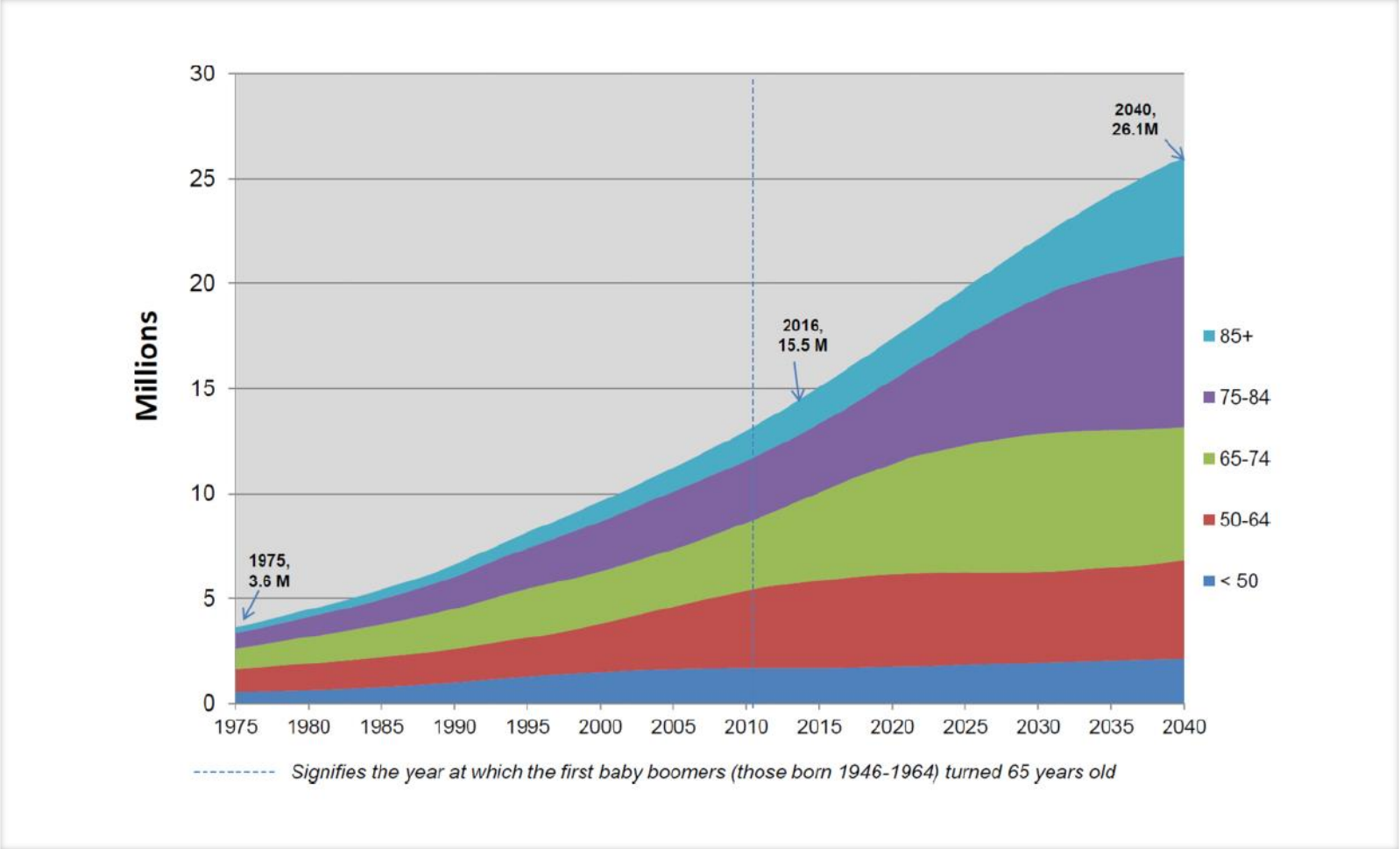
THE WOMEN'S HEALTH INITIATIVE

Plenary 4: Disparities in cancer survivorship

Chair: Elizabeth Cespedes-Feliciano, Kaiser Permanente Division of Research

Older survivors are an increasingly diverse and growing population that WHI-LILAC data is uniquely situated to address



Bluethmann et al. CEBP 2016 25(7): 1029 –1036

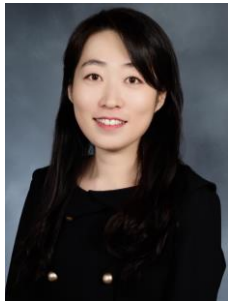
Disparities in cancer survivorship

Alexandra Binder

Impact of cancer and its treatments on epigenetic and functional aging

Sowmya Vasan

Deficits accumulation index in WHI: disparities by race



Eunji Choi

Neighborhood deprivation and deficit accumulation score: TLC

Xiaochen Zhang

Guideline-concordant breast cancer treatment by age and in urban and rural survivors in WHI

WOMEN'S HEALTH INITIATIVE

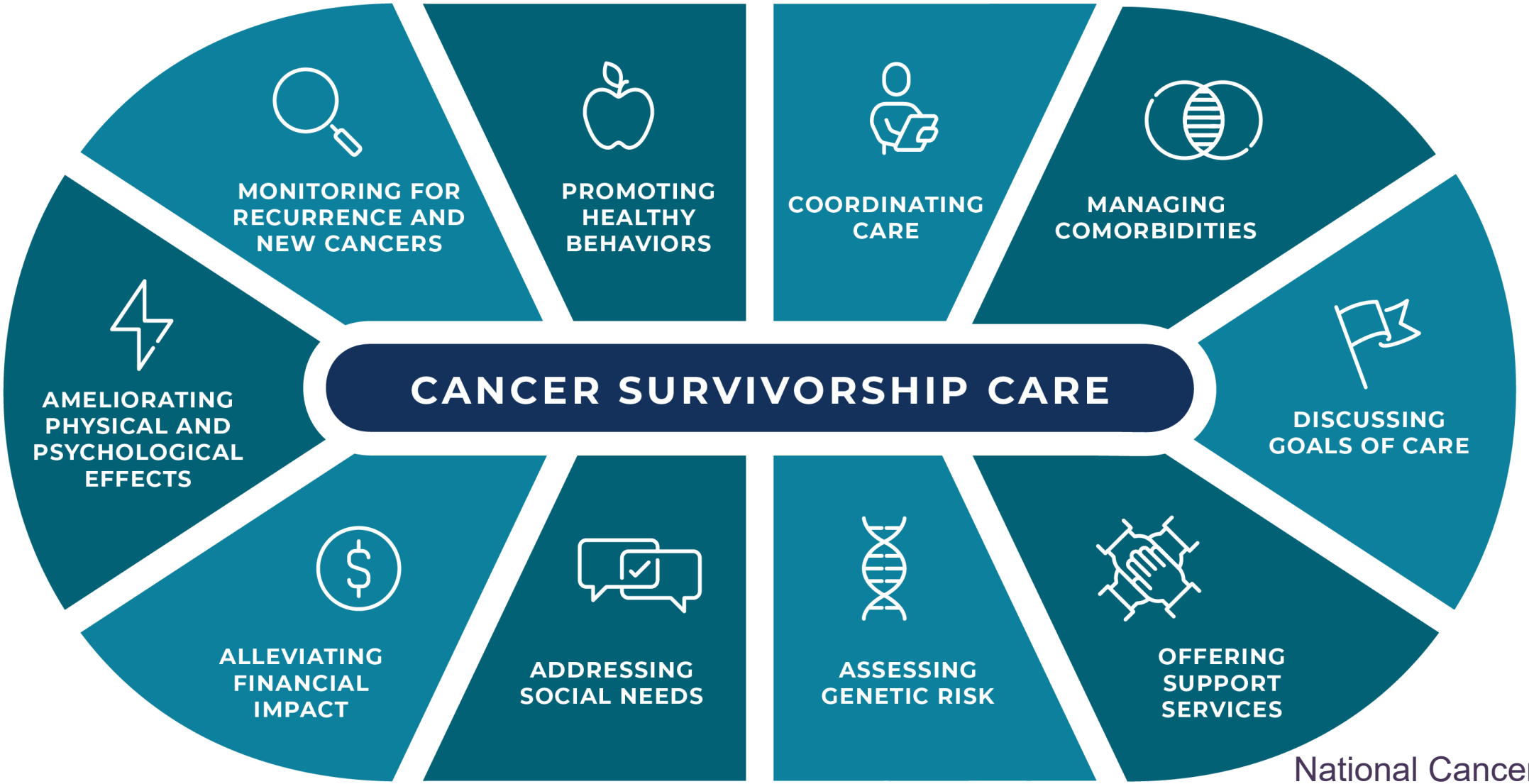
Life and Longevity After Cancer (LILAC)
A national resource for studies of cancer and aging

Impact of cancer and its treatments on epigenetic and functional aging: understanding trajectories and potential interventions

UNIVERSITY OF HAWAI'I CANCER CENTER

Alexandra M. Binder, ScD, ScM

Associate Professor of Cancer Epidemiology
University of Hawai'i Cancer



National Cancer Institute

Nā Wahine Hula `Akala, meaning "Pink Ladies of Hula," is a hula group composed of cancer survivors, or in their words, "***thrivers***"

Long-term health

There is growing evidence that cancer survivors are at risk of accelerated aging trajectories relative to individuals of a similar age without a history of cancer

What are the indicators of risk of accelerated aging trajectories among cancer survivors?

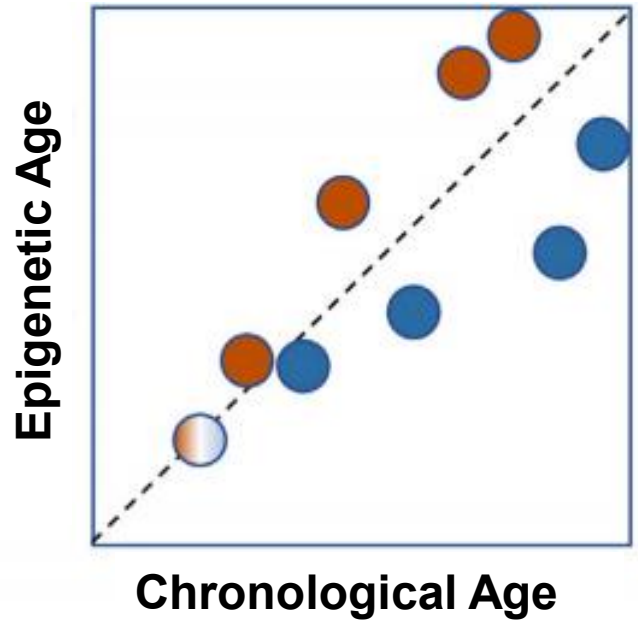
- DNA methylation/epigenetic age clocks
- Physical function (e.g., grip strength, gait speed)
- Comorbidity burden
- Sarcopenia or low muscle mass
- Geriatric assessment

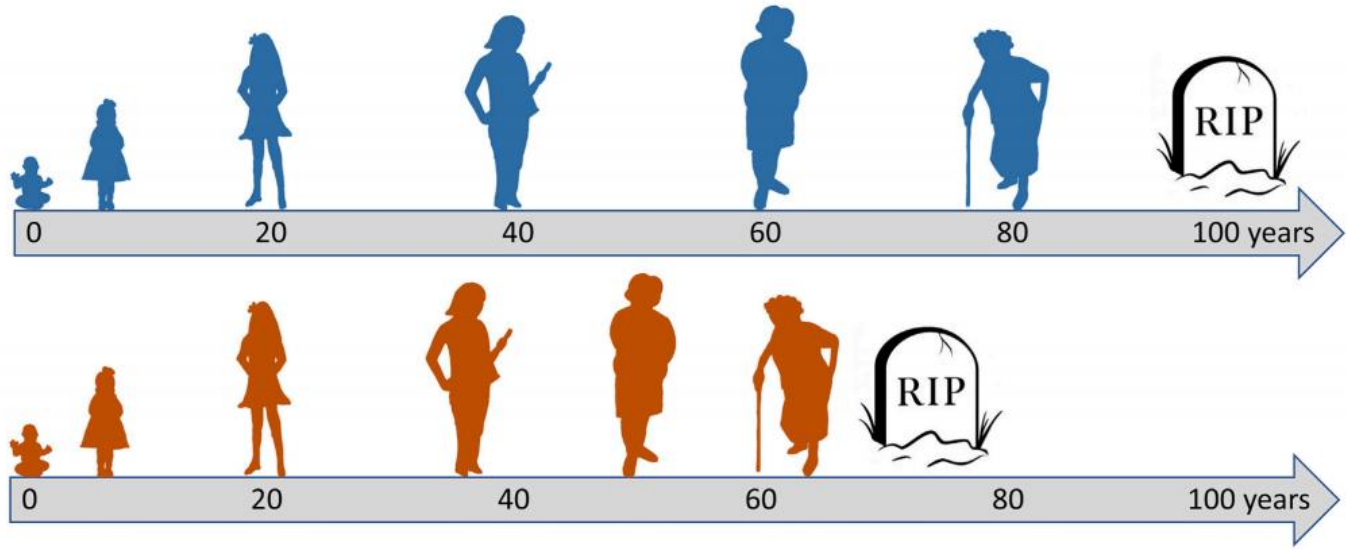
How can we use this information for supportive care strategies?

- Tailor exercise and nutrition interventions
- Predict and prevent treatment-related toxicities
- Stratify patients for enhanced follow-up

EPIGENETIC CLOCKS

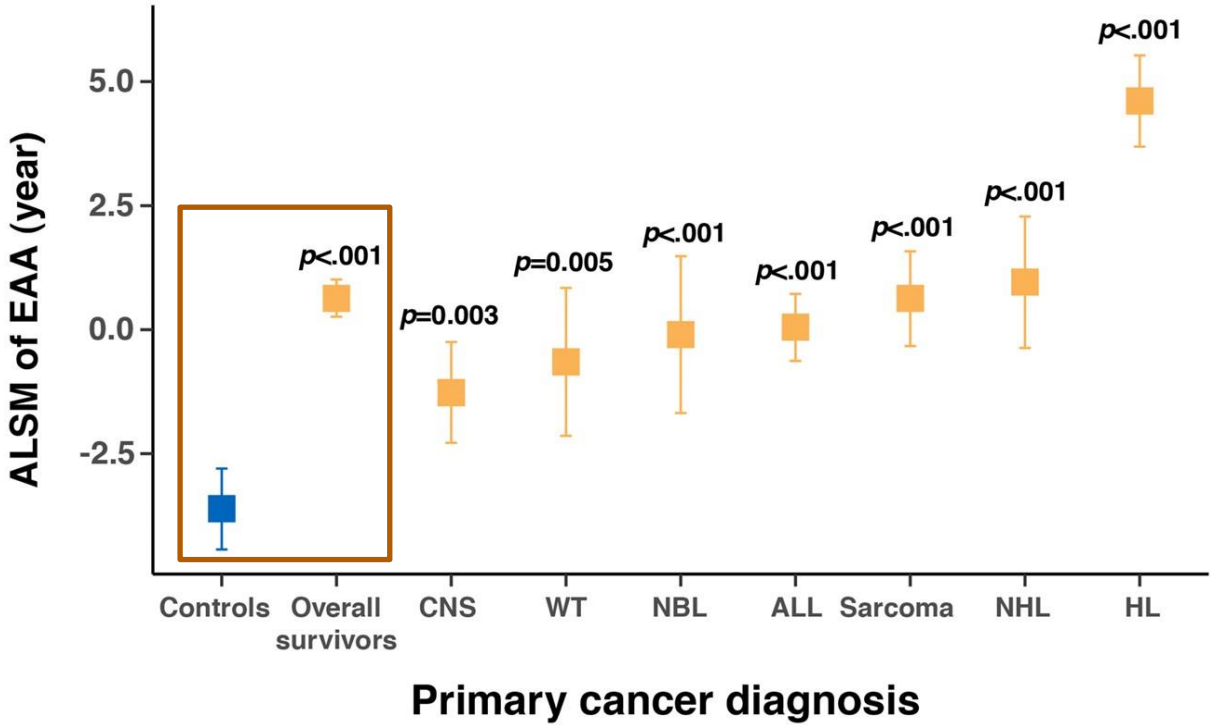
- Epigenetic clocks are a composite measure of DNA methylation across certain CpG loci that provides a surrogate measure of biologic age or rate of biologic aging
- Well replicated associations with morbidity and mortality across cohorts





Field *et al* (2018) Mol Cell Review

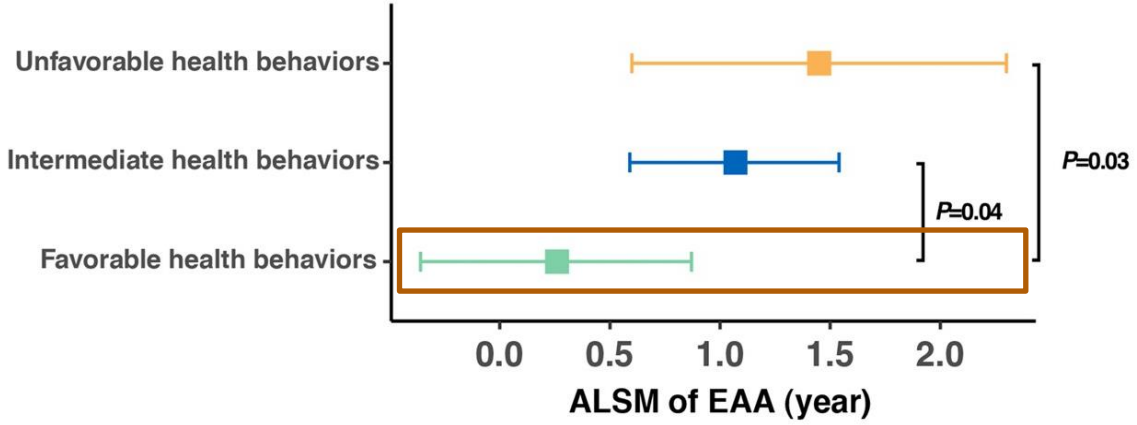
Higher AgeAccel documented among cancer survivors compared to age-matched individuals without cancer



