

Jan 1, 2025 Volume 7-1 Winter 2025

Topics:

- **Longevity - Parts I and II**
- **Debunking Myths**
- **Office Updates**

YOUR HEALTH: Longevity – Part I

All Humans wish for a long lifespan and, most importantly, a commensurate health span. The finality of life is the “great equalizer” of humanity, an intricate part of who we are as a species and a major daily motivator, as we all wake up ready to “seize the day” and honor “carpe diem”.

This aspiration for “longevity” is so old, and so much a part of us, that the earliest surviving manuscripts recount mythical long-lived figures. Sumerian mythology, written around 4000 BC in rudimentary ancient cuneiform characters, already described Enki, a major God associated with water, wisdom, magic, and immortality. And even in my endless Pampas, I heard of Gilgamesh, the legendary king of Uruk, who embarked on a journey to find eternal life. Babylonians later appropriated the epic tale and further explored the theme of immortality and the search for eternal life.

Hindu mythology describes the sage Vyasa, as having lived for thousands of years. And we are all familiar with the Book of Genesis’ story of Methuselah, who traces his genealogy back to Adam, is the grandfather of Noah and dies at age 969 in the year of the Great Flood (brought about by Noah’s construction of the Ark, and confirming that no good deed shall go unpunished from the earliest days of humanity!).

“The superior man is modest in his speech, but exceeds in his actions.”

Confucius

“It is impossible for a man to learn what he thinks he already knows.”

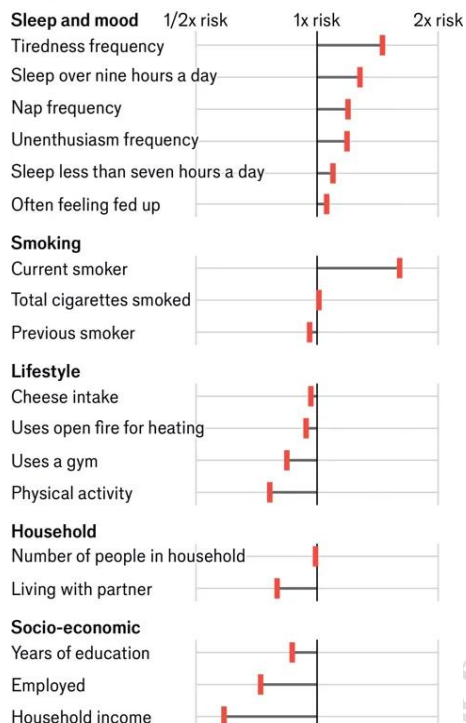
Epictetus

My informed patients have been reading and wondering about all the “buzz” and frenzy surrounding “Longevity”. Numerous “gurus” provide daily advice through books, articles, podcasts and videos, on how to extend our time on planet Earth. Numerous supplements, monitoring devices, and biologic markers are touted and

Risky business

Effect of factors on risk of mortality

In separate models*



*Controlling for age, education, ethnicity, income, location and sex (unless the factor is already included in model)

Source: "Integrating the environmental and genetic architectures of aging and mortality", M. A. Argentieri et al., *Nature Medicine*, 2025

promoted in that quest for "immortality". And since Medicine and Preventive Medicine are very much at the heart of "life extension", we feel the "heat" and responsibility in summarizing some of the science and clarifying some of the "myths" (which you realize are more interminable than life itself).

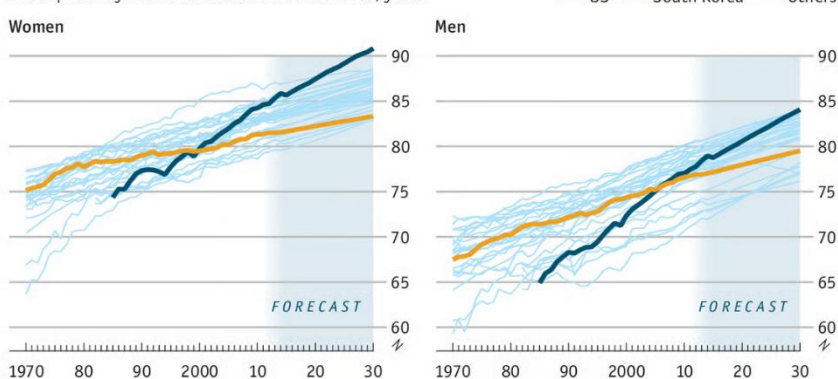
We should make clear from the outset that "longevity" supplements and medications have not been formally tested in humans, in part because the FDA and the agencies in charge of drug approval do not recognize "aging" as a treatable condition. Also because some of these molecules are in the public domain, without incentives for the private pharmaceutical industry, although that is starting to change, with the launch of [TAME](#) (Targeting Ageing with Metformin Trial) which will follow 3000 Americans in their 60-70's to see if the drug aids survival supported by NIH.

Arguably, embracing healthy choices to improve quality of life, healthspan, and possibly lifespan is our responsibility. Barring accidents or rare conditions, most humans today should be able to live well into their 80s and 90s. The contribution of genetics beyond the late 80's becomes progressively more important.

As we become older and "seasoned", if we remain healthy, we can contribute to the development of our children, grandchildren, and communities with all the accumulated wisdom and perspective only experience provides. We must remember that most

Live long and prosper

Life expectancy at birth in selected rich countries, years



Source: "Future life expectancy in 35 industrialised countries", by M. Ezzati et al. *The Lancet*, February 2017

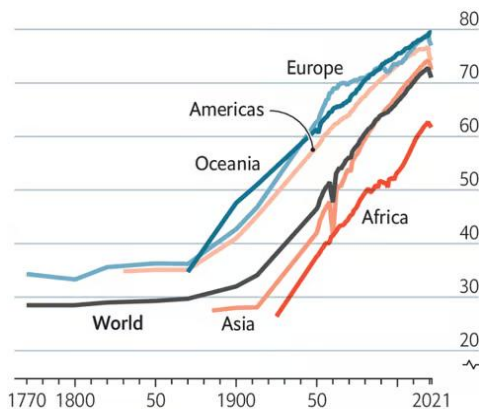
Economist.com

chronic conditions, such as hypertension, type II diabetes, obesity, vascular disease (including vascular dementia), hypercholesterolemia, etc, are intrinsically related to a sedentary lifestyle and inadequate diet over decades, which lead to

the poor metabolic consequences we have discussed over many "Medical Bits".

Three months more every year

Life expectancy at birth, years



Source: Our World in Data

Surprisingly, some physicians and healthcare systems claim to be able to increase your “longevity” by 5-10 years. You know that extending your longevity depends on **YOU** and your healthy choices over your lifetime. Do not believe any of those simple pitches to grab your wallet!

For those of you who want to [read one paragraph](#) and move on to the long daily reading list and other pleasurable endeavors, the quick answer to your Longevity question is what you already know:

There is no magic pill! Increasing longevity takes hard work!

1. Eat the right way and embrace a Mediterranean diet.
2. Avoid concentrated sweets and all sugary drinks (anything that tastes sweet is probably not good for you, as even artificial edulcorants are known to trigger insulin release and precipitate a negative metabolic response).
3. Accept intermittent fasting as much as you can tolerate, trying to approximate 14 without much caloric intake (breakfasting with a few almonds or nuts and getting most of your nutrition at dinner time gets you close to the goal).
4. Exercise daily. Both aerobic/cardiovascular and resistance exercises help.
5. Get “uncomfortable” by exercising and fasting daily.
6. Meditate.
7. Foster meaningful relationships with family, friends, and even strangers.
8. And LASTLY, as we are addressing in Longevity Part II.

Several molecules have been associated with increased longevity and stress resistance in model organisms such as yeasts, nematodes, flies, mice, and even humans! Some compounds are currently in preclinical and clinical trials by the National Institute on Aging's Interventions Testing Program.

We will briefly discuss some of these proposed “longevity agents and promoters”:

Several molecules have been associated with longevity based on current research. Key molecules and pathways include:

1. **Sirtuins (SIRT1, SIRT2, SIRT3, etc.):** These proteins are involved in cellular regulation, including DNA repair, metabolism, and stress resistance, and have been shown to extend lifespan in various model organisms.
2. **Insulin/Insulin-like Growth Factor (IGF) Signaling Pathway:** Reduced activity in this pathway is associated with increased lifespan in multiple species. Key components include IGF-1 and its receptor.
3. **Forkhead Box (FOXO) Proteins:** These transcription factors, particularly FOXO3a, play a crucial role in longevity by regulating genes involved in stress resistance, metabolism, and cell cycle control.
4. **Mechanistic Target of Rapamycin (mTOR):** Inhibition of mTOR signaling has been linked to increased lifespan and healthspan, primarily through effects on autophagy and protein synthesis.

5. **AMP-activated Protein Kinase (AMPK)**: This enzyme is involved in energy homeostasis and promotes longevity by enhancing autophagy and mitochondrial function.
6. **Nicotinamide Adenine Dinucleotide (NAD⁺)**: NAD⁺ levels decline with age, and boosting NAD⁺ through precursors like nicotinamide mononucleotide (NMN) has been shown to extend lifespan in animal models.
7. **Klotho**: This protein regulates multiple pathways, including insulin sensitivity and oxidative stress, and its overexpression is associated with extended lifespan in mice.
8. **Polyphenols (e.g., resveratrol, quercetin)**: These naturally occurring compounds mimic the effects of caloric restriction and have been shown to extend lifespan in various model organisms.
9. **Apolipoprotein E (APOE)**: Specifically, the APOE2 genotype has been associated with exceptional longevity in humans.

