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Fueling a Healthy Future: Clinical Insights for a Longer Life

ADVANCING WELLNESS THROUGH MEDICAL RESEARCH AND CARE

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Objectives

- Define healthy aging
- Outline the biology of aging
- Review clinical manifestations of aging
- Estimating/measuring age and longevity
- Review evidence-based interventions to support healthy aging

The Difference Between Living Longer and Living Well

Understanding Lifespan

Lifespan is the total years a person lives, regardless of health or quality during those years.

Defining Healthspan

Healthspan is the portion of life spent in good health, free from chronic disease or frailty.

Lifespan vs Healthspan Gap

Many people live longer but experience a gap of declining health and reduced quality of life.

Goal of Longevity Health

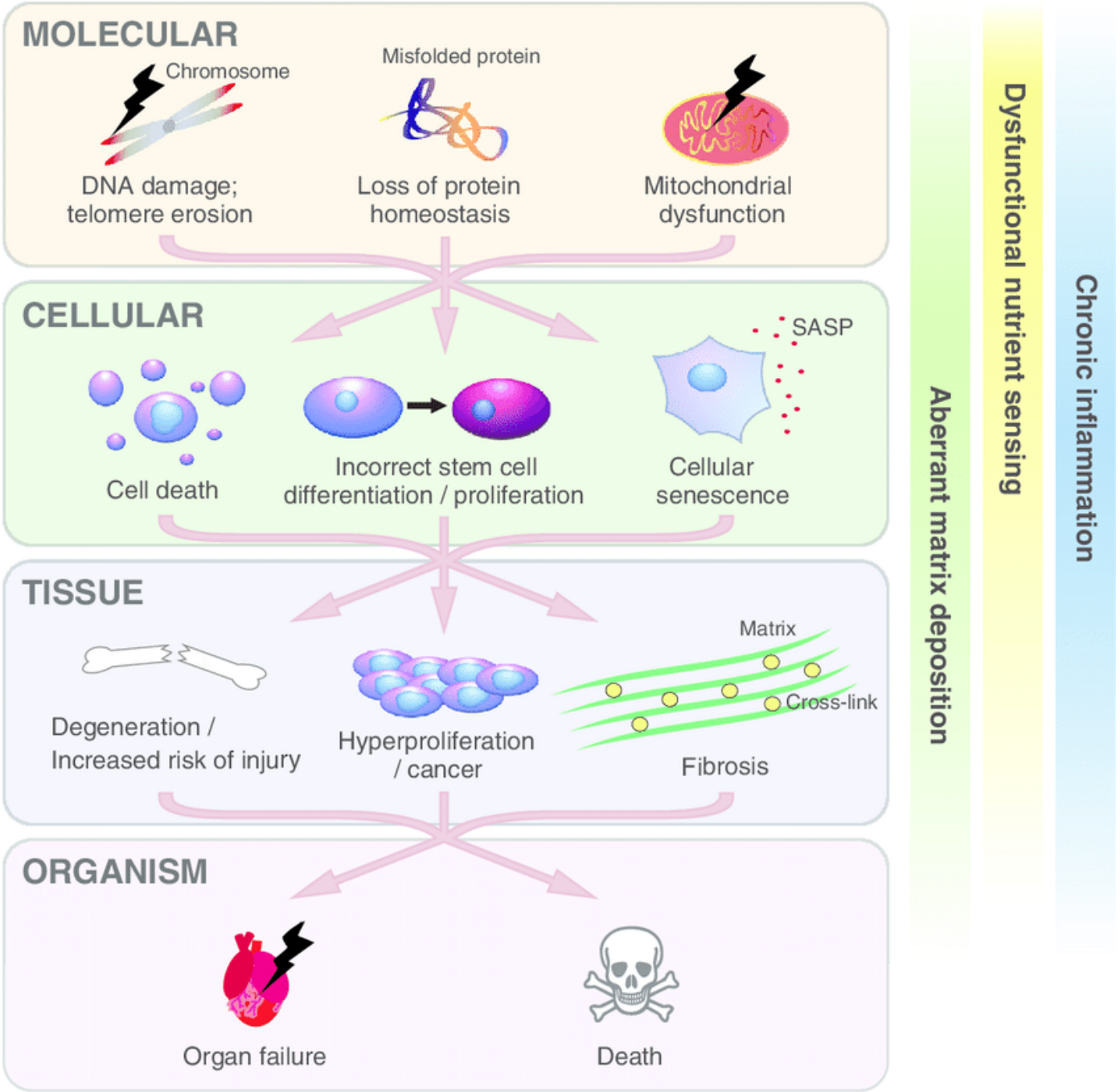
The focus is on extending healthspan to match lifespan, improving life quality in later years.

Chronological Age vs Biological Age

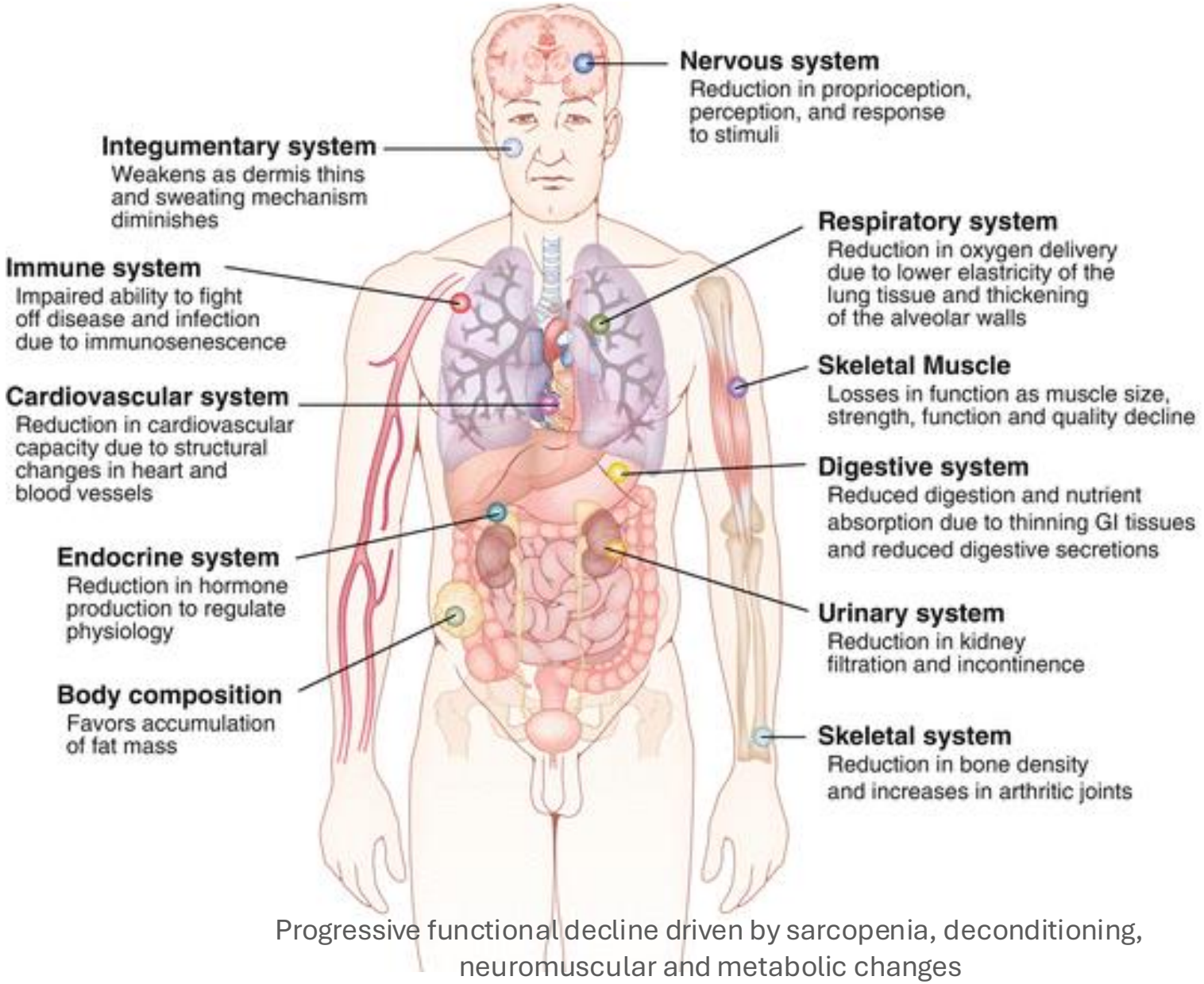
- **Chronological Age:**
  - Measured by calendar years since birth
  - Does not account for individual health status
  - Commonly used in demographics and legal contexts

- **Biological Age:**
  - Reflects physiological and functional status
  - Influenced by genetics, lifestyle, and environment
  - Can be estimated using biomarkers and aging clocks

Biological Mechanisms of Aging



Physiological Decline with Aging



- Muscle Mass & Strength
- Cardiorespiratory Fitness
- Balance & Mobility
- Bone Density
- Metabolic Flexibility
- Neuromotor Speed

Progressive functional decline driven by sarcopenia, deconditioning, neuromuscular and metabolic changes

Aging and Bone Loss

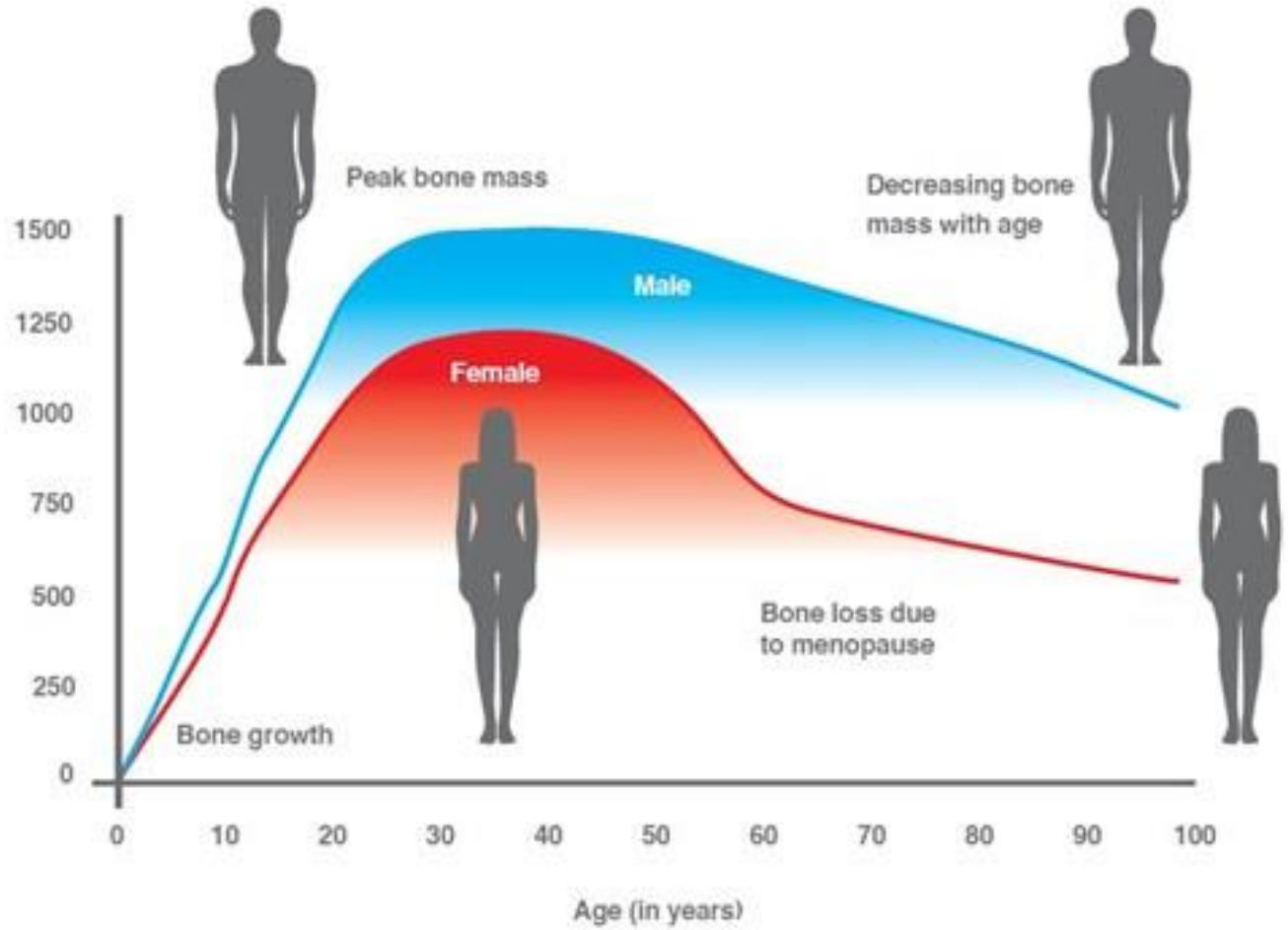


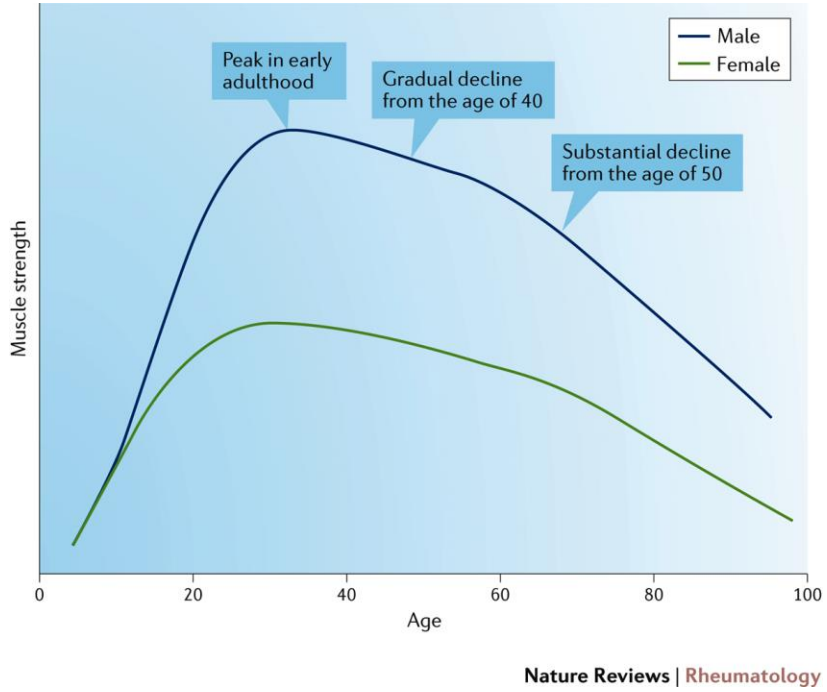
Table 1. Common Risk Factors for Osteoporosis

Nonmodifiable	Modifiable
Older age	Low levels of calcium and vitamin D
Female gender	Reduced intake of vegetables and fruits
Menopause	Increased intake of caffeine, sodium, or protein
Family history	Sedentary lifestyle
Small frame or low body weight	Smoking
History of broken bones or height loss	Increased use of alcohol

Source: Reference 4.

