Cardio-Oncology: Life Lessons After Cancer

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Disclosures

No conflicts of interest

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Objectives

- Cardiovascular toxicity risks
- Surveillance and monitoring
- Long-term follow-up and prevention of chronic complications
- Life after cancer

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What is Onco-Cardiology / Cardio-Oncology?

- Bridging discipline aiming to **maximize anti-cancer effects** while **minimizing cardiovascular toxicity**

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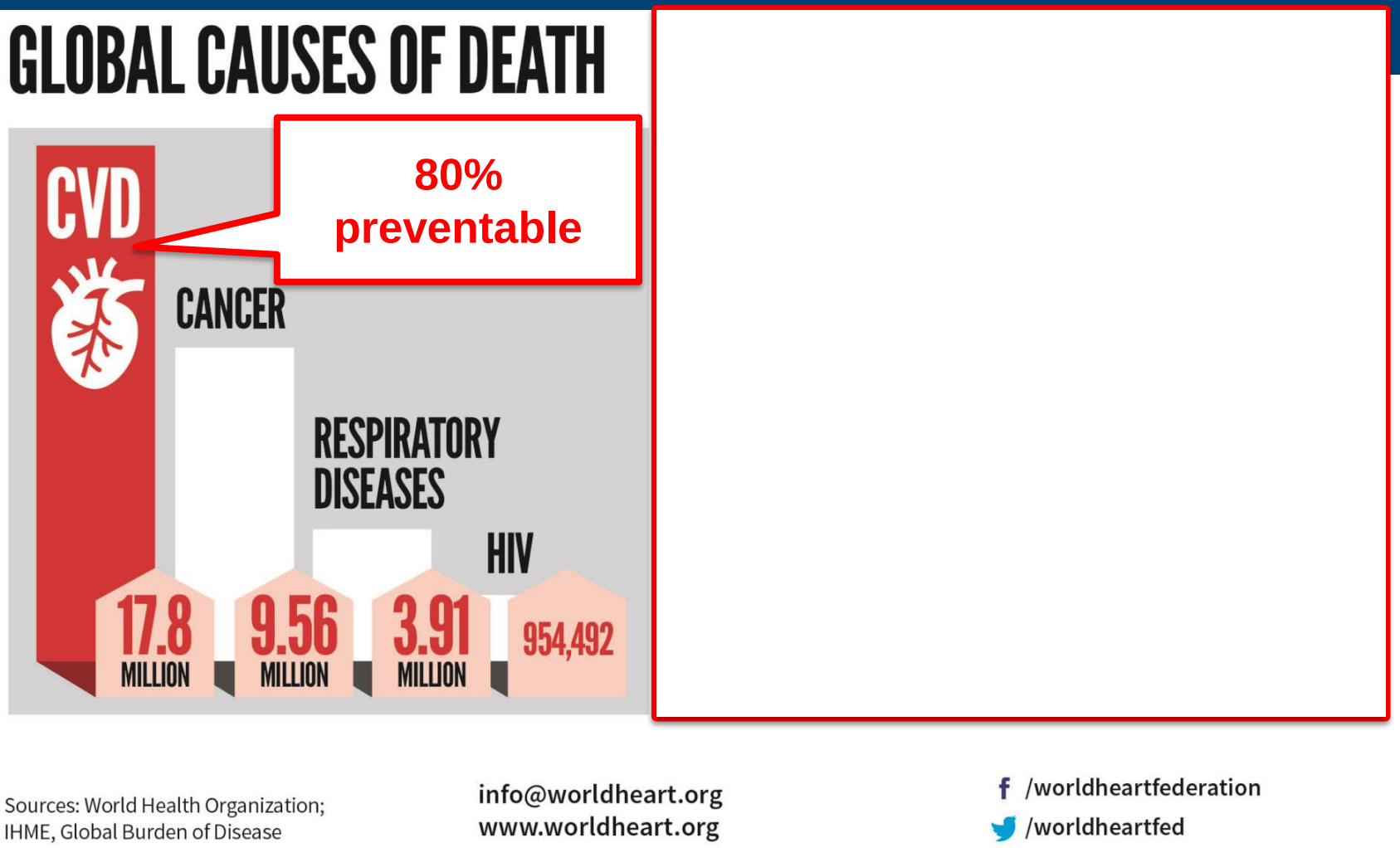
Why?



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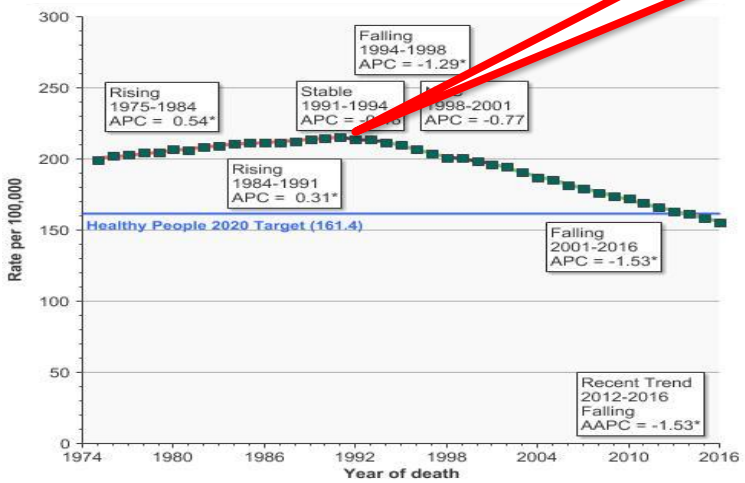
Cancer Survival

Smoking bans started 1995

US Death Rates for all Cancers 1975-2016



seer.cancer.gov

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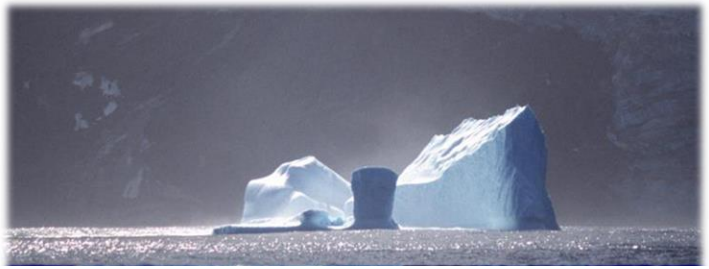
Cardiotoxic Effects of Cancer Therapy