Qin *et al* (2020) JNCI

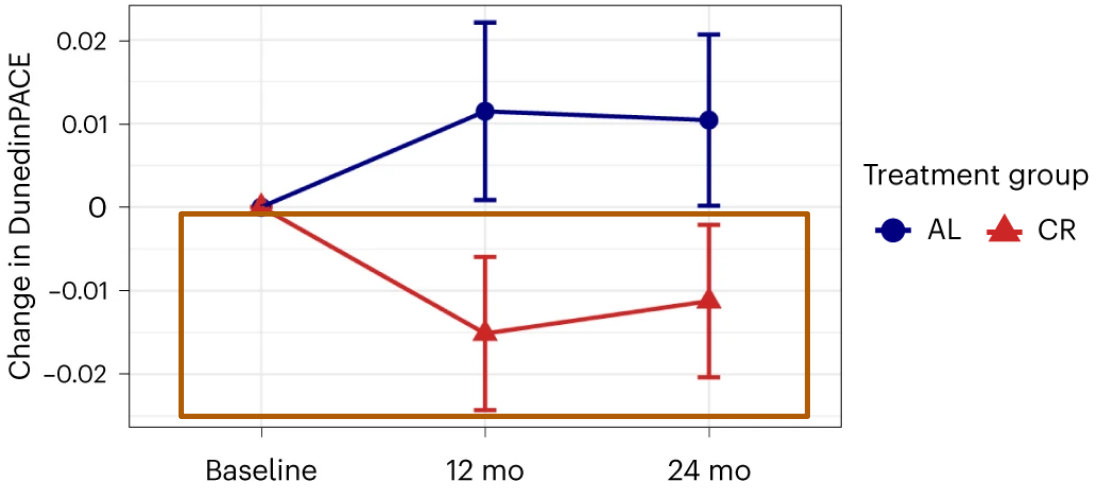
More favorable health behaviors are associated with lower AgeAccel among cancer survivors

Overall health behavior based on diet, smoking and alcohol use, resistance training and physical activity



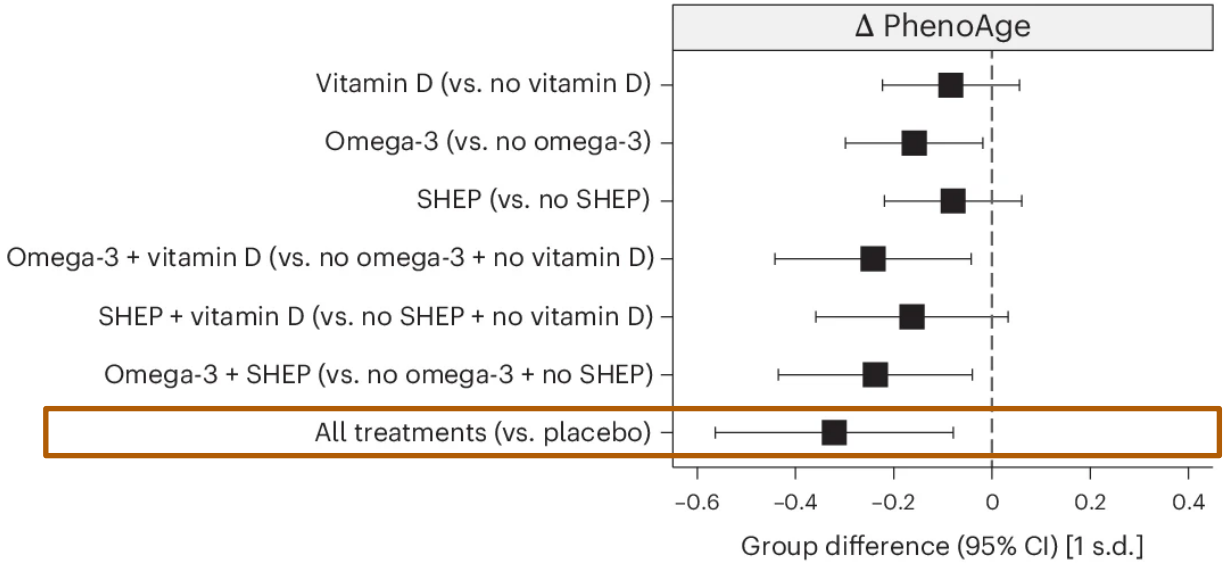
Interventional studies have shown that diet and exercise programs may attenuate epigenetic aging relative to those assigned to control arms

CALERIE: randomized to 25% caloric restriction or ad libitum control diet for 2 yrs



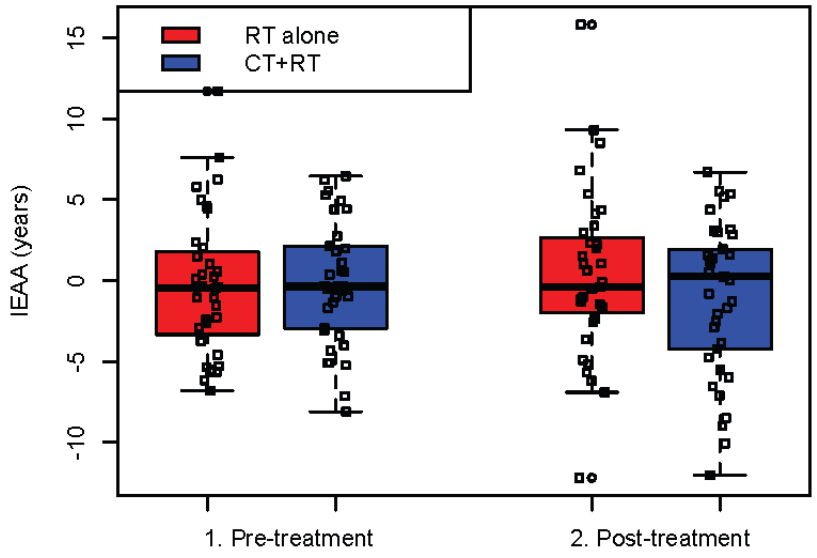
Waziry *et al* (2023) Nature Aging

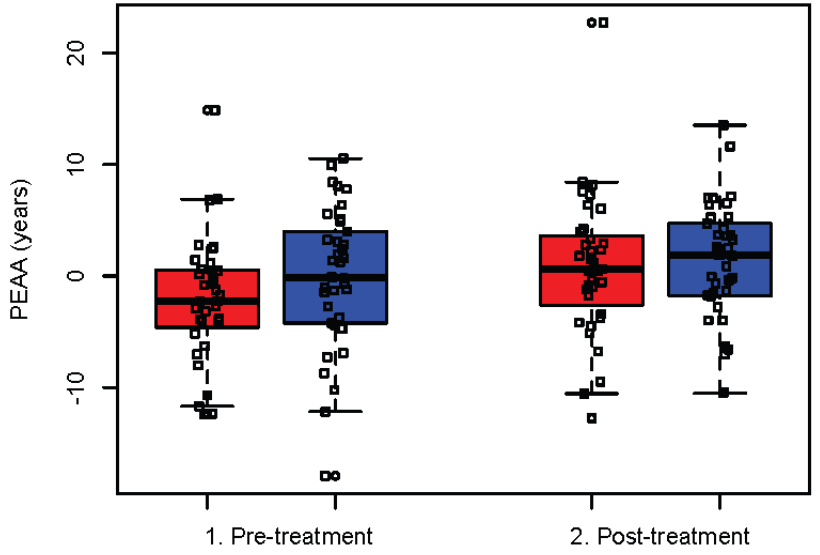
DO-HEALTH: effect of vitamin D and/or omega-3 and/or a home exercise program over 3 yrs

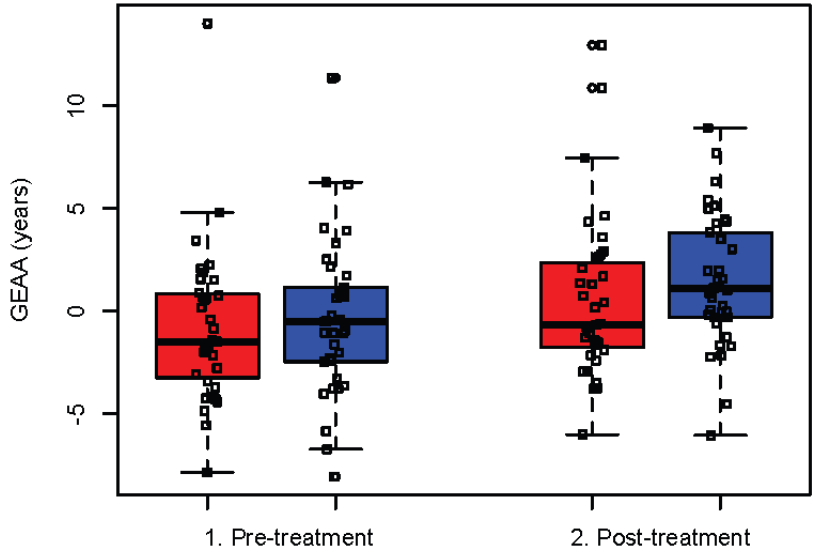


Bischoff-Ferrari *et al* (2025) Nature Aging

- Disparity in epigenetic age acceleration among cancer survivors is thought to be driven, in part, by exposure to systemic or targeted cancer therapies
- Longitudinal studies of breast cancer patients suggests that this acceleration at least partially occurs over the course of cancer treatment, and may vary by assigned treatment



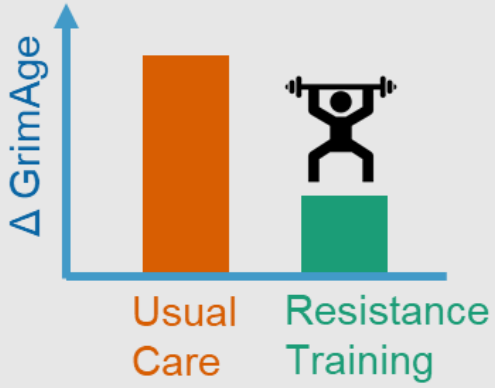


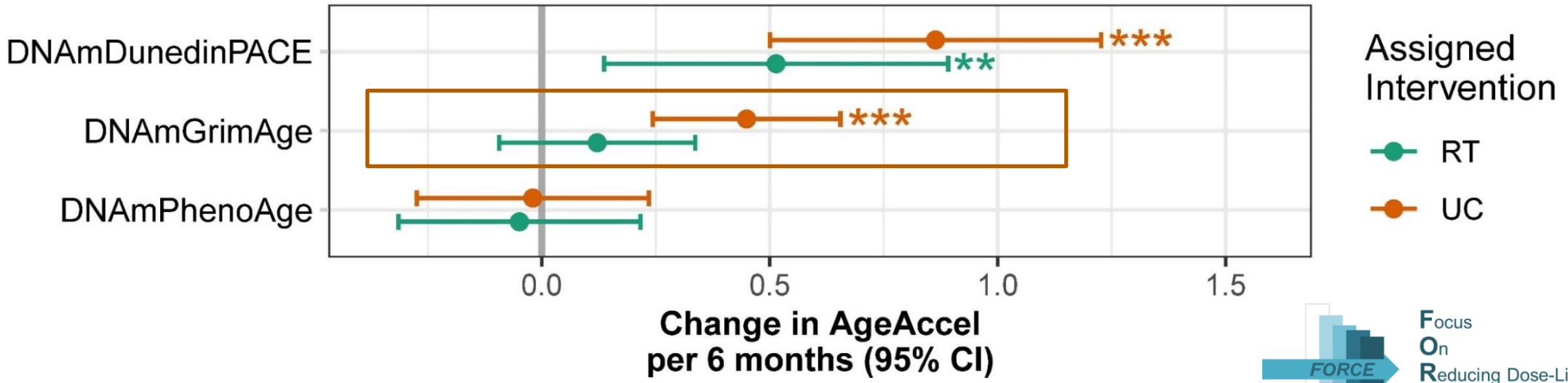


Sehl *et al* (2020) npj Breast Cancer

Assigned resistance training significantly modified the rate of change in GrimAgeAccel over chemotherapy

RT reduced the change in GrimAge over chemotherapy





Binder *et al*; unpublished;
please do not duplicate or distribute

FORCE
Focus On Reducing Dose-Limiting Toxicities in Colon Cancer with Resistance Exercise

Long-Term Trajectories of Accelerated Biological Aging and Functional Decline Associated with Breast Cancer and its Treatment

R01CA283839
MPIs: Feliciano and Binder

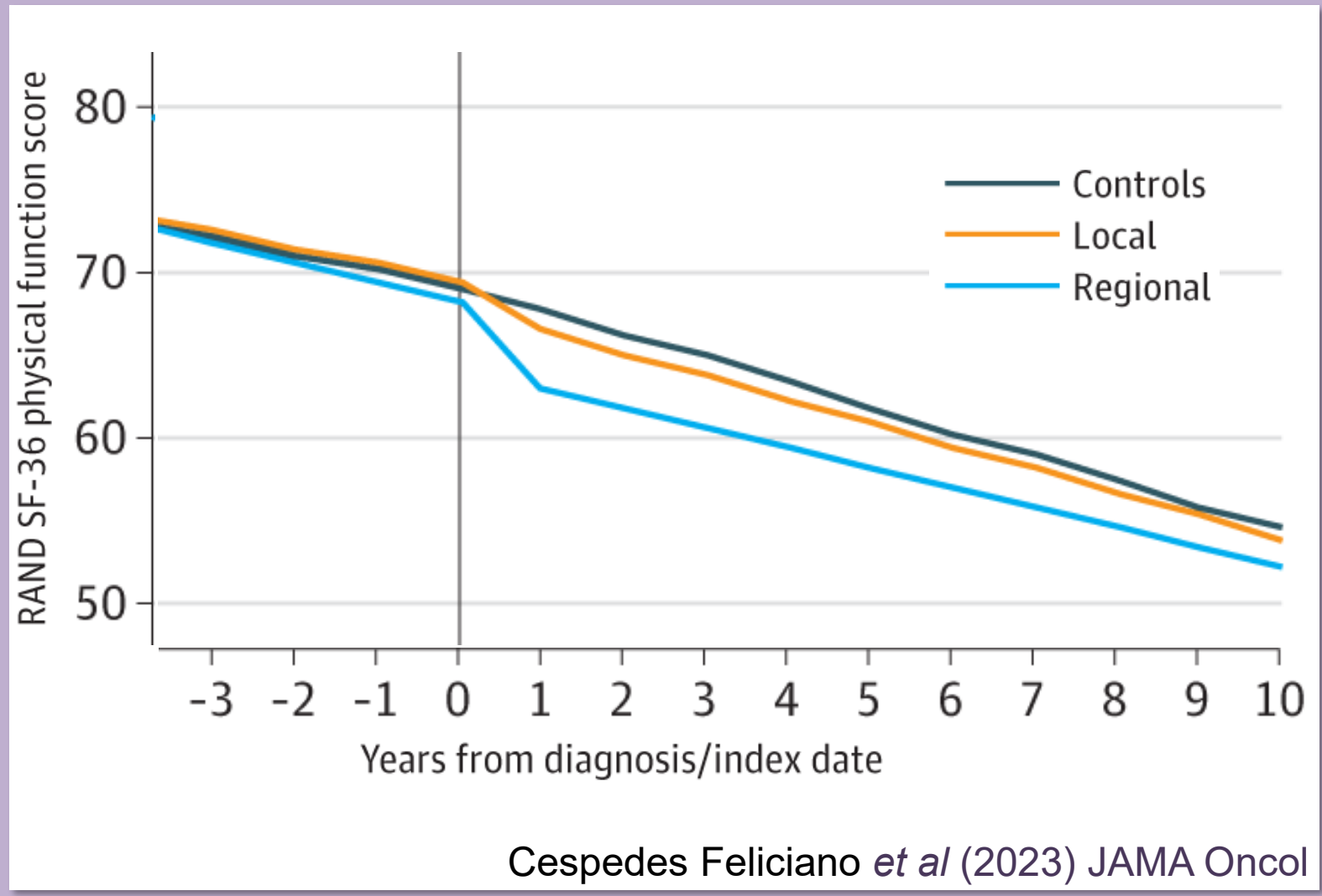
SCOPE

- Identify patients at risk for long-term function impairment due to cancer and its treatment
- Understand the intersection between biological and functional aging among cancer survivors

WHI & LILAC

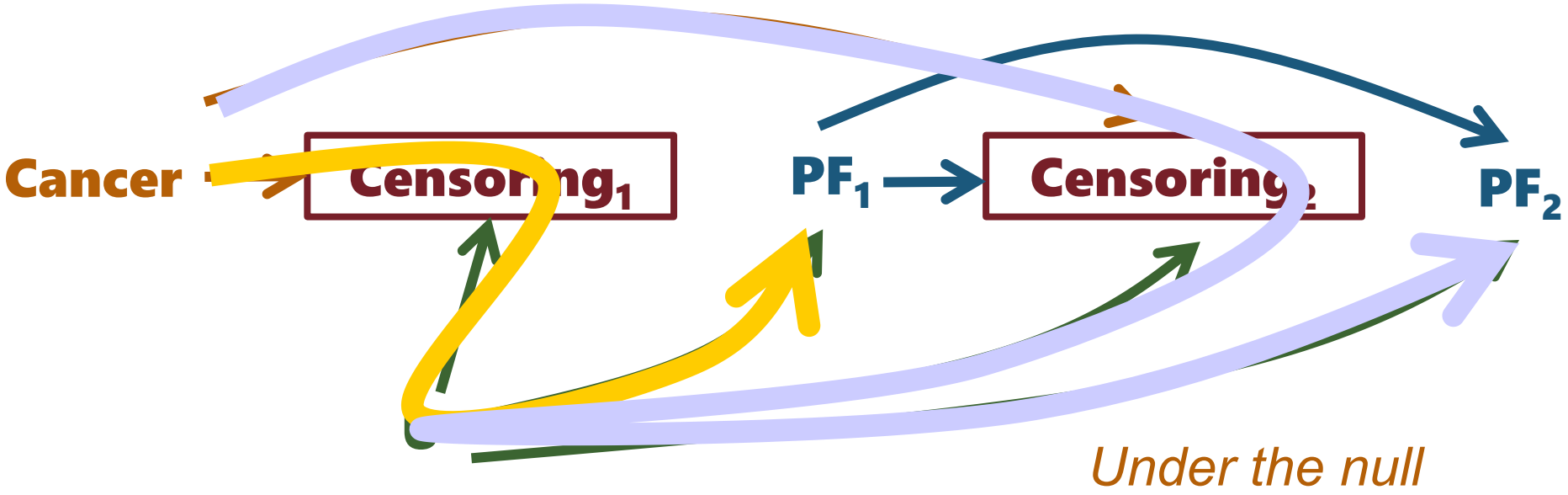
- Annual assessments of functional status
- Objective physical performance at home visits
- Longitudinal blood collection over 30 years
- Chemotherapy data

- ***Building on these results***:
  - Cleaning and modeling impact of treatment type and intensity
  - Accounting for differential loss to follow-up



