Lab Briefings Webinar

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May 14, 2025

WashU Medicine

Beyond the Label

Novel Applications of Cardiac Biomarkers

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CardinalHealth

Disclosures

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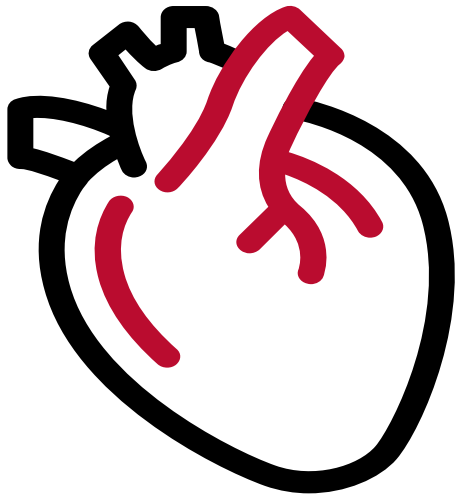
Abbott Laboratories
Beckman Coulter
Roche Diagnostics
Sebia
The Binding Site
Siemens Healthineers
Cepheid
Qiagen

Consulting & Advisory Boards

Werfen
Abbott Laboratories
Cytovale
Roche Diagnostics
BD

Learning Objectives



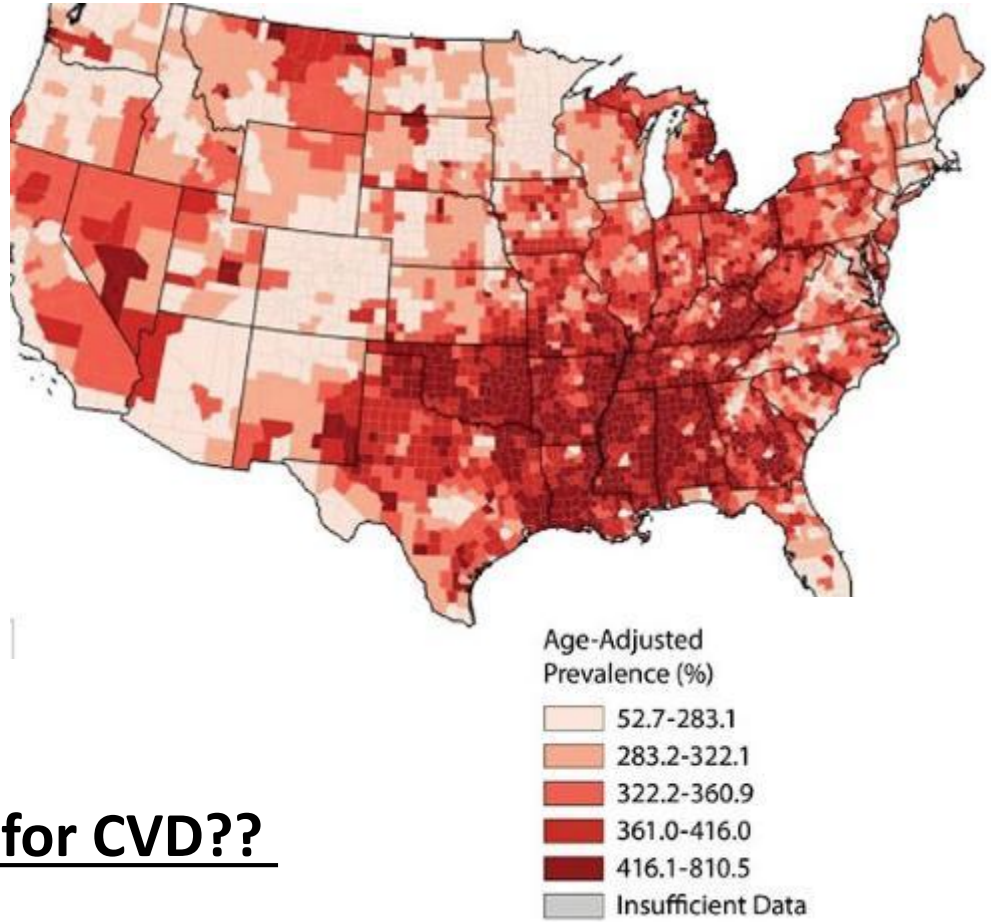
01 Explain the primary clinical applications of troponin and natriuretic peptides.

02 Evaluate the emerging and non-traditional uses of cardiac biomarkers in clinical practice.

03 Recognize key limitations and gaps in the literature related to biomarker cutpoints and clinical study design.

Cardiovascular disease (CVD) is leading cause of US mortality

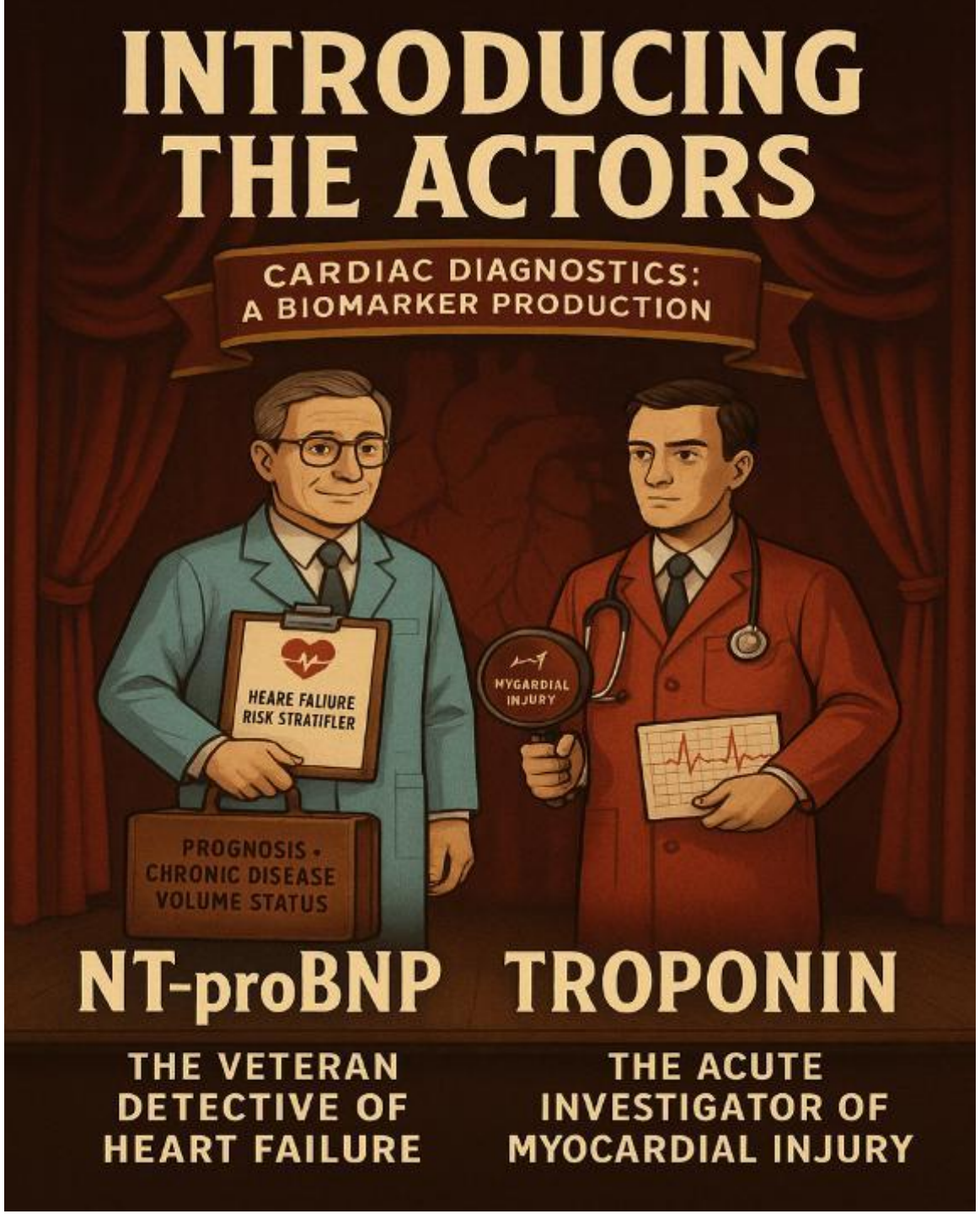
- 702,880 people in 2022 died from CVD
  - ~20% of all deaths in 2022
- Primarily due to myocardial infarction (MI), heart failure (HF), and arrhythmia
- Risk factors: diabetes, obesity, inactivity, excessive alcohol use



Can we use biomarkers to detect patients at risk for CVD??

CDC. About heart disease . https://www.cdc.gov/heart-disease/about/index.html

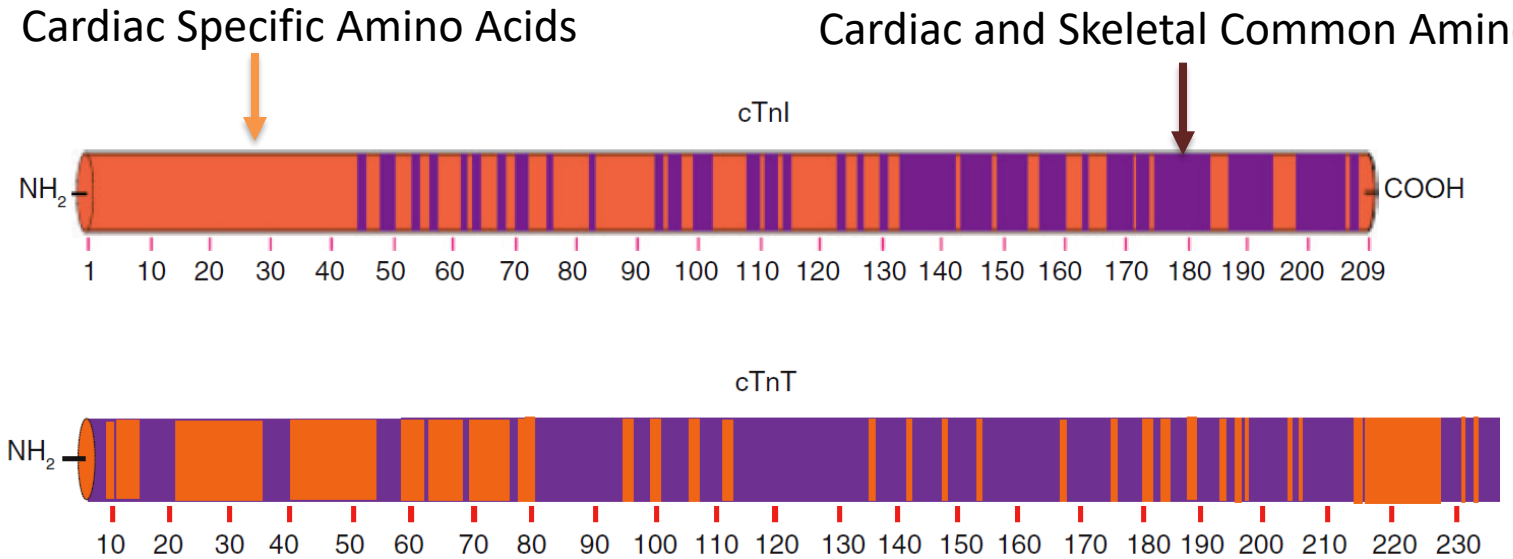
Introducing the Biomarkers



Cardiac troponin (cTn) is associated with cardiac injury

- cTns are **cardiac tissue specific**
  - Not expressed in any other tissue

- cTn assays **are specific** for myocardial injury



Diagnosis 2019; 6(3): 189–201

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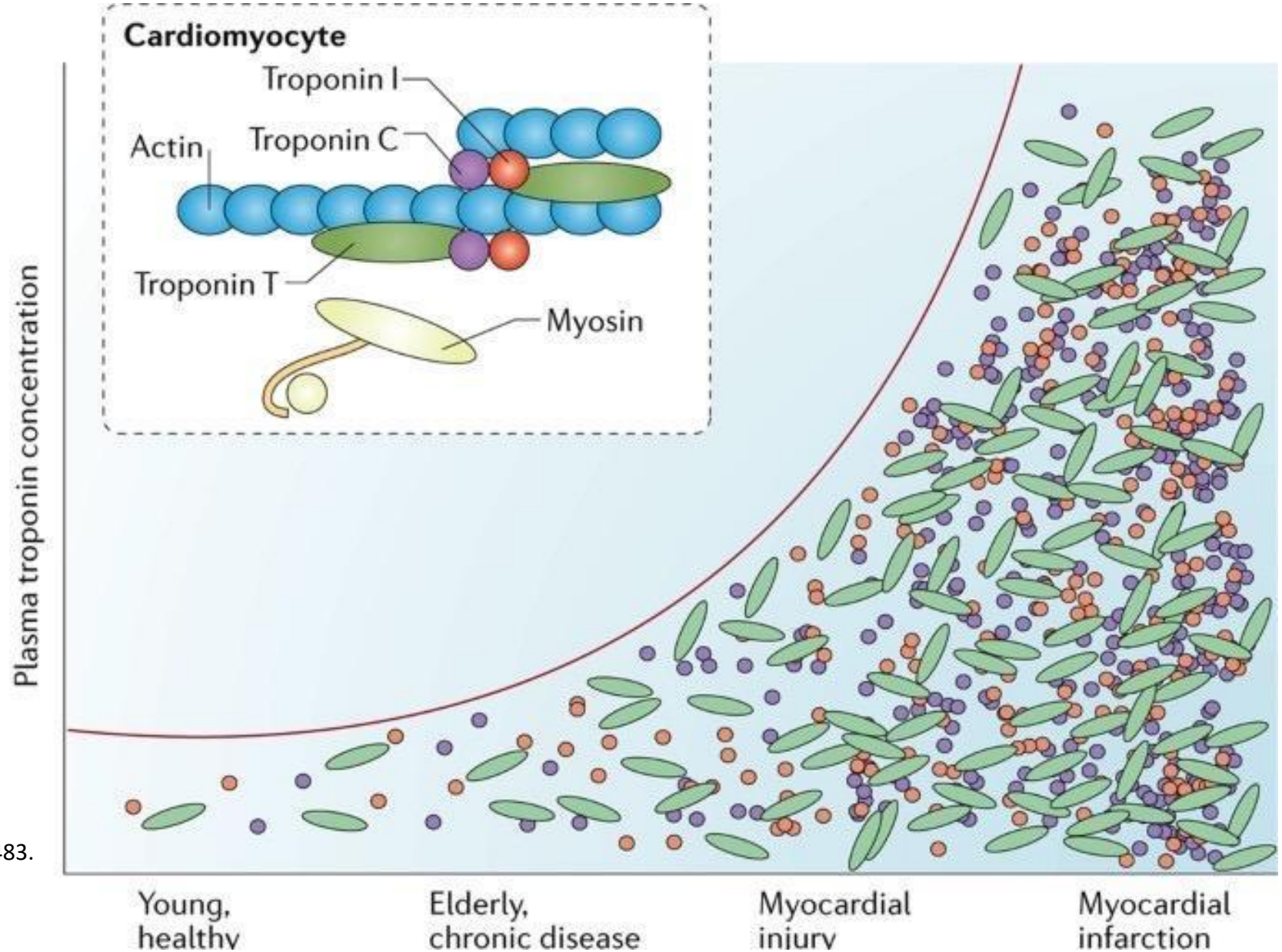
Troponin function and elevation after injury



Nat Reviews Cardiology 2017;14:472-483.

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Myocardial Injury = Elevated cTn

Criteria for myocardial injury

Detection of an elevated cTn value above the 99th percentile URL is defined as myocardial injury. The injury is considered acute if there is a rise and/or fall of cTn values.

99th % URL = 99th percentile upper reference limit

Myocardial Infarction = acute myocardial injury + Ischemia

J Am Coll Cardiology 2018;72: 2231-64.

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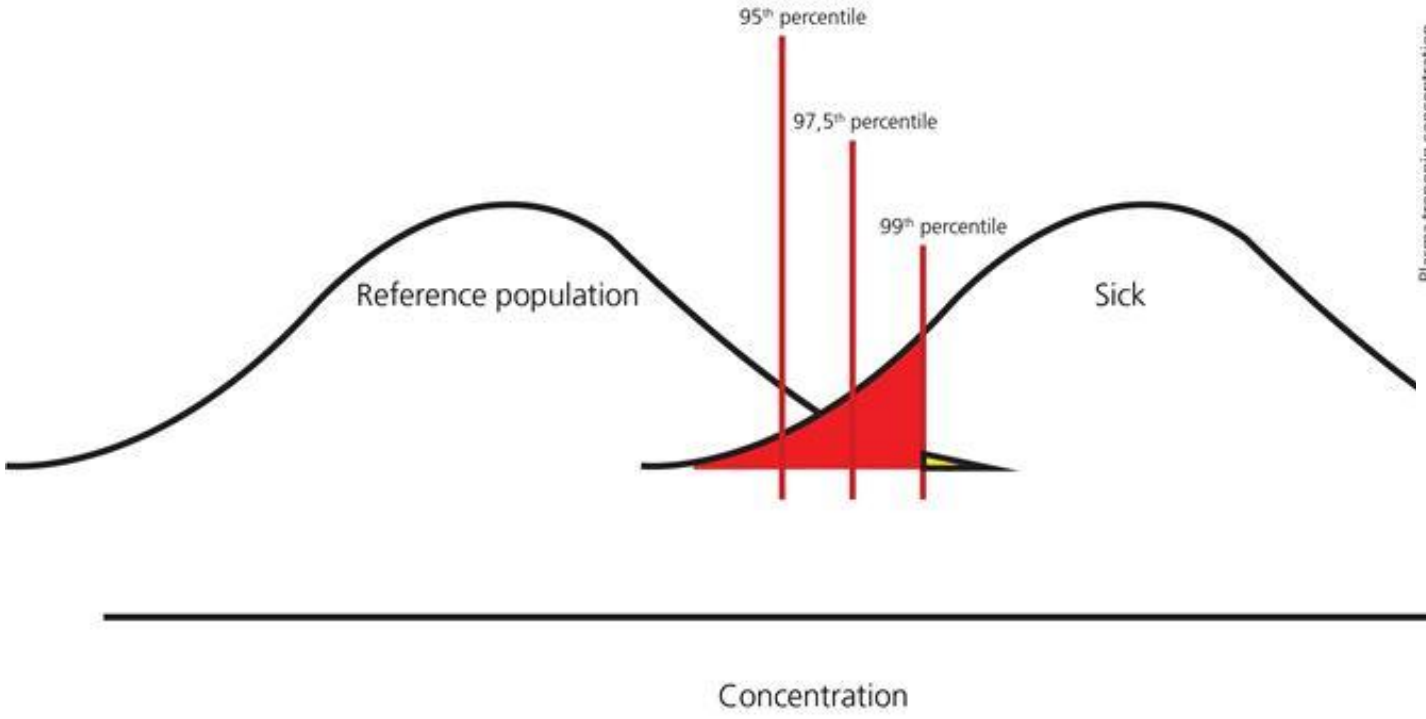
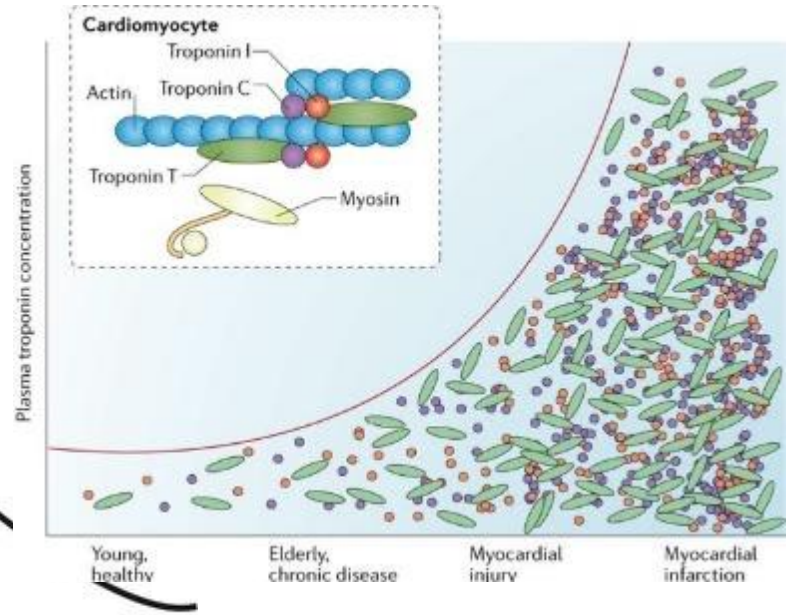
Defining "Healthy" and the 99th % URL?

99th % is universally endorsed as reference cutoff for myocardial injury

- Higher cutoff = missed diagnoses
- Lower cutoff = decreased specificity





Clin Chem 2022;68: 1022-30.

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IFCC Recommendations for deriving the 99th % URL

- 400 males
- 400 females
- 4 lots of reagent
- 18—80 years old

Clin Chem 2022;68: 1022-30.

Table 1. Conditions that should be excluded from the reference population.

Condition	Screening tool
All known cardiovascular or cardiac diseases	Reported in questionnaire
Treatment for hyperlipidemia	Medication reported in questionnaire
Treatment for hypertension	Medication reported in questionnaire
Subclinical heart disease	Exclude if NT-proBNP >125 ng/L or BNP >35 ng/L (38)
Diabetes	Treatment (including diet) reported in questionnaire Exclude if HbA1c ≥48 mmol/mol (≥6.5%), fasting glucose ≥7.1 mmol/L (126 mg/dL), 2 hour plasma glucose during oral tolerance test (100 g) or a randomly measured glucose ≥11.1 mmol/L (200 mg/dL) (39)
Chronic renal disease	eGFR <60 mL/min/1.73 m^2 or urine albumin/creatinine ratio > 3 mg/mmol (>30 mg/g) (40)
Abnormal BMI	<18 m^2/kg or >35 m^2/kg
Smoking	Reported in questionnaire
Chronic disease that could affect the heart (cancer, lung, liver, unstable or nontreated thyroid disease, autoimmune diseases)	Reported in questionnaire
Recent acute hospitalization (within the last 3 months)	Reported in questionnaire
Pregnancy	Reported in questionnaire
For biotin sensitive assays only: Ongoing treatment with biotin (within one week)	Reported in questionnaire

NT-proBNP, N terminal pro brain natriuretic peptide; BNP, Brain natriuretic peptide; HbA1c, Hemoglobin A1c; eGFR, estimated glomerular filtration rate.

Reference intervals will depend on the population assessed

And the instrument that you use…

Sex-Specific 99th Percentile Upper Reference Limits for High Sensitivity Cardiac Troponin Assays Derived Using a Universal Sample Bank

Fred S. Apple,[a,*] Alan H. B. Wu,[b] Yader Sandoval,[c] Anne Sexter,[d] Sara A. Love,[a] Gary Myers,[e] Karen Schulz,[f] Show-Hong Duh,[g] and Robert H. Christenson[g]

	Abbott Architect		Roche 801		Siemens Vista		Ortho Clinical Vitros	
	Male 99%	Female 99%	Male 99%	Female 99%	Male 99%	Female 99%	Male 99%	Female 99%
Manufacturer	34	16	22	14	55	33	19	16
Universal Sample Bank	20	13	16	10	68	44	16	5

426 men and 417 women

Exclusions: questionnaire for CVD, NTproBNP > 125 ng/L, eGFR < 60 ml/min/1.73 m^2

Clin Chem 2020;66:434-444.
Am J of Med 2016;129:354-365.

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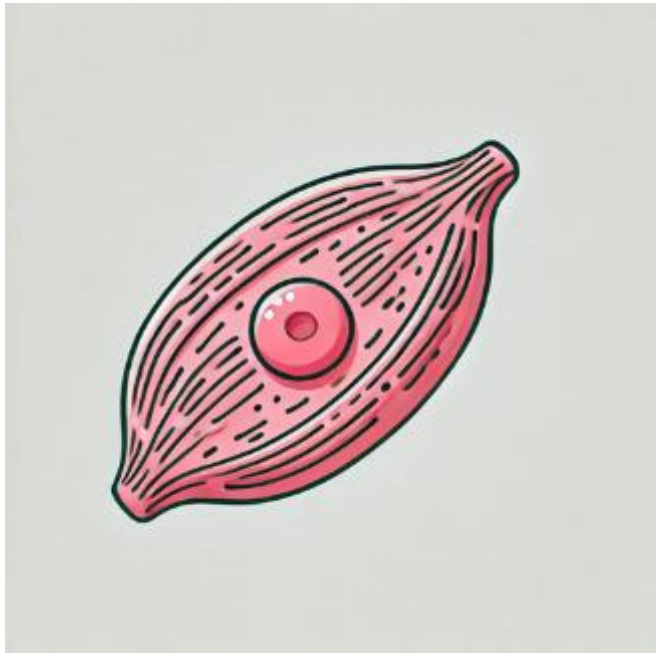
Take home for troponin elevations

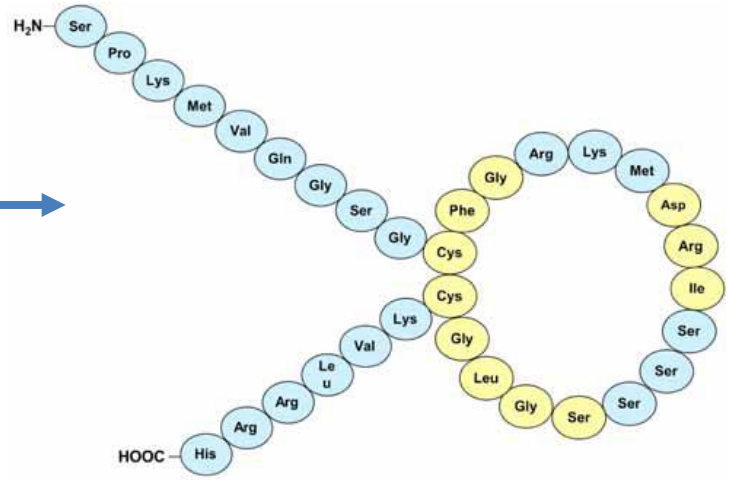
- Troponin elevation is due to myocardial injury
- Definition of elevation may vary based on a host of variables
- 99th% Upper reference limit varies dramatically between assays

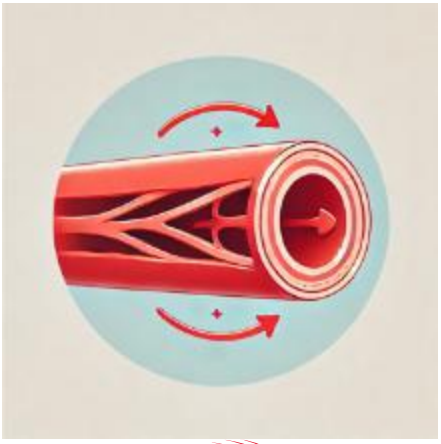
Natriuretic Peptides (NPs) and Myocardiocyte Stretch



Stretch

BNP Release





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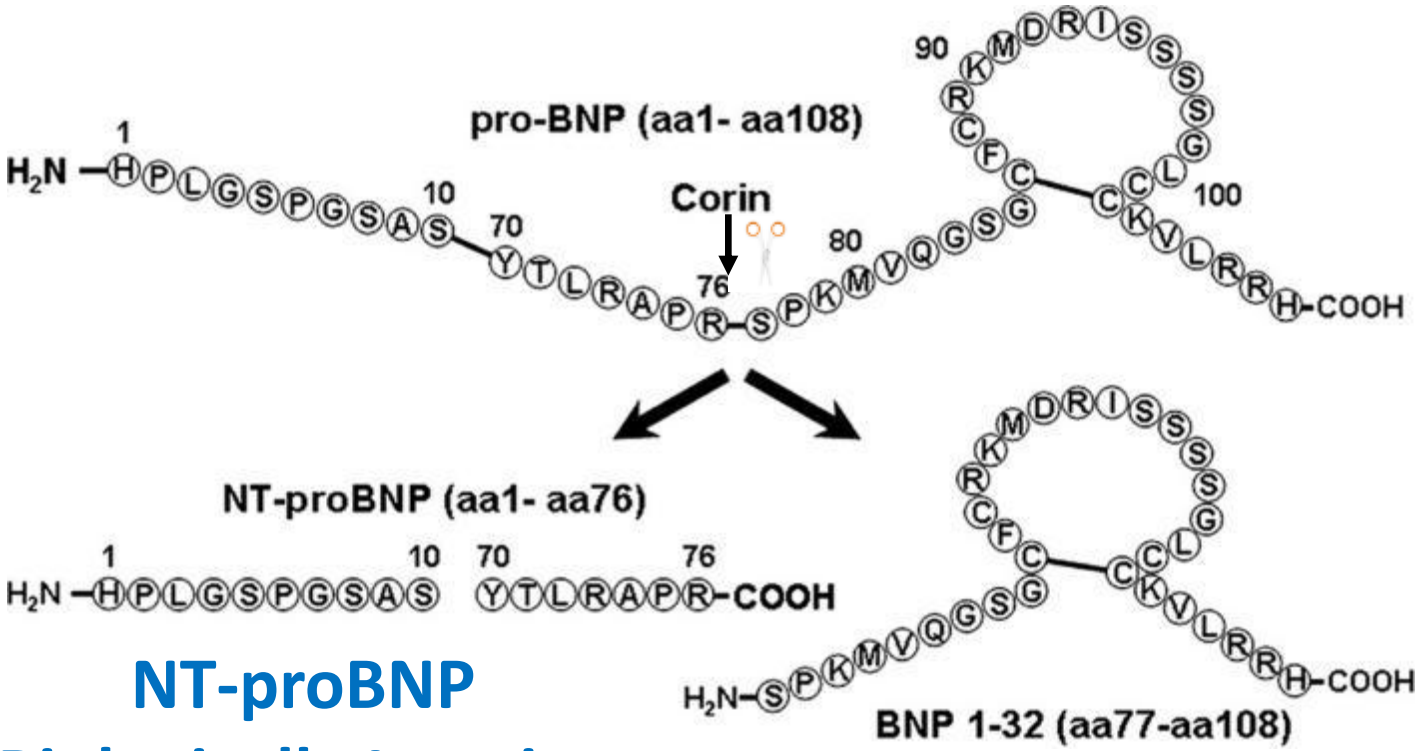
NP Biochemistry



NT-proBNP
Biologically Inactive

BNP
Biologically Active

Produced 1:1 Molar ratio

Heublein D M et al. Hypertension. 2007;49:1114-1119

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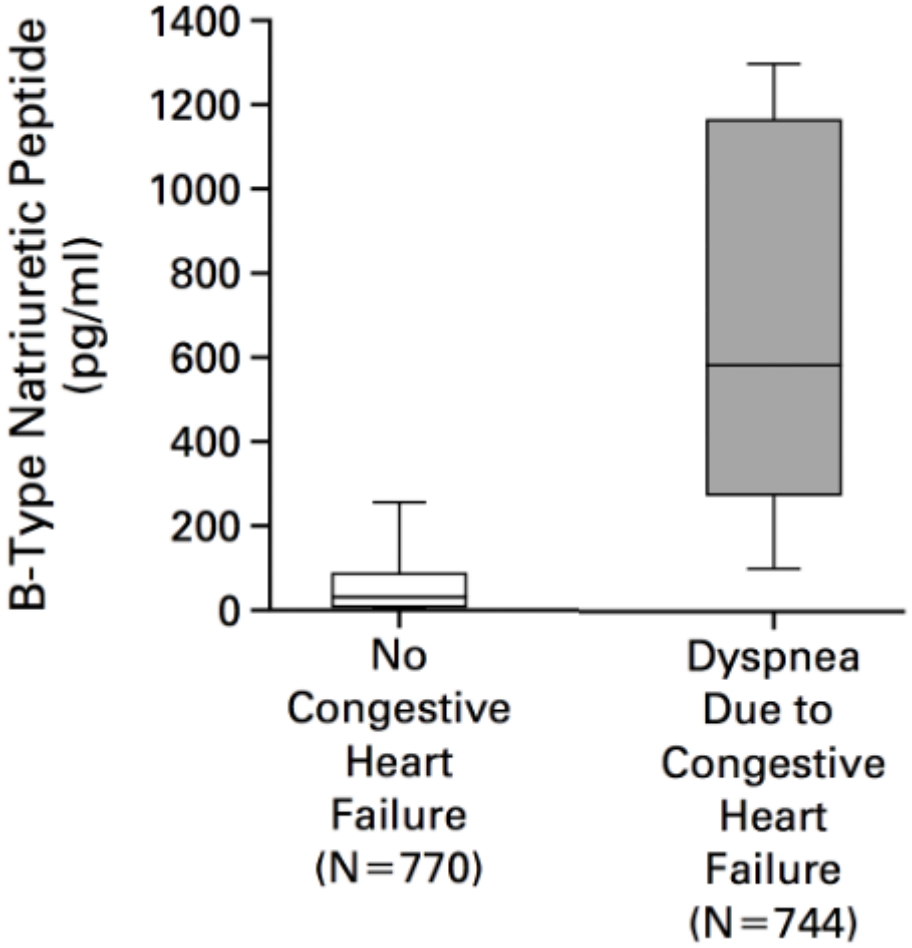
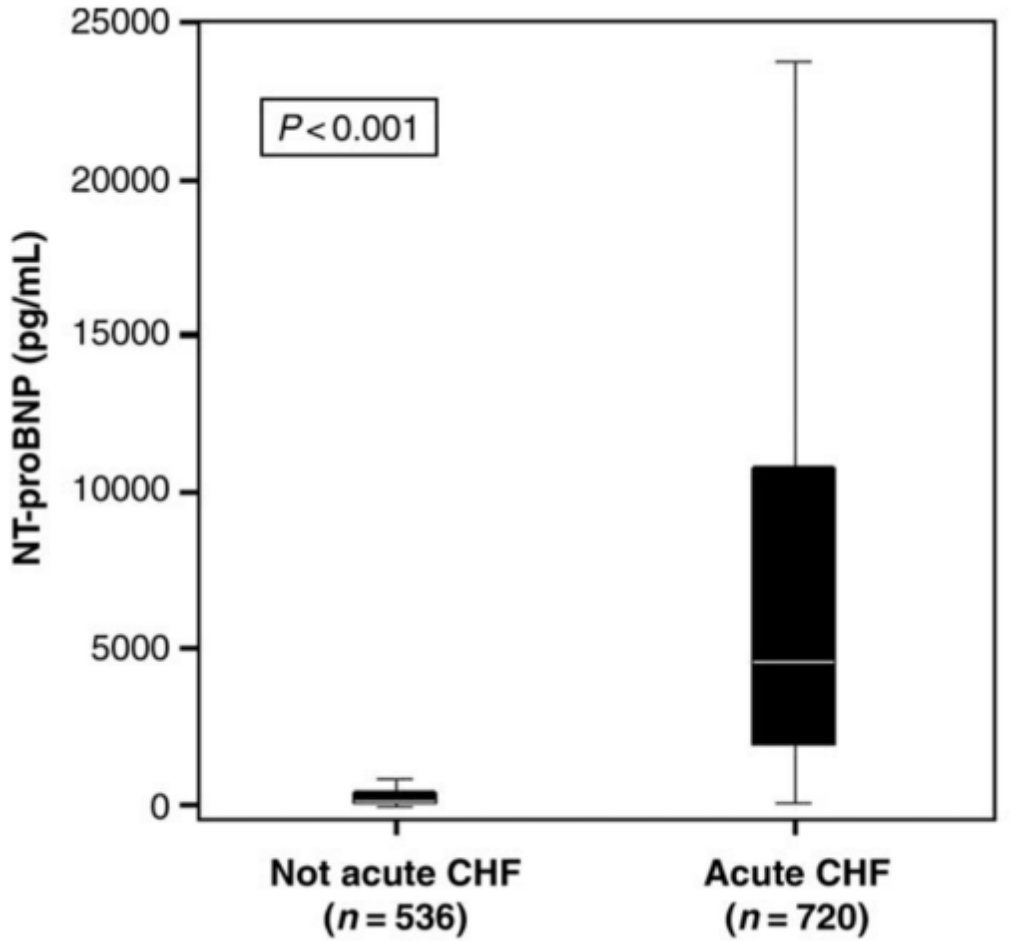
Performance of NP's for Diagnosis of Heart Failure



BNP: Sensitivity =90%, specificity= 76%

Maisel AS *et al.* NEJM. 2002; 347:161-7.



