



Penn Medicine

Thalheimer Center for Cardio-Oncology

Cardio-oncology:

PROVIDING MULTIDISCIPLINARY, MULTISPECIALTY EXPERT CARE FOR
PATIENTS LIVING WITH AND BEYOND CANCER

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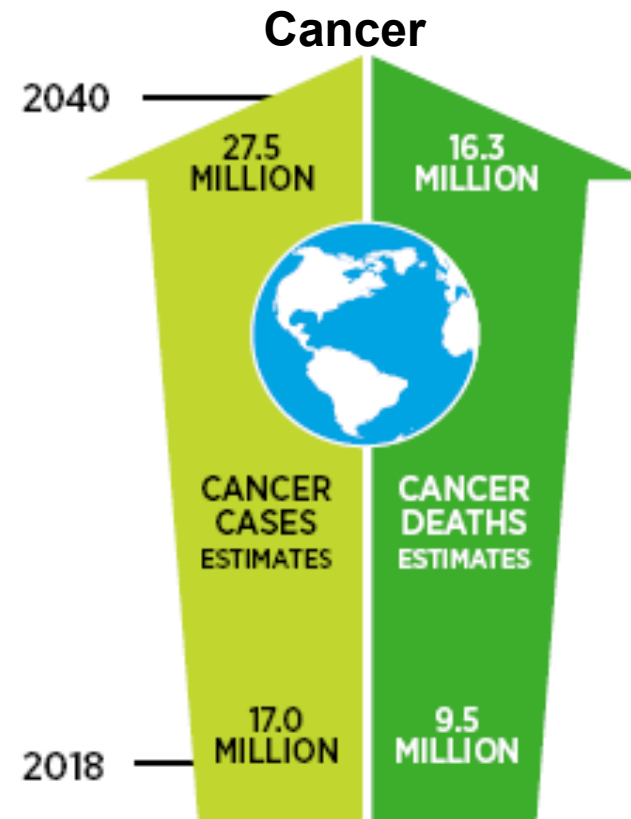
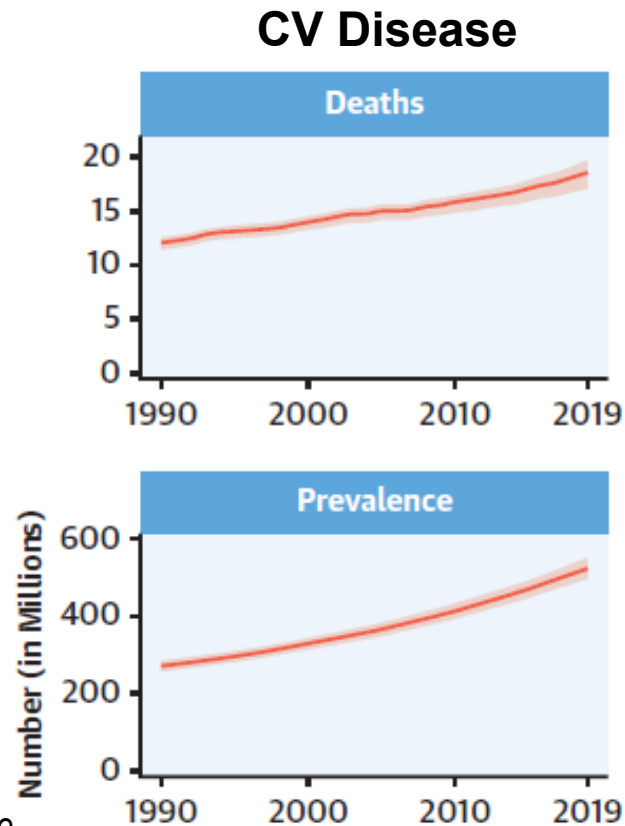
July 17, 2023

Outline

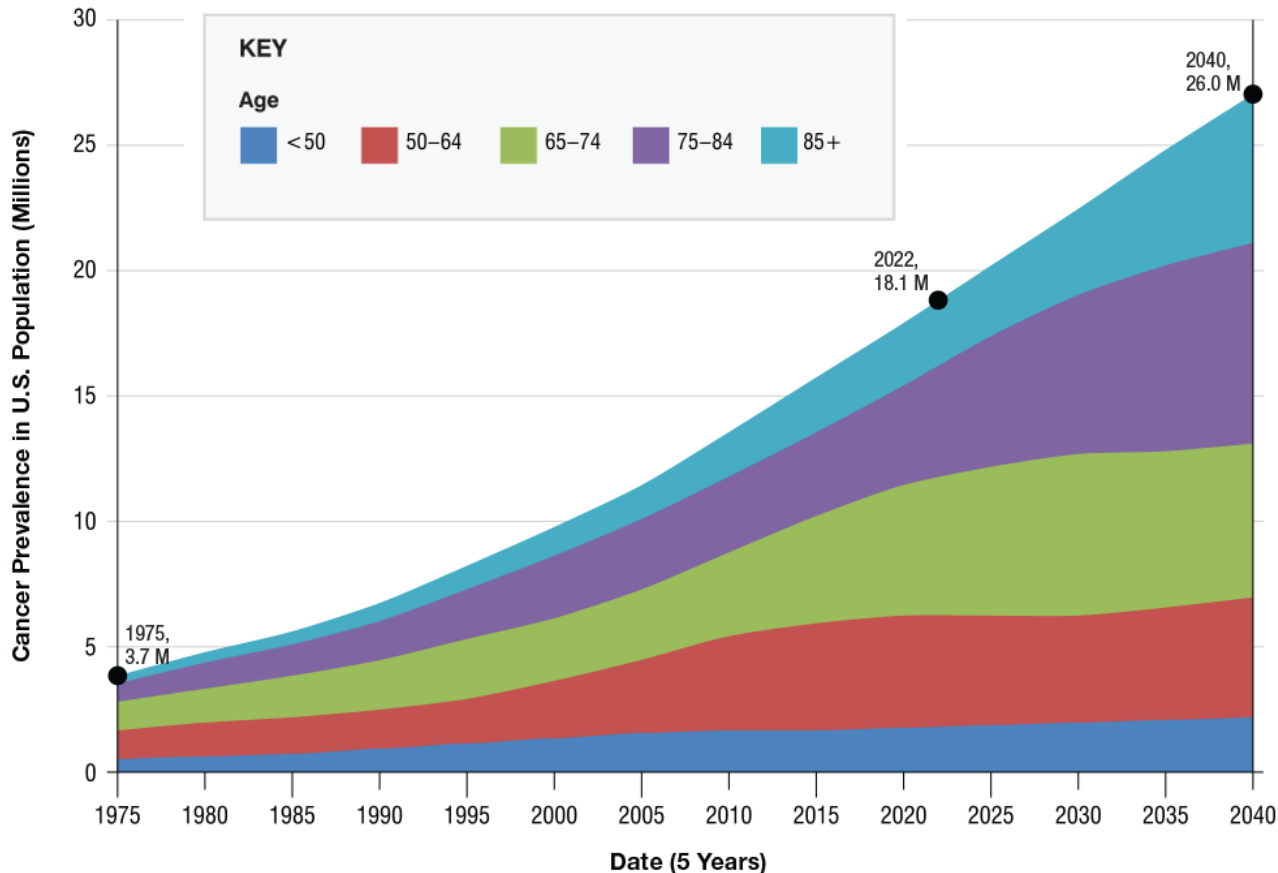
- **Why is cardio-oncology important?**
- **What are our fundamental goals in cardio-oncology care?**
- **What are our priorities and actionable strategies to achieve our goals?**
- **Summary**

