Avian epigenetic clocks: state of the art and call to action

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Abstract

DNA methylation-based epigenetic clocks are powerful biomarkers of chronological and biological age, estimating age from CpG-specific methylation patterns that integrate developmental history, environmental exposure, physiological stress, and stochastic epigenetic change. Despite rapid advances in mammals, avian epigenetic clocks remain scarce, limiting comparative inference and our understanding of how avian ageing varies across ecological and evolutionary contexts. Here, we review existing avian epigenetic clocks and evaluate their performance for age estimation and biological inference. We argue that birds provide a uniquely powerful system for resolving what epigenetic age represents, due to unique qualities such as external embryonic development, rapid postnatal growth, long-term field studies, and nucleated erythrocytes that enable minimally invasive longitudinal sampling. Together with variation in lifespan and life-history strategies, and expanding genomic and physiological resources, these features position birds as an ideal system for linking developmental environments to epigenetic ageing trajectories. We conclude that integrating epigenetic clocks into avian research will improve age estimation, demographic inference, and conservation applications, while enabling mechanistic tests of how development, environment, and physiology shape ageing. We call for broader taxonomic coverage, longitudinal datasets of known-age individuals, biological validation, standardized methodology and reporting to fully realize this potential.

KEYWORDS: epigenetic clock, bird, life-history evolution, ageing, development

WHY BIRDS MATTER FOR EPIGENETIC AGEING RESEARCH

Birds are increasingly recognized as powerful systems for the study of ageing (Harper & Holmes, 2021). Many species are unusually long-lived for their body size despite high metabolic rates and body temperatures (Austad, 2011; Holmes & Ottinger, 2003; Travin & Feniouk, 2016), challenging simple relationships between metabolism and lifespan and suggesting enhanced mechanisms of somatic maintenance (Austad & Fischer, 1991; Ricklefs, 2010). Avian cells can also exhibit increased resistance to oxidative stress and other cytoprotective adaptations (Castiglione et al., 2020; Harper & Holmes, 2021), while work on telomeres, neurogenesis, and life-history variation has established birds as valuable comparative models of ageing (Barnea & Pravosudov, 2011; Wilbourn et al., 2018). Yet a fundamental challenge remains: how can we quantify not only how old an individual is, but how rapidly it is ageing biologically?

DNA methylation (DNAm)-based epigenetic clocks offer one potential solution. These statistical models estimate age or ageing-related phenotypes from DNAm patterns at selected CpG sites (Horvath, 2013). First-generation clocks are trained primarily to predict chronological age and have been developed for a variety of taxa (Horvath & Raj, 2018; Tangili et al., 2023). Whereas second-generation clocks, developed largely for humans and other mammals, incorporate outcomes such as lifespan, mortality risk, or physiological decline to better capture variation in biological ageing (see Levine et al., 2018; Lu et al., 2019). Some clocks are species- or tissue-specific, while others reveal striking evolutionary conservation, such as pan-mammalian clocks which can predict age across 185 species with high accuracy (Lu et al., 2023). Together, these advances demonstrate that DNAm contains a robust signature of ageing, but leave a more difficult question unresolved: what does variation in epigenetic age actually represent?

Epigenetic age acceleration - the extent to which an individual's biological age, as measured by an epigenetic clock, deviates from that expected for its chronological age - provides one approach to addressing this question. Epigenetic age acceleration is commonly quantified as either (i) the difference between epigenetic and chronological age (Marioni et al., 2015) or (ii) as the residual from a regression of epigenetic on chronological age (Horvath et al., 2014), which accounts for the relationship between the two across the study population. Positive values indicate that individuals appear epigenetically older than expected, and negative values younger. Age acceleration has been associated with health, disease, and mortality in humans (Horvath et al., 2014; Marioni et al., 2015; Oblak et al., 2021), and emerging wildlife studies link it to ecological and social conditions, including social dominance rank in wild baboons (Anderson et al., 2021) and captivity in king penguins (Cristofari et al., 2026). Thus, variation around expected epigenetic age offers a potential means of quantifying why same-aged individuals differ in biological state and longevity.

Birds offer unusual opportunities to determine the origin and consequences of ageing rate and lifespan variation. External development and experimentally accessible nestlings enable early-life processes to be manipulated directly. Long-term studies of individually marked birds provide known-age individuals with detailed environmental and fitness histories, allowing epigenetic trajectories to be linked to later-life fitness and senescence. Nucleated erythrocytes further enable repeated, minimally-invasive DNAm sampling within individuals, providing rare opportunities to distinguish within-individual ageing from cross-sectional differences among age classes. Combined with extraordinary diversity of avian lifespans (Wasser & Sherman, 2010) and life-history strategies (Robinson et al., 2010), these features allow epigenetic ageing to be studied experimentally, longitudinally, and comparatively across the lifespan.

Despite their promise as ageing models, birds remain strikingly under-represented in epigenetic clock research (Tangili et al., 2023), with validated clocks currently available for only a small number of species (N=5, Table 1; Cristofari et al., 2026; De Paoli-Iseppi et al., 2019; Gerber et al., 2025; Haller et al., 2025; Raddatz et al., 2021). Expanding avian epigenetic clocks offers benefits in both directions: epigenetic clocks can provide avian researchers with high-resolution tools for age estimation and biological-age inference, while avian systems can help resolve what epigenetic age represents and how conserved its underlying biology is across vertebrates. Here, we review emerging literature on avian epigenetic clocks and consider how experimental, longitudinal, and comparative approaches can advance our understanding of the developmental and ecological origins of biological ageing.

