Universities-Communities:
strengthening cooperation

Aging is not a death sentence or how to live a better life during the third age

Prof., Dr. Sci. Biol., Victoria Rodinkova
Professor of the Department of Pharmacy at the National Pirogov Memorial Medical University, Ukraine (VNMU)
Head of the Laboratory of Allergenic Environmental Factors' Investigation at VNMU,
Board Member of the Ukrainian Fulbright Circle,
Member of the Scientific Council of the National Research Foundation of Ukraine,
Deputy Member of the Parliament of the Vinnytsia Region

AGEING

Process that comprises progressive physiological changes in an organism that lead to senescence – a decline of biological functions and of the organism's ability to adapt to metabolic stress.

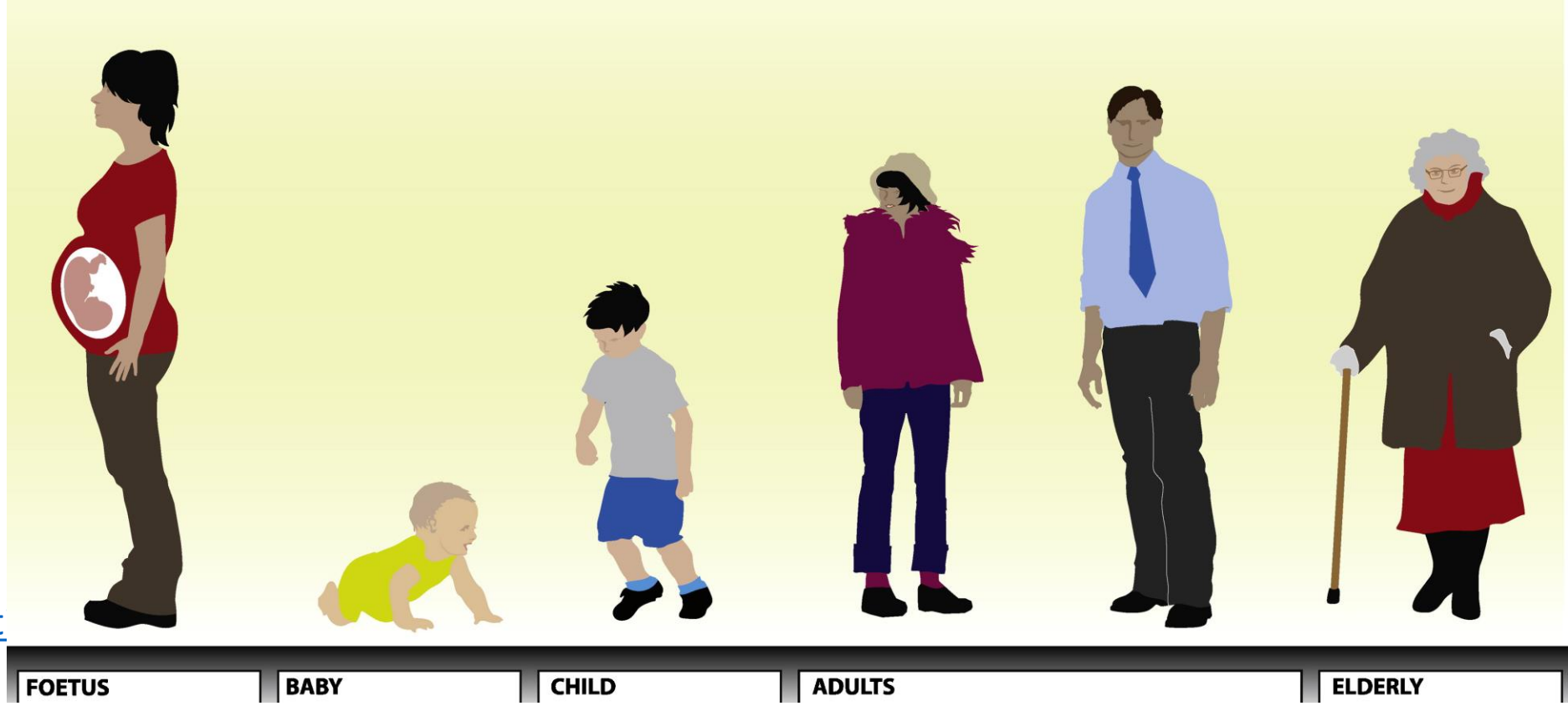
Aging goes on over the entire adult life span of any living thing and takes place in a cell, an organ, or the total organism with the passage of time.

https://www.britannica.com/science/aging-life-process

https://de.freepik.com/vektoren-kostenlos/menschliches-lebenszyklus-set_5972384.htm

Lifespan is determined by the aging rate. Aging disturbances touch homeostasis maintenance, metabolic reactions, and transduction of intra- and intercellular signals. Senescent cells, damaged organelles, and macromolecules are accumulated; epigenetic changes; and genetic instability occur.

Genetic structure of longevity



https://link.springer.com/art.1134/S2079059717040074

Ageing considers genes and signaling pathways that regulate stress response, metabolism, the growth of cells and the body, preservation of genome and proteome integrity, qualitative and quantitative mitochondrion composition, inflammatory response, apoptosis, selection of viable cells, and circadian rhythms. These changes are known collectively as the hallmarks of aging.

Hallmarks of ageing

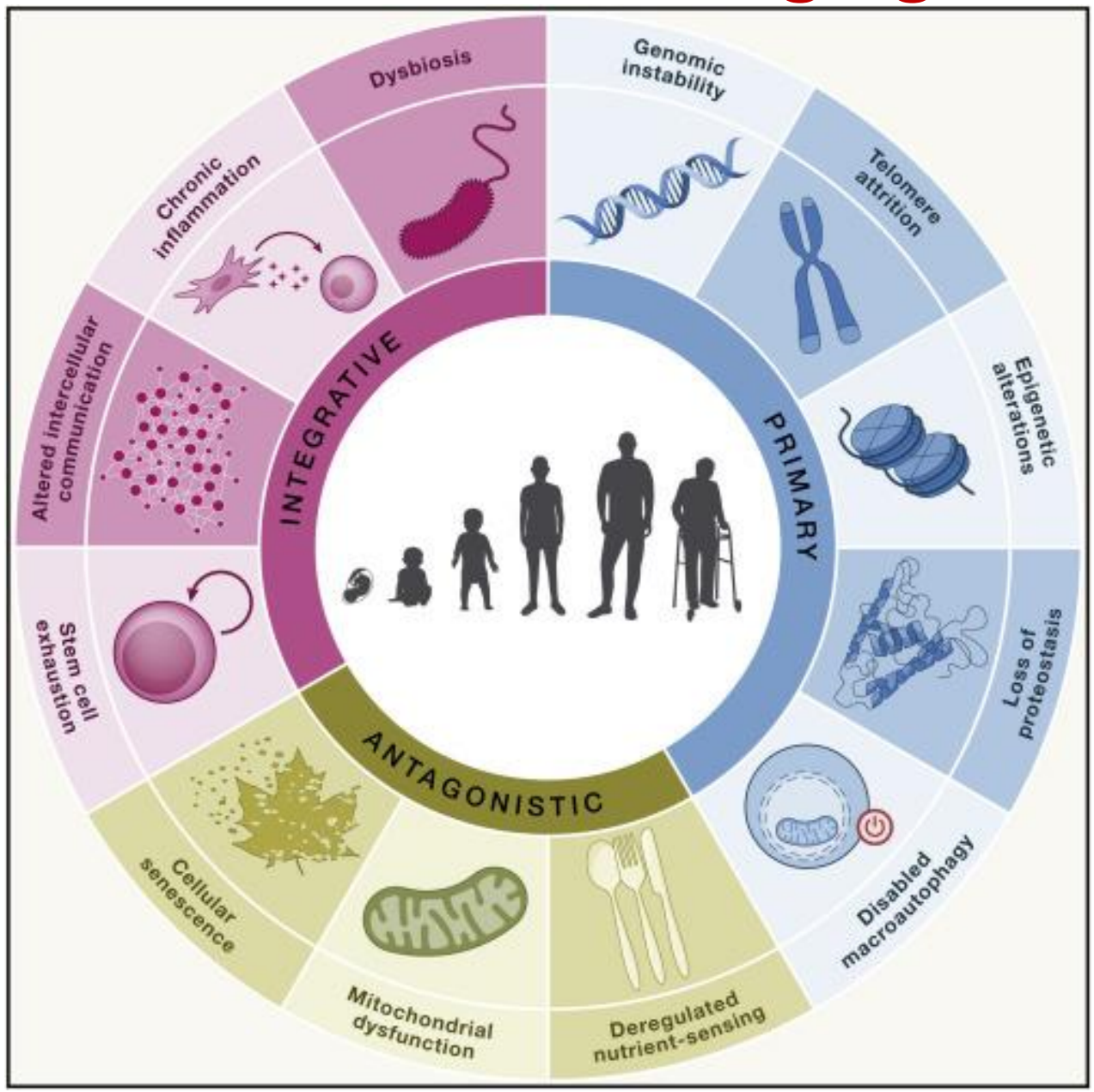
Hallmarks of aging

A global view at the candidate hallmarks of aging allows grouping them into three categories:

- primary hallmarks,
- antagonistic hallmarks,
- integrative hallmarks.

Primary hallmarks are all unequivocally negative. Antagonistic hallmarks have opposite effects depending on their intensity. At low levels, they mediate beneficial effects, but at high levels, they become deleterious. This is the case for senescence, which protects the organism from cancer, but in excess can promote aging; similarly, reactive oxygen species (ROS) mediate cell signaling and survival, but at chronic high levels can produce cellular damage; likewise, an optimal nutrient-sensing and anabolism is obviously important for survival but in excess and during time can become pathological.