Cespedes Feliciano *et al* (2023) JAMA Oncol

- Selective attrition describes left censoring that is differential by exposure status, and is expected when exposure is associated with rates of morbidity and mortality
- This is highly likely when exposure is a history of cancer, particularly when focused on older populations

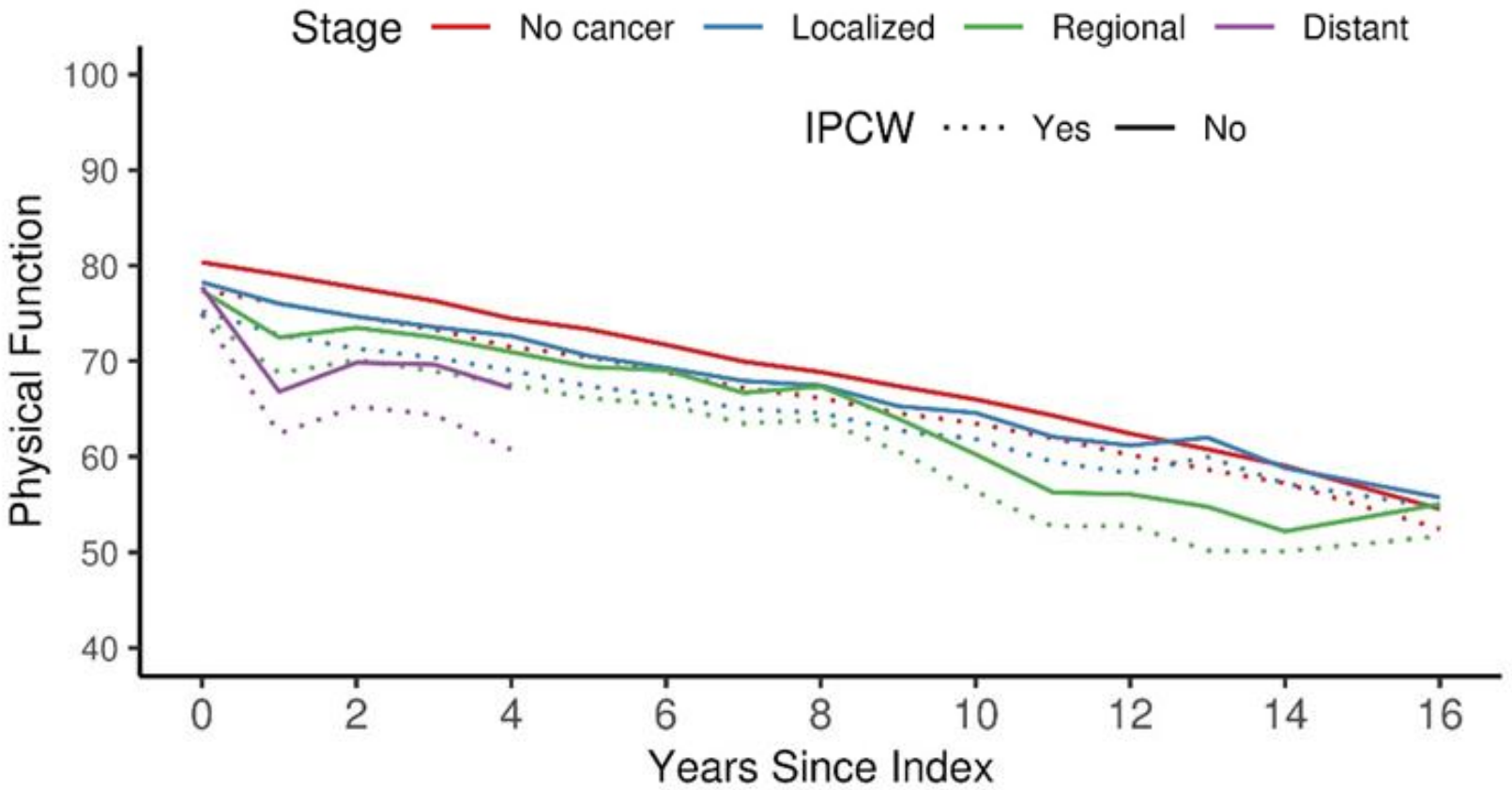


Under the null

Although selective attrition does not inherently impact internal validity, it creates a foundation for potential selection bias, which arises by conditioning on a common effect

A number of factors could impact both physical function and mortality rates, many of which are relevant to our considerations of disparities in cancer survivorship

Not accounting for selection bias overestimates trajectory of physical function and underestimated the difference in trajectories for the more advanced stages

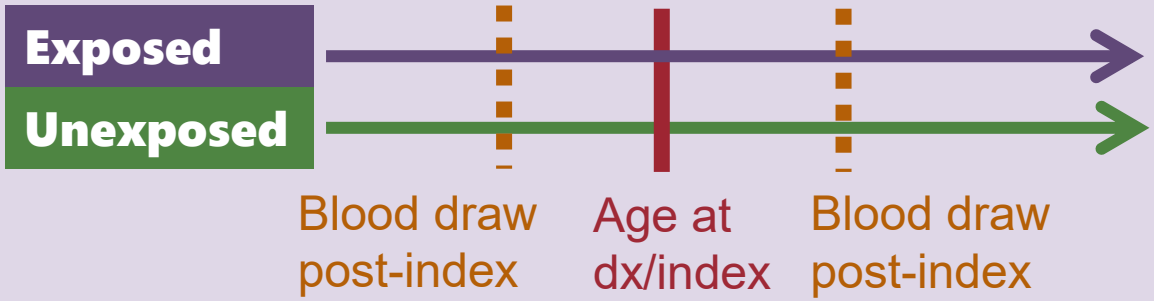


Banack *et al*; unpublished;
please do not duplicate or distribute

Epigenetic Source Population

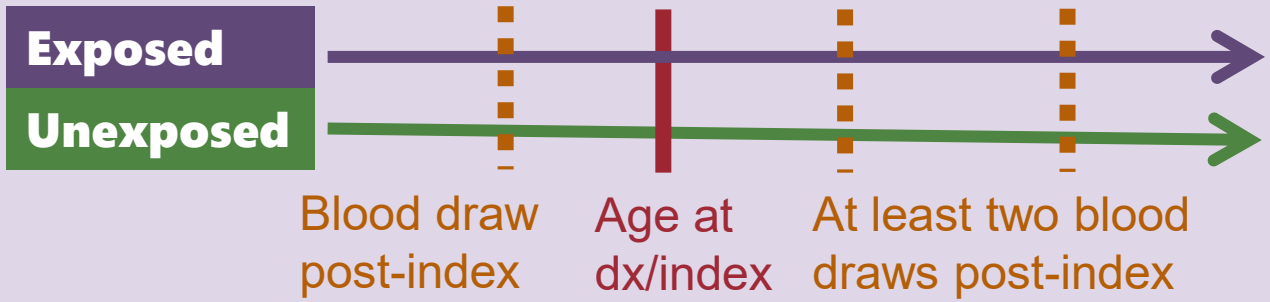
Exposed	WHI participants diagnosed with local or regional cases of first incident invasive breast cancer who lived at least five years
Unexposed	WHI participants without an invasive cancer diagnosis up to the age of diagnosis of a matched exposed participant

Group A



Our sampling scheme aims to ensure that those in Group A are representative of all eligible exposed and matched unexposed among the source population, regardless of the availability of blood collections

Group B



Instead of prioritizing generalizability, our sampling for Group B focuses on the unique opportunity to evaluate long-term, longitudinal trends in epigenetic aging after diagnosis

IMPACT

Together, our aims will:

- Advance our understanding long-term effects of cancer and its treatments on trajectories of biologic and functional aging, and the relationship between biologic and function aging
- Investigate whether rates of aging differ by type/intensity of treatment

Our study will integrate:

- Longitudinal comparison of survivors to women without a cancer history
- Consideration of survival bias in analysis
- Inclusion of multiple longitudinal epigenetic age assessments, including two post-treatment

Identify survivors at greatest risk for accelerated aging to inform supportive care strategies to improve long-term health and wellbeing

THANK YOU

WHI/LILAC Study Collaborators
Elizabeth Cespedes Feliciano, Bette Caan, Garnett Anderson, Andrea LaCroix, Sophia Fuller, Adrienne Castillo, Sowmya Vasan, Hailey Banack, Roberta Ray

NIH NATIONAL CANCER INSTITUTE

Funding Sources: National Cancer Institute
R01CA283839; MPIs: Feliciano; Binder A
U01CA173642; MPIs: Anderson, Caan, Paskett

The WHI program is funded by the National Heart, Lung, and Blood Institute, National Institutes of Health, U.S. Department of Health and Human Services through contracts 75N92021D00001, 75N92021D00002, 75N92021D00003, 75N92021D00004, 75N92021D00005

Deficits Accumulation Index in WHI: Disparities by race in cancer survivor and non-cancer controls

-Sowmya Vasan
Fred Hutchinson Cancer Center

WHI Investigator Meeting 2025
May 2nd, 2025

What to expect

- A quick overview of Deficits Accumulation Index (DAI).
- Overall characteristics of DAI at Baseline: among all WHI participants and within the cancer survivorship (LILAC) cohort, and how they differ by:
  - Race, Ethnicity
  - Cancer Survivorship Status

Background

- Frailty is a state of increased vulnerability resulting from age-associated decline in physiologic reserve and function.
- There is no single universally accepted way to measure frailty.
  - Comprehensive Geriatric Assessments, Fried Phenotypic Frailty score
- Rockwood et al. (2011) proposed the Deficit Accumulation Index (DAI), a frailty index based on the health deficit accumulation model, for use in epidemiologic studies.
  - Condenses many health deficits into one continuous score that represents the overall health of an individual.
  - Ranges from 0 to 1, with a lower score indicating lower frailty.
- Theou et al. (2023) published a paper outlining best practices for creating DAI.
  - Candidate health deficits are checked for missingness, age associations and correlations with each other.
  - DAI is calculated as the percentage of the selected deficits present in an individual.

Operationalizing DAI in WHI

- Guided by Theou et al. (2023) we developed the DAI among all WHI participants at baseline.
- The DAI included a list of 55 deficits spanning six different health domains.
- The baseline DAI score among all WHI participants ranged from (0 - 0.69) with a mean of 0.14 and a median of 0.13.

Presence and History of Diseases	General Health	Physical Health and Function
- Individual CVD conditions (MI, Stroke/TIA, Heart failure, Angina, PAD, Revascularization, Atrial fibrillation, DVT) - Cancer - Osteoporosis - Liver disease - COPD/Chronic bronchitis/Emphysema - Gall bladder problems - Stomach or intestinal ulcer - Kidney or bladder stones - Colon or polyp removal - Diverticulitis - Thyroid problems (Nodule. Underactive, Goiter) - Glaucoma - Cataract - Arthritis (Rheumatoid, Other) - Treated Diabetes - Treated Hypertension - High cholesterol requiring pills	- Heartburn - Low back pain - Skin dryness or scaling - Dizziness - Forgetfulness - Tremors (shakes) - Clumsiness - Urinary incontinence - General aches or pains - Pain or burning while urinating - Cough or wheezing - Decreased appetite - General health - Syncope or blackouts - Sleep Disturbance scale - Hospitalized in the past 2 years	- Fracture - Hearing loss - Physical Function construct - Role limitations due to Physical Problems - Intestine removed - Any trouble seeing that is uncorrected by lenses - Joint pain or stiffness - Pain Construct
Activities of Daily Living	**Functional and Emotional Well-being**	**Polypharmacy**
- Activities of Daily Living construct	- Role limitations due to Emotional Problems	- Polypharmacy (intake of >= 5 medications)

Life and Longevity After Cancer Study (LILAC)

- WHI-LILAC is a cancer survivorship study funded by NCI.
- The study enrolled WHI participants diagnosed with cancer from 8 cancer sites.
- One of the aims was to establish an age-matched cancer-free group to compare how cancer and its treatment influence aging and related health conditions.
  - Each case was matched with up to 5 cancer free controls.
  - Matching factors included: Age at enrollment, Enrollment date, CT/OS enrollment, HT trial enrollment, LLS-I enrollment.

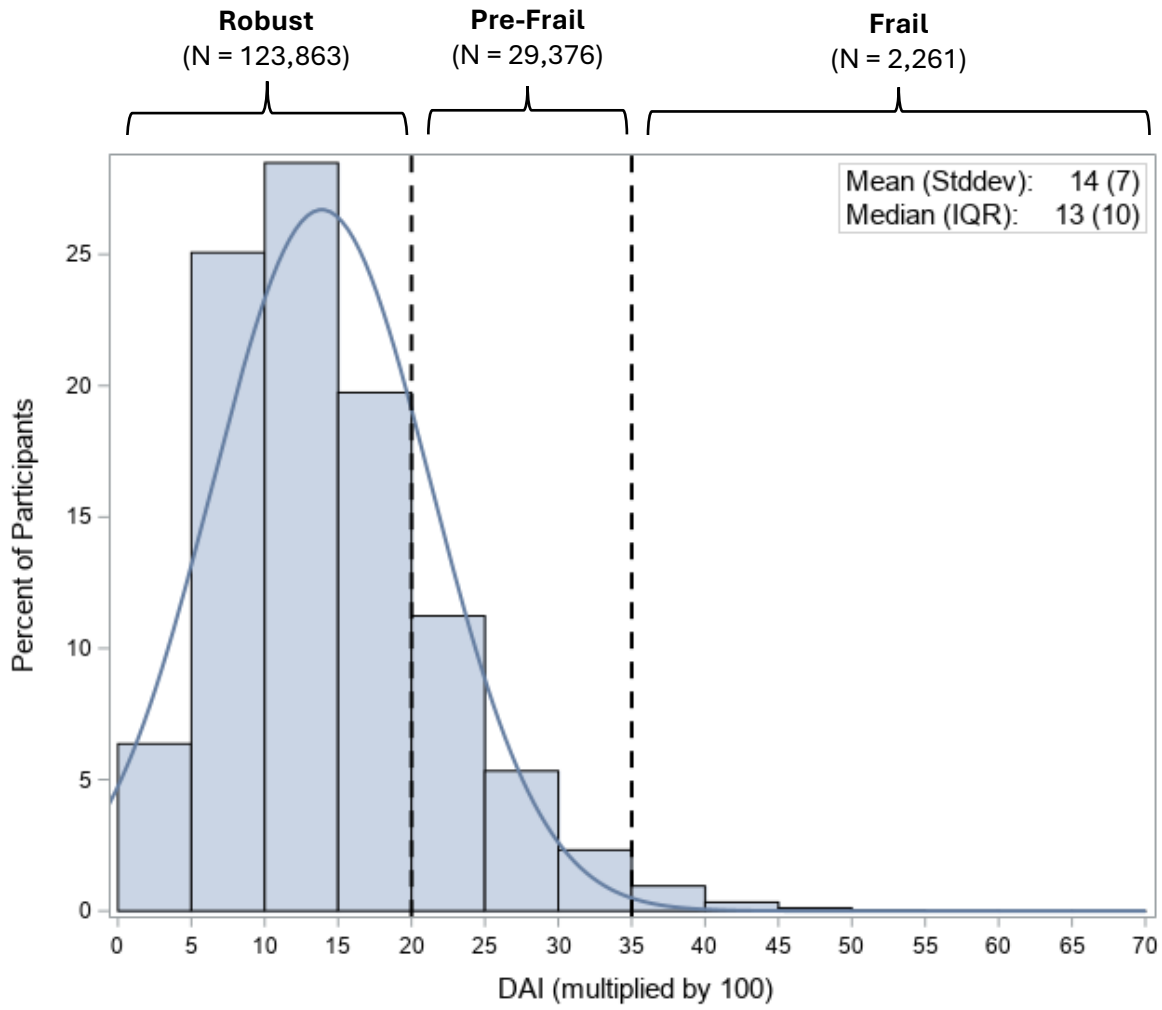
Life and Longevity After Cancer Study (LILAC)

- There are **13,412 LILAC cases** (as of March 2020).
- They were matched to a total of **66,144 cancer-free controls**.
- Among them:
  - 96.60% matched to 5 controls
  - 1.46% matched to 4 controls
  - 0.92% matched to 3 controls
  - 0.60% matched to 2 controls
  - 0.37% matched to 1 control
  - 0.05% had no matched controls

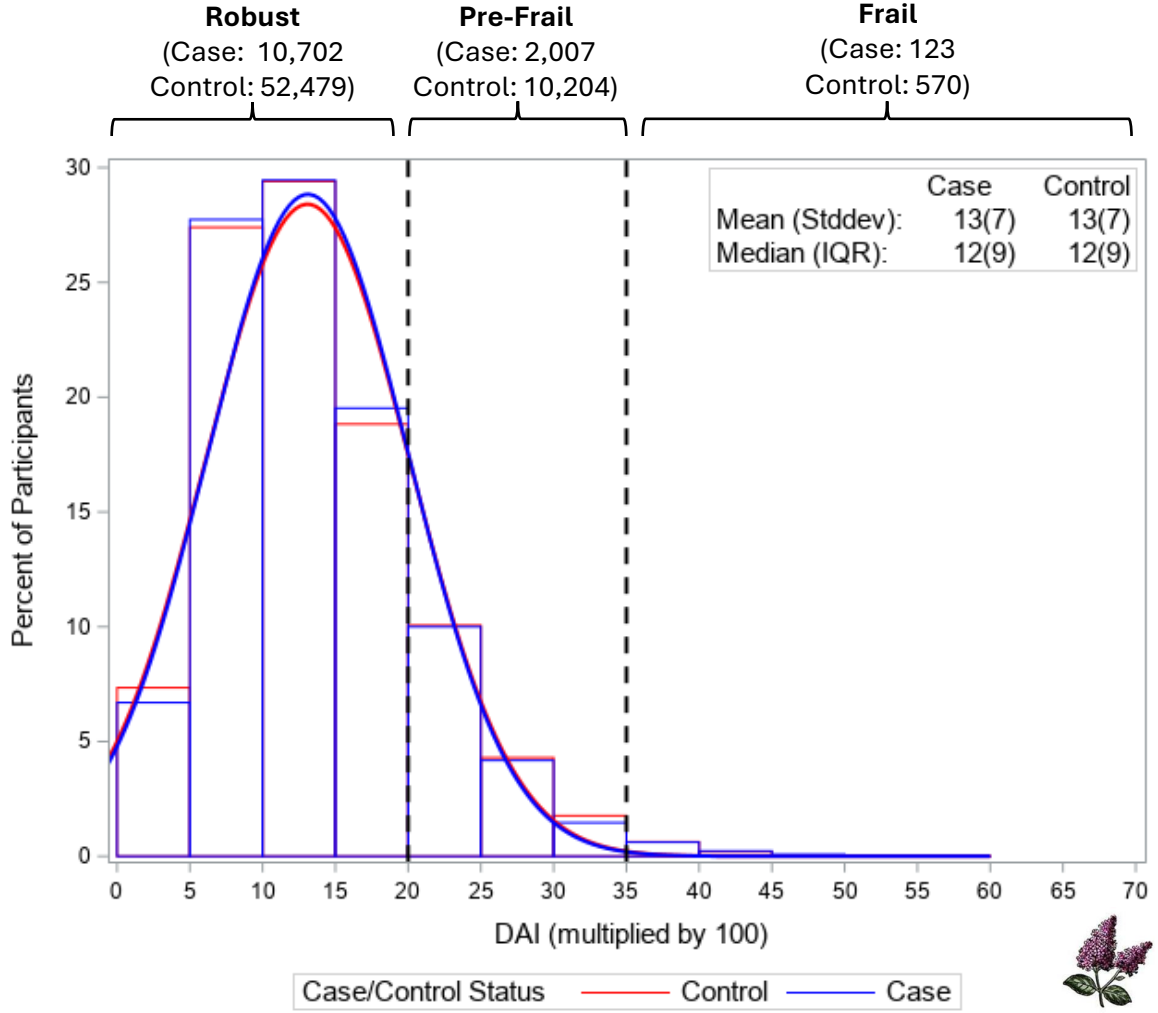
	Cancer case N (%)	Matched cancer-free control N (%)
Race		
White	12,257 (91.4)	57,644 (87.1)
Black	664 (4.9)	4,872 (7.4)
Asian/Native Hawaiian/Other PI	211 (1.6)	1,715 (2.6)
American Indian/Alaska Native	28 (0.2)	199 (0.3)
More than one race	130 (1.0)	787 (1.2)
Unknown/Not reported	122 (0.9)	927 (1.4)
Ethnicity		
Hispanic/Latino	284 (2.1)	2,470 (3.7)
Not Hispanic/Latino	13,060 (97.4)	63,351 (95.8)
Unknown/Not reported	68 (0.5)	323 (0.5)

