in addition to the chromosome's extremes (i.e., the telomeres *sensu stricto*). Not all the telomere measurement techniques consider these ITSs, and their number or presence may be species-specific or vary among individuals or

populations within a species (Foote et al., 2013). In addition, their biological implications at the organismal level remain unclear. Other biological characteristics, such as the change with age or the within-individual repeatability, have also been shown to be sensitive to the method employed in telomere estimation (Atema et al., 2019; Kärkkäinen et al., 2021; Remot et al., 2021). Therefore, these technical limitations could influence any inferences about past stress exposure or future long-term consequences for a given telomere length if not considered beforehand.

Furthermore, it is important to stress that an individual's telomere length represents an equilibrium between telomere loss and the activity of the telomere repair and maintenance mechanisms (see Box 1), and the latter two are rarely quantified in wildlife or wild-derived organisms (e.g., Kesäniemi et al., 2019). As discussed in Section 3, some genotoxic agents are often expected to induce telomere elongation, which is probably linked to the upregulation of some repair machinery. Therefore, in many cases it remains difficult to interpret the telomere dynamics (shortening or lengthening) without an understanding of the regulatory mechanisms' beneath. In wildlife, the observed outcome in terms of telomere length in response to anthropogenic disturbances could indicate an upregulation/downregulation of the telomere protecting mechanisms, but also just inadequate repair (i.e., direct telomere attrition). Combining telomere length estimates together with metrics of their maintenance, protection, or repair, such as telomerase or oxidative stress, will provide a step forward when evaluating the responses of wildlife to anthropogenic actions and simultaneously facilitate adequate evaluation of telomeres as a biomarker in this context (Kesäniemi et al., 2019; Matzenbacher et al., 2019; Figure 4). Moreover, the implications for individuals' health and fitness of environmentally induced telomere elongation, or lack of telomere loss, are still unknown (Sebastiano et al., 2020), and this represents a promising research avenue for future environmental, evolutionary and ecological studies (Criscuolo et al., 2018; Smith et al., 2021).

6 | CONCLUSIONS

It is increasingly acknowledged that molecular and physiological tools are useful for evaluating wildlife health and performance in response to anthropogenic disturbances. Although the implementation of telomeres in this context is relatively recent, and the number of available studies is still small, our synthesis and meta-analysis do confirm that, overall, wildlife telomere length is negatively affected by human-derived disturbances. This is a promising step towards implementing telomere assessment in an applied context. However, we have also detected some important limitations that need to be considered to definitively evaluate telomere length as a biomarker of the impact of anthropogenic disturbances on wildlife. These limitations reside in the lack of experimental studies assessing the effects, in terms of telomere length, on exposure to realistic levels of disturbance. Moreover, only a handful of studies have explored the link between telomere length and the subsequent organismal fitness and performance in anthropogenic scenarios, which makes any inference of the consequences of a given telomere length difficult. Finally, we ignore the relative importance for telomere length of the mechanisms involved in their maintenance, protection, repair or damage in response to anthropogenic stressors. We will not be able to evaluate the use of telomeres as a health and fitness biomarker in natural populations until all these aspects are thoroughly covered. Although some of the most recent research in the field has moved in a promising direction, we hope this work can serve as a steppingstone for further work in this respect.

ACKNOWLEDGEMENTS

We thank R. I. A. Stewart for comments and improvements in language and structure and A. Sánchez-Tójar and P. Capilla-Lasheras for their help with the meta-analytic models. We also thank Pierre Blévin, Pablo Sabat, Agnès Saulnier and Hannah Watson for providing data or information. P.B. was supported by a Marie-Sklodowska-Curie Individual Fellowship (797879-METAGE project). P.S. was supported by a Leverhulme Trust Research Project awarded to Professors Pat Monaghan and Colin Selman (RPG-2017-061) and a Basque Government Postdoctoral Fellowship (POS-2020-1-0007) during the writing of the study.

AUTHOR CONTRIBUTIONS

The authors contributed equally to the data compilation, analyses and writing of this article.

OPEN RESEARCH BADGES

This article has earned an Open Data Badge for making publicly available the digitally-shareable data necessary to reproduce the reported results. The data is available at the Dryad Digital Repository (https://doi.org/10.5061/dryad.p2ngf1vs8).

DATA AVAILABILITY STATEMENT

Data used in the meta-analysis are publicly available in the Dryad Digital Repository at https://doi.org/10.5061/dryad.p2ngf1vs8.

ORCID

Pablo Salmón https://orcid.org/0000-0001-9718-6611

REFERENCES

Asterisks (*) indicate references that have been only included in the systematic review (Table 1) and (**) also in the meta-analysis.

Angelier, F., Costantini, D., Blévin, P., & Chastel, O. (2018). Do glucocorticoids mediate the link between environmental conditions and telomere dynamics in wild vertebrates? A review. *General and Comparative Endocrinology*, *256*, 99–111. https://doi.org/10.1016/j.ygcen.2017.07.007

Angelier, F., Weimerskirch, H., Barbraud, C., & Chastel, O. (2019). Is telomere length a molecular marker of individual quality? Insights from a long-lived bird. *Functional Ecology*, *33*(6), 1076–1087. https://doi.org/10.1111/1365-2435.13307

Arnold, K. E., Brown, A. R., Ankley, G. T., & Sumpter, J. P. (2014). Medicating the environment: Assessing risks of pharmaceuticals to wildlife and ecosystems. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *369*(1656), 20130569. https://doi.org/10.1098/rstb.2013.0569

Asghar, M., Hasselquist, D., Hansson, B., Zehtindjiev, P., Westerdahl, H., & Bensch, S. (2015). Hidden costs of infection: Chronic malaria accelerates telomere degradation and senescence in wild birds. *Science*, *347*(6220), 436–438. https://doi.org/10.1126/science.1261121

Asghar, M., Palinauskas, V., Zaghdoudi-Allan, N., Valkiūnas, G., Mukhin, A., Platonova, E., Färnert, A., Bensch, S., & Hasselquist, D. (2016). Parallel telomere shortening in multiple body tissues owing to malaria infection. *Proceedings of the Royal Society B: Biological Sciences*, *283*(1836), https://doi.org/10.1098/rspb.2016.1184

Atema, E., Mulder, E., van Noordwijk, A. J., & Verhulst, S. (2019). Ultralong telomeres shorten with age in nestling great tits but are static in adults and mask attrition of short telomeres. *Molecular Ecology Resources*, *19*(3), 648–658. https://doi.org/10.1111/1755-0998.12996

Au, D. W. T., Mok, H. O. L., Elmore, L. W., & Holt, S. E. (2009). Japanese medaka: A new vertebrate model for studying telomere and telomerase biology. *Comparative Biochemistry and Physiology. Toxicology & Pharmacology: CBP*, *149*(2), 161–167. https://doi.org/10.1016/j.cbpc.2008.08.005

Aubert, G., Hills, M., & Lansdorp, P. M. (2012). Telomere length measurement-caveats and a critical assessment of the available technologies and tools. *Mutation Research*, *730*(1–2), 59–67. https://doi.org/10.1016/j.mrfmmm.2011.04.003

Barnes, R. P., Fouquerel, E., & Opresko, P. L. (2019). The impact of oxidative DNA damage and stress on telomere homeostasis. *Mechanisms of Ageing and Development*, *177*, 37–45. https://doi.org/10.1016/j.mad.2018.03.013

Barrett, E. L. B., Burke, T. A., Hammers, M., Komdeur, J., & Richardson, D. S. (2013). Telomere length and dynamics predict mortality in a wild longitudinal study. *Molecular Ecology*, *22*(1), 249–259. https://doi.org/10.1111/mec.12110

Bates, J. T., Fang, T., Verma, V., Zeng, L., Weber, R. J., Tolbert, P. E., Abrams, J. Y., Sarnat, S. E., Klein, M., Mulholland, J. A., & Russell, A. G. (2019). Review of acellular assays of ambient particulate matter oxidative potential: Methods and relationships with composition, sources, and health effects. *Environmental Science & Technology*, *53*(8), 4003–4019. https://doi.org/10.1021/acs.est.8b03430

