Review

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Lessons from Geroscience to End Smoking and Promote Healthy Aging

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Abstract

Smoking acts as an aging accelerant, and smokers can lose up to a decade of life expectancy to tobacco. This difference from non-smokers has long been reflected in the life insurance industry's higher premiums for smokers. However, as well as reducing risks of chronic disease and mortality, quitting smoking or switching to non-combustible tobacco harm reduction (THR) nicotine products significantly improve both longevity and healthy aging outcomes. The biology of aging, and how knowledge might extend health span (the healthy, functional years of life) through interventions that increase resilience, is being assessed in the interdisciplinary field of geroscience. Research employing biomarkers of aging (such as epigenetic clocks and telomere length) indicates rejuvenation effects when smokers quit or switch to THR. Nevertheless, the use of THR as a gerotherapeutic option is not well understood. Aligning THR, and specifically the use of "clean" non-combustible nicotine products, with geroscience goals by treating smoking not only as a cause of disease but as a modifiable driver of aging, presents new opportunities for public health. For example, aging outcomes, such as Parkinson's disease, cognitive aging and physical function, could be integrated into smoking cessation trials using THR and provide new ways to measure benefits. Concepts, such as intrinsic capacity—encompassing an individual's physical and cognitive functional ability—already offer practical metrics. Findings could be articulated in terms of achievable goals that might resonate anew with the public and policymakers and encourage THR uptake. This article applies insights from geroscience to tobacco control strategies to illustrate how "success" could be broadened beyond diseases avoided and deaths averted to encompass extended lifespan with improved health outcomes.

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Introduction

Smoking has long been recognized as a major threat to longevity. Longitudinal cohort studies in the mid-20th century first quantified the toll of tobacco on lifespan, revealing stark differences in survival between smokers and non-smokers.[1] In the 1950s, life insurance actuaries had already observed significantly shorter life expectancies among smokers.[2] Subsequent large-scale studies confirmed these early warnings: prolonged cigarette smoking eventually kills over half of persistent smokers and cuts an average of roughly ten years off an individual's life compared to a never-smoker.[3] However, with mounting evidence indicating smoking as a leading cause of multiple non-communicable diseases, by the late 20th century public messaging had become focused on disease-specific effects and shifted away from loss of life expectancy. Instead, research and interventions became targeted, such as lung-cancer screening programs or medications for prevention of heart disease in smokers.

Most smoking-attributable deaths stem from a short list of chronic illnesses: cancers (chiefly lung cancer), chronic respiratory diseases (especially chronic obstructive pulmonary disease, COPD), and cardiovascular diseases (such as coronary heart disease and stroke). Global estimates reinforce this: as of 2019, tobacco was responsible for over 7–8 million deaths annually worldwide, with the largest

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fractions due to lung cancer, COPD, ischemic heart disease, and stroke.[4] Smokers also face elevated risk for dozens of other conditions – from blindness and osteoporosis to peripheral vascular disease.

If smokers can be persuaded to quit in their 30s–50s, they can regain several years of life expectancy. Jha and colleagues[5] calculated that smokers who quit by around age 40 years regained 90% of potential life-years lost had they continued smoking. Le and colleagues[6] found that smokers who had smoked throughout adulthood up to age 35 were predicted to lose 9.1 years of life on average if they continued. However, if they quit smoking at that age, they could regain an average of 8.0 years' life expectancy. In addition to lifespan, the growing specialty of geroscience explores ways to extend the health span – the healthy, functional years of life – by considering holistically how the aging process drives chronic diseases.[7] Geroprotective interventions might include drugs and lifestyle changes to address biological rather than chronological age. Yet, despite the systemic aging effects of smoking, the use of tobacco harm reduction (THR) as a gerotherapeutic option has not by widely explored in geroscience studies.

In this paper I explore returning longevity to the focus of smoking cessation strategies and the use of "clean" non-combustible nicotine THR products, such as e-cigarettes, heated tobacco, and oral pouches, with emphasis on the aspect of increased health span. I propose roles for THR products to aid quitting and switching and highlight how geroscience data can support messaging for the public and policymakers.

