Az egészséges öregedés táplálkozástudományi vonatkozásai

Dr. Péter Szabolcs MD, PhD
vezető orvosigazgató
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My way

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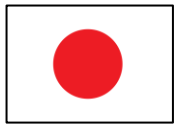

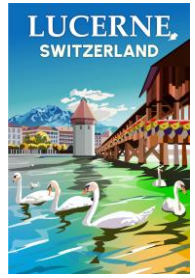

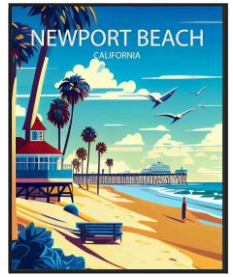

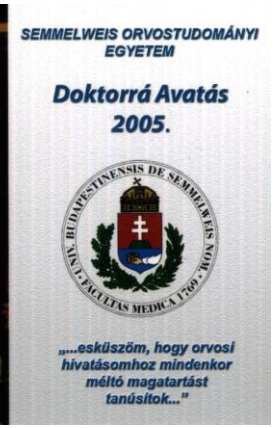

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Proud of our history

DSM established as Dutch State Mines

1902

Commercial production baker yeast

1869

Development, production and sales of penicillin

1946

First naphtha cracker

1963

Last coal mine closes

1974

DSM listed on stock exchange

1989

Acquisition of Gist-Brocades; growth of fine-chemicals business accelerates

1998

Acquisition of Roche Vitamins and Fine Chemical Division; life-sciences portfolio doubles

2003

EU approval for Bovaer®

DSM Protective Materials transferred

Sale of Engineering Materials announced

2022

2023

dsm-firmenich is born!

1895

Philippe Chuit and Martin Naef start perfumery business in Geneva

1934

Becomes Firmenich & Cie

1939

Leopold Ružička jointly awarded Nobel Prize in chemistry

1962–1980

Global expansion accelerates in Europe, Asia, and Latin America

1988

New corporate headquarters in Geneva

2007

First sustainability report

2020

100% renewable electricity worldwide

DRT acquisition

World's first AI-created flavor & laundry care fragrance

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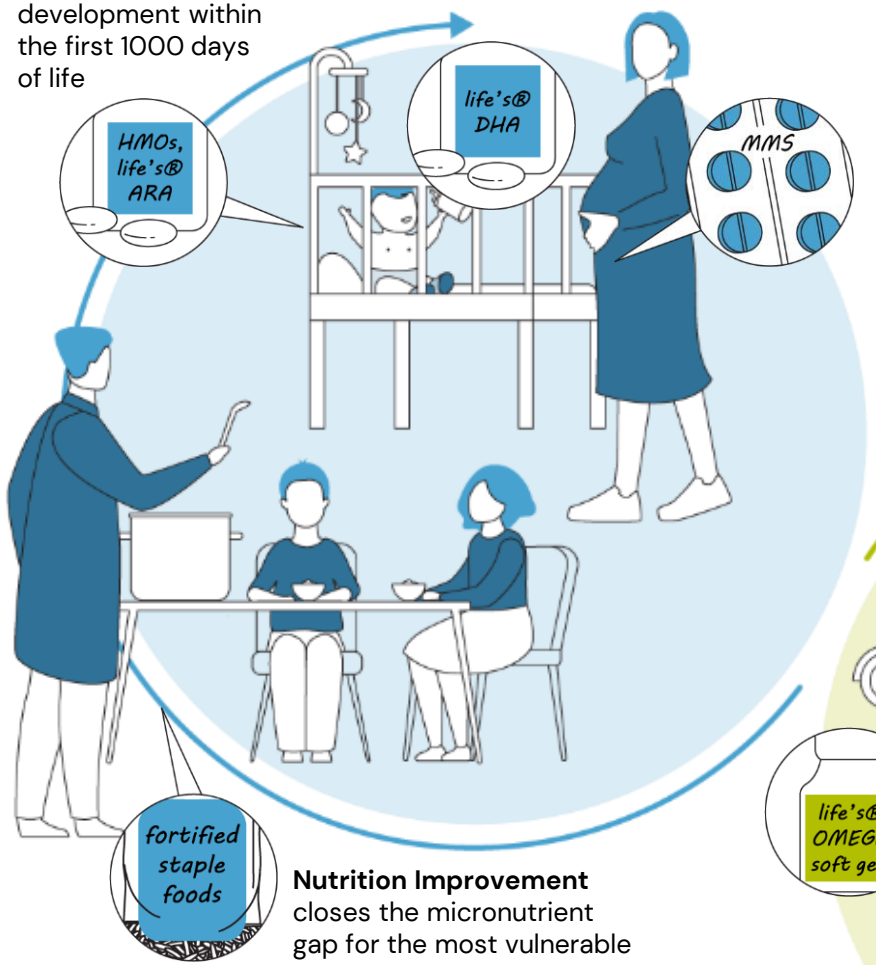
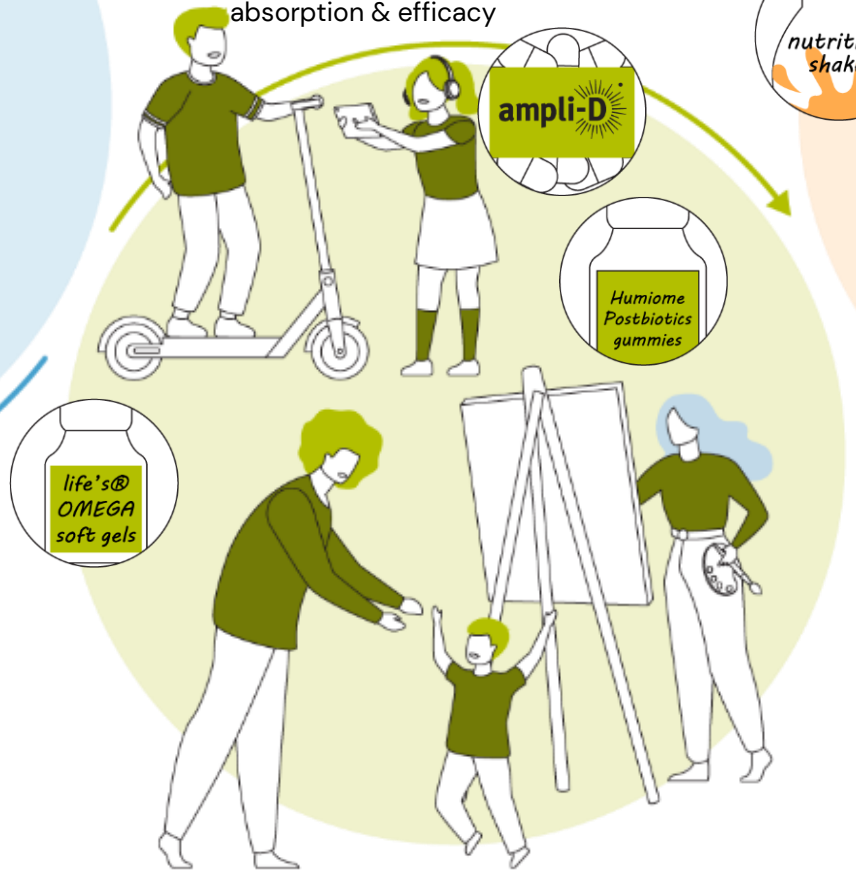
In dsm-firmenich, we keep the world's growing population healthy

Early Life Nutrition supports optimal development within the first 1000 days of life

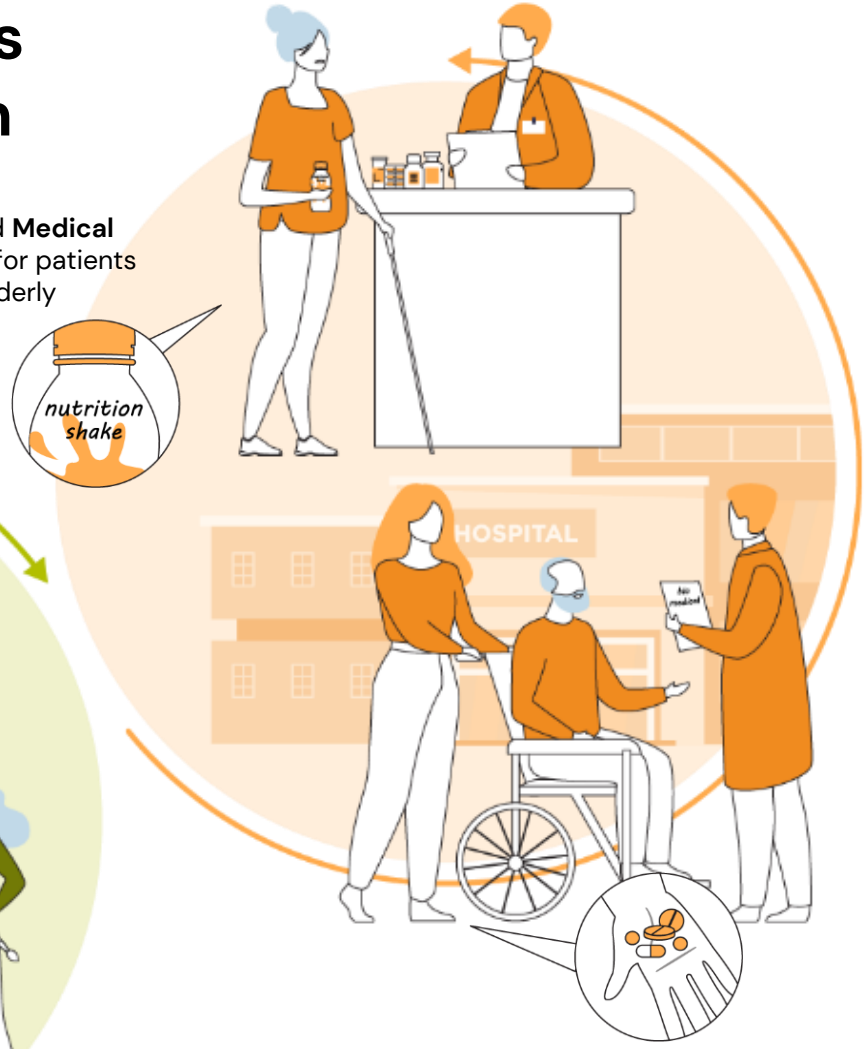


Nutrition Improvement closes the micronutrient gap for the most vulnerable

Attractive innovations & formats in **Dietary Supplements** to enhance absorption & efficacy



Insight-led **Medical Nutrition** for patients and the elderly



Pharma co-creates purposeful and safe therapeutics

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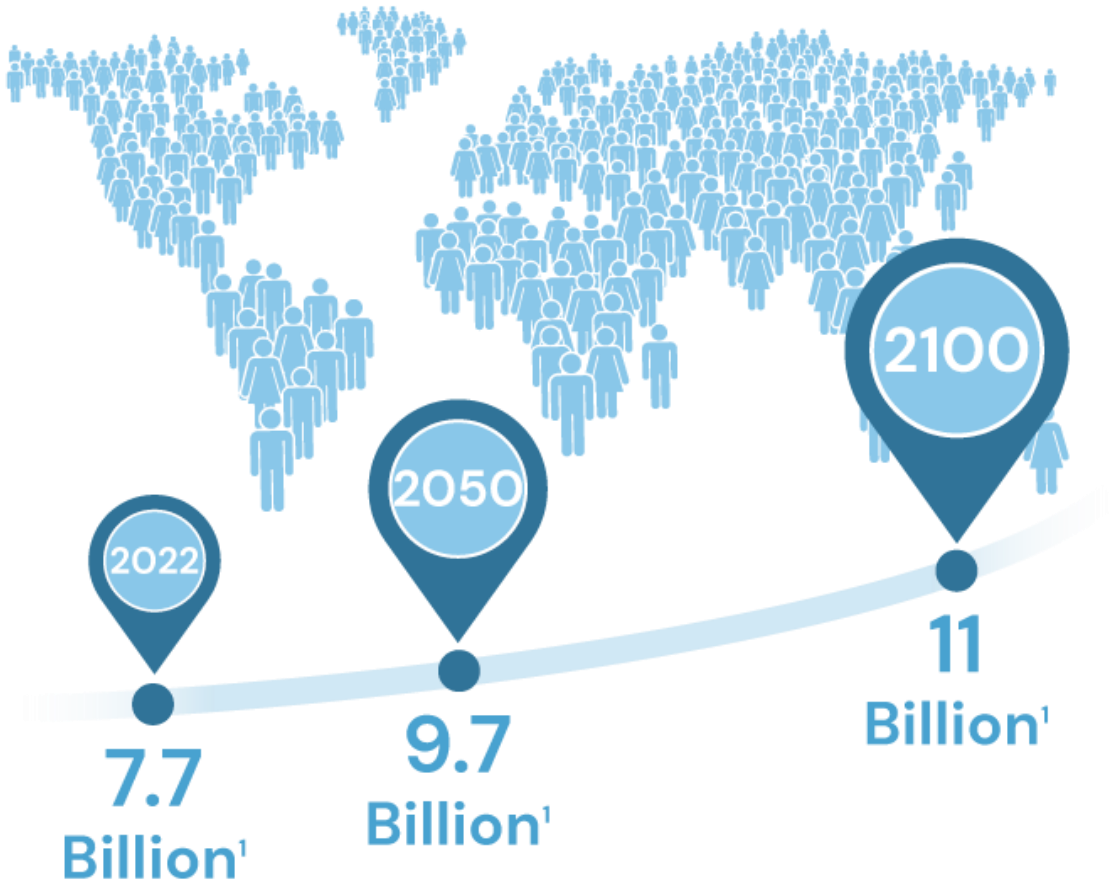
The world's population is growing and ageing

The world's population[1]...



By 2050[4]...

140 million births per year[2]

1 in 10 babies is born prematurely[3]

1 in 6 AGED 65+

AGED 80+ **1 in 20** (2022: 1 in 60)

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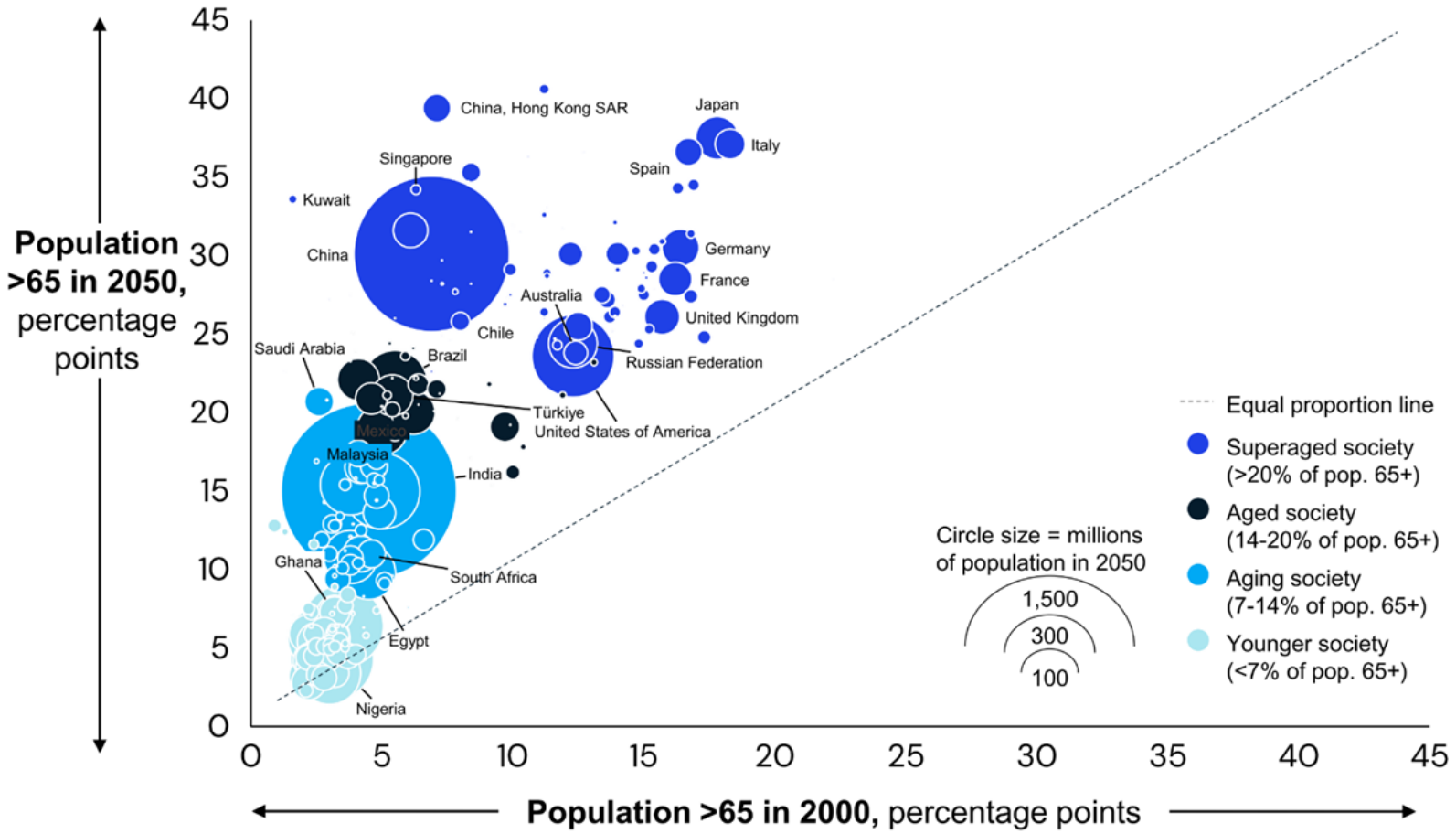
By 2050, the absolute number of adults 65+ will reach 1.6bn or roughly 16.5% of the global population



In the vast majority of countries, the **share of population >65 is expected to grow significantly** to 2050

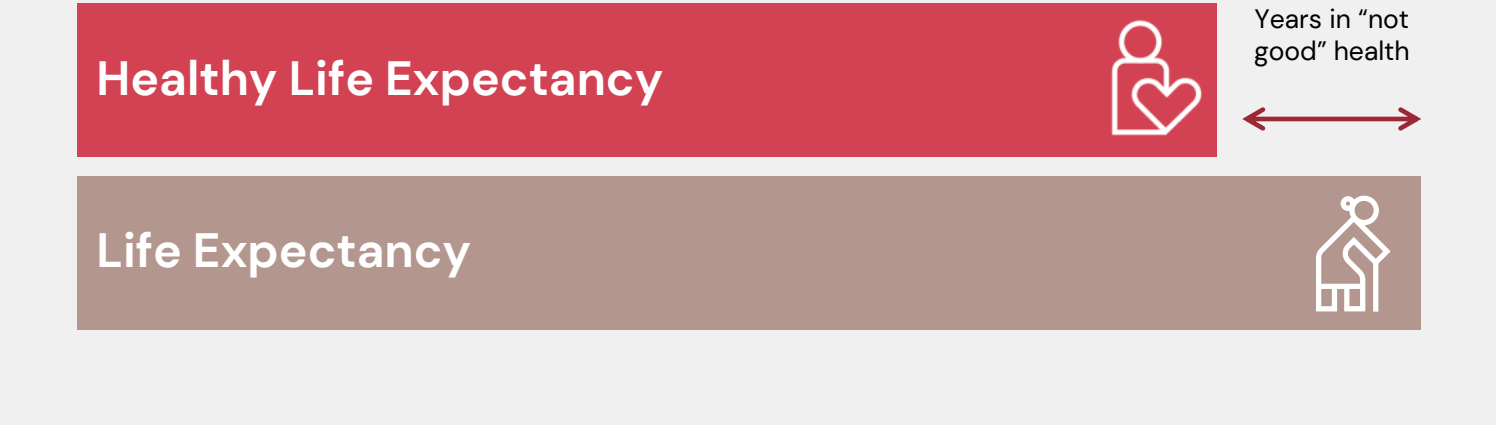
While this growth in life expectancy is no doubt cause for celebration, our society will require **fundamental rethinks across our social, economic, and healthcare systems** as the aging population increases demand for resources

World population prospects 2022, United Nations

As life expectancy increases, a significant 10-year gap between lifespan and health span highlights the need to focus on improving health expectancy

10

One of humanity's greatest achievements is the dramatic increase in life expectancy. However, living longer often comes with age-related challenges—metabolic issues, heart conditions, and decreased mobility. Currently, **there is a gap of roughly 10 years between how long we live and how long we stay healthy.**



Our goal is to close this gap, extending our healthy years so we can continue doing what we love—staying active, fulfilled, and deeply connected with the people who matter most.

