Cardiologia (e ricerca in cardiologia) trasversale

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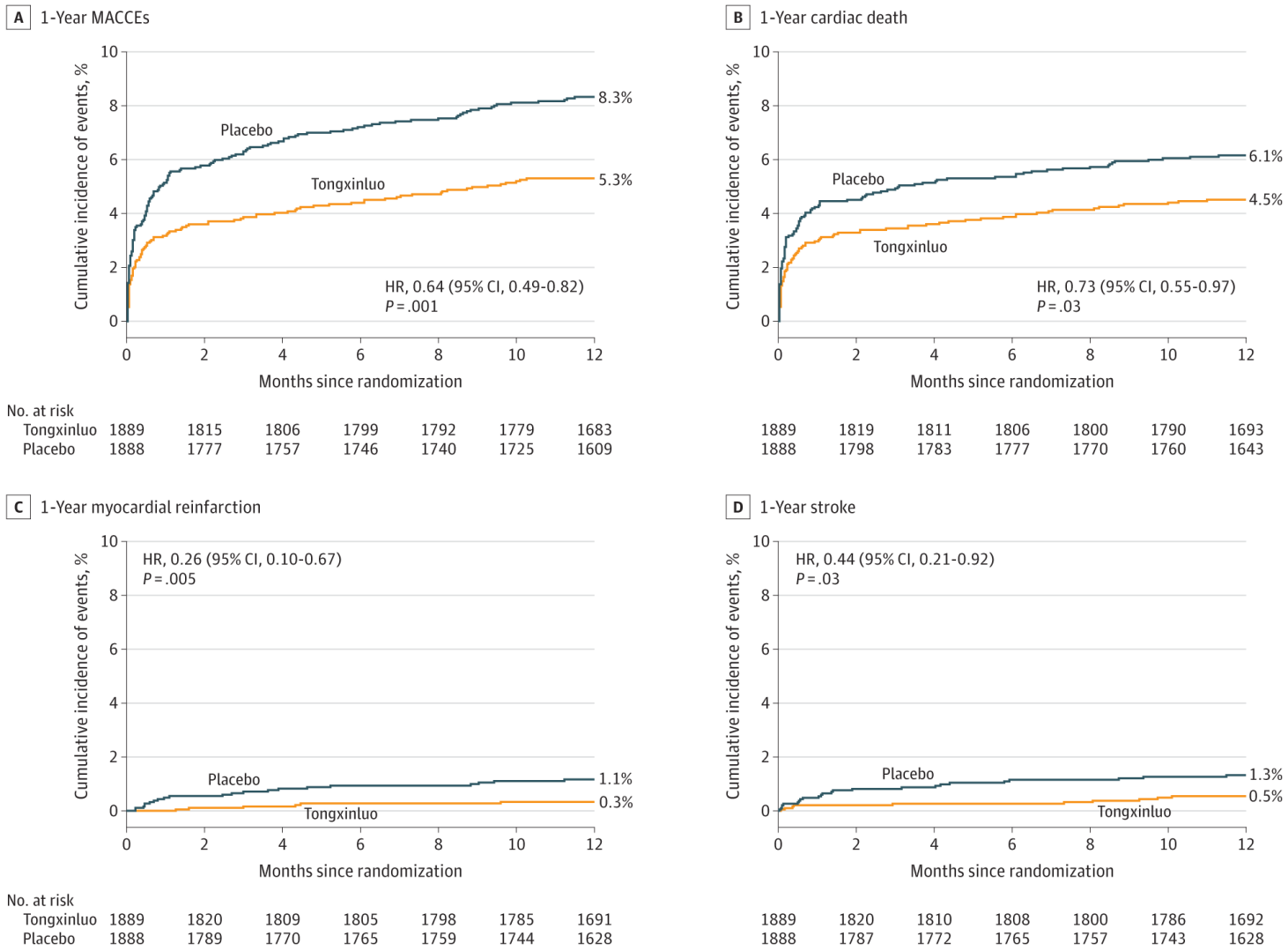
Genova

OSPEDALE POLICLINICO SAN MARTINO
Sistema Sanitario Regione Liguria

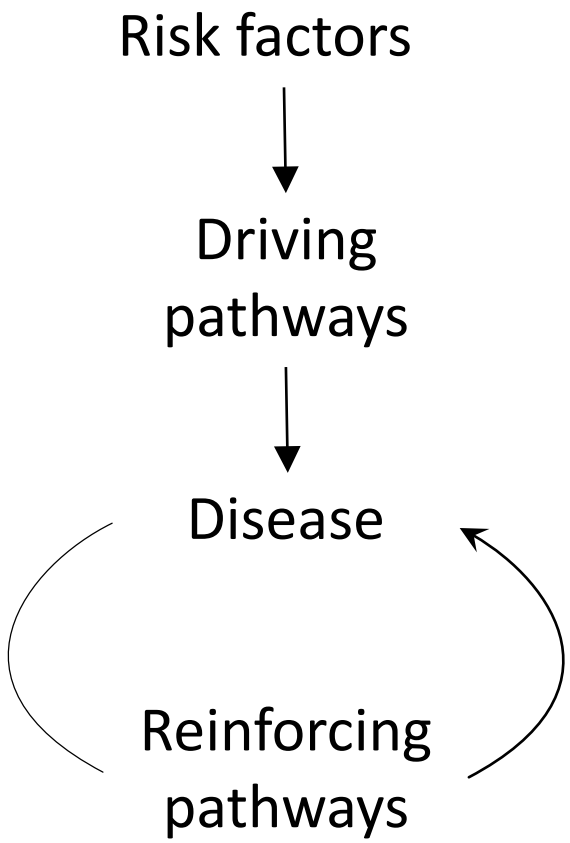
CTS-AMI

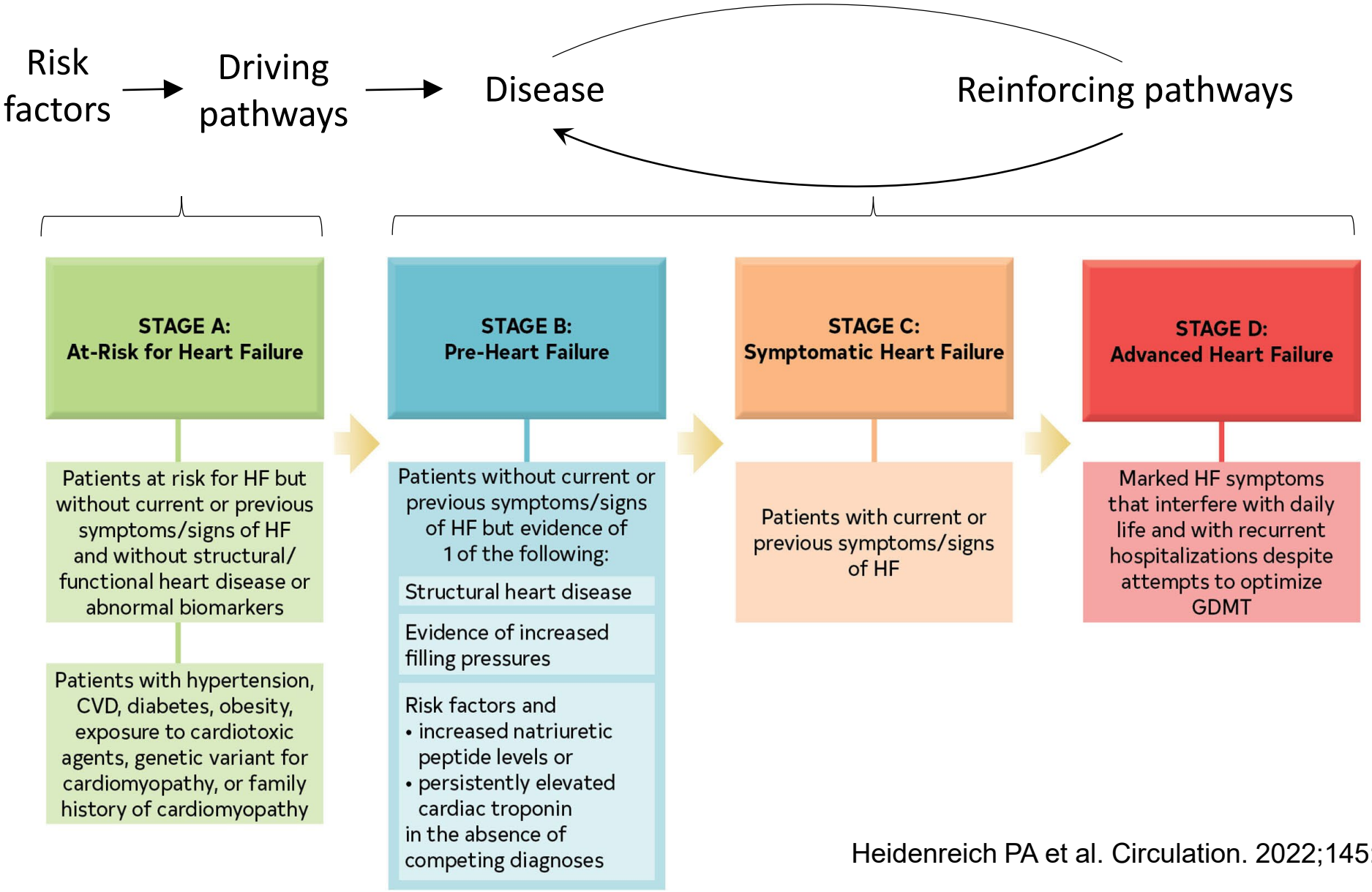
- 3797 patients with STEMI within 24 hours of symptom onset from 124 hospitals in China
- randomized 1:1 to Tongxinluo vs placebo orally for 12 months, in addition to STEMI guideline-directed treatments
- 3777 included in the primary analysis

"The Tongxinluo capsule is a traditional Chinese medicine compound of multiple plant and insect products. Despite the clinical benefit demonstrated in this trial, the active ingredient(s) and the exact mechanism of action remain to be established."

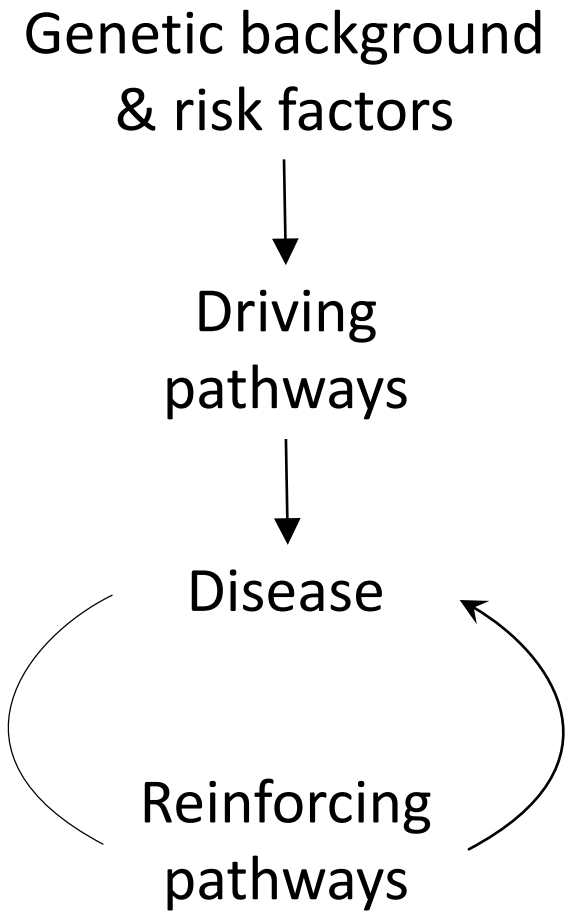


Yang Y et al. JAMA. 2023;330:1534-45


Risk factors
Driving pathways
Disease
Reinforcing pathways



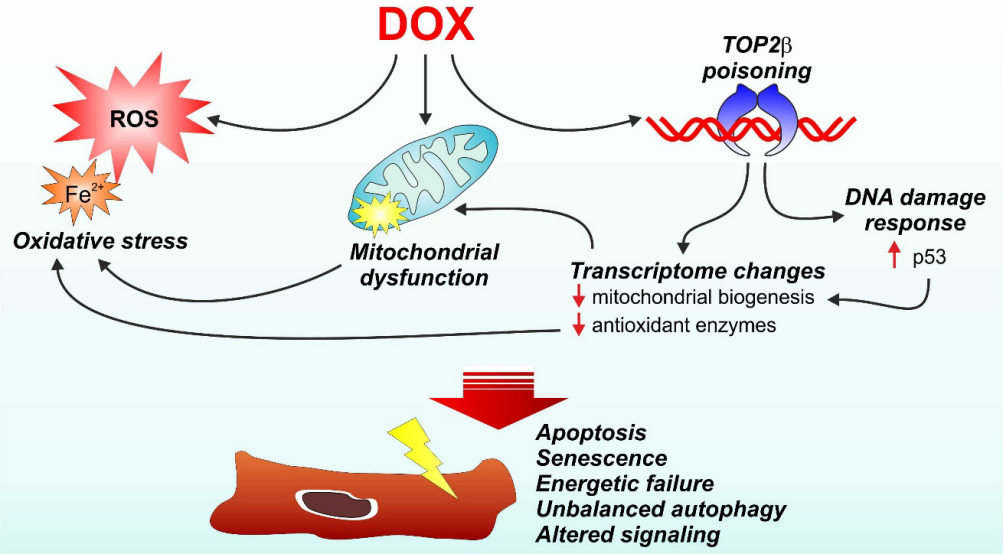
Heidenreich PA et al. Circulation. 2022;145:e895–e1032


