

Multicomponent Interventions in a Geroscience Context

AGS/NIA Optimizing Resilience

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Buck



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Live better longer.

Disclosures

- Component Health, Ltd: Co-founder, stockholder
- Selah Therapeutics, Ltd: Co-founder, stockholder
- BPOZ: Co-founder, stockholder
- Junevity: Scientific Advisory Board
- Virta Health: former Scientific Advisory Board

AGING

A central diagram with the word 'AGING' in large red letters at the top. Below it, several colorful arrows (purple, blue, pink, red, orange, yellow, green) point outwards to various health conditions listed in colored boxes. The conditions include cardiovascular diseases, neurological disorders, respiratory issues, musculoskeletal problems, and metabolic conditions.

Atherosclerosis
Heart Attack
Stroke

Glaucoma
Macular
Degeneration

Emphysema
Pneumonia

Alzheimer's
Parkinson's
Delirium

Cancer

Sarcopenia

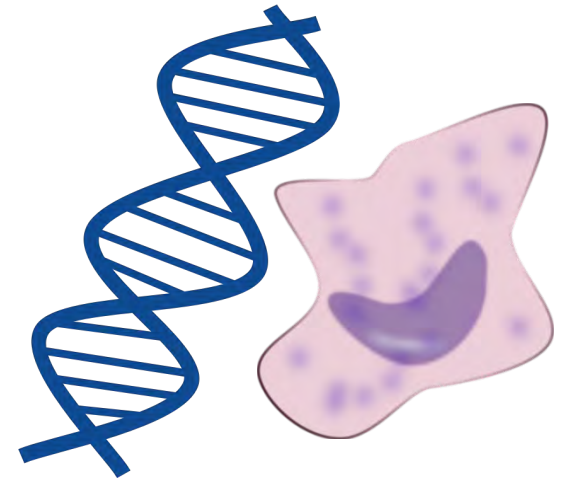
Type 2 Diabetes

Osteoarthritis
Osteoporosis



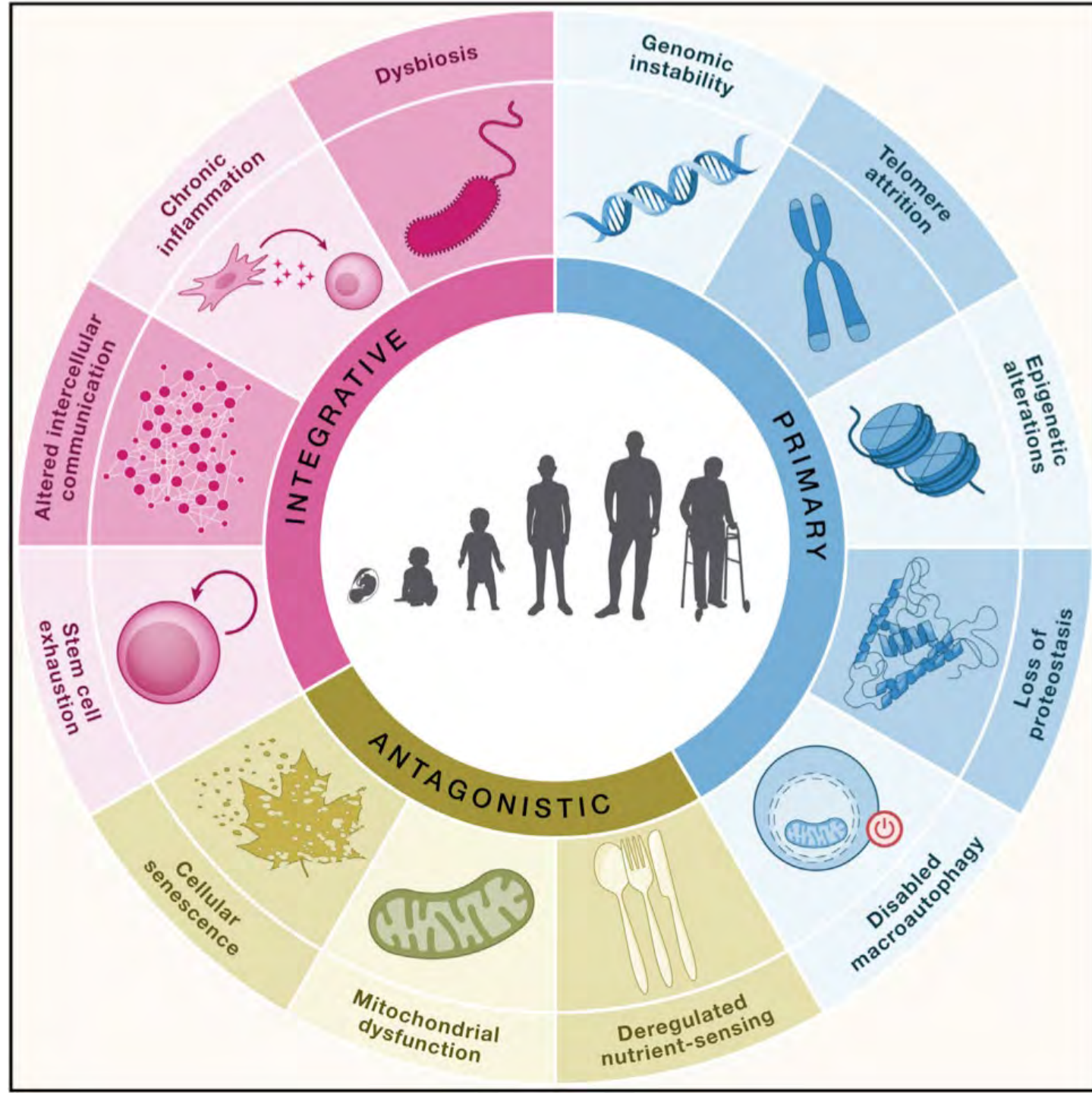
Age is a Not a Number

...Aging is Biology



Aging phenotypes are driven by specific, modifiable molecular mechanisms...

The "Hallmarks of Aging"



López-Otín, PMID 36599349

The Geroscience Hypothesis:





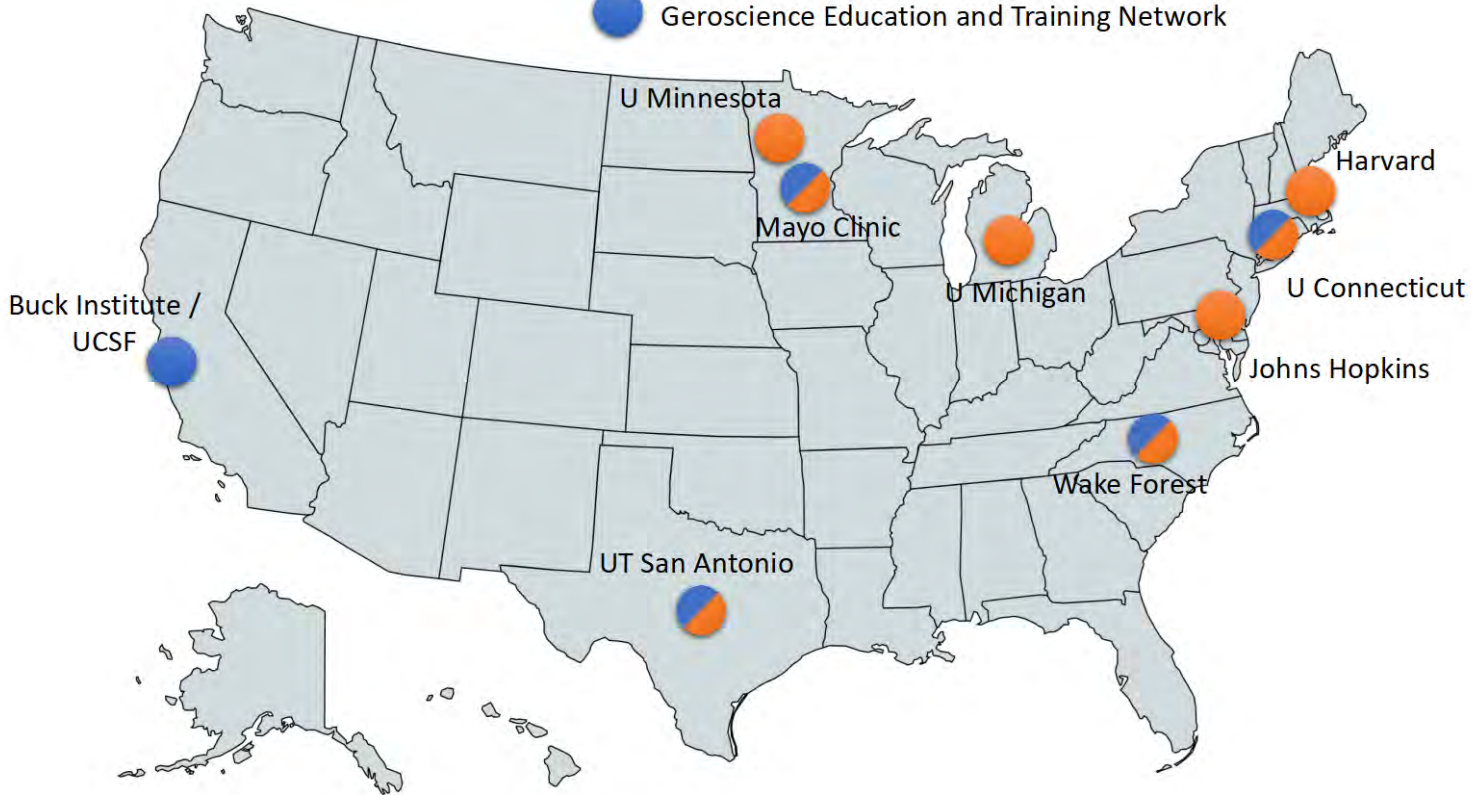
Interventions that target fundamental mechanisms of aging (**gerotherapeutics**) will prevent, mitigate, or treat *multiple* diseases and conditions of aging *simultaneously*