Garmany, A. and A. Terzic (2024). "Global Healthspan-Lifespan Gaps Among 183 World Health Organization Member States." JAMA Netw Open 7(12)

What is healthy ageing?

WHO defines healthy ageing as “the process of developing and maintaining the functional ability that **enables wellbeing in older age**.”

Functional ability is about having the capabilities that enable all people to be and do what they have reason to value. This includes a person’s ability to:

- meet their basic needs;
- learn, grow and make decisions;
- be mobile;
- build and maintain relationships; and
- contribute to society

https://www.who.int/news-room/fact-sheets/detail/ageing-and-health

Advancements in aging science are transforming how we think about longevity, shifting the focus from treating symptoms to addressing root causes

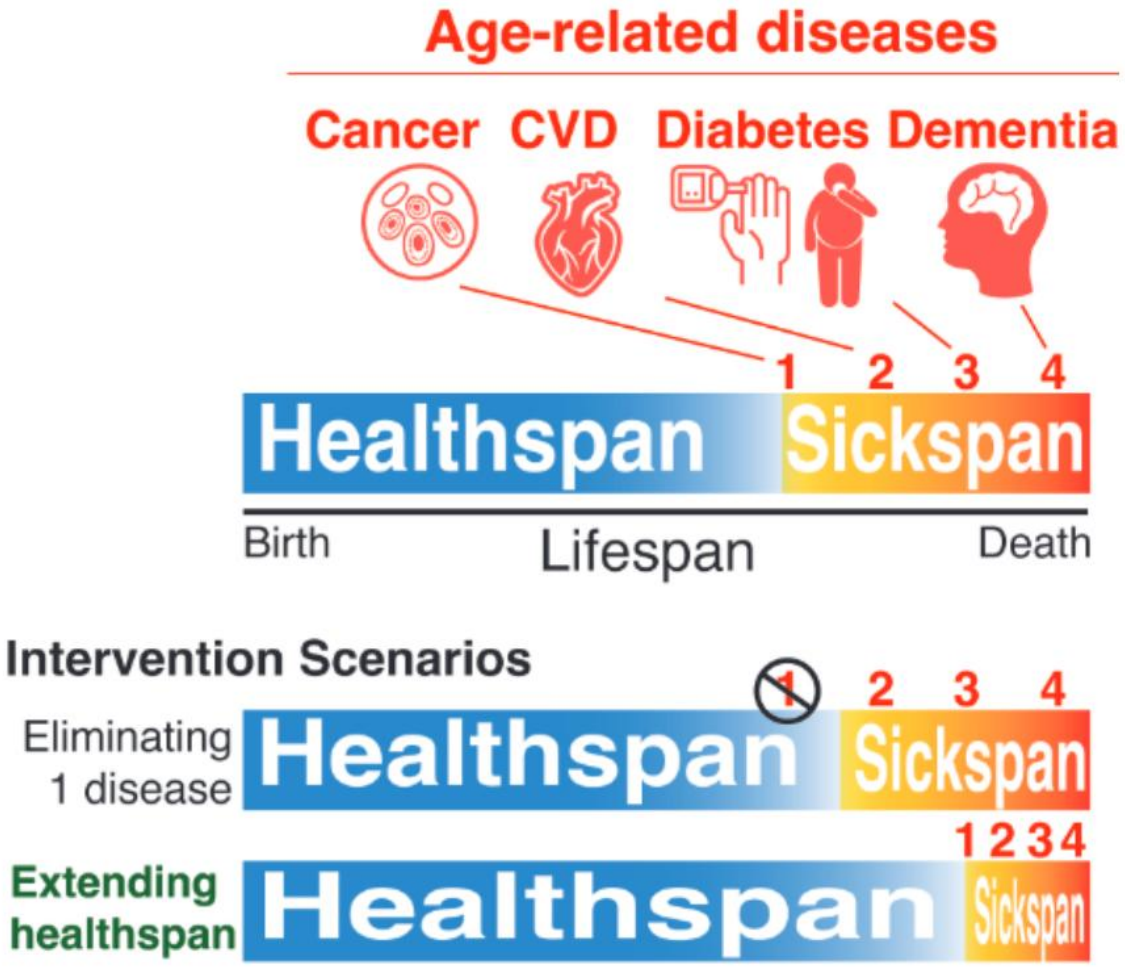
- **A Disruptive Approach**: Theories like the geroscience hypothesis are challenging traditional approaches. Instead of treating individual age-related issues such as heart disease, Alzheimer's, or cancer separately, the focus shifts to addressing the **core mechanisms of aging** itself.

- **A Holistic Focus:** Aging is the single biggest risk factor for many chronic conditions. By targeting fundamental biological processes—like cellular senescence, inflammation, and mitochondrial dysfunction—we aim to **address the root cause**, rather than managing each condition in isolation.

- **Measuring the Aging Process**: Emerging tools like the "biological clocks" are now enabling us to measure the aging process more accurately. Although their reliability remains debated, these tools are improving, offering potential for precise interventions in the future.

Kennedy, B. K., et al. (2014). "Geroscience: Linking Aging to Chronic Disease." Cell 159(4): 709-713.
Partridge, L. (2014). "Intervening in ageing to prevent the diseases of ageing." Trends in Endocrinology & Metabolism 25(11): 555-557.5
Lu, A. T., et al. (2019). "DNA methylation GrimAge strongly predicts lifespan and healthspan." Aging (Albany NY) 11(2): 303-327
Moqri, M., et al. (2023). "Biomarkers of aging for the identification and evaluation of longevity interventions." Cell 186(18): 3758-3775

Geroscience hypothesis
Treat ageing biology rather than individual age-related diseases



Ruckstuhl, M. M., et al. (2023). Swiss Med Wkly

The aging process: From cellular damage to functional decline
A framework for interventions

Biological Aging *(root mechanisms)*

- Molecular damage
- Defective repair
- Energy exhaustion
- Signal/noise reduction

Phenotypic Aging *(phenotypes that change)*

- Body Composition
- Energetics
- Homeostatic Mechanisms
- Brain health

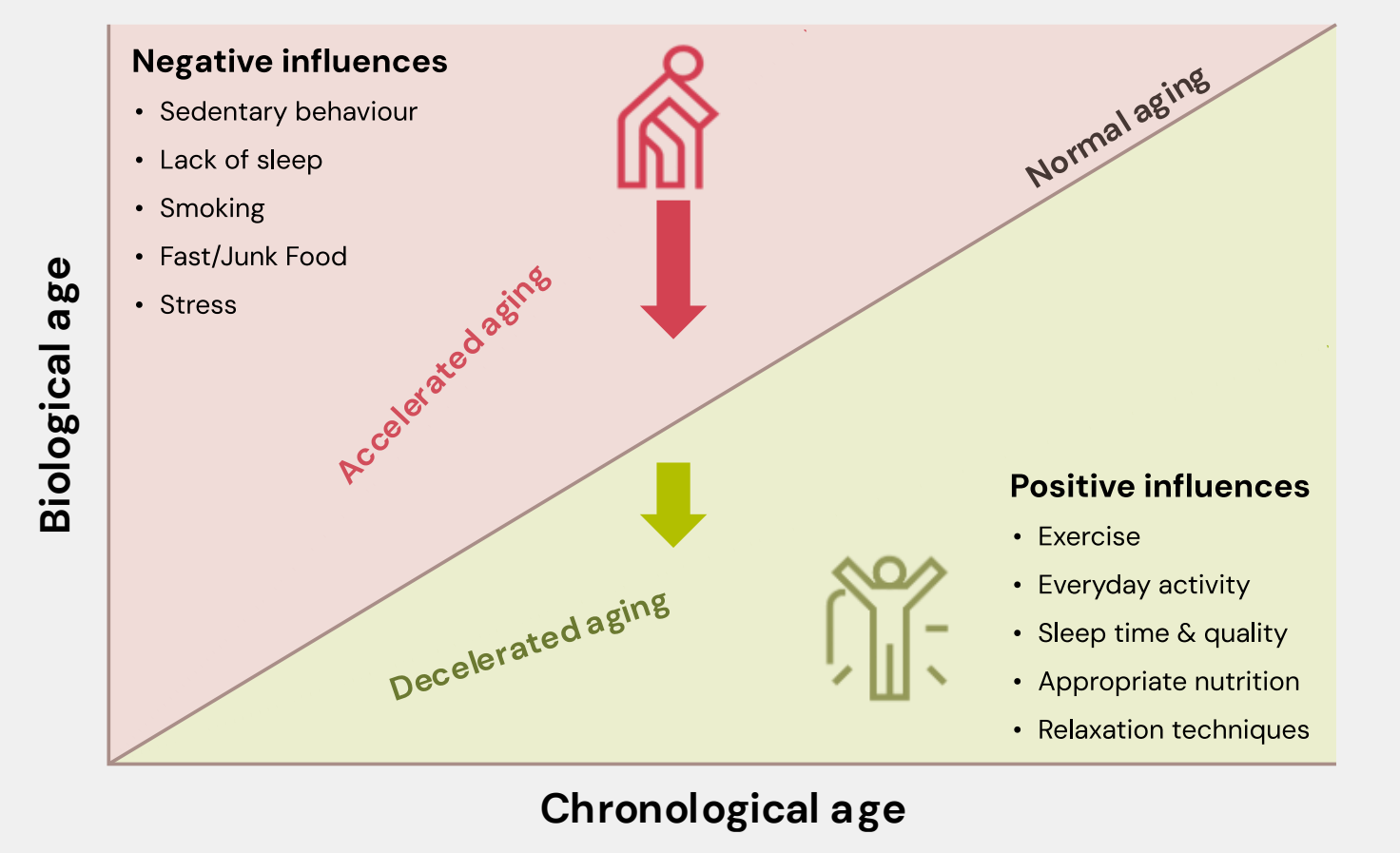
Functional Aging *(impact on daily life)*

- Cognitive Function
- Physical Function
- Mood
- Mental Health

- Aging unfolds in three stages: biological → phenotypic → functional.
- Functional decline (e.g., mobility loss, cognitive impairment) is the final stage and often occurs only after biological and phenotypic buffers are exhausted
- **Early interventions can target biological and phenotypic aging to prevent functional loss**

Modified from Ferrucci et al. Time and the Metrics of Aging. Circ Res. 2018 Sep 14;123(7):740-744.

Insights from biological age measurements
Evaluating the impact of healthy aging interventions



- Chronological and biological age don't always match. Chronological age is the number of years you've lived, while biological age shows how your body is aging.
- Biological age refers to the physiological age of a person, which can be modified with lifestyle interventions.
- Factors like nutrition, environment, and lifestyle—exercise, for example—can either speed up or slow down biological aging, helping us stay healthier as we age.
- Biological age is a strong predictor of health, disease and all-cause mortality.
- In places called "Blue Zones," people tend to live longer, healthier lives. These regions follow nutrient-rich diets, like the Mediterranean diet, known for promoting health and longevity.

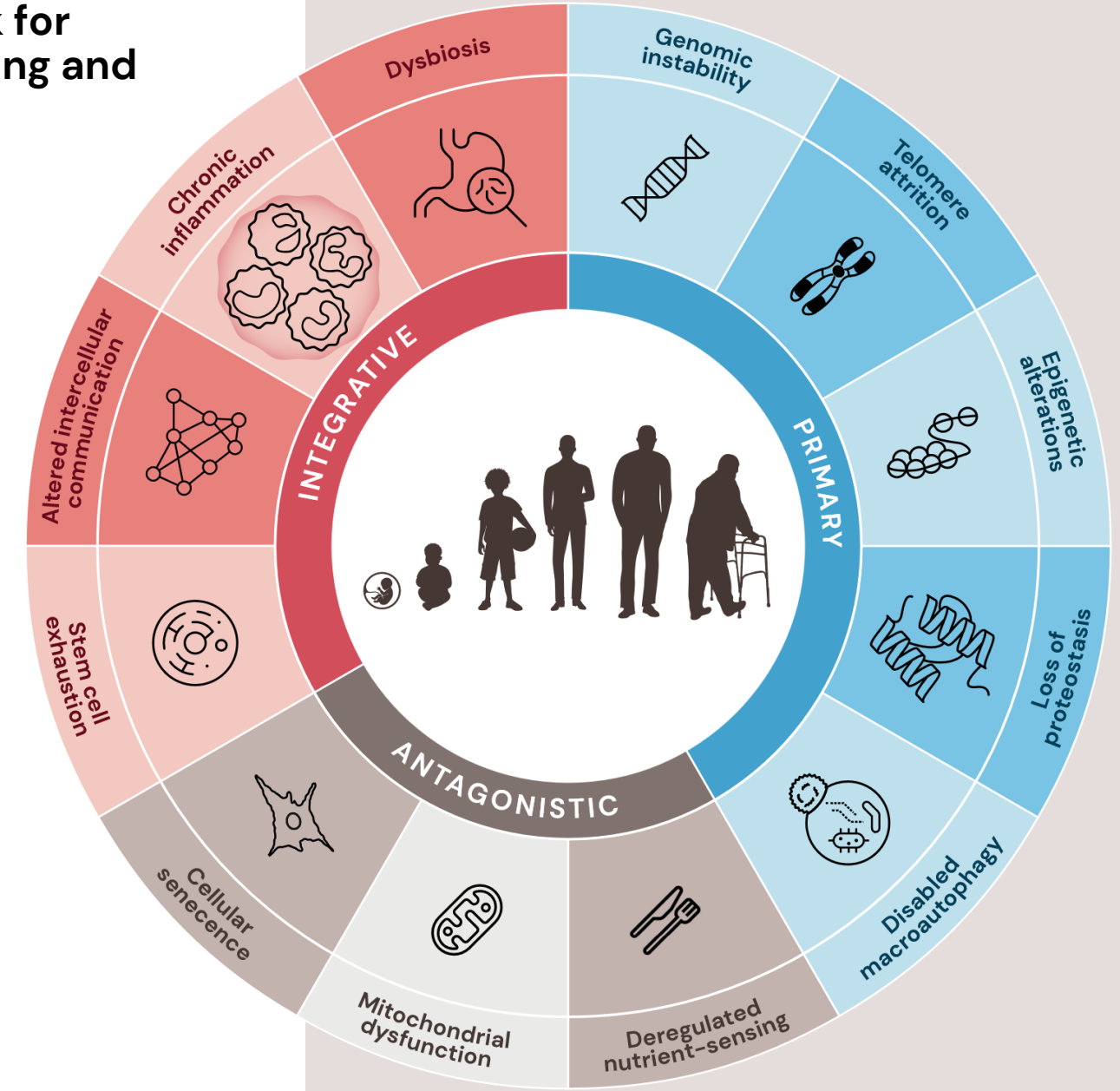
Measuring biological age through advanced biomarkers like **aging clocks** provides a groundbreaking opportunity to accurately assess the effectiveness of interventions aimed at extending health span

Haupt, S., et al. (2022). "The Impact of Exercise on Telomere Length, DNA Methylation and Metabolic Footprints." Cells 11(1): 153

The hallmarks of aging offer a scientific framework for understanding the biological processes driving aging and identifying points for intervention

- The process of aging is complex, but researchers have simplified it by identifying key mechanisms, known as **hallmarks of aging, that contribute to it.**
- This framework helps us **understand aging** and guides potential **interventions**.
- The hallmarks categorize aging mechanisms into three groups: primary (causes of damage), antagonistic (responses to damage), and integrative (systems that coordinate cellular responses), highlighting their **interconnections and complexity**, but in a simple way.

- **Opportunity to decelerate, or reverse ageing with targeted interventions on the hallmarks**



López-Otín, C., et al. (2023). "Hallmarks of aging: An expanding universe." Cell 186(2): 243-278.

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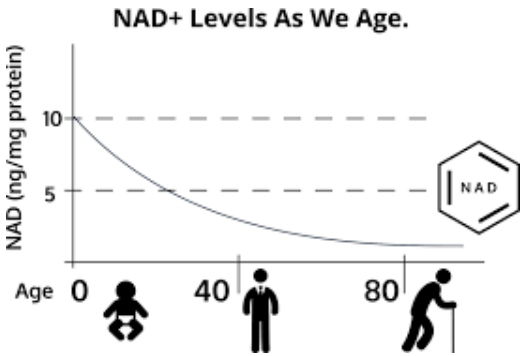
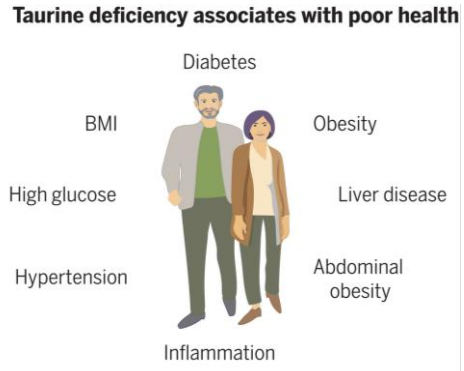
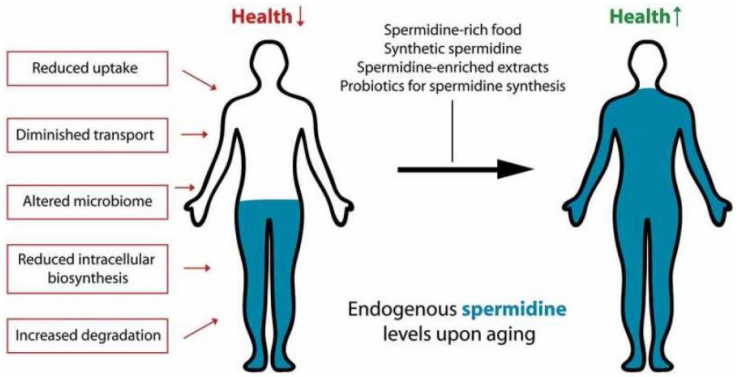
Nutrient deficiencies exacerbates hallmarks of ageing
Cellular nutrition for age-associated cellular decline



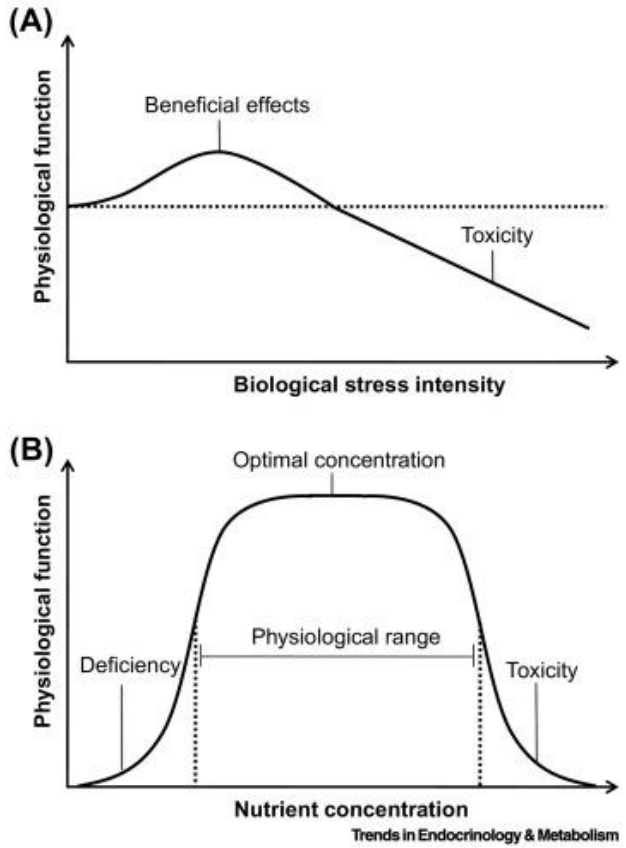




Triage theory: nutrients shortage triggers a built-in rationing mechanism that favors the function of enzymes needed for immediate survival and reproduction (survival enzymes) while sacrificing those needed to protect against future damage for long term health (longevity enzymes).