THE CURRENT STATE OF AVIAN EPIGENETIC CLOCKS

Epigenetic clocks have now been developed to predict chronological age for several avian species using approaches ranging from targeted to whole-genome methylation sequencing (Table 1, Cristofari et al., 2026; De Paoli-Iseppi et al., 2019; Gerber et al., 2025; Haller et al., 2025; Raddatz et al., 2021). Although avian clock development remains limited compared to mammals, existing clocks collectively demonstrate that age-associated DNAm signatures are detectable across avian taxa and life histories.

Across these avian epigenetic clocks, age prediction errors (i.e., mean/median absolute deviation between epigenetic and chronological age over the whole dataset) are small in absolute terms, ranging from ~1 day to ~2.5 years (Table 1). Scaled to maximum lifespan, these values suggest remarkably high accuracy: ~0.03% in domestic chickens (~3.4 days of a ~30-year lifespan), ~0.05% in chestnut-crowned babblers, ~2–3% in great tits, and up to ~9% in king penguins (~2.5 years of a 27-year lifespan). However, these estimates can overstate performance because many clocks are trained using relatively narrow age ranges, often focused on early development or young adulthood.

When prediction error is evaluated relative to the training age range rather than maximum lifespan, accuracy declines substantially; for example, prediction error in chicken approaches ~10% across individuals aged 3-35 days. Clock performance should therefore be interpreted relative to the ages represented during training and validation. Even so, epigenetic clocks can provide substantially finer age resolution than morphological traits such as plumage, body size, or wing length, which are frequently coarse, stage-dependent, and unreliable beyond early life.

Existing avian studies also provide early evidence that epigenetic age varies with biological state. In great tits, rapid postnatal growth induced by brood size reduction was associated with epigenetic age acceleration, linking early-life growth dynamics to DNAm ageing trajectories (Haller et al., 2025). In king penguins, captive individuals exhibited higher epigenetic age acceleration than wild ones, potentially reflecting changes in growth, metabolic, and cardiac-related pathways (Cristofari et al., 2026). In chickens, experimentally-induced inflammation altered epigenetic ageing profiles, implicating immune activation and physiological stress in modulating DNAm age estimates (Raddatz et al., 2021). Although these first-generation clocks were trained primarily on chronological age, such findings suggest that their prediction can retain some information associated with biological ageing driven by growth, environment, and physiological state. Second-generation avian clocks could help distinguish DNAm variation that predicts chronological age from variation that predicts biologically meaningful differences among same-aged individuals.

Although avian clocks remain few, existing studies suggest they are beginning to capture biologically meaningful variation beyond chronological age alone. Understanding what this variation represents - and whether it reflects causes, consequences or correlates of ageing and lifespan - is therefore a key next step.

Table 1. Information on the experimental design, methods for DNA methylation quantification and validation approaches used to develop the existing avian epigenetic clocks (N=5). Species-specific maximum lifespan information was derived from the AnAge database (https://genomics.senescence.info/species/index.html).

Reference	Species	Wild or Captive	Tissue	Maximum Lifespan (years)	Age Range	Sample Size	Method	R^2	MAD	Validation Approach
De Paoli-Iseppi et al. 2019	Short-tailed shearwater (*Ardenna tenuirostris*)	wild	blood	38	0-21 years	42	DREAM	0.587	-	Elastic net
Raddatz et al. 2021	Domestic chicken (*Gallus gallus domesticus*)	captive	muscle, ileum, jejunum, spleen	30	3-35 days	36	WGBS	-	3.4 days (RMSE)	Elastic net
Haller et al. 2025	Great tit (*Parus major*)	wild	blood	15.4	Development clock:6-15 days, Ageing clock:0.-6 years	Development clock:67, Ageing clock:122	epiGBS	Development clock:0.792, Ageing clock: 0.706	Development clock:1.06 days, Ageing clock: 0.4 years	Elastic net
Gerber et al 2025	chestnut-crowned babbler (*Pomatostomus ruficeps*)	wild	blood	8.3	0-19 days	56	EM-seq	0.903	1.6 days	Elastic net
Cristofari et al. 2026	King peguin (*Aptenodytes patagonicus*)	both	blood	27	1-38 years	64	EM-Seq	0.91	2.48 years (RMSE)	Elastic net

LEVERAGING AVIAN EPIGENETIC CLOCKS TO STUDY AGEING

Mechanistic interpretations of epigenetic age. A central challenge in epigenetic clock research is determining what epigenetic age represents mechanistically. Age-related DNAm changes could contribute directly to functional decline, reflect downstream consequences of ageing, or arise from correlated processes such as developmental programmes, environmental exposures, stochastic epigenetic drift, or declining epigenetic maintenance (Bell et al., 2019; Horvath & Raj, 2018; López-Otín et al., 2023). Indeed, emerging mammalian studies suggest that CpGs predictive of age are not necessarily those implicated causally in ageing-related traits (Ying et al., 2024).

Distinguishing cause from consequence ultimately requires experimental manipulation. Mammalian studies have begun to test this through genetic and epigenetic interventions; for example, partial cellular reprogramming can reverse epigenetic-age signatures alongside other age-related phenotypes (Browder et al., 2022; Mitchell et al., 2024). Mammals currently offer more developed and scalable genetic tools for direct mechanistic manipulation, although avian approaches including CRISPR, primordial germ cell manipulation, and *in ovo* electroporation continue to advance (Cooper et al., 2018; Williams et al., 2018). Birds offer complementary opportunities for causal inference: developmental conditions, physiology, and environments can be manipulated in natural populations to identify drivers of variation in epigenetic ageing and test whether this variation predicts subsequent outcomes. Thus, while mammalian systems currently provide greater power to test whether specific epigenetic changes drive ageing, birds are particularly suited to identify ecological causes and consequences of epigenetic ageing.