Bauch, C., Becker, P. H., & Verhulst, S. (2014). Within the genome, long telomeres are more informative than short telomeres with respect to fitness components in a long-lived seabird. *Molecular Ecology*, *23*(2), 300–310. https://doi.org/10.1111/mec.12602

Beaulieu, M., & Costantini, D. (2014). Biomarkers of oxidative status: Missing tools in conservation physiology. *Conservation Physiology*, *2*(1), cou014. https://doi.org/10.1093/conphys/cou014

Bhattacharjee, P., Das, A., Giri, A. K., & Bhattacharjee, P. (2020). Epigenetic regulations in alternative telomere lengthening: Understanding the mechanistic insight in arsenic-induced skin cancer patients. *Science of the Total Environment*, *704*, 135388. https://doi.org/10.1016/j.scitotenv.2019.135388

***Biard, C., Brischoux, F., Meillère, A., Michaud, B., Nivière, M., Ruault, S., Vaugoyeau, M., & Angelier, F. (2017). Growing in cities: An urban penalty for wild birds? A study of phenotypic differences between urban and rural great tit chicks (Parus major). *Frontiers in Ecology and Evolution*, *5*, https://doi.org/10.3389/fevo.2017.00079

Blackburn, E. H. (1991). Structure and function of telomeres. *Nature*, *350*(6319), 569–573. https://doi.org/10.1038/350569a0

Blackburn, E. H., Epel, E. S., & Lin, J. (2015). Human telomere biology: A contributory and interactive factor in aging, disease risks, and protection. *Science*, *350*(6265), 1193–1198. https://doi.org/10.1126/science.aab3389

Blasco, M. A. (2007). The epigenetic regulation of mammalian telomeres. *Nature Reviews Genetics*, *8*(4), 299–309. https://doi.org/10.1038/nrg2047

***Blévin, P., Angelier, F., Tartu, S., Bustamante, P., Herzke, D., Moe, B., Bech, C., Gabrielsen, G. W., Bustnes, J. O., & Chastel, O. (2017). Perfluorinated substances and telomeres in an Arctic seabird: Cross-sectional and longitudinal approaches. *Environmental Pollution*, *230*, 360–367. https://doi.org/10.1016/j.envpol.2017.06.060

***Blévin, P., Angelier, F., Tartu, S., Ruault, S., Bustamante, P., Herzke, D., Moe, B., Bech, C., Gabrielsen, G. W., Bustnes, J. O., & Chastel, O. (2016). Exposure to oxychlordane is associated with shorter telomeres in arctic breeding kittiwakes. *Science of the Total Environment*, *563–564*, 125–130. https://doi.org/10.1016/j.scitotenv.2016.04.096

Boonekamp, J. J., Bauch, C., Mulder, E., & Verhulst, S. (2017). Does oxidative stress shorten telomeres? *Biology Letters*, *13*(5), 20170164. https://doi.org/10.1098/rsbl.2017.0164

Boonekamp, J. J., Mulder, G. A., Salomons, H. M., Dijkstra, C., & Verhulst, S. (2014). Nestling telomere shortening, but not telomere length, reflects developmental stress and predicts survival in wild birds. *Proceedings of the Royal Society B: Biological Sciences*, *281*(1785), https://doi.org/10.1098/rspb.2013.3287

Bousman, S., Schneider, G., & Shampay, J. (2003). Telomerase activity is widespread in adult somatic tissues of Xenopus. *Journal of Experimental Zoology. Part B, Molecular and Developmental Evolution*, *295*(1), 82–86. https://doi.org/10.1002/jez.b.7

Brooks, T. M., Mittermeier, R. A., da Fonseca, G. A. B., Gerlach, J., Hoffmann, M., Lamoreux, J. F., Mittermeier, C. G., Pilgrim, J. D., & Rodrigues, A. S. L. (2006). Global biodiversity conservation priorities. *Science*, *313*(5783), 58. https://doi.org/10.1126/science.1127609

Brum, F. T., Graham, C. H., Costa, G. C., Hedges, S. B., Penone, C., Radeloff, V. C., Rondinini, C., Loyola, R., & Davidson, A. D. (2017). Global priorities for conservation across multiple dimensions of mammalian diversity. *Proceedings of the National Academy of Sciences*, *114*(29), 7641. https://doi.org/10.1073/pnas.1706461114

Bryan, T. M., Englezou, A., Dalla-Pozza, L., Dunham, M. A., & Reddel, R. R. (1997). Evidence for an alternative mechanism for maintaining telomere length in human tumors and tumor-derived cell lines. *Nature Medicine*, *3*(11), 1271–1274. https://doi.org/10.1038/nm1197-1271

Burger, J., Fossi, C., McClellan-Green, P., & Orlando, E. F. (2007). Methodologies, bioindicators, and biomarkers for assessing gender-related differences in wildlife exposed to environmental chemicals. *Environmental Research*, *104*(1), 135–152. https://doi.org/10.1016/j.envres.2006.08.002

Burraco, P., Lucas, P. M., & Salmón, P. (2021). Telomeres in a spatial context: A tool for understanding ageing pattern variation in wild populations. *Ecography*. https://doi.org/10.1111/ecog.05565

Burraco, P., Orizaola, G., Monaghan, P., & Metcalfe, N. B. (2020). Climate change and ageing in ectotherms. *Global Change Biology*, *26*(10), 5371–5381. https://doi.org/10.1111/gcb.15305

Cadet, J., Courdavault, S., Ravanat, J.-L., & Douki, T. (2005). UVB and UVA radiation-mediated damage to isolated and cellular DNA. *Pure and Applied Chemistry*, *77*(6), 947–961. https://doi.org/10.1351/pac200577060947

Cai, M., Liu, Z., Yu, P., Jiao, Y., Chen, Q., Jiang, Q., & Zhao, Y. (2020). Circadian rhythm regulation of the oxidation–antioxidant balance in Daphnia pulex. *Comparative Biochemistry and Physiology Part B: Biochemistry and Molecular Biology*, *240*, 110387. https://doi.org/10.1016/j.cbpb.2019.110387

Callahan, C. L., Pavuk, M., Birnbaum, L. S., Ren, X., Olson, J. R., & Bonner, M. R. (2017). Serum polychlorinated biphenyls and leukocyte telomere length in a highly-exposed population: The Anniston Community Health Survey. *Environment International*, *108*, 212–220. https://doi.org/10.1016/j.envint.2017.08.018

Calow, P., & Forbes, V. E. (1998). How do physiological responses to stress translate into ecological and evolutionary processes? *Comparative Biochemistry and Physiology Part A: Molecular & Integrative Physiology*, *120*(1), 11–16. https://doi.org/10.1016/S1095-6433(98)10003-X

Ceballos, G., Ehrlich, P. R., & Raven, P. H. (2020). Vertebrates on the brink as indicators of biological annihilation and the sixth mass extinction. *Proceedings of the National Academy of Sciences*, *117*(24), 13596–13602. https://doi.org/10.1073/pnas.1922686117

Cesare, A. J., & Reddel, R. R. (2010). Alternative lengthening of telomeres: Models, mechanisms and implications. *Nature Reviews. Genetics*, *11*(5), 319–330. https://doi.org/10.1038/nrg2763

Chamberlain, S. A., Hovick, S. M., Dibble, C. J., Rasmussen, N. L., Van Allen, B. G., Maitner, B. S., Ahern, J. R., Bell-Dereske, L. P., Roy, C. L., Meza-Lopez, M., Carrillo, J., Siemann, E., Lajeunesse, M. J., & Whitney, K. D. (2012). Does phylogeny matter? Assessing the impact of phylogenetic information in ecological meta-analysis. *Ecology Letters*, *15*(6), 627–636. https://doi.org/10.1111/j.1461-0248.2012.01776.x

Chapman, P. M. (2002). Integrating toxicology and ecology: Putting the "eco" into ecotoxicology. *Marine Pollution Bulletin*, *44*(1), 7–15. https://doi.org/10.1016/S0025-326X(01)00253-3