Insurance Industry Insights

Intriguingly, one of the earliest sectors to act on smoking's mortality risk was the life insurance industry. Initially, and for several decades despite clear actuarial data on smokers' shortened lifespan, insurers were reluctant to adjust premiums or publicly acknowledge the risk.[2] Only after the United States Surgeon General's landmark 1964 report on smoking and health[8] did this silence break. In the same year, State Mutual, an insurance company in Massachusetts, MA, became the first insurer to offer a non-smoker discount on life insurance, effectively penalizing smokers with higher premiums.[2] Before long, differentiated underwriting for smokers and non-smokers became the industry norm. This change incentivized smoking cessation by rewarding quitters with lower rates and signaled that smoking was a quantifiable risk factor with financial implications. Some insurers even experimented with temporary smoker rates that could be lowered after a period of cessation.

Tobacco Harm Reduction: New Tools and New Evidence

In the 21st century, the landscape of tobacco use is being reshaped by the advent of THR products, including e-cigarettes, heated tobacco, Swedish snus, and oral nicotine pouches. These alternative nicotine-delivery methods do not involve combustion, thereby avoiding most of the toxins present in cigarette smoke. Their rise has opened new avenues to study the benefits of switching away from combustible cigarettes. Many of these products have become popular only in the past 10–15 years, meaning that long-term epidemiological evidence is still maturing. Traditional cohort studies may require decades to observe differences in disease outcomes from chronic conditions, such as cancer or COPD. However, use of real-world evidence and studies adopting alternative approaches, such as measurement of disease biomarkers, have provided encouraging findings in much shorter time periods. Smokers who switch completely to THR products have shown significant improvements in indicators of health risk. For example, smokers who transitioned to vaping in observational studies have shown reduced exposure to carcinogenic toxicants and improved respiratory symptoms.[9] A Cochrane review provided high-certainty evidence that nicotine e-cigarettes are more effective for smoking cessation than NRT.[10] This superior efficacy, coupled with toxicological studies showing that e-cigarettes have only a small fraction of the risks of smoking, has cemented the role of THR products as a pragmatic toolkit to reduce smoking-related disease. The United Kingdom has already integrated vaping into its stop-smoking services, and even the broader public health community is recognizing that "nicotine without smoke" can save lives.[11] In the

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United States, the National Institute on Drug Abuse supports THR as a more achievable goal that smoking abstinence and is funding relevant research.[12] However, while 39 e-cigarettes have received marketing approval for commercial sale, none has yet been submitted for approval as quitting aids.

Perhaps more profoundly, the emergence of THR has prompted scientists to develop biomarker-based methods to gauge health improvements much earlier than waiting for smokers to either die or be diagnosed as having a disease. It can take at least 20 years of follow-up to show lower rates of lung cancer or COPD definitively among people who switched to vaping or heated tobacco. By contrast, in a recent article, Yach and Scherer discussed how biomarkers of exposure and effect can supplement epidemiology to evaluate reduced-risk products.[13] These include biomarkers of toxicant exposure and early indicators of harm (e.g., inflammation and endothelial dysfunction). In clinical trials, smokers who switch to THR products have shown sharp reductions in exposure biomarkers (often approaching those of a complete quitter) and improvements in blood pressure, lung function, and cholesterol.[14,15] Biomarker panels range from simple cotinine tests to complex gene expression profiles. Even health providers and insurers have begun to consider this evolving science, recognizing the lower risk profile of former smokers who have switched.[13]

Some research is also examining biomarkers related to aging in the context of smoking cessation and switching. One example is measurement of the length of telomeres – the protective DNA end caps that shorten as cells age. Telomere length is often considered a marker of biological aging, and it is known that they shorten faster with continued exposure to cigarette smoke. Deb et al.[16] found that smokers have shorter leukocyte telomeres than age-matched non-smokers, and that quitting can slow this premature telomere attrition. By measuring such aging-related biomarkers, researchers hope to detect benefits of cessation or THR (e.g., slowed cellular aging) long before traditional endpoints of aging appear – perhaps even decades earlier. In short, the THR era has sparked a new scientific approach that bridges toxicology, epidemiology, and gerontology, allowing early estimation of years of life saved by quitting or switching.