Agents proposed and undergoing evaluation:

- a. **Metformin.**
- b. **Nicotinamide.**
- c. **Rapamycin,**
- d. **Mifepristone**
- e. **Quercetin**
- f. **Resveratrol,**
- g. **Curcumin.**
- h. **Spermidine.**
- i. **Sulforaphane**
- j. **L-serine** and lipids with more double bonds (lower mortality risk).
- k. **Omega-3 polyunsaturated fatty acids (PUFAs),**
- l. **Short-chain fatty acids (SCFAs),**
- m. **Sphingolipids, Hexosylceramides, ether-linked phosphocholines**
- n. **Polyphenols, and nutrients such as ergothioneine, pyrroloquinoline quinone (PQQ), queuine, lutein, zeaxanthin, lycopene, α - and β -carotene, β -cryptoxanthin, and astaxanthin** are proposed as "longevity vitamins".

LONGEVITY

LONGEVITY refers to the capacity to live longer than the average lifespan for the species. This brings about the deep concept of time, with its Newtonian scalar vector (moving forward) and relativity spacetime coordinates. We all have a rudimentary understanding of time, as the progression of events from the past to the present and into the future, realizing that it is the fourth dimension of space (a bit more complicated to comprehend for our three-dimensional world perception).

Time is intertwined with the three dimensions of space to form spacetime and is an integral part of the fabric of our Universe. Einstein demonstrated that time can slow down or speed up, depending on relative velocity and gravitational fields. For physicists, time is a "measure of space", and its preferred direction is forward (due to the increase in Entropy, or disorder / randomness). But math and quantum mechanics physicists inform us that time can behave in unexpected ways.

Over the past two decades, the “longevity” field has grown exponentially! According to some estimates, humans spend more than \$50 billion annually on some forms of “anti-aging” treatments. Most focus on “appearance,” such as cosmetic surgeries, Botox, creams, and dyes. None of those deal with the all-important goal of “slowing down the clock”. But that may be starting to change, as there are now more than 700 biotechnology companies working on different aspects of this growing field, and over 250,000 articles have been published in the last 15 years.

Why do we age differently, and what can we learn from other species and analyze biology?

Most complex life is made of the same building blocks (carbohydrates, lipids, proteins, and nucleic acids), and yet, a mayfly lives for a day, a mouse for 2 years, and a similar-sized bat for 40 years. Tortoises can live for 200 years, and whales and sharks can survive for several centuries. Long-living species have a slow metabolism, stable environments, excellent DNA repair mechanisms, and a low risk of becoming “prey”.

The underlying mechanisms of aging involve general decay at the cellular level and the body’s dwindling ability to remove old and dysfunctional cells and proteins. When we are healthy, our organs function like a well-tuned orchestra, and dynamic and active homeostasis is maintained. Aging impairs rhythmic physiologic processes and adaptation, leading to diminishing physiologic reserves available to meet new biologic challenges, leading to “homeostenosis”, pushing our biology to the brink of the “precipice”.

NORMAL AGING

Aging does not seem to be a homogeneous decline. Some organs in the same person age at different rates. A Danish twin study found that genetics accounted for 25% of the variation in longevity among twins, and environmental factors, for more than 50%. But after age 90, genetics becomes more important.

Cardiovascular System

Vascular elasticity decreases, and arteries become stiff. Blood pressure rises. The left ventricle thickens, leading to diastolic stiffness and limiting maximal cardiac output and exercise tolerance. There is a marked decrease in the maximum heart rate in response to exertion (220-age), which cannot be modified by exercise. Even if the resting left ventricular ejection fraction (LVEF) does not change in healthy elderly individuals, there are smaller increases in LVEF in response to exercise. We know that older hearts have impaired early left ventricular filling, becoming more dependent on atrial systole (explains why atrial fibrillation may lead to heart failure in the elderly). All of these changes lead to a decrease in maximum O₂ utilization (VO₂max) and maximal work on exercise testing.

Respiratory System

Almost 1/3 of the surface area for gas exchange is lost over the lifespan, and anatomic “dead” space (non-functional lung tissue) increases. There is a loss of elastic tissue with decreased expiratory lung recoil, which may limit the speed of lung emptying and may lead to dynamic excessive lung inflation during exercise. Diffusion capacity (lung efficiency) declines about 5%

per decade, leading to a mismatch between lung ventilation and blood perfusion, worsening tolerance of hypoxia, particularly at high altitudes (worse in women). The chest wall also becomes stiffer with a reduction in chest wall compliance by 1/3 by age 75. The Functional vital capacity (FVC) decreases by ~ 220 ml/decade. The Forced Expiratory Volume in 1 s (FEV1) decreases by ~ 250 ml/decade. The Residual Volume (air left in the lung at the end of exhalation) rises by 10% per decade.

Cough is less vigorous, muco-ciliary clearance is slower and less effective, and peak aerobic capacity declines by 6% per decade in the 30s, but it can drop by almost 20% per decade beyond the 70s.

Renal System

Kidney mass declines by 25-30% between 30 and 80, but it becomes steeper after age 50, with loss of nephrons (functional unit) and decline in filtration rate by 7.5-10 ml/min per decade, although there is significant variability. The older kidney is more sensitive to toxic agents, with decreased ability to acidify and concentrate the urine, and releases more aldosterone, leading to hypertension. Also, the production of klotho decreases (an important protein with aging implications).

Gastrointestinal System

The oral mucosa thins with age. Gums recede. Salivary gland production declines, and the propulsion of the food bolus to the pharynx is altered, along with the strength and coordination of the tongue, leading to less effective mastication, decreased food clearance, and increased risk of aspiration. Sleep apnea becomes more common.

Esophageal propulsion of food is also slower, and the sensation of distension and tissue damage becomes impaired. The stomach is frequently the target of chronic gastritis, and up to 50% of older people may be infected with *Helicobacter Pylori*. The endocrine stomach function may also suffer.

The small intestine suffers villus atrophy with the consequent loss of surface area, with the loss of micronutrients, and up to 15% of senior community residents have bacterial overgrowth, with an impact on absorption.

The large intestine loses colonic propulsive motility and 1/2 of those older than 65 suffer from constipation.

The loss of sensory neurons in the bowel decreases responsiveness and also lowers pain intensity. Diverticuli are present in over 65% in the US population. The risk of colon cancer rises with aging. The barrier function of the colon may become compromised with increased permeability to toxins and contributing to a proinflammatory state or "inflammaging". The liver mass decreases by 20-40% with aging, and blood flow declines by 50% by the 10th decade of life.

Genito-urinary System

Aging leads to an increase in urinary incontinence, infections, erectile dysfunction, and more difficult sexual performance for both sexes. Incontinence is related to declining detrusor muscle force, bladder capacity, and sphincter pressure. The increased post-voiding residual inside the bladder, reduced ability to withhold voiding, and nocturia (nocturnal urination) are related to decreased brain dopamine rather than local bladder abnormalities.

The absence of estrogen in women results in a shortened urethra, a lower urethral closing pressure, and alterations in the local flora, leading to more frequent infections. We are all familiar with the age-related prostatic enlargement and the vascular, neurologic, and endocrine changes that lead to more challenging sexual performance for older men.

We have reviewed the consequences of Menopause and Andropause in prior “Bits”.

Musculoskeletal System

Muscle mass decreases by approximately 30-50% in adults with muscle becoming infiltrated by fat and connective tissue, with greater loss from legs and fast-twitch fibers. There is a loss of innervation, and the number of motor neurons declines, with greater than 50% loss in grip strength and other measures of muscle force. And as you well know, older muscles are easily fatigued and recovery after use or injury is slower, due to a defect in satellite cells, inadequate nerve recovery and altered “energetics”, as older muscle has decreased ability to generate ATP (energy) through both, the glycolytic (anaerobic) and oxidative (aerobic) pathways. Testosterone may help slow down this process, but long-term studies have shown that physical activity and training raise Testosterone, and safer and more effective than the pharmacologic administration of T.

Bone

We are all familiar with the bone loss affecting the elderly and the increased risk of fractures. There is a progressive decline in the number and function of Osteoblasts (bone forming cells), but Osteoclasts (bone recycling cells) remain unchanged. The overall decline in bone mass has been quantified at about 0.5% annually.

Central Nervous System

Even if your name is Albert Einstein, your brain volume decreases annually after age 65, with the greatest loss in the frontal and temporal lobes, with greater loss of white vs. gray matter (and probably one of the reasons his brightest insights and discoveries were attained in his 20s and 30s). Blood flow also declines by 5-20%. Neuronal loss is most prominent in the largest neurons of the cerebellum and cerebral cortex. There is also a loss of synapses, but new connections and new neurons are formed throughout our lifespans. In standardized testing, the old brain works harder, requiring more neurons and energy for a given task, reflecting the loss of functional reserve. Processing speed declines, and executive function (planning, monitoring, attention, and self-preserving behavior) declines, particularly after age 70. Of course, social deprivation, environmental changes, smoking, alcohol, limited education, and lack of sleep can aggravate or exacerbate the pace of decline.

