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## Metatrend #14: Increased Human Healthspan

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Today's blog is brought to you by Abundance360, my year-round leadership program designed for founders, executives, and investors who are ready to create meaningful impact and leave a legacy.

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How long do you think you'll live?

What if we could add an additional ten, twenty, thirty \*healthy\* years to your life?

Could replacement human organs be bioengineered from scratch, available on demand?

How long until no human being dies from cancers, Alzheimer's, heart disease, or any disease of aging—because we've learned to effectively *prevent* them with next-generation, AI-powered diagnostics or vaccines?

For the first time in history, billions of dollars of venture capital and thousands of brilliant scientists are committed to extending the human *healthspan*: the number of years we live without developing debilitating diseases.

In today's blog, we'll dive into the extraordinary research happening in the booming field of aging science. We'll zoom into 3 concrete ways your healthspan will be extended in the coming decade, and probe into the ethical and economic implications of emerging therapies which will add decades of *healthy* years to your life.

With the convergence of genome sequencing, CRISPR technologies, AI, quantum computing, cellular medicines, and an abundance of capital flowing into aging research, the healthspan revolution is set to become one of the biggest opportunities of the decade ahead.

***Let's dive in!***

*(This blog is written by Peter H. Diamandis, MD and Raiany Romanni)*

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## **THE SEARCH FOR A FOUNTAIN OF HEALTH**

The medical advancements of centuries past were far more effective at extending *lifespan* than they were at increasing our years of vitality and youth.

Inventions like pacemakers, chemotherapies, and even mRNA vaccines, guarantee that millions of chronically ill adults are routinely kept alive *past* their healthspan. An extreme, but sadly familiar manifestation of this phenomenon to millions of Americans is the

existence of ventilators, which can keep patients breathing long after their brain activity has ceased.

In the 20<sup>th</sup> century, we engineered more than a doubling in average life expectancy. But we failed to devise a corresponding increase in *healthspan*, causing our medical systems to become chronically overburdened.

Instead of dying suddenly at the age of 40 by infectious diseases, most of us today will go on to live into our 80's or longer, *decades* past retirement; and one day, be diagnosed with one of the gradually debilitating diseases of aging.

But what if those debilitating diseases of aging—cancer, heart disease, Alzheimer's—could be prevented altogether, making your final decades of life productive and joyful?

Two profound examples give me hope. Bowhead whales can make it to 200 years of age and are incredibly resistant to the diseases of aging. Greenland sharks can make it up to 500, and can give birth to baby sharks at age 200.

If they can live that long, why can't we?

It is either a software or a hardware problem, and the technologies required to address both are coming on-line this decade.

The good news is that game-changing biotech and pharmaceutical solutions are currently in Phase 1, 2, or 3 clinical trials and are likely to reach consumers in the coming decade, many of which have the potential to add an additional 10 years or more to our healthspan.

Examples of the companies working on this (of which I'm either a founder or an advisor) include: **Vaxxinity** which is combating heart disease and strokes with a PCSK9 vaccine; **Celularity** which is using placenta-derived stem-cell and natural killer cells to augment vitality and immunity; **Immunis** which is delivering stem-cell derived precursors and growth factors; and **Elevian** whose rGDF-11 product has been shown to promote recovery and regeneration in a number of preclinical models of age-related diseases.

And of course, these represent only a small fraction of the potential breakthroughs on the horizon. With a "Longevity Mindset" you understand that that the gift of an additional healthy decade is more than just those extra ten years—it is also the continued exponential advances in AI, CRISPR, gene therapy, and DNA reading and writing that will get you additional healthy follow-on years.

This is best described by my friend and mentor Ray Kurzweil: "Science will soon be able to extend your life by more than a year for every year you are alive." The concept is called **longevity escape velocity**. I believe we will reach this point by 2033.

Professor George Church of Harvard Medical School agrees, "Today science is adding one year of life for every four years that we're alive. But I think age-reversal advances could mean that we reach longevity escape velocity within a decade or two."

Professor Church goes on to say, "It is quite possible that some of the people alive today will see no upper limit [to their lifespan]."