Massudi, H., et al. (2012 PLoS One
Singh, P., et al. (2023).Science
Madeo, F., et al. (2019). Autophagy

Increasing organism ability to respond to stress via hormesis

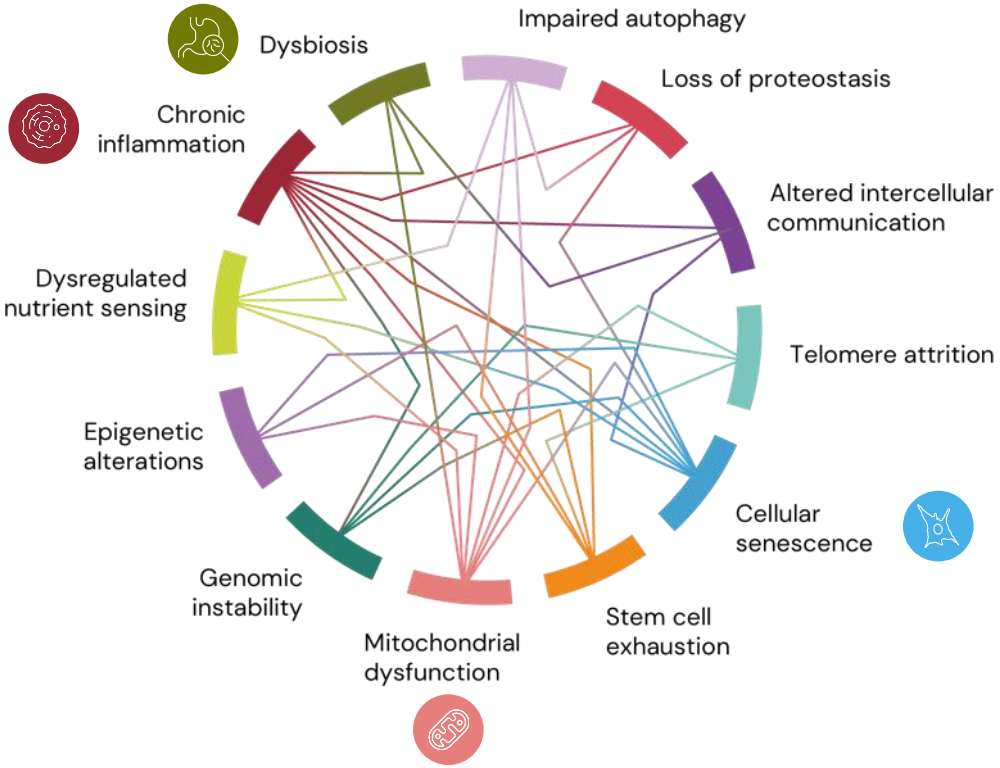


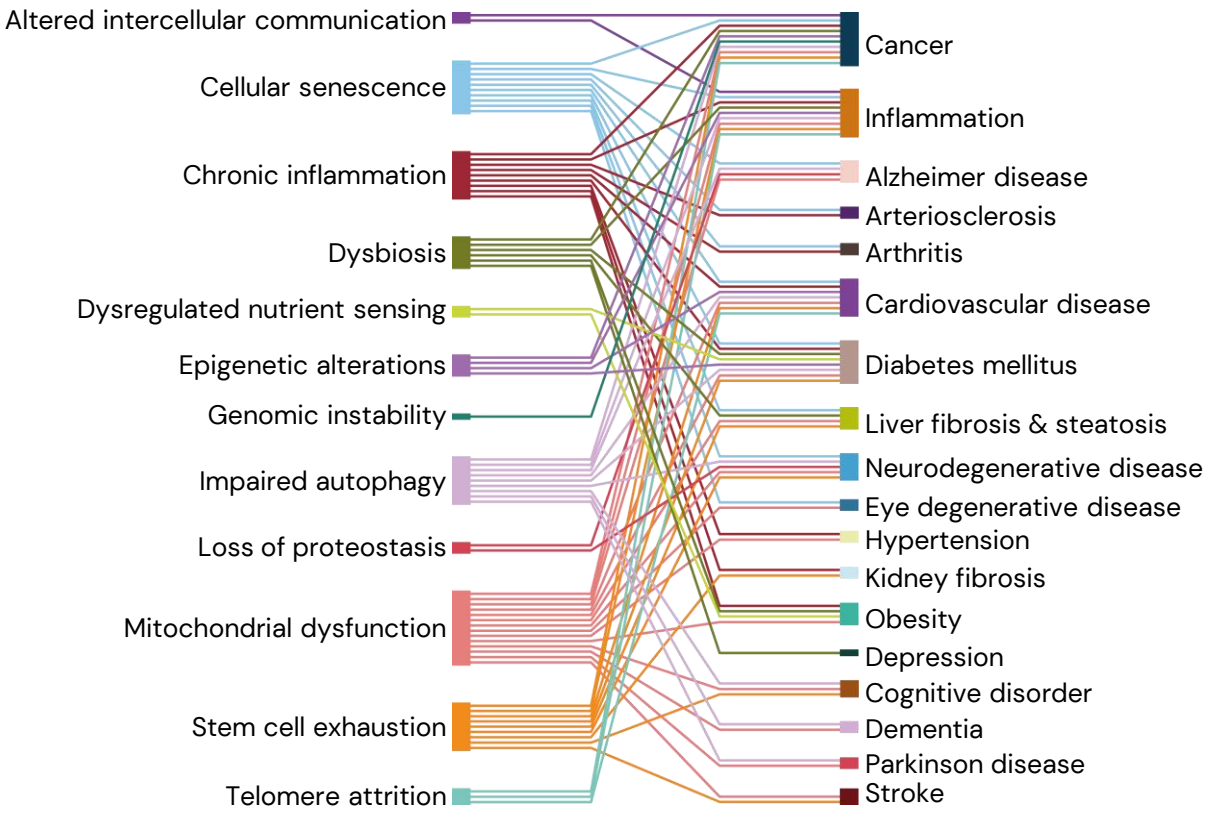
Hormesis: Biological stress may be beneficial at low intensity through activation of stress respone processes that aim to maintain homeostasis. The production of endogenous antioxidant enzymes by biological stress triggered by e.g. phytochemicals protects the organism from subsequent more intense oxidative stress.

Compound	Source	Mechanism	Major finding
Berberine	Chinese goldthread, dietary supplement	Autophagy↑	Lifespan↑ in flies; improvement of T2DM markers in humans
Curcumin	Turmeric spice, dietary supplement	Autophagy↑	Lifespan↑ in fruit flies (but failed to affect lifespan in mice); inflammation↓, hypertension↓ and ROS↓ in humans
Caffeine	Coffee	AMPK↑, mTOR↓, autophagy↑	Lifespan↑ in nematodes; CVD↓, cognitive impairment↓ and mortality↓ in humans
EGCG	Green tea, dietary supplement	SIRT1↑, FOXO↑, autophagy↑, Nrf2↑	Lifespan↑ in rats; cardiovascular disease↓, cancer↓, and neuroprotection↑ in humans
Emodin	Plants	Sir2.1↑, AMPK↑	Lifespan↑ in nematodes; insulin sensitivity↑ in mice
Fisetin	Fruits, vegetables	DAF-16/FOXO↑, ROS↓, CRP↓	Lifespan↑ in nematodes; inflammation↓ in humans
Glucosamine	Dietary supplement	AMPK↑, autophagy↑	Lifespan↑ in nematodes and mice; mortality↓ in humans
Polyphenols	Coffee	AMPK↑, mTOR↓, autophagy↑	CVD↓, cognitive impairment↓, and mortality↓ in humans
Polysaccharides	*Ganoderma lucidum* and *Hirsutella sinensis*	Prebiotic, intestinal integrity↑	Obesity↓, inflammation↓, diabetes↓ in HFD-fed mice
Quercetin	Vegetables, dietary supplement	AMPK↑, autophagy↑, senescence↓	Lifespan↑ in mice; hypertension↓ in humans
Resveratrol	Red wine, dietary supplement	IGF-1↓, AMPK↑, PGC-1α↑, autophagy↑	Lifespan↑ in HFD-fed mice; improved markers for Alzheimer's disease, cancer, CVD, T2DM in humans
Spermidine	Soybeans, natto, fungi	Autophagy↑	Lifespan↑ in mice; mortality↓ in humans
Sulforaphane	Broccoli, Brussels sprouts	Nrf2↑, antioxidant enzymes↑	Neuroprotection↑ in rats

Martel, J., et al. (2019) Trends Endocrinol Metab **30**(6): 335-346.

Decoding the interconnected mechanisms of aging, we can develop holistic strategies to slow its progression and improve health expectancy





The interconnected nature of these hallmarks means that a decline in one area can adversely affect others.

Understanding these relationships is crucial for developing strategies to promote healthy aging and mitigate the impact of age-related conditions.

Tenchov, R., et al. (2024). "Polyglutamine (PolyQ) Diseases: Navigating the Landscape of Neurodegeneration." ACS Chem Neurosci 15(15): 2665-2694.

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By narrowing our focus to four critical hallmarks, we can deliver solutions that provide measurable benefits and address the evolving needs of consumers across demographics

At dsm-firmenich, we've identified four key hallmarks of aging—mitochondrial dysfunction, cellular senescence, chronic inflammation, and dysbiosis—that present opportunities for nutritional interventions to enhance Health Expectancy.

Cellular Senescence

One aspect of cellular senescence is the presence of "zombie cells." These are cells that stop dividing but persist in the body.

They release harmful substances that damage surrounding cells.

Dysbiosis

An imbalance or disruption in the gut microbiota, the community of microorganisms in our digestive system, can affect digestion, immune function, and overall health.

As we age, this imbalance becomes more common.

Mitochondrial Dysfunction

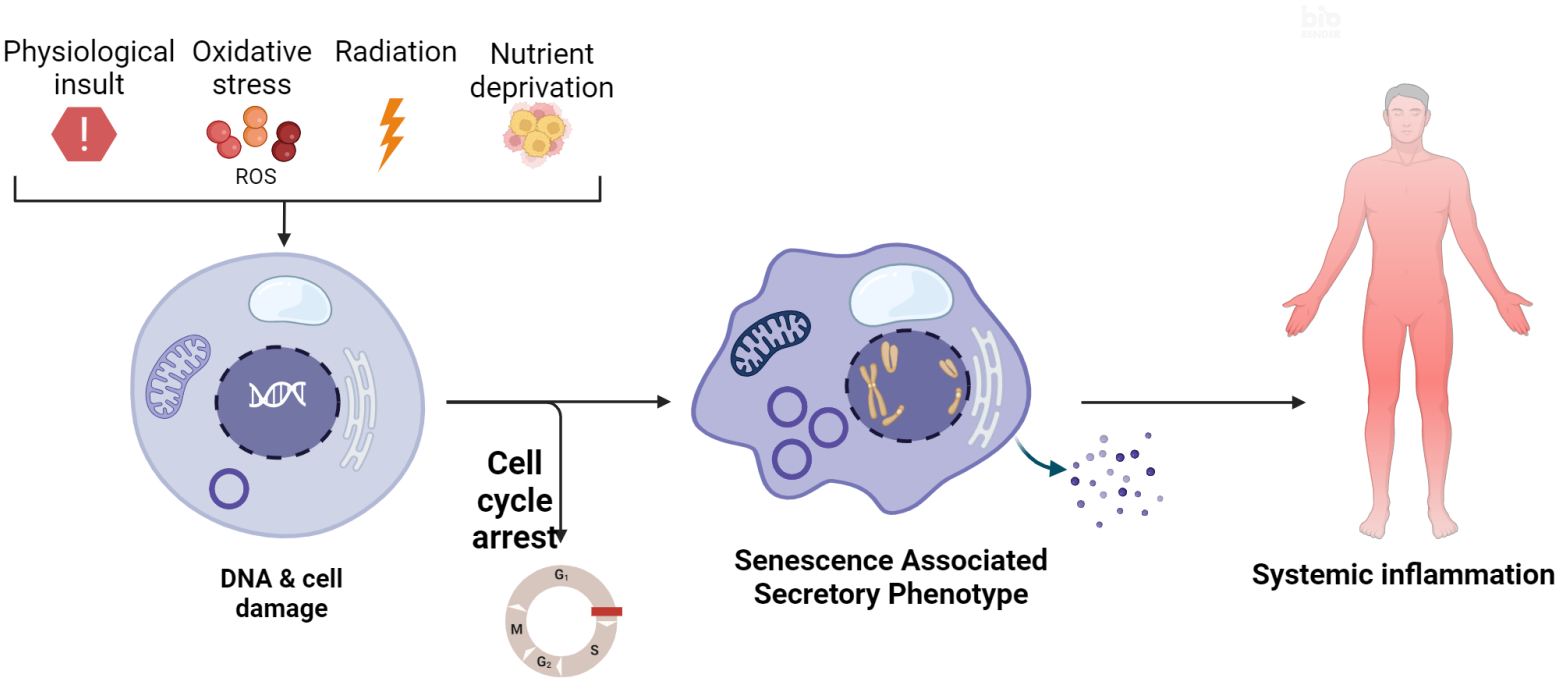
Mitochondria, the powerhouses of our cells, generate the energy required for essential functions.

As we age, their energy production declines, and their ability to manage oxidative stress weakens, leading to reduced cellular function.

Chronic Inflammation

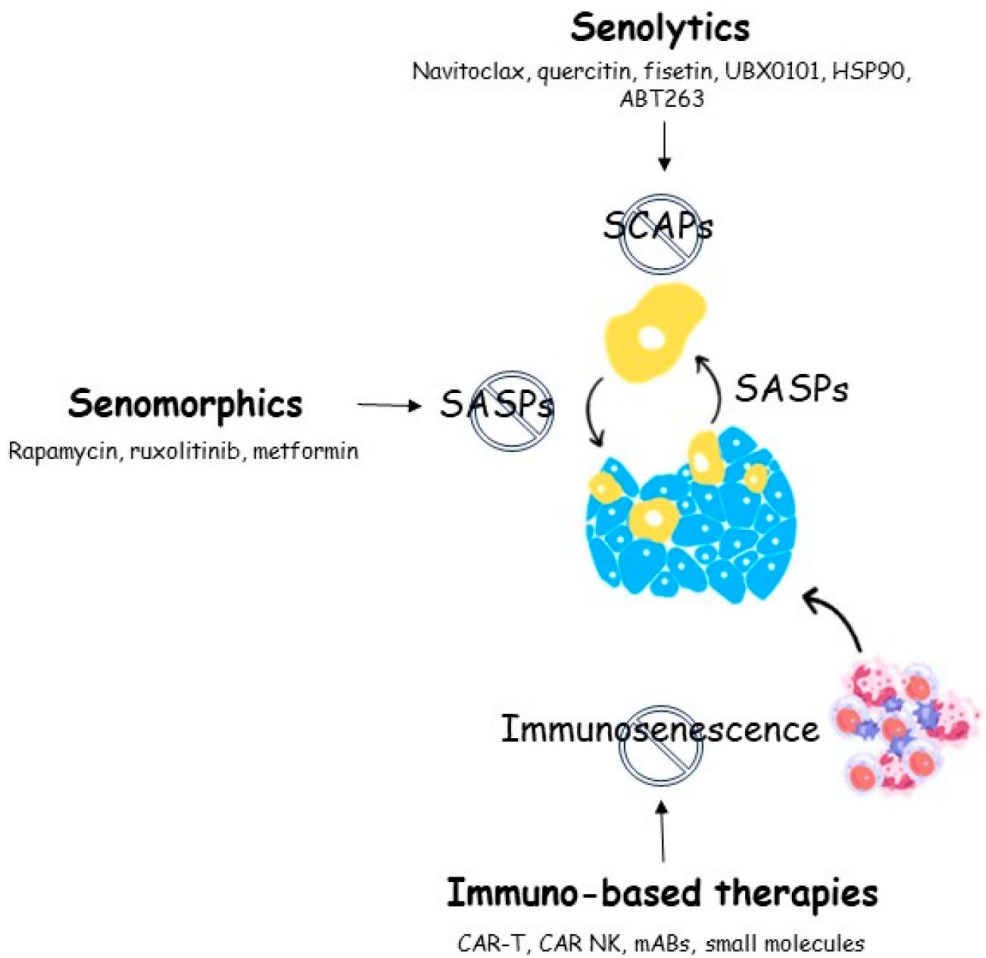
Elevated persistent low-level inflammation which triggers an exaggerated inflammatory response, resulting in cumulative damage to tissues and organs.