Genetic background
& risk factors
Driving
pathways
Disease
Reinforcing
pathways

CCT study

277 women treated for breast cancer between 2010 and 2015

- 64%: doxorubicin-based chemotherapy
- 18%: trastuzumab-based chemotherapy
- 18%: doxorubicin + trastuzumab-based chemotherapy

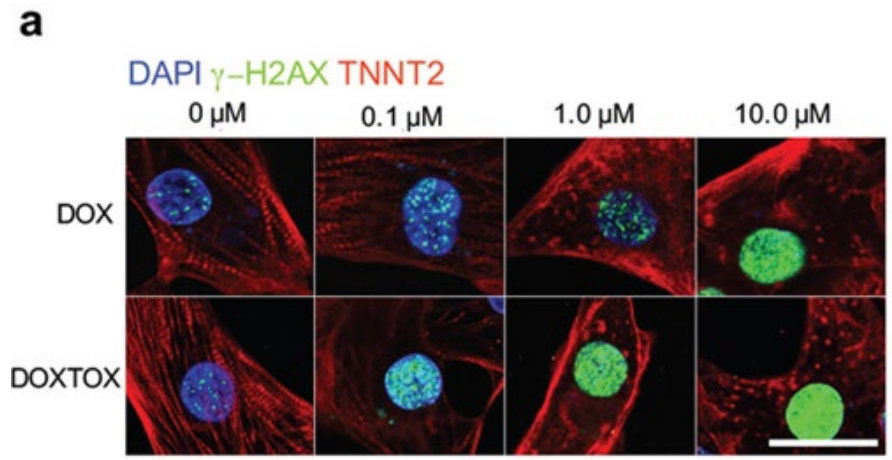


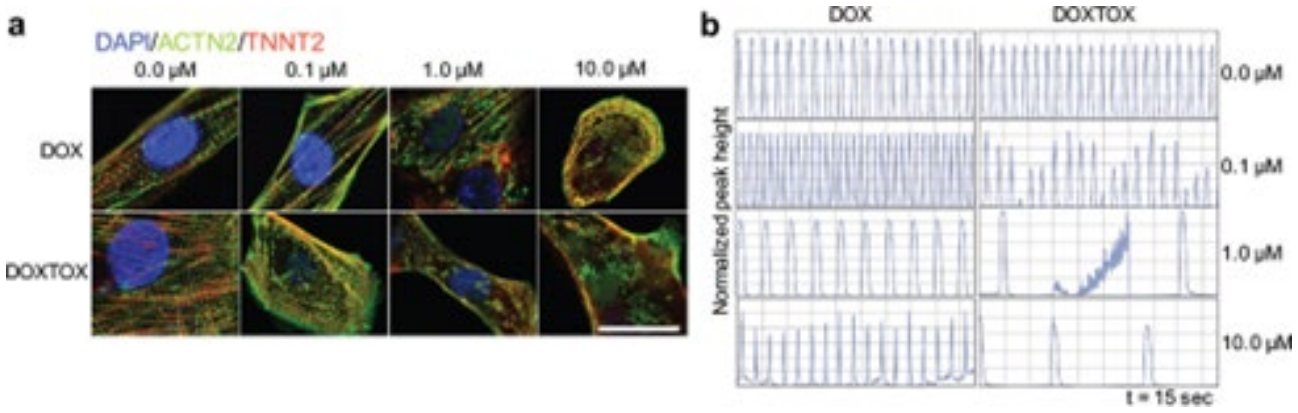
Mercurio V, …, Ameri P. J Card Fail. 2016;22:449-58

- ✓ 42/229 (18%): ↓ LVEF ≥10% to <50%
- ✓ both during and after therapy
- ✓ median time to LVEF decline: 7 mo

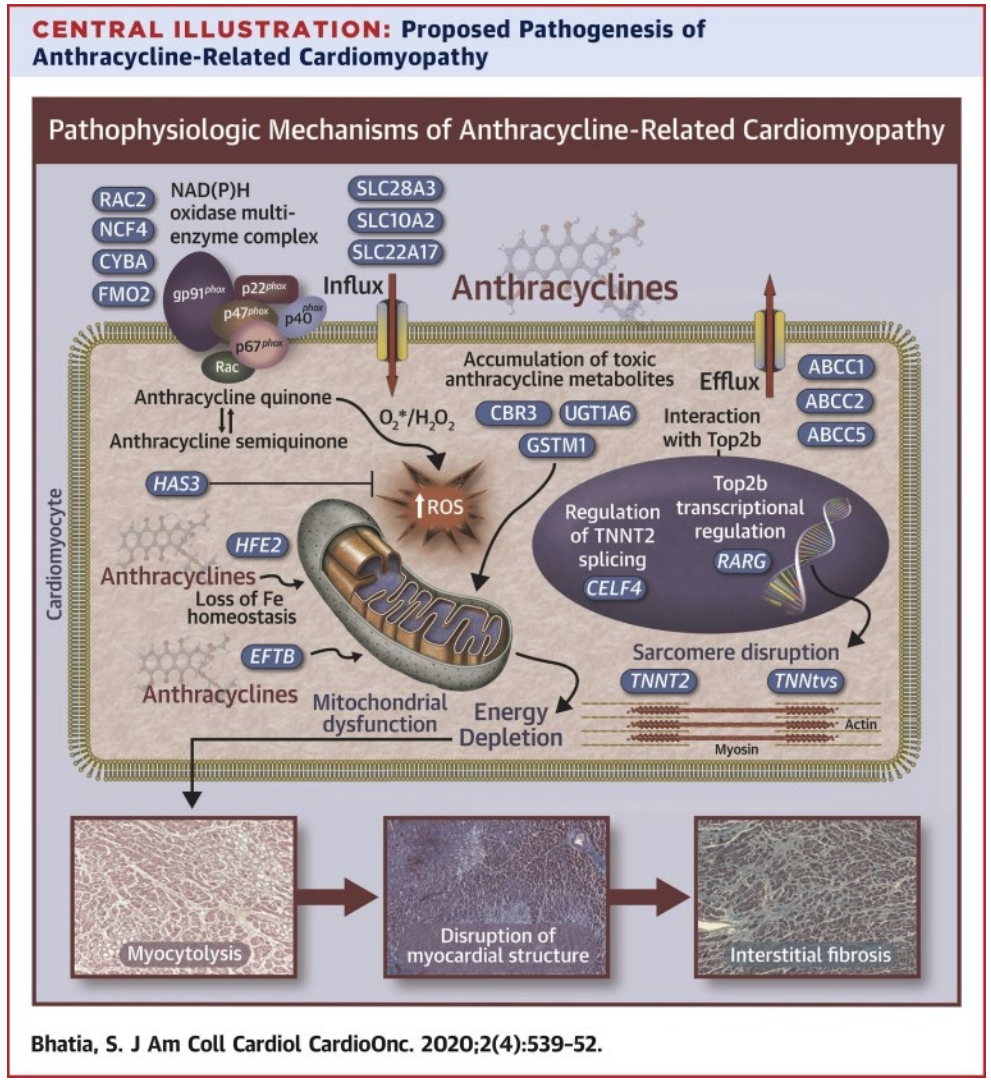
- ✓ 20 (48%) w/ LVEF decline had sympyoms
- ✓ 14 (33%) interrupted or discontinued cancer therapy