Skin

Our skin loses elasticity and dries up. The superficial layer (epidermis) becomes thinner, the dermo-epidermal junction (interface between superficial and deeper layers) flattens and results in increased fragility unable to tolerate “shear stress” and resulting in bleeding into the space between the dermis and the epidermis (those bluish – reddish spots that appear over your arms and legs after minimal trauma). The blood supply declines, with delayed wound healing, and dermal collagen declines by up to 75%. Sensory perception decreases, and the atrophy of subdermal fat leads to the wrinkles and sagging we all recognize.

Eye

The eyelids become more relaxed. Lacrimal tear production declines. The conjunctiva and lens yellow. UV-light exposure accelerates oxidation of the lens protein and leads to “cataracts” with the consequent decreased transmission of blue light. The iris becomes more rigid and less responsive to light changes. The production of aqueous humor and vitreous humor declines. The retina becomes thinner due to the loss of neurons and retinal vessels, and with progressive loss of photoreceptors. As a result, the older eye faces many challenges, with loss of contrast sensitivity (discrimination between object and background), which is important when designing dwellings and environments for the elderly.

Hearing

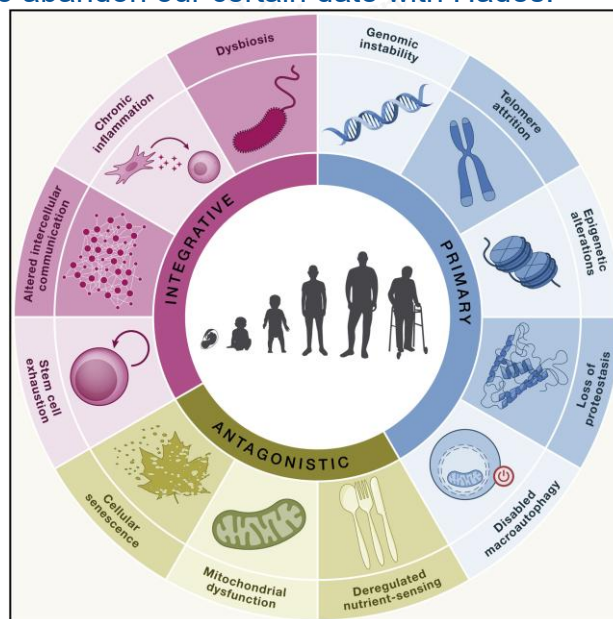
Cerumen becomes drier, leading to a higher risk of wax impaction. The inner ear is invariably affected to various degrees with loss of hair cells in the transducer (Organ of Corti, responsible for converting the mechanical impulses into electrical signals that travel to the auditory brain centers). Cochlear neurons are lost, leading to hearing loss, especially at higher frequencies. Thus, it’s recommended that the message be rephrased with different words instead of repeating in a louder voice.

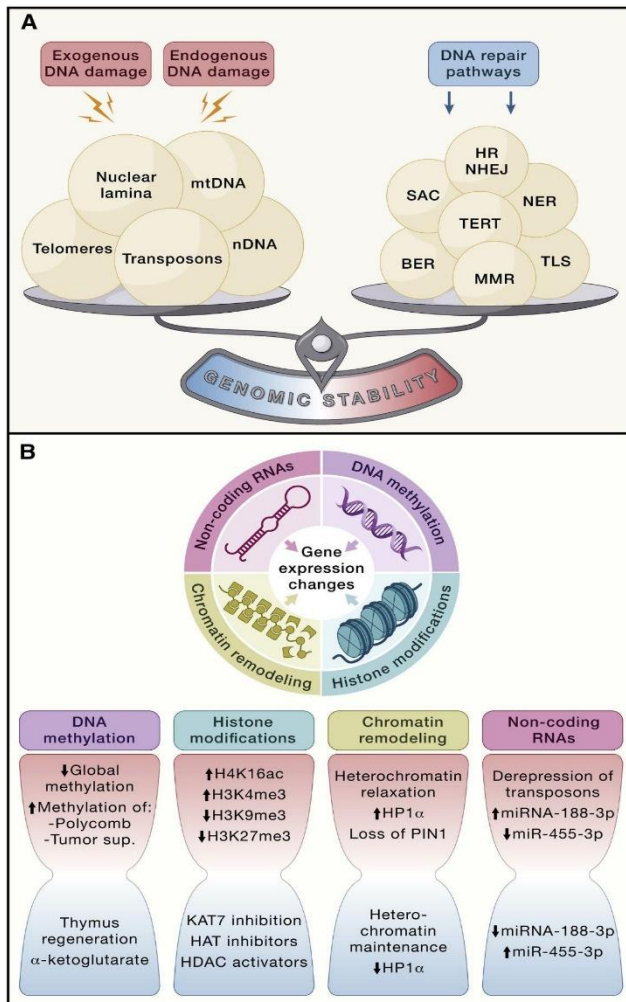
Immune System

We have discussed immune-senescence in multiple other “Bits”, addressing the decline in immune function responsible for the increased susceptibility to infectious diseases, malignancies, and autoimmune disorders.

Most important mechanisms leading to aging

This is the subject of intense research and likely to change substantially over the next few years, but not enough to abandon our certain date with Hades.





1. Damage to genetic material or “genomic instability”, due to DNA damage by UV radiation and reactive O₂ species produced by our energy organelles called mitochondria. Our DNA is damaged thousands of times daily and most is repaired immediately, but some repairs are inadequate and these DNA imperfections accumulate over time leading to an increased risk of cancers, reduced cell function and cell senescence with loss of organ function as we age.

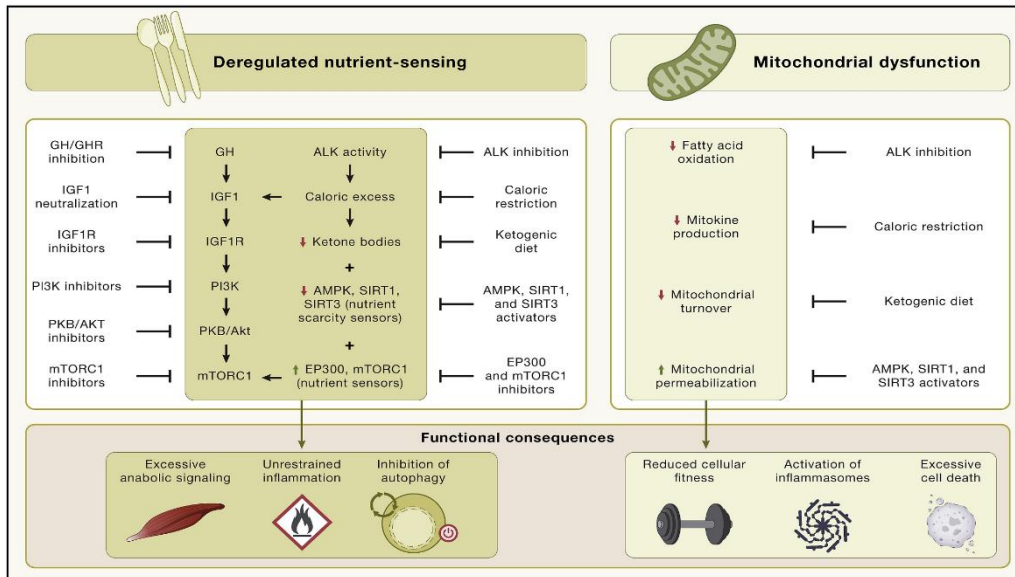
2. Telomere degradation. Telomeres are the shoelaces that keep our chromosomes intact. Every time a cell divides, telomeres shorten, eventually pushing the cells into a resting phase and halting division and replication, limiting those cells lifespan. An enzyme called telomerase can prevent shortening and restore telomere length, but the only cells expressing this enzyme are our stem cells and of course, cancer cells are characterized by high telomerase activity and “immortality”.

3. Epigenetic changes. Our genome encodes information through more than 3 billion nucleotide base pairs and chemical modifications/histone proteins that package our DNA. The accumulated chemical modifications are known as the epigenome, which is dynamic and changes in response to diet, drugs, stress, and aging. One of these forms of adaptation is DNA methylation, and some patterns can predict a person’s biological age (‘epigenetic clock’) and serve as a

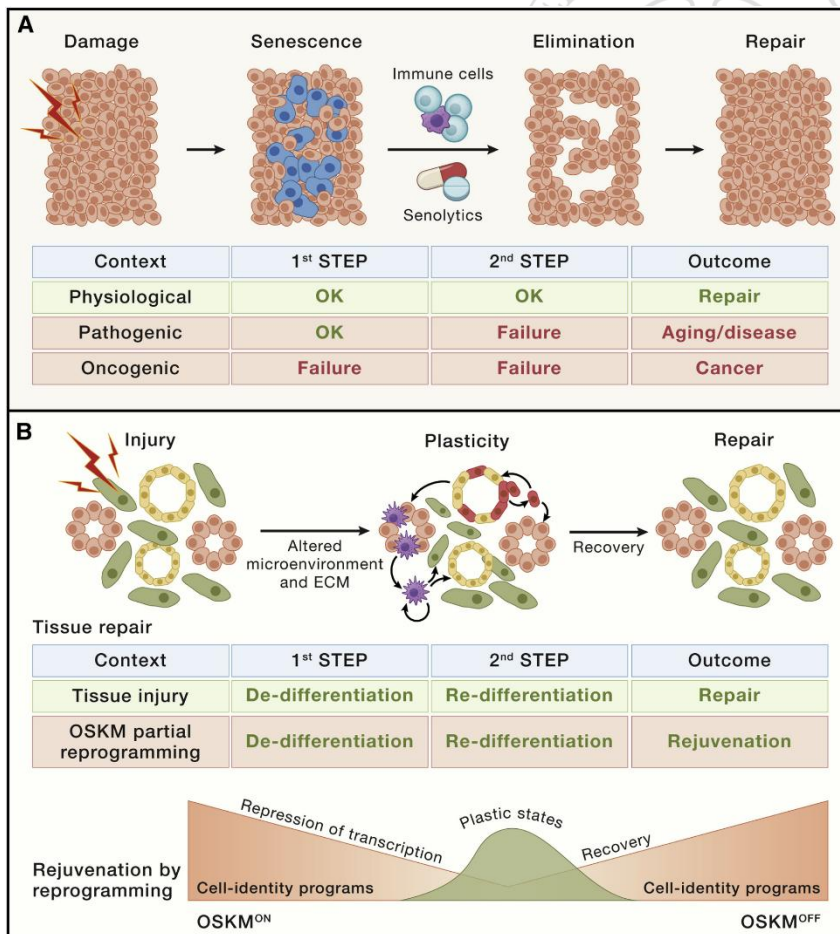
biomarker but also a potential target to modify lifespan.

