THE WOMEN'S HEALTH INITIATIVE

WHI Early Career Award and presentation

Alexi Vasbinder, University of Washington School of Nursing

Leveraging WHI Data to Advance Knowledge in Cardio-Oncology

Alexi Vasbinder, PhD, RN
Assistant Professor
School of Nursing
University of Washington
WHI Investigator Meeting
May 1st, 2025

SCHOOL OF NURSING
UNIVERSITY of WASHINGTON

Cancer survivorship

- Estimated 18.1 million cancer survivors in the United States in 2022
  - >26 million by 2040; 73% over 65y
- Largely due to improvements in cancer treatments and aging population
- Cancer survivors experience many adverse events:
  - High symptom burden
  - Reduced quality of life
  - Increased morbidity & mortality

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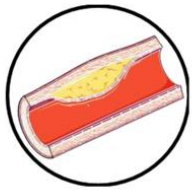
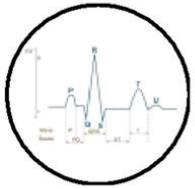
  - High symptom burden
  - Reduced quality of life
  - Increased morbidity & mortality
  - **Cardiotoxicity/cardiovascular disease**

Treatment-related cardiotoxicities

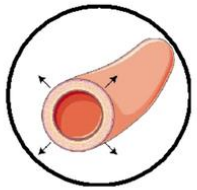
Valve Disease
Radiation, Anthracyclines, Endocrine Tx



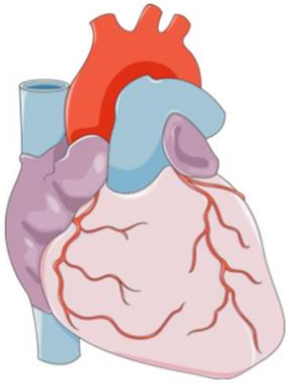
Atherosclerosis
Radiation, Endocrine Tx, Alkylating Agents, TKIs

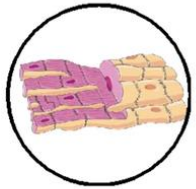


Abnormal Conduction
Radiation, Anthracyclines, Endocrine Tx, Alkylating Agents, Antimetabolites, ICIs, TKIs, Taxanes

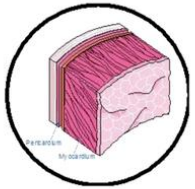


Vasospasm, Myocardial Ischemia
Taxanes, Endocrine Tx, Alkylating Agents, Antimetabolites, TKIs, Anti-tumor ab, Anti-CD20 Ab, PIs





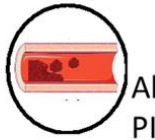
Cardiomyopathies
Radiation, Anthracyclines, Endocrine Tx, Alkylating Agents, Antimetabolites, ICIs, TKIs, HER2 Ab



Pericardial Disease
Radiation, Anthracyclines, Endocrine Tx, Alkylating Agents, ICIs

Myocarditis
Antracyclines, Alkylating agents, ICIs

Thrombosis
Alkylating Agents, Endocrine Tx, PIs, TKIs, AntiMT agents



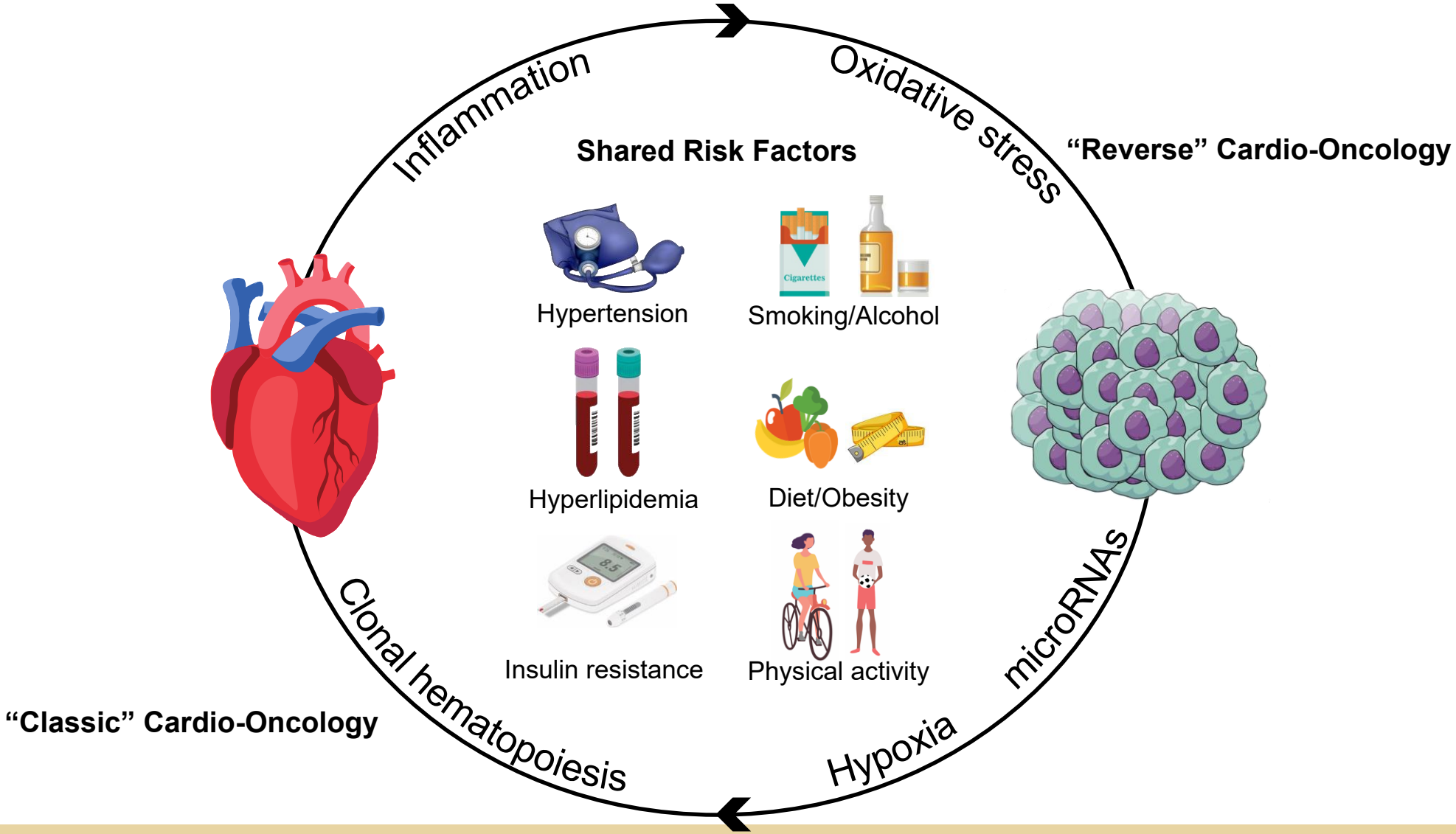
Hypertension
Alkylating Agents, PIs, TKIs, AntiMT agents

Vasculitis
ICIs

Vasospasm
Alkylating Agents, Antimetabolites, AntiMT agents

Stenosis
Endocrine Tx, TKIs

Intersection between cardiovascular disease and cancer



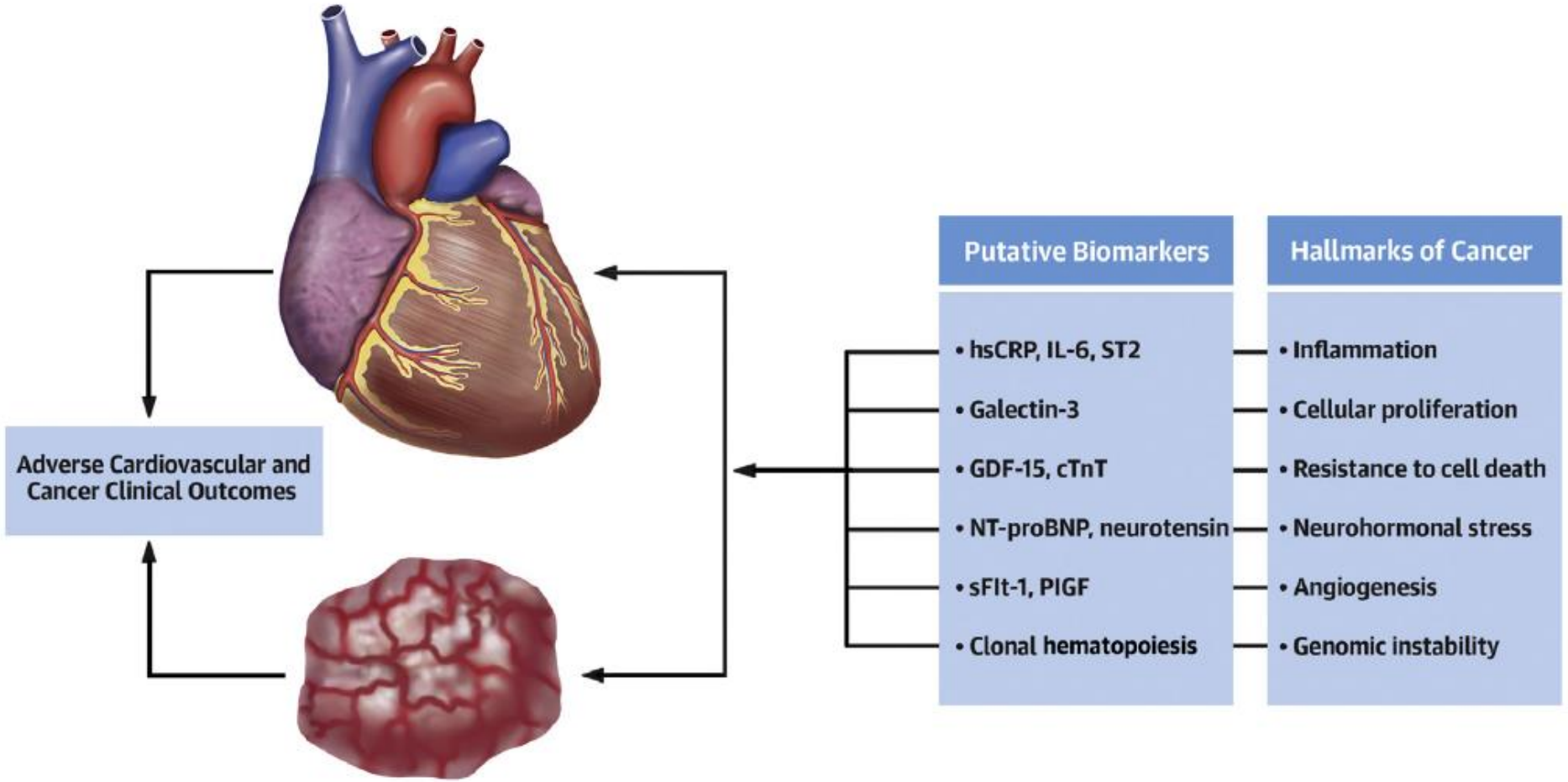
Raychauduri et al. *Frontiers in Oncology.* 2023;12