Early-life environments and the developmental origins of ageing. Early-life conditions can have consequences that persist long after development, shaping adult survival, reproduction, and senescence (Barker, 2004; Cooper and Kruuk, 2018; Wada & Coutts, 2021), yet the mechanisms linking early conditions to ageing trajectories remain poorly understood. Across vertebrates, early-life adversity can leave persistent biological signatures, including accelerated telomere attrition and reduced lifespan (Boonekamp et al., 2014; Heidinger et al., 2012; Nettle et al., 2013) while in humans it is associated with accelerated epigenetic ageing and elevated later-life disease and mortality risk (Huang et al., 2019; Levine et al., 2018; Marioni et al., 2015; Schlomer, 2024; Tehranifar et al., 2013). An important unresolved question is therefore whether variation in adult biological ageing is partly established during development.

DNAm provides a plausible mechanism through which early environments could become biologically embedded and exert lifelong effects on the phenotype. The methylome undergoes extensive remodelling during development (Moore et al., 2013), and avian experiments show that rearing conditions can alter DNAm, although effects vary among

studies (Ruuskanen, 2024). Brood size manipulations have altered methylation in great tits and zebra finches (Jimeno et al., 2019; Sepers et al., 2021; Sheldon et al., 2018; Tangili, Palsbøll, et al., 2026), while cross-fostering of wild house wrens identified methylation differences associated with rearing environment and glucocorticoid physiology (von Holdt et al., 2023). However, a larger great tit brood-size experiment detected little immediate genome-wide DNAm response despite effects on nestling condition (Sepers, Mateman, et al., 2023), and cross-fostering suggests that much early-life DNAm variation may reflect genetic or brood-of-origin effects rather than rearing environment (Sepers, Chen, et al., 2023). Intriguingly, follow-up of experimentally manipulated great tits after fledging revealed substantial DNAm differences between brood-size treatments (Sepers et al., 2024). Together, these studies show that developmental conditions can shape the methylome, but that effects may be context-dependent or emerge later in development.

Epigenetic clocks provide a way to test whether these developmental effects extend to ageing trajectories, but epigenetic age during development requires careful interpretation. Rapid post-hatching growth is accompanied by fast, non-linear DNAm change, meaning clocks trained on nestlings may capture rapid developmental remodeling rather than the slower, more linear epigenetic ageing observed later in life. Accordingly, separate developmental and adult clocks have been developed in great tits (Haller et al., 2025) and found that nestlings from reduced broods were biologically older compared to control nestlings, although they are known to have higher fitness. Therefore, an epigenetically “older” nestling may be developmentally advanced rather than biologically aged. The critical question is therefore whether environmentally induced differences disappear after development or persist and alter subsequent ageing trajectories - a distinction that can be tested by longitudinally following experimentally manipulated, known-age birds across their lifespan.

Comparative life-history evolution. Birds exhibit exceptional variation in lifespan (Wasser & Sherman, 2010) and pace-of-life strategies, providing a natural framework for comparative ageing research. This diversity raises a central question for epigenetic clock research: do age-associated DNAm changes represent conserved molecular signatures of ageing, or are they systematically shaped by evolved life-history strategies across species? Cross-species analyses can test whether DNAm ageing patterns are conserved across avian lineages or scale predictably with maximum lifespan, as observed in mammals (Bertucci-Richter & Parrott, 2023; Li et al., 2024; Mayne et al., 2019). Similar macroevolutionary structure is evident in other ageing traits, including telomere dynamics, which covary with lifespan across bird species (Tangili et al., 2026; Tricola et al., 2018), suggesting that ageing biomarkers may reflect both conserved biological processes and evolved differences in life-history strategy.

These considerations motivate a pan-avian epigenetic clock framework: a standardized comparative system enabling direct comparison of DNAm ageing trajectories across species. This framework would disentangle whether exceptional longevity arises from uniformly slower epigenetic ageing, shifts in specific DNAm trajectories, or enhanced epigenetic maintenance mechanisms operating across lineages, and whether life-history strategies are encoded in shared or divergent epigenetic signatures. However, progress is constrained by a key methodological limitation. Most mammalian epigenetic clocks rely on standardized platforms such as the HorvathMammalMethylChip40 (Arneson et al., 2022), which targets ~37,000 conserved CpG sites and enables robust cross-species comparisons (Lu et al., 2023). The absence of an equivalent avian platform limits comparability across species and hinders the development of truly comparative epigenetic ageing models. Developing a conserved avian CpG panel or analogous standardized sequencing framework would therefore be a critical step toward pan-avian epigenetic clock construction, comparative studies, and evolutionary inference.

Sex differences in longevity and ageing rates. Sex differences in lifespan and ageing rates add an important layer of biological complexity for epigenetic clock design. In birds, females are the heterogametic sex (ZW) and often exhibit shorter lifespans than males (Tower & Arbeitman, 2009), consistent with broader evidence that the homogametic sex tends to live longer across taxa (Xirocostas et al., 2020). Although the study of sex chromosome DNAm in relation to ageing is still in its infancy, growing evidence now points to a role of sex chromosome DNAm in ageing processes of both in humans and birds. In humans, hypermethylation of Y-linked CpGs has been linked to mortality risk (Lund et al., 2020), while there are only a few X-linked CpG sites whose DNAm significantly changes with age (Acevedo et al., 2015). Most recently, X and Y chromosome dosage has been found to influence epigenetic aging (Zhang et al., 2025). In birds, many age-related CpGs are found on sex chromosomes, suggesting a potential contribution to sex-specific ageing trajectories and longevity (Tangili et al., 2025). Birds therefore offer a powerful comparative system for disentangling the role of sex chromosome DNAm in ageing, given their contrasting ZW system relative to mammalian XY sex determination. These findings highlight that sex chromosomes should not be excluded from (avian) epigenetic clock construction, and that explicitly modeling sex-linked variation may improve age prediction and better capture biologically meaningful differences in ageing and lifespan.