Beyond Smoking Cessation – The Nicotine Paradox

Paradoxically, long-term smokers have a significantly lower risk of Parkinson's disease than never-smokers, with protective effects being suggested for nicotine.[17,18] Research suggests that nicotine may have neuroprotective properties: in animal models it reduces neuroinflammation and oxidative stress, and small clinical trials in patients with early Parkinson's disease or mild cognitive impairment have shown improvements in motor and cognitive performance.[17] Any potential benefit of nicotine never outweighs the harms of smoking, but it raises the prospect that smoke-free nicotine use could help to preserve brain function in aging individuals. The potential benefits of maintaining nicotine intake should be investigated in geroscience studies as well as smoking cessation.

Geroscience: Targeting Aging Processes for Health Span

The past decade has seen the rise of geroscience, which is an interdisciplinary field that seeks to understand the biology of aging and apply that knowledge to extend health span (the healthy, functional years of life). Geroscience starts from the insight that aging itself is the single biggest risk factor for most chronic diseases, including cancer, heart disease and age-related neurological and cognitive disorders (the very diseases also elevated by smoking). Rather than tackling diseases in isolation, geroscientists aim to slow the aging process, thereby delaying the onset or progression of multiple diseases at once – an appealing strategy. The goals of geroscience range from deciphering fundamental mechanisms, such as cellular senescence, DNA damage, chronic inflammation, and other hallmarks of aging, to developing geroprotective interventions, which might include drugs and lifestyle regimens, that retard those mechanisms and improve resilience. In practical terms, a successful geroscience intervention might allow a person to live to 90 or 100 years in good health

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instead of suffering multiple morbidities in their 70s or 80s. Notably, geroscience considers aging in terms of biology, meaning that a person might be biologically "older" or "younger" than their chronological age. Interventions aim is to maintain young biological age, slow progression or reduce it.

Several candidate interventions are being tested in humans. A flagship effort is the TAME Trial (Targeting Aging with Metformin), which aims to investigate whether the generic diabetes drug metformin can reduce multimorbidity in older adults. Metformin was chosen due to promising observational data showing beneficial effects in relation to type 2 diabetes (reduced cardiovascular effects and extended lifespan), cancer (reduced incidence and mortality) and possibly cognitive impairment, hinting at broad antiaging effects.[19] Other compounds, like sirolimus and its derivatives and senolytics that kill senescent cells, are also under study,[20,21] although data in humans remain sparse. Nevertheless, momentum in the field is palpable.

New institutional players have emerged, such as the Hevolution Foundation (Riyadh, Saudi Arabia), which is a $1-billion-plus initiative that funds aging biology and geroscience research globally. In 2022, Hevolution partnered with the American Federation for Aging Research (New York, NY, USA) to launch new investigator awards in aging biology. These fund dozens of young scientists to study topics ranging from cellular senescence to novel gerotherapeutics. For instance, some grants have explicitly encouraged work on compounds like metformin and sirolimus as potential longevity enhancers. Similarly the XPRIZE Healthspan award is offering $101 million to the team that develops a "proactive, accessible therapeutic that restores muscle, cognition, and immune function" in 10–20 years among people aged 65–80 years.[22] Smoking cessation and the use of THR may well be one of the most effective ways to achieve these outcomes.

In addition, cohorts in studies dedicated to aging research are expanding. For example, studies from the UK Biobank (https://www.ukbiobank.ac.uk/projects/prospective-studies-of-ageing-and-age-related-diseases/) and the U.S. Health and Retirement Study (https://hrs.isr.umich.edu/about) will provide rich longitudinal data to study how various exposures (including smoking) impact aging trajectories. To date they do not explicitly address the impact of smoking nor the benefits of cessation and THR.