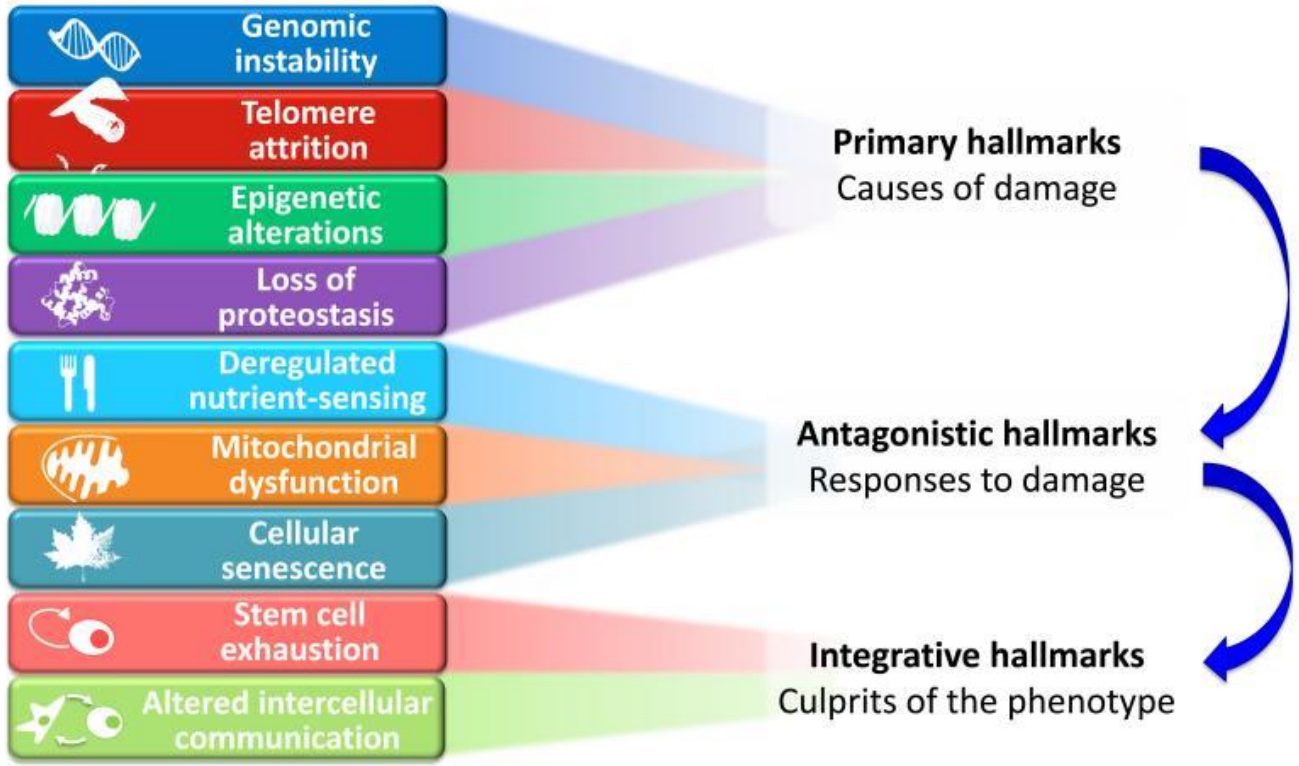
The integrative hallmarks, stem cell exhaustion and altered intercellular communication directly affect tissue homeostasis and function.



https://www.sciencedirect.com/science/article/abs/pii/S0092867422013770, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3836174/

The primary hallmarks could be the initiating triggers whose damaging events progressively accumulate with time. The antagonistic hallmarks, being in principle beneficial, become progressively negative in a process that is partly promoted or accelerated by the primary hallmarks. Finally, the integrative hallmarks arise when the accumulated damage caused by the primary and antagonistic hallmarks cannot be compensated by tissue homeostatic mechanisms. These hallmarks co-occur during aging and are interconnected, understanding their exact causal network can help to slow aging down.

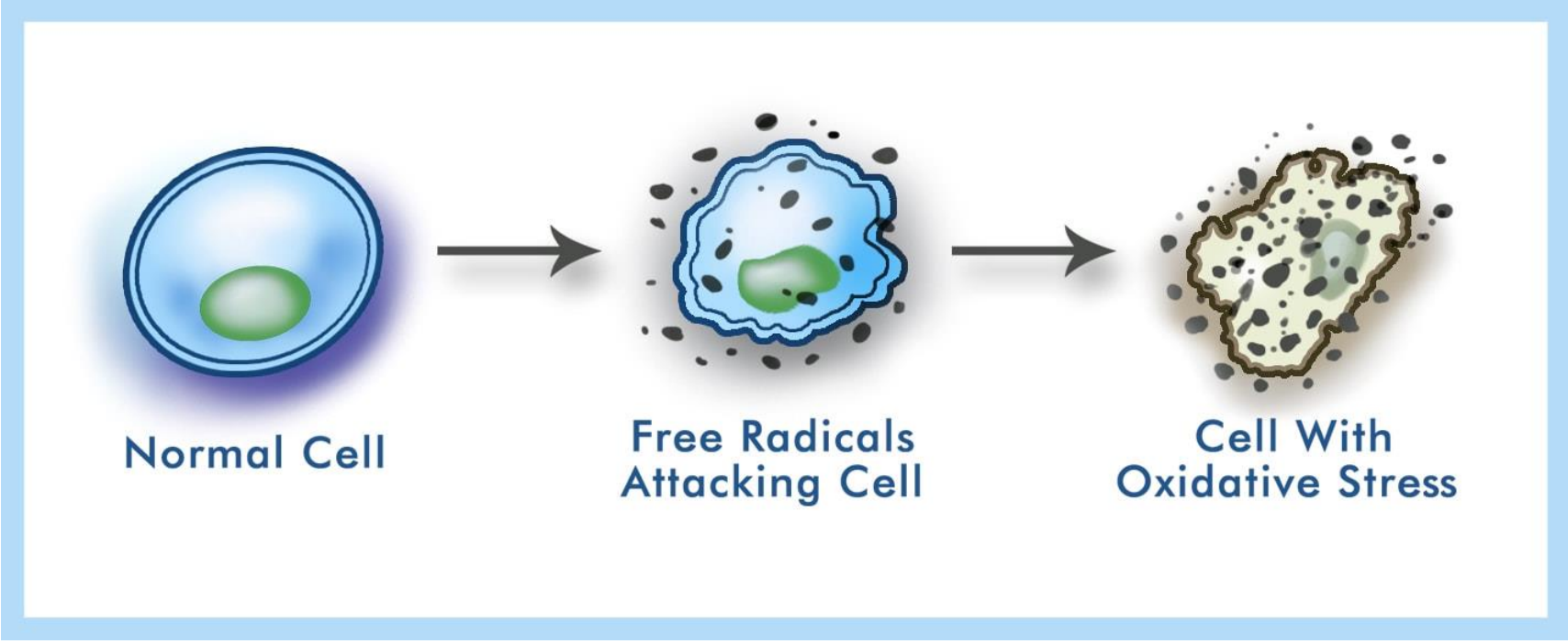
Hallmarks of aging



https://www.sciencedirect.com/science/article/abs/pii/S0092867422013770

- Genes involved in DNA repair, telomere preservation and regulation of free radicals have been identified as contributing to longevity, and when impaired, exacerbate the cellular aging of senescence. This gives the future potential of improving longevity by targeting these genes and activating or deactivating them accordingly.

Epigenetics and its changes over age



https://www.sciencedirect.com/science/article/abs/pii/S0092867422013770

The redistribution of energy resources from one pathway to another can induce or inhibit the “longevity program,” improving stress resistance and slowing down senescence. Approaches to slowing aging and achieving healthy longevity are based on the geroprotective potential of the regulation of the examined genes.

- These trends include heterochromatin recovery;
- retrotransposition suppression;
- aneuploidy elimination;
- restoration of lysosome acidity;
- telomere extension;
- suppression of chronic inflammation;
- elimination of protein crosslinks;
- elimination of senescent cells;
- recovery of NAD^+ levels;
- inhibition of cell harmful signaling (mTOR, S6K, TGFβ, and AT1 signals);
- and controlled activation of the longevity program genes (*FOXO*, *AMPK*, *PGC1α*, and *NRF2)*.

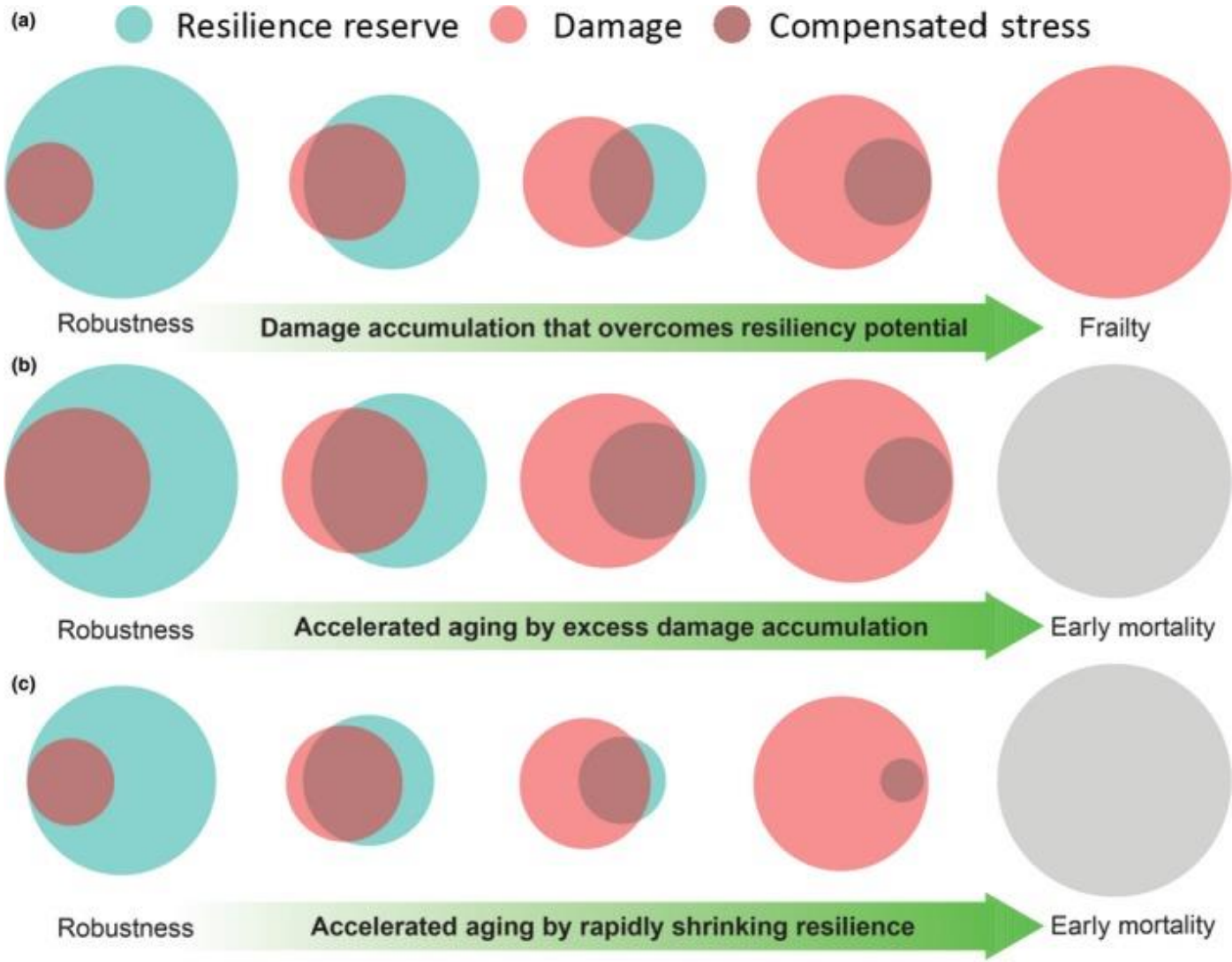
How to slow aging down

https://link.springer.com/article/10.1134/S2079059717040074

Normal aging and different pathways to accelerated aging

Robust resilience at a young age fully compensates damage (a). Over time, damage accumulates that is not fully compensated by resilience. Toward the end of life, resiliency is overwhelmed, and new stresses cause fast, unopposed damage accumulation that leads to frailty and eventually to death.