Cardiomyopathy



Anti-metabolites
Anthracyclines
Radiation therapy

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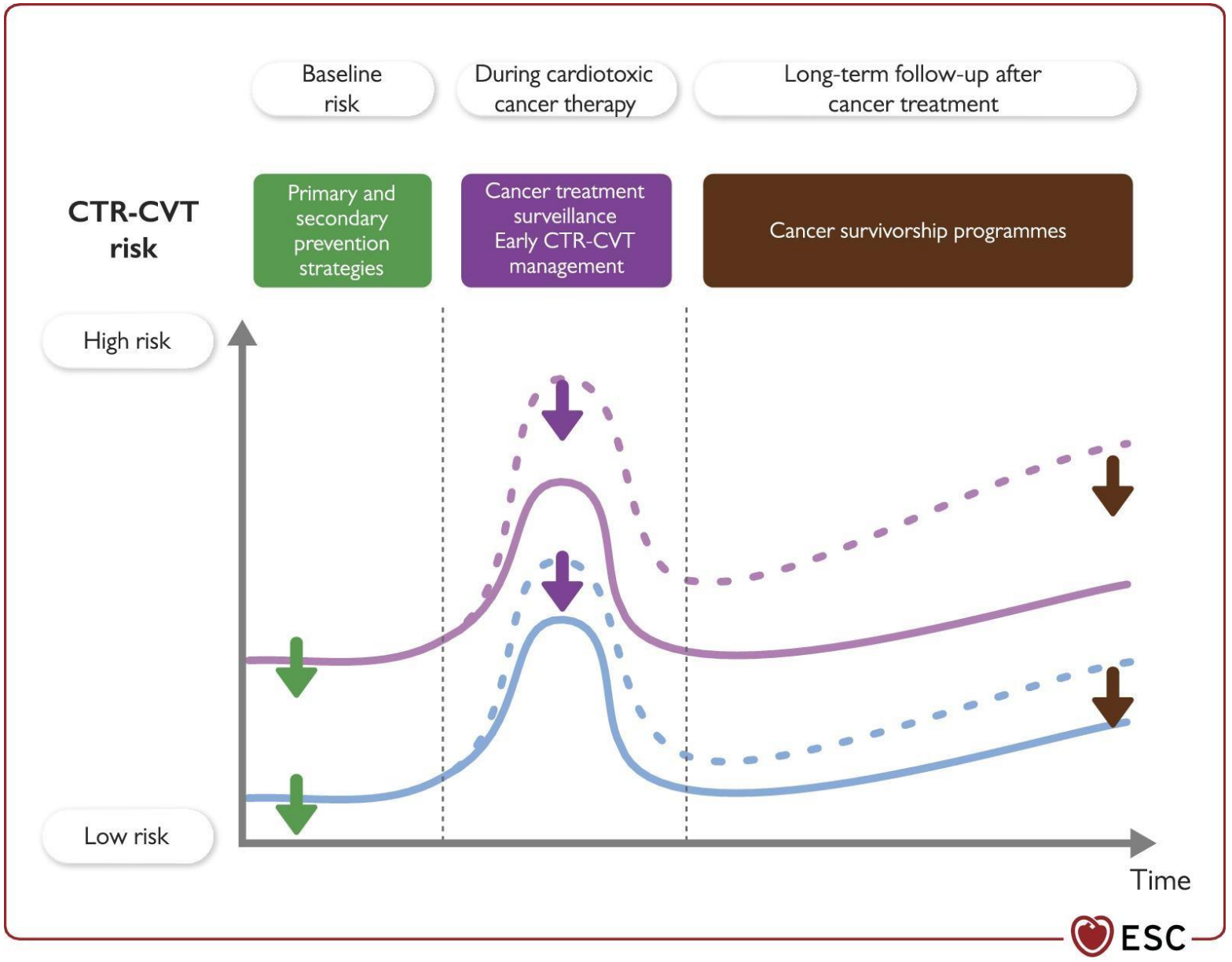
Dynamics of Cardiovascular Toxicity Risk



CTR-CVT, cancer therapy-related cardiovascular toxicity

Eur Heart J. 2022 Nov 1;43(41):4229-4361. doi: 10.1093/eurheartj/ehac244.

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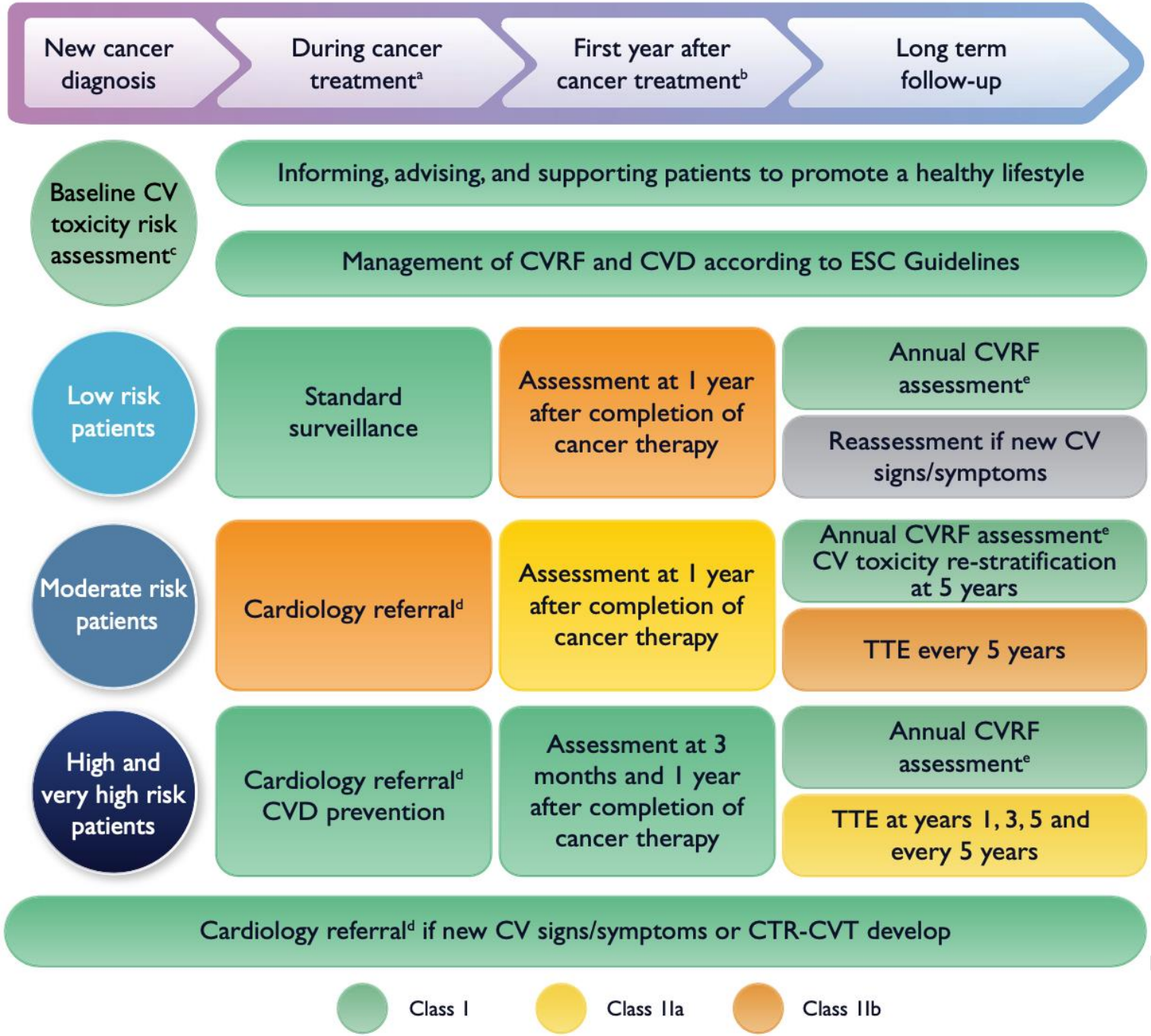

Cardiovascular Risk

- Baseline
- During
- Early after-
- Long term after cancer treatment

Eur Heart J. 2022 Nov 1;43(41):4229-4361. doi: 10.1093/eurheartj/ehac244.

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Patients at High-Risk

2016

- Treatment that includes any of the following:
  - High-dose anthracycline (eg, doxorubicin $\geq$ 250 mg/m^2, epirubicin $\geq$ 600 mg/m^2)
  - High-dose radiotherapy (RT; $\geq$ 30 Gy) where the heart is in the treatment field
  - Lower-dose anthracycline (eg, doxorubicin $<$ 250 mg/m^2, epirubicin $<$ 600 mg/m^2) in combination with lower-dose RT ($<$ 30 Gy) where the heart is in the treatment field
- Treatment with lower-dose anthracycline (eg, doxorubicin $<$ 250 mg/m^2, epirubicin $<$ 600 mg/m^2) or trastuzumab alone, and presence of any of the following risk factors:
  - Multiple cardiovascular risk factors ($\geq$ two risk factors), including smoking, hypertension, diabetes, dyslipidemia, and obesity, during or after completion of therapy
  - Older age ($\geq$ 60 years) at cancer treatment
  - Compromised cardiac function (eg, borderline low left ventricular ejection fraction [50% to 55%], history of myocardial infarction, $\geq$ moderate valvular heart disease) at any time before or during treatment
- Treatment with lower-dose anthracycline (eg, doxorubicin $<$ 250 mg/m^2, epirubicin $<$ 600 mg/m^2) followed by trastuzumab (sequential therapy)

J Clin Oncol. 2017 Mar 10;35(8):893-911. doi: 10.1200/JCO.2016.70.5400. Epub 2016 Dec 5. PMID: 27918725.

