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RESTING HEART RATE AS A BIOMARKER OF BIOLOGICAL AGING: A REVIEW AND SYNTHESIS

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ABSTRACT

Research objectives: The objective of this study was to synthesise evidence on resting heart rate (RHR) and heart rate variability (HRV) as biomarkers of biological aging, with a focus on their relationships to multisystem physiological decline across cardiovascular, metabolic, autonomic, and inflammatory domains.
Methods: A structured literature search was conducted. Included publications comprised population-based cohorts, mechanistic studies, biomarker analyses, and autonomic assessments evaluating associations between RHR, HRV, biological aging markers, morbidity, and mortality.
Key findings: Elevated RHR consistently aligned with signatures of accelerated aging, including adverse cardiometabolic profiles, reduced autonomic flexibility, and increased inflammatory activation. Higher RHR was associated with older brain age, diminished functional resilience, and biomarker patterns characteristic of inflammaging, such as heightened interleukin-6 and tumour necrosis factor-α. Lower RHR corresponded to slower biological aging trajectories. HRV analyses complemented these findings, linking reduced parasympathetic activity and lower variability with diminished physiological adaptability and greater aging burden.
Conclusions: RHR emerges as a robust, multidimensional biomarker that integrates signals of cumulative physiological decline and reliably identifies individuals exhibiting accelerated biological aging. Its consistent associations with molecular, functional, and clinical indicators of aging highlight its value as a practical, noninvasive tool for assessing multisystem health status.

KEYWORDS

Resting Heart Rate, Biological Aging, Heart Rate Variability, Autonomic Function, Inflammaging, Multisystem Physiology

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Introduction

Understanding the determinants of biological aging and their measurable correlates has become a central objective in contemporary preventive cardiology and population health sciences. Among routinely collected physiological parameters, few offer as direct and integrative a window into systemic function as resting heart rate. Resting heart rate (RHR) is a fundamental physiological parameter derived from the intrinsic activity of the sinoatrial node and modulated by autonomic, metabolic, and endocrine inputs (MacDonald et al., 2020). As a core component of cardiovascular homeostasis, it reflects the dynamic balance between sympathetic and parasympathetic regulation and responds to changes in physical fitness, stress load, systemic inflammation, and metabolic status (Cao et al., 2025). RHR integrates information from autonomic balance, basal metabolic activity, vascular function, and systemic inflammatory tone, providing a macroscopic reflection of organism-level homeostasis (Gaye et al., 2024). This broad physiological embedding has prompted growing interest in RHR as a candidate marker of biological aging. Emerging work in geroscience highlights that aging cannot be characterized by isolated molecular or clinical indices but rather by coordinated alterations across multiple regulatory systems. The clinical significance of RHR extends beyond routine monitoring, serving as an important predictor of all-cause mortality, cardiometabolic risk, and cardiorespiratory fitness (Speed et al., 2023). Large-scale population studies have demonstrated compelling associations between RHR and health outcomes across diverse demographics. Research involving over 500,000 individuals shows that every 10 beats per minute increase in RHR corresponds to significantly higher mortality risk - 22% greater hazard in men and 19% in women for all-cause mortality (Raisi-Estabragh et al., 2020, 2022). Perhaps most striking is the relationship between RHR and lifespan: individuals with resting heart rates above 90 bpm show an average lifespan of approximately 70 years, while those with rates below 60 bpm live an average of 79 years - a remarkable 9-year difference (Gaye et al., 2024). Integration of RHR into the conceptual framework of

biological aging is therefore justified: heart rate may reflect the aggregate burden of aging-related physiological decline and serve as a convenient, reproducible metric in both clinical and epidemiological settings. Building on these insights, this review aims to synthesize current evidence positioning RHR and heart rate variability (HRV) as integrative biomarkers of biological aging, examine their mechanistic underpinnings, and evaluate their potential utility for clinical and preventive applications.

Methods

Given the conceptual nature of this work, a narrative review approach was employed to capture the multidimensional aspects of RHR in the context of biological aging. The review focuses on integrating mechanistic, clinical, and epidemiological data rather than performing quantitative synthesis, thereby allowing a broader exploration of converging evidence across diverse scientific disciplines. A structured literature search was performed in the following databases: PubMed/MEDLINE, Embase, Web of Science, Scopus, and ScienceDirect. Searches were conducted without time restrictions to capture both classical epidemiological evidence and emerging data from digital and geroscience research. Supplementary manual searches of reference lists and citation tracking of key studies were also undertaken. The search combined controlled vocabulary and keywords related to: “resting heart rate”, “heart rate variability”, “biological aging”, “longevity”, “inflammaging”, “epigenetic age”, “autonomic nervous system”, “frailty”, “biomarkers of aging”, and “wearable devices”. Boolean operators (AND, OR) were applied to ensure sensitivity, and only English-language studies involving human participants were included. Included works comprised original research articles, cohort and population-based studies, meta-analyses, and high-impact narrative or conceptual reviews that addressed the relationship between RHR and biological aging indicators. Studies restricted to acute illness, pediatric populations, or pharmacological interventions without mechanistic discussion were excluded. Priority was given to investigations reporting longitudinal outcomes, multi-system biomarkers, or integration of RHR into molecular and physiological aging frameworks.

