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Global Healthspan Summit 2023: closing the gap between healthspan and lifespan

On 29–30 November 2023, the inaugural Global Healthspan Summit, convened in Riyadh by the nonprofit Hevolution Foundation, provided a dynamic platform that united experts from diverse sectors to foster collaborative discussions on aging research, innovative healthcare strategies and the healthspan ecosystem. This Meeting Report encapsulates the multifaceted insights that were garnered from the perspectives of science, economics and society.

The geroscience hypothesis addresses aging as a risk factor for most chronic diseases and emphasizes the interplay between lifestyle factors and genetics in determining healthspan. It posits that the manipulation of aging will delay the appearance or severity of many chronic diseases because these diseases share the same underlying major risk factor: age[1]. Although akin to lifespan, healthspan refers to the length of time that a person is healthy — not just alive. The current medical frame of reference refers to chronological age when describing age as a risk factor, but there is a need to distinguish immutable chronological age from variable biological age. Biological aging represents a dynamic complex system that requires multiple approaches to unravel its various etiological pathways and determine how they intersect over time. Interventions — in terms of medicinal modalities and environmental constructs — must be discovered and tested to optimize healthspan. There are socioeconomic and moral imperatives for public health to focus on healthspan, which requires a radical transition from reactive treatment to proactive health maintenance and disease prevention. However, despite myriad benefits, the regulatory and public health landscape remains challenging, as there are scientific hurdles and public and professional skepticism regarding geroscience and healthspan optimization.

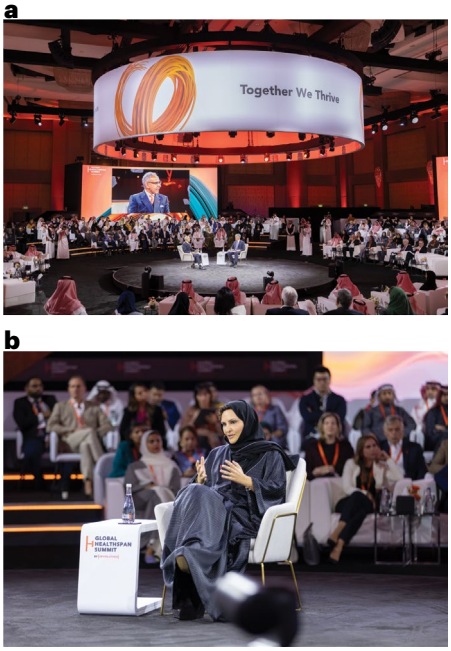

Fig. 1 | Snapshots of discussions at the Global Healthspan Summit in Riyadh, Saudi Arabia. **a**, M.K., chief executive officer of Hevolution Foundation, discusses the future of health ecosystems with Jonathan Symonds, GSK Board of Directors Chair. **b**, H.A.S., Hevolution Foundation Vice President of Organizational Strategy & Development, discusses the promise of a 'healthspanned' society.

Biomarker discovery remains a linchpin for basic, translational and clinical research

The summit unfolded a rich tapestry of discussions that encompassed aging pathways, biomarkers and interventions, including outstanding issues and potential solutions. Topics spanned the therapeutic potential of senolytics, senomorphics and artificial intelligence (AI)-driven systems for composite biomarker discovery to the importance of molecular resilience and imperative for a healthspan ecosystem. Many agreed the dearth of validated translatable biomarkers of biological age and aging is hindering basic research and the discovery and translation of potential interventions into the clinic.

The interpretation of biomarker-derived biological age is limited due to unknowns about the causal relationship between these biomarkers and aging mechanisms. Using epigenome-wide Mendelian randomization of large-scale genetic data, Vadim Gladyshev and his team at Harvard Medical School identified CpG sites that are causal to aging-related traits, including healthspan-related ones such as the frailty index[2]. They found known epigenetic clocks were not enriched for these sites. The causality-enriched sites were segregated into those that contributed to aging and those that protected against it. Although 'aging-contributive' sites were similar in number to 'aging-protective' sites, the net effect of the combined sites was aging-contributive. DNA methylation changes that accumulated at the aging-contributive sites were associated with age-related damage that contributes to mortality risk, whereas adaptations that accumulated at the aging-protective sites were associated with longer lifespan. There was only a weak association between aging-contributive and aging-protective changes, which suggests that damaging changes may primarily reflect downstream effects of aging rather than causing them (whereas protective changes may be causal to healthy longevity). This was further supported by the reversal of damaging changes, but not protective ones, by rejuvenating cell reprogramming in aged-induced pluripotent stem cells. This comprehensive map of human CpG sites that are causal to aging traits could be used to further inform understandings of aging-accelerating events, the discovery of causal aging biomarkers and the assessment of novel aging-protective interventions.