National Geroscience Networks



**TRANSLATIONAL
GEROSCIENCE NETWORK**

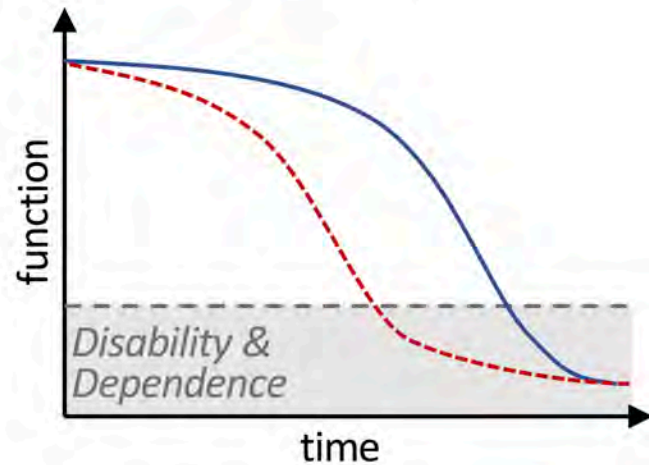
-  The Geroscience Network
-  Geroscience Education and Training Network



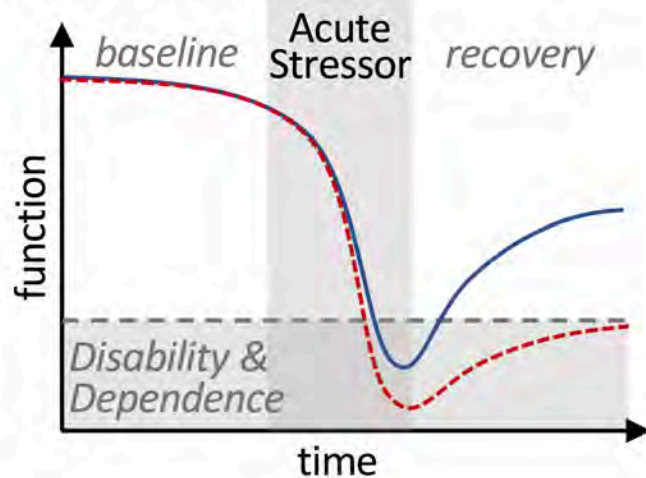
**Geroscience
Education & Training
Network**

Geroscience Clinical Trials to Change Practice

A. Extending Healthspan



B. Enhancing Resilience



Age associated decline in Intrinsic Capacity
(WHO, ICD-11 code MG2A)

Multimorbidity
(MACE-like composite)

Geriatric Syndromes
(frailty, sarcopenia, mobility disability, cognitive impairment, incontinence, etc.)

