HEVOLUTION

THE GLOBAL HEALTHSPAN REPORT

A New Agenda for Global Health





Foreword

The reality of ageing today is an unforgiving one: people are living longer yet are spending more years in poor health than ever before. This paradox is a testament to both the successes and the severe limitations of our current healthcare paradigm. We believe this can and must change. Everyone has the right to age well. Every person should live better not just longer.

Launched in 2021, Hevolution Foundation is a first of its kind global non-profit organization that provides grants and early-stage investments to incentivize independent research and entrepreneurship in the emerging field of healthspan science.

Our mission is to extend healthy lifespan for the benefit of all humanity by driving efforts to understand the processes of ageing. We want to increase the number of safe and effective treatments entering the market, compress the timeline of drug development using the latest tools and technologies, and increase accessibility to therapeutics that extend healthy lifespan.



Since our launch two years ago, Hevolution has been on an impressive trajectory, committing over \$200 million in global funding to help reshape and accelerate discoveries and tangible contributions to healthy ageing research and development. We have also established a fast-moving investment team based in Boston, Massachusetts, extending Hevolution's operational footprint globally and amplifying its engagement with the broader life sciences ecosystem that now includes a short list of companies that are potential investment candidates this year. We are proud to work with leading scientific institutions around the world to expand the emerging field of healthspan science such as the U.S. National Academy of Medicine, the Buck Institute, the American Federation for Aging Research, and multiple universities worldwide, including nine across The Kingdom of Saudi Arabia, in addition to The United States of America, The Netherlands, Austria, and Australia.

Our success is inseparable from our partnerships, because humanity achieves its greatest potential through collaboration. Indeed, engagement is a critical part of our work. It helps us to identify gaps, share valuable insights, unite diverse perspectives, and offer practical recommendations to help quide our collaborative efforts to deliver healthspan for all.

To that end, we are delighted to share our first Global Healthspan Report: A New Agenda for Global Health. This report synthesizes the findings of our global survey of 4,000 citizens and domain specialists from over 20 countries, two workshops with experts in London and Boston, and a series of in-depth interviews with scientists, investors, practitioners and policy experts. We are so pleased to bring together this group of experts to share their views and perspectives. We hope this report, published at our Global Healthspan Summit in Riyadh, serves as a clarion call for advancing the healthspan agenda for all.

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Abbreviations & Acronyms

Aged society An aged society is one where 14% of the population will be over 65.
BMI body mass index
CAGR compound annual growth rate
CRISPR clustered regularly interspaced short palindromic repeats
DALYs disability adjusted life years
FDA Food and Drug Administration (United States)
G20 Group of 20
GCC Gulf Cooperation Council
IMF International Monetary Fund

GDP

gross domestic product

MENA Middle East and North Africa

mRNA messenger ribonucleic acid

NAM

National Academy of Medicine (United States)

NCD noncommunicable disease

NHS National Health Service (United Kingdom)

NIH National Institute of Health (United States)

WHO World Health Organisation



Healthspan science is flourishing, thanks to innovations in medical research and new ways of understanding human biology.

The evidence base is building for novel approaches to tackling the diseases of ageing. Early diagnostic innovations, such as AI-powered liquid biopsies, promise to catch killer diseases before they take hold. Senolytics can target damaged cells before they wreak havoc on the body. mRNA vaccines and cell and gene therapy hold promise for stopping diseases from emerging in the first place. Leading the research agenda are a growing pool of investors and scientists who are boldly questioning the common assumption of chronic disease as an inevitable consequence of ageing. Their efforts are essential; nearly two in three health professionals we surveyed (63%) believe health systems will not be financially viable by 2030 without a breakthrough in healthy longevity science.

To capitalise on progress, scientific research into expanding healthspan needs enabling reforms on how therapies are tested, approved, and reimbursed.

Our survey found scientists were most optimistic about the impact of stem cells on longevity (63%), but large shares also marked AI, next-generation vaccines, genomic editing, advanced biomarker detection and therapies targeting senescence. The business case is compelling; 97% of financial professionals believe healthy longevity investments can yield greater financial returns than traditional healthcare investments. But as a highly regulated sector, pharmaceutical research and investment is heavily influenced by the incentives laid out by regulators. To encourage bold R&D, medical agencies and payers (insurance companies or governments) need to craft a pro-innovation regulatory and approval environment that rewards innovations that prevent, rather than treat, disease, and that recognise the clinical validity of 'pre-disease' states and new biomarkers.



Emerging economies face a worrying rise in unhealthy ageing; with the right actions now, they can learn lessons from the mistakes of the developed economies – and be innovation leaders in their own right.

Our survey found that citizens in emerging markets are strongly in favour of innovation and reforms to enable healthy longevity, from willingness to use longevity therapies and services to rethinking policy areas like pension age. As their health systems are less entrenched, these countries, home to most of the world's population, can build the infrastructure required for a 'healthspan society' including a greater role for digital technology and preventive approaches. Their regulatory approaches could also challenge conventions and norms, fostering responsible innovation in the healthspan field.



Health system reform is often glacial; ambition and policy leadership will now be key to tackle the crisis of unhealthy ageing.

Most policy professionals in our survey believe that healthy longevity requires a new approach, but a similar majority (75%) would prefer to be a "fast follower" rather than a leader when it comes to approving longevity therapies. This shows the need for policy leadership for countries to show vision and provide the path for others to advance. Globally, coordination and collaboration on best practices to support preventative health is essential; international organisations and standards-setting bodies can aid in this and leverage networks like the G20.

Executive Summary

Antibiotics, vaccines, agricultural productivity, and public health policies all helped significantly increase human lifespan in developed economies over the 20th century. These hard-won additional years are frequently blighted with chronic disease and morbidity. In both developed and emerging economies, 'unhealthy longevity' is weighing heavily on the individual, as well as health systems, economies, and societies at large.

The 'healthspan' agenda – which emphasises the extension of healthy life years, not simply lifespan – is moving from the field of geroscience into the spheres of public health, policy, and economics. Thanks to breakthroughs in science and digital technologies, and radical new approaches to how we organise work, pensions, and education, countries can finally make healthspan achievable for all citizens.

But the shift is systemic and complex, requiring new ways of thinking and breaking away from conventions and the status quo, stretching from how medical research is conducted to health service design. This Hevolution Foundation report, drawing from a global survey of citizens and experts, two expert workshops and an interview program with leading thinkers in science, investment, and policy, outlines the key calls to action for enabling the healthspan transition.

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About the Surveys

To inform the report and complement its research, interview program and workshops, Hevolution Foundation commissioned two global surveys, the findings of which are described in this report.



20 Countries Were Covered

Africa

Nigeria South Africa

Asia-Pacific

Australia China India Japan Singapore

Europe

France Germany United Kingdom

Latin America Brazil

Data for the citizen survey was collected between June 16, 2023 and July 27, 2023 via online surveys.

Data for the healthcare professionals survey was collected June 15, 2023 and July 14, 2023 using computer assisted telephone interviews methodology

4,000 Citizens



1,000 Healthcare **Professionals**



Bahrain Egypt Kuwait Oman Qatar Saudi Arabia United Arab Emirates

Middle East

North America

Canada

United States

Igniting the Healthspan Revolution

Antibiotics, vaccines, improved food production technologies and investments in sanitation and public health all helped dramatically lengthen human lifespan in Western countries over the 20th century, and promise to lift the six billion inhabitants of developing countries to look forward to the same (1).

These hard-won additional years are frequently blighted with chronic disease and morbidity from what longevity thought leader Peter Attia has dubbed the 'four horsemen' - atherosclerotic disease, cancer, neurodegenerative disease and foundational disease, a spectrum ranging from insulin resistance to fatty liver disease. These together account for 80% of deaths of those over 50 who do not smoke (2). "Through most of human evolution, lifespan has been between 20 and 30 years," says Dr Nir Barzilai, director of the Institute for Aging Research at the Albert Einstein College of Medicine. "In the last 150 years, we did something incredible: we tripled our lifespan. In doing this, we got diseases that haven't been part of the previous 100,000 years of human evolution."

The burden of 'unhealthy longevity' on individuals, their families and health systems is immense – and set to worsen. Globally, disability adjusted life years, a metric that includes years of life lost to time lived in a state of ill health, increased by 32% between 1990 and 2019, and is expected to have increased by 55% between 2004 and 2030 (3,4).

An estimated 20% of healthcare spending growth will be attributed to ageing by 2025 (5). Rising costs coincide with economic stagnation common to ageing economies, including slower GDP growth, smaller working age populations and tighter government budgets (6). Fertility rates are falling too, a demographic time bomb as tomorrow's workforce shrinks ever further (7).

The outlook for emerging economies is more dire. Falling fertility in emerging economies is doubly significant because the family network shoulders a considerable share of the care burden for older people, and it is shrinking. The number of people aged 60 and over in China will rise from 254 million in 2019 to 402 million by 2040, making up 28% of the population. An estimated 14 million of them will need long-term care by 2030, and there will not be enough young people to shoulder the informal support that the country has implicitly relied on (8). Several Asian economies are also 'prematurely aging', meaning their population is growing old in ways that typify demographic trends in much higher income countries. Thailand, for instance, reached the threshold for an aged society in 2021 (14% of the population aged 65 or over) yet unlike aged societies like Japan and South Korea, Thailand is not yet a developed country (9).