One of the most significant advances in geroscience has been the development of biomarkers of aging – measurable indicators that reflect biological age or functional capacity better than chronological age. These include molecular measures, such as analysis of DNA methylation patterns to estimate biological age (also known as "epigenetic clocks"), protein and metabolite signatures of aging, inflammation markers like (e.g., IL-6), and physical indicators like gait speed or muscle strength. For example, the GrimAge epigenetic clock can predict mortality risk, and has shown that heavy smokers reach an advanced epigenetic age earlier than non-smokers.[23] Similarly, chronic smokers often exhibit higher levels of inflammatory cytokines and a more rapidly declining lung function than former and never smokers, indicating accelerated aging. On the flip side, these biomarkers offer a way to test the effects of anti-aging interventions in a feasible timeframe. Rather than waiting 30 years to see whether a drug lowers mortality, researchers can see within a 1–2 years if epigenetic aging has slowed.

Composite metrics for functional health are already available. These underpin efforts to address ways of measuring the effects of interventions that increase health span. The World Health Organization proposed the concept of intrinsic capacity as a holistic measure of an individual's functional age.[24] Unlike disease diagnoses, intrinsic capacity directly gauges an older person's functional ability in daily life. Thus, this measurement is essentially a composite of all the physical and mental capacities an individual can draw on. Intrinsic capacity is assessed across multiple domains (cognitive, vitality, locomotor, psychological, and sensory). Research has shown that intrinsic capacity tends to decline with age and, importantly, lifestyle factors significantly influence its trajectory.[25] Higher physical activity and a healthy body weight correlate with better intrinsic capacity profiles over time. Not surprisingly, tobacco use is associated with worse intrinsic capacity trajectories, reflecting the broad multisystem impairment associated with smoking. A lifelong heavy

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smoker might have the lung function, cognition, and muscle strength of someone 10 years older. Intrinsic capacity scores, therefore, provide an effective way to link geroscience and public health. It is now being validated as an endpoint for use in longitudinal studies and geroprotective trials.[26]

Bridging Smoking and Aging Research

There is a compelling case for closer collaboration between the tobacco control and geroscience fields. For one, geroscientists need to account fully for smoking as a key variable that can confound studies of aging. If a cohort study seeks to identify determinants of healthy aging but fails to stratify by smoking status, it may mistake effects of smoking for those of normal aging. Smoking accelerates many aspects of aging – onset of diseases, frailty, and even measurable aging at the cellular level. Smokers not only die younger on average than non-smokers, they also tend to experience age-related disabilities about a decade earlier.[27] To isolate the true impact of novel antiaging interventions, researchers must either exclude smokers or, better yet, include smoking status in study designs as a critical stratifier, for which adjustments are made in their analyses. Many ongoing aging studies (e.g., epigenetic clock research) do adjust for smoking, and it has been shown that smoking leaves a distinctive epigenetic signature. But, more integration of tobacco epidemiology into geroscience models is needed.

Conversely, tobacco researchers could use geroscience tools to better understand benefits of smoking cessation, including the use of THR products. Traditional smoking studies focus on short-term improvements in disease outcomes, like better lung function within 1 year of quitting. With the addition of geroscience biological age markers and functional measures, recovery may be captured in a more holistic way.

One powerful illustration of what might be learned comes from the seminal work of Jha and colleagues[5] on smoking cessation and life expectancy. In a large cohort in the United States of America, smokers who quit by around age 40 years regained most (90%) of the life-years they would have lost by continuing. Those who quit between ages 35–44 lived about 9 years longer than those who continued smoking, nearly reaching the lifespan of never-smokers. Even quitting at age 50 or 60 still added about 4–6 years of life relative to never quitting. Le and colleagues[6] presented very similar figures in their study using 2018 census data in the United States. Smokers who had smoked throughout adulthood up to age 35 were predicted to lose 9.1 years of life on average if they continued. However, if they quit smoking at that age, they could regain an average of 8.0 years' life expectancy. These dramatic benefits underscore that it is never too late to quit smoking. An intriguing question is: what if a smoker doesn't quit nicotine, but switches to a THR product in mid-life? The intuitive expectation is that switching completely to a non-combustible nicotine source would substantially mitigate risk, since most harm comes from smoke rather than nicotine. Epidemiological data are still emerging, but evidence from snus users in Sweden[28] and heated tobacco users in Japan[29] suggests long-term switchers have much lower rates of smoking-related diseases. Quantifying life gain, for instance in a 40-year-old who switches completely to clean nicotine, should be a priority and combine the expertise of epidemiologists and geroscientists.