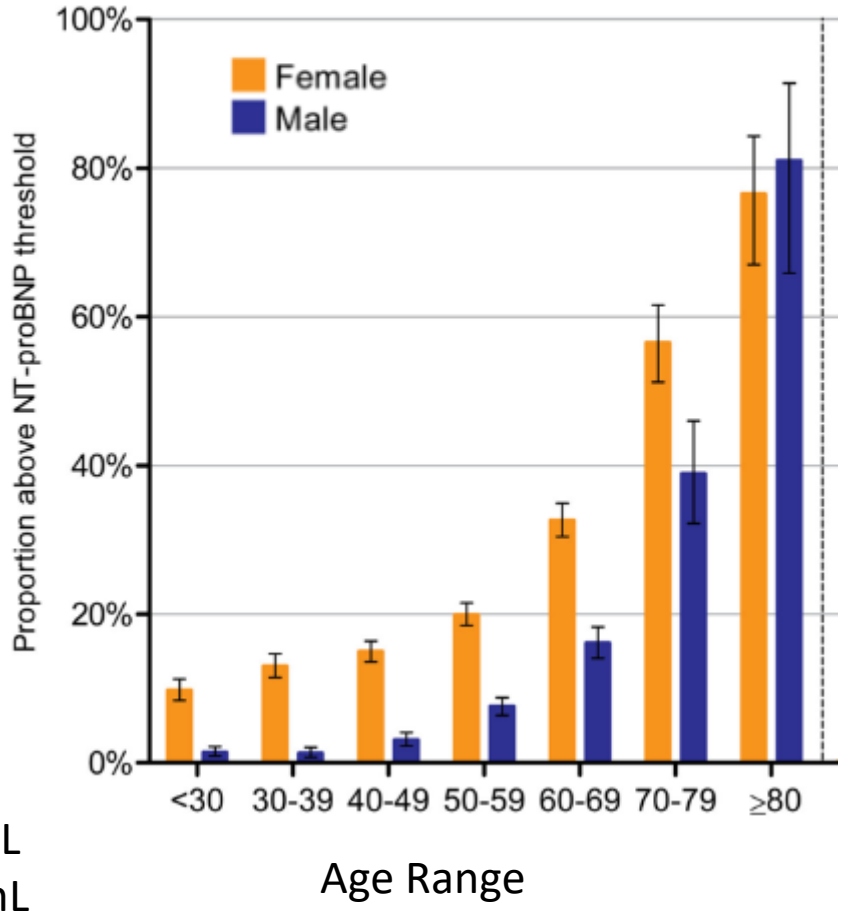
NT-proBNP: Sensitivity = 90%, Specificity = 84%

Januzzi JL *et al.* Eur. Heart Journal. 2006; 27:330-7.

Identifying the ideal NP thresholds

Table 7 Natriuretic peptide levels supporting definition of heart failure

	Ambulatory	Hospitalized/ decompensated
BNP, pg/ml	≥35	≥ 100
NT-proBNP, pg/ml	≥ 125	≥ 300



NT-proBNP Manufacturer Reference interval = Males < 75 = 64 pg/mL
Females < 75 = 95 pg/mL

Bozkurt B et al. Eur J Heart Fail. 2021; 23:352–380

Welsh P et al. Circulation Heart Failure. 2022;10:e009427

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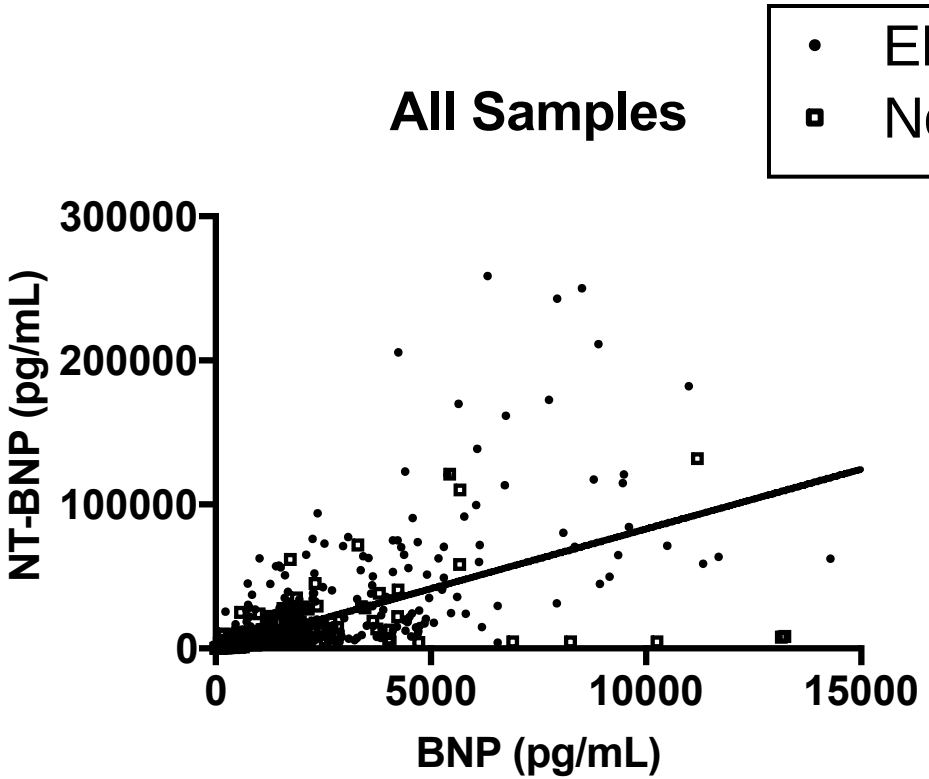
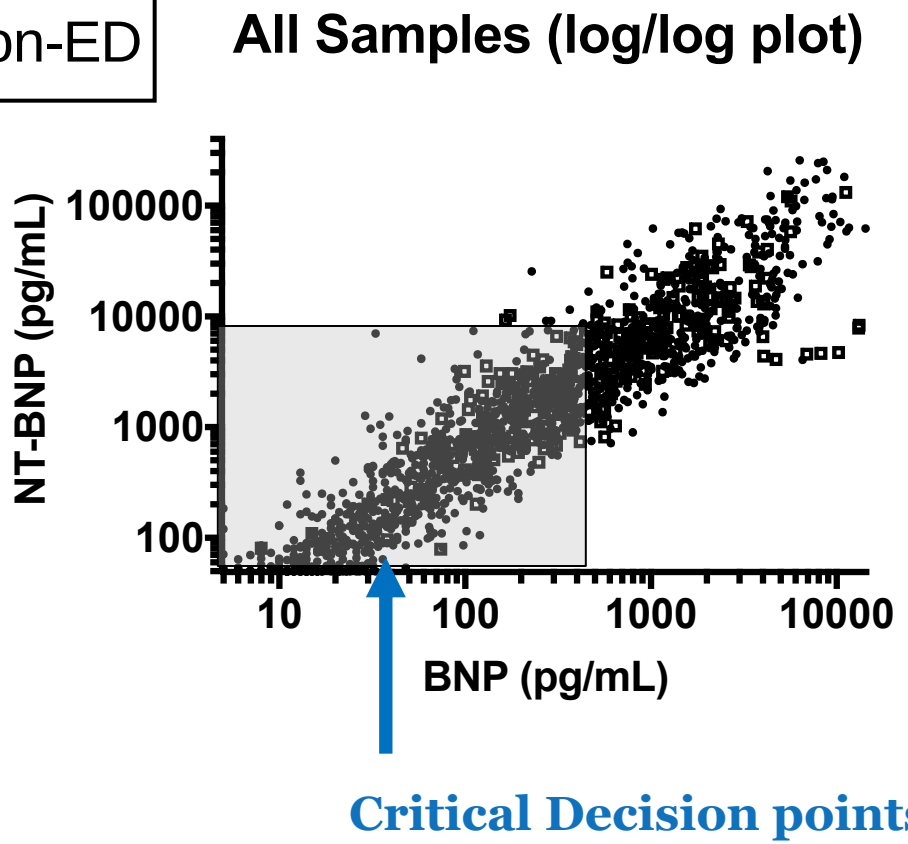
Modest correlation between BNP and NT-proBNP



Spearman Correlation r = 0.71



Critical Decision points

Kappa (95% CI)
0.70 (.69-.72)

933 (72%)	Concordant
340 (26%)	Partially Discordant
23 (2%)	Fully Discordant

Farnsworth CW et al. Clin Biochem 2018;59:50-55.

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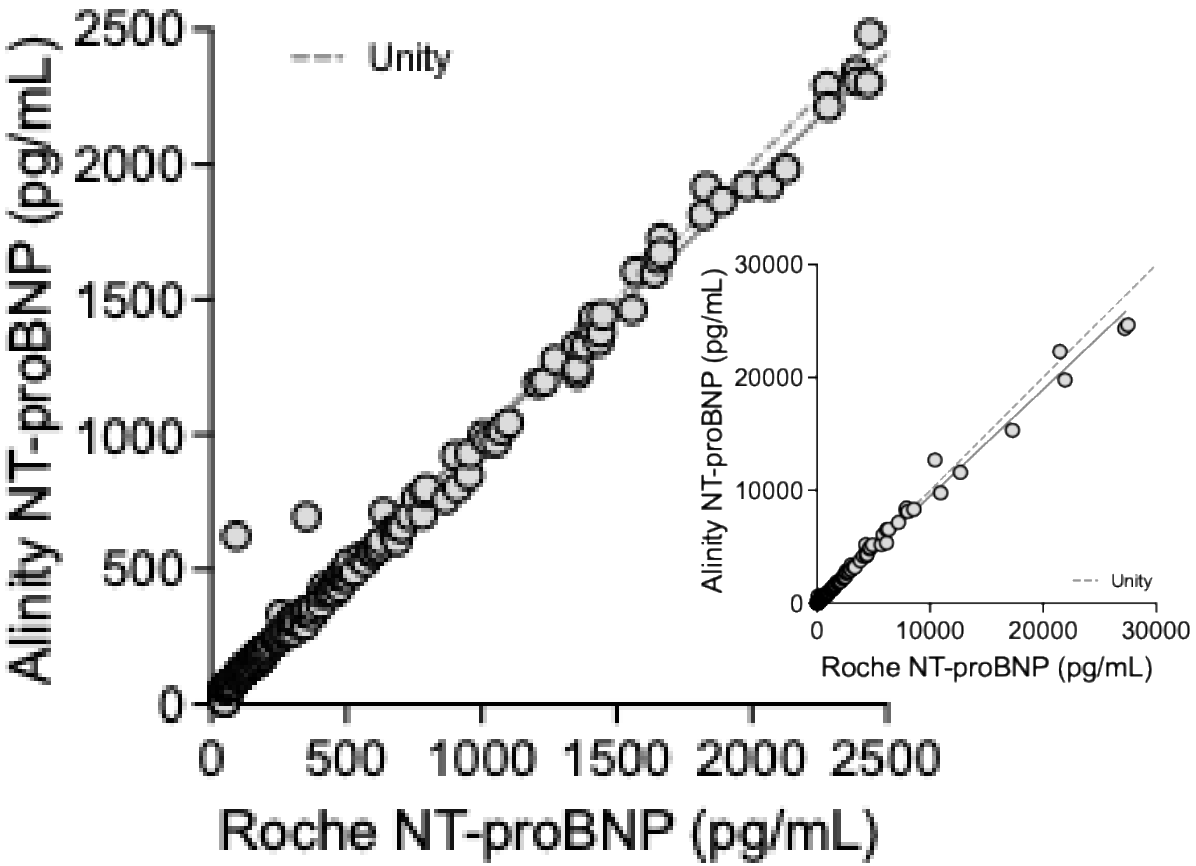
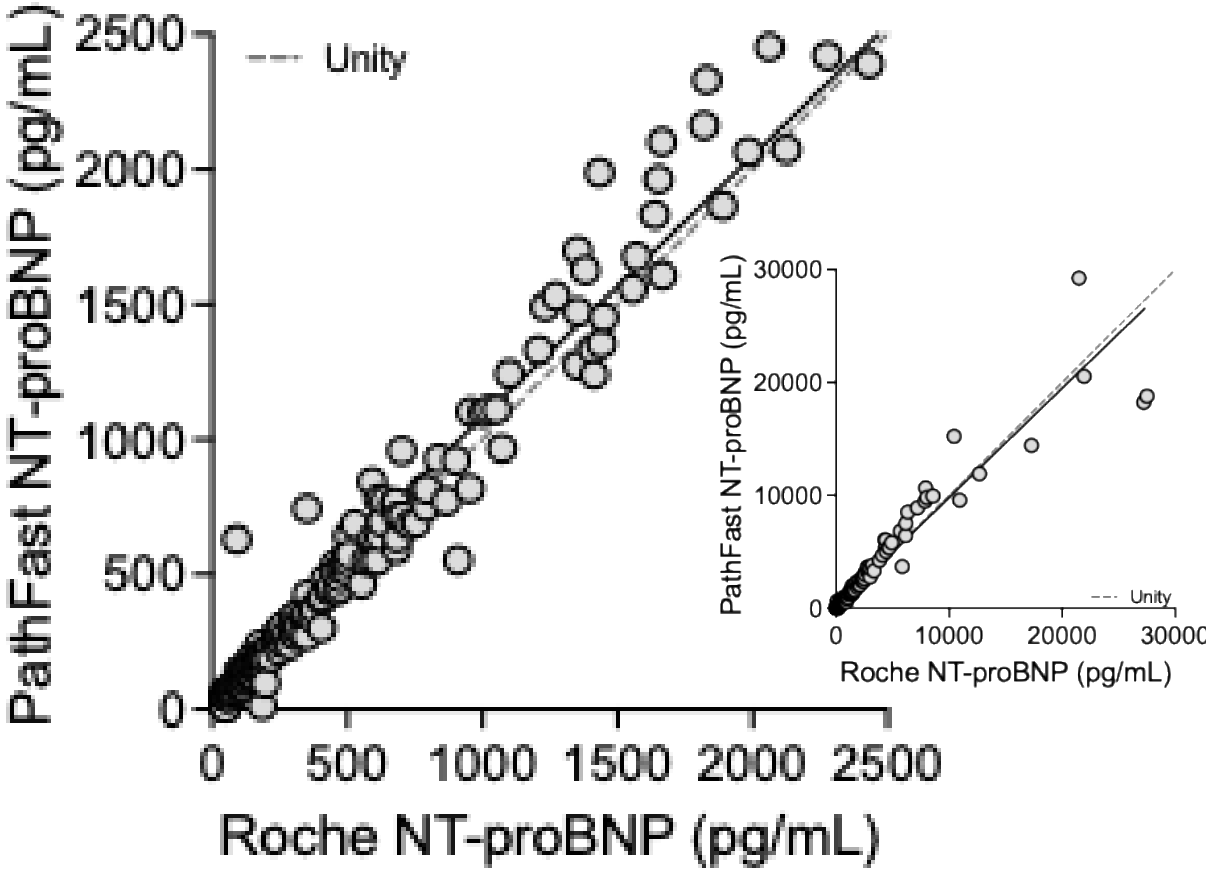
Excellent correlation between NT-proBNP assays





Spearman Correlation R = 0.99

Farnsworth Lab, unpublished data

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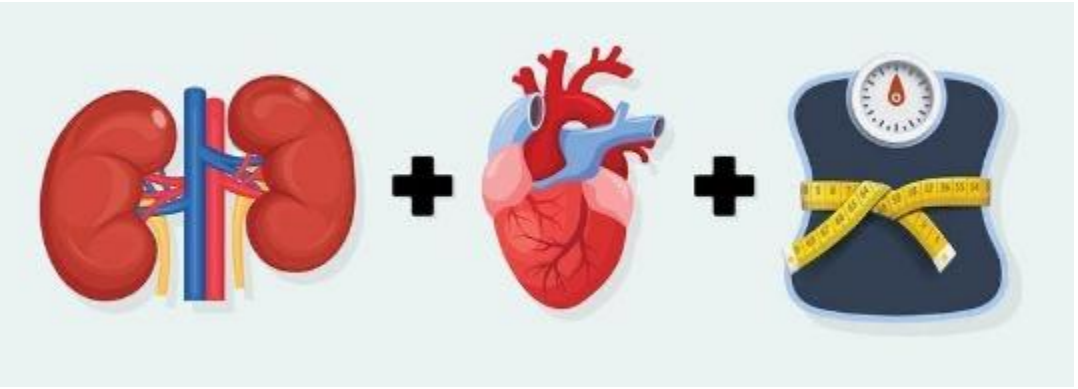
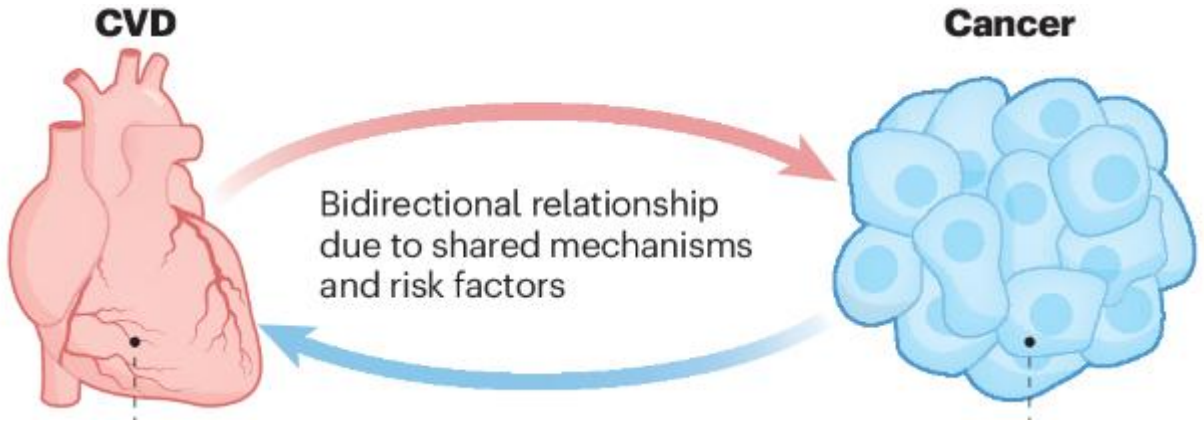
Take home for NP elevations

- NP elevation is due to cardiomyocyte stretch
- Definition of elevation may vary based on a host of variables
- Excellent agreement between NT-proBNP assays
- Limited correlation between BNP and NT-proBNP assays

Utility of Cardiac Biomarkers:



Cardiovascular-Kidney-Metabolic Syndrome



Cardio-Oncology

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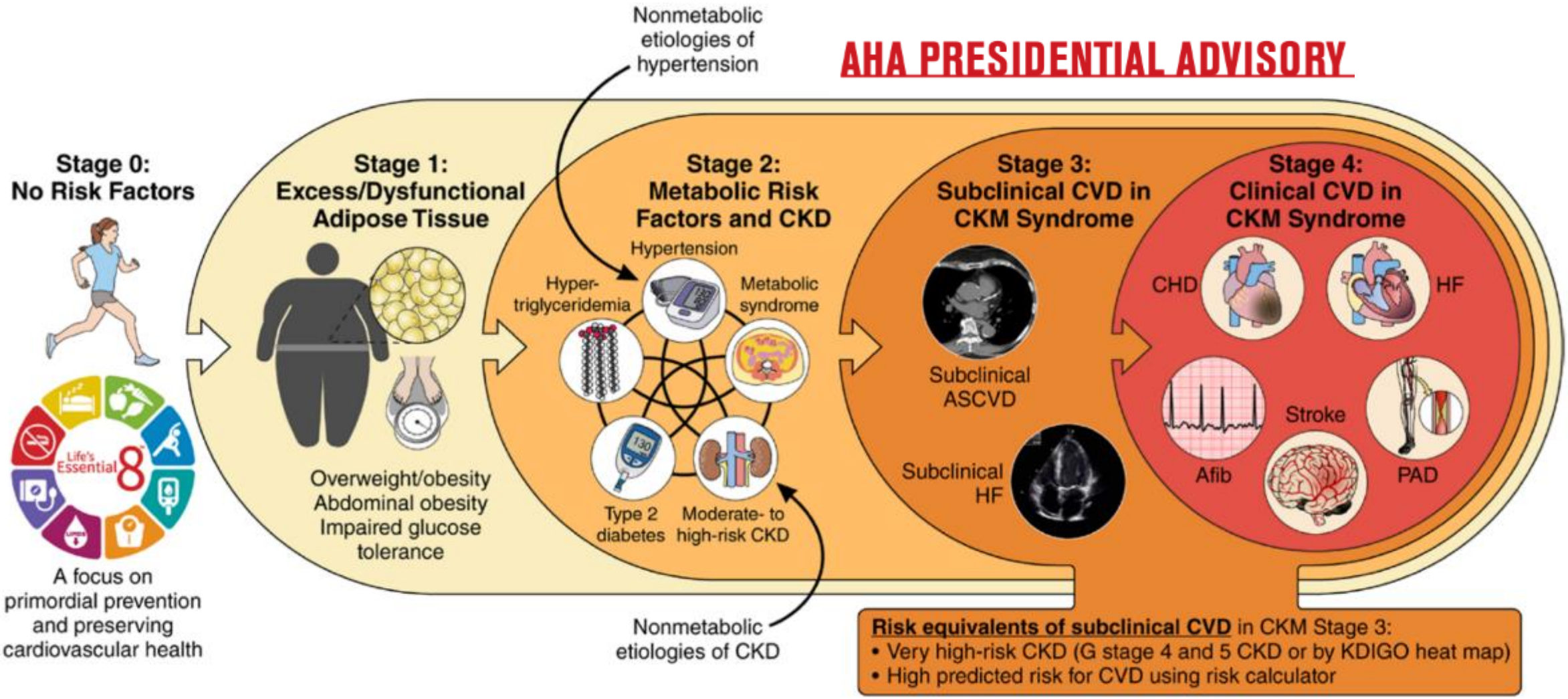
Use case 1: Cardiovascular-Kidney-Metabolic (CKM) Syndrome



Ndumele CE et al.. 2023:148:1606-35.

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Biomarkers are supported by multiple consensus documents

Circulation
Volume 148, Issue 20, 14 November 2023; Pages 1636-1664
https://doi.org/10.1161/CIR.0000000000001186

AHA SCIENTIFIC STATEMENTS

A Synopsis of the Evidence for the Science and Clinical Management of Cardiovascular-Kidney-Metabolic (CKM) Syndrome: A Scientific Statement From the American Heart Association

Subclinical HF diagnosed by:

"Elevated cardiac biomarkers (NT-proBNP ≥125 pg/mL, hs-troponin T ≥14 ng/L for women and ≥22 ng/L for men, hs-troponin I ≥10 ng/L for women and ≥12 ng/L for men"

…..

Ndumele CE et al.. 2023:148:1606-35.

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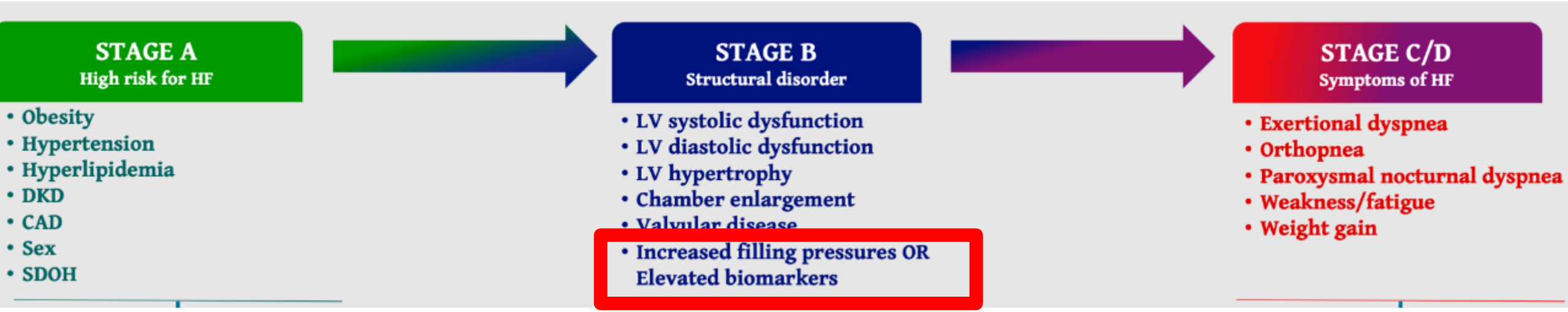
American Diabetes Association Consensus Statement

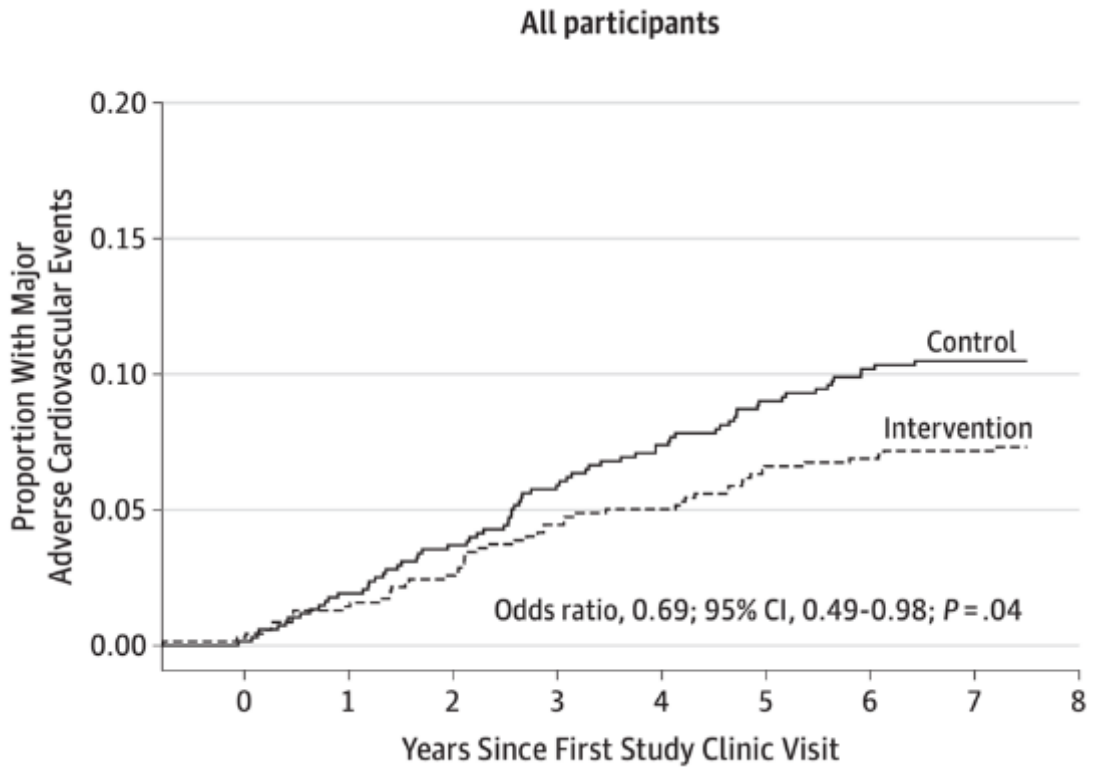


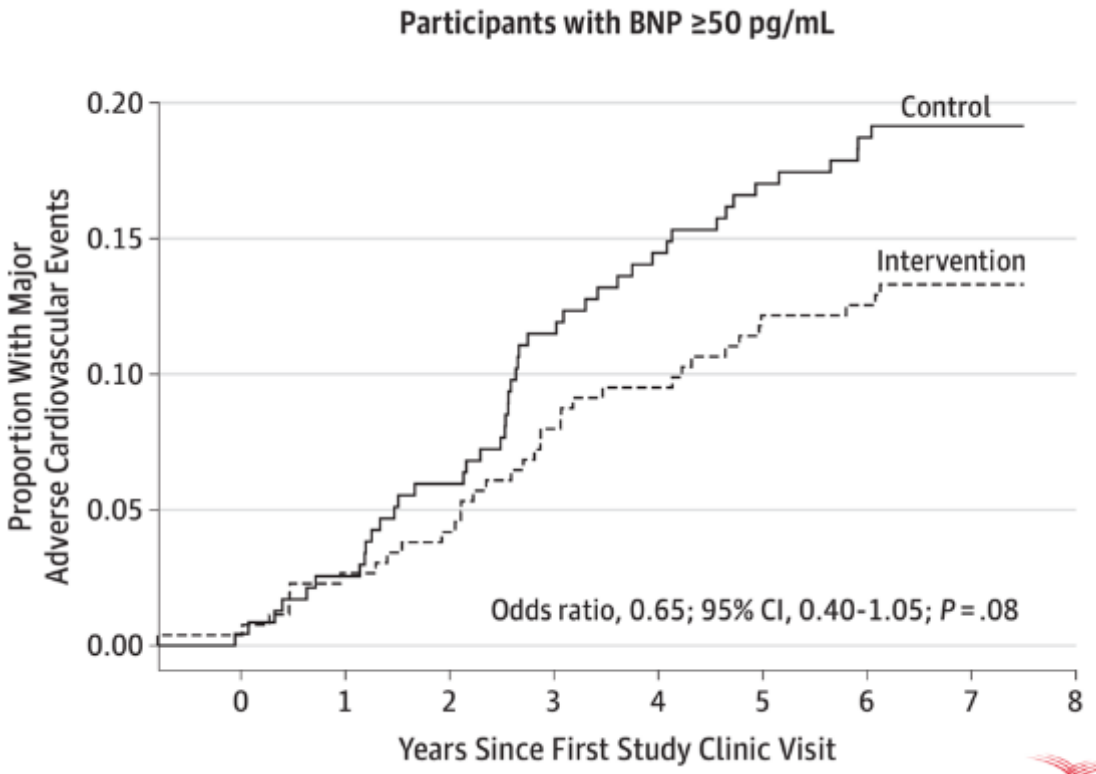
"…the biomarker thresholds for clinical use include a BNP ≥50 pg/mL, NT-proBNP ≥125 pg/mL and a hs-cTn > 99th% URL"

Pop-Busui R et al. Diabetes Care 2022:45:1670-90.

