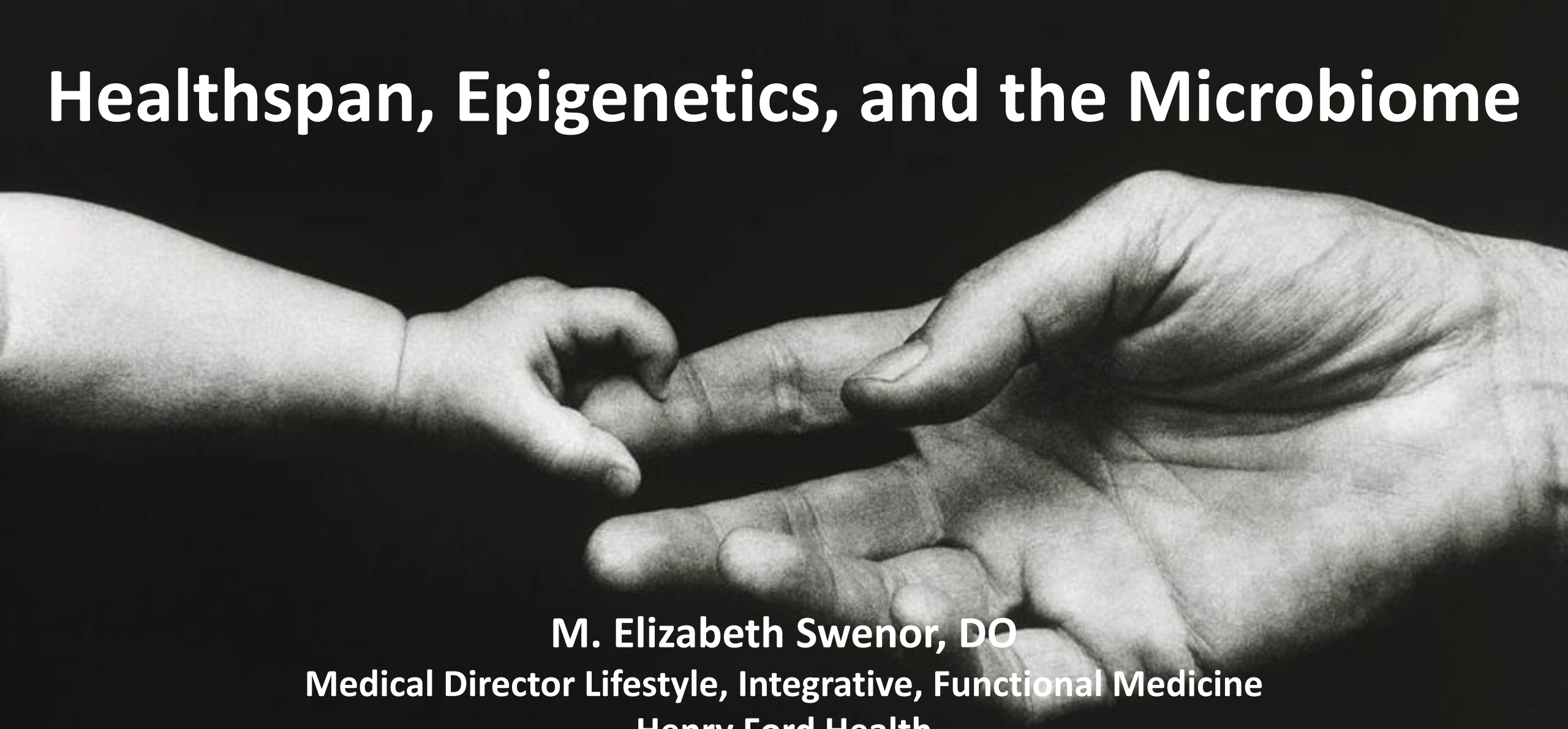
Healthspan, Epigenetics, and the Microbiome



M. Elizabeth Swenor, DO
Medical Director Lifestyle, Integrative, Functional Medicine
Henry Ford Health

May 21, 2025

I have no financial disclosures

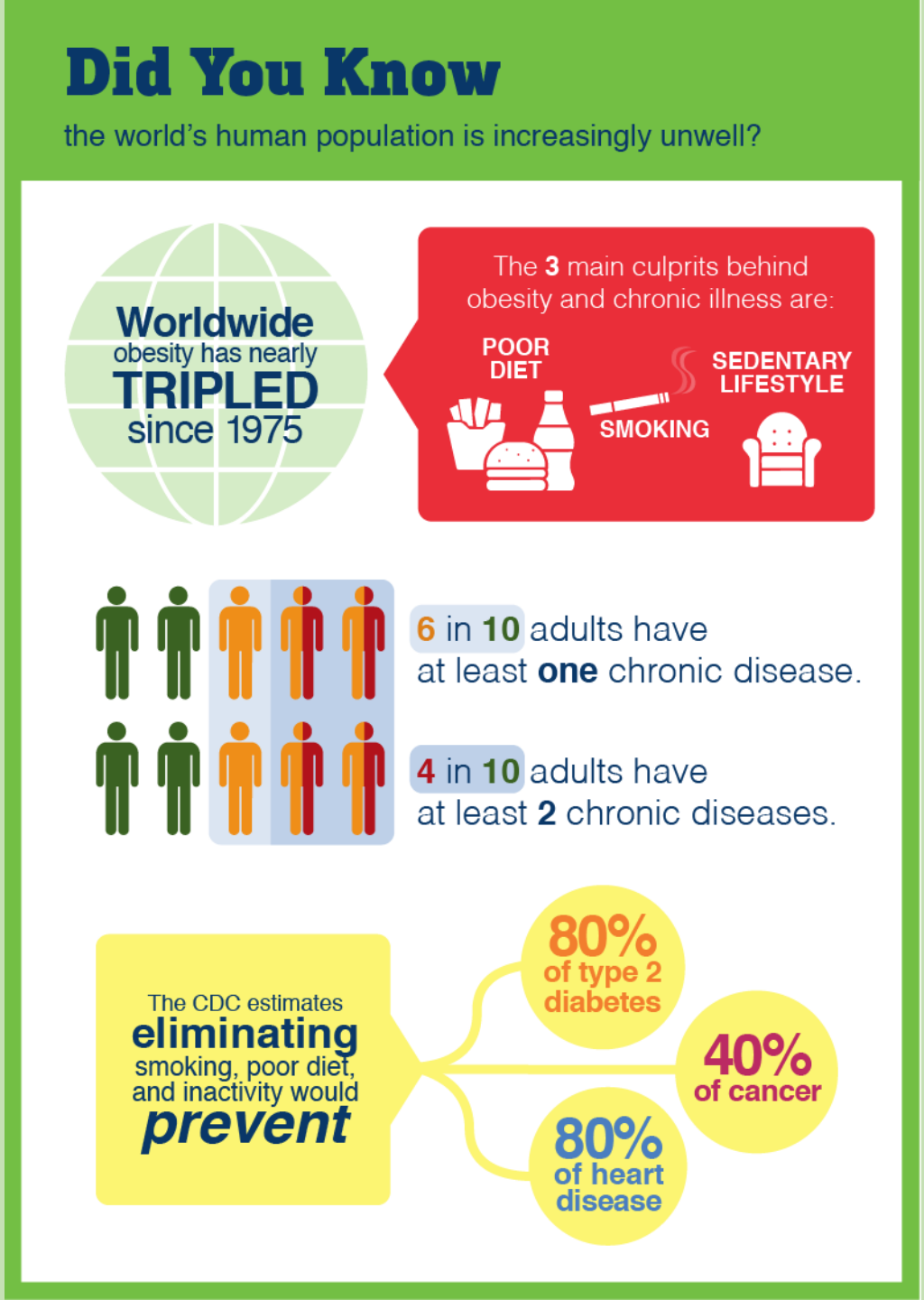
Objectives

1. Define Epigenetics, Lifespan, Healthspan, Transgenerational Inheritance, and the Human Microbiome

2. Discuss lifestyle modification for optimizing human healthspan, microbiota health, and reducing health risks of stress driven aberrant epigenetic changes

Human Microbiome Interplay

Chronic diseases are responsible for 7 in 10 deaths each year.



Most chronic diseases can be prevented by eating well, being physically active, avoiding tobacco and excessive drinking, and getting regular health screenings.