CV Disease and Cancer are Two Leading Causes of Morbidity and Mortality Worldwide

- **CV Disease:** ~523 million prevalent cases and ~18 million deaths in 2019
- **Cancer:** ~17.2 million incident cases and ~9.9 million cancer deaths in 2019

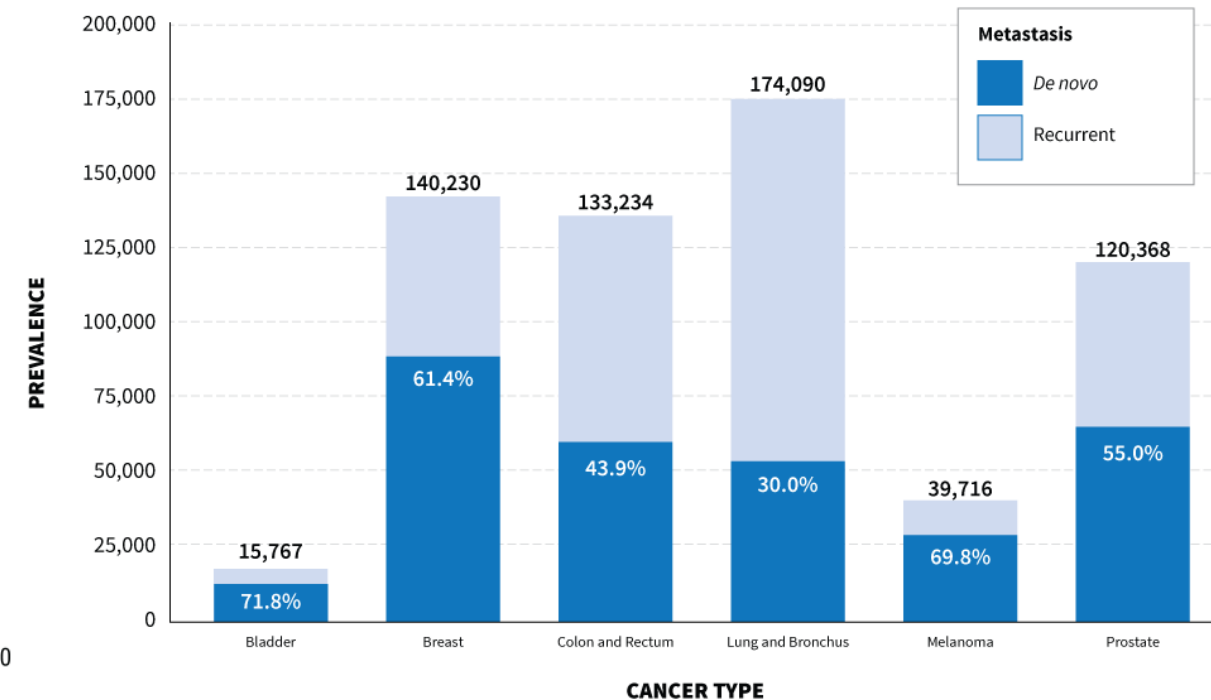


There is a Growing Population of Aging US Cancer Survivors At Risk for Cardiovascular Disease



> 12 million greater than 65 years of age

Estimated Numbers of Individuals Living with Metastatic Cancer in the U.S.

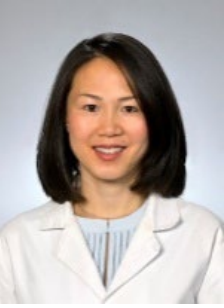


Miller, et al. *CA Cancer J Clin.* 2022.

Bluethmann, et al. *Cancer Epidemiol Biomarkers Prev.* 2016 Penn Medicine

Gallicchio, et al. *JNCI.* 2022.

The Burden of CV Risk Factors in Cancer Patients is Substantial and Under-Treated



- Cross-sectional analysis of 90,494 US Veterans with prostate cancer, stratified by CV disease history (~15-21%) and androgen deprivation therapy (ADT)
 - 79% HTN; 68% hyperlipidemia; 28% diabetes
- CV risk factor assessment incomplete in 32%;
- Risk factors not controlled in 54%;
- Despite uncontrolled risk factors, 29% not on CV medications
- ADT not associated with CV risk factor assessment, control or medications
- **Why is this important? CV risk factors associated with increased risk of CV disease in cancer survivors, greater than non-cancer comparators; underdiagnosis and undertreatment pervasive across survivors**

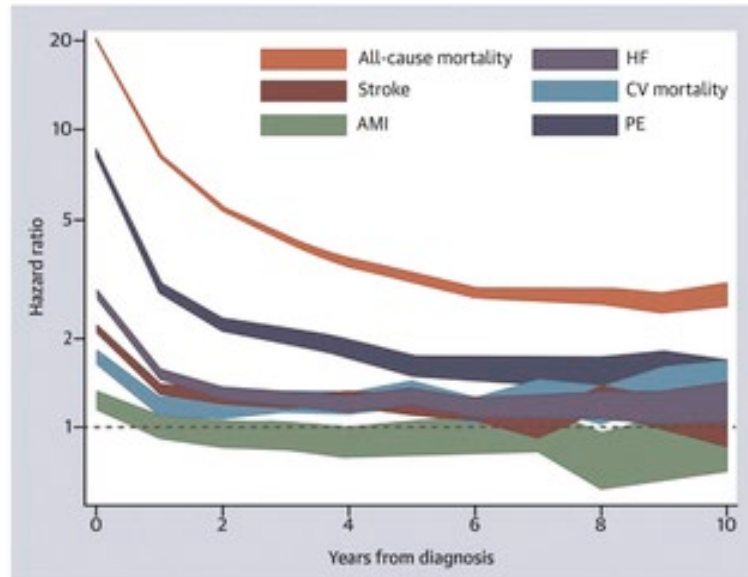
Sun, Narayan, Ky, et al. JAMA Network Open. 2021.