STOP-HF Trial: BNP screening improves outcomes

- 1,374 patients with CVD risk factors
- Randomized to Standard of care vs. screening with BNP
  - BNP ≥ 50 pg/mL referred to cardiovascular specialist





Lewwidge M et al, JAMA. 2013:310:66-74.

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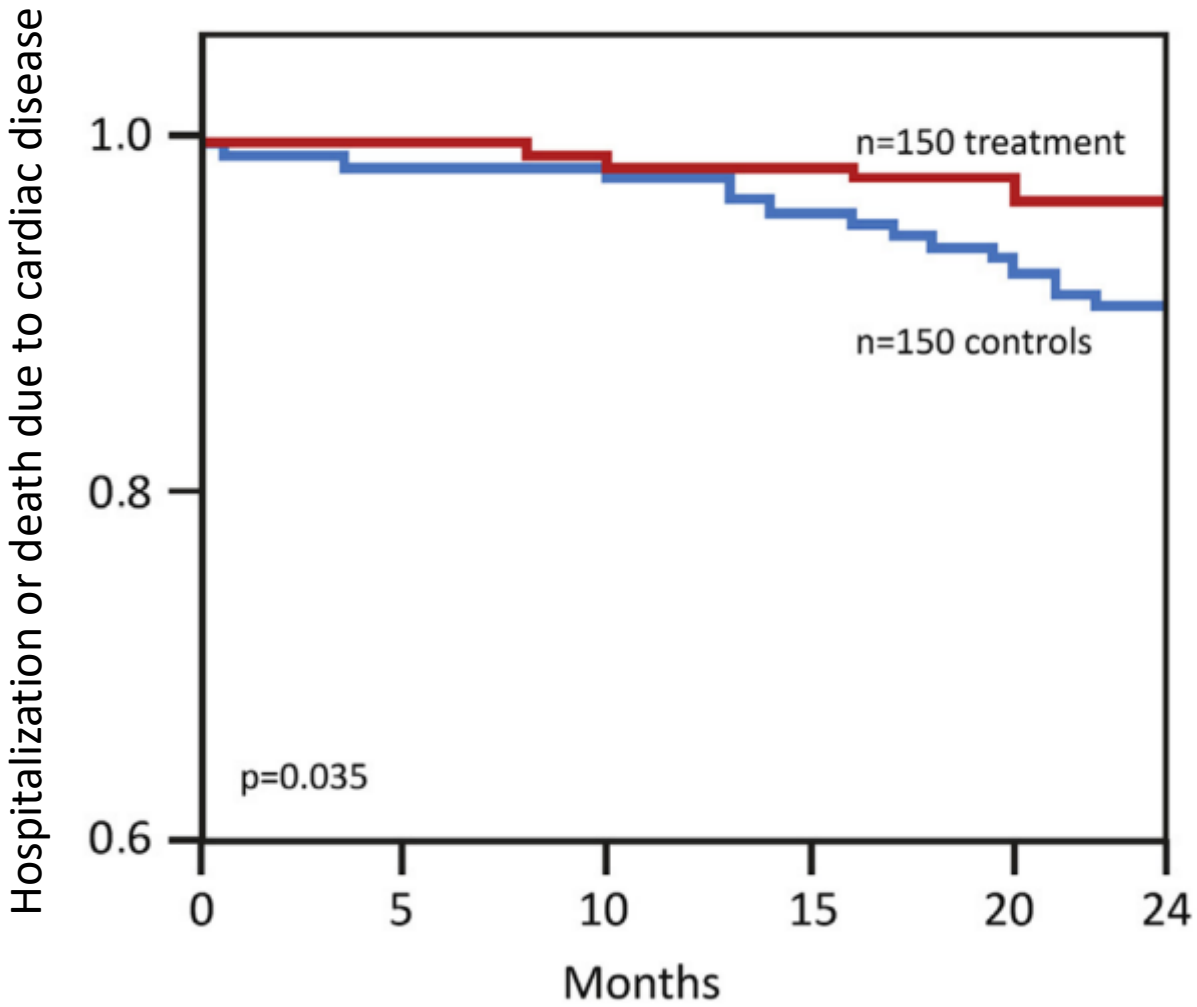
PONTIAC study: Reduced cardiac events in diabetics

- 300 patients with Type 2 Diabates
- NT-proBNP > 125 pg/mL
- Standard of care treatment vs. up-titration of renin-angiotensin system (RAS) antagonists and betablockers



Reduced hospitaliation / death. Hazard Ratio of 0.351 (0.127-0.975)

Huelsmann M et al, JACC. 2013;08:1365-72.

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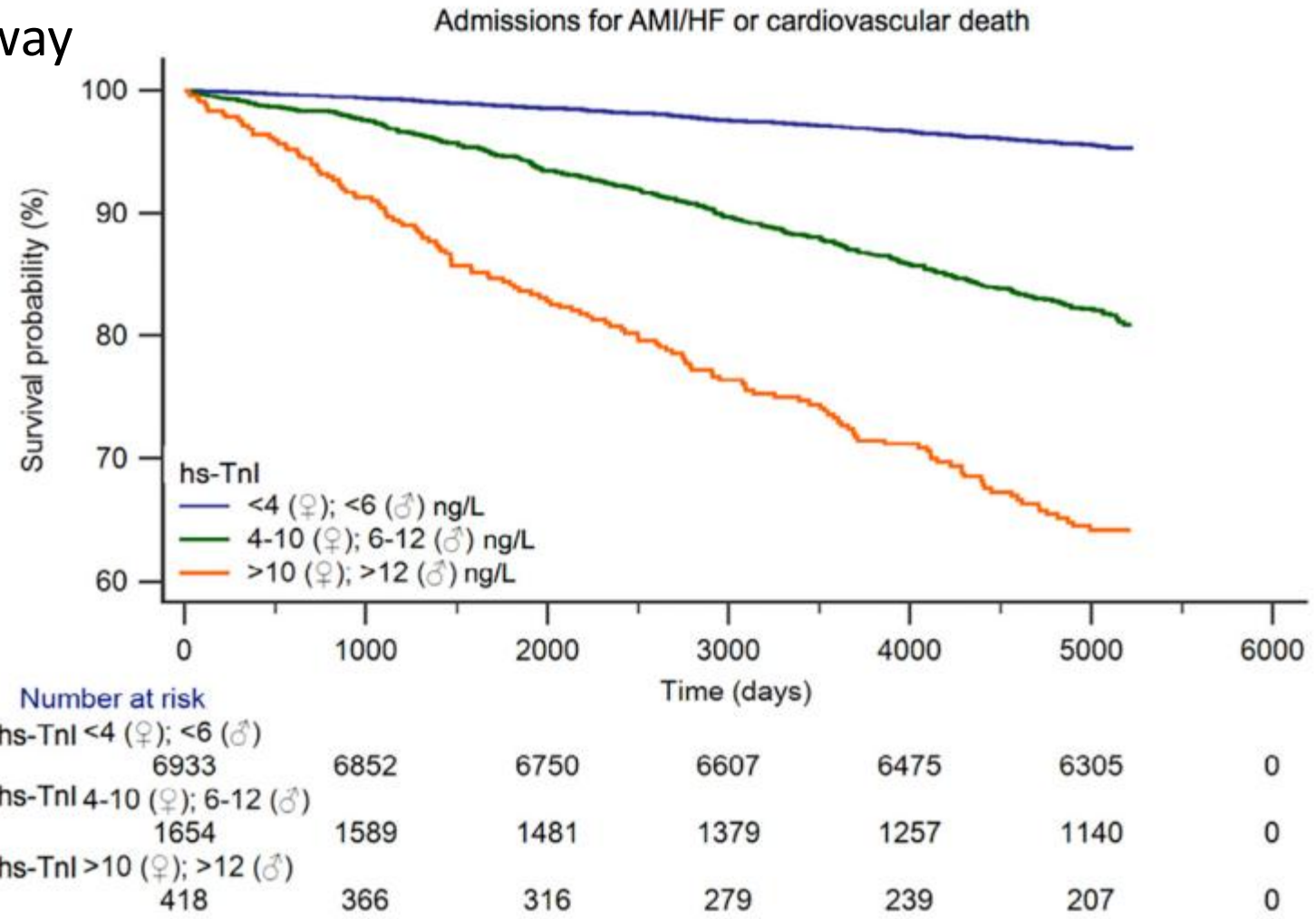
Measurable cTn = worse outcomes in healthy outpatients

- 9005 healthy subjects from Norway
- All samples tested for hs-cTnI
- Pts. w/ known CVD excluded
- 99th % males = 34 ng/L
- 99th % females = 16 ng/L

> 10 ng/L females
> 12 ng/L males



Sigurdardottir FJ et al. Amer J of Cardiol. 2018:121;949-55.

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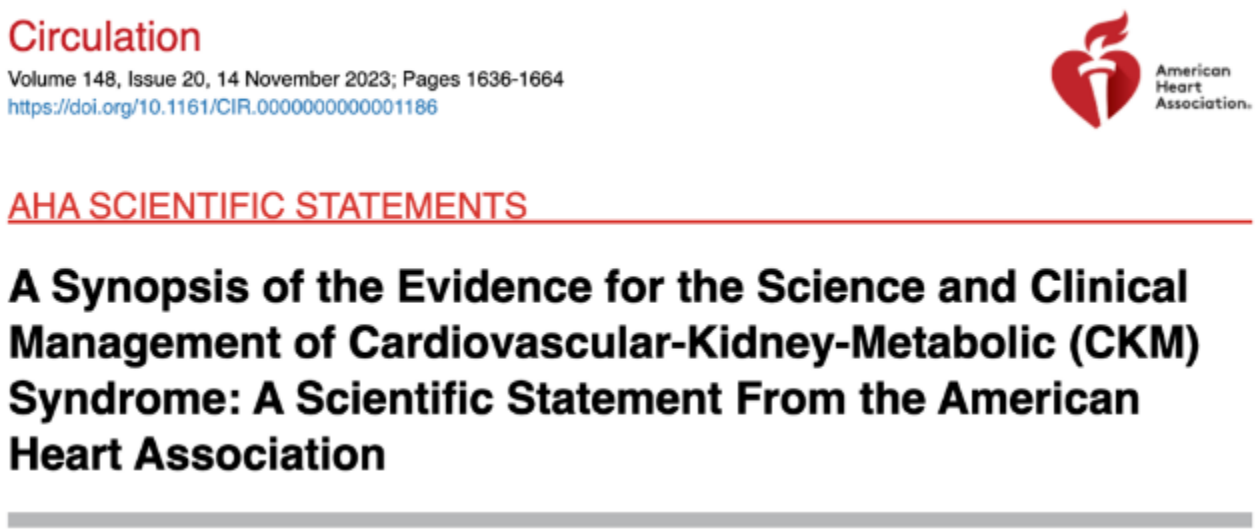
Cardiovascular-Kidney-Metabolic (CKM) Syndrome



"there is limited clarity on how best to target cardiac biomarker measurements in the population, the frequency of such testing, and appropriate next diagnostic steps (eg, echocardiograms) when elevated cardiac biomarkers are identified. " **.....**

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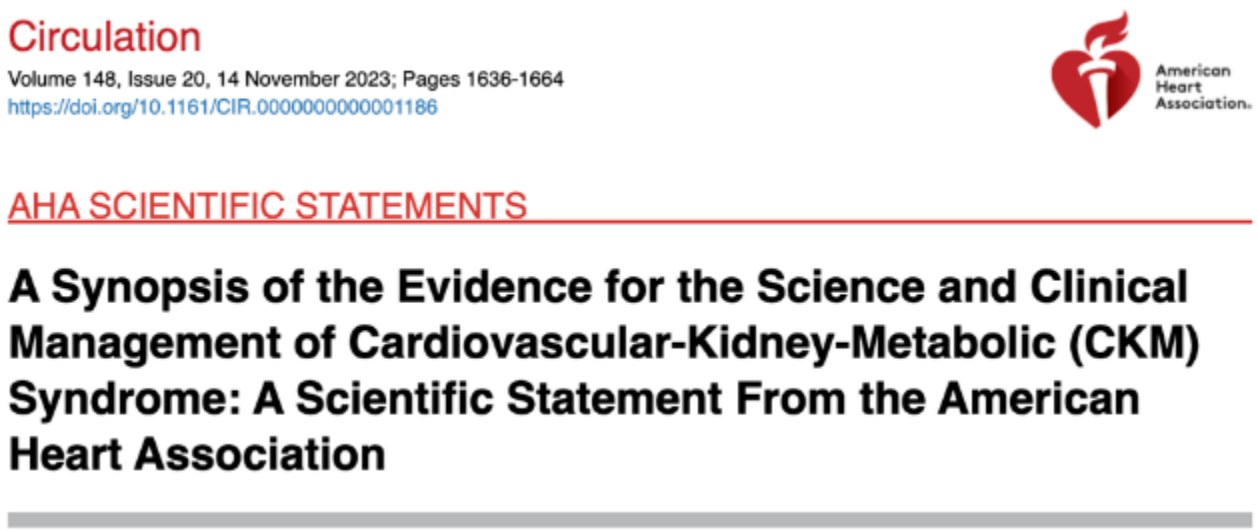

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American Heart Association.

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Are risk-based screening strategies effective?

Ndumele CE et al.. 2023:148:1606-35.

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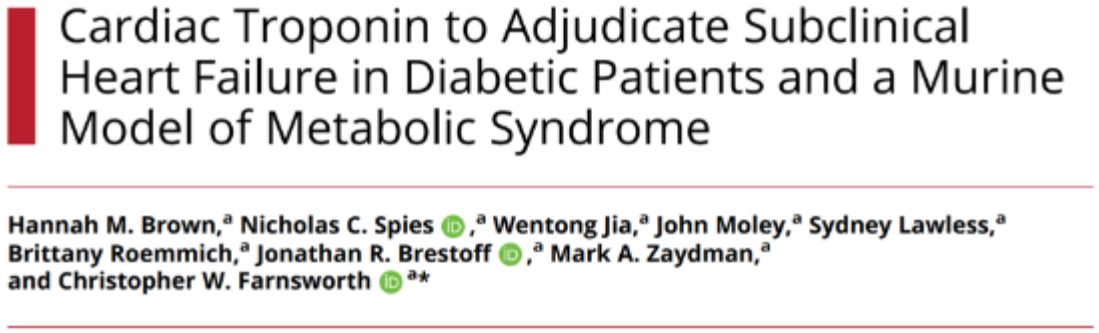
What are the risk factors for elevated troponin?

- 1,304 outpatients w/ physician ordered A1c
- Measured high sensitivity cTnI
- Clinical data obtained from medical record



Cardiac Troponin to Adjudicate Subclinical Heart Failure in Diabetic Patients and a Murine Model of Metabolic Syndrome

Hannah M. Brown,[a] Nicholas C. Spies ,[a] Wentong Jia,[a] John Moley,[a] Sydney Lawless,[a] Brittany Roemmich,[a] Jonathan R. Brestoff ,[a] Mark A. Zaydman,[a] and Christopher W. Farnsworth [a]*

Brown H et al, JALM. 2024:09:06:913-26.

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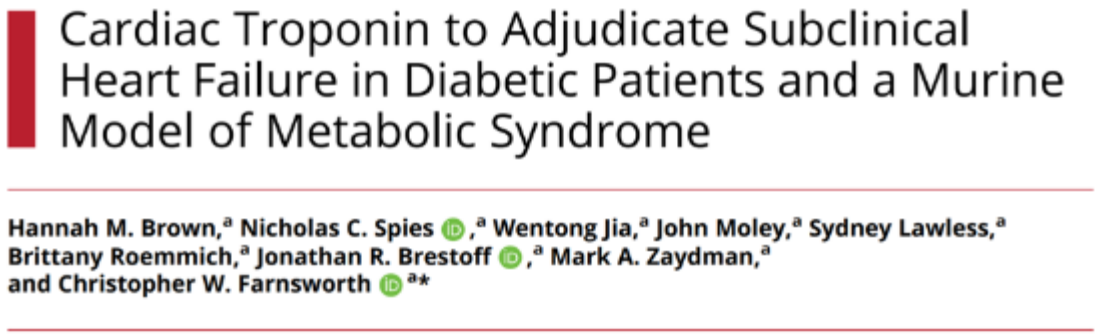
What are the risk factors for elevated troponin?

- 1,304 outpatients w/ physician ordered A1c
- Measured high sensitivity cTnI
- Clinical data obtained from medical record

59 (8.0%) of females had cTnI > 10 ng/L
31 (4.2%) of females had cTnI > 99th% URL (sex specific)

88 (15.7%) of males had cTnI > 12 ng/L
23 (4.1%) of males had cTnI > 99%URL (sex specific)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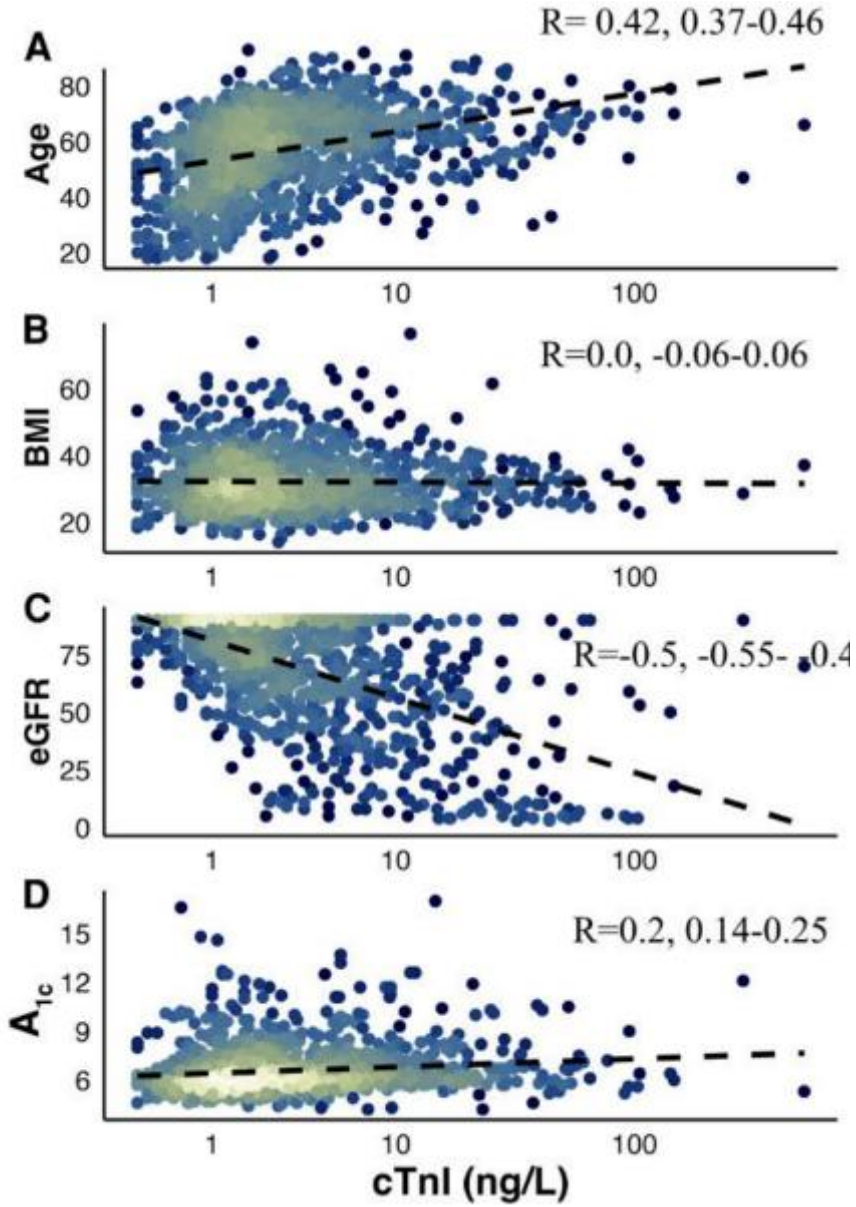
Age, eGFR, A1c, and prior CVD associated with elevated cTnI



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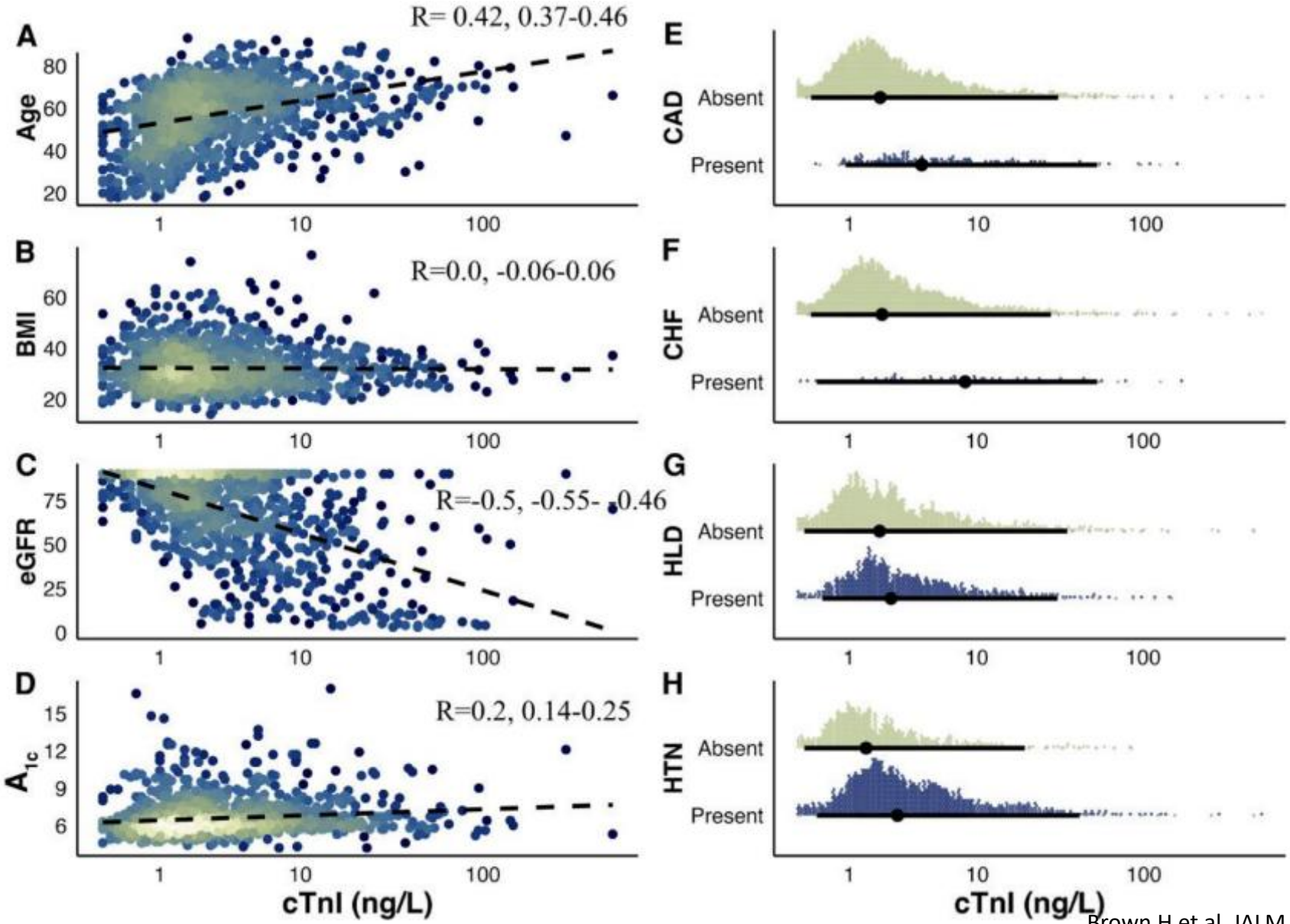

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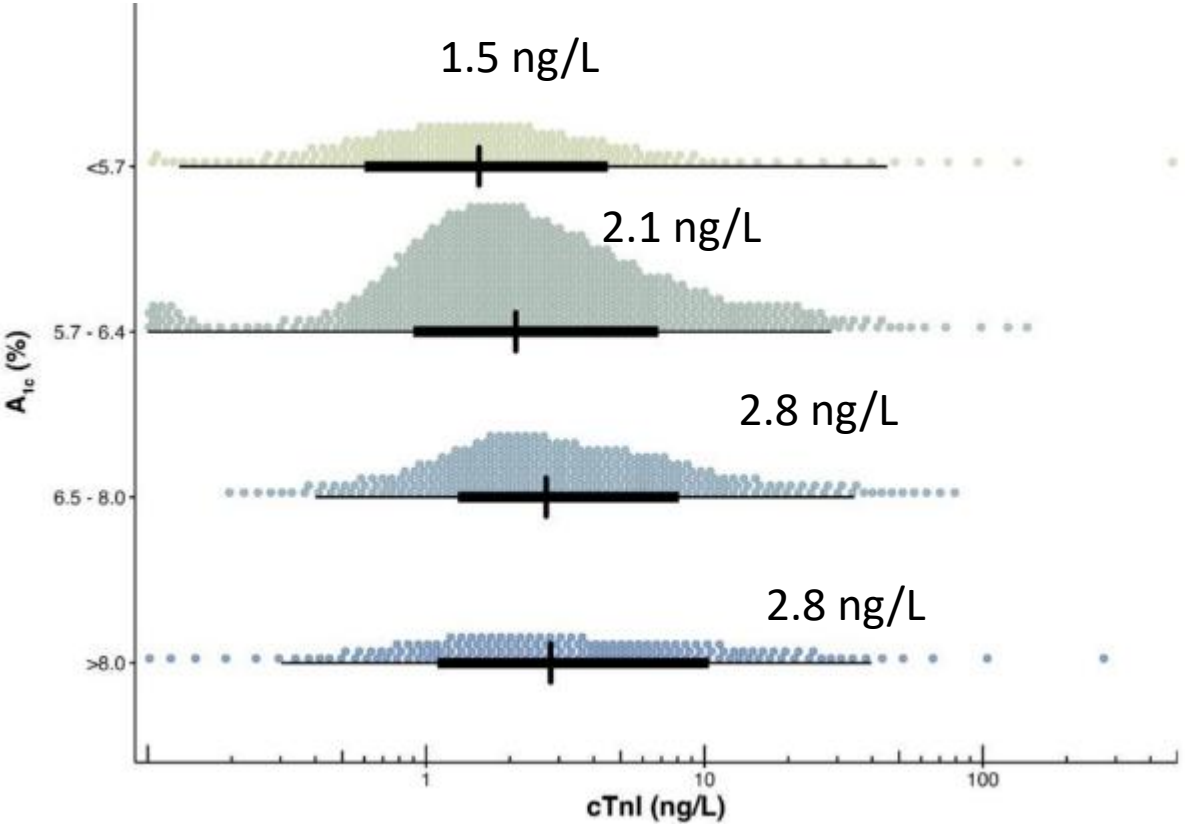
Increased A1c and hyperglycemia associated with elevated cTnI



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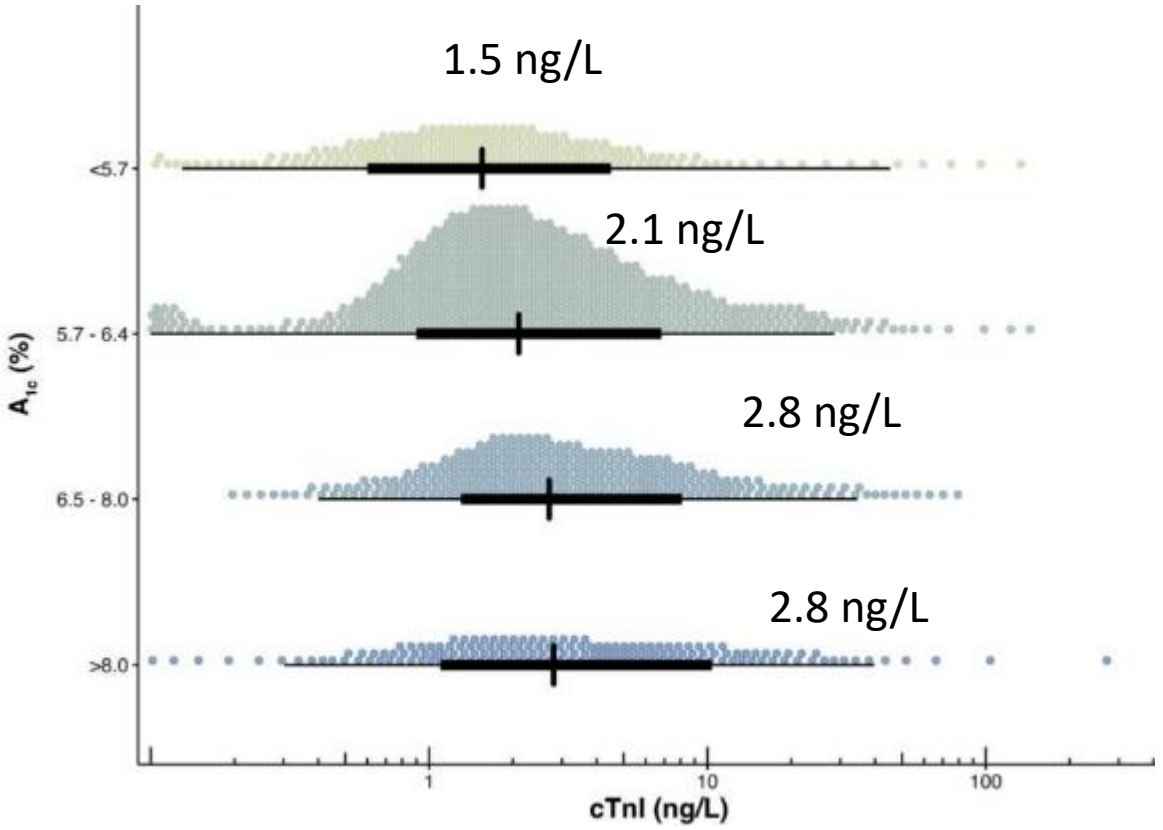

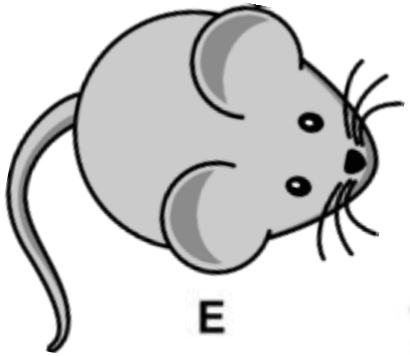

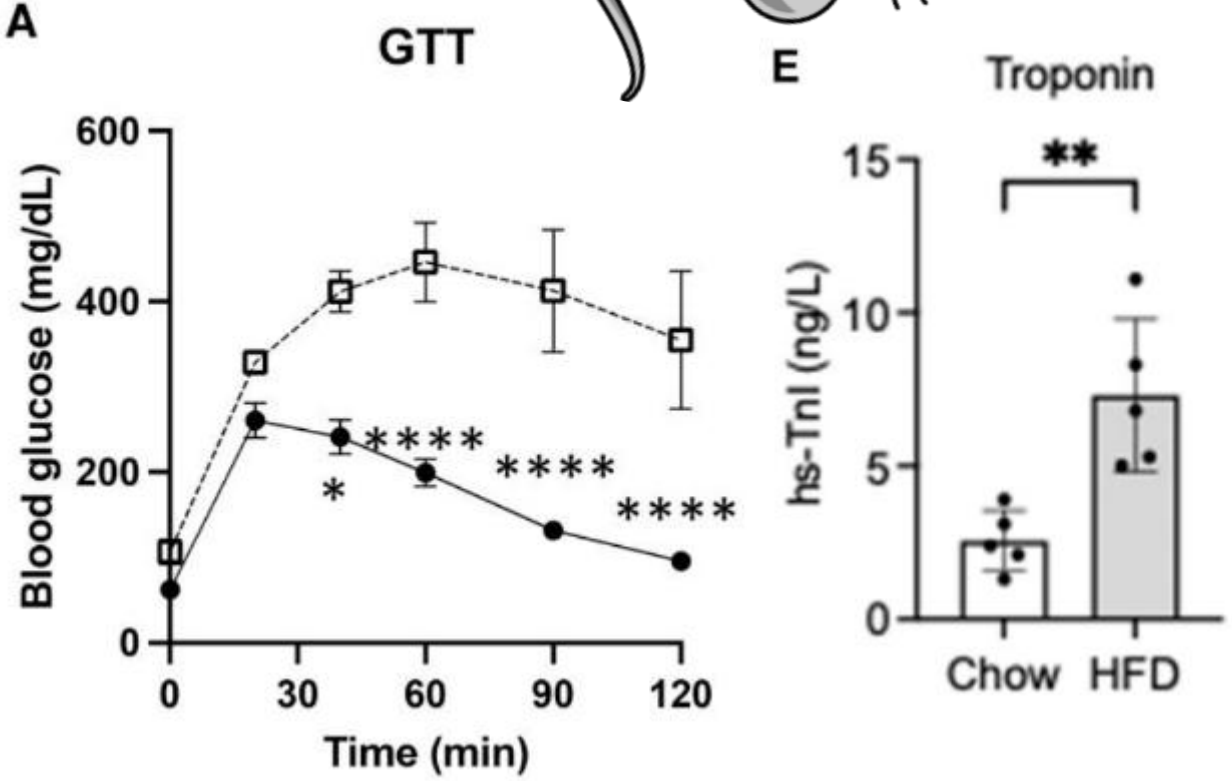

Brown H et al, JALM. 2024:09:06:913-26.