Distribution of Baseline DAI

All WHI Participants (N = 155,500)

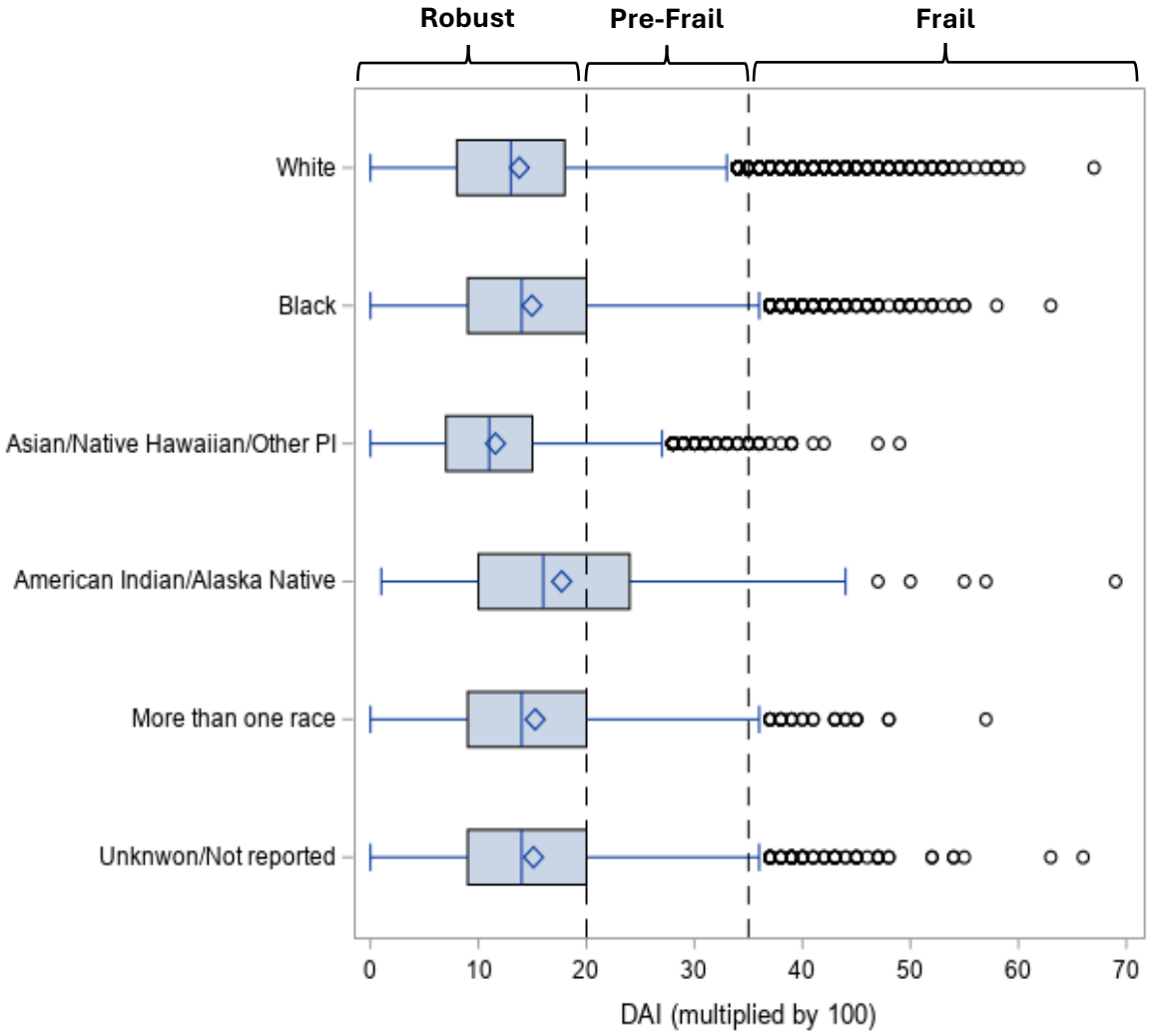


LILAC cases (N = 12,832) & matched controls (N = 63,253)



Distribution of Baseline DAI by Race

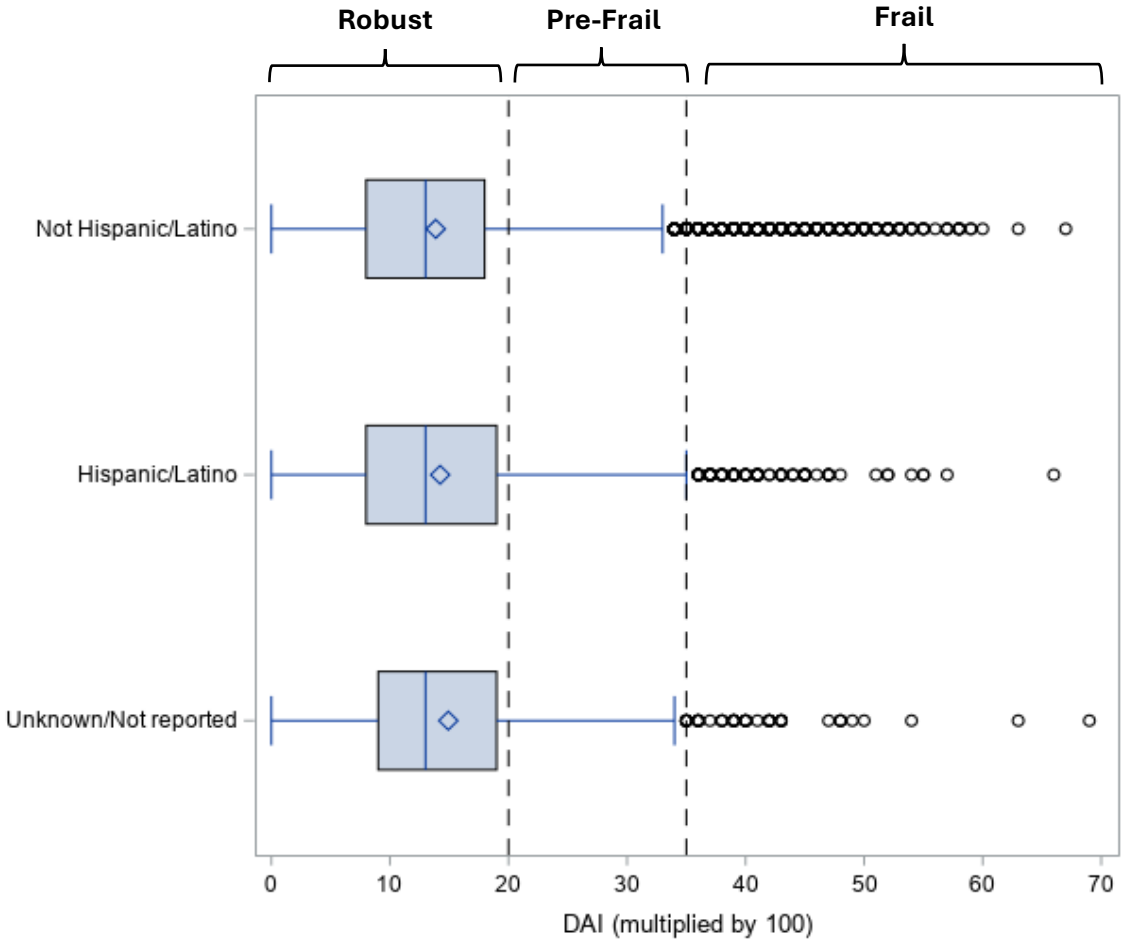
All WHI Participants (N = 155,500)



	N (%)	Mean (Stddev)
White	132,331 (85.1)	13.8 (7.3)
Black	13,731 (8.8)	15.0 (8.4)
Asian/Native Hawaiian/Other PI	4,103 (2.6)	11.6 (6.4)
American Indian/Alaska Native	514 (0.3)	17.7 (9.8)
More than one race	1,823 (1.2)	15.3 (7.9)
Unknown/Not reported	2,998 (1.9)	15.1 (8.7)

Distribution of Baseline DAI by Ethnicity

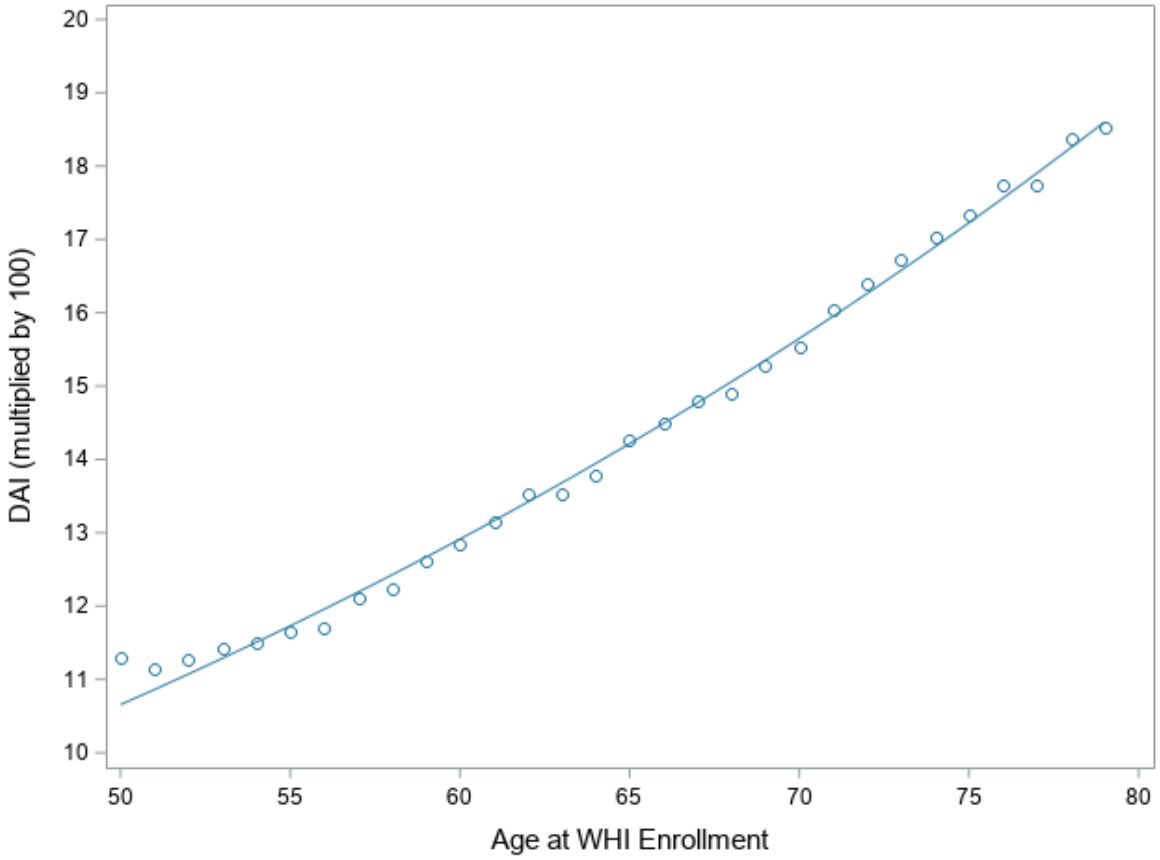
All WHI Participants (N = 155,500)



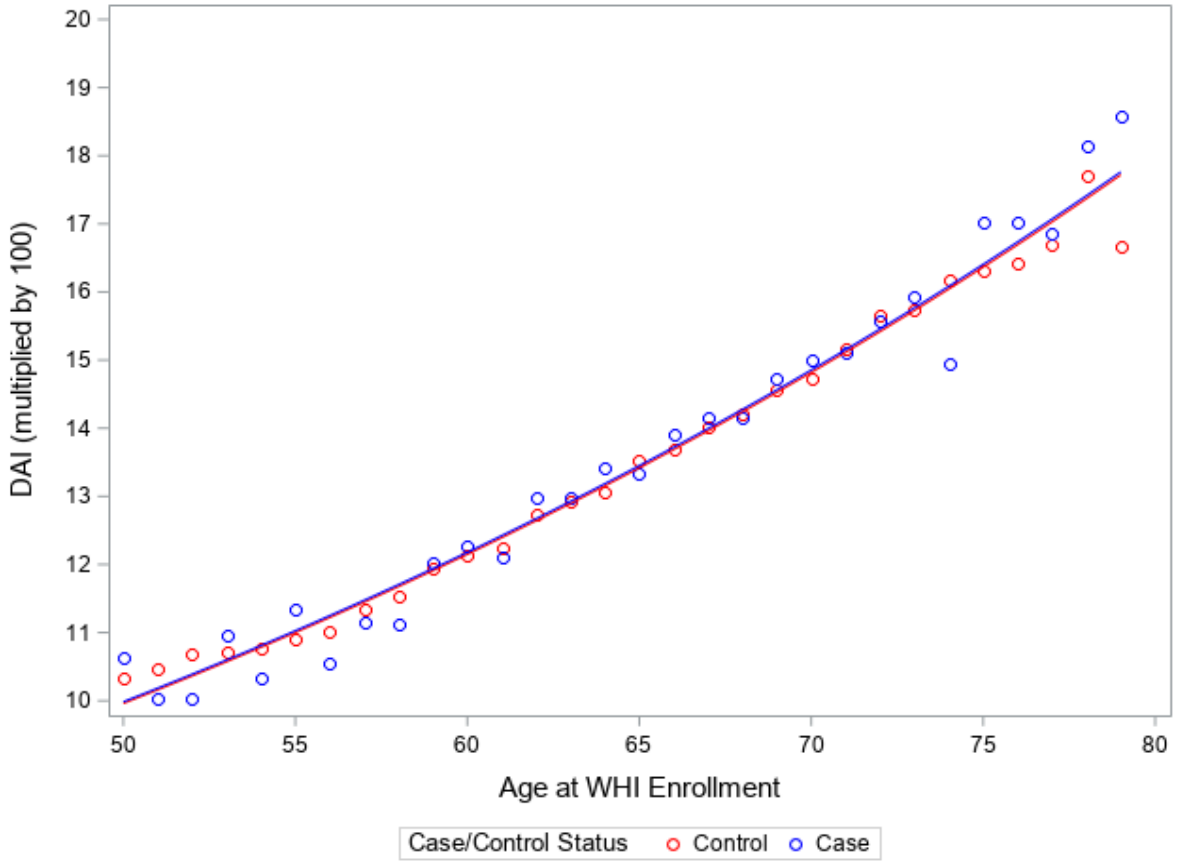
	N (%)	Mean (Stddev)
Not Hispanic/Latino	147,329 (94.8)	13.9 (7.4)
Hispanic/Latino	6,831 (4.4)	14.2 (8.0)
Unknown/Not reported	1,340 (0.9)	14.9 (9.0)

Average DAI by Age

All WHI Participants (N = 155,500)

