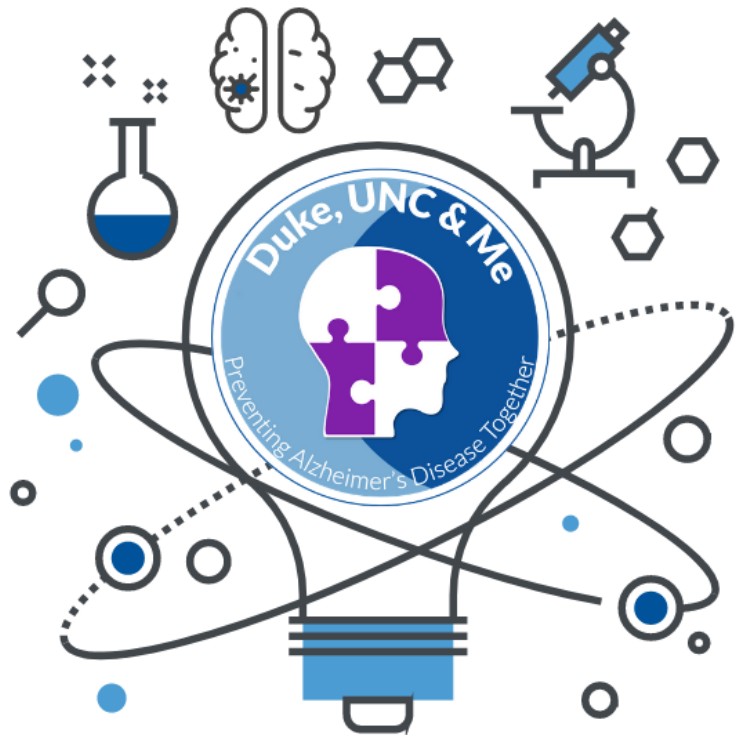


Comorbidity and ADRD: Innocent bystanders or accomplices?



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March 5, 2025

 **Duke University**
School of Medicine

 **UNC** | SCHOOL OF
MEDICINE



National Institute on Aging: Duke/UNC ADRC, Duke Pepper Center, Duke Roybal Center, AGING Initiative, multiple investigator-initiated projects

Veterans Administration – Durham VA GRECC

AGS Board of Directors

Co-Chair, Alzheimer's Association AUC Panel on Blood-Based Biomarkers

Consultant: DrivenData



- 1) Define “multiple chronic conditions (MCCs)” and its significance in 21st century health
- 2) Discuss the role of chronic conditions in biological aging and loss of resilience to health stressors
- 3) Consider MCC in the context of aging brain/ADRD
- 4) Set the stage for our consideration of the interface between Alzheimer’s disease and MCCs



The Case of B

87 year-old woman presents for consult at Duke Geriatrics Evaluation and Treatment Clinic

Patient's Health Goal:

“I'm not here because I want to live forever...but I hope you can help me live better.”

Family Chief Concern:

functional and cognitive decline





Issues at Presentation

Memory and cognitive changes

Multiple Falls

Chronic Pain

Sleep disturbance

Polypharmacy/Side effects

Social isolation

Low energy

Urinary incontinence

Unintentional weight loss

Anxiety



The Medical History: 60s

- “First retirement” at age 58: middle school principal
- Earned a PhD and a pilot’s license in her 60s
- Interests: world travel, avid reader, being outdoors



The Medical History: 70s

- “Second retirement” at age 72: college professor
- Mild chronic obstructive pulmonary disease (COPD) and osteoarthritis worsened in her 70s
- Decreased activity
- Weight gain exacerbated arthritis and shortness of breath
- Had to cut back on NSAIDs due to chronic kidney disease



The Medical History: 80s

- Neovascular age-related macular degeneration (AMD) diagnosed at age 82
- Hearing impairment
- Frequent falls (~weekly)
 - Persistent back pain after vertebral fracture one year ago
 - Tramadol and opioids worsen cognition and balance
- Mild cognitive changes noted in last 2-3 years

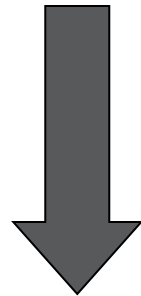


Multiple Chronic Conditions (MCC)



Age 56

Osteoarthritis
COPD
Macular Degeneration
Cognitive Impairment
Hearing Impairment
Osteoporosis
Chronic Kidney Disease
Depression