4. Impaired “proteostasis”. Proteins are the most important building blocks in our cells, and mediate most chemical reactions and proper cell function. Cellular systems regulate protein synthesis, folding, and degradation. Damaged proteins are recycled by the proteasome or through a process of autophagy which become ineffective as we age, leading to accumulation of misfolded proteins (characteristic feature of neurodegenerative diseases such as Alzheimer’s, Parkinson’s, Multiple System atrophy and others. Activation of the proteasome or autophagy can extend lifespan in animal models.
5. Impaired nutrient perception. Reduced food intake without malnutrition – Dietary Restriction – extends lifespan in multiple species. Our cells regulate growth and metabolism to the perceived availability of nutrients. Insulin and mTOR (mechanistic target of rapamycin) are important signaling systems. The latter is preserved across multiple species and classes of organisms, and its job is to balance the need for growth and reproduction with the available nutrients. When food is available, mTOR is activated and the cell/organism goes into growth mode, producing new proteins and replicating. When nutrients dwindle, mTOR is suppressed and cells go into “recycling” mode, triggering autophagy, breaking down cellular components with conservation of energy. There are

two separate complexes: mTOR complex 1 and mTOR complex 2. The longevity-related benefits appear to be related to inhibition of complex 1.



slows down our energy power plants, allowing the accumulation of reactive oxygen species and free radicals.

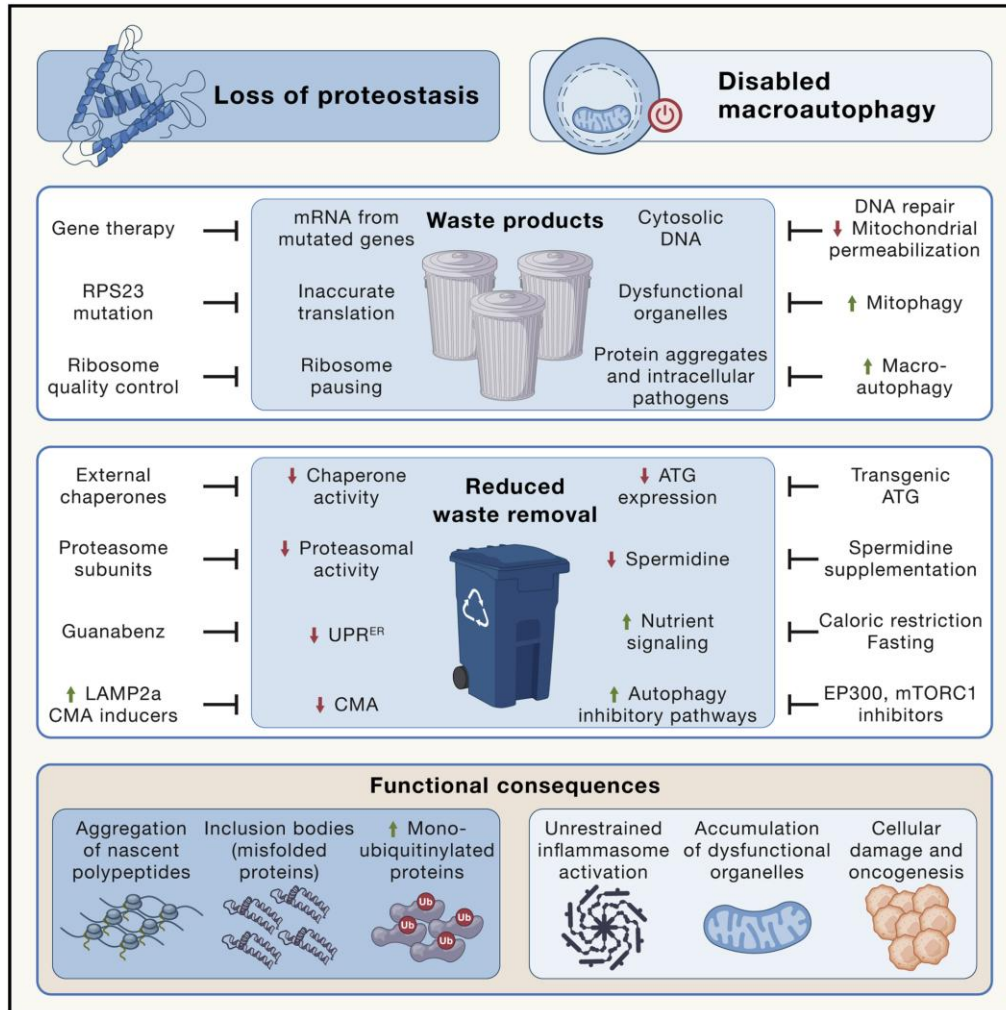


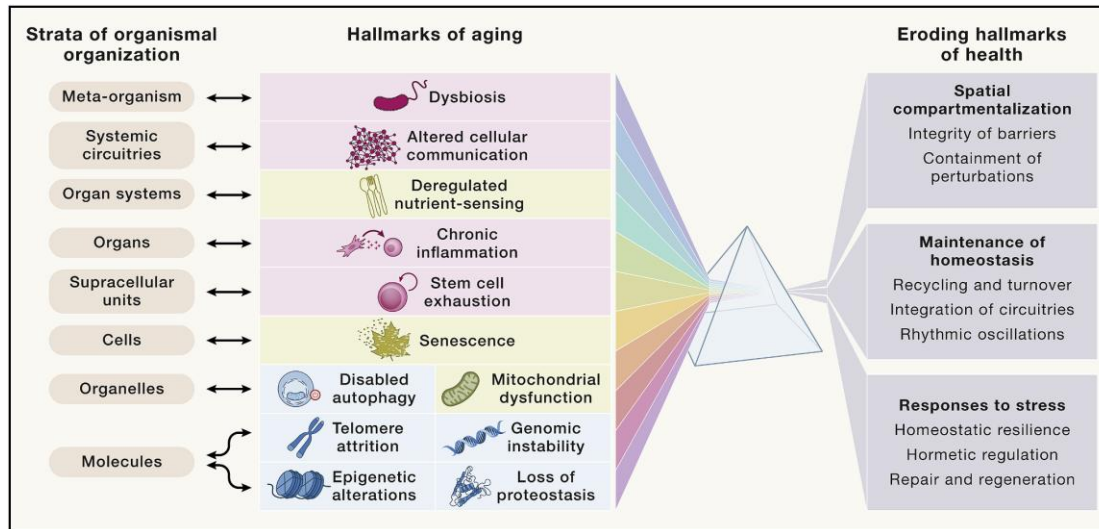
6. Mitochondria are the cell's energy factory or power plant, using oxygen to efficiently "burn" fuel in a process called mitochondrial aerobic respiration. They have their own DNA (mtDNA) which regulate the proteins needed for the process of fuel utilization and efficient production of energy (ATP). Aging damages mitochondrial DNA and

7. Cellular senescence. Stress and cumulative damage may lead the cells to enter a state of senescence. Cells stop dividing, lose original function and release inflammatory cytokines and mediators impacting surrounding cells and organic function. There are many triggers for cellular senescence, including telomere shortening, DNA damage and mitochondrial dysfunction and now new drugs are being tested to silence these senescent cells (called senolytics) and potentially improve aging.

8. Stem cell exhaustion. The cells in our tissues lose the ability to divide once they reach their final destination and identity, but stem cells have the ability to divide and differentiate into different cell types and are important to repair tissues and organs. Aging results in stem cell depletion leading to a limited ability to repair organ damage. New research indicates that old stem cells can be "rejuvenated" leading to improved organ function.

9. Altered intra and intercellular communication is another hallmark of aging.
10. Degraded autophagy: the body's breakdown of unwanted cell components deteriorates with aging.
11. Chronic inflammation at low levels is a hallmark of aging.
12. Dysbiosis (imbalance) of intestinal flora: There is good evidence that centenarians have a healthier flora and microbiome.