Senescent cells accumulate with age and drive ageing



- With ageing some cells lose the ability to divide and grow entering a state of cell cycle arrest called **senescence**
- Senescent cells release factors that contribute to increased **inflammation** and diseases
- **Senolytics** eliminate senescent cells, promoting tissue regeneration

Senescent cells can be removed with nutritional interventions



Nutritional Senotherapeutic	Effects
	Senomorphics
Resveratrol	Inhibits NF-κB and activates Nrf-2; increases OXPHOS and SIRT1 activation; acts on FOXO and IGF pathway
Genistein	Regulation of FOXO3
Isoflavone	Modulation of apoptosis pathways
Kaempferol	Acts on inhibition of NF-κB through IRAK1/IKB-α
Apigenin	Acts on inhibition of NF-κB through IL-1rα modulation acting on IRAK1/p38MAPK
EGCG	Inhibition of AMPK activation through the modulation of AKT/PI3k/mTOR signalling pathway. Inhibition of ROS, SASPs, NF-κB, and COX
Fisetin	Antioxidant and anti-inflammatory action through modulation of NF-κB and Nrf-2
Curcumin	Anti-inflammatory activity on NF-κB and antioxidative effects on Nrf-2.
Piperlongumine	Antioxidant activity inhibiting ROS production

Calabro, A., et al. (2024). Int J Mol Sci **25**(3)

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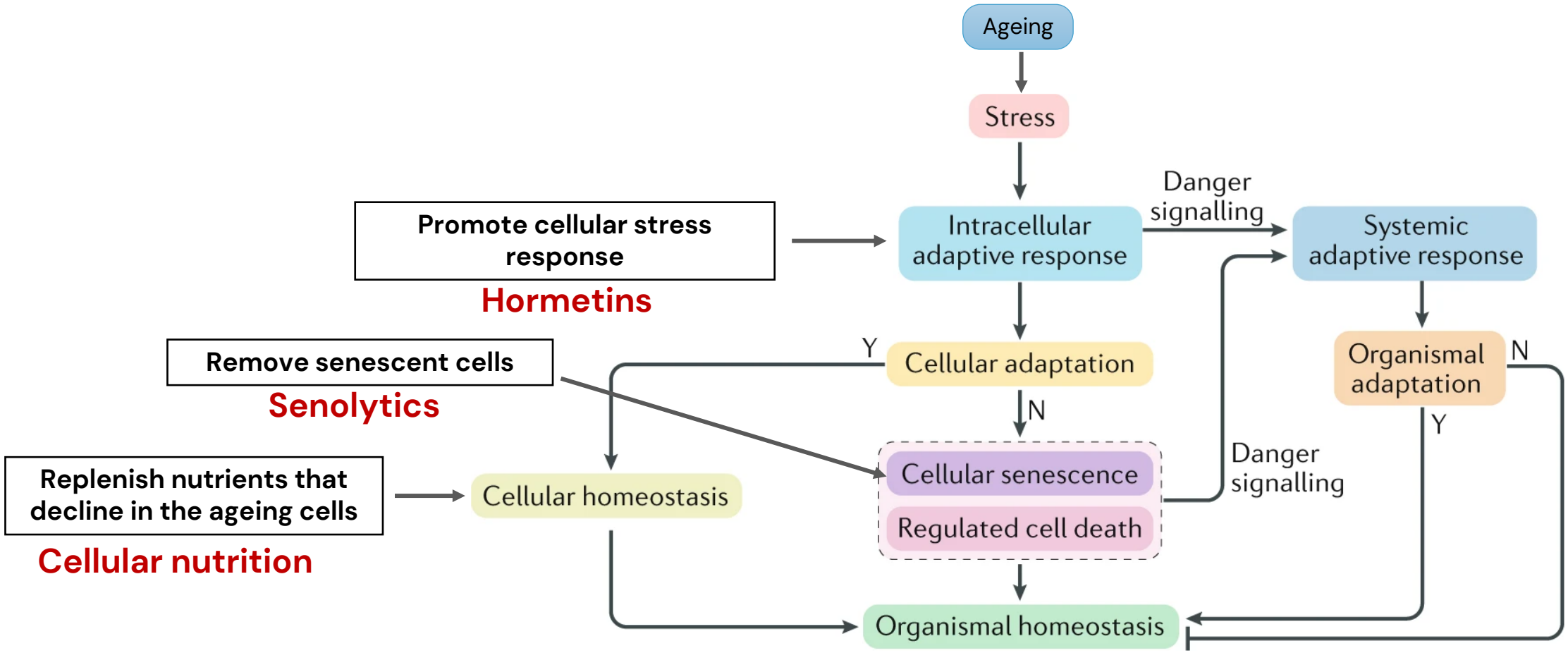
Nutritional strategies to support cellular health



Modified from: Galluzzi, L., et al. (2018). Nat Rev Mol Cell Biol

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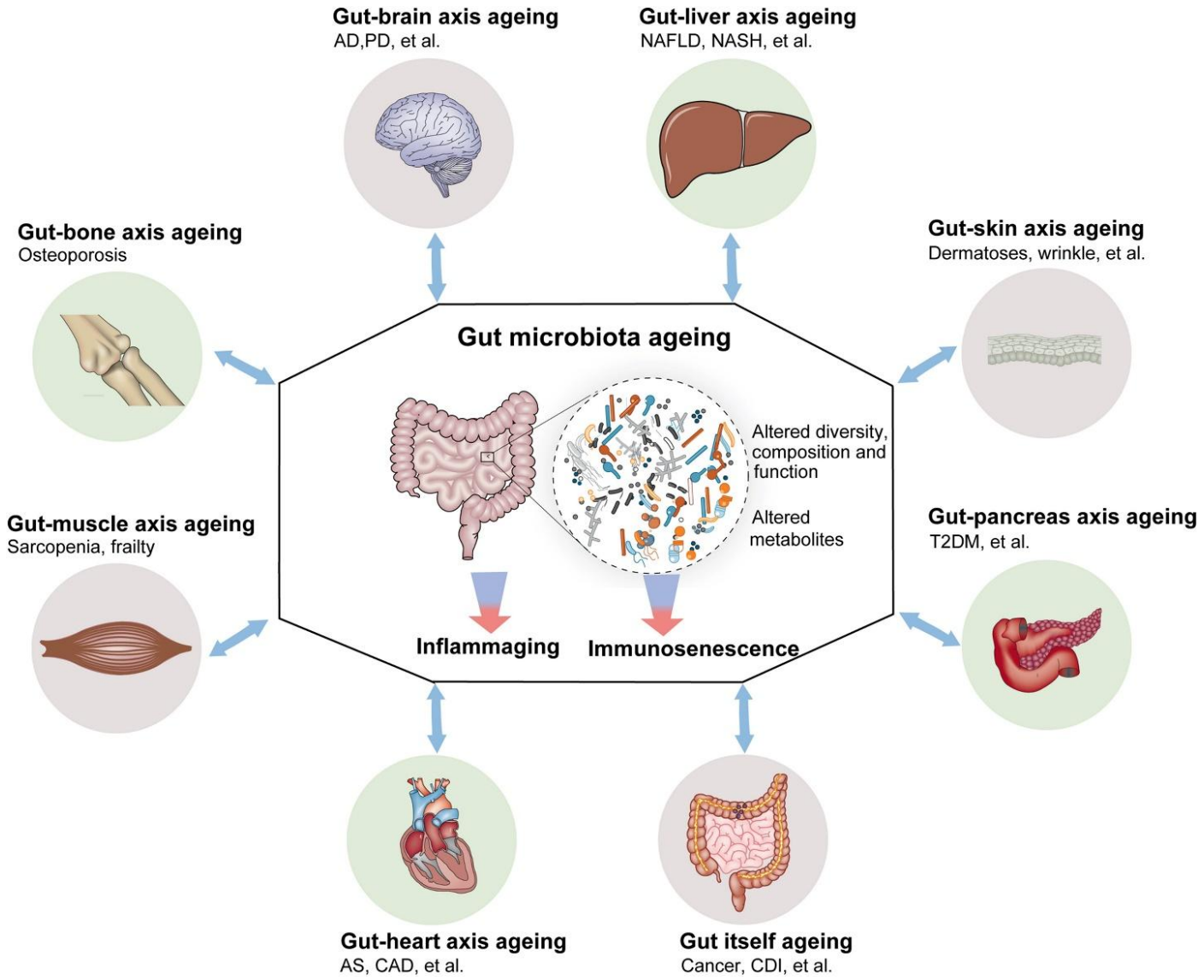
Microbiome in ageing



Ghosh, T. S., et al. (2022). Nature Reviews Gastroenterology & Hepatology

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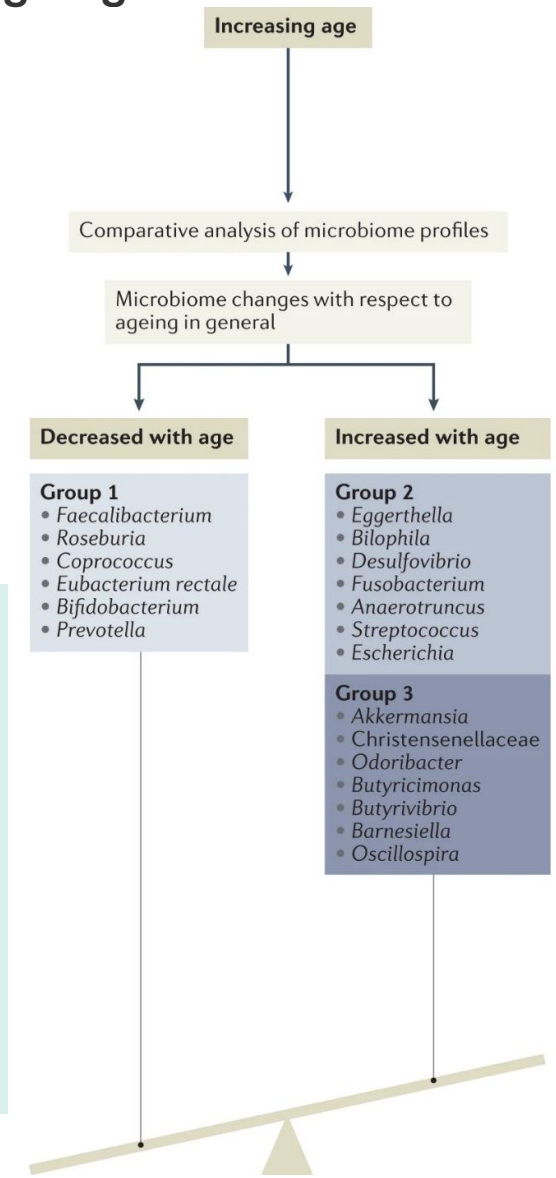
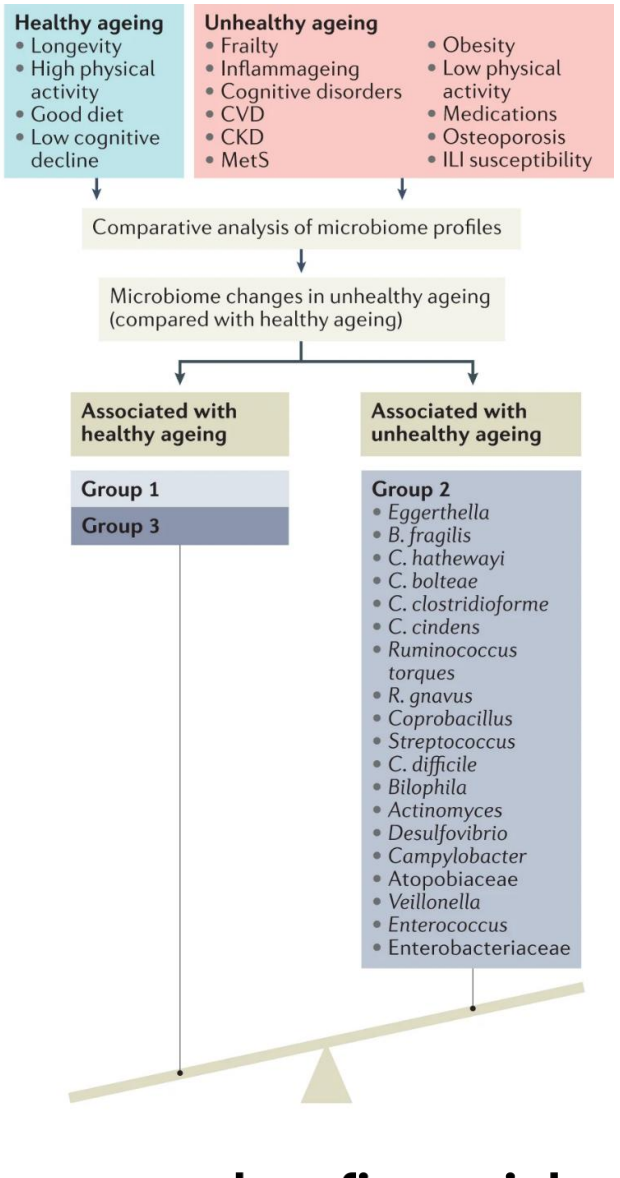
Gut Microbiome as a modulator of healthy ageing
Microbes associated with healthy and unhealthy ageing

- Some commensals decrease with age, specially during unhealthy ageing. (Group 1)
- Pathobionts increases with ageing, especially in unhealthy ageing (Group 2)
- Some taxonomic checkpoints become more abundant with age but are lost during unhealthy ageing (Group 3)

The gut microbiota of centenarians exhibits:

- higher microbial diversity
- higher abundance of some healthy bacterial species, such *Akkermansia*, *Lactobacillus* and many SCFA-producing bacteria
- *Lactobacillus* produces L- ascorbic acid and may thus control oxidative damage in centenarians





Ghosh, T. S., et al. (2022). Nature Reviews Gastroenterology & Hepatology

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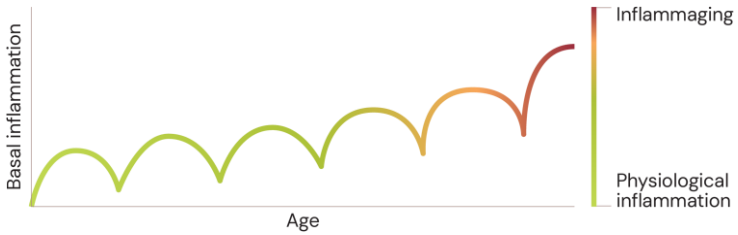
Defining inflammaging: the Silent Driver of Aging

While acute inflammation is a necessary and beneficial response to injury or infection, chronic inflammation can be detrimental, leading to various diseases

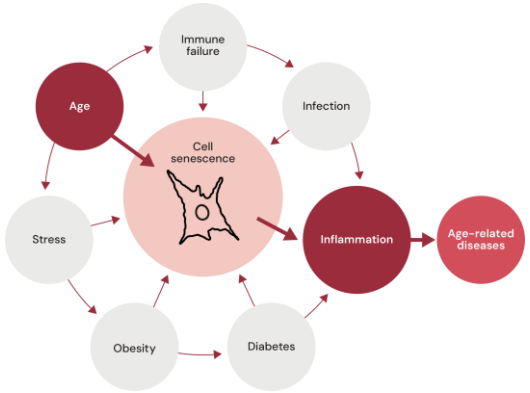
Not acute inflammation[1]

- **Duration and Resolution:** Acute inflammation is a short-term response that resolves quickly, whereas chronic inflammation is prolonged and can persist for months or years.
- **Outcomes:** Acute inflammation aims to restore tissue to its pre-injury state, whereas chronic inflammation often leads to tissue destruction and fibrosis.



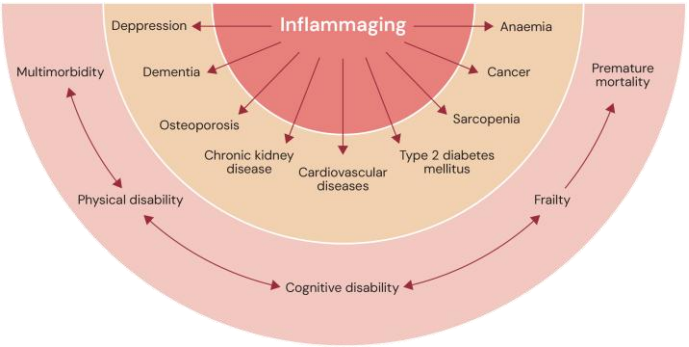
Underlying mechanisms[2]

- Associated with oxidative stress, cellular senescence and aging-related decline of immune function.
- Characterized by increased levels of pro-inflammatory cytokines in the bloodstream, such as IL-6, TNF-α, and CRP.



Health consequences[3]

- The pro-inflammatory environment is perpetuated as the body struggles to manage persistent infections and cellular damage.
- Contributing to the onset of various diseases, including cancer, metabolic and cardiovascular disorders.



Chronic inflammation arises when acute inflammation fails to resolve, often due to persistent infections, cellular damage or immune system dysregulation. Understanding these mechanisms is essential for developing effective interventions for healthy longevity

1. Franceschi C. Nat Rev Endocrinol. 2018 Oct;14(10):576-590.
2. Teissier T. et al. Cells. 2022 Jan 21;11(3):359.
3. Ferrucci L, Fabbri E. Nat Rev Cardiol. 2018 Sep;15(9):505-522.

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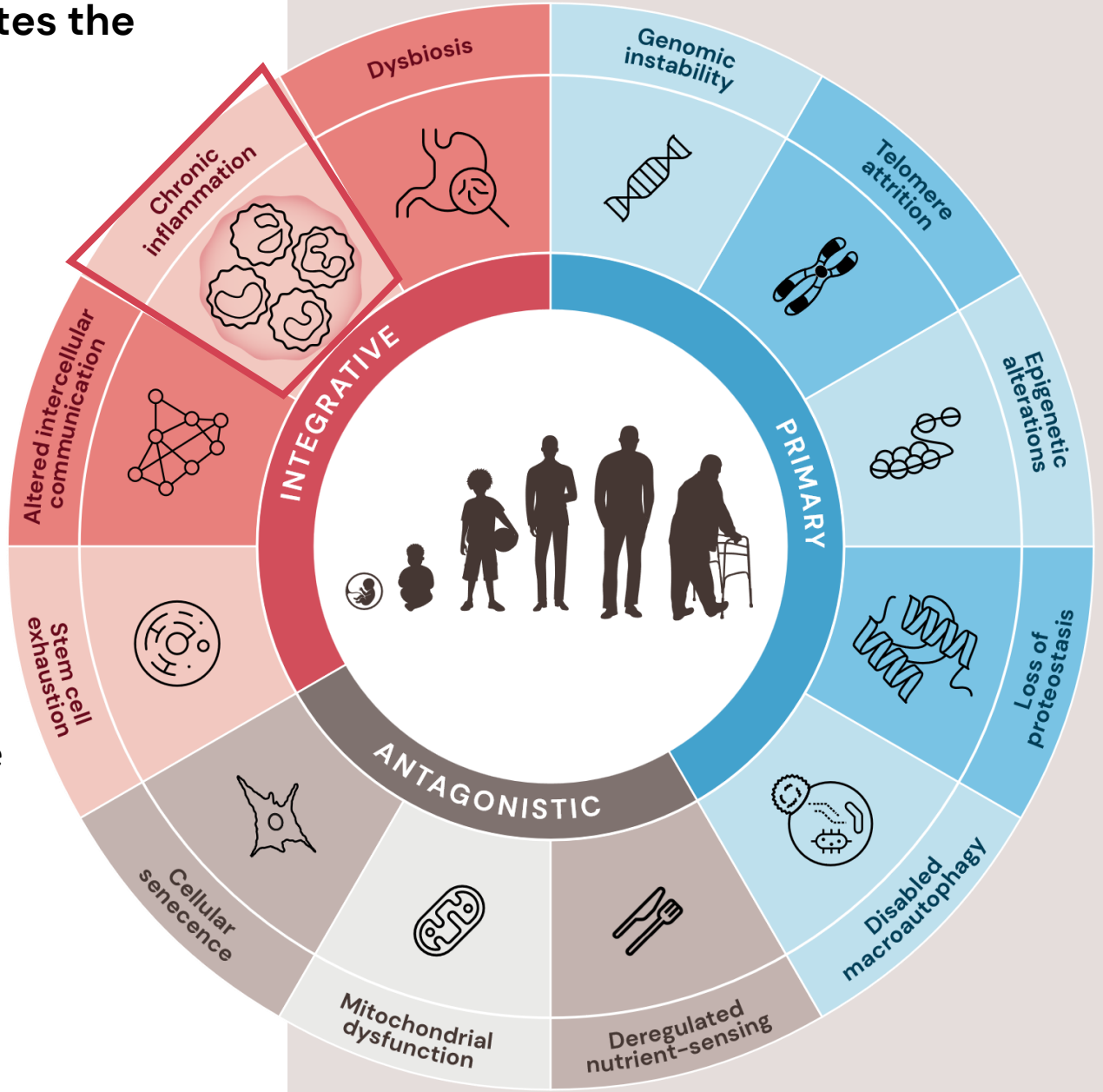
Chronic inflammation: a pivotal hallmark that dictates the pace of aging

- Chronic inflammation is characterized by a **persistent low-grade** inflammatory response that can last for months or years, leading to organ damage and contributing to various age-related diseases
- Due to its association with aging, it is also termed **inflammaging** and arises when the accumulated damage inflicted by the primary and antagonistic hallmarks of aging cannot be compensated anymore
- It involves complex interactions between the immune system and various cellular processes coordinating body's response to damage and disease
- **Dietary solutions** that alleviate inflammation can play a preventive role on the development of age-related conditions such as cardiovascular diseases, cancer and type 2 diabetes



López-Otín, C., et al. (2023). "Hallmarks of aging: An expanding universe." Cell 186(2): 243-278.