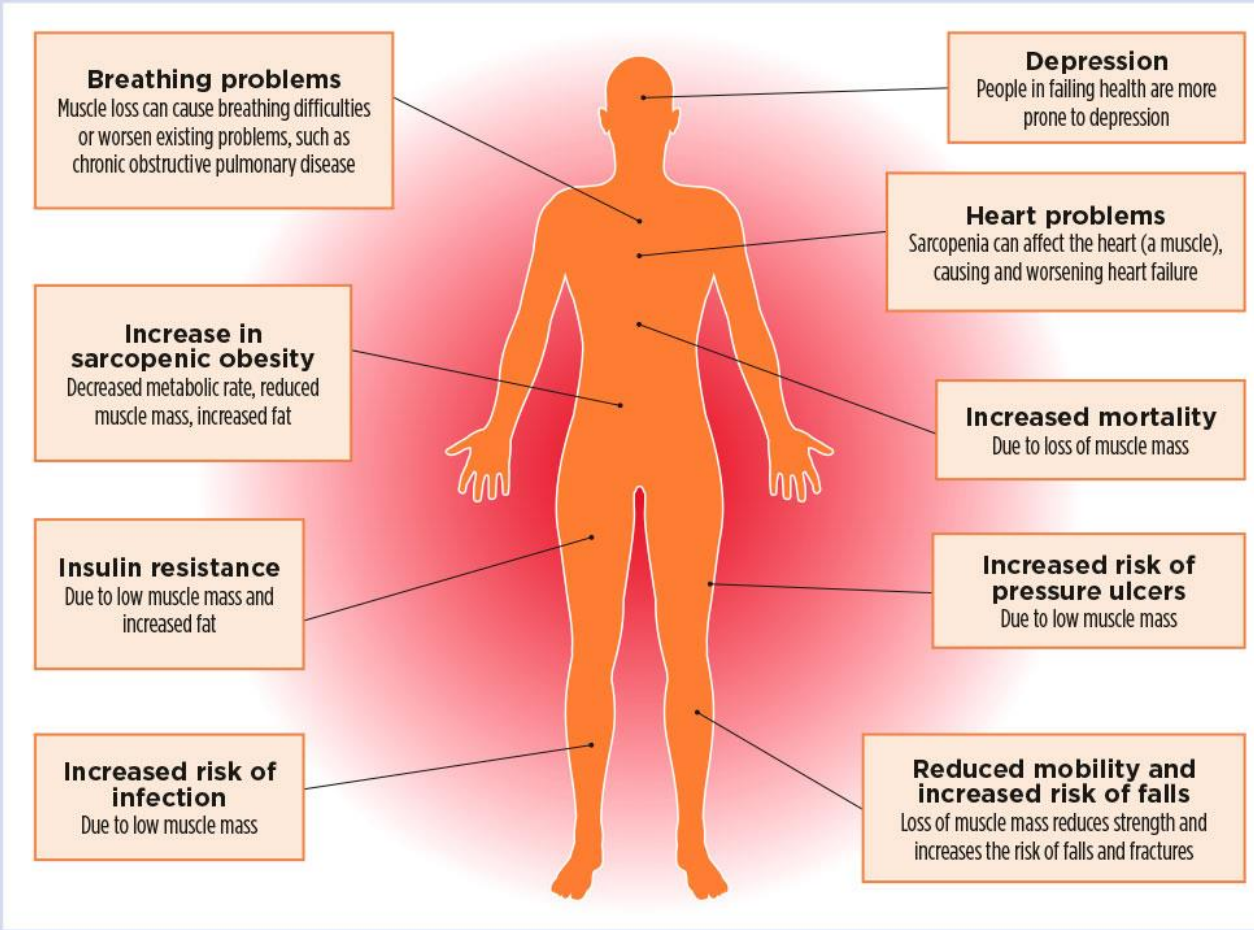
Loss of Muscle Mass with Aging

Figure 1 Grip strength across the lifecourse



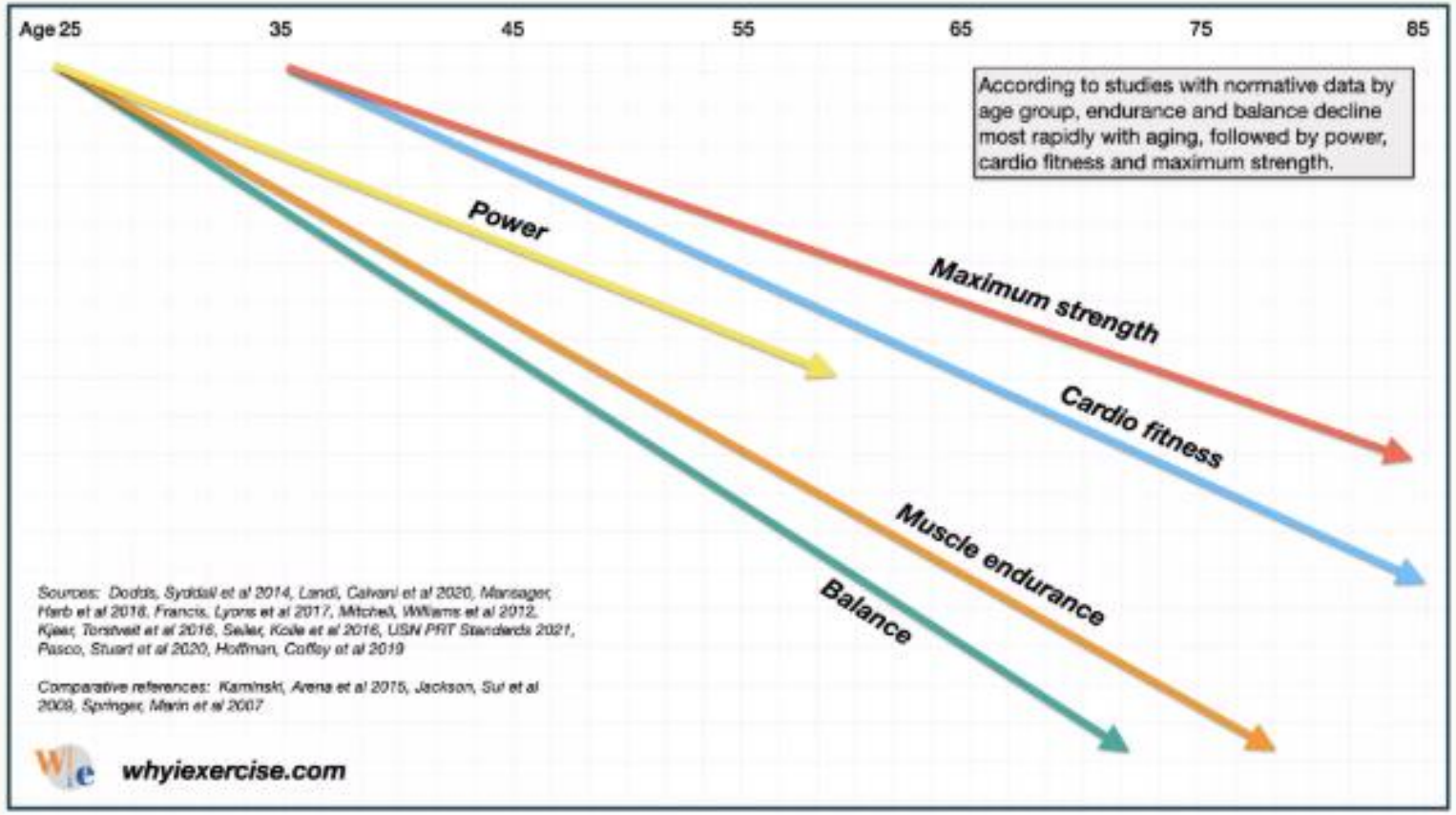
Dennison, E. M. *et al.* (2017) Epidemiology of sarcopenia and insight into possible therapeutic targets *Nat. Rev. Rheumatol.* doi:10.1038/nrrheum.2017.60

Fig 3. **Impacts of sarcopenia**



Adapted from: Holdoway and Ashworth (2021)

Decline in Human Performance with Aging



Balance and muscle endurance decline with aging more rapidly than maximum strength and cardio fitness.