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  - High-dose radiotherapy (RT; ≥ 30 Gy) where the heart is in the treatment field
  - Lower-dose anthracycline (eg, doxorubicin < 250 mg/m^2, epirubicin < 600 mg/m^2) in combination with lower-dose RT (< 30 Gy) where the heart is in the treatment field
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2022

+ Immunotherapy

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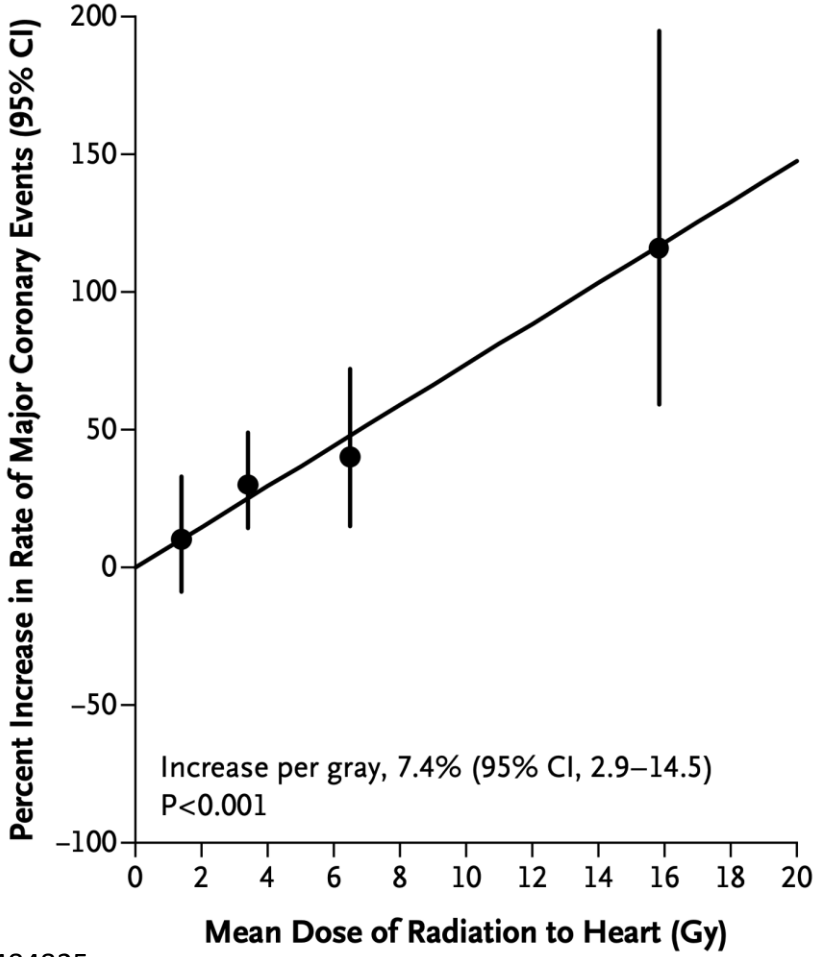
Linear Increase of Major Coronary Events with Mean Radiation Dose to the Heart

2168 women

Mean heart dose to the heart
0.03 Gy-27.72 Gy

Increased risk starting at 5 years, continuing to increase after 20 years



Darby SC et al. N Engl J Med. 2013 Mar 14;368(11):987-98. doi: 10.1056/NEJMoa1209825. PMID: 23484825.

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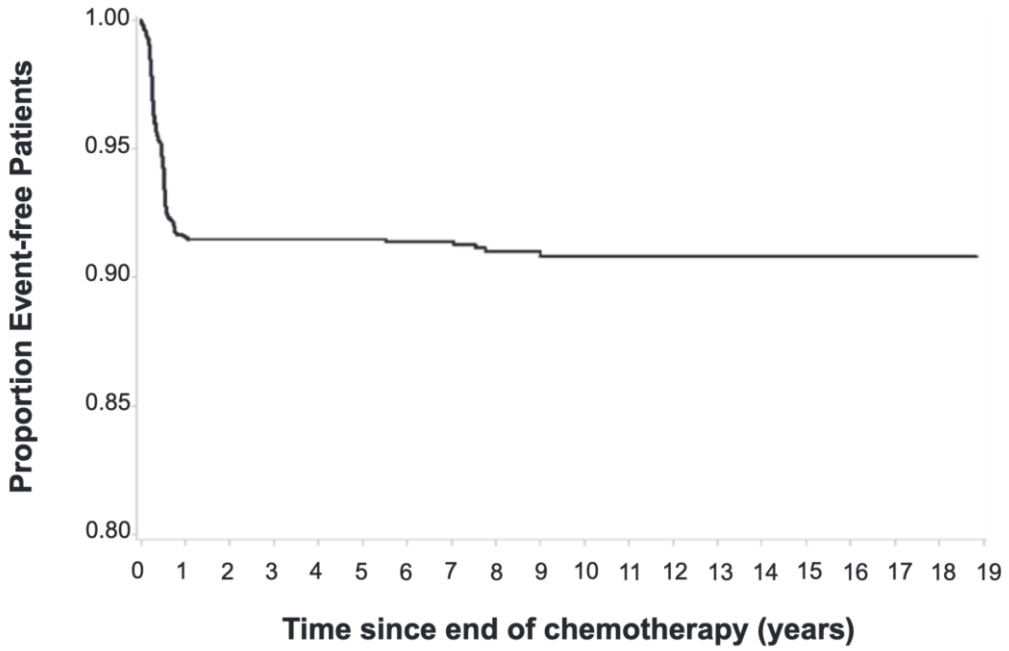
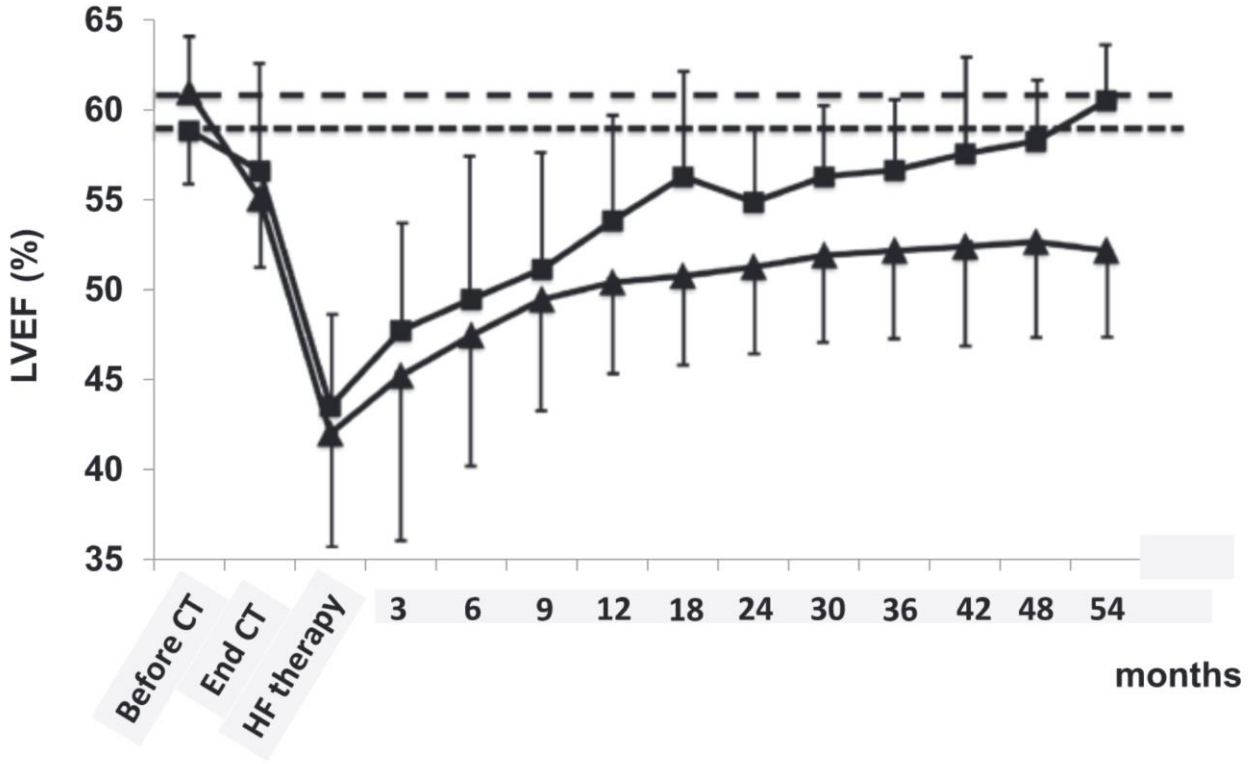
Early Detection of Anthracycline Cardiotoxicity and Improvement with HF Therapy





Cardinale D et al. Circulation. 2015 Jun 2;131(22):1981-8. doi: 10.1161/CIRCULATIONAHA.114.013777. Epub 2015 May 6. PMID: 25948538.