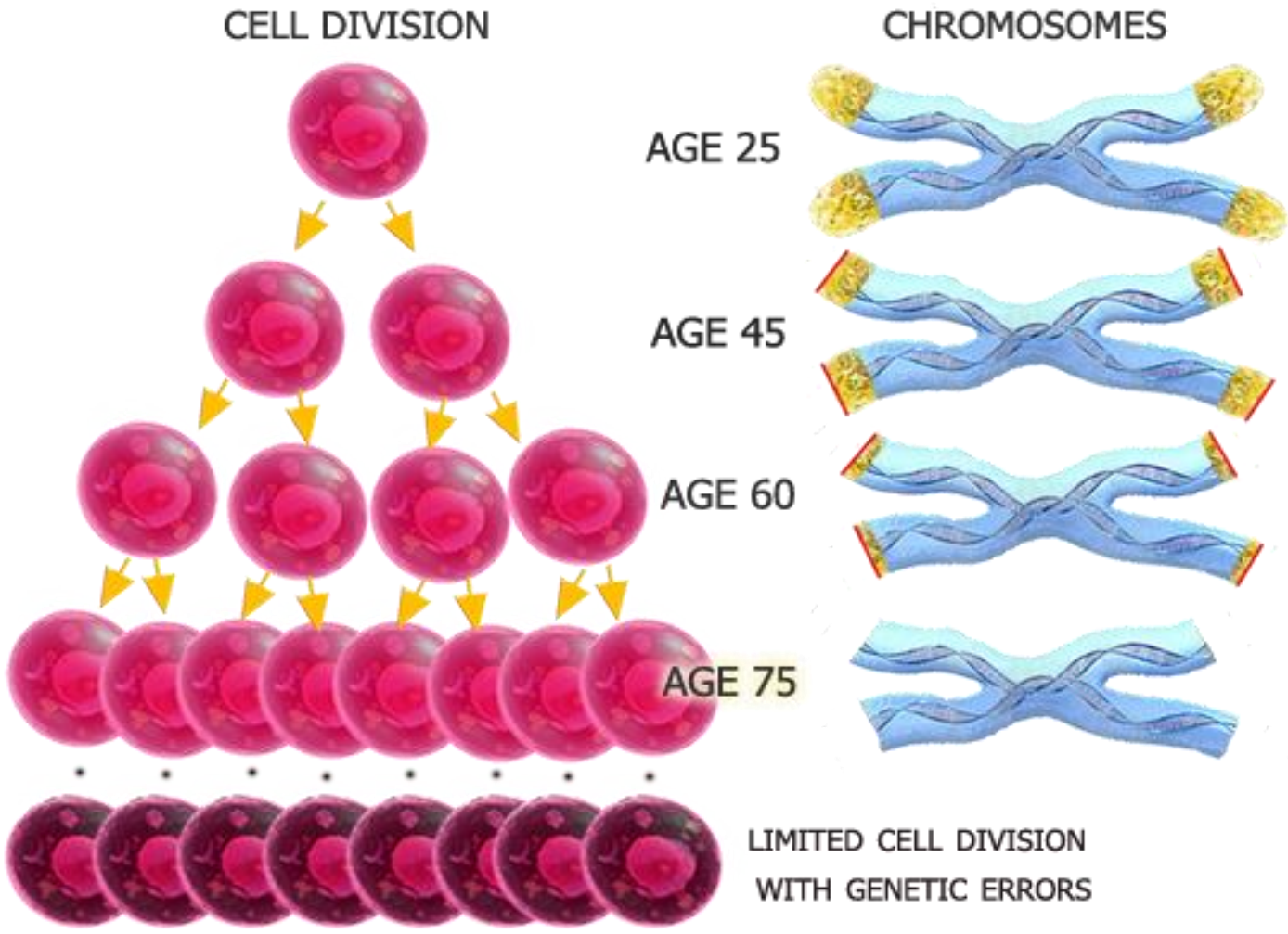
Accelerated aging may occur either because of faster rates of damage accumulation (b) or because of rapid shrinking and eventual collapse of resilience (c).



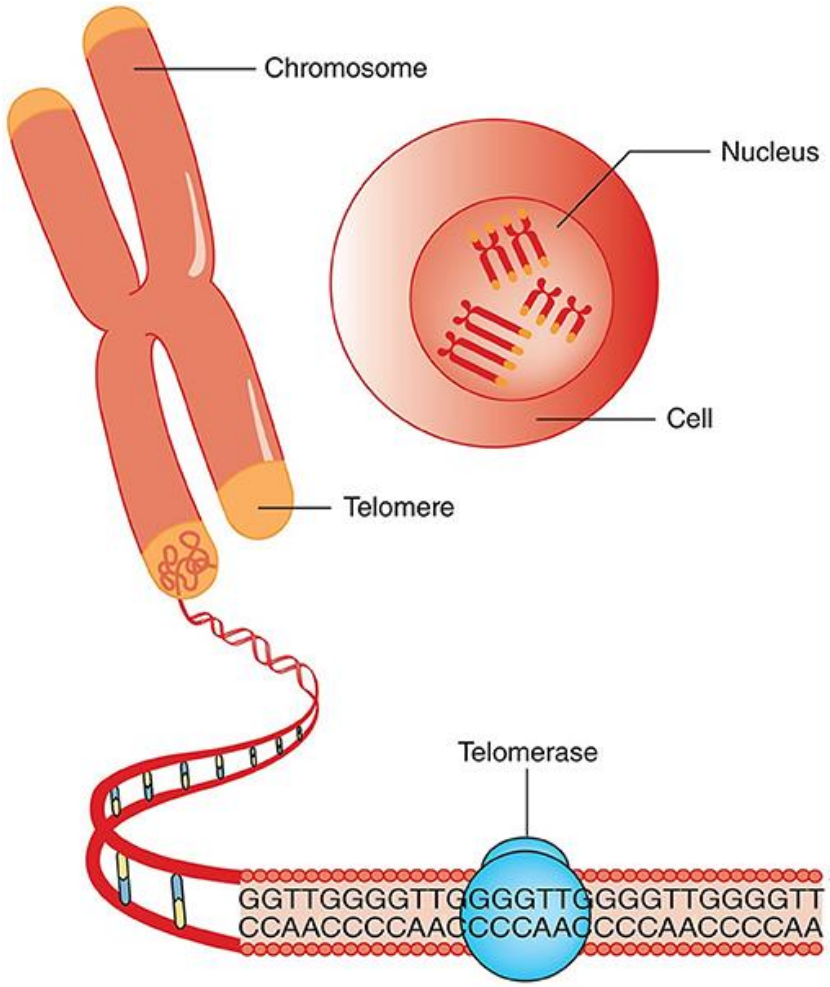
https://www.britannica.com/science/aging-life-process,
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6996955/

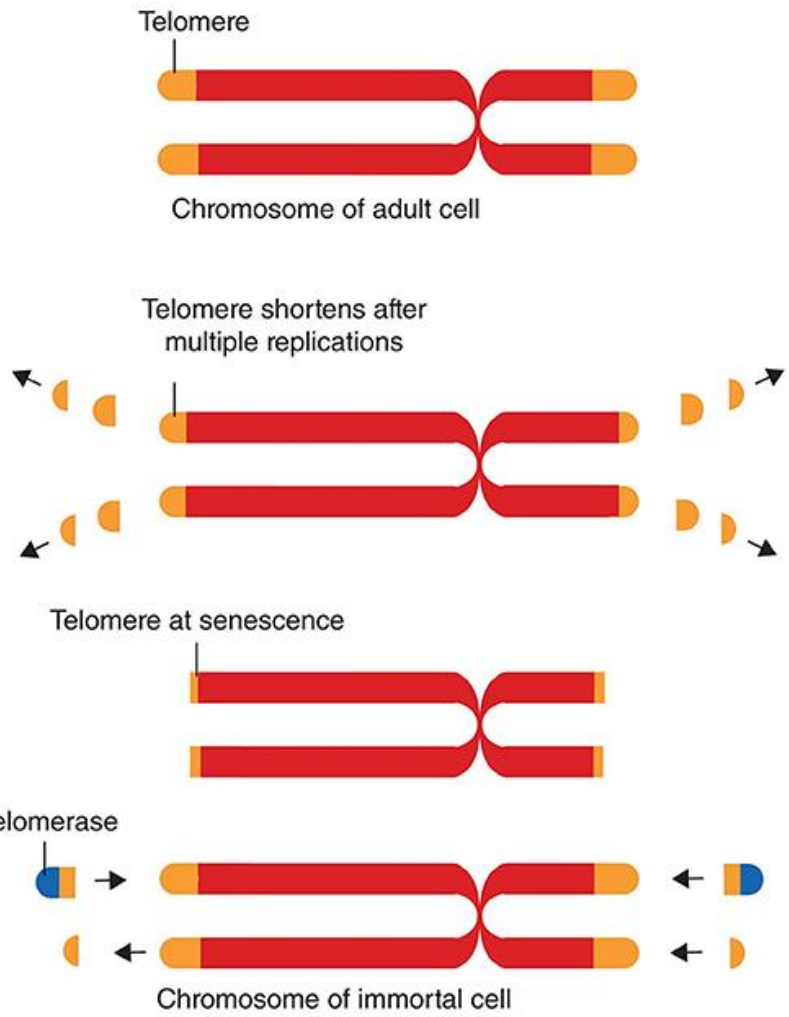
Hayflick limit

- is the limit of somatic cell division, named after its discoverer, Leonard Heyflick. In 1965, Heyflick observed that dividing human cells in cell culture die after about 50 divisions and show signs of senescence as they approach this limit. For most human cells, the Heiflick limit is 52 divisions.
- The Hayflick limit is associated with the shortening of telomeres at each somatic cell division.
- Telomeres shorten because DNA polymerase is unable to replicate the ends of the DNA molecule (telomeres are sometimes shortened by some other factors). When, after a certain number of divisions, the telomeres disappear completely, the cell usually freezes in a certain stage of the cell cycle or starts a program of apoptosis, that is, programmed death.