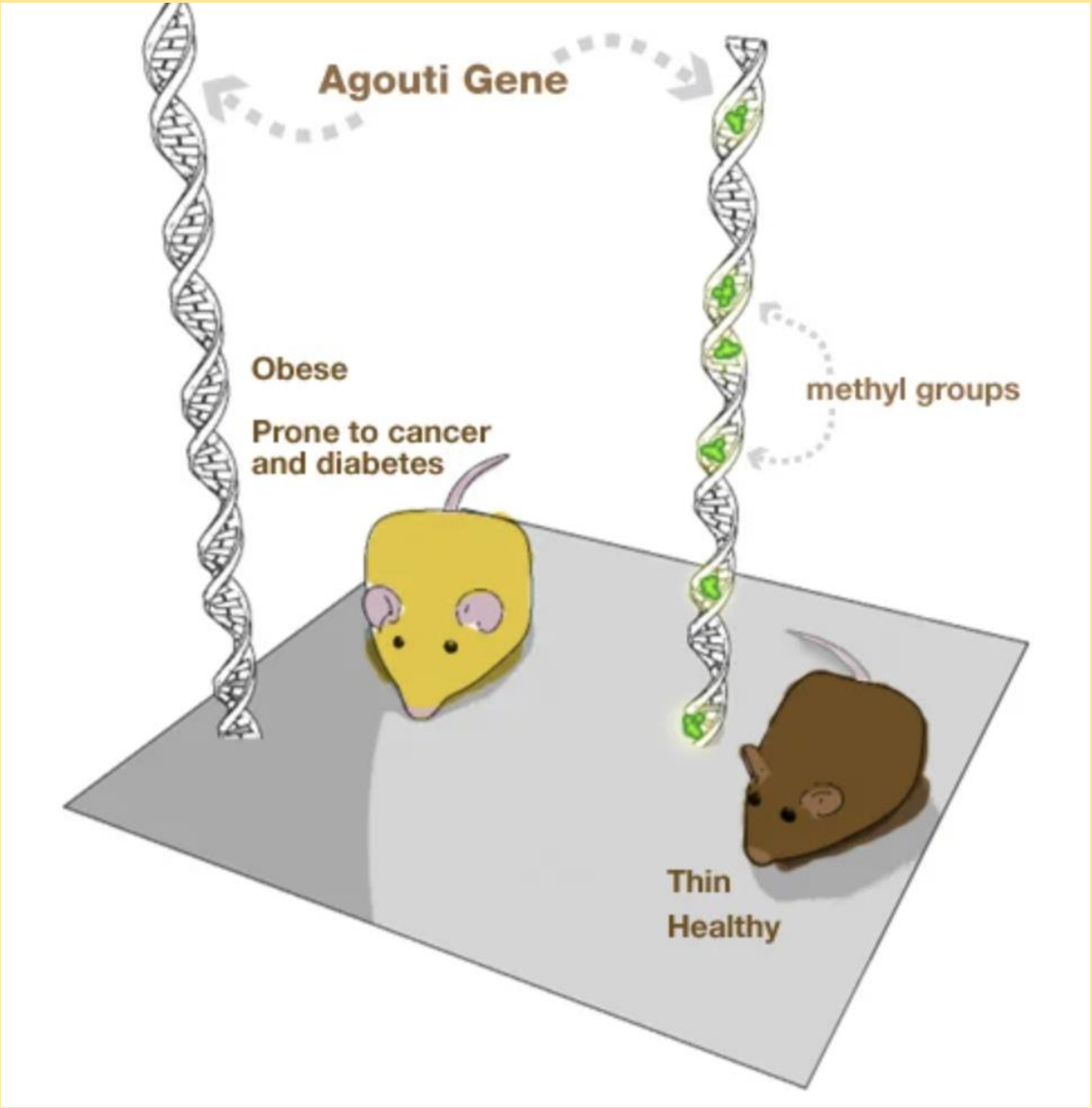
Sarah 62 yo Caucasian Female
CC: morbid obesity, fatigue, weight gain, uncontrolled T2DM, Crohn's disease with diarrhea and bloating

PMHX

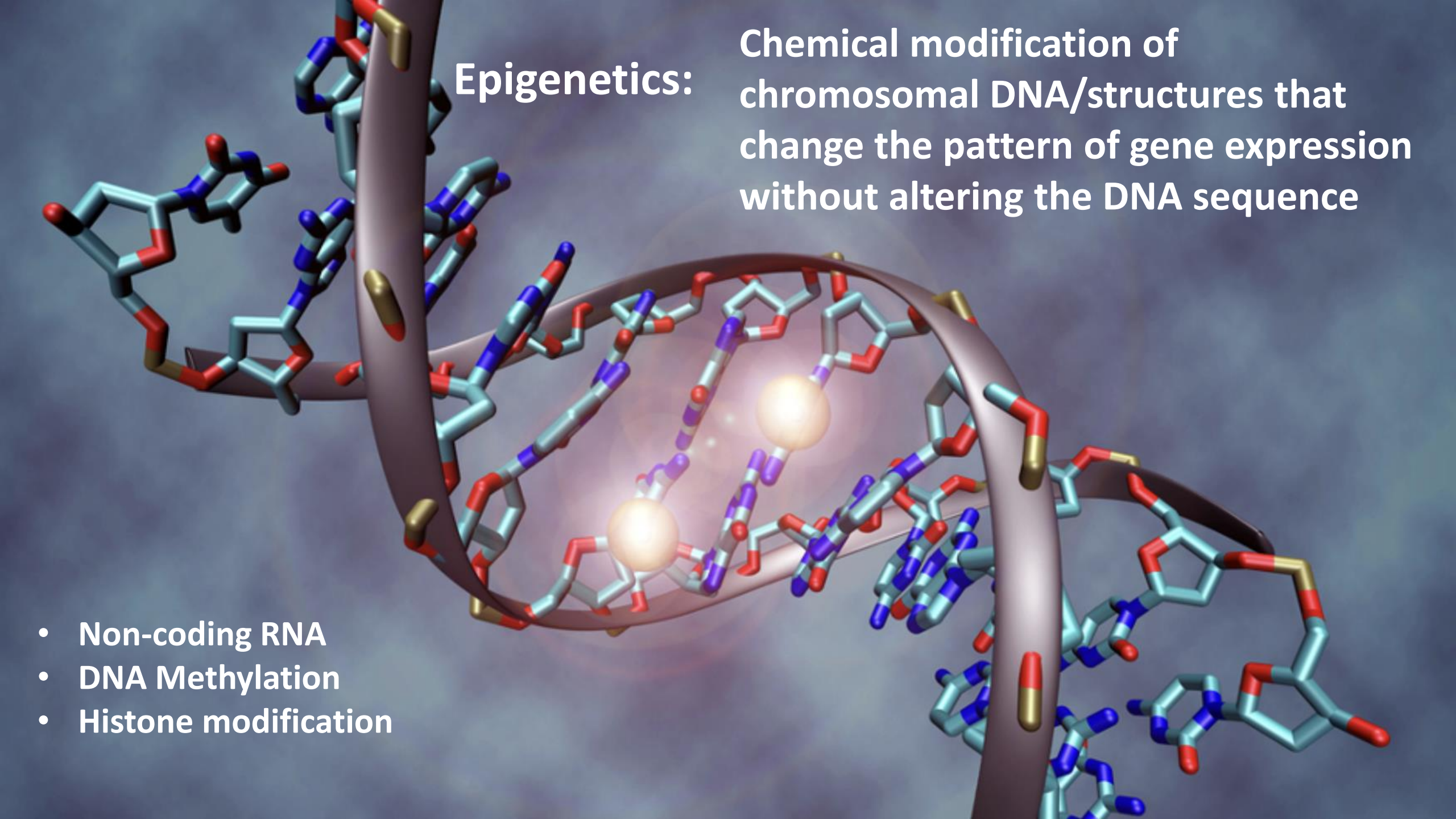
- Age 45 -NSTEMI- 99% stenosis mid-RCA and LAD stenosis
- 250 pounds. BMI 44.3
- Hypertension
- Hyperlipidemia
- Hashimoto's hypothyroidism
- T2DM HbA1C 8.5 non complaint with prescription medications
- Crohn's disease
- Lupus
- Psoriasis
- Depression, anxiety, insomnia with daytime hypersomnolence
- Low Vitamin B12 and D3, Low magnesium

Your DNA is NOT Your Destiny (Epigenetics)