Measuring Success in New Ways

By incorporating geroscience measures, THR outcomes can be broadened. Traditionally, "success" has been measured by diseases avoided and deaths averted. But studies could also measure outcomes like cognitive aging and physical function. For example, a trial could test whether older smokers who switch to vaping maintain better intrinsic capacity over time (e.g., slower declines in gait speed, memory, or muscle strength) than those who continue smoking. The highlighting of such improvements might resonate with the public and policymakers by linking quitting to positive aging and independence in later life, rather than, for example, quitting being only about preventing a heart attack. It also aligns with WHO's emphasis on functional ability during aging and echoes calls in medicine to shift focus from simply extending lifespan to improving health span.

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Policy Synergies and a Shared Research Agenda

The convergence of geroscience and tobacco control has practical implications for policy and research. First, aging and tobacco studies can integrate data. Large aging cohorts could collect detailed smoking and nicotine-use data and, vice versa, smoking cessation trials could include aging biomarkers and functional assessments. Collaborative analyses could yield new insights, such as identifying whether ex-smokers receiving nicotine-replacement therapy have different aging trajectories from ex-smokers who are completely nicotine-free. Second, regulatory science can evolve: agencies evaluating antiaging therapeutics and those overseeing new nicotine products might harmonize approaches. for instance, by considering biological aging markers as evidence in regulatory assessments of nicotine-only products. Third, insurers might benefit from more nuanced risk stratification using geroscience and THR data. Currently, many insurers still classify users of THR products as "tobacco users," and charge them the same high premiums as smokers, despite evidence of reduced risk. However, a 2024 industry report highlights the increasing complexities in products, regulations, and patterns of use, and encourages research and inspiration into technologies, biomarkers, and so on, to assess actuarial risk more reliably.[30]

Public health experts argue that insurers and wellness programs should "accept the science" by treating non-combustible nicotine users more leniently than smokers.[31] Insurers could even partner with geroscientists to develop aging-based risk metrics, illuminating how a 50-year-old ex-smoker biologically rejuvenates after cessation. In the long run, such incentives could save both lives and health-care costs, as fewer smokers develop expensive chronic diseases in midlife.

Finally, there is a need for shared research protocols and data between the traditionally separate realms of tobacco research and aging research. Tobacco companies and their academic collaborators have conducted many short-term studies of switching to THR products, generating data on biomarkers, lung function, etc. Meanwhile, academic geroscientists have cohorts and trials measuring longevity-related endpoints. The embedding of a THR arm into a geroscience trial or the other way around could greatly accelerate discovery. The private and public sectors both have roles: industry can provide products, technology, and funding while public institutions can ensure unbiased analysis and broad dissemination of findings. With transparency and independent oversight to overcome historical mistrust, the potential gains are huge.

Conclusions

Leveraging lessons from geroscience offers a fresh lens through which to reinvigorate the fight against smoking – shifting expectation away from solely preventing disease and death towards promoting healthy longevity and brain health. With the inclusion of geroscience data, benefits of quitting smoking or switching completely to THR products can be articulated in novel ways that might resonate with the public and policymakers. The synergy goes both ways. For geroscience, smoking remains a critical but controllable accelerant of aging that must be accounted for, and studying "natural" smoking cessation can give insights into resilience and recovery that could inform antiaging therapeutics. For tobacco control, geroscience provides new measures of "success". As we stand at the intersection of these fields, the message is one of optimism: by applying cutting-edge aging science to the world's leading preventable cause of death, a transformative innovation could not only add to life but also add life to the later years of millions of people.