Multicomponent Interventions Improve Complex Outcomes

INTERVENTION DURATION: 2 YEARS

Structured lifestyle intervention: 38 facilitated peer team meetings over 2 years, with education, goal-setting, and accountability to support the health behaviors below

Physical exercise:

Aerobic, resistance, and stretching and balance exercise primarily at a community facility, with support through facilitated peer group meetings

Nutrition:

Encouragement to follow the MIND diet, with support through peer group meetings and telephone contacts with the interventionist

Cognitive and social challenge:

Computer cognitive training at home and regular participation in intellectually and socially engaging activities through peer group meeting support

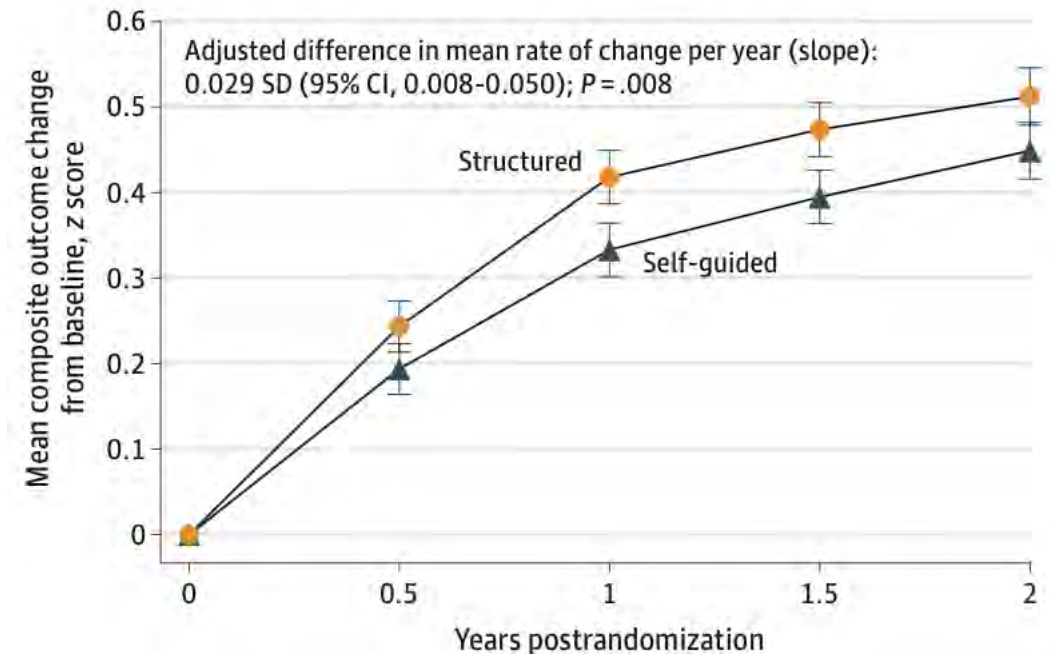
Guideline-based health coaching:

Medical advisor appointments every 6 months to review monthly pressure monitoring results, blood laboratory results provided at clinic visits, and goal-setting