Age 87

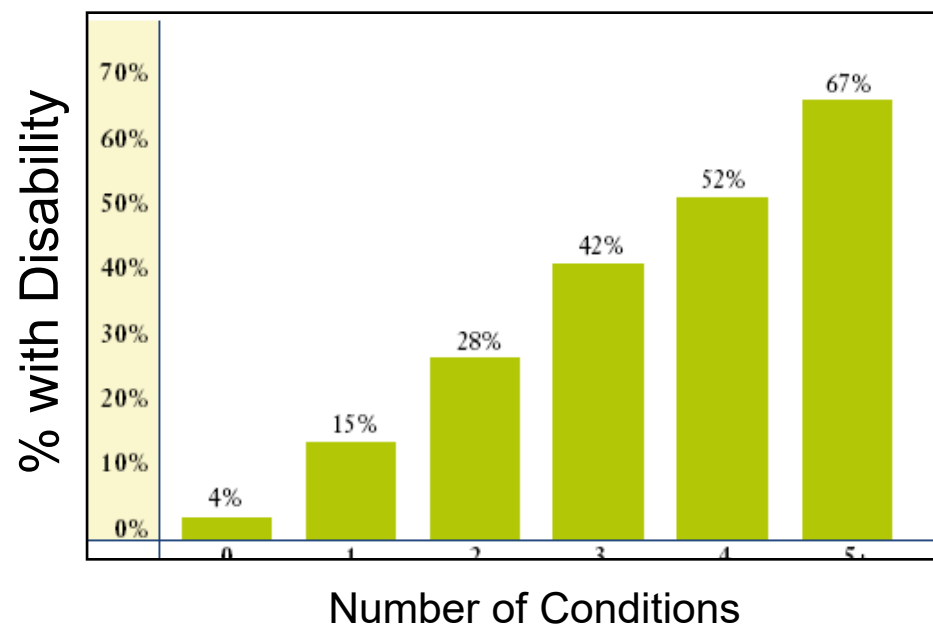
Loss of Independence and Quality of Life

Multiple Chronic Conditions (MCC)

Definition: Co-occurrence of two or more chronic conditions that impact health or require treatment

~96% of Medicare dollars go to the 2/3 of Beneficiaries who have MCC.

More chronic conditions
= increasing threat to
independence.



Multiple Chronic Conditions (MCC):

The “new normal” in 21st Century medicine

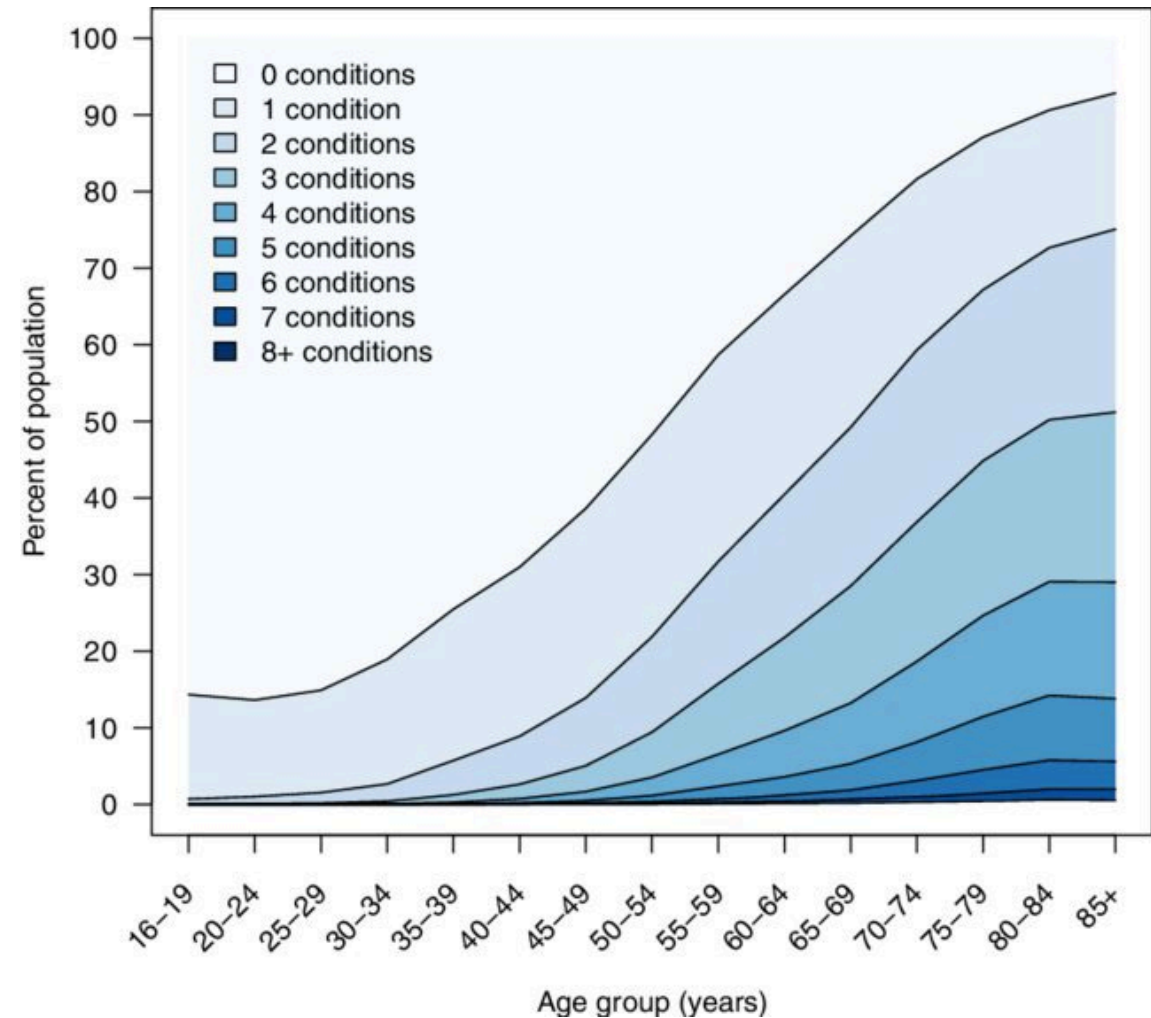
- A by-product of modern medical success
 - Life expectancy has increased
 - Many previously deadly conditions converted to “chronic” conditions
- Aging baby boomers
- Rise in obesity and metabolic syndrome