APPLICATIONS OF EPIGENETIC CLOCKS IN AVIAN ECOLOGY AND CONSERVATION

Chronological age estimation for demography and population ecology. Many ecological studies rely on minimum age categories unless individuals are followed from hatching or exhibit clear age-specific morphology. Once validated in independent datasets, epigenetic clocks enable continuous age estimation from cross-sectional samples,

allowing population age structure and age-specific patterns of survival, recruitment, reproduction, and senescence to be inferred without decades of intensive monitoring (e.g., Eichenberger et al., 2026; Heydenrych et al., 2021; Roman et al., 2024). Compared to categorical approaches (e.g., “second-year” vs “after-second-year”), epigenetic clocks provide higher-resolution age estimates that may reveal late-life demographic patterns such as actuarial senescence and terminal investment, which are often difficult to detect in wild systems (Nussey et al., 2013). Incorporating clock-derived ages into capture-mark-recapture or integrated population models could reduce bias from unknown age at first capture, a longstanding challenge in estimating age-specific survival and senescence (Gaillard & Lemaître, 2020; Lebreton et al., 1992; Schaub & Abadi, 2011). In addition, clocks can enable age estimation in less-frequently observed classes, including juveniles, floaters, and non-breeders, improving inference on full population structure. Clocks further allow rapid detection of demographic shifts following environmental change and retrospective analysis of archived samples (Eichenberger et al., 2026). More broadly, epigenetic clocks transform age from a latent demographic variable to a directly measurable trait, enabling stronger tests of age-structured ecological and evolutionary theory in the wild.

Health, disease, welfare, and livestock. In agricultural mammals, epigenetic biomarkers are increasingly being explored as tools to evaluate health, welfare, and production efficiency (Clarke et al., 2021; Hayes et al., 2021), with potential applications in selective breeding for robustness and longevity (Wang and Ibeagha-Awemu, 2021). Although poultry-specific applications of epigenetic clocks remain in their early stages, intensive production systems may be especially well-suited for these approaches given their rapid turnover and high economic sensitivity to variation in performance and health. Poultry are exposed to chronic stressors, including high stocking densities, controlled photoperiods, strong artificial selection for rapid growth, alongside routine immunological and veterinary interventions (Ncho et al., 2025). These conditions can induce sustained inflammatory and metabolic changes that are likely to be reflected in DNAm dynamics (Pértille et al., 2020; Raddatz et al., 2021; Ratan et al., 2023). In this context, epigenetic age acceleration may serve as an integrative biomarker of cumulative physiological burden, capturing trade-offs between productivity and somatic maintenance in systems where selection for growth and feed efficiency may come at the expense of long-term physiological robustness.

Conservation and wildlife management. Epigenetic clocks could inform conservation at both demographic and biological levels. Where ages are unknown, reconstructed age structure could help identify which life stages constrain populations - for example, distinguishing poor recruitment from elevated adult mortality - and guide stage-specific management. Age estimates could also inform captive breeding, translocation, and reintroduction by characterizing the demographic composition of managed populations (Anastasiadi et al., 2026; Newediuk et al., 2025). However, translating these applications

to routine management will require cheaper, scalable DNAm ageing assays, as epigenetic ageing remains relatively costly even when an appropriate clock already exists. Beyond chronological age, epigenetic age acceleration could indicate biological state, revealing whether anthropogenic pressures such as habitat degradation, pollution, or climate extremes are associated with accelerated ageing. Such biomarkers could help identify vulnerable populations or evaluate management interventions, although links with fitness will require validation. Archived tissues and museum collections could extend both applications retrospectively, reconstructing demographic and biological responses to environmental change. Together, epigenetic clocks could move from describing individual age to diagnosing when, where, and potentially why populations are under pressure..

BOX 1. Open questions in the study of epigenetic clocks in ecology and evolution

Key questions that will determine how epigenetic clocks can move from age predictors towards tools for understanding biological ageing in natural populations.

1. **What do epigenetic clocks measure?** Do clock-associated DNAm changes causally contribute to ageing, reflect its downstream consequences, or track correlated developmental and environmental history?
2. **When are ageing trajectories established?.** Do early-life environments produce persistent changes in epigenetic ageing, and are these adaptive, neutral, or deleterious?
3. **How systemic is epigenetic age?** To what extent does tissue-specific DNAm reflect organism-wide ageing, and how does tissue choice alter relationships of DNAm with ageing and fitness?
4. **How environmentally sensitive are epigenetic clocks?** How do ecological conditions, populations, and life histories influence epigenetic age, and how much apparent variation reflects biology versus methodological artefacts?
5. **How transferable are clocks?** When can clocks be applied across species or populations, and what minimal calibration is required to correct systematic bias?
6. **Can epigenetic age predict fitness?** Can clocks move beyond chronological age estimation to predict survival, reproductive senescence, or remaining lifespan in wild populations?

BOX 2. Building an avian epigenetic clock: a practical guide

Clock design depends on the biological question, species, life stage, and intended application. Here, we highlight avian-specific considerations; for comprehensive guidance of wildlife clock construction and validation, see Newediuk et al. (2025).

1. Decide what the clock should measure. Use first-generation clocks for chronological age estimation and second-generation clocks trained on health, function, or survival to more directly capture biological ageing. Age acceleration can capture variation among same-aged individuals, but chronological-age clocks may retain little signal of biological ageing. In wild birds, where mortality and longitudinal health can be difficult to measure, reproductive performance, frailty, or physiological decline may provide useful alternatives.

2. Build a representative training dataset. Use known-age individuals spanning the intended prediction range. Both sample size (Mayne et al., 2021; Tangili et al., 2023) and a representative age structure matter: abundant, precisely-aged nestlings should not overwhelm scarcer older birds. Rapid, non-linear DNAm change during development may favour separate developmental and adult clocks or age transformations (Horvath, 2013). Avoid confounding age with technical variation and factors like sex, population, year, season, or major life-history states (e.g., breeding, moult, and migration).