Narayan HK et al. Circulation. 2017;135:1397-412

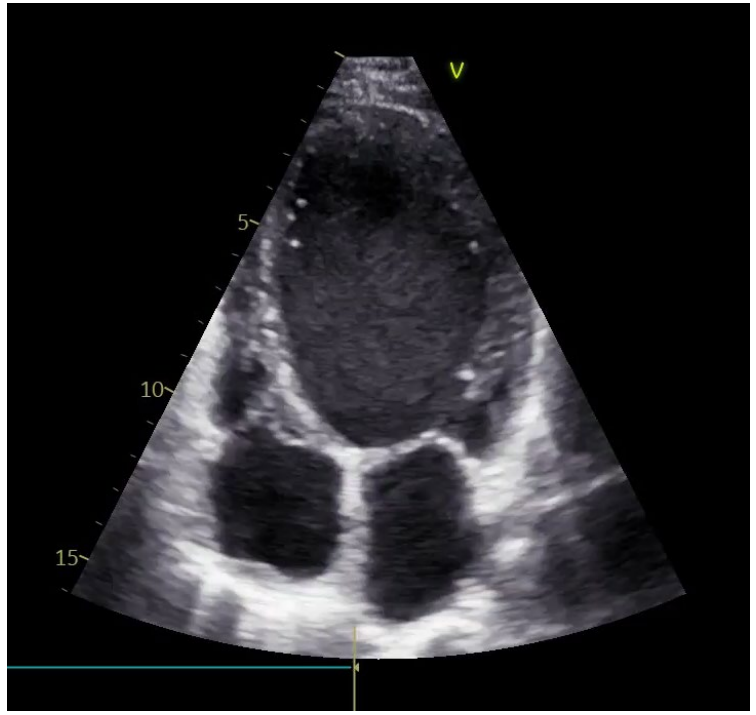




Burridge PW et al. Nat Med. 2016;22:547-56



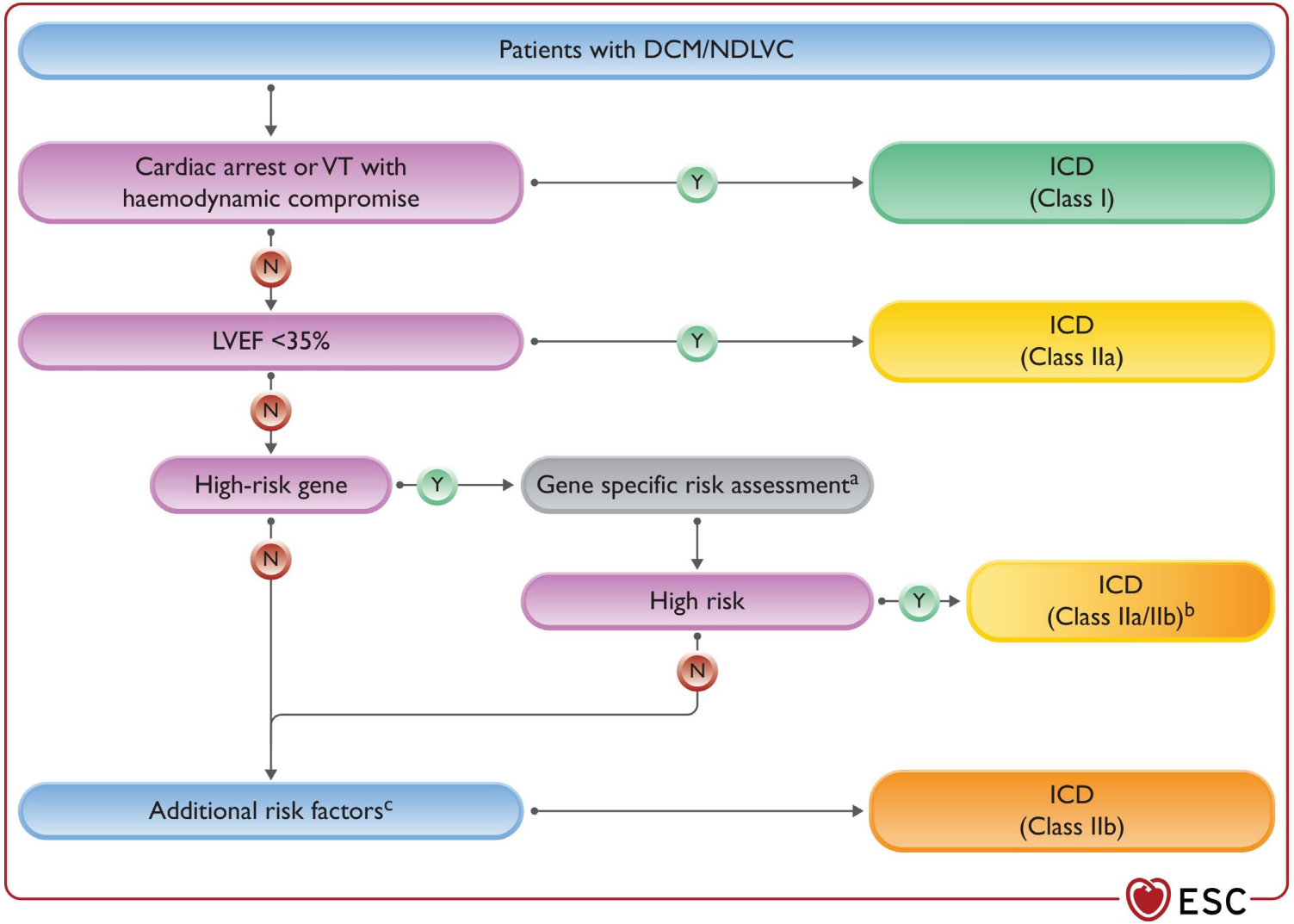
Bhatia, S. J Am Coll Cardiol CardioOnc. 2020;2(4):539-52.



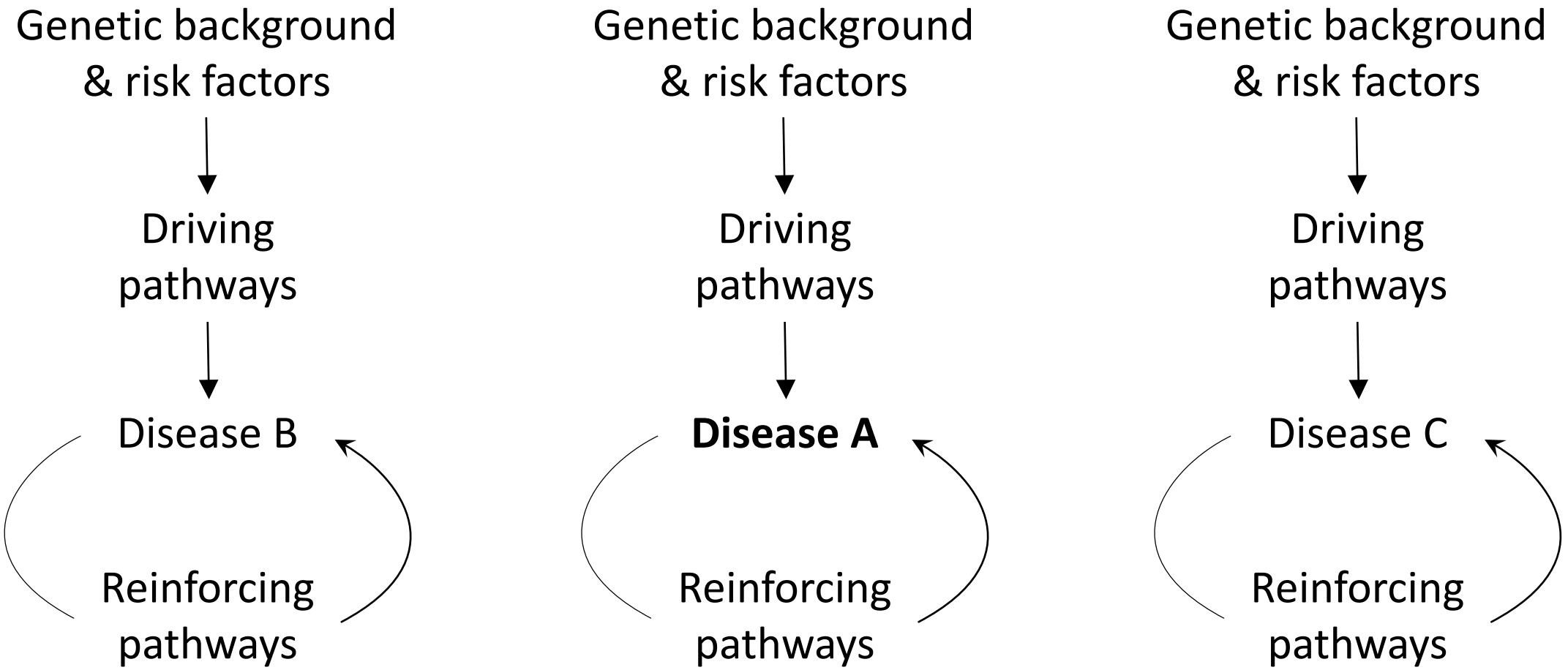
Dilated cardiomyopathy

LV dilation (LVID >58/52 mm, LVEDVi ≥75/62 mL/m^2) and systolic dysfunction (LVEF <50%) unexplained solely by abnormal loading conditions or CAD

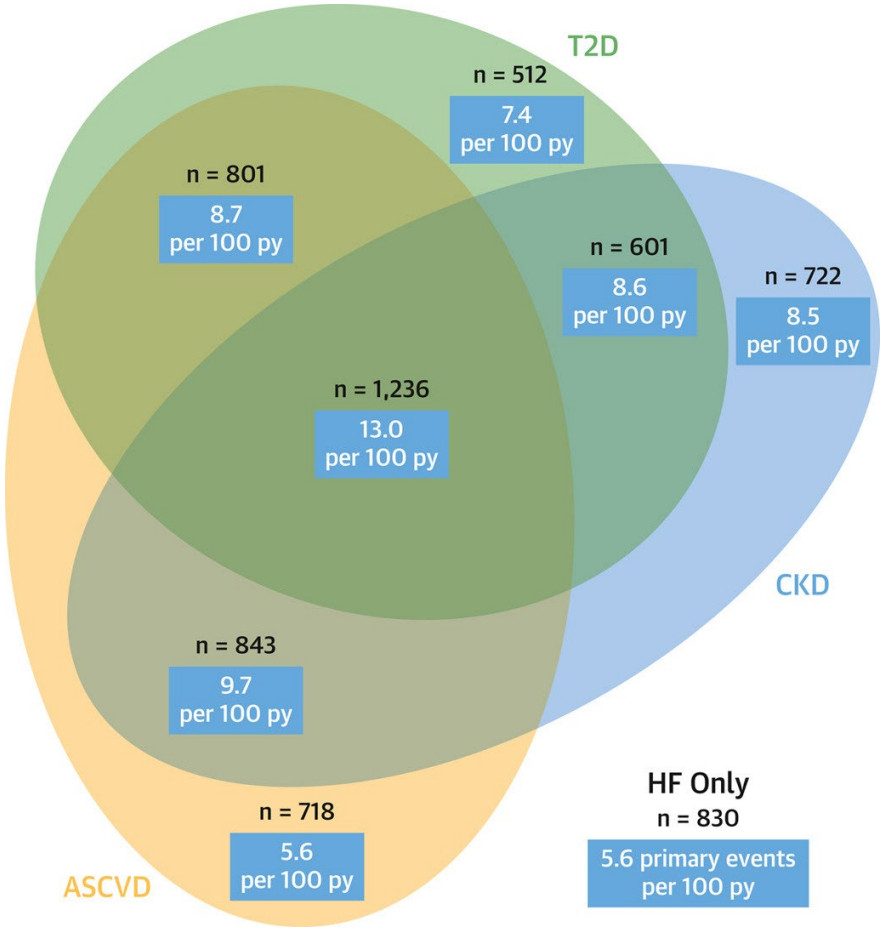
Arbelo E et al. Eur Heart J. 2023;44:3503-3626



High-risk genes: *PLN*, *DSP*, *LMNA*, *FLNC*, *EMD*, *TMEM43*, *RBM20*
Risk factors: syncope, LGE on CMR, NVST, PVCs, male sex, specific gene variants


Genetic background & risk factors
Driving pathways
Disease B
Reinforcing pathways
Genetic background & risk factors
Driving pathways
Disease A
Reinforcing pathways
Genetic background & risk factors
Driving pathways
Disease C
Reinforcing pathways