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Cardiotoxic Effects of Cancer Therapy

Cardiomyopathy

Hypertension

CAD, vasospasm

Arrhythmias

Valvular disease

Pericardial disease

Arterial/venous thrombosis

Anti-metabolites
Anthracyclines
Radiation therapy

Hormonal therapies
Molecular targeted therapies
- Tyrosine Kinase Inhibitors
- Proteasome inhibitors

Bone marrow transplant
Immune checkpoint inhibitors
Genetically engineered therapies
- Chimeric antigen receptor T-cells

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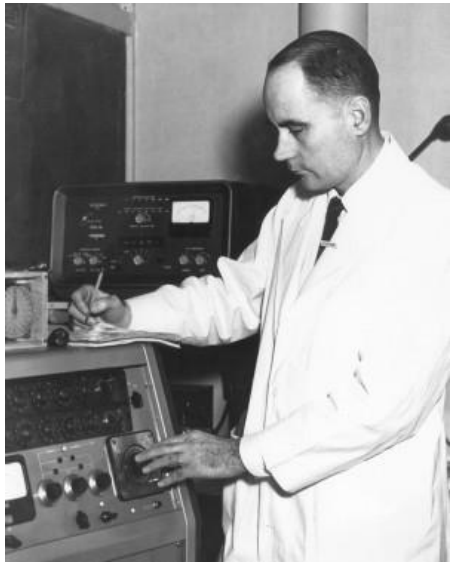
The Beginning

- 1950's bone marrow transplantation (BMT) - pioneered in by E. Donnall Thomas
- 1990 Nobel Prize in Physiology or Medicine
- 1957-2012 > 1million patients transplanted

INTRAVENOUS INFUSION OF BONE MARROW IN PATIENTS RECEIVING RADIATION AND CHEMOTHERAPY*

E. Donnall Thomas, M.D.,† Harry L. Lochte, Jr., M.D.,‡ Wan Ching Lu, Ph.D.,§ and Joseph W. Ferrebee, M.D.¶

Cooperstown, New York, and Boston, Massachusetts



Thomas ED, et al. N Engl J Med. 1957 Sep 12;257(11)
https://www.nobelprize.org/prizes/medicine/1990/thomas/biographical/

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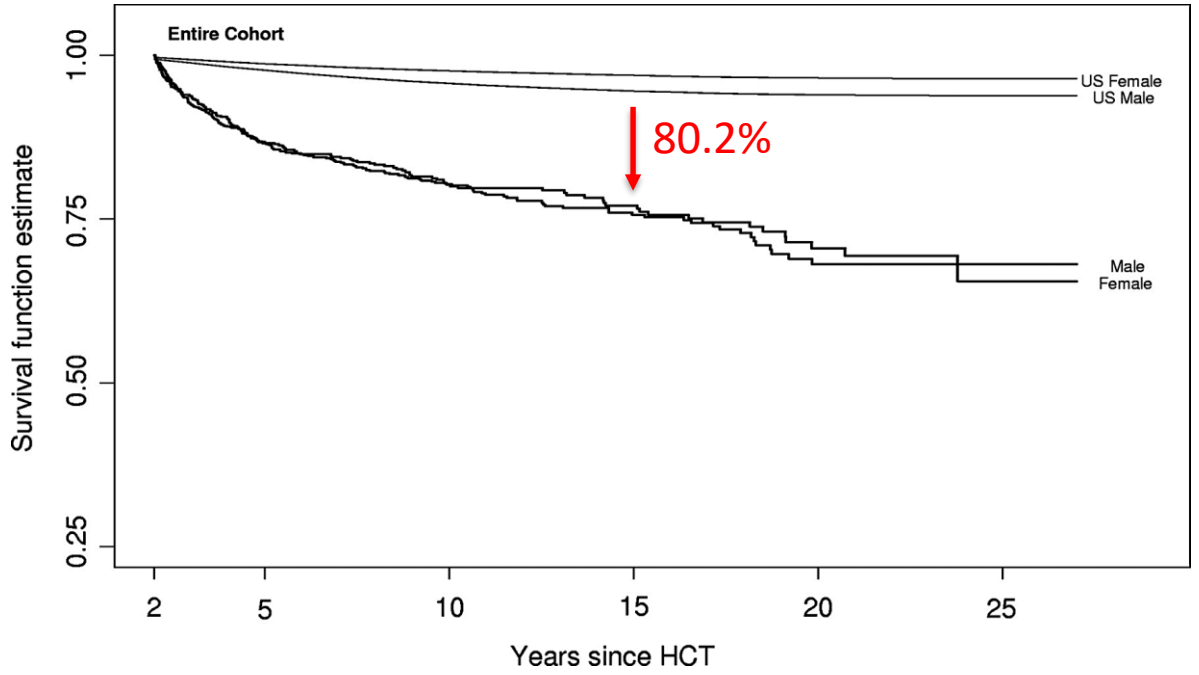
Long-term Survival after HSCT

- Bone Marrow Transplant Survivor Study
  - 1479 individuals, >2 years survival
  - Median age 25.9 years
  - Median follow-up 9.5 years
  - Survival 80.2% at 15 years
  - Standardized mortality ratio 2.2



>240,000 survivors in 2020
>500,000 survivors in 2030

Bhatia S et al. Blood. 2007 Nov 15;110(10):3784-92.