Why Your DNA Isn't Your Destiny | **Jan. 18, [2010]**



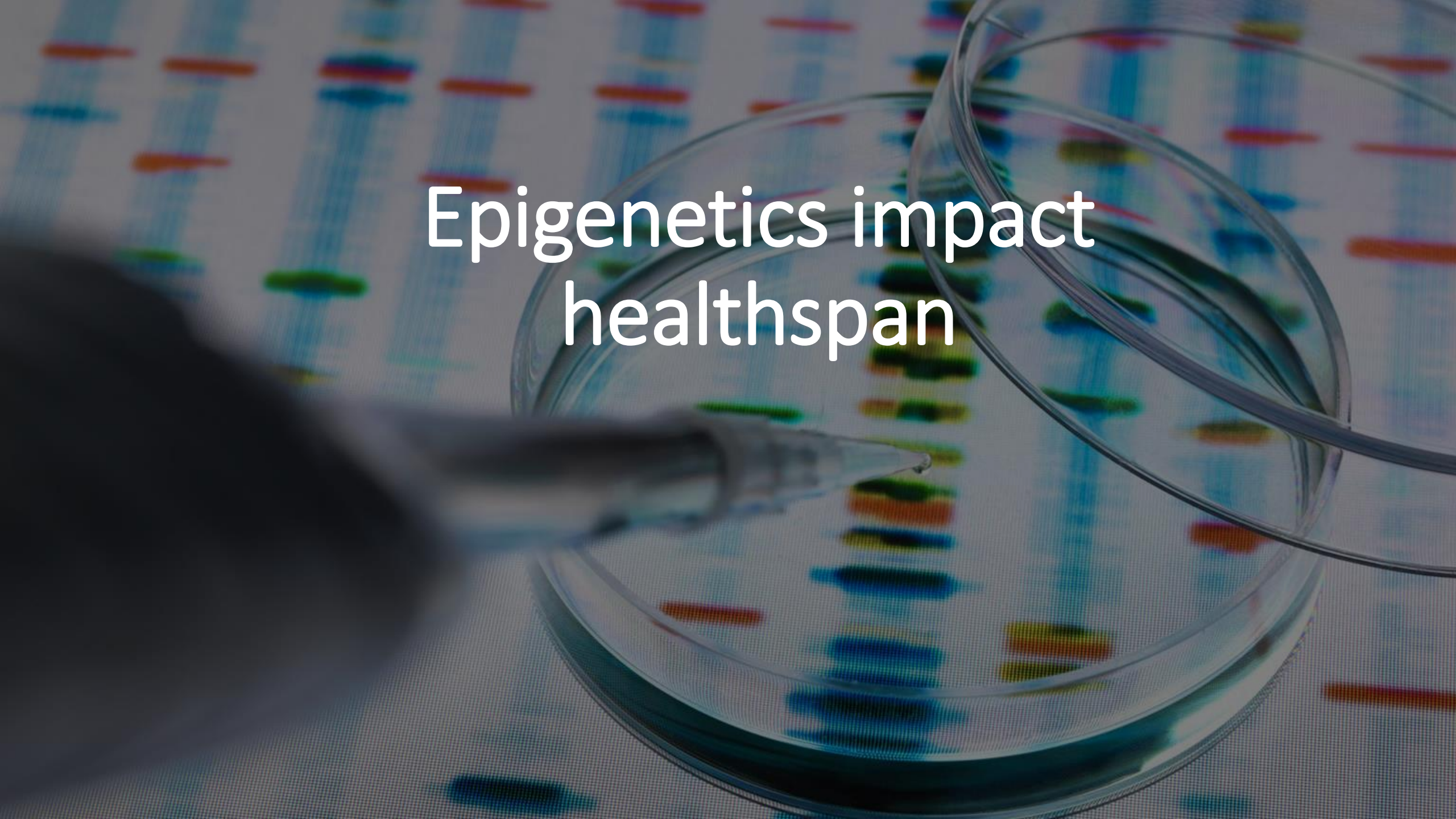
2000, Randy Jirtle, Professor Duke University



Epigenetics:

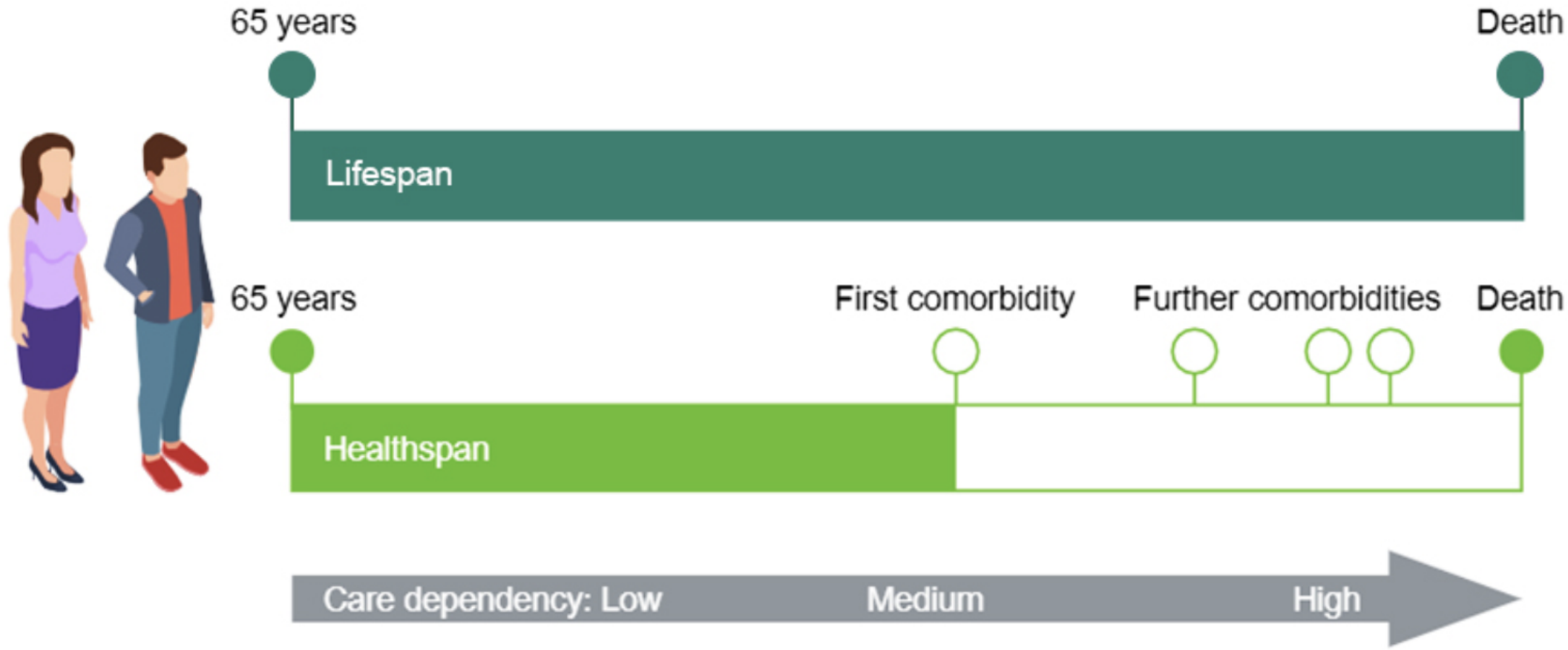
Chemical modification of chromosomal DNA/structures that change the pattern of gene expression without altering the DNA sequence

- Non-coding RNA
- DNA Methylation
- Histone modification


Epigenetics impact
healthspan

Healthspan

The period of life spent in good health, free from the chronic diseases and disabilities of aging