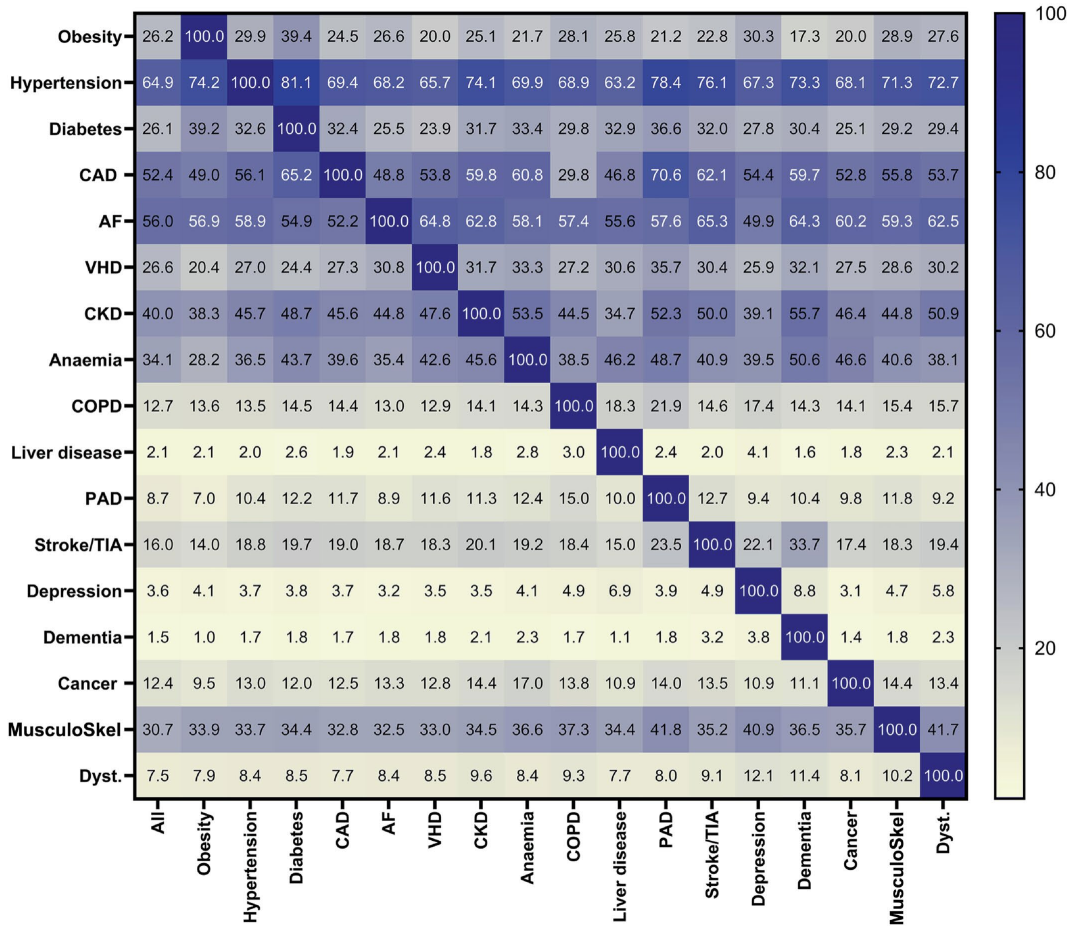
DELIVER



Ostrominski JW et al. JACC Heart Fail. 2023;11:1491-1503

Swedish Heart Failure Registry

- 91,463 patients between 2000 and 2021

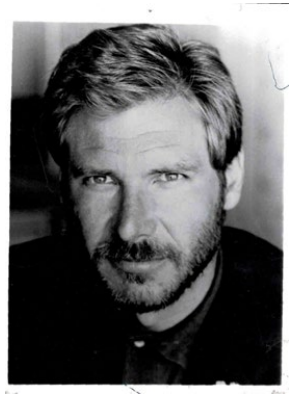


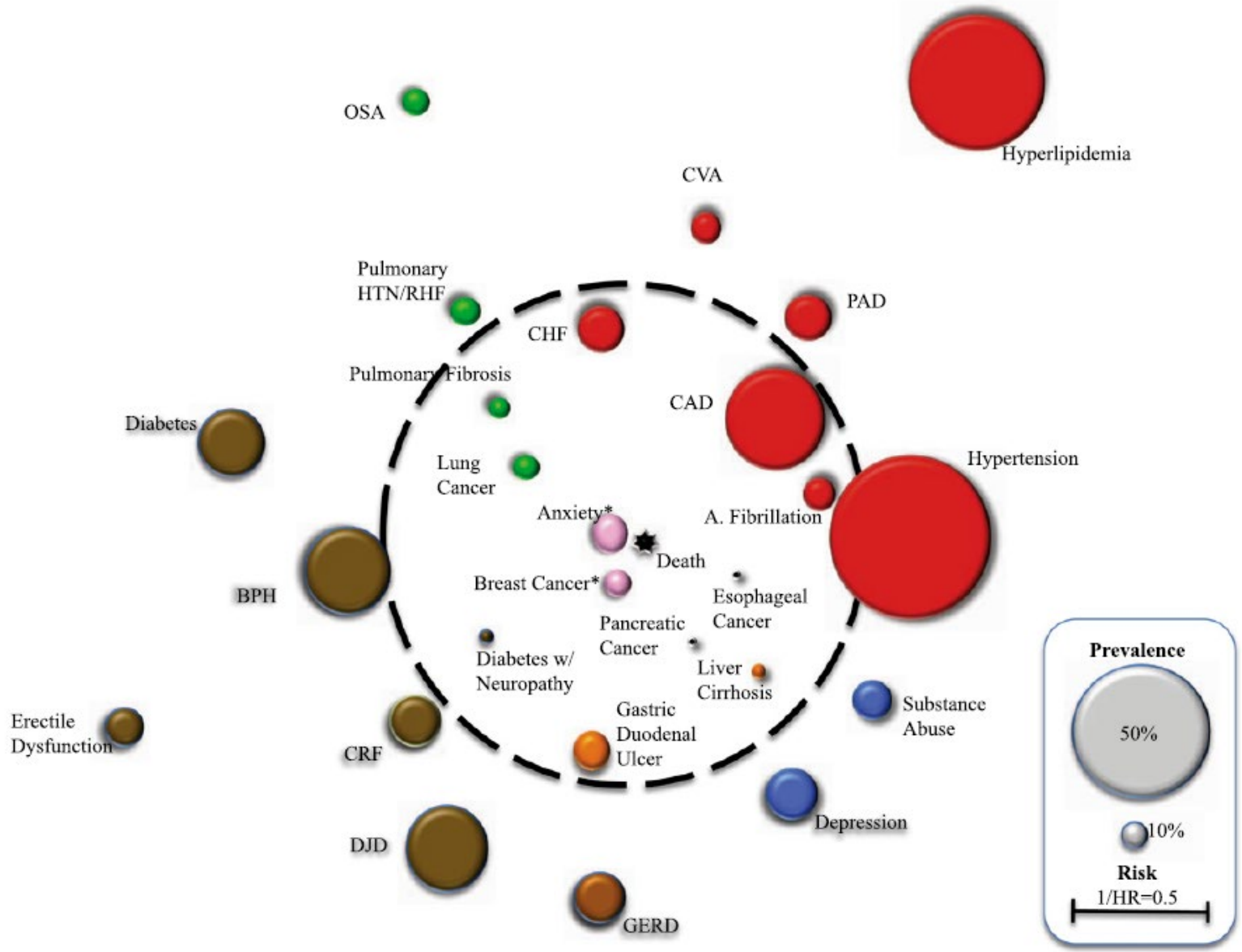
Tomasoni D et al. Eur J Heart Fail. 2024;26:854-68

Age	<50 / 50-59 / 60-69 / 70-79 / ≥80 years
Myocardial infarction	No / yes
Chronic heart failure	No / yes
Peripheral vascular disease	No / yes
CVA or TIA	No / yes
Dementia	No / yes
COPD	No / yes
Connective tissue disease	No / yes
Diabetes mellitus	No or diet-controlled, uncomplicated, end-organ damage

Peptic ulcer disease	No / yes
Liver disease	No, mild, moderate to severe
Hemiplegia	No
Moderate to severe CKD	No / yes
Solid tumor	No / localized / metastatic
Leukemia	No / yes
Lymphoma	No / yes
AIDS	No / yes

Charlson ME et al. J Chronic Dis. 1987;40:373-83

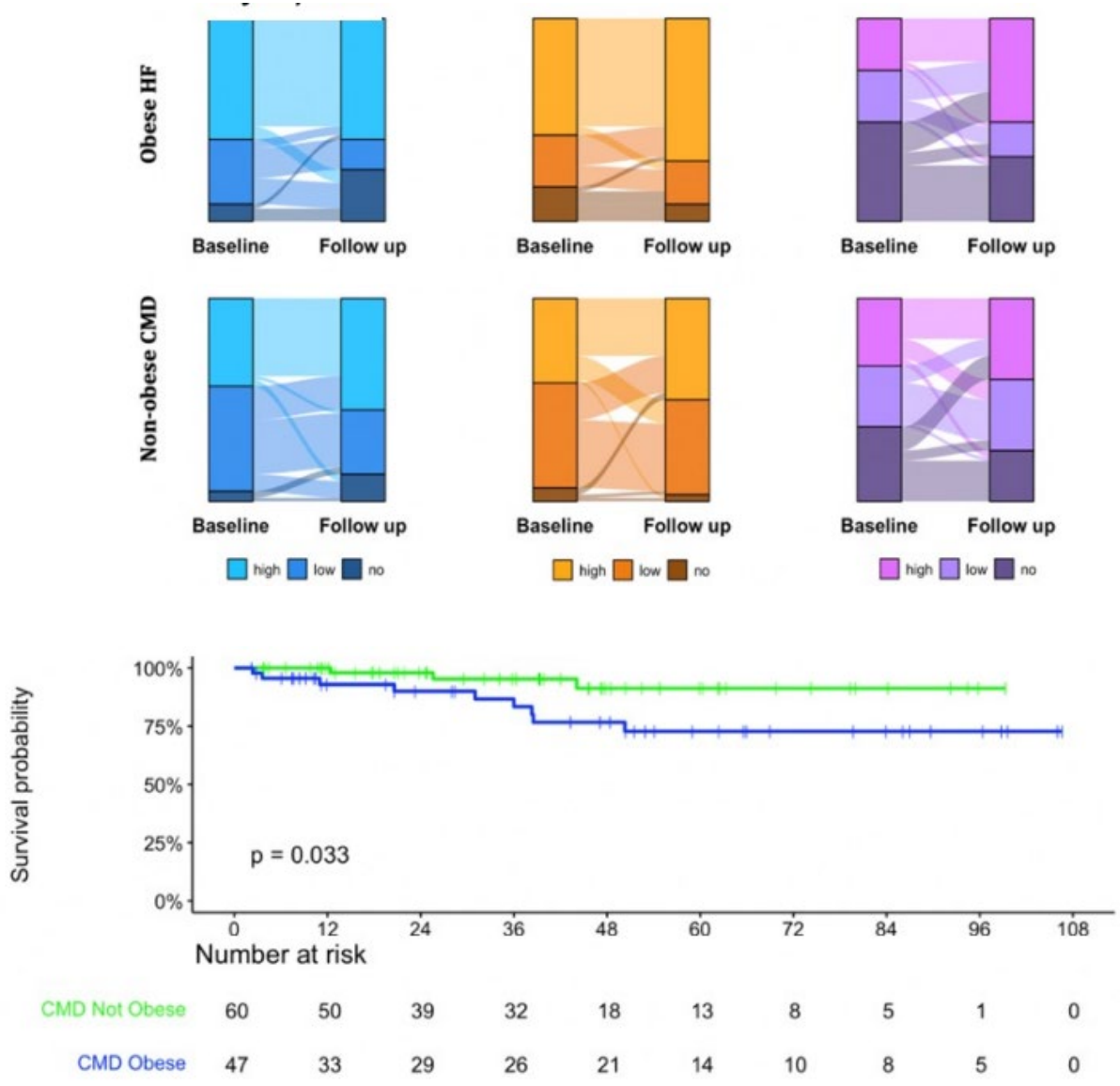




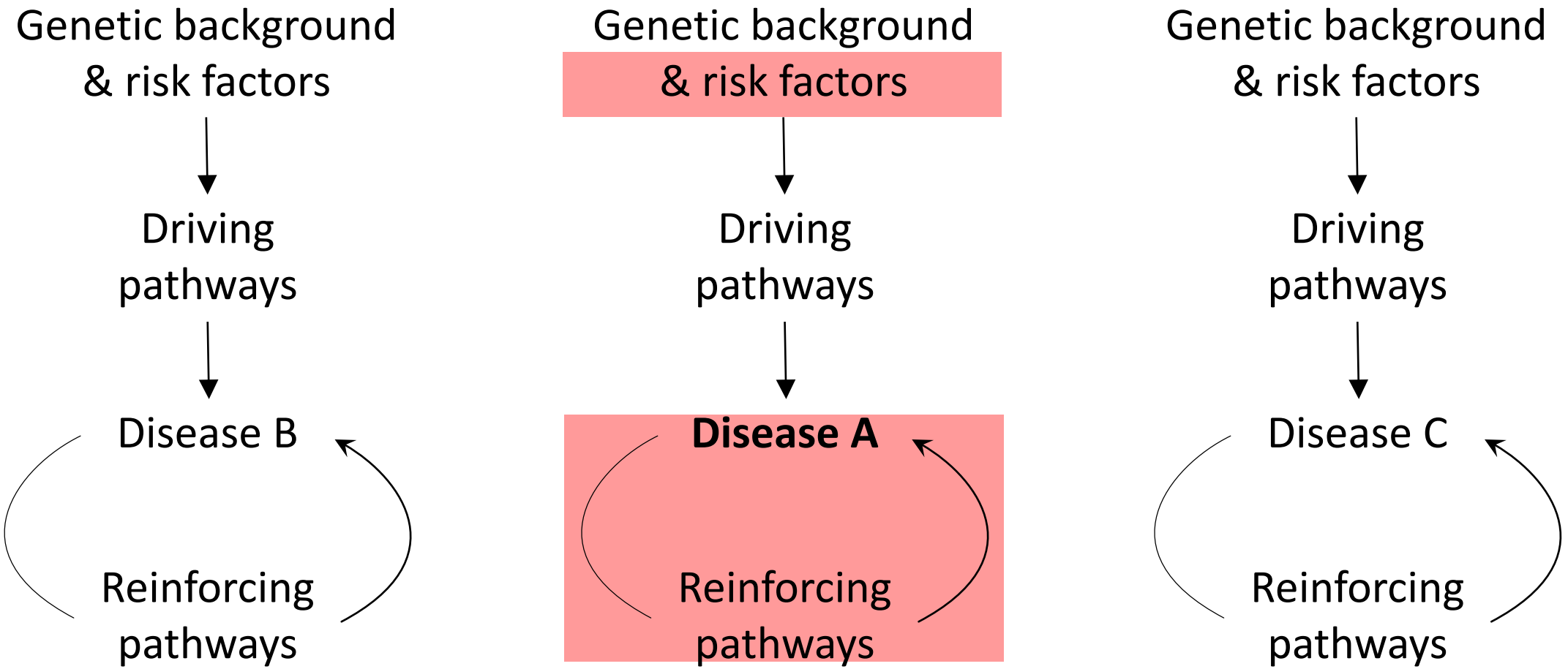
Divo M et al. Am J Respir Crit Care Med 2012;186:155-61