Prevalence of MCC is age-related



27% of US Population
~64% of those age 65+

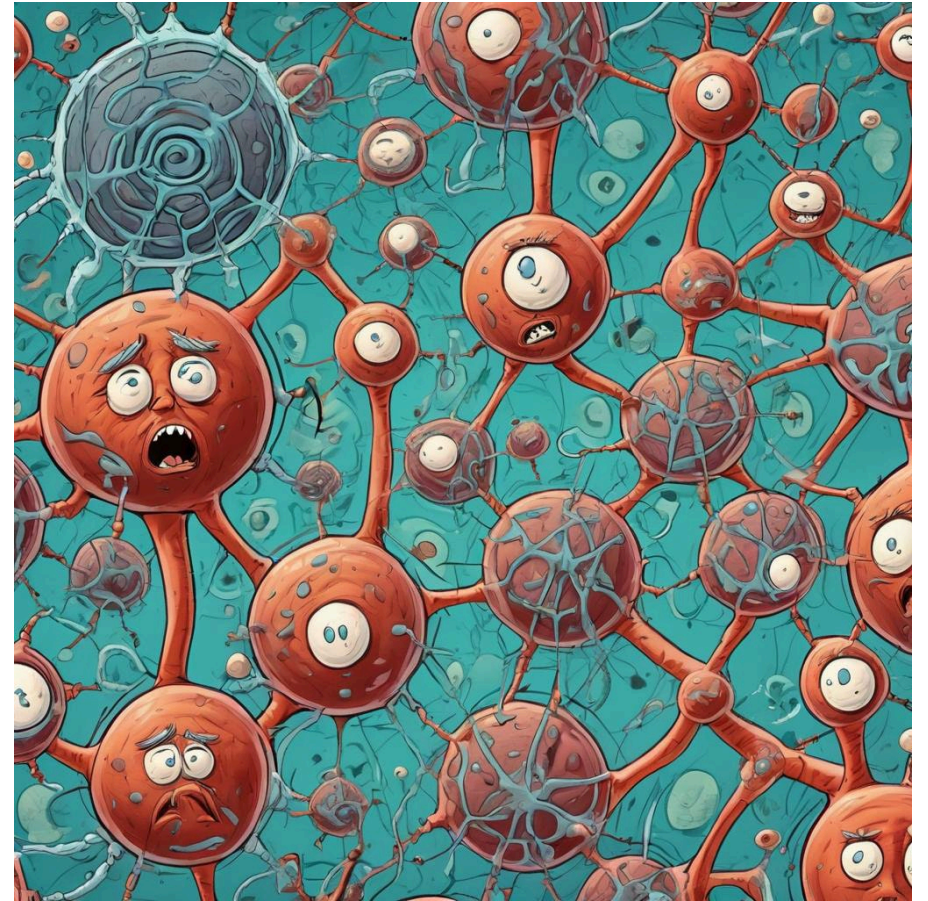
- Comparable rates in men and women in mid-life; more prevalent in women in late-life
- More common in:
 - VA users
 - deprived areas
 - minoritized racial/ethnic groups
 - lower SES