WHI contributions to cardio-oncology

1. Explore molecular mechanisms of CV risk in cancer survivors
    - Biomarkers and epigenetics
2. Characterize risk of CV events in cancer survivors
    - Evaluate CV risk factors, CV risk scores, social determinants of health, health disparities
3. Evaluate role of reverse cardio-oncology
    - Estimate risk of cancer after CVD
    - Explore pathways of shared risk factors

Molecular mechanisms in cardio-oncology

Biomarkers and shared mechanisms



Narayan, V. et al. J Am Coll Cardiol. 2020;75(21):2726-37.

Biomarkers and radiation-induced CVD

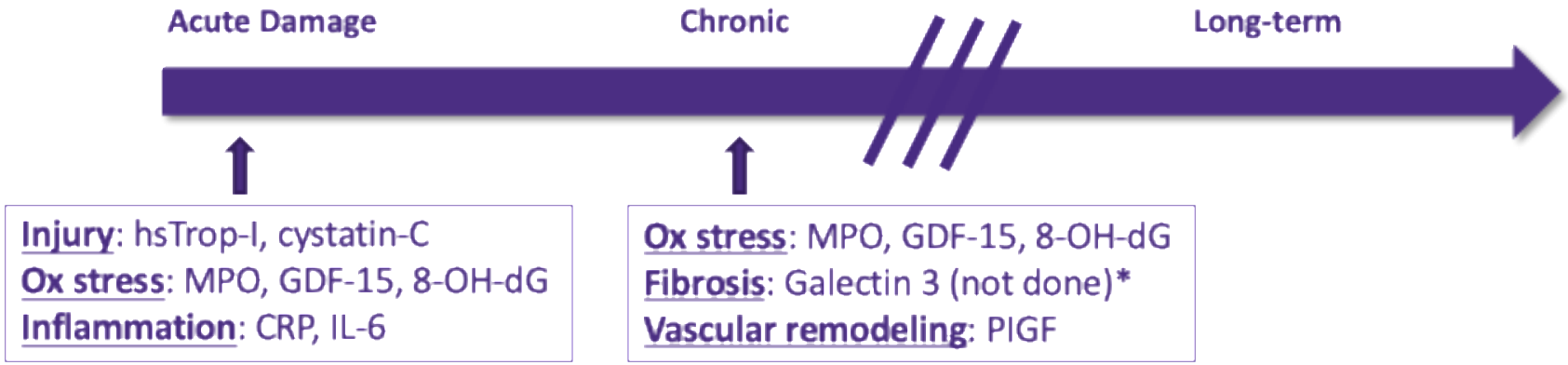
Ancillary study (AS622; PI: Vasbinder)

Journal of Cardiovascular Translational Research
https://doi.org/10.1007/s12265-022-10320-2

ORIGINAL ARTICLE

Chronic Oxidative Stress as a Marker of Long-term Radiation-Induced Cardiovascular Outcomes in Breast Cancer

Alexi Vasbinder[1] · Richard K. Cheng[2] · Susan R. Heckbert[3] · Hilaire Thompson[1] · Oleg Zaslavksy[1] · Rowan T. Chlebowski[4] · Aladdin H. Shadyab[5] · Lisa Johnson[6] · Jean Wactawski-Wende[7] · Gretchen Wells[8] · Rachel Yung[9] · Lisa Warsinger Martin[10] · Electra D. Paskett[11] · Kerryn Reding[1]



F31NR018588, PI: Vasbinder; R21HL152149, PI: Reding

NIH National Institute of Nursing Research
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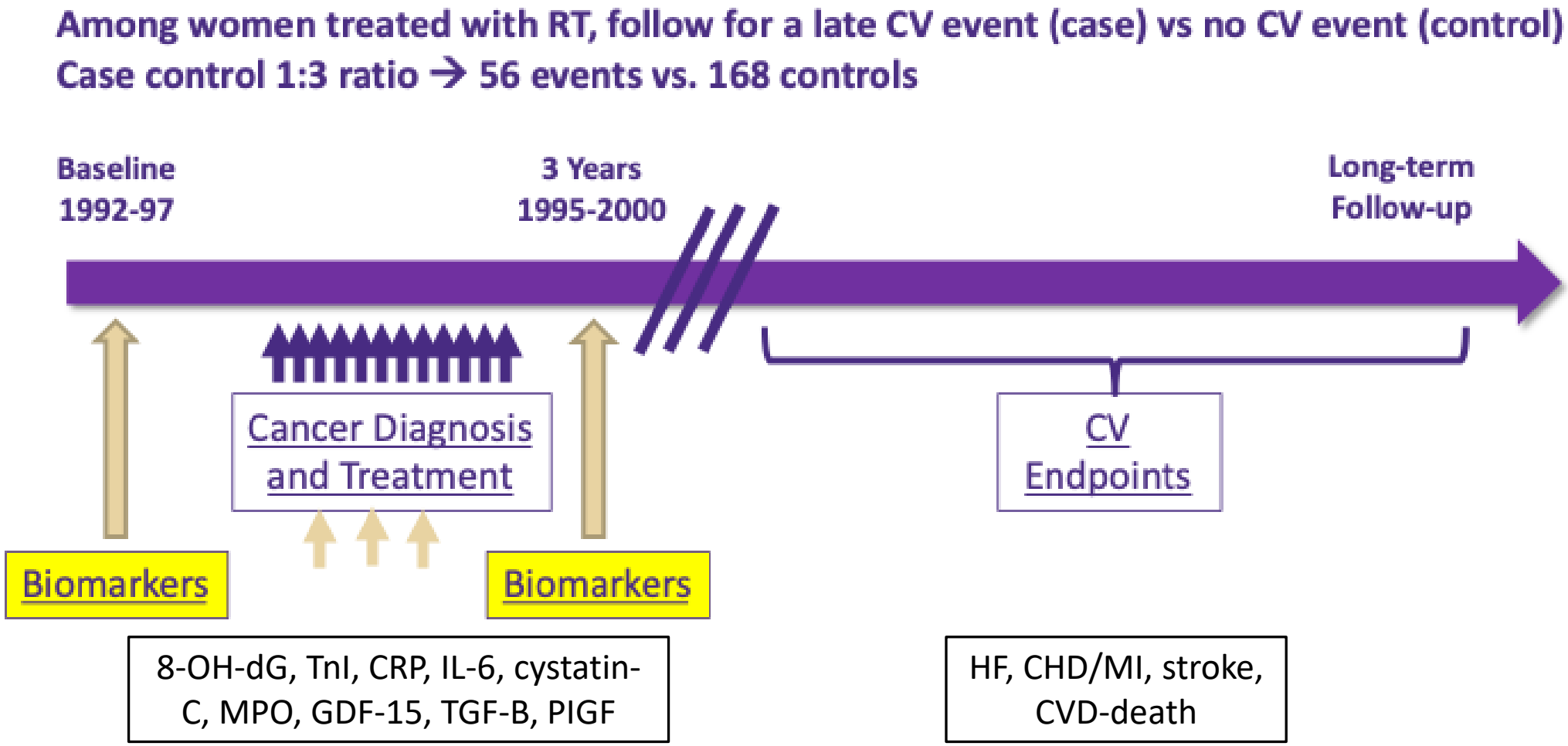
Vasbinder et al. *JTCR.* 2023;16:403-413