3. Exploit avian blood - but consider tissue specificity. Nucleated erythrocytes make small blood samples DNA-rich and enable longitudinal sampling. Develop and apply clocks in the same tissue where possible. Non-proliferative tissues may better capture cumulative ageing but cannot usually be repeatedly sampled (Tangili et al., 2023).

4. Match the DNAm platform to the goal. Whole-genome approaches (WGBS/EM-seq) maximize discovery and accuracy (Gerber et al., 2025) but can constrain sample size through cost; reduced-representation approaches (e.g., RRBS/epiGBS) trade coverage for scalability and accuracy; targeted assays or arrays/panels efficiently measure predefined CpGs. In heterogeneous wild populations, sample size may outweigh exhaustive coverage of the genome. For comparative clocks, prioritise platforms that reliably measure conserved CpGs across species.

5. Validate the clock - and the biology. Assess performance on individuals not used to train the clock, using independent validation where possible or cross-validation when sample size is limited. Report prediction error (e.g., MAE or RMSE) alongside R^2 or Pearson's correlation and evaluate performance across relevant groups and life stages. Interpret error biologically: a few days may be trivial for adults but substantial for nestlings. For biological-ageing clocks, additionally validate predictions against independent ageing outcomes.

6. Make clocks reusable and comparative. Report methodological choices in details and share data, metadata, and code to support accessibility, transparency, reproducibility, and cross-species comparison.

A CALL TO ACTION

Despite recent progress, epigenetic clocks exist for only a small fraction of avian diversity. Existing studies demonstrate that age-associated patterns can be detected across several bird species, can predict age with high accuracy, and in some cases, offer insights on biological ageing. Going forward, greater coordination across avian systems will be essential for comparative studies which will aim to determine which epigenetic signatures of ageing are conserved and which reflect differences in development, ecology and life history. Achieving this will require substantially broader taxonomic coverage, longitudinal datasets of known-age individuals, biological validation, and standardized methodologies and reporting across avian studies of epigenetic aging. Combined with the experimental tractability, developmental diversity, and ecological breadth of avian systems, this comparative framework could establish birds, alongside mammals, as a core system for epigenetic ageing research, extending our understanding of biological ageing across vertebrate diversity and ultimately across the tree of life.

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REFERENCES

Acevedo, N., Reinius, L. E., Vitezic, M., Fortino, V., Söderhäll, C., Honkanen, H., Veijola, R., Simell, O., Toppari, J., Ilonen, J., Knip, M., Scheynius, A., Hyöty, H., Greco, D., & Kere, J. (2015). Age-associated DNA methylation changes in immune genes, histone modifiers and chromatin remodeling factors within 5 years after birth in human blood leukocytes. *Clinical Epigenetics*, *7*(1), 34. https://doi.org/10.1186/s13148-015-0064-6

Anastasiadi, D., Kasmi, Y., Stransky, C., Casas, L., Eschbach, E., & Piferrer, F. (2026). An Epigenetic Clock for Accurate Age Prediction in Atlantic Cod Populations for Improved Fisheries Management. *Molecular Ecology Resources*, *26*(3), e70109. https://doi.org/10.1111/1755-0998.70109

Anderson, J. A., Johnston, R. A., Lea, A. J., Campos, F. A., Voyles, T. N., Akinyi, M. Y., Alberts, S. C., Archie, E. A., & Tung, J. (2021). High social status males experience accelerated epigenetic aging in wild baboons. *eLife*, *10*, 1–22. https://doi.org/10.7554/ELIFE.66128

Austad, S. N. (2011). Candidate bird species for use in aging research. *ILAR Journal*, *52*(1), 89–96.

Austad, S. N., & Fischer, K. E. (1991). Mammalian aging, metabolism, and ecology: Evidence from the bats and marsupials. *Journal of Gerontology*, *46*(2), B47–B53.

Barker, D. J. (2004). The developmental origins of adult disease. *Journal of the American College of Nutrition*, *23*(sup6), 588S-595S.

Barnea, A., & Pravosudov, V. (2011). Birds as a model to study adult neurogenesis: Bridging evolutionary, comparative and neuroethological approaches. *European Journal of Neuroscience*, *34*(6), 884–907.

Bell, C. G., Lowe, R., Adams, P. D., Baccarelli, A. A., Beck, S., Bell, J. T., Christensen, B. C., Gladyshev, V. N., Heijmans, B. T., & Horvath, S. (2019). DNA methylation aging clocks: Challenges and recommendations. *Genome Biology*, *20*(1), 249.

Bertucci-Richter, E. M., & Parrott, B. B. (2023). The rate of epigenetic drift scales with maximum lifespan across mammals. *Nature Communications*, *14*(1), 7731.

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), 20133287. https://doi.org/10.1098/rspb.2013.3287

Browder, K. C., Reddy, P., Yamamoto, M., Haghani, A., Guillen, I. G., Sahu, S., Wang, C., Luque, Y., Prieto, J., & Shi, L. (2022). In vivo partial reprogramming alters age-associated molecular changes during physiological aging in mice. *Nature Aging*, *2*(3), 243–253.

Castiglione, G. M., Xu, Z., Zhou, L., & Duh, E. J. (2020). Adaptation of the master antioxidant response connects metabolism, lifespan and feather development pathways in birds. *Nature Communications*, *11*(1), 2476.

Clarke, S., Caulton, A., McRae, K., Brauning, R., Couldrey, C., & Dodds, K. (2021). Beyond the genome: A perspective on the use of DNA methylation profiles as a tool for the livestock industry. *Animal Frontiers*, *11*(6), 90–94.