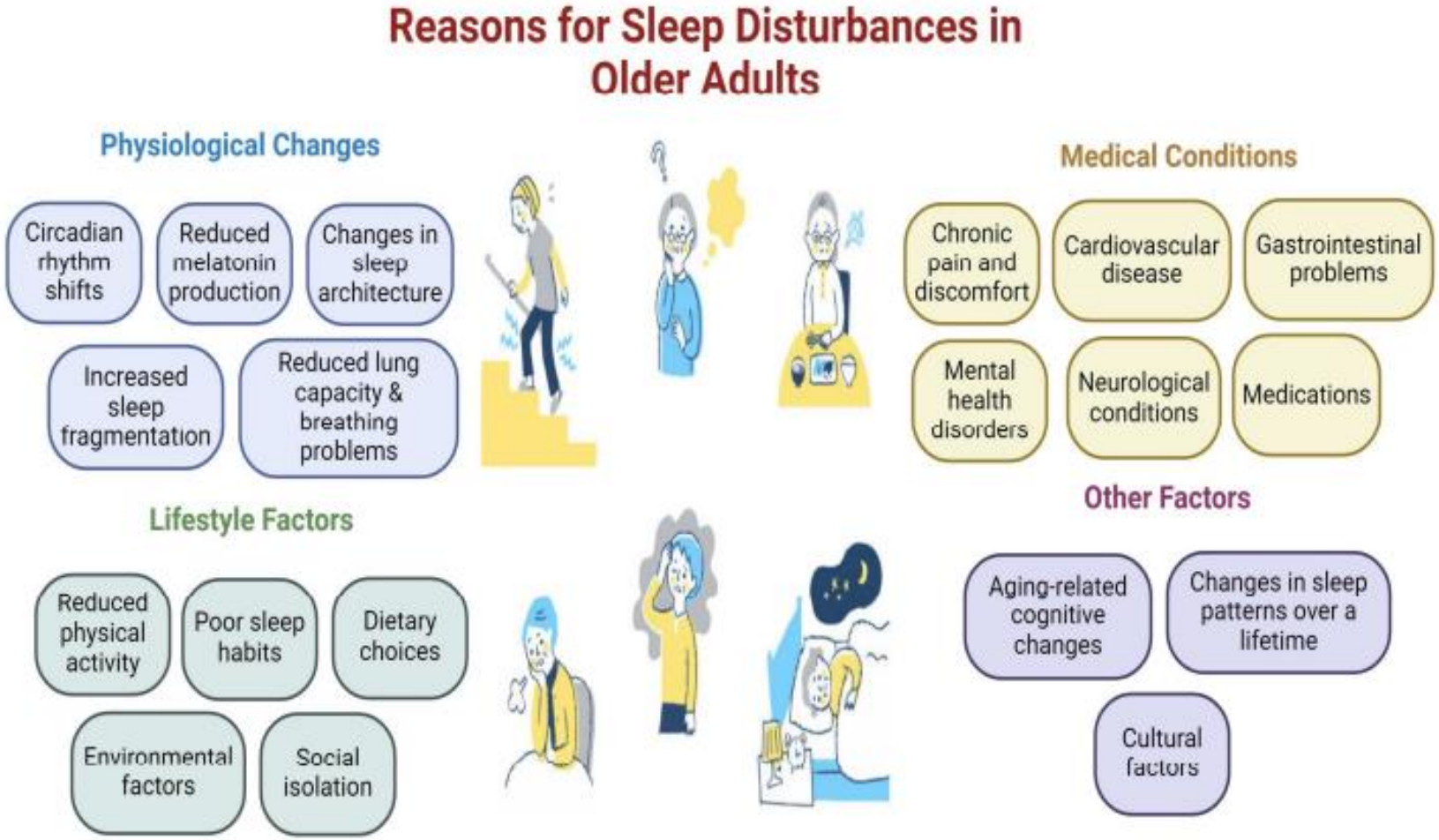
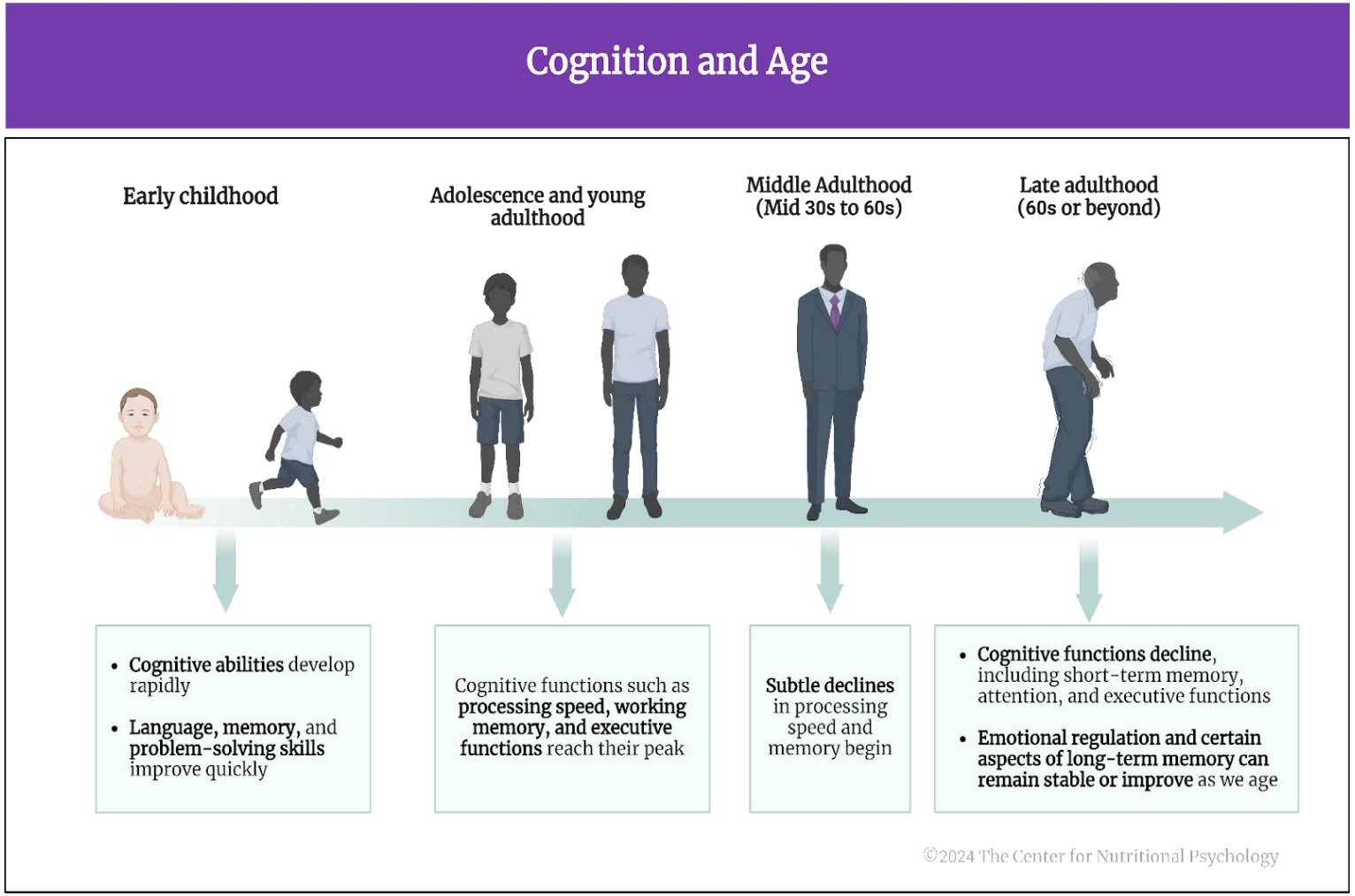
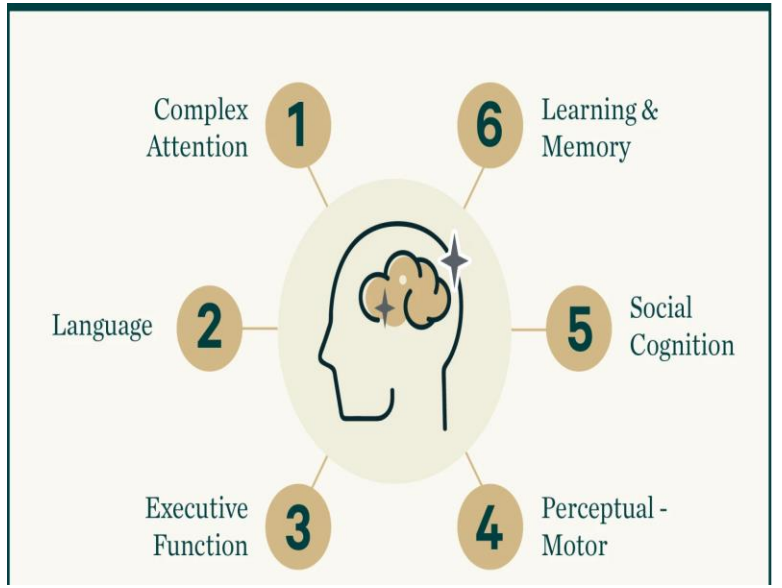
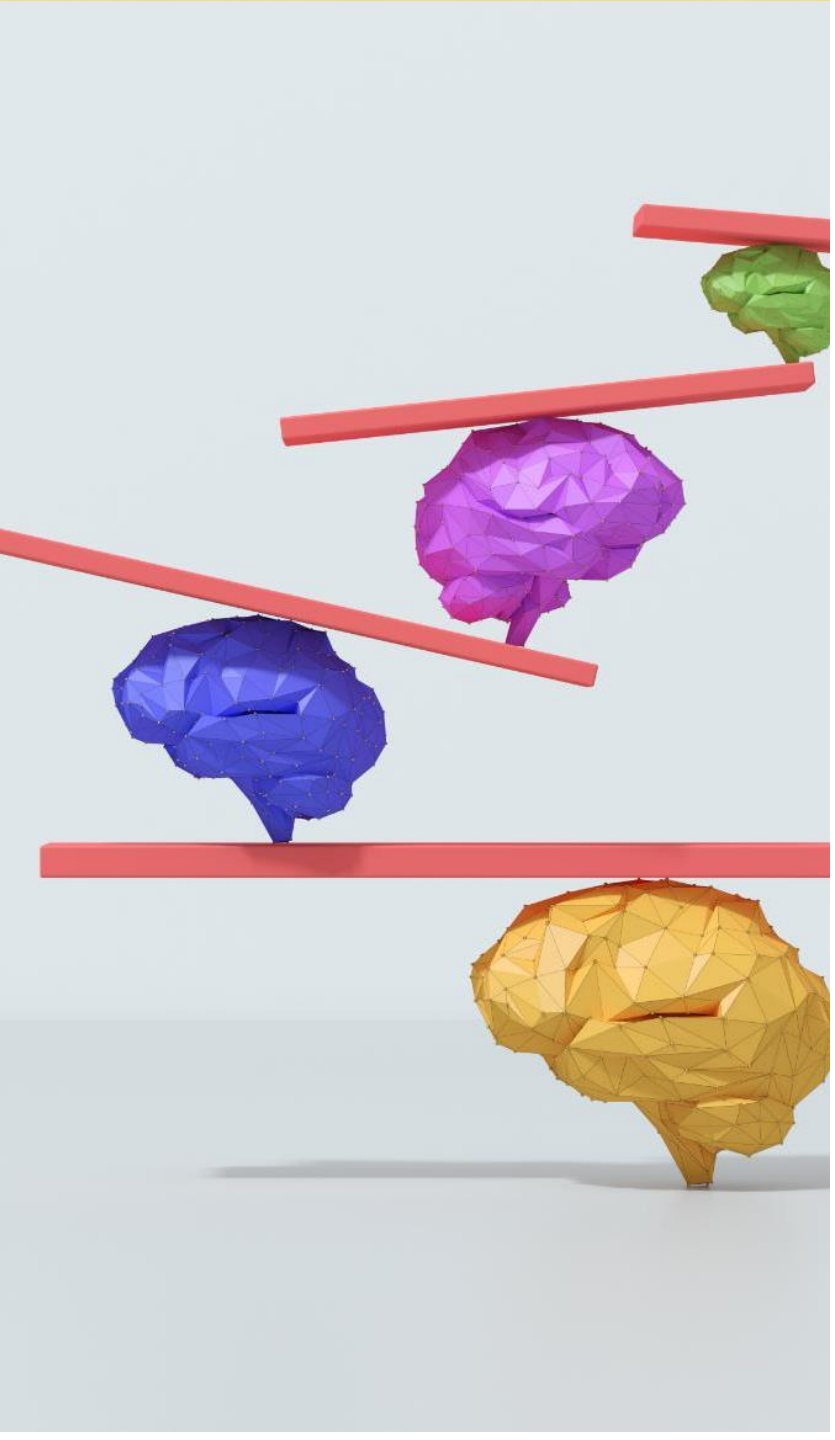


Figure 2: Factors of sleep deprivation in older adults: Sleep disturbances in older adults can arise from physiological changes, and medical conditions. Additionally, lifestyle choices, including inactivity or poor sleep hygiene, and factors like age-related cognitive decline can further impact their sleep quality.

Cognitive Decline with Aging







Biological and Physical Drivers of Mental Health in Aging

Brain Aging and Mental Health

Aging decreases neuroplasticity and increases neuroinflammation, affecting mood and cognition.

Vascular and Cognitive Health

Cerebrovascular disease links to cognitive impairment and depression through vascular health deterioration.

Physical Health Impact

Chronic illnesses and mobility issues increase stress and reduce independence in aging individuals.

Protective Role of Fitness

Cardiorespiratory fitness and muscle strength improve blood flow, sleep, and resilience to stress.

Psychosocial and Environmental Drivers of Mental Health in Aging

Psychological Adaptation

Emotional regulation and coping strategies help older adults manage stress and reduce anxiety during aging.

Social Connection Benefits

Meaningful relationships and strong support networks protect against loneliness and cognitive decline in older adults.

Environmental and Care Factors

Access to quality healthcare and supportive environments enables autonomy and well-being in aging populations.

The Four Horsemen of Longevity

- Accounts for 80% of deaths in older adult nonsmokers
- Develop slowly and silently over decades
- Detecting and modifying risk as early as possible is key

Increasing Risk of CVD and Dementia with Aging

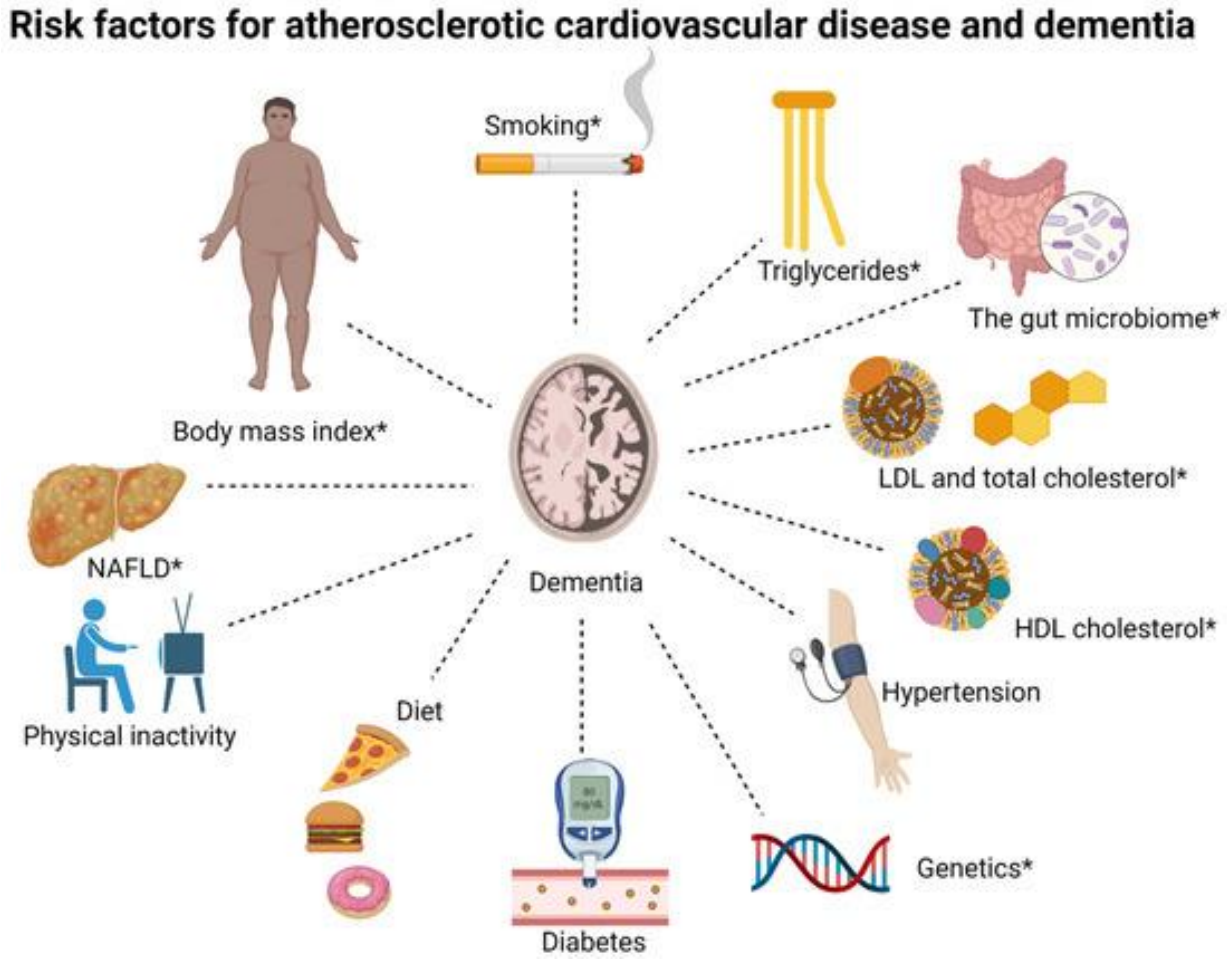
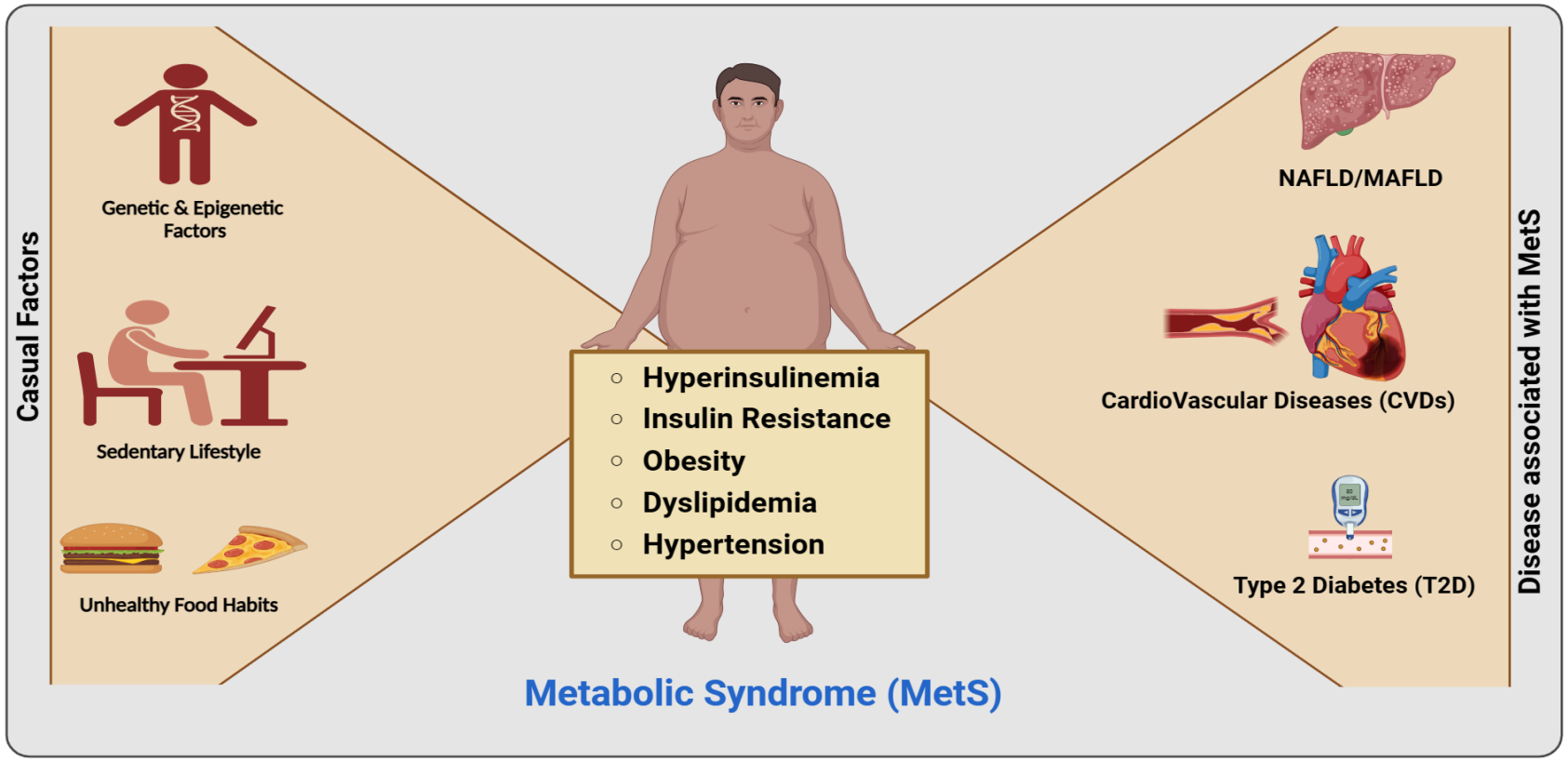