Schiøtz et al. BMC Public Health (2017) 17:422

MCCs and Aging Biology

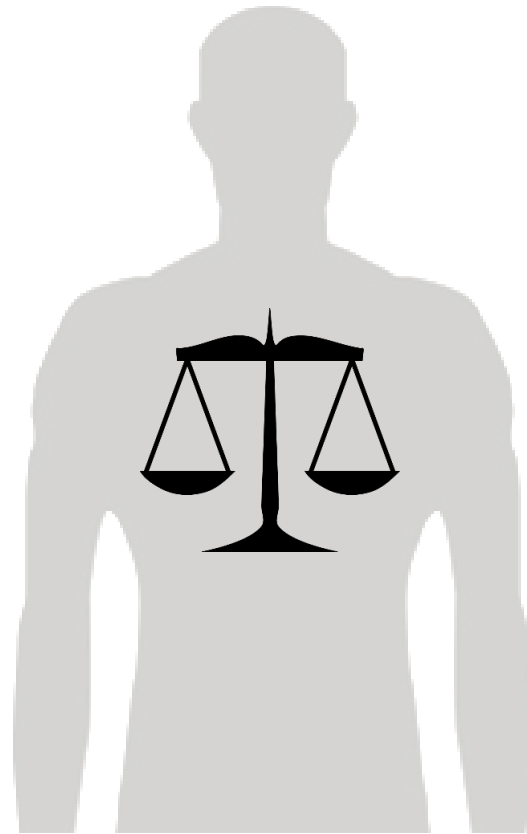
GenCraft prompt: “complicated web of aging cells and disease and cycles of failing health.” Cartoon style



Human health is a constant balancing act



Biological Resilience = The ability of a biological system to maintain or regain equilibrium in response to perturbations or health stressors.



Every person is a complex dynamic system



Interconnected Systems and Sub-systems constantly moving, transitioning, and adapting to changing environments and new stressors