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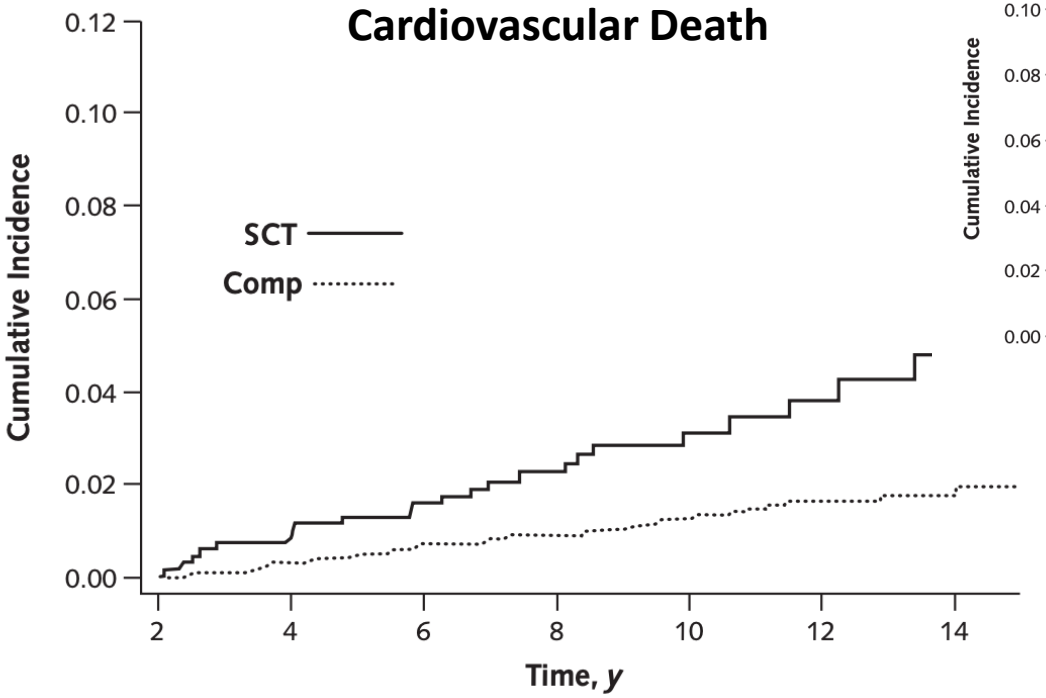
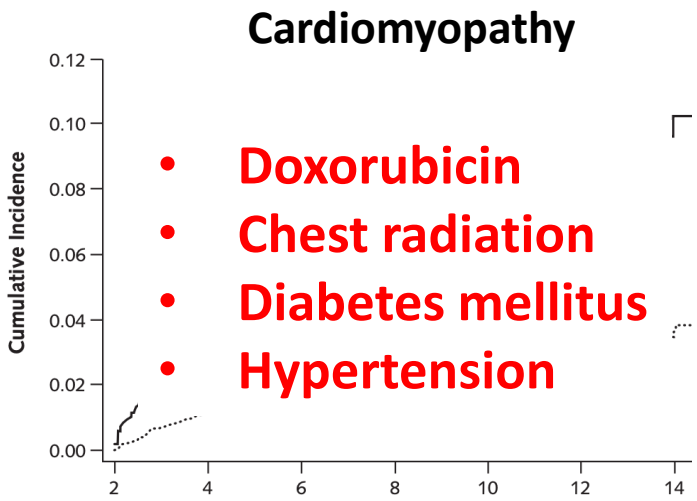
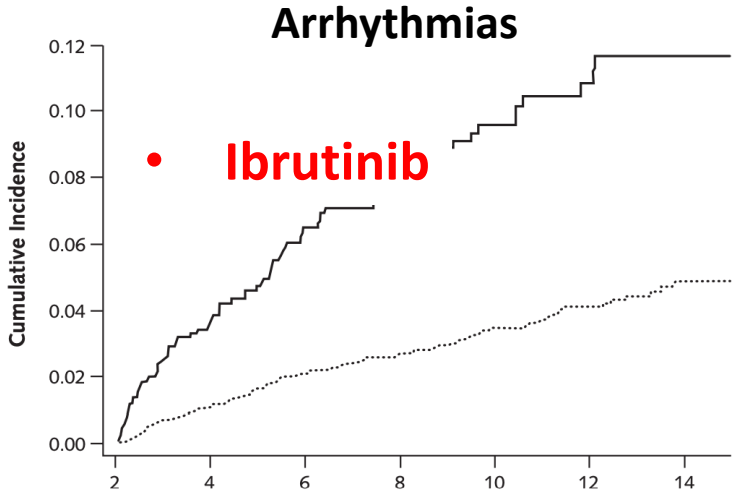
Cardiovascular Complications of HSCT

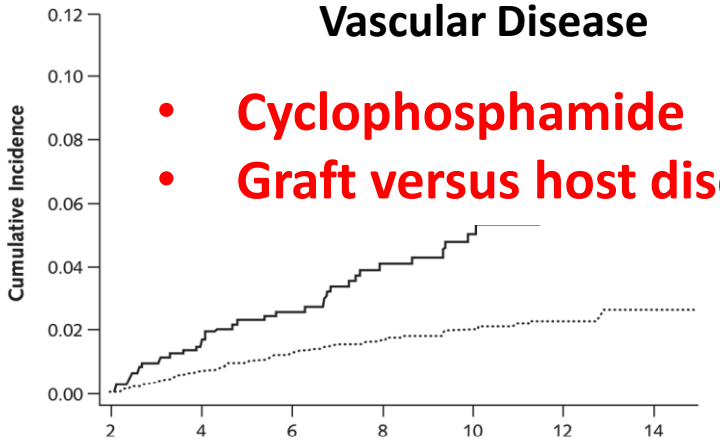




- Doxorubicin
- Chest radiation
- Diabetes mellitus
- Hypertension



- Ibrutinib



- Cyclophosphamide
- Graft versus host disease

- Fred Hutchinson Cancer Research Center
  - 1481 individuals, >2 years survival

Chow EJ et al. Ann Intern Med. 2011 Jul 5;155(1):21-32

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Cardiotoxic Effects of Cancer Therapy

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Hypertension

CAD, vasospasm

Arrhythmias

Valvular disease

Pericardial disease

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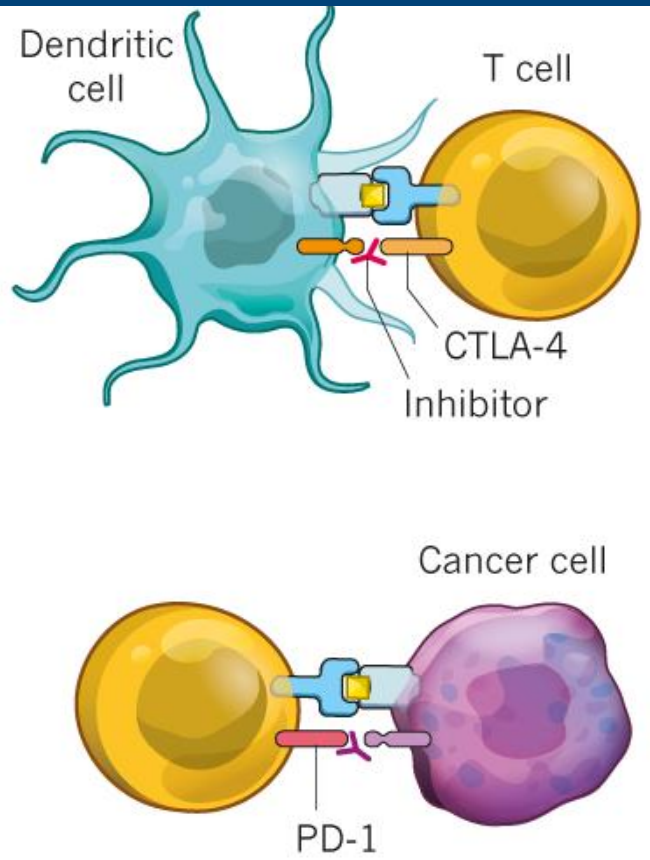
Immune Checkpoint Inhibitors (ICI)



Medicine 2018

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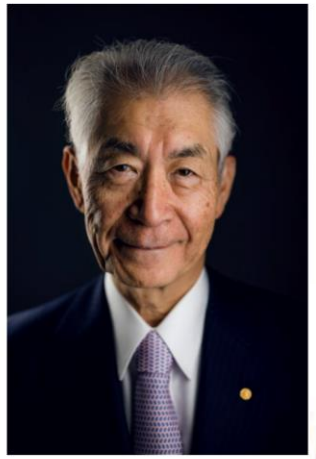
James P. Allison

Prize share: 1/2



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Tasuku Honjo

Prize share: 1/2

The Nobel Prize in Physiology or Medicine 2018 was awarded jointly to James P. Allison and Tasuku Honjo "for their discovery of cancer therapy by inhibition of negative immune regulation."