POINTER-US

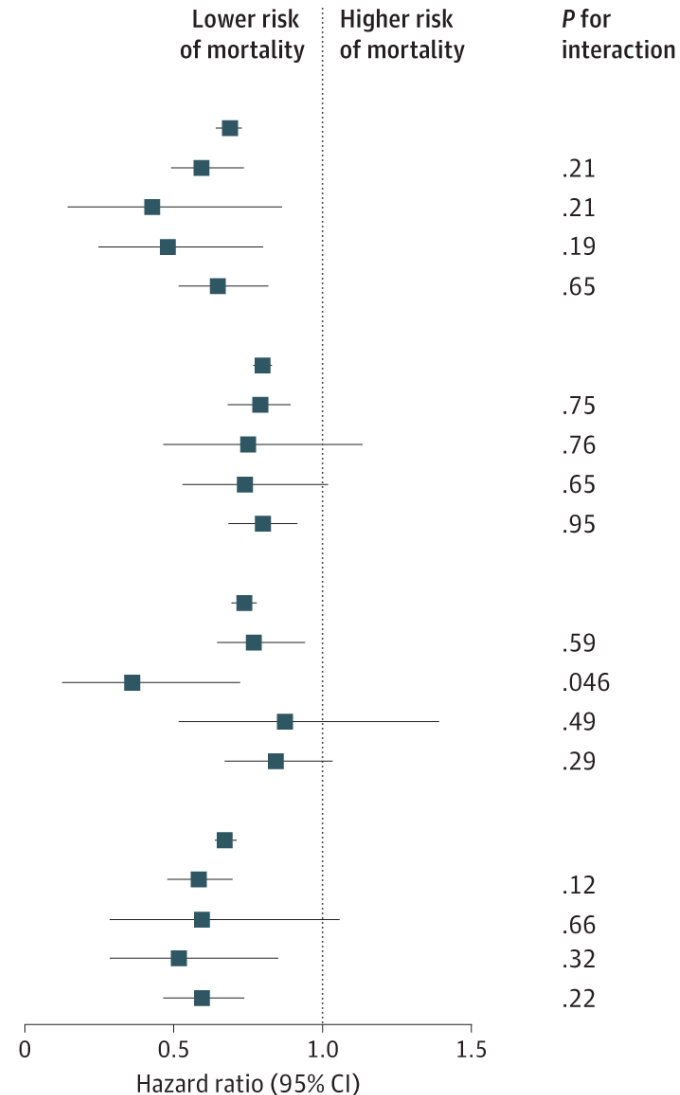
A multi-domain lifestyle intervention improves cognitive function in older adults in US (average age 68)
Baker et al., JAMA 2025

See also:
FINGER (Finland)
SMARRT (US)
CORDIOPREV (Spain)
...many others...



There Are Many Effective “Healthy Eating Patterns” – How?

Healthy eating score, race and ethnicity	Cases/ person-years	Hazard ratio (95% CI)
HEI-2015		
Non-Hispanic White	29 291/2 197 702	0.75 (0.72-0.78)
Racial and ethnic minority group	1972/145 442	0.68 (0.60-0.79)
Hispanic	217/18981	0.55 (0.33-0.89)
Non-Hispanic Black	346/25 515	0.59 (0.41-0.84)
Other	1409/100946	0.72 (0.62-0.85)
AMED		
Non-Hispanic White	29 291/2 197 702	0.84 (0.82-0.86)
Racial and ethnic minority group	1972/145 442	0.83 (0.75-0.91)
Hispanic	217/18981	0.80 (0.58-1.10)
Non-Hispanic Black	346/25 515	0.79 (0.63-1.01)
Other	1409/100946	0.84 (0.75-0.93)
HPDI		
Non-Hispanic White	29 291/2 197 702	0.79 (0.76-0.82)
Racial and ethnic minority group	1972/145 442	0.82 (0.72-0.95)
Hispanic	217/18981	0.50 (0.32-0.78)
Non-Hispanic Black	346/25 515	0.90 (0.62-1.30)
Other	1409/100946	0.87 (0.74-1.02)
AHEI		
Non-Hispanic White	29 291/2 197 702	0.74 (0.72-0.77)
Racial and ethnic minority group	1972/145 442	0.67 (0.59-0.76)
Hispanic	217/18981	0.68 (0.44-1.04)
Non-Hispanic Black	346/25 515	0.62 (0.44-0.88)
Other	1409/100946	0.68 (0.58-0.79)



Healthy Eating Index 2015
 Alternate Mediterranean Diet Score
 Healthful Plant-Based Diet Index
 Alternate Healthy Eating Index

Sodium?
 Fish?
 Sugar?
 Legumes?
 Red meat?
 More good foods?
 Fewer bad foods?
 Etc etc...