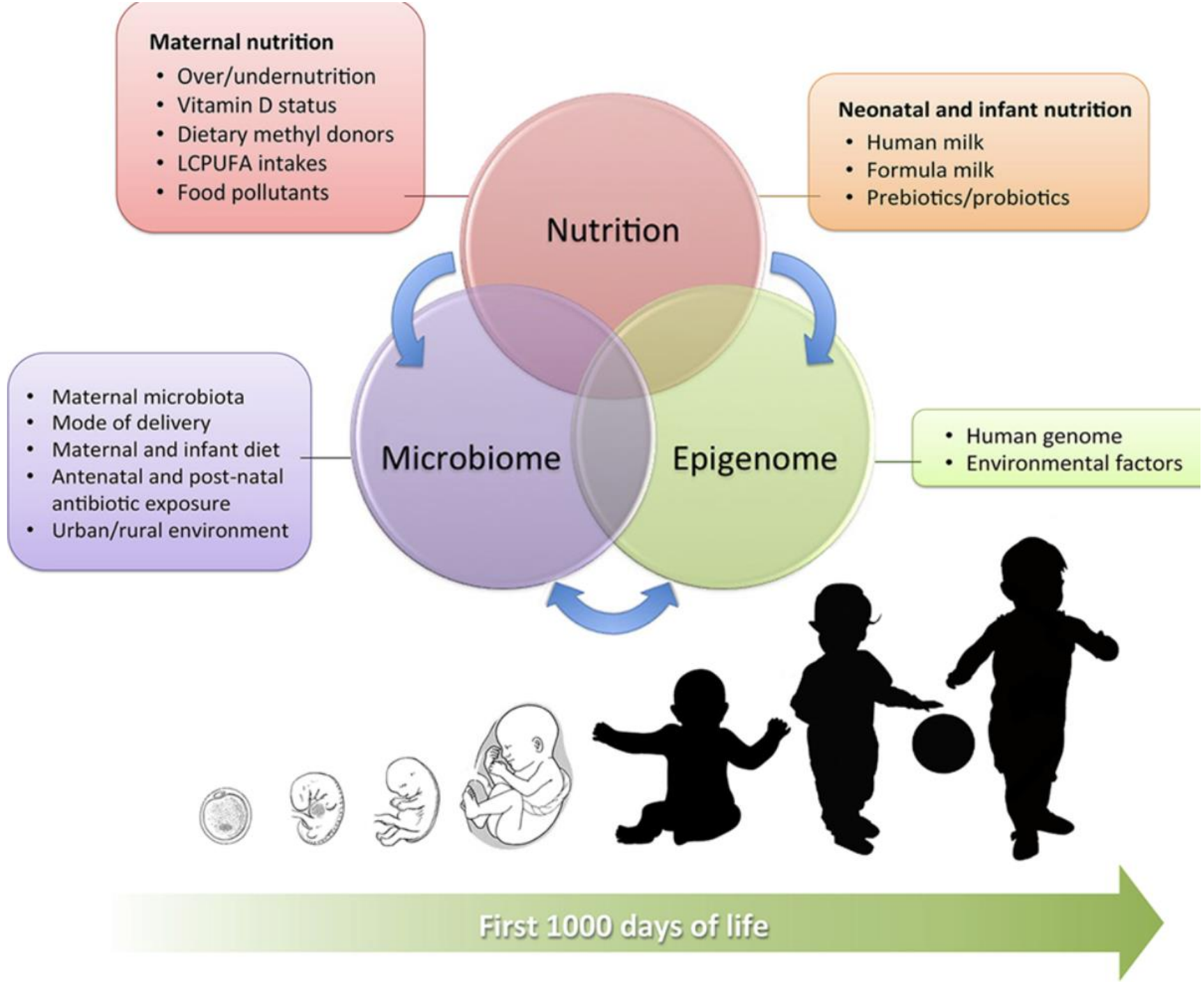


Remaining lifespan after 65 years of age is characterised by a sharp decrease in healthspan approximately halfway between 65 years and death. The further you progress towards the end of your lifespan the more likely you acquire comorbidities which increase your care dependency.

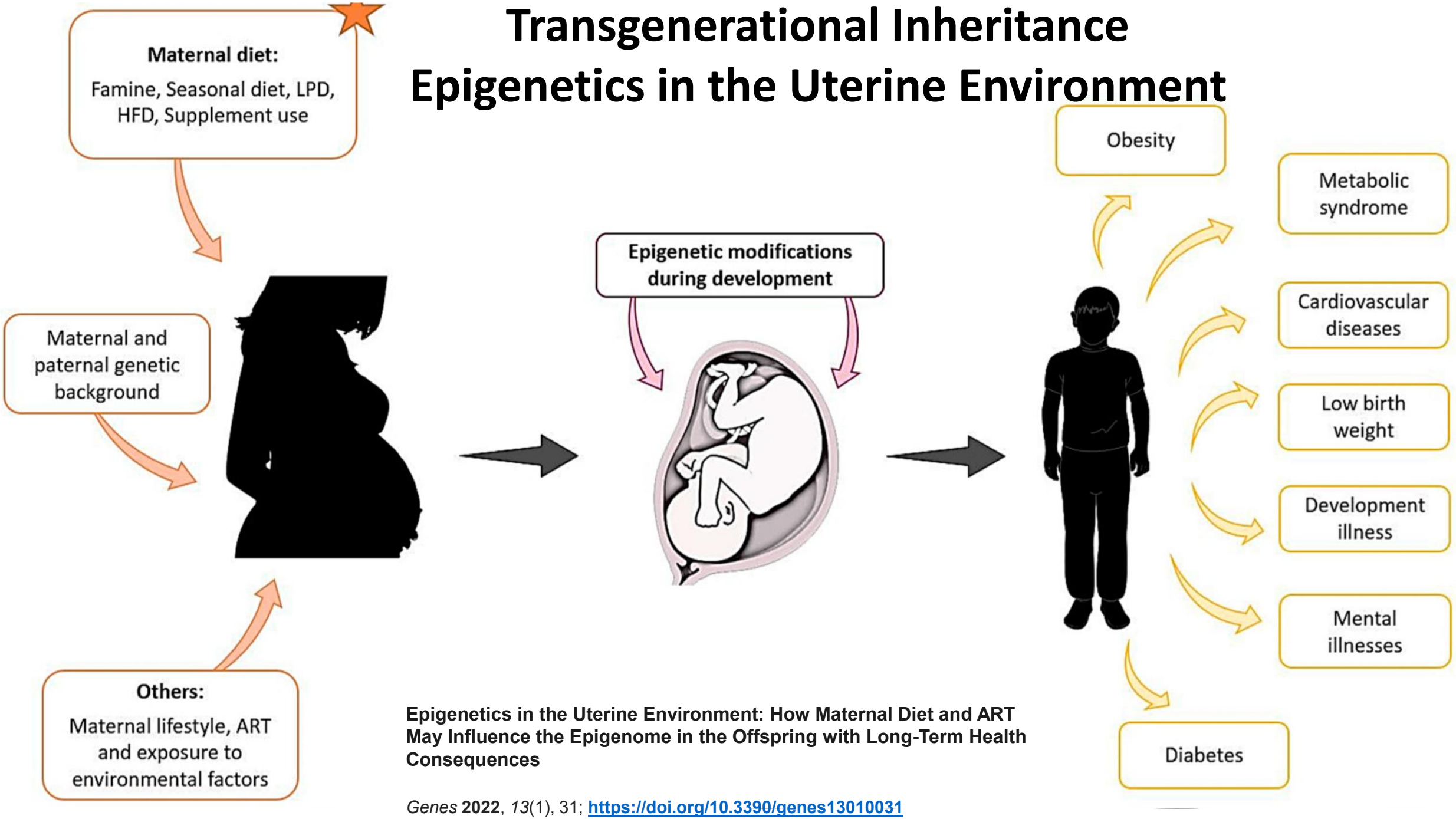
In 2025, the gap between lifespan and healthspan is a significant concern, particularly in the US, where it stands at 12.4 years, the highest among WHO members. Globally, this gap has been increasing, with the average healthspan-lifespan difference at 9.6 years in 2019, a 13% increase from 2000. The US also faces the greatest chronic disease burden.

Lifestyle, exposure to toxins, dietary intake, Stress, exercise all impact simultaneously epigenetic transgenerational inheritance

- Mother – 1st generation
- Fetus – 2nd generation
- Reproductive Cells – 3rd generation
- Microbiota/microbiome- influences all 3 generations


Maternal nutrition
• Over/undernutrition
• Vitamin D status
• Dietary methyl donors
• LCPUFA intakes
• Food pollutants
Neonatal and infant nutrition
• Human milk
• Formula milk
• Prebiotics/probiotics
Nutrition
Microbiome
Epigenome
• Maternal microbiota
• Mode of delivery
• Maternal and infant diet
• Antenatal and post-natal antibiotic exposure
• Urban/rural environment
• Human genome
• Environmental factors
First 1000 days of life

Transgenerational Inheritance
Epigenetics in the Uterine Environment



Epigenetics in the Uterine Environment: How Maternal Diet and ART May Influence the Epigenome in the Offspring with Long-Term Health Consequences

Genes **2022**, *13*(1), 31; https://doi.org/10.3390/genes13010031

DNA Methylation in Cancer: Epigenetic View of Dietary and Lifestyle Factors

Lifestyle choices significantly impact cancer survival through epigenetic mechanisms, specifically by influencing DNA methylation, histone modifications, and microRNA expression

By influencing these epigenetic mechanisms, lifestyle interventions could potentially:

- **Reduce cancer risk by preventing epigenetic changes that lead to tumor development.**
- **Improve cancer treatment outcomes by enhancing the effectiveness of therapies or reducing drug resistance.**
- **Improve overall survival by promoting healthy cellular processes and reducing the severity of disease.**

Epigenet Insights. 2023 Sep 15;16:25168657231199893. doi: 10.1177/25168657231199893

Changes in prostate gene expression in men undergoing an intensive nutrition and lifestyle intervention

Epidemiological and prospective studies indicate that comprehensive lifestyle changes may modify the progression of prostate cancer.