The primary aim of this narrative review is to synthesize current evidence on resting heart rate as an integrative biomarker reflecting biological aging processes across multiple physiological systems. The review seeks to explore how RHR relates to systemic aging mechanisms, including inflammation, autonomic imbalance, oxidative stress, and metabolic decline, and to evaluate its potential as a noninvasive, population-level indicator of healthspan.

Results

Resting heart rate as a biomarker of biological aging

The growing body of research positions resting heart rate as a valuable biomarker that reflects biological aging processes beyond simple chronological age. RHR is now recognized among the multitude of individual markers associated with accelerated biological aging, alongside established indicators like glycated hemoglobin, triglycerides, and inflammatory markers (Lohman et al., 2021). This recognition stems from RHR's ability to capture information about multiple physiological systems that deteriorate with aging. Recent studies using advanced aging biomarkers demonstrate significant correlations between RHR and epigenetic age acceleration. Wearable device data shows that RHR correlates significantly with PCPhenoAge acceleration, suggesting that changes in heart rate can capture portions of biological aging at the molecular level (Sugden et al., 2023). This relationship extends to brain aging, where higher RHR (>80 bpm) associates with older brain age even among middle-aged adults, while RHR below 60 bpm correlates with younger brain age and smaller brain age gaps (Wang et al., 2025). The mechanisms linking RHR to biological aging appear multifactorial. Cross-species analysis reveals that RHR explains additional variance in lifespan beyond somatic mutation rates, suggesting it may directly influence aging processes or represent underlying mechanisms like metabolic rate that drive longevity (Garger et al., 2023). The strong correlation between faster heart rates and cardiac aging provides evidence that RHR effects may be mediated through promotion of adverse cardiovascular remodeling (Raisi-Estabragh et al., 2020, 2022). Importantly, RHR trajectories established early in life appear to persist into the seventh decade, suggesting that heart rate patterns may serve as long-term indicators of aging processes (O’Hare et al., 2018). The practical implications are significant: due to its ease of measurement and strong associations with health outcomes, RHR may serve as a preliminary health indicator to detect undiagnosed diseases and monitor biological aging, potentially making it a new target for better health outcomes (Gaye et al., 2024; Park et al., 2020). Beyond cardiovascular mechanisms, recent evidence indicates that RHR also reflects the integrated behavior of multisystem biomarkers that define the biological age phenotype. In Large-scale cluster analysis, identified 26 distinct biomarker signatures of aging combining inflammatory, metabolic,

endocrine, and renal indices, which showed independent predictive power for morbidity and mortality (Sebastiani et al., 2017). Individuals characterized by low inflammation and favorable renal function exhibited reduced biological aging rates, paralleling the phenotype observed in individuals with low RHR. Moreover, population-based research supports a bidirectional link between RHR and inflammatory pathways (Mao et al., 2023). Mao et al. demonstrated that in adults aged ≥65 years, elevated RHR was linearly associated with increased circulating interleukin-6, tumor necrosis factor-α, and vascular adhesion molecules, canonical mediators of chronic low-grade inflammation and endothelial dysfunction. Such findings place RHR within the broader inflammaging framework, whereby autonomic imbalance and metabolic strain contribute to systemic inflammatory activation that accelerates vascular and cognitive aging. Similarly, the DunedinPACE framework quantified the pace of biological aging using longitudinal data on 19 organ-system biomarkers, demonstrating that faster aging trajectories correspond to higher resting heart rate, lower fitness, and cognitive decline by midlife (Elliott et al., 2021). These findings suggest that RHR may act as a macroscopic, integrative signal mirroring cumulative multisystem dysregulation.

Population based evidence of RHR and health outcomes

Extensive population-based research has established robust associations between resting heart rate and multiple health outcomes across diverse demographic groups. Meta-analyses incorporating over 1.2 million participants demonstrate that each 10 beats per minute increase in RHR corresponds to a 9% higher risk of all-cause mortality and 8% higher risk of cardiovascular mortality in the general population (Zhang et al., 2023). These associations remain consistent even after adjusting for traditional cardiovascular risk factors, suggesting RHR provides independent prognostic information beyond conventional markers. What more, all-cause mortality risk is consistently higher in individuals with higher RHR. Large cohort analyses have shown that even within what is considered a “normal” range, those at the upper end face shorter life expectancy (Vazir et al., 2018). The magnitude of risk associated with elevated RHR is substantial across different thresholds. Individuals with resting heart rates above 80 bpm show a 45% increased risk of all-cause mortality compared to those in the lowest heart rate category, while cardiovascular mortality risk increases by 33 (Raisi-Estabragh et al., 2020; Zhang et al., 2023). More striking findings emerge at higher heart rate ranges: participants with baseline RHR above 75 bpm demonstrate approximately twofold higher risk of all-cause death, cardiovascular disease, and coronary heart disease compared to those below 55 bpm (Chen et al., 2019). Conversely, a lower RHR is often observed in healthy longevity cohorts, aligning with cross-species observations that slower heart rates correlate with longer lifespans (Jensen, 2019). The relationship between RHR and health outcomes extends beyond mortality to include functional capacity and cognitive decline. Higher resting heart rates associate with worse functional status and increased risk of future functional decline in older adults, independent of existing cardiovascular disease (Imahori et al., 2022; Ogliari et al., 2015; Yashin et al., 2013). Participants in the highest heart rate tertile (71-117 bpm) show nearly 80% higher risk of decline in activities of daily living compared to those with lower heart rates (Ogliari et al., 2015). Importantly, RHR trajectories over time provide additional prognostic information. Individuals with stable heart rates between ages 50-60 show 44% decreased cardiovascular disease risk compared to those with increasing RHR during this period (Chen et al., 2019). However, the relationship may be more complex than previously thought, with some studies identifying a U-shaped association where both very low (below 60 bpm) and elevated heart rates predict adverse outcomes, suggesting an optimal range of 60-70 bpm for cardiovascular health (Cui et al., 2021). These population-based findings demonstrate that RHR serves as an inexpensive and reliable risk predictor across healthy populations and those with existing cardiovascular disease, with associations that vary by sex, age, and baseline health status (Jensen et al., 2013; Raisi-Estabragh et al., 2020).