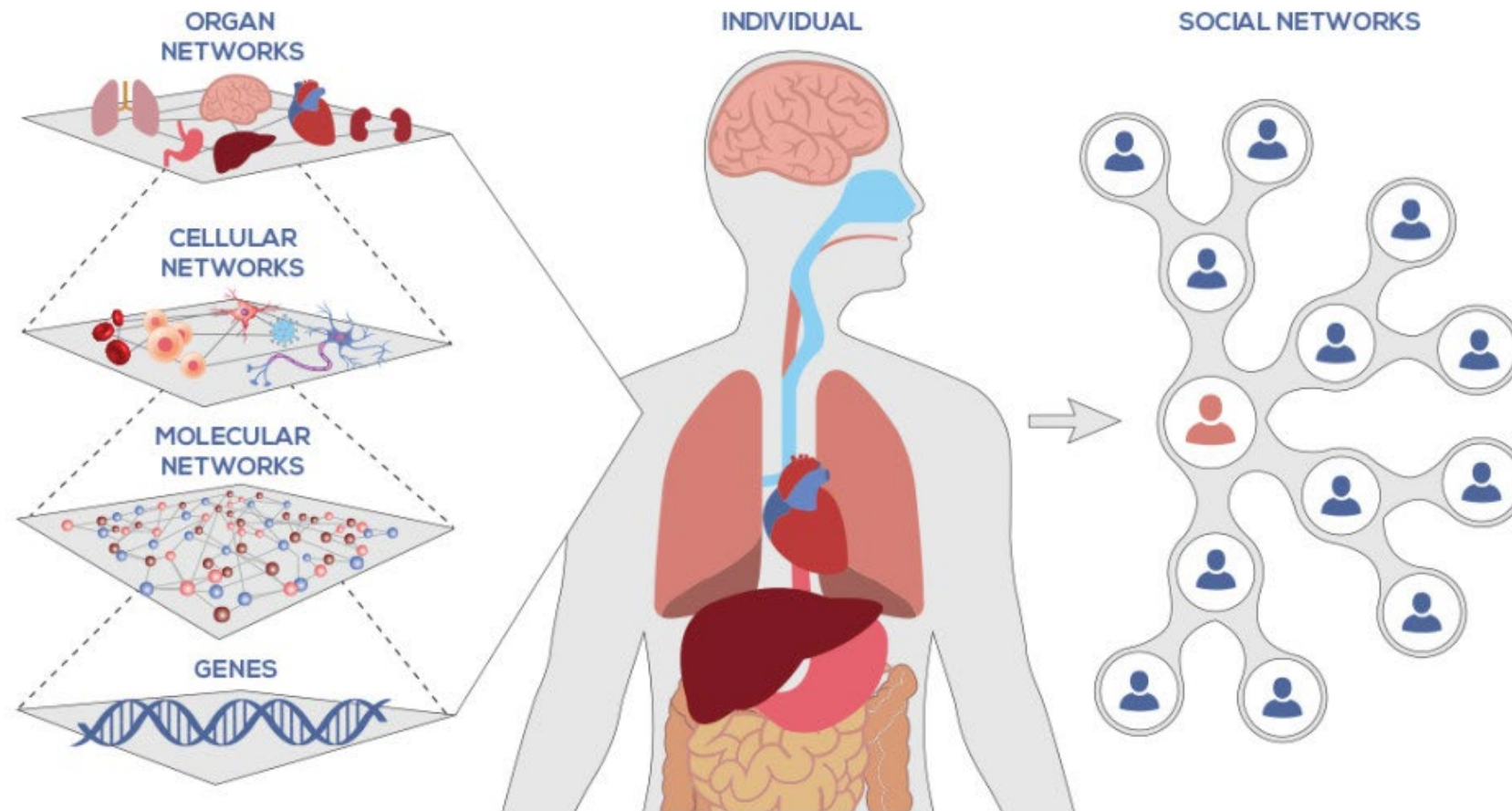


Image by: Institute for Systems Biology, Seattle, WA



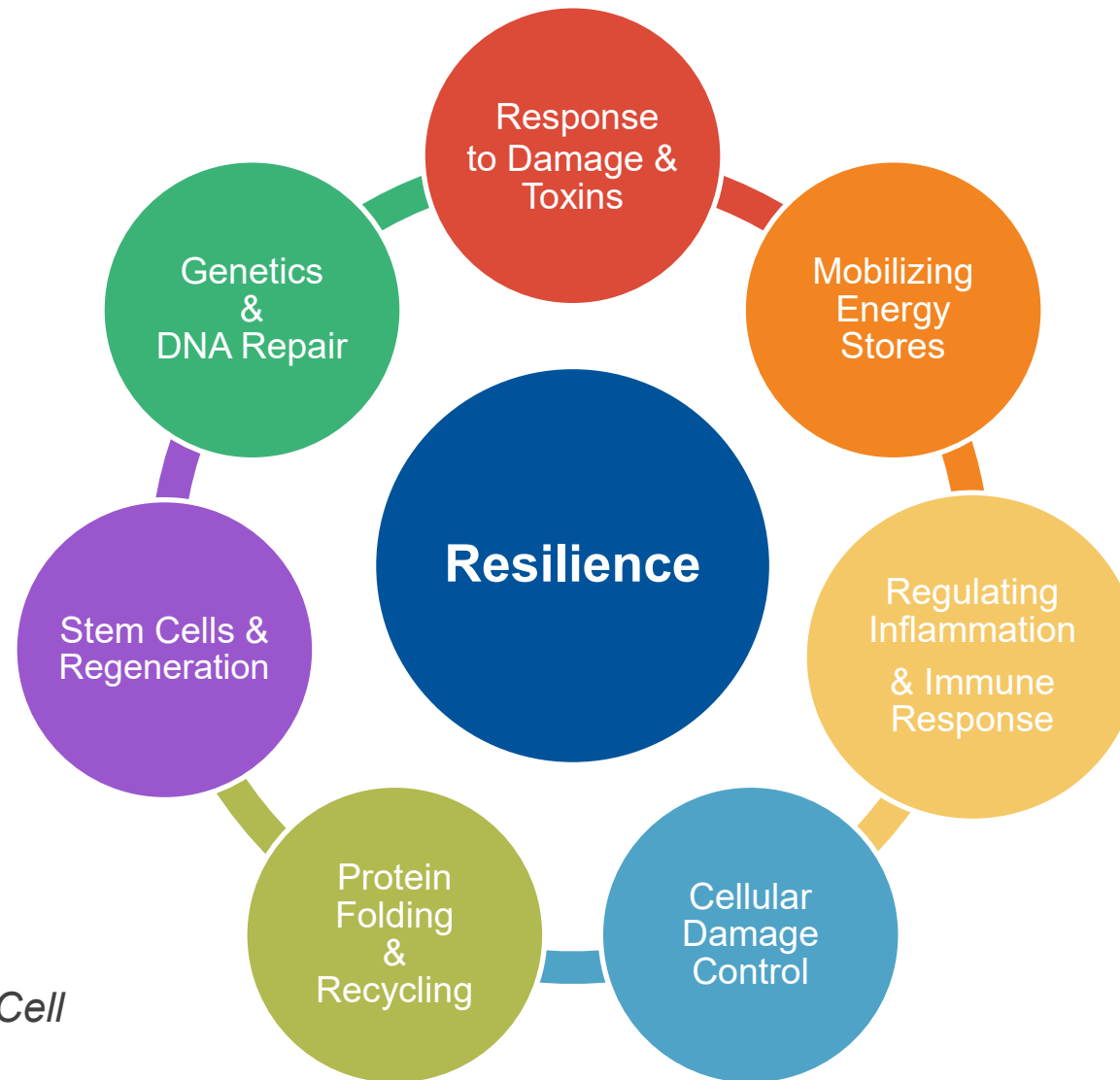
A vicious cycle

Injury or disease in any sub-system or organ can diminish biologic resilience...



and lower resilience makes us vulnerable to the next disease...