Chatelain, M., Drobniak, S. M., & Szulkin, M. (2020). The association between stressors and telomeres in non-human vertebrates: A meta-analysis. *Ecology Letters*, *23*(2), 381–398. https://doi.org/10.1111/ele.13426

Cheron, M., Angelier, F., Ribout, C., & Brischoux, F. (2021). Clutch quality is related to embryonic development duration, hatchling body size and telomere length in the spined toad (Bufo spinosus). *Biological Journal of the Linnean Society*, *133*(1), 135–142. https://doi.org/10.1093/biolinnean/blab035

Cheron, M., Costantini, D., Angelier, F., Ribout, C., & Brischoux, F. (2022). Aminomethylphosphonic acid (AMPA) alters oxidative status during embryonic development in an amphibian species. *Chemosphere*, *287*, 131882. https://doi.org/10.1016/j.chemosphere.2021.131882

Cleaver, J. E., Brennan-Minnella, A. M., Swanson, R. A., Fong, K.-W., Chen, J., Chou, K.-M., Chen, Y.-W., Revet, I., & Bezrookove, V. (2014). Mitochondrial reactive oxygen species are scavenged by Cockayne syndrome B protein in human fibroblasts without nuclear DNA damage. *Proceedings of the National Academy of Sciences of the United States of America*, *111*(37), 13487–13492. https://doi.org/10.1073/pnas.1414135111

Cohen, J. (2013). *Statistical power analysis for the behavioral sciences*. Academic press.

Correia-Melo, C., Hewitt, G., & Passos, J. F. (2014). Telomeres, oxidative stress and inflammatory factors: Partners in cellular senescence? *Longevity & Healthspan*, *3*, 1. https://doi.org/10.1186/2046-2395-3-1

Criscuolo, F., Smith, S., Zahn, S., Heidinger, B. J., & Haussmann, M. F. (2018). Experimental manipulation of telomere length: Does it reveal a corner-stone role for telomerase in the natural variability of individual fitness? *Philosophical Transactions of the Royal Society B: Biological Sciences*, *373*(1741), 20160440. https://doi.org/10.1098/rstb.2016.0440

de Lange, T. (2005). Shelterin: The protein complex that shapes and safeguards human telomeres. *Genes & Development*, *19*(18), 2100–2110. https://doi.org/10.1101/gad.1346005

de Wit, C. A. (2002). An overview of brominated flame retardants in the environment. *Chemosphere*, *46*(5), 583–624. https://doi.org/10.1016/s0045-6535(01)00225-9

Debes, P. V., Visse, M., Panda, B., Ilmonen, P., & Vasemägi, A. (2016). Is telomere length a molecular marker of past thermal stress in wild fish? *Molecular Ecology*, *25*(21), 5412–5424. https://doi.org/10.1111/mec.13856

Dietz, R., Letcher, R. J., Desforges, J.-P., Eulaers, I., Sonne, C., Wilson, S., Andersen-Ranberg, E., Basu, N., Barst, B. D., Bustnes, J. O., Bytingsvik, J., Ciesielski, T. M., Drevnick, P. E., Gabrielsen, G. W., Haarr, A., Hylland, K., Jenssen, B. M., Levin, M., McKinney, M. A., … Víkingsson, G. (2019). Current state of knowledge on biological effects from contaminants on arctic wildlife and fish. *Science of the Total Environment*, *696*, 133792. https://doi.org/10.1016/j.scitotenv.2019.133792

Diffenbaugh, N. S., & Field, C. B. (2013). Changes in ecologically critical terrestrial climate conditions. *Science*, *341*(6145), 486. https://doi.org/10.1126/science.1237123

Dioni, L., Hoxha, M., Nordio, F., Bonzini, M., Tarantini, L., Albetti, B., Savarese, A., Schwartz, J., Bertazzi, P. A., Apostoli, P., Hou, L., & Baccarelli, A. (2011). Effects of short-term exposure to inhalable particulate matter on telomere length, telomerase expression, and telomerase methylation in steel workers. *Environmental Health Perspectives*, *119*(5), 622–627. https://doi.org/10.1289/ehp.1002486

***Dorado-Correa, A. M., Zollinger, S. A., Heidinger, B., & Brumm, H. (2018). Timing matters: Traffic noise accelerates telomere loss rate differently across developmental stages. *Frontiers in Zoology*, *15*(1), 29. https://doi.org/10.1186/s12983-018-0275-8

Dupoué, A., Rutschmann, A., Le Galliard, J. F., Clobert, J., Angelier, F., Marciau, C., Ruault, S., Miles, D., & Meylan, S. (2017). Shorter telomeres precede population extinction in wild lizards. *Scientific Reports*, *7*(1), 16976. https://doi.org/10.1038/s41598-017-17323-z

Duquette, C. A., Loss, S. R., & Hovick, T. J. (2021). A meta-analysis of the influence of anthropogenic noise on terrestrial wildlife communication strategies. *Journal of Applied Ecology*, *58*(6), 1112–1121. https://doi.org/10.1111/1365-2664.13880

Eastwood, J. R., Hall, M. L., Teunissen, N., Kingma, S. A., Hidalgo Aranzamendi, N., Fan, M., Roast, M., Verhulst, S., & Peters, A. (2019). Early-life telomere length predicts lifespan and lifetime reproductive success in a wild bird. *Molecular Ecology*, *28*(5), 1127–1137. https://doi.org/10.1111/mec.15002

Eastwood, J. R., Mulder, E., Verhulst, S., & Peters, A. (2018). Increasing the accuracy and precision of relative telomere length estimates by RT qPCR. *Molecular Ecology Resources*, *18*(1), 68–78. https://doi.org/10.1111/1755-0998.12711

***Eckbo, N., Le Bohec, C., Planas-Bielsa, V., Warner, N. A., Schull, Q., Herzke, D., Zahn, S., Haarr, A., Gabrielsen, G. W., & Borgå, K. (2019). Individual variability in contaminants and physiological status in a resident Arctic seabird species. *Environmental Pollution*, *249*, 191–199. https://doi.org/10.1016/j.envpol.2019.01.025

Epel, E. S., Blackburn, E. H., Lin, J., Dhabhar, F. S., Adler, N. E., Morrow, J. D., & Cawthon, R. M. (2004). Accelerated telomere shortening in response to life stress. *Proceedings of the National Academy of Sciences of the United States of America*, *101*(49), 17312–17315. https://doi.org/10.1073/pnas.0407162101

Factor-Litvak, P., & Susser, E. (2015). The importance of early life studies of telomere attrition. *Paediatric and Perinatal Epidemiology*, *29*(2), 144–145. https://doi.org/10.1111/ppe.12181

Foote, C. G., Vleck, D., & Vleck, C. M. (2013). Extent and variability of interstitial telomeric sequences and their effects on estimates of telomere length. *Molecular Ecology Resources*, *13*(3), 417–428. https://doi.org/10.1111/1755-0998.12079

Forbes, V. E., Palmqvist, A., & Bach, L. (2006). The use and misuse of biomarkers in ecotoxicology. *Environmental Toxicology and Chemistry*, *25*(1), 272–280. https://doi.org/10.1897/05-257R.1

Fumagalli, M., Rossiello, F., Clerici, M., Barozzi, S., Cittaro, D., Kaplunov, J. M., Bucci, G., Dobreva, M., Matti, V., Beausejour, C. M., Herbig, U., Longhese, M. P., & d'Adda di Fagagna, F. (2012). Telomeric DNA damage is irreparable and causes persistent DNA-damage-response activation. *Nature Cell Biology*, *14*(4), 355–365. https://doi.org/10.1038/ncb2466

Giraudeau, M., Angelier, F., & Sepp, T. (2019). Do telomeres influence pace-of-life-strategies in response to environmental conditions over a lifetime and between generations? *BioEssays*, *41*(3), e1800162. https://doi.org/10.1002/bies.201800162

Gomes, N. M. V., Shay, J. W., & Wright, W. E. (2010). Telomere biology in Metazoa. *FEBS Letters*, *584*(17), 3741–3751. https://doi.org/10.1016/j.febslet.2010.07.031

Gormally, B. M. G., & Romero, L. M. (2020). What are you actually measuring? A review of techniques that integrate the stress response on distinct time-scales. *Functional Ecology*, *34*(10), 2030–2044. https://doi.org/10.1111/1365-2435.13648

Grafen, A. (1989). The phylogenetic regression. *Philosophical Transactions of the Royal Society of London. B, Biological Sciences*, *326*(1233), 119–157.