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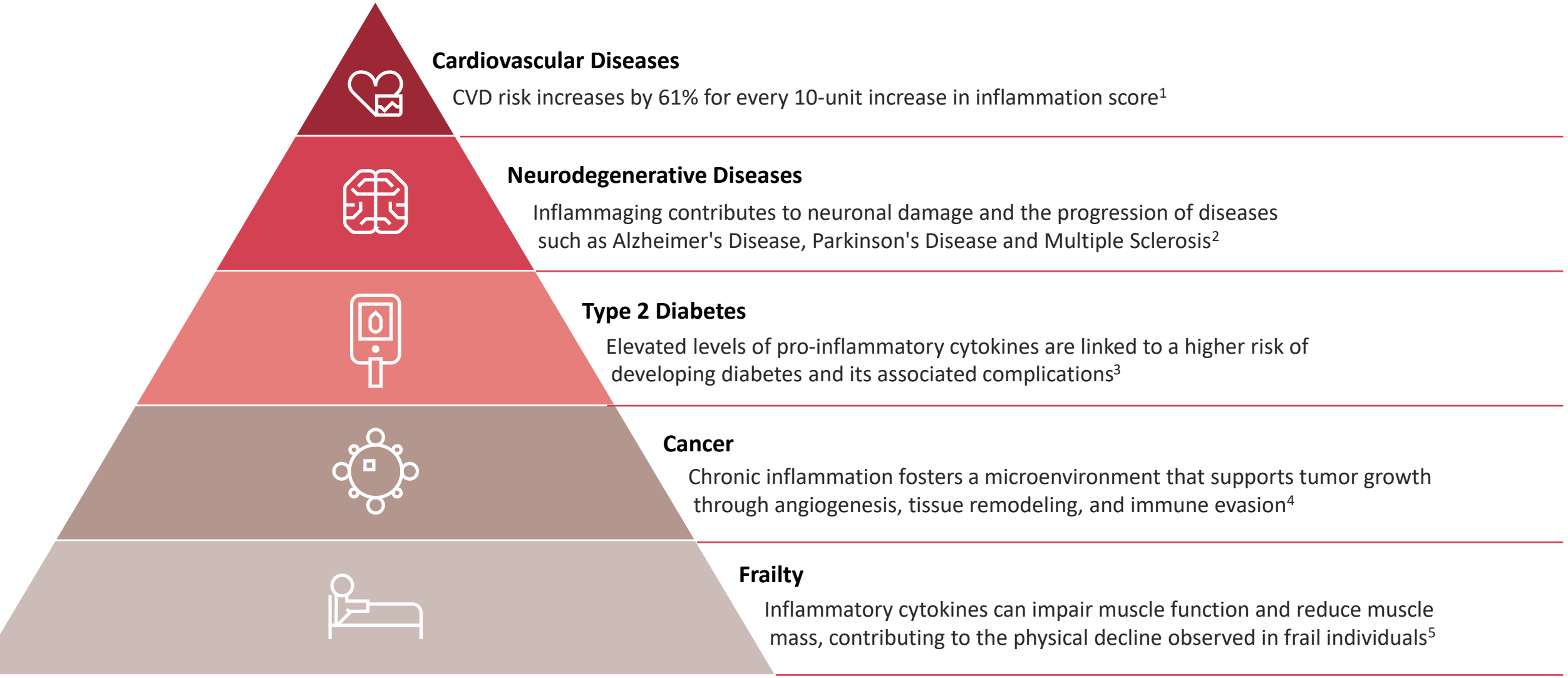
Inflammaging is increasingly recognized as a key factor in the development and progression of age-related diseases



Cardiovascular Diseases

CVD risk increases by 61% for every 10-unit increase in inflammation score[1]

Neurodegenerative Diseases

Inflammaging contributes to neuronal damage and the progression of diseases such as Alzheimer's Disease, Parkinson's Disease and Multiple Sclerosis[2]

Type 2 Diabetes

Elevated levels of pro-inflammatory cytokines are linked to a higher risk of developing diabetes and its associated complications[3]

Cancer

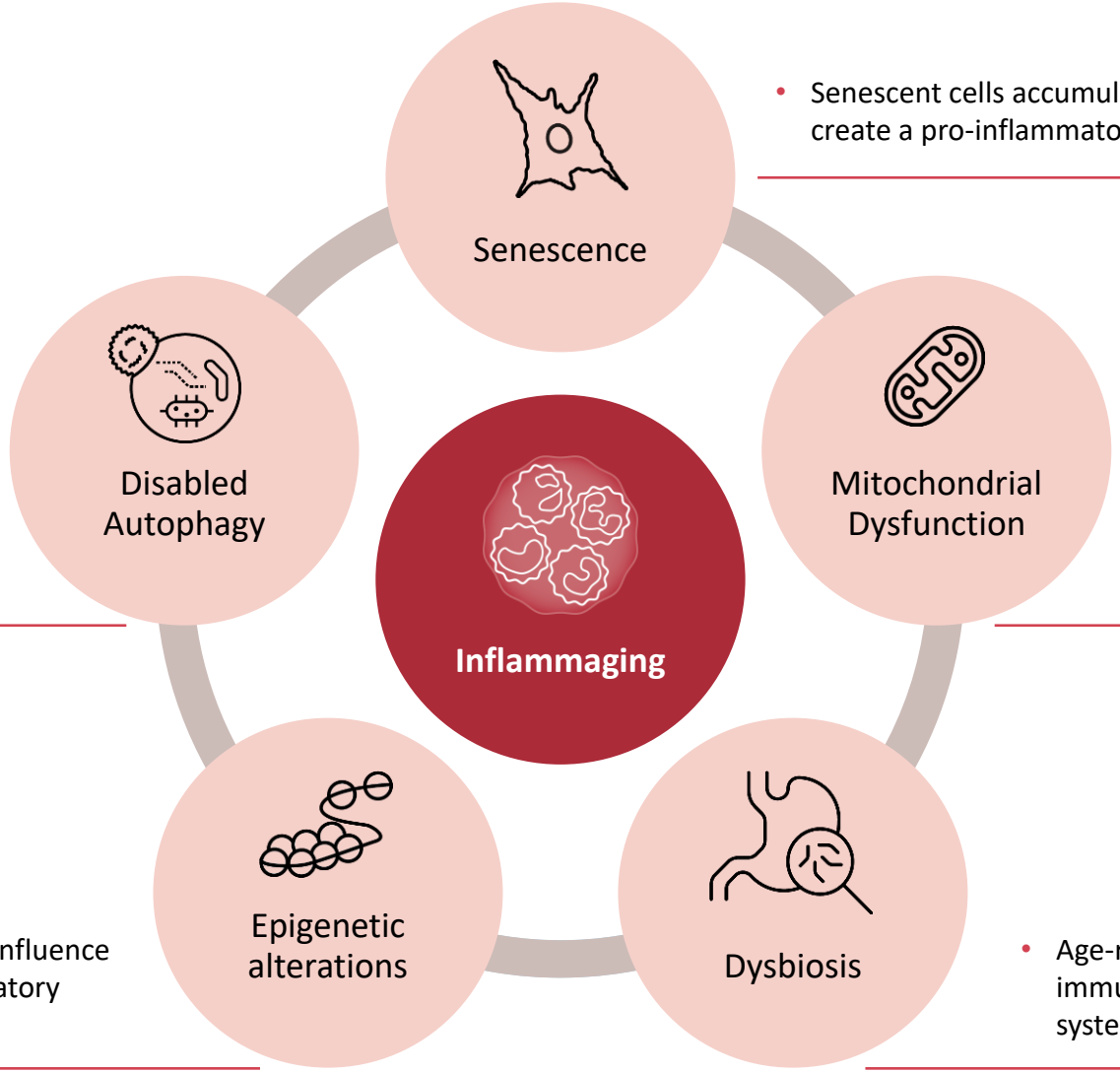
Chronic inflammation fosters a microenvironment that supports tumor growth through angiogenesis, tissue remodeling, and immune evasion[4]

Frailty

Inflammatory cytokines can impair muscle function and reduce muscle mass, contributing to the physical decline observed in frail individuals[5]

1. Zhao HQ et al. Front Nutr. 2025 Feb 20;12
2. Kempuraj, D., et al. Front. Cell. Neur. 2024;18
3. Liu C,. Et al. Cytokine. 2016 Oct;86:100-109
4. Nigam M. et al. Biomed Pharmacother. 2023 Aug;164:115015.
5. Soysal P. et al. Ageing Res Rev. 2016 Nov;31:1-8.

Other Hallmarks of Aging Contribute to Inflammaging



- Senescent cells accumulate with age and secrete factors that create a pro-inflammatory environment

- Mitochondrial dysfunction leads to increased production of reactive oxygen species (ROS), which can damage cellular components and contribute to inflammation

- Age-related changes of the gut microbiota alter the immune system and the gut barrier, which increases systemic inflammation

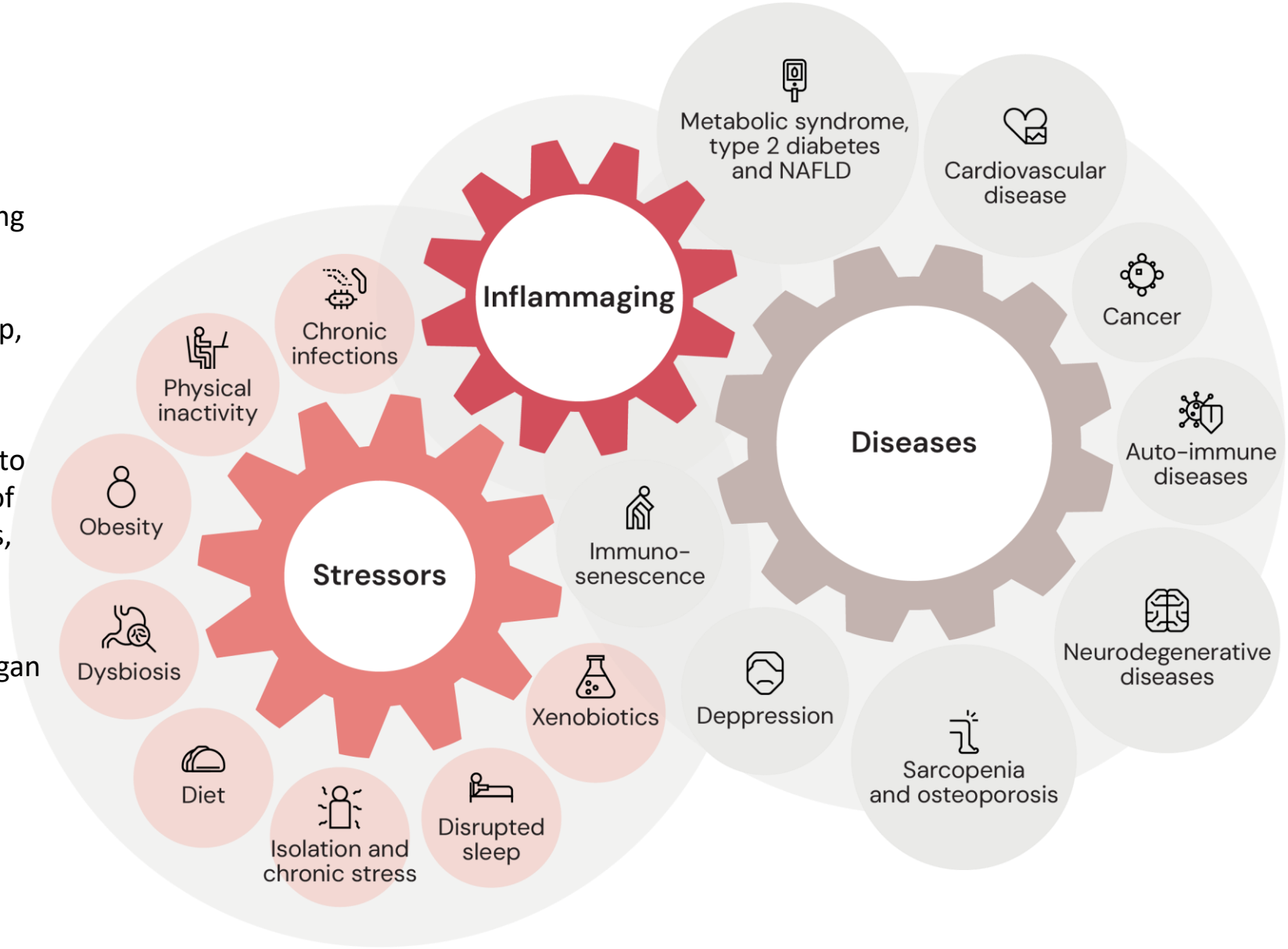
- Epigenetic changes, such as DNA methylation, influence gene expression and are implicated in inflammatory pathways

- Cellular cleanup mechanisms become less efficient with aging, resulting in accumulation of “cellular waste”, which triggers pro-inflammatory signals

Inflammaging at the crossroad of stress and disease

Causes and consequences

- **Chronic stress** is known to enhance inflammaging by influencing the production of inflammatory mediators through physiological and behavioral pathways, such as negative emotions, poor sleep, and unhealthy diet
- **Immunosenescence** (aging of immune system) reduces the efficiency of the immune response to resolve inflammation, leading to an imbalance of pro-inflammatory and anti-inflammatory signals, which contributes to chronic inflammation
- A persistent pro-inflammatory environment increases cell and tissue damages, leading to organ dysfunction and **diseases**



Furman D. et al. Nat Med. 2019 Dec;25(12):1822-1832.

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Understanding the molecular mechanisms of chronic inflammation to develop supplementation strategies

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DO-HEALTH trial

Vitamin *D*3 – *O*mega3 – *H*ome *E*xercise – He*ALTH*y Ageing and Longevity Trial

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DO-HEALTH represents the largest healthy aging study in Europe

First subject entered DO-HEALTH.
2012

2014-2017
Intervention start - end in DO-HEALTH. DSM produces and donates all supplement materials for DO HEALTH intervention

Various publications on physiological and clinical outcomes in DO-HEALTH
2020-2024

2024-2025
Expansion of research into the newest outcomes related to aging (biological clocks)

Positive impact on biological aging published in Nature Aging
2025

Principal Investigator DO-HEALTH:
Prof. Heike Bischoff-Ferrari

Where: 7 centers across 5 countries

5 primary endpoints:
Reducing the risk of incident non-vertebral fractures; of functional decline; of blood pressure increase; of cognitive decline; and the rate of any infection.

Bischoff-Ferrari HA et al. JAMA. 2020; 324(18):1855-1868
Gagesch M et al. J Frailty Aging. 2022;11(1):18-25
Bischoff-Ferrari HA et al. Am J Clin Nutr.2022; 115(5):1311-1321
Bischoff-Ferrari HA et al. Front Aging. 2022; 3:8526433

Treatment arms in the DO-HEALTH Trial

Vitamin ***D***3 – ***O***mega3 – ***H***ome ***E***xercise – He***ALTH***y Ageing and Longevity Trial

DO-HEALTH

Study Overview:
- **Who: 2,152 seniors (aged 70+)** living in the community
- **Type:** Randomized, double-blind, placebo-controlled trial

Monitoring:
- 4 clinic visits
- 9 phone check-ins (every 3 months)

2x2x2 Factorial Design, daily for 3 years

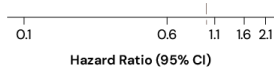
1	Vitamin D3 (2000IU)	Omega-3 (1g)	SHEP	5	Vitamin D3 (2000IU)	Omega-3 (1g)	Flexibility
2	Vitamin D3 (2000IU)	Placebo	SHEP	6	Vitamin D3 (2000IU)	Placebo	Flexibility
3	Placebo	Omega-3 (1g)	SHEP	7	Placebo	Omega-3 (1g)	Flexibility
4	Placebo	Placebo	SHEP	8	Placebo	Placebo	Flexibility

SHEP – Simple Home Exercise program – Strength & balance exercise program.
High quality control group – Flexibility exercise program 3 times/week for 30mins
Subjects were allowed an additional 800IU of Vitamin D daily

Previous publications from DO-HEALTH study showed positive additive effects of the interventions on aging related outcomes

A study published in 2022 analyzed time-to-development of any verified invasive cancer over a follow-up of 3 years[1]

Treatment	Treatment Event / Total	Control Event / Total	Hazard Ratio (95%CI)	P values
Vit D	36 / 1074	45 / 1081	0.76 (0.49 – 1.18)	p=0.225
Omega-3	32 / 1073	49 / 1084	0.7 (0.44 – 1.09)	p=0.115
SHEP	35 / 1081	46 / 1076	0.74 (0.48 – 1.15)	p=0.183
Omega-3 + Vit D	15 / 529	28 / 537	0.53 (0.25 – 1)	p=0.051
Vit D + SHEP	11 / 539	21 / 539	0.56 (0.3 – 1.04)	p=0.068
Omega-3 + SHEP	12 / 539	26 / 542	0.52 (0.28 – 0.97)	p=0.039
Vit D + Omega-3 + SHEP	4 / 264	12 / 270	0.39 (0.18 – 0.85)	p=0.017

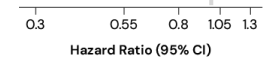


Key Findings: Additive effects of Vitamin D, Omega-3 and exercise with a significant **reduction in incidence of cancer by 61%.**

61%

In 2023, an article in the *Journal of Frailty & Aging* focused on frailty assessment in older adults. Additive effect of Vitamin D, Omega-3 and exercise[2]

Treatment	Treatment Incidence	Control Incidence	Odds Ratio (95%CI)	P Values
Vit D vs **No Vit D**	333 / 528 (63.1%)	363/535 (67.9)	0.81 (0.62-1.07)	P=0.134
Omega-3 vs **No Omega-3**	334 / 520 (64.2%)	362 / 543 (66.7%)	0.84 (0.64-1.11)	P=0.221
SHEP vs **No SHEP**	343 / 540 (63.5%)	353 / 523 (67.5%)	0.89 (0.67-1.16)	P=0.379
Omega-3 + Vit D vs **No Omega-3 + Vit D**	160 / 251 (63.8%)	189 / 266 (71.1%)	0.69 (0.46-1.01)	P=0.059
Vit D + SHEP vs **No Vit D + SHEP**	166 / 264 (62.9%)	186 / 259 (71.8%)	0.72 (0.49-1.06)	P=0.097
Omega-3 + SHEP vs **No Omega-3 + SHEP**	164 / 266 (61.7%)	183 / 269 (68.0%)	0.75 (0.51-1.10)	P=0.135
Vit D + Omega-3 + SHEP vs **Placebo**	80 / 126 (63.5%)	96 / 130 (73.9%)	0.61 (0.38-0.98)	P=0.041



Key Findings: Additive effects of Vitamin D, Omega-3 and exercise with a significant **reduction in the incidence of pre-frailty by 39%.**

39%

1. Front Aging. 2022 Apr 25;3:852643. doi: 10.3389/fragi.2022.852643
2. Gagesch M. et al. (2023) Effects of Vitamin D, Omega-3 Fatty Acids and a Home Exercise Program on Prevention of Pre-Frailty in Older Adults: The DO-HEALTH Randomized Clinical Trial. J Frailty Aging.12(1):71-77.