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References

1. Doll R, Peto R, Boreham J, Sutherland I. Mortality in relation to smoking: 50 years' observations on male British doctors. BMJ. 2004 Jun 24;328:1519.
2. University of Alabama. The Life Insurance Industry's Long, Strange Silence about Smoking and Cancer – The Center for the Study of Tobacco and Society [Internet]. [cited 2025 Sep 3]. Available from: https://csts.ua.edu/life-insurance-long-strange-silence-about-smoking-and-cancer/
3. Doll R, Peto R, Wheatley K, Gray R, Sutherland I. Mortality in relation to smoking: 40 years' observations on male British doctors. BMJ. 1994 Oct 8;309(6959):901–11.
4. Reitsma MB, Kendrick PJ, Ababneh E, Abbafati C, Abbasi-Kangevari M, Abdoli A, et al. Spatial, temporal, and demographic patterns in prevalence of smoking tobacco use and attributable disease burden in 204 countries and territories, 1990–2019: a systematic analysis from the Global Burden of Disease Study 2019. The Lancet. 2021 Jun;397(10292):2337–60.
5. Jha P, Ramasundarahettige C, Landsman V, Rostron B, Thun M, Anderson RN, et al. 21st-Century Hazards of Smoking and Benefits of Cessation in the United States. N Engl J Med. 2013 Jan 24;368(4):341–50.
6. Le TTT, Mendez D, Warner KE. The Benefits of Quitting Smoking at Different Ages. American Journal of Preventive Medicine. 2024 Nov 1;67(5):684–8.
7. Addie S, Kohanski R, Ferrucci L, Carter C, Carrington-Lawrence S. Considering the Future of Geroscience: Goals and Opportunities Stemming From the Fourth Geroscience Summit. J Gerontol A Biol Sci Med Sci. 2024 Sep 1;79(9):glae179.
8. US Department of Health, Education and Welfare. Smoking and Health:: report of the surgeon general of the public health service [Internet]. US Department of Health, Education and Welfare; 1964 [cited 2025 Jan 14]. Available from: https://www.scribd.com/document/199073624/Smoking-and-Health
9. Goniewicz ML, Miller CR, Sutanto E, Li D. How effective are electronic cigarettes for reducing respiratory and cardiovascular risk in smokers? A systematic review. Harm Reduct J. 2020 Nov 23;17:91.
10. Hartmann-Boyce J, Ordóñez-Mena JM, Livingstone-Banks J, Fanshawe TR, Lindson N, Freeman SC, et al. Behavioural programmes for cigarette smoking cessation: investigating interactions between behavioural, motivational and delivery components in a systematic review and component network meta-analysis. Addiction. 2022 Aug;117(8):2145–56.
11. Abrams DB, Glasser AM, Villanti AC, Pearson JL, Rose S, Niaura RS. Managing nicotine without smoke to save lives now: Evidence for harm minimization. Prev Med. 2018 Dec;117:88–97.
12. Volkow N. Toward the development of e-cigarettes as smoking-cessation therapeutics | National Institute on Drug Abuse (NIDA) [Internet]. 2025 [cited 2025 Sep 11]. Available from: https://nida.nih.gov/about-nida/noras-blog/2025/09/toward-development-of-e-cigarettes-as-smoking-cessation-therapeutics
13. Yach D, Scherer G. Applications of biomarkers of exposure and biological effects in users of new generation tobacco and nicotine products: Tentative proposals. Drug Test Anal. 2023;15(10):1127–32.
14. Lüdicke F, Picavet P, Baker G, Haziza C, Poux V, Lama N, et al. Effects of Switching to the Tobacco Heating System 2.2 Menthol, Smoking Abstinence, or Continued Cigarette Smoking on Biomarkers of Exposure: A Randomized, Controlled, Open-Label, Multicenter Study in Sequential Confinement and Ambulatory Settings (Part 1). Nicotine Tob Res. 2018 Jan 5;20(2):161–72.
15. Edmiston JS, Webb KM, Wang J, Oliveri D, Liang Q, Sarkar M. Biomarkers of Exposure and Biomarkers of Potential Harm in Adult Smokers Who Switch to e-Vapor Products Relative to Cigarette Smoking in a 24-week, Randomized, Clinical Trial. Nicotine Tob Res. 2022 Jul 1;24(7):1047–54.
16. Deb S, Berei J, Miliavski E, Khan MJ, Broder TJ, Akurugo TA, et al. The Effects of Smoking on Telomere Length, Induction of Oncogenic Stress, and Chronic Inflammatory Responses Leading to Aging. Cells. 2024 Jan;13(11):884.
17. Barreto GE, Iarkov A, Moran VE. Beneficial effects of nicotine, cotinine and its metabolites as potential agents for Parkinson's disease. Front Aging Neurosci [Internet]. 2015 Jan 9 [cited 2025 Sep 4];6. Available from: https://www.frontiersin.org/journals/aging-neuroscience/articles/10.3389/fnagi.2014.00340/full