Alexandra Bause (Apollo Health Ventures) and Jorge Conde (Andreessen Horowitz) noted that composite biomarkers would be most informative for personalizing interventions. Stephen Kritchevsky (Wake Forest University) discussed using dynamic biomarkers as surrogate end points and described the two-pronged end-point selection strategy of the TAME trial[3]. One was an age-related disease end point that could be extrapolated further to biological aging and the other was an easily

measured and reliable standard end point that regulators would accept. He also discussed with John Beard (Columbia University) the potential utility of composite outcome measures such as intrinsic capacity, which was recently included in the latest International Classification of Diseases (ICD-11), as clinical end points[4].

Competition fosters collaboration and catalyzes healthspan realization

The Biomarkers of Aging Challenge was announced to find predictive biomarkers of age, time of death, and aging outcomes such as multimorbidity, using 500 methylation-profiled blood samples and curated outcomes data and electronic medical records, with cash prizes amounting to US $200,000 over the next 2 years[5]. The launch of the ambitious XPRIZE Healthspan competition, led by Jamie Justice, was also announced at the summit: this is a seven-year, $101-million global initiative to revolutionize human aging, supported by Hevolution as the leading funder. The competition aims to facilitate the creation of the healthspan industry by spurring regulatory recognition through the achievement of solutions that reverse functional loss in muscle, immunity and cognition in individuals aged 65 to 80. Teams will be provided funding and support to transform winning solutions into businesses and therapeutics. Feedback was solicited on proposed end points, which enabled stakeholders to collaborate on much-needed consensus definitions and measurements of aging. Entrants discussed cooperation and complementary research, and global participation with nationally sponsored teams and the announcement of winners at the World Expo 2030 in Riyadh were hopefully anticipated.

Aging societies promise a dividend of longer, healthier and more productive lives

Leading economists and scientists discussed aging societies, and acknowledged the need for collaboration across sectors and disciplines to achieve healthspan — especially as the global population surpassed 8 billion. Declining birth rates and increasing life expectancy prompted questions about resource scarcity and economic sustainability. Andrew Scott from the London Business School argued for reframing the negative narrative around aging societies to emphasize their promise and celebrate the benefits of young and middle-aged people living longer, with global life expectancy exceeding 70.

Research by Scott and his collaborators has shown that healthspan is more valuable economically and personally than is lifespan. Using a value of statistical life economic model (which places a monetary value on gains from longer life, better health and changes in the rate of aging), he found that compressing the period of morbidity to improve health in older age was more valuable than further increases in life expectancy[6]. The economic value of gains from an extra year of healthy life expectancy always exceeded those from an extra year of life expectancy. Targeting biological aging instead of individual diseases offered potentially larger economic gains than eradicating individual diseases, with an attenuation of aging that increased life expectancy by 1 year being worth $38 trillion and by 10 years, $367 trillion. The more progress that is made in improving biological aging, the greater the value of further improvements. Moreover, individual gains would aggregate synergistically and benefit all ages in society and future generations. These findings assumed widespread access to healthy aging interventions. To reap the three-dimensional healthspan dividend of longer, healthier and more productive lives, Scott proposed applying the same drivers that increased life expectancy in the first place: ingenuity, investment, innovation and institutions.