453 down-regulated transcripts after the intervention

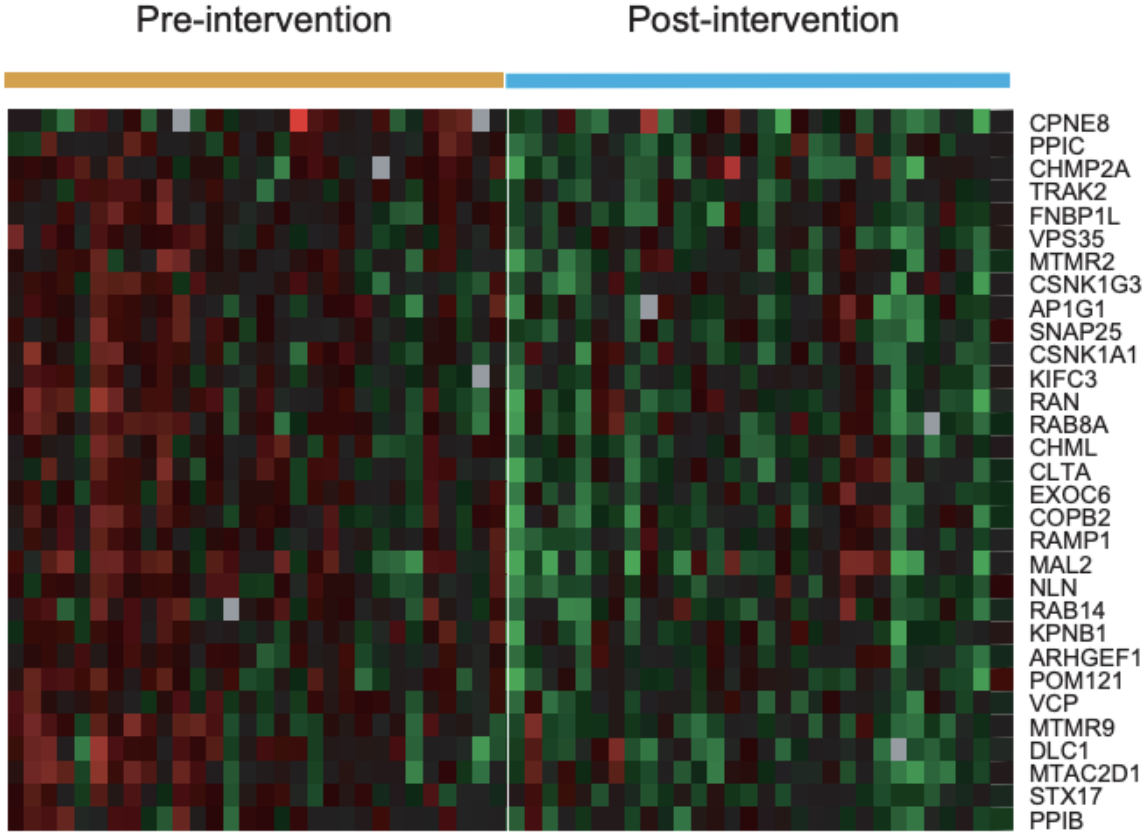
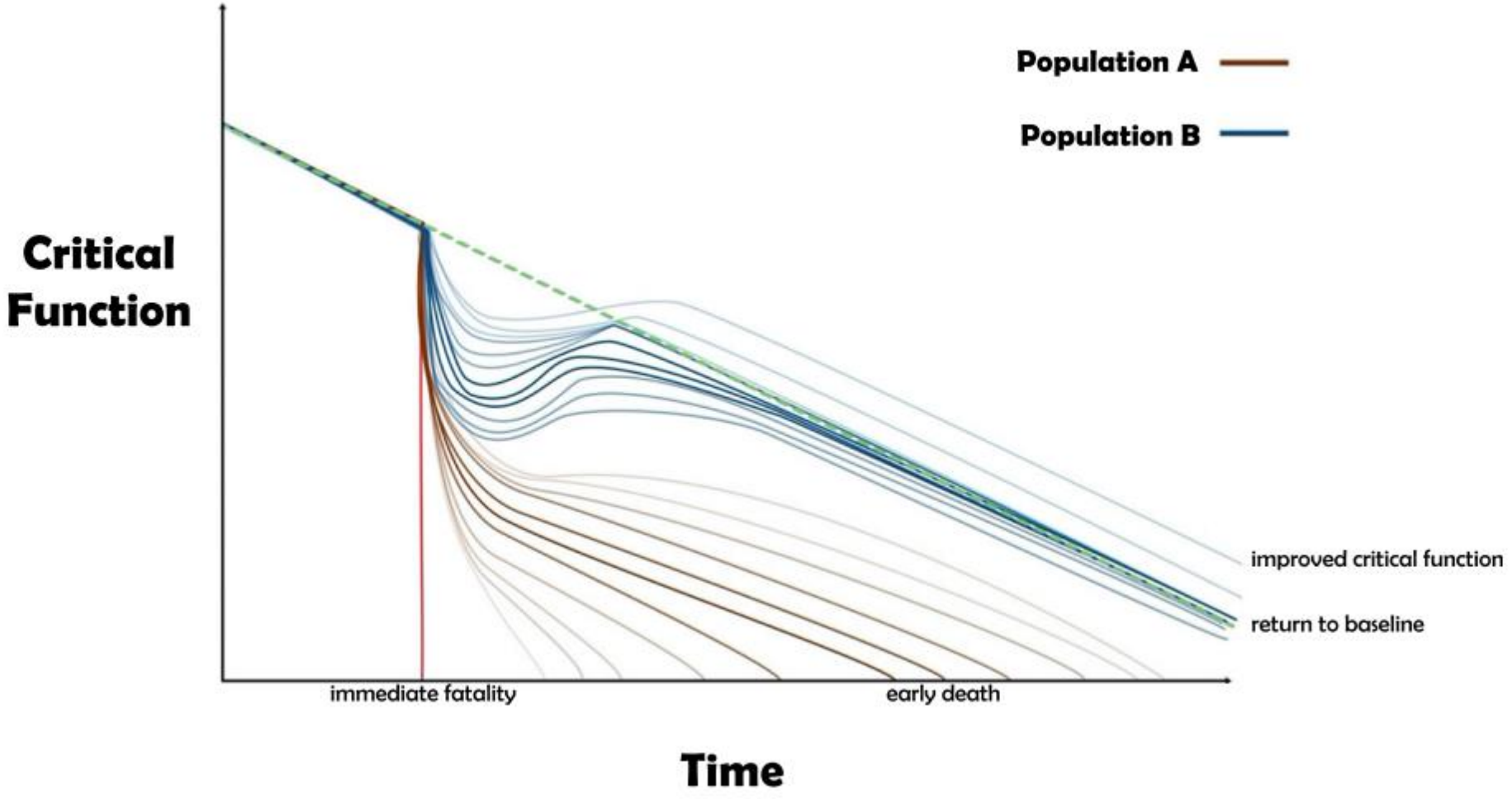


Fig. 4. Heat map of the gene ontology group "Intracellular Protein Traffic" illustrating the down-regulation of these 31 transcripts. Pre- and postcomprehensive diet and lifestyle intervention samples are indicated.