Figure 1. Overview of shared risk factors between dementia and atherosclerotic cardiovascular disease, discussed in this review. LDL, low-density lipoprotein; HDL, high-density lipoprotein; NAFLD, non-alcoholic fatty liver disease. The associations for some risk factors differ between Alzheimer's disease and non-Alzheimer dementia, specifically, body mass index, triglycerides, HDL cholesterol, NAFLD, the gut microbiome, smoking, and genetics (these are marked by *).

Int. J. Mol. Sci. 2022, 23(17), 9777; https://doi.org/10.3390/ijms23179777

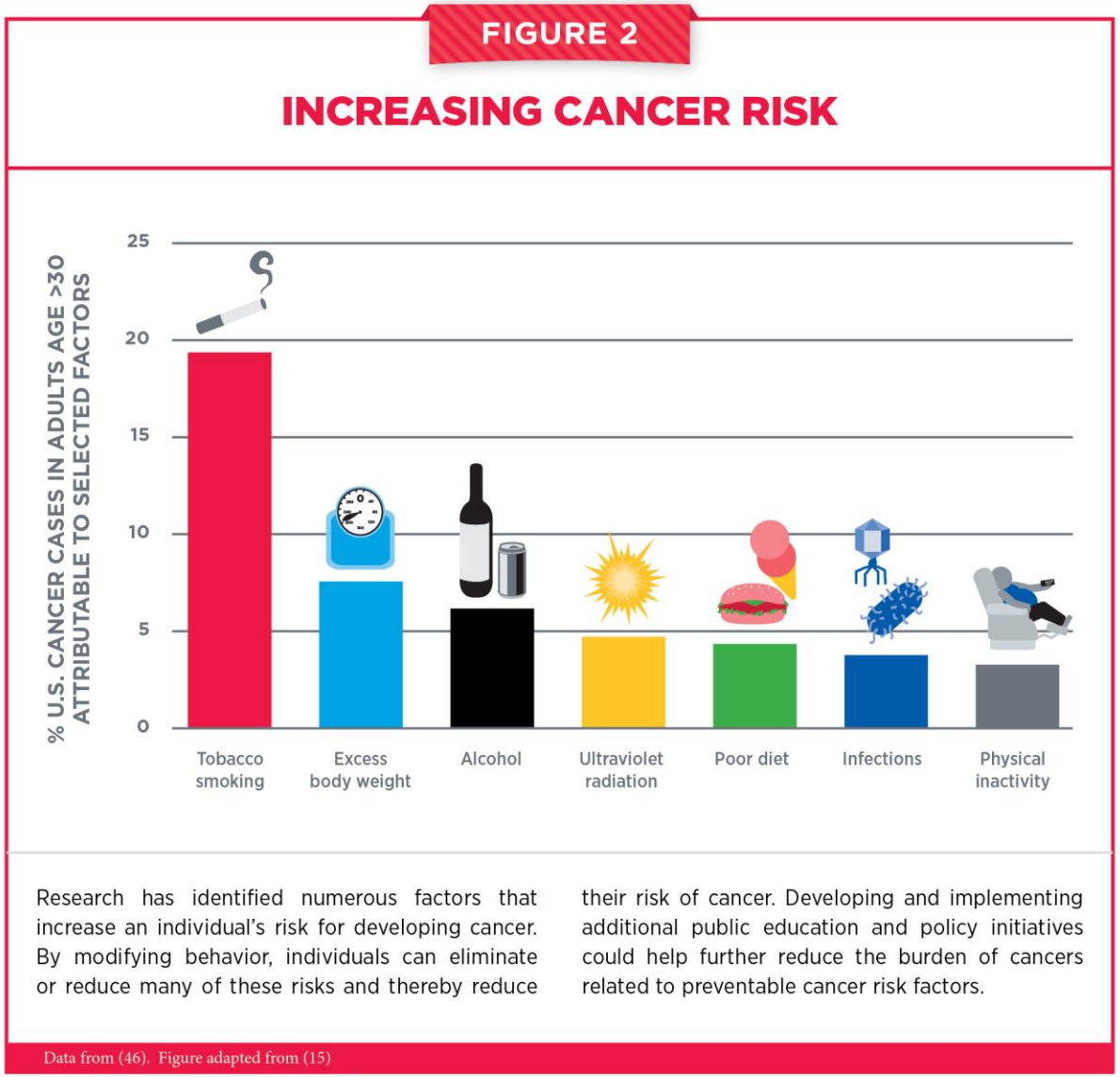
Increased Risk of Metabolic Disorders with Age

Metabolic Syndrome : Casual Factors, Diagnosis and associated diseases



Increased Cancer Risk with Aging

- Accumulation of DNA damage and mutations
- Declining immune surveillance
- Cellular senescence & chronic inflammation
- Longer exposure to carcinogens
- Metabolic dysfunction as an accelerant



American Association for Cancer Research (AACR) Cancer Progress Report 2019

Measuring Longevity

Biomarkers of aging

Blood-based

Fasting insulin
Insulin-like growth factor 1
Hemoglobin A1c
Interleukin-6
Tumor necrosis factor α receptor II
High sensitivity c-reactive protein
N-terminal B-type natriuretic peptide
Growth differentiating factor 15
Cystatin C

Physiological

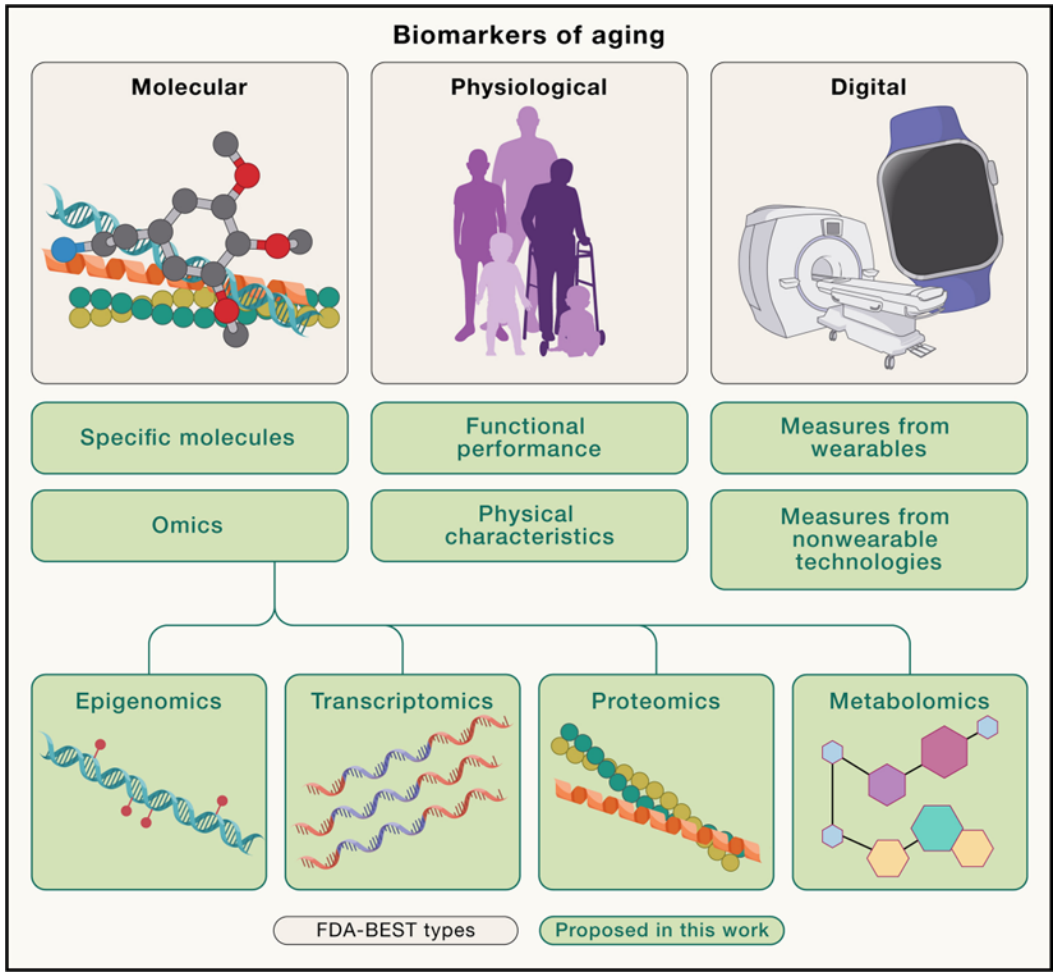
Gait speed
Grip strength
Pulse wave velocity
Heart rate variability
Blood pressure

Neurological

Mini-mental state exam
Hearing test

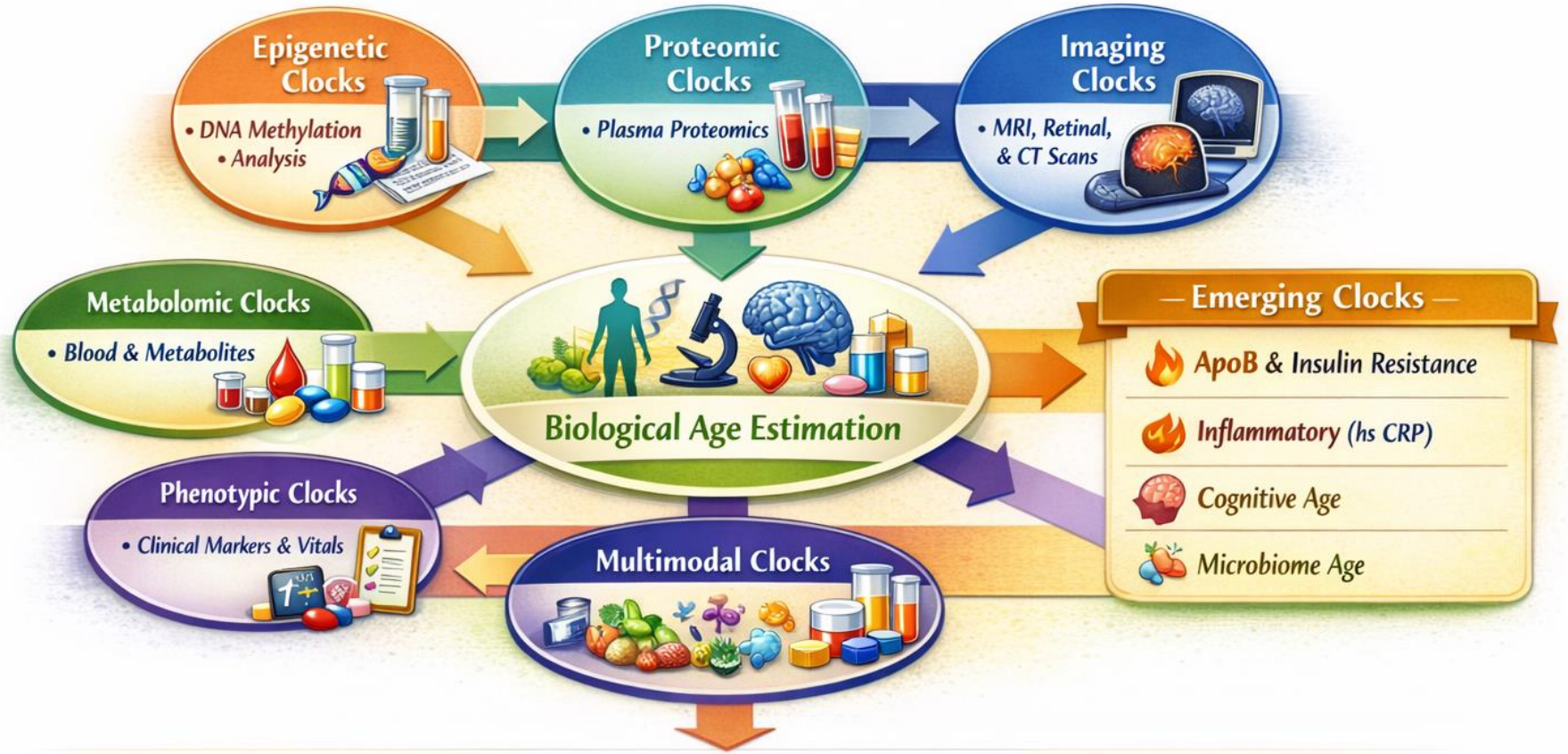
AI-driven age prediction

DNA methylation
Blood biochemistry
Transcriptomics
Metabolomics
Proteomics
Microbiome
Facial photographs



AI Approaches to Age Estimation

Methods for Predicting Biological Age and Healthspan



Longevity Health Blood Biomarkers

Laboratory Test Categories & Key Tests

Lipids & Apolipoproteins

- Total Cholesterol, LDL-C
- HDL-C
- Triglycerides
- ApoB
- Lp(a)
- Small LDL-P
- HDL Map

Metabolic & Glucose

- HbA1c
- Glucose
- Insulin
- HOMA-IR

Inflammation & Oxidation

- hs-CRP
- Lp-PLA$_2$ Activity
- OXPL-apoB

Fatty Acid Balance

- Omega-3 Index
- Omega-6/Omege-3 Ratio
- EPA & DHA

Cardiac & Kidney

- NT-proBNP
- Cystatin C
- eGFR & BUN

Vitamins & Nutrients

- Vitamin D
- B$_{12}$ & Folate
- CoQ10

Hormones

- Testosterone
- Estradiol
- Cortisol
- IGF-1

Thyroid Function

- TSH
- Free T4
- Free T3

Iron & CBC

- Ferritin
- Hemoglobin
- RDW
- WBC & Differential

Specialty Tests

- Cystatin C; eGFR
- BUN; eGFR

Advanced blood testing to assess cardiovascular, metabolic, hormonal, and micronutrient health.