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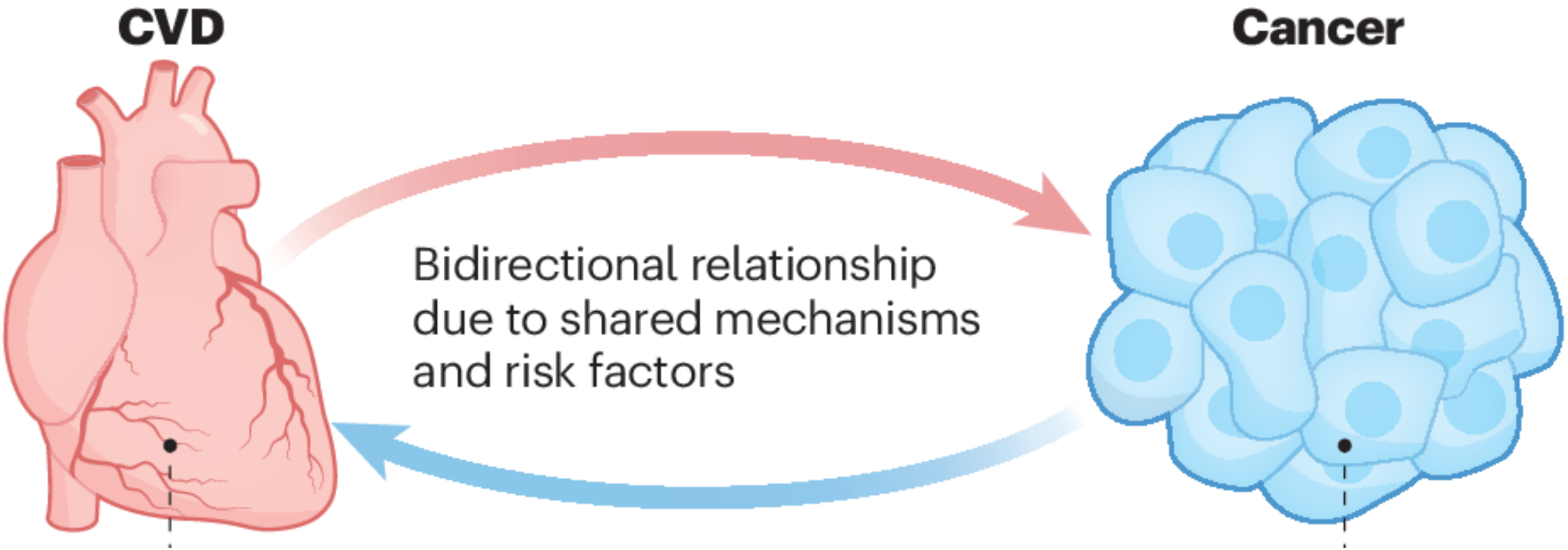
Utility of cardiac markers in CKM syndrome

1. Both BNP/NT-proBNP and cTn prognosticate outcomes and progression to HF
2. Ideal thresholds for each have not been fully elucidated
3. The risk factors that warrant screening in diabetics/pre-diabetics are not fully known
4. The frequency of screening (and who to screen) is not yet fully elucidated

Use Case 2: Cardiac biomarkers in cardio-oncology

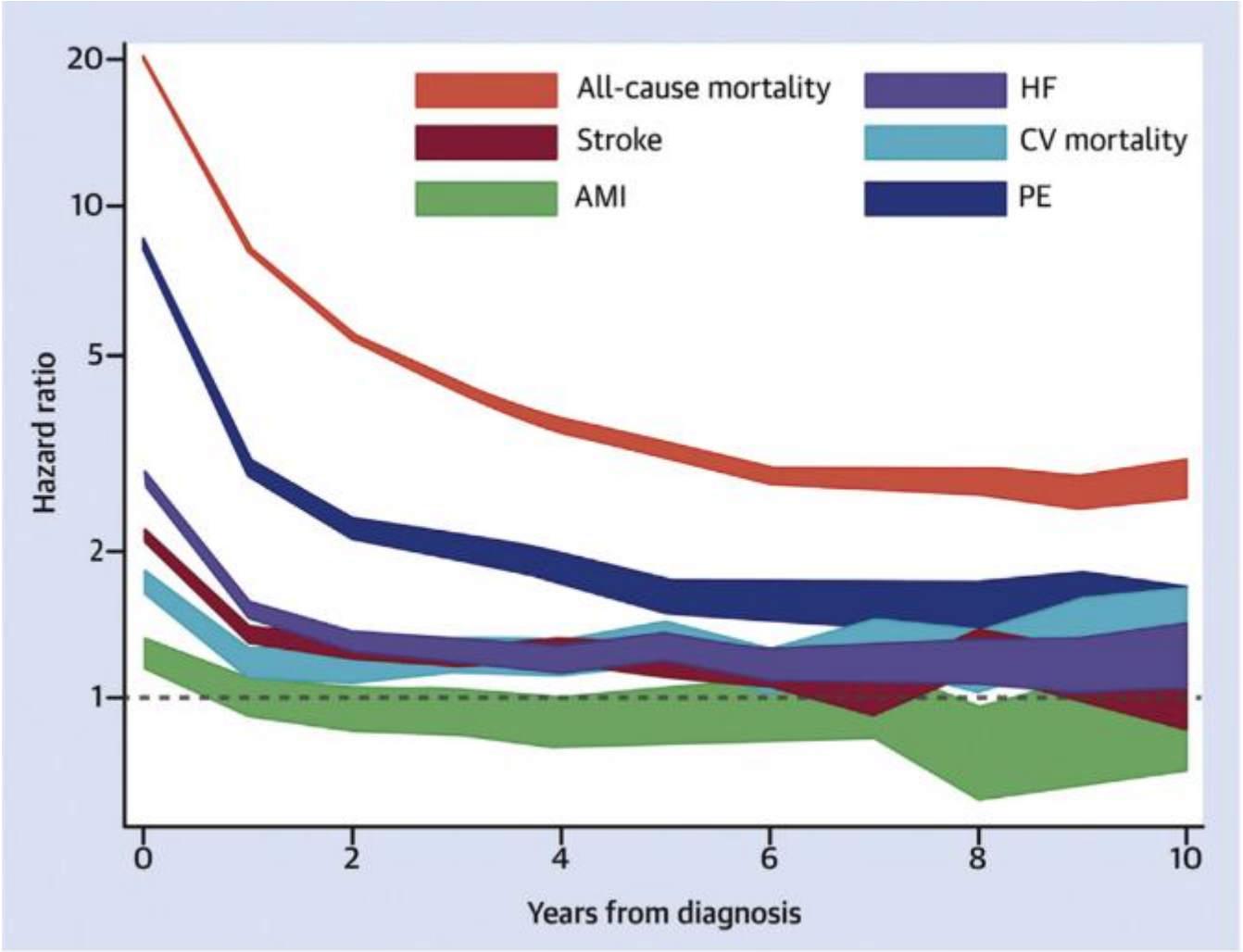


CardinalHealth

Cancer survival is associated with cardiovascular disease (CVD)

- Retrospective cohort study
  - 4,519,243 adults, Canada
  - Compared those with cancer to those without
  - Risk for cardiovascular events

- Survivors of most cancers have increased risk for CVD

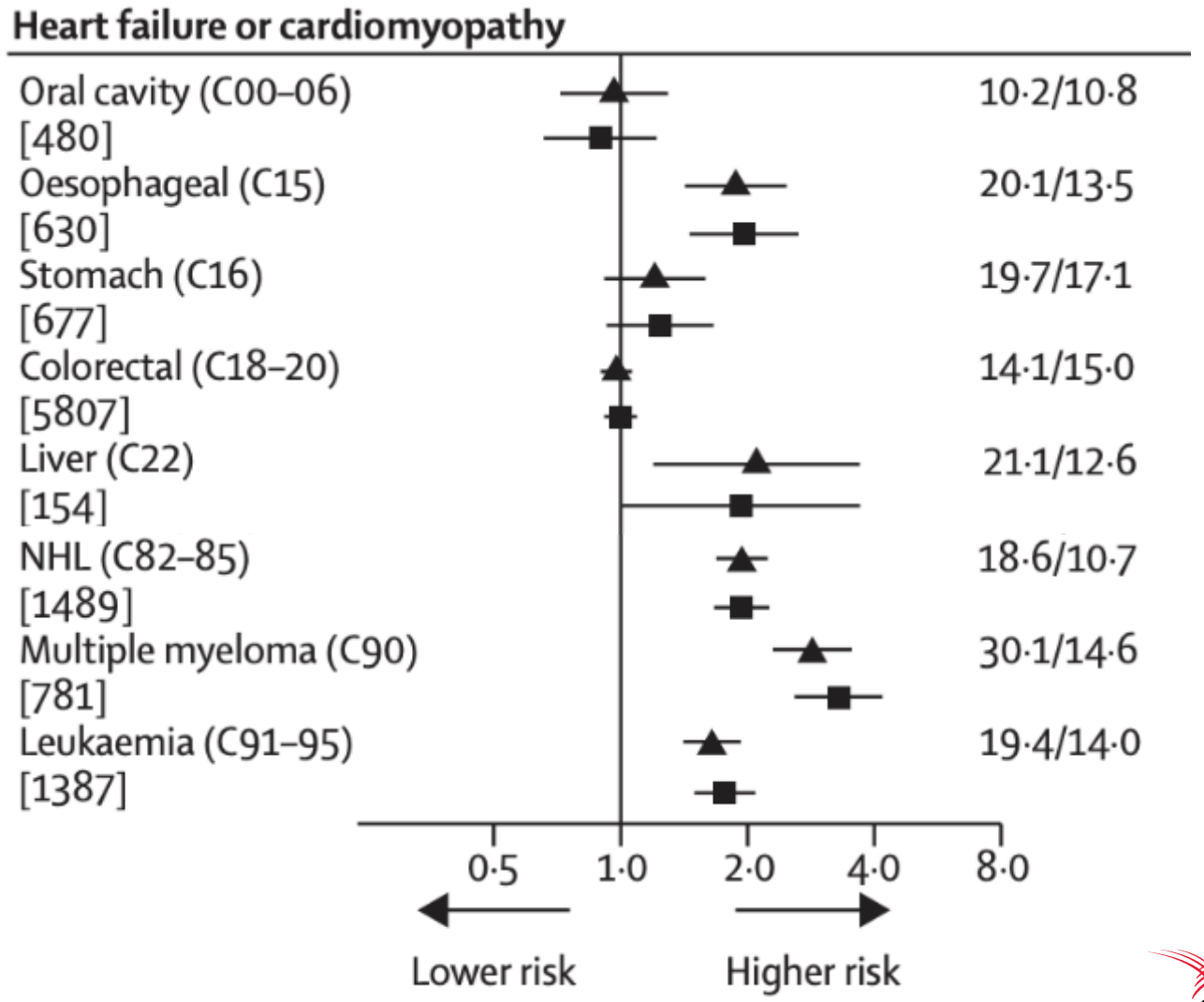


Paterson DI, J Am Coll Cardiol CardioOnc. 2022 Mar, 4 (1) 85–94

CardinalHealth

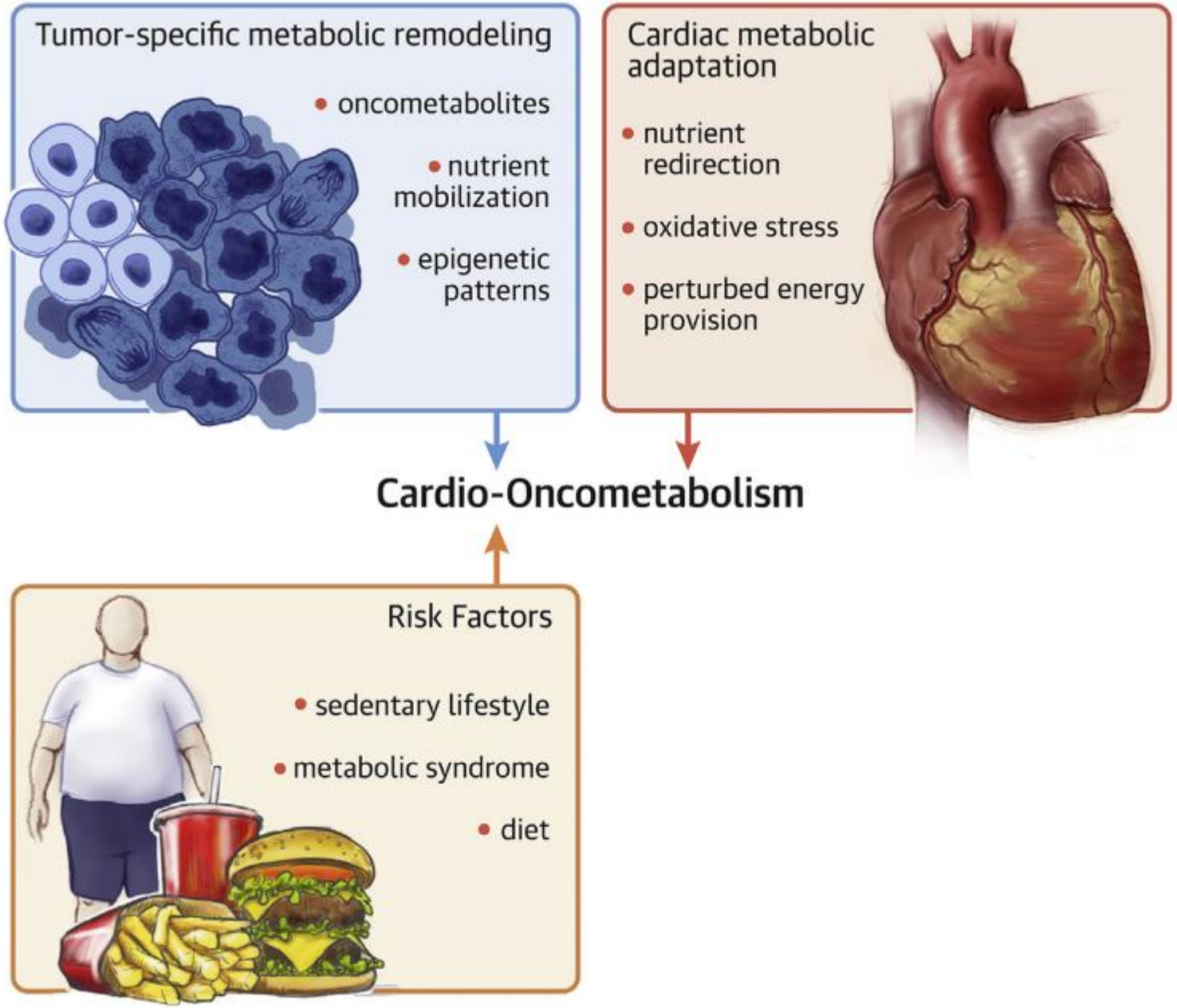
Increased heart failure and cardiomyopathy in cancer survivors

- 108,215 cancer survivors (with at least 1 year of follow-up)
- 523,541 age and sex matched controls
- Substantial variation between cancer sites / types



Strongman H, Lancet 2019;394:1041-54.

CV toxicity associated with cancer risk factors and treatment



Karlstaedt A et al. J Am Coll Cardiol Basic Trans Science 2021;6:705-18.

CardinalHealth

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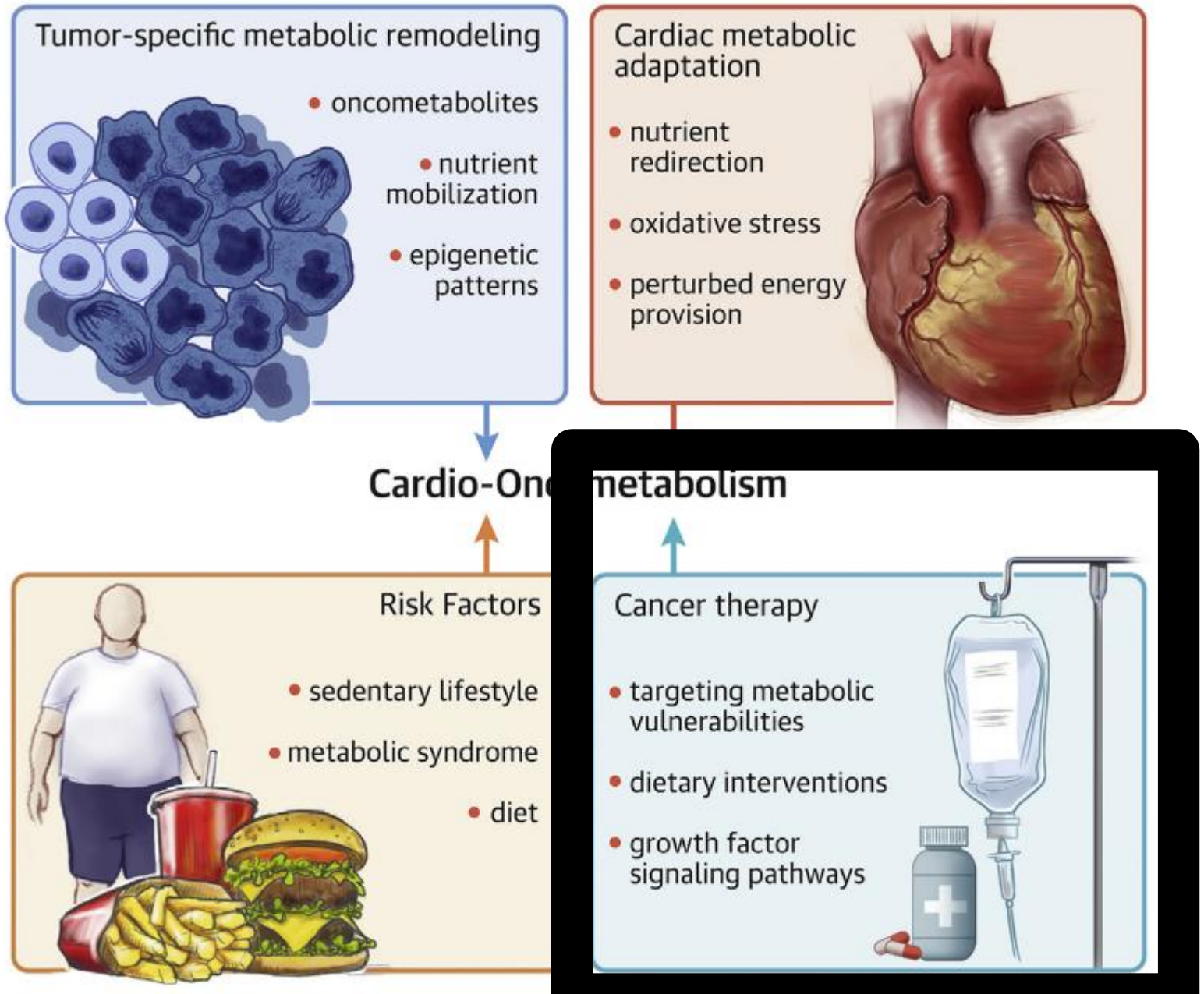

Karlstaedt A et al. J Am Coll Cardiol Basic Trans Science 2021;6:705-18.

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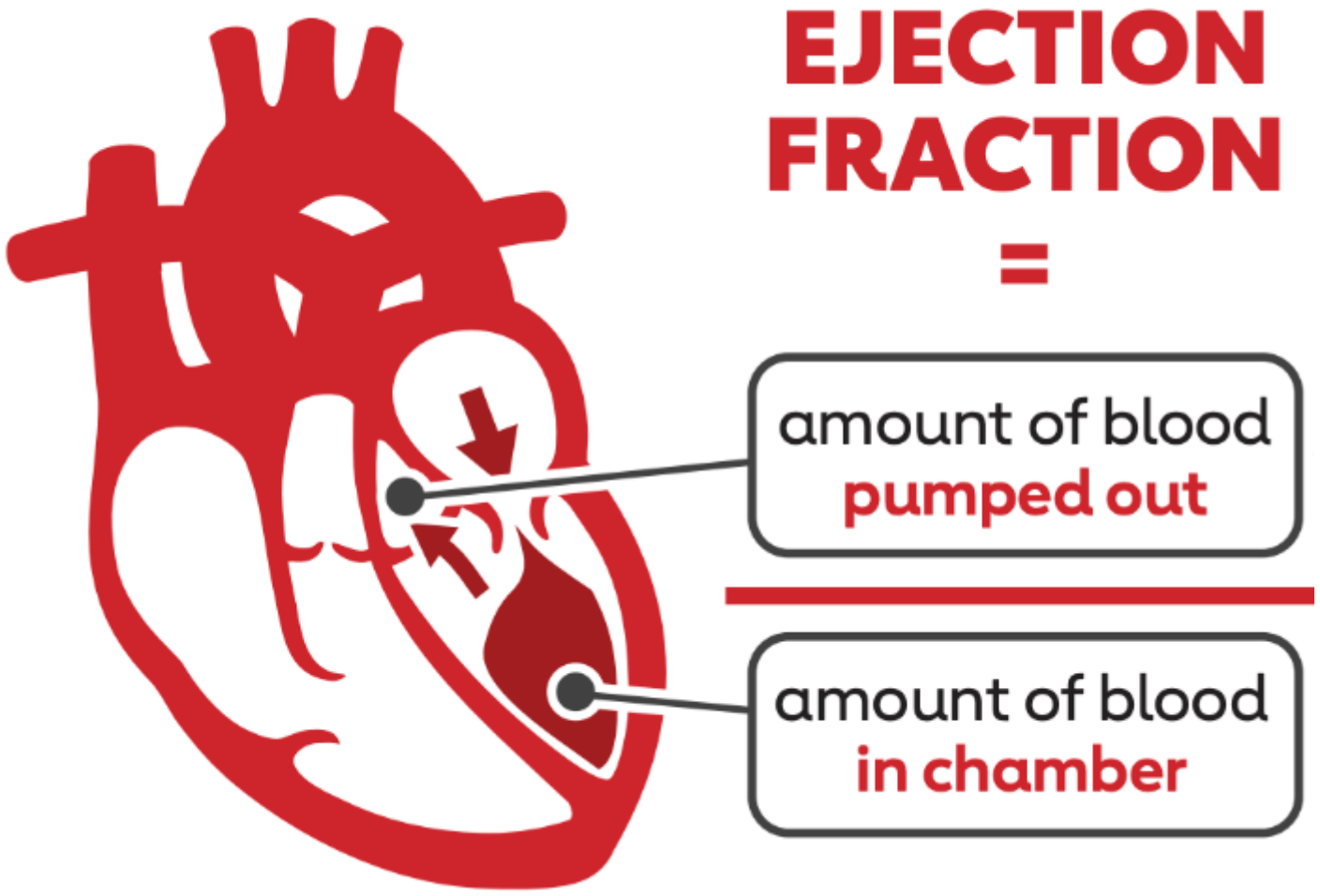
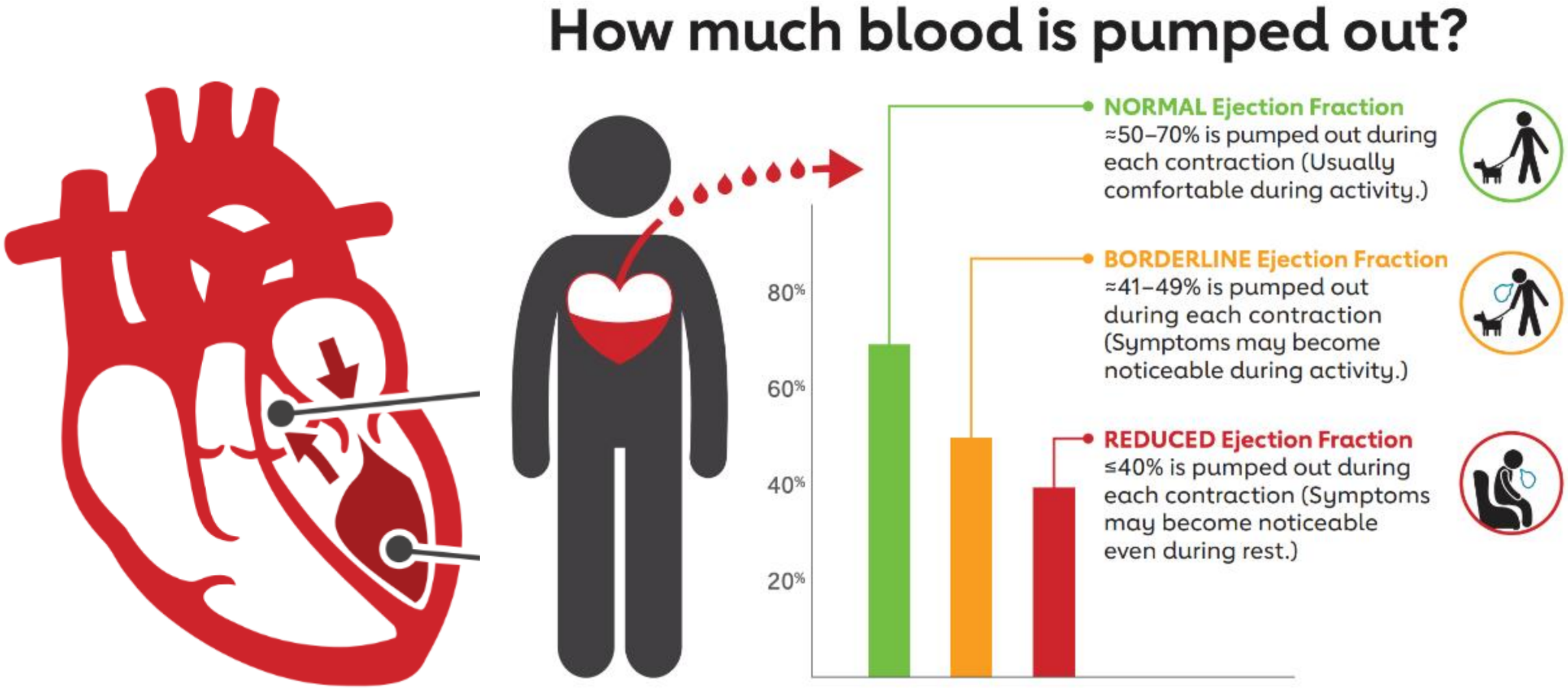
Left ventricular ejection fraction (LVEF) and cardiac dysfunction