Shan et al., JAMA Intern Med 2023

Geroscience: Synthesizing Pleiotropic Effects of Multicomponent Interventions

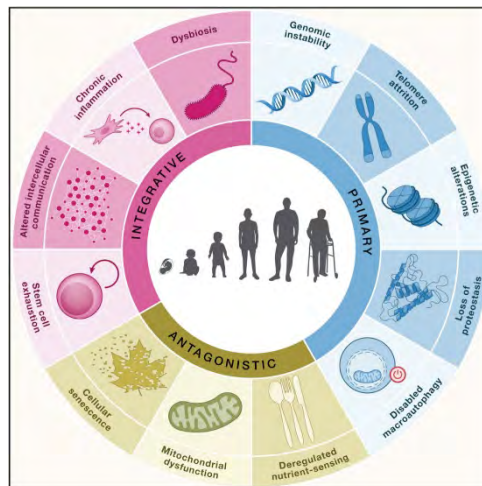
Letter to the Editor

J Nutr Health Aging.2023;27(3):238-239

Published online March 10, 2023, <https://doi.org/10.1007/s12603-023-1897-1>

Healthy Eating Patterns: A Stealthy Geroscience-Guided Approach to Enhancing the Human Healthspan

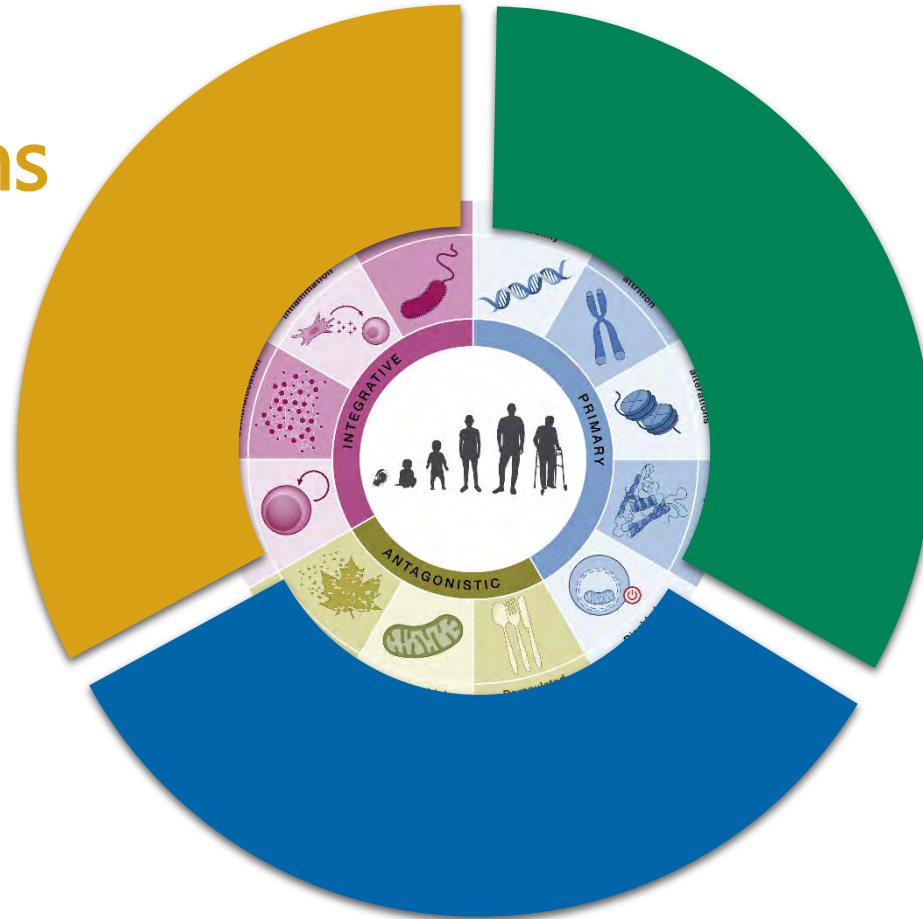
I.M. Al-Naggar^{1,2}, J.C. Newman^{3,4}, G.A. Kuchel¹



“healthy eating patterns... may share a set of positive interactions with downstream aging mechanisms through common elements such as AMPK (AMP-activated protein kinase) activation (small meal size), mTOR inhibition (moderate protein intake), autophagy activation (polyunsaturated fats), or microbial epigenetic modifiers (soluble fiber from nuts and legumes).”