Heart rate variability and aging

Heart rate variability represents a sophisticated measure of autonomic nervous system function that provides deeper insights into aging processes than resting heart rate alone. HRV indices mirror global, sympathetic, and parasympathetic activities of the autonomic nervous system, with low HRV values typically indicating compromised health and increased mortality (Eggenberger et al., 2020). The physiological principle underlying HRV's importance is that healthy systems oscillate within a range of states, allowing flexible adaptation to various inputs, whereas dysregulated systems become locked in specific patterns similar to low HRV (Eggenberger et al., 2020). The relationship between HRV and aging follows a consistent pattern across populations, with autonomic regulation of blood pressure and cardiac rhythm progressively declining with increasing age (Schumann & Bär, 2022). Research demonstrates a clear decrease with age in the main parasympathetic HRV variables, as well as in the standard deviation of RR intervals and low frequency heart rate oscillations (Hernández-Vicente et al., 2020). Population-level studies confirm that HRV reduces

moderately with age, representing what appears to be a natural exhaustion of allostatic systems related to aging (Altini & Plews, 2021; Hernández-Vicente et al., 2020). The clinical significance of HRV in aging extends beyond cardiovascular health to encompass cognitive function and overall physiological resilience. Changes in HRV patterns provide a sensitive and early indicator of possible health declines, with efficient autonomic mechanisms characterized by high HRV signaling good adaptation to intrinsic and extrinsic factors (Rodrigues et al., 2022; Vanderlei et al., 2009). Notably, HRV serves as a promising early biomarker of cognitive impairment in older populations, with both increased sympathetic activity and decreased parasympathetic activity associated with worse cognitive performance across multiple domains (Forte et al., 2019; Rodrigues et al., 2022). Recent advances in HRV analysis have introduced the concept of "autonomic age gap" - a metric quantifying individual deviation between machine-learning-estimated biological age and chronological age based on autonomic nervous system function (Schumann et al., 2025). This approach demonstrates that comprehensive analysis of heart rhythm data can yield robust biomarkers for cardiovascular risk stratification, with biological age predictions significantly associated with increased mortality and elevated cardiovascular disease risk (Manimaran et al., 2025). The preservation of HRV appears critical for successful aging, with studies of centenarians showing that healthy longevity depends on maintenance of autonomic function, particularly parasympathetic HRV function, despite early age-related decreases (Olivieri et al., 2024). Persistently high HRV in older subjects represents a marker predictive of longevity, while very low HRV values can predict early mortality even in exceptionally long-lived individuals (Hernández-Vicente et al., 2020; Olivieri et al., 2024).

Preventive implications

The clinical utility of resting heart rate as a health biomarker extends far beyond simple monitoring, offering significant opportunities for preventive healthcare strategies. Due to its ease of measurement and strong associations with health outcomes, RHR may serve as a preliminary health indicator to detect undiagnosed cardiometabolic diseases, potentially making lowering RHR a new target for better health outcomes (Park et al., 2020). The modifiable nature of factors influencing RHR - including aerobic fitness, physical activity, body mass, smoking, drinking, sleep duration, and stress - aligns perfectly with general health recommendations, suggesting that interventions targeting these lifestyle components can simultaneously improve RHR and overall health (Park et al., 2020). Heart rate variability offers even more sophisticated clinical applications, particularly in the realm of early health screening and cognitive assessment. HRV can be considered a promising early biomarker of cognitive impairment in older populations, with both increased sympathetic activity and decreased parasympathetic activity associated with worse cognitive performance across multiple domains (Forte et al., 2019; Rodrigues et al., 2022). Changes in HRV patterns provide sensitive and early indicators of possible health declines, with efficient autonomic mechanisms characterized by high HRV signaling good adaptation to intrinsic and extrinsic factors (Rodrigues et al., 2022; Vanderlei et al., 2009). This positions periodic HRV assessments as particularly beneficial for monitoring cognitive health and providing indications for preventative exercise measures in older citizens (Eggenberger et al., 2020). Advanced applications of heart rhythm analysis are emerging through artificial intelligence approaches that estimate biological age based on autonomic nervous system function. The "autonomic age gap" - a metric quantifying individual deviation between machine-learning-estimated biological age and chronological age - demonstrates significant associations with increased mortality and elevated cardiovascular disease risk, highlighting its potential as a sensitive marker for early risk detection and longitudinal health monitoring (Manimaran et al., 2025; Schumann et al., 2025). These methods offer affordable and convenient approaches to biological age estimation, providing opportunities for early stratification of individuals at risk of accelerated aging (Bashkirtser et al., 2021). The practical implementation of RHR monitoring has proven feasible even in remote settings, as demonstrated during the COVID-19 pandemic when smartphone applications successfully measured RHR dynamics and revealed differential responses based on pre-pandemic fitness levels (Gonzales et al., 2023). Beyond biomarker applications, autonomic modulation represents a promising therapeutic target for cognitive health preservation, with time-domain HRV metrics showing potential for integration into multimodal screening approaches and preventive cognitive screening strategies (Kim, 2018; Maduro et al., 2025).