Comprehensive Longevity Assessment

Key Tests and What They Measure

Cardiovascular Health

- **EKG** Heart Rhythm
- **ABI** PAD Screening
- **CT CAC Score** Coronary Plaque
- **Echocardiogram** Structure & Function
- **VO_2 Max Testing** Cardiopulmonary Fitness
- **Carotid Ultrasound** Vascular Assessment

Metabolic & Body Composition

- **DEXA** Bone Density
- **DEXA FIT**
- *Body Composition / Visceral Fat*

Genetic Risk

- Whole Genome Sequencing
- Polygenic Risk Scores DM, CAD, Alzheimer's

Neurologic

- Cognivue Cognitive Assessment
- Cognitive Screening

Respiratory / Sleep

- Pulmonary Function Tests
- Lung Capacity & Airway

Sensory Health

- **Audiometry** Hearing Assessment
- **Vision Testing** Eye & Vision Evaluation

Oncology / Early Detection

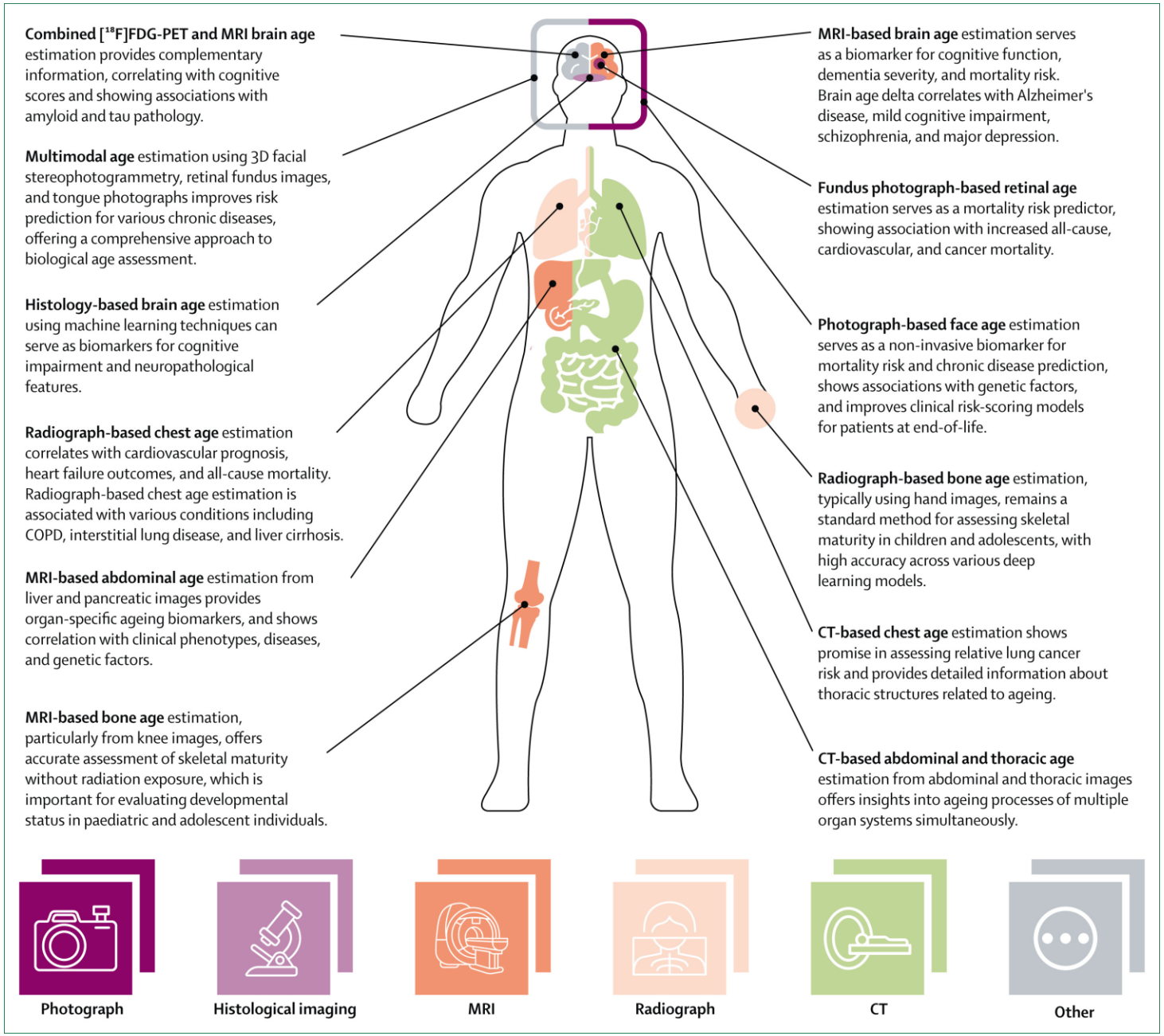
- **Chest X-Ray** Thoracic Imaging
- **Mammogram** Breast Cancer Screening

Early Detection

- **Galleri** Multi-Cancer Screening Test

- *Liver FibraScan*
- **Cologuard** Stool DNA CRC Screening
- **Microbiome Analysis** Digestive Health

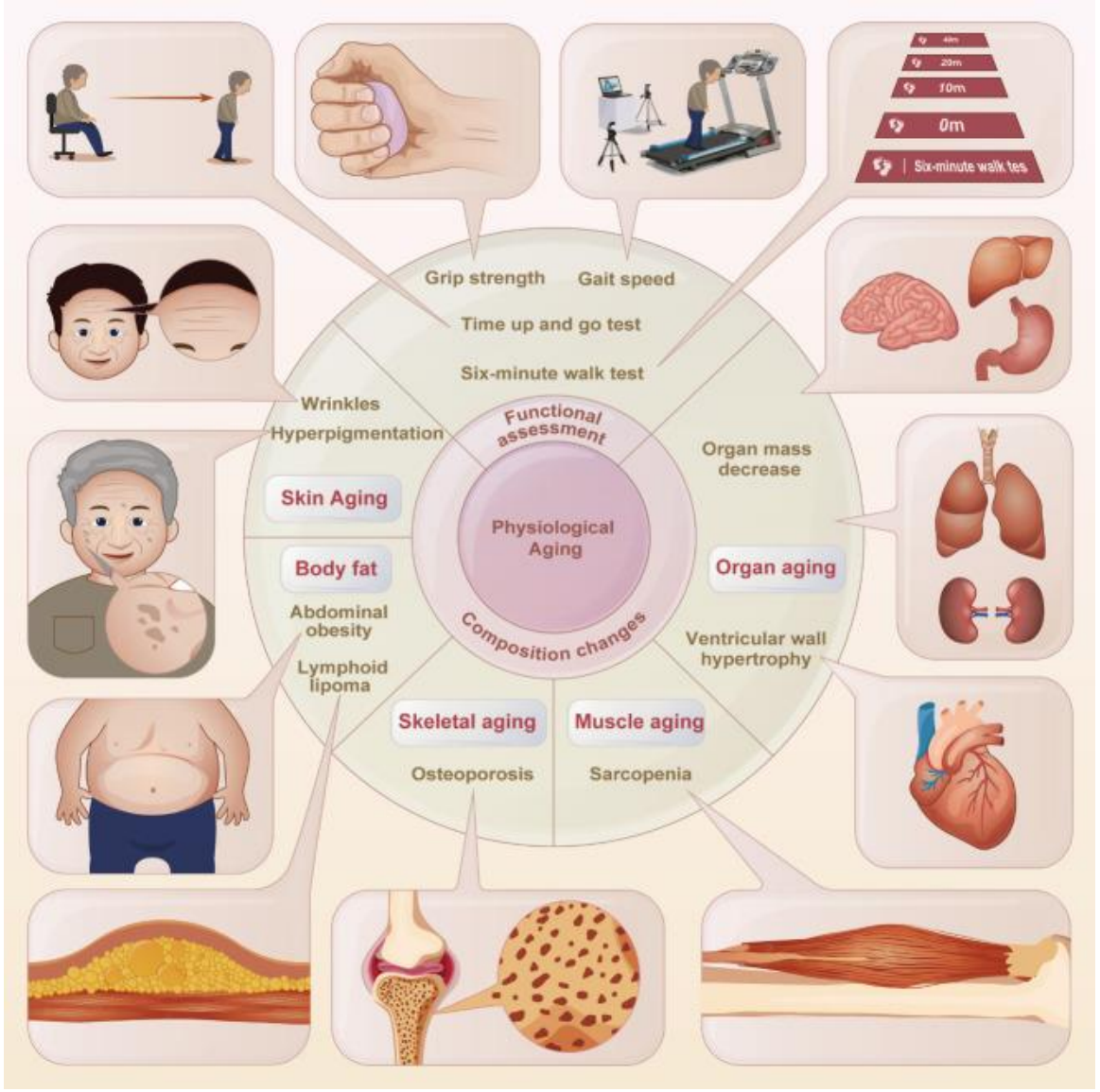
Together, these assessments identify early disease risk, functional decline, and modifiable drivers of aging—before symptoms appear.



AI-Based Imaging Biomarkers of Aging

Imaging biomarkers of ageing: a review of artificial intelligence-based approaches for age estimation
The Lancet Healthy Longevity, 2025; 6

Physiological and Functional Markers of Aging



whyiexercise.com

VO2 MAX AND SURVIVAL

VO2 max *(percentile score)*	10-Year Survival Rate*	Risk of death *(from any cause)*
Top 2%	97%	↓ 80%
Top 25%	96%	↓ 76%
Top 50%	93.5%	↓ 64%
Lower 50%	91%	↓ 49%
Bottom 25%	77%	Highest risk

*Ten-year survival measured from middle age (50s).
Based on fitness testing and long-term follow up of over 120,000 people!

Source: Mandsager, Harb, Cremer et al 2018.

Wearable Technology for Longevity

Devices for Tracking Health, Fitness, and Aging Biomarkers

Heart Rate & HRV

- Heart Rate Monitoring
- Heart Rate Variability (HRV)
- Resting Heart Rate
- HRV Trends & Recovery

Sleep Tracking

- Sleep Stages & REM
- Sleep Duration & Efficiency
- Sleep Apnea Detection
- Sleep Scores

Continuous Glucose Monitoring

- Real-Time Glucose Levels
- Glucose Trends
- Time in Range
- Dietary Response

Activity & Fitness

- Step Counting
- Exercise Performance
- VO_2 Max Estimation
- Calories Burned

Sleep & Circadian

- Sleep Efficiency
- AHI / ODI
- HRV
- Sleep Duration & Regularity

Respiratory & Oxygenation

- Step Count
- Exercise Volume
- VO_2 Max Estimation
- Calories Burned

Respiratory & Oxygenation

- Oxygen Saturation (SpO_2)
- Respiratory Rate
- Breathing Patterns
- Altitude Adaptation

Sleep & Circadian

- Sleep Efficiency
- AHI / ODI
- HRV
- Sleep Duration & Regularity

Wearables provide actionable data for optimizing health, fitness, and aging biomarkers.

Sleep & Longevity

How Sleep Impacts Aging and Healthspan

Sleep Metrics Mapped to Biomarkers

Key Sleep Metrics and Their Impact on Longevity Biomarkers

<6 hrs or >9 hrs:

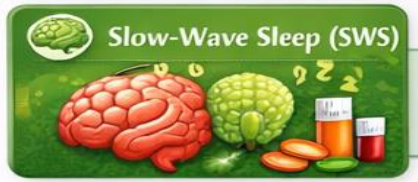
- ↑ Insulin Resistance & HbA1c
- ↑ Blood Pressure
- ↑ CRP & Inflammation
- ↑ ApoB / LDL Particles

<85% Efficiency:

- ↑ hs-CRP & Cytokines
- ↑ Heart Rate (↓ HRV)
- ↑ Heart Rate (↓ HRV)
- ↑ Fragmented Sleep Patterns

Elevated AHI / ODI:

- ↑ hs-CRP & Oxidative Stress
- ↑ Blood Pressure Variability
- ↑ NT-proBNP
- ↑ Blood Pressure Variability

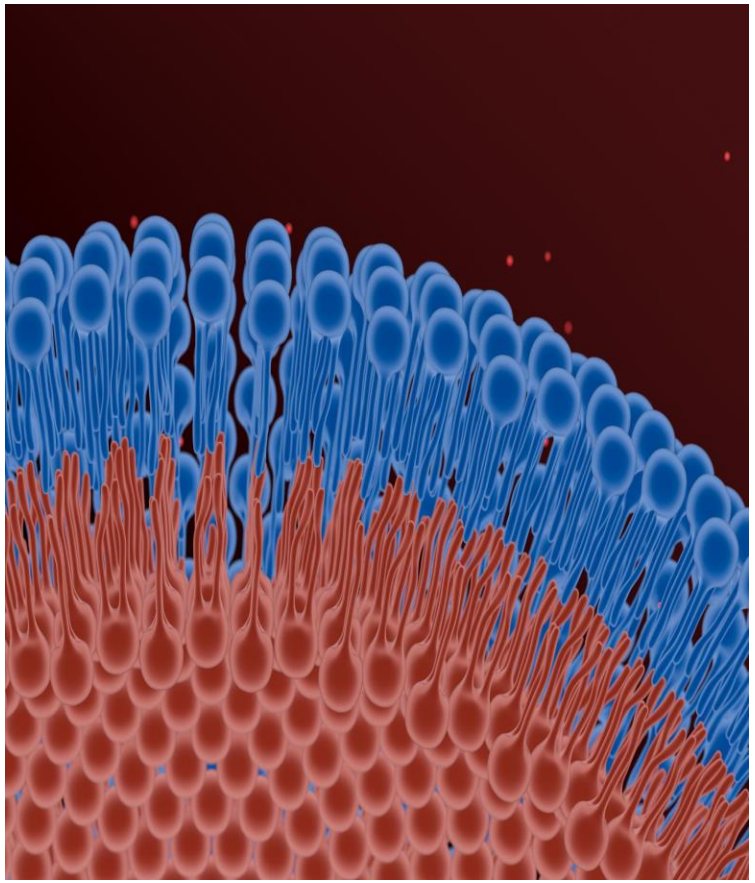


Reduced SWS:

- ↑ β-Amyloid & Tau Buildup
- ↑ Alzheimer's Risk
- ↓ Glymphatic Clearance
- ↓ Insulin Sensitivity
- ↑ Alzheimer's Risk
- ↓ Glymphatic Clearance

Sleep Disturbances Elevate Biomarkers Linked to Metabolic Dysfunction, Vascular Aging, and Cognitive Decline.