> "IN THE LAST 150 YEARS, WE DID SOMETHING INCREDIBLE: WE TRIPLED OUR LIFESPAN. IN DOING THIS, WE GOT DISEASES THAT HAVEN'T BEEN PART OF THE 100,000 YEARS OF HUMAN EVOLUTION"

- DR NIR BARZILAI

Founding Director, Institute for Aging Research, Albert Einstein College of Medicine Gulf countries, meanwhile, have a median population that is relatively young, and yet there is evidence of an increased incidence of diseases traditionally associated with ageing (10). In Oman, for instance, almost 20% of all colorectal cancer patients were diagnosed under the age of 40, partly attributed to changes to lifestyle and adoption of Western diets (11). "The primary health care challenge in [Saudi Arabia] is cardiovascular diseases," says Salman AlAsiry, Vice President of Law, Ethics, & Compliance at Hevolution Foundation.

THE HEALTHSPAN IMPERATIVE

Healthspan – a concept referring to years of life lived in good health, rather than simply being alive – is a concept that is moving from the field of geroscience (12) to wider public health, biotech and policy circles, as the unsustainable trajectory of this every-growing number chronically ill older people becomes evident everywhere. As a testament to its importance, the National Academy of Medicine in the US has selected healthy longevity one of the grand challenges. "Of all the issues that face the world and humanity, population ageing and healthy longevity are especially important," says Dr Victor Dzau, president of the National Academy of Medicine.

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"OF ALL THE ISSUES THAT FACE THE WORLD AND HUMANITY, THE AGEING POPULATION AND HEALTHY LONGEVITY IS VERY IMPORTANT"

-DR. VICTOR J. DZAU

President, National Academy of Medicine, United States



Current healthcare systems are poorly set up to respond to this new paradigm. In 1948 when the NHS was founded, a baby boy had a life expectancy of 65.86 years and that of a baby girl was 70.29 (13). Now, the average across both males and females is 81.77 years (14). According to Lord David Prior of Brampton, a member of the UK House of Lords and former chairman of England's National Health Service (NHS), developed economy health systems are skewed towards acute and 'sick-care', rather than prevention and supporting elderly people with chronic disease. "We've got a massive investment in legacy institutions of a late stage sick care system," says Lord Prior. "We have invested in hospitals at the expense of primary care, social care and public health."

Emerging economies, meanwhile, face a twin challenge of supporting growing numbers of older people with chronic disease, while still battling a high infectious disease burden with conditions like tuberculosis, HIV/AIDS and malaria, all in a context of lower incomes and smaller public budgets.

The outlook might seem gloomy, but projections are not laws. The decisions we take now will impact how our societies adapt to demographic change. Growing older need not mean growing sicker, as evidenced by how the health of centenarians varies across countries, especially in the so-called 'blue zones', defined as regions of the world with higher than usual numbers of healthy older people. Demographic ageing does not inevitably cause an exponential rise in

healthcare costs (15). Advances in technology and preventative healthcare can postpone the onset of ill health before death, with periods of morbidity becoming 'compressed' into shorter periods (16). "Healthspan has been the objective of medicine since Greek times, and suddenly we have new tools and new understanding at our disposal," says Lord Prior of the UK House of Lords.

By expanding healthspan, older citizens can be productive, active, and contributing members of societies. But achieving healthspan requires ambition and innovation, from challenging norms and assumptions about biological ageing to revising medical curricula to emphasize preventive health insights which today's medics are barely taught. It requires harnessing the latest advances in wearable technology, artificial intelligence, early diagnostics, drug repurposing, and exploring frontier ideas like stem cell therapy, mRNA vaccines for chronic disease and drug development areas like senolytics, which can tackle the process of cell ageing itself. It will be a society-wide reform, going far beyond biotechnology and healthcare actors, to include labour markets, advertising and branding, and education. If achieved, expanding human healthspan will also raise new questions about everything from intergenerational equity to reforms to the retirement age, while at the same time accommodating cultural and religious differences on the scope of medical research into ageing and longevity.

Health systems of the developed world were designed for a far-gone age, focused on acute care, infectious disease and hospital-based interventions. Combined with the power of vaccines, antibiotics and sanitation, they were successful in lengthening life expectancy in the 19th and 20th century. "The traditional health system, based upon diseasebased interventions, has got us living to 70 or 80," says Andrew Scott, Professor of Economics at London Business School. "But a system designed around the model for infectious disease interventions can't cope with the second longevity revolution, which is about changing how we age."

'Healthspan' marks a paradigm shift in medicine and policy that targets both adding more years to life and more active life into those years. Ambitious but essential, the healthspan vision requires far-reaching changes to health systems, from drug development to the structure and distribution of health services. One such pivot is towards prevention. "The older population has 2-4 times more chronic disease that is responsible for increased disease burden and significant

"A SYSTEM DESIGNED AROUND THE MODEL FOR INFECTIOUS DISEASE INTERVENTIONS CAN'T COPE WITH THE SECOND LONGEVITY **REVOLUTION, WHICH IS ABOUT CHANGING HOW WE AGE"**

- PROFESSOR ANDREW J. SCOTT Professor of Economics, London Business School

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consumption of healthcare resources and facilities," says Dr Dzau at the National Academies of Medicine. "A population health approach is key. Prevention needs to happen further upstream."

Primary and secondary care spending constitute the majority of health spending with just 2 to 3% on average directed at prevention, according to Professor Scott. The focus is intervening on the consequences of ageing. Yet, by a large majority, prevention is seen as the most effective lever to achieve healthy longevity. Nearly two thirds of citizens (64%) in our survey agree that influencing lifestyle and diet was the strategy that would help most to rapidly extend healthy human lifespan. Indeed, under a healthspan paradigm, the citizen becomes a central actor at the heart of the prevention system, with the majority of medical experts (52%) believing that the main consequence of a healthspan system would be to empower individuals to manage their own health. This means designing a health system that puts the individual in command.

Figure 1

"Which of the following strategies do you think will help most rapidly extend healthy human lifespan?" (Citizen responses)



Delivering this change will require a shift in outlook and training, such as moving more nurses and doctors to local community bases so it's "easier to just pop in and talk to people," says Professor Scott. Upskilling will also be needed. As explored in the London Hevolution Foundation workshop, medical education needs to incorporate preventive and lifestyle education, which has played a minor role in conventional curricula.

Medics are not taught enough about preventive approaches and the role of nutrition, sleep, and stress during their training. A Lancet analysis showed that nutrition is insufficiently incorporated into medical curricula across countries, settings and years of study (17). A 2021 survey of US and UK medical schools found that students received an average of 11 hours of nutrition training, part of which is typically student-run (18). This shows there is significant need for more policies to embed preventative care in the healthcare system if we are to move towards a prevention-focused approach to health. For instance, Resolution 959, introduced by the American College of Preventive Medicine and passed in 2017 by the American Medical Association House of Delegates, is a commitment to support policies that incentivise or fund the inclusion of lifestyle medicine education in undergraduate, graduate and continuing medical education (19).

Professional incentives are also often geared towards acute care and surgical specialty - thus towards promoting the status quo. To enable a shift towards preventative care, medical curricula must evolve to bring areas like nutrition and lifestyle to the fore, so that prospects for a career in that space become more attractive.

Technology will be a powerful ally in achieving a prevention-focused health system. For consumers, there are now a range of affordable, effective wearables that track activity, diet and sleep, while social networks incentivise and reward healthy decisions by making them more fun and social, such as sharing of runs and 'personal bests' on Strava. These promote self-monitoring and goal-setting, and are associated with improved physiological outcomes such as a reduced BMI, reduced blood

Figure 2

"What do you think would be the main consequence (Medical experts responses)



pressure, and improved psychosocial outcomes such as depression and anxiety (20, 21).

A study on the long-term benefits of using trackers such as continuous blood glucose monitors indicates beneficial effects on parameters like blood sugar levels (22) while online health communities have improved patient outcomes and increased empowerment (23). But such tools are often confined to the already healthy, better off citizens in society, and need to be made more commonly available.

As clinical evidence grows, those who regulate, approve and reimburse digital health technologies will likely see value in shrinking the 'ill' years of life, which currently weigh heavily on health systems and the public purse. "Healthcare providers will be happy to pay once they see how healthspan is extended," predicts Dr Barzilai of the Albert Einstein College of Medicine.

Health system reform is a challenging endeavour akin to changing an engine while a vehicle is moving. But there are signs that, with political will and given pressing needs, legacy institutions can shake out of their inertia and make greater use of technology. Telemedicine and virtual consultations are a case in point. These were technically possible for years prior to the outbreak of COVID-19, offering more convenience and service efficiency for patients and medical staff, but



"What do you think would be the main consequences of healthy longevity for healthcare systems?"

a combination of inertia and regulatory obstacles prevented adoption. That changed under necessity during lockdowns, and digital consultation has now become more accepted. In the first months of the COVID-19 pandemic, the number of teleconsultations skyrocketed to as high as 50% of all doctor consultations in Denmark and Spain, for example (24). Nine countries (Estonia, Hungary, Iceland, Ireland, Korea, Luxembourg, Mexico, Turkey and the United States) which previously only allowed in-person medical consultations also adapted their policies.

Though triggered by a crisis, the changes look set to remain. Some 40% of patients now prefer telemedicine to in-person consultations (24). England's NHS is increasingly rolling out 'virtual wards' that can monitor patients at home or in care homes, greatly reducing pressure on overstretched hospitals (25). This shows change is possible, and reforms that facilitate the uptake of preventive and health management technologies, from consumers to clinical actors, could play a major role in bringing greater agility to the current system.