Greider, C. W., & Blackburn, E. H. (1989). A telomeric sequence in the RNA of Tetrahymena telomerase required for telomere repeat synthesis. *Nature*, *337*(6205), 331–337. https://doi.org/10.1038/337331a0

Griffith, J. D., Comeau, L., Rosenfield, S., Stansel, R. M., Bianchi, A., Moss, H., & de Lange, T. (1999). Mammalian telomeres end in a large duplex loop. *Cell*, *97*(4), 503–514. https://doi.org/10.1016/S0092-8674(00)80760-6

***Grunst, A. S., Grunst, M. L., Bervoets, L., Pinxten, R., & Eens, M. (2020). Proximity to roads, but not exposure to metal pollution, is associated with accelerated developmental telomere shortening in nestling great tits. *Environmental Pollution*, *256*, 113373. https://doi.org/10.1016/j.envpol.2019.113373

***Grunst, M. L., Grunst, A. S., Pinxten, R., & Eens, M. (2020). Anthropogenic noise is associated with telomere length and carotenoid-based coloration in free-living nestling songbirds. *Environmental Pollution*, *260*, 114032. https://doi.org/10.1016/j.envpol.2020.114032

***Grunst, M. L., Raap, T., Grunst, A. S., Pinxten, R., & Eens, M. (2019). Artificial light at night does not affect telomere shortening in a developing free-living songbird: A field experiment: Artificial light at night and telomere dynamics. *Science of the Total Environment*, *662*, 266–275. https://doi.org/10.1016/j.scitotenv.2018.12.469

Gutiérrez-Castillo, M. E., Roubicek, D. A., Cebrián-García, M. E., De Vizcaya-Ruíz, A., Sordo-Cedeño, M., & Ostrosky-Wegman, P. (2006). Effect of chemical composition on the induction of DNA damage by urban airborne particulate matter. *Environmental and Molecular Mutagenesis*, *47*(3), 199–211. https://doi.org/10.1002/em.20186

***Han, X., Zhang, Q., Fan, L., Yang, L., & Liu, Z. (2018). The influence of oxygen on the development of *Nanorana parkeri* tadpoles. *Asian Herpetological Research*, *9*(1), 6.

Harley, C. B., Futcher, A. B., & Greider, C. W. (1990). Telomeres shorten during ageing of human fibroblasts. *Nature*, *345*(6274), 458–460. https://doi.org/10.1038/345458a0

Harrison, X. A. (2014). Using observation-level random effects to model overdispersion in count data in ecology and evolution. *PeerJ*, *2*, e616. https://doi.org/10.7717/peerj.616

Hartwig, A. (2010). Mechanisms in cadmium-induced carcinogenicity: Recent insights. *BioMetals*, *23*(5), 951–960. https://doi.org/10.1007/s10534-010-9330-4

Haussmann, M. F., & Vleck, C. M. (2002). Telomere length provides a new technique for aging animals. *Oecologia*, *130*(3), 325–328. https://doi.org/10.1007/s00442-001-0827-y

Heidinger, B. J., Blount, J. D., Boner, W., Griffiths, K., Metcalfe, N. B., & Monaghan, P. (2012). Telomere length in early life predicts lifespan. *Proceedings of the National Academy of Sciences of the United States of America*, *109*(5), 1743–1748. https://doi.org/10.1073/pnas.1113306109

Hendry, A. P., Gotanda, K. M., & Svensson, E. I. (2017). Human influences on evolution, and the ecological and societal consequences. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *372*(1712), 20160028. https://doi.org/10.1098/rstb.2016.0028

Higgins, J. P. T., Thompson, S. G., Deeks, J. J., & Altman, D. G. (2003). Measuring Inconsistency in meta-analyses. *BMJ*, *327*(7414), 557–560. https://doi.org/10.1136/bmj.327.7414.557

Hinchliff, C. E., Smith, S. A., Allman, J. F., Burleigh, J. G., Chaudhary, R., Coghill, L. M., Crandall, K. A., Deng, J., Drew, B. T., Gazis, R., Gude, K., Hibbett, D. S., Katz, L. A., Laughinghouse, H. D., McTavish, E. J., Midford, P. E., Owen, C. L., Ree, R. H., Rees, J. A., … Cranston, K. A. (2015). Synthesis of phylogeny and taxonomy into a comprehensive tree of life. *Proceedings of the National Academy of Sciences*, *112*(41), 12764–12769. https://doi.org/10.1073/pnas.1423041112

Hochella, M. F., Mogk, D. W., Ranville, J., Allen, I. C., Luther, G. W., Marr, L. C., Yang, Y. (2019). Natural, incidental, and engineered nanomaterials and their impacts on the Earth system. . *Science*, *363*(6434). https://doi.org/10.1126/science.aau8299

Hoffmann, S., Spitkovsky, D., Radicella, J. P., Epe, B., & Wiesner, R. J. (2004). Reactive oxygen species derived from the mitochondrial respiratory chain are not responsible for the basal levels of oxidative base modifications observed in nuclear DNA of Mammalian cells. *Free Radical Biology & Medicine*, *36*(6), 765–773. https://doi.org/10.1016/j.freeradbiomed.2003.12.019

Huang, H., Wang, Q., He, X., Wu, Y., & Xu, C. (2019). Association between polyfluoroalkyl chemical concentrations and leucocyte telomere length in US adults. *Science of the Total Environment*, *653*, 547–553. https://doi.org/10.1016/j.scitotenv.2018.10.400

Huggett, R. J. (2018). *Biomarkers: Biochemical, physiological, and histological markers of anthropogenic stress*. CRC Press.

***Ibáñez-Álamo, J. D., Pineda-Pampliega, J., Thomson, R. L., Aguirre, J. I., Díez-Fernández, A., Faivre, B., Figuerola, J., & Verhulst, S. (2018). Urban blackbirds have shorter telomeres. *Biology Letters*, *14*(3), 20180083. https://doi.org/10.1098/rsbl.2018.0083

***Injaian, A. S., Gonzalez-Gomez, P. L., Taff, C. C., Bird, A. K., Ziur, A. D., Patricelli, G. L., Haussmann, M. F., & Wingfield, J. C. (2019). Traffic noise exposure alters nestling physiology and telomere attrition through direct, but not maternal, effects in a free-living bird. *General and Comparative Endocrinology*, *276*, 14–21. https://doi.org/10.1016/j.ygcen.2019.02.017

Jacobs, J. J. L., & de Lange, T. (2004). Significant Role for p16INK4a in p53-Independent Telomere-Directed Senescence. *Current Biology*, *14*(24), 2302–2308. https://doi.org/10.1016/j.cub.2004.12.025

Jimenez Villarreal, J., Murillo Ortiz, B., Martinez Garza, S., Rivas Armendáriz, D. I., Boone Villa, V. D., Carranza Rosales, P., Betancourt Martínez, N. D., Delgado Aguirre, H., & Morán Martínez, J. (2018). Telomere length analysis in residents of a community exposed to arsenic. *Journal of Biochemical and Molecular Toxicology*, *33*(1), e22230. https://doi.org/10.1002/jbt.22230

Kärkkäinen, T., Bize, P., & Stier, A. (2020). Correlation in telomere lengths between feathers and blood cells in pied flycatchers. *Journal of Avian Biology*, *51*(4). https://doi.org/10.1111/jav.02300

Kärkkäinen, T., Briga, M., Laaksonen, T., & Stier, A. (2021). Within-individual repeatability in telomere length: A meta-analysis in nonmammalian vertebrates. *Molecular Ecology*. https://doi.org/10.1111/mec.16155

***Kesäniemi, J., Lavrinienko, A., Tukalenko, E., Boratyński, Z., Kivisaari, K., Mappes, T., Milinevsky, G., Møller, A. P., Mousseau, T. A., & Watts, P. C. (2019). Exposure to environmental radionuclides associates with tissue-specific impacts on telomerase expression and telomere length. *Scientific Reports*, *9*(1), 850. https://doi.org/10.1038/s41598-018-37164-8

*Kirby, R., Johnson, H. E., Alldredge, M. W., & Pauli, J. N. (2019). The cascading effects of human food on hibernation and cellular aging in free-ranging black bears. *Scientific Reports*, *9*(1), 2197. https://doi.org/10.1038/s41598-019-38937-5

Koricheva, J., Gurevitch, J., & Mengersen, K. (2013). *Handbook of meta-analysis in ecology and evolution*. Princeton University Press.