Ledford, Nature, 2018

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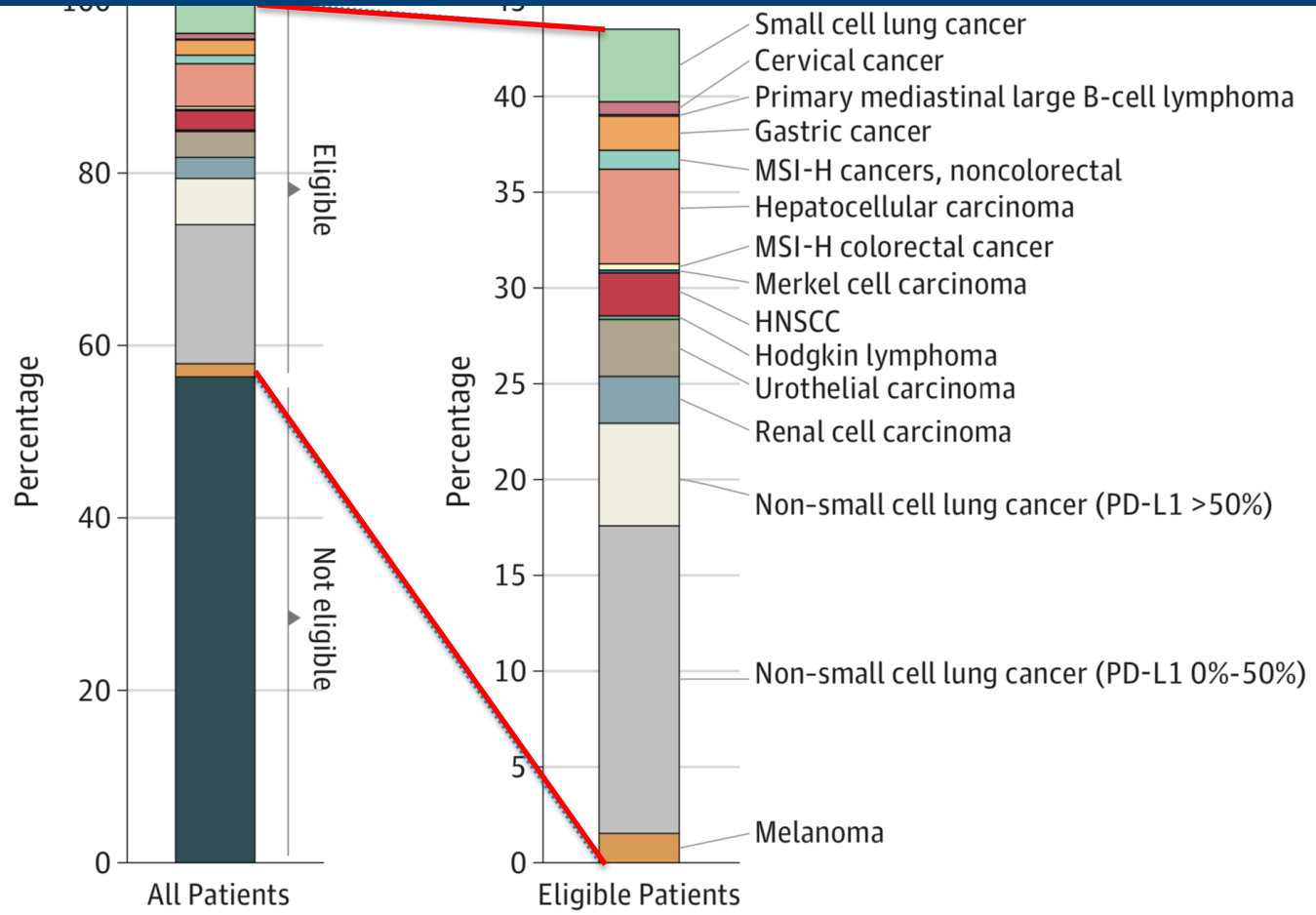
Increased Survival with ICI Therapy

- **Survival 52% at 5 years in patents with stage III-IV melanoma**
- **First line of therapy from 1.5% in 2011 to 43.6% of cancers in 2018**



Larkin, NEJM, 2019; Haslam, Jama Network Open, 2019; Upadhaya, Nat Rev Drug Discov, 2020

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Increased Survival with ICI Therapy

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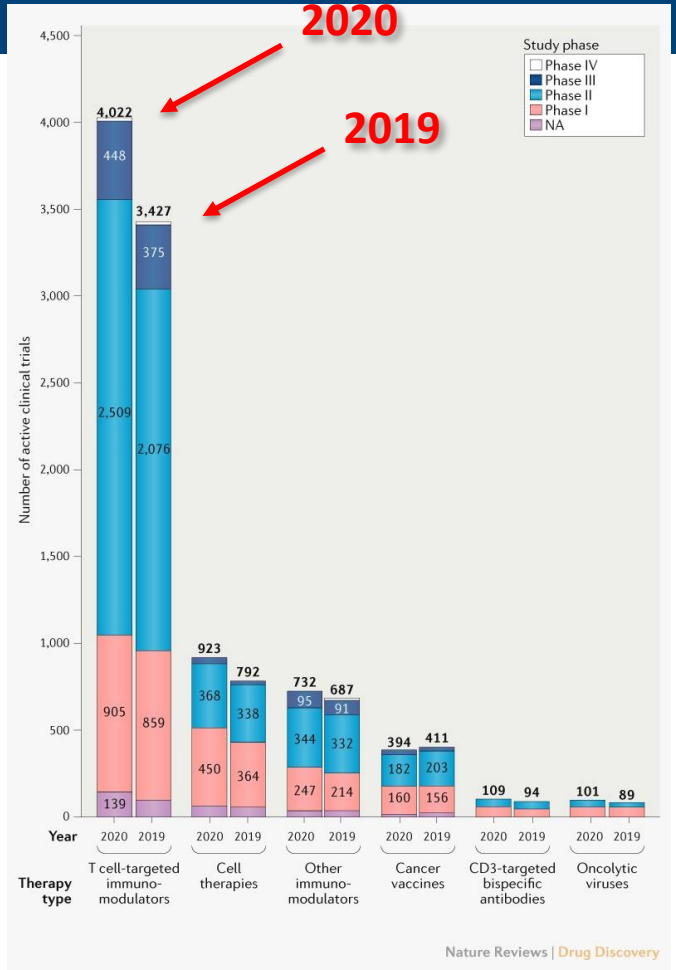
- **More than 4000 active clinical trials in 2020**



Larkin, NEJM, 2019; Haslam, Jama Network Open, 2019; Upadhaya, Nat Rev Drug Discov, 2020