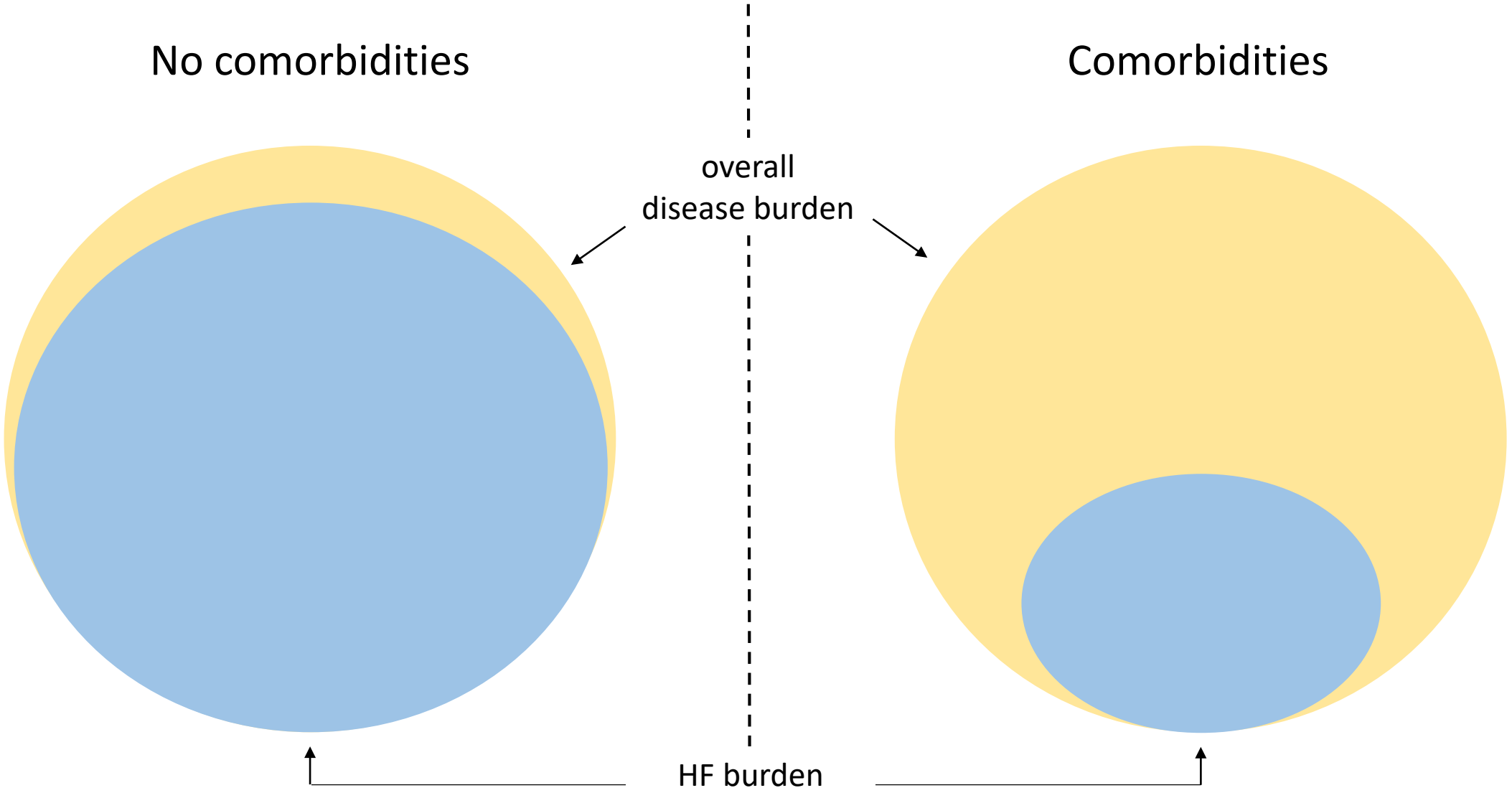
Table. Patient characteristics at baseline.

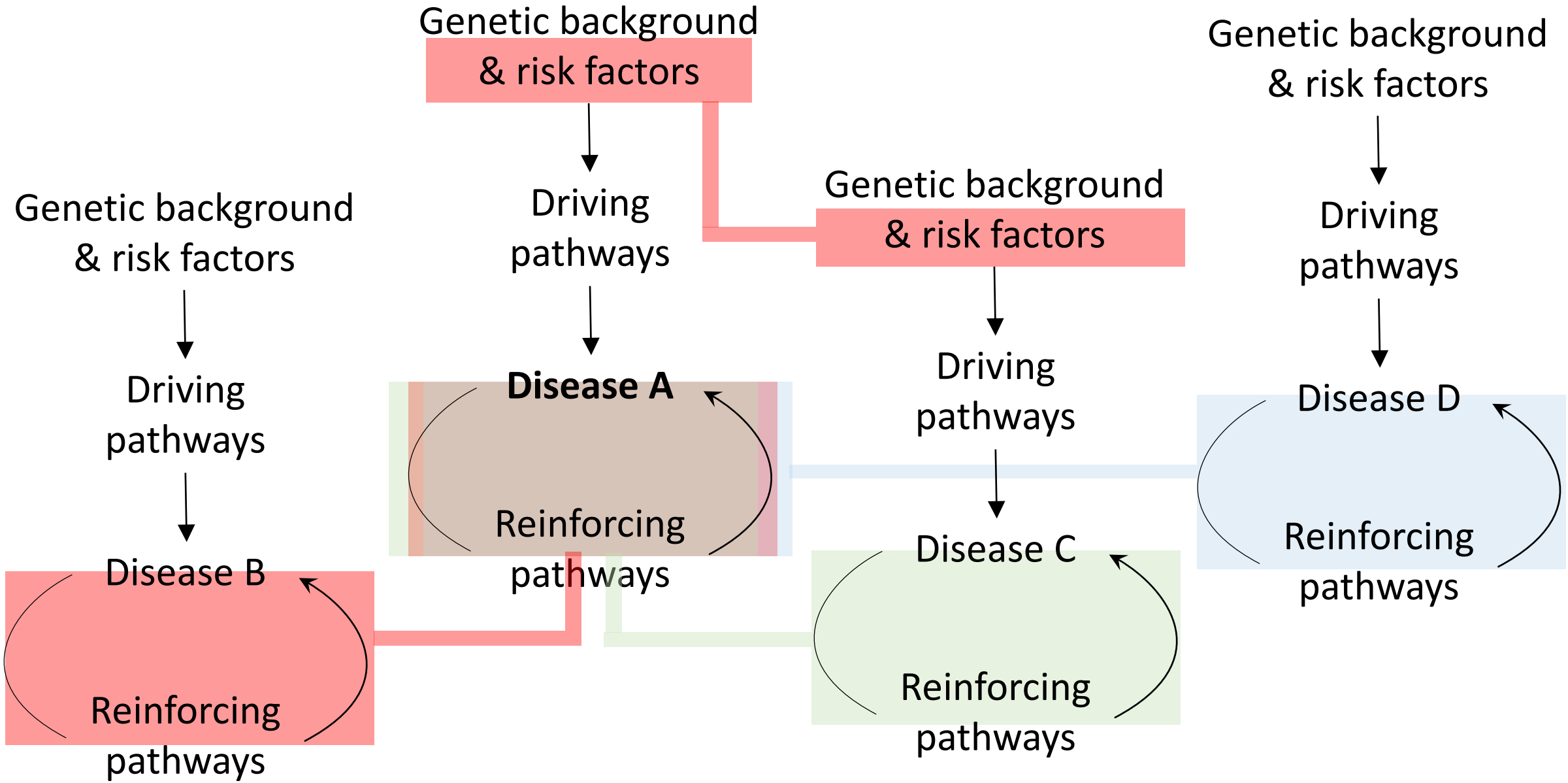
	Overall N = 107	Non_Obese_CMD N = 60	Obese_CMD N = 47	P
Male	81 (76%)	39 (65%)	42 (89%)	**0.004**
Age, years	57 ± 10	55 ± 10	59 ± 10	**0.03**
LVEF, %	34 ± 9	32 ± 9	36 ± 9	**0.03**
BMI, kg/m2	29 ± 6	25 ± 3	34 ± 5	**<0.001**
Hypertension	46 (43%)	16 (27%)	30 (64%)	**<0.001**
eGFR, mL/min/1.73m2	80 ± 22	83 ± 24	76 ± 20	0.07
Dislipidemia	32 (30%)	12 (21%)	20 (43%)	**0.02**
Diabetes	16 (15%)	4 (6.7%)	12 (26%)	**0.007**
Smoking	70 (65%)	36 (60%)	34 (72%)	0.2
Alcohol abuse	23 (21%)	12 (20%)	11 (23%)	0.7
COPD	14 (13%)	3 (5.0%)	11 (24%)	**0.004**
History of AF	25 (23%)	10 (17%)	15 (32%)	0.07
NYHA class				0.7
I-II	97 (91%)	55 (92%)	42 (89%)	
III-IV	10 (9.3%)	5 (8.3%)	5 (11%)	
NT-proBNP, pg/mL	991 [520; 2387]	1577 [793; 2836]	634 [453; 2254]	0.16
Systolic blood pressure	124 ± 17	121 ± 18	128 ± 14	**0.02**
Heart rate	70 ± 15	68 ± 15	72 ± 14	0.10
End-diastolic LV diameter	63 ± 7	63 ± 7	63 ± 7	0.9
RV basal diameter	38 ± 7	37 ± 6	40 ± 8	0.1
TAPSE	21 ± 4	20 ± 4	22 ± 4	0.2



Bianchi L et al. HFA congress 2024


Genetic background
& risk factors
Driving
pathways
Disease B
Reinforcing
pathways
Genetic background
& risk factors
Driving
pathways
Disease A
Reinforcing
pathways
Genetic background
& risk factors
Driving
pathways
Disease C
Reinforcing
pathways