Stroke Volume

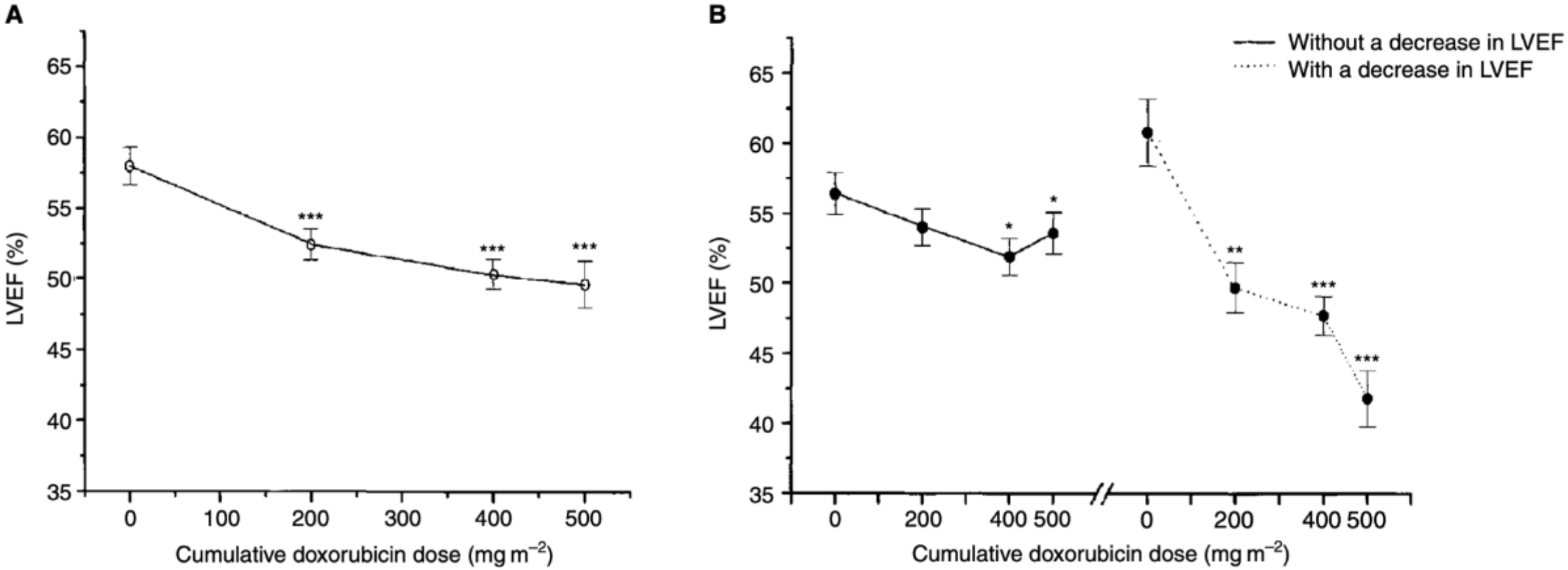
End-diastolic Volume

Left ventricular ejection fraction (LVEF) and cardiac dysfunction



Effects of doxorubicin on cardiac function

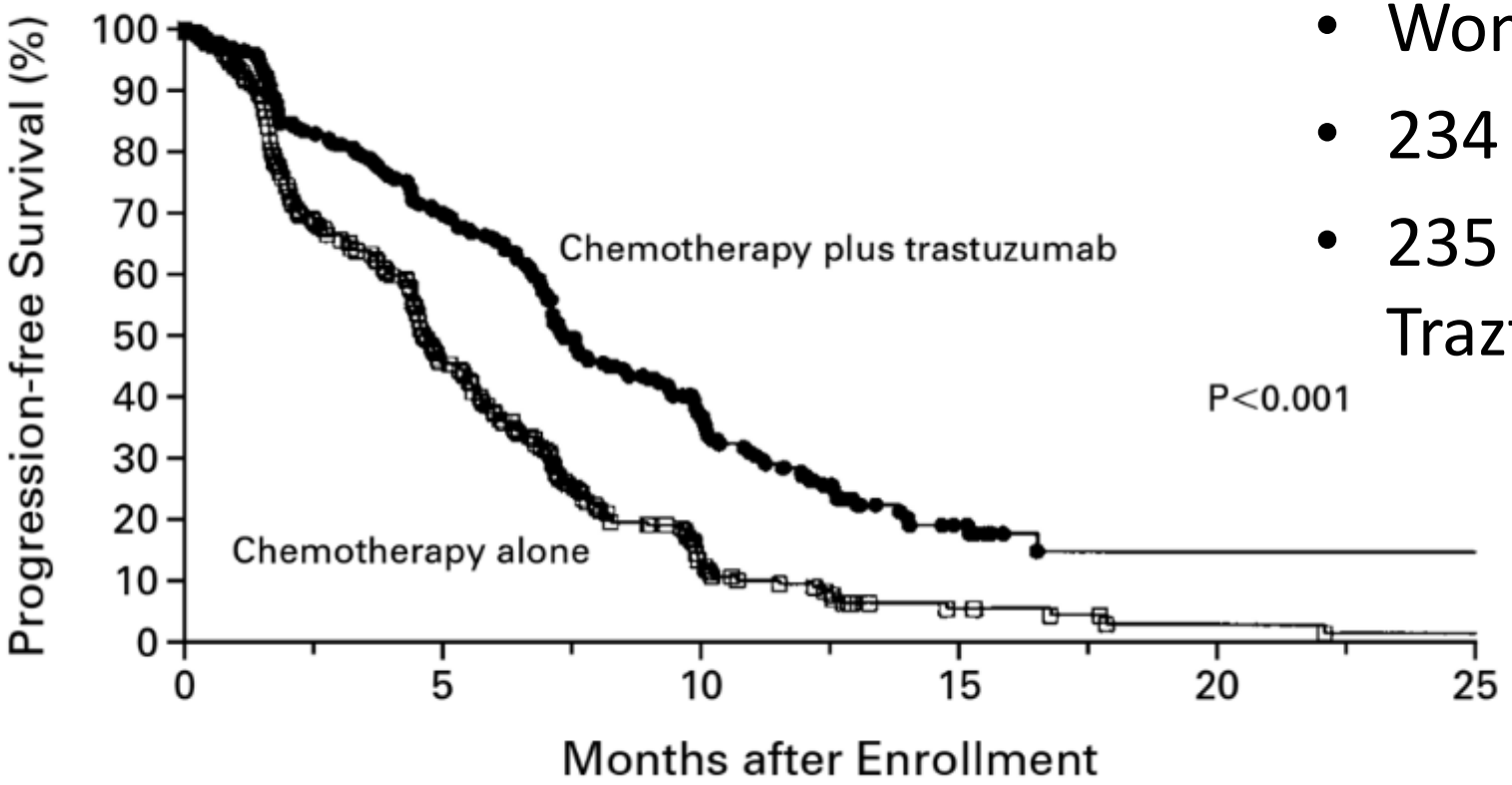
- Thirty adult patients with non-Hodgkins Lymphoma
- All administered doxorubicin, monitoring for LVEF changes



Nnousiainen T et al. Br J Cancer 2002:86:1697

CardinalHealth

Trastuzumab increases risk of cardiac dysfunction



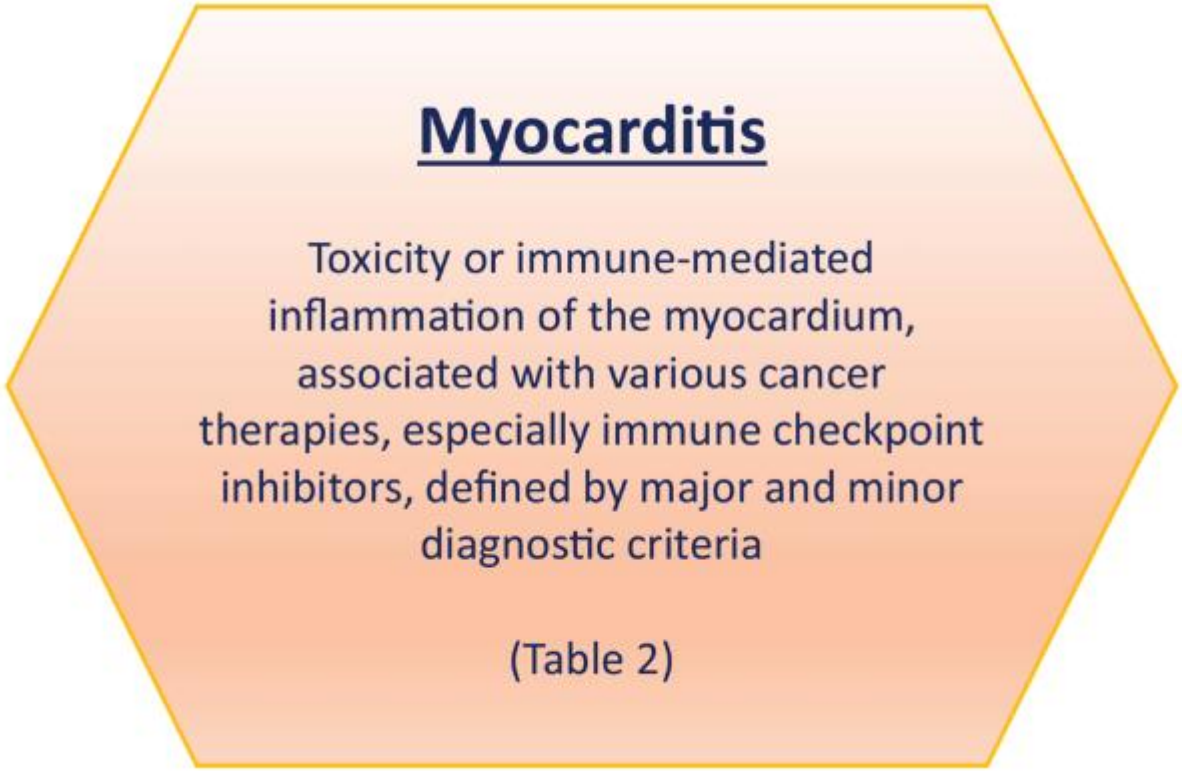
- Women with HER2+ breast cancer
- 234 Women- standard chemo
- 235 women- standard chemo + Traztuzumab

- ~27% of patients on trastuzumab + anthracycline experienced cardiac dysfunction

Slamon DJ NEJM 2001;344:783-792.

Cancer therapy-related myocarditis

- Inflammation of the myocardium or middle layer of the heart
- Symptoms:
  1. Fatigue
  2. Shortness of breath
  3. Chest pain
  4. Irregular heartbeat



ESC European Society of Cardiology
European Heart Journal (2022) 43, 280–299
https://doi.org/10.1093/eurheartj/ehab674
SPECIAL ARTICLE

Defining cardiovascular toxicities of cancer therapies: an International Cardio-Oncology Society (IC-OS) consensus statement

AHA- https://www.heart.org/en/health-topics/myocarditis

CardinalHealth

Diagnosis of cancer therapy-related myocarditis

- **Histological-** inflammatory cell infiltrates w/ cardiomyocyte loss

- **Clinical Diagnosis-** Troponin elevation (new or change from baseline) with 1 major or two minor criterion

  - Major- Diagnostic Cardiac Magnetic Resonance Imaging
  - Minor- Clinical syndrome, arrythmia, decreased systolic function, other immune related events (I.e, Myasthenia)

errmann J Eur Heart Jour. 2022;43:280-99.

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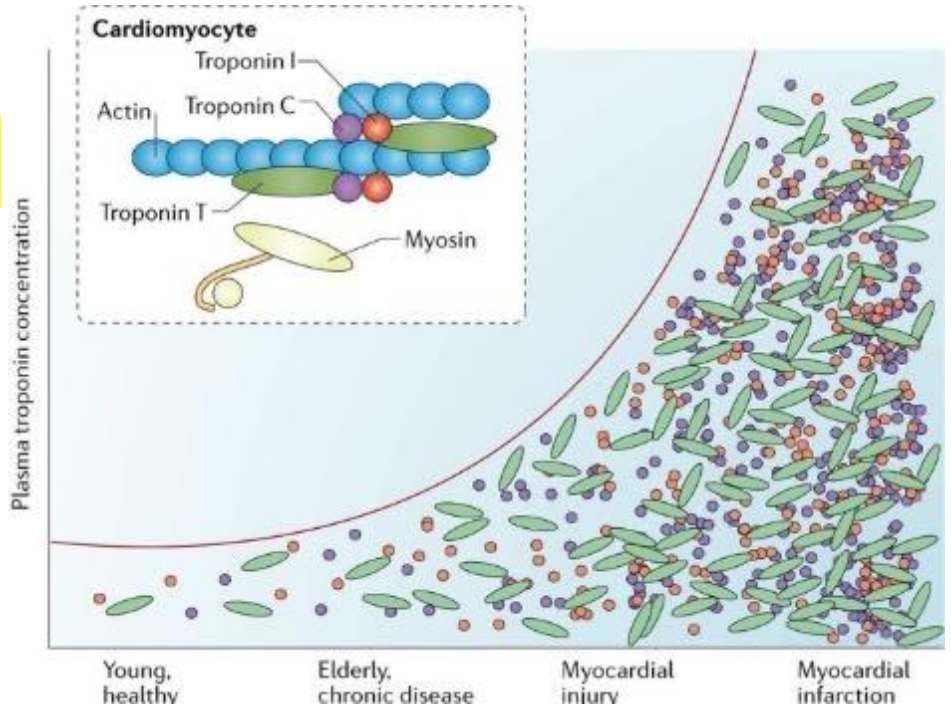
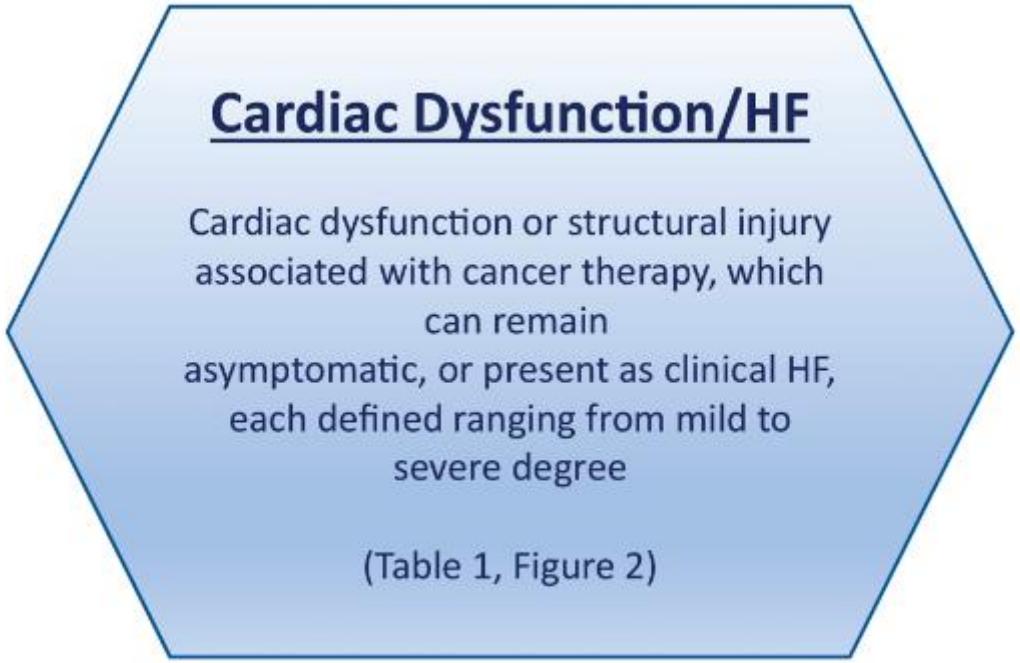


Herrmann J Eur Heart Jour. 2022;43:280-99.

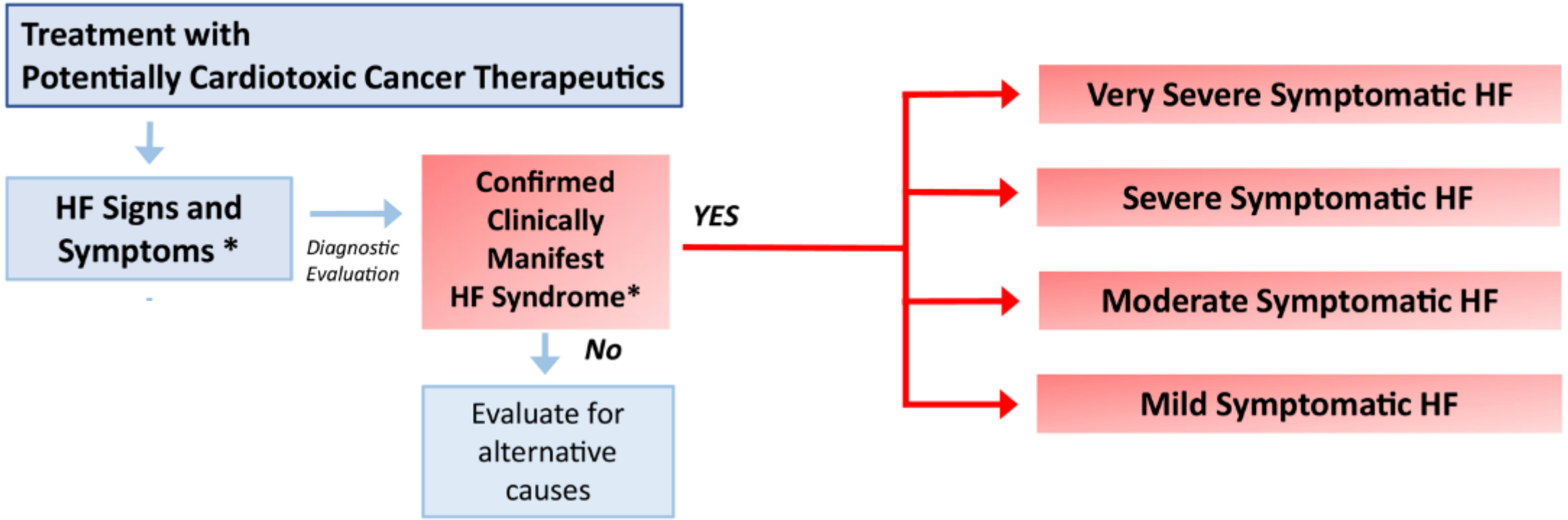
CardinalHealth

Cancer therapy associated cardiac dysfunction / heart failure

- Impact of cardiac structure or function from cancer therapy
- May be symptomatic or asymptomatic
- Commonly caused by
  - Anthracyclines
  - HER-2 targeting agents
  - Kinase inhibitors
  - Proteosome inhibitors



Algorithm for cancer therapy-related cardiac dysfunction (CTRCD)



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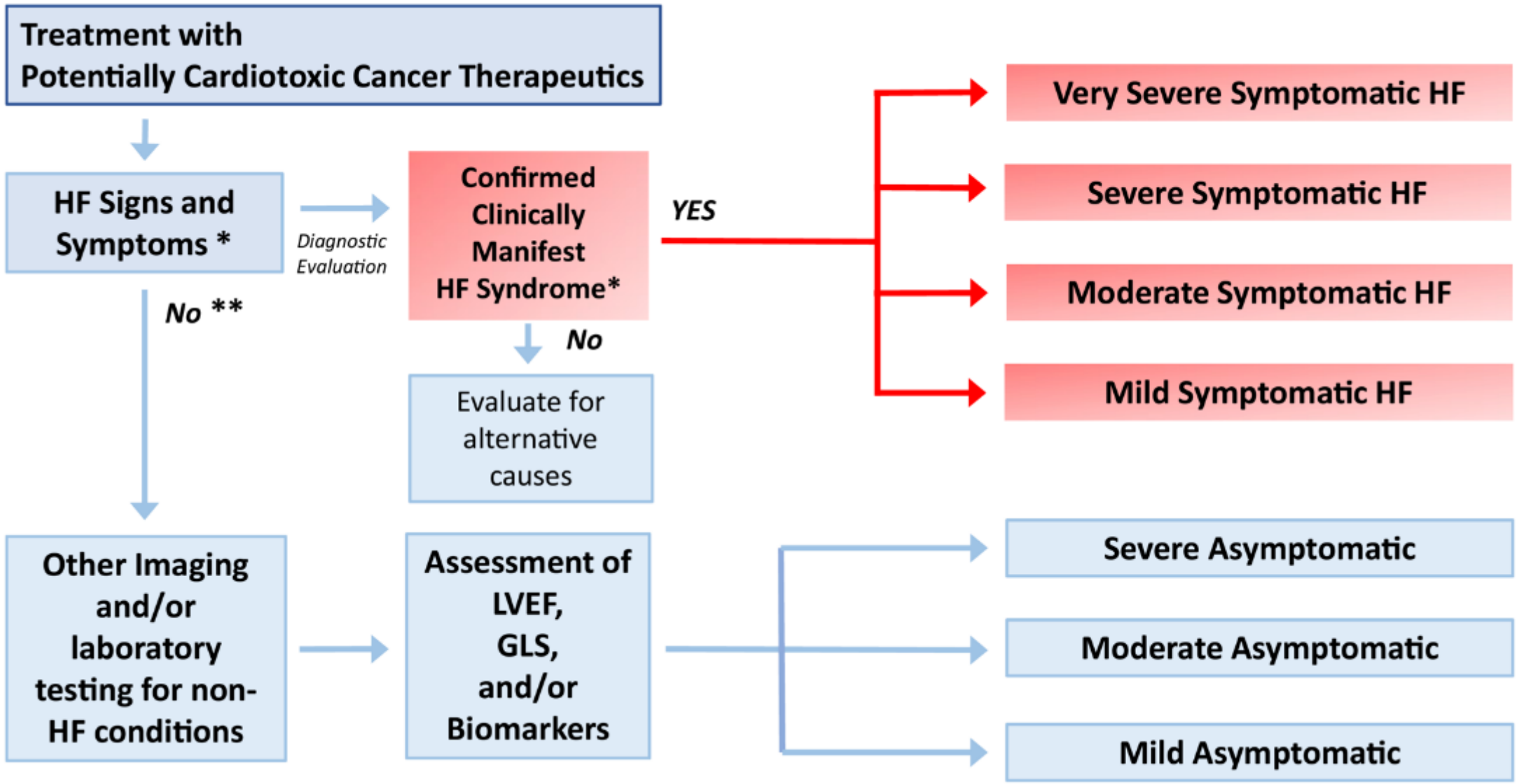
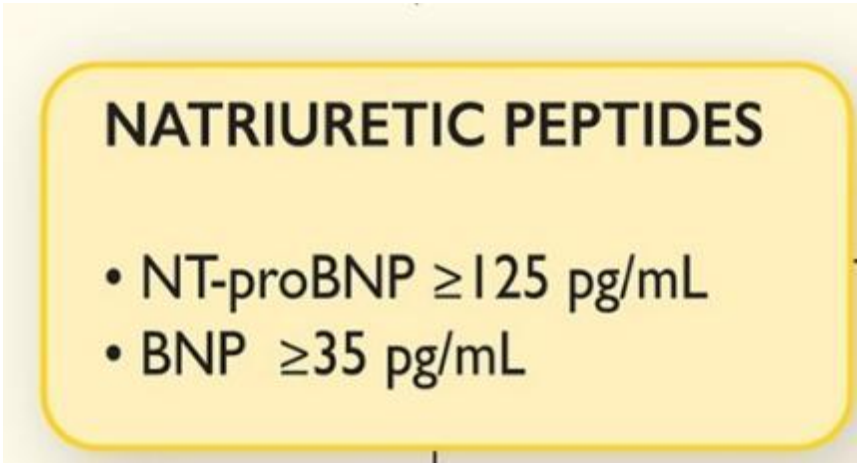


Herrmann J Eur Heart Jour. 2022;43:280-99.

Criteria for CTRCD

IC-OS 2021 Consensus	
Asymptomatic CTRCD (with or without additional biomarkers, LVEF values are based on 2D echocardiography)	**Mild** LVEF ≥50% AND new relative decline in GLS by >15% from baseline AND/OR new rise in cardiac biomarkers§



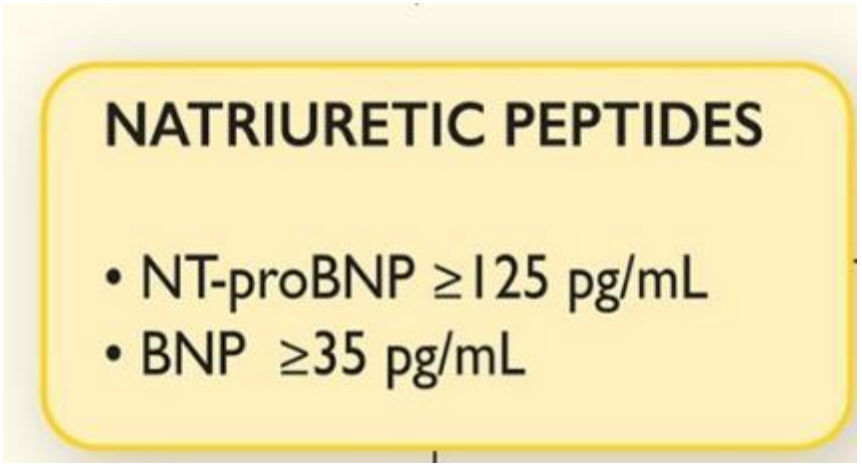
Maisel AS *et al.* NEJM. 2002; 347:161-7.
Roberts E BMJ 2015:350:h910.
Herrmann J Eur Heart Jour. 2022;43:280-99.

CardinalHealth

Criteria for CTRCD

IC-OS 2021 Consensus

Asymptomatic CTRCD (with or without additional biomarkers, LVEF values are based on 2D echocardiography)	**Mild**	**Moderate**	**Severe**
	LVEF ≥50% AND new relative decline in GLS by >15% from baseline AND/OR new rise in cardiac biomarkers§	New LVEF reduction by ≥10 percentage points to an LVEF of 40-49% New LVEF reduction by <10 percentage points to an LVEF of 40-49% AND new relative decline in GLS by >15% from baseline AND/OR new rise in cardiac biomarkers§	New LVEF reduction to <40%



Maisel AS *et al.* NEJM. 2002; 347:161-7.
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Herrmann J Eur Heart Jour. 2022;43:280-99.

CardinalHealth

Criteria for CTRCD

IC-OS 2021 Consensus

Asymptomatic CTRCD (with or without additional biomarkers, LVEF values are based on 2D echocardiography)

Mild

LVEF ≥50%

AND new relative decline in GLS by >15% from baseline

AND/OR new rise in cardiac biomarkers§

Moderate

New LVEF reduction by ≥10 percentage points to an LVEF of 40-49%

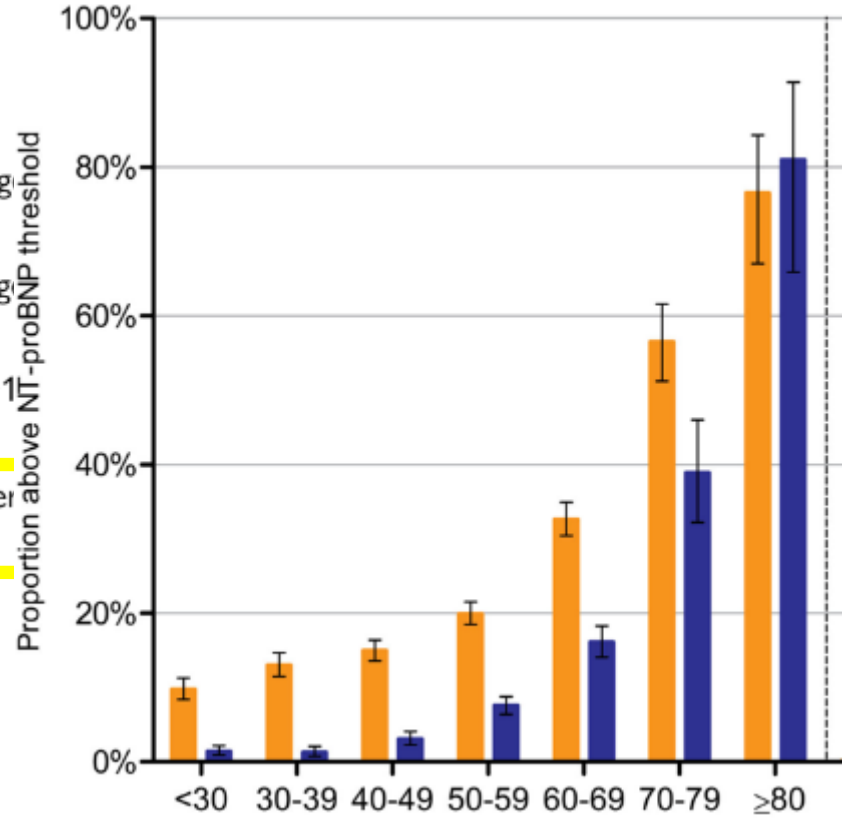
New LVEF reduction by <10 percentage points to an LVEF of 40-49%

AND new relative decline in GLS by >1 from baseline

AND/OR new rise in cardiac biomarker

NATRIURETIC PEPTIDES

- NT-proBNP ≥125 pg/mL
- BNP ≥35 pg/mL



Maisel AS *et al.* NEJM. 2002; 347:161-7.

Roberts E BMJ 2015:350:h910.

Herrmann J Eur Heart Jour. 2022;43:280-99.

CardinalHealth

Utility of biomarkers at baseline prior to treatment

Recommendation Table 3 — Recommendation for cardiac biomarker assessment prior to potentially cardiotoxic therapies

Recommendation	Class[a]	Level[b]
Baseline measurement of NP[c] and/or cTn[d] is recommended in all patients with cancer at risk of CTRCD if these biomarkers are going to be measured during treatment to detect CTRCD.[e,53,55]	I	C

ESC European Society of Cardiology European Heart Journal (2022) 43, 4229–4361 https://doi.org/10.1093/eurheartj/ehac244

ESC GUIDELINES

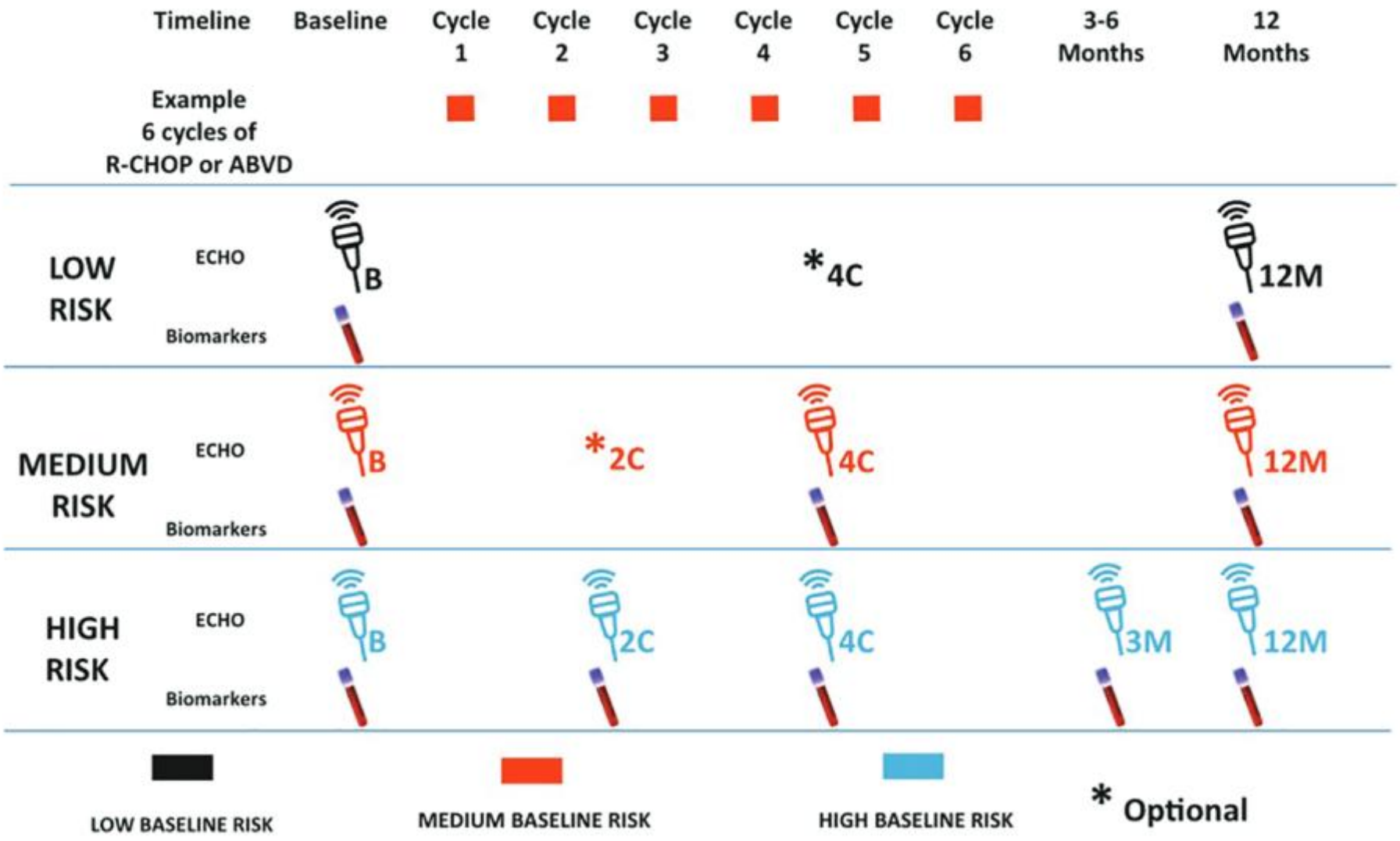
2022 ESC Guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS)

Developed by the task force on cardio-oncology of the European Society of Cardiology (ESC)

Lyon AR. European Heart Journal 2022;43:4229-361.