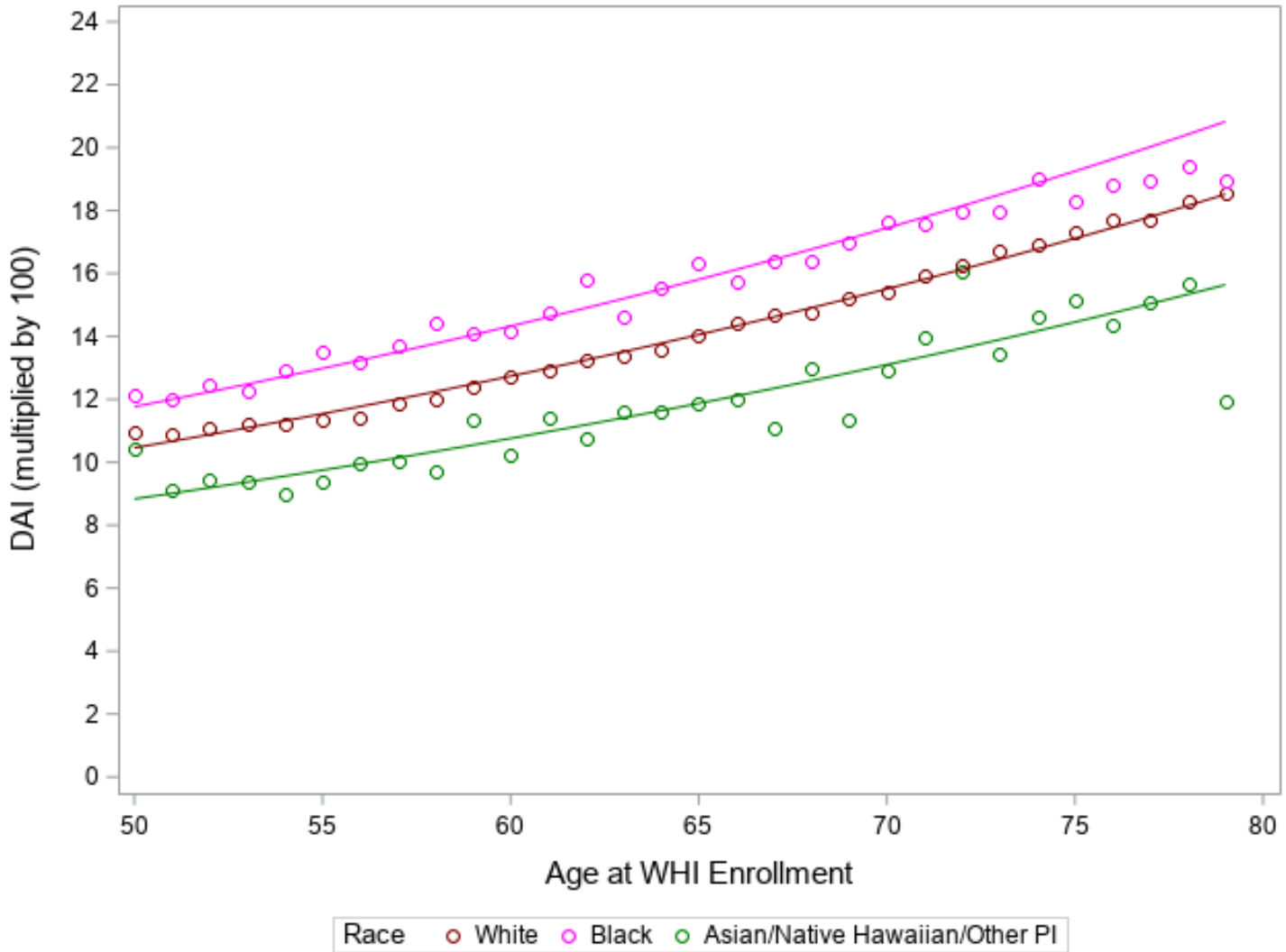


LILAC cases (N = 12,832) & matched controls (N = 63,253)



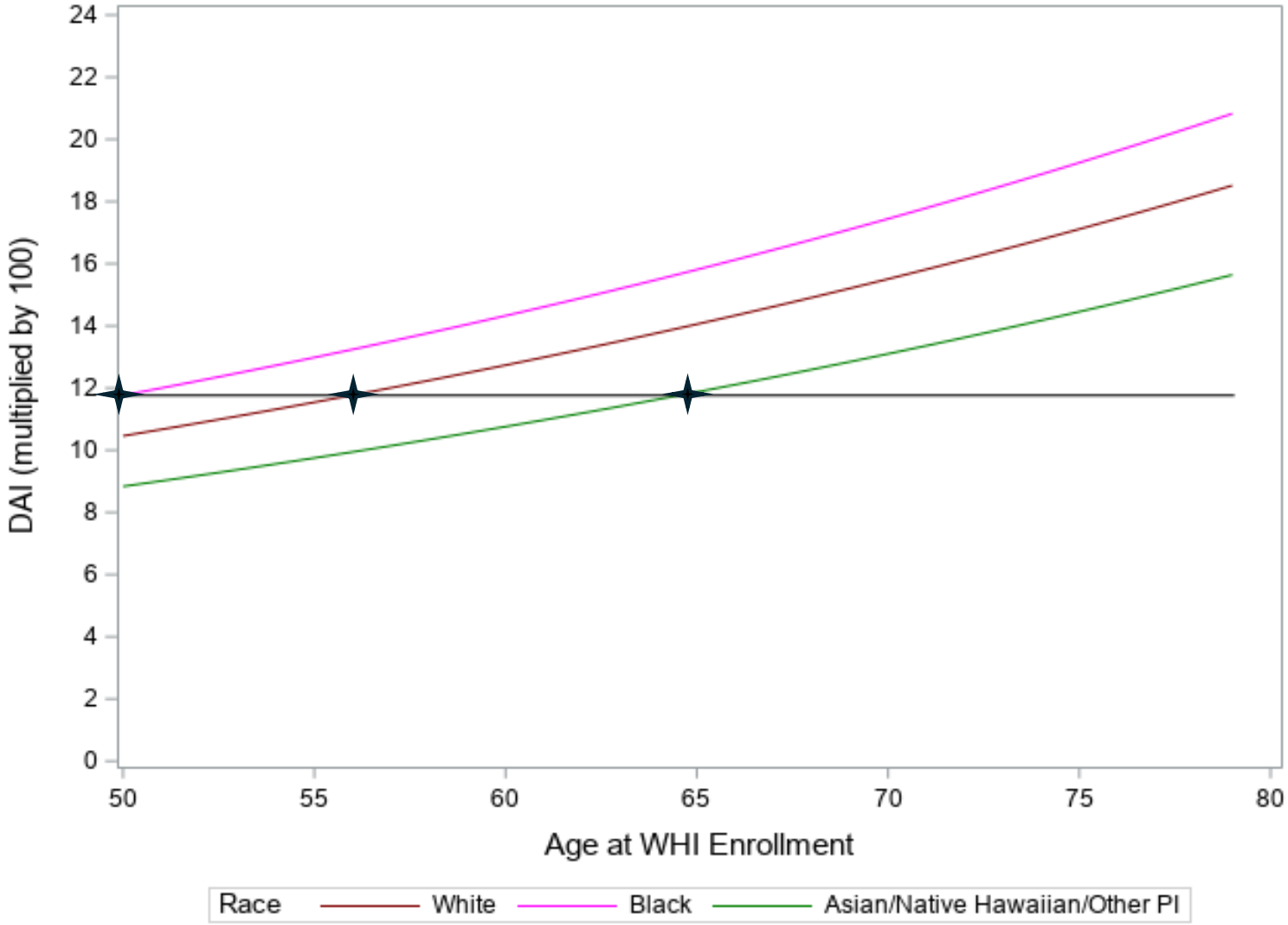
Average DAI by Age & Race

All WHI Participants (N = 155,500)



Average DAI by Age & Race

All WHI Participants (N = 155,500)

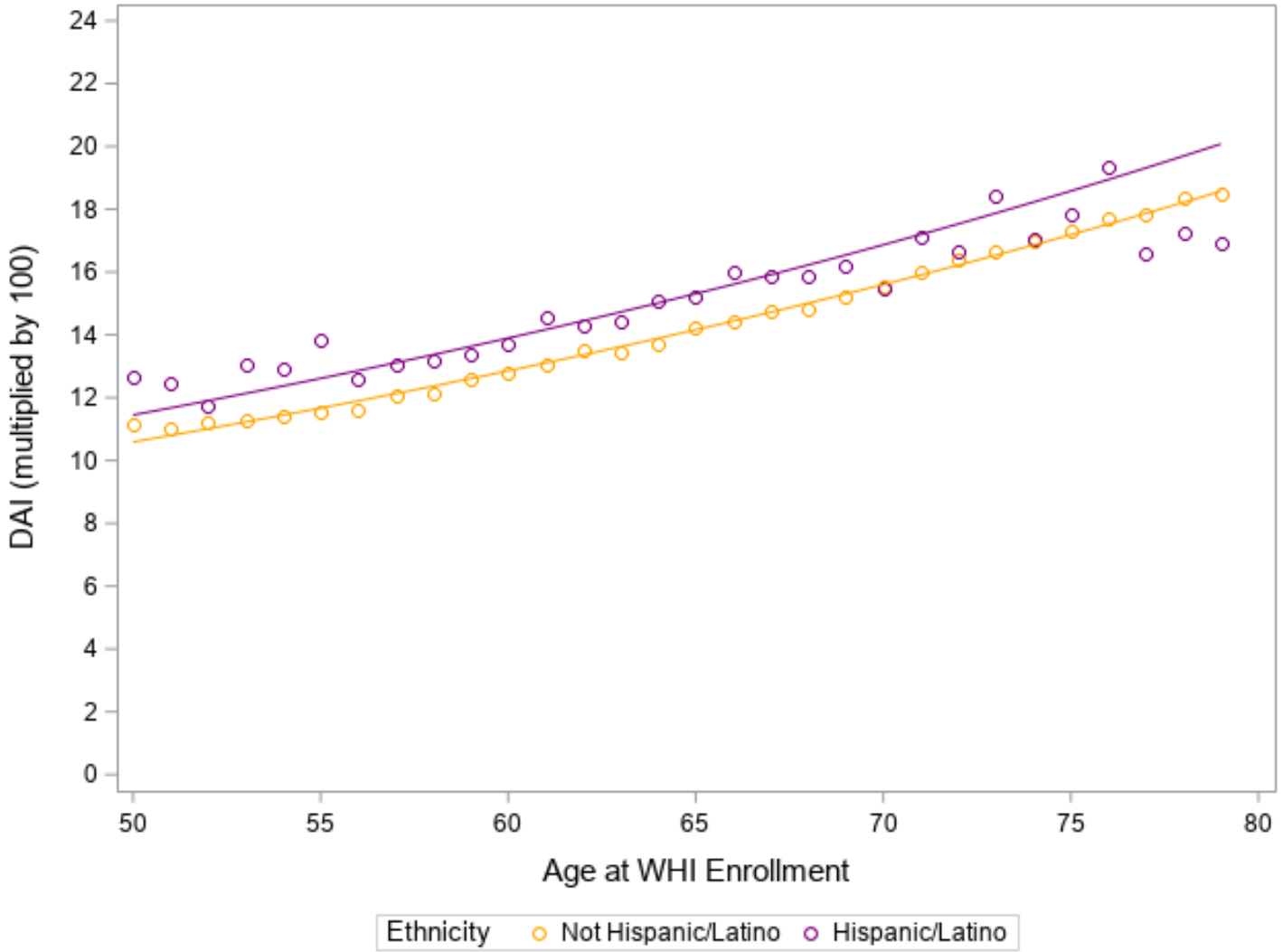


On average, a 50-year-old Black participant has the same frailty as a:

- 57-year-old white participant
- 65-year-old Asian participant

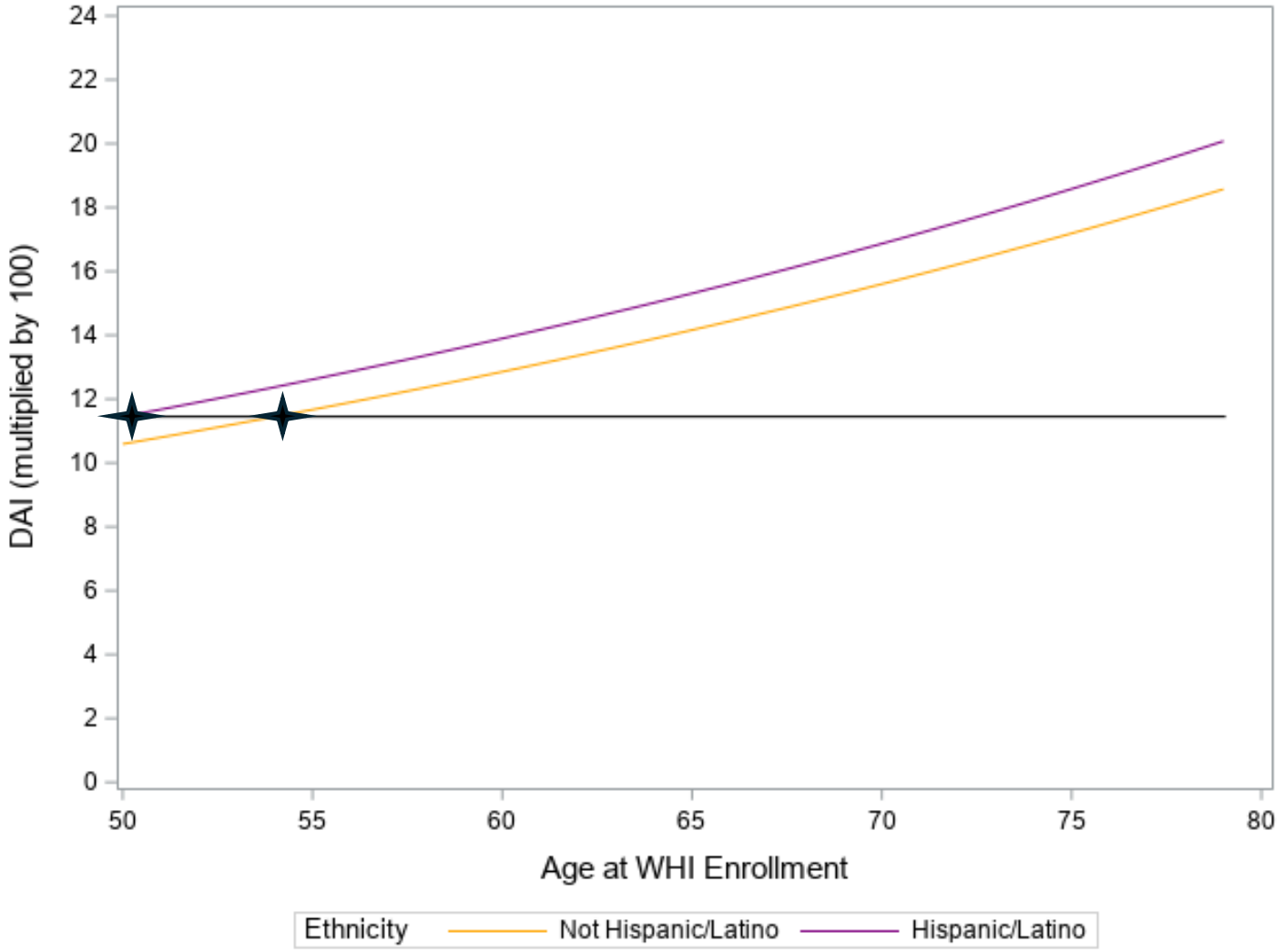
Average DAI by Age & Ethnicity

All WHI Participants (N = 155,500)



Average DAI by Age & Ethnicity

All WHI Participants (N = 155,500)



On average, a 50-year-old Hispanic/Latino participant has the same frailty as a 55-year-old Not Hispanic/Latino participant

Association Between Baseline Frailty Status and All-Cause Mortality by Race Categories

	All WHI Participants (N = 155,500)		Interaction By Race Categories					
			White (N = 132,331)		Black (N = 13,731)		Asian/Native Hawaiian/Other PI (N = 4,103)	
	# Deaths	HR (95% CI)	# Deaths	HR (95% CI)	# Deaths	HR (95% CI)	# Deaths	HR (95% CI)
Per 0.05 increase in score		1.17 (1.16, 1.17)		1.17 (1.16, 1.18)		1.15 (1.14, 1.17)		1.14 (1.10, 1.18)
By Frailty Domains								
Robust (0 - <0.2)	62,432	Ref	54,591	Ref	4,703	Ref	1,478	Ref
Pre-Frail (0.2 - <0.35)	22,071	1.49 (1.47, 1.51)	18,748	1.40 (1.47, 1.52)	2,216	1.46 (1.38, 1.53)	294	1.41 (1.24, 1.60)
Frail (>= 0.35)	1,968	2.19 (2.10, 2.30)	1,532	2.19 (2.08, 2.30)	293	2.17 (1.92, 2.45)	15	1.93 (1.16, 3.22)

Cox Proportional Hazards model were stratified by Age at WHI enrollment (5-yr interval), all Trial arms, OS participation and WHI Extension 1 & 2 participation. All model are adjusted for Age at WHI enrollment.
All discovered deaths (as of Dec 31st, 2022) are used to define All-cause mortality.

Association Between Frailty Status and All-Cause Mortality by Case& Control Status and Race Categories in the LILAC cohort

	Interaction By Race Categories		
	White HR (95% CI)	**Black** HR (95% CI)	**Asian/Native Hawaiian/Other PI** HR (95% CI)
Per 0.05 increase in continuous score			
Case	1.16 (1.14, 1.18)	1.16 (1.10, 1.23)	1.24 (1.05, 1.46)
Control	1.18 (1.17, 1.19)	1.16 (1.13, 1.19)	1.15 (1.09, 1.22)
By Frailty domains			
Case			
Robust (0 - <0.2)	Ref	Ref	Ref
Pre-Frail & Frail (>=0.2)	1.48 (1.40, 1.57)	1.82 (1.46, 2.26)	1.81 (0.99, 3.33)
Control			
Robust (0 - <0.2)	Ref	Ref	Ref
Pre-Frail & Frail (>=0.2)	1.57 (1.52, 1.61)	1.56 (1.43, 1.71)	1.53 (1.24, 1.88)

Cox Proportional Hazards model were stratified by Age at WHI enrollment (5-yr interval), all Trial arms, OS participation and WHI Extension 1 & 2 participation. All model are adjusted for Age at WHI enrollment. All discovered deaths (as of Dec 31st, 2022) are used to define All-cause mortality.

Summary

- The distribution of DAI at baseline is similar to what we observe in other cohorts.
  - No differences by Case/Control Status.
  - There were small but significant differences by race and ethnicity.
- There is a positive association of DAI with age and differences by race and ethnicity.
- Risk of all-cause mortality was higher in pre-frail and frail than robust women; results were similar across race categories.
- Risk of all-cause mortality was higher in pre-frail and frail Black or Asian/Native Hawaiian/Other PI participants who go on to develop cancer compared to cancer free controls.

Future Directions

- To create DAI longitudinally across WHI follow-up.
- Test for association of DAI with cancer specific mortality.
- Examine trajectories of DAI overall and by LILAC cancer status.
- Create DAI as a resource for Investigators use in their research.