Role of the Gut Microbiome in Healthspan and Aging



- Microbiome's Role in Aging
  - Regulate metabolism, immunity, and inflammation, influencing aging process and healthspan
- Changes in Microbial Diversity
  - Microbial diversity decreases with age, chronic disease, and medication, associating with inflammation and age-related conditions
- Microbiome Measurements
  - Diversity, beneficial bacteria, metabolic activity, and pathogens
- Microbiome Testing and Healthspan
  - Microbiome analysis aids personalized interventions, supporting healthspan but not proven to extend lifespan directly

Genetic Testing for Longevity

Assessing Genetic Risk to Inform Health and Longevity

Genetic Foundations

- **Whole Genome Sequencing**
- Full DNA Analysis
- Rare Genetic Mutations

ApoE Genotyping

- **ApoE e2 / e3 / e4**
- Brain & Lipid Metabolism

Polygenic Risk Scores (PRS)

- Cumulative Risk Assessment
- Multiple SNPs Combined
- Relative Risk Estimates

Key Genetic Risk Areas

- *Cardiovascular Disease*
- *Cancer Susceptibility*
- *Neurodegenerative Risk*
- *Metabolic Health (Diabetes)*

Single Gene Disorders

- Rare Hereditary Diseases
- Carrier Screening

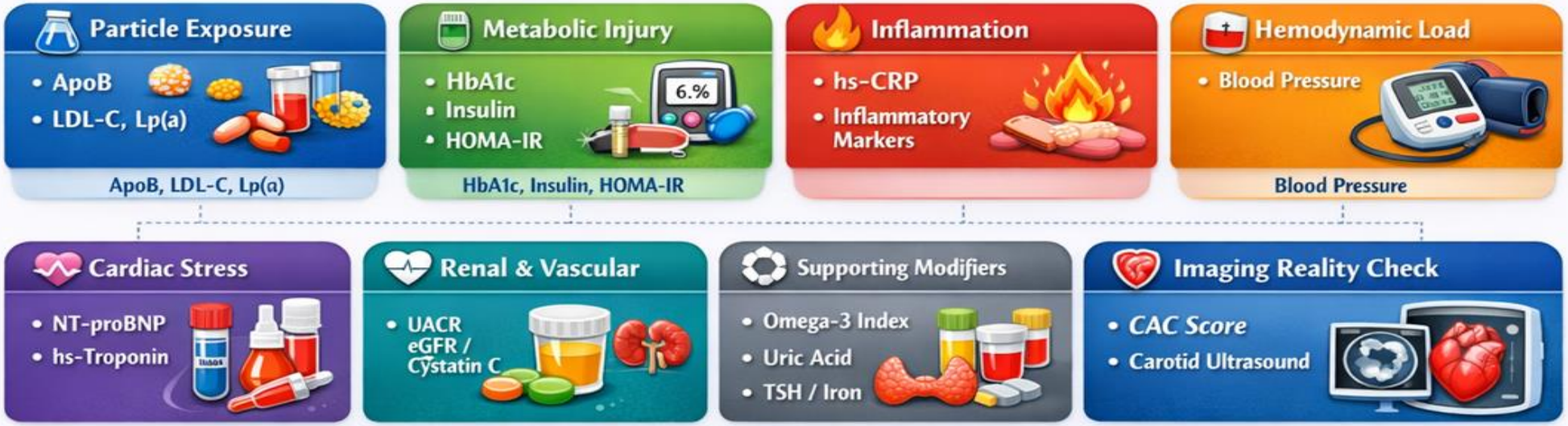
Genetic Counseling & Action

- Risk Interpretation
- Targeted Prevention Strategies

Using genetic insights to guide personalized health and longevity interventions.

Cardiac Measurements of Longevity

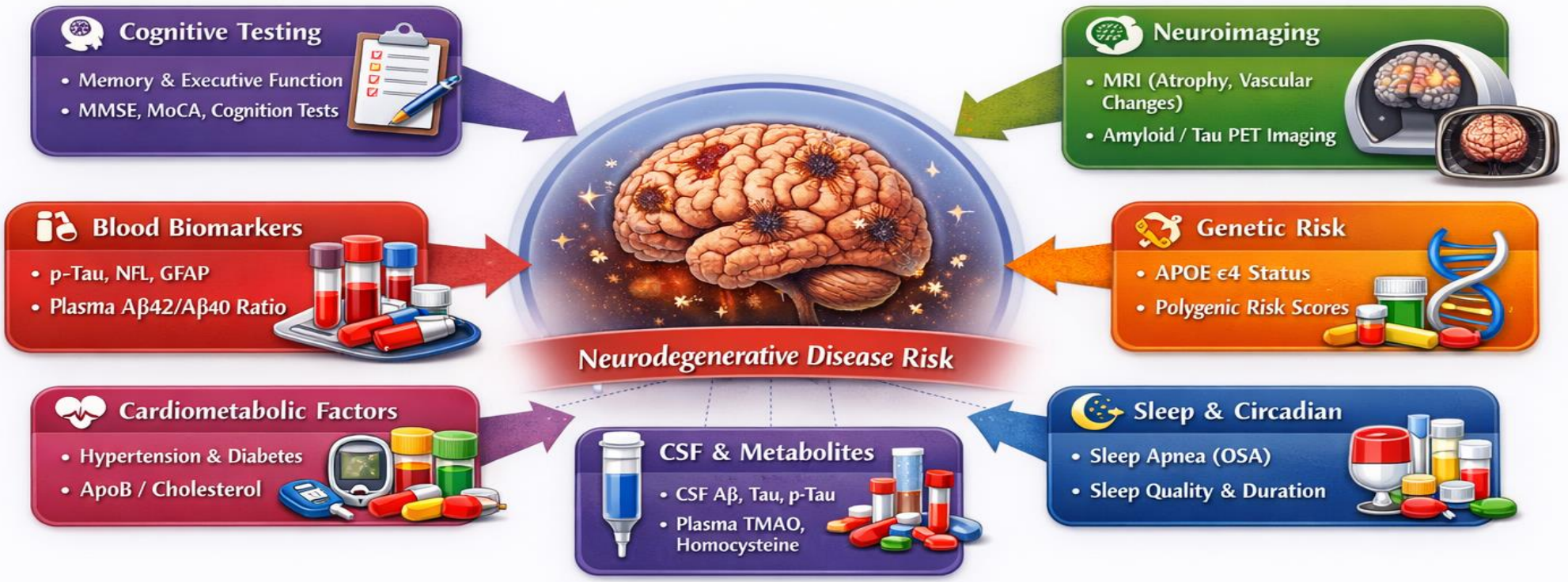
Quantifying atherosclerosis biology across the artery-first model



Measuring particle burden, metabolic injury, inflammation, and stress—long before clinical events occur.

Evidence-Based Measurements of Neurodegenerative Disease Risk

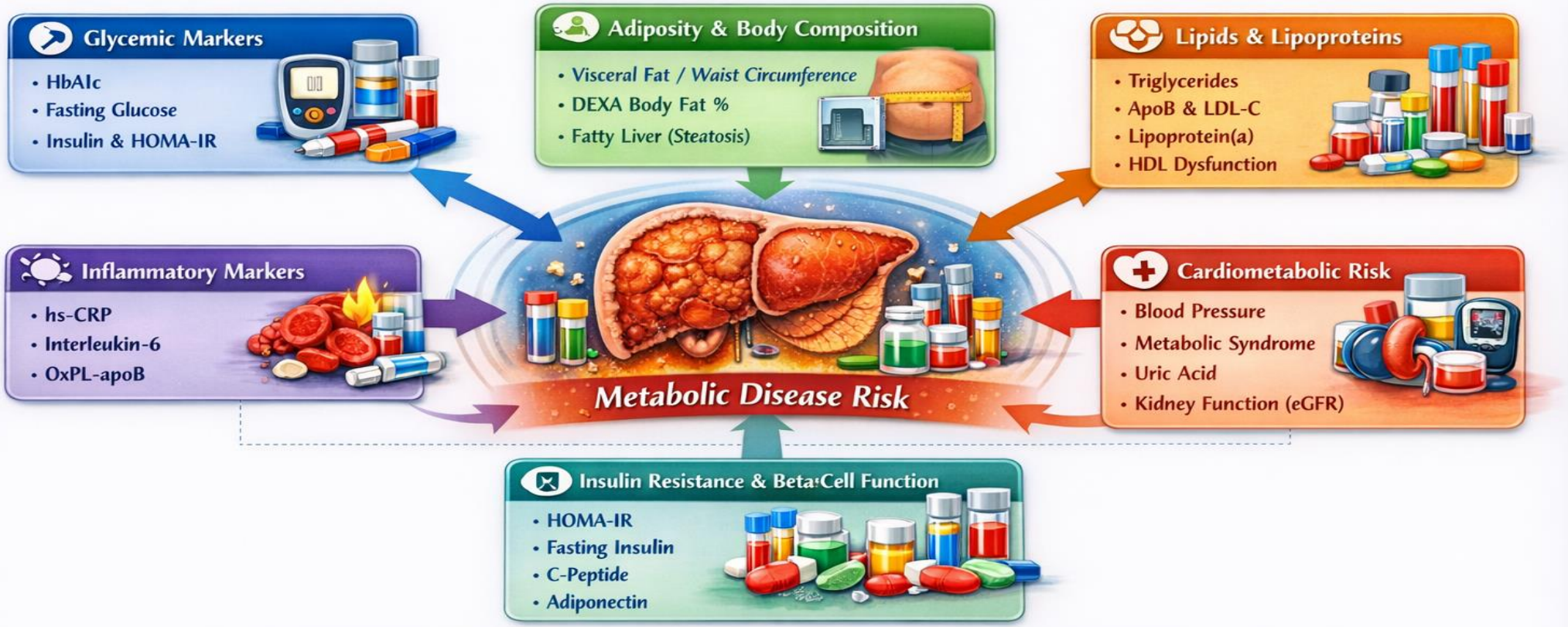
Key Clinical Assessments and Biomarkers Linked to Cognitive Decline



Multi-domain assessment is key to evaluating neurodegenerative risk.

Evidence-Based Measurements of Metabolic Disease Risk

Key Clinical Assessments and Biomarkers Linked to Metabolic Dysfunction



Assessing the multi-factorial drivers of metabolic disease and its impact on healthspan.

Goals and Objectives of Longevity Interventions

Core Mission
- Extend healthspan over lifespan
- Delay chronic disease

Preserve Cognitive Function
- Prevent/delay cognitive decline
- Reduce dementia risk
- Maintain independence

Prevent ASCVD
- Reduce lifetime ApoB exposure

Preserve Metabolic Health
- Prevent insulin resistance
- Maintain healthy body composition

Reduce Chronic Inflammation
- Target systemic inflammatory markers

Maintain Physiologic Reserve
- Muscle mass and VO_2 reserve

Optimize Foundational Behaviors
- Sleep
- Physical activity
- Nutrition
- Stress regulation

Early Detection & Tracking
- Risk assessments
- Biomarker tracking

Personalized Prevention
- Genetics & biomarkers

Evidence-Based Sleep Interventions & Longevity

Targeted Approaches to Improve Sleep and Health Outcomes

Improving sleep positively impacts cardiovascular, metabolic, and cognitive healthspan.

Evidence-Based Diets for Longevity

Nutritional Patterns Linked to Healthspan and Reduced Mortality

Nutrition for Longevity

Emphasize Plant-Based Foods

Consuming ample vegetables, fruits, whole grains, and lean proteins supports health and longevity.

Limit Unhealthy Ingredients

Minimize processed foods, added sugars, unhealthy fats, alcohol and excess sodium for better long-term health.