www.pnas.orgcgidoi10.1073pnas.0803080105

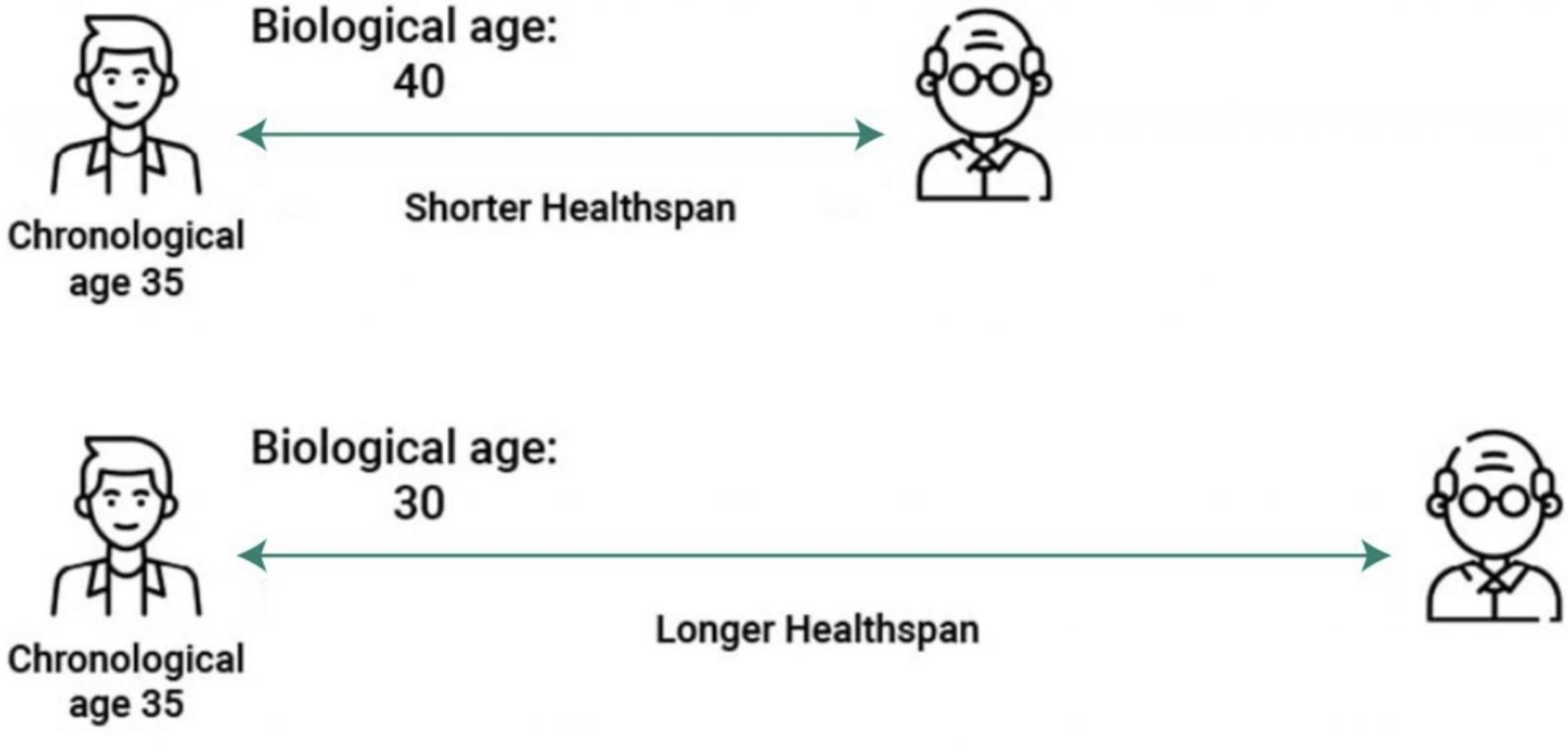
RESILIENCE DETERMINES HEALTHSPAN



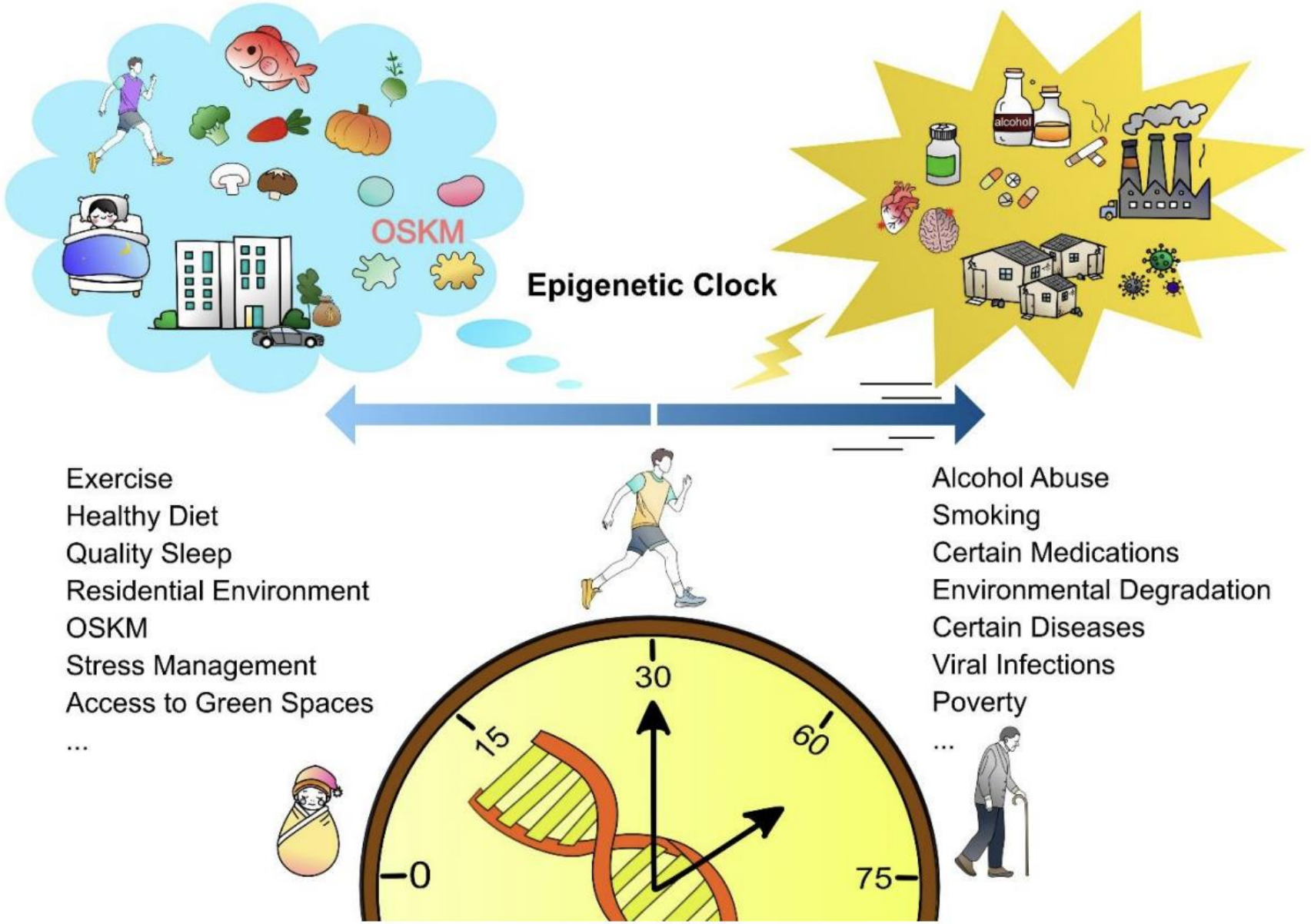
Klasa et al. BMC Geriatrics (2021) 21:51

- Resilience contributes to longevity at all ages
- Nurturing your body, brain, and social connections builds resilience.
- Healthy eating (mostly plants), physical activity, and regular sleep can improve resiliency.
- The gut microbiota is an “organ” with frontline exposure is vulnerable to one’s diet, environmental exposure, sleep, and stress which greatly impacts resiliency.
- Impaired resilience leads to chronic disease, dysbiosis, frailty, and mortality.

Front Microbiol. 2020; 11: 572921. doi: 10.3389/fmicb.2020.572921

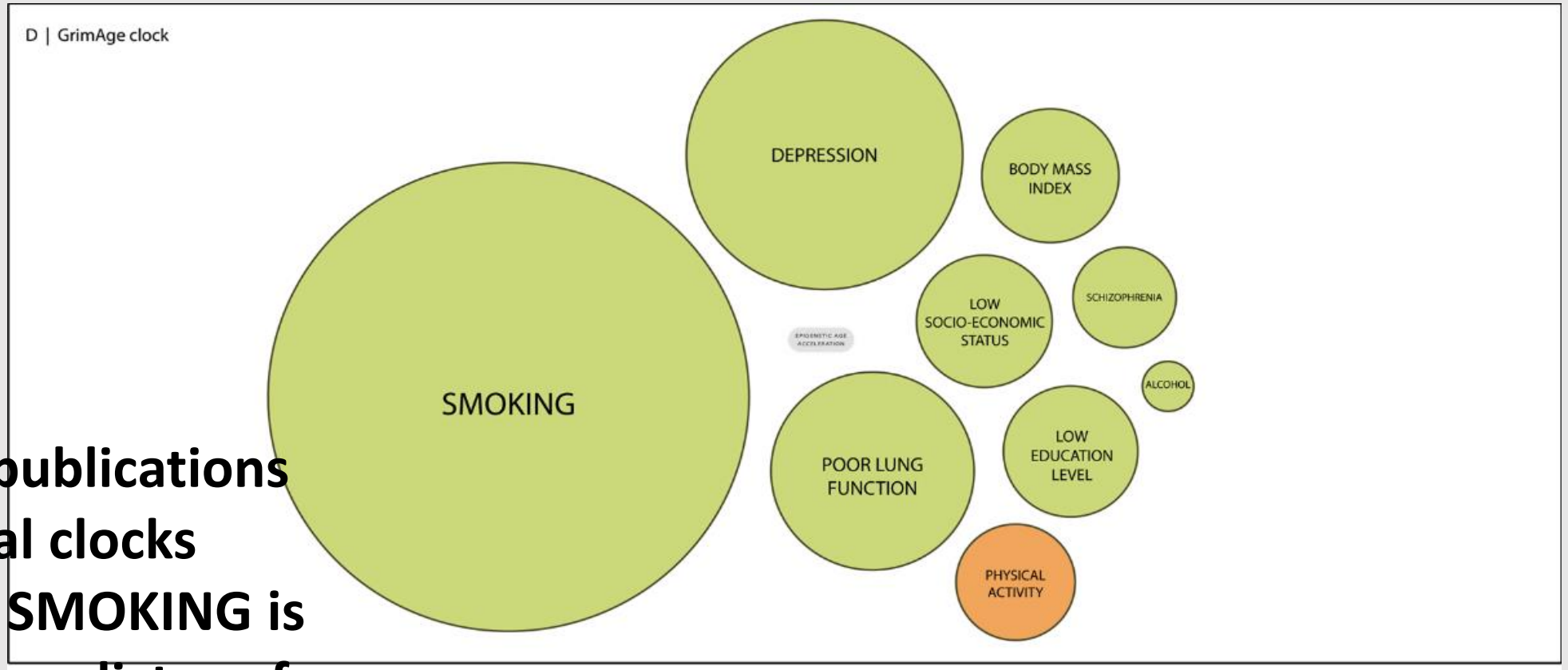

Biological age:
40
Chronological
age 35
Shorter Healthspan
Biological age:
30
Chronological
age 35
Longer Healthspan

Epigenetic Clocks: Beyond Biological Age, Using the Past to Predict the Present and Future



Aging and disease ›› DOI: 10.14336/AD.2024.1495

A systematic review of biological, social and environmental factors associated with epigenetic clock acceleration



Over 156+ publications on biological clocks report that SMOKING is the largest predictor of accelerated aging.