- This limit has been found in cultures of all fully differentiated cells of both humans and other multicellular organisms. The maximum number of divisions varies slightly depending on the type of cells and depending on the organism.
- Cells like cancer, stem cells and spermatocytes have an enzyme telomerase restoring telomeres and making these cells <u>immortal.</u>

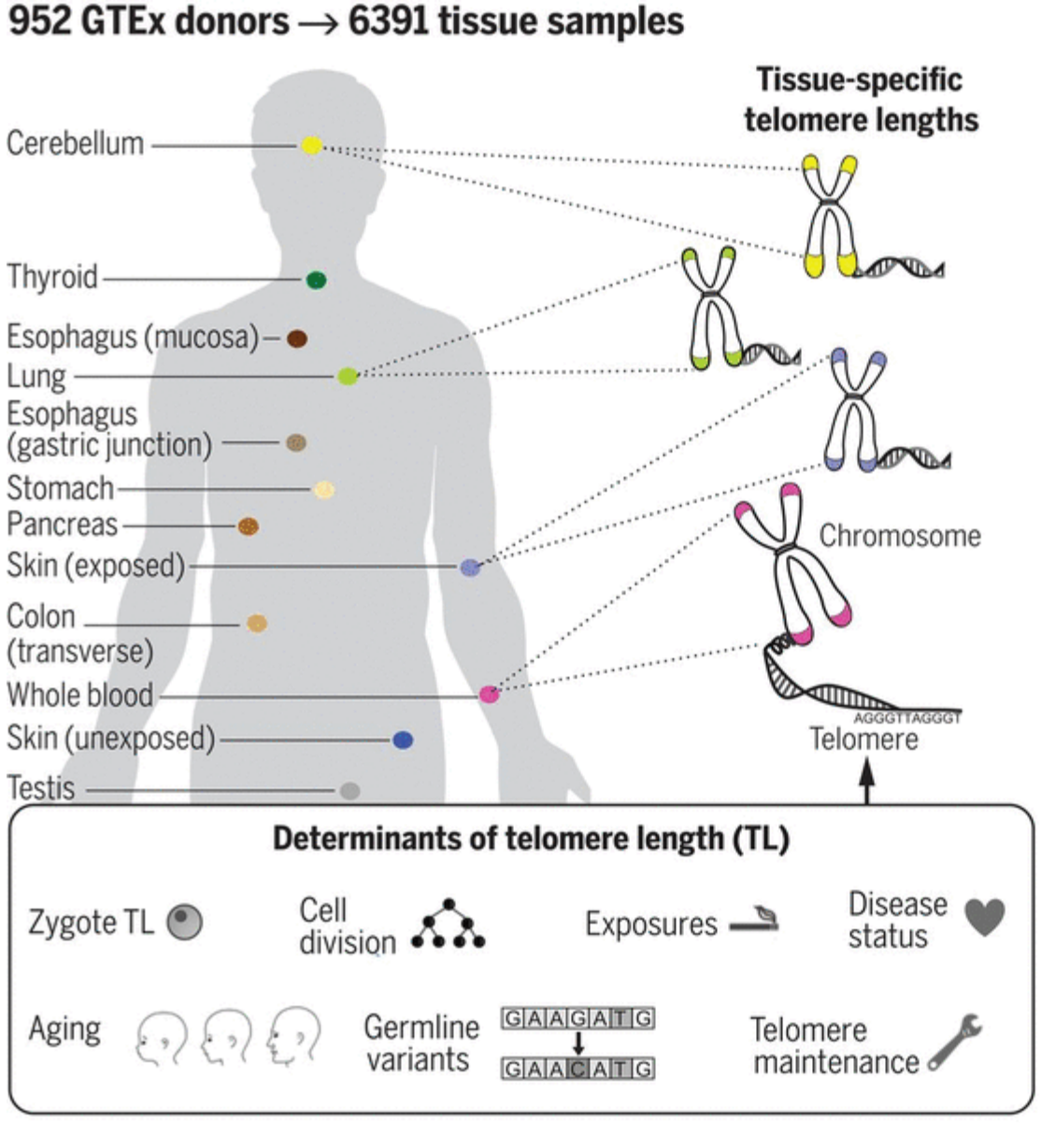


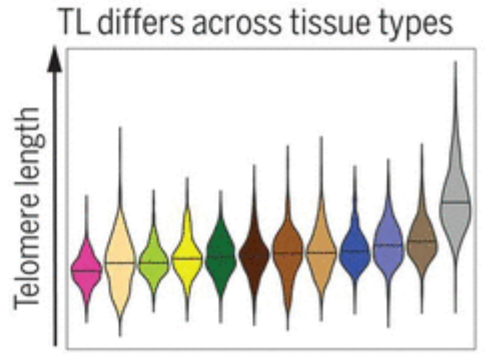


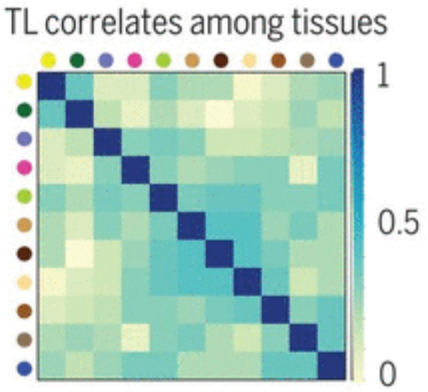
https://www.frontiersin.org/articles/10.3389/fgene.2020.630186/full

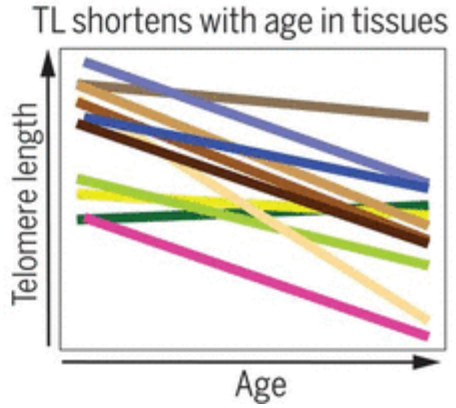
Human health and telomere length

The difference in the length of people's telomeres can indicate the general state of their health, as well as obesity, socioeconomic status and the environment in which a person developed in the uterus and lived in early childhood.





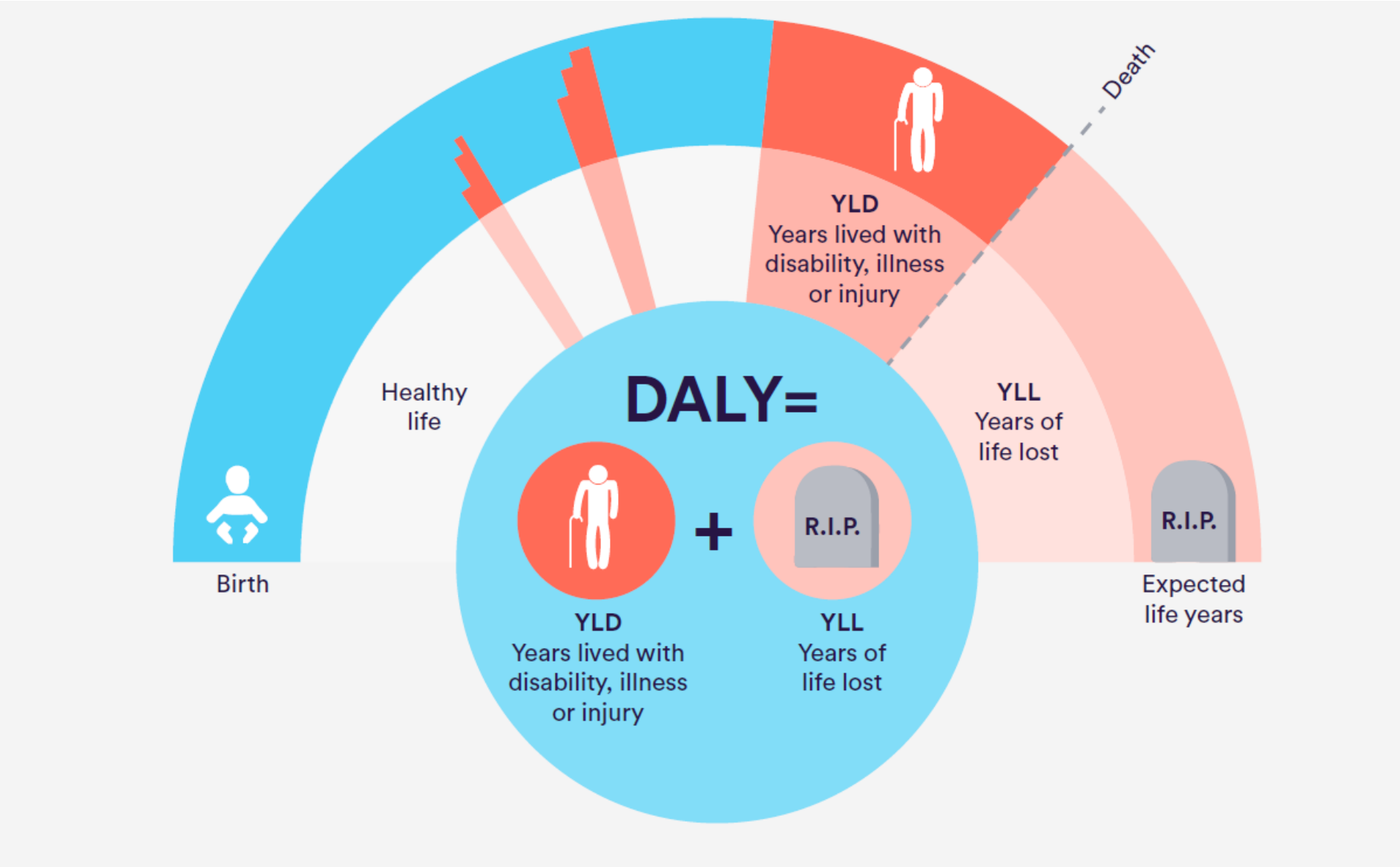




https://www.science.org/doi/10.1126/science.aaz6876

No one wants to spend their precious final years in ill-health, known as disability-adjusted life-years (DALYs), and instead the focus of the growing longevity industry is on improving healthy life expectancy. Health is influenced by genetic, lifestyle and environmental factors.