No comorbidities
Comorbidities
overall
disease burden
HF burden


Genetic background
& risk factors
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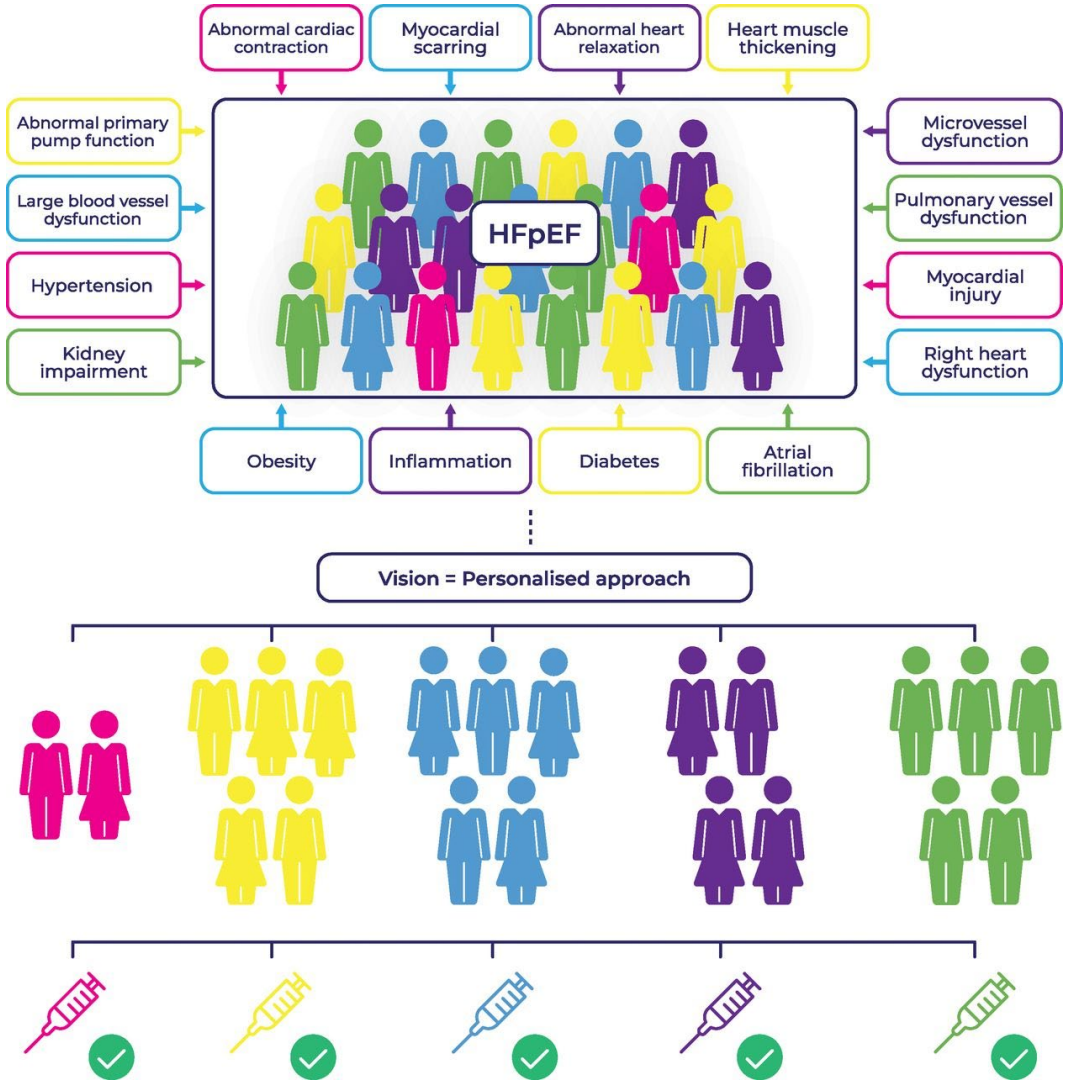
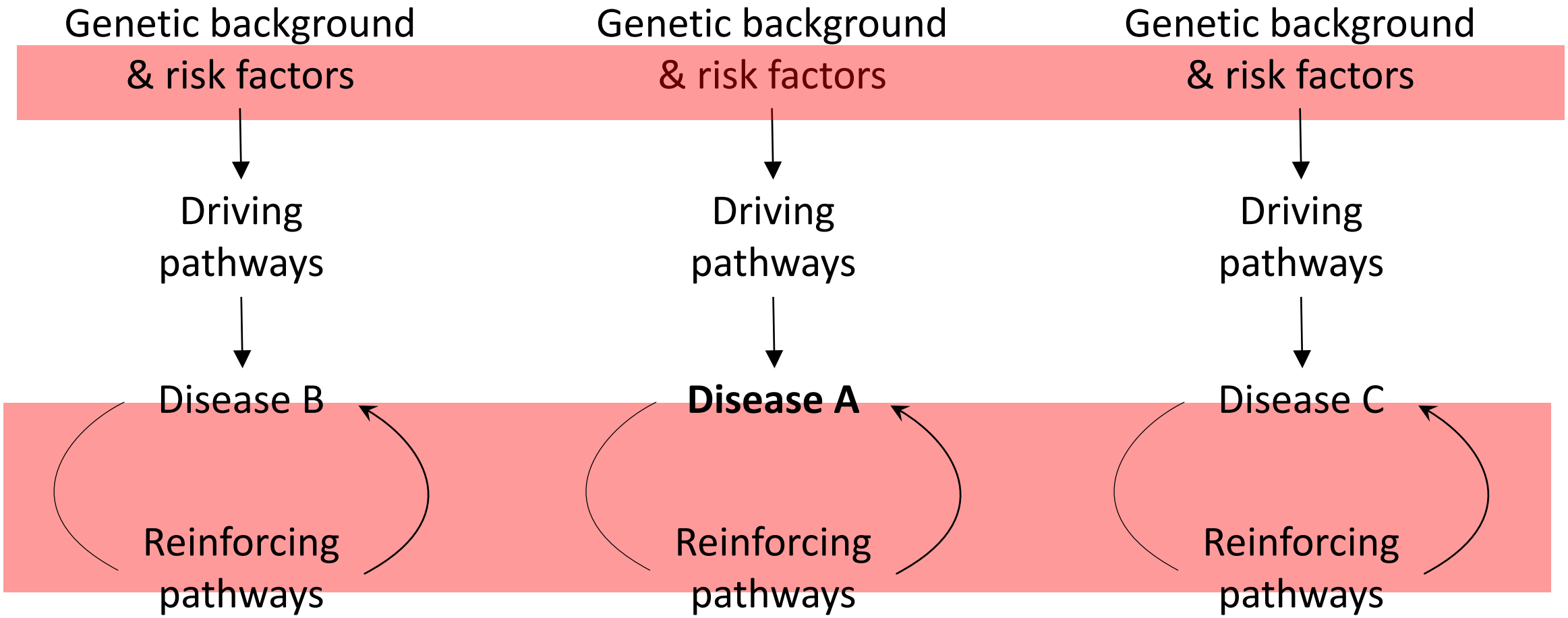
Disease A
Reinforcing
pathways
Genetic background
& risk factors
Driving
pathways
Disease B
Reinforcing
pathways
Genetic background
& risk factors
Driving
pathways
Disease C
Reinforcing
pathways
Genetic background
& risk factors
Driving
pathways
Disease D
Reinforcing
pathways



Jasinska-Piadlo A, Campbell P. Heart. 2023;109:874-83


Genetic background & risk factors
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Driving pathways
Driving pathways
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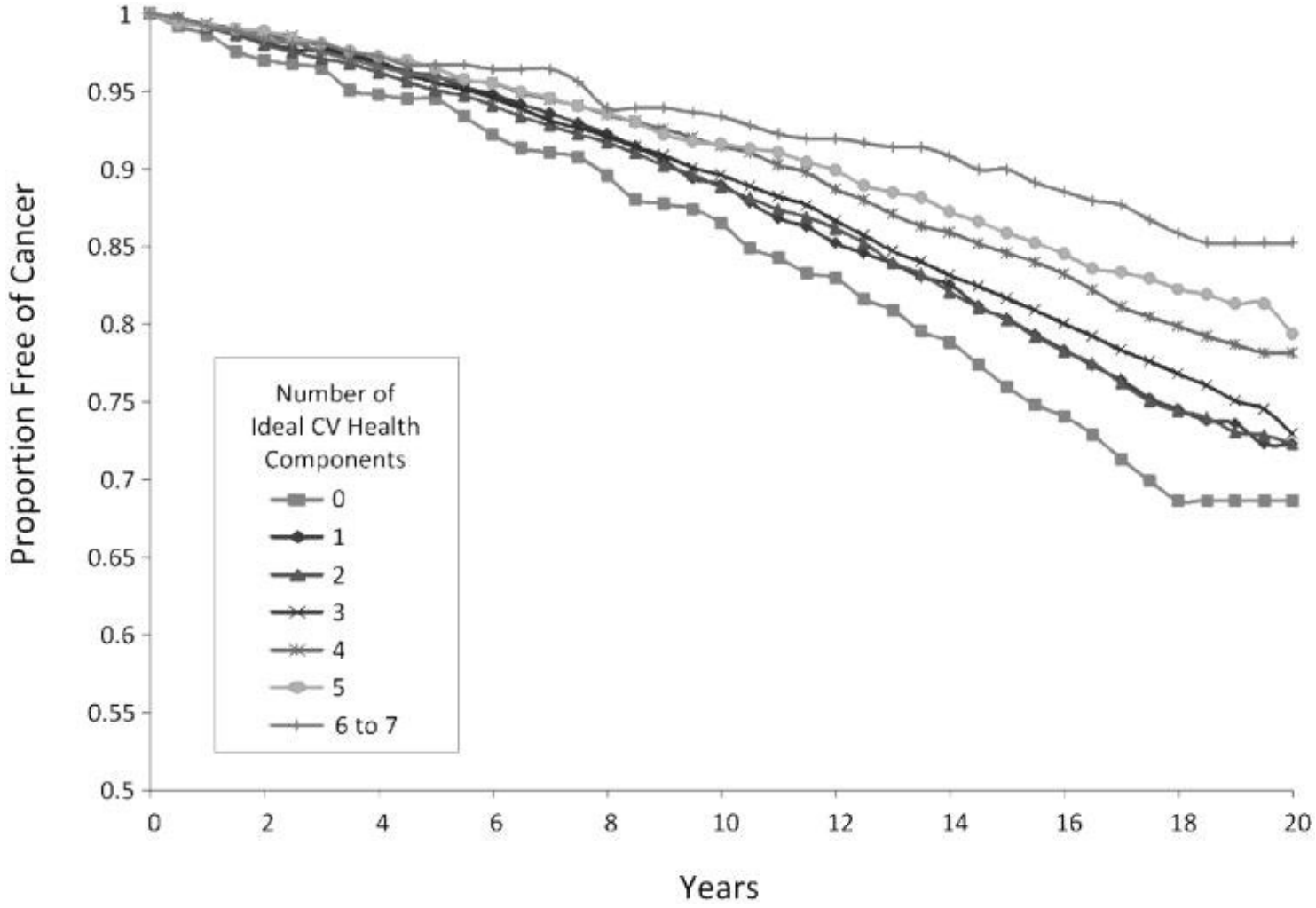
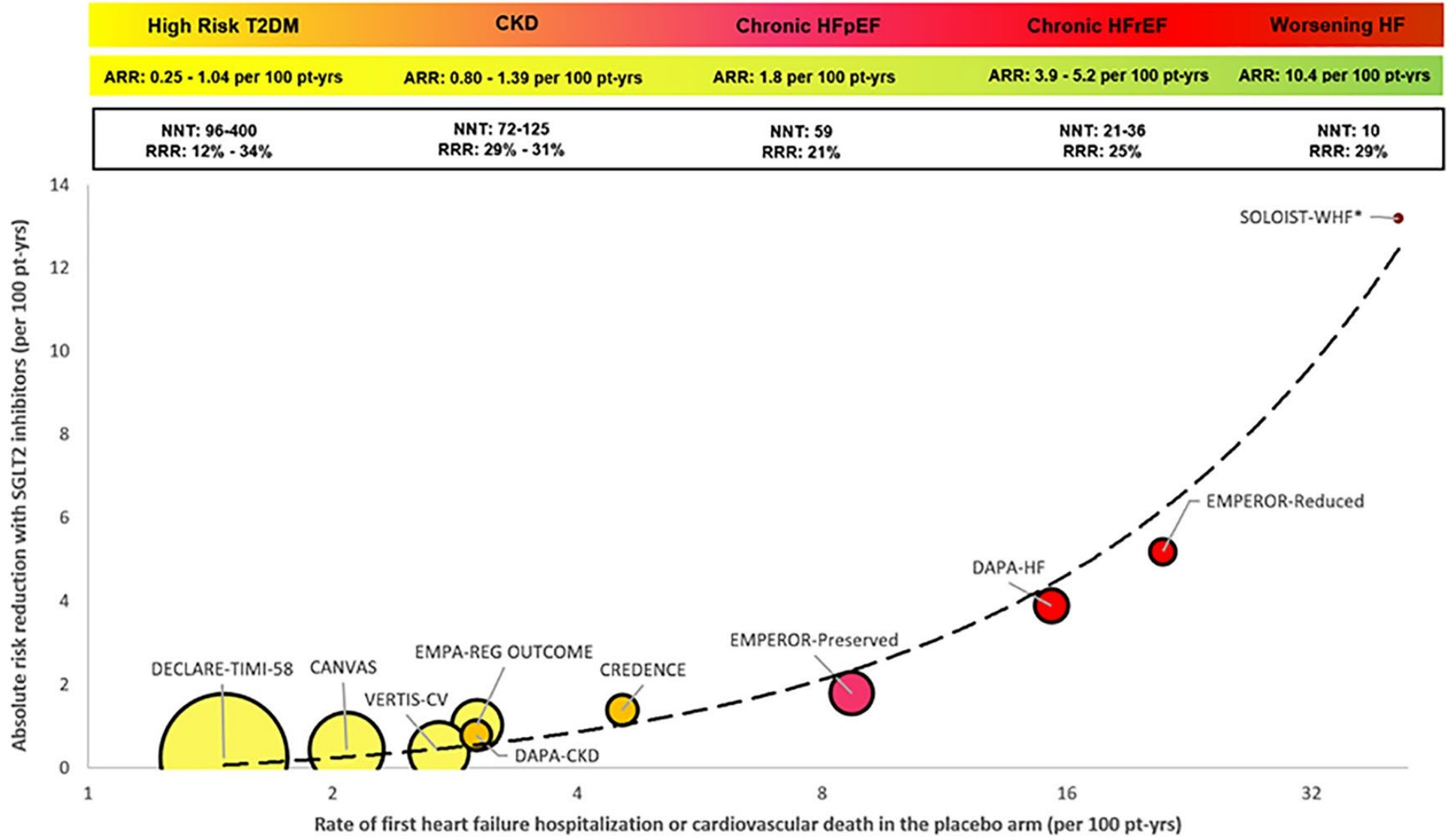
Disease B
Disease A
Disease C
Reinforcing pathways
Reinforcing pathways
Reinforcing pathways