Ageing Research Reviews 69 (2021) 101348

Major Lifestyle Recommendations
For Increasing Healthspan and Reducing Biological Age

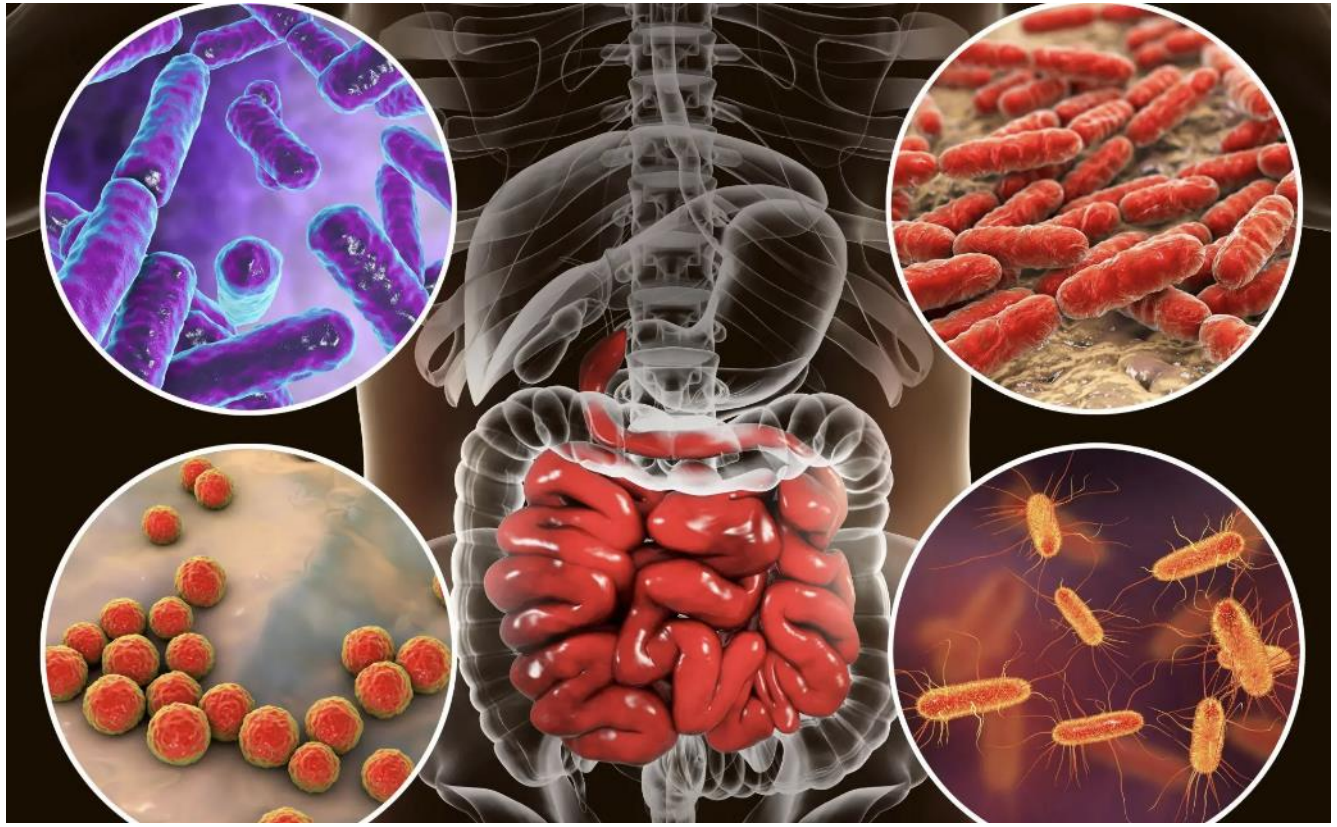
Int J Environ Res Public Health. 2019 Jul; 16(13): 2356.
Published online 2019 Jul 3. doi: 10.3390/ijerph16132356
PMCID: PMC6651499
PMID: 31277270

Smoking-Related DNA Methylation is Associated with DNA Methylation Phenotypic Age Acceleration: The Veterans Affairs Normative Aging Study

Yang Yang,[1] Xu Gao,[2] Allan C. Just,[3] Elena Colicino,[3] Cuicui Wang,[4] Brent A. Coull,[5] Lifang Hou,[6] Yinan Zheng,[6] Pantel Vokonas,[7] Joel Schwartz,[4] and Andrea A. Baccarelli[2,*]

Smokers demonstrated a higher aging ratio, and both male and female smokers were predicted to be twice as old as their chronological age as compared to nonsmokers.

The results were carried out based on the blood profiles of 149,000 adults.



Cross-talk between gut microbiota and tobacco smoking: a two-sample Mendelian randomization study

BMC Medicine volume 21, Article number: 163 (2023)

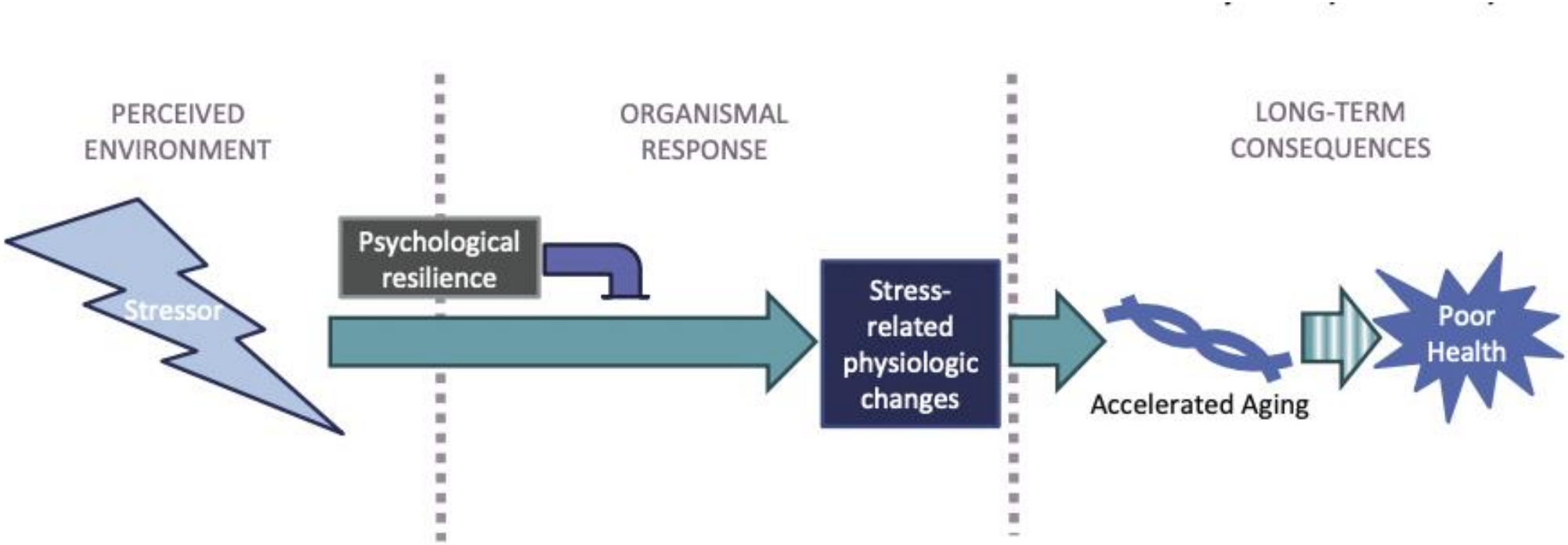
Smoking affects the gut microbiota by:

- **Raising the pH of the intestinal environment**
- **Inducing chronic low-grade inflammation and inflammatory related diseases**
- **Promoting damaging oxidative stress which increases systemic inflammation**


STRESS
ANXIOUS
Betrayed
RELATIONSHIP PROBLEM
DISCRIMINATED
HEALTH PROBLEM
TROUBLE
DEATH
IMPOTENCE
EMOTIONAL
PSYCHOLOGICAL
lost
HARDSHIP
PENNILESS
AGITATION
NEGATIVITY
DOUBT
FIGHTING
TRAUMA
MOODY
LOSS
OVERDUE BILLS
DEPRESSION
HEADACHE
IRRITATED
CHEATED
LONELINESS