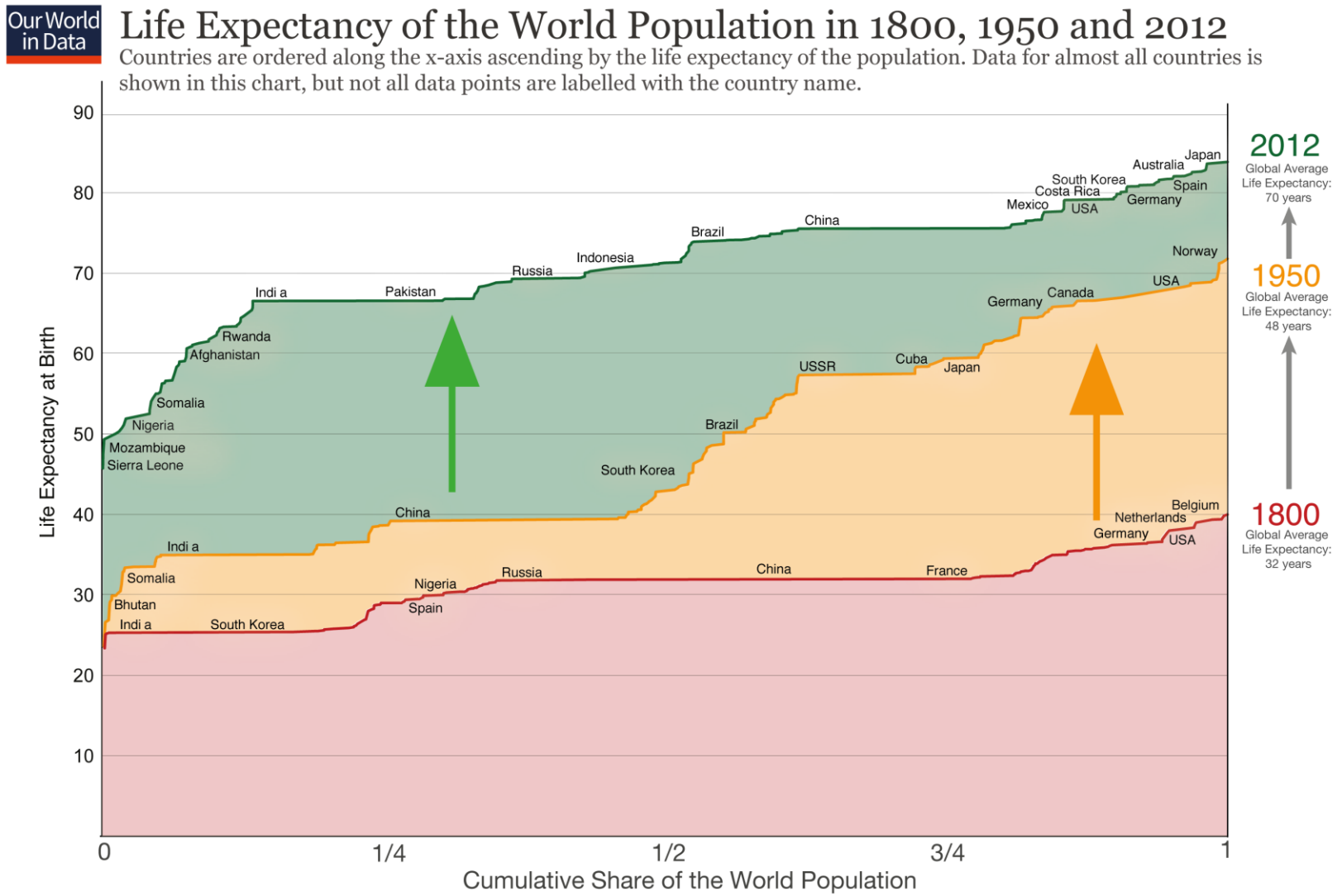
DISABILITY-ADJUSTED LIFE-YEARS



https://www.nuffieldtrust.org.uk/resource/using-dalys-to-understand-young-people-s-health

Genetics of biological ageing and longevity

- Life expectancy, or the number of years an individual can expect to live from birth, is influenced by location, sex, lifestyle, genetics and socioeconomic status. Average life expectancy has been rapidly increasing globally and is above 70 years now.
- The maximum human lifespan is thought to be around 120-150 years, although this upper limit has never been reached.



https://longevity.technology/lifestyle/to-what-extent-is-longevity-determined-by-genetics/

Data source: The data on life expectancy by country and population by country are taken from Gapminder.org.
The interactive data visualisation is available at OurWorldinData.org. There you find the raw data and more visualisations on this topic.

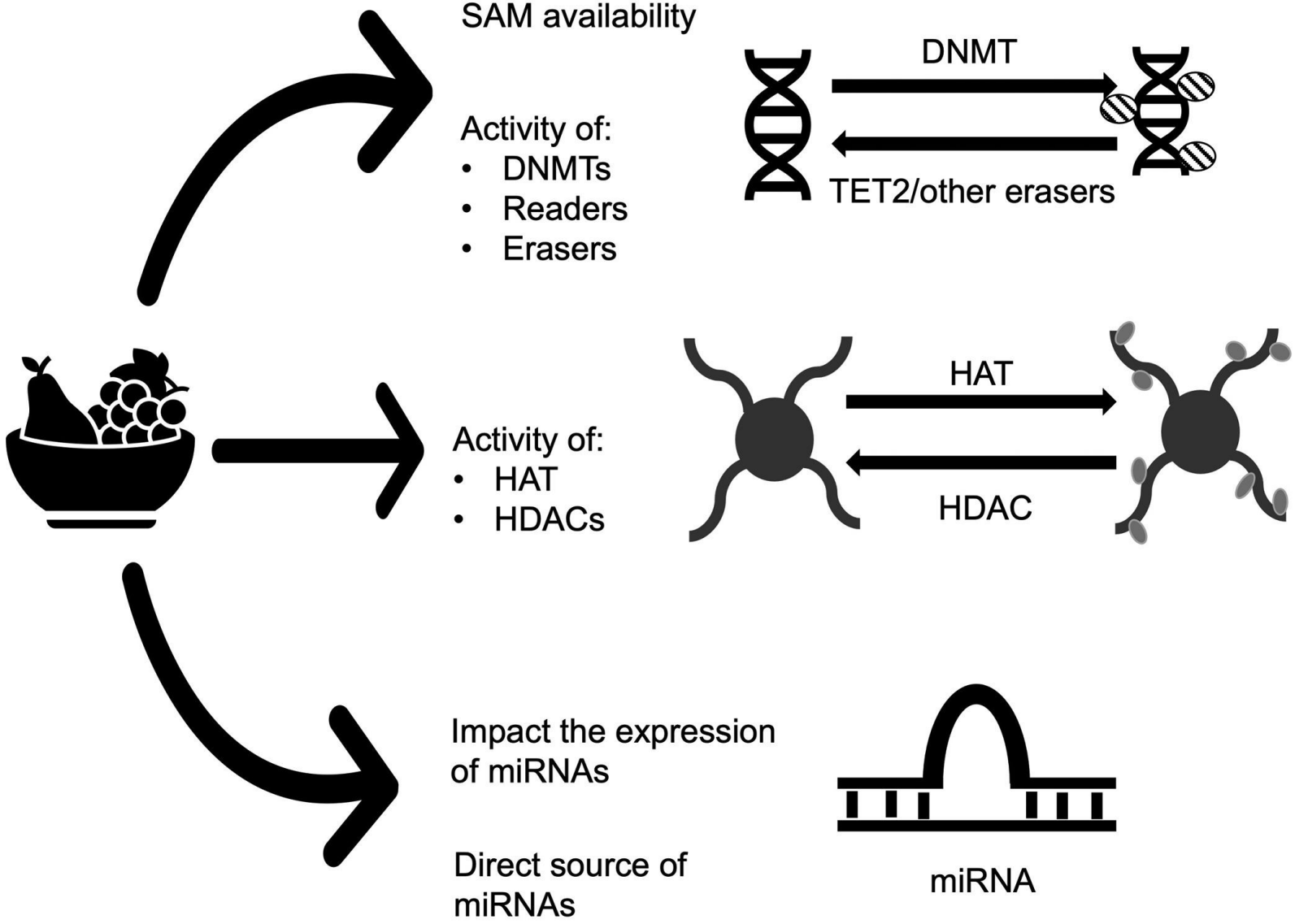
As Life expectancy increases, healthy ageing is essential

Responding to external factors like nutrition, behaviour, stress and physical activity can change how our genes are expressed, leading to targeted therapies.

For example, caloric restriction mimetics are supplements that mimic the effect of fasting on the body, targeting pathways that induce antiaging.

Nutrigemonics: Genes are not destiny

Dietary compounds have been shown to contribute directly to the alterations in DNA methylation, histone modifications and miRNA mechanisms and also via regulating the expression and activity of enzymes that modulate these mechanisms – the epigenetic writers, readers and erasers. These enzymes already are target for pharmacological interventions in a variety of cancers and with the recent identification of epigenetic targets of nutraceuticals, they are seen as potential dietary epigenomic modifiers in disease prevention.



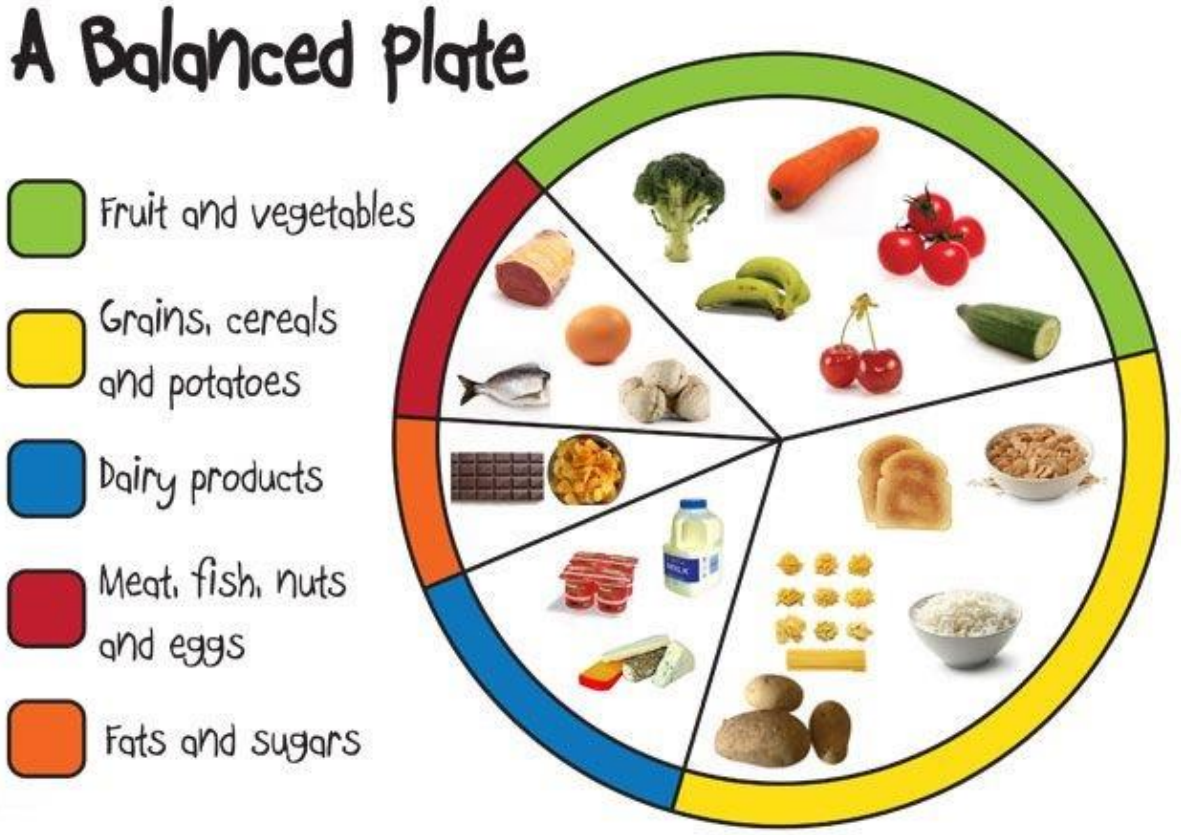
SAM, S-adenosyl-methionine; HAT, histone acetylase; HDAC, histone deacetylase; DNMTs, DNA methyl transferases; TET2, ten-eleven translocation enzyme 2.

https://www.sciencedirect.com/science/article/pii/S006526602100016X

Why diet is important ?

•Diet along with physical activity plays a key role in the development of noncommunicable chronic diseases that are responsible for > 70% of all deaths globally (World Health Organisation, 2018). Diet is also one of the key modifiable factors that can reduce the risk of developing these diseases. Nutritionists have traditionally focused on diet plans as a preventative measure to various diseases. However, most of these have been of limited success and these rarely take into account the genetically determined inter-individual variability in food metabolism. There are multiple interactions between food and genes that should be taken into account while choosing the diet.

•Gene-diet interactions are bi-directional and impact the health and disease status of the individual. The research in these interactions have led to two rapidly expanding branches of science; Nutrigenetics and Nutrigenomics.