CardinalHealth

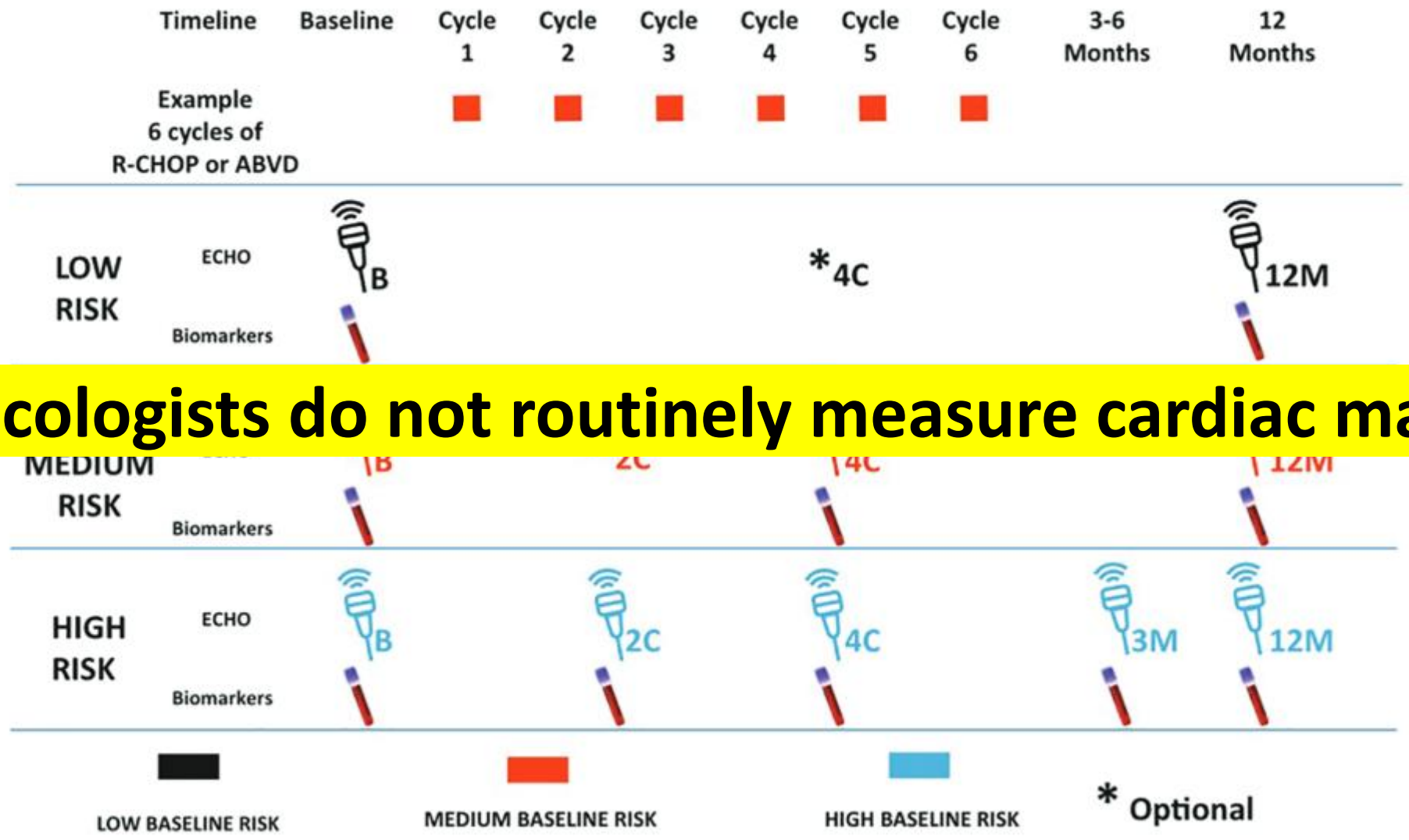
ESC recommendations for serial monitoring



Pudil R,. *Eur J Heart Fail* 2020;**22**:1966–83.

CardinalHealth

ESC recommendations for serial monitoring



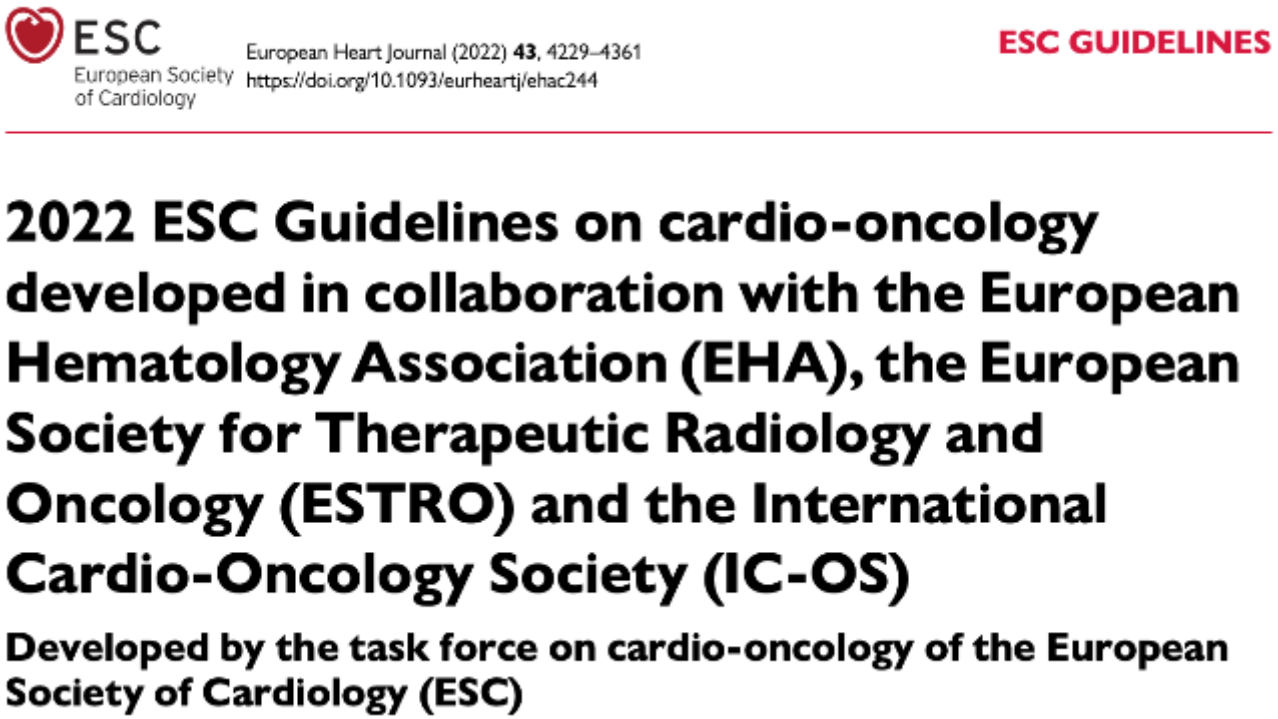
Most oncologists do not routinely measure cardiac markers

Pudil R,. *Eur J Heart Fail* 2020;**22**:1966–83.

CardinalHealth

What are the correct thresholds for ruling in / out CTRCD?

"It is important to consider that generally accepted cut-offs and reference values of CV biomarkers have not been established for patients with cancer or for those who receive cancer therapies."



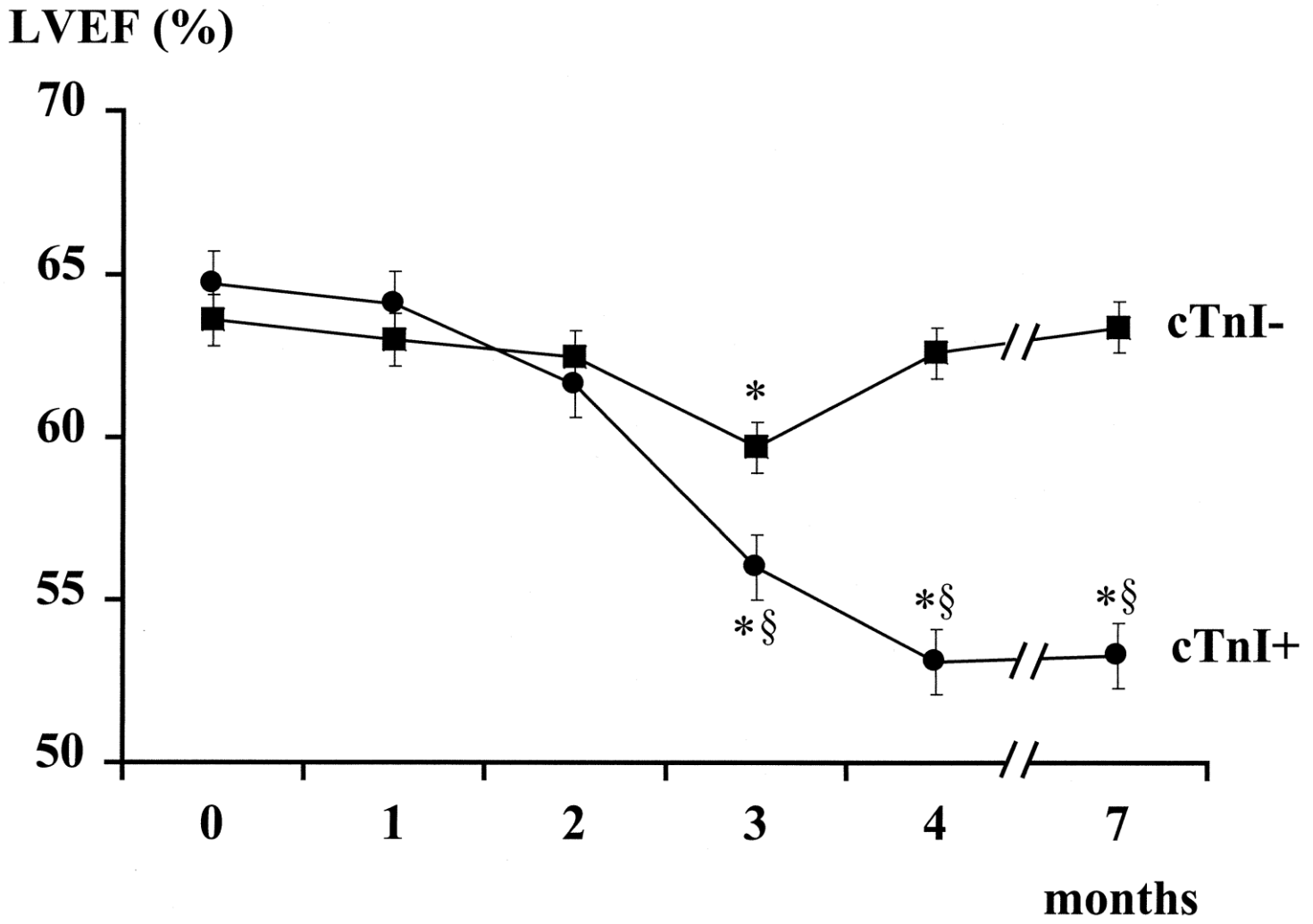
Lyon AR. European Heart Journal 2022;43:4229-361.

CardinalHealth

Elevated cTnI associated with LV Dysfunction

- 204 patients with cancer
- cTnI measured every cycle
- 45 with cTnI > 0.4 ng/mL
- 139 with cTnI ≤ 0.4 ng/mL

- 0.4ng/mL= 400 ng/L

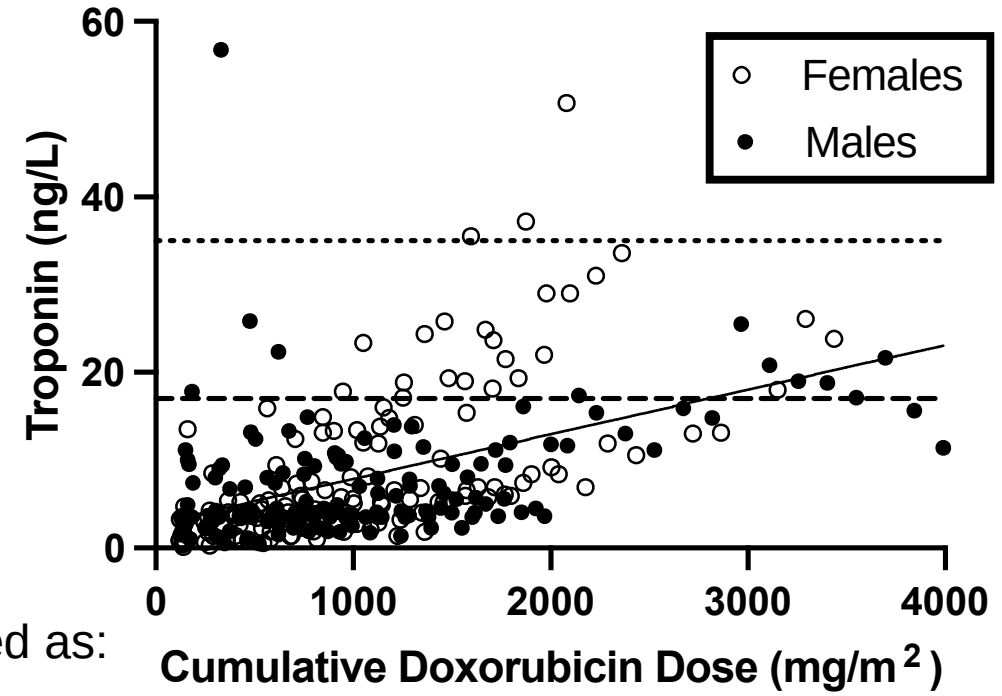


Cardinale D. *J Am Coll of Cardiol* 2000:36:517-22.

CardinalHealth

Do elevated or a change in biomarkers predict CTCRD?

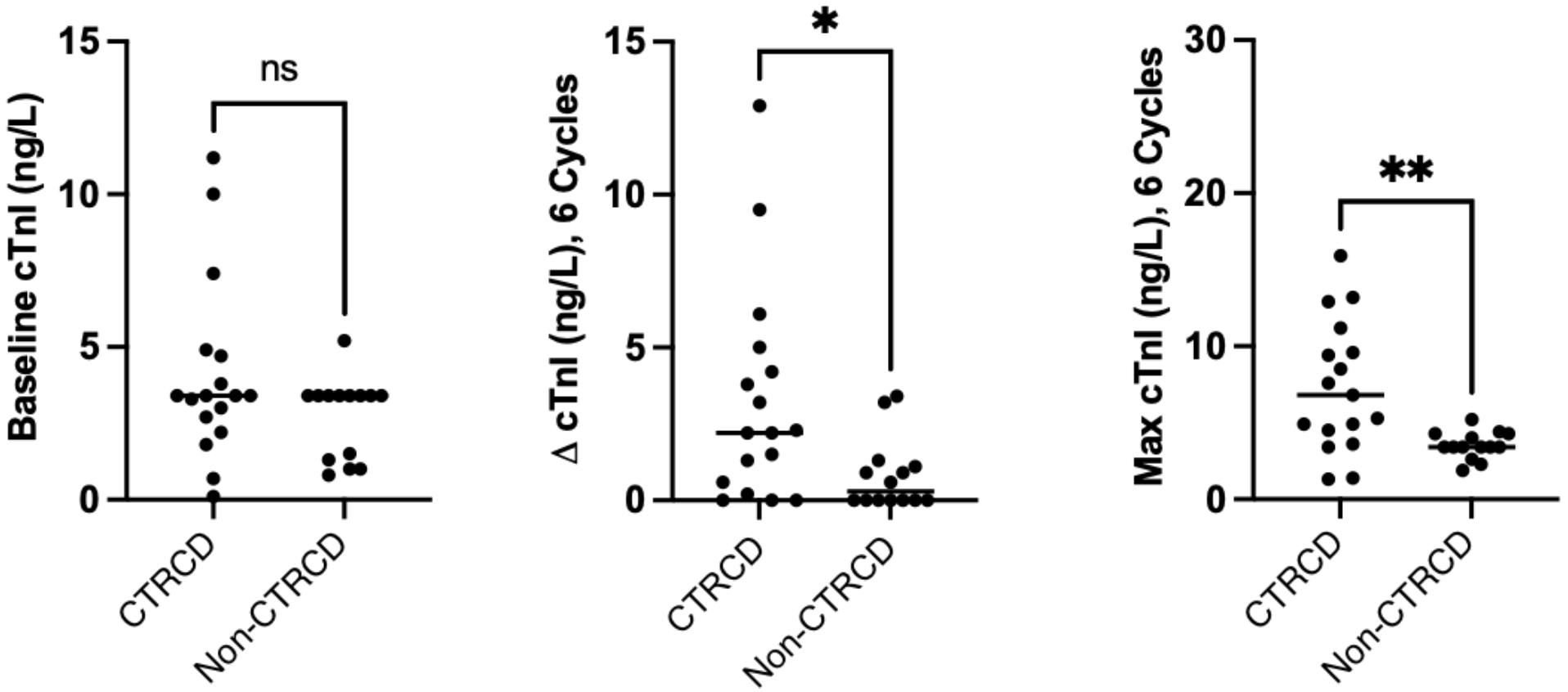
- Patients with metastatic or unresectable sarcoma (previously untreated)
- Doxorubicin (cycles of 75 mg/m^2 every 21 days)
- Dexrazoxane initiated cycle 1 and
  - continued through the duration of the study,
  - administered with each dose of doxorubicin
  - 10:1 ratio to doxorubicin (750 mg/m^2)
- 62 patients with biomarkers enrolled
- Cancer therapy related cardiac dysfunction (CTRCD) defined as:
  - 10% reduction in LVEF & < 50%



Spearman R = 0.57 (95% CI, 0.48-0.65)

Krone R, Mitchell J, Van Tine B, Farnsworth CW, Unpublished Data

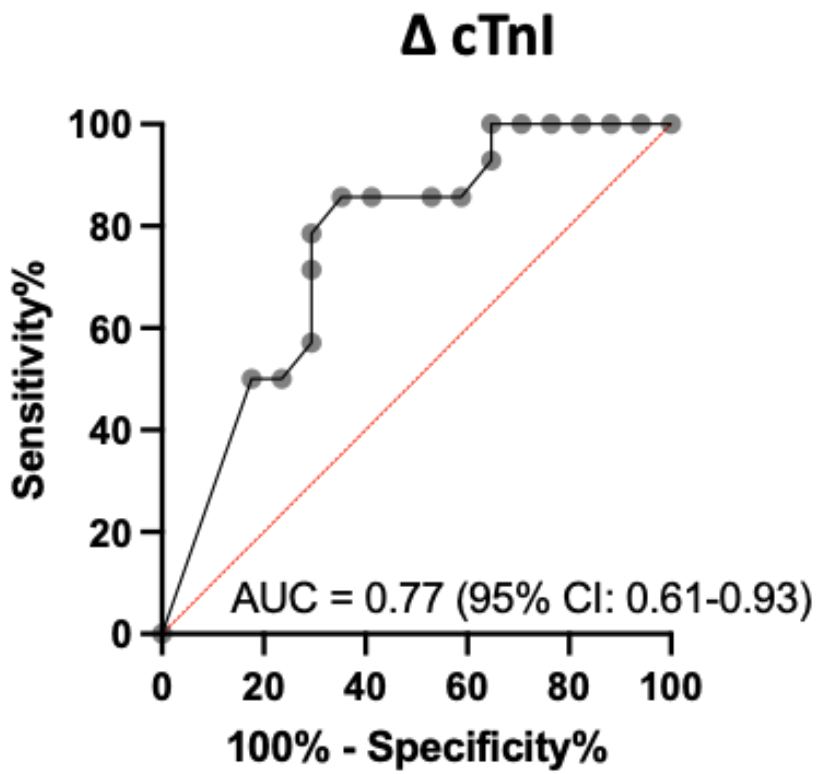
Change in cTnI and max cTnI predict cardiotoxicity

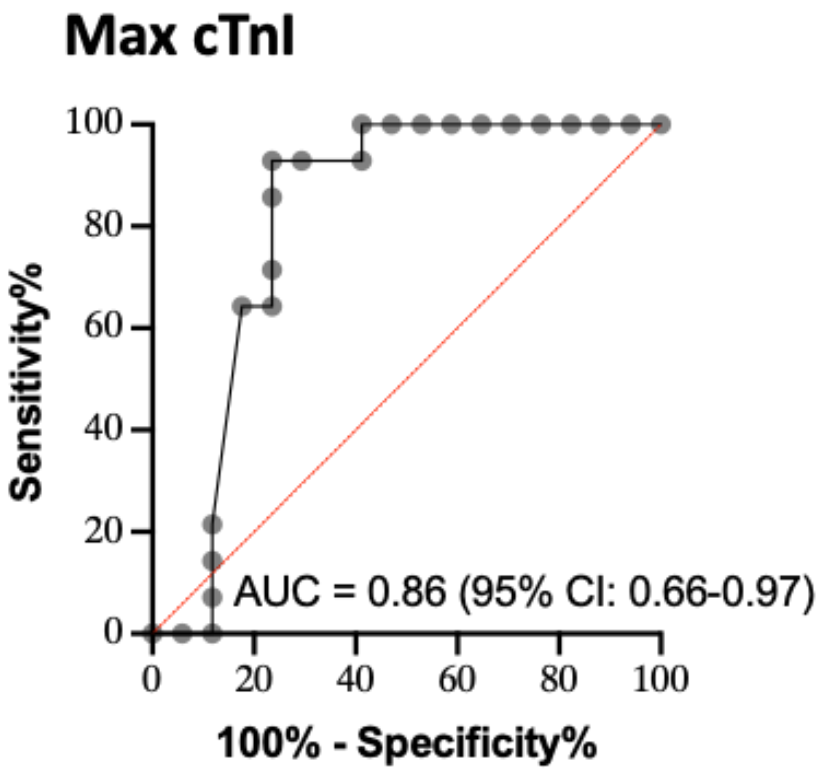


Krone R, Mitchell J, Van Tine B, Farnsworth CW, Unpublished Data

CardinalHealth

Small changes in cTnI predicts cardiotoxicity





Δ cTnI of 3 ng/L = Sensitivity 85.7 (60.0-97.5)
Specificity 47.1 (21.6-64.0)

cTnI ≥ 5 ng/L = Sensitivity 92.9 (68.5-99.6)
Specificity 70.6 (46.9-86.7)

Krone R, Mitchell J, Van Tine B, Farnsworth CW, Unpublished Data

CardinalHealth

Study Design

- 80 patients with any history of cancer on current chemotherapy
- Referred to cardio-oncology
- Study design: patients enrolled at baseline (any point in chemotherapy)
  - Visited clinic every 3 months for appointments and blood draw
  - Echocardiogram performed at baseline and every 6 months
- **Hypothesis:** cardiac biomarkers will predict CTRCD (physician dx. or drop in EF by ≥10%)

Mitchell J, Farnsworth CW, Unpublished Data

Study Design

Demographics	
N=	80
Male (%)	35 (43.8%)
White (%)	63 (78.8%)
Age (IQR)	63 (54-72)
Median # Timepoints (IQR)	8 (3-9)
# CTRCD	**25 (31%)**
# Died	22 (27.5%)

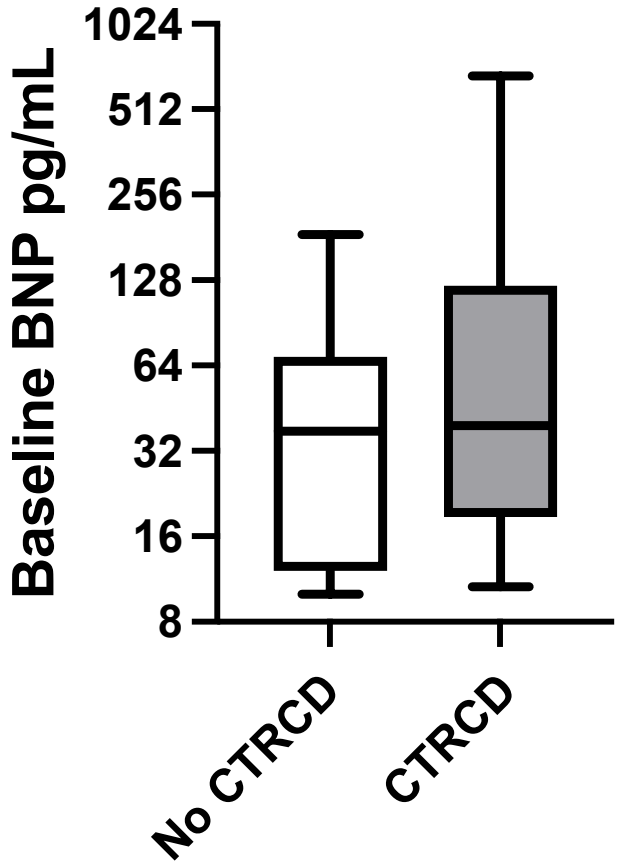
45% with CTRCD died within 2 years vs. 25% in those without CTCRD (p= 0.18)

- Hypothesis: cardiac biomarkers will predict CTRCD (physician diagnosis or drop in EF by ≥10%)

64 Mitchell J, Farnsworth CW, Unpublished Data

CardinalHealth

No difference in baseline biomarkers in patients with CTRCD



Mitchell J, Farnsworth CW, Unpublished Data

CardinalHealth

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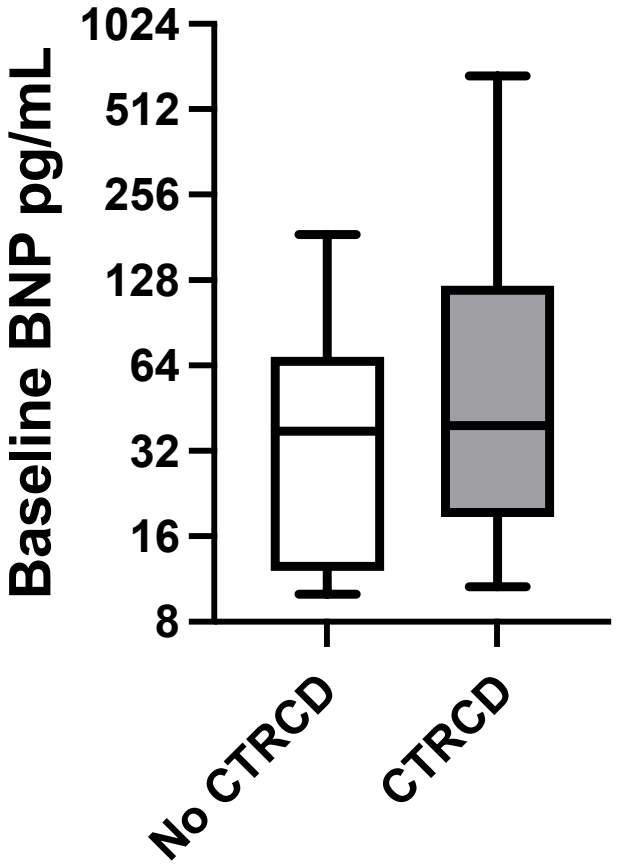

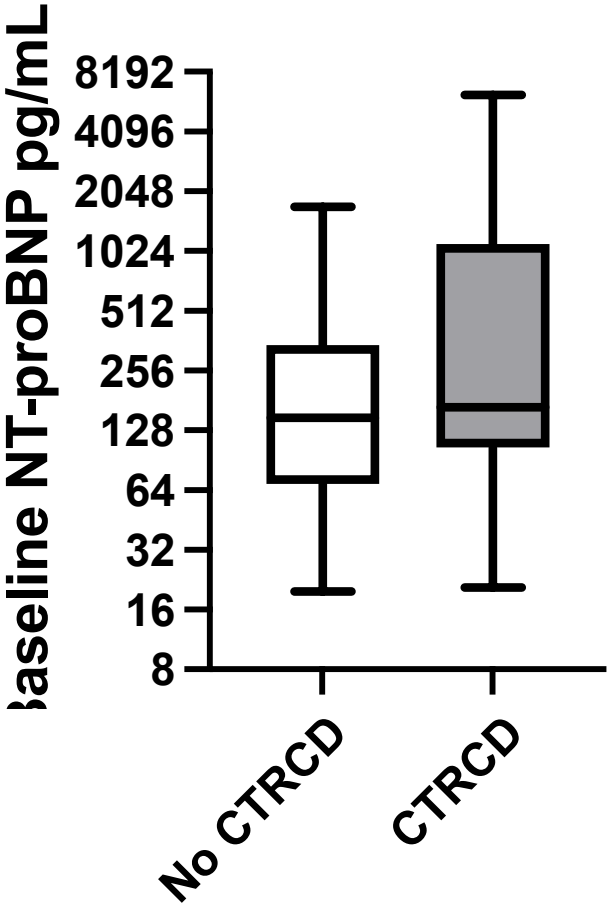

Mitchell J, Farnsworth CW, Unpublished Data

CardinalHealth

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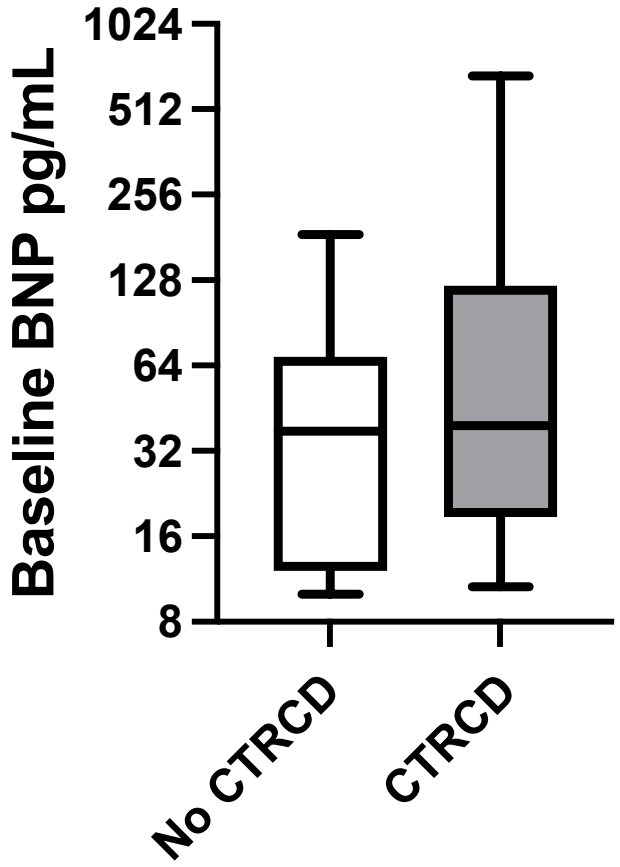
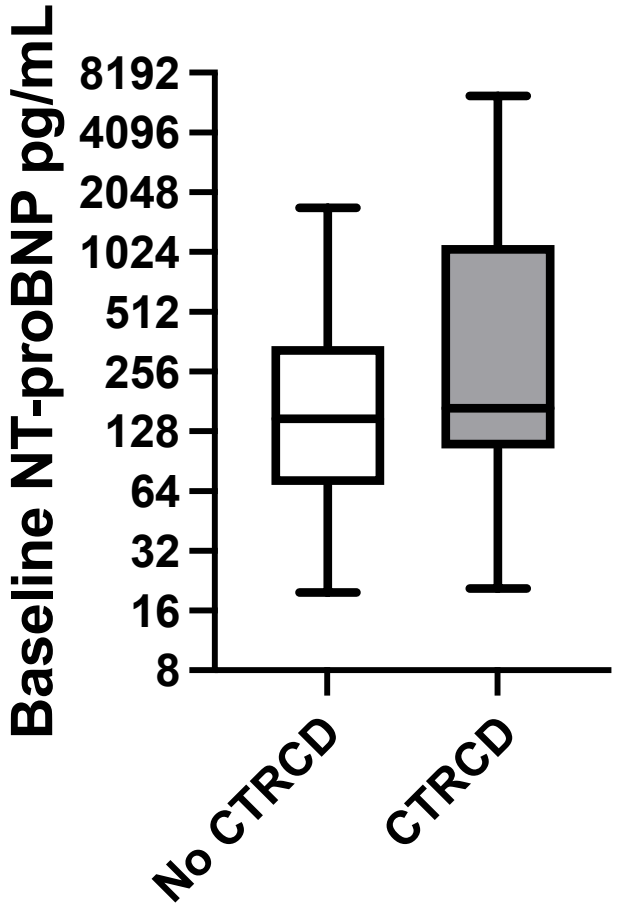
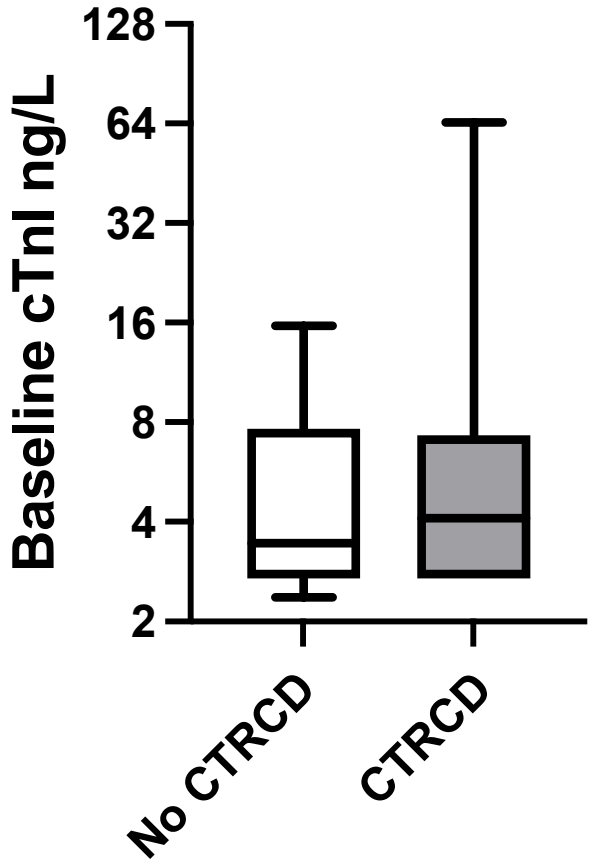