Hydration and Eating Patterns

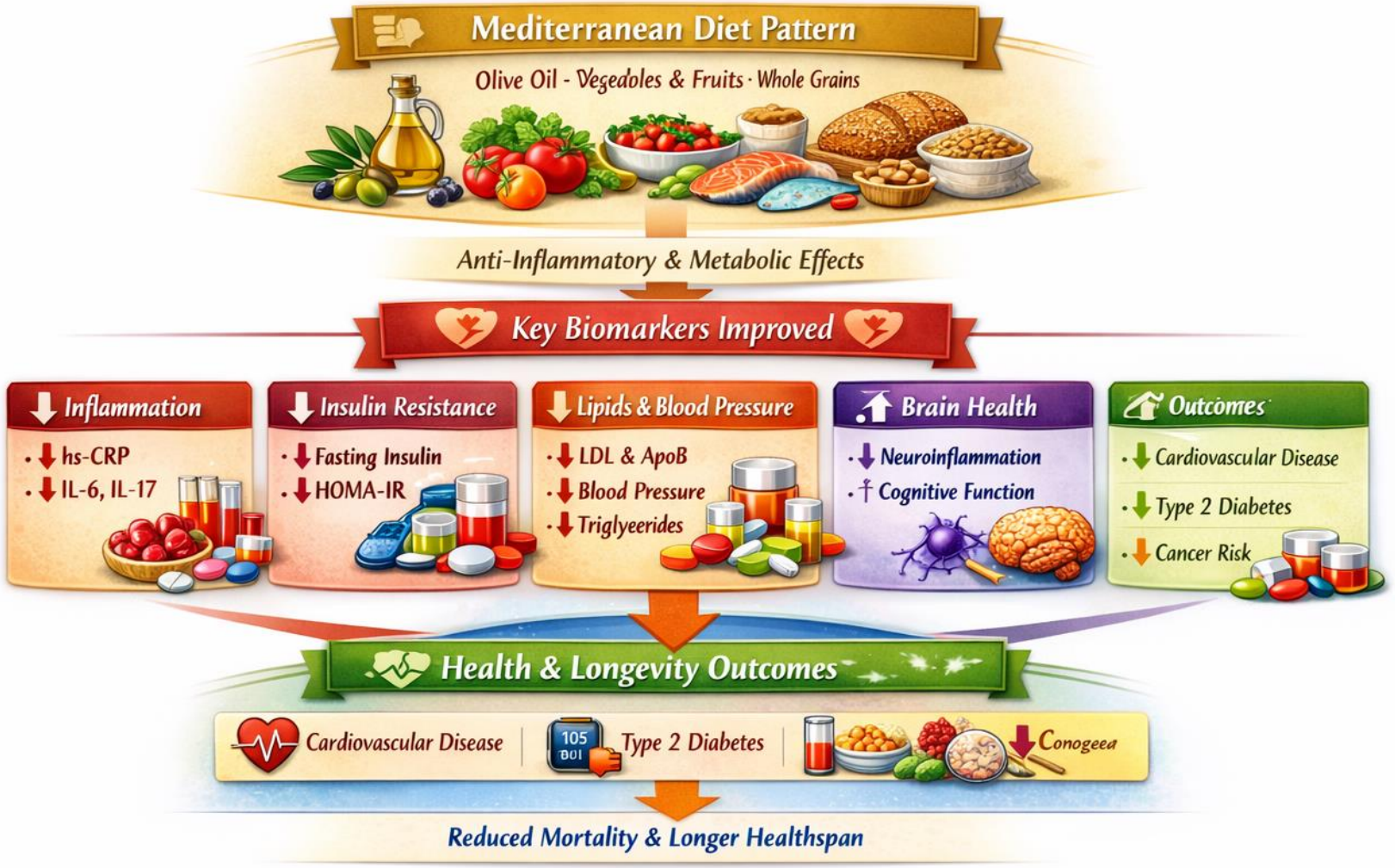
Stay hydrated, practice portion control, and consider time-restricted eating for longevity benefits.

Adopt Healthy Diet Models

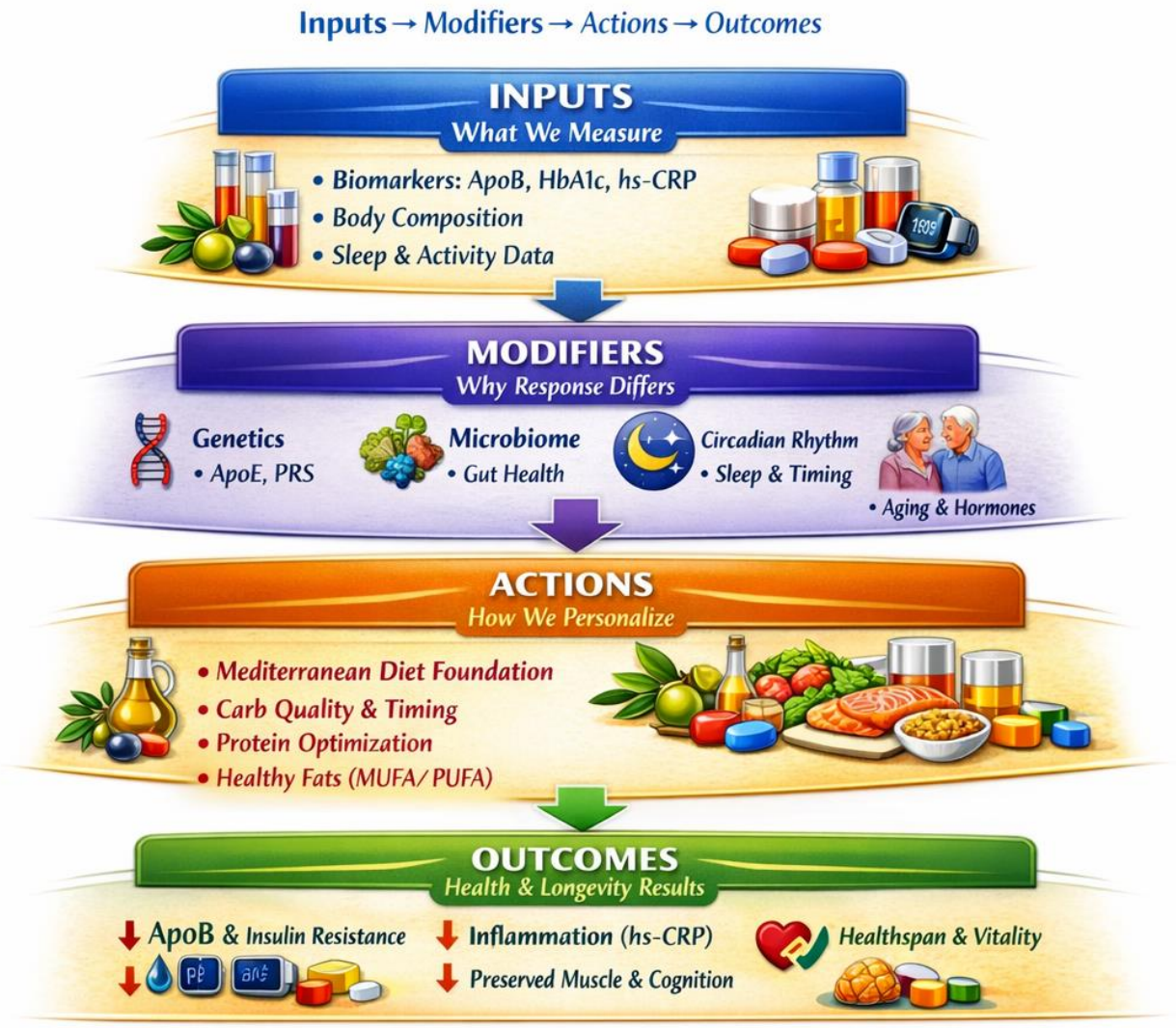
Patterns like the Mediterranean or Okinawa diets promote sustainable health and increased lifespan.

Mediterranean Diet: *From Nutrition to Outcomes*

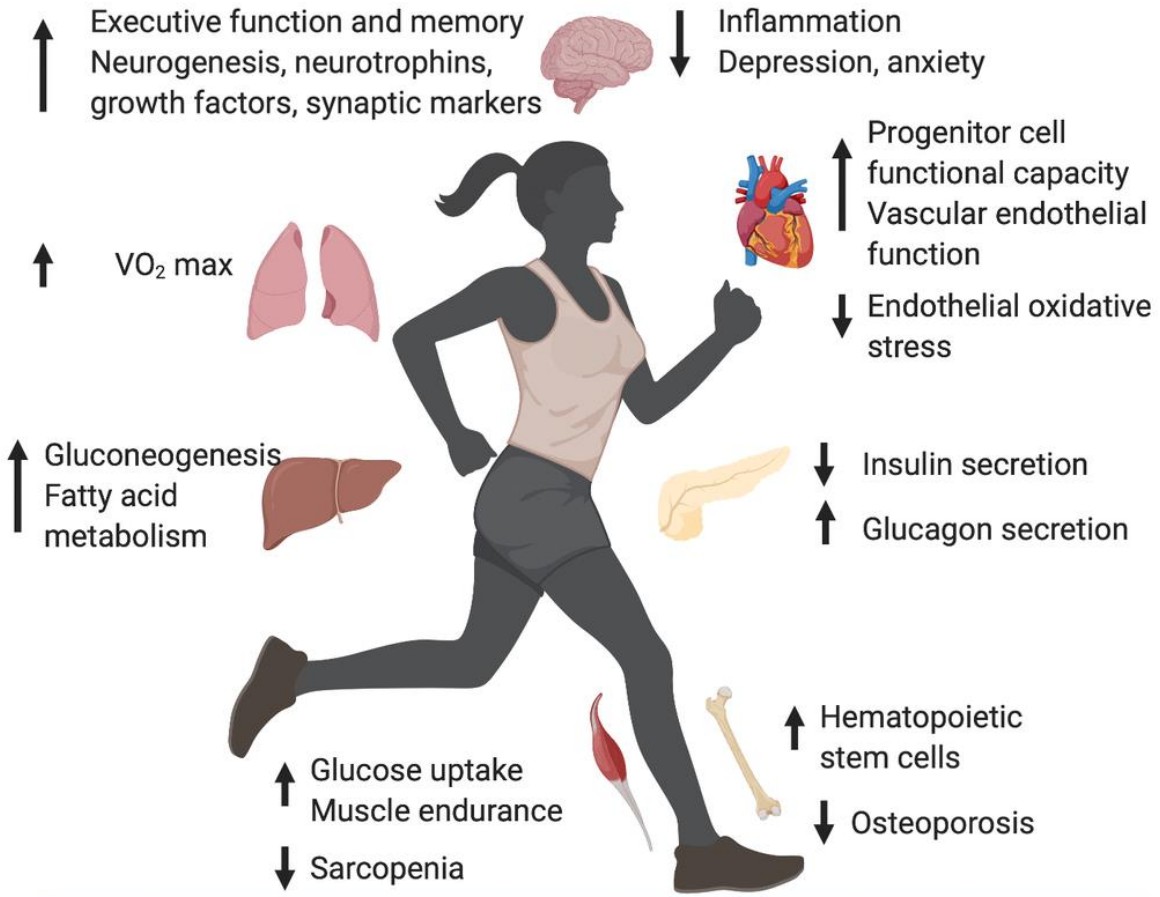
How the Mediterranean Diet Impacts Biomarkers and Health Outcomes



Precision Nutrition Embedded in the Mediterranean Diet



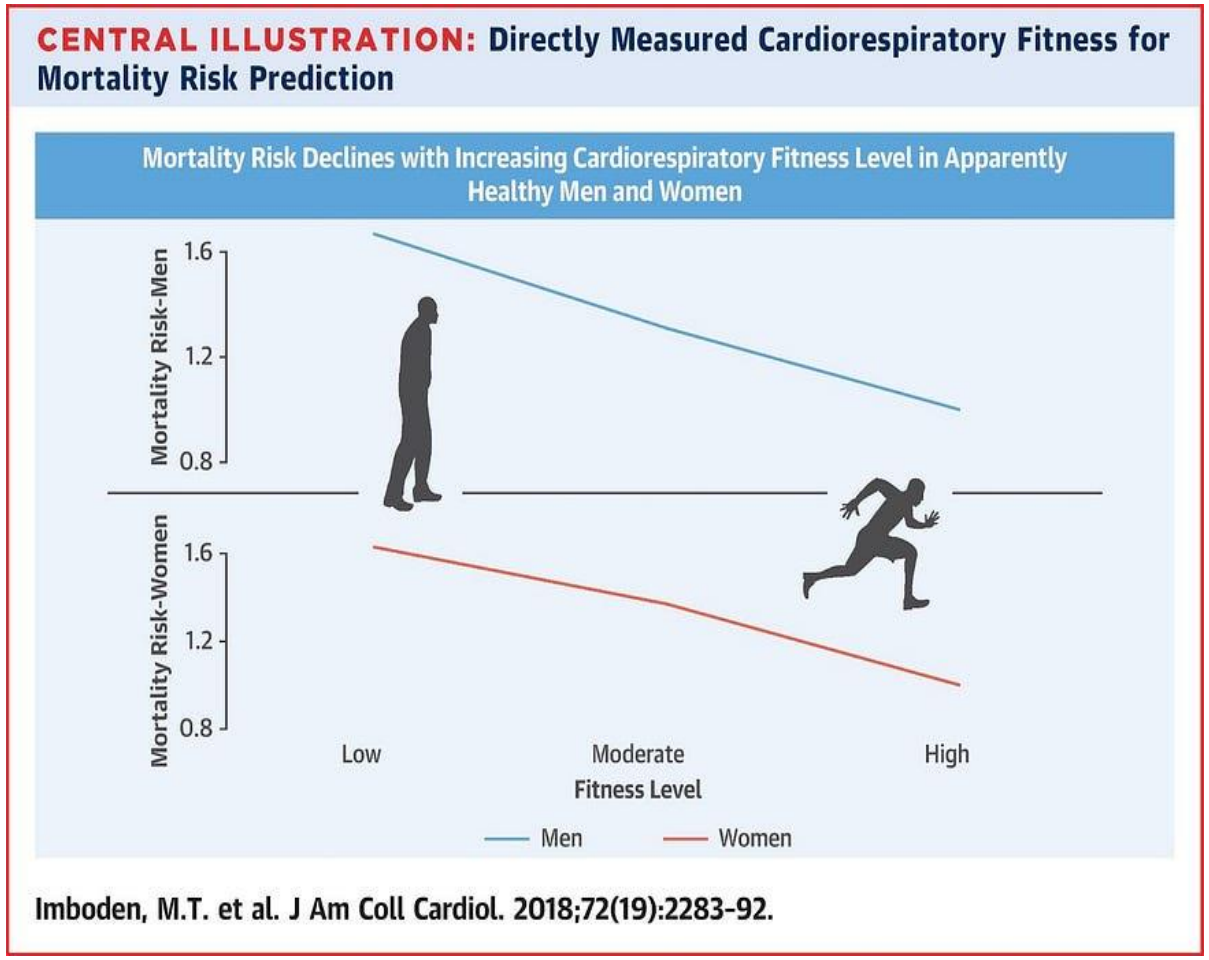
Impact of Exercise on Longevity



Longevity effects: exercise >150 but <2000 minutes/week.
Combination of aerobic and resistance exercise

→

- ↑ Independence with Activities of Daily Living
- ↑ Quality of life
- ↑ Physical function
- ↑ Aerobic capacity
- ↑ Muscle strength
- ↑ Muscle quality
- ↓ Fall risk
- ↓ Frailty