Cooper, C. A., Doran, T. J., Challagulla, A., Tizard, M. L., & Jenkins, K. A. (2018). Innovative approaches to genome editing in avian species. *Journal of Animal Science and Biotechnology*, *9*(1), 15.

Cooper, E. B., & Kruuk, L. E. (2018). Ageing with a silver-spoon: A meta-analysis of the effect of developmental environment on senescence. *Evolution Letters*, *2*(5), 460–471.

Cristofari, R., Davis, L. R., Bardon, G., Nitta Fernandes, F. A., Figueroa, M. E., Franzenburg, S., Gauthier-Clerc, M., Grande, F., Heidrich, R., Hukkanen, M., Le Maho, Y., Ollikainen, M., Paciello, E., Rampal, P., Stenseth, N. C., Trucchi, E., Zahn, S., Le Bohec, C., & Meyer, B. S. (2026). Lifestyle change accelerates epigenetic ageing in King penguins. *Nature Communications*, *17*(1), 3795. https://doi.org/10.1038/s41467-026-70527-8

De Paoli-Iseppi, R., Deagle, B. E., Polanowski, A. M., McMahon, C. R., Dickinson, J. L., Hindell, M. A., & Jarman, S. N. (2019). Age estimation in a long-lived seabird

(Ardenna tenuirostris) using DNA methylation-based biomarkers. *Molecular Ecology Resources*, *19*(2), 411–425.

Eichenberger, F., Carroll, E. L., Garrigue, C., Jarman, S., Steel, D. J., Robbins, J., Rendell, L., & Garland, E. C. (2026). Changes in age-related sexual selection in a humpback whale population recovering from exploitation. *Current Biology*, *36*(5), 1115–1127.

Gaillard, J., & Lemaître, J. (2020). An integrative view of senescence in nature. *Functional Ecology*, *34*(1), 4–16.

Gerber, L., Schrey, A. W., Anderson, S. C., Jain, E., & Liebl, A. L. (2025). Sequencing method matters: Differential performance of DNA methylation data acquisition in epigenetic clock calibration. *Journal of Avian Biology*, *2025*(5), e03498.

Gluckman, P. D., & Hanson, M. A. (2004). Living with the past: Evolution, development, and patterns of disease. *Science*, *305*(5691), 1733–1736.

Haller, A., Risse, J., Sepers, B., & van Oers, K. (2025). Independent avian epigenetic clocks for ageing and development. *Molecular Ecology Resources*, *25*(7), e14128.

Harper, J. M., & Holmes, D. J. (2021). New perspectives on avian models for studies of basic aging processes. *Biomedicines*, *9*(6), 649.

Hayes, B. J., Nguyen, L. T., Forutan, M., Engle, B. N., Lamb, H. J., Copley, J. P., Randhawa, I. A., & Ross, E. M. (2021). An epigenetic aging clock for cattle using portable sequencing technology. *Frontiers in Genetics*, *12*, 760450.

Heidinger, B. J., Blount, J. D., Boner, W., Griffiths, K., Metcalfe, N. B., & Monaghan, P. (2012). Telomere length in early life predicts lifespan. *PNAS*, *109*(5), 1743–1748.

Heydenrych, M. J., Saunders, B. J., Bunce, M., & Jarman, S. N. (2021). Epigenetic measurement of key vertebrate population biology parameters. *Frontiers in Ecology and Evolution*, *9*, 617376.

Holmes, D., & Ottinger, M. (2003). Birds as long-lived animal models for the study of aging. *Experimental Gerontology*, *38*(11–12), 1365–1375.

Horvath, S. (2013). DNA methylation age of human tissues and cell types. *Genome Biology*, *14*(10), 3156.

Horvath, S., & Raj, K. (2018). DNA methylation-based biomarkers and the epigenetic clock theory of ageing. *Nature Reviews Genetics*, *19*(6), 371–384.

Huang, R.-C., Lillycrop, K. A., Beilin, L. J., Godfrey, K. M., Anderson, D., Mori, T. A., Rauschert, S., Craig, J. M., Oddy, W. H., & Ayonrinde, O. T. (2019). Epigenetic age acceleration in adolescence associates with BMI, inflammation, and risk score for middle age cardiovascular disease. *The Journal of Clinical Endocrinology & Metabolism*, *104*(7), 3012–3024.

Hutchinson, G. E. (1991). Population studies: Animal ecology and demography. *Bulletin of Mathematical Biology*, *53*, 193–213.

Jimeno, B., Hau, M., Gómez-Díaz, E., & Verhulst, S. (2019). Developmental conditions modulate DNA methylation at the glucocorticoid receptor gene with cascading effects on expression and corticosterone levels in zebra finches. *Scientific Reports*, *9*(1), 1–11. https://doi.org/10.1038/s41598-019-52203-8

Lebreton, J.-D., Burnham, K. P., Clobert, J., & Anderson, D. R. (1992). Modeling survival and testing biological hypotheses using marked animals: A unified approach with case studies. *Ecological Monographs*, *62*(1), 67–118.

Levine, M. E., Lu, A. T., Quach, A., Chen, B. H., Assimes, T. L., Bandinelli, S., Hou, L., Baccarelli, A. A., Stewart, J. D., Li, Y., Whitsel, E. A., Wilson, J. G., Reiner, A. P., Aviv, A., Lohman, K., Liu, Y., Ferrucci, L., & Horvath, S. (2018). An epigenetic biomarker of aging for lifespan and healthspan. *Aging*, *10*(4), 573–591. https://doi.org/10.18632/aging.101414

Li, C. Z., Haghani, A., Yan, Q., Lu, A. T., Zhang, J., Fei, Z., Ernst, J., Yang, X. W., Gladyshev, V. N., & Robeck, T. R. (2024). Epigenetic predictors of species maximum life span and other life-history traits in mammals. *Science Advances*, *10*(23), eadm7273.