Armenian, Ky, Chao, et al. JCO. 2016.

Chow, et al. JAHA. 2022.

The Burden of CV Disease and CV Mortality in Cancer Patients is Substantial

CENTRAL ILLUSTRATION: Cardiovascular Risk by Time From Cancer Diagnosis



CENTRAL ILLUSTRATION: Does Cardiovascular Mortality Overtake Cancer Mortality During Cancer Survivorship?

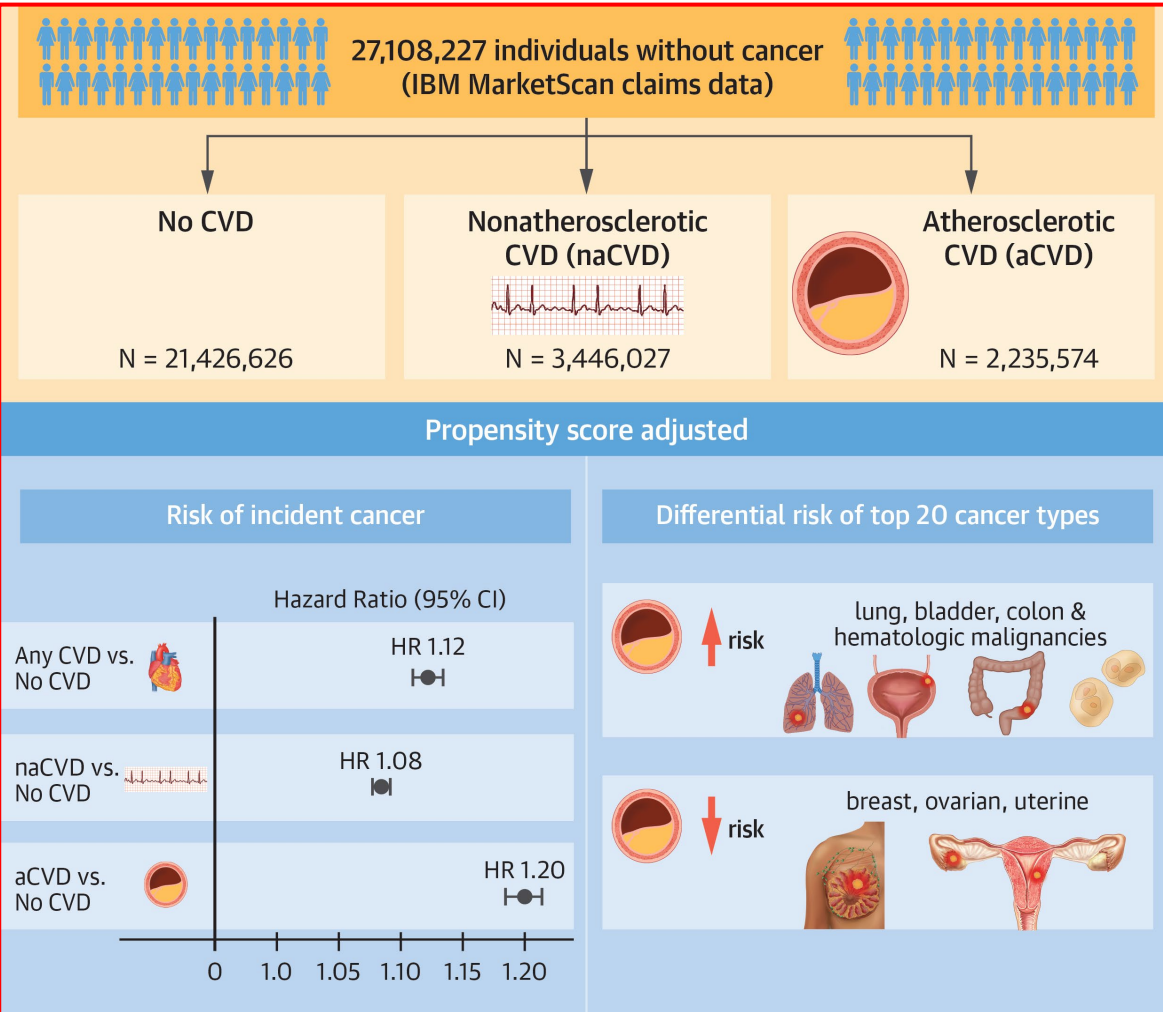
Crossover point in years when cardiovascular disease mortality rate equals mortality rate from primary cancer, by age group at diagnosis

Cancer site	Age group at diagnosis		
	40 to 59 yrs	60 to 79 yrs	≥80 yrs
Prostate			8.9 (7.4-16.7)
Leukemia			6.3 (2.9-13.1)
Colorectal		8.6 (8.1-13.9)	5.4 (4.7-9.3)
Lung		17.4 (12.9-26.6)	10.6 (7.4-22.4)
Melanoma		8.5 (6.8-14.6)	1.9 (1.5-4.5)
Breast		12.7 (11.6-21.6)	7.1 (6.3-12.6)
Bladder		4.8 (2.9-9.1)	2.6 (2.4-3.9)
Non-Hodgkin lymphoma		15.4 (10.8-24.8)	4.7 (3.1-9.9)
Uterus	11.0 (8.2-20.8)	7.1 (6.6-13.0)	3.9 (3.5-8.8)

- 224,016 participants with new cancer; median follow-up 11.8 years
- Compared to controls: CV mortality risk 1.3; Stroke: 1.4; Heart Failure: 1.2