Geroscience: Biological resilience has a molecular basis



...and all of these molecular pathways exhibit decline with age (over time), even in the absence of serious disease.

Adapted from Kennedy et al. *Cell* 159; 2014



MCCs and Aging Brain

GenCraft prompt: “Brain on a human body with organs that look connected to the brain.” Realistic style



MCCs are prevalent in people living with dementia



>95% of people with ADRD have 1 or more additional chronic condition

A person with ADRD, compared to a peer without dementia, is >3.8 times as likely to have 6+ chronic conditions

Percentage of People with Alzheimer's or Another Dementia Who Also Have . . .

Hypertension	56%
Heart Disease	46%
Chronic Kidney Disease	46%
Diabetes	37%
Congestive Heart Failure	34%
COPD	20%
Stroke	13%
Cancer	10%

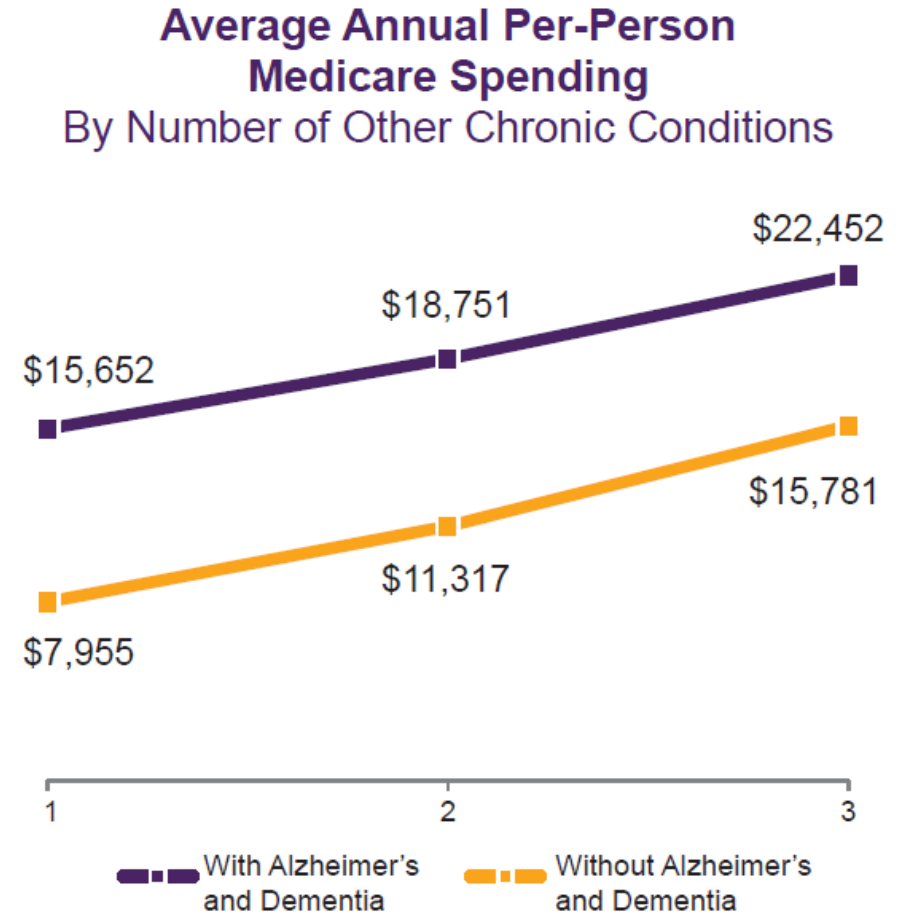


MCC is associated with high care costs and complications in people with dementia

-risk:benefit ratios

MCC impacts the detection of AD-related pathology

MCC likely plays a role in the development of pathology and dementia



The biggest risk factor for Alzheimer's disease is age.



We propose that certain age- or disease-related change(s) at the cellular level are necessary to *initiate* the pathology of Alzheimer's disease.

If so, the changes likely begin in early- and mid-life.



My grandmother's story: Conclusions

Memory and cognitive changes

Multiple Falls

Chronic Pain

Sleep disturbance

Polypharmacy/Side effects

Social isolation

Low energy

Urinary incontinence

Unintentional weight loss

Anxiety



My Grandmother's Story

• Interventions

- Medication list simplified
 - Special attention to pain and sleep concerns
 - Reducing medications likely to affect cognition
- One new medication: SSRI
- Referral to Physical Therapy
- Referral to Vision Rehabilitation
- Living will, goals of care reviewed
(ePrognosis 5-year mortality risk: 47-52%)



18 months later

- Depression symptoms responded to medication (SSRI)
- Mobility improved
- Cognition returned to near baseline
- Using new visual assistive equipment to write letters, use computer, manage self-care

My grandmother died about 2 weeks after this picture was taken.