Discussion

The accumulated findings indicate that resting heart rate (RHR) constitutes a multidimensional biomarker of biological aging that reflects not merely cardiovascular workload, but the coordinated deterioration of metabolic, inflammatory, autonomic, and vascular pathways that shape aging trajectories. Individuals with persistently low RHR show phenotypic features of slower biological aging, whereas elevated RHR consistently associates with accelerated decline across molecular, functional, and organ-system domains. The biological plausibility of these associations is supported by convergent mechanistic evidence positioning RHR at the intersection of several aging-related processes. Chronic, low-grade inflammation is a hallmark of aging and may partly link elevated RHR to biological aging. Individuals with higher resting heart rates tend to have higher circulating inflammatory markers such as C-reactive protein (CRP) and interleukin-6 (Nanchen et al., 2013). One hypothesis is that sympathetic overactivity (often indicated by higher RHR) can injure vascular walls and trigger a neurohormonal inflammatory cascade, releasing cytokines like TNF-α and IL-6 (Goorakani et al., 2020a). Over time, this persistent inflammation and oxidative stress can lead to arterial stiffness and atherosclerotic plaque formation, processes that both accelerate cardiovascular aging and impair organ perfusion, including in the brain, potentially explaining cognitive links (Thayer et al., 2010). Thus, an elevated RHR may both reflect and contribute to an inflammatory milieu that promotes aging-related tissue damage.

Aging is accompanied by a shift in autonomic balance, generally characterized by reduced parasympathetic (vagal) tone and a relative dominance of sympathetic activity. This manifests as a decline in heart rate variability and, in many individuals, a higher resting pulse. Autonomic nervous system (ANS) imbalance is implicated in multiple age-related chronic conditions. A high RHR is a simple physiologic marker of this imbalance, essentially a sign of lower vagal and/or heightened sympathetic stimulation. Autonomic dysregulation can accelerate biological aging by increasing stress hormone levels (e.g. cortisol and catecholamines), raising blood pressure and blood glucose, and promoting pro-inflammatory gene expression. Consistent with this, low heart rate variability predicts frailty, disability, and mortality in older adults (Ogliari et al., 2015). By contrast, interventions that improve vagal tone (exercise, meditation, beta-blockade) often lower RHR and are associated with healthier aging profiles. Overall, an elevated RHR may be both an outcome of age-related ANS changes and an active contributor to further wear-and-tear on organ systems via sustained adrenergic signaling.

RHR is fundamentally a measure of the body's basal metabolic "speed," which ties it to mitochondrial function and metabolic signaling pathways. Higher resting heart rates indicate increased cardiac energy expenditure at rest; this may reflect systemic metabolic stress or inefficiency. Indeed, cross-species comparisons attribute the inverse relationship between heart rate and lifespan to differences in metabolic rate (smaller animals with faster resting heart rates burn energy quicker and accumulate damage sooner). In humans, a high RHR is often associated with features of metabolic syndrome including insulin resistance, dyslipidemia, and obesity. Increment in RHR has been linked to higher odds of obesity in longitudinal studies, and RHR is a predictor of incident metabolic syndrome (Goorakani et al., 2020). Mechanistically, hyperactive sympathetic signaling can impair insulin sensitivity and glucose control: elevated catecholamines raise heart rate and also drive hepatic glucose release and hyperinsulinemia, eventually causing insulin resistance (Anselmino et al., 2010; Grassi et al., 2009). Over years, this metabolic strain can contribute to pancreatic β-cell aging, vascular glycation damage, and other degenerative changes. Moreover, mitochondrial dysfunction - core element of cellular aging - may both result from and contribute to high RHR. Mitochondrial DNA damage and reduced respiratory efficiency force the heart to pump faster at rest to meet tissue energy needs. Reciprocally, chronic tachycardia increases myocardial oxygen demand and oxidative stress, potentially exhausting mitochondrial reserves in cardiac myocytes. In this way, RHR intersects with metabolic and mitochondrial pathways, serving as a macro-level indicator of how hard the body's cells are working to maintain homeostasis.

Vascular endothelial cells experience continuous mechanical and chemical stress, which accumulates with age. An elevated RHR exposes the endothelium to more frequent pulsatile shear stress and potentially less diastolic perfusion time, contributing to earlier fatigue of endothelial function. High RHR has been tied to markers of endothelial dysfunction (e.g. lower nitric oxide availability, higher plasma von Willebrand factor) in population studies (Nanchen et al., 2013). As noted, sympathetic activation and inflammation accompanying high RHR can reduce endothelial nitric oxide synthase activity and promote oxidative injury to the endothelium. Over time this leads to arterial stiffening and hypertension, creating a vicious cycle where stiff arteries further elevate pulse pressure and heart rate. Epidemiologically, RHR correlates with arterial stiffness indices and atherosclerotic burden (Demir et al., 2019). Endothelial cell senescence, often driven by telomere attrition and oxidative damage is accelerated in the context of chronic tachycardia due to these stresses. Therefore, a high

resting heart rate can be viewed as a marker of an accelerated cardiovascular aging process, integrating multiple insults from hemodynamic strain to inflammatory injury of the vessel lining.