Koricheva, J., & Kulinskaya, E. (2019). Temporal instability of evidence base: A threat to policy making? *Trends in Ecology & Evolution*, *34*(10), 895–902. https://doi.org/10.1016/j.tree.2019.05.006

Kruk, P. A., Rampino, N. J., & Bohr, V. A. (1995). DNA damage and repair in telomeres: Relation to aging. *Proceedings of the National Academy of Sciences of the United States of America*, *92*(1), 258–262. https://doi.org/10.1073/pnas.92.1.258

Le Vaillant, M., Viblanc, V. A., Saraux, C., Le Bohec, C., Le Maho, Y., Kato, A., Criscuolo, F., & Ropert-Coudert, Y. (2015). Telomere length reflects individual quality in free-living adult king penguins. *Polar Biology*, *38*(12), 2059–2067. https://doi.org/10.1007/s00300-015-1766-0

Liu, J., Tan, Y., Song, E., & Song, Y. (2020). A critical review of polychlorinated biphenyls metabolism, metabolites, and their correlation with oxidative stress. *Chemical Research in Toxicology*, *33*(8), 2022–2042. https://doi.org/10.1021/acs.chemrestox.0c00078

Liu, Y., Wang, J., Huang, Z., Liang, J., Xia, Q., Xia, Q., & Liu, X. (2021). Environmental pollutants exposure: A potential contributor for aging and age-related diseases. *Environmental Toxicology and Pharmacology*, *83*, 103575. https://doi.org/10.1016/j.etap.2020.103575

Louzon, M., Coeurdassier, M., Gimbert, F., Pauget, B., & de Vaufleury, A. (2019). Telomere dynamic in humans and animals: Review and perspectives in environmental toxicology. *Environment International*, *131*, 105025. https://doi.org/10.1016/j.envint.2019.105025

***Louzon, M., Zahn, S., Capelli, N., Massemin, S., Coeurdassier, M., Pauget, B., Gimbert, F., & de Vaufleury, A. (2020). Impact of ageing and soil contaminants on telomere length in the land snail. *Ecotoxicology and Environmental Safety*, *201*, 110766. https://doi.org/10.1016/j.ecoenv.2020.110766

Luke, B., & Lingner, J. (2009). TERRA: Telomeric repeat-containing RNA. *The EMBO Journal*, *28*(17), 2503–2510. https://doi.org/10.1038/emboj.2009.166

Lustig, A., Shterev, I., Geyer, S., Shi, A., Hu, Y., Morishita, Y., Nagamura, H., Sasaki, K., Maki, M., Hayashi, I., Furukawa, K., Yoshida, K., Kajimura, J., Kyoizumi, S., Kusunoki, Y., Ohishi, W., Nakachi, K., Weng, N.-P., & Hayashi, T. (2016). Long term effects of radiation exposure on telomere lengths of leukocytes and its associated biomarkers among atomic-bomb survivors. *Oncotarget*, *7*(26), 38988–38998. https://doi.org/10.18632/oncotarget.8801

Lv, Y.-Z., Yao, L., Wang, L., Liu, W.-R., Zhao, J.-L., He, L.-Y., & Ying, G.-G. (2019). Bioaccumulation, metabolism, and risk assessment of phenolic endocrine disrupting chemicals in specific tissues of wild fish. *Chemosphere*, *226*, 607–615. https://doi.org/10.1016/j.chemosphere.2019.03.187

Madliger, C. L., Love, O. P., Hultine, K. R., & Cooke, S. J. (2018). The conservation physiology toolbox: Status and opportunities. *Conservation Physiology*, *6*(coy029). https://doi.org/10.1093/conphys/coy029

Madliger, C. L., Semeniuk, C. A. D., Harris, C. M., & Love, O. P. (2015). Assessing baseline stress physiology as an integrator of environmental quality in a wild avian population: Implications for use as a conservation biomarker. *Biological Conservation*, *192*, 409–417. https://doi.org/10.1016/j.biocon.2015.10.021

Martens, D. S., Cox, B., Janssen, B. G., Clemente, D. B. P., Gasparrini, A., Vanpoucke, C., Lefebvre, W., Roels, H. A., Plusquin, M., & Nawrot, T. S. (2017). Prenatal air pollution and newborns' predisposition to accelerated biological aging. *JAMA Pediatrics*, *171*(12), 1160–1167. https://doi.org/10.1001/jamapediatrics.2017.3024

Mather, K. A., Jorm, A. F., Parslow, R. A., & Christensen, H. (2011). Is telomere length a biomarker of aging? A review. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, *66*(2), 202–213. https://doi.org/10.1093/gerona/glq180

***Matzenbacher, C. A., Da Silva, J., Garcia, A. L. H., Cappetta, M., & de Freitas, T. R. O. (2019). Anthropogenic effects on natural mammalian populations: Correlation between telomere length and coal exposure. *Scientific Reports*, *9*(1), 6325. https://doi.org/10.1038/s41598-019-42804-8

McLennan, D., Armstrong, J. D., Stewart, D. C., Mckelvey, S., Boner, W., Monaghan, P., & Metcalfe, N. B. (2017). Shorter juvenile telomere length is associated with higher survival to spawning in migratory Atlantic salmon. *Functional Ecology*, *31*(11), 2070–2079. https://doi.org/10.1111/1365-2435.12939

***Meillère, A., Brischoux, F., Ribout, C., & Angelier, F. (2015). Traffic noise exposure affects telomere length in nestling house sparrows. *Biology Letters*, *11*(9), 20150559. https://doi.org/10.1098/rsbl.2015.0559

Meyer, J. N., Leung, M. C. K., Rooney, J. P., Sendoel, A., Hengartner, M. O., Kisby, G. E., & Bess, A. S. (2013). Mitochondria as a target of environmental toxicants. *Toxicological Sciences*, *134*(1), 1–17. https://doi.org/10.1093/toxsci/kft102

Michonneau, F., Brown, J. W., & Winter, D. J. (2016). rotl: An R package to interact with the Open Tree of Life data. *Methods in Ecology and Evolution*, *7*(12), 1476–1481. https://doi.org/10.1111/2041-210X.12593

Molbert, N., Agostini, S., Alliot, F., Angelier, F., Biard, C., Decencière, B., Leroux-Coyau, M., Millot, A., Ribout, C., & Goutte, A. (2021). Parasitism reduces oxidative stress of fish host experimentally exposed to PAHs. *Ecotoxicology and Environmental Safety*, *219*, 112322. https://doi.org/10.1016/j.ecoenv.2021.112322

***Molbert, N., Angelier, F., Alliot, F., Ribout, C., & Goutte, A. (2021). Fish from urban rivers and with high pollutant levels have shorter telomeres. *Biology Letters*, *17*(1), 20200819. https://doi.org/10.1098/rsbl.2020.0819

Moll, R. J., Cepek, J. D., Lorch, P. D., Dennis, P. M., Tans, E., Robison, T., Millspaugh, J. J., & Montgomery, R. A. (2019). What does urbanization actually mean? A framework for urban metrics in wildlife research. *Journal of Applied Ecology*, *56*(5), 1289–1300. https://doi.org/10.1111/1365-2664.13358