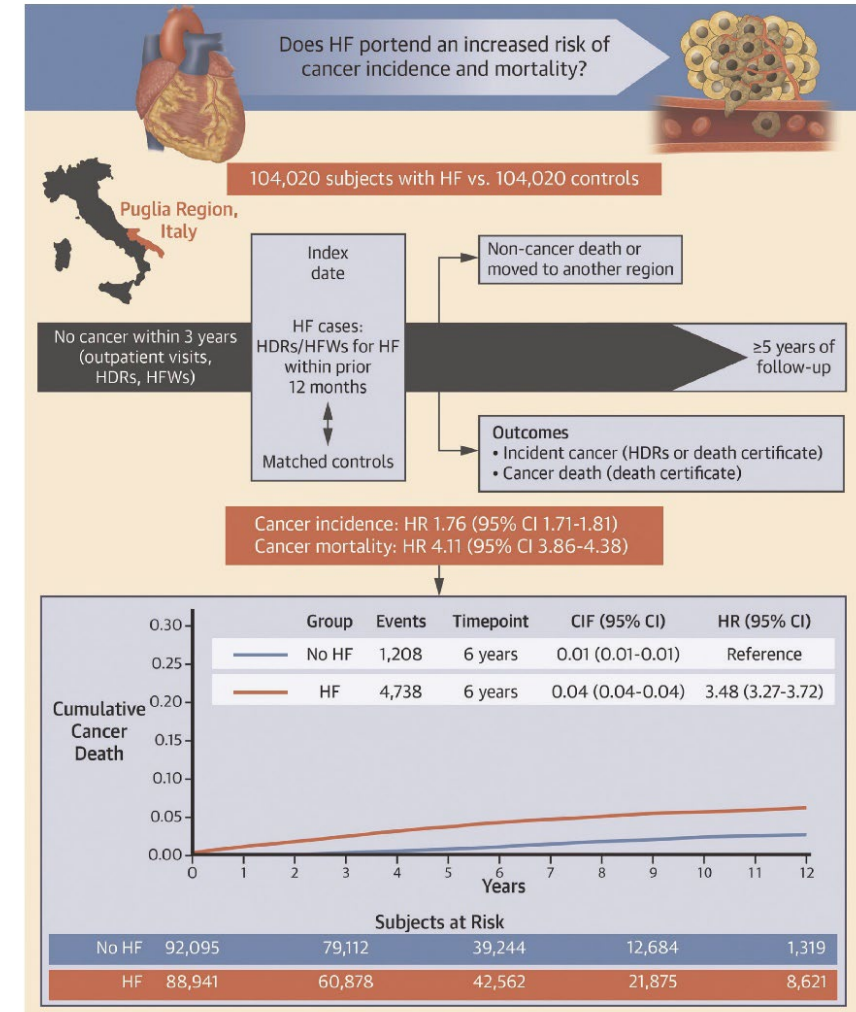
- 104,028 participants with first cancer; median follow-up 4.8 years
- CV mortality > primary cancer mortality in many 60-79 years; all ≥80 years

The Burden of Cancer and Cancer Mortality in CVD Patients is Substantial



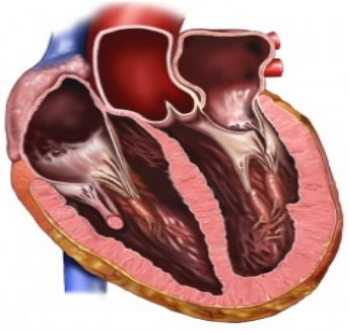
Bell, Nead, et al. JACC CardioOnc. 2023.

CENTRAL ILLUSTRATION: Cancer Incidence and Mortality Are Increased in HF Patients

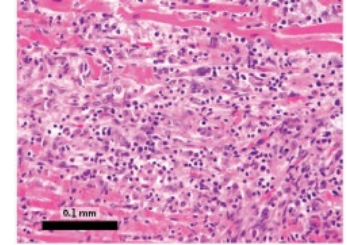
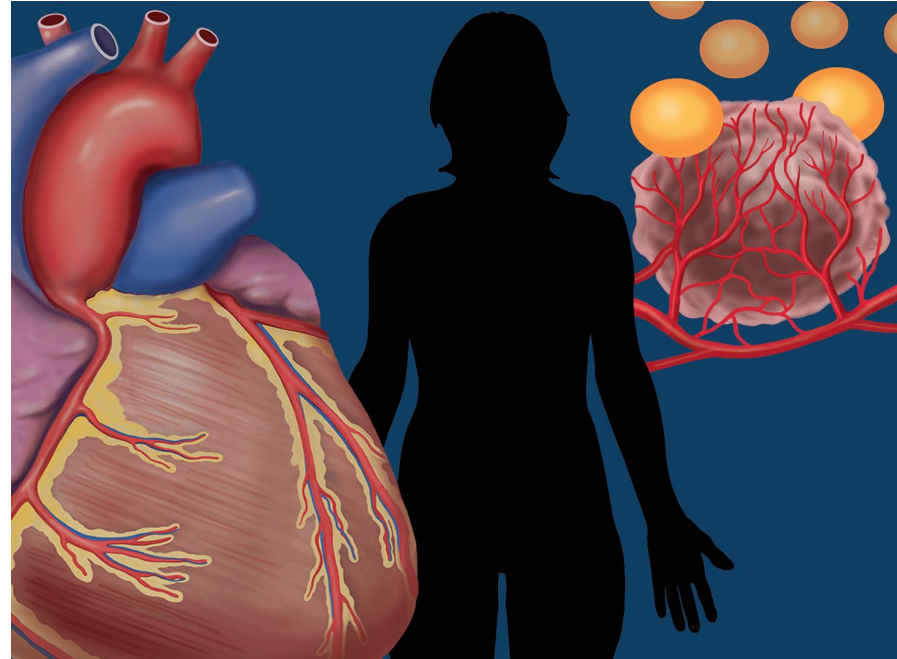


Bertero, E. et al. J Am Coll Cardiol CardioOnc. 2022;4(1):98-109.

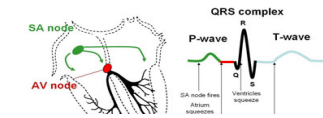
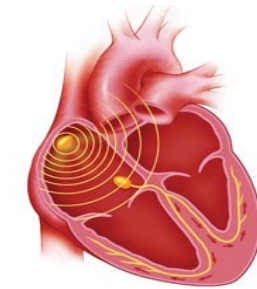
Cancer Therapies Can Have Broad Cardiotoxic Effects



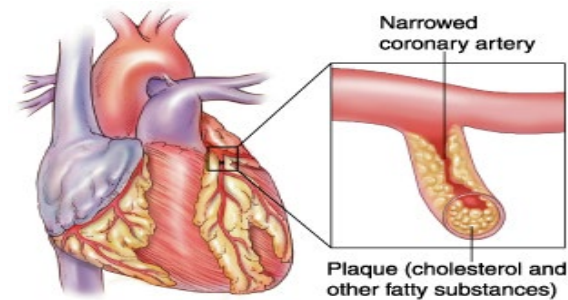
Heart Failure with reduced or preserved EF, Valvular Disease, Pulmonary Hypertension, Pericardial Disease