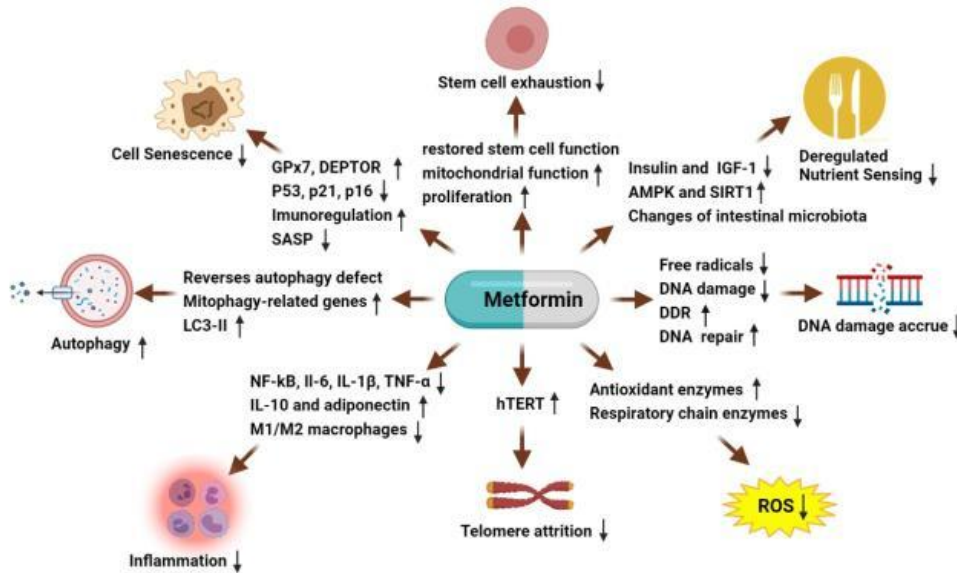


Molecules Associated with Increased Longevity:

Metformin, a widely prescribed medication for type 2 diabetes and prediabetes, has attracted so much attention for its potential to extend lifespan and promote healthy aging, even in individuals without diabetes. Research in animal models and humans suggests that metformin may influence several fundamental aging pathways and biological processes.

- **Reduction of Oxidative Stress:** Metformin decreases the production of mitochondrial reactive oxygen species (ROS), protecting proteins and DNA from oxidative damage. This reduction in oxidative stress is a critical factor in delaying cellular aging and extending lifespan.
- **Improvement of Insulin Sensitivity and Metabolic Regulation:** Metformin enhances insulin sensitivity, particularly in the liver, by activating pathways such as AMPK (AMP-activated protein kinase). Improved insulin sensitivity is associated with increased lifespan and reduced risk of age-related diseases.
- **Regulation of Nutrient Sensing Pathways:** Metformin modulates key nutrient-sensing pathways, including the inhibition of mTOR (mechanistic target of rapamycin) and activation of AMPK. These pathways are central to the aging process, and their modulation mimics some effects of calorie restriction, a well-established intervention for lifespan extension.
- **Reduction of Advanced Glycation End Products (AGEs):** By facilitating glucose utilization and lowering blood glucose levels, metformin reduces the accumulation of AGEs, which are linked to protein dysfunction and cellular aging¹.
- **Enhancement of Autophagy and Proteostasis:** Metformin promotes autophagy, the cellular process that removes damaged proteins and organelles, by activating AMPK and inhibiting mTOR. This helps maintain protein homeostasis (proteostasis) and delays cellular senescence.

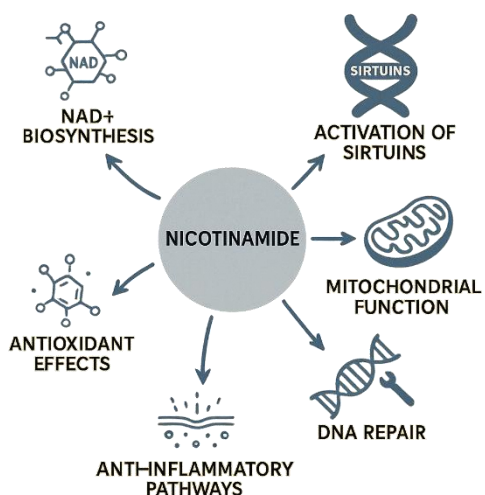
- Maintenance of Telomere Stability: Metformin has been shown to help preserve telomere length, a marker of cellular aging, possibly through the activation of SIRT1 and reduction of oxidative stress.
- Reduction of Inflammation: Metformin inhibits age-related inflammatory pathways, including NF- κ B signaling, and reduces pro-inflammatory cytokines, contributing to healthier tissue function with age.



- Delaying Cellular Senescence: Studies indicate that metformin delays the onset of cellular senescence, reducing the burden of dysfunctional cells that accumulate with age.

- Epidemiological studies in humans suggest that metformin use is associated with reduced all-cause mortality, lower incidence of cancer, and improved cognitive outcomes, even beyond its effects on blood sugar regulation.

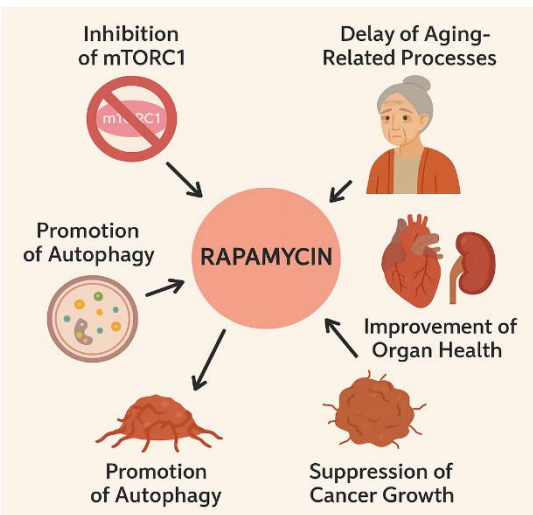
Nicotinamide, (NAM), a form of vitamin B3, is a precursor to nicotinamide adenine dinucleotide (NAD⁺), a critical coenzyme involved in various cellular processes, including energy metabolism, DNA repair, and cell signaling. Nicotinamide helps improve longevity primarily by increasing NAD⁺ levels, which decline with age and are associated with age-related diseases.



Studies have shown that supplementation with NAD⁺ precursors, including nicotinamide, can enhance NAD⁺ levels, thereby improving cellular function and healthspan. For instance, nicotinamide supplementation has been demonstrated to improve aspects of healthspan in mice, such as glucose homeostasis and reducing hepatic steatosis and inflammation, although it did not extend lifespan in these models. Additionally, nicotinamide has been shown to extend the replicative lifespan of human cells by reducing reactive oxygen species (ROS) levels and oxidative damage, and decelerating telomere shortening. Furthermore, NAD⁺ precursors, including nicotinamide, have shown potential in mitigating age-related conditions and improving physiological functions in preclinical models, but human clinical trials are still needed to fully establish the efficacy and safety of nicotinamide supplementation for improving longevity. In summary,

nicotinamide contributes to longevity by boosting NAD⁺ levels, which supports various cellular functions and mitigates age-related physiological decline

Rapamycin, is an inhibitor of the mechanistic target of rapamycin (mTOR), and has been shown to improve longevity by modulating the mTOR signaling pathway, which is crucial in regulating cell growth, metabolism, and aging. The inhibition of mTOR, particularly mTOR Complex 1 (mTORC1), has been demonstrated to extend lifespan and delay age-related diseases in various model organisms, including yeast, nematodes, fruit flies, and mice.



Rapamycin's efficacy in extending lifespan is attributed to its ability to reduce the rate of aging and improve age-related diseases by inhibiting the mTOR pathway. This inhibition helps in delaying the aging of multiple organ systems, including the nervous, urinary, digestive, circulatory, and immune systems. Additionally, rapamycin has been shown to extend both mean and maximum lifespan in genetically heterogeneous mice, suggesting its potential applicability across different genetic backgrounds.

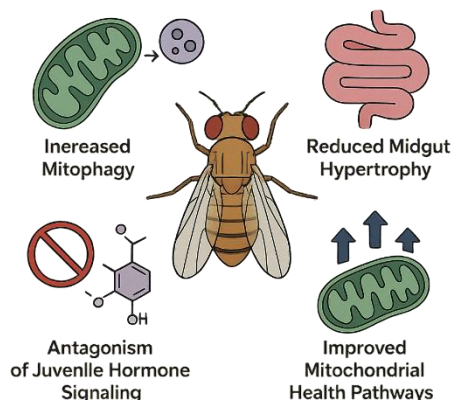
However, the chronic use of rapamycin is associated with significant side effects, such as immunosuppression and metabolic disruptions, primarily due to the inhibition of mTOR Complex 2 (mTORC2).^[2-3] To mitigate these side effects, intermittent dosing regimens and the development of rapamycin analogs (rapalogs) that selectively inhibit mTORC1 are being

explored. These strategies aim to harness the geroprotective effects of rapamycin while minimizing adverse outcomes.

In summary, rapamycin may improve longevity by inhibiting the mTOR pathway, particularly mTORC1, thereby delaying aging and extending lifespan. Careful consideration of dosing regimens and potential side effects will be crucial for its clinical application in humans.