Dr. Billie Bagby

January 25, 1920 – May 25, 2009

- Recall goals of care:

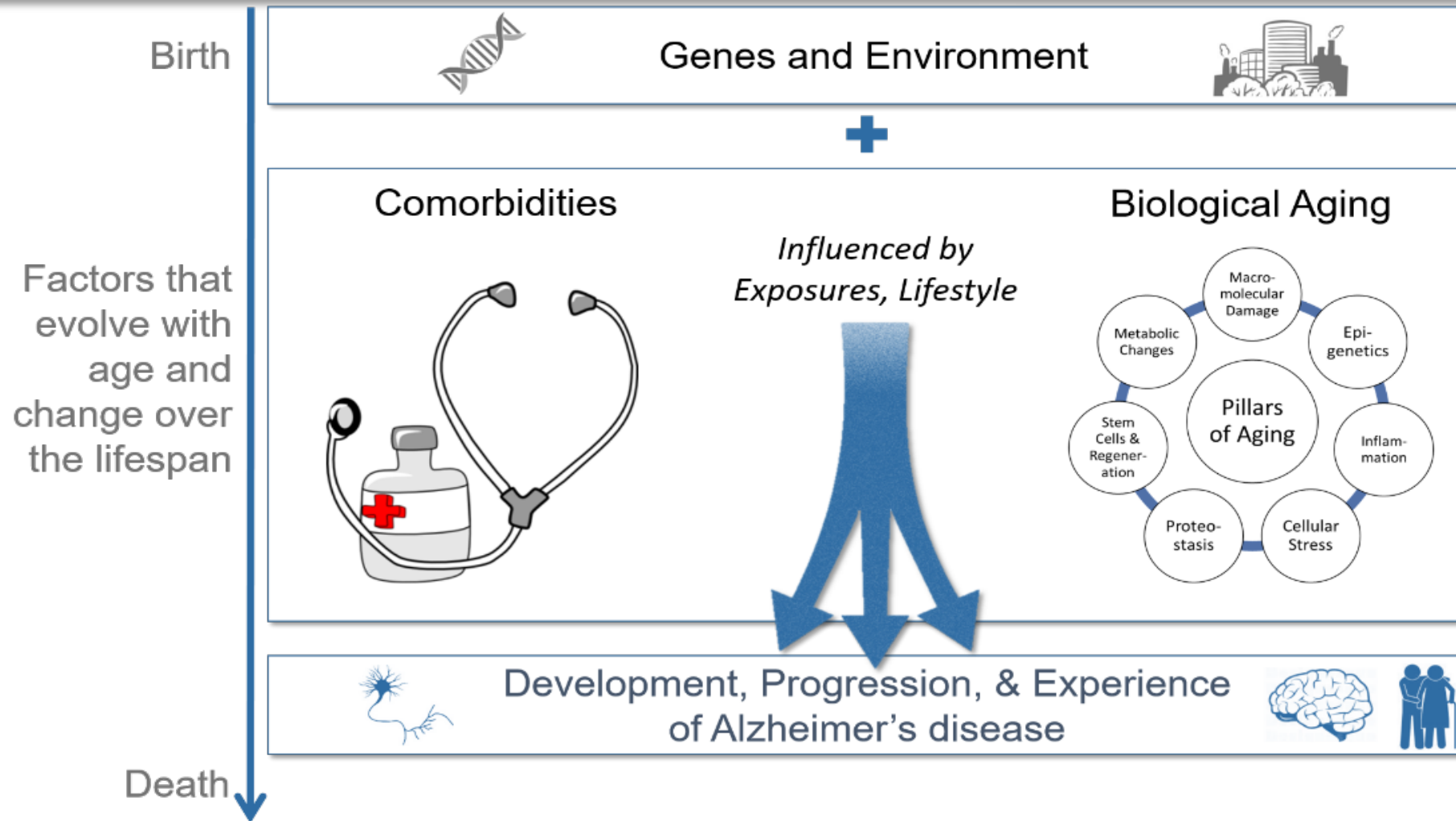
“I don’t care about living longer, but can you help me live better?”

If she presented today, would goals of care be served if her care plan included:

- Blood-based biomarkers for AD
- Lumbar puncture or PET scan
- Lecanemab



Alzheimer's disease: a disease of aging, not the aged



Unlike most ADRCs, the Duke/UNC ADRC focuses on people who do NOT have MCI or dementia.