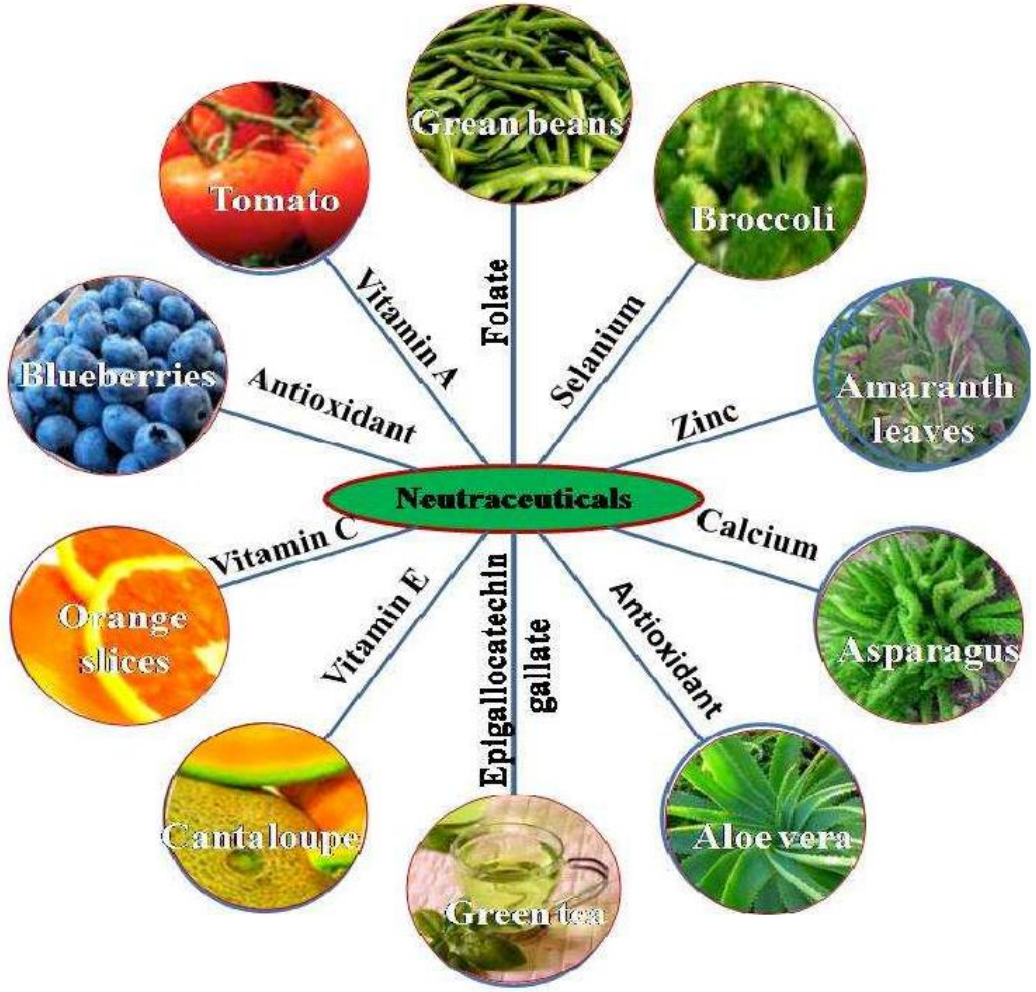


https://www.sciencedirect.com/science/article/pii/S006526602100016X , The Importance Of Healthy Eating – Our Aim | Clowns Nursery, https://www.clownsnursery.co.uk/the-importance-of-healthy-eating/

A class of nutraceuticals that has gained far more attention in the last decade is the plant-based foods. Plant-based foods are an important component of a healthy diet and studies suggest that regular intake of fruit and vegetables reduce the risk of chronic diseases and mortality. Plant food contains carbohydrates, amino acids, fatty acids, vitamins and secondary metabolites, which include biologically active chemical substances which include terpenoid/isoprenoid, phenolic, and nitrogen or sulfur-containing compounds.

Effectiveness of these compounds relies on their bioavailability (the fraction of ingested nutrient or bioactive compound that reaches the systemic circulation and ultimately utilized) and bio-accessibility (the quantity of a compound that is released from its matrix in the gastrointestinal tract, becoming available for absorption) and both of these functions vary greatly depends on multiple exogenous and endogenous factors including genetic variants.

Plant-derived nutraceuticals



Green Mediterranean diet reshapes DNA methylation, boosts metabolism

The study highlights that a polyphenol-rich MED diet can significantly regulate DNA methylation patterns by increasing key epigenetic drivers such as folic acid and vitamin B-12. Furthermore, polyphenols present in the diet have high potency in regulating one-carbon metabolism with consequences in autoimmune responses.

Green Mediterranean diet reshapes DNA methylation, boosts metabolism

Download PDF Copy

By Dr. Sanchari Sinha Dutta, Ph.D. May 30 2023

A study published in the journal *Metabolism* describes the effect of a polyphenol-rich Mediterranean diet on epigenetic regulation.

Study: A polyphenol-rich green Mediterranean diet enhances epigenetic regulatory potential: the DIRECT PLUS randomized controlled trial. Image Credit: Antonina Vlasova / Shutterstock

Background

Chronic low-grade inflammation is considered a major hallmark of various metabolic diseases, including obesity. Therefore, lifestyle interventions, such as a healthy diet and physical activity, are vital in managing body weight and reducing morbidity and mortality risks related to metabolic diseases.

Plant-based polyphenols with high antioxidant properties are known to have beneficial

ADVERTISEMENT

Trending Stories | Latest Interviews | Top Health Articles

Adopting 8 healthy habits could add decades to a person's life

Effects of turmeric supplementation in individuals with metabolic syndrome and diabetes

MIT expert calls for a total overhaul of the U.S. health insurance system

https://www.news-medical.net/news/20230530/Green-Mediterranean-diet-reshapes-DNA-methylation-boosts-metabolism.aspx?utm_source=azonetwork_newsletter&utm_medium=email&utm_campaign=genomics_newsletter_12_june_2023

Personal genomics

Personal genomics is an area of genomics focusing specifically on the sequencing and analysis of one person's genome, and then giving them their genomic information.

The Human Genome Project sequenced DNA pooled from a range of individuals, to create an average or 'reference' genome. However, every genome is unique, and, with the development of DNA sequencing technologies, it is now becoming practical and affordable for individuals to choose to get their genomes sequenced. This is called personal genomics.

Medical Genomics (Genomic Medicine)

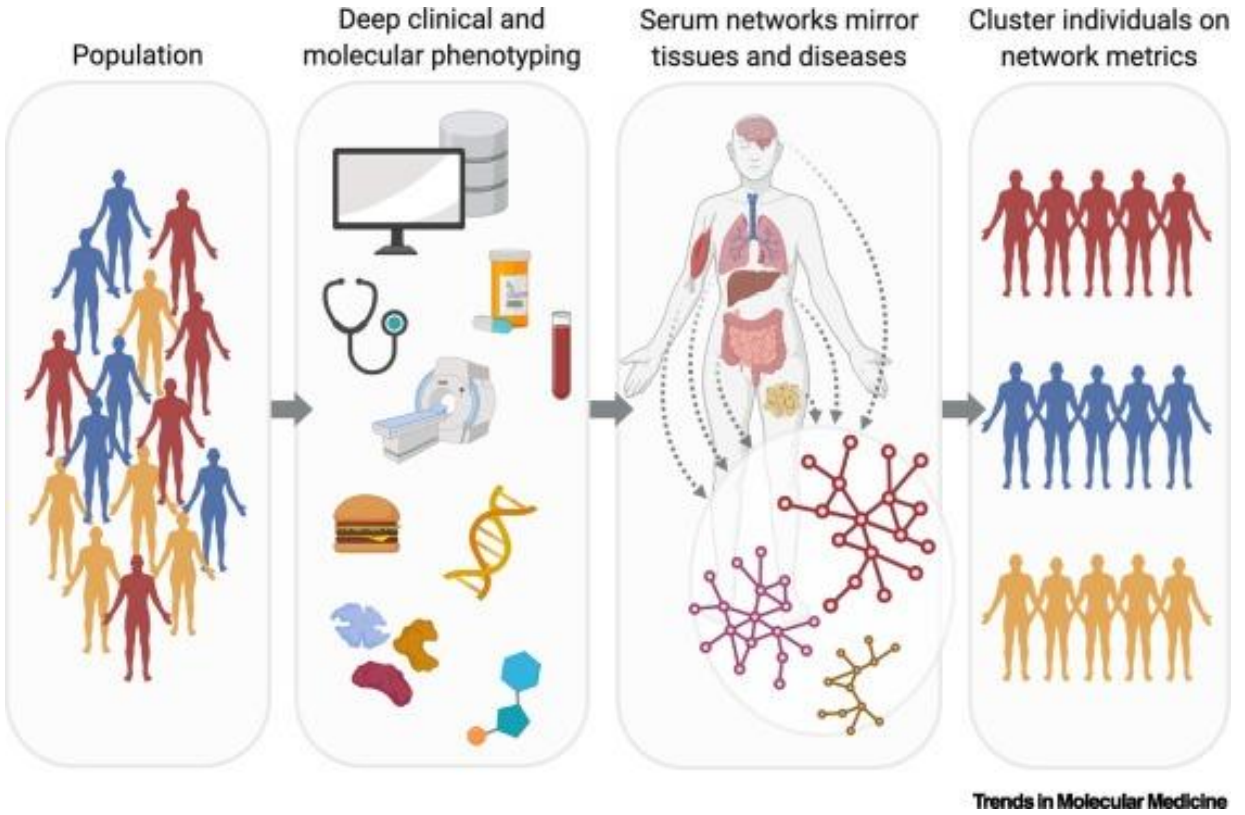
Genomic medicine is a medical discipline that involves using a person's genomic information as part of their clinical care. Other similar terms include individualized medicine, personalized medicine and precision medicine. For some conditions, genomic information can be used to help diagnose disease, predict outcomes and guide treatment.