Morinha, F., Magalhães, P., & Blanco, G. (2020). Different qPCR master mixes influence telomere primer binding within and between bird species. *Journal of Avian Biology*, *51*(2). https://doi.org/10.1111/jav.02352

Muñoz-Lorente, M. A., Cano-Martin, A. C., & Blasco, M. A. (2019). Mice with hyper-long telomeres show less metabolic aging and longer lifespans. *Nature Communications*, *10*(1), 1–14. https://doi.org/10.1038/s41467-019-12664-x

Münzel, T., Sørensen, M., & Daiber, A. (2021). Transportation noise pollution and cardiovascular disease. *Nature Reviews Cardiology*, *18*(9), 619–636. https://doi.org/10.1038/s41569-021-00532-5

Nakagawa, S., & Cuthill, I. C. (2007). Effect size, confidence interval and statistical significance: A practical guide for biologists. *Biological Reviews*, *82*(4), 591–605. https://doi.org/10.1111/j.1469-185X.2007.00027.x

Nakagawa, S., Gemmell, N. J., & Burke, T. (2004). Measuring vertebrate telomeres: Applications and limitations. *Molecular Ecology*, *13*(9), 2523–2533. https://doi.org/10.1111/j.1365-294X.2004.02291.x

Nakagawa, S., Lagisz, M., Jennions, M. D., Koricheva, J., Noble, D. W. A., Parker, T. H., Sánchez-Tójar, A., Yang, Y., & O'Dea, R. E. (2021). Methods for testing publication bias in ecological and evolutionary meta-analyses. *Methods in Ecology and Evolution*, *13*(1), 4–21. https://doi.org/10.1111/2041-210X.13724

Nakagawa, S., Lagisz, M., O'Dea, R. E., Rutkowska, J., Yang, Y., Noble, D. W. A., & Senior, A. M. (2021). The orchard plot: Cultivating a forest plot for use in ecology, evolution, and beyond. *Research Synthesis Methods*, *12*(1), 4–12. https://doi.org/10.1002/jrsm.1424

Nakagawa, S., & Santos, E. S. A. (2012). Methodological issues and advances in biological meta-analysis. *Evolutionary Ecology*, *26*(5), 1253–1274. https://doi.org/10.1007/s10682-012-9555-5

Nakagawa, S., & Schielzeth, H. (2013). A general and simple method for obtaining R2 from generalized linear mixed-effects models. *Methods in Ecology and Evolution*, *4*(2), 133–142. https://doi.org/10.1111/j.2041-210x.2012.00261.x

Nussey, D. H., Baird, D., Barrett, E., Boner, W., Fairlie, J., Gemmell, N., Hartmann, N., Horn, T., Haussmann, M., Olsson, M., Turbill, C., Verhulst, S., Zahn, S., & Monaghan, P. (2014). Measuring telomere

length and telomere dynamics in evolutionary biology and ecology. *Methods in Ecology and Evolution*, *5*(4), 299–310. https://doi.org/10.1111/2041-210X.12161

Ohmer, M. E. B., Costantini, D., Czirják, G. Á., Downs, C. J., Ferguson, L. V., Flies, A., Franklin, C. E., Kayigwe, A. N., Knutie, S., Richards-Zawacki, C. L., & Cramp, R. L. (2021). Applied ecoimmunology: Using immunological tools to improve conservation efforts in a changing world. *Conservation. Physiology*, *9*(1), coab074. https://doi.org/10.1093/conphys/coab074

Oikawa, S., Tada-Oikawa, S., & Kawanishi, S. (2001). Site-specific DNA damage at the GGG sequence by UVA involves acceleration of telomere shortening. *Biochemistry*, *40*(15), 4763–4768. https://doi.org/10.1021/bi002721g

Olsson, M., Wapstra, E., & Friesen, C. (2018). Ectothermic telomeres: It's time they came in from the cold. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *373*(1741), 20160449. https://doi.org/10.1098/rstb.2016.0449

*Uuyang, J. Q., Jong, M., Grunsven, R. H. A., Matson, K. D., Haussmann, M. F., Meerlo, P., Visser, M. E., & Spoelstra, K. (2017). Restless roosts: Light pollution affects behavior, sleep, and physiology in a free-living songbird. *Global Change Biology*, *23*(11), 4987–4994. https://doi.org/10.1111/gcb.13756

Paradis, E., & Schliep, K. (2019). ape 5.0: An environment for modern phylogenetics and evolutionary analyses in R. *Bioinformatics*, *35*(3), 526–528.

Parolini, M., Colombo, G., Valsecchi, S., Mazzoni, M., Possenti, C. D., Caprioli, M., Dalle-Donne, I., Milzani, A., Saino, N., & Rubolini, D. (2016). Potential toxicity of environmentally relevant perfluorooctane sulfonate (PFOS) concentrations to yellow-legged gull Larus michahellis embryos. *Environmental Science and Pollution Research*, *23*(1), 426–437. https://doi.org/10.1007/s11356-015-5248-2

Parolini, M., De Felice, B., Mondellini, S., Caprioli, M., Possenti, C. D., & Rubolini, D. (2021). Prenatal exposure to triclosan induced brain telomere shortening in a wild bird species. *Environmental Toxicology and Pharmacology*, *87*, 103718. https://doi.org/10.1016/j.etap.2021.103718

Peixoto, M. S., de Oliveira Galvão, M. F., & Batistuzzo de Medeiros, S. R. (2017). Cell death pathways of particulate matter toxicity. *Chemosphere*, *188*, 32–48. https://doi.org/10.1016/j.chemosphere.2017.08.076

Pepper, G. V., Bateson, M., & Nettle, D. (2018). Telomeres as integrative markers of exposure to stress and adversity: A systematic review and meta-analysis. *Royal Society Open Science*, *5*(8), 180744. https://doi.org/10.1098/rsos.180744

***Petitjean, Q., Jean, S., Côte, J., Larcher, T., Angelier, F., Ribout, C., Perrault, A., Laffaille, P., & Jacquin, L. (2020). Direct and indirect effects of multiple environmental stressors on fish health in human-altered rivers. *Science of the Total Environment*, *742*, 140657. https://doi.org/10.1016/j.scitotenv.2020.140657

Power, M. L., Power, S., Bertelsen, M. F., Jones, G., & Teeling, E. C. (2021). Wing: A suitable nonlethal tissue type for repeatable and rapid telomere length estimates in bats. *Molecular Ecology Resources*, *21*(2), 421–432. https://doi.org/10.1111/1755-0998.13276

*Powolny, T., Bassin, N., Crini, N., Fourel, I., Morin, C., Pottinger, T. G., Massemin, S., Zahn, S., & Coeurdassier, M. (2020). Corticosterone mediates telomere length in raptor chicks exposed to chemical mixture. *Science of the Total Environment*, *706*, 135083. https://doi.org/10.1016/j.scitotenv.2019.135083

Qian, W., Kumar, N., Roginskaya, V., Fouquerel, E., Opresko, P. L., Shiva, S., Watkins, S. C., Kolodieznyi, D., Bruchez, M. P., & Van Houten, B. (2019). Chemoptogenetic damage to mitochondria causes rapid telomere dysfunction. *Proceedings of the National Academy of Sciences*, *116*(37), 18435–18444. https://doi.org/10.1073/pnas.1910574116

R Core Team (2018). *R: A language and environment for statistical computing*. R Foundation for Statistical Computing.