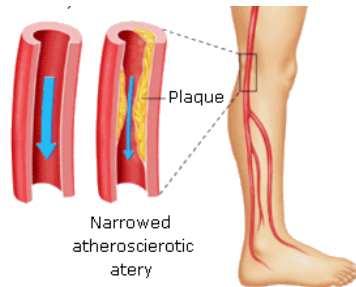
Myocarditis



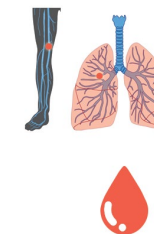
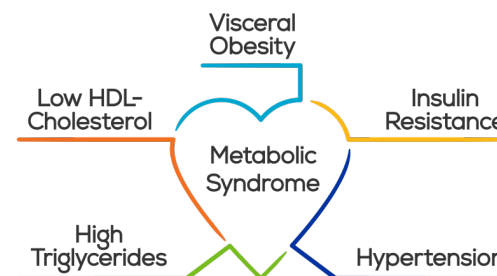
Arrhythmia, Long QT



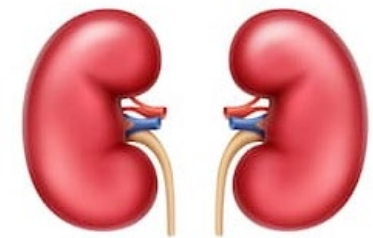
Atherosclerosis, Acute Coronary Syndrome, Coronary Vasospasm, Dyslipidemia



Peripheral Arterial Disease



Bleeding/Thrombosis



Hypertension

What Are Our Goals in the Care of Our Patients Living With and Beyond Cancer?

Provide equitable, evidence-based care so our patients can live longer, healthier lives

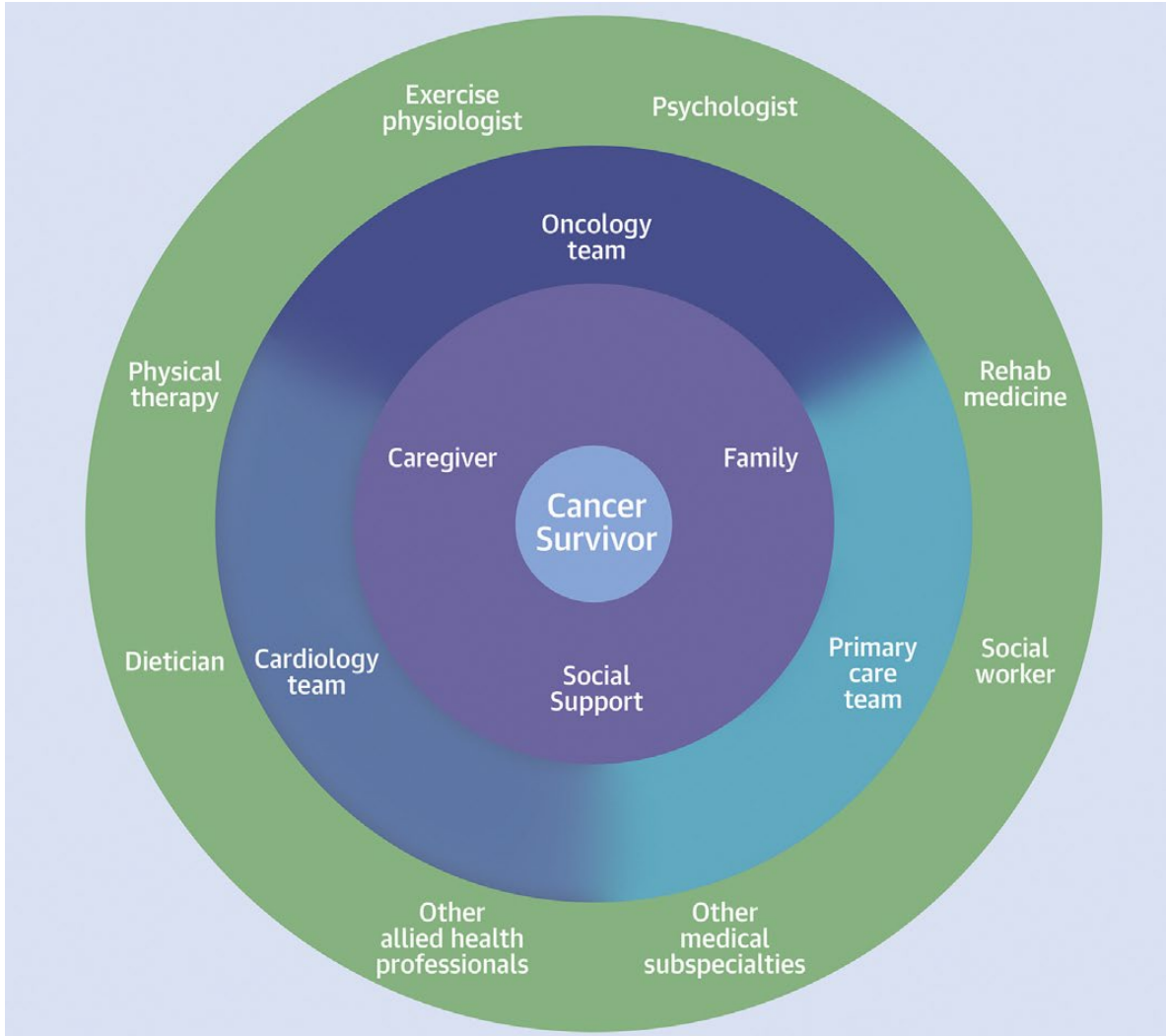
Build evidence-based, effective, collaborative care delivery models at the practice and system-level

Advance science in precision phenotyping and CV risk reduction throughout the lifespan

Mitigate inequities in CV disease in cancer patients to provide inclusive care

Educate the next generation of physicians, advanced practice providers, and scientists by training an effective, empathic, and resilient careforce