Genomic information is only one piece of the puzzle of why some people get a disease and some don't. But it's a piece we can measure very accurately that can help us in treating and even preventing diseases. Other factors are also important, such as the habits people practice and the possibly harmful things they're exposed to in their environment over their lifetime. Scientists are learning more and more about how all these factors work together in keeping us healthy or causing disease, and are beginning to apply this knowledge in targeted ways that can individualize or personalize the care that doctors provide to do a better job at choosing the right test or treatment for the right patient at the right time. This is what makes genomically directed medicine truly precision medicine.

https://www.genome.gov/genetics-glossary/Genomic-Medicine

Precision medicine

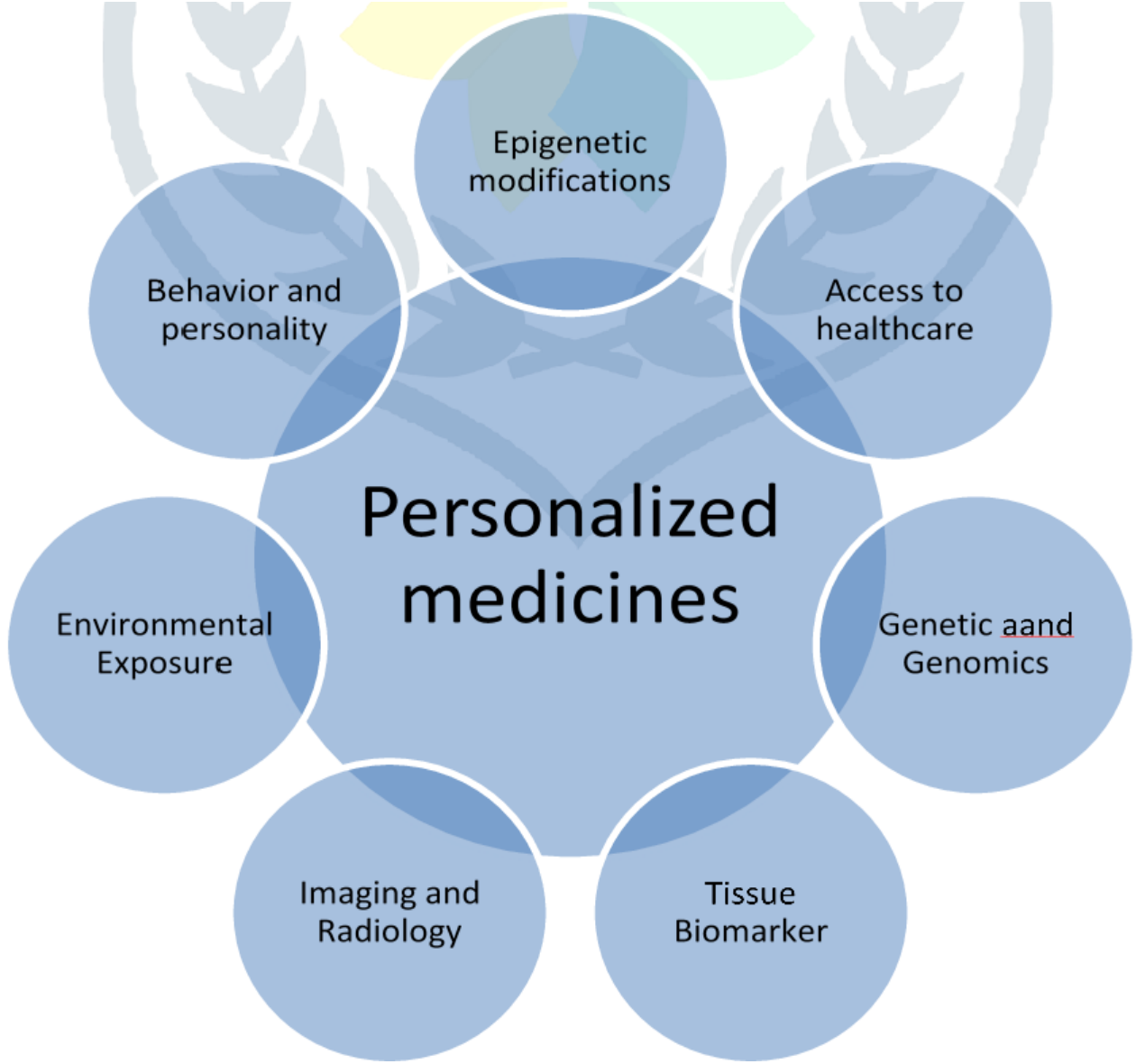
- Precision medicine (generally considered analogous to personalized medicine or individualized medicine) is an innovative approach that uses information about an individual's genomic, environmental and lifestyle information to guide decisions related to their medical management. The goal of precision medicine is to provide more a precise approach for the prevention, diagnosis and treatment of disease.
- Precision medicine or precision healthcare is medical care that takes advantage of large data sets of individuals such as their genome or their entire electronic health record to tailor their healthcare to their unique attributes. It is common sense that no two individuals are the same, and so they should not get the same healthcare. Precision healthcare embodies that simple idea.



https://www.genome.gov/genetics-glossary/Precision-Medicine

Personalized medicine

is an emerging practice of medicine that uses an individual's genetic profile to guide decisions made in regard to the prevention, diagnosis, and treatment of disease. Knowledge of a patient's genetic profile can help doctors select the proper medication or therapy and administer it using the proper dose or regimen. Personalized medicine is being advanced through data from the Human Genome Project.

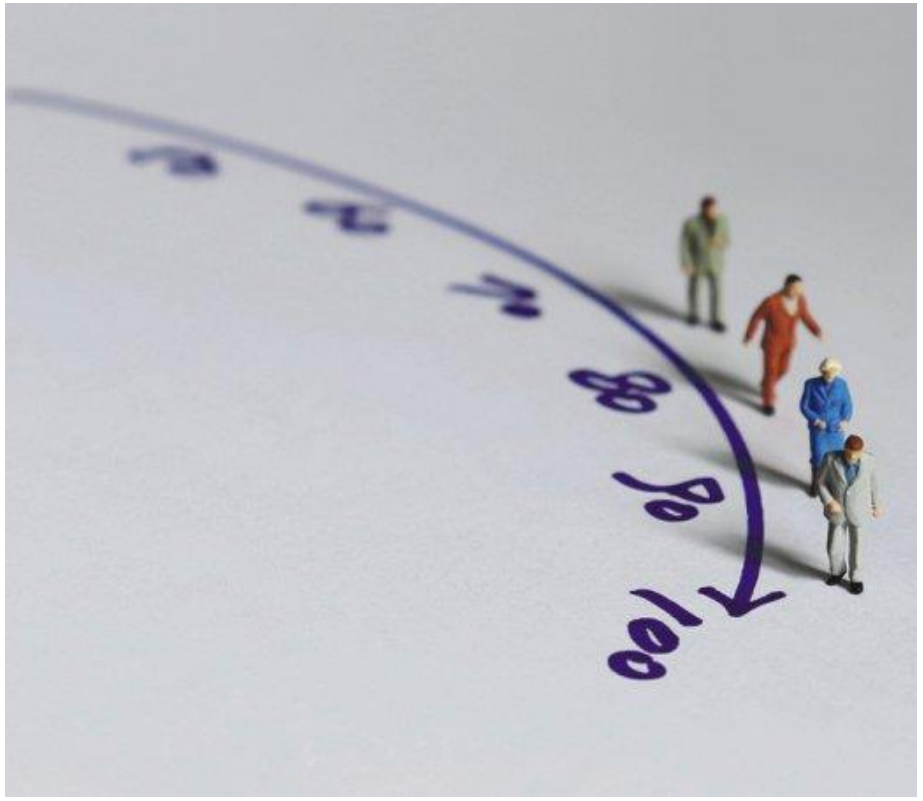


https://www.genome.gov/genetics-glossary/Personalized-Medicine, https://www.semanticscholar.org/paper/Personalized-Medicine-%E2%80%93-A-Valuable-Tool-in-Dhingra-Chopra/da85665482e309a9be9844f70c656cc97288acf1

What is so super about ageing?

Modern science says:

- Cells of the nervous system renew
- Graying of hairs is irreversable
- age-related cognitive decline is not inevitable. adults classified as superagers exist
- Limits of age periods are expanding



https://www.nih.gov/nih-style-guide/age#:~:text=The%20following%20are%20the%20American%20Medical%20Associations%E2%80%99%20age,years%20or%20older%29%20Older%20adults%20%2865%20and%20older%29%2A – age classification

What is so super about ageing?

Research data on ageing show that age-related cognitive decline is not inevitable. Studies have identified a remarkable group of older adults who display a youthful memory function—superagers. Their phenotype includes several previously unobserved differences between superagers and typical older adults across multiple domains, including motor skills and mental health. Traditionally, superagers have been defined using delayed recall performance on verbal list learning tasks on which superagers aged between 65–80 years or older perform equivalently to middle-aged adults (50–60 years old), adults aged 30–44 years, or young adults (18–32 years old).

The authors report less grey matter loss in multiple brain regions typically associated with learning and memory, primarily in the medial temporal lobe, which is consistent with previous research. Previous studies have reported greater cortical thickness and better brain network functional connectivity in the anterior mid-cingulate cortex in superagers than in age-matched peers. Resilience to Alzheimer's disease in superageing is observed, although the mechanisms underlying this resilience remain unknown.

https://www.thelancet.com/journals/lanhl/article/PIIS2666-7568(23)00103-4/fulltext

Using a computer model, evolutionary biologists at the HUN-REN Centre for Ecological Research (Hungary) have demonstrated that under the right circumstances, senescence can support the response to the directional selection and assist the adaptation to the changed environmental factors.

Széchenyi Terv Plusz Építsük együtt Magyarországot!
Magyarország Kormánya
Az Európai Unió finanszírozásával NextGeneration EU

2023. 11. 13.

SENESCENCE CAN ACCELERATE EVOLUTION

https://ecolres.hu/en/hun-ren-cer-scientists-prove-that-senescence-can-accelerate-evolution/
https://bmcbiol.biomedcentral.com/articles/10.1186/s12915-023-01716-w

The Secrets to Successful Aging

U.S. INTERNATIONAL CANADA ESPAÑOL 中文

The New York Times

1. For successful aging, recognize one's issues and adapt accordingly.
2. longevity starts with nutrition. The more your gut microbiome changes, the better.
3. 'Cognitive Super-Agers' may hold clues to how we can keep our brains in shape.
4. The sweet spot for longevity lies around 7,000 steps a day (or 30 minutes of exercise).
5. Older couples are thriving while 'living apart together.'
6. Reducing stress and avoiding jerks is important