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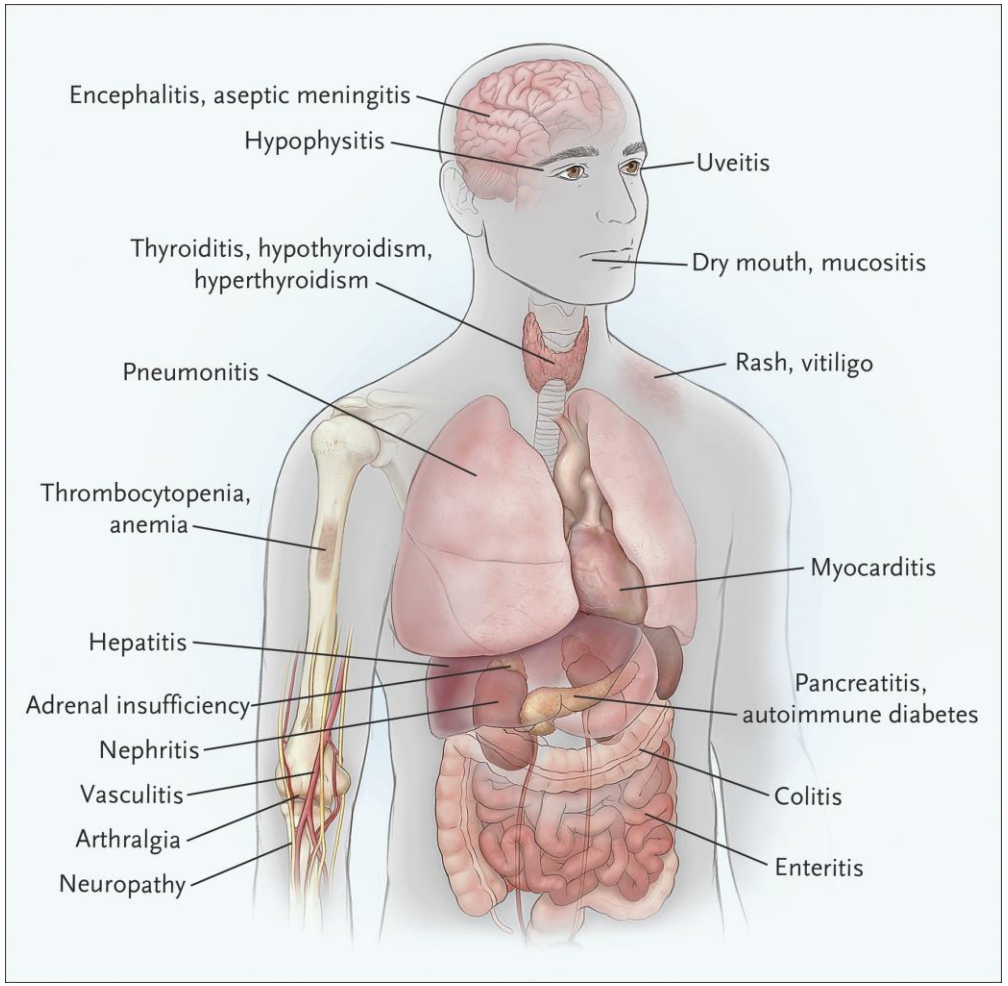
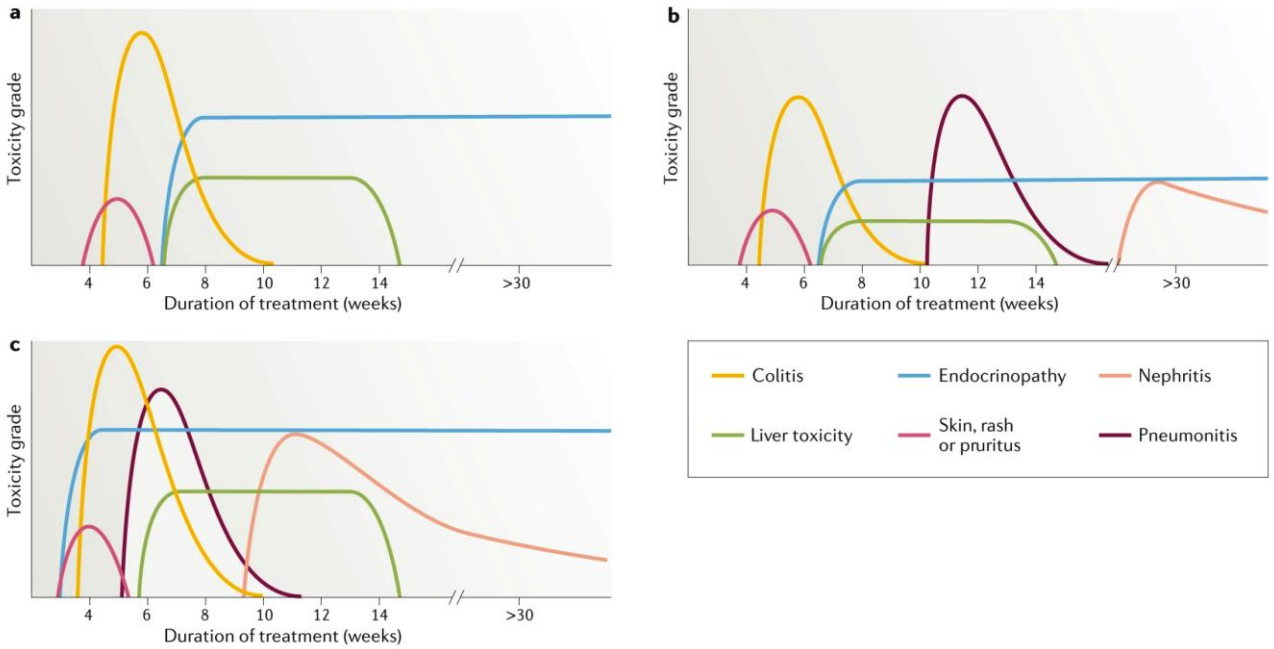
ICI-associated immune related adverse events





Postow, NEJM, 2018; Salem, The Lancet, 2018

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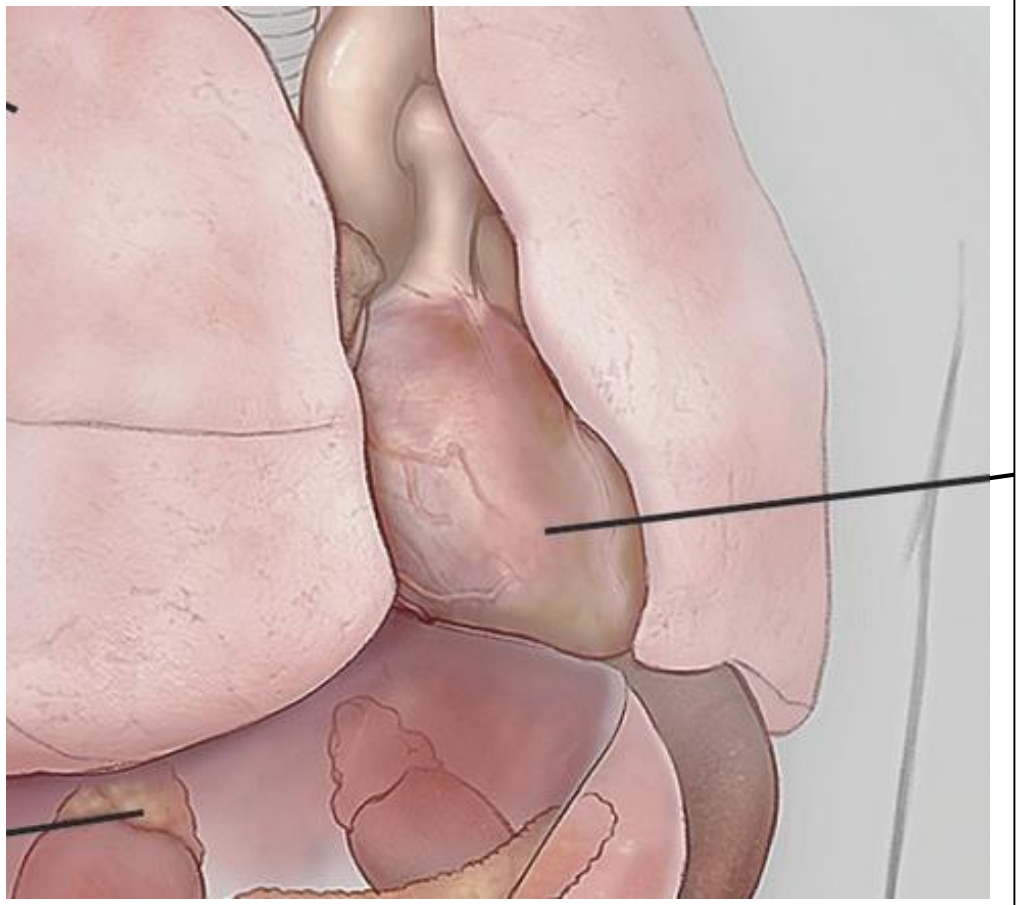

Cardiovascular toxicities

- Myocarditis
- Pericardial disease
- Vasculitis
- Stress cardiomyopathy (Takotsubo)
- Atherosclerosis

Johnson, NEJM, 2016; Escudier, Circulation, 2017; Postow, NEJM, 2018; Salem, Lancet Oncol, 2018; Drobni, Circulation, 2020