Priority: Build Evidence-based, Effective, Collaborative Care Delivery Models

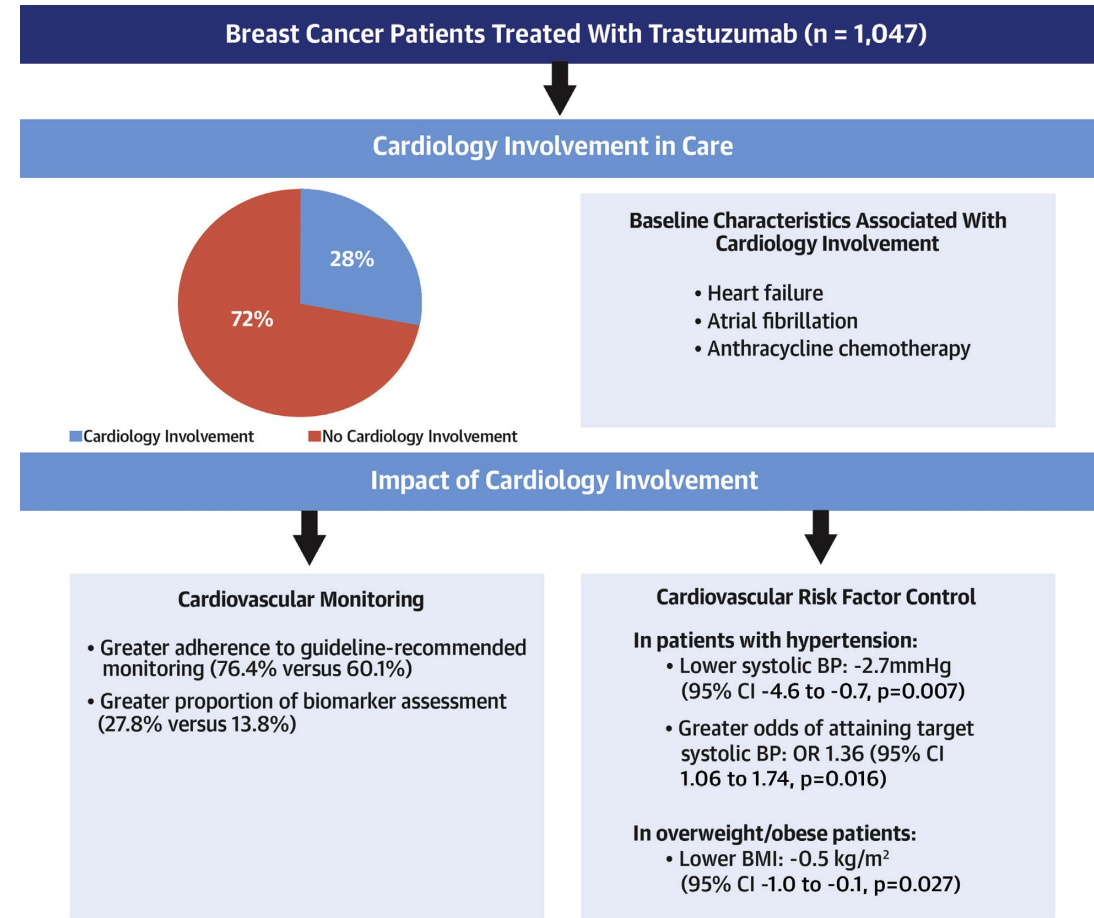


- Develop patient-centric care models at the practice and system-level that are efficient and effective
- Define and equip the gatekeeper for the care of the cancer survivor
- Empower the patient and the careforce to collaborate in care

Oncology team	Shared areas	Primary care and cardiovascular care
• Cancer care • Response to therapy • Monitor for adverse events/side effects	• Communication • Prevention of frailty • Use of technology • Financial resources • Opportunities for research in communication and shared care	• Non-cancer comorbidities • Medication adherence • Lifestyle/behaviors

Actionable Strategies to Achieve Our Goal

- Inform the efficacy of various care team models through evidence
 - NCT03935282, AH-HA: Weaver
 - Greater referral to primary care with EHR-based CV assessment tool (39% vs 25%) and greater reporting (98% vs 55%) and discussion of CV risk factors
 - NCT04258813, ONE TEAM, Oeffinger
 - Care coordination with the primary care physician and patient empowerment
- Establish the impact of cardiology and cardio-oncology care



Actionable Strategies to Achieve Our Goal

- Leverage scalable technology and behavioral economics to advance care (e.g. nudge units)
 - Cluster RCT of 158 clinicians, 28 primary care centers, 4,131 patients: 7.2% increase in statin prescription in patient + clinician nudge compared to usual care
- Overcome geographic and racial inequities in access to care
 - US census tracts with NH Blacks (OR 2.37), Hispanic/Latino (OR 1.30), worse poverty (OR 1.12) had higher odds of losing health care facilities between 2000-2014

Priority: Advance Science in Precision Phenotyping and CV Risk Reduction throughout the Lifespan

Advance actionable science so our patients with and beyond cancer can live longer, healthier lives

- To define the epidemiology of CV disease in the modern treatment era (*When, who, why?*)
- To determine who is at risk for CV disease through detailed phenotyping (*Integrate multi-omics with machine learning strategies to understand disease*)
- To develop innovative cardioprotective strategies and target cardioprotection according to risk (*COG ALTE1621 Armenian, Bhatia, ASCO 2023*)
- To translate our understanding of the basic mechanisms of CV disease and cancer to our patients so we can deliver augmented clinical care (*CHIP, inflammation, and the immune system*)

Priority: Mitigate Inequities in CV Disease in Cancer Patients to Provide Inclusive Care

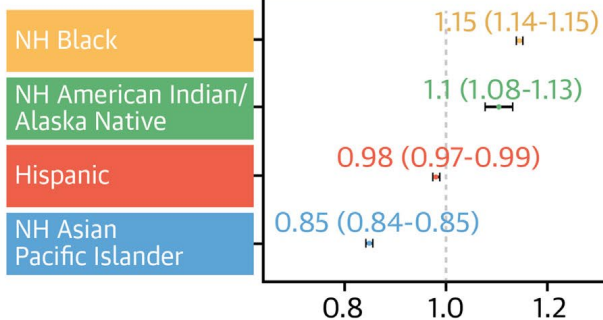
Racial and Ethnic Disparities in All-Cause and Cardiovascular Mortality Among Cancer Patients in the U.S.

3,674,511 Patients from SEER Database (2000-2018)

- 73.6% Non-Hispanic (NH) White
- 11.0% NH Black
- 9.0% Hispanic
- 6.1% NH Asian/Pacific Islander
- 0.4% NH American Indian/Alaska Native

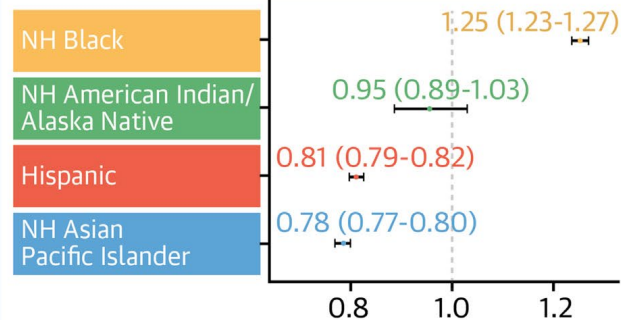
All-Cause Mortality (ref: NH White)

Adjusted HR (95% CI)