The Healthspan Science Frontier

Prevention can delay the onset of noncommunicable disease, but cannot entirely eradicate it. Genetic and environmental stresses, and the march of time, statistically increase risk. Even those sceptical that the overall lifespan of humans can be expanded recognize the possibility of 'compressing' the period of life in ill-health to the final months or years.

Optimists believe biotech and pharmaceutical innovation, from stem cells and breakthroughs in early diagnostics to mRNA-based vaccines for chronic disease, could bring curative breakthroughs for conditions that have so far eluded a cure, like dementia and cancer. Indeed, most professionals in the healthy longevity field expect a breakthrough in longevity research within the next 5 years. They also see those breakthroughs as necessary: nearly two in three health professionals we surveyed (63%) believe health systems will not be financially viable by 2030 without a breakthrough in healthy longevity science.

Figure 3

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"To what extent do you agree with the following: without breakthrough in healthy longevity, our healthcare systems will not be financially viable by 2030." (Medical experts responses)



'Pills for living longer' are no longer the stuff of science fiction: the humble statin has saved thousands of lives including in those who lead healthy lifestyles overall but are at risk with the passing of time. Lord Prior of the UK House of Lords says the pharmaceutical and biotech industry should not be underestimated as an engine of change in bringing new therapies to market. "If you look at who rose to the challenge of COVID, it wasn't primarily the traditional healthcare service," he says. "They treated people who got the symptoms of the disease, but it was the pharma industry - it was BionTech, Moderna, Pfizer, AstraZeneca – who came up with a vaccine in under a year and now these new mRNA vaccines can be produced in under 60 days."

The healthspan science field is now advancing across several fronts, from stem cells and gene editing to repurposing mainstream drugs which confer surprising healthspan benefits. Our survey found scientists were most optimistic about the impact of stem cells on longevity (63%), but large shares also marked AI, next-generation vaccines, genomic editing, advanced biomarker detection and therapies targeting cellular senescence.

Figure 4

"When do you believe that breakthroughs in longevity research will significantly impact society?" (Expert and citizen reponses)



A Breakthrough is **Expected this Decade**

Half of healthy longevity professionals expect a breakthrough in longevity research within the next 5 years (most healthy longevity professionals expect it within the next decade)

Big Pharma is believed to be the number one driver in all regions, but the belief is significantly greater in Brazil, the Middle East and Europe

Improving social benefits is believed to be the most important objective of longevity research for both citizens and healthy longevity professionals

Figure 5

"Which scientific breakthroughs do you believe will have the most significant impact on the longevity field in the next 10 years?" (Scientists responses)



STEM CELLS

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Stem cell research is by far the most impactful field, our survey found. Stem cells are found in the developing fetus and are undifferentiated cells from which cells with specialised functions are generated, such as brain cells, blood cells, muscle cells or bone cells (26). Many adult tissues also contain stem cells with the ability to differentiate into tissue-specific cell types. These lose their potential for self-renewal and tissue generation (27). Clinical trial results from studies of stem cell transplantations on frailty and facial skin ageing have been positive (27). Stem cells in conjunction with genetic functions create a shield of protection to withstand erosion by ageing and may result in longevity (28).

Preserving the functions of stem cells for longer could have significant impacts on slowing the ageing process. Currently, stem cell research is strictly regulated in many countries due to ethical concerns. However, regulatory reforms are starting to emerge, with the potential to facilitate new avenues and therapeutic uses. Japan has adopted a policy of regulatory reform, aiming to stimulate business and speed up the approval process for stem cell therapies (29). Businesses

and patient groups in the US and UK have advocated for similar approaches (30).

The Middle East is an emerging hub for stem cell research. Jordan has been leading the way for the regulation of stem cell research, passing laws in 2014 that allow the use of human embryonic stem cells from permissible sources - including excess eggs from in vitro fertilisation, which are banned from use in many other countries - by government organisations and publicly funded academic institutions (31). Other countries in the region have since moved in the same direction, with a centre established in the UAE developing COVID-19 treatments using stem cells (32).

TACKLING CELLULAR SENESCENCE

Senolytics and senomorphics are drugs that kill or modify the behaviour of senescent cells, which have stopped replicating (33) and which contribute to ageing by secreting bioactive molecules with mostly deleterious functions. Senolytics have shown promise in treating age-related diseases such as diabetic kidney disease and idiopathic pulmonary fibrosis. "It may take only one dose of senolytics to get rid of those senescent cancerharboring cells that are susceptible to senolytics, because senescent cells generally do not divide," says Dr James Kirkland, President of the American Federation for Ageing Research.

"There are at least 40 conditions that senolytics appear to delay, prevent, alleviate or treat in preclinical models. These are things like osteoporosis, osteoarthritis, diabetes, complications of obesity, complications of chemotherapy, cancer development and cancer recurrence. There are several hundred senolytic candidates discovered now since we discovered the first ones." According to Dr Kirkland, the study of senescent cells is relevant across various ageing treatments, including metformin, a diabetes drug. "Metformin works in part by inhibiting production of the things that senescent cells use to damage those around them," he says.

"THERE ARE AT LEAST 40 CONDITIONS THAT SENOLYTICS APPEAR TO DELAY, PREVENT, ALLEVIATE OR TREAT IN PRECLINICAL MODELS"

- DR. JAMES KIRKLAND

President, American Federation for Ageing Research

GENETIC AND EPIGENETIC MODIFICATION

Epigenetic mechanisms – cellular processes that regulate and change gene expression without directly bringing about gene mutations – are a second target in healthspan research (34). Certain practices that influence ageing, such as dietary restriction, work in part by causing epigenetic modifications. (35). A number of pharmaceutical companies are currently working on reproducing genetic processes that slow ageing. Merck is developing a CETP inhibitor for cardiovascular disease. Ionis is developing an APOC3 inhibitor. A third project is an IGF1 receptor antibody, developed by several pharmaceuticals to fight cancer; in preclinical studies on animals, they lived 10% longer and were much healthier.

For Dr Barzilai at the Albert Einstein College of Medicine, this sector is poised for growth as the global health data ecosystem expands. "Two-thirds of the drugs approved by the FDA last year were based on genetic findings in humans," says Dr. Barzilai. "If we had the genome sequencing and electronic medical records of all 8 billion people in the world, we'd be able to treat every disease in the world."

Gene editing is another way of exploring the role of genetics in the ageing process. CRISPRbased gene editing can be used to promote healthspan by identifying and silencing genes that affect ageing (36). Studies in mice with a mutation that causes progeria – a rare, fatal, genetic disease that causes symptoms of early ageing - have shown that a CRISPR-like technique corrected the mutation and prevented the heart damage typical of the disease. Treated mice lived more than twice as long as untreated animals (37). Gene editing has been a particularly fast-changing area of research. "From an investment point of view, we see medical progress as a slow process of chipping away," says Dr Andrew Levin, Partner & Managing Director at RA Capital Management. "But mRNA and editing systems have changed a fair bit, at a steeper curve than you'd normally expect."

DRUG REPURPOSING

If the allure of breakthrough novel therapies is understandable, there is also a surprising level of optimism that existing drugs could deliver healthspan benefits. Our survey found that 86% of medical professionals believe repurposing existing drugs for healthy longevity applications is a viable approach to enhancing the field.

Among top candidates are rapamycin and metformin, with about one third of respondents being highly optimistic that they can be repurposed for healthspan benefits. The former is an FDA-approved drug used to prevent organ transplant rejection and in cystic lung disease (38), and has been found to slow ageing in worms, flies, and mice, by inhibiting the activity of TORC1, a protein complex that senses nutrients inside every cell (39). The same type of drug was found to improve immune function in elderly patients (40). It is currently in veterinary clinical trials to assess its ability to slow ageing in dogs (41). Metformin is a FDA-approved drug that has been used successfully to treat diabetes and occasionally helps to treat symptoms of polycystic ovary syndrome (42). It has been shown to delay ageing in animals and influence fundamental ageing factors that underlie age-related conditions in humans.

"Two studies, one in the New England Journal of Medicine and one in the Lancet, showed that giving a COVID patient metformin within three days of infection prevented hospitalisation, death, and long COVID by over 40%," says Dr Barzilai. "Metformin changes immunity and cell formation, and that's why it has the potential to prevent age related disease." The American Federation for Ageing Research is conducting an ongoing clinical trial called TAME (43). Dr Barzilai believes that once metformin is approved for ageing by the FDA, "the acceleration of what biotechs will be able to do will be amazing."

THE AI ENABLER

Cutting across each healthspan field is the capability of contemporary artificial intelligence, which was the second most-cited breakthrough innovation opportunity in our survey. Al can identify patterns within complex data sets including genomic, proteomic, metabolic and physiological ageingrelated data and unveil mechanistic relationships. It can identify biomarkers of age which would allow targeted treatment, optimises the development of new compounds and improves selection of appropriate treatments by predicting treatment outcomes (44).

Al offers significant positive implications for drug development. "This is the most exciting time in medical science in a generation," says Lord Prior of the UK House of Lords. "The understanding of how molecular biology works at a cell and gene level, and the application of generative AI to simulate the behaviour of human cells, opens up the field of regenerative medicine in a way that would have been inconceivable three, four or five years ago. Cancer vaccines, cell therapies where you can, for example, reprogram cells to produce dopamine, these are extraordinary potential breakthroughs."