López-Otín, C., Blasco, M. A., Partridge, L., Serrano, M., & Kroemer, G. (2023). Hallmarks of aging: An expanding universe. *Cell*, *186*(2), 243–278. https://doi.org/10.1016/j.cell.2022.11.001

Lu, A. T., Quach, A., Wilson, J. G., Reiner, A. P., Aviv, A., Raj, K., Hou, L., Baccarelli, A. A., Li, Y., & Stewart, J. D. (2019). DNA methylation GrimAge strongly predicts lifespan and healthspan. *Aging (Albany NY)*, *11*(2), 303.

Lund, J. B., Li, S., Christensen, K., Mengel-From, J., Soerensen, M., Marioni, R. E., Starr, J., Pattie, A., Deary, I. J., Baumbach, J., & Tan, Q. (2020). Age-dependent DNA methylation patterns on the Y chromosome in elderly males. *Aging Cell*, *19*(2), e12907. https://doi.org/10.1111/acel.12907

Marioni, R. E., Shah, S., McRae, A. F., Chen, B. H., Colicino, E., Harris, S. E., Gibson, J., Henders, A. K., Redmond, P., Cox, S. R., Pattie, A., Corley, J., Murphy, L., Martin, N. G., Montgomery, G. W., Feinberg, A. P., Fallin, M. D., Multhaup, M. L., Jaffe, A. E., … Deary, I. J. (2015). DNA methylation age of blood predicts all-cause mortality in later life. *Genome Biology*, *16*(1), 25. https://doi.org/10.1186/s13059-015-0584-6

Mayne, B., Berry, O., Davies, C., Farley, J., & Jarman, S. (2019). A genomic predictor of lifespan in vertebrates. *Scientific Reports*, *9*(1), 1–10.

Mayne, B., Berry, O., & Jarman, S. (2021). Optimal sample size for calibrating DNA methylation age estimators. *Molecular Ecology Resources*, *21*(7), 2316–2323.

Mitchell, W., Goeminne, L. J., Tyshkovskiy, A., Zhang, S., Chen, J. Y., Paulo, J. A., Pierce, K. A., Choy, A. H., Clish, C. B., & Gygi, S. P. (2024). Multi-omics characterization of partial chemical reprogramming reveals evidence of cell rejuvenation. *Elife*, *12*, RP90579.

Ncho, C. M., Berdos, J. I., Gupta, V., Rahman, A., Mekonnen, K. T., & Bakhsh, A. (2025). Abiotic stressors in poultry production: A comprehensive review. *Journal of Animal Physiology and Animal Nutrition*, *109*(1), 30–50.

Nettle, D., Monaghan, P., Boner, W., Gillespie, R., & Bateson, M. (2013). Bottom of the heap: Having heavier competitors accelerates early-life telomere loss in the European starling, Sturnus vulgaris. *Plos One*, *8*(12), e83617.

Newediuk, L., Richardson, E., Bohart, A., Roberto-Charron, A., Garroway, C., & Jones, M. (2025). *Designing epigenetic clocks for wildlife research*. Life Sciences. https://doi.org/10.32942/X2NW5C

Nussey, D. H., Froy, H., Lemaitre, J.-F., Gaillard, J.-M., & Austad, S. N. (2013). Senescence in natural populations of animals: Widespread evidence and its implications for bio-gerontology. *Ageing Research Reviews*, *12*(1), 214–225.

Pértille, F., Ibelli, A. M. G., Sharif, M. E., Poleti, M. D., Fröhlich, A. S., Rezaei, S., Ledur, M. C., Jensen, P., Guerrero-Bosagna, C., & Coutinho, L. L. (2020). Putative epigenetic biomarkers of stress in red blood cells of chickens reared across different biomes. *Frontiers in Genetics*, *11*, 508809.

Raddatz, G., Arsenault, R. J., Aylward, B., Whelan, R., Böhl, F., & Lyko, F. (2021). A chicken DNA methylation clock for the prediction of broiler health. *Communications Biology*, *4*(1), 76.

Ratan, P., Rubbi, L., Thompson, M., Naresh, K., Waddell, J., Jones, B., & Pellegrini, M. (2023). Epigenetic aging in cows is accelerated by milk production. *Epigenetics*, *18*(1), 2240188.

Ricklefs, R. E. (2010). Insights from comparative analyses of aging in birds and mammals. *Aging Cell*, *9*(2), 273–284.

Robinson, W. D., Hau, M., Klasing, K. C., Wikelski, M., Brawn, J. D., Austin, S. H., Tarwater, C., & Ricklefs, R. E. (2010). Diversification of Life Histories in New World Birds. *The Auk*, *127*(2), 253–262. https://doi.org/10.1525/auk.2010.127.2.253

Roman, L., Mayne, B., Anderson, C., Kim, Y., O'Dwyer, T., & Carlile, N. (2024). A novel technique for estimating age and demography of long-lived seabirds (genus Pterodroma) using an epigenetic clock for Gould's petrel (Pterodroma leucoptera). *Molecular Ecology Resources*, *24*(7).

Ruuskanen, S. (2024). Early-life environmental effects on birds: Epigenetics and microbiome as mechanisms underlying long-lasting phenotypic changes. *Journal of Experimental Biology*, *227*. https://doi.org/10.1242/jeb.246024

Schaub, M., & Abadi, F. (2011). Integrated population models: A novel analysis framework for deeper insights into population dynamics. *Journal of Ornithology*, *152*(Suppl 1), 227–237.