Exercise Prescription for a Healthier Life

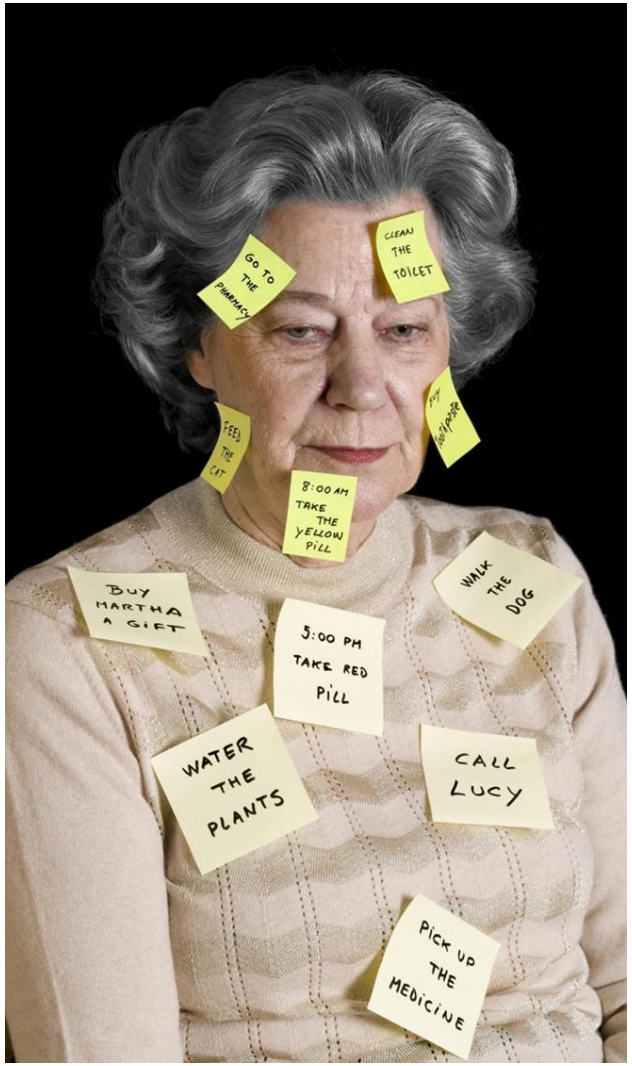
1. Aerobic Exercise
   - Enough: 30-45min, 5 days/week
   - Optimal:45-90 min most days
2. High Intensity Training
   - 1-2 times/week, 6 minutes total
3. Strength Training
   - Enough-2 days/week
   - Optimal-3 plus days/week

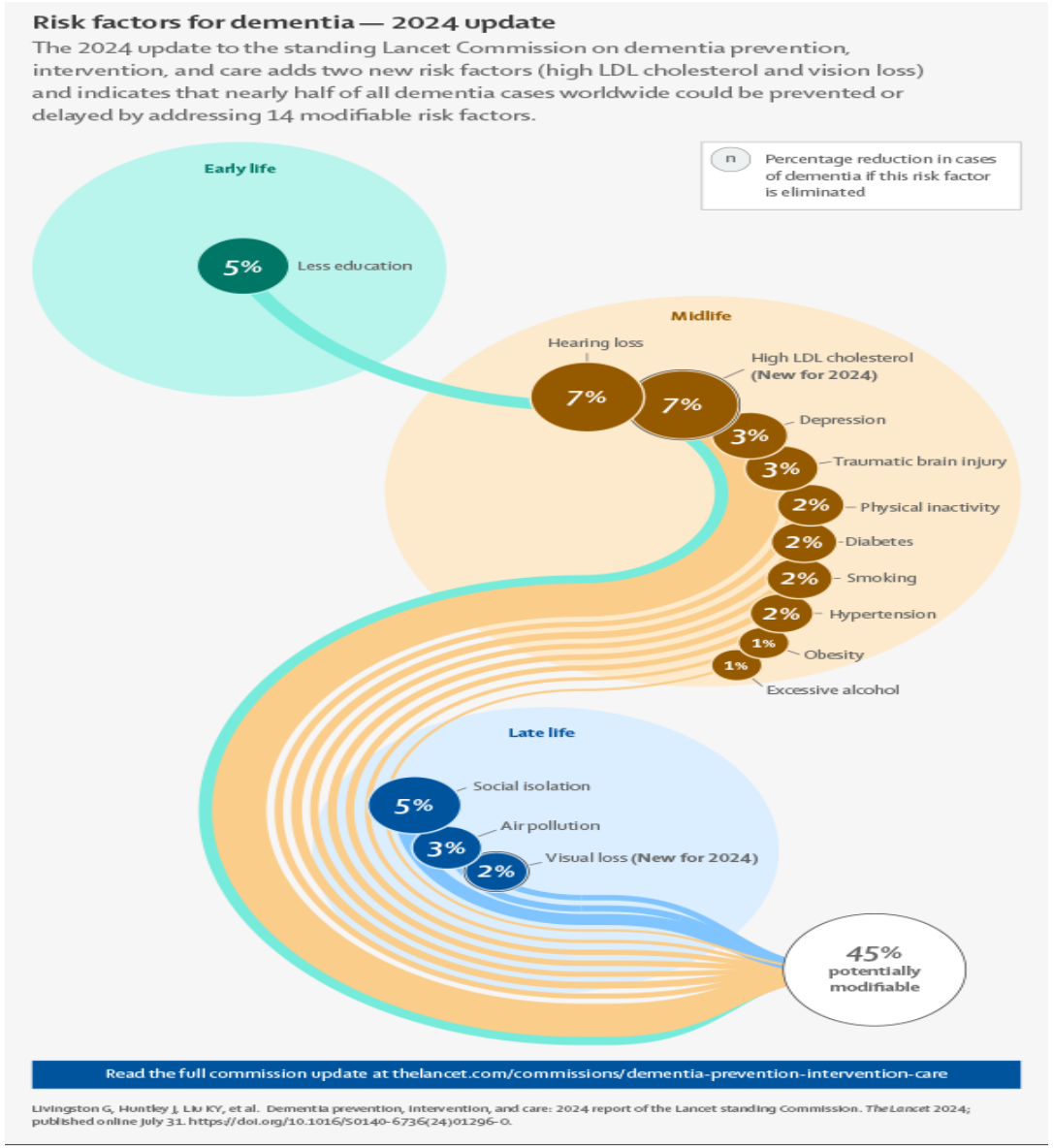
Impact on Biomarkers

- Reduced insulin resistance, APO B, and inflammation
- Improved Vo2 max and lean muscle mass

Dementia Prevention

Modifiable Risk Factors





Optimizing Brain Health To Improve Longevity

10 ways to reduce your risk of dementia

Alzheimer Society

Be physically active each day

Get moving! Any physical activity is better than none at all.

Protect and support your hearing

Hearing loss in midlife can increase dementia risk by an average of 90%. Use hearing aids if needed – they help reduce that risk.

Stay socially active

Stay connected and engaged with your family, friends and community. Social isolation in later life can increase dementia risk by an average of 60%.

Manage your medical conditions

In collaboration with your health-care provider, try to manage complex conditions such as diabetes and obesity as best you can.

Quit smoking

Get support in quitting or reducing smoking. Even in later life, these steps can improve your brain health and reduce your dementia risk.

Seek support for depression

Depression is more than just feeling sad. Seeking depression treatment and support will help improve your mood and brain functioning.

Drink less alcohol

Drinking more than 12 standard drinks a week in midlife increases dementia risk by an average of 20%. If you need help in quitting or limiting alcohol, speak with your health-care provider.

Protect your heart

Working with your health-care provider, monitor and manage your blood pressure and heart health. What's good for the heart is also good for the brain!

Avoid concussion and traumatic brain injury

Steer clear of activities where you might put your brain at risk of harm. Play, travel and work safe!

Aim to get quality sleep

Work toward sleeping well for 6 to 8 hours each night. If you experience sleep apnea or other sleep issues, talk to your health-care provider for treatment options.

The more actions you take, the better! Learn more at alzheimer.ca/ReduceYourRisk.

Enhancing Mental Health and Cognitive Resilience with Aging

Exercise

Sleep

Nutrition

Cognitive Engagement

Social Connection & Purpose

Stress Regulation & Psychological Flexibility

Physical Health Optimization

Drugs with Potential Anti-Aging Properties

Promising Medications for Longevity

Medication	Primary Use	Longevity Mechanism	Research Status
Rapamycin	Immunosuppressant	Inhibits mTOR (a protein that regulates cell growth and aging)	Highly promising in animals; human trials for aging are ongoing.
Metformin	Type 2 Diabetes	Activates AMPK, improves insulin sensitivity, and reduces inflammation	Most studied in humans; TAME Trial is specifically testing its anti-aging effects.
Acarbose	Type 2 Diabetes	Slows carbohydrate digestion, preventing blood sugar spikes	Shown to extend lifespan in male mice significantly.
SGLT2 Inhibitors	Type 2 Diabetes	Lowers blood sugar and reduces cardiovascular risk	Ranked highly for "gerotherapeutic" potential by experts like Nir Barzilai.
GLP-1 Agonists	Weight Loss / Diabetes	Reduces inflammation and targets metabolic mechanisms of aging	Emerging area of interest for its broad multi-disease protection.
Atorvastatin	High Cholesterol	Lowers "bad" cholesterol and reduces systemic inflammation	Associated with increased lifespan in large-scale observational data.
Sildenafil	Erectile Dysfunction	Improves vascular health and blood flow	Observed association with lower mortality risk in UK Biobank data.
17α-Estradiol	Hormone Replacement	Mimics estrogen's protective effects without feminizing side effects	Extended lifespan in male mice; currently being studied for human metabolic health.

Supplements for Longevity

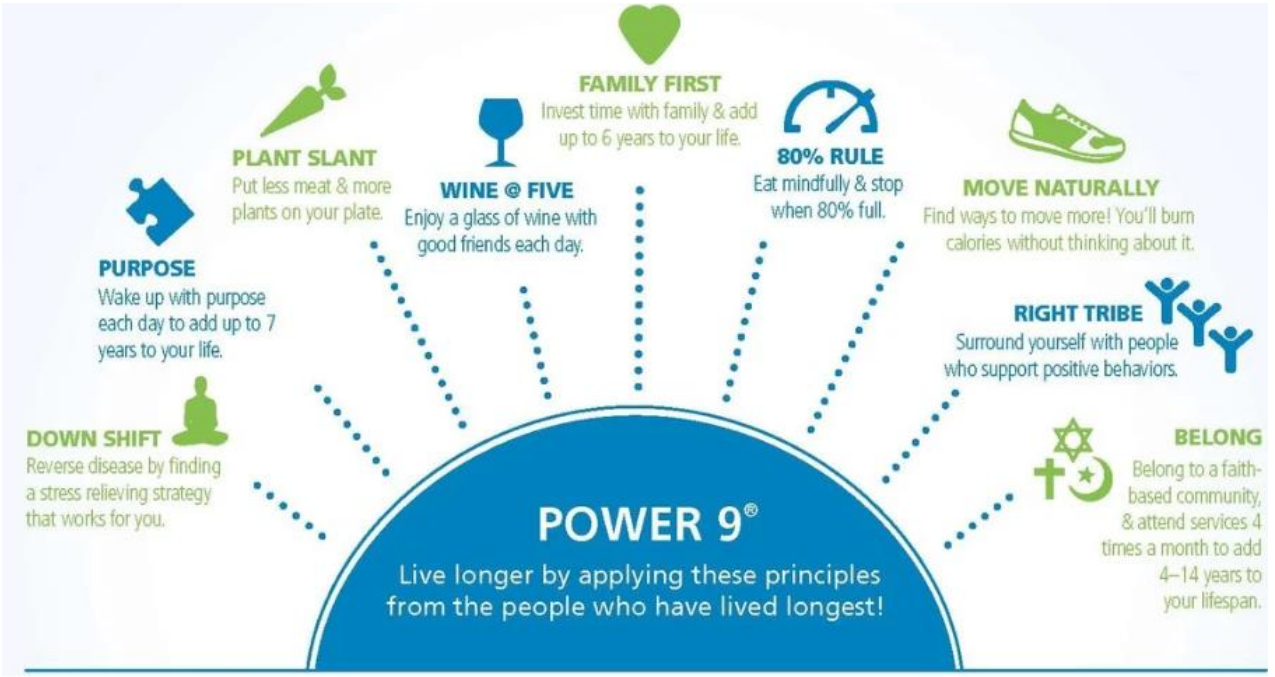
Supplement	Mortality Evidence	Best Use Case
Omega-3 (EPA)	✅ ✅	ASCVD risk
Vitamin D	✅ (conditional)	Deficiency, cancer mortality
Magnesium	✅ (dietary)	Low intake, metabolic risk
Protein	❌ (healthy) / ✅ (frail)	Sarcopenia
Multivitamin	❌	Cognitive support
NAD^+ boosters	❌	Not recommended
Resveratrol	❌	Not recommended

Nonpharmacological and Plasma Interventions

Intervention	Human Evidence	Longevity Signal	Clinical Recommendation
Young plasma transfusion	Very limited (small observational and perioperative studies)	❌ None	Do not use outside clinical trials
Therapeutic plasma exchange (TPE)	Randomized and controlled human studies; disease-specific trials	⚠️ Biomarker improvement only	Experimental / investigational use only
Standard blood transfusion	Extensive evidence for medical indications	❌ None	Use only for standard medical care
Plasma fractions / extracellular vesicles	Preclinical and early translational research	⚠️ Theoretical	Research-stage only
Hyperbaric Oxygen Therapy	Small prospective trial in humans showed telomere lengthening	No evidence yet of increased lifespan	

Intervention	Human Aging Biomarkers	Mortality Evidence
Statins	❌	✅✅✅
SGLT2 inhibitors	❌	✅✅✅
Metformin (IR/T2DM)	❌	✅✅
HBOT	✅✅✅	❌
TPE (plasmapheresis)	✅✅	❌
NAD^+ boosters	❌	❌

Lessons from Blue Zones



Summary

- Longevity focuses on improving healthspan
- Aging is a complex process that occurs at a molecular level impacted by genetics, environment and lifestyle
- Biomarkers, genetic testing and diagnostic imaging provide a good estimate of longevity
- Longevity is most significantly impacted by adopting a healthy lifestyle that includes regular exercise, good sleep hygiene, healthy eating, social connection and stress reduction

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Thank You