Scaling up AI in healthcare will require regulatory frameworks - of which there are few at the moment worldwide, though this is starting to change. In October 2023, the WHO released a series of considerations for regulation of AI for health, aiming to provide a framework for countries. The WHO report emphasises transparency and documentation, risk management, clarity of intended use, a commitment to data quality and protection, and fostering collaboration between regulatory bodies, research bodies, medical practitioners and patients (45). This will support countries in establishing safe and effective AI regulations for healthcare.

Investing In Healthspan

The task of backing scientific research into healthspan medicine is falling to a large extent on biotech investors as public funding options, like those of the National Institutes of Health (NIH), tend to focus on specific disease verticals, rather than targeting ageing biology per say. Dr. Jan Adams, partner at Apollo Health Ventures views the strategy of targeting the so-called 'hallmarks of ageing' as "a vertical in its own right", distinguishing it from traditional approaches to healthcare investment.

Figure 6

The Hallmarks of Ageing



"THIS IS THE MOST EXCITING TIME IN MEDICAL SCIENCE IN A GENERATION"

- RT. HON. LORD DAVID PRIOR OF BRAMPTON

Former Chairman of NHS, United Kingdom

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The investment case for healthy longevity is clear to finance professionals

97% of finance professionals believe that healthy longevity investments can yield greater financial returns than traditional healthcare investments

Artificial intelligence (44%) is the most invested field, followed by stem cells (25%) and immunotherapy (23%)

Corporate partnerships (53%) are the most popular source of funding for longevity research followed by PE (46%), VC (39%) and internal R&D (39%)

The fear of missing out on the next wave of healthcare innovation is strongest in the Middle East (39% vs 26% average)

Figure 7

What are your company's motivations for investing in healthy longevity? (Finance professionals response)



A growing pool of investors is spotting opportunities to build businesses in the healthy ageing space. The economic opportunity is vast. The economic value of slowing down biological ageing and improving health alongside a 1-year increase in life expectancy is \$37 trillion (46). One estimate puts the commercial market for 'delaying human death' at \$610 billion by 2025 (47). A recent and prominent sign of growing awareness came with the \$3 billion financing of Altos Labs, a company with a stellar scientific team (48). Our survey confirms that investors see longterm commercial potential with 97% of financial professionals believing healthy ageing investments can yield greater financial returns than traditional healthcare investments.

Major new markets can open quickly, as

evidenced by recent breakthroughs in a class of appetite-suppressing GLP-1 agonist class of drugs, which mimic the GLP-1 hormone produced by the body to indicate satiety. Sales of GLP-1 drugs are expected to top \$18 billion this year (49).

"The biotech industry has been reluctant to go after large populationdiseases, wide not because of the lack of business opportunity but the intractability of the clinical development

"WE'RE OBSERVING **A GROWING INTEREST ON THE PART OF INVESTORS TO FIND** A WAY TO PARTICIPATE IN ADDRESSING LARGE **MARKETS: DISEASES** WITH MILLIONS OF PATIENTS"

- STEPHEN BERENSON

programme without surrogate biomarkers and the capital required to do it right," says Mr Berenson, Managing Partner at Flagship Pioneering. "But now that [Eli Lilly and Novo Nordisk] have shown extraordinary success, we're observing a growing interest on the part of investors to find a way to participate in addressing large markets: diseases with millions of patients."

For some investors, the healthy ageing opportunity is also the next chapter in the consumer wellness market, a segment which reached \$1.5 trillion in 2021 according to McKinsey (50). About 492 million "smart wearable" units were shipped in 2022 (51). The fitness trackers market size was valued at \$7.5 billion US in 2022 and will reach \$16.91 billion US in 2028, with a CAGR of 14.32%

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(52). The suite of wearable technologies is now expanding to those which can monitor deeper indicators like heart rate, blood pressure and blood glucose with increasing precision, often based on subscription fee models. The supplements opportunity is a draw for some investors and startups, especially given the reported evidence of repurposed drugs like metformin (53), although care is needed to ensure proper governance, regulations and safety.

"Improving overall wellness rather than increasing the length of life is a relatively new concept," says Dr Levin of RA Capital. "As an investor, my theory is that we'll see a shift to more of a commercial based model in terms of quality of life. People pay for the gym and cosmetic procedures and other things to make their body

Managing Partner, Flagship Pioneering

and mental health feel better and look better. and that's how I see the healthy longevity field going."

The early, even presymptomatic diagnostics space is another domain biotech attracting investors, as product innovations show potential to catch killer diseases at a far earlier stage. Harbinger Health, a liquid biopsy and AI startup, has developed an algorithm that can detect cancer with 82% sensitivity (54).

"One Flagship company currently in stealth mode is trying to come up with a scientifically rigorous way of identifying pre-disease states and then identifying therapies, treatments, vaccinations that can catch something in a pre-disease state and at least delay the onset," says investor Stephen Berenson, Managing Partner at Flagship Pioneering, a fund which also backed Harbinger Health. The company has identified early biomarkers for disease states like nonalcoholic liver disease. "I think early diagnosis is one of the stronger themes in terms of impacting longevity and wellness," says Dr Levin of RA Capital.

Investors call for enabling reforms to unlock more capital and support startups. An important area for innovation is for regulators and payors to recognise and reimburse innovations that target prevention or pre-disease states, which today is not common outside of certain well-studied preventatives such as vaccines. This could include expanding the definitions of medical devices to include devices that assist preventative care, for instance, and developing metrics to approve and fund companies developing therapies that spot the earliest signs of conditions like cancer, dementia and diabetes, when outcomes could be modified, delayed or even eradicated. In addition to regulatory and payor innovation, these types of interventions will require clinical demonstration of benefit, with innovative clinical trial designs and endpoints.

"There needs to be an evolution of the way these treatments would be paid for," says Mr Berenson of Flagship Pioneering. "Today, at least in the US environment, it's hard for somebody to get paid for supplying a treatment to a predisease state. We have to create a framework for qualifying pre-disease states as being eligible for reimbursement." Jan Adams agrees that facilitating investment in pre-disease identification and prevention should be a priority. "We need to find early symptoms and get approvals based on biomarkers," he says. "Neurodegeneration might be where this starts as a template, in areas like Alzheimer's or ALS, and this could be a sandbox."

Regulatory frameworks for AI are also evolving, as it can be classified as a medical device with important implications for allowing individuals to access and pay for AI health services. Used for diagnosis, prognosis, screening, and supporting treatment, AI medical devices can relieve pressure on the health system (55).

"IMPROVING OVERALL WELLNESS RATHER THAN **INCREASING THE LENGTH OF LIFE IS A RELATIVELY NEW CONCEPT**"

- DR. ANDREW LEVIN

Partner & Managing Director, RA Capital Management

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In the US, the FDA has set premarket requirements for AI or machine learning-enabled medical devices, expanding the current regulatory framework to ensure the safety and effectiveness of AI products on the market. Approved devices include wearable seizure monitors, glucose monitors, and a mobile application to detect heart rhythms (56).

The regulatory landscape is evolving for AI that uses adaptive algorithms, which learn from real time data, rather than "locked" algorithms. The FDA is now considering a new product lifestyle-based regulatory framework in order to allow for modifications from real-world learning and adaptation, while still ensuring that the product's safety and effectiveness are maintained throughout its lifecycle (57). This expansion of medical device regulation, once adopted, could expand the capacity for innovation from medical device manufacturers.

With 52% of investors expecting a breakthrough in healthy longevity research in the near future and 97% of investors expecting better financial return from healthy longevity investments, it is easy to see why there is a tremendous interest from the investment community.

One driver to be careful about will be hubris, especially among tech investors or founders not familiar with the highly regulated healthcare field. The ghost of Theranos looms as a warning of the dangers of over-hyping. "Tech investors have a very different cultural mindset," says Dr Levin of RA Capital. "The tech mindset is that tech can do anything, we can solve any problem." Dr Levin cites the example of a company that had built an impressive diagnostic tool for Alzheimer's disease, but that was impractical to roll out at scale - and which offered limited impact given there is no cure for the condition.

Still, it is important to encourage a wider pool of investors into the space. Boston workshop participants proposed a strategic multidisciplinary alliance to showcase investor interest in the healthspan domain to provide the patient capital needed to support investment. For if startups are hard and risky, biology is harder.

The Healthspan Society

Achieving a longer and healthier life for all citizens would be a triumph of medicine, technology and health policy. The implications this would have on society are profound. Demographic transition is an engine of wrenching social and economic change, bringing both opportunities and challenges.

The pursuit of longevity science specifically raises questions about ethics, values and principles that will vary across cultures and contexts. For example, around 70% of participants - both citizens and healthcare professionals- express concerns about the ethical implications of longevity science, while two thirds of citizens believe that longevity research would increase socio economic inequalities.

The Hevolution Foundation survey also found regional differences on nearly every aspect of it - from willingness to buy products or services to attitudes about whether it would require reforms to retirement age. Health regulators, investors and companies must be attuned to citizen attitudes



to emerging science; ignoring public opinion was a key reason for the controversies and pushback related to genetically modified food.

One important finding from the survey is that demand for longevity products and service was the highest in emerging markets, with 52% of Brazilian and 45% of African citizens expressing interest (vs. 32% globally). Another is that concerns over the ethics of longevity research, though real, are not necessarily a barrier to demand. While Middle Eastern citizens are more likely to question the pursuit of longevity medicine because it goes against their beliefs (25% vs 12% average) and because we should not tinker with nature (40% vs 34% average), their interest in longevity products is nevertheless in line with global averages while their willingness to pay for it is higher (28% would be willing to spend 4-6 months of income on longevity therapies vs. 23% average)

Tackling existing diseases is seen as a prerequisite to longevity science. But the space is creating major unease too.