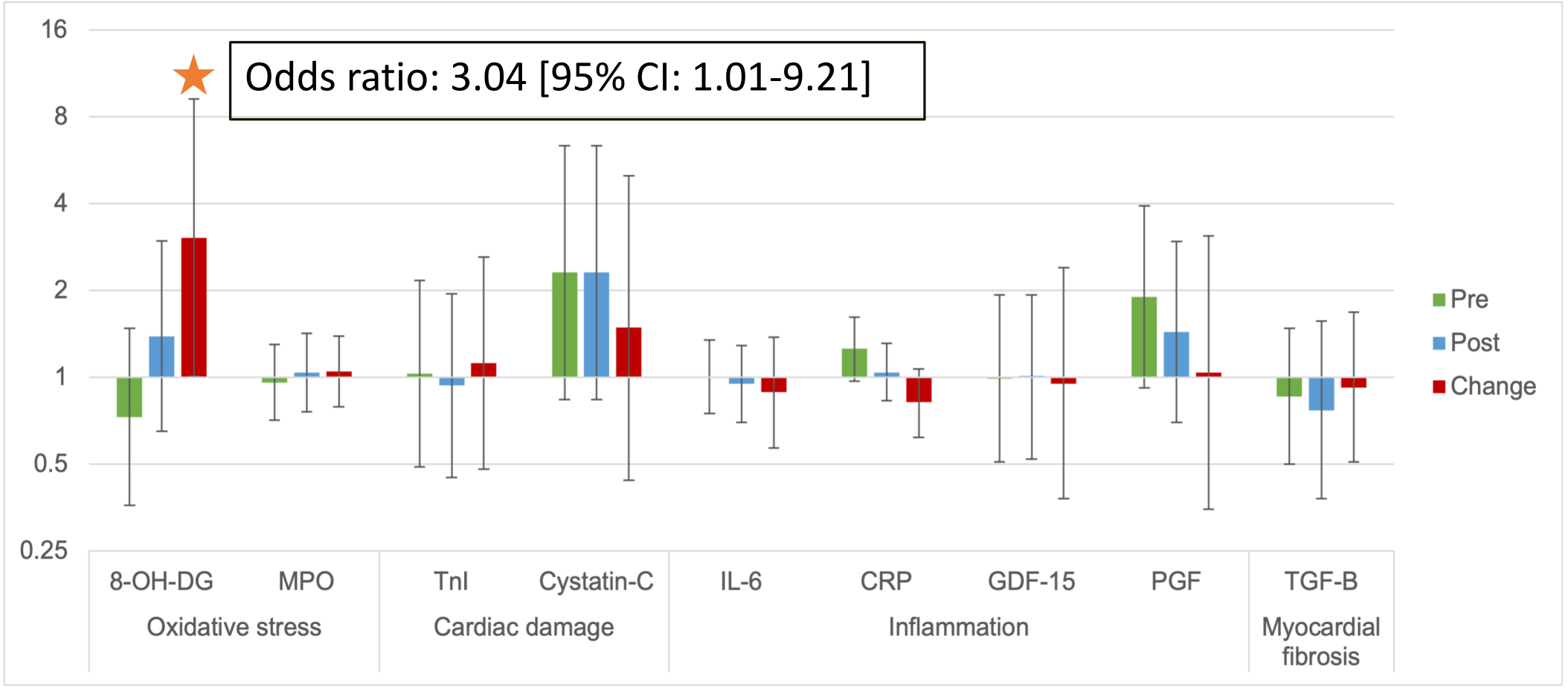
Biomarkers and radiation-induced CVD



Vasbinder et al. *JTCR.* 2023;16:403-413

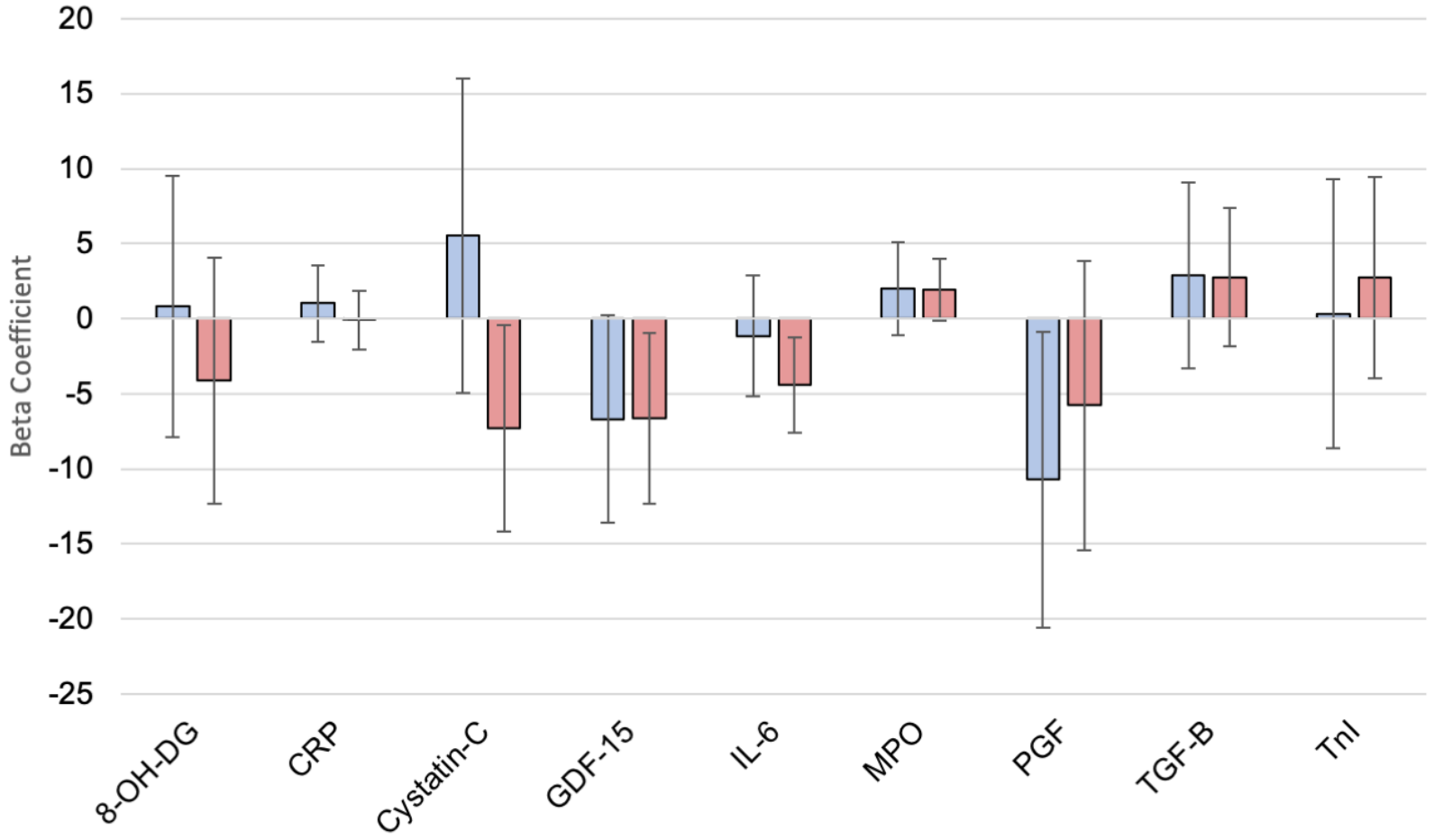
Biomarkers and radiation-induced CVD

8-OH-dG was associated with 3x greater risk of CV events after breast cancer



Vasbinder et al. *JTCR.* 2023;16:403-413

Biomarkers and radiation-induced fatigue

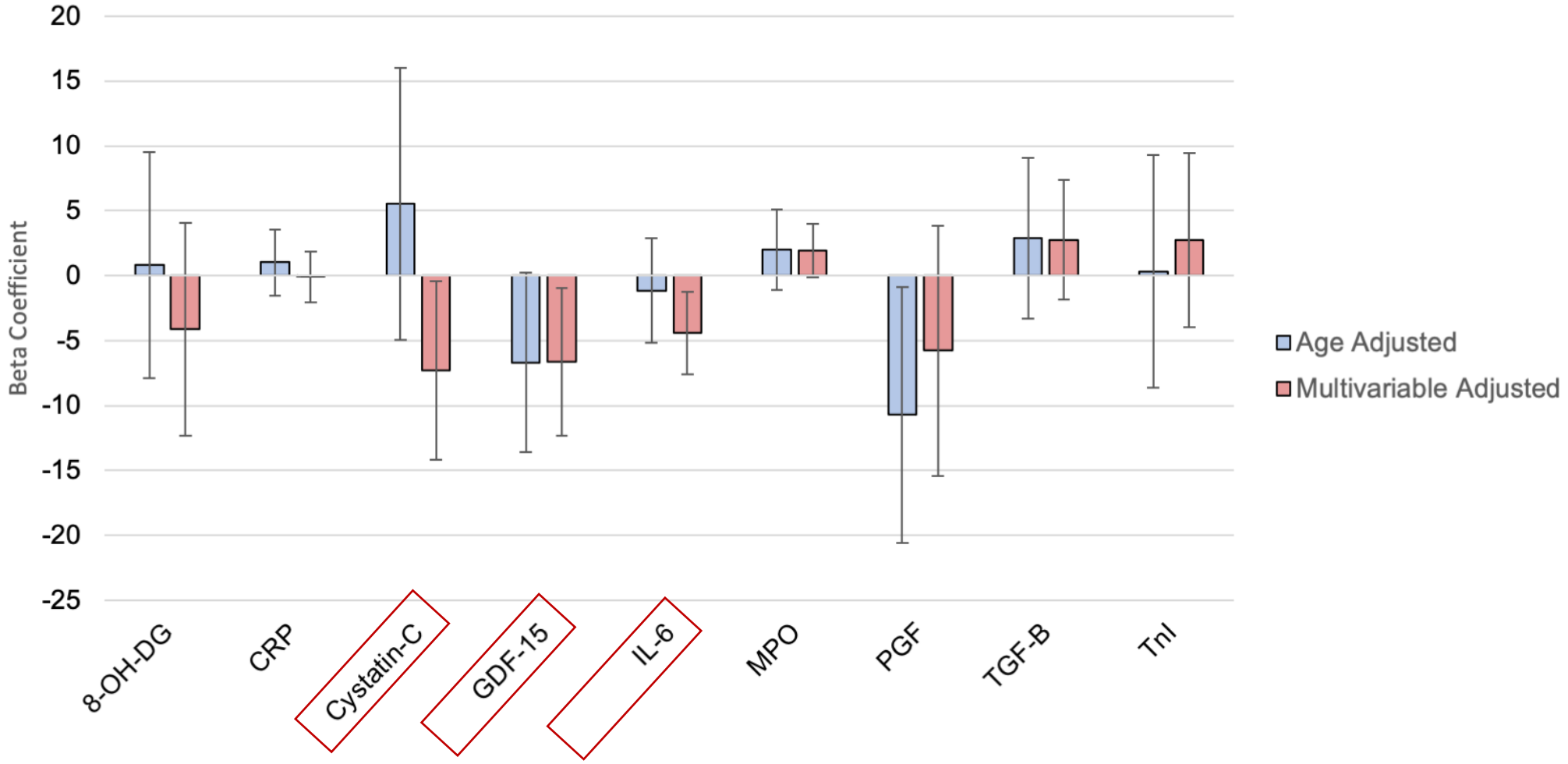


*Each biomarker was recorded as the ratio of the post-BC value relative to the pre-BC biomarker and log transformed to base 2