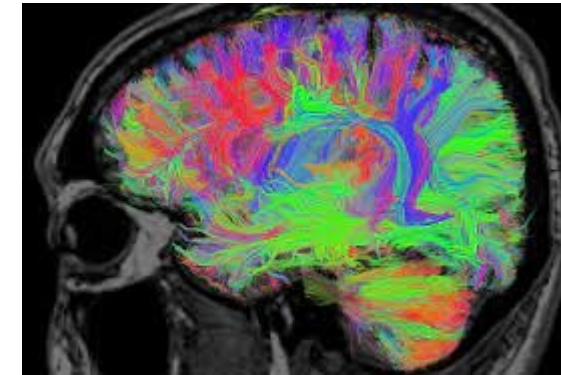
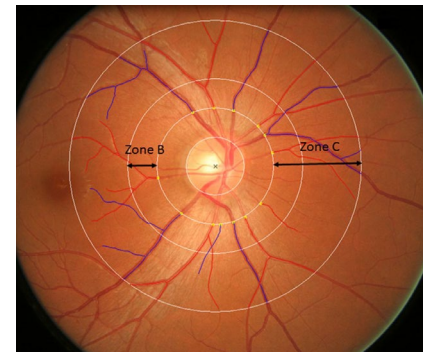


Our participants are younger and more diverse

- Represent urban and rural populations of North Carolina
- Biofluids and data from age 25 to 80
- Peri-menopausal women

Data and samples relevant to MCC

- Retinal imaging, high-res MRI
- Plasma and CSF
- Sensory and mobility measures
- Subsets with actigraphy, menopause data



Actively recruiting!

- ~20% UREGs; ~30% from rural zip codes; > 80% donated CSF



Memory & Aging Longitudinal Cohort: Target is 420 people age 45-80

- At least 2/3 have parent with Alzheimer's disease or a known APOEε4 gene
- 320 with normal cognition at time of enrollment

Currently at n= 335 and counting...

Young Cohort: Target is 100 people age 25-44 for a one-time visit

- Family history of dementia or APOEε4 gene

Currently at 47 and counting...



Legend: all data

HELP

NEWS

Age at screening

42	20 ≤ x < 50
79	50 ≤ x < 64
78	64 ≤ x < ∞
199	Total

Sex

80	M
156	F
236	Total

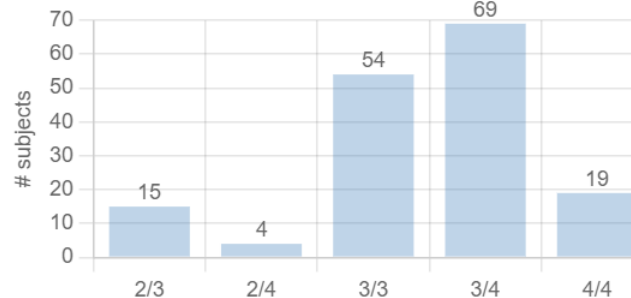
Selector panel Click this bar to query a subgroup of subjects ▾

< All Demographics Diagnosis Biomarkers Bios >

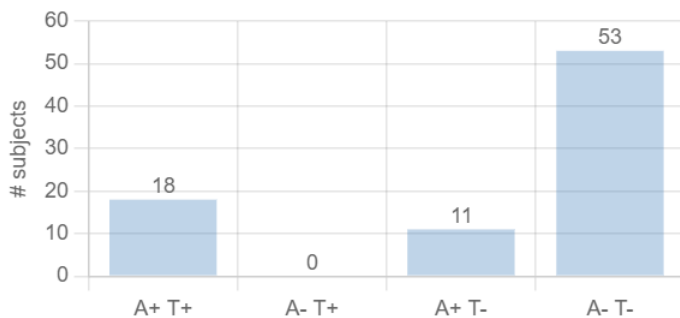
MRI scans



APOE



CSF biomarkers



Race

179	White
44	Black
3	Asian
4	Other
7	Unknown
237	Total

APOE

15	2/3
4	2/4
54	3/3
69	3/4
19	4/4
161	Total





- The LEARNING Collaborative has created an online curriculum of self-directed PowerPoint presentations, downloadable teaching slides, podcasts, and live webinars with the aim of filling educational and training gaps in multiple chronic conditions research

Curriculum Domains

Data, Measures, and Measurements Sarah Berry, MD, MPH & Michael Steinman, MD	Patient, Family Caregiver, and Other Stakeholder Engagement Alyce Adams, PhD & Libby Hoy
Research Design Heather Allore, PhD & David Reuben, MD	Useful Analytic Approaches Terrence Murphy, PhD & Karen Bandeen-Roche, PhD
Inclusion Across the Lifespan, Health Equity, and Vulnerable Populations Barrett Bowling, MD & Ana Quiñones, PhD	Integrating Research Into a Learning Healthcare System Leah Hanson, PhD & Jeff Williamson, MD
Being a MCCs Researcher Albert Siu, MD, MSPH & Heather Whitson, MD	Basics of MCCs and Aging Cynthia Boyd, MD & Jay Magaziner, PhD

Register Today for Free Access to
the MCC Core Curriculum and
Resources

<https://mccresearch.agscocare.org>