Lifestyle and Social Interventions

- Physical Activity
- Nutrition
- Social Connection
- Mental Activity
- Purpose
- Smoking/Alcohol



Geriatric Care Principles

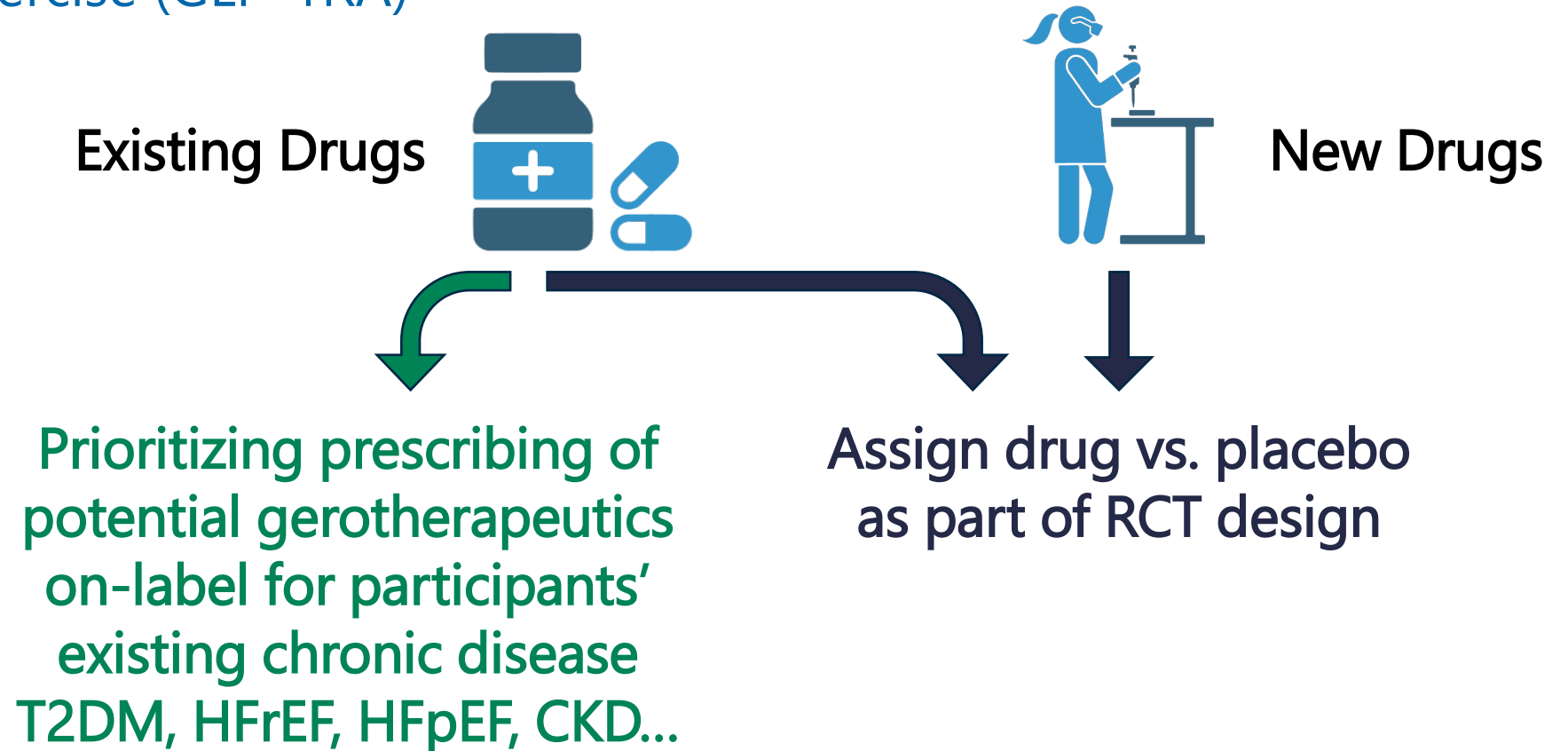
- Age-Friendly Hospitals
- Polypharmacy
- Multimorbidity
- Function-Based Care
- Preventative Care
- Advanced Care Planning

Gerotherapeutic Medicines

Integrating Gerotherapeutics with Multicomponent Interventions

Rationales:

- “Unlock” response to lifestyle
- Synergy with e.g. exercise (GLP-1RA)
- Additive effect