Taken together, these mechanistic pathways reinforce the interpretation of RHR as a macroscopic integrator of multisystem aging rather than a narrow cardiovascular metric. The convergence of inflammatory activation, autonomic imbalance, metabolic-mitochondrial strain, and endothelial deterioration suggests that RHR mirrors the cumulative biological debt accrued across organ systems over the life course.

Limitations of the study

The studies included in this synthesis vary substantially in methodological rigor, analytic approaches, and measurement standards. Many relied on single-point RHR assessments rather than longitudinal trajectories, limiting inferences about temporal dynamics. Confounding by fitness level, medication use, sleep quality, and subclinical disease remains a significant challenge, as these factors influence both heart rate and aging biomarkers. Several mechanistic findings are largely associative and cannot confirm causality. Moreover, heterogeneity in HRV methodology (time-domain, frequency-domain, and nonlinear metrics) complicates direct comparison across studies.

Future research directions

Future work should prioritize large-scale, longitudinal designs capable of disentangling causal pathways linking resting heart rate to biological aging. Studies integrating RHR, HRV, and multimodal biomarkers such as epigenetic clocks, proteomic and metabolomic signatures, vascular imaging, and mitochondrial function are needed to clarify whether RHR is primarily a proxy marker or an active driver of multisystem decline. Quantifying how changes in RHR over time relate to dynamic shifts in biological age will be essential.

Conclusions

Resting heart rate emerges from the accumulated evidence as a robust, multidimensional indicator of biological aging that integrates the functional status of cardiovascular, metabolic, autonomic, and inflammatory systems. Its associations with molecular aging signatures, cognitive and functional decline, and long-term morbidity underscore its value as a practical, non-invasive marker capturing the pace of multisystem physiological deterioration. Heart rate variability further refines this perspective by providing granular insight into autonomic resilience, enabling more sensitive detection of early dysregulation that precedes clinical disease. Together, these measures highlight the central role of autonomic–cardiometabolic interactions in shaping aging trajectories. Given their accessibility, low cost, and strong prognostic performance, RHR and HRV represent promising tools for early risk stratification, long-term monitoring, and evaluation of preventive interventions. Their integration into biological aging frameworks may support more precise identification of individuals at risk of accelerated decline and offer a pathway toward personalized strategies aimed at preserving physiological function across the lifespan.

REFERENCES

1. Altini, M., & Plews, D. (2021). What Is behind Changes in Resting Heart Rate and Heart Rate Variability? A Large-Scale Analysis of Longitudinal Measurements Acquired in Free-Living. *Sensors*, *21*(23), 7932. https://doi.org/10.3390/s21237932
2. Anselmino, M., Ohrvik, J., Rydén, L., & Euro Heart Survey Investigators. (2010). Resting heart rate in patients with stable coronary artery disease and diabetes: A report from the euro heart survey on diabetes and the heart. *European Heart Journal*, *31*(24), 3040–3045. https://doi.org/10.1093/eurheartj/ehq368
3. Cao, Y., Li, S., Zha, Y., Yan, X., Jia, J., Luo, Y., & Chi, A. (2025). Effects of different incremental treadmill exercise protocols on the autonomic nervous system in healthy college students: A comparative study based on heart rate variability analysis. *Frontiers in Physiology*, *16*, 1579929. https://doi.org/10.3389/fphys.2025.1579929
4. Chen, X., Barywani, S. B., Hansson, P.-O., Östgärd Thunström, E., Rosengren, A., Ergatoudes, C., Mandalenakis, Z., Caidahl, K., & Fu, M. L. (2019). Impact of changes in heart rate with age on all-cause death and cardiovascular events in 50-year-old men from the general population. *Open Heart*, *6*(1), e000856. https://doi.org/10.1136/openhrt-2018-000856
5. Cui, X., Mandalenakis, Z., Thunström, E., Fu, M., Svärdsudd, K., & Hansson, P.-O. (2021). The impact of time-updated resting heart rate on cause-specific mortality in a random middle-aged male population: A lifetime follow-up. *Clinical Research in Cardiology*, *110*(6), 822–830. https://doi.org/10.1007/s00392-020-01714-w
6. Demir, V., Yılmaz, S., Ede, H., & Turan, Y. (2019). Correlation of Resting Heart Rate with the Severity and Complexity of Coronary Artery Disease: A Single-Center Retrospective Study. *International Journal of Preventive Medicine*, *10*(1). https://doi.org/10.4103/ijpvm.IJPVM_347_18