*Adjusted for age, education, smoking, BMI, stage, pre-cancer emotional wellbeing, physical function, pain, sleep disturbance, and fatigue

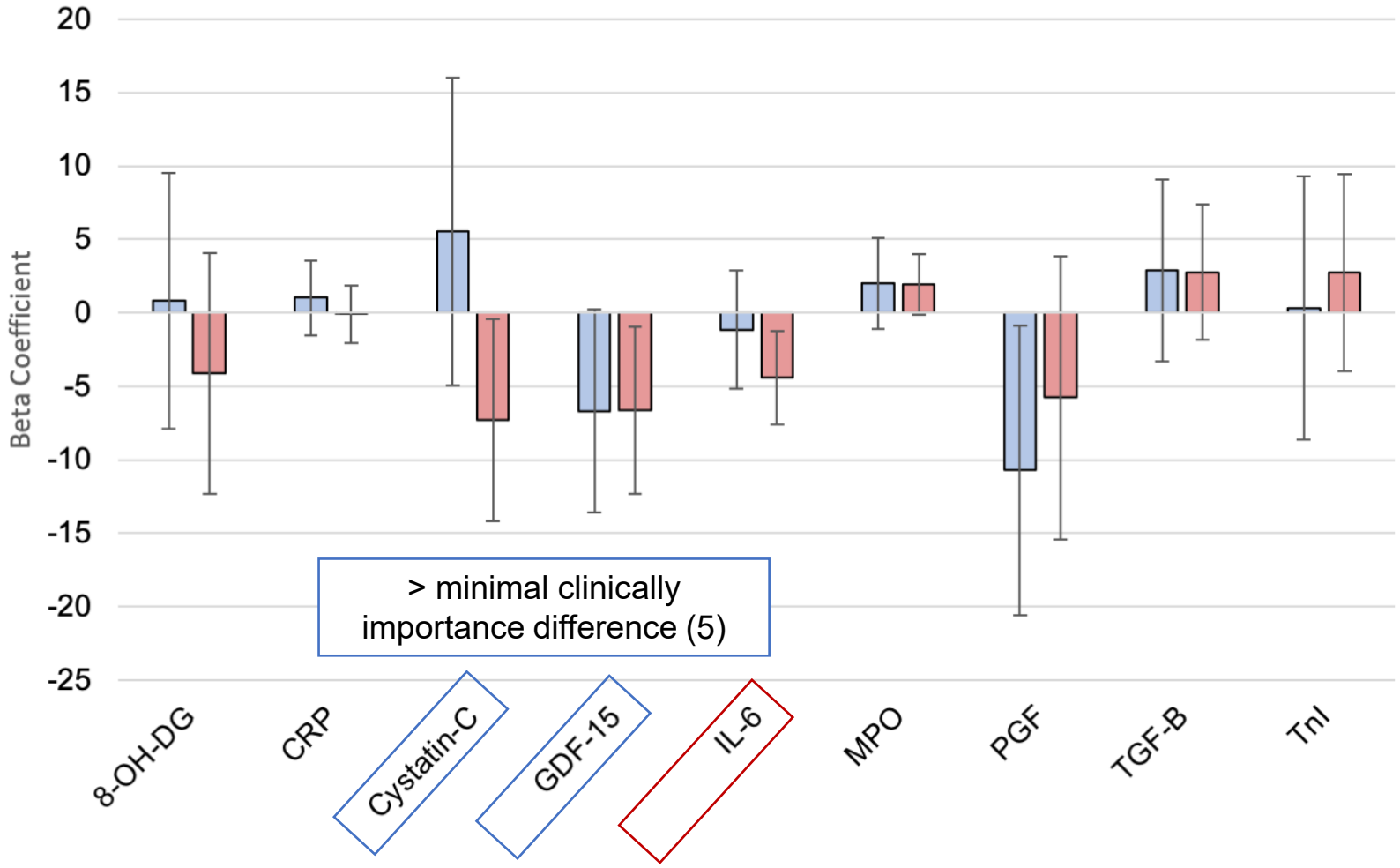
Vasbinder et al. *Biol Res Nurs*. 2022;24(4):472-483