Acknowledgements

- NCI (LILAC, Grant: U01CA173642)
- NHLBI (WHI, Contract: 75N92021D00001)
- Dr. Garnet Anderson (LILAC & WHI PI, Fred Hutchinson Cancer Center)
- Dr. Electra Paskett (LILAC PI, The Ohio State University)
- Dr. Bette Caan (LILAC PI, Kaiser Permanente Northern California)
- Dr. Judith Carroll (LILAC Investigator, UCLA)
- Madeleine Clarke (Fred Hutchinson Cancer Center)

Weill Cornell Medicine
Meyer Cancer Center

The Impact of Neighborhood Deprivation on Increasing Deficit Accumulation Frailty in Older Breast Cancer Survivors and Non-Cancer controls

The Thinking and Living with Cancer Study

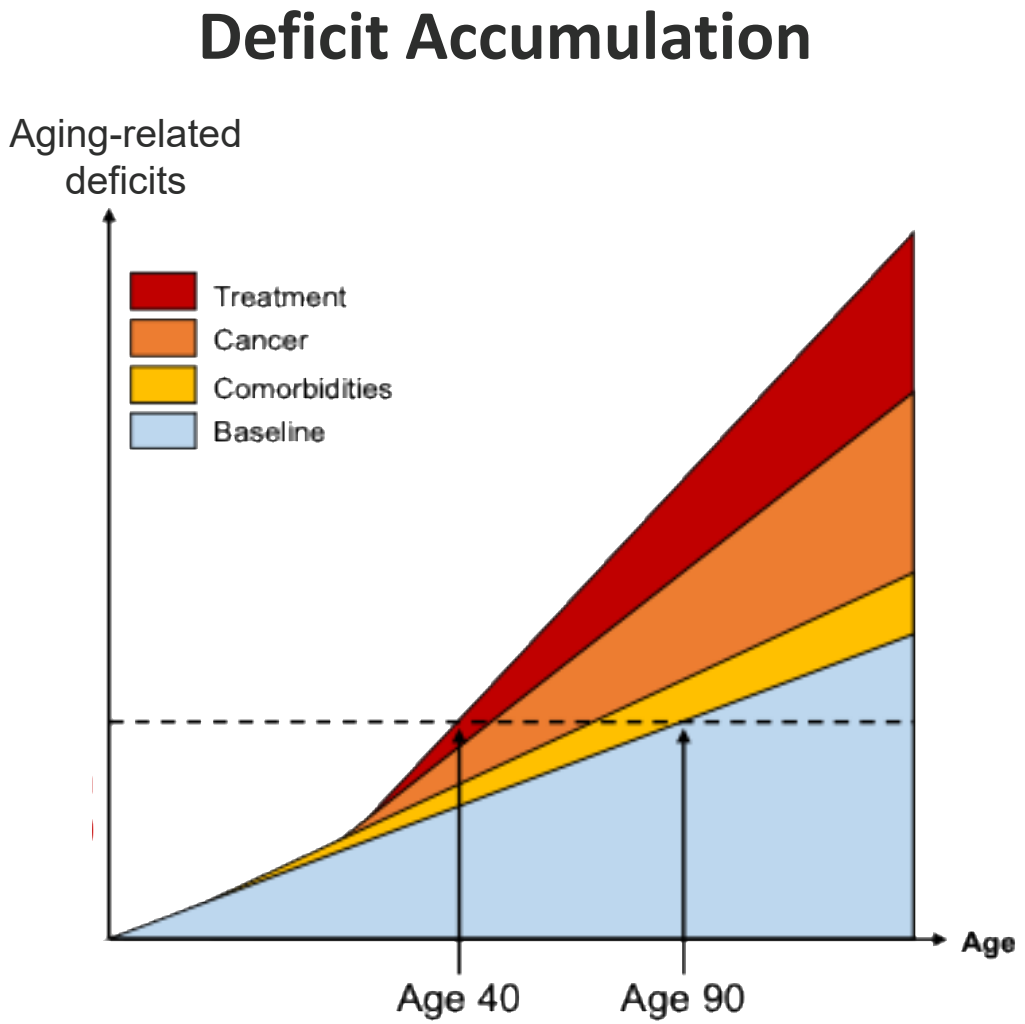
Eunji Choi
Assistant Professor

May 2, 2025
WHI Investigator Meeting

We're Changing Medicine.

Background

- Frailty, a state of increased vulnerability to adverse health outcomes and death.
    - The concept of frailty as deficit accumulation focuses on a state of poor health due to cumulative age-related deficits across multiple systems.
- Cancer and treatments are drivers of aging.
- It is important to compare aging trajectories between cancer and non-cancer control.



Background

- Where people live influences their health outcomes.
- Area Deprivation Index (ADI)
    - A composite measure that aggregates neighborhood-level socioeconomic factors.
- Previous studies have examined the impact of neighborhood deprivation on DAFI change solely on either cancer survivors or non-cancer adults.

Domain	17 ADI-Items
Income (4)	Below poverty level
	Below 150% of poverty level
	Income disparity
	Median family income
Employment (2)	Unemployment
	White collar occupation
Education (2)	High school diploma or higher
	<9 years of education
Housing (4)	Owner-occupied housing
	Median monthly mortgage
	Median gross rent
	Median home value
Household (4)	Single-parent households
	Without a telephone
	Without a motor vehicle
	Without complete plumbing
Crowding (1)	Crowding (>1 person/room)

Objective

- Investigate the longitudinal relationship between neighborhood deprivation using ADI and increase in deficit accumulation over time in the older (≥60) female breast cancer survivors (BCS) compared to non-cancer controls.

- Hypothesis:
  - Those in more deprived areas may be at higher risk for DAFI increase
  - The influence of neighborhood deprivation on DAFI increase may differ between cancer survivors and non-cancer controls.

Methods

- Study population

THE TLC STUDY

THINKING & LIVING WITH CANCER

Dr. Jeanne Mandelblatt

Dr. Judith Carroll

Women enrolled in TLC with at least 1 follow-up in 9/2/2010 – 5/2/2023 (N = 1004)
Non-cancer (n=464), Breast cancer (n=540)

Exclusion Criteria	Breakdown by case-control	
	Non-cancer	Breast cancer
No information of baseline frailty (n=47)	16	31
Not geocoded (n=16)	6	10
Missing frailty at follow-up (n = 30)	8	22

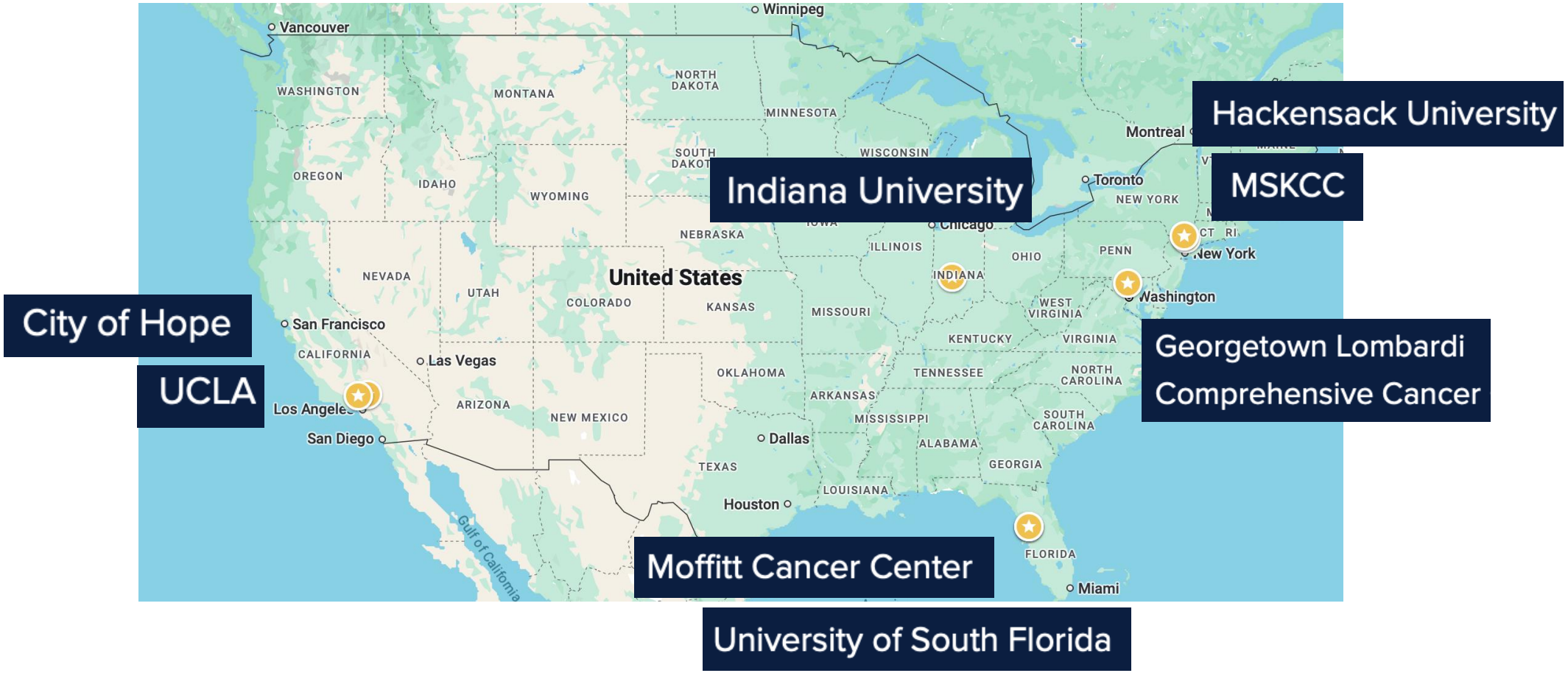
Study cohort (N = 911)
Non-cancer (n=434), Breast cancer (n=477)

Controls are frequency matched at baseline by age, education, race, and enrollment site.

Methods

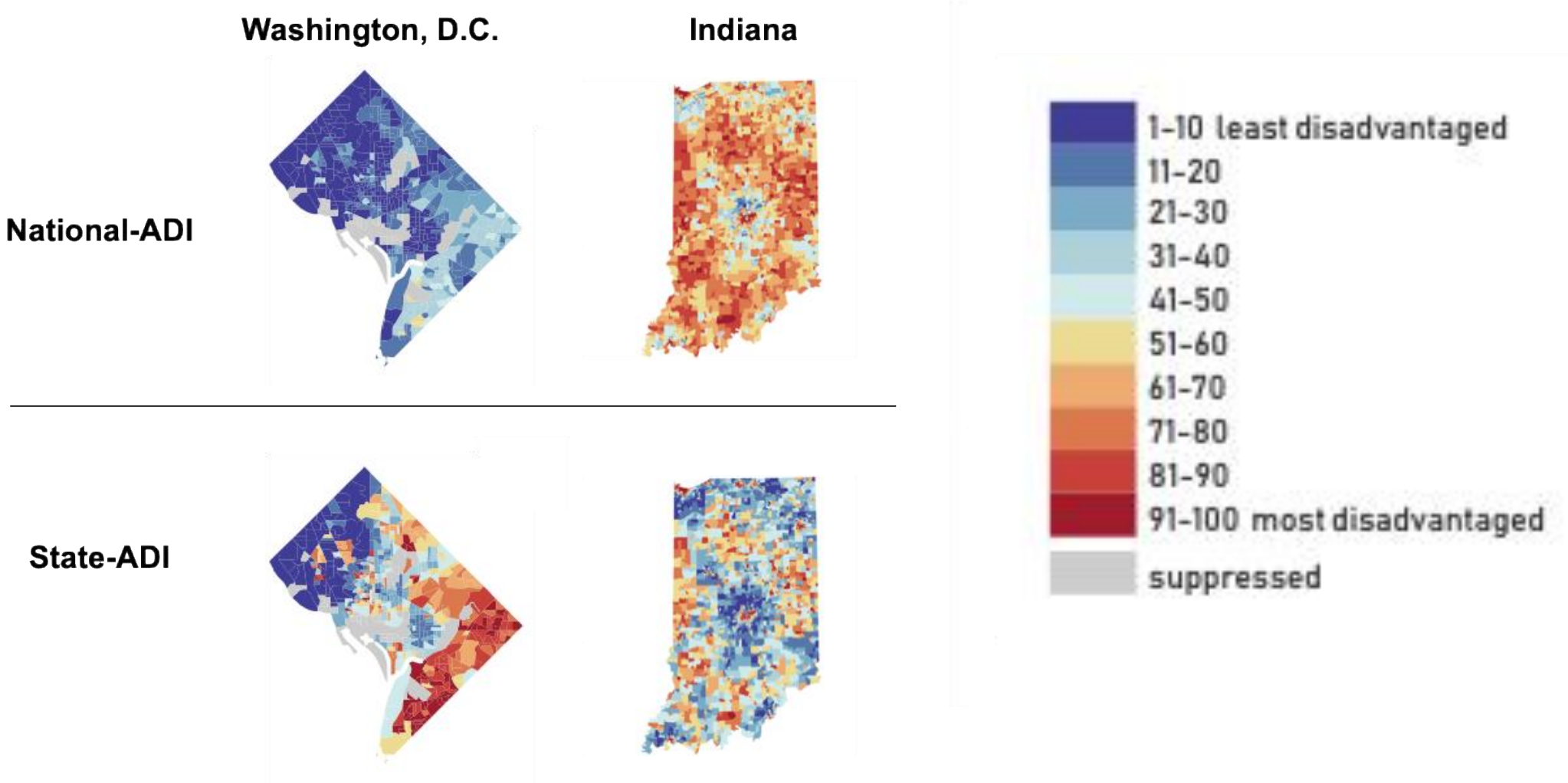
- **Primary Outcome**
  - A clinically meaningful increase (0.06) in a 48-item DAFI score over time
- **Key Exposures:** Neighborhood deprivation
  - Area Deprivation Index (ADI) 2015, 2020, 2022 closest to enrollment
  - State-level ADI (1-10 rankings) → Tertile based on TLC women
- **Statistical Analysis**
  - Cause-specific Cox model to account for competing risk of death
  - Cumulative incidence of DAFI increase using Aalen-Johansen estimator
  - Low intra-class correlation in women who shared the same census block and high singleton block (92%), a clustering block was not included.

TLC Sites



There were 13 community practices and hospital sites involved across these areas.
UCLA did not recruit participants; it contributed solely by providing laboratory services.

ADI in two TLC states



Results

Participant Characteristics

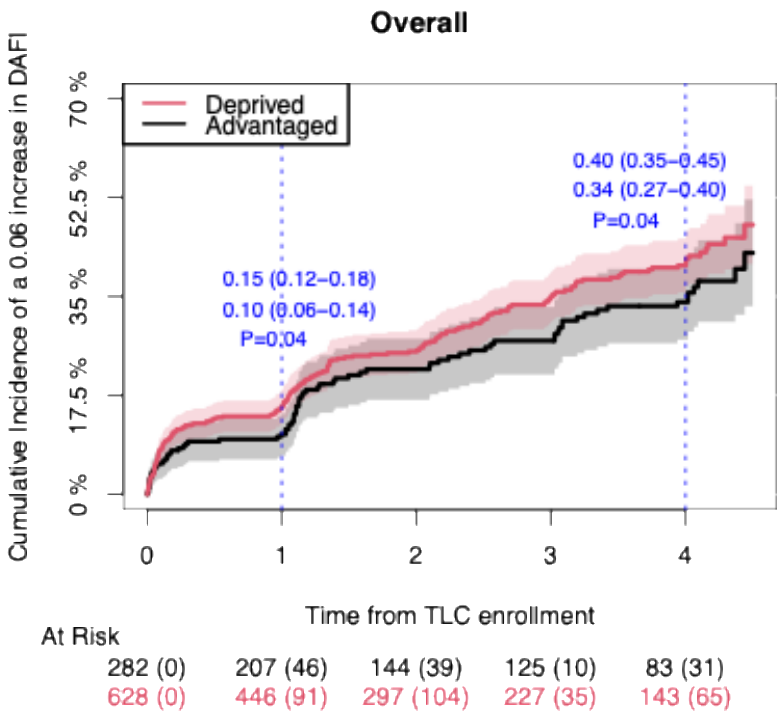
Deprived

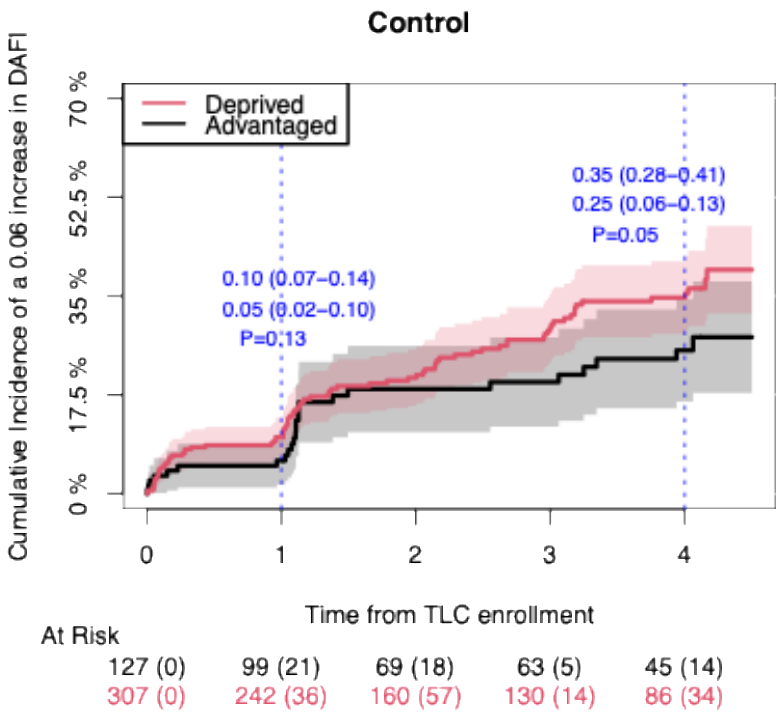
Factors	Total	Tertiles of Area Deprivation Index (ADI)			*P*-value
		1st	2nd	3rd	
Total N (row %)	911 (100.0%)	282 (31.0%)	263 (28.9%)	366 (40.2%)	
Breast cancer status					
No (non-cancer controls)	434 (47.6%)	127 (45.0%)	127 (48.3%)	180 (49.2%)	0.56
Yes (Breast cancer survivors)	477 (52.4%)	155 (55.0%)	136 (51.7%)	186 (50.8%)	
Patient age at enrollment					
Mean (SD)	67.9 (±6.2)	68.0 (±6.0)	67.3 (±5.9)	68.2 (±6.4)	0.22
Race					
White	753 (82.7%)	254 (90.1%)	208 (79.1%)	291 (79.5%)	<.01
Black	68 (7.5%)	10 (3.5%)	19 (7.2%)	39 (10.7%)	
Hispanic	51 (5.6%)	8 (2.8%)	18 (6.8%)	25 (6.8%)	
Other	39 (4.3%)	10 (3.5%)	18 (6.8%)	11 (3.0%)	
Education					
High school graduate	115 (12.6%)	19 (6.7%)	30 (11.4%)	66 (18.0%)	<.01
College graduate	252 (27.7%)	49 (17.4%)	74 (28.1%)	129 (35.2%)	
Graduate school or more	544 (59.7%)	214 (75.9%)	159 (60.5%)	171 (46.7%)	
Social well-being at enrollment					
Good (FACT-G[a]≥16)	345 (37.9%)	107 (37.9%)	96 (36.5%)	142 (38.8%)	0.85
Poor	566 (62.1%)	175 (62.1%)	167 (63.5%)	224 (61.2%)	
Site					
Georgetown	192 (21.1%)	103 (36.5%)	36 (13.7%)	53 (14.5%)	<.01
Memorial Sloan Kettering	156 (17.1%)	65 (23.0%)	47 (17.9%)	44 (12.0%)	
Moffit Cancer Center	251 (27.6%)	22 (7.8%)	91 (34.6%)	138 (37.7%)	
City of Hope	136 (14.9%)	27 (9.6%)	50 (19.0%)	59 (16.1%)	
John Theurer Cancer Center	36 (4.0%)	8 (2.8%)	11 (4.2%)	17 (4.6%)	
Indiana University	140 (15.4%)	57 (20.2%)	28 (10.6%)	55 (15.0%)	
Baseline deficit accumulation at enrollment					
Robust (DAI: <0.2)	722 (79.3%)	234 (83.0%)	221 (84.0%)	267 (73.0%)	<.01
Pre-Frail (DAI: 0.2-0.34)	173 (19.0%)	44 (15.6%)	39 (14.8%)	90 (24.6%)	
Frail (DAFI: >0.34)	16 (1.8%)	4 (1.4%)	3 (1.1%)	9 (2.5%)	
Clinically significant DAFI increase (a 0.06 increment) during follow-up					
Yes	279 (30.6%)	80 (28.4%)	85 (32.3%)	114 (31.1%)	0.87
No	632 (69.4%)	202 (71.6%)	178 (67.7%)	252 (68.9%)	