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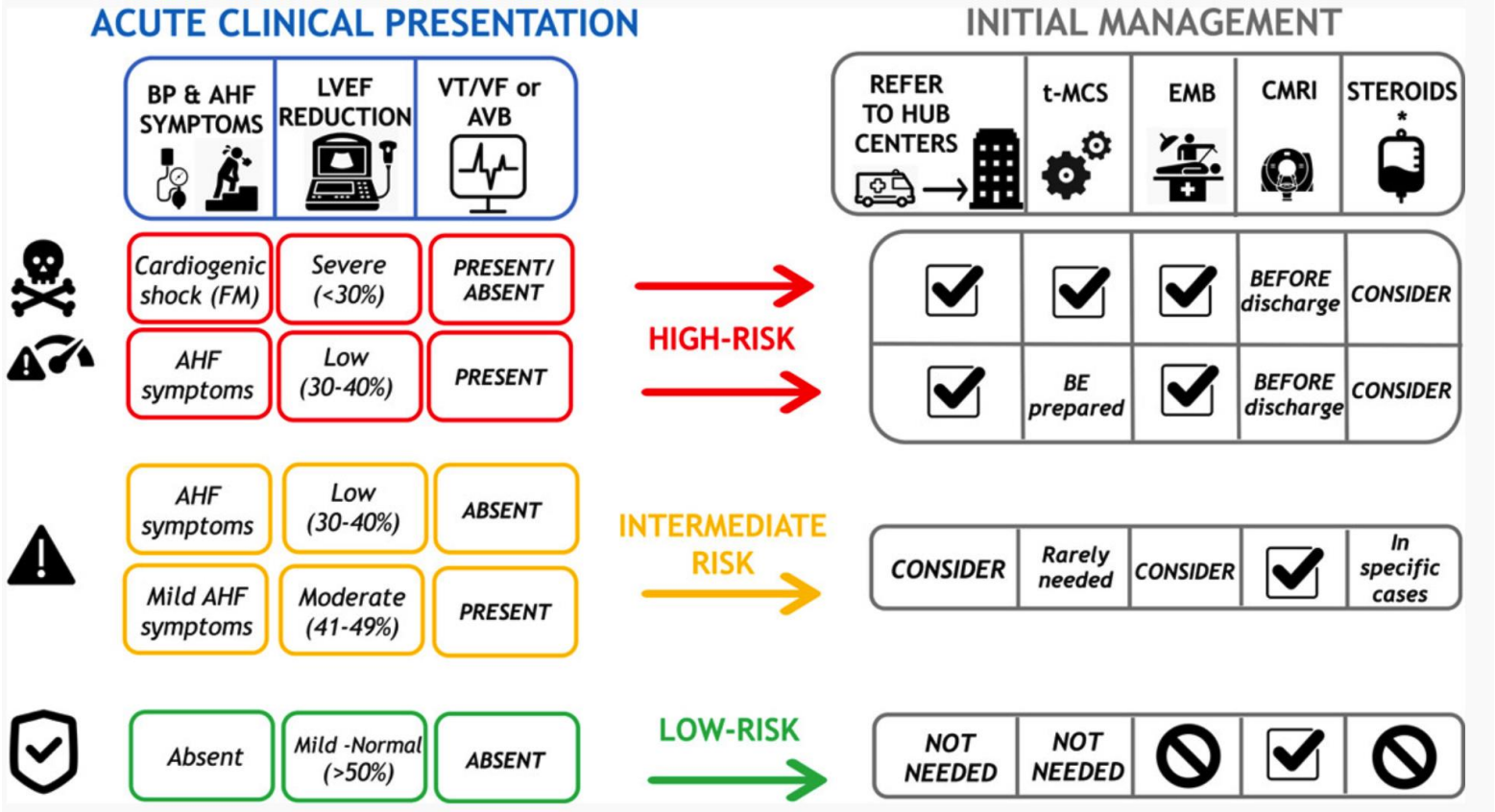
Risk based approach to acute myocarditis



Amirati et al, Circ Heart Fail, 2020

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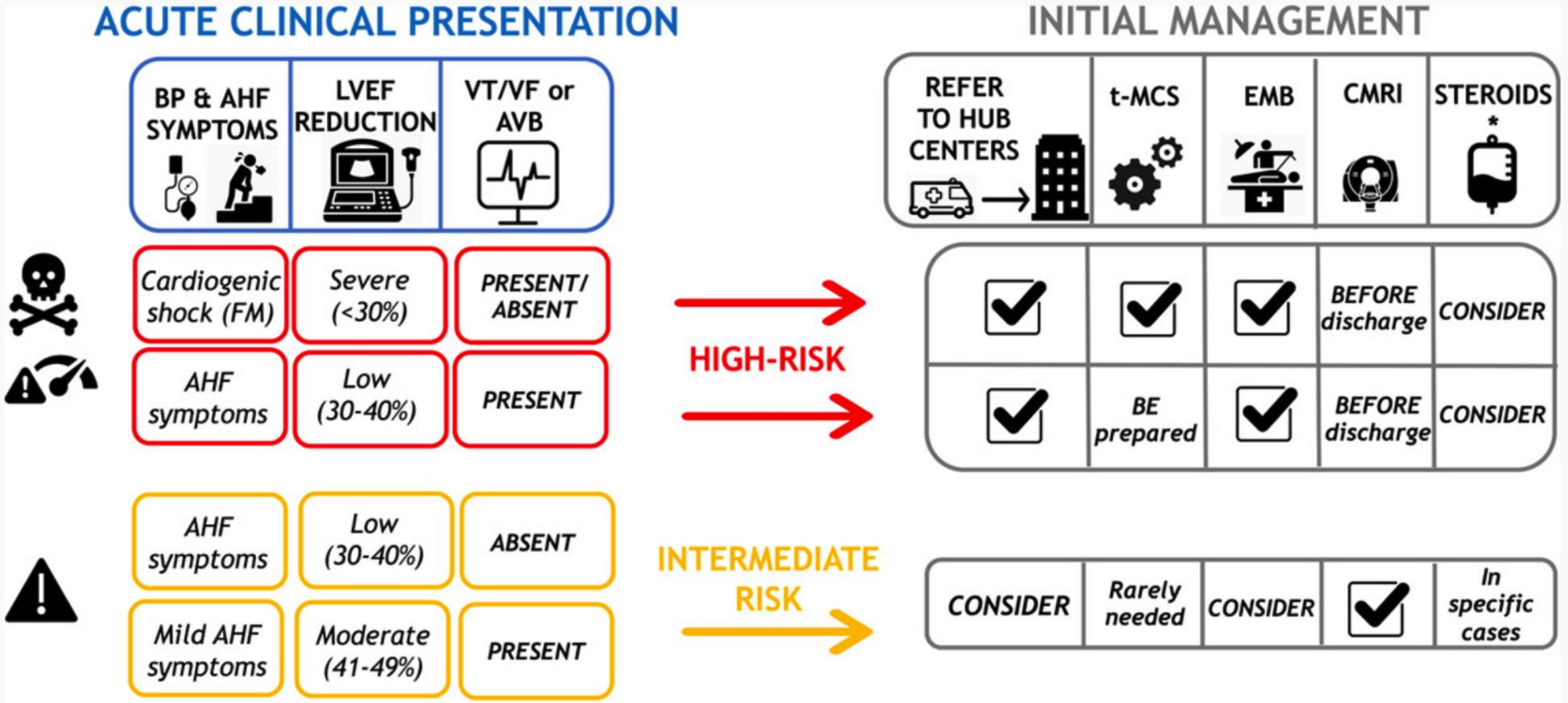

Amirati et al, Circ Heart Fail, 2020

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Which Patients Require Surveillance in First Year after Anticancer Treatment?

- ≥ High baseline CV risk
- High-risk anticancer treatment
- ≥ Moderate anticancer therapy related complications
- New CV symptoms or abnormal tests at the end of anticancer therapy

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Objectives

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- Long-term follow-up and prevention of chronic complications
- Life after cancer

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After Cancer Experience Program

ACE adult appointments

We facilitate transition to adult survivorship services where the personalized comprehensive care continues. Within the adult primary care survivorship clinic, ACE patients are able to have a targeted survivorship visit, or have both their primary care and survivorship needs taken care of by our team. Our goal is to ensure all components of survivorship care are addressed at your visit (acute concerns, late and long term effects, and preventive health). Working closely with the UTSW Simmons Comprehensive Cancer Center, survivors of cancer are able to access expanded support services such as social work, exercise, behavioral health/psychology/ and nutrition. We have locations for our adult program that include:

Ft Worth: Primary Care Cancer Survivorship Clinic

Address:
400 W Magnolia Ave
Ft Worth, TX 76104
817-645-3900
(The clinic is located within the Moncrief Cancer Institute on the first floor)

Dallas: Primary Care Cancer Survivorship Clinic

Address:
5939 Harry Hines Blvd; Ste 303
Dallas, TX 75390
214-645-3900
(The clinic is located within the Family Medicine Practice Office)

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Director, Cardio-Oncology Program
.

Kathleen Zhang, M.D.

Alvin Chandra, M.D.

- Expedited consultations to minimize delays in cancer treatment
- Flexible scheduling options to coordinate timely office visits and cardiac testing
- Telemedicine consults to improve patient access and safety
- Close partnership with hematology and oncology experts to provide individualized care

UT Southwestern
Medical Center

utswmed.org/cardio-onc 214-645-0402 cardio-onc@utsouthwestern.edu

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