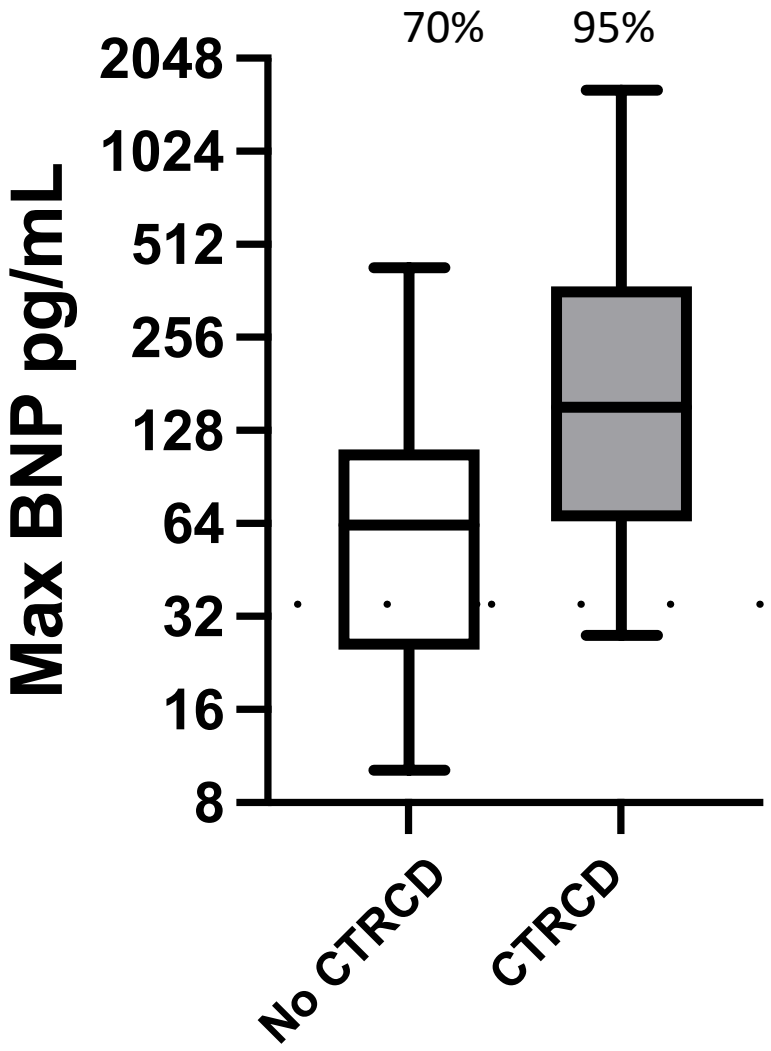


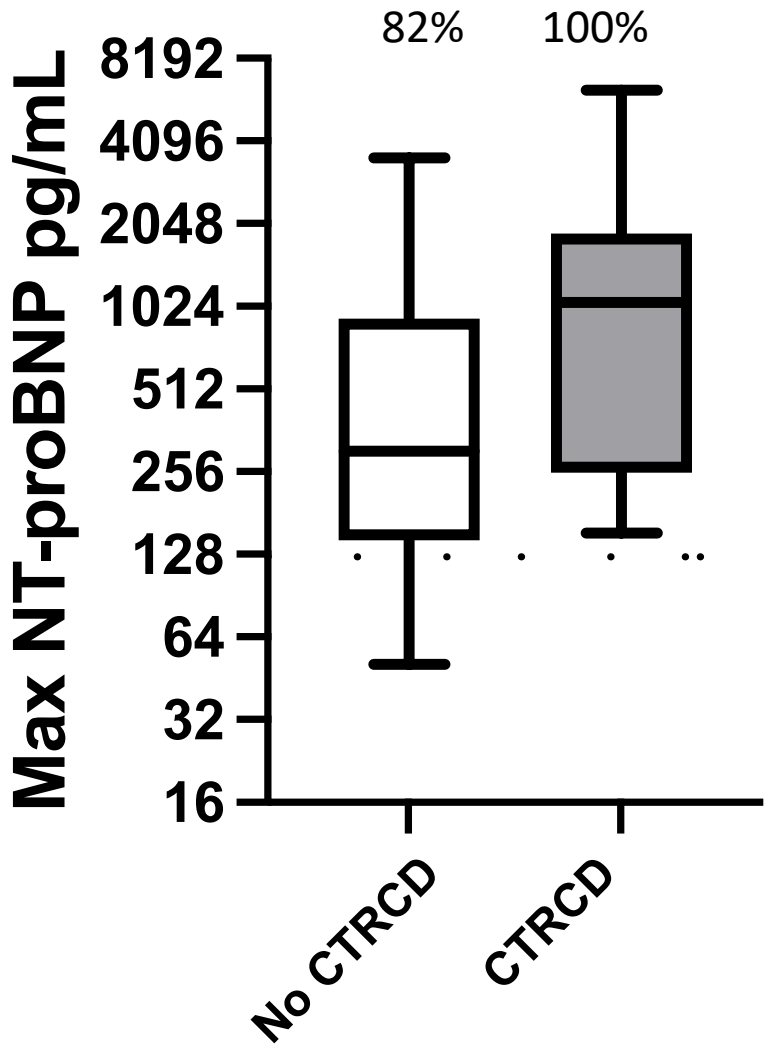


Mitchell J, Farnsworth CW, Unpublished Data

CardinalHealth

Most patients have NPs above guideline endorsed thresholds





NT-proBNP ≥125 pg/mL

Sensitivity = 63.6 (43.0-80.3)

Specificity = 45.7 (32.2-59.8)

BNP ≥35 pg/mL

Sensitivity = 59.1 (38.7-76.7)

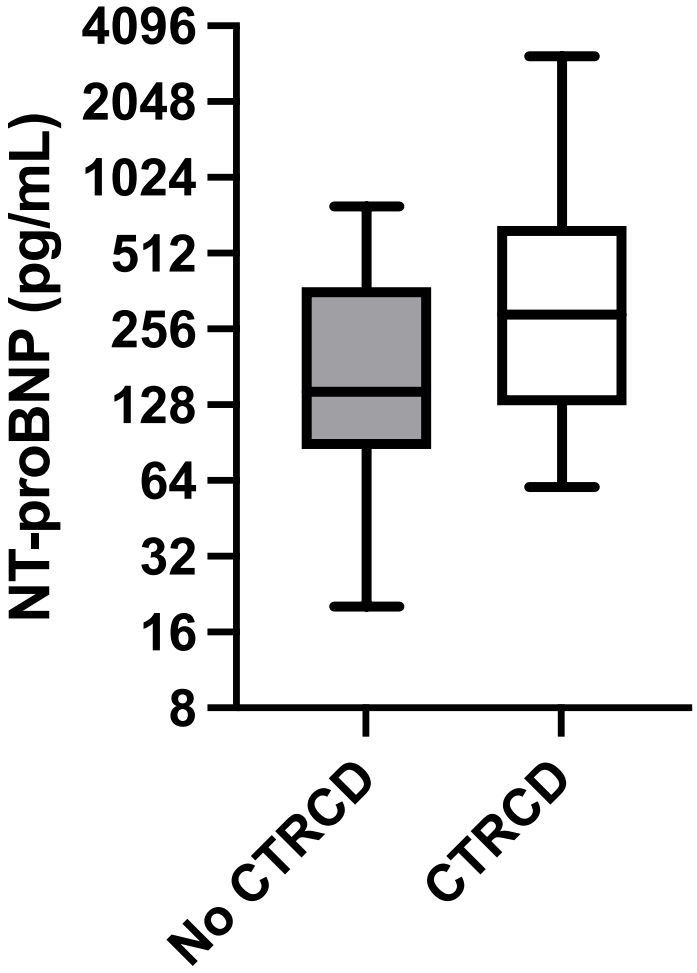
Specificity = 45.7 (32.2-59.8)

68 Mitchell J, Farnsworth CW, Unpublished Data

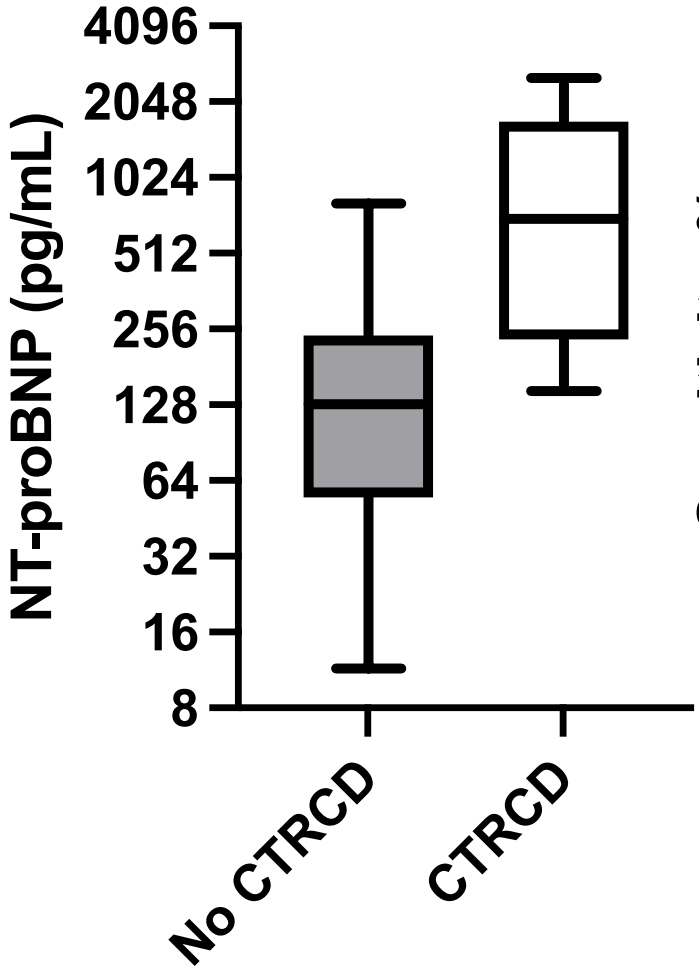
CardinalHealth

NT-proBNP most useful for diagnosis at cycle

1 Cycle pre-Dx

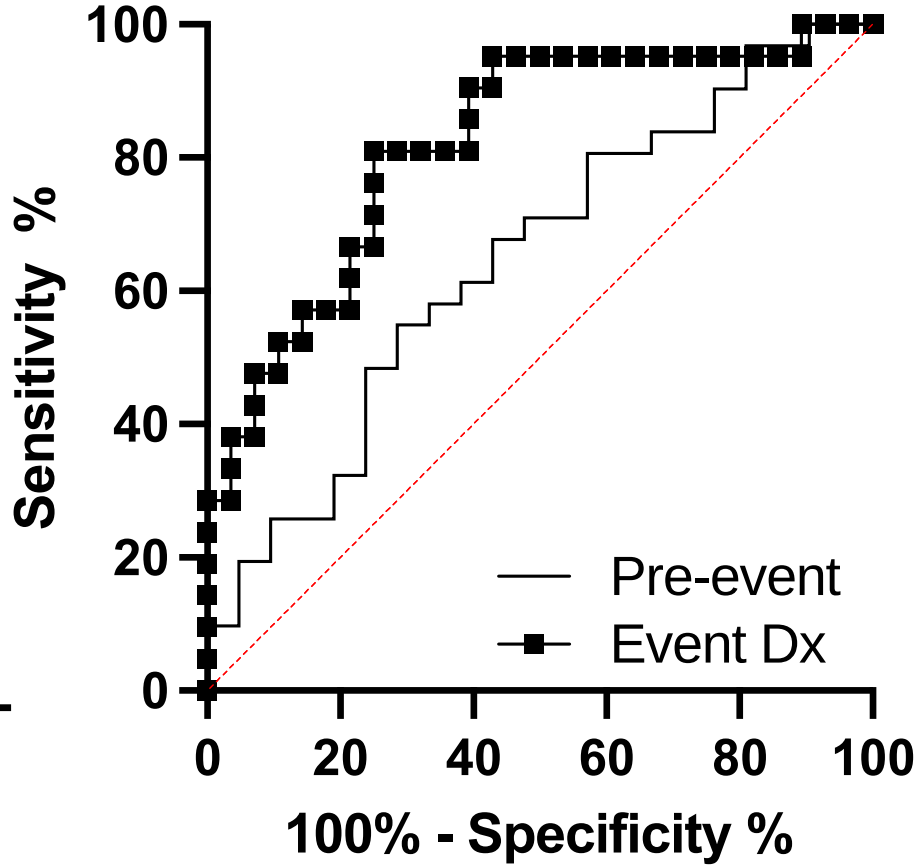


Cycle of Dx



Pre-event AUC: 0.65 (0.49-0.8)

Event-Dx AUC: 0.82 (0.7-0.94)



225 pg/mL

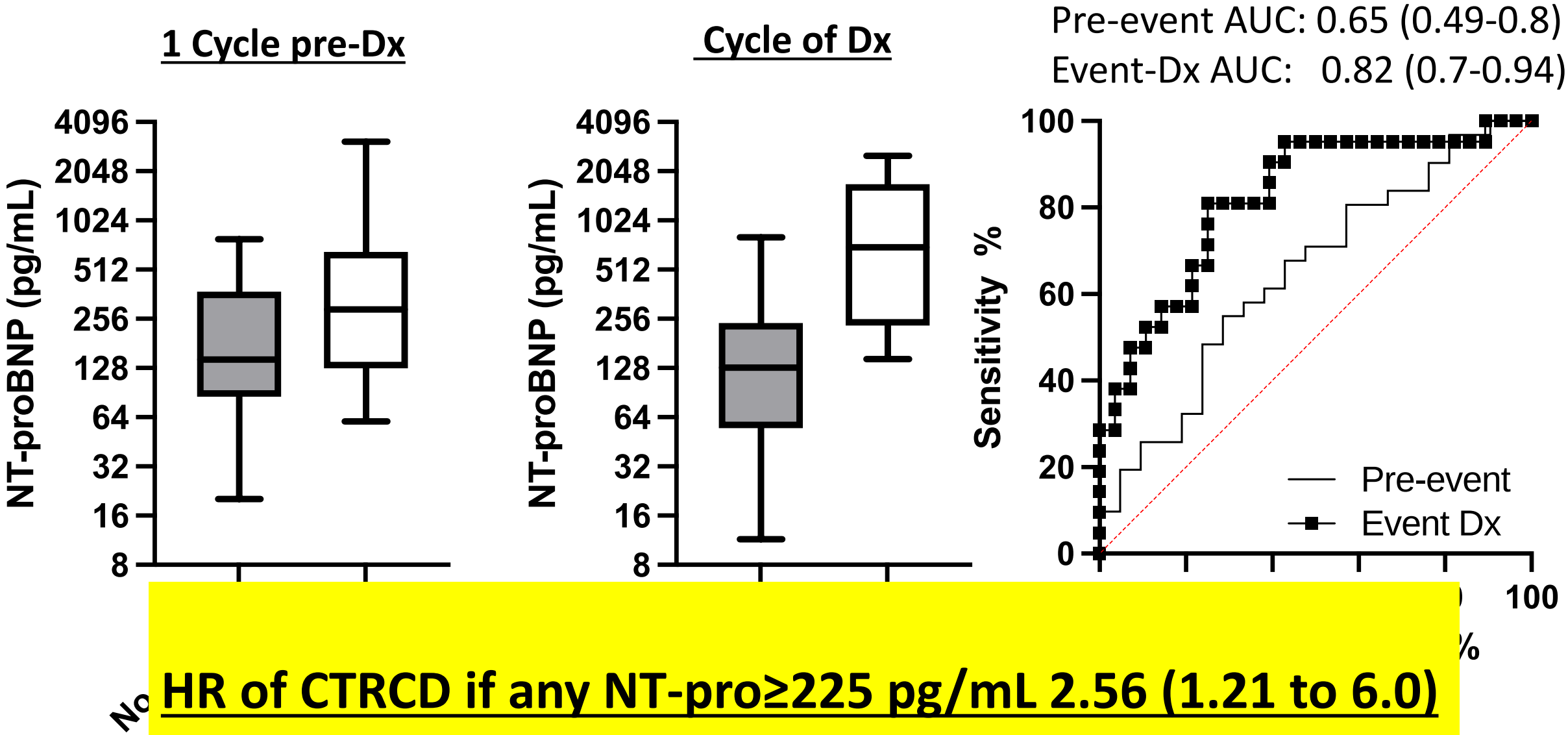
Sensitivity: 81% (60-92)

Specificity: 75% (56-87)

Mitchell J, Farnsworth CW, Unpublished Data

CardinalHealth

NT-proBNP most useful for diagnosis at cycle



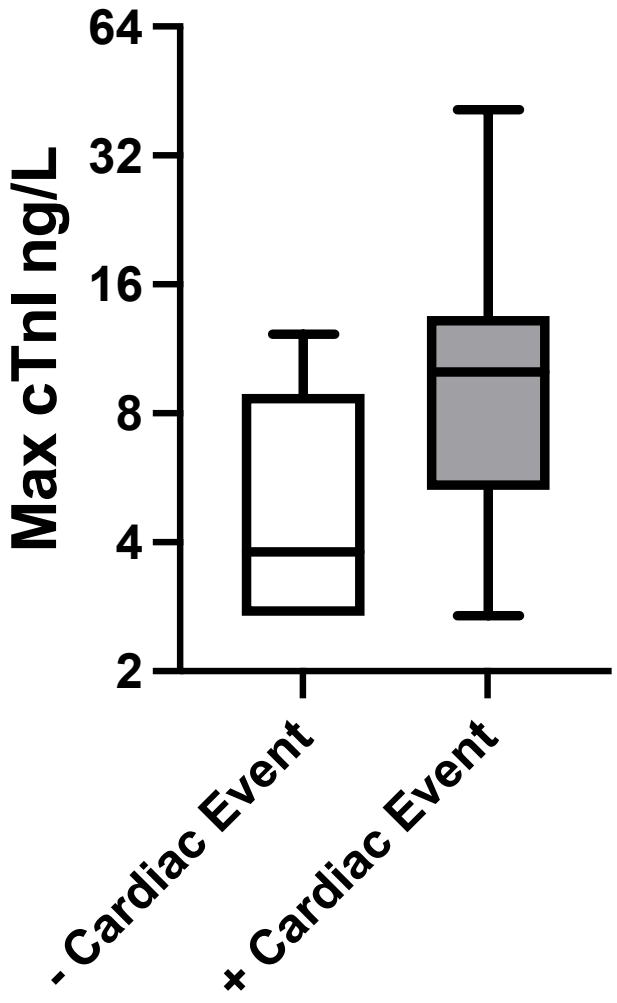
HR of CTRCD if any NT-pro≥225 pg/mL 2.56 (1.21 to 6.0)

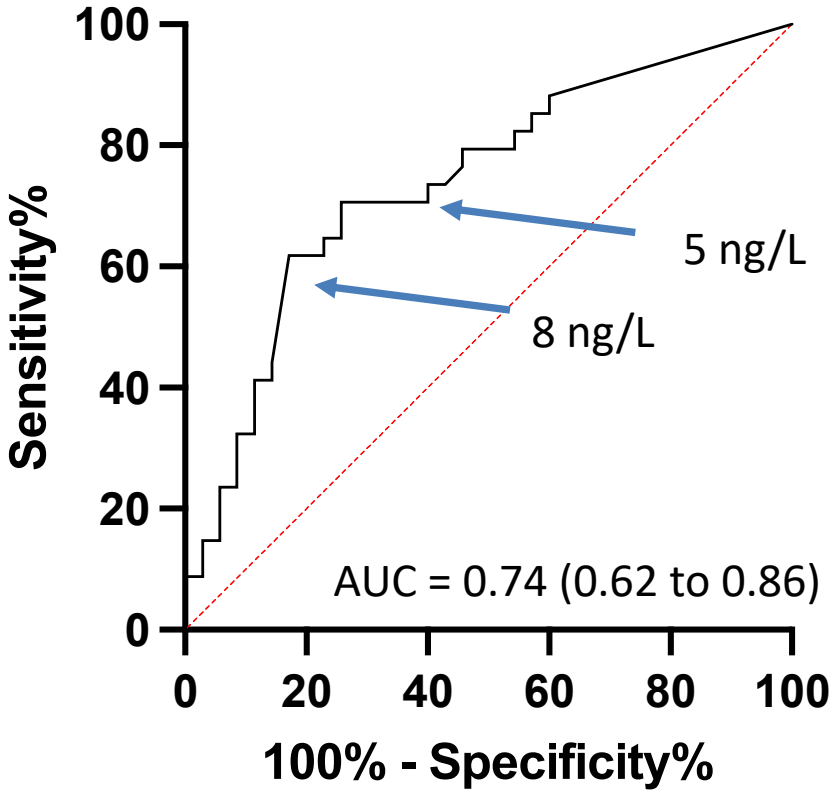
Specificity: 75% (56-87)

Mitchell J, F

CardinalHealth

Max cTnI is useful for predicting cardiac events





cTnI ≥ 8 ng/L

Sensitivity = 71%

Specificity = 74%

HR of cardiac event:

cTnI ≥ 8 ng/L 2.53 (1.52 to 4.35)

Cardiac event = stroke, arrhythmia, ACS, HF

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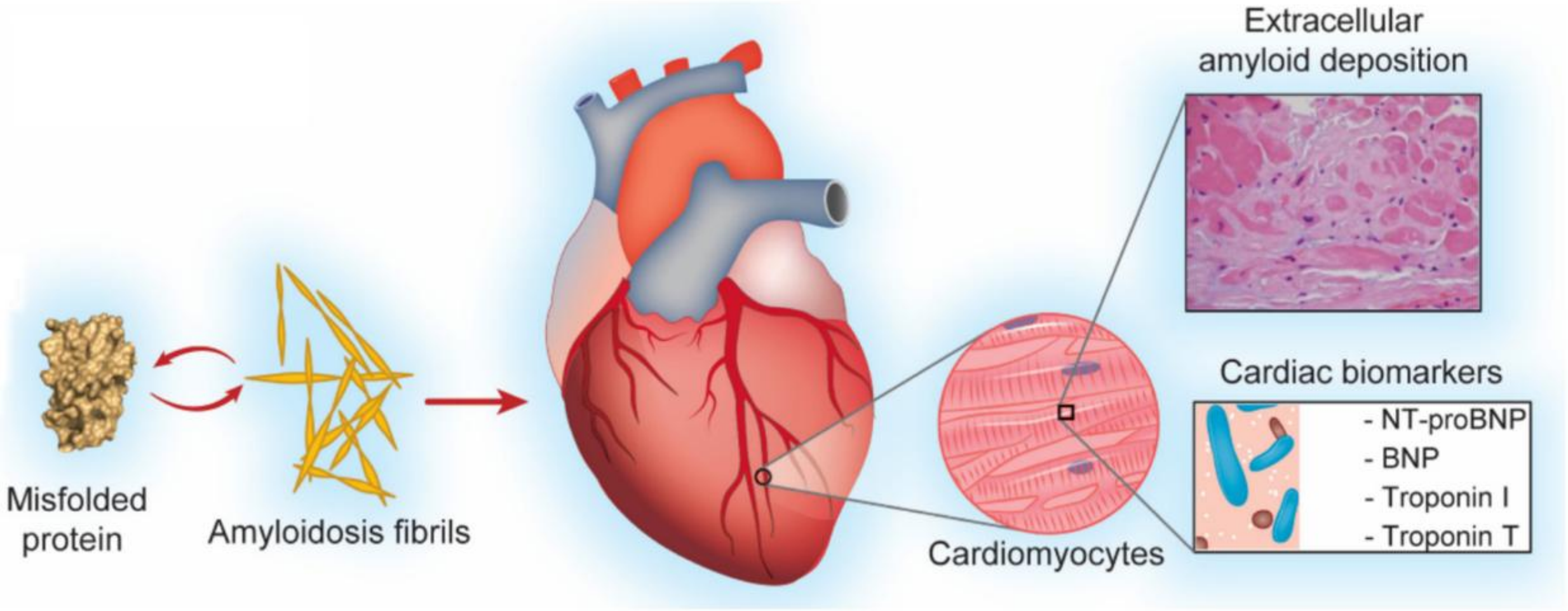
Utility of cardiac markers in Cardio-oncology

1. Several therapy types (conventional, targeted, immunotherapies) are associated with cardiotoxicity
2. cTn and NPs are endorsed by consensus statements
3. cTn and NP thresholds for predicting cardiac dysfunction / diagnosis are likely imperfect
4. Ideal cutoffs will likely be cancer dependent and context dependent (i.e., untreated, previously treated, referred)

Utility of cardiac markers for staging amyloidosis



Pregenzer-Wenzler A et al. JACC Heart Failure 2020;8:701-11

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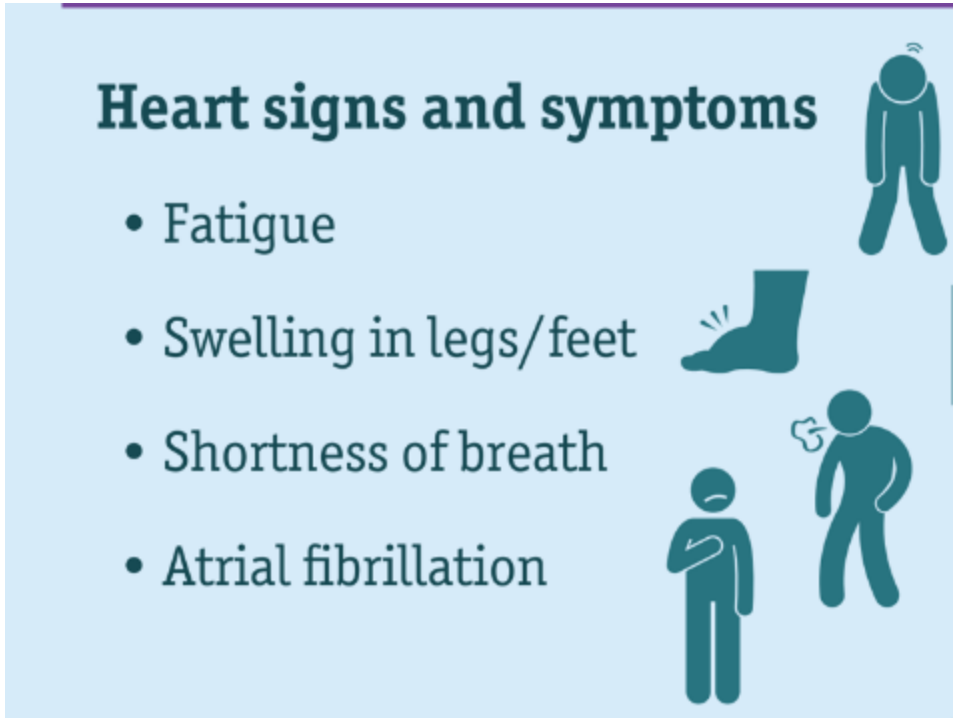
Utility of cardiac markers for staging cardiac amyloidosis



Blood and urine tests to look for monoclonal proteins

If found, it may be light chain **(AL) amyloidosis** – a medical emergency

- A blood specialistv (hematologist) treats this

A heart PYP scan to see if there is amyloid (PYP = pyrophosphate)

If yes, it's likely transthyretin **(ATTR) amyloidosis**

- A cardiologist treats this
- Genetic testing is needed

Other needed tests

https://www.cardiosmart.org/topics/cardiac-amyloidosis

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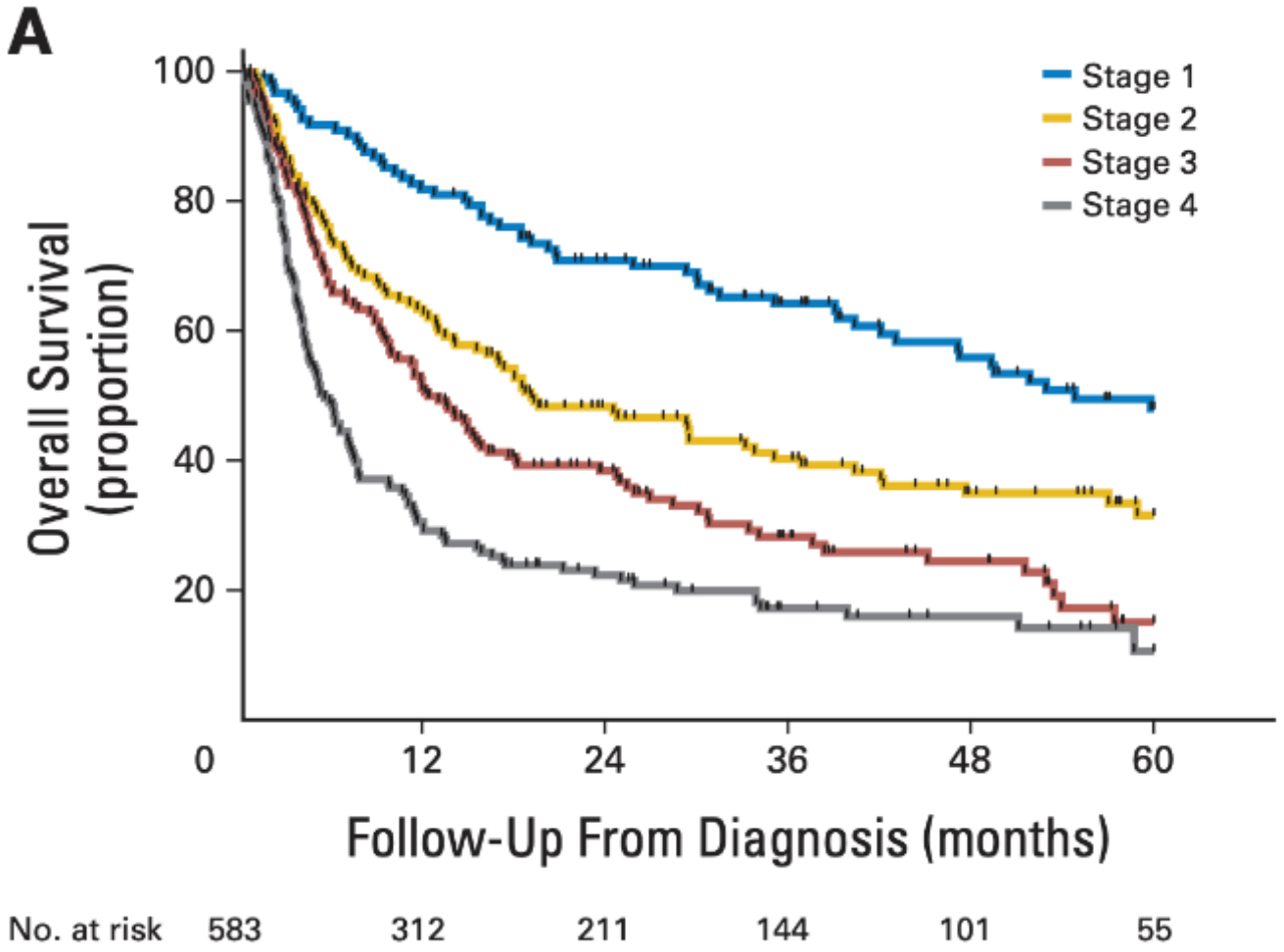
Utility of cardiac markers for staging cardiac amyloidosis

Assigned a score of 1 for each:

- FLC-diff 18 mg/dL
- cTnT ≥ 25 ng/L
- NT-ProBNP ≥ 1,800 pg/mL



Kumar S et al. Jour of Clinical Oncology 2012;30:689-95.