Reichert, S., Criscuolo, F., Verinaud, E., Zahn, S., & Massemin, S. (2013). Telomere length correlations among somatic tissues in adult zebra finches. *PLoS One*, *8*(12), 1–7. https://doi.org/10.1371/journal.pone.0081496

Reichert, S., Froy, H., Boner, W., Burg, T. M., Daunt, F., Gillespie, R., Griffiths, K., Lewis, S., Phillips, R. A., Nussey, D. H., & Monaghan, P. (2017). Telomere length measurement by qPCR in birds is affected by storage method of blood samples. *Oecologia*, *184*(2), 341–350. https://doi.org/10.1007/s00442-017-3887-3

Reichert, S., & Stier, A. (2017). Does oxidative stress shorten telomeres in vivo? A review. *Biology Letters*, *13*(12). https://doi.org/10.1098/rsbl.2017.0463

Remot, F., Ronget, V., Froy, H., Rey, B., Gaillard, J.-M., Nussey, D. H., & Lemaitre, J.-F. (2021). Decline in telomere length with increasing age across nonhuman vertebrates: A meta-analysis. *Molecular Ecology*. https://doi.org/10.1111/mec.16145

Richter, T., & von Zglinicki, T. (2007). A continuous correlation between oxidative stress and telomere shortening in fibroblasts. *Experimental Gerontology*, *42*(11), 1039–1042. https://doi.org/10.1016/j.exger.2007.08.005

Rochette, P. J., & Brash, D. E. (2010). Human telomeres are hypersensitive to UV-Induced DNA damage and refractory to repair. *PLOS Genetics*, *6*(4), e1000926. https://doi.org/10.1371/journal.pgen.1000926

Rohatgi, A. (2021). *Webplotdigitizer: Version 4.5*. https://automeris.io/WebPlotDigitizer

Rollings, N., Friesen, C. R., Whittington, C. M., Johansson, R., Shine, R., & Olsson, M. (2019). Sex- And tissue-specific differences in telomere length in a reptile. *Ecology and Evolution*, *9*(11), 6211–6219. https://doi.org/10.1002/ece3.5164

Saaristo, M., Brodin, T., Balshine, S., Bertram, M. G., Brooks, B. W., Ehlman, S. M., McCallum, E. S., Sih, A., Sundin, J., Wong, B. B. M., & Arnold, K. E. (2018). Direct and indirect effects of chemical contaminants on the behaviour, ecology and evolution of wildlife. *Proceedings of the Royal Society B: Biological Sciences*, *285*(1885), 20181297. https://doi.org/10.1098/rspb.2018.1297

***Sabat, P., Bozinovic, F., Contreras-Ramos, C., Nespolo, R. F., Newsome, S. D., Quirici, V., Maldonado, K., Peña-Villalobos, I., Ramirez-Otarola, N., & Sanchez-Hernandez, J. C. (2019). The interplay between ambient temperature and salt intake affects oxidative status and immune responses in a ubiquitous Neotropical passerine, the rufous-collared sparrow. *Comparative Biochemistry and Physiology Part A: Molecular & Integrative Physiology*, *234*, 50–59. https://doi.org/10.1016/j.cbpa.2019.04.016

***Salmón, P., Nilsson, J. F., Nord, A., Bensch, S., & Isaksson, C. (2016). Urban environment shortens telomere length in nestling great tits, Parus major. *Biology Letters*, *12*(6), https://doi.org/10.1098/rsbl.2016.0155

***Salmón, P., Nilsson, J. F., Watson, H., Bensch, S., & Isaksson, C. (2017). Selective disappearance of great tits with short telomeres in urban areas. *Proceedings of the Royal Society B: Biological Sciences*, *284*(1862), https://doi.org/10.1098/rspb.2017.1349

Salomons, H. M., Mulder, G. A., Van De Zande, L., Haussmann, M. F., Linskens, M. H. K., & Verhulst, S. (2009). Telomere shortening and survival in free-living corvids. *Proceedings of the Royal Society B: Biological Sciences*, *276*(1670), 3157–3165. https://doi.org/10.1098/rspb.2009.0517

***Sánchez-Virosta, P., Espín, S., Ruiz, S., Panda, B., Ilmonen, P., Schultz, S. L., Karouna-Renier, N., García-Fernández, A. J., & Eeva, T. (2020). Arsenic-related oxidative stress in experimentally-dosed wild great tit nestlings. *Environmental Pollution*, *259*, 113813. https://doi.org/10.1016/j.envpol.2019.113813

Sánchez-Tójar, A., Lagisz, M., Moran, N. P., Nakagawa, S., Noble, D. W. A., & Reinhold, K. (2020). The jury is still out regarding the generality of adaptive 'transgenerational' effects. *Ecology Letters*, *23*(11), 1715–1718. https://doi.org/10.1111/ele.13479

Sanders, D., Frago, E., Kehoe, R., Patterson, C., & Gaston, K. J. (2021). A meta-analysis of biological impacts of artificial light at night. *Nature Ecology & Evolution*, *5*(1), 74–81. https://doi.org/10.1038/s41559-020-01322-x

***Sapozhnikova, Y. P., Koroleva, A. G., Yakhnenko, V. M., Tyagun, M. L., Glyzina, O. Y., Coffin, A. B., & Sukhanova, L. V. (2020). Molecular and cellular responses to long-term sound exposure in peled (*Coregonus peled*). *The Journal of the Acoustical Society of America*, *148*(2), 895. https://doi.org/10.1121/10.0001674

Sardon Puig, L., Valera-Alberni, M., Cantó, C., & Pillon, N. J. (2018). Circadian rhythms and mitochondria: Connecting the dots. *Frontiers in Genetics*, *9*, 452. https://doi.org/10.3389/fgene.2018.00452

***Saulnier, A., Bleu, J., Boos, A., El Masoudi, I., Ronot, P., Zahn, S., Del Nero, M., & Massemin, S. (2020). Consequences of trace metal cocktail exposure in zebra finch (*Taeniopygia guttata*) and effect of calcium supplementation. *Ecotoxicology and Environmental Safety*, *193*, 110357. https://doi.org/10.1016/j.ecoenv.2020.110357

***Scholten, B. D., Beard, A. R., Choi, H., Baker, D. M., Caulfield, M. E., & Proppe, D. S. (2020). Short-term exposure to unmanned aerial vehicles does not alter stress responses in breeding tree swallows. *Conservation Physiology*, *8*(coaa080). https://doi.org/10.1093/conphys/coaa080

***Sebastiano, M., Angelier, F., Blévin, P., Ribout, C., Sagerup, K., Descamps, S., Herzke, D., Moe, B., Barbraud, C., Bustnes, J. O., Gabrielsen, G. W., & Chastel, O. (2020). Exposure to PFAS is associated with telomere length dynamics and demographic responses of an arctic top predator. *Environmental Science & Technology*, *54*(16), 10217–10226. https://doi.org/10.1021/acs.est.0c03099

Senior, A. M., Grueber, C. E., Kamiya, T., Lagisz, M., O'Dwyer, K., Santos, E. S. A., & Nakagawa, S. (2016). Heterogeneity in ecological and evolutionary meta-analyses: Its magnitude and implications. *Ecology*, *97*(12), 3293–3299. https://doi.org/10.1002/ecy.1591

Senthilkumar, P. K., Klingelhutz, A. J., Jacobus, J. A., Lehmler, H., Robertson, L. W., & Ludewig, G. (2011). Airborne polychlorinated biphenyls (PCBs) reduce telomerase activity and shorten telomere length in immortal human skin keratinocytes (HaCat). *Toxicology Letters*, *204*(1), 64–70. https://doi.org/10.1016/j.toxlet.2011.04.012

Shay, J. W. (2016). Role of telomeres and telomerase in aging and cancer. *Cancer Discovery*, *6*(6), 584–593. https://doi.org/10.1158/2159-8290.CD-16-0062

Shin, J.-Y., Choi, Y. Y., Jeon, H.-S., Hwang, J.-H., Kim, S.-A., Kang, J.-H., Chang, Y.-S., Jacobs, D. R., Park, J. Y., & Lee, D.-H. (2010). Low-dose persistent organic pollutants increased telomere length in peripheral leukocytes of healthy Koreans. *Mutagenesis*, *25*(5), 511–516. https://doi.org/10.1093/mutage/geq035

Shoeb, M., Meier, H. C. S., & Antonini, J. M. (2020). Telomeres in toxicology: Occupational health. *Pharmacology & Therapeutics*, *220*, 107742. https://doi.org/10.1016/j.pharmthera.2020.107742

Sishc, B. J., Nelson, C. B., McKenna, M. J., Battaglia, C. L., Herndon, A., Idate, R., Liber, H. L., & Bailey, S. M. (2015). Telomeres and Telomerase in the Radiation Response: Implications for Instability, Reprograming, and Carcinogenesis. *Front Oncology*, *24*(5), 257. https://doi.org/10.3389/fonc.2015.00257