Biomarkers and radiation-induced fatigue



Vasbinder et al. *Biol Res Nurs*. 2022;24(4):472-483

Biomarkers and radiation-induced fatigue

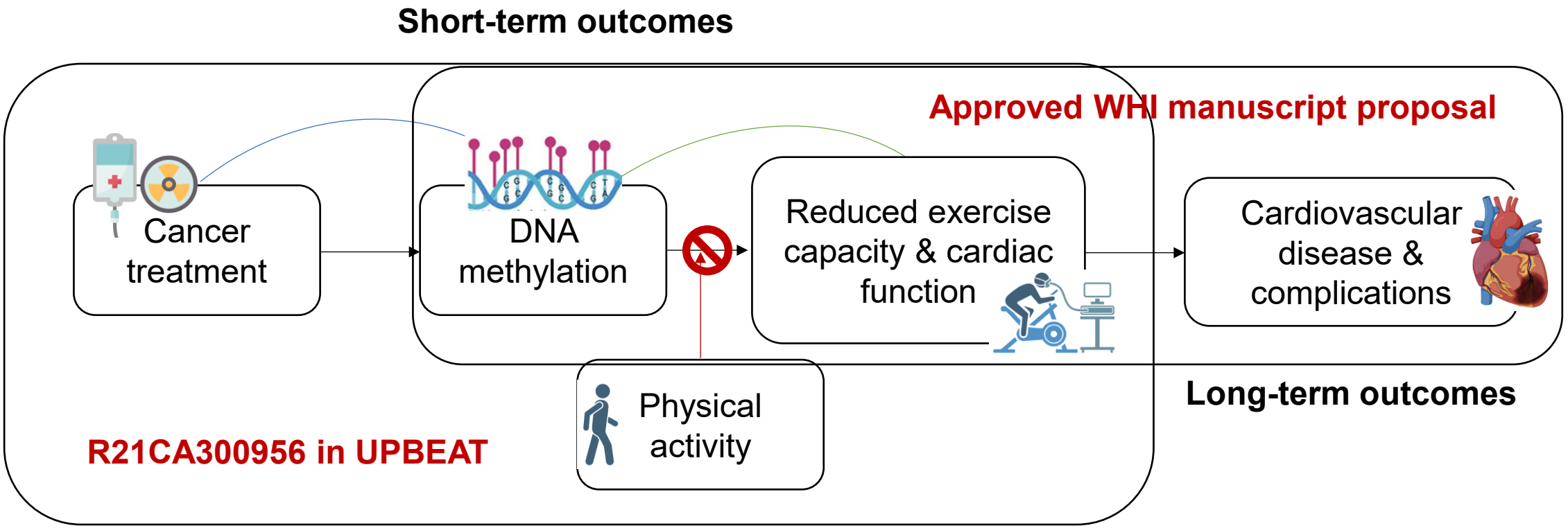


1. Inflammation plays a role in fatigue in women treated with radiation

2. Fatigue could be associated with underlying cardiovascular function or changes in body composition

Vasbinder et al. *Biol Res Nurs*. 2022;24(4):472-483

Future studies – epigenetics and CV risk

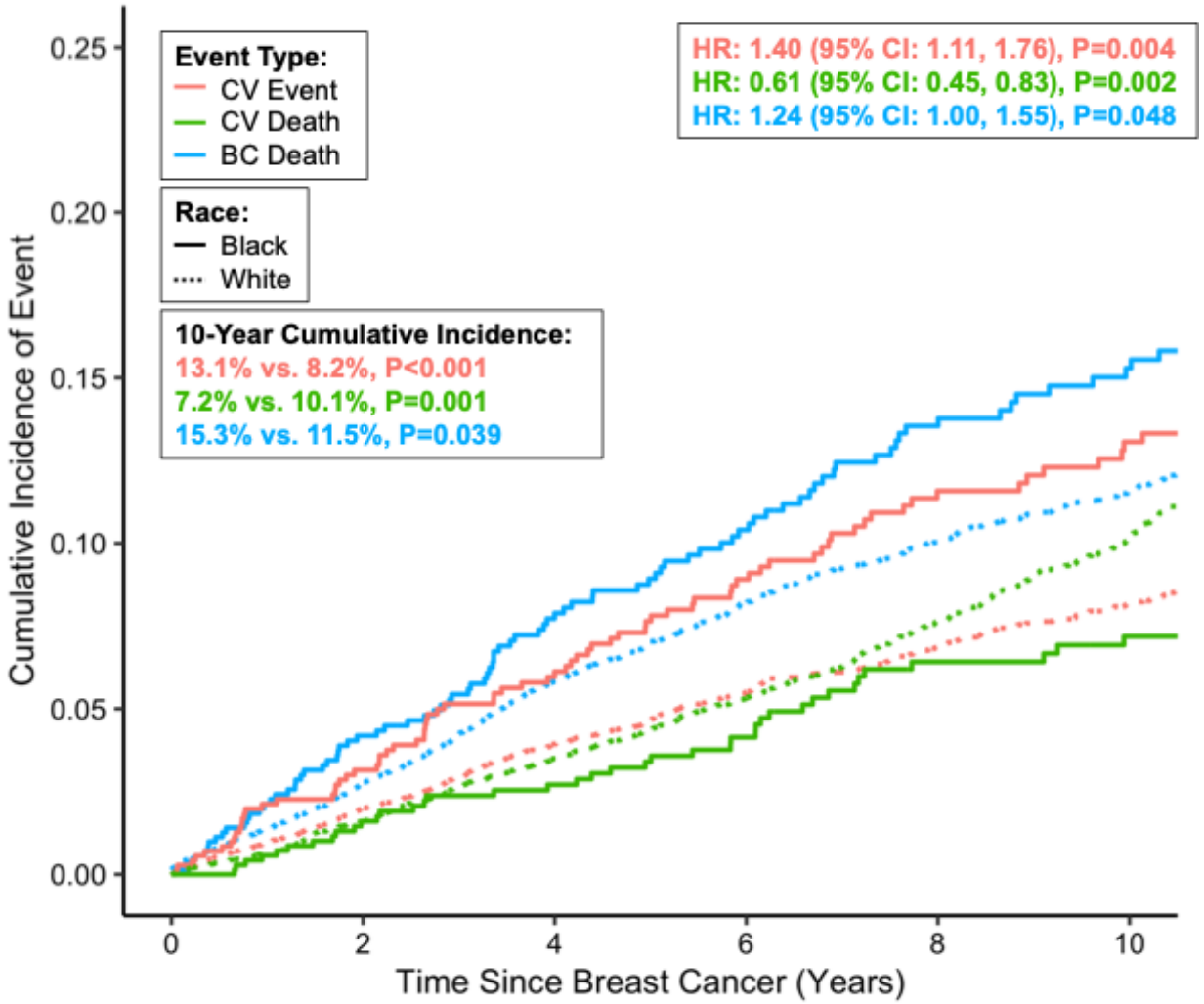


NIH NATIONAL CANCER INSTITUTE

Characterizing risk of CV events in cancer survivors

Incidence of CV events after breast cancer (disparities)

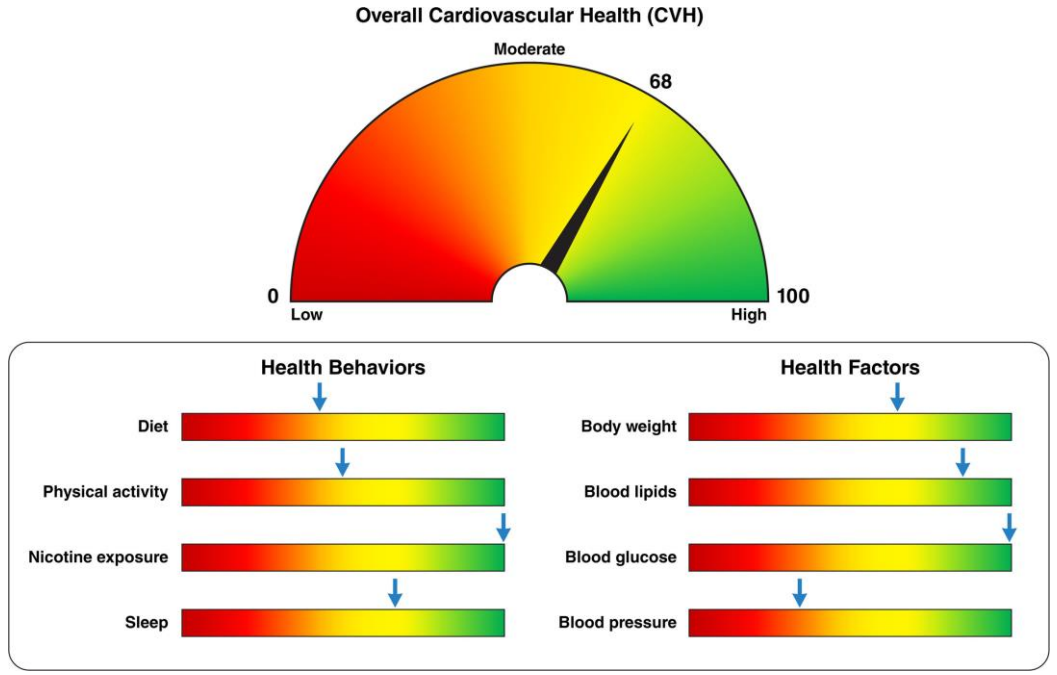
- N=8,410 (mean at dx 70.6; 8.1% Black; median follow-up 16.2 years; 74.7% local cancer)
- Cumulative incidence curves accounting for competing risks
- Models adjusted for age, stage, triple negative BC, BMI, diabetes, and hypertension



Reding et al. *Under Review*

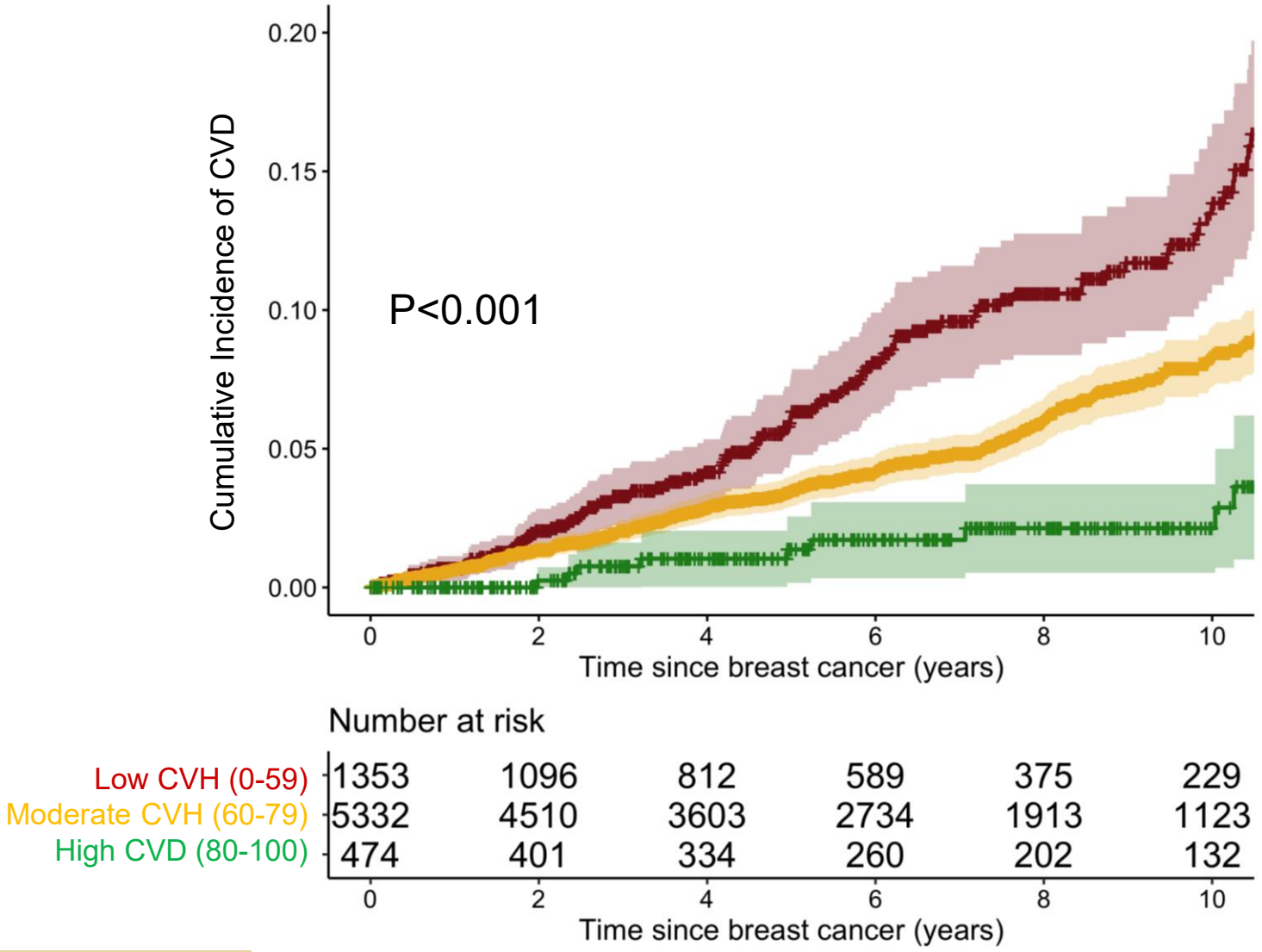
Life's Essential 8 and CVD after breast cancer

- To examine the clinical utility of the American Heart Association Life's Essential 8 Score in predicting the risk of cardiovascular events after breast cancer
  - Diagnosed with stage I-III breast cancer
  - Free of prevalent CVD prior to breast cancer
  - Complete LE8 scoring variables
- LE8 Score: diet, physical activity, avoidance of nicotine, sleep, weight, lipid levels, blood glucose, and blood pressure
  - Low (0-49 points), moderate (50-79 points), and high (80-100 points) cardiovascular health



Wadden et al. *JACC:CardioOncology.* 2024;6(5):746-757

Incidence of CVD by LE8 categories



10-year cumulative incidence

Low (0-49): 16.2%
Moderate (50-79): 9.1%
High (80-100): 1.5%

Median follow-up: 6 years

Wadden et al. *JACC:CardioOncology.* 2024;6(5):746-757

Association between LE8 and CVD risk

	Model 0		Model 1		Model 2	
	sHR (95% CI)	P-value	sHR (95% CI)	P-value	sHR (95% CI)	P-value
LE8, per 10 points	0.79 (0.74, 0.85)	<0.001	0.82 (0.76, 0.89)	<0.001	0.82 (0.76, 0.89)	<0.001
LE8, categorical		<0.001		<0.001		
Low	1.0 [ref]		1.0 [ref]		1.0 [ref]	
Moderate	0.59 (0.48, 0.71)	<0.001	0.62 (0.50, 0.77)	<0.001	0.62 (0.50, 0.77)	<0.001
High	0.32 (0.19, 0.54)	<0.001	0.42 (0.25, 0.72)	0.002	0.42 (0.25, 0.73)	0.002
C-index		**0.57**		**0.74**		**0.74**