Equitable healthspan is a moral imperative for the benefit of all

Examining the ethical dimensions of pursuing healthspan, Arthur Caplan (New York University Grossman School of Medicine) and Julian Savulescu (National University of Singapore (NUS)) discussed the definition of aging as a disease — Caplan proposed the notion as early as 1981 (ref. 7); the perils of healthspan inequity; and ethical approaches and frameworks, such as collective reflective equilibrium[8], for resolving ethical issues. They outlined gaps in determining the ethical goals and societal implications of healthspan interventions and emphasized the moral imperative for universal rather than elite access. The COVID-19 pandemic demonstrated that exclusivity founded on patents and intellectual property rights hindered local manufacturing, fair pricing and access. To avoid socioeconomic disparities in healthspan, incentives (such as funding contingent on intellectual property waivers) and disincentives (such as heavy taxation on interventions that lack equitable access) could be implemented. However, this assumes an approach — egalitarianism — that has yet to be agreed upon. The pandemic also underscored the need for basic infrastructure to enable local manufacturing and distribution, echoed by H. Balkhy from the World Health Organization.

Managing public expectations responsibly and establishing robust ethical guidelines for healthspan studies would be crucial, including participant diversity and the possibility of expanding research into pediatric populations, for instance, with preventive interventions. Understanding stakeholders' healthspan conceptions should inform the formulation of ethical goals and guidelines. Societal expectations about healthspan and its ethical principles may be quantified through the deployment of online experimental platforms such as the 'Moral Machine'[9] that are designed to explore moral dilemmas. Integrating such data with ethical theory would inform the development of ethical policies to guide healthspan provision and ethical frameworks to resolve dilemmas.

Entrepreneurship and strategic investment will catalyze the healthspan revolution

The summit explored roles and routes to entrepreneurship, investment and funding to advance geroscience and healthspan interventions into the clinic and market. As an impact investor, Hevolution outlined its mission-driven approach with criteria that focus on strategic alignment, novel intellectual property and commercial viability, as well as risk mitigation strategies that leverage their internal scientific team and global network. Emerging trends and areas for investment focused on research and development that addresses hallmarks of aging, such as chronic inflammation, frailty and cognitive changes. Hevolution launched the Breakthrough Innovation Alliance as a collaborative program that is aimed at curating and supporting high-potential ideas that could be translated into practical development programs to seed the next generation of transformative interventions and companies.

Debates on the maturity of biotechnology targets and assets highlighted translation and scalability challenges, and the need for meaningful personalized precision interventions at a population level. Advice to entrepreneurs included goal setting to drive stakeholder alignment and support; aiming to 'fail fast' to refocus on more successful projects; focusing on reaching clear value inflection points; communicating honestly with investors to set expectations and overcome challenges together; diversifying funding sources in a

nondilutive fashion; attracting researchers at low cost through open-source projects; obtaining human data as early as possible to demonstrate proof of concept; considering geographical arbitrage opportunities to improve cost efficiency; formalizing agreements with peer-reviewed journals to publish negative results; and staying resilient. Recommendations for investors included leveraging being a nonprofit organization to start other nonprofit organizations; microfunding multiple projects to better tolerate failure; and considering investing in very early-stage research and development for high-impact interventions and higher returns, despite higher risk.

Digital innovation will democratize clinical trials and healthcare

Discussions on the challenges and positive effects of digital technologies showcased the application of AI for longitudinal data analysis, intervention development and patient selection. Platforms to integrate electronic medical records, real-world data and evidence worldwide were described, for training AI models, enabling large population-wide research studies and facilitating global access to clinical trials. Andrea Britta Maier (NUS) and Laura Niedernhofer (University of Minnesota), both of whom are investigating healthspan-related processes[10,11], argued that decentralized clinical trials and clinical trial networks would provide the means for recruiting sufficiently large and diverse populations to identify high-impact interventions quickly and cost efficiently. Jonathan Symonds from GSK highlighted the need for technological innovation to address the scale of data required for predictive risk assessments, preventive and early interventions, and the identification of healthy high-risk individuals as well as patients.

AI-based platforms are being developed to fully characterize individuals for research. Eric Verdin (Buck Institute) described their machine-learning bioinformatic platform that integrates multiomics (including proteomics, metabolomics and transcriptomics) with data from wearables and electronic medical records to study the mechanisms of aging, identify causal relationships and predict ways to improve human health[12]. This platform is being applied by a research team led by Lee Hood at the Center for Phenomic Health.