In 2004 Ray Kurzweil wrote a milestone book called *Fantastic Voyage: Live Long Enough to Live Forever*. In the book, Kurzweil described *bridge one* as a set of near-term life-extending solutions—like a sugar-free diet and muscle-mass-increasing exercise—that

should be followed until eventually *bridge-two interventions*—like cellular reprogramming, synthetic organs, and stem cell therapies—are safely and routinely available in the clinical setting.

Our job, then, is to stay healthy and free of accidents long enough in order to intercept many of the bridge-two therapies expected later this decade.

Helping you cross “*bridge one*” is also the goal of Fountain Life, a company I co-founded and serve as Executive Chairman. With cutting-edge diagnostics services like full-body and brain MRI and the AI-powered, coronary (Clearly) CT scan, and a 150-gigabit digital upload of your body, the goal is to spot any actionable, life-threatening disease at inception when it most effectively and easily treatable.

The healthspan revolution is fast arriving.

How will *you* prepare yourself for it? What will you do with an extra ten, twenty, thirty years of *healthy* life?

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## 2023 A360 SUMMIT SPEAKER SNAPSHOT

Here's a sneak peek of the A360 speaker lineup. This will be an exciting year!

**Note:** *At the time of this email, we have 34 remaining spots to attend the Summit live in March.*

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## Tony Robbins

#1 *New York Times* bestselling author and life & business strategist. He is a leading philanthropist and through his 1 Billion Meals Challenge, he has provided over 945 million meals in the last 8 years and is ahead of schedule to provide 1 billion meals by 2025.



## Andrew Yang

2020 Democratic presidential candidate and 2021 New York City mayoral candidate. He is the Founder of Humanity Forward, and his *New York Times* bestselling book *The War on Normal People* helped introduce the idea of universal basic income (UBI) into the political mainstream.



## Jacqueline Novogratz

Founder and CEO of Acumen, whose mission is to change the way the world tackles poverty. She is a *New York Times* bestselling author and was named by *Insider* as a top 30 global leader working on climate solutions.



## Mark Hyman, MD

Family physician and internationally recognized thought leader in the field of functional medicine. He is a fourteen-time *New York Times* bestselling author, and Board President for Clinical Affairs of The Institute for Functional Medicine.

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# 3 WAYS YOUR HEALTHSPAN WILL BE EXTENDED

## 1. The Information Theory of Aging

When we are born, when we are 20, 50 or 80 years old, our genome sequence is identical. In other words, our genetic information—the 3.2 billion letters from our mother and father—doesn't change over time.

If that's the case, why do we look different as we age? Why do we develop diseases later in life?

While our genes don't change, what does change is the *expression* of our genes—in other words, which genes are turned on and which genes are turned off—also known as our epigenome (“epi” coming from the Greek word for “above”).

This nascent field of epigenetics made a leap forward on January 12, 2023 when a landmark paper was published in the prestigious scientific journal *Cell*, by Harvard geneticist David Sinclair. In this paper, Dr. Sinclair and his colleagues showed that epigenetic change is a major cause of mammalian aging—and tweaking the epigenetic information of mice can actively speed up or *reverse* the effects of aging.

According to the *Cell* paper authored by Dr. Sinclair and his team, they were able to not only age mice on an accelerated timeline, but also reverse the effects of aging and restore some of the biological markers of youthfulness in the animals. This reversibility supports Sinclair's theory that the primary causes of aging are not mutations in DNA, but rather errors in epigenetic instructions.



Dr. Sinclair has long held the belief that aging is a result of losing crucial instructions that cells need to function, which he refers to as the "Information Theory of Aging." He states, "Underlying aging is information that is lost in cells, not just the accumulation of damage. That's a paradigm shift in how to think about aging."

These latest findings appear to back up his theory, and Sinclair likens it to how software programs depend on hardware, but can sometimes become corrupted and require a reboot. He adds, "If the cause of aging was because a cell became full of mutations, then age reversal would not be possible. But by showing that we can reverse the aging process, that shows that the system is intact, that there is a backup copy and the software needs to be rebooted."

In his book *Lifespan*, Dr. Sinclair brilliantly points out that if we cloned a 65-year-old, the clone wouldn't be *born old*—which says a lot about how their genetic sequence or information remains intact, even if this 65-year-old's genetic expression and cell regulation mechanisms are presently malfunctioning. Genetic mutations, in other words, seem not to corrupt our essential hardware. There is, as Dr. Sinclair points out, a "back-up copy" within all of us, which remains retrievable.