75% of citizens and 69% of healthy longevity professionals agree or somewhat agree with the statement: "I am concerned with the ethical issues associated with longevity science"

In fact, 96% of policy experts believe we need an international agreement on the ethics and practice of healthy longevity research

Distributive impacts are also a concern — half of all healthy longevity professionals and citizens believe longevity research will solely benefit the wealthiest individuals in society

Figure 9

Interest in healthy longevity across regions (Citizen responses)

How familiar are you with the concept of healthy longevity?

Answers	Total	North America	Brazil	Middle East	Europe	Asia-Pacific	Africa
Unfamiliar	31%	33%	23% ۲	35%	38% 7	25% 🖻	31%
Somewhat familiar (I have heard of the term)	39%	39%	47% 7	35%	39%	37%	35%
Familiar	23%	21%	23%	20%	18%	28% 7	26%
Very Familiar	6%	6%	6%	5%	5%	8%	7%
Expert	1%	‹1%	‹1%	5%	5%	2%	۰1%

antly lower than average 🎽

Figure 8

Concerns about longevity science

To what extent do you agree/disagree with the following statements:



Healthy Longevity Professionals

Asia-Pacific citizens show one of the highest levels of interest

Asia-Pacific citizens match Brazilian citizens for previous consumption of longevity treatments and have a similar level of familiarity with longevity as a concept

Asia-Pacific medical professionals encounter patients interested in longevity treatments more often than peers in other regions (36% on weekly basis vs 19% average / 19% on daily basis vs 10% average)

42% of them are also very likely to prescribe a proven anti-ageing therapeutic (if available) within 5 years, compared to 23% on average

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Significantly higher than average 🤊

As for Europe, it is by far and large the toughest market from a perception and consumer perspective. Consumers have the lowest interest in and willingness to pay for longevity-related products. 59% are 'probably not' or 'definitely not' interested in longevity services/products versus a global average of 38% and two thirds don't want to pay for it (vs. 45% average). The notion of 10 additional healthy years also fails to intrigue Europeans: 41% of European consumers are not interested in such a therapy versus a 25% global average. This may be due to cultural values around work in Europe that have led to resistance such as the multiple demonstrations against raising the pension age. Ironically, though, Europe, thanks to its world-leading biotech and pharmaceutical ecosystem, is likely to play a key role in longevity science, with 27% of scientists expecting the continent to be a 'very developed' research hub by 2030, second only to North America. This is not necessarily bad news: a combination of low demand and expected high supply is an export opportunity for the old continent.

THE HEALTHSPAN ECONOMY

A longer-living, healthier population would require social and economic changes which many citizens believe their countries are ill-prepared for. More than 70% of those polled in our survey believe their country is not yet ready to support a longerliving healthier population, when considering the full spectrum of implications from pensions to agefriendly employment. The finding shows that living better for longer is not an unalloyed good without reforms to public finances, employment norms, and equal opportunity.

Indeed, many countries are already experiencing a top-heavy age distribution with fewer and fewer workers supporting more older people, an unsustainable trajectory. Our survey reveals pockets of strong resistance to retirement age reforms, although views vary across contexts. Over half (55%) of respondents from North America and Europe believe that the retirement age should not change even if the person's average healthspan is extended by 10 years, while only 27% of Africans believe so, compared to an average

Figure 11

Preferred retirement age across regions (Citizen responses)

Answers	Total	North America	Brazil	Middle East	Europe	Asia-Pacific	Africa
It should stay as it currently is	40%	55% 7	42%	33% ك	55% 7	29% ك	27% 🛛
Retirement age should be increased by 2 years	7%	7%	8%	6%	8%	10%	6%
Retirement age should be increased by 5 years	19%	14% 🗵	13% 🔰	25%7	10% 🖌	25% 7	30% 7
Retirement age should be increased by 7 years	4%	2%	1%	4%	3%	6%	6%
Retirement age should be increased by 10 years	9%	5%	6%	11%	4%	12%	14% 7
Retirement age should be tied to average lifespan for the country	21%	17%	31% 7	21%	21%	19%	17%
		Significantly lower than average 🕥		Significantly higher than average 🔻			

of 40% across regions. African respondents were also the most likely to say that the retirement age should be raised by 5 (30%) or even 10 (14%) years, followed by those in Asia-Pacific and the Middle East. Respondents in Brazil were far more likely to think retirement age should be tied to the average lifespan for the country (31% vs. 21% global average).

To avoid politically contentious retirement age reforms, it is crucial to encourage and reward people for staying in the workforce for longer – which their better health should make possible. Encouraging healthy older people to work beyond the current pension age would both support wellbeing and purpose, and allow societies to sidestep the tough choice between an unsustainable share of non-working people, which is unfair to younger generations, or politically divisive reforms to pension age which would be unfair to the older ones - although the pursuit of full employment of people above the current state pension age could maintain the current agedependency ratio (58).

To achieve this intergenerational balancing act, Professor Scott at London Business School emphasises the importance of 'age-friendly jobs' defined as those that people can perform without excessive physical effort, and which offer greater autonomy and flexibility to balance work and caring

Figure 10 Readiness for longer-living, healthy population

Do you think your country is ready to support a longer-living healthier population in the following categories? (Citizen responses)



responsibilities across the overall workforce. "The good news is that the labour market is shifting that way for all sorts of reasons," says Professor Scott. "We're seeing a decline in manufacturing, new technologies, and flexible working. Age-friendly jobs have grown very rapidly, and everyone likes these jobs, not just older people."

PUTTING HEALTHSPAN TO WORK

People spend most of their waking hours working, which makes employers an influential societal force - for good or ill. Unhealthy working environments, whether psychological issues like high stress and burnout or physical factors such as lack of convenient access to healthy food and physical activity facilities, can over time lead to health issues including obesity, diabetes, some cancers and musculoskeletal issues. The mental health impacts of work are now receiving greater attention both due to rising levels of anxiety and stress and the consensus over the impact of mental health on physical wellbeing, such as the relationship between stress and cardiovascular disease. Workrelated stress, depression, and anxiety have been steadily increasing since 2018, even before the COVID-19 pandemic (59). Over 80% of US workers have reported experiencing workplace stress (60).

Employers can support workforce health in many ways. Inactivity, including sitting at work, is



linked to obesity, diabetes, and cardiovascular disease. Employers can encourage physical activity programmes in the workplace, like offering open floor plans, treadmills, or standing desks or encouraging 'standing meetings', provided they cater for those with any disabilities (61). Our London workshop participants proposed that corporations could commit to specific healthspan targets.

An Economist Impact study found that to contribute to reducing stress, workplaces can support workers having a social life at work, improve work-life balance and offer flexible working; they should also take regular surveys and ask questions to know what their employees need and identify those who may be in 'silent' suffering. Workplace mental health training can lead to a significant reduction in work-related sickness absence and might even be a magnet for talent; 59% of workers in one survey said they would consider taking a job with a company that offered better wellbeing benefits than their current employer (62).

Managers are in a position to provide support and encouragement to employees. A study by The Lancet of an Australian workplace found that implementing a 4-hour mental health training programme for managers improved confidence in interactions between managers and employees about mental illness and reduced rates of sick leave (63). 52% of US workplaces now offer corporate wellness programs, which can include meditation, mindfulness training, counselling, and resting rooms; these companies report a 67% increase in employee satisfaction (64).

Employers can also drive a shift in culture, combating ageism and hiring bias, for example, by looking at older workers as a key part of the talent pool (65). Hiring more workers over 50 and retaining them for longer will provide models of opportunity for other older people and younger generations, helping more people envision themselves working for longer and improving the mental and social enrichment of older workers. Conversely, there could be an opposite problem of older people staying in post for longer, limiting the churn and turnover that otherwise allows younger workers to ascend the ranks. The key will be to redesign the workforce and organisational hierarchies to allow people to work for longer without suppressing the careers of those below them.

Beyond their role as employers, the private sector writ large can play a constructive role in the healthspan society through means like advertising and product development. Participants at the Hevolution workshop in London emphasised the key role that brands and advertisers have in tackling ageist bias and stigma and in supporting an age-inclusive society. Multiple industries, from 'athleisure' and consumer technology to cosmetics, have already evolved their advertising to be more inclusive of diverse populations, including older consumers. In 2015, for instance, Apple announced a new iPad in Japan specifically marketed to the elderly, with simplified interfaces and larger text. At the launch, CEO Tim Cook spoke about the growing elderly population worldwide and the importance of maintaining a culture of respect for the elderly, and stated that Apple would eventually explore similar initiatives in the US and other countries (66).

More recently, absorbent underwear brand Depend made ads featuring young-looking models using their product in everyday situations, in order to challenge the association between incontinence and old age. This maintains dignity for elderly customers and reduces shame for younger customers. Nike embraced a new marketing strategy for its CruzrOne sneaker, a "shoe for the slower runner", in a video featuring Nike co-founder Phil Knight, who talks about his enjoyment of running at a slow pace without explicitly mentioning that he is in his 80s. This focus on running speed rather than age is inclusive and appealing to all customers (67).

Joseph Coughlin, founder and director of the AgeLab at the Massachusetts Institute of Technology, has argued that a marketing tactic emphasizing old age is unlikely to attract either young or old consumers, and a neutral strategy inclusive of all ages - for an "ageless lifestyle" - is best. In other words, focusing on customers' actual needs rather than their assumed age is not just inclusive, it's also good business (67).