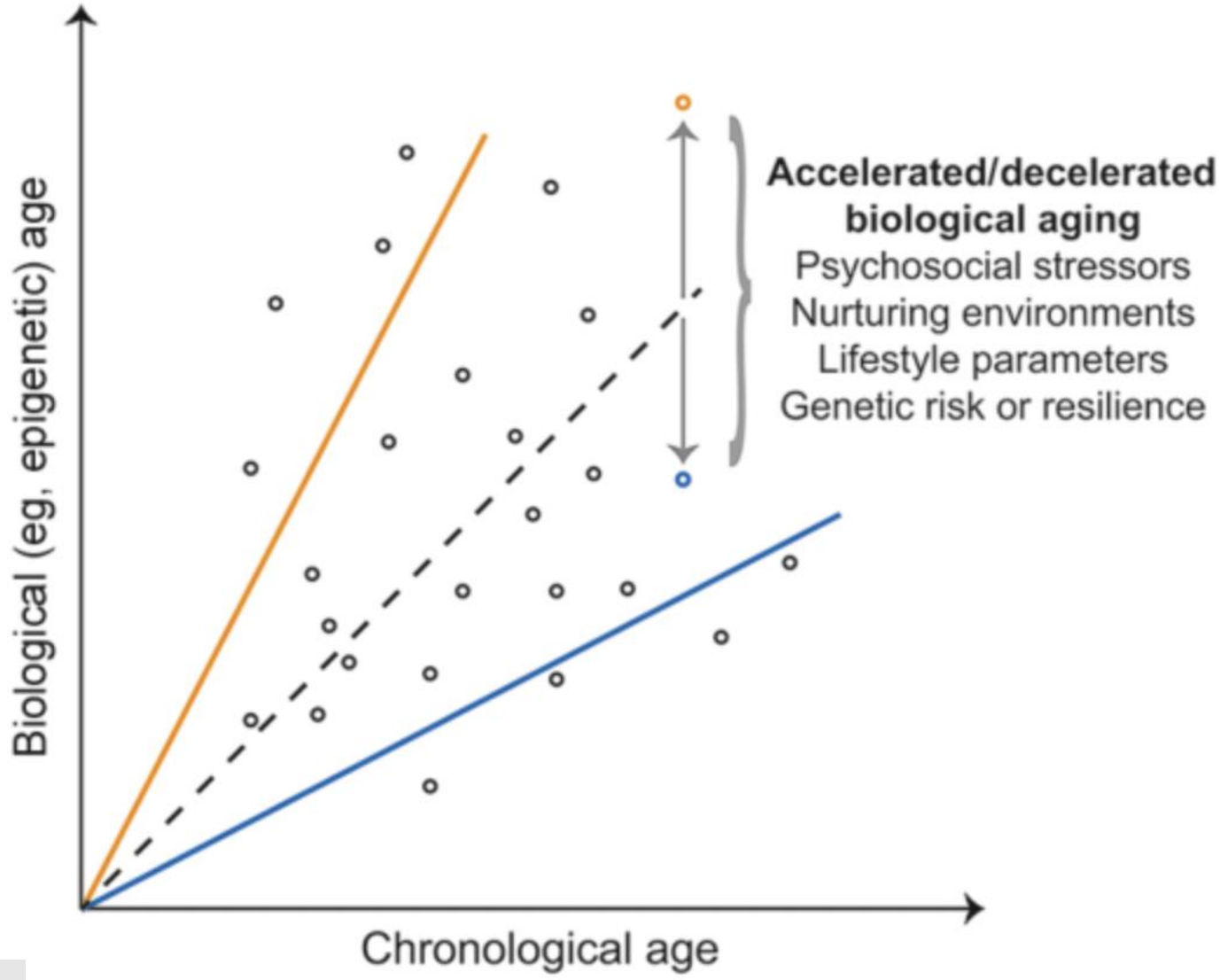
Psychological and biological resilience modulates the effects of stress on epigenetic aging

Translational Psychiatry (2021) 11:601



Cumulative life-time stress is associated with accelerated epigenetic aging

Personal life stress had greater impact in older compared to younger participants



Dialogues Clin Neurosci. 2019 Dec; 21(4): 389–396.
Epigenetics as a key link between psychosocial stress and aging: concepts, evidence, mechanisms

Anthony S. Zannas, MD

BGM bidirectional communication system:

- Neuroendocrine
- Neuronal
- Immune

Diet

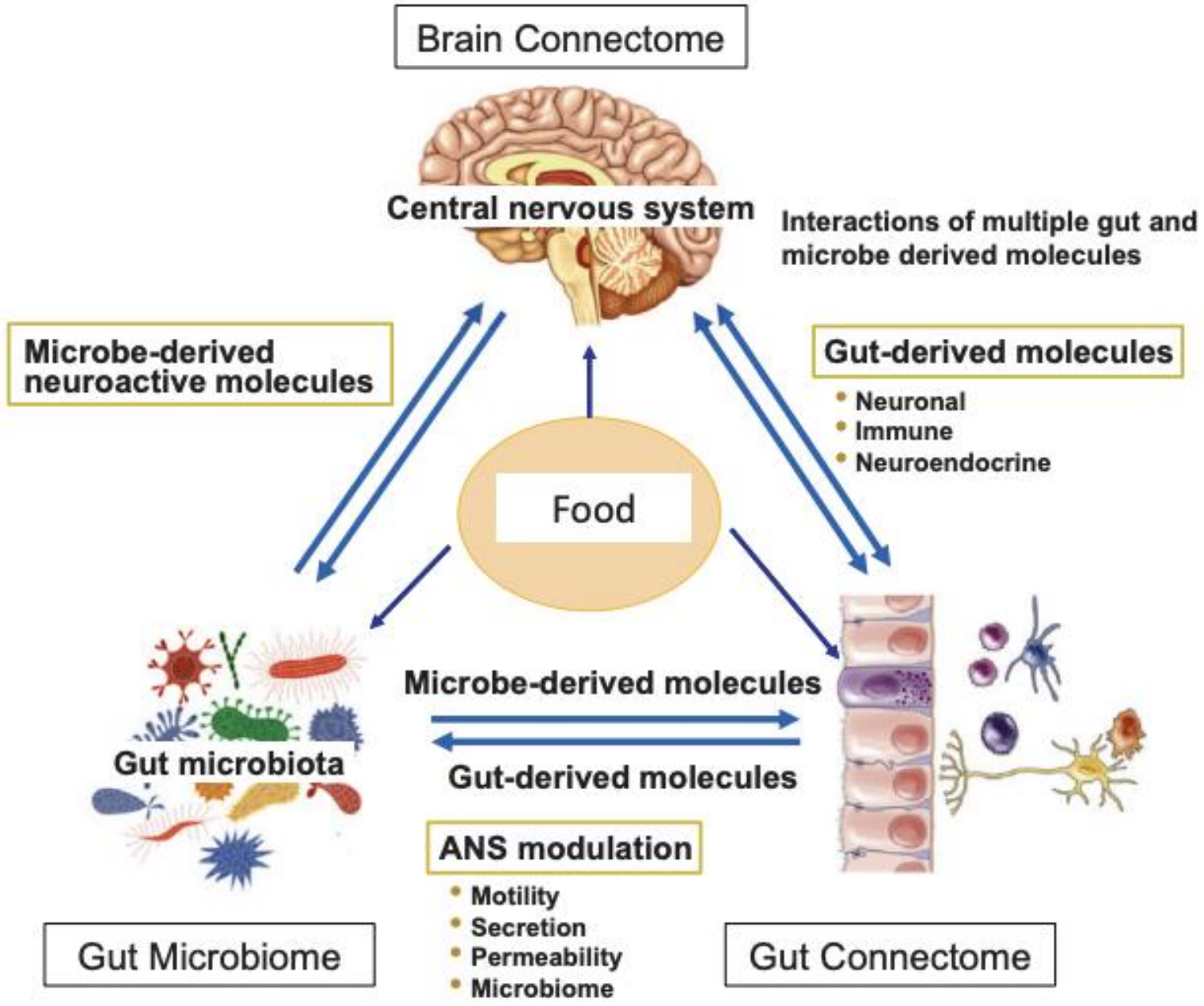
- Modulates the microbiome
- Modulates structure and function of the brain through these communication channels

Preclinical and Clinical Studies focusing on dietary habits of psychiatric and neurologic disorders

- Depression
- Cognitive decline, dementia
- Parkinson's Disease
- Autism Spectrum Disorder
- Epilepsy
- -Anxiety
- -Eating disorders
- -ADHD

Clinical studies have demonstrated that the diet induced anti-inflammatory effects mediated by microbial metabolites from dietary fiber and polyphenols have an impact on brain health, structure, and function.

Translational Psychiatry (2022) 12:164 ; https://doi.org/10.1038/s41398-022-01922-0



Translational Psychiatry (2022) 12:164 ; https://doi.org/10.1038/s41398-022-01922-0