7. Department of Research and Innovation, Edem Medical Center, Strilky, Ukraine, Bashkirtsev, O., Sagan, V., National Technical University of Ukraine «Igor Sikorsky Kyiv Polytechnic Institute, Kyiv, Ukraine, Mawi International, Clearwater, Florida, USA, Gaevska, V., Department of Research and Innovation, Edem Medical Center, Strilky, Ukraine, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine, Zimba, O., Danylo Halytsky Lviv National Medical University, Lviv, Ukraine, & Department of Research and Innovation, Edem Medical Center, Strilky, Ukraine. (2021). BIOLOGICAL AGE ESTIMATION BASED ON HEART RATE VARIABILITY: A PILOT STUDY. *Proceedings of the Shevchenko Scientific Society. Medical Sciences*, *65*(2). https://doi.org/10.25040/ntsh2021.02.21
8. Eggenberger, P., Annaheim, S., Kündig, K. A., Rossi, R. M., Münzer, T., & De Bruin, E. D. (2020). Heart Rate Variability Mainly Relates to Cognitive Executive Functions and Improves Through Exergame Training in Older Adults: A Secondary Analysis of a 6-Month Randomized Controlled Trial. *Frontiers in Aging Neuroscience*, *12*, 197. https://doi.org/10.3389/fnagi.2020.00197
9. Elliott, M. L., Caspi, A., Houts, R. M., Ambler, A., Broadbent, J. M., Hancox, R. J., Harrington, H., Hogan, S., Keenan, R., Knodt, A., Leung, J. H., Melzer, T. R., Purdy, S. C., Ramrakha, S., Richmond-Rakerd, L. S., Righarts, A., Sugden, K., Thomson, W. M., Thorne, P. R., … Moffitt, T. E. (2021). Disparities in the pace of biological aging among midlife adults of the same chronological age have implications for future frailty risk and policy. *Nature Aging*, *1*(3), 295–308. https://doi.org/10.1038/s43587-021-00044-4
10. Forte, G., Favieri, F., & Casagrande, M. (2019). Heart Rate Variability and Cognitive Function: A Systematic Review. *Frontiers in Neuroscience*, *13*, 710. https://doi.org/10.3389/fnins.2019.00710
11. Garger, D., Meinel, M., Dietl, T., Hillig, C., Garzorz-Stark, N., Eyerich, K., De Angelis, M. H., Eyerich, S., & Menden, M. P. (2023). The impact of the cardiovascular component and somatic mutations on ageing. *Aging Cell*, *22*(10), e13957. https://doi.org/10.1111/acel.13957
12. Gaye, B., Valentin, E., Xanthakis, V., Perier, M.-C., Celermajer, D. S., Shipley, M., Marijon, E., Song, R. J., Empana, J.-P., Ramachandran, V. S., & Jouven, X. (2024). Association between change in heart rate over years and life span in the Paris Prospective 1, the Whitehall 1, and Framingham studies. *Scientific Reports*, *14*(1), 20052. https://doi.org/10.1038/s41598-024-70806-8
13. Gonzales, T. I., Jeon, J. Y., Lindsay, T., Westgate, K., Perez-Pozuelo, I., Hollidge, S., Wijndaele, K., Rennie, K., Forouhi, N., Griffin, S., Wareham, N., & Brage, S. (2023). Resting heart rate is a population-level biomarker of cardiorespiratory fitness: The Fenland Study. *PLOS ONE*, *18*(5), e0285272. https://doi.org/10.1371/journal.pone.0285272
14. Goorakani, Y., Sedigh Rahimabadi, M., Dehghan, A., Kazemi, M., Chijan, M. R., Bijani, M., Shahraki, H. R., Davoodi, A., Farjam, M., & Homayounfar, R. (2020a). Correlation of resting heart rate with anthropometric factors and serum biomarkers in a population-based study: Fasa PERSIAN cohort study. *BMC Cardiovascular Disorders*, *20*(1), 319. https://doi.org/10.1186/s12872-020-01594-y
15. Goorakani, Y., Sedigh Rahimabadi, M., Dehghan, A., Kazemi, M., Chijan, M. R., Bijani, M., Shahraki, H. R., Davoodi, A., Farjam, M., & Homayounfar, R. (2020b). Correlation of resting heart rate with anthropometric factors and serum biomarkers in a population-based study: Fasa PERSIAN cohort study. *BMC Cardiovascular Disorders*, *20*(1), 319. https://doi.org/10.1186/s12872-020-01594-y
16. Grassi, G., Arenare, F., Quarti-Trevano, F., Seravalle, G., & Mancia, G. (2009). Heart rate, sympathetic cardiovascular influences, and the metabolic syndrome. *Progress in Cardiovascular Diseases*, *52*(1), 31–37. https://doi.org/10.1016/j.pcad.2009.05.007
17. Hernández-Vicente, A., Hernando, D., Santos-Lozano, A., Rodríguez-Romo, G., Vicente-Rodríguez, G., Pueyo, E., Bailón, R., & Garatachea, N. (2020). Heart Rate Variability and Exceptional Longevity. *Frontiers in Physiology*, *11*, 566399. https://doi.org/10.3389/fphys.2020.566399
18. Imahori, Y., Vetrano, D. L., Xia, X., Grande, G., Ljungman, P., Fratiglioni, L., & Qiu, C. (2022). Association of resting heart rate with cognitive decline and dementia in older adults: A population-based cohort study. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*, *18*(10), 1779–1787. https://doi.org/10.1002/alz.12495
19. Jensen, M. T. (2019). Resting heart rate and relation to disease and longevity: Past, present and future. *Scandinavian Journal of Clinical and Laboratory Investigation*, *79*(1–2), 108–116. https://doi.org/10.1080/00365513.2019.1566567
20. Jensen, M. T., Suadicani, P., Hein, H. O., & Gyntelberg, F. (2013). Elevated resting heart rate, physical fitness and all-cause mortality: A 16-year follow-up in the Copenhagen Male Study. *Heart*, *99*(12), 882–887. https://doi.org/10.1136/heartjnl-2012-303375
21. Kim, J. (2018). ASSOCIATION BETWEEN TINNITUS AND MENTAL HEALTH AMONG KOREAN ADOLESCENTS: THE KOREA NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY. *CENTRAL EUROPEAN JOURNAL OF PUBLIC HEALTH*, *26*(1), 65–70. https://doi.org/10.21101/cejph.a4514
22. Lohman, T., Bains, G., Berk, L., & Lohman, E. (2021). Predictors of Biological Age: The Implications for Wellness and Aging Research. *Gerontology and Geriatric Medicine*, *7*, 23337214211046419. https://doi.org/10.1177/23337214211046419