INTERGENERATIONAL RELATIONS

Changes to lifespan have already had ripple effects on younger cohorts. Longer life expectancy combined with more years of ill health places a heavy burden on middle aged children, who find themselves 'trapped' between caring for parents and young children at the same time as they enter their prime earning years leading to the so-called 'sandwich' generation (68). Lengthening healthspan could flip the script by allowing older people to continue to support themselves and even make a fuller contribution to caring for grandchildren.

Multigenerational households are already common in many Asian countries. In 2020, around 80% of elderly widows and widowers in India lived with their children, while 45% of elderly couples lived with their children (69). These households are mutually beneficial for older and younger people. In countries where multigenerational living is common, older people in such environments have demonstrated lower risks of acute and chronic illness (70). Two thirds of older people in South Korea, and a third in India and the Philippines, regularly support or care for a member of their family, while in Latin America, older people in multigenerational households share retirement benefits with other family members (71).

In the West, people are typically placed in care facilities in their advanced age, but Dr Dzau believes this can bring risks including social

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isolation and, as seen during the pandemic, the potential for the spreading of infections. He believes multigenerational homes offer a smarter approach, citing the case of Singaporean housing, where older people often live in units within multigenerational housing, combining privacy and sociality, autonomy with support.

In countries where these living arrangements are less common, there are initiatives to encourage intergenerational connectivity through other means. Programme-based intergenerational interactions show positive associations with older adults' physical health, cognitive function, and wellbeing. Engagement in intergenerational activities is linked with increased physical and social wellbeing. (72). One of these programmes, Humanitas Deventer, an intergenerational care home in the Netherlands, offers affordable housing to students in exchange for contributing to the social care of elderly neighbours. Students' attitudes towards ageing have shifted and older individuals felt as if they exited the "sick role" traditionally experienced in care homes (73).

Supporting intergenerational connectivity at scale might require policy and infrastructure changes, however. In the UK, for example, it can be difficult to find affordable housing that can accommodate a large household. Potential solutions include connectable flats with shared kitchens (74). "We've really got to design things intergenerationally, so old and young people are living in cities close together and cities don't become financially prohibitive for younger people," says Professor Scott. One idea proposed by participants to the Hevolution Foundation workshop in Boston revolved around the encouragement of volunteerism as a mechanism to promote healthy ageing and combat ageism in communities. Participants also put forward an idea for the creation of a national service program connecting the aged population and youth to improve intergenerational connectivity.

A Leapfrog Opportunity?

On current trends, the health outlook is worrying as low- and middle-income countries face a double burden. Rising consumption of Western diets and processed foods, and a reduction in physical activity due to urbanisation and the migration away from physical agricultural activities, have contributed to rising obesity, diabetes and heart diseases. Diabetes in Africa is projected to increase as populations become more urban (75). Obesity rates in Latin America are among the highest in the world, reaching 28.9% in Mexico in 2021, and are increasing faster than any other region (76, 77). Dementia will devastate millions of lives in the years ahead; by 2050, prevalence will increase nearly 300%, mostly driven by low and middle-income countries (78).

Some emerging economies are also acutely vulnerable to the health threats of climate change and the worsening environment. In Southeast Asia, air pollution is the main cause of NCDs (79). The Middle East and North Africa (MENA) region is vulnerable to rising temperatures, with Oman, Qatar, Saudi Arabia, and UAE projected to have high future heat mortality burdens. In such a context, healthy ageing will be key to successful adaptation (80).

While these trajectories are a source of concern, emerging markets do have opportunities to 'leapfrog' the kinds of legacy challenges that impinge reforms in developed markets. "The potential for developing nations lies in their freedom from the constraints of entrenched legacy healthcare systems," says Michael Torres, Chief Communications Officer at the Hevolution Foundation. "These established healthcare systems are massive and often slow to adapt. Emerging and developing countries can learn from this established model to forge innovative and agile healthcare ecosystems. Conversely, the challenge for developed nations lies in transitioning from an

intervention-minded healthcare model to a more proactive, prevention-oriented approach."

Participants to the Hevolution Foundation workshop in London identified several key advantages for emerging market healthcare systems in the healthspan transition. An important one is time: many emerging markets have yet to fully engage in their demographic shift, many have a decade to go, which is enough time to institute system change. Emerging economies also have fewer investments in physical infrastructure, which means lower sunk costs and weaker vested interests in the status quo health system. This puts them in an ideal situation to innovate, becoming sources of 'reverse innovation'. London workshop participants noted the analogy of M-PESA, the mobile banking platform that emerged in Kenya and spread to other countries across Africa and the developed world (81). "There's a willingness to explore innovative approaches in emerging markets," says Dr Al Saud, Vice President of Organisational Strategy and Development at Hevolution Foundation. "Not just customers, but also governments need to be willing to carry out these potentially high-risk challenges. Compared to developed countries, emerging markets are more open to innovation."

A more pro-innovation attitude was evident in our survey, which found stronger interest among emerging market respondents in areas like willingness to pay for longevity therapies. When asked the question "Are you interested in using longevity-enhancing products or services?" 52% of Brazilian consumers and 45% of Africans responded "definitely/probably", compared to only 13% of Europeans. African and Brazilian consumers also rank significantly higher in willingness to pay up to 1 month of income for a therapy that could extend healthspan by 10 years.

Emerging economies have another advantage: access to technologies that were not available at a corresponding point in developed economies' earlier phases. Take diagnostics as one example. Digital and virtual tools like symptom checkers and imaging are bringing advanced healthcare services to remote areas (82). Drone technology is helping deliver medical supplies to marginalised regions. Rwanda, for instance, has pioneered the adoption of drones for health, through a partnership with American drone startup Zipline to deliver blood and medical supplies such as vaccines to remote villages (83). Rwanda's three-year contract with Zipline, which grants them provisions to deliver vaccines and medicine, will help make new medicines accessible to all and could overcome the access inequality challenge that leads to rural health outcomes being significantly worse (84).

Digital infrastructure and electronic health data could help emerging economies leapfrog the clunky, silo-riven health data system that bedevils developed economies. India, for instance, began transitioning to an open digital health ecosystem with the launch of the National Digital Health Mission

Figure 12

"Are you interested in using longevity-enhancing products or services?" (Citizen responses)



Brazilian citizens have more appetite for longevity therapies than citizens in other regions.

Most Brazilians (52%) are at least probably interested in using longevity related products versus 13% of Europeans and 17% of North Americans

They also show above average familiarity with healthy longevity, willingness to pay for treatments and previous consumption of treatments not available over the counter

Compared to other regions, Brazilians (and North Americans) would use healthy life years gained to retire earlier (27% vs 21% average)

A New Agenda For Global Health

Figure 13

"How much would you be willing to pay for a therapy that could potentially extend your health span by 10 years?" (Citizen responses)



(NDHM) in 2020. Similar digital public infrastructure has revolutionised financial systems in the past, like India's Unified Payments Interface (UPI). This has the potential to lead to an unprecedented change in products and delivery models in Indian healthcare (85). This initiative aims to give Indians digital health IDs that will store their medical records and streamline healthcare by making it easier for doctors to access patients' records (86).

Dr Dzau also urges societies and communities to take advantage of the opportunities presented by digital technology. Increasing Internet and broadband access among low-income and other marginalized populations, for example by utilizing community health workers, could help reduce the digital divide by ensuring broad and equitable benefits of such tools.

R&D CHALLENGERS

Emerging markets could also power new advances in medical research. To date, pharmaceutical innovation has been centered in Europe and North America, built on established ecosystems of universities, research institutions, venture capital and large pharmaceutical companies able to take ideas through the long, costly and risky drug development process. That is changing as a subset of emerging economies with the requisite capital, research and innovation capabilities start pushing the frontiers of medicine.

"When I first joined this industry, one of the things I found very intriguing was how global the industry was," notes Mr. Berenson, whose company Flagship Pioneering is beginning to establish its Asia Pacific presence through an office in Singapore, a country which is "making a single, serious run at this...the field will become more global and societies with the wherewithal will want to be masters of their own destiny."

The likes of Singapore, Taiwan, and Korea, as well as developed economies from outside North America and Europe like Australia, have all become challengers in innovation capacity and production, including in digital health (87) and pharmaceutical manufacturing (88). Over the past five years, life sciences deal activity has expanded to include

"IN THE NEXT TEN TO TWENTY YEARS, THE OPPORTUNITIES IN SCIENCE AND TECHNOLOGY ARE GOING TO BE IN EMERGING MARKETS"

- H.R.H. PRINCESS DR. HAYA BINT KHALED BIN BANDAR AL SAUD

Vice President of Organisational Strategy and Development, Hevolution Foundation

more companies headquartered in China and South Korea and biopharma drug development is rising rapidly in China-headquartered companies, whose share now exceeds that of Europe (89). Meanwhile, India's 'generics' industry has earned it the title of 'pharmacy of the world' (90).

"In the next ten to twenty years, the opportunities in science and technology are going to be in emerging markets," says Dr. Al Saud, who believes Saudi Arabia could be among the leading players. "I believe Saudi Arabia's contribution is going to be both on the scientific research front and on regulatory frameworks. You need to be bold when investing in research. Usually, government funding focuses on basic research in universities, but we need governmental institutions to actually focus on translational science, on how to move science off the bench and on to human applications."