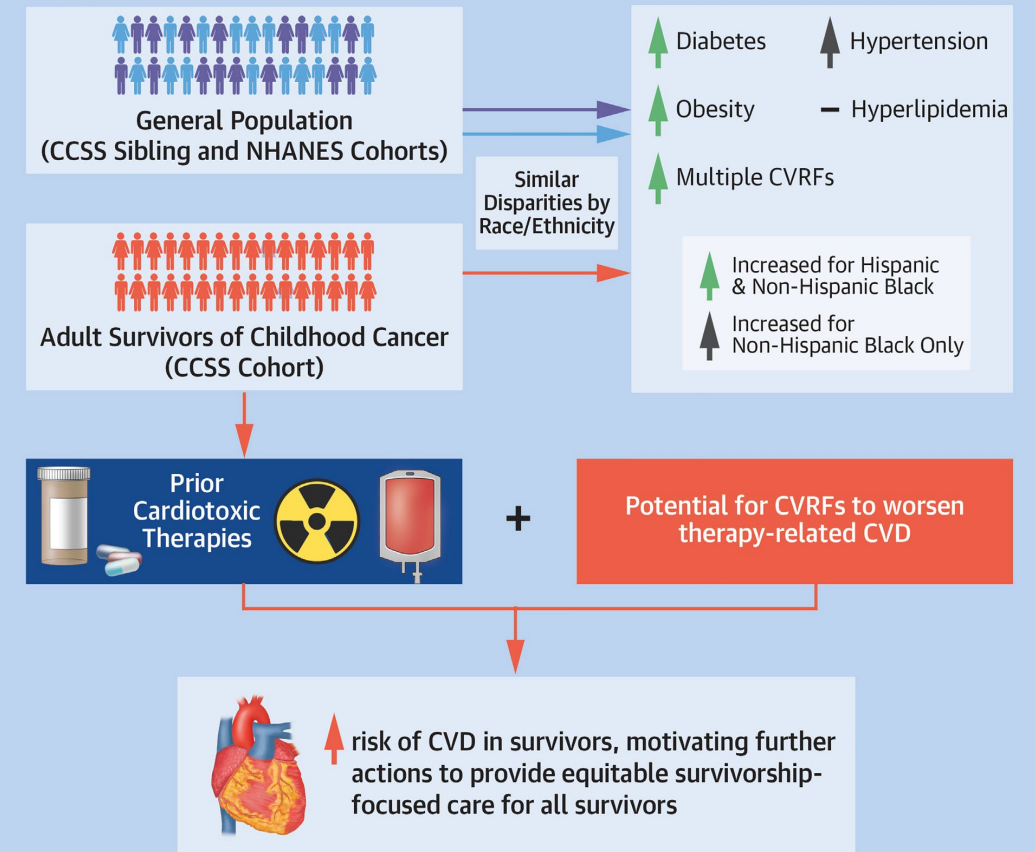


CVD Mortality (ref: NH White)

Subdistribution HR (95% CI)

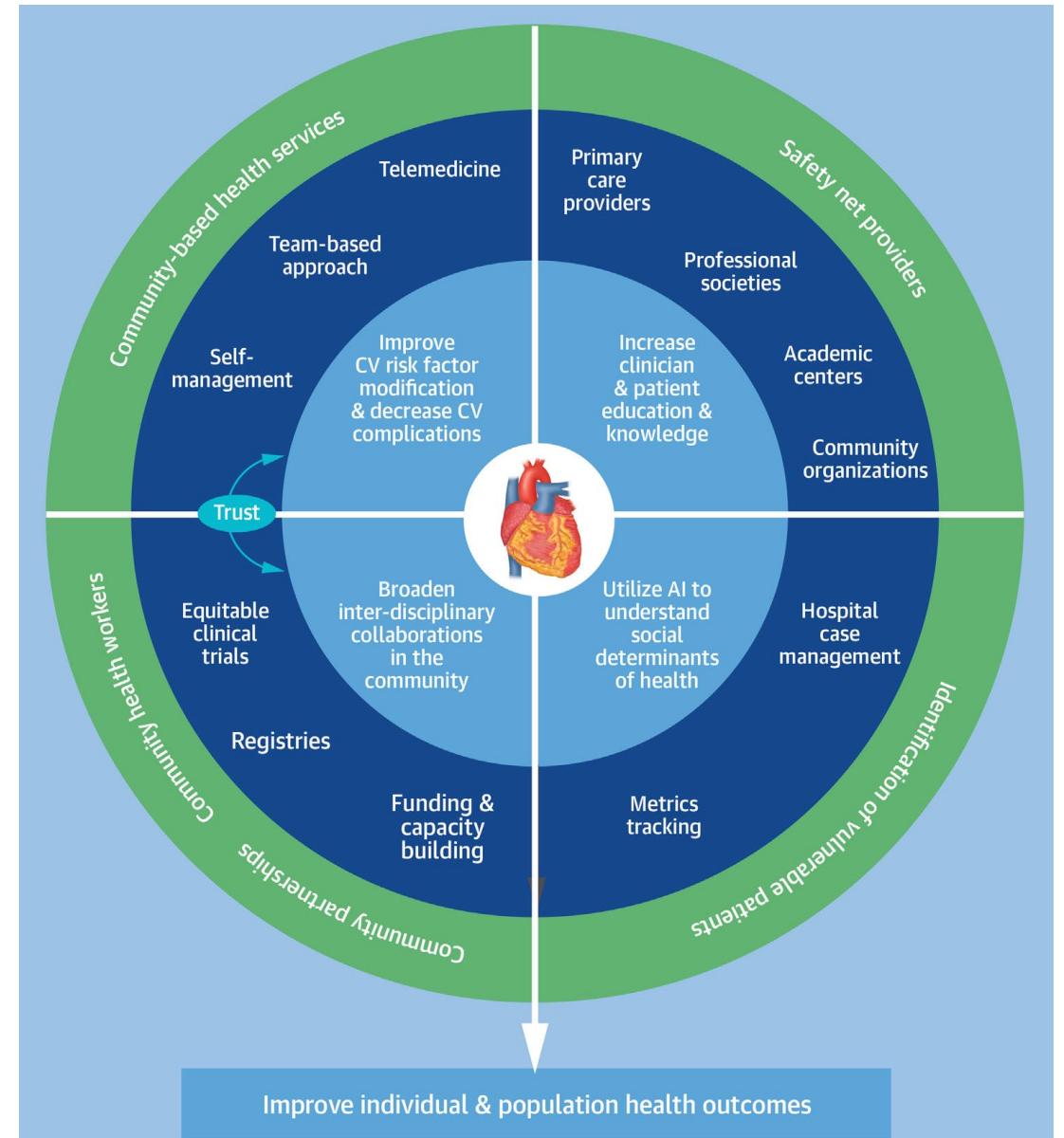


Disparities in CV Risk Factors (CVRFs) Among Adult Survivors of Childhood Cancer Compared With the General Population