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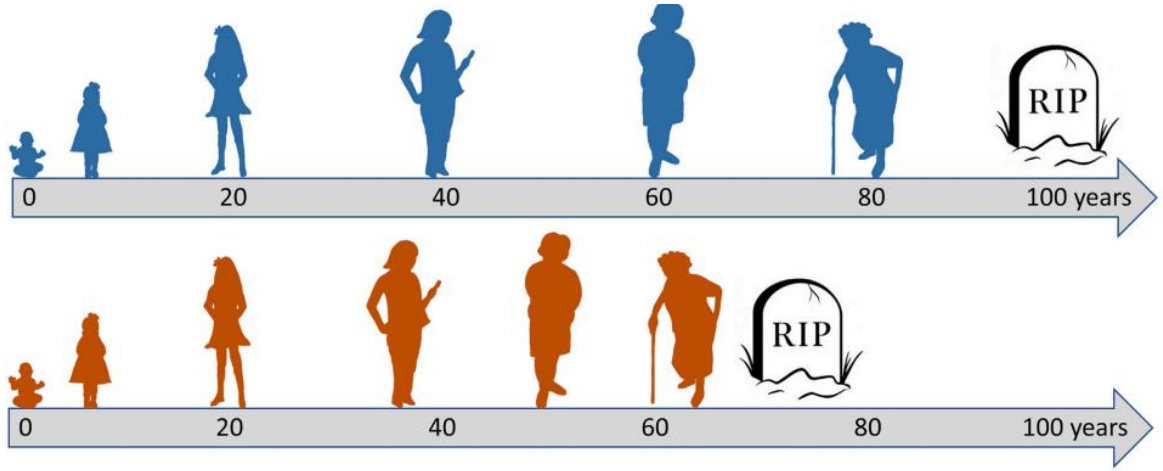
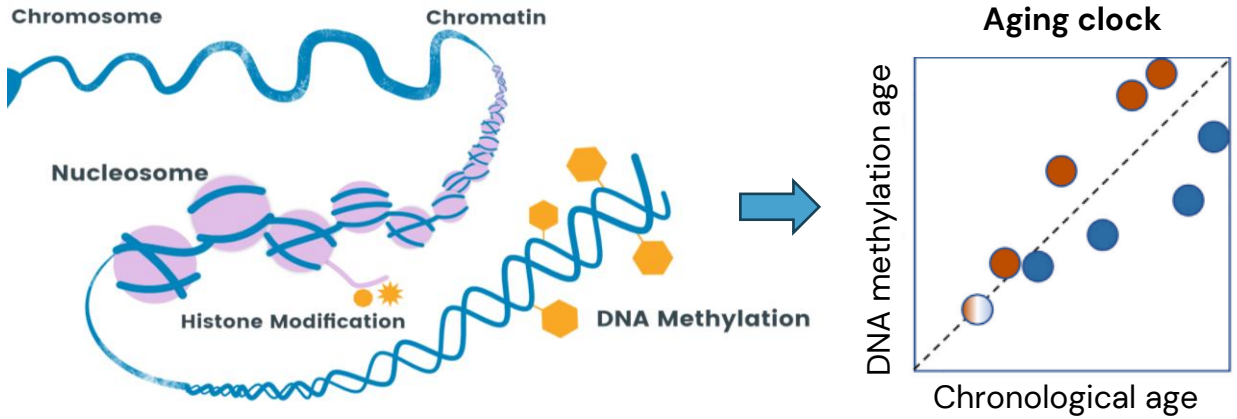
DNA methylation clocks provide a sophisticated measure of biological age

DNA methylation (or epigenetic) clocks measure multiple changes in DNA methylation that are associated with aging and risk of diseases and mortality





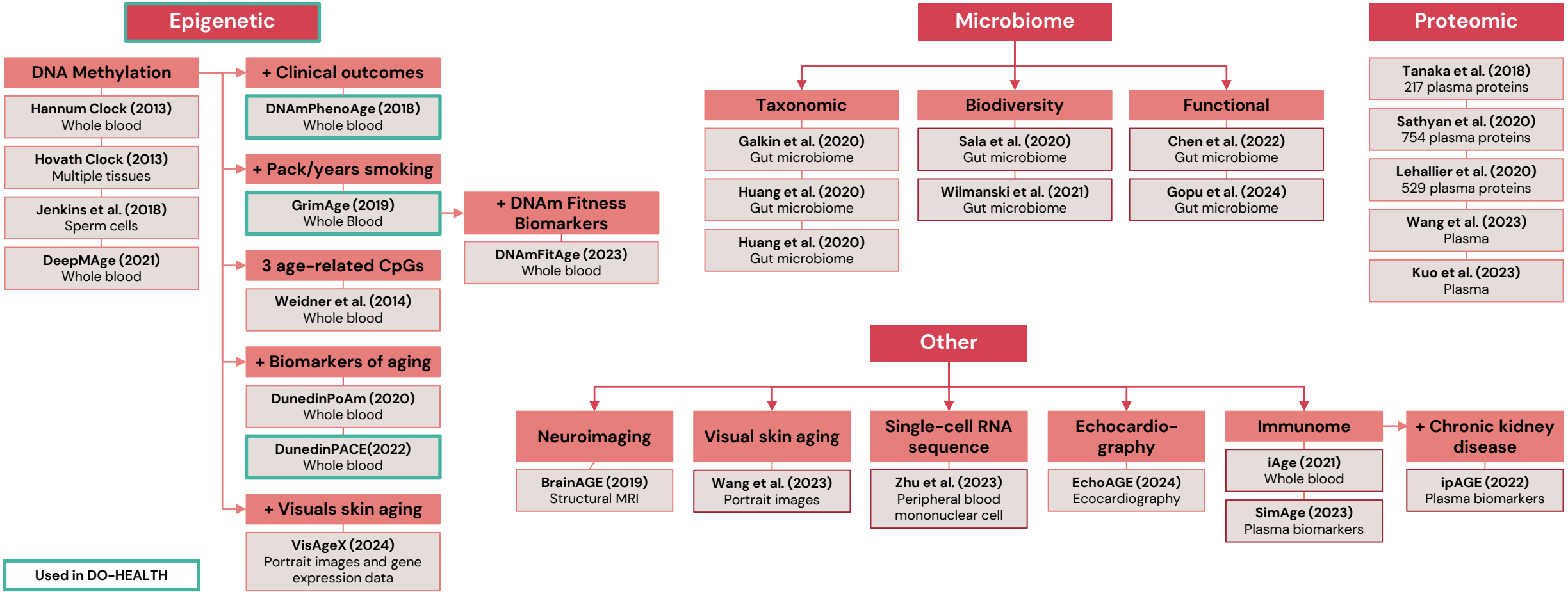
- DNA methylation is a process where DNA is tagged with methyl groups in specific regions of the DNA (CpG sites) to regulate gene expression
- Using machine learning algorithms, scientists have identified techniques crucial for constructing the DNA methylation clocks.
- The differences between various DNA methylation clocks lie in how their algorithms are constructed:
  - First-generation: estimate **chronological age** by correlating DNA methylation patterns with chronological age data (HorvathAge)
  - Second-generation: predict **biological age** and health outcomes, offering more comprehensive insights into aging (PhenoAge, GrimAge)
  - Third generation: measures the **rate of aging** (DunedinPACE)

Field AE et al. 2018. DNA Methylation Clocks in Aging: Categories, Causes, and Consequences. Molecular Cell.

Aging clocks

AI-driven biomarkers for predicting biological age and health outcomes

Aging clocks are computational models designed to measure biological age and aging rate based on age-related markers including epigenetic, proteomic, metabolic changes, among others.



Min M et al. 2024. Critical review of aging clocks and factors that may influence the pace of aging. Front Aging.

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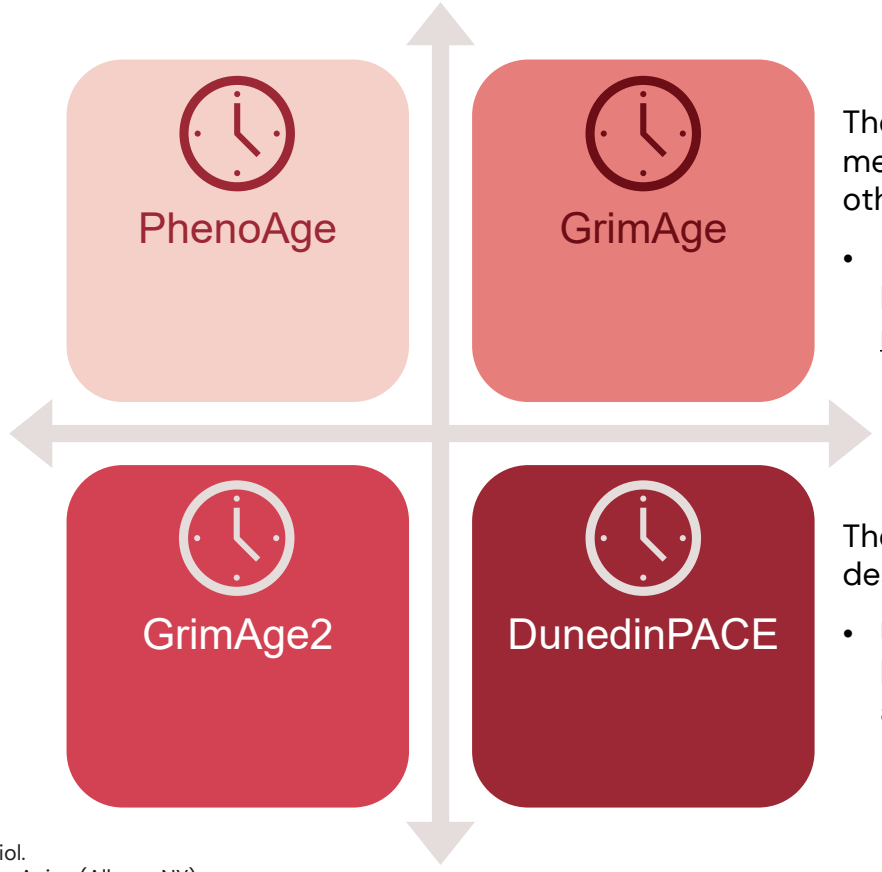
The DO-HEALTH Bio-Age trial included 777 of the 2,157 DO-HEALTH participants with DNAm measures at baseline and 3 years.

In a subset of participants (Swiss group), four epigenetic clocks (PhenoAge, GrimAge, GrimAge2, and DunedinPACE) were employed to assess biological age.
Those clocks analyzed DNA changes that occur as we age, in combination with clinical biomarkers.

The **PhenoAge clock** uses a combination of DNA methylation and clinical biomarkers.

- Incorporating **9 clinical biomarkers** related to inflammation, metabolism, and organ function.
- This clock is particularly useful in assessing overall health risks and life expectancy.[1]



The **GrimAge clock** integrates both DNA methylation data and biomarkers for smoking and other aging-related factors

- Predicts lifespan and age-related diseases based on DNA methylation patterns related to mortality and health risk.[2]

The **GrimAge2** clock is an updated version of the GrimAge clock, improving upon its ability to predict mortality and age-related diseases.[3]

The **DunedinPACE** clock is an epigenetic measure designed to estimate how quickly a person is aging.

- Unlike other clocks, DunedinPACE focuses on biological processes linked to functional decline and overall health.[4]

1. Horvath S. 2013. DNA methylation age of human tissues and cell types. Genome Biol.
2. Lu et al. 2019. DNA methylation GrimAge strongly predicts lifespan and healthspan. Aging (Albany NY).
3. Lu et al. 2022. DNA methylation GrimAge version 2. Aging (Albany NY).
4. Belsky et al. 2022. DunedinPACE, a DNA methylation biomarker of the pace of aging. Elife

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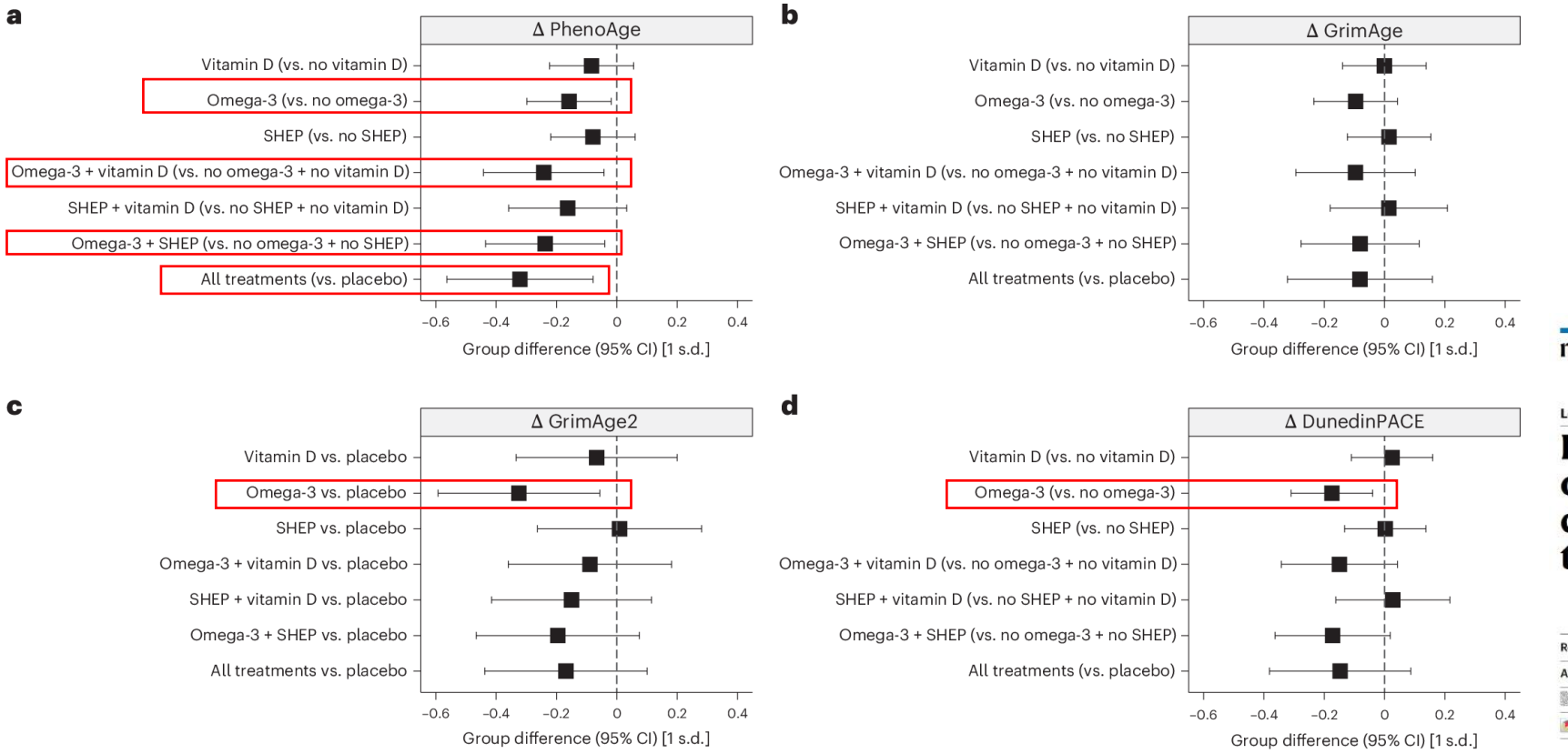
Omega-3 and vit D supplementation can slow down the aging process

- Clinically proven to slow down biological aging with an additional protective effect when the combination of life's® Omega and Quali-D® is taken with exercise.
- Omega-3 supplementation alone significantly reduces biological age



How much?
Rejuvenation was
2.9 – 3.8 months
over 3 years


nature aging
Letter
https://doi.org/10.1038/s43587-024-00793-y

Individual and additive effects of vitamin D, omega-3 and exercise on DNA methylation clocks of biological aging in older adults from the DO-HEALTH trial

Received: 7 August 2024
Accepted: 4 December 2024
Check for updates

Heike A. Bischoff-Ferrari, Stephanie Gängler, Maud Wieczorek, Daniel W. Belsky, Joanne Ryan, Reto W. Kressig, Hannes B. Stähelin, Robert Theiler, Bess Dawson-Hughes, René Rizzoli, Bruno Vellas, Laure Rouch, Sophie Guyonnet, Andreas Egli, E. John Orav, Walter Willett & Steve Horvath

Bischoff-Ferrari, Heike A., et al. "Individual and Additive Effects of Vitamin D, Omega-3 and Exercise on DNA Methylation Clocks of Biological Aging in Older Adults from the DO-HEALTH Trial." Nature Aging, February 3, 2025.

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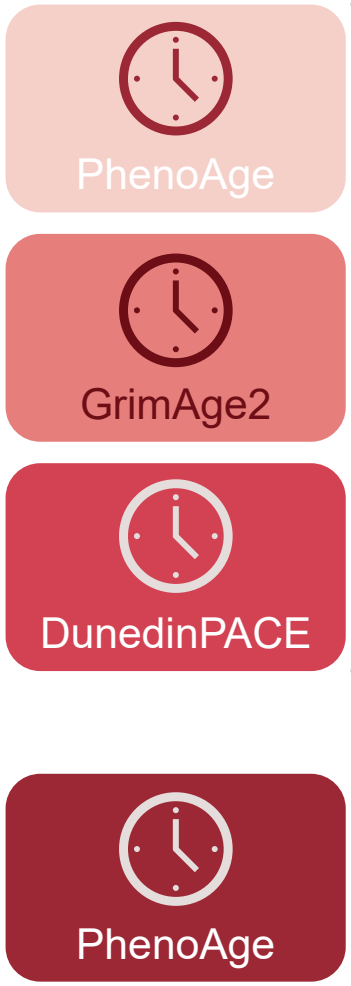
Omega-3 and vitamin D supplementation and SHEP can slow down biological aging

Consistent effects of omega-3 on three aging clocks and additive effects of the combination of omega-3 with vitamin D on PhenoAge

- In this cohort (Swiss subgroup, **n=777**), participants were generally healthy adults with a mean age at the baseline of 75 years old.
- Four established DNA methylation clocks (PhenoAge, GrimAge, GrimAge2, and DunedinPACE), which are indicators of biological age and predictors of morbidity and mortality, were used to assess the impact of the interventions on aging.
- This research demonstrates that simple lifestyle changes, such as omega-3 and vitamin D supplementation or physical exercise, can reduce biological age.
- These results were observed in a very healthy population, suggesting that the effects may be even greater in other groups. Ongoing studies are exploring this further.
- This outcome was made possible by the advancement of aging clocks, enabling a broader and more comprehensive analysis of data.



Omega-3 alone helped slow down the aging process according to these three aging clocks

On top, an additive effect was observed for the combination of Omega-3 and vitamin D with the PhenoAge clock

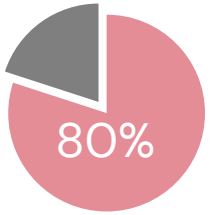
Bischoff-Ferrari, Heike A., et al. "Individual and Additive Effects of Vitamin D, Omega-3 and Exercise on DNA Methylation Clocks of Biological Aging in Older Adults from the DO-HEALTH Trial." Nature Aging, February 3, 2025.