23. MacDonald, E. A., Rose, R. A., & Quinn, T. A. (2020). Neurohumoral Control of Sinoatrial Node Activity and Heart Rate: Insight From Experimental Models and Findings From Humans. *Frontiers in Physiology*, *11*, 170. https://doi.org/10.3389/fphys.2020.00170
24. Maduro, P. A., Maduro, L. A. R., Lima, P. E., Silva, A. C. C., Silva, R. D. C. M. D., Rocha, A. S. L., Ribeiro, M. J. S., Matoso, J. M. D., Bavaresco Gambassi, B., & Schwingel, P. A. (2025). Cardiac Autonomic Modulation and Cognitive Performance in Community-Dwelling Older Adults: A Preliminary Study. *Neurology International*, *17*(5), 74. https://doi.org/10.3390/neurolint17050074
25. Manimaran, G., Puthusserypady, S., Dominguez, H., & Bardram, J. E. (2025). Cardiovascular Risk Assessment via Sleep Patterns and ECG-Based Biological Age Estimation. *Journal of Clinical Medicine*, *14*(10), 3339. https://doi.org/10.3390/jcm14103339
26. Mao, M., Liu, R., Dong, Y., Wang, C., Ren, Y., Tian, N., Tang, S., Hou, T., Cong, L., Wang, Y., Du, Y., & Qiu, C. (2023). Resting heart rate, cognitive function, and inflammation in older adults: A population-based study. *Aging Clinical and Experimental Research*, *35*(11), 2821–2829. https://doi.org/10.1007/s40520-023-02576-8
27. Nanchen, D., Stott, D. J., Gussekloo, J., Mooijaart, S. P., Westendorp, R. G. J., Jukema, J. W., Macfarlane, P. W., Cornuz, J., Rodondi, N., Buckley, B. M., Ford, I., Sattar, N., de Craen, A. J. M., & Group, on behalf of the P. (2013a). Resting heart rate and incident heart failure and cardiovascular mortality in older adults: Role of inflammation and endothelial dysfunction: the PROSPER study. *European Journal of Heart Failure*, *15*(5), 581–588. https://doi.org/10.1093/eurjhf/hfs195
28. Nanchen, D., Stott, D. J., Gussekloo, J., Mooijaart, S. P., Westendorp, R. G. J., Jukema, J. W., Macfarlane, P. W., Cornuz, J., Rodondi, N., Buckley, B. M., Ford, I., Sattar, N., de Craen, A. J. M., & Group, on behalf of the P. (2013b). Resting heart rate and incident heart failure and cardiovascular mortality in older adults: Role of inflammation and endothelial dysfunction: the PROSPER study. *European Journal of Heart Failure*, *15*(5), 581–588. https://doi.org/10.1093/eurjhf/hfs195
29. Ogliari, G., Mahinrad, S., Stott, D. J., Jukema, J. W., Mooijaart, S. P., Macfarlane, P. W., Clark, E. N., Kearney, P. M., Westendorp, R. G. J., De Craen, A. J. M., & Sabayan, B. (2015). Resting heart rate, heart rate variability and functional decline in old age. *Canadian Medical Association Journal*, *187*(15), E442–E449. https://doi.org/10.1503/cmaj.150462
30. Ogliari, G., Mahinrad, S., Stott, D. J., Jukema, J. W., Mooijaart, S. P., Macfarlane, P. W., Clark, E. N., Kearney, P. M., Westendorp, R. G. J., de Craen, A. J. M., & Sabayan, B. (2015). Resting heart rate, heart rate variability and functional decline in old age. *CMAJ: Canadian Medical Association Journal = Journal de l'Association Medicale Canadienne*, *187*(15), E442–E449. https://doi.org/10.1503/cmaj.150462
31. O'Hare, C., Kuh, D., & Hardy, R. (2018). Association of Early-Life Factors With Life-Course Trajectories of Resting Heart Rate: More Than 6 Decades of Follow-up. *JAMA Pediatrics*, *172*(4), e175525. https://doi.org/10.1001/jamapediatrics.2017.5525
32. Olivieri, F., Biscetti, L., Pimpini, L., Pelliccioni, G., Sabbatinelli, J., & Giunta, S. (2024). Heart rate variability and autonomic nervous system imbalance: Potential biomarkers and detectable hallmarks of aging and inflammaging. *Ageing Research Reviews*, *101*, 102521. https://doi.org/10.1016/j.arr.2024.102521
33. Park, E., Kim, H., Choi, I., Han, H., Han, K., Jung, H., & Im, G. (2020). Psychiatric Distress as a Common Risk Factor for Tinnitus and Joint Pain: A National Population-Based Survey. *CLINICAL AND EXPERIMENTAL OTORHINOLARYNGOLOGY*, *13*(3), 234–240. https://doi.org/10.21053/ceo.2019.00563
34. Raisi-Estabragh, Z., Cooper, J., Judge, R., Khanji, M. Y., Munroe, P. B., Cooper, C., Harvey, N. C., & Petersen, S. E. (2020). Age, sex and disease-specific associations between resting heart rate and cardiovascular mortality in the UK BIOBANK. *PLOS ONE*, *15*(5), e0233898. https://doi.org/10.1371/journal.pone.0233898
35. Raisi-Estabragh, Z., Salih, A., Gkontra, P., Atehortúa, A., Radeva, P., Boscolo Galazzo, I., Menegaz, G., Harvey, N. C., Lekadir, K., & Petersen, S. E. (2022). Estimation of biological heart age using cardiovascular magnetic resonance radiomics. *Scientific Reports*, *12*(1), 12805. https://doi.org/10.1038/s41598-022-16639-9
36. Rodrigues, E., Lima, D., Barbosa, P., Gonzaga, K., Guerra, R. O., Pimentel, M., Barbosa, H., & Maciel, Á. (2022). HRV Monitoring Using Commercial Wearable Devices as a Health Indicator for Older Persons during the Pandemic. *Sensors*, *22*(5), 2001. https://doi.org/10.3390/s22052001
37. Schumann, A., & Bär, K.-J. (2022). Autonomic aging – A dataset to quantify changes of cardiovascular autonomic function during healthy aging. *Scientific Data*, *9*(1), 95. https://doi.org/10.1038/s41597-022-01202-y
38. Schumann, A., Gupta, Y., Gerstorf, D., Demuth, I., Olecka, M., Gaser, C., & Bär, K.-J. (2025, April 17). *The autonomic age gap: A machine learning approach to assess biological-calendar age deviations*. https://doi.org/10.1101/2025.04.16.25325919
39. Sebastiani, P., Thyagarajan, B., Sun, F., Schupf, N., Newman, A. B., Montano, M., & Perls, T. T. (2017). Biomarker signatures of aging. *Aging Cell*, *16*(2), 329–338. https://doi.org/10.1111/acel.12557
40. Speed, C., Arneil, T., Harle, R., Wilson, A., Karthikesalingam, A., McConnell, M., & Phillips, J. (2023). Measure by measure: Resting heart rate across the 24-hour cycle. *PLOS Digital Health*, *2*(4), e0000236. https://doi.org/10.1371/journal.pdig.0000236