Model 0: LE8 + WHI CT/OS

Model 1: Model 0 + age at diagnosis, race, income

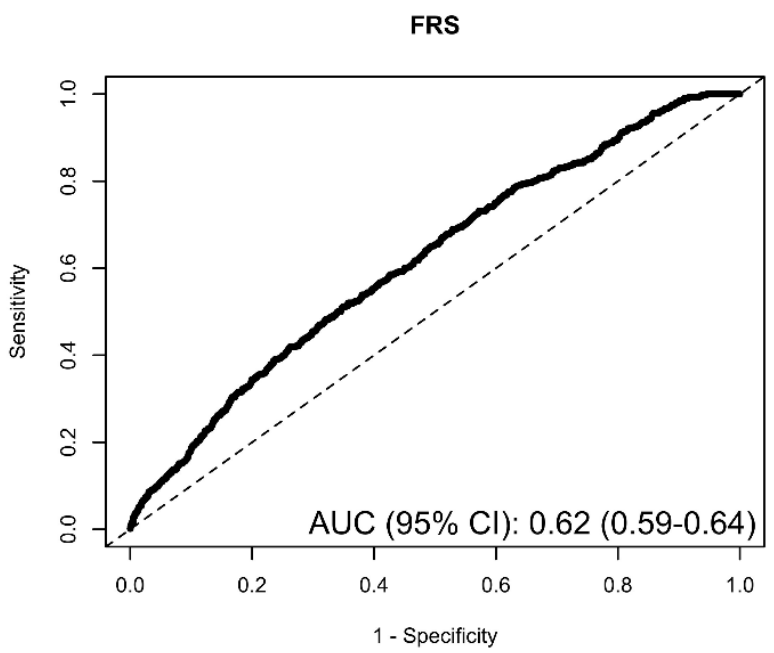
Model 2: Model 1 + cancer stage

Wadden et al. *JACC:CardioOncology.* 2024;6(5):746-757

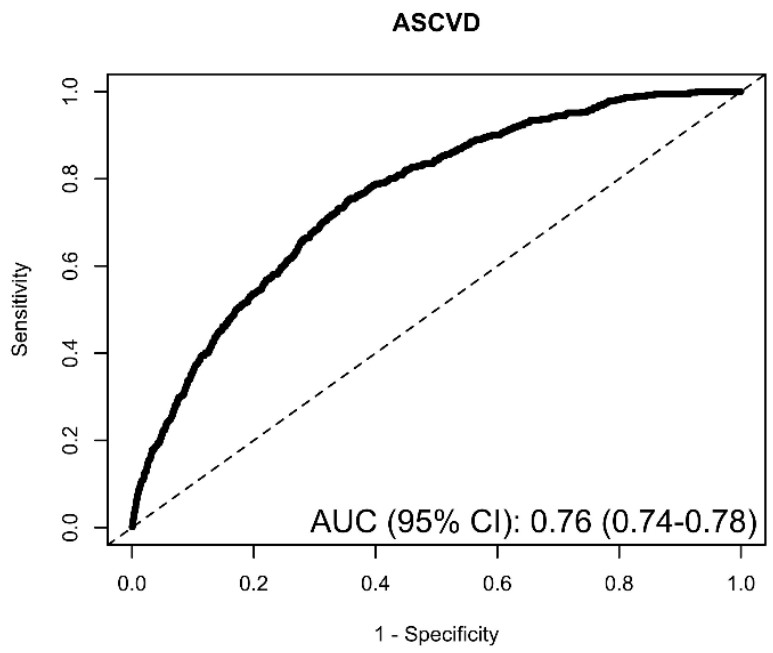
Comparing CV risk scores

ASCVD had AUC 0.76 for predicting CV events in breast cancer survivors

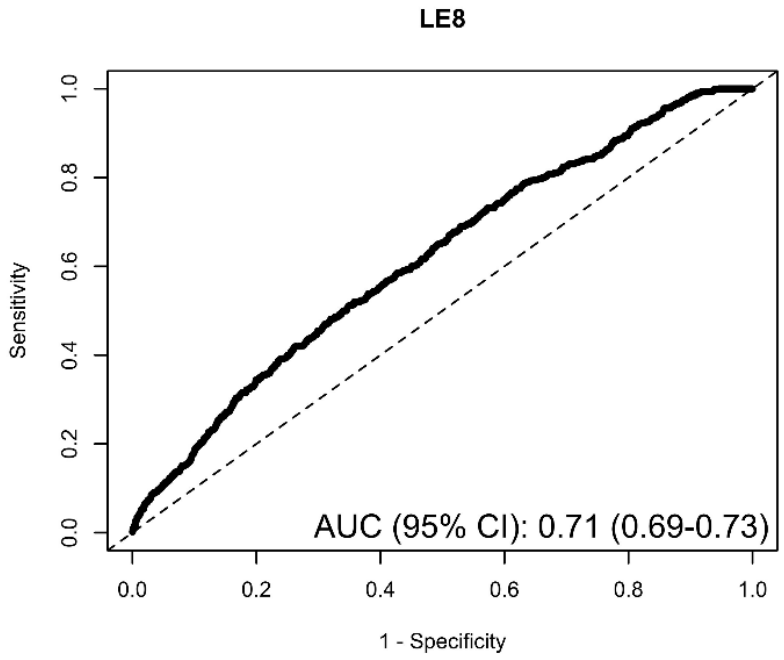
Framingham Risk Score



ASCVD Risk Score



Life's Essential 8



*Approved manuscript

Wadden et al. *In preparation*

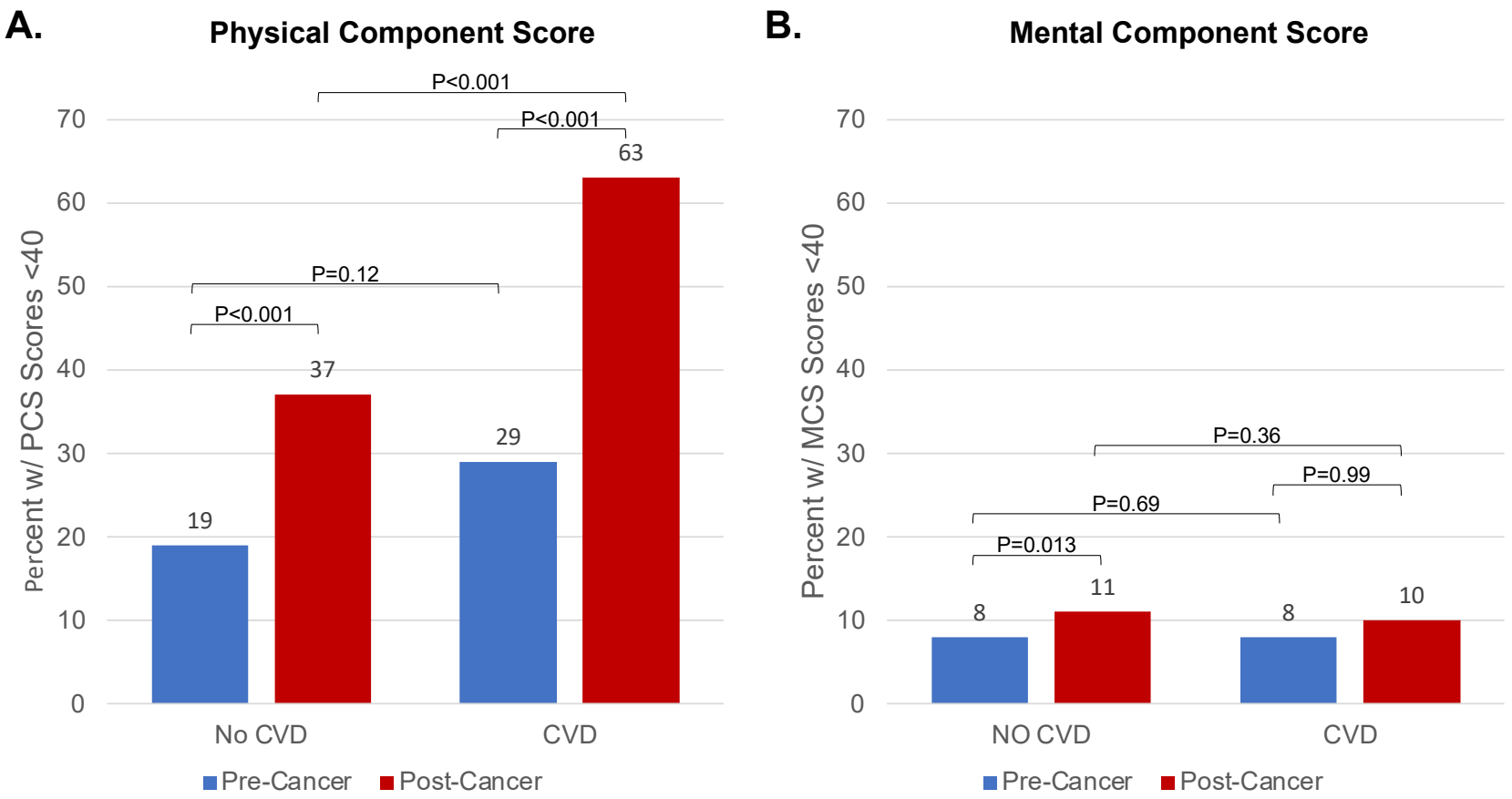
Quality of life after CVD in breast cancer