Atherosclerosis Risk In Communities (ARIC) study

- 13,253 subjects



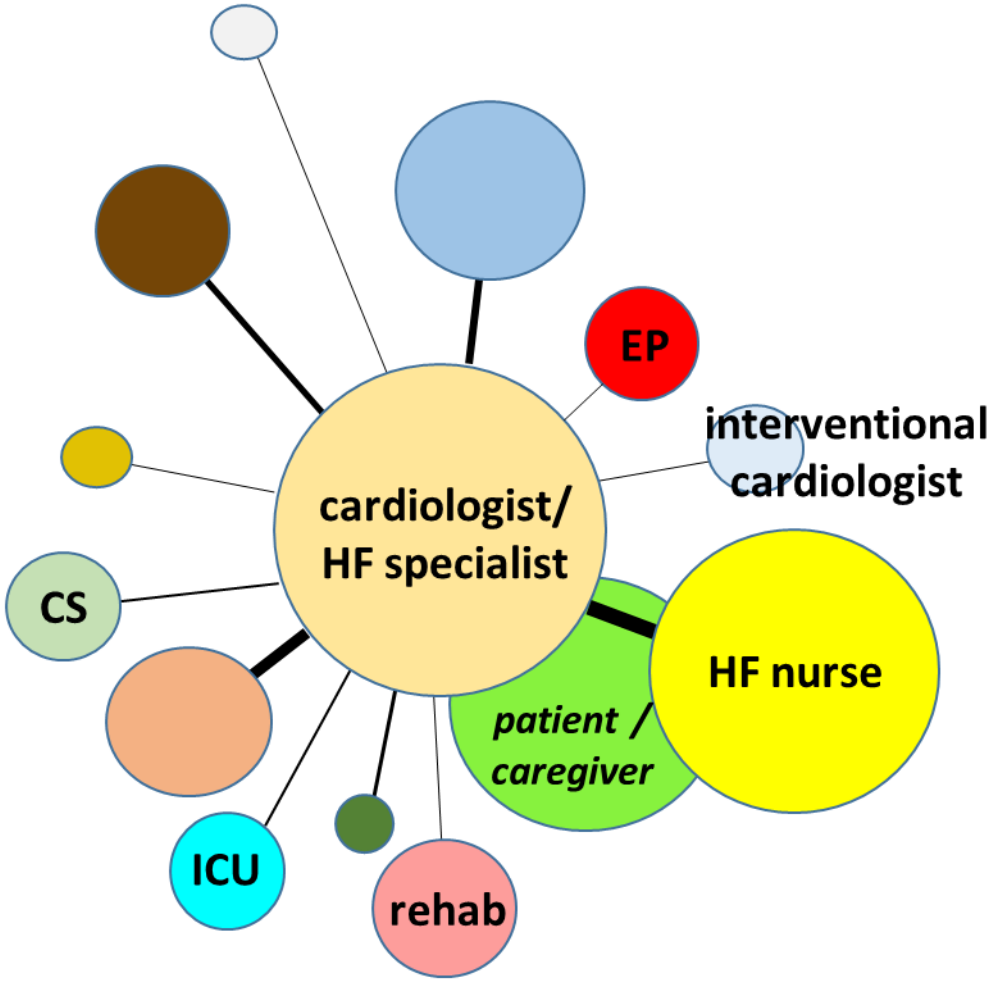
Rasmussen-Torvik LJ et al. Circulation. 2013;127:1270-5

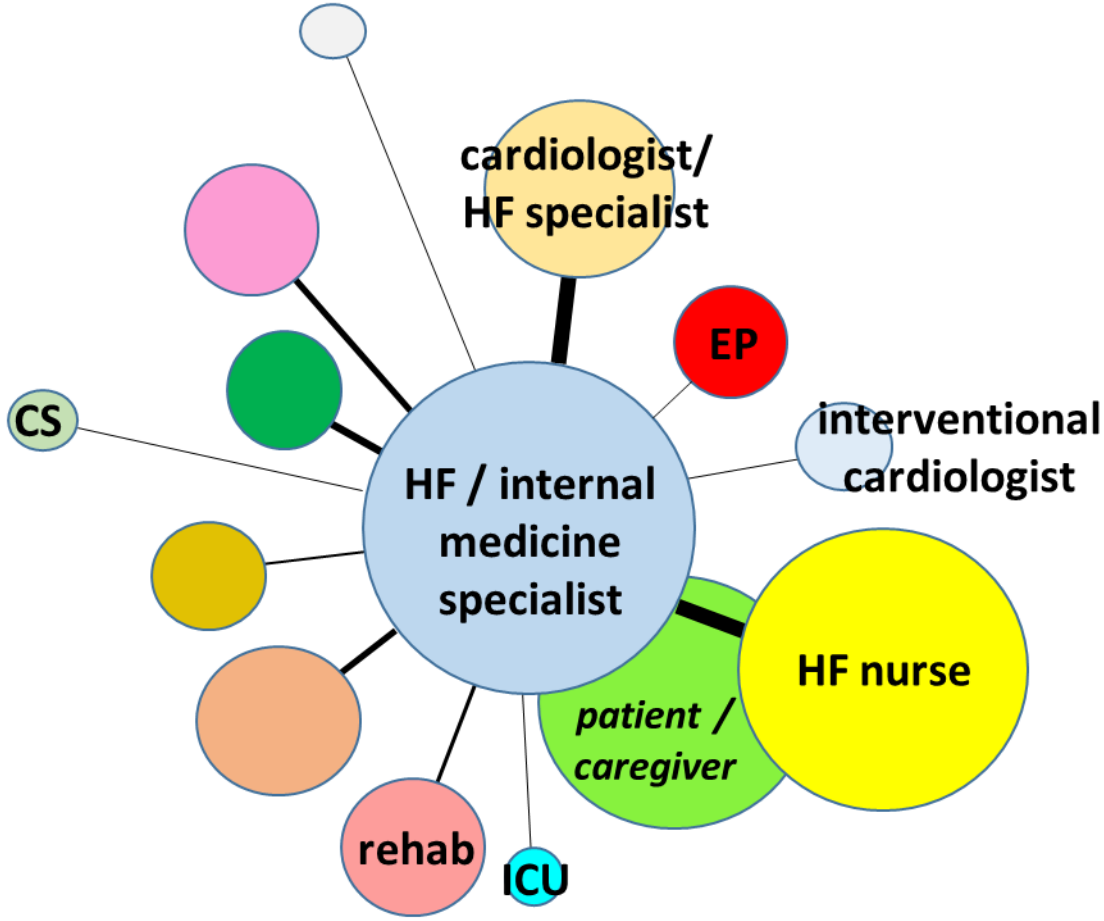


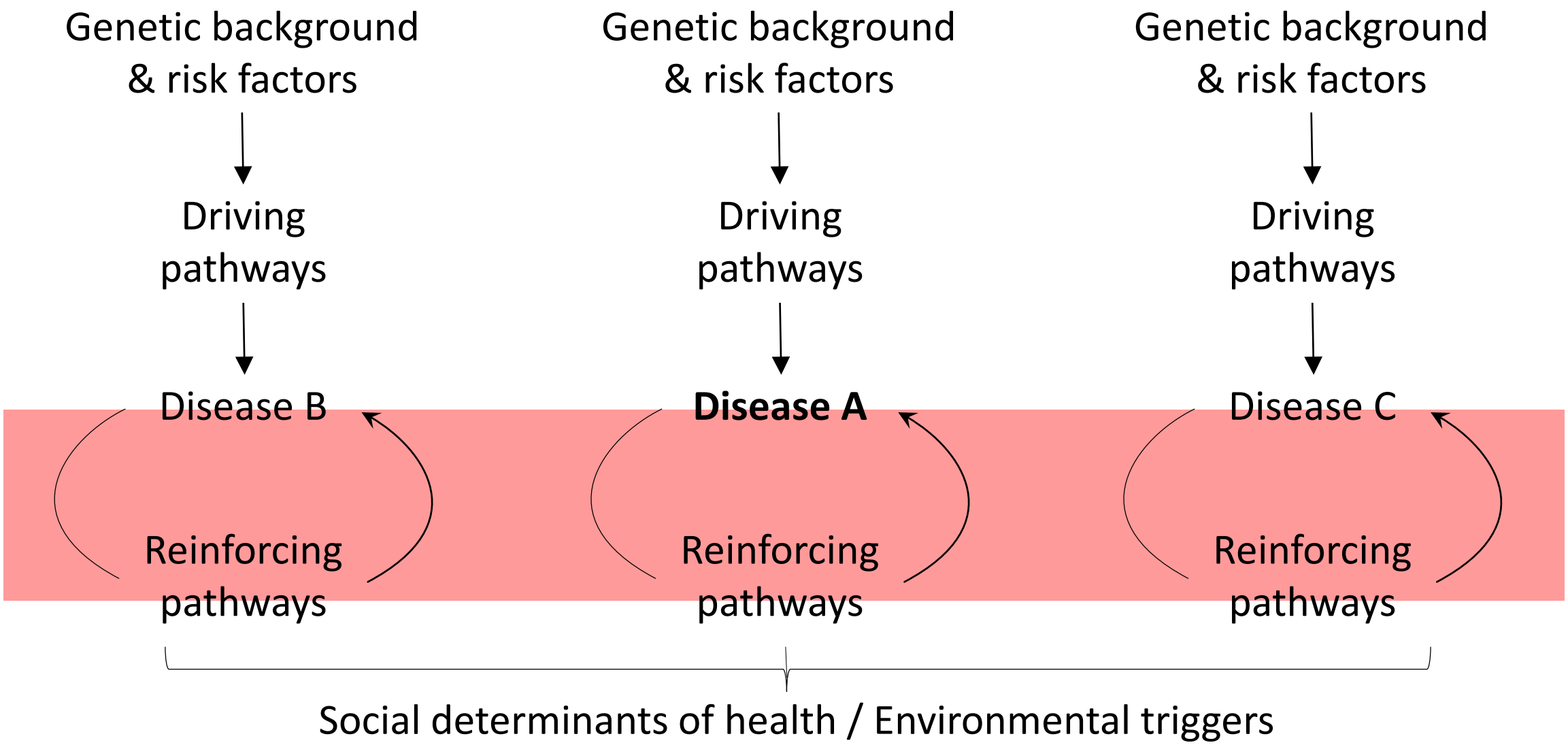
Butler J et al. Eur Heart J. 2021;42:4887-90

How do SGLT2i work in patients with heart failure?