Innovations from the Kingdom could include R&D investment and modernised drug development and clinical trial approaches. Regulatory innovations have enabled countries outside of Europe and North America to become hubs for healthspan science; for example, Australia enacted reforms to the clinical trial process that supported expedited trial processes and streamlined trial standards (91). During the pandemic, Australia was able to fast-track funding, ethical approvals, trial registration and publication (92)."I believe that Saudi Arabia will go in that direction and adopt similar regulations, so that we can support innovation through taking risks and investing in science and implementing regulatory reform to support drug development," says Dr Al Saud.

Mr AlAsiry of Hevolution Foundation agrees that regulatory reforms to drug approval is one

route for progress in Saudi Arabia. "Under the current regulations, a great deal of time and requirements are needed before approval, for multiple reasons," he says. "I think there is an opportunity for [Saudi Arabia] to learn from global best practices and develop a progressive drug approval policy that does not compromise safety and risk." Streamlining the framework for drug trials will also allow Saudi Arabia to tap into its vast network of hospitals and research centres to find potential trial participants and attract pharmaceutical companies by facilitating clinical research (93).

Jan Adams agrees that emerging markets could become global players, but argues that they need to differentiate themselves to become real innovation hubs. "Money is a commodity, it's not enough to find an edge. Can you create an ecosystem that delivers specific tools or populationwide data sets that you can tap into that others don't have, like a biobank and longitudinal data? In addition to money, talent and infrastructure, you need to add something that facilitates innovation and product development."

He believes Saudi Arabia has the potential to be an innovation sandbox, especially in terms of disease burden of the population. Adams also believes funders in Western countries as of lately are mostly focused on specific diseases, especially cancer. New entrants like KSA could spot the "blue ocean areas, and channel the money into emerging areas like ageing which established players are not geared to".

> "MONEY IS A COMMODITY, IT'S NOT ENOUGH TO FIND AN EDGE [...] IN ADDITION TO MONEY, TALENT AND INFRASTRUCTURE, YOU NEED TO ADD SOMETHING THAT FACILITATES INNOVATION AND PRODUCT DEVELOPMENT"

- DR. JAN ADAMS Partner, Apollo Health Ventures

Policy Leadership

Ensuring emerging market perspectives are part of the healthspan agenda – and supporting their research and innovation ecosystems – can help deliver a truly global movement, rather than the developed economies-dominated norms of the past. Participants at both the London and Boston workshops stressed the need for global coordination and collaboration.

Global coalitions are networks for lesson sharing, agenda-setting and resourcing to support healthspan policies and programmes – as well as fora for agreeing on new international norms. The scandal of the gene-edited twins in China shows how important global coordination is for ensuring responsible medical innovation (94). According to our survey, 96% of policy experts believe we need an international agreement on the ethics and practice of healthy longevity.

International coordination will also be necessary to mainstream the concept of healthspan into the policy agenda. At the Boston workshop, participants proposed that putting this issue on the agenda of finance ministers of the G20 would help accelerate global awareness and action, given the looming fiscal disaster of a 'business as usual' scenario. A precedent exists, as shown by the introduction of sustainable finance into the G20 finance targets and through the Sustainable Finance Working Group (95). London workshop participants agreed with the importance of the G20 as a platform, noting that this could also be an opportunity for emerging markets to lead as the next two years will see a G20 presidency from Brazil (2024) and South Africa (2025). Indeed, Brazil has already proven itself a major player in reshaping global health policy, having passed legislation in the 1990s giving citizens the right to universal

access to HIV treatment, forcing pharmaceutical companies to radically reform drug pricing (96).

International organisations play a lead role in influencing government policy to lead on the healthspan agenda. One idea at the London workshop, for instance, was to have the IMF include longevity considerations into Article 4 country reviews to create incentives for governments to track and report progress on the issue.

There are pre-existing international alliances to tackle diseases of ageing too, although these remain focused on conventional disease categories. The Global Group of Heads of State and Government for the prevention and control of noncommunicable diseases (NCDs), established in 2022, is aiming to invest resources and prioritising noncommunicable diseases in healthcare systems across the world, for example. Norway has been a frontrunner in investing in the fight against NCDs as part of its aid, as the first WHO donor country to include NCDs in its international development strategy. Ghana, which has taken on an important role in the group, has implemented tobacco demand-reduction measures and introduced guidelines for NCD management (97).

But new alliances and actors will be key to drive progress and tackle neglected areas. "I am very grateful to the Hevolution Foundation for having identified Healthy Longevity as the area that needs much more support and investment, says Dr Dzau at NAM. Its focused and pioneering investment in the field is having a signature impact. We need many more philanthropic entrants and investors to join Hevolution in this space to bring their expertise and resources to work towards healthy longevity equity worldwide."

GOVERNING FOR CHANGE

Central governments will be indispensable to achieving healthspan. As research funders, they can catalyse R&D. Public funding has already driven advances in basic and applied science in areas like cancer and dementia, conditions which are draining billions of dollars from health systems (78).

As regulators, central governments can nurture innovation by reforming procurement, approval and reimbursement policies. The US Orphan Drug Act in the 1980s was one such transformation, offering grants, tax credits and marketing exclusivity for R&D in rare diseases, incentivising R&D by the pharmaceutical sector and changing lives for patients (98). The pandemic put regulatory innovation in the front seat on a new scale. In the US, Operation Warp Speed invested \$18 billion and guaranteed purchase of nearly 500 million doses, helping pull vaccine candidates through the development process through more flexible approval and data requirements (99). The UK's Vaccine Task Force won plaudits for its venture capital-style approach to procurement, placing big bets on unproven approaches. This required busting through bureaucracy and institutional resistance and backing approaches like mRNA vaccines, which had faced years of scepticism from the medical mainstream (100).

Of course, the pandemic was a unique window of time that cannot be replicated easily. But it shows that policy leadership and ambition

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can deliver transformational outcomes at speed without compromising human health. The majority of policy professionals in our survey agree that healthy longevity requires such a new approach, yet few are willing to lead: 75% would prefer to be a "fast follower" rather than a leader when it comes to approving longevity therapies. This points to an important gap in leadership - and to a major opportunity for those who decide to fill this gap.

Governments can also influence healthspan through nudges and incentives on citizens. Tobacco control policies prove that government steps can impact consumer choices and directly improve health outcomes. The evidence for smokefree legislation impacting cardiovascular health, in particular admissions for heart attacks, is positive. Ten studies, from countries including the US, Italy, and Canada, found a significant drop in hospital admissions for heart attacks following the introduction of smokefree legislation (101). In the UK, the 2007 ban on indoor smoking in public places was linked to a 2.4% drop in hospital admissions for heart attacks in the following year, and the drop since then could be as high as 40% (102). New Zealand recently introduced a steadilyrising smoking age law ensuring tobacco cannot be sold to anyone born in 2009 or after (103).

Andrew Scott at London Business School expects governments to build on the precedent of tobacco control in other areas. Sugar taxes have

become more common globally, for example, and evidence suggests they have been effective in reducing demand through higher prices (104). The WHO has promoted a sugary drinks tax for disease prevention, with the aim of reducing diabetes, obesity, heart disease, stroke, and cancer, and 85 countries currently implement some form of this tax (105). Researchers at the University of Cambridge found that the UK's sugary drinks tax led to an 8% drop in obesity among girls in Year 6. Funds raised by the tax have been allocated to child health measures such as breakfast clubs, sports, and PE in schools. (106). Doctors have recommended extending the sugary drink tax to other foods high in sugar and salt (107).

Government impact on lifestyle can also be facilitative; in particular, investing in optimal nutrition for children to provide the best foundation for lifelong metabolic and cardiovascular health. In children, poor diet quality raises the risks of non-communicable diseases in adulthood, making healthy food for children in low-income communities an essential area of focus (108).

Universal free school meals programmes have improved food security in the US and the UK. In a study of two schools in London, staff observed that students who had changed from packed or bought-offsite lunches to universal free school meals were more likely to be eating healthier and more nutritious food (109). In Latin America, obesity prevention strategies that have shown some positive results include front-of-package labelling, school environment/meal regulations/ programmes, food marketing regulation, beverage tax and programmes to improve the level of physical activity (76). The WHO also recommends policies for improving physical education in schools to improve metabolic and musculoskeletal health in children, including training teachers in physical activity promotion, creation of appropriate spaces, materials and resources, encouragement of innovation, and partnerships with community organisations (110). Yet physical education classes have been in decline, and twenty percent of adolescents across 54 countries have reported never attending physical education classes (111). Rates of physical inactivity are higher in high- and middle-income countries, suggesting that more people may become inactive as more countries transition from lower to higher income (111).

Social determinants - from income and education levels to housing - influence both lifespan and healthspan, with studies showing they affect more than 50% of health outcomes (112). This has been vividly illustrated in so-called 'ZIP code' studies that reveal how individual life expectancy or likelihood of disease can differ by years within a single country, even in the wealthiest countries. Studies in England conducted between 2017 and 2019 found a 10.5 year gap in male life expectancy at birth within the country, with the highest in Westminster at 84.9 years and the lowest in Blackpool at 74.4 years (113). In the US, there are similar gaps: in 2020, average life expectancy at birth in California was 79 while in Mississippi it was 71.9 (114). There is an even starker gap when compared to Native American communities, with the lowest life expectancy in the country found in Lakota County, South Dakota at 66.8 years (118).