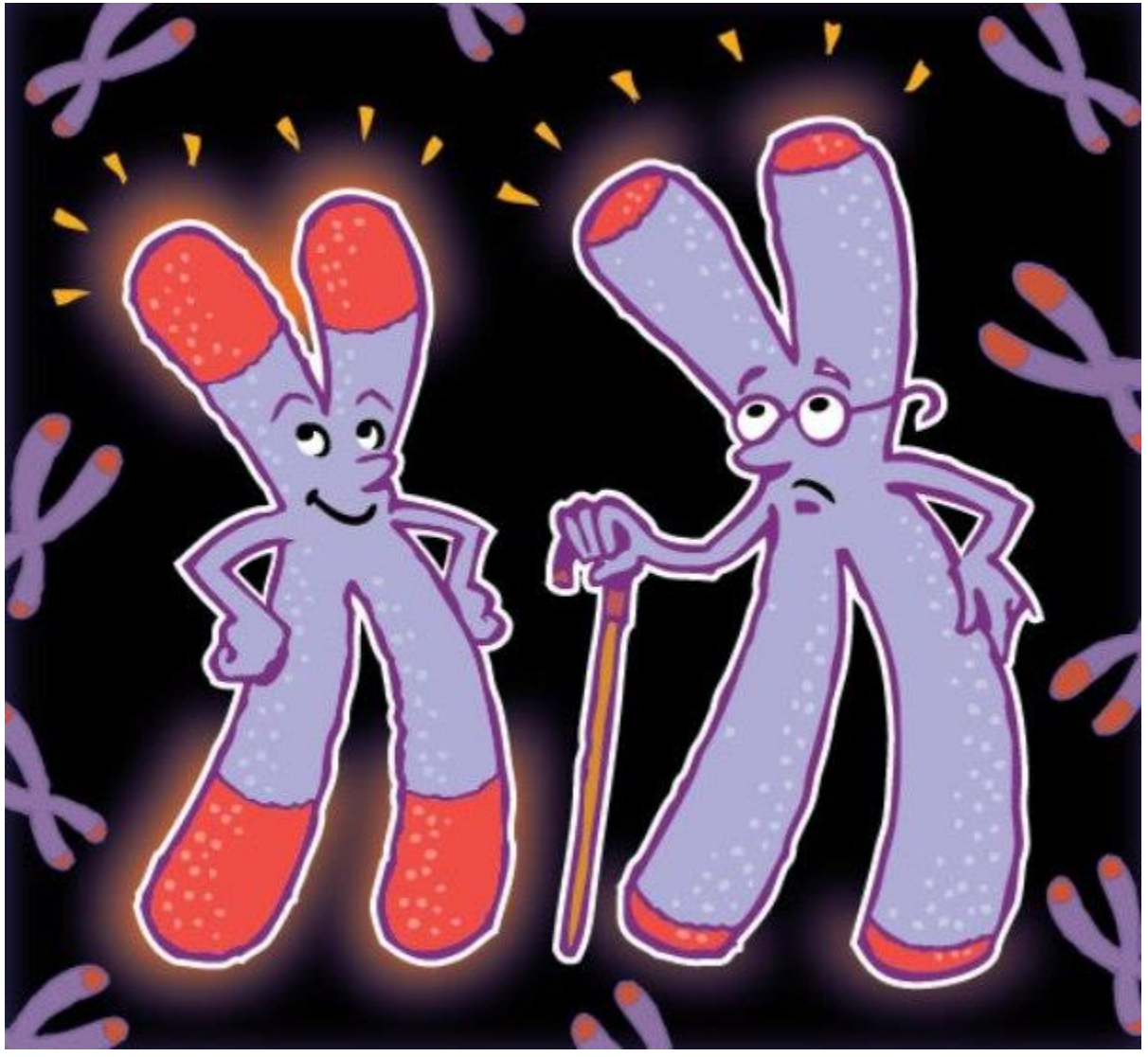
https://www.nytimes.com/2021/12/31/well/live/aging-advice.html

“Science is showing that while chronological aging is inevitable, biological aging is malleable. There's a part of it that you can fight, and we are getting closer and closer to winning that fight”.

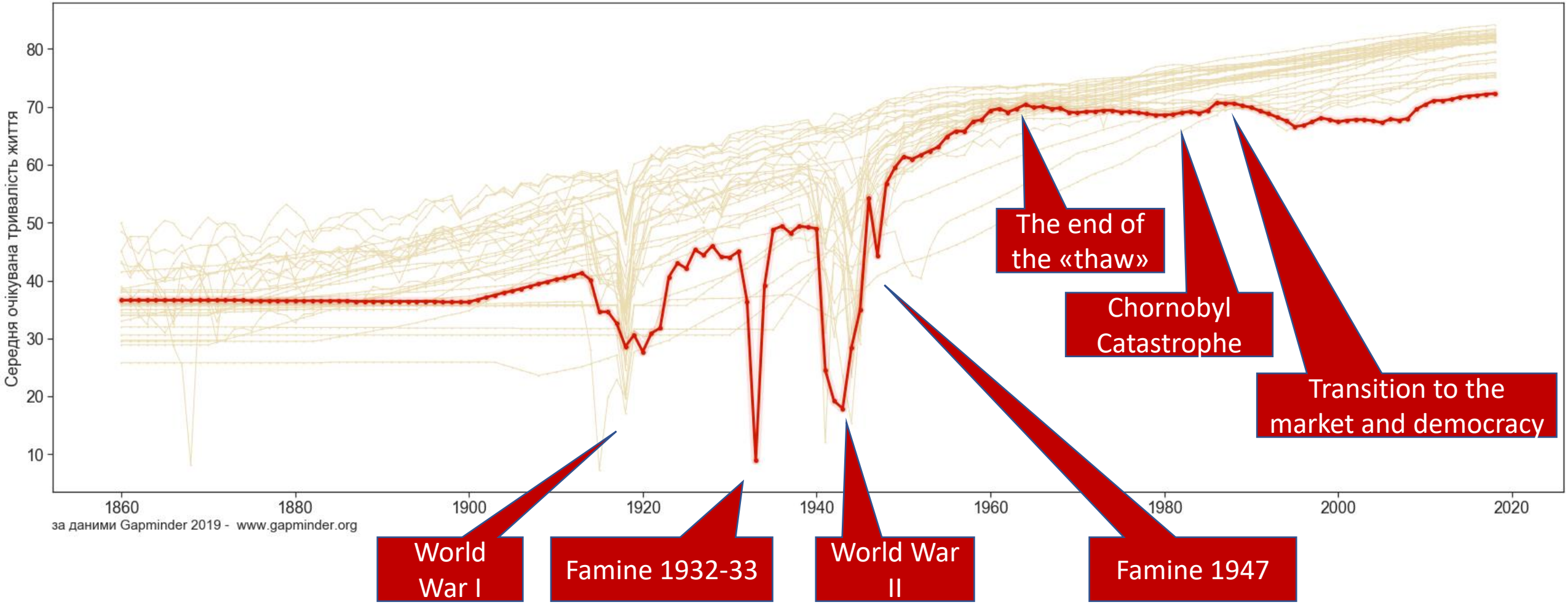
Eric Verdin, MD, Buck Institute
President and CEO

https://www.dailydemocrat.com/2020/07/06/our-shields-are-up-but-they-grow-weaker-as-we-age/

THANK YOU FOR ATTENTION!

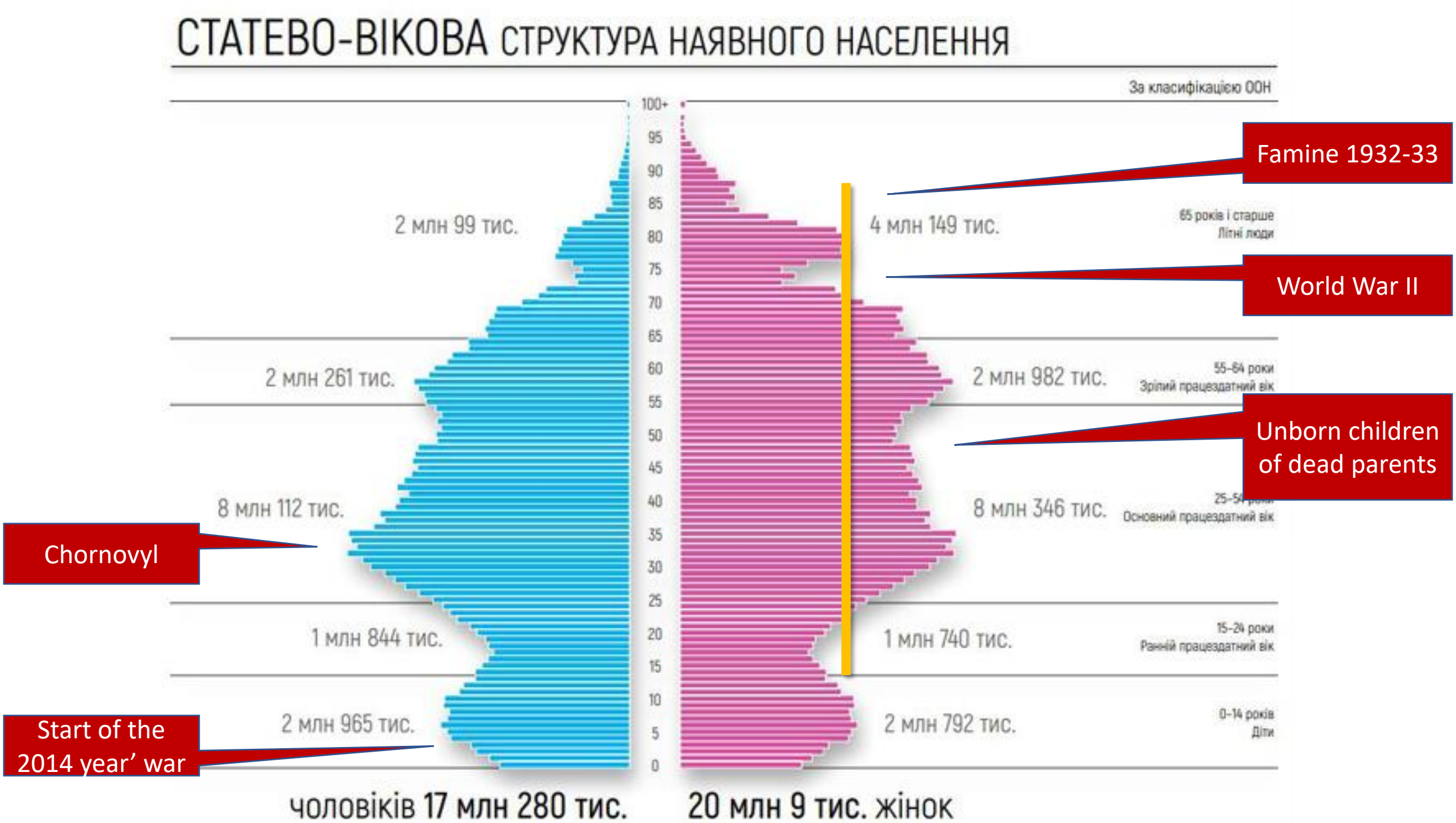


Ukraine* and other European countries. Average life expectancy at birth. 1860-2020



За горизонтами видимості: стратегічні виклики для України. Безпека, культура та управлінська спроможність проти загроз середини XXI століття.
Євген Глібовицький. Лекція, 16 грудня 2020

* Дані з Російської імперії/СРСР; українське населення територій Османської імперії, Австро-Угорщини, міжвоєнної Польщі, Чехословаччини та Румунії не включені; Крим 1954-2013


СТАТЕВО-ВІКОВА СТРУКТУРА НАЯВНОГО НАСЕЛЕННЯ
За класифікацією ООН
100+
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
2 млн 99 тис.
4 млн 149 тис.
65 років і старше
Літні люди
2 млн 261 тис.
2 млн 982 тис.
55–64 роки
Зрілий працездатний вік
8 млн 112 тис.
8 млн 346 тис.
25–54 роки
Основний працездатний вік
1 млн 844 тис.
1 млн 740 тис.
15–24 роки
Ранній працездатний вік
2 млн 965 тис.
2 млн 792 тис.
0–14 років
Діти
чоловіків 17 млн 280 тис.
20 млн 9 тис. жінок
Famine 1932-33
World War II
Unborn children of dead parents
Chornovyl
Start of the 2014 year’ war

Russian aggression against Ukraine.
Losses of Ukrainian population are ongoing…..

United Nations | Department of Economic and Social Affairs

World Population Prospects 2019

UN predicted in 2019 that population of Ukraine will increase due to migration processes promoted by economical reasons in neighboring countries and climate change

https://population.un.org/wpp/Publications/Files/WPP2019_Volume-I_Comprehensive-Tables.pdf

https://population.un.org/wpp2019/Graphs/900

Multicultural society is expected in Ukraine

Life Expectancy Prospects in Ukraine and in the world