Mifepristone, has been shown to improve longevity in certain experimental models, particularly in female

Mifepristone Increases Longevity



Drosophila melanogaster. The primary mechanism involves its ability to counteract the life span-shortening effects of mating and male sex peptide (SP). Mating and SP transfer induce inflammation and metabolic shifts that reduce life span. Mifepristone mitigates these effects by antagonizing juvenile hormone (JH) signaling, which is implicated in these detrimental processes.

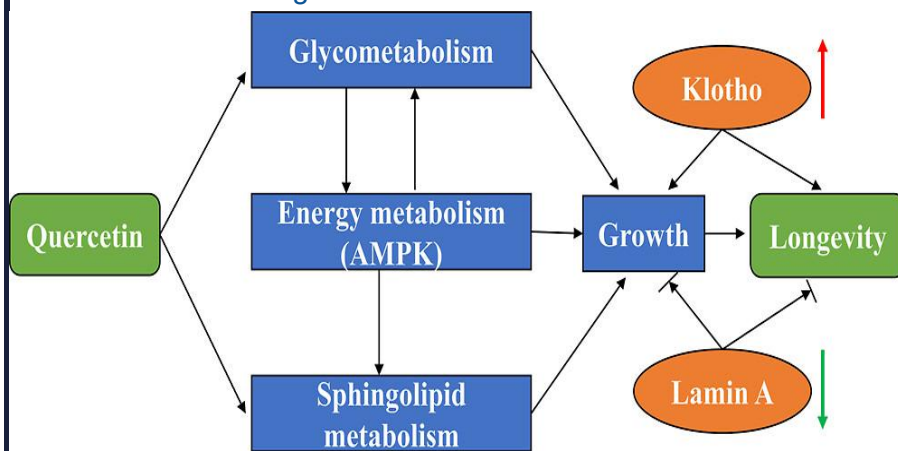
In mated female *Drosophila*, mifepristone has been observed to increase life span by reducing inflammation and altering metabolic pathways. Specifically, it decreases the expression of genes involved in protein degradation, amino acid metabolism, and immune response, while increasing the expression of genes associated with somatic maintenance and turnover.¹ Additionally,

mifepristone has been shown to reduce midgut hypertrophy and lipid metabolism dysregulation caused by mating.

Furthermore, mifepristone has demonstrated life span extension in virgin female *Drosophila* on both regular and high-fat diets, suggesting its potential benefits are not solely dependent on mating status.^[2] The drug's effects on longevity are also linked to its ability to modulate metabolic pathways, including reducing tryptophan breakdown and mimicking dietary restriction effects.

In summary, mifepristone improves longevity in *Drosophila* primarily by antagonizing juvenile hormone signaling, reducing inflammation, and modulating metabolic pathways that are adversely affected by mating and dietary factors.

Quercetin, is a flavonoid with significant potential in improving longevity through various mechanisms. It exhibits antioxidant, anti-inflammatory, and anti-apoptotic properties, which are crucial in mitigating aging-related cellular damage.



One of the primary mechanisms by which quercetin enhances longevity is through the activation of Sirtuin 1 (SIRT1), a NAD-dependent deacetylase enzyme. SIRT1 plays a vital role in regulating cellular senescence and multiple aging-related processes, including oxidative stress, inflammatory response, mitochondrial function, autophagy, and apoptosis. Quercetin's ability to modulate SIRT1 activity has been shown to provide neuroprotective effects and

improve mitochondrial function, thereby contributing to increased lifespan and healthspan.

Additionally, quercetin has been demonstrated to prolong lifespan and enhance stress tolerance in model organisms such as *Caenorhabditis elegans* by modulating insulin-like signaling (ILS) and p38-mitogen-activated protein kinase (MAPK) pathways. These pathways are involved in reducing oxidative stress and improving cellular resilience.

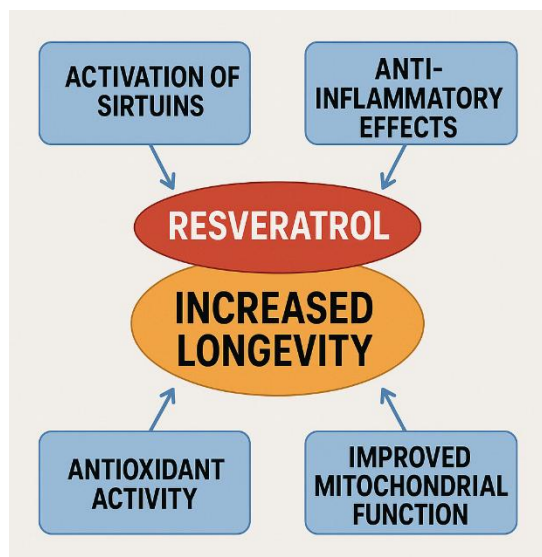
Furthermore, quercetin's antioxidant properties help in reducing oxidative damage, which is a major contributor to aging. It has been shown to decrease reactive oxygen species (ROS) levels and improve mitochondrial function in aged human dermal fibroblasts, thereby restoring cellular health and function.

In summary, quercetin improves longevity by activating SIRT1, modulating key signaling pathways, and reducing oxidative stress, which collectively contribute to enhanced cellular function and resilience against aging-related damage

Resveratrol, a polyphenolic compound found in foods such as grapes, red wine, and blueberries, has been studied for its potential to improve longevity through several mechanisms.

Resveratrol is believed to enhance longevity primarily by activating sirtuin 1 (SIRT1), a highly conserved family of histone deacetylases involved in metabolism, stress response, and genomic stability. Activation of

SIRT1 by resveratrol mimics the effects of caloric restriction, which has been associated with lifespan extension in various model organisms. Additionally, resveratrol exerts its anti-aging effects through several other pathways:



1. **Oxidative Stress Reduction:** Resveratrol has potent antioxidant properties, reducing oxidative damage to DNA, proteins, and lipids, which are critical factors in the aging process.

2. **Anti-inflammatory Effects:** Chronic inflammation is a hallmark of aging, and resveratrol has been shown to mitigate inflammatory responses, thereby potentially delaying the onset of age-related diseases.

3. **Mitochondrial Function:** Resveratrol improves mitochondrial function and biogenesis, which are essential for maintaining cellular energy homeostasis and reducing age-related decline in cellular function.

4. **Regulation of Apoptosis:** By modulating apoptotic pathways, resveratrol helps in maintaining cellular integrity and preventing premature cell death.

While these mechanisms suggest a promising role for resveratrol in promoting longevity, it is important to note that the evidence from human clinical trials remains inconclusive, and more research is needed to establish effective dosages and long-term safety.

Curcumin, a polyphenolic compound derived from the rhizomes of *Curcuma longa*, has been shown to have several mechanisms that may contribute to improved longevity. Curcumin exhibits potent antioxidative and anti-inflammatory properties, crucial in mitigating the cellular damage associated with aging. Curcumin has been demonstrated to extend the lifespan of various model organisms, including *Caenorhabditis elegans*, *Drosophila melanogaster*, and mice. This lifespan extension is associated with enhanced superoxide dismutase (SOD) activity and reduced levels of malondialdehyde (MDA) and lipofuscin, which are markers of oxidative stress and cellular aging. Additionally, curcumin modulates key signaling pathways involved in aging, such as the insulin/IGF-1 signaling (IIS), mammalian target of rapamycin (mTOR), protein kinase A (PKA), and forkhead box O (FOXO) pathways. Curcumin also influences the activity of sirtuins and AMP-activated protein kinase (AMPK), which are proteins involved in cellular metabolism and longevity. By modulating these proteins, curcumin can enhance cellular stress resistance and promote autophagy, thereby delaying the onset of age-related diseases. Furthermore, curcumin has been shown to have senolytic properties, meaning it can selectively eliminate senescent cells, which accumulate with age and contribute to tissue dysfunction and inflammation. This elimination of senescent cells can improve tissue function and potentially extend lifespan.

In summary, curcumin improves longevity through its antioxidative and anti-inflammatory effects, modulation of key aging-related signaling pathways, enhancement of cellular stress resistance, and senolytic activity.

Spermidine, is a natural polyamine that has been shown to have significant effects on longevity. The mechanisms through which spermidine exerts its beneficial effects include the induction of autophagy, modulation of metabolic processes, and reduction of oxidative stress.

1. **Autophagy Induction:** Spermidine stimulates autophagy, a cellular process that degrades and recycles damaged cellular components, which is crucial for maintaining cellular homeostasis and function. This process has been linked to increased lifespan in various model organisms, including yeast, flies, worms, and mice. Autophagy helps in reducing cellular damage and improving tissue function, which are critical factors in aging.
2. **Cardioprotection:** Spermidine has cardioprotective effects, including reducing cardiac hypertrophy and preserving diastolic function in aged mice. It enhances cardiac autophagy, mitophagy, and mitochondrial respiration, which are essential for maintaining heart health and function. Epidemiological studies have also shown that higher dietary spermidine intake is associated with reduced cardiovascular disease incidence and mortality in humans.
3. **Metabolic Regulation:** Spermidine has been shown to protect against metabolic dysfunction, particularly in the context of overnutrition. It increases lipolysis in visceral fat and modulates the expression of metabolic regulators such as fibroblast growth factor 21 (FGF21). These effects contribute to improved metabolic health and potentially extend lifespan.
4. **Reduction of Oxidative Stress:** Spermidine inhibits oxidative stress by promoting the deacetylation of histone H3, which suppresses the generation of reactive oxygen species and necrosis. This reduction in oxidative stress is crucial for preventing cellular damage and extending lifespan.
5. **Epidemiological Evidence:** A prospective population-based study demonstrated that higher spermidine intake is linked to lower all-cause mortality. The study found that individuals with higher dietary spermidine intake had a significantly reduced risk of death, suggesting a strong association between spermidine consumption and increased survival in humans.