 doi:10.20944/preprints202510.0660.v1

18. Nicholatos JW, Francisco AB, Bender CA, Yeh T, Lugay FJ, Salazar JE, et al. Nicotine promotes neuron survival and partially protects from Parkinson's disease by suppressing SIRT6. Acta Neuropathologica Communications. 2018 Nov 8;6(1):120.
19. Barzilai N, Crandall JP, Kritchevsky SB, Espeland MA. Metformin as a Tool to Target Aging. Cell Metab. 2016 Jun 14;23(6):1060–5.
20. Lee DJW, Kuerec AH, Maier AB. Targeting ageing with rapamycin and its derivatives in humans: a systematic review. The Lancet Healthy Longevity. 2024 Feb 1;5(2):e152–62.
21. Zhang L, Pitcher LE, Prahalad V, Niedernhofer LJ, Robbins PD. Targeting cellular senescence with senotherapeutics: senolytics and senomorphics. The FEBS Journal. 2023;290(5):1362–83.
22. XPRIZE. $101M XPRIZE Healthspan to Drive Healthier Aging for All [Internet]. 2023 [cited 2025 Sep 4]. Available from: https://www.xprize.org/prizes/healthspan/articles/xprize-hevolution-solve-fshd-launch-101-million-healthspan-largest-history
23. Lu AT, Quach A, Wilson JG, Reiner AP, Aviv A, Raj K, et al. DNA methylation GrimAge strongly predicts lifespan and healthspan. Aging (Albany NY). 2019 Jan 21;11(2):303–27.
24. WHO. Healthy ageing and functional ability [Internet]. [cited 2025 Sep 4]. Available from: https://www.who.int/news-room/questions-and-answers/item/healthy-ageing-and-functional-ability
25. Bernal MC, Batista E, Martínez-Ballesté A, Solanas A. A functional approach to model intrinsic capacity in ageing trajectories. Sci Rep. 2025 Mar 6;15(1):7878.
26. Beyene MB, Visvanathan R, Ahmed M, Benyamin B, Beard JR, Amare AT. Development and validation of an intrinsic capacity score in the UK Biobank study. Maturitas [Internet]. 2024 Jul 1 [cited 2025 Sep 8];185. Available from: https://www.maturitas.org/article/S0378-5122(24)00071-9/fulltext
27. Zaninotto P, Head J, Steptoe A. Behavioural risk factors and healthy life expectancy: evidence from two longitudinal studies of ageing in England and the US. Sci Rep. 2020 Apr 24;10(1):6955.
28. Clarke E, Thompson K, Weaver S, Thompson J, O'Connell G. Snus: a compelling harm reduction alternative to cigarettes. Harm Reduct J. 2019 Nov 27;16(1):62.
29. Lee PN, Djurdjevic S, Weitkunat R, Baker G. Estimating the population health impact of introducing a reduced-risk tobacco product into Japan. The effect of differing assumptions, and some comparisons with the U.S. Regulatory Toxicology and Pharmacology. 2018 Dec 1;100:92–104.
30. Wyman O, Marsh & McLennan Advantage Insights. Insurer perspectives on smoking risks [Internet]. Marsh & McLennan Advantage Insights; 2019 [cited 2025 Sep 11]. Available from: https://www.marshmclennan.com/assets/insights/publications/2019/oct/20191030_Insure_Perspectives_on_Smoking_Risks.pdf
31. Consumer Choice Center. Fixing what's broken: practical consumer-friendly insurance reforms to save money [Internet]. Consumer Choice Center; 2024 [cited 2025 Sep 4]. Available from: https://consumerchoicecenter.org/wp-content/uploads/2024/11/Insurance-reform-fixing-whats-broken.pdf