## **2. The (other) hallmarks of aging**

From mitochondrial dysfunction to senescent cell build-up and stem cell exhaustion, the 9 hallmarks of aging seem to be interlinked and, more importantly, reversible.

In the coming decade, a combination of Senolytic medicines, natural killer cells, and vaccines will be used eliminate senescent "zombie" cells which cause age-related inflammation. Cell therapy (the addition of autologous and allogeneic stem cells) will be used to replace or augment a patient's stem cell population. Technologies such as *wnt* pathway modifiers, endo-vaccines, and supplementation of

NMN/NAD+ are among other treatments that will be used in the clinical setting to extend your healthspan.

BioAge, a California-based company led by Kristen Fortney, recently announced positive Phase 1b clinical data for BGE-105 (a potent small-molecule agonist of the apelin receptor APJ), showing significant prevention of muscle atrophy relative to placebo in volunteers aged 65 or older. The company's approach is compelling because muscle atrophy—loss of muscle mass and strength—is a universal feature of human aging, which accelerates the risk of co-morbidity and significantly shortens lifespan.

“The strategy of aging reversal treatments,” Professor George Church shared with Tony Robbins and me, for our 2022 book *Life Force*, “is to test them against various diseases that have nothing in common other than they happen to be diseases of aging in the same animal. If a single treatment can reverse a multitude of age-related diseases, then you have an age-reversal treatment.”

### **3. Organs on demand**

Crossing *bridge one* towards limitless human healthspan is hopefully the goal for many of us, but for some who are in organ failure, breakthroughs are a matter of life and death.

In 2023, a person dies almost *every hour* while waiting for an organ transplant. Nearly *1 million* Americans lose their lives every year because of heart failure.

The ability to safely and effectively manufacture, deploy and transplant organs at scale would transform our health system in the short term, offering patients the chance to live for another ten, twenty, thirty years—and to capitalize on the extraordinary technology that arises in this interim.

Martine Rothblatt, a trailblazing entrepreneur whose disruptive work I've commended in my previous books, envisions a future where organ supply is *unlimited*. Famous for devising a first-of-its-kind drug for a fatal lung disease from scratch to save her daughter's life, Martine is now determined to engineer a future where—should her daughter need it—lungs and other organs would be easily transplantable.

And this future isn't far off. In 2022, a 57-year-old man lived for *two months* past heart failure with a pig's heart. By 2024, Dr. Rothblatt's biotechnology company, United Therapeutics, hopes to have formal trials for xenotransplantation (of pig organs into humans) underway.

Dean Kamen, founder of the Advanced Regenerative Manufacturing Institute (ARMI), similarly aims to “make practical the large-scale manufacturing of engineered tissues and tissue-related technologies, to benefit existing industries and grow new ones.” This is a tall order, but not overly demanding to Kamen, whose previous inventions add up to over 1,000 patents across industries.

ARMI, a non-profit based in Manchester, New Hampshire, was recently awarded a \$44 million federal grant to establish a biofabrication cluster designed to engineer tissues and organs—bringing the institute's total funding close to *\$400 million*. (By the way, ARMI will be one of our stops during my Platinum Longevity Trip this fall, for which a few spaces remain available.)

A future where organs can be quickly 3D-printed or xenotransplanted is not just realistic—it is *in the making*.

## THE MORALITY OF IMMORTALITY

If aging is either a software or a hardware problem, then that means it is solvable.

And if we solve it, it is quite likely we will get to live *a lot* longer.

A ten-year-old's chances of dying, for example, are of 1 in 10,000 every year. This means without the effects of aging, the average ten-year-old would live to be roughly 10,000—barring catastrophic or existential risks.

Because of humanity's emerging *underpopulation* problem (yes, we're actually in danger of under population versus over population), this is good news.

The population replacement rate, which is the average number of children per family for each generation to replace itself, is roughly 2.1. Yet *only 2 countries* in the Organization for Economic Co-Operation and Development (OECD) had a total fertility rate at or over 2.1 in 2020.