***Sletten, S., Bourgeon, S., Bårdsen, B.-J., Herzke, D., Criscuolo, F., Massemin, S., Zahn, S., Johnsen, T. V., & Bustnes, J. O. (2016). Organohalogenated contaminants in white-tailed eagle (*Haliaeetus albicilla*) nestlings: An assessment of relationships to immunoglobulin levels, telomeres and oxidative stress. *Science of the Total Environment*, *539*, 337–349. https://doi.org/10.1016/j.scitotenv.2015.08.123

Smith, S., Hoelzl, F., Zahn, S., & Criscuolo, F. (2021). Telomerase activity in ecological studies: What are its consequences for individual physiology and is there evidence for effects and trade-offs in wild populations. *Molecular Ecology*. https://doi.org/10.1111/mec.16233

***Stauffer, J., Panda, B., Eeva, T., Rainio, M., & Ilmonen, P. (2017). Telomere damage and redox status alterations in free-living passerines exposed to metals. *Science of the Total Environment*, *575*, 841–848. https://doi.org/10.1016/j.scitotenv.2016.09.131

Sudyka, J., Arct, A., Drobniak, S., Dubiec, A., Gustafsson, L., & Cichoń, M. (2014). Experimentally increased reproductive effort alters telomere length in the blue tit (*Cyanistes caeruleus*). *Journal of Evolutionary Biology*, *27*(10), 2258–2264. https://doi.org/10.1111/jeb.12479

Timbrell, J. A. (1998). Biomarkers in toxicology. *Toxicology*, *129*(1), 1–12. https://doi.org/10.1016/s0300-483x(98)00058-4

Turbill, C., Ruf, T., Smith, S., & Bieber, C. (2013). Seasonal variation in telomere length of a hibernating rodent. *Biology Letters*, *9*(2), 20121095. https://doi.org/10.1098/rsbl.2012.1095

Victorelli, S., & Passos, J. F. (2017). Telomeres and cell senescence—Size matters not. *EBioMedicine*, *21*, 14–20. https://doi.org/10.1016/j.ebiom.2017.03.027

Viechtbauer, W. (2010). Conducting Meta-Analyses in R with the metafor Package. *Journal of Statistical Software*, *36*, 1–48. https://doi.org/10.18637/jss.v036.i03

Von Zglinicki, T. (2002). Oxidative stress shortens telomeres. *Trends in Biochemical Sciences*, *27*(7), 339–344. https://doi.org/10.1016/S0968-0004(02)02110-2

Vriens, A., Nawrot, T. S., Janssen, B. G., Baeyens, W., Bruckers, L., Covaci, A., De Craemer, S., De Henauw, S., Den Hond, E., Loots, I., Nelen, V., Schettgen, T., Schoeters, G., Martens, D. S., & Plusquin, M. (2019). Exposure to environmental pollutants and their association with biomarkers of aging: A multipollutant approach. *Environmental Science & Technology*, *53*(10), 5966–5976. https://doi.org/10.1021/acs.est.8b07141

Wang, Q., Zhan, Y., Pedersen, N. L., Fang, F., & Hägg, S. (2018). Telomere length and all-cause mortality: A meta-analysis. *Ageing Research Reviews*, *48*, 11–20. https://doi.org/10.1016/j.arr.2018.09.002

***Watson, H., Bolton, M., & Monaghan, P. (2015). Variation in early-life telomere dynamics in a long-lived bird: Links to environmental conditions and survival. *Journal of Experimental Biology*, *218*(5), 668–674. https://doi.org/10.1242/jeb.104265

Whitehead, A., Clark, B. W., Reid, N. M., Hahn, M. E., & Nacci, D. (2017). When evolution is the solution to pollution: Key principles, and lessons from rapid repeated adaptation of killifish (*Fundulus heteroclitus*) populations. *Evolutionary Applications*. *10*(8), 762–783. https://doi.org/10.1111/eva.12470

Wikelski, M., & Cooke, S. J. (2006). Conservation physiology. *Trends in Ecology and Evolution*, *21*(1), 38–46. https://doi.org/10.1016/j.tree.2005.10.018

Wilbourn, R. V., Moatt, J. P., Froy, H., Walling, C. A., Nussey, D. H., & Boonekamp, J. J. (2018). The relationship between telomere length and mortality risk in non-model vertebrate systems: A meta-analysis. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *373*(1741), 20160447. https://doi.org/10.1098/rstb.2016.0447

Wiley, C. D., Velarde, M. C., Lecot, P., Liu, S. U., Sarnoski, E. A., Freund, A., Shirakawa, K., Lim, H. W., Davis, S. S., Ramanathan, A., Gerencser, A. A., Verdin, E., & Campisi, J. (2016). Mitochondrial dysfunction induces senescence with a distinct secretory phenotype. *Cell Metabolism*, *23*(2), 303–314. https://doi.org/10.1016/j.cmet.2015.11.011

Wilking, M., Ndiaye, M., Mukhtar, H., & Ahmad, N. (2013). Circadian rhythm connections to oxidative stress: Implications for human health. *Antioxidants & Redox Signaling*, *19*(2), 192–208. https://doi.org/10.1089/ars.2012.4889

Witkin, E. M. (1976). Ultraviolet mutagenesis and inducible DNA repair in Escherichia coli. *Bacteriological Reviews*, *40*(4), 869–907. https://doi.org/10.1128/br.40.4.869-907.1976

Wood, E. M., & Young, A. J. (2019). Telomere attrition predicts reduced survival in a wild social bird, but short telomeres do not. *Molecular Ecology*, *28*(16), 3669–3680. https://doi.org/10.1111/mec.15181

Yeager, M., Machiela, M. J., Kothiyal, P., Dean, M., Bodelon, C., Suman, S., Wang, M., Mirabello, L., Nelson, C. W., Zhou, W., Palmer, C., Ballew,

B., Colli, L. M., Freedman, N. D., Dagnall, C., Hutchinson, A., Vij, V., Maruvka, Y., Hatch, M., … Chanock, S. J. (2021). Lack of transgenerational effects of ionizing radiation exposure from the Chernobyl accident. *Science*, *372*(6543), 725–729. https://doi.org/10.1126/science.abg2365

Yoshida, K., Misumi, M., Kubo, Y., Yamaoka, M., Kyoizumi, S., Ohishi, W., Hayashi, T., & Kusunoki, Y. (2016). Long-Term Effects of Radiation Exposure and Metabolic Status on Telomere Length of Peripheral Blood T Cells in Atomic Bomb Survivors. *Radiation Research*, *186*(4), 367–376. https://doi.org/10.1667/RR14389.1

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 B: Biological Sciences*, *373*(1741), 20160452. https://doi.org/10.1098/rstb.2016.0452

Yuan, J., Liu, Y., Wang, J., Zhao, Y., Li, K., Jing, Y., Zhang, X., Liu, Q., Geng, X., Li, G., & Wang, F. (2018). Long-term persistent organic pollutants exposure induced telomere dysfunction and senescence-associated secretary phenotype. *The Journals of Gerontology: Series A*, *73*(8), 1027–1035. https://doi.org/10.1093/gerona/gly002

Zhang, T.-C., Schmitt, M. T., & Mumford, J. L. (2003). Effects of arsenic on telomerase and telomeres in relation to cell proliferation and apoptosis in human keratinocytes and leukemia cells in vitro. *Carcinogenesis*, *24*(11), 1811–1817. https://doi.org/10.1093/carcin/bgg141

Zhang, Y., & Wong, H. S. (2021). Are mitochondria the main contributor of reactive oxygen species in cells? *Journal of Experimental Biology*, *224*(jeb221606). https://doi.org/10.1242/jeb.221606

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

How to cite this article: Salmón, P., & Burraco, P. (2022). Telomeres and anthropogenic disturbances in wildlife: A systematic review and meta-analysis. *Molecular Ecology*, 31, 6018–6039. https://doi.org/10.1111/mec.16370