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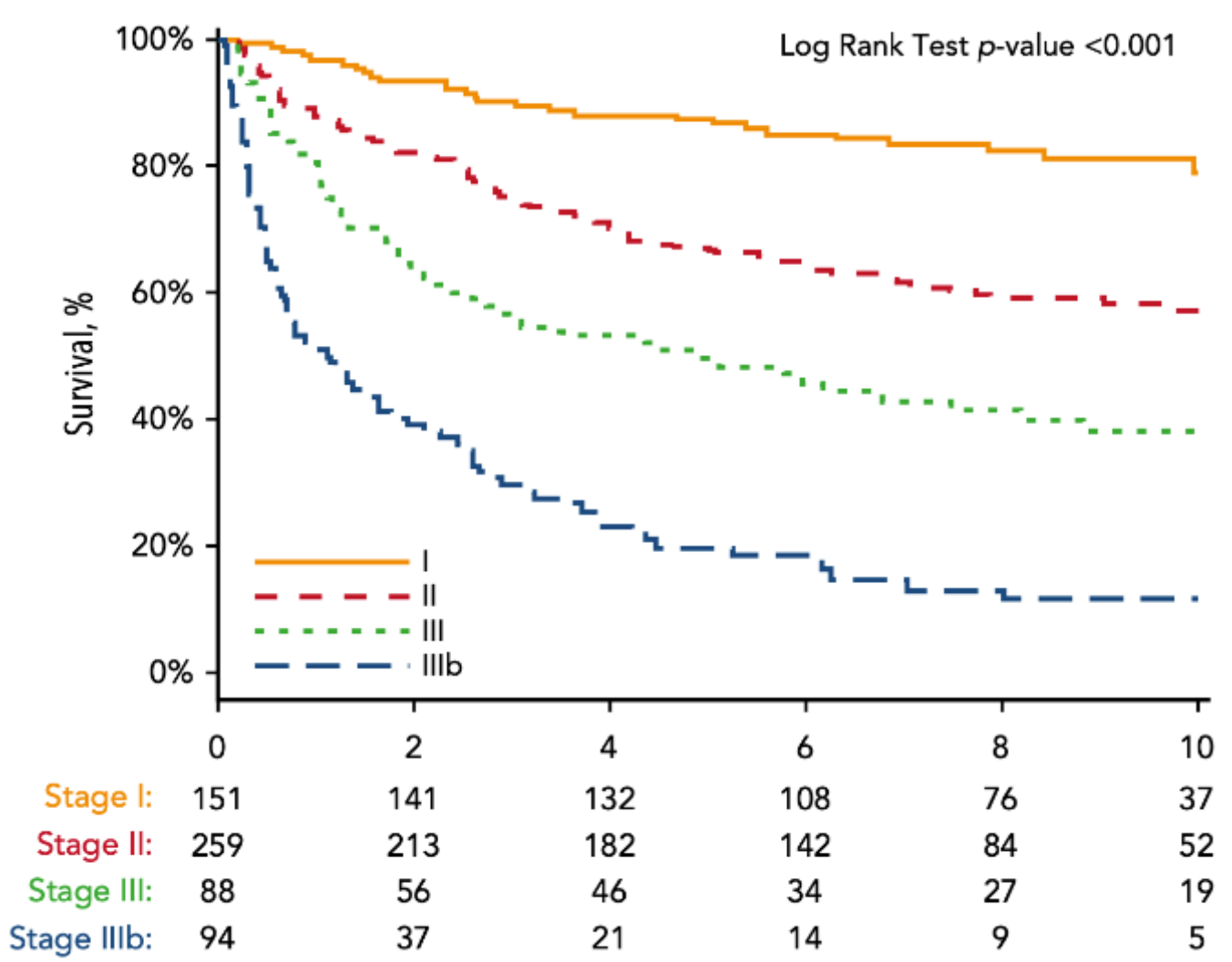
cTnI and BNP can be used to stage amyloidosis

Boston University Staging System

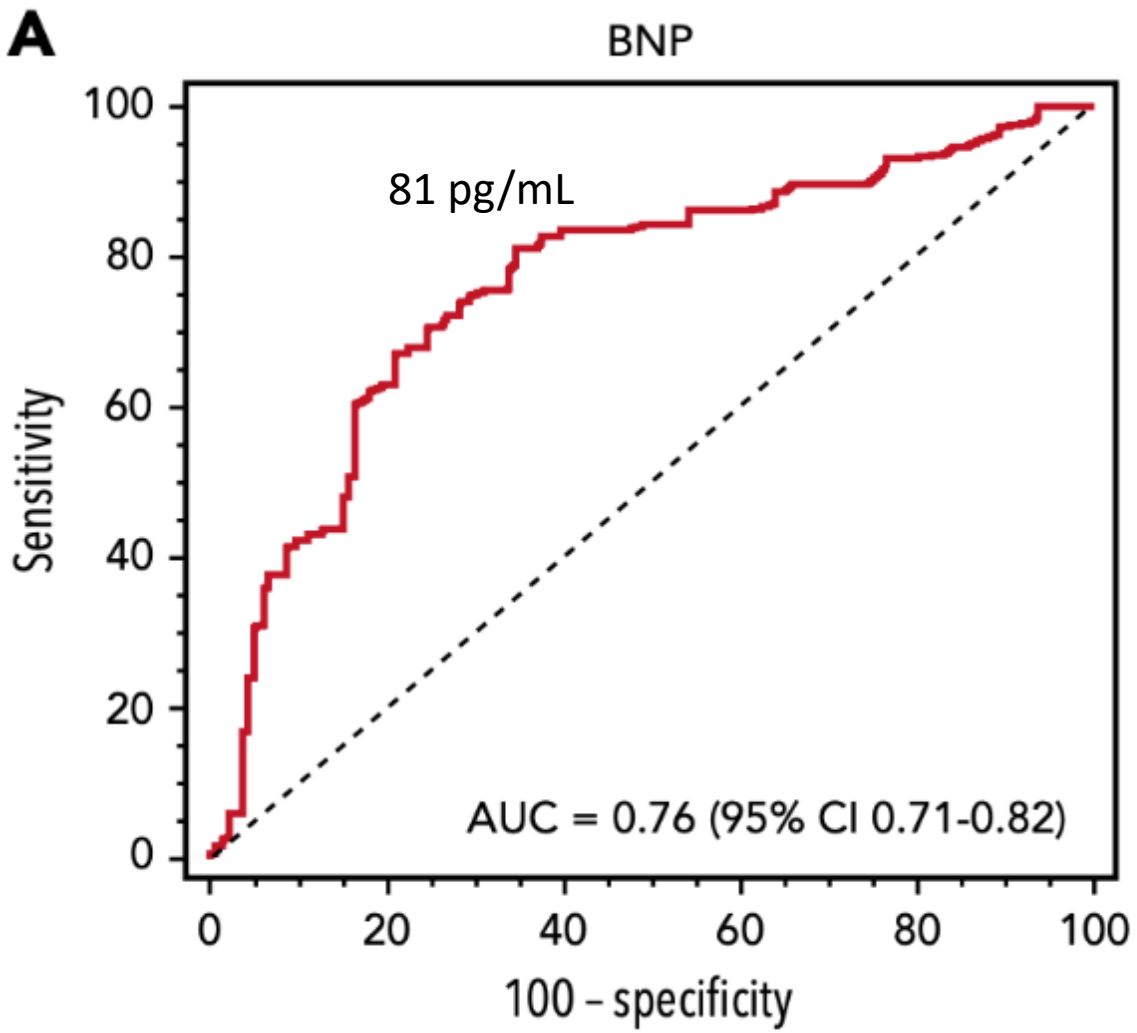
- FLC-diff 18 mg/dL
- cTnI > 100 ng/L,
- BNP > 81 pg/mL
- Stage III- BNP> 700 pg/mL

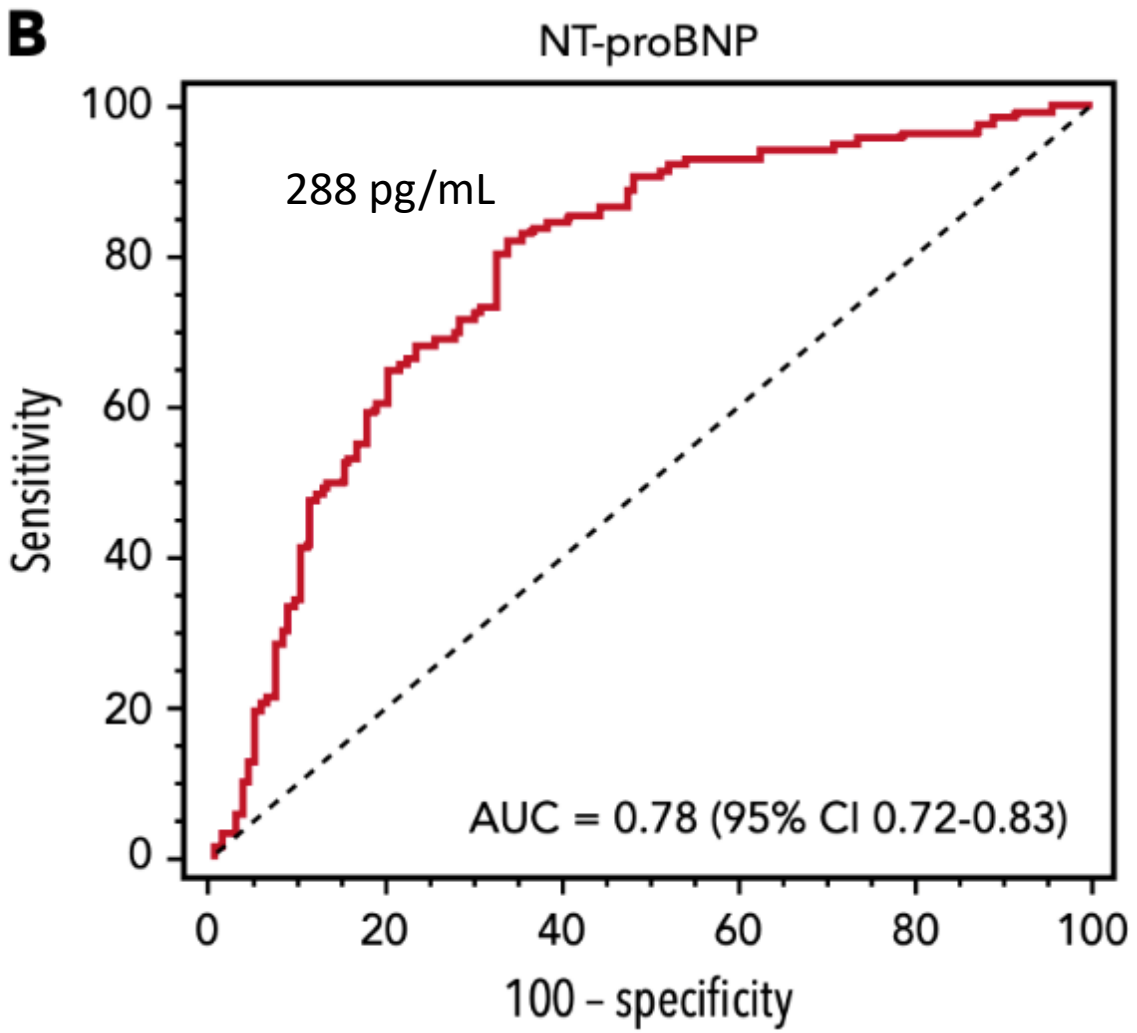
	Mayo Stage I	Mayo Stage II	Mayo Stage III
BU Stage I	94	10	0
BU Stage II	15	92	1
BU Stage III	0	1	36



Lilleness B et al. Blood 2019;133:215-223.

NP assays perform comparably for determining cardiac involvement





Lilleness B et al. Blood 2019;133:215-223.

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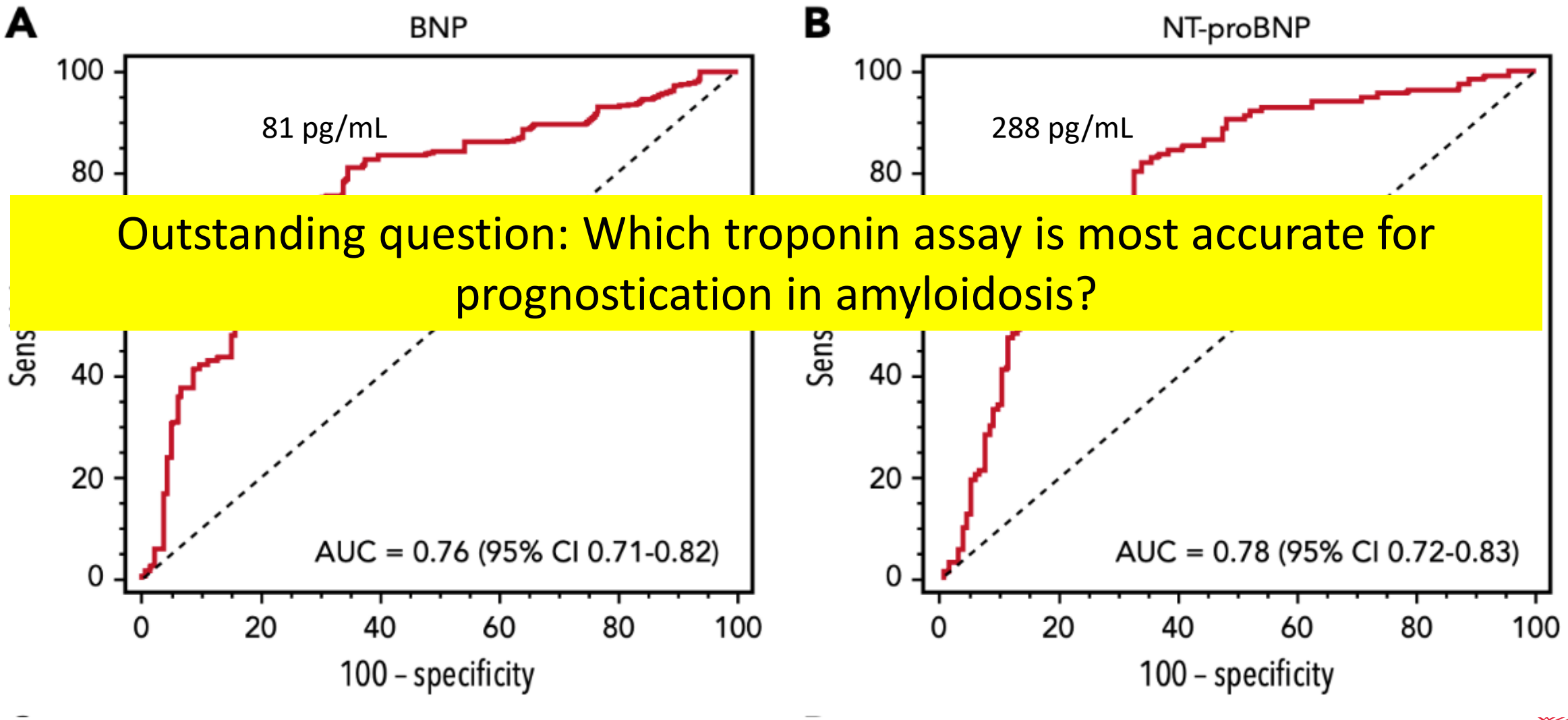
NP assays perform comparably for determining cardiac involvement



Outstanding question: Which troponin assay is most accurate for prognostication in amyloidosis?

Lilleness B et al. Blood 2019;133:215-223.

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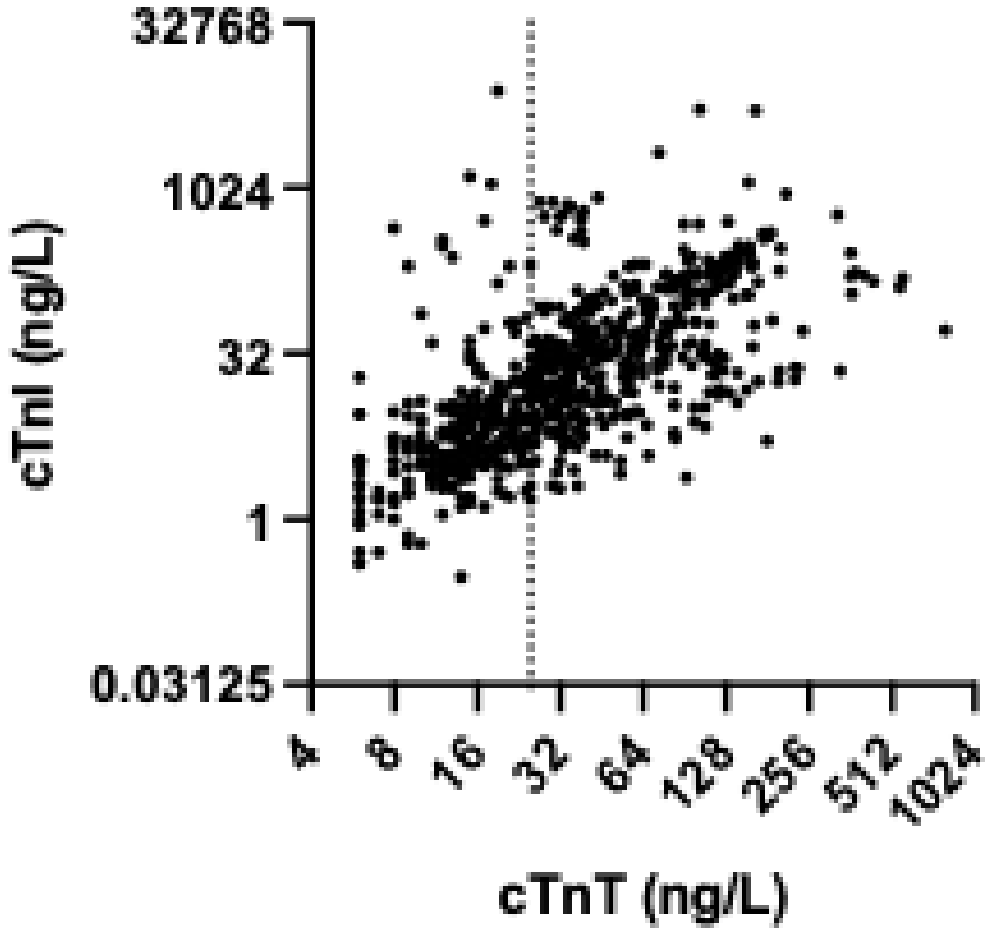
Study Design

- 692 specimens from ~300 patients with physician diagnosed or c/f cardiac amyloidosis
- Physician ordered NT-proBNP, cTnT

- Chart review for:
  - DX date, comorbidities, EF, global, lab values (eGFR, FLC)
- Staged using Mayo criteria
- Remnant sample tested for
  - hs-cTnI, BNP, Galectin 3



Farnsworth unpublished data

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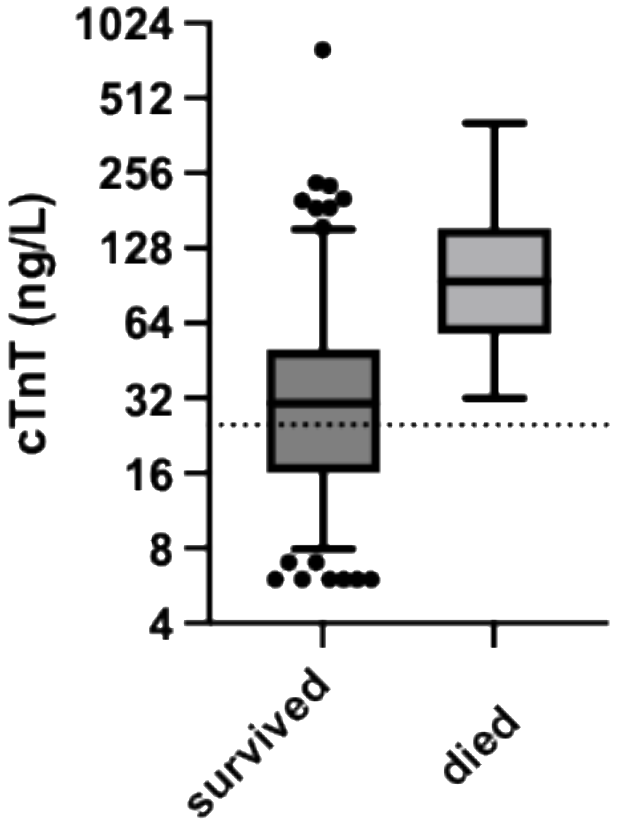
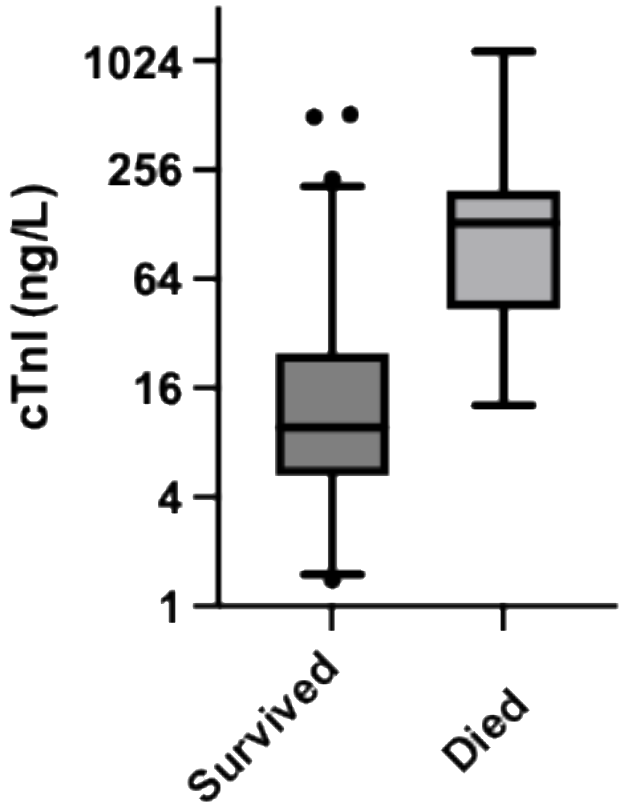
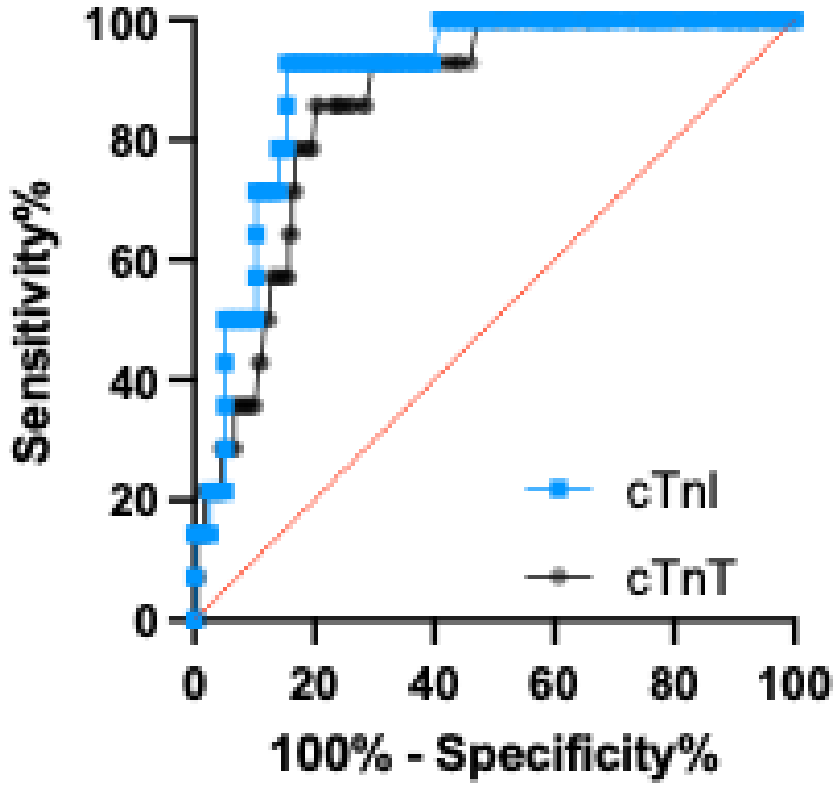
cTnI and cTnT have similar prognostic capabilities







Sensitivity = 100%
Specificity = 44.4%

Sensitivity = 92.9%
Specificity = 84.6%

cTnI AUC = 0.9 (0.83-0.97)
cTnT AUC = 0.86(0.79-0.94)

N = 162 patients with 2+ years of outcomes

Farnsworth unpublished data

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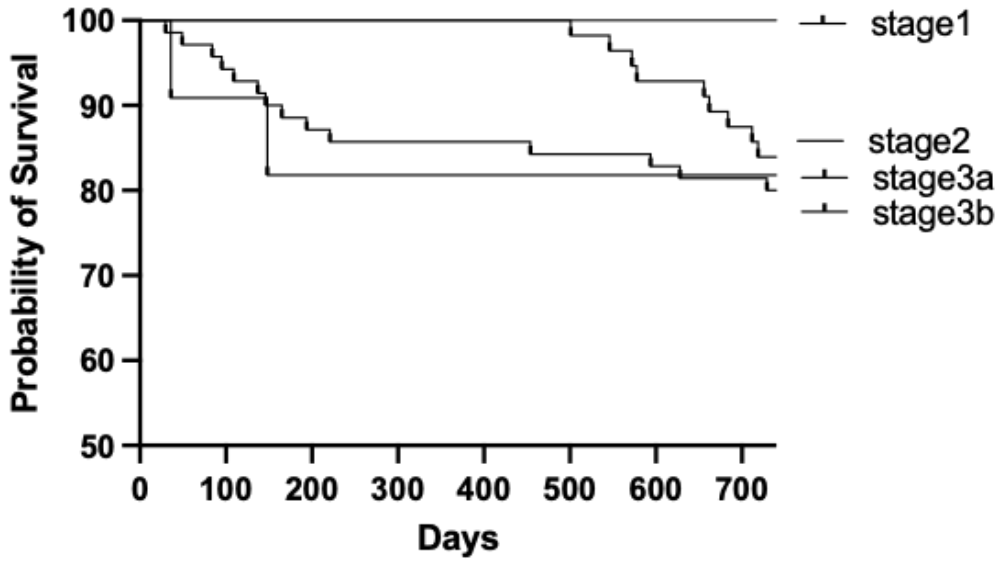
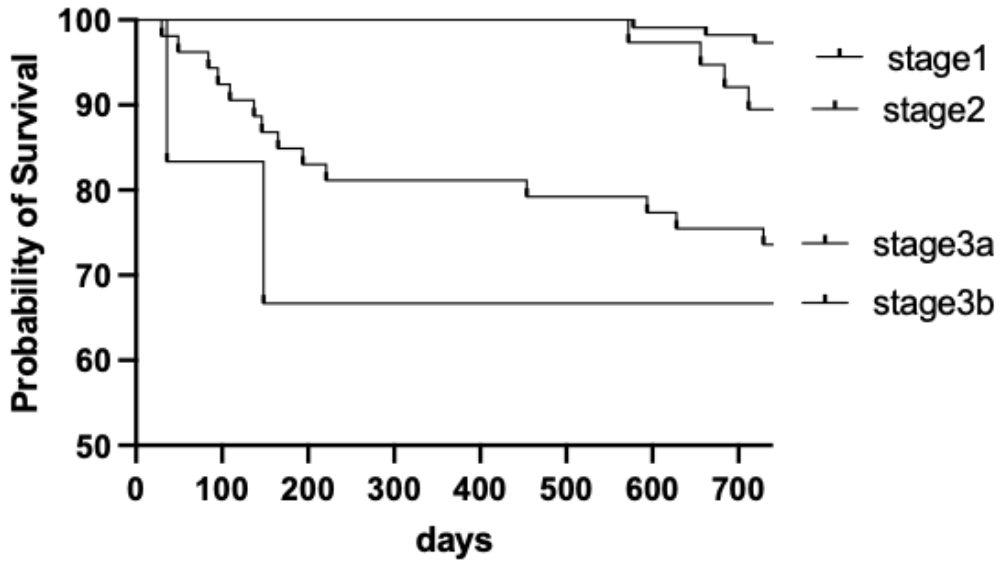
cTnI and cTnT have similar prognostic performance

Mayo Based cTnT Score



Mayo Based cTnI Score



N = 212 specimens from 96 patients with 2+ years of outcomes

Farnsworth unpublished data

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Take home points from Amyloidosis

- cTn and NPs show up in both staging criteria for amyloidosis
- Mayo and Boston seem to perform comparably
- BNP/NT-proBNP and cTnI/cTnT have comparable performance for predicting outcomes in amyloidosis

Final conclucions

01 cTn and NPs, previously used for acute care have emerged in multiple guidelines for ambulatory patients

02 Guidelines use cTn and Np for diagnosing structure heart damage, assessing risk of cardiovascular disease, and prognosticating outcomes

03 While helpful, more studies are needed to better define the cutoffs used, time intervals of screening, and populations to screen

WashU Medicine

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Thank you!

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Questions?