Schlomer, G. L. (2024). Epigenetic age acceleration and reproductive outcomes in women. *Evolution and Human Behavior*, *45*(1), 91–98. https://doi.org/10.1016/j.evolhumbehav.2023.11.003

Sepers, B., Chen, R. S., Memelink, M., Verhoeven, K. J., & Van Oers, K. (2023). Variation in DNA methylation in avian nestlings is largely determined by genetic effects. *Molecular Biology and Evolution*, *40*(4), msad086.

Sepers, B., Erven, J. A. M., Gawehns, F., Laine, V. N., & Van Oers, K. (2021). Epigenetics and Early Life Stress: Experimental Brood Size Affects DNA Methylation in Great Tits (Parus major). *Frontiers in Ecology and Evolution*, *9*, 609061. https://doi.org/10.3389/fevo.2021.609061

Sepers, B., Mateman, A. C., Gawehns, F., Verhoeven, K. J., & van Oers, K. (2023). Developmental stress does not induce genome-wide DNA methylation changes in wild great tit (Parus major) nestlings. *Molecular Ecology*, *32*(14), 3960–3974.

Sepers, B., Verhoeven, K. J., & van Oers, K. (2024). Early developmental carry-over effects on exploratory behaviour and DNA methylation in wild great tits (Parus major). *Evolutionary Applications*, *17*(3), e13664.

Sheldon, E. L., Schrey, A. W., Ragsdale, A. K., & Griffith, S. C. (2018). Brood size influences patterns of DNA methylation in wild Zebra Finches (*Taeniopygia guttata*). *The Auk*, *135*(4), 1113–1122. https://doi.org/10.1642/AUK-18-61.1

Tangili, M., Mulder, E., Jimeno, B., Briga, M., & Verhulst, S. (2026). Telomere dynamics, not absolute telomere length, predicts lifespan in adult zebra finches. *Journal of Evolutionary Biology*, voag034. https://doi.org/10.1093/jeb/voag034

Tangili, M., Palsbøll, P., & Verhulst, S. (2026). Inferences from epigenetic information in an ecological context: A case study of early-life environmental effects

on DNA methylation in zebra finches. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *381*(1955), 20250025. https://doi.org/10.1098/rstb.2025.0025

Tangili, M., Slettenhaar, A. J., Sudyka, J., Dugdale, H. L., Pen, I., Palsbøll, P. J., & Verhulst, S. (2023). DNA methylation markers of age(ing) in non-model animals. *Molecular Ecology*, *32*(17), 4725–4741. https://doi.org/10.1111/mec.17065

Tangili, M., Sudyka, J., Furni, F., Palsbøll, P. J., & Verhulst, S. (2025). Sex-Chromosome-Dependent Ageing in Female Heterogametic Methylomes. *Molecular Ecology*, *34*(22), e70147. https://doi.org/10.1111/mec.70147

Tehranifar, P., Wu, H.-C., Fan, X., Flom, J. D., Ferris, J. S., Cho, Y. H., Gonzalez, K., Santella, R. M., & Terry, M. B. (2013). Early life socioeconomic factors and genomic DNA methylation in mid-life. *Epigenetics*, *8*(1), 23–27.

Tower, J., & Arbeitman, M. (2009). The genetics of gender and life span. *Journal of Biology*, *8*(4), 38. https://doi.org/10.1186/jbiol141

Travin, D., & Feniouk, B. (2016). Aging in birds. *Biochemistry (Moscow)*, *81*(12), 1558–1563.

Tricola, G. M., Simons, M. J., Atema, E., Boughton, R. K., Brown, J., Dearborn, D. C., Divoky, G., Eimes, J. A., Huntington, C. E., & Kitaysky, A. S. (2018). The rate of telomere loss is related to maximum lifespan in birds. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *373*(1741).

von Holdt, B. M., Kartzinel, R. Y., van Oers, K., Verhoeven, K. J., & Ouyang, J. Q. (2023). Changes in the rearing environment cause reorganization of molecular networks associated with DNA methylation. *Journal of Animal Ecology*, *92*(3), 648–664.

Wada, H., & Coutts, V. (2021). Detrimental or beneficial? Untangling the literature on developmental stress studies in birds. *Journal of Experimental Biology*, *224*(19), jeb227363.

Wang, M., & Ibeagha-Awemu, E. M. (2021). Impacts of epigenetic processes on the health and productivity of livestock. *Frontiers in Genetics*, *11*, 613636.

Wasser, D. E., & Sherman, P. W. (2010). Avian longevities and their interpretation under evolutionary theories of senescence. *Journal of Zoology*, *280*(2), 103–155. https://doi.org/10.1111/j.1469-7998.2009.00671.x

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.

Williams, R. M., Senanayake, U., Artibani, M., Taylor, G., Wells, D., Ahmed, A. A., & Sauka-Spengler, T. (2018). Genome and epigenome engineering CRISPR toolkit for in vivo modulation of cis-regulatory interactions and gene expression in the chicken embryo. *Development*, *145*(4), dev160333.

Xirocostas, Z. A., Everingham, S. E., & Moles, A. T. (2020). *The sex with the reduced sex chromosome dies earlier: A comparison across the tree of life*. 113001 bytes. https://doi.org/10.5061/DRYAD.TMPG4F4VK

Ying, K., Liu, H., Tarkhov, A. E., Sadler, M. C., Lu, A. T., Moqri, M., Horvath, S., Kutalik, Z., Shen, X., & Gladyshev, V. N. (2024). Causality-enriched epigenetic age uncouples damage and adaptation. *Nature Aging*, *4*(2), 231–246.

Zhang, J., Teoli, J., Rey, B., Vieira, C., Lemaitre, J., Plotton, I., Marais, G. A. B., & Horvath, S. (2025). Epigenetic Clock Analysis of Sex Chromosome Aneuploidies. *Aging Cell*, *24*(11), e70243. https://doi.org/10.1111/acel.70243