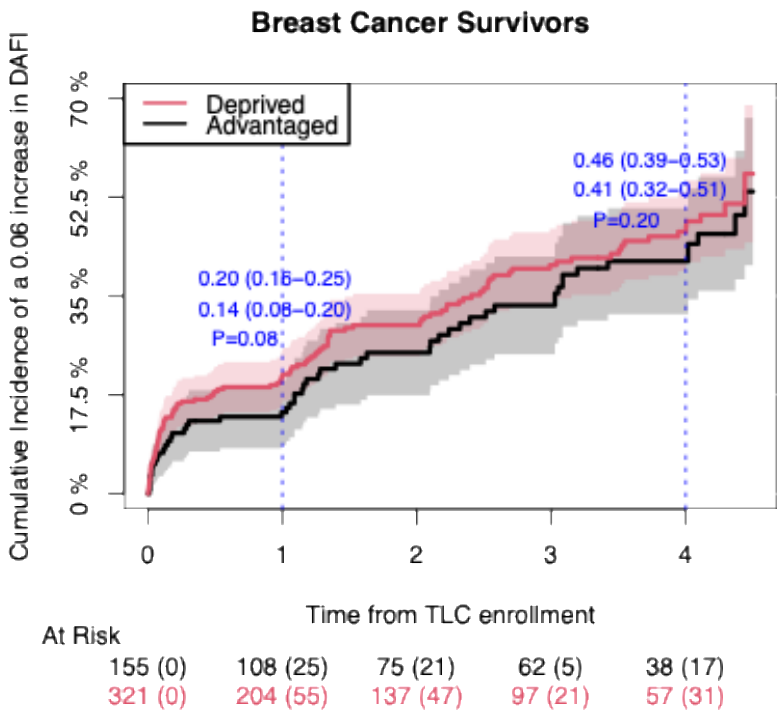
Neighborhood Deprivation and DAFI Increase

Factors	Adjusted Hazard Ratio (95% CI)	P-value
Area Deprivation Index (ADI)		
1st tertile (Least deprived)	Ref	
2nd tertile	1.38 (1.01-1.89)	0.04
3rd tertile (Most deprived)	1.46 (1.07-1.94)	0.01
Age at enrollment	1.03 (1.01-1.05)	0.01
Race		
White	Ref	
Black	0.74 (0.43-1.26)	0.27
Hispanic	0.53 (0.28-1.01)	0.05
Other	1.04 (0.60-1.78)	0.88
Breast cancer status		
No (non-cancer controls)	Ref	
Yes (breast cancer survivors)	1.69 (1.32-2.17)	<.001
Social well-being[b] at enrollment		
Poor (Score≥16)	Ref	
Good	0.81 (0.63-1.04)	0.09
DAFI status at enrollment		
Robust (DAI: <0.2)	Ref	
Pre-frail (DAI: 0.2-0.34)	0.85 (0.62-1.15)	0.29
Frail (DAI: >0.34)	1.30 (0.57-3.00)	0.52
Education Attainment		
High school graduate	Ref	
College graduate	0.98 (0.63-1.51)	0.91
Graduate school or more	1.32 (0.89-1.96)	0.15

DAFI Increase among All Women by Cancer Status





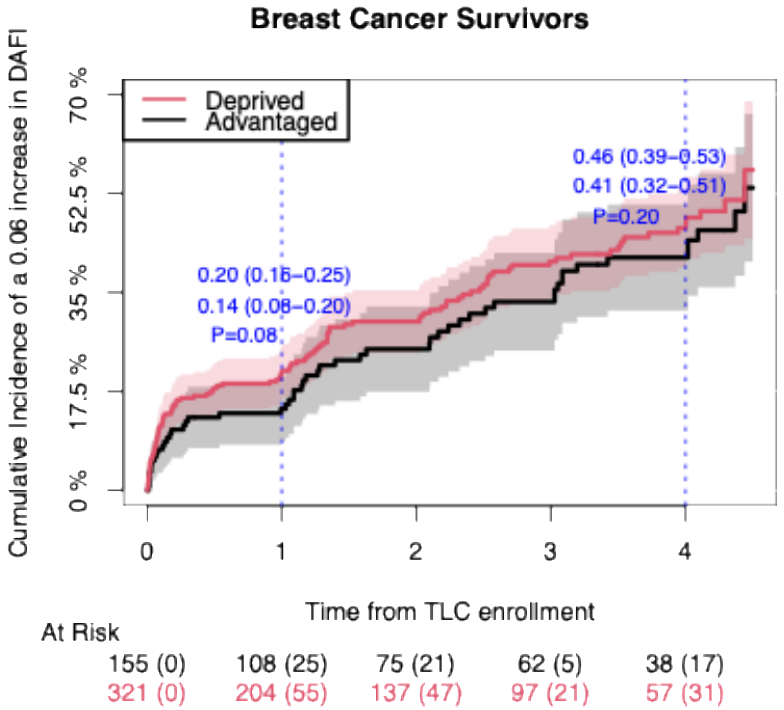


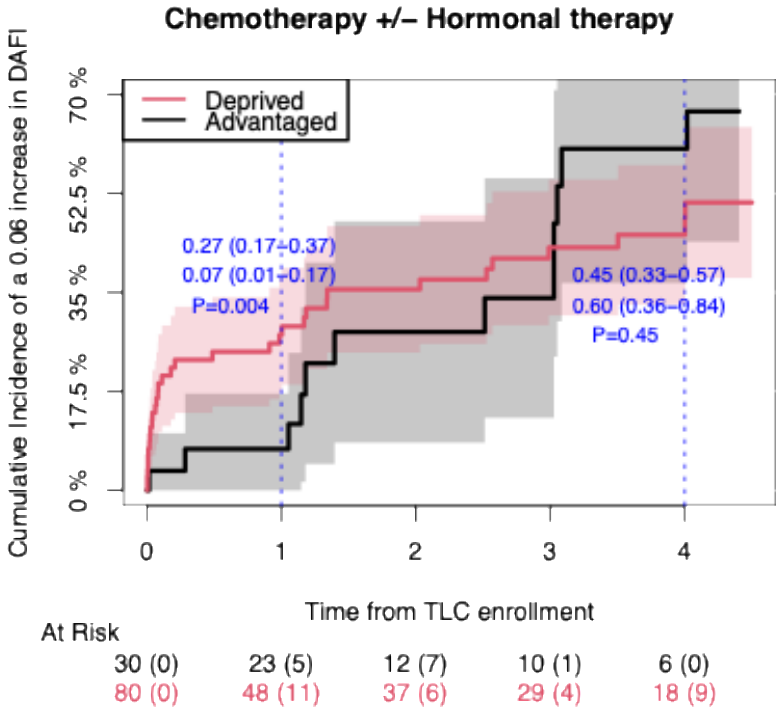
The cumulative incidence of DAFI increase was higher in deprived areas across all follow-up times.

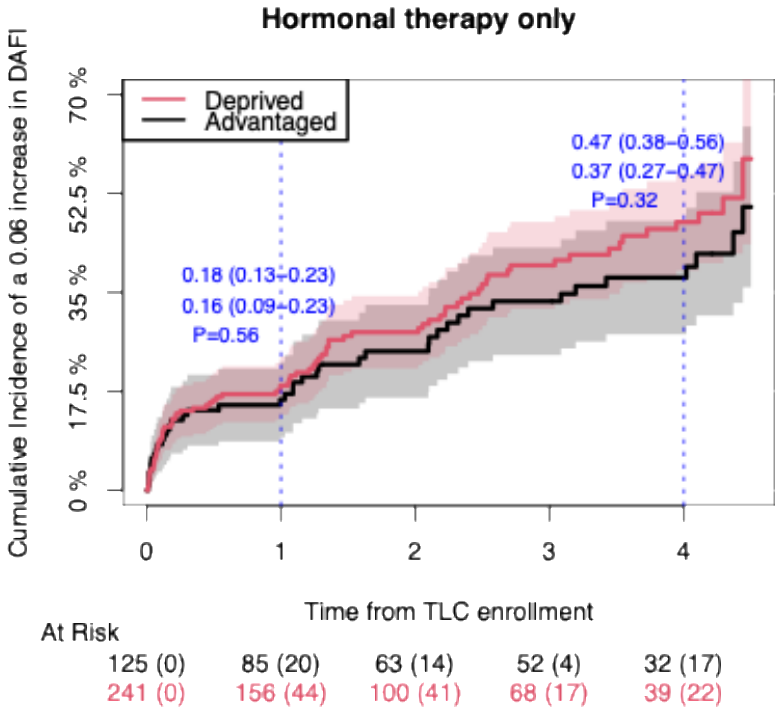
Sustained, long-term effect of living deprived areas on DAFI increase

Overall higher DAFI increase than non-cancer controls but no significant difference by ADI; Cancer and/or treatment may negate ADI impact on DAFI increase

DAFI Increase among BCS by Treatment







An immediate, short-term effect of ADI on DAFI increase among chemotherapy-treated BCS

Similar patterns as non-cancer controls

Discussions

- Women residing in more deprived neighborhoods faced a higher risk of an increase in DAFI in this multi-site, longitudinal study of older BCS and non-cancer controls over five years.
- Non-cancer controls experienced a long-term impact from living in more deprived areas on DAFI increase over time.
- The influence of neighborhood deprivation may be diminished among BCS, as the significant impact of cancer diagnosis and/or treatment on DAFI increase appears to negate it.
    - However, neighborhood deprivation appears to have an acute, short-term impact on chemotherapy-treated BCS.

- Non-cancer controls
  - The gap in cumulative DAFI increase by neighborhood deprivation progressively widened over time
  - A cumulative burden of chronic stressors from the neighborhood, potentially including concerns about neighborhood safety, environmental exposures, and associated financial or occupational strain at the individual level.
- BCS
  - The strong impact of cancer diagnosis and treatment on DAFI increase may counteract the effect on neighborhood deprivation on DAFI increase.
  - Chemotherapy-treated BCS experienced the largest short-term DAFI increase when living in more deprived areas.
  - This pattern suggests that the negative effects of chemotherapy may be intensified by restricted access to supportive care, inadequate symptom management, and limited healthcare resources in disadvantaged communities.

Discussions

- Our findings underscore the importance of longitudinal DAFI assessment in both BCS and non-cancer controls.
    - Such assessments may help identify patients on a trajectory toward DAFI progression, thus informing interventions such as physical therapy referrals, durable medical equipment, or in-home services.
- The robust association between neighborhood deprivation and DAFI increase, even after adjusting for key individual-level adjustment factors suggests that ADI captures influences beyond individual-level factors.
    - This underscores the need to examine underlying neighborhood-level contributors driving these disparities.

Discussions

- Limitations
  - Residential history data were unavailable.
  - There may be left-censoring due to the exclusion of individuals at high risk of frailty or mortality from eligibility in the TLC study.
  - TLC sample is more educated and predominantly White compared to the broader population.
  - While this study focused on area-level social determinants (i.e., neighborhood deprivation), exploring both individual and area-level social determinants of aging will be crucial.

Future Directions

- Future validation studies leveraging larger datasets, such as SEER-Medicare, may provide more robust long-term estimates grounded in real-world, representative populations.
- Investigating the interplay of individual-level and area-level social determinants of health (SDOH) on DAFI and other aging outcomes.
  - Using an integrated cohorts from three, large cohorts of BCS: Leading Pathways (Hispanic women), Detroit Research on Cancer Survivors (ROCS; Black women), and TLC (White women).
- WHI & LILAC (Annual assessments of functional status, objective physical performance at home visits, blood collection over 30 years, and treatment data)

Thank you!


Dr. Jeanne Mandelblatt


Dr. Traci Bethea


Dr. Jaeil Ahn


Wanting Zhai


Dr. Judith Carroll


Dr. Harvey Cohen


Dr. Tim A. Ahles


Dr. Zev Nakamura


Dr. Yiwey Shieh

- Research reported in this poster was supported by the NIA of the NIH under Award Number RO1CA129769, R35CA197289 (PI: Mandelblatt), K01AG088449 (PI: Choi).
- Contact: euc4006@med.cornell.edu; @AEunjiChoi

Guideline-concordant breast cancer treatment by rural/urban and age groups in the WHI cohort

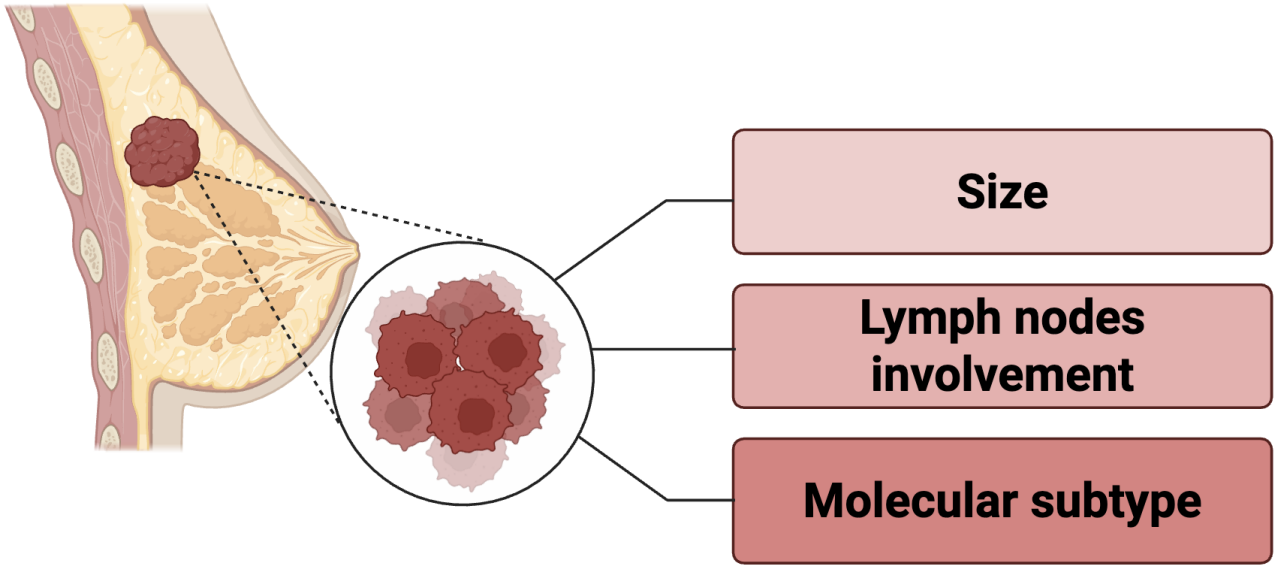
Xiaochen Zhang, PhD, MPH, MBBS

May 2nd, 2025

The Ohio State University

Treatment guidelines for breast cancer

Tumor characteristics



Patient characteristics & preference

Guideline concordant breast cancer treatment

- Better survival outcomes
- Receipt of guideline-concordant treatment (GCT)
  - Stage I-III breast cancer: 58-63% non-concordant
  - Early-stage breast cancer: 28-32% non-concordant

Undertreatment may lead to preventable deaths

  - Racial and ethnic minorities, rural
  - Older women
    - Competing comorbidities, frailty, functional status
    - Underrepresented in clinical trials, tolerability of systemic therapy

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2015
Invasive Breast Cancer

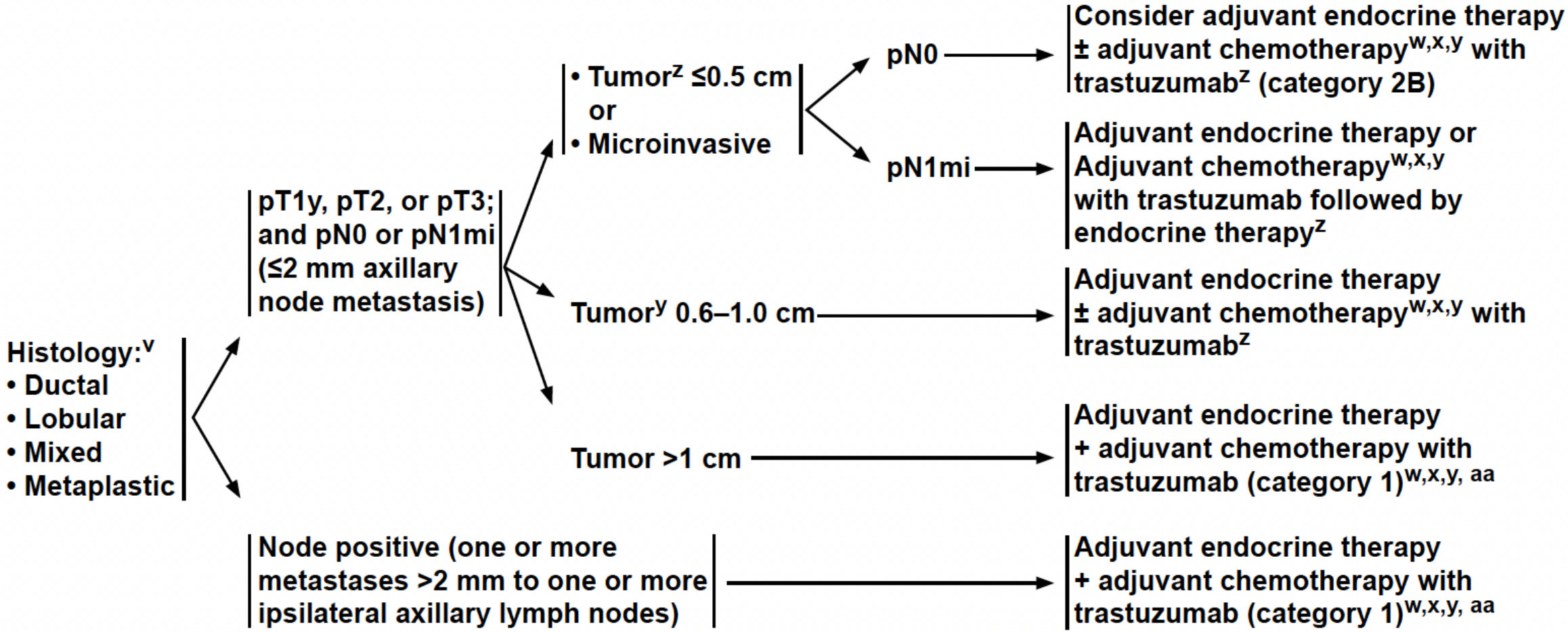
LOCOREGIONAL TREATMENT OF CLINICAL STAGE I, IIA, OR IIB DISEASE OR T3, N1, M0

Lumpectomy with surgical axillary staging (category 1)[j,k,l]