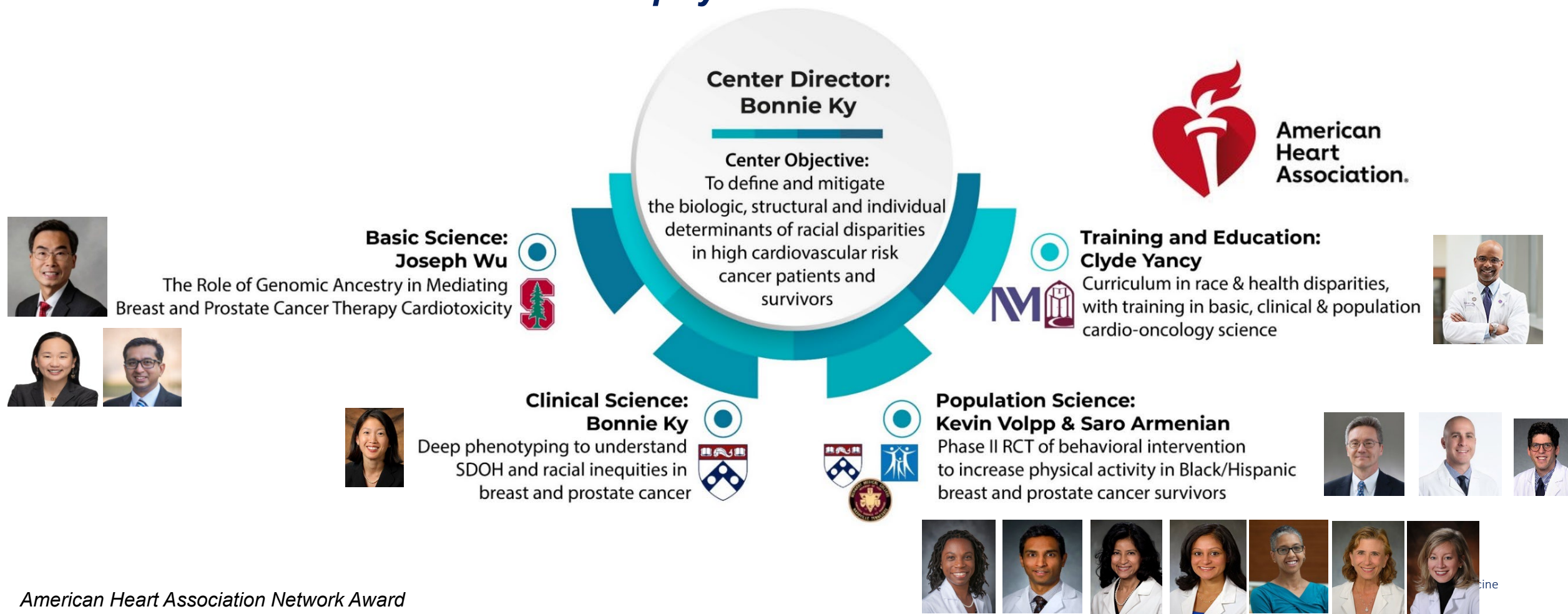
Actionable Strategies to Achieve Our Goal

- Determine how CV risk might differ according to ancestry
- Determine how the SDoH impact CV disease in our patients with cancer
- Improve accessibility of historically marginalized populations to clinical trials
- Develop strategies to mitigate disparities to ensure equitable, accessible, inclusive care to our patients and survivors



Ongoing Work: Understanding and Overcoming Disparities in Cardio-Oncology

Fundamental Goals: Understand and reduce racial disparities experienced by vulnerable patients with cancer and heart disease; provide the highest level of training to physician scientists



Priority: Train the Next Generation of Physicians, Scientists, and Multi-disciplinary Care Team

- Strengthen the pipeline of young investigators, clinicians, and care team with a focus on diversity and inclusivity
- Build a strong community based on advancement of rigorous science and patient centeredness
- Design programs that couple scientific training with active clinical training



JACC: CardioOncology Pulse

Implementation of Cardio-Oncology Training for Cardiology Fellows

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Cardio-Oncology Education and Training JACC Council Perspectives



Jose A. Alvarez-Cardona, MD,^{a,*} Jordan Ray, MD,^{b,*} Joseph Carver, MD,^c Vlad Zaha, MD, PhD,^d Richard Cheng, MD,^e Eric Yang, MD,^f Joshua D. Mitchell, MD,^a Keith Stockerl-Goldstein, MD,^g Lavanya Kondapalli, MD,^h Susan Dent, MD,ⁱ Anita Arnold, DO,^j Sherry Ann Brown, MD,^k Monica Leja, MD,^l Ana Barac, MD, PhD,^m Daniel J. Lenihan, MD,^a Joerg Herrmann, MD,ⁿ for the Cardio-Oncology Leadership Council



Actionable Strategies to Achieve Our Goal

- Develop evidence-based individual and programmatic clinical training standards and metrics for accreditation
- Invest in the early career investigator through targeted incentives
- Address stressors in the careforce (burnout, administrative burden)
- Establish formal collaborations across multiple organizations, including academic institutions, industry, professional societies, funding agencies, and the government to advance science, care and education

Summary: Our Priorities in the Care of Our Patients Living With and Beyond Cancer

Build evidence-based, effective, collaborative care delivery models at the practice and system-level

Advance science in precision phenotyping and CV risk reduction throughout the lifespan

Mitigate inequities in CV disease in cancer patients to provide inclusive care

Educate the next generation of physicians, advanced practice providers, and scientists by training an effective, empathic, and resilient careforce

My Hope for Cardio-Oncology

Bonnie Ky, MD, MSCE, *Editor-in-Chief, JACC: CardioOncology*

I often reflect on my hope for our field of cardio-oncology. My earnest desire is that we are cohesively driven by the common mission of providing the best possible care for our cancer patients and survivors, so that they can live longer, healthier, and fulfilling lives. Evidence-based care. Empathic care. Accessible care. Inclusive care.

How can we accomplish this as a field? As a community? As a physician, scientist, advanced practice provider, trainee, patient, person?

Fundamentally, we need to be driven by science. Innovative, rigorous, team science drives actionable knowledge for our patients. As important, we need to be driven by empathy. There are many joys in life, but also much sadness and suffering. We need to support each other, the pipeline of investigators and clinicians, and strive to listen and act with compassionate understanding of each other.