- To examine whether incident CVD after breast cancer is an independent predictor of health-related quality of life
    - Diagnosed with stage I-III breast cancer
    - Free of prevalent CVD prior to breast cancer
    - SF-36 measured prior to and after breast cancer
- Quality of life: SF-36 physical (PCS) and mental component scores (MCS)
    - Poor PCS and MCS scores < 40 points
- CVD defined as composite of coronary heart disease, heart failure, and stroke

Vasbinder et al. *J Cancer Surviv.* 2025

Quality of life after CVD in breast cancer

- N=2,866; mean age 67.2
- 63 women had CVD between BC diagnosis and collection of post-cancer SF-36
- **Women had significantly poorer physical QOL after cancer**



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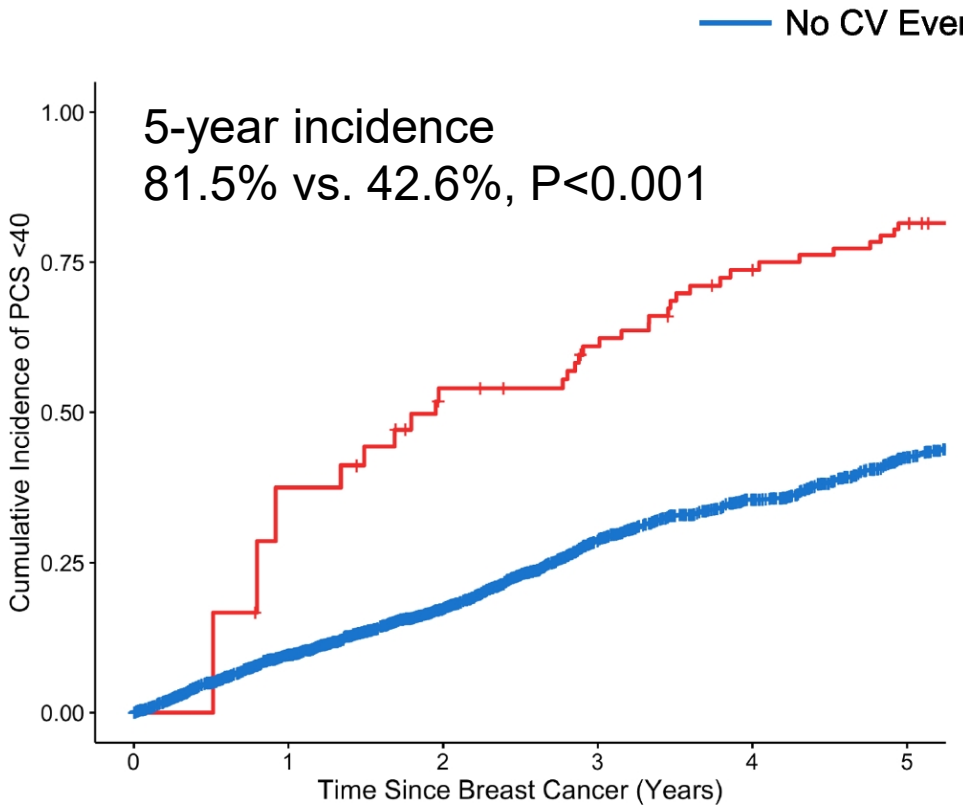
Quality of life after CVD in breast cancer

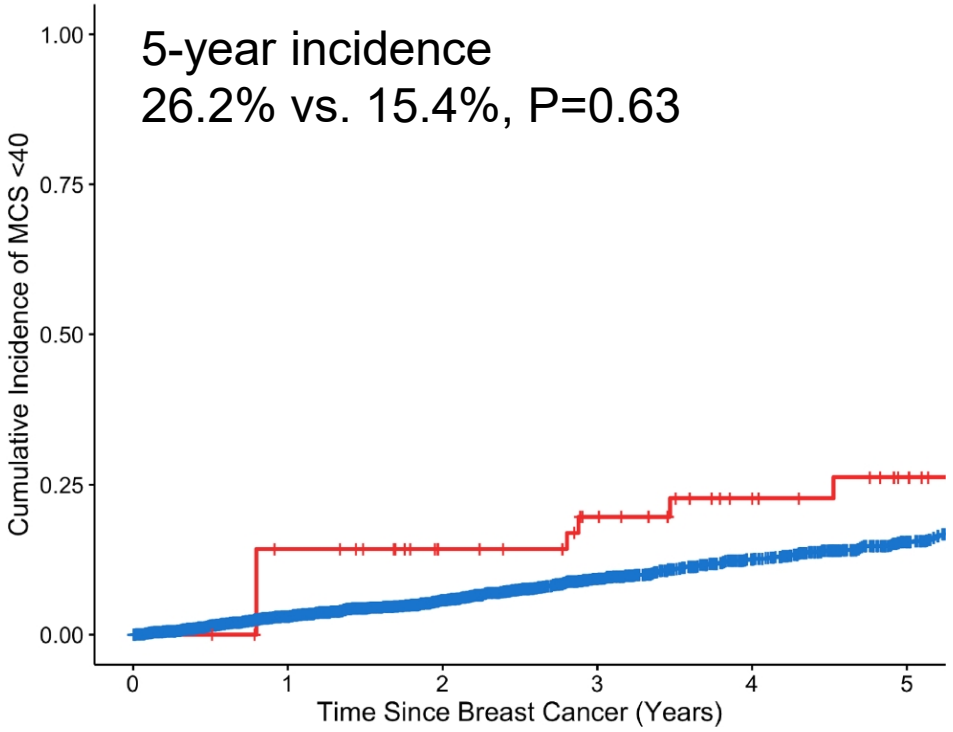
Women who experience CV events have a higher rate of poor physical QOL

A. Physical Component Score



B. Mental Component Score

PCS or MCS < 40



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Quality of life after CVD in breast cancer

	Events	HR (95% CI)	P-value
Physical Component Score	1072	1.88 (1.36, 2.59)	**<0.001**
Mental Component Score	310	1.05 (0.46, 2.40)	0.90
SF-36 Domain Subscales			
Physical Component			
Physical Function	869	1.89 (1.36, 2.64)	**0.002**
Role Physical	1058	2.00 (1.43, 2.78)	**<0.001**
Bodily Pain	907	1.75 (1.21, 2.53)	**0.003**
General Health	664	2.57 (1.78, 3.71)	**<0.001**
Mental Component			
Vitality	651	2.24 (1.50, 3.35)	**<0.001**
Mental Health	274	1.65 (0.83, 3.29)	0.15
Social Function	457	2.03 (1.22, 3.37)	**0.007**
Role Emotional	553	1.56 (0.93, 2.64)	0.09

Vasbinder et al. *J Cancer Surviv.* 2025

Evaluating reverse cardio-oncology

Reverse cardio-oncology

ESC European Society of Cardiology

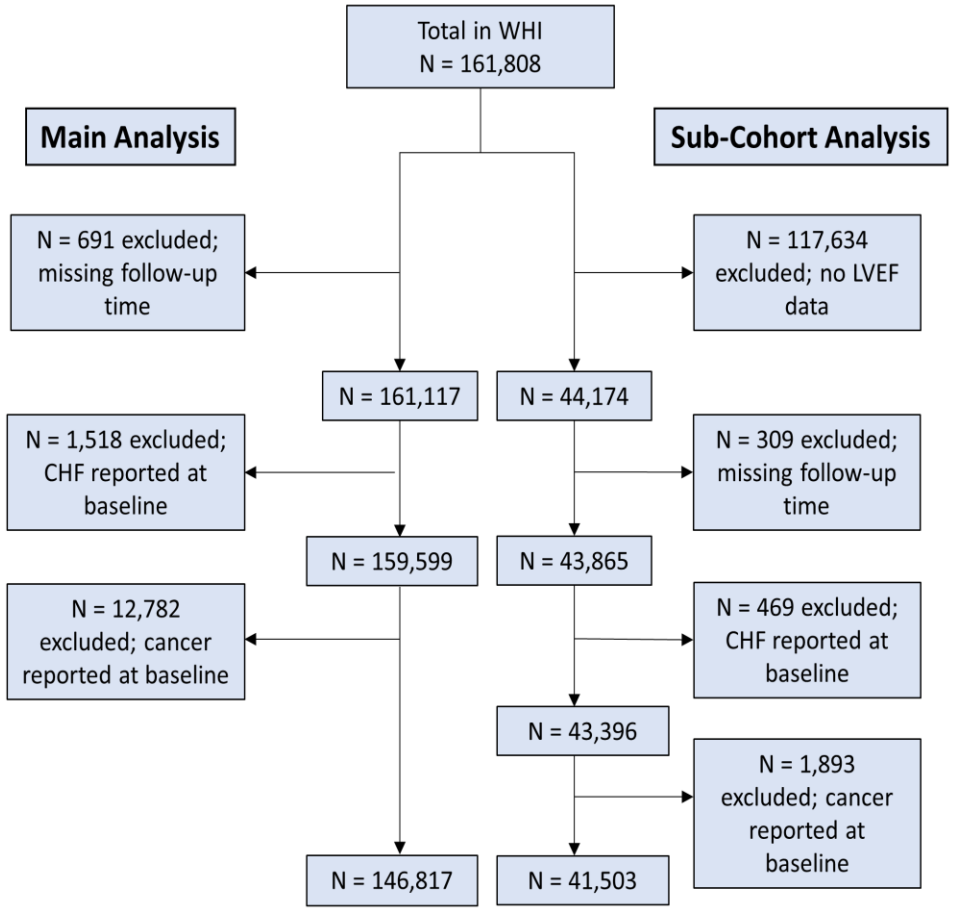
European Journal of Heart Failure (2021)
doi:10.1002/ejhf.2207

RESEARCH ARTICLE

The association between heart failure and incident cancer in women: an analysis of the Women's Health Initiative