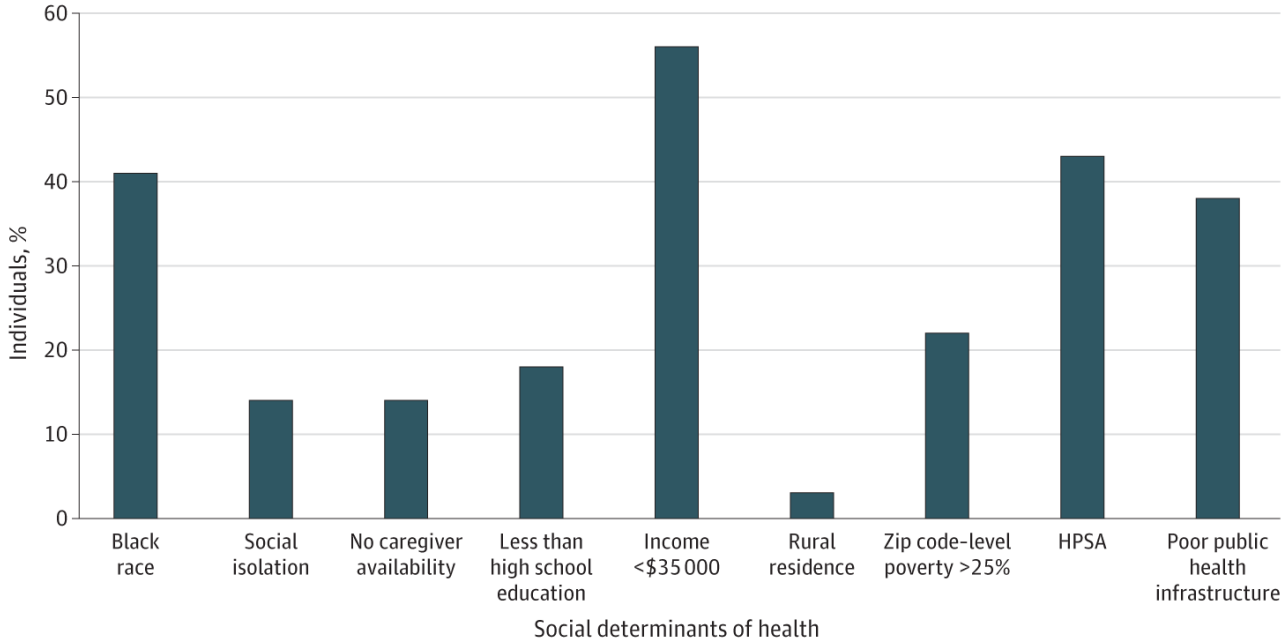
- mild caloric depletion:
  - reduced body weight
  - induction of nutrient deprivation signaling
- renal effects:
  - (increased diuresis)
  - improved intrarenal hemodynamics
  - early proximal tubule reconfiguration → reduced glucotoxicity and oxidative stress, favorable modulation of apical transporters
  - increased erythropoietin
- reduced microbiome formation of uremic toxins
- glucometabolic/hormonal balance
- direct cardiac effects?


EP
interventional cardiologist
cardiologist/ HF specialist
CS
HF nurse
patient / caregiver
ICU
rehab

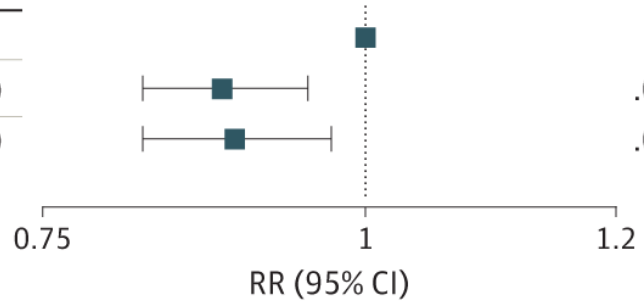

cardiologist/ HF specialist
EP
CS
interventional cardiologist
HF / internal medicine specialist
HF nurse
patient / caregiver
rehab
ICU


Genetic background & risk factors
Driving pathways
Disease B
Reinforcing pathways
Genetic background & risk factors
Driving pathways
Disease A
Reinforcing pathways
Genetic background & risk factors
Driving pathways
Disease C
Reinforcing pathways
Social determinants of health / Environmental triggers

- 1,000 patients admitted for HF between 2009 and 2017 at 549 US hospitals
- median age 77.8 [71.5-84.0] years, 479 (47.9%) women, 414 (41.4%) Black, and 492 of 876 (56.2%) with low income hospitalized



Income <$35 000	RR (95% CI)	*P* value
Model	1 [Reference]	
Age-adjusted	0.88 (0.82-0.95)	.001
Fully adjusted	0.89 (0.82-0.97)	.005



Zhang DT et al. JAMA Netw Open. 2023;6:e2344070

Hypothesis

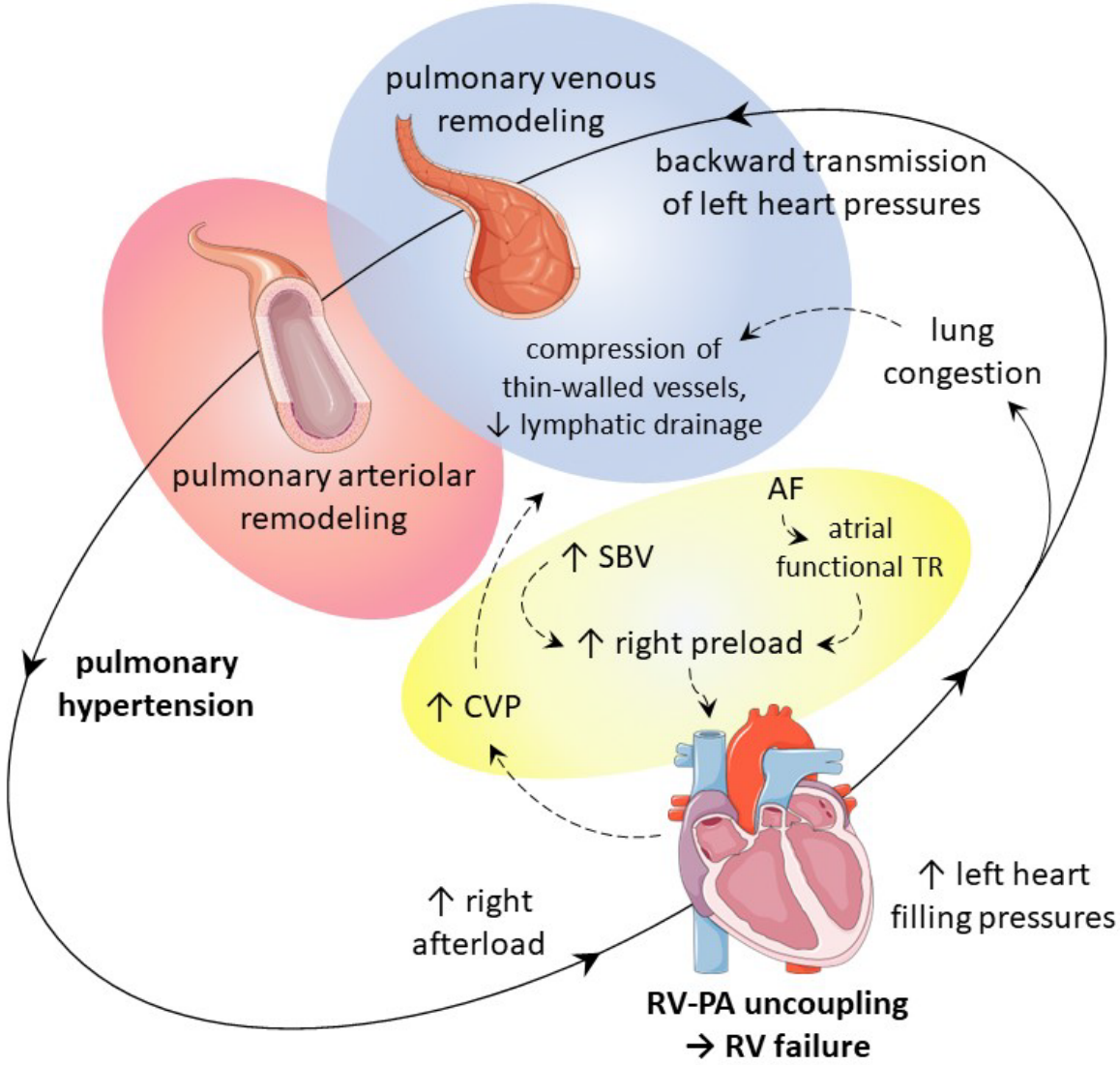
↓

Experiments

↓

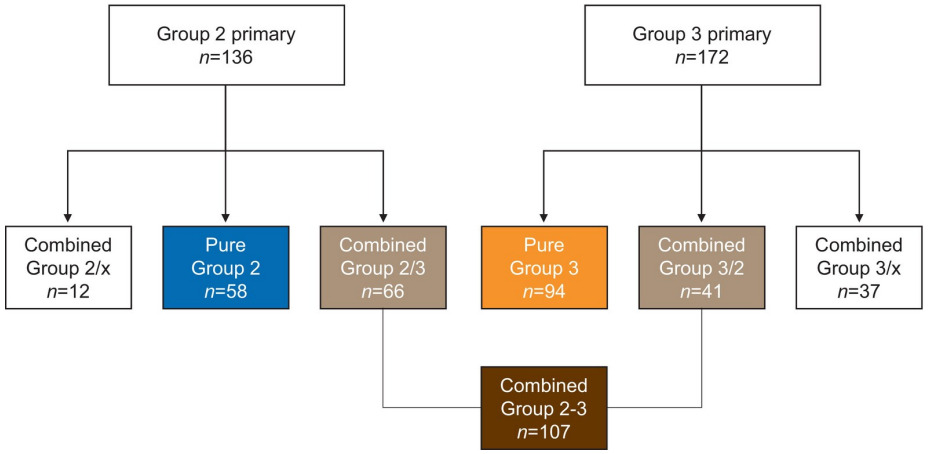
Confirmation or confutation

- *feasible*
- *verifiable*
- *fundamental principle of EBM*

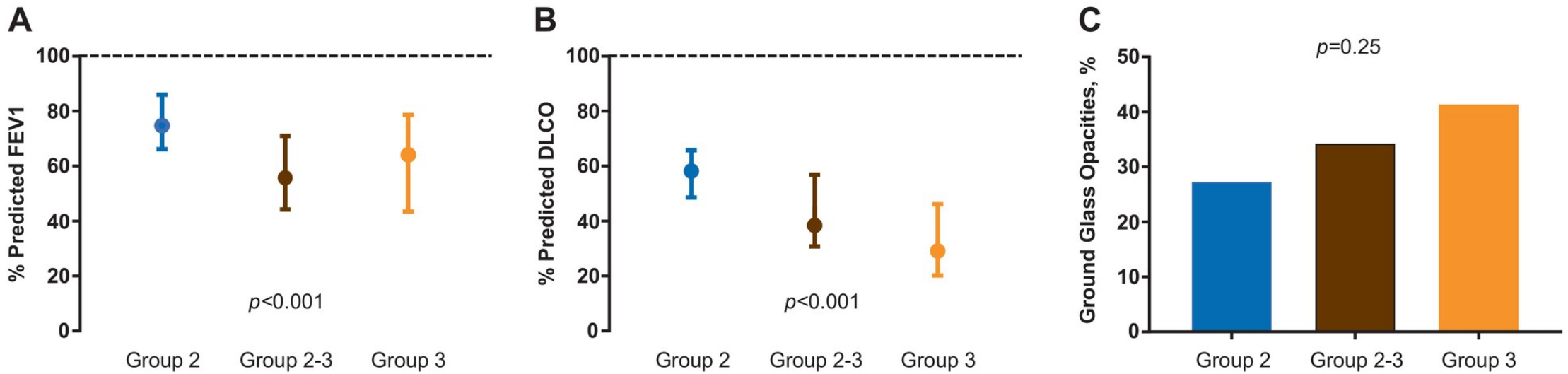


Ameri P et al. Eur J Heart Fail. 2024;26:707-29

PVDOMICS



- G2, PH associated with LHD:
  mPAP ≥25 mmHg, mean PAWP >15 mmHg, and: PVR >3.0 WU if CO >4 L/min; or DPG >7 mmHg if CO ≤4 L/min; or TPG >12 mmHg
- G3, PH associated with lung disease/hypoxaemia:
  mPAP ≥25 mmHg, PAWP ≤15 mmHg



Borlaug BA et al. Eur J Heart Fail. 2024; doi:10.1002/ejhf.3302

Hypothesis

↓

Experiments

↓

Confirmation or confutation

- *feasible*
- *verifiable*
- *fundamental principle of EBM*

Data availability

↓

Data patterns

↓

Recurring trends

⇣