Digital technologies may also democratize some diagnostics and interventions. For instance, Khizer Khaderi (Stanford Medicine) devised the vision performance index (VPI), which uses natural human–technology interaction to assess visual, cognitive and motor function on the basis of five psychometric domains[13]. Incorporation of the VPI application programming interface into video games enabled evaluation of the visual function of players, which may help to monitor age-related ocular diseases such as cataracts and macular degeneration. This technology may also facilitate the collection of data from up to about 3.5 billion players globally for the development of healthspan markers, diagnostics and interventions. Khizer Khaderi also discussed a subsequent study of lifestyle factors and screentime, using over 100 psychometric measures, informed a VPI application programming interface version that can assess visual, cognitive and motor function holistically while working symbiotically with players to protect and nudge them toward behaviors such as screen breaks and exercise. However, this application would rely on numerous players being willing to donate their psychometric data altruistically (as people already do with blood).

The need to transform the healthcare system

Regulators, payers and governments resist the system-wide transformation and reevaluation of health priorities that are required to shift the paradigm from 'sick-care' to healthcare. Jonathan Symonds stressed that governments need to recognize the economic case for investing in healthspan. James Bethell (UK Parliament) agreed on the need to pivot resource allocation from treatment to prevention, to combat the drivers of disease early and reduce the burden of chronic disease and comorbidity in older people. Healthcare in its current socioeconomic and political framework is unsustainable and can only advance through preventive healthcare. A lack of accounting technology to ascribe value to early interventions – despite their high impact and low risk – hinders the investment case. James Bethell is working with the Milken Institute to help to define the healthspan ecosystem and requisite systemic changes. Diane Ty (Milken Institute) and John Beard also argued for wider societal change, including the eradication of ageism and misconceptions about aging, aging societies and aging individuals[14].

Conclusion

Hevolution's Global Healthspan Summit[15] offered a platform for high-level discussions that encompassed all areas of aging science, with talks that blended scientific advancements, collaborative academia–industry endeavors, economic imperatives, and societal and ethical considerations (Fig. 1). The summit showcased the current landscape of aging research and underscored the necessity for interdisciplinary collaboration, visionary investments and paradigm shifts to pave the way for a healthier and more productive future for aging societies. Participants, speakers and panelists were inspired by the meeting of minds; one industry leader remarked that, in the future, they might look back and marvel at their attendance of such an historic event. Hevolution committed to being a driving force in shaping the healthspan trajectory with one of us (M.K.) concluding the summit by rallying all attendees to become 'hevolutionaries' and join the healthspan revolution.

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References

1. Sierra, F. & Kohanski, R. *Geroscience* **39**, 1–5 (2017).
2. Ying, K. et al. *Nat. Aging* **4**, 231–246 (2024).
3. Justice, J. N. et al. *Geroscience* **40**, 419–436 (2018).
4. de Souto Barreto, P. et al. *Nat. Aging* **3**, 1474–1479 (2023).
5. Biomarkers of Aging Consortium, Methuselah Foundation & VoLo Foundation. Biomarkers of Aging Challenge. *agingconsortium.org*, https://www.agingconsortium.org/challenge (accessed 18 December, 2023).
6. Scott, A. J., Ellison, M. & Sinclair, D. A. *Nat. Aging* **1**, 616–623 (2021).
7. Caplan, A. L. in *Concepts of Health and Disease: Interdisciplinary Perspectives* (eds Caplan A. L. et al.) 725–737 (Addison-Wesley, Advanced Book Program/World Science Division, 1981).
8. Savulescu, J., Gyngell, C. & Kahane, G. *Bioethics* **35**, 652–663 (2021).
9. Awad, E. et al. *Nature* **563**, 59–64 (2018).
10. Goh, J., Wong, E., Soh, J., Britta Maier, A. & Kennedy, B. K. *FEBS J.* **290**, 649–668 (2023).
11. Gurkar, A. U. et al. *Nat. Aging* **3**, 776–790 (2023).
12. Yurkovich, J. T. et al. *Nat. Rev. Genet.* https://doi.org/10.1038/s41576-023-00674-x (2023).
13. Ahmed, Y. et al. *Ophthalmol. Sci.* **4**, 100349 (2024).
14. Dunning, L., Ty, D., Shah, P. & McDermott, M. *Geriatrics (Basel)* **8**, 58–73 (2023).
15. Hevolution Foundation. Global Healthspan Summit. *hevolution.com*, https://www.hevolution.com/en/ghs (accessed 19 December 2023).

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Competing interests

The authors declare no competing interests.