Forman and Pignolo, J Gerontol 2024
Forman et al., JACC 2023

Toulouse IHU / Buck Institute: X Prize Semifinalist



Bruno Vellas,
MD, PhD
IHU Toulouse

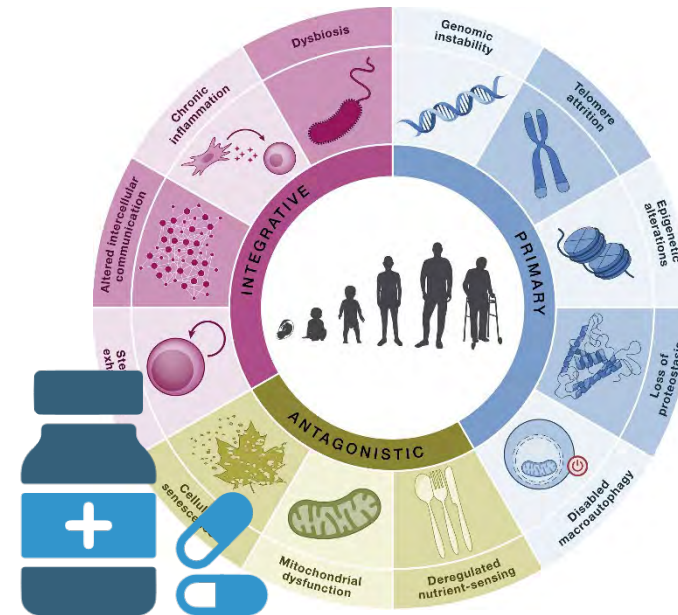
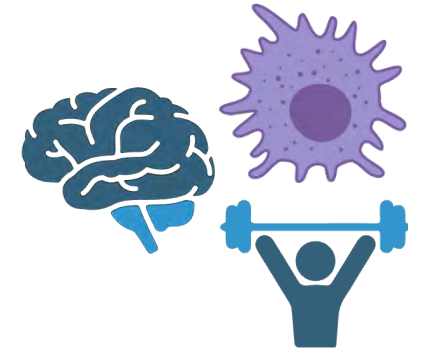
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Goal: Improve cognitive, muscle, immune domains by 10-20 years within 1 year among 50-80 year olds



ICOPE INTENSE Pilot: Clinic-Based

Mobility/Exercise:

- in-person 45 min 3x per week
- 150 min at home per week
- aerobic/walking, resistance, flexibility

Cognitive:

- in-person 60 min 2x per week
- pen/paper cognitive training + education
- Luminosity at home

Nutrition/Vitality:

- Focus on overweight/obese
- Individual dietician advice
- Ensure-like high-protein supplementation if sarcopenic or low protein intake
- Folate, B12, D, Omega 3
- *Geroscience-based supplement compounds*

Mood:

- CBT-I, sleep, mindfulness interventions
- 1 hour orientation, 15 min per week
- Mindfulness app used at home
- screen for and treat depression

Sensory:

- Screen, assess and treat hearing and vision impairments
- Refer to specialists as needed

Clinical (ICOPE):

- Referrals for vision, hearing, cognition
- Assess social and physical environment
- Personalized clinical care plan

Knowledge Gaps and Research Opportunities

Do multicomponent interventions alter aging mechanisms?

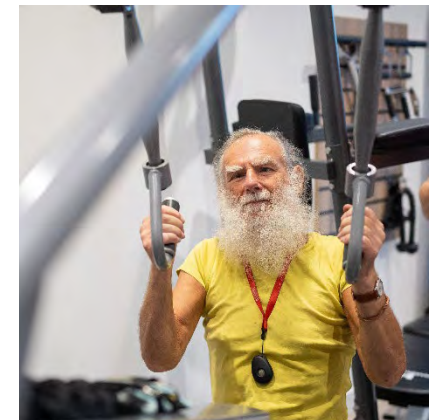
Do multicomponent interventions improve multiple outcomes and/or geroscience outcomes (Intrinsic Capacity, multimorbidity, resilience)?

To what extent do geriatric care, multicomponent interventions, and gerotherapeutics complement each other?

Do varied multicomponent interventions share common molecular effector mechanisms, and if so what are the most important?

Can multicomponent interventions be optimized for aging/geroscience outcomes, and/or personalized?

What are the molecular mechanisms by which gerotherapeutics enable response to multicomponent interventions?



Thank you!

Relevant Collaborators

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Images:



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Sid Madhavan, PhD
Sawyer Peralta



Live better longer.