Back in April 2021, when I interviewed Elon Musk for the launch of the \$100M Carbon Removal XPRIZE, I asked him his concern on the topic of population. He shook his head and said, "Earth is going to face a massive population collapse over the next 20 to 30 years... this would be civilization's way of dying with a whimper."

More than ever, we need to increase our productive and healthy lifespan. If we don't, we are likely to face a significant shortage of labor. So, not only will longer healthy lives allow us to spend more time with loved ones and fulfill our bucket list dreams—it also has the potential for enormous value to society.

From an economic standpoint, our achievement of longer—but not much healthier—lives over the previous century has been costly. Retirement pensions were implemented in the 1910's, when deadly infectious diseases were the norm; the average life expectancy was less than 50; and the governmental bet was that most retirees would only be supported for a short period of time.

Today, the United States spends over *a trillion dollars* every year on Social Security.

Greece spends a whopping 17% of its GDP on retirement pensions.

In an impressive study, researchers from Harvard, Oxford, and London Business School showed that to extend the *healthy* lifespan of the global population by just one year would add **\$38 trillion dollars** to the global economy.

Imagine the societal benefits and economic value of increasing healthy lifespan by *ten to twenty years*.

The most precious resource of the 21<sup>st</sup> century is the persistent and passionate human mind. Companies and organizations investing in longevity understand this. The Hevolution Foundation exceeded all investment commitments in the field so far, by pledging up to \$1 billion dollars *yearly* to advance aging science. Altos Labs, backed by Jeff Bezos, recently committed \$3 billion dollars to aging research.

And it isn't all private money moving this field forward. The Biden Administration deserves accolades for their proposed \$6.5 billion Advanced Research Projects Agency for Health, referred to as ARPA-H, modeled on the Advanced Research Projects Agency (ARPA) arm

of the U.S. Defense Department, which in the 1960s gave America ARPANET, the precursor to today's global internet. It's proposed that ARPA-H would aim to deliver breakthrough treatments for diseases like Alzheimer's, cancer, and diabetes.

Coupled with AI, the human mind is set to reinvent the very concept of health in the 21<sup>st</sup> century.

As Alex Zhavoronkov has shared with us, the AI-powered reinvention of the drug discovery process is resulting in “an explosion in potential drug targets and a much more efficient testing process,” allowing their team to do “with fifty people what a typical drug company does with five thousand.”

Just as the cost of genome sequencing has been demonetizing at a rate five times faster than Moore's Law—becoming >1,000,000x CHEAPER over the past 23 years—aging therapies are sure to become democratized, alongside an exponential increase in computing power.

What if, in the near future, AI could generate novel drugs to target age-related diseases, overnight, ready for clinical trials—disrupting the ten-year average drug-discovery cycle?

Insilico Medicine is aiming for just that, and its recent Phase I results on an AI-discovered, first-in-its-class drug to treat idiopathic pulmonary fibrosis (IPF) are no less than disruptive. IPF currently affects 5 million people worldwide, with no approved treatment. Insilico is now leveraging its recently announced research collaboration with Sanofi (worth up to \$1.2 billion) to redefine the standards of the AI-powered biopharmaceutical industry.

Finally, an increasing abundance of private and governmental capital flowing into longevity, coupled with converging, exponential technologies, will ensure that emerging aging therapies can be demonetized and democratized, making them accessible to the world's most vulnerable populations.

## FINAL THOUGHTS

As exponential technologies continue to accelerate, and more capital flows into aging research, the diseases of aging will become increasingly preventable.

As organs on demand become a near-future reality, and epigenetic reprogramming therapies enter human trials, aging will eventually be seen as a treatable, multi-factorial disorder.

Since there is nothing more valuable to anyone than extra decades of health, it is my strong belief that capital will continue to flow into this field at accelerating rates and the goal of adding 30+ healthy years to the average human lifespan will eventually become a reality.

Besides all of us who have taken care of ourselves sufficiently to benefit from these health-extending therapeutics, insurance companies and governments are both poised to benefit tremendously from this shift.

Other than AI, the increase in human healthspan is set to be the biggest opportunity of the decade ahead.

What will YOU do to ensure you unlock an additional thirty years (or more) of healthy life?

In our next blog in this Metatrend series (#15 of 20), we'll explore **Demonetized, Democratized & Preventative Healthcare**.

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