Douglas J. Leedy[1], Kerryn W. Reding[2,3], Alexi L. Vasbinder[2], Garnet L. Anderson[3], Ana Barac[4], Jean Wactawski-Wende[5], Aladdin H. Shadyab[6], Charles B. Eaton[7], Wayne C. Levy[1], LiHong Qi[8], and Richard K. Cheng[1]*

Figure 1: Flow Diagram of Study Population



Leedy et al. *Eur J Heart Failure.* 2021;23(10):1712-1721

Incident heart failure and risk of cancer

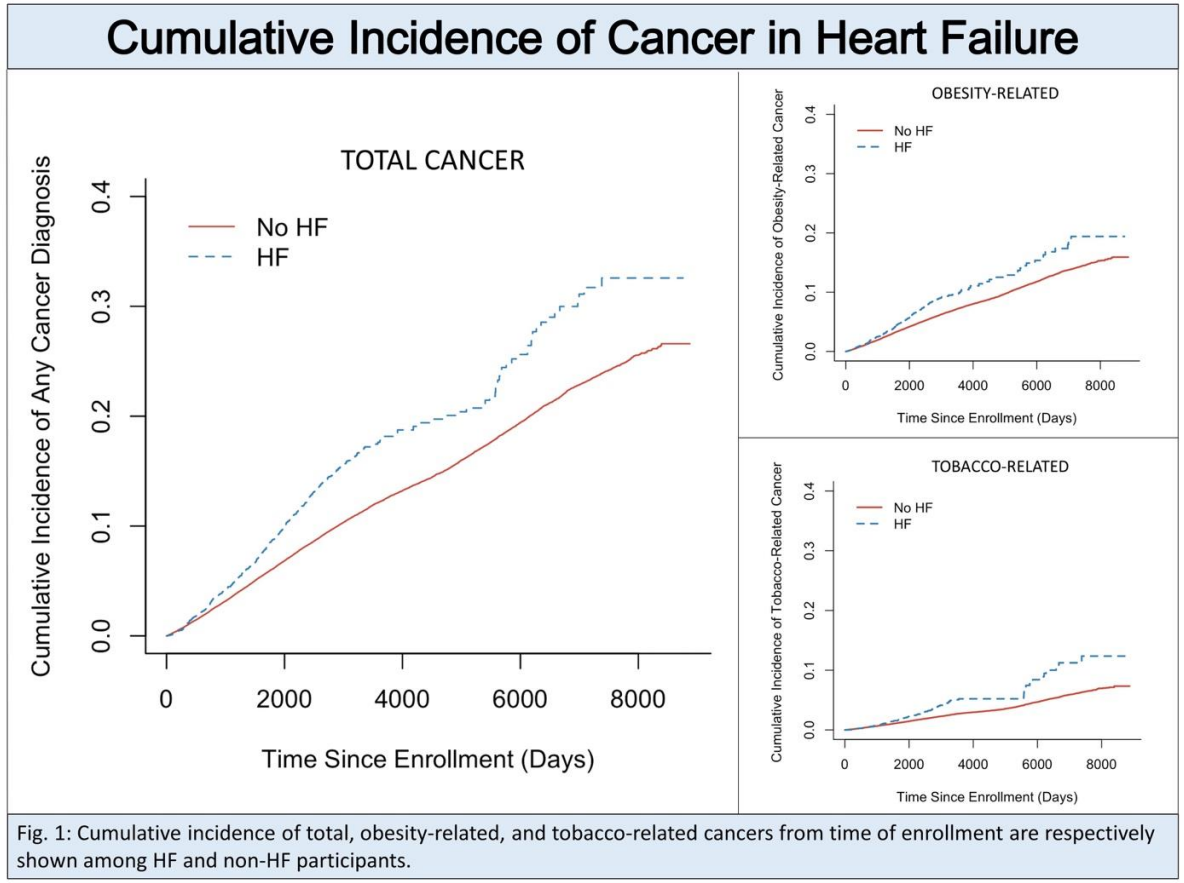


Fig. 1: Cumulative incidence of total, obesity-related, and tobacco-related cancers from time of enrollment are respectively shown among HF and non-HF participants.

Incident heart failure is associated with higher risk of cancer (even after adjusting for screening behaviors)

Association of Overall Heart Failure with Incident Total and Site-Specific Cancers

	Model 2 (+Demographics/Comorbidities)			Model 3 (+Screening variable)		
	Number of events	HR (95% CI)	p-value	Number of events	HR (95% CI)	p-value
Total	14,811	1.33 (1.16, 1.54)	<0.001	14,401	1.46 (1.29, 1.66)	<0.001
Obesity-related	8,688	1.21 (0.99, 1.47)	0.057	8.463	1.24 (1.02, 1.51)	0.032
Tobacco-related	3,216	1.59 (1.23, 2.05)	<0.001	3,110	1.51 (1.16, 1.97)	0.002

Leedy et al. *Eur J Heart Failure.* 2021;23(10):1712-1721

Incident heart failure and risk of cancer

Association with heart failure appears to be driven by HFpEF

Association of HFpEF and HFrEF with Incident Total Cancers						
	Age-Adjusted			Fully-Adjusted		
	Number of events	HR (95% CI)	p-value	Number of events	HR (95% CI)	p-value
Total	7,292			5,868		
No HF	6,753	1.0 (reference)			1.0 (reference)	
Any HF	539	1.37 (1.19, 1.58)	<0.001		1.33 (1.13, 1.55)	<0.001
HFpEF	253	1.45 (1.18, 1.79)	<0.001		1.39 (1.10, 1.75)	0.005
HFrEF	169	1.08 (0.83, 1.41)	0.564		1.04 (0.78, 1.39)	0.787
Unknown EF	117	1.68 (1.26, 2.23)	<0.001		1.64 (1.21, 2.22)	0.001

Leedy et al. *Eur J Heart Failure.* 2021;23(10):1712-1721

Incident heart failure and risk of cancer

Source	Number at risk (n=)	HR (95% CI)
Present Study	3,272	1.28 (1.11-1.48)[a]
Selvaraj et al,[17] 2018	1,420	1.02 (0.84-1.25)
Hasin et al,[10] 2016	228	1.71 (1.07-2.73)
Banke et al,[6] 2016	9,307	1.24 (1.15-1.33)
Hasin et al,[7] 2013	596	1.68 (1.13-2.50)

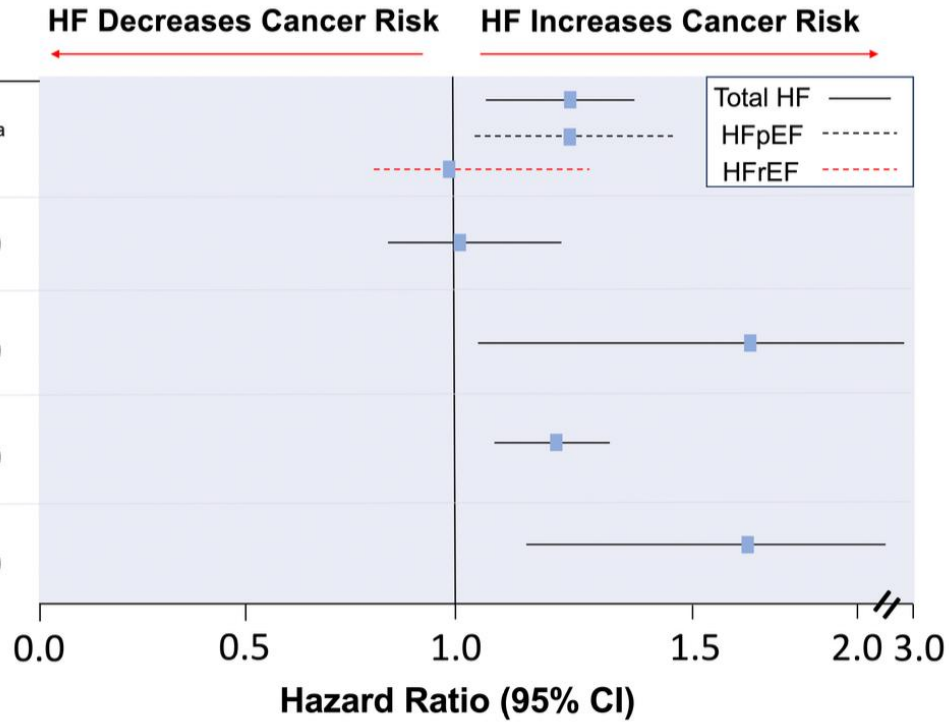


Figure 3 Studies investigating the association of heart failure (HF) with incident cancer. Hazard ratios (HR) and 95% confidence intervals (CI) are shown from studies evaluating the risk of incident cancer among patients with HF. HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction. [a]HR for HFpEF and HFrEF 1.28 (1.06–1.67) and 0.99 (0.78–1.34), respectively. [b]Number of participants in each study with HF at risk of developing cancer.

Leedy et al. *Eur J Heart Failure.* 2021;23(10):1712-1721

Final remarks

- WHI has been instrumental in uncovering cardiovascular risks among cancer survivors (Cardio-Oncology Working Group within Cancer SIG)

- Findings inform risk prediction, prevention strategies, and highlight health disparities

- Shifting from discovery to actionable prevention/management
  - Testing modifiable risk factors (i.e., frailty)
  - Innovative methods to simulate interventions (i.e., physical activity)

Acknowledgments

Co-investigators

Kerryn Reding
Richard Cheng
Ana Barac
Doug Leedy
Michael Simon
Michael LaMonte
Hyunhae Lee
Chi-shan Tsai
Sophia Larson
Elena Wadden
Paola Encabo Gonzalo
Christina Dieli-Conwright
Roberta Ray
Susan Heckbert
Rachel Yung
Susan Heckbert
Oleg Zaslavsky
Roberta Ray
Electra Paskett
Aladdin Shadyab
Nazmus Saquib
Lisa Warsinger Martin
Marcia Stefanick
Joe Larson
Lisa Johnson
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Thank you for all your support!!!