Importance of omega-3 fatty acid supplementation

- Omega-3 fatty acids (particularly EPA & DHA) have been extensively studied for their anti-inflammatory properties
- However, the majority of the world's population do not consume adequate amounts of EPA & DHA

Omega-3 FA intake is low around the world

- 80% of people worldwide have low levels of EPA and DHA [1]



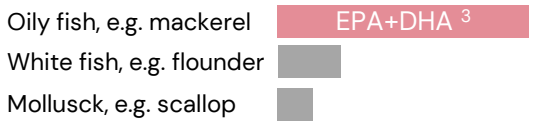
- Regional differences [2]:

  High: Japan, Scandinavia

  Very low: North, Central & South America, Europe, Middle East, Southeast Asia, Africa

Role for supplementation

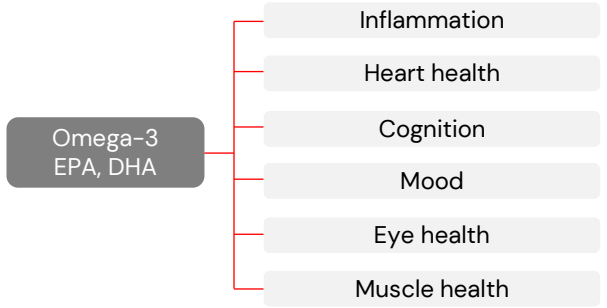
- It is a challenge to meet EPA+DHA recommendations by diet alone
- Even those who consume fish regularly can have a low omega-3 index



- Supplements are an efficient way to boost omega-3 fatty acid intake[4]

Multisystem Protector

Omega-3 fatty acids are important for many health conditions associated with aging [5,6]



1. GOED GOED-HCP-web
2. Stark KD et al. Progress in Lipids Research 2016;63:132-152
3. USDA FoodData Central Food Search Food Search | USDA FoodData Central
4. Harvard Health Omega-3 foods: Incorporating healthy fats into your diet - Harvard Health
5. Troesch B et al. Nutrients 2020;12(9):2555
6. Djuricic I and Calder PC. Nutrients 2021;13:2421

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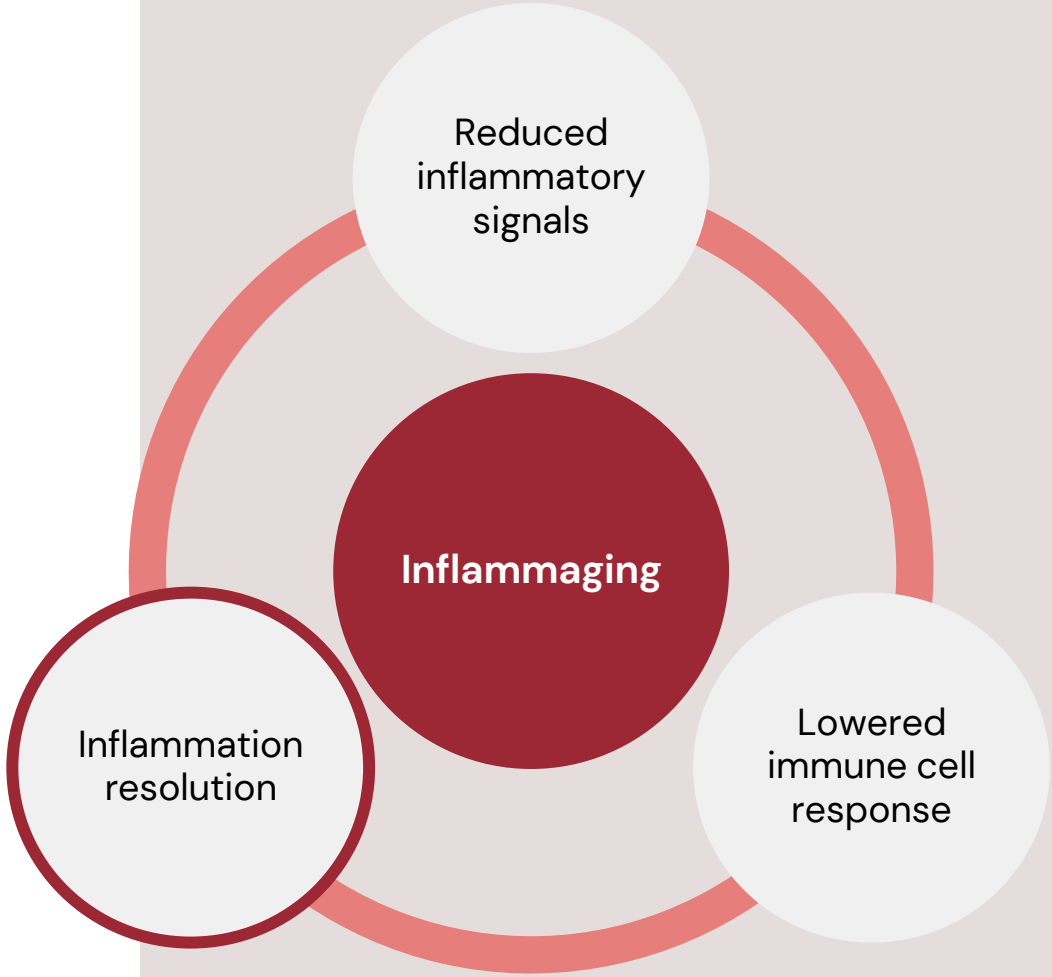
Omega-3 fatty acids: Established anti-inflammatory support system

Signals, response and resolution [1,2]

- Omega-3 fatty acids influence inflammation through a variety of mechanisms
- Many are mediated by, or at least associated with, changes in fatty acid composition of inflammatory cell membranes, which modifies fluidity, signaling leading to altered gene expression, and the pattern of inflammatory mediator production
- Established for modulating inflammatory response → e.g. cytokines, **eicosanoids,** adhesion molecules, cell response
- More recently a more complex role for omega-3 fatty acids has emerged for **inflammation resolution** → involves **specialized pro-resolving mediators (SPM)**



1. Calder PC. Brit J Clinical Pharmacology 2012;75(3):645-662 (figure)
2. Calder PC. Nutrients 2010;2:355-374

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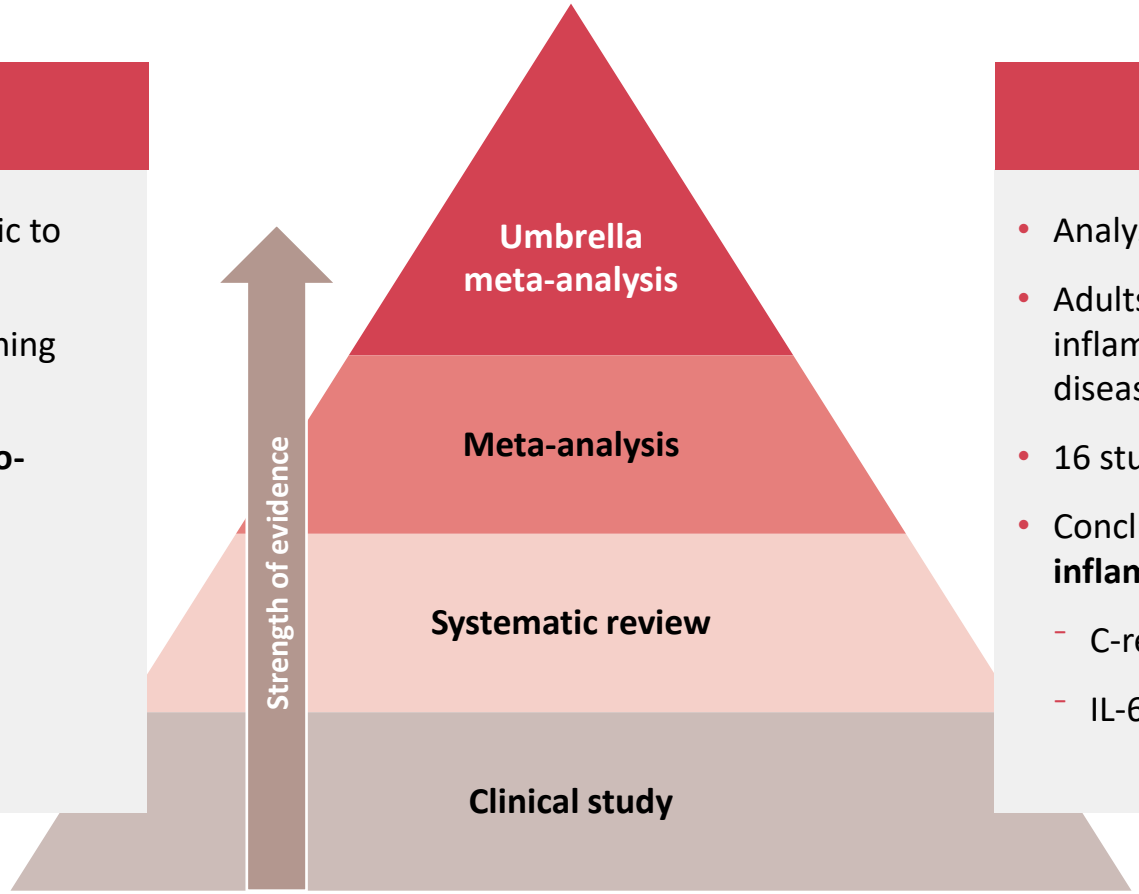
Omega-3s and inflammation: state of clinical knowledge

Due to the extensive number of clinical studies, meta-analyses are available

Umbrella meta-analysis

- Meta-analysis of meta-analyses, specific to omega-3 FAs
- 32 meta-analyses were included, spanning various conditions
- Conclusion: **significant reduction in pro-inflammatory biomarkers**
  - C-reactive protein (≤ 55y & > 55y)
  - TNFα (> 55yr)
  - IL-6 (≤ 55 yr & > 55 yr)



Meta-analysis

- Analysis on 2 specific inflammatory markers
- Adults 45+ yr, with chronic low-grade inflammation, but excluding inflammatory disease
- 16 studies were included
- Conclusion: **significant reduction in pro-inflammatory biomarkers**
  - C-reactive protein
  - IL-6

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Vitamin D levels decline with aging, but need increases, emphasizing the importance of supplementation

- Older adults have a higher risk for Vitamin D deficiency, as production and metabolism changes
- Production of active Vitamin D is reduced by 50% due to age-related decline in renal function [3]

Factors contributing to a decline in status [1,2,3,4]

- Poor & changing diet
- Decreased sun exposure
- Reduced skin production capacity
- Decreased renal activation of VitD
- Decreased VitD receptor expression
- Drug interactions affecting absorption & metabolism

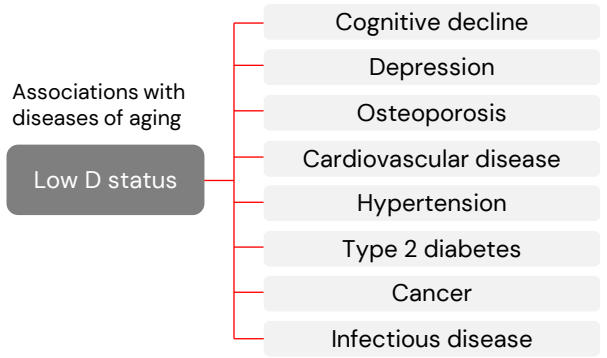
Need increases [5]

- Some national bodies have higher VitD recommendations for older adults, e.g.

  USA: 15 ug/d 18-70 yr → 20 ug/d 70+ yr
- Food sources naturally rich in VitD are limited
- Supplementation is an easy way to achieve VitD sufficiency

Multisystem Protector [2,4]

- VitD has diverse biological actions, with benefits beyond bone health, due to the widespread presence of VitD receptors (VDR) throughout the body



1. Giustina et al. Endocrine 2023 79:31-44.
2. Meehan et al. J Aging Gerontol 2014;2(2):60-71.
3. Gallagher. Endocrinol Metab Clin North Am 2013;42(2):319-332
4. Kupisz-Urbanska et al. Nutrients 2021;13:1247
5. Vitamin D - Health Professional Fact Sheet

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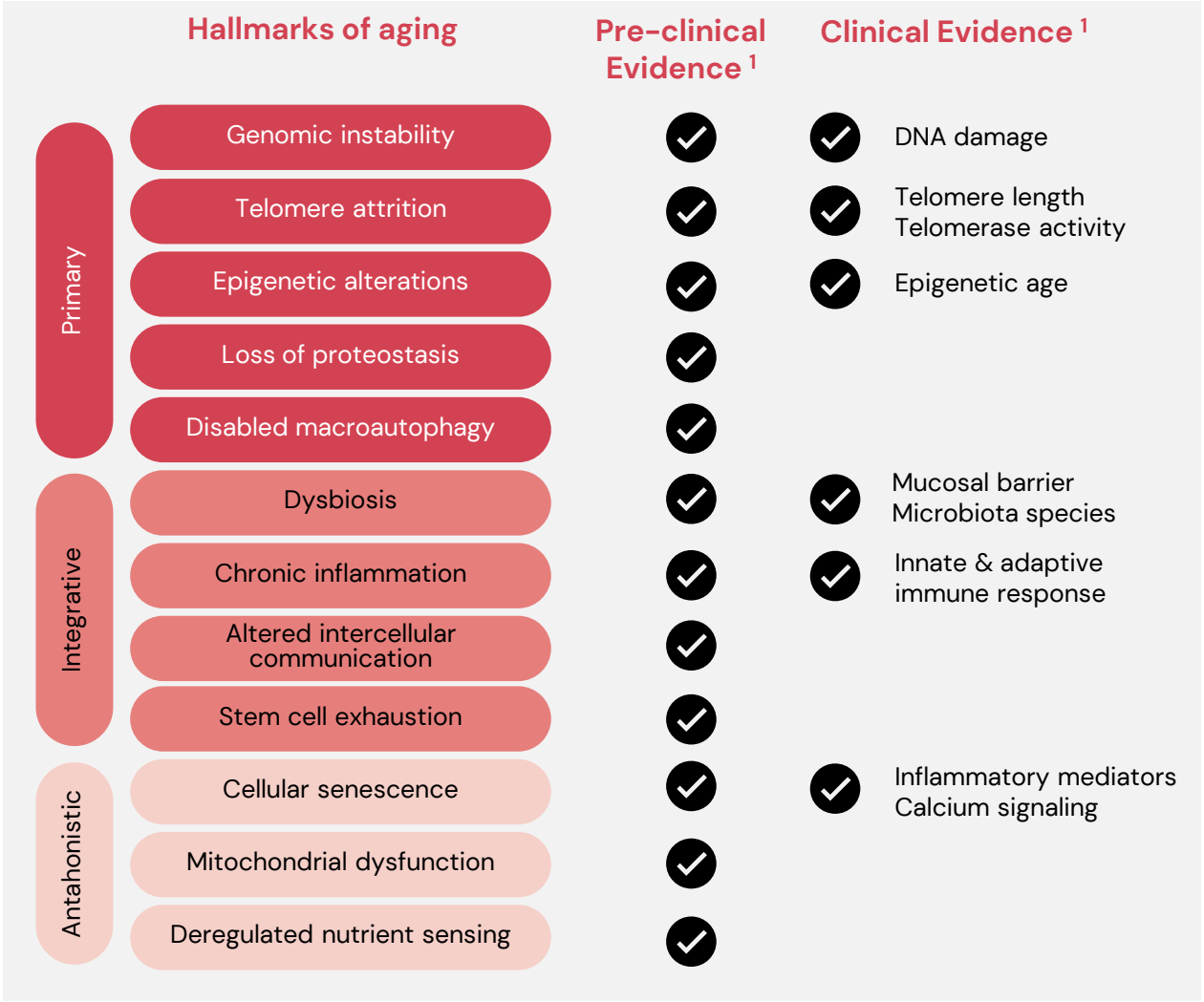
Targeting the Hallmarks of Aging with Vitamin D: State of clinical evidence

- Preclinical evidence supports Vitamin D and Vitamin D receptors as molecules targeting the **entire hallmarks of aging** network; clinical evidence is emerging (mostly disease) [1]
- Low Vitamin D status raises **biological age** at the epigenetic level; improved with supplementation [2]
- Vitamin D is renowned for its positive impact on **musculoskeletal health** (e.g. falls, fracture) [2]. In the aging process, decline in physical performance is the **first phenotypical feature** of accelerated aging [3]
- Vitamin D supplementation may **reduce mortality** in older adults; reported in a Cochrane review of 56 trials [4].



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2. Bischoff-Ferrari HA. BMJ. 2009; 339:b3692
3. Vetter VM et al. Geroscience 2022;44(3):1847
4. Bjelakovic Cochrane Database of Systematic Reviews 2014

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What if you could reclaim a season every three years?

Age Slower by dsm-firmenich is backed by DO-HEALTH, the largest human healthy aging trial, providing strong evidence for science-based prevention to extend health expectancy.

2 flavored Softgels with *life's®OMEGA 60 and* Quali®-D

Brand	Ingredient	Dose per 2 softgels
Quali®-D	**Vitamin D**	**2000 IU**
life's®OMEGA 60	**Total DHA + EPA as FA in a 2:1 ratio**	**1000mg**

Recommended daily dosage: Adults take **2 Softgels daily.**

life's™ OMEGA | Quali-D™

Used in the DO-HEALTH Study

Powered by:

life's®OMEGA helped reduce signs of aging by an average of 3 months over a 3-year study*.

Even better results were observed when it was combined with **Quali®-D**.

Study Publication: Bischoff-Ferrari, Heike A., et al. "Individual and Additive Effects of Vitamin D, Omega-3 and Exercise on DNA Methylation Clocks of Biological Aging in Older Adults from the DO-HEALTH Trial." Nature Aging, February 3, 2025.

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DO-HEALTH is the largest trial to date to show that interventions can slow biological aging, not only in mice, but also in humans.