In summary, spermidine improves longevity through autophagy induction, cardioprotection, metabolic regulation, and reduction of oxidative stress. These effects are supported by both preclinical and epidemiological studies

Sulforaphane is a bioactive compound derived from cruciferous vegetables, such as broccoli, and has been shown to have several mechanisms that may contribute to improved longevity.

1. **Insulin/IGF-1 Signaling Pathway:** Sulforaphane has been demonstrated to inhibit the DAF-2-mediated insulin/IGF-1 signaling pathway, which is associated with increased nuclear translocation of the FOXO transcription factor homolog DAF-16. This leads to the upregulation of target genes that enhance stress resistance and lifespan.
2. **Nrf2 Pathway Activation:** Sulforaphane activates the Nrf2 pathway, which induces the expression of antioxidant and cytoprotective genes. This activation helps mitigate oxidative stress and inflammation, both of which are critical factors in aging and age-related diseases.
3. **Epigenetic Modulation:** Sulforaphane has epigenetic effects, such as inhibiting histone deacetylases (HDACs) and DNA methyltransferases, which can modify gene expression patterns associated with aging and longevity.
4. **Mitochondrial Function and Metabolic Health:** Sulforaphane has been shown to improve mitochondrial function and metabolic health, which are essential for maintaining cellular energy balance and reducing age-related decline in muscle and cardiac function.

5. Gut Microbiome Modulation: Sulforaphane can positively influence the gut microbiome, promoting a composition that supports better intestinal barrier function and anti-inflammatory effects, which are beneficial for healthy aging.

Collectively, these mechanisms suggest that sulforaphane can promote longevity and healthspan by enhancing stress resistance, reducing oxidative damage, and improving metabolic and mitochondrial functions.

L-serine has been shown to have potential benefits in improving longevity through several mechanisms. Firstly, L-serine plays a crucial role in cellular functions such as protein synthesis, neurotransmission, and the synthesis of sphingolipids and phospholipids, which are essential for maintaining cellular integrity and function.

Additionally, L-serine supplementation has been demonstrated to reduce oxidative stress and inflammation, which are key contributors to aging and age-related diseases. For instance, long-term administration of L-serine in aging mice has been shown to decrease oxidative stress markers and inflammatory cytokines, while increasing antioxidant levels such as superoxide dismutase and glutathione. This reduction in oxidative stress and inflammation can potentially mitigate age-related damage and improve overall healthspan.

Moreover, L-serine has been implicated in the activation of SIRT1, a protein that is associated with increased fatty acid oxidation and improved mitochondrial function. Enhanced SIRT1 activity has been linked to improved insulin sensitivity and metabolic health, which are important factors in promoting longevity. Furthermore, L-serine deficiency has been shown to exacerbate inflammation and oxidative stress via the microbiota-gut-brain axis in aging models, suggesting that adequate levels of L-serine are necessary to maintain homeostasis and prevent age-related decline.^[4]

In summary, L-serine may improve longevity by reducing oxidative stress and inflammation, enhancing mitochondrial function, and supporting overall cellular health.

and lipids with more double bonds (lower mortality risk).

Omega-3 polyunsaturated fatty acids (n-3 PUFAs), have been shown to improve longevity through several mechanisms.

Firstly, higher levels of circulating n-3 PUFAs, particularly eicosapentaenoic acid (EPA) and docosapentaenoic acid (DPA), are associated with a lower risk of unhealthy aging. A prospective cohort study demonstrated that older adults with higher cumulative levels of these fatty acids had an 18% lower risk of unhealthy aging, defined as survival without chronic diseases and the absence of cognitive and physical dysfunction. Secondly, n-3 PUFAs have anti-inflammatory properties that contribute to their longevity benefits. They reduce systemic immune inflammation, which mediates the association between serum n-3 PUFAs and reduced biological aging. This effect is partly due to the modulation of inflammatory cytokines and the enhancement of anti-inflammatory pathways. Additionally, n-3 PUFAs help maintain telomere length, which is a marker of cellular aging. Studies indicate that n-3 PUFAs can reduce oxidative stress and inflammation, thereby slowing telomere attrition and promoting genomic stability.

Moreover, n-3 PUFAs promote energy metabolism and lipid homeostasis, which are crucial for slowing organ aging. They act as agonists of peroxisome proliferator-activated receptor α (PPAR α), enhancing fatty acid β -oxidation and ATP production, thus preserving organ function and retarding the aging process. In summary, Omega-3 polyunsaturated fatty acids improve longevity by reducing the risk of chronic diseases, modulating inflammation, maintaining telomere length, and promoting energy metabolism.

Short-chain fatty acids (SCFAs), primarily acetate, propionate, and butyrate, are produced by the fermentation of dietary fibers by gut microbiota. These SCFAs have been shown to play significant roles in promoting longevity through various mechanisms.

Firstly, SCFAs contribute to the maintenance of redox homeostasis by activating nuclear erythroid 2-related factor 2 (Nrf2), which helps protect against oxidative and mitochondrial stress. This cytoprotective role is crucial in suppressing inflammation and carcinogenesis, both of which are associated with aging.

Secondly, SCFAs have been linked to improved metabolic function. They enhance insulin sensitivity, increase energy expenditure, and promote mitochondrial function, which are essential for metabolic health and longevity. Additionally, SCFAs stimulate G-protein-coupled receptors (GPCRs) and inhibit histone deacetylases (HDACs), leading to beneficial epigenetic modifications that support healthy aging. Furthermore, studies on centenarians have shown that higher levels of SCFAs are associated with better cognitive function, reduced local inflammation, and overall health-span-promoting processes. This suggests that SCFAs play a role in the metabolic remodeling that characterizes exceptional longevity.

In summary, SCFAs help improve longevity by maintaining redox homeostasis, enhancing metabolic function, and promoting anti-inflammatory and epigenetic modifications. These effects collectively contribute to healthier aging and increased lifespan.

Sphingolipids, play a significant role in improving longevity through several mechanisms. These bioactive lipids, including ceramide, sphingosine, and sphingosine-1-phosphate (S1P), are involved in regulating cell survival, proliferation, differentiation, and stress responses, which are critical for aging and longevity.

One key mechanism is the regulation of lysosomal function. Sphingolipids tightly control lysosomal homeostasis, which is crucial for cellular waste management and recycling processes. Dysregulation of lysosomal function is associated with aging and age-related diseases, suggesting that maintaining lysosomal integrity through sphingolipid regulation can promote longevity. Additionally, sphingolipids interact with the insulin-like growth factor (IGF) signaling pathway, particularly the IGF-I-Akt-mTOR pathway, which is known to modulate aging and longevity. This pathway integrates various metabolic signals and influences gene expression to enhance stress resistance and cellular metabolic profiles, contributing to increased lifespan.

Furthermore, specific sphingolipid species have been identified as longevity metabolites. For instance, in *Caenorhabditis elegans*, the acyl chain-specific sphingolipid C22 glucosylceramide is required for proper lysosomal function and autophagic processes, which are essential for lifespan regulation.

In humans, a unique plasma sphingolipidome profile characterized by higher levels of complex glycosphingolipids and lower levels of ceramide species has been associated with exceptional longevity. This suggests that structural glycosphingolipids may play a more significant role in achieving a centenarian condition than signaling sphingolipids. In summary, sphingolipids contribute to longevity by maintaining lysosomal function, modulating key signaling pathways like IGF-I-Akt-mTOR, and through specific lipid profiles that support cellular health and stress resistance.

Hexosylceramides and ether-linked phosphocholines have been implicated in promoting longevity through several mechanisms.

Hexosylceramides, a type of glycosphingolipid, have been associated with slower biological aging. Higher levels of hexosylceramides are linked to a deceleration in biological aging metrics, such as DNA methylation-based aging markers, suggesting a protective role against age-related cellular damage.^[1]

Additionally, studies have shown that centenarians exhibit increased levels of hexosylceramides, indicating their potential role in achieving exceptional longevity.^[2]

Ether-linked phosphocholines, a subclass of phospholipids, are also associated with longevity. These lipids are known for their antioxidant properties, which help in reducing oxidative stress, a key factor in aging. Research has demonstrated that higher levels of ether-linked phosphocholines are present in individuals with exceptional longevity, suggesting that these lipids contribute to a plasma lipidome that is more resistant to oxidative damage and lipid peroxidation.^[3-4] This resistance to oxidative stress is crucial for maintaining cellular integrity and function over time.

In summary, hexosylceramides and ether-linked phosphocholines are beneficial in improving longevity by slowing biological aging and enhancing resistance to oxidative stress, respectively. These findings are supported by lipidomic studies in both population-based cohorts and centenarians.

Polyphenols: These compounds exhibit antioxidant and anti-inflammatory properties, which help mitigate oxidative stress and inflammation, key contributors to aging. They also influence cellular processes such as autophagy, proteostasis, and mitochondrial function, which are critical for maintaining cellular health and delaying aging.