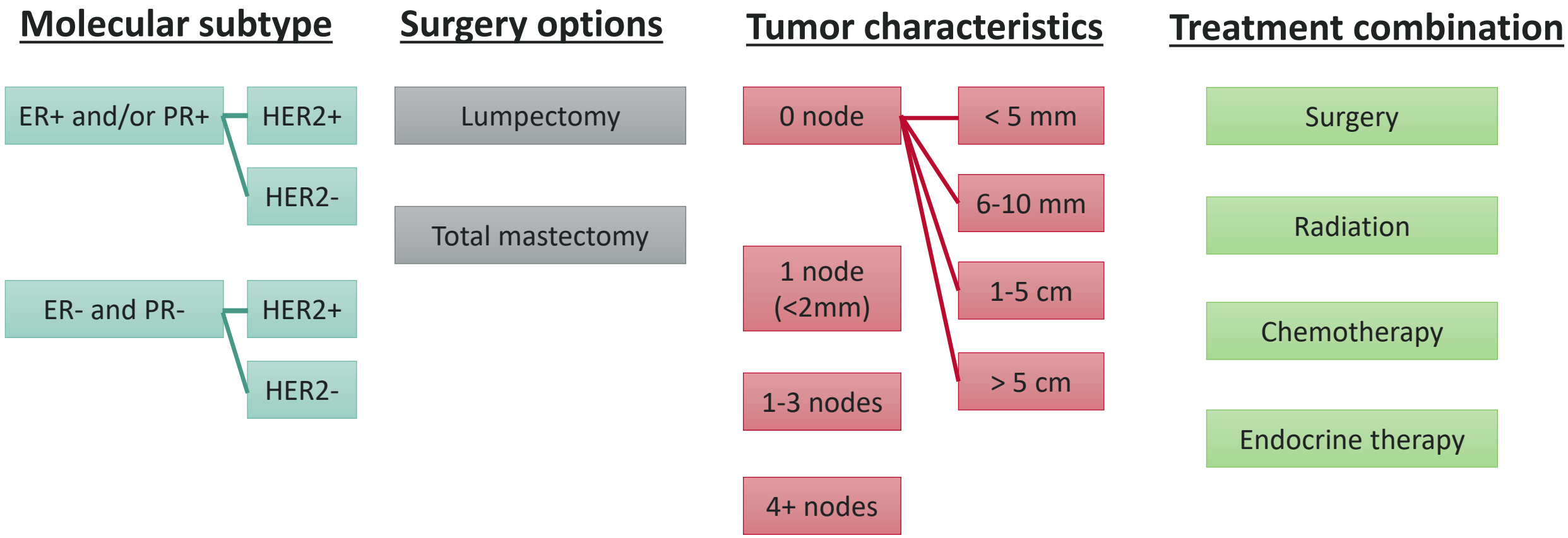
or

- ≥4 positive[o] axillary nodes → Radiation therapy to whole breast with or without boost[p] to tumor bed (category 1), infraclavicular region, and supraclavicular area. Strongly consider radiation therapy to internal mammary nodes[q] (category 2B). It is common for radiation therapy to follow chemotherapy when chemotherapy is indicated.
- 1–3 positive axillary nodes → Radiation therapy to whole breast with or without boost[p] (to tumor bed (category 1). Strongly consider radiation therapy to infraclavicular supraclavicular area, internal mammary nodes[q] (category 2B). It is common for radiation therapy to follow chemotherapy when chemotherapy is indicated.
- Negative axillary nodes → Radiation therapy to whole breast with or without boost[p] to tumor bed or consideration of partial breast irradiation (PBI) in selected patients.[p,r] It is common for radiation therapy to follow chemotherapy when chemotherapy is indicated.[s]

SYSTEMIC ADJUVANT TREATMENT - HORMONE RECEPTOR-POSITIVE - HER2-POSITIVE DISEASE[b]



NCCN guideline concordant treatment algorithm



Example: 2015 NCCN guideline concordant algorithm

Hormone Receptor	HER2	# of Positive node	Tumor size	Surgery	Radiation	Chemo	Endocrine therapy
ER+ and/or PR+	HER2 +	0	≤0.5 cm	partial mastectomy	radiation	with/out adjuvant chemo	with/out adjuvant endocrine
				mastectomy	-	with/out adjuvant chemo	with/out adjuvant endocrine
			0.6-1 cm	partial mastectomy	radiation	with/out adjuvant chemo	adjuvant endocrine
				mastectomy	-	with/out adjuvant chemo	adjuvant endocrine
			1-5 cm	partial mastectomy	radiation	adjuvant chemo	adjuvant endocrine
				mastectomy	-	adjuvant chemo	adjuvant endocrine
			> 5cm	partial mastectomy	radiation	adjuvant chemo	adjuvant endocrine
				mastectomy	with/out radiation	adjuvant chemo	adjuvant endocrine
		1 node (<2mm axillary node)		partial mastectomy	radiation	with/out adjuvant chemo	adjuvant endocrine
				mastectomy	with/out radiation	with/out adjuvant chemo	adjuvant endocrine
		1-3 positive nodes		partial mastectomy	radiation	adjuvant chemo	adjuvant endocrine
				mastectomy	radiation	adjuvant chemo	adjuvant endocrine
		≥4 positive nodes		partial mastectomy	radiation	adjuvant chemo	adjuvant endocrine
				mastectomy	radiation	adjuvant chemo	adjuvant endocrine

Data utilized

The LILAC Study

Life and Longevity after Cancer

WOMEN'S HEALTH INITIATIVE

- Women who participated in WHI LILAC study
  - Diagnosed with breast cancer (localized stage) between 2008-2015
  - Form 340, 342 (breast cancer abstraction) or CMS, F122/130/33
- Outcome: Receipt of GCT
  - Surgery, radiation therapy, chemotherapy, and endocrine therapy
  - Form 342 or CMS
- Rural/urban residency (RUCA code): Urban 1-3 vs. Rural 4-10
- Age at diagnosis: ≤70 vs. >70 yrs

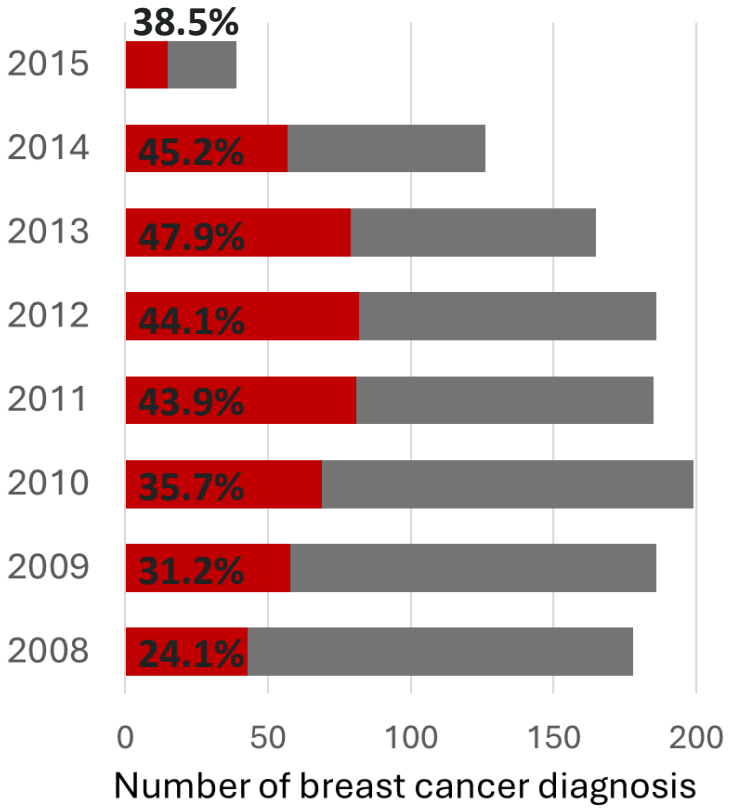
Results: participants characteristics

Overall: n=1264

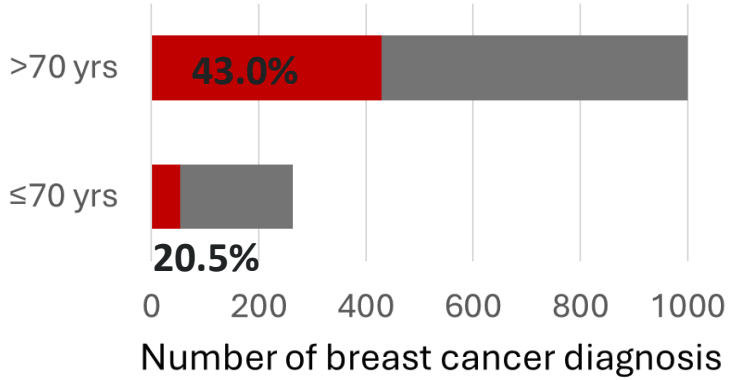
Guideline concordant: n=780 (61.7%)

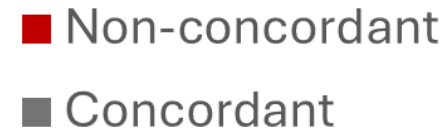
Non-concordant: n=484 (38.3%)

Diagnosis Year

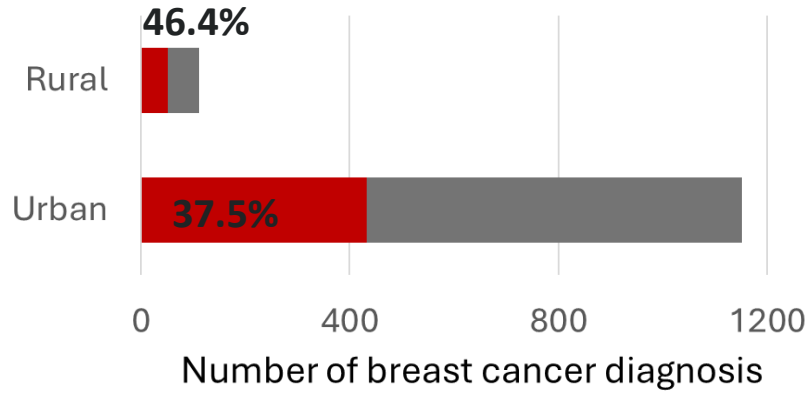


Age at diagnosis





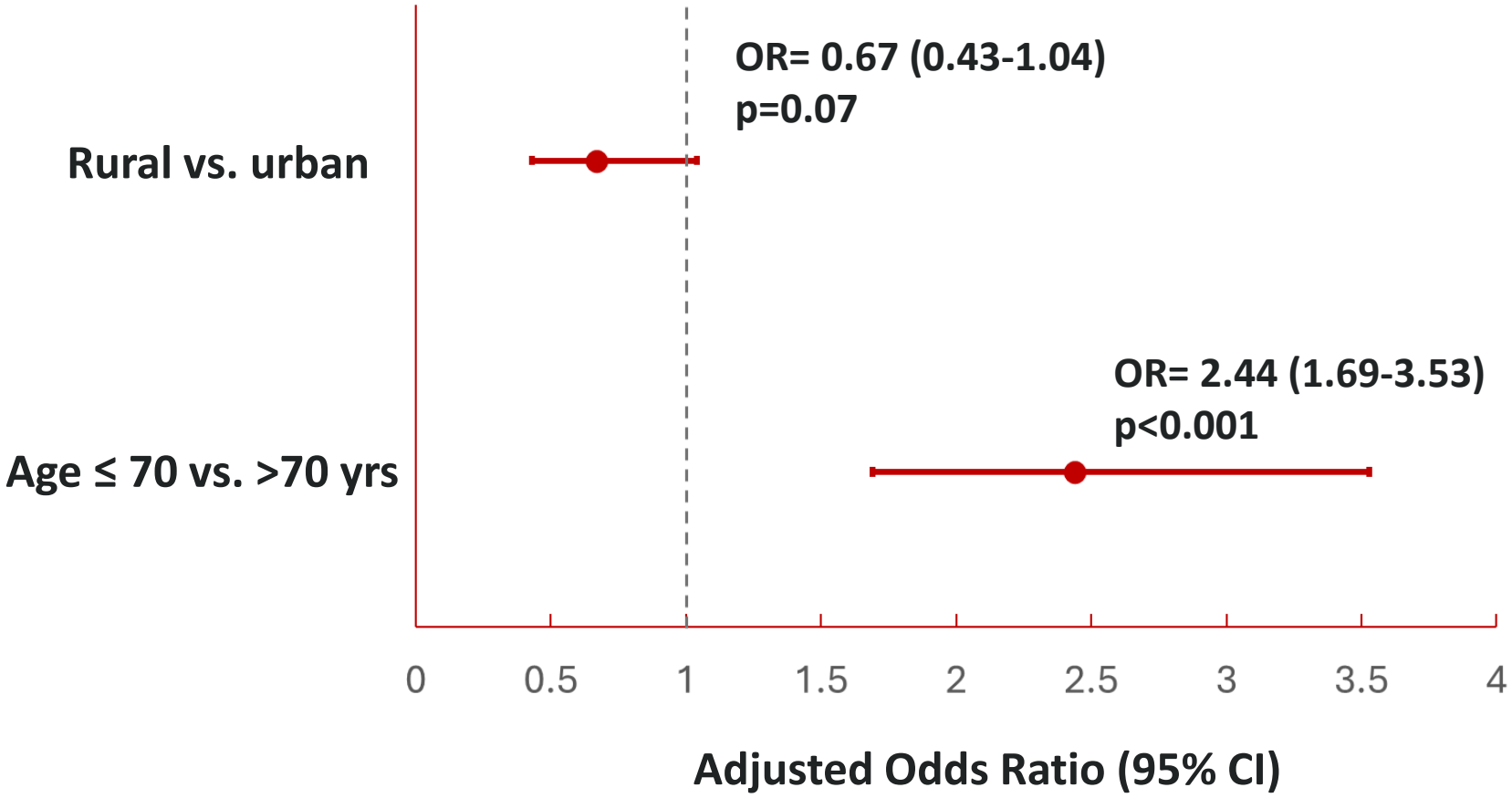
Rural/urban



Results: clinical characteristics

Variable	Overall n=1264	Non-concordant n=484 (38.3%)	Concordant n=780 (61.7%)	P-value
Time from dx to LILAC				<0.001
<1 year	85	38 (7.9)	47 (6.0)	
1-5 years	1004	404 (83.5)	600 (76.9)	
5-10 years	175	42 (8.7)	**133 (17.1)**	
Number of nodes examined				<0.001
0	130	88 (18.2)	**42 (5.4)**	
1-3	834	292 (60.3)	542 (69.5)	
4+	300	104 (21.5)	196 (25.1)	
Subtype				0.23
ER or PR +, HER2 +	75	36 (7.4)	39 (5.0)	
ER or PR -, HER2 +	24	11 (2.2)	13 (1.7)	
ER or PR +, HER2 -	1079	405 (82.8)	674 (90.0)	
ER or PR -, HER2 -	86	37 (7.6)	49 (6.3)	
Size (mm), median [IQR]	12 [8-17]	12 [8-17]	11 [7-17]	0.23
Number of comorbidities*				0.69
0	106	37 (7.6)	69 (8.8)	
1	281	105 (21.7)	176 (22.6)	
2	379	142 (29.3)	237 (30.4)	
3+	498	200 (41.3)	298 (38.2)	

Results: age, rural/urban residence, and GCT



OR>1 indicates that group is **more likely** to have received GCT than the reference group

Model adjusted for diagnosis year, race, ethnicity, education level, marital status, number of lymph nodes examined, time from diagnosis to LILAC enrollment, and number of comorbidities.

Take home message

- Women who were diagnosed ≤70 yrs were **MORE** likely to receive GCT
  - Smaller tumor size, fewer comorbidities, higher % of private insurance
  - Clinical practice: individual's health conditions and providers perspective
  - Risk and benefit assessment are needed to facilitate clear guidelines for older women to improve quality of life and longevity
- Women who lived in rural area were **LESS** likely to receive GCT
  - Older, other potential factors (insurance, comorbidities)
  - Future research should utilize effective approaches to expand access to care for rural breast cancer patients

Strengths

- Wide range of age at diagnosis → ≤70 vs. >70 yrs
- Continuous data collection for cancer diagnosis (self-report and adjudicated)
- Large sample size: explore whether age group modifies the association between GCT and rural/urban residency

Limitation

- May not have as many women with recent diagnosis (after 2015), who lived in rural areas
- Only included localized cancer, 0 positive lymph nodes → generalizability
- Clinical and treatment data are limited to what was collected in the survey
- CMS rules to avoid reporting small cells: forced to combine categories for some variables

Next steps

- Finalize analysis with adjudicated data on clinical and treatment information
- Interaction: age group x rural/urban residency
- Survival outcome: association between GCT and overall survival, and by rural/urban residency

Future direction

- Expand to other cancer sites (e.g., colorectal, lung)
- Other cohorts with more recent diagnosis, wider range of age at diagnosis (35-80 yrs), various racial/ethnic groups

Thank you

Acknowledgement

Eric McLaughlin, MS- Statistician, OSU
Jingbo Yi, MPH- PhD student, OSU
Sara Myers, MD- Breast surgeon, OSU
Erin Burke, MD- Breast surgeon, OSU
Maryam Lustberg, MD- Medical oncologist, Yale
Allison Quick, MD- Radiation oncologist, OSU
Electra D. Paskett, PhD- PI, MW Regional Center

Lindsey Bull- WHI Coordinating Center
Ananya Roy- WHI Coordinating Center