Professor Steve Horvath
Pioneer of DNA methylation clocks

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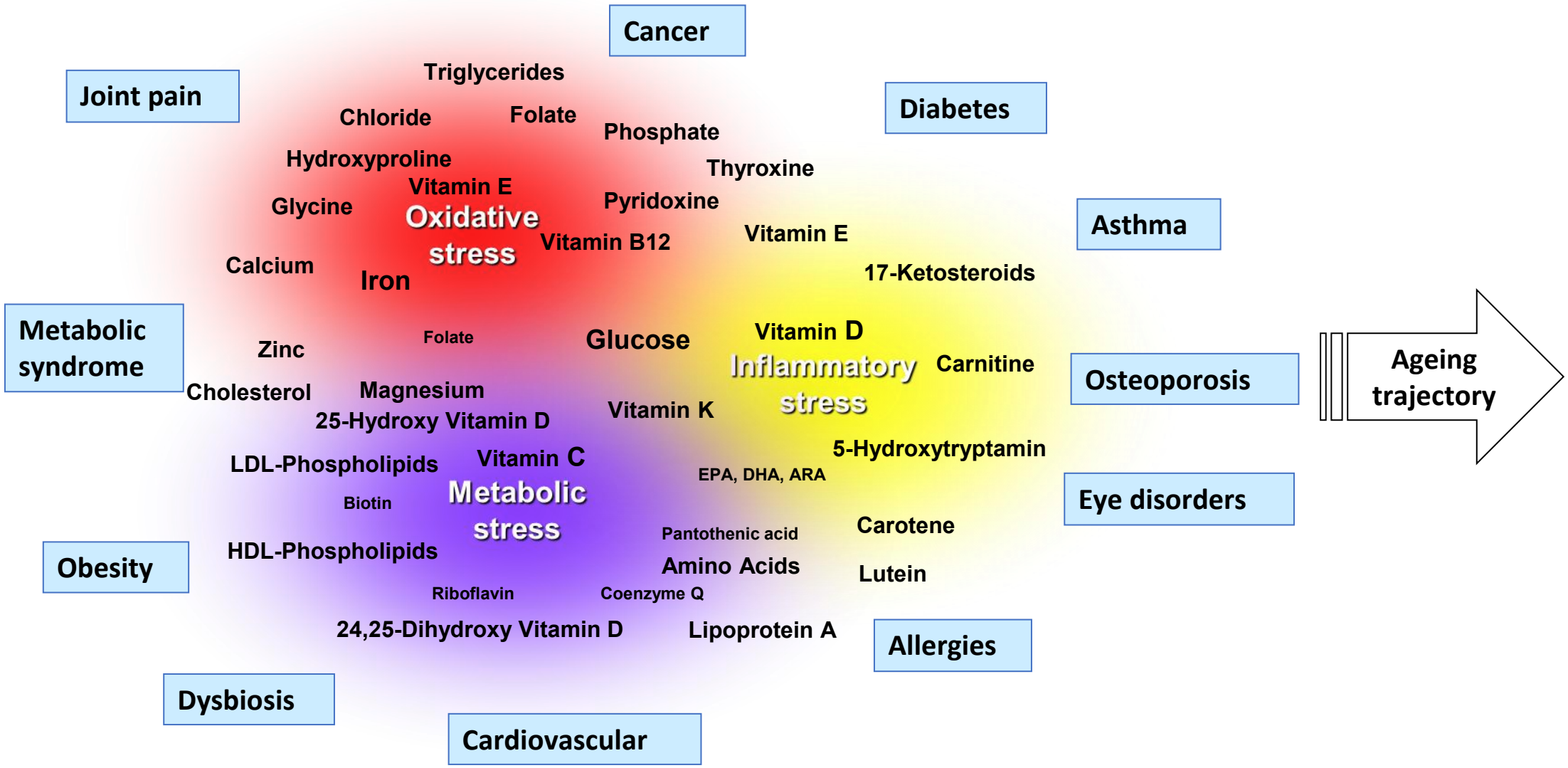
An optimal supply and balance of all essential nutrients is key for homeostasis, chronic disease prevention – to be complemented with additional ingredients for healthy ageing

- Genetics
- **Nutrition**
- Lifestyle
- Environment
- Life-course events



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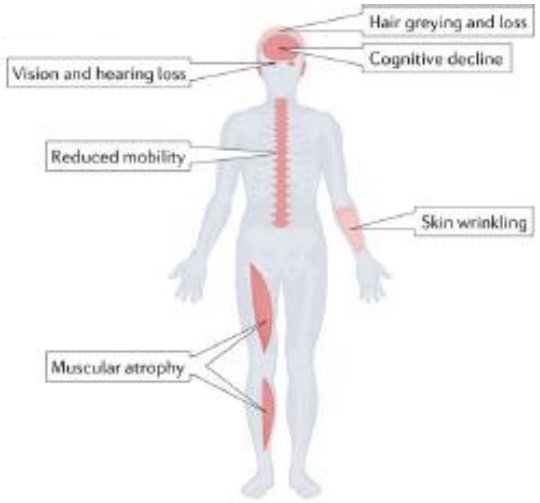
Biomarkers of ageing are indispensable tools for research in healthy ageing

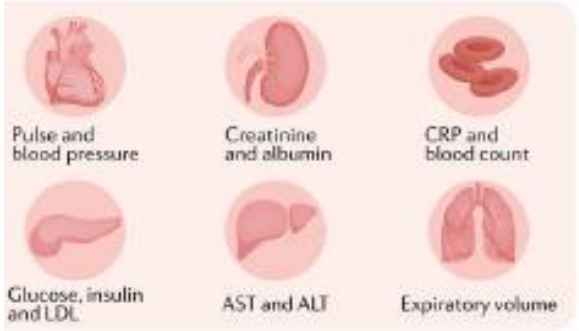
Measures biological age

Measures age-related function decline

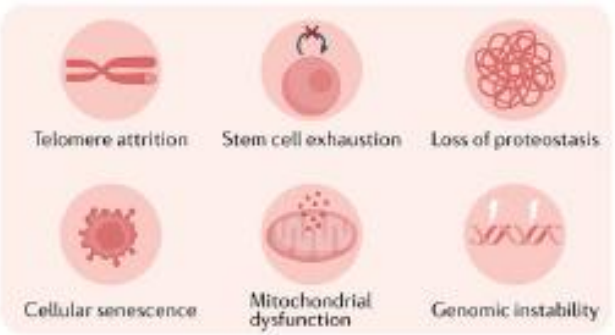
Visible aging biomarkers



Health and disease biomarkers



Cellular & molecular biomarkers



Composite biomarkers

Predictive biomarkers

Diagnostic biomarkers

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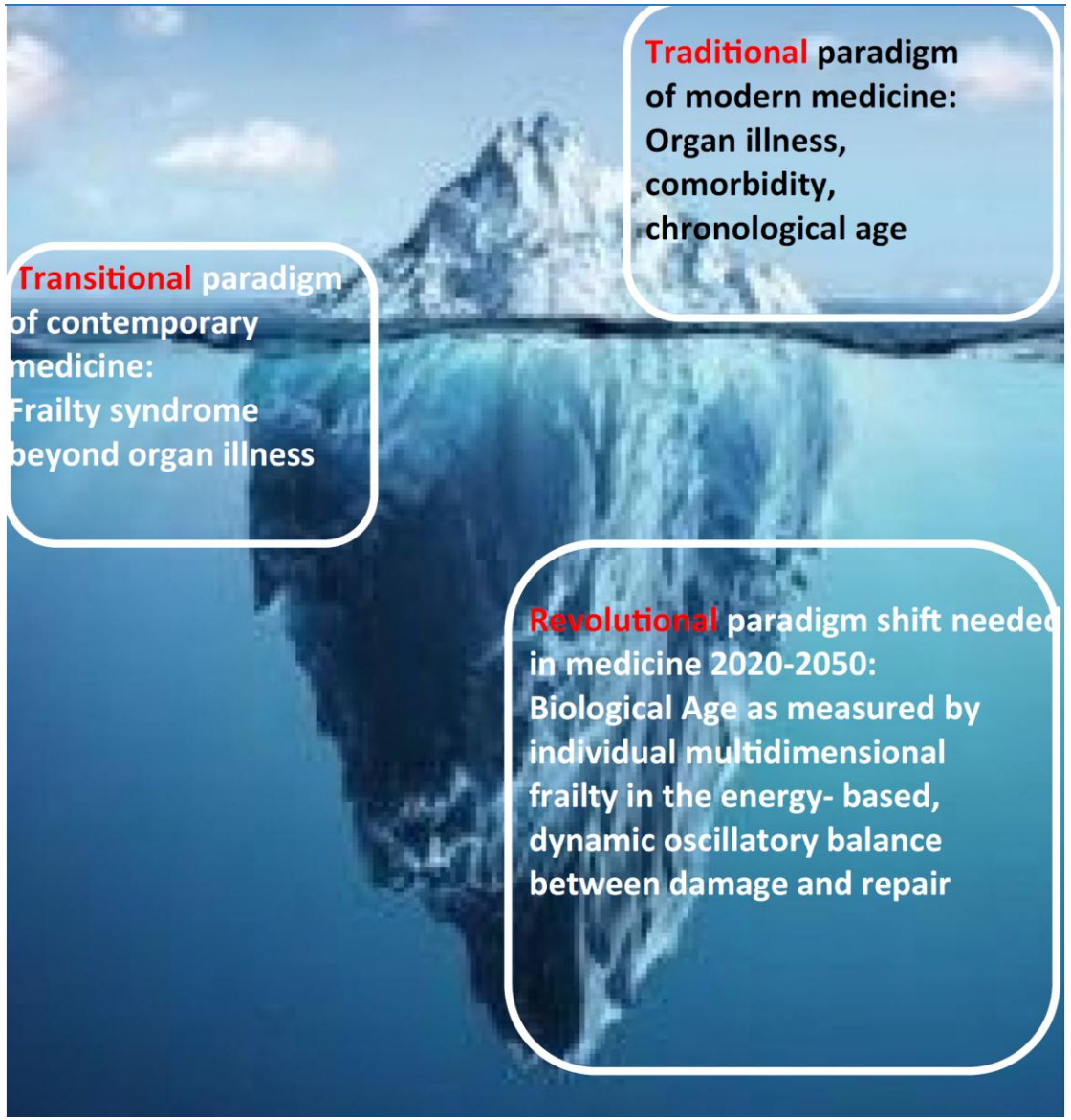
Measuring biological age in clinical trials



Polidori, M. C. and L. Ferrucci (2023). Aging Clin Exp Res

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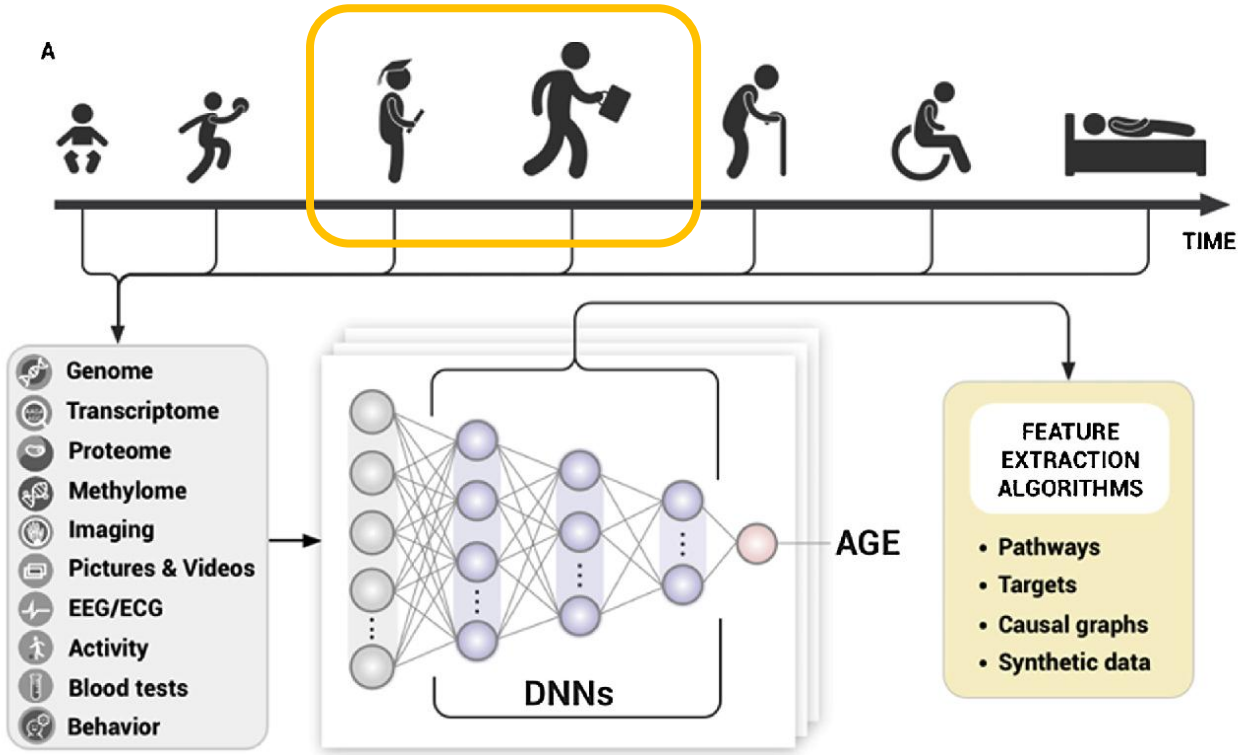
Leveraging AI for Healthy Ageing Through Nutrition

Biomarker Analysis:
- AI assesses biomarkers from various sources to predict health risks.
- Early identification enables proactive intervention and personalized care.

Synergistic Nutrients:
- AI identifies combinations of nutrients that optimize health outcomes.
- Promotes understanding of how nutrients work together to support healthy aging.

Nutrient Tracking Apps:
- AI tracks nutrient intake, offering insights into deficiencies or excesses.

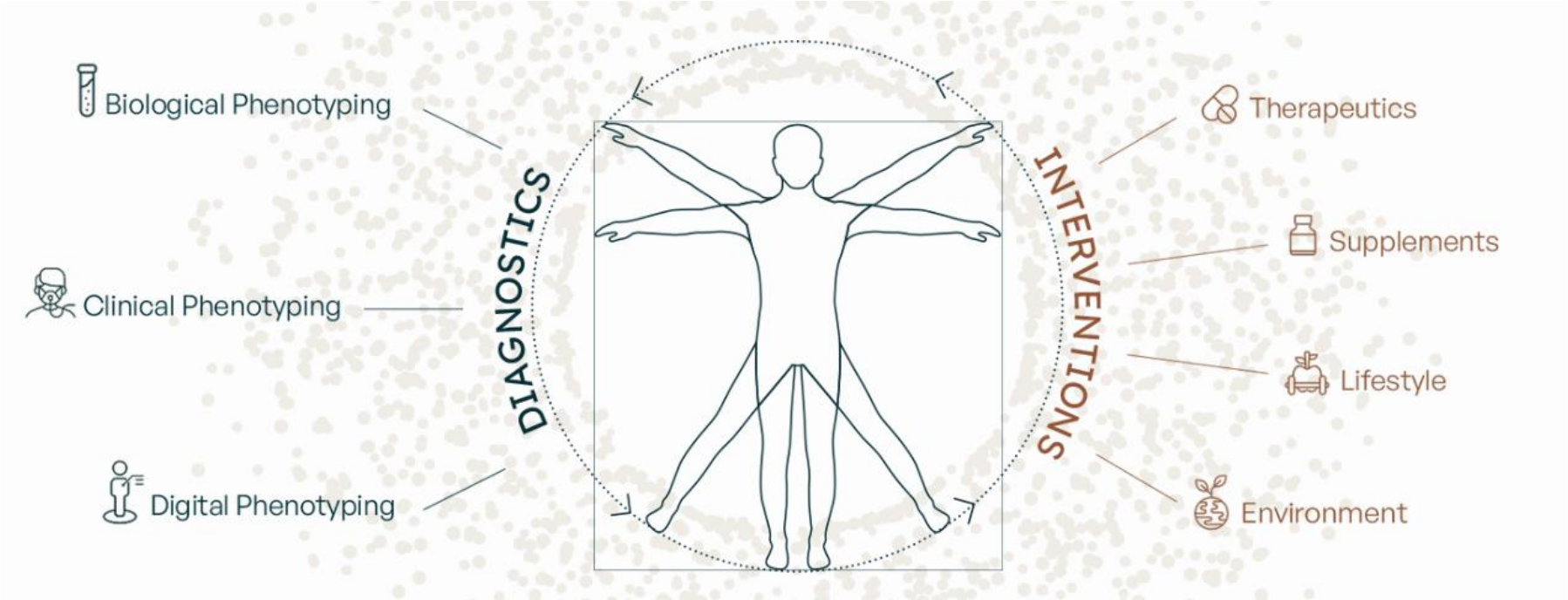
Early Intervention:
- Identifying early signs of potential health issues through AI analysis, enabling timely intervention with preventative measures.



Zhavoronkov A, et al., Ageing Res Rev. 2019; Theodore Armand TP, et al., J Pers Med. 2024

Longevity clinics are emerging around the world

Mission: to delay biological age and enhance healthspan



How:

- Advanced diagnostics identifying potential issues before they become evident
- Personalized lifestyle recommendations
- Nutrition and supplements guidance

Summary and Take-Home Message

- The population is living longer, but not always healthier. Today, most of us will spend our last 10 years of life battling ill health.
- New, cutting-edge research shows that it is possible to increase our health expectancy, i.e., the number of years we live in good health, by targeting the processes of aging at a cellular and system level—making our senior years not just longer, but some of our best.
- To effectively slow aging and increase health expectancy, it is critical to understand how the different aspects of aging are connected and address them in a unified way.
- There is a need to build longevity solutions that unite efficacy across various hallmarks of ageing and deploy systems view on the ageing process.
- These solutions should integrate well-established ingredients with emerging ones, addressing health at all levels —from molecules to cells, tissues, and organs—and should be clinically validated

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Hallmark	Definition
Genomic instability	Accumulation of DNA damage and the loss of ability to repair damage
Telomere attrition	Telomere shortening with each cell division cycle, compromising genomic integrity
Epigenetic alterations	Changes to how genes are expressed over time, triggered by environmental influences
Loss of proteostasis	Reduced regulation, causing reduced cell viability and misfolded proteins
Disabled macro-autophagy	Decline in cellular ability to deliver damaged organelles and proteins for degradation
Stem cell exhaustion	Decline in tissue renewal as well as impaired tissue repair upon injury
Altered intercellular communication	Loss, misinterpretation, or ignoring of the signaling between cells, interrupting normal tissue function and repair
Chronic inflammation	Increase in inflammatory cytokines and biomarkers with immune decline
Dysbiosis	Disruption in gut bacterial composition, distribution, and activities
Extracellular matrix (ECM) changes	Deposition, degradation, and modification of ECM components
Deregulated nutrient sensing	Cellular inability to sense what nutrients are at hand and communicate with other systems
Mitochondrial dysfunction	Functional deterioration, causing an increase in reactive oxygen species
Cellular senescence	Cessation of cell division while metabolically still active, damaging other healthy tissues
Psychosocial isolation	Enfeeblement of social and affective bonds, as well as their psychological or psychiatric consequences

McKinsey & Company: Healthspan science may enable healthier lives for all (2025)

Term	Explanation
Biomarker	A measurable indicator of a biological state, such as the presence or progression of a disease or a response to a treatment
Biomedicine	A branch of medical science that applies principles from biology, physiology, and molecular science to understand, diagnose, and treat human diseases
Biotechnology	A multidisciplinary field that uses living organisms and their components to develop products and services
Digital twin	A real-time virtual replica of a physical object or system used for monitoring, analysis, and simulation
Disease burden	Disability-adjusted life years lost attributable to certain diseases or risk factors
Endpoint	An event or outcome that can be measured objectively to determine whether the intervention being studied is beneficial
Foundation model	A large, general-purpose AI model trained on broad data and adaptable to many specific tasks
Geroscience	An interdisciplinary field that seeks to understand the biological mechanisms of aging and how they contribute to age-related diseases. Its central premise (geroscience hypothesis) is that therapeutically addressing aging biology can prevent or delay the onset of age-related diseases, mitigate their severity, or even treat and reverse them
Hallmarks of aging	A set of cellular and molecular changes that contribute to the process of biological aging
Healthspan	Number of years that a person lives in good or great health and free of significant illness or disease
Healthy longevity	The ability to live longer while maintaining good physical, cognitive, and emotional health—essentially, extending healthspan, not just lifespan
Intrinsic capacity	Introduced by the World Health Organization and defined as "the composite of all the physical and mental capacities that an individual can draw on at any point in time"; intrinsic capacity encompasses five key domains[59]:
	1. Cognition: Assessed using tools such as the Mini-Mental State Examination
	2. Locomotion (mobility): Evaluated through tests such as the Short Physical Performance Battery
	3. Vitality (energy balance): Often measured by nutritional assessments including the Mini Nutritional Assessment
	4. Psychological: Assessed using scales such as the Geriatric Depression Scale
	5. Sensory (vision and hearing): Evaluated through standard sensory function tests
Knowledge graph	A structured network of entities and their relationships that helps organize and interpret data meaningfully
Multimodal data	Information that combines different types of data or sensory inputs, such as text, images, video, and audio, for a more comprehensive understanding
Multiomics data	The integration of data from multiple "omics" disciplines, such as genomics, transcriptomics, proteomics, and metabolomics, to gain a more comprehensive understanding of biological systems
Phenotypic data	All kinds of clinical information regarding patients' disease symptoms, as well as relevant demographic data, such as age, ethnicity, and sex
Preventive lifestyle	A proactive approach to health that focuses on reducing the risk of disease and promoting long-term well-being through regular habits and behaviors
Public health	The science and art of preventing disease, prolonging life, and promoting health on a population level through organized efforts and informed choices of society, organizations, and individuals

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