Education is a critical intervention to lower geographic disparities given the close linkages between education level and health overall. Universal pre-kindergarten education, improving graduation rates, and tax benefits for keeping children in school, have all been shown to have positive health impacts for communities. Blitzer and Johnson (116) emphasise the link between education and preventative healthcare in the US and the need for partnerships between health and education policy experts.

There is also a role for education about preventative health for people of all ages, continuing public education initiatives into adulthood. The Japanese government launched the National Health Promotion Movement known as Health Japan 21 in 2000, aimed at preventing and controlling lifestyle-related NCDs through intervention in workplaces and local communities as well as schools (117). The initiative's midterm evaluation in 2018 found that healthy life expectancy had increased (118). In Saudi Arabia, ministries coordinate across government to emphasise the importance of a healthy lifestyle, ensuring that the design of living spaces takes into consideration the population's need for sports, exercise, clean air, and more. "I think we've made a great deal of progress by making sure that the overall environment is conducive to a healthier lifestyle," says Mr AlAsiry of Hevolution Foundation.

Conclusion An Action Agenda for Healthspan

Over the last century, breakthroughs in medical science, and the fruits of economic growth, have combined to triple life expectancy relative to human evolutionary norms. But these hard-won additional years of life are frequently marred by chronic diseases which are taking a heavy and unsustainable toll on both rich and emerging economies alike. The global survey found over half of healthcare professionals simply do not believe health systems will be financially viable by 2030 without a breakthrough in longevity science and over 80% of citizens do not believe their country is ready to support a longer-living, health population. Tackling diseases of ageing requires a new paradigm, from medical research and drug development to employment and welfare.

While there is no magic bullet solution, and contexts vary, the international workshops, global survey and expert interview programme point to several calls to action for a new, bold agenda for achieiving healthspan for all in our lifetime.

Healthspan science is flourishing, thanks to innovations in medical research and new ways of understanding human biology. The evidence base is building for novel approaches to tackling the diseases of ageing. Early diagnostic innovations, such as liquid biopsies, powered by AI, promise to catch killer diseases before they take hold while senolytics can target damaged cells before they wreak havoc on the body. mRNA vaccines and cell and gene therapy may hold promise for stopping diseases from emerging in the first place. Leading the research agenda are a growing pool of investors and scientists who are boldly questioning the common assumption of chronic disease as an inevitable consequence of ageing.

To capitalise on progress, healthspan science needs enabling reforms to how medical therapies are tested, approved, and reimbursed. As a highly regulated sector, medical research and investment is heavily influenced by the incentives of regulators. To encourage bold R&D, medical agencies, and payers (insurance companies or governments) need to craft a pro-innovation regulatory and approval environment that rewards innovations that prevent, rather than treat, disease, and recognise the clinical validity of 'pre-disease' states and new biomarkers.

Emerging markets face a worrying rise in unhealthy ageing; with the right actions now, they can learn lessons from the mistakes of developed economies - and be innovation leaders. Citizens in emerging markets are strongly in favour of innovation and reform to enable healthy longevity, from willingness to use longevity therapies and services to their appetite to reform policy areas like pension age. As their health systems are less entrenched, these economies can build the infrastructure required for a 'healthspan society' with a greater role for digital technology, data and preventive approaches. Additionally, their regulations are evolving, with fewer vested interests and legacy norms, providing more emerging economies the opportunity to become hubs for new approaches to drug and technology development.

Employers must play an active role in encouraging healthspan, investing in workforce health and challenging labour market norms that

bias against older populations. If people are living longer and healthier lives, the traditional phases of the working life must be reimagined. The survey shows many people are willing to retire later if their healthy lifespan is extended. This requires more dynamic, flexible work environments and 'age-friendly' jobs, defined as those that people can perform without excessive physical effort and offering the flexibility to take time off to care for or spend time with familities, learn new skills, retrain for new roles for take breaks between phases of work. Employers must also challenge ageism in hiring and consider ways to make the workplace a healthier and more appealing place for older people. These changes will help older people maintain purpose and social connection and help countries avoid the politically contentious choice between raising retirement ages to cope with more older people. or placing more financial burden on young people to support older citizens.

Young people must not be forgotten in the healthspan economy - building flexible workplaces and preventative health will benefit people of all ages. A society with longer lives may mean more young people are living in multigenerational households or caring for family members; this is already a norm in many emerging economies - in developed economies, policies may be needed to foster intergenerational relations which have psychological and social benefits for young people, and widen their horizons and social circles. More flexible jobs will make it easier for working-age people to balance work and family responsibilities as well as leisure time and continuing education.

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Young people also need to be engaged early in their own lifestyle choices. Preventative healthcare means that people will be living healthier lifestyles throughout their whole lives, which will reduce NCDs like diabetes and obesity that have significant impacts on the young. These benefits must be emphasised early, through the education system.

Governments must show policy leadership to advance the healthspan agenda. The majority of policy professionals in the survey believe that healthy longevity requires a new approach, but a similar majority (75%) would prefer to be a "fast follower" rather than a leader when it comes to approving longevity therapies. This shows the need for policy leadership for countries to show vision and provide the path for others to advance. Globally, coordination and collaboration on best practices to support preventative health is essential; international organisations and standards-setting bodies can aid in this and leverage networks like the G20. To incentivise better choices, governments can build on the success of policies like tobacco control, and invest resources and attention to nutrition and physical activity in the education system.

Disclaimer: The views expressed in this report do not necessarily express the views of the Hevolution Foundation.

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Glossary

Aged society

An aged society is one where 14% of the population will be over 65.

Age-dependency ratio

This is the ratio of dependents—people younger than 15 or older than 64—to the working-age population (15–64); data are shown as the number of dependents per 100 working-age population.

Ageing society

An ageing society is one in which 7% (or more) of the population is over age 65.

Biomarker

A naturally occurring molecule, gene, or characteristic by which a particular biological process or disease can be identified.

Centenarians

People living to or over the age of 100.

CRISPR

A segment of DNA containing short repetitions of base sequences, involved in an organism's defence mechanisms against viruses. It can be used in genetic engineering to edit the base pairs of a gene.

Digital consultation

A remote medical appointment that is conducted online.

Disability-adjusted life years (DALYs)

According to the World Health Organization's Global Health Observatory, "one DALY represents the loss of the equivalent of one year of full health. DALYS for a disease or health condition are the sum of the years of life lost due to premature mortality (YLLs) and the years lived with a disability (YLDs) due to prevalent cases of the disease or health condition in a population."

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Emerging markets

An economy that is experiencing economic growth and transitioning into a developed market, but does not yet meet its standards. According to the Corporate Finance Institute, it is characterised by market volatility, growth and investment potential, high rates of economic growth, and low-middle income per capita.

Epigenetics

Cellular processes that regulate and change gene expression without directly bringing about gene mutations.

Genomic editing

A type of genetic engineering in which an organism's DNA is inserted, deleted, modified or replaced in the genome.

GCC countries

Gulf Cooperation Council countries are Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and the United Arab Emirates.

Healthspan

The number of years that someone lives or can be expected to live in good health.

Healthy life expectancy (HALE) at birth

The World Health Organization's Global Health Observatory defines HALE as "the average number of years that a person can expect to live in 'full health' by taking into account years lived in less than full health due to disease and/or injury."

Leapfrogging

Leapfrogging occurs when a nation bypasses traditional stages of development to jump directly to the latest technologies or explore an alternative path of technological development involving emerging technologies with new benefits and new opportunities.

Life expectancy (LE) at birth

The World Health Organization's Global Health Observatory defines life expectancy at birth as "the average number of years that a newborn is expected to live, if he or she were to pass through life exposed to the sex- and age-specific death rates prevailing at the time of his or her birth, for a specific year, in a given country, territory, or geographic area."

Liquid biopsy

According to the NIH, "Liquid biopsy provides the opportunity of detecting, analyzing and monitoring cancer in various body effluents such as blood or urine instead of a fragment of cancer tissue."

Morbidity

Morbidity is the state of being symptomatic or unhealthy for a disease or condition.

M-PESA

A mobile phone-based money transfer, payments, and micro-financing service, launched in Kenya in 2007.

mRNA

A form of nucleic acid, which helps the human genome which is coded in DNA to be read by the cellular machinery. It has been used in innovative vaccines and medicines to generate an immune response.

Neurodegeneration

Degeneration of the nervous system caused by the loss of function of neurons in the brain. Neurodegenerative diseases include multiple sclerosis, Alzheimer's, and Parkinson's.

Noncommunicable diseases (NCDs)

Also known as chronic diseases, they are diseases that tend to be of long duration and are the result of a combination of genetic, physiological, environmental and behavioural factors rather than transmissible factors like viruses.

Primary care

The day-to-day healthcare given by a health provider.

Secondary care

Care provided by a specialist provider or specialist facility to whom a patient has been referred by their primary health provider.

Senescence

A state in which cells have stopped replicating and contribute to ageing by prohibiting tissue repair.

Senolytics

Drugs or therapies that work to remove senescent cells from the body.

Stem cells

Cells with unique abilities to self-renew, and can be found in embryos and various adult organs. They have great potential for replacing defective or damaged cells resulting from various disorders and injuries.

Vertical

A group of companies that focus on a shared niche or specialized market spanning multiple industries.

Virtual wards

Also known as hospitals at home, they allow patients to get the care they need at home safely and conveniently, rather than being in hospital."

Wearable technologies

Any technology that is designed to be used while worn, such as smart watches and smart glasses.

Western diet

The NIH defines the Western diet as low in fruits and vegetables, high in fat and sodium, and consisting of large portions, high calories, and excess sugar.

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