Ergothioneine: This sulfur-containing amino acid acts as a potent antioxidant and cytoprotectant. It scavenges reactive oxygen and nitrogen species, chelates metals, and regulates Nrf2 activity, which is crucial for cellular defense mechanisms. High levels of ergothioneine are associated with reduced cardiovascular and overall mortality risks, and its deficiency is linked to increased oxidative stress and inflammation.

Pyrroloquinoline Quinone (PQQ): PQQ supports mitochondrial biogenesis and function, which are essential for energy production and cellular health. It also exhibits antioxidant properties, reducing oxidative damage and promoting longevity.

Queuine: This bacterial metabolite is involved in tRNA modification, which is crucial for protein synthesis and cellular function. Its role in maintaining cellular homeostasis and reducing oxidative stress contributes to longevity.

Carotenoids (lutein, zeaxanthin, lycopene, alpha- and beta-carotene, beta-cryptoxanthin, astaxanthin): These compounds are known for their antioxidant properties, protecting cells from oxidative damage. They also have anti-inflammatory effects and support eye health, skin health, and cognitive function, all of which are important for healthy aging.

In summary, these nutrients and polyphenols contribute to longevity by reducing oxidative stress, inflammation, and supporting cellular health through various mechanisms. Their intake through diet or supplementation can help mitigate age-related diseases and promote healthy aging.

DEBUNKING MYTHS: Q & A

1. Are people with Shellfish Allergy intolerant of IV Contrast? It was previously believed that patients with shellfish allergies should not receive intravenous contrast due to a higher risk of anaphylactoid reactions. However, research has shown that the risk of contrast reactions is not higher.
2. Anticoagulation in Atrial Fibrillation: Another myth was that patients with atrial fibrillation of less than 48 hours' duration do not require anticoagulation before cardioversion. Current evidence suggests that anticoagulation should be considered to reduce the risk of thromboembolic events, regardless of the duration of atrial fibrillation.^[1]
3. CT Scan Before Lumbar Puncture in Suspected Meningitis: It was commonly believed that a CT scan should be performed before a lumbar puncture in patients with suspected acute bacterial meningitis to avoid herniation. However, this practice is inefficient and unnecessary.
4. β -Blockers in Respiratory Disease: There was a longstanding belief that β -blockers should be avoided in patients with respiratory diseases such as asthma or COPD. Modern studies have demonstrated that β -blockers can be safely used in these patients and may even reduce the risk of cardiac events.
5. MMR Vaccine and Autism: The myth that the measles-mumps-rubella (MMR) vaccine causes autism has been thoroughly debunked despite our Secretary of HHS long-held beliefs. Extensive research has shown no link between the MMR vaccine and autism spectrum disorders, and this has been supported by numerous studies and medical organizations.^[2-4]

These examples highlight the importance of evidence-based medicine in dispelling myths and improving clinical practice.

In addition to the previously mentioned myths, modern medicine and research have debunked several other widely held medical myths:

1. **Starving a Fever:** The belief that fasting when feverish can increase the pace of recovery is a myth. Adequate nutrition and hydration are essential for recovery from illness, and there is no evidence to support the idea that fasting benefits febrile patients.^[1]
2. **Showering After Sex Prevents Pregnancy:** This is a common misconception. Showering or douching after intercourse does not prevent pregnancy, as sperm can reach the cervix within minutes of ejaculation.^[1]
3. **Calcium Intake and Bone Health:** The myth that high calcium intake alone ensures bone health has been challenged. While calcium is important, other factors such as vitamin D, physical activity, and overall diet play crucial roles in maintaining bone health.^[2]
4. **Dietary Fat and Obesity:** The notion that all dietary fat leads to obesity and is detrimental to vascular health is overly simplistic. Research has shown that the type of fat consumed is more important, with unsaturated fats being beneficial for cardiovascular health.^[2]
5. **Fiber and Health:** Not all fiber is equally beneficial. The myth that all fiber, whether naturally occurring or artificially added, is beneficial has been debunked. Whole foods containing natural fiber are more beneficial than processed foods with added fiber.^[2]

6. Food Calories and Weight Gain: The idea that food calories translate to body weight through a simple linear relationship is a myth. Factors such as metabolism, the thermic effect of food, and individual variability play significant roles in how calories are processed and stored.^[2]

2. Routine Prostate-Specific Antigen (PSA) Screening: PSA screening was widely recommended for early detection of prostate cancer. However, evidence from large trials such as the PLCO and ERSPC showed that routine PSA screening leads to overdiagnosis and overtreatment without significantly reducing mortality. This has led to more conservative screening guidelines.^[2-3]

3. Vitamin D and Calcium Supplementation for Fracture Prevention: Public health policies often recommended high doses of vitamin D and calcium supplements to prevent fractures in older adults. Recent meta-analyses have shown that these supplements do not significantly reduce fracture risk in community-dwelling adults, leading to revised guidelines.^[2-3]

4. Low-Fat Diets for Heart Disease Prevention: Public policy once strongly advocated for low-fat diets to prevent heart disease. However, research has shown that the type of fat consumed is more important than the total fat intake. Diets rich in unsaturated fats are now recommended over low-fat diets.^[4]

5. Antibiotics for Upper Respiratory Infections: It was common practice to prescribe antibiotics for upper respiratory infections, despite most being viral in origin. Overuse of antibiotics has contributed to antibiotic resistance, prompting guidelines to recommend against routine antibiotic use for these conditions.^[2-3]

These examples highlight the importance of evidence-based medicine in shaping public health policies and clinical guidelines.

HelpfulNot Helpful

References

Should we all take medical supplements? MYTH!

As we discussed in the past, almost 60% of Americans consumes vitamins, minerals, botanicals, live microorganisms, probiotics and dietary supplements (spending about 55 billion in 2020) to prevent or treat various (mostly) imaginary ailments and “conditions” (infections of all sorts, memory loss, lack of energy, heart disease, aging, degenerative bone disease, etc.) you may want to read the Dietary Supplement Listing Act of 2022 and will realize why it’s always best to “keep it simple” and if not proven, do not use them.

The [FDA reports](#) that there are more than 95,000 supplements on the market today and the vast majority have not been tested for safety or effectiveness.

What are the exceptions where supplements may be beneficial?

1. Laboratory testing has demonstrated a deficiency of specific vitamins or minerals (Only to be tested in particular situations).
2. Vegan individuals are frequently deficient in Vitamin B12, as animal sources are rich in B12. Also, patients who had a gastric or terminal ileal resection.
3. Individuals with Inflammatory Bowel Disease (UC or CD) or GI conditions with associated malabsorption syndromes may need fat-soluble vitamins (A-D-E-K).
4. All Cystic Fibrosis patients.
5. Most patients with prior Bariatric Surgery.
6. Pregnant women need to add Folic Acid and Prenatal Vitamins with iron.
7. [Multivitamins](#) might slow cognitive decline, but more research is necessary.
8. [AREDS](#) supplements (Vitamins C, E, Copper, Lutein and Zeaxanthin) may slow vision loss in those with age-related macular degeneration.

There is no MAGIC PILL and NO SUBSTITUTE FOR EXERCISE and a HEALTHY PROTEINACEOUS DIET!

If you have 10 minutes, enjoy this [time-lapse of the Entire Universe](#).

If you have 6 more minutes, the [massive expanse of our Universe](#) and the magnificent insignificance of humanity will delight you.

As you look up at the sky in awe to observe our Solar Eclipse of the decade, remember that Thales of Miletus' eclipse prediction in the spring of 585 BC arguably launched science and doomed superstition.

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Embrace fitness! Exercise is candy to our muscles and they need daily intermittent activity to remain metabolically healthy!

Remember that every woman benefits from Pelvic Floor exercises and should be part of their routine.

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It lowers your BP, stress and raises pain threshold and well-being.

RESOURCES ON THE WEB.

You know that the only certainty in life, is death and the only fountains of youth proven by science and experience are love, exercise, laughter, humor and a positive attitude!

35 SIMPLE HEALTH TIPS

OFFICE UPDATES

As you know, we have opened our Premier Medicine – Concierge Internal Medicine and Consultative Pulmonary Medicine practice and moved to our office at the Barlow Building, 5454 Wisconsin Ave, Suite 1710 on April 11th.

Ashley Alvarez is our secretary and front desk supervisor, ready to assist with your scheduling needs at aalvarez@premier-medicine.com or by calling our office at 301-637-5555.

Brenda Perez is our office manager who can troubleshoot any insurance problems or office matters at bperez@premier-medicine.com

Emily Swearingen (Emily.swearingen@premier-medicine.com) is one of our Medical Assistants always and our Respiratory Technician, always willing to help in between her marathon running, as she works towards Medical School acceptance in 2026.

Olivia Dragovits (odragovits@premier-medicine.com) is one of our Medical Assistants and in charge of SMD / Signature MD matters, always ready to help as well, as she works towards her Medical School acceptance in 2026.

Irene Rieder is our wonderful new Nurse Practitioner – joined us on Feb 1st and an integral part of the practice already!

Some of our former assistants, whom you know, continue to make progress towards their medical degrees. Patty Zhao graduated from UVa in 2024. Emily Ferguson is graduating next week from Jefferson University in PA and getting married!

Simran Singh is now in her third year medical school at the University of Buffalo.

Samantha Morales is married and now a third-year student at the University of South Carolina School of Medicine.

Andrew Fookes at Georgetown University is advancing to his third year as well!