41. Sugden, C., Du Preez, F. B., Olivier, L. R., & Deffur, A. (2023). *Wearable-ome meets epigenome: A novel approach to measuring biological age with wearable devices*. https://doi.org/10.1101/2023.04.11.536462
42. Thayer, J. F., Yamamoto, S. S., & Brosschot, J. F. (2010). The relationship of autonomic imbalance, heart rate variability and cardiovascular disease risk factors. *International Journal of Cardiology*, *141*(2), 122–131. https://doi.org/10.1016/j.ijcard.2009.09.543
43. Vanderlei, L. C. M., Pastre, C. M., Hoshi, R. A., Carvalho, T. D. D., & Godoy, M. F. D. (2009). Noções básicas de variabilidade da frequência cardíaca e sua aplicabilidade clínica. *Revista Brasileira de Cirurgia Cardiovascular*, *24*(2), 205–217. https://doi.org/10.1590/S0102-76382009000200018
44. Vazir, A., Claggett, B., Cheng, S., Skali, H., Shah, A., Agulair, D., Ballantyne, C. M., Vardeny, O., & Solomon, S. D. (2018). Association of Resting Heart Rate and Temporal Changes in Heart Rate With Outcomes in Participants of the Atherosclerosis Risk in Communities Study. *JAMA Cardiology*, *3*(3), 200–206. https://doi.org/10.1001/jamacardio.2017.4974
45. Wang, Z., Chen, N., Cao, S., Gao, L., Geok, S. K., & Liu, J. (2025). The effects of balance training on physical fitness and skill-related performance in basketball players: A systematic review. *BMC Sports Science, Medicine and Rehabilitation*, *17*(1), 108. https://doi.org/10.1186/s13102-025-01164-9
46. Yashin, A. I., Arbeev, K. G., Wu, D., Arbeeva, L. S., Kulminski, A., Akushevich, I., Culminskaya, I., Stallard, E., & Ukraintseva, S. V. (2013). How lifespan associated genes modulate aging changes: Lessons from analysis of longitudinal data. *Frontiers in Genetics*, *4*. https://doi.org/10.3389/fgene.2013.00003
47. Zhang, Y., Xie, H., He, Z., Zhang, F., Li, L., Wang, N., & Mao, D. (2023). Medical Therapy of Hearing Impairment and Tinnitus with Chinese Medicine: An Overview. *CHINESE JOURNAL OF INTEGRATIVE MEDICINE*, *29*(8), 761–768. https://doi.org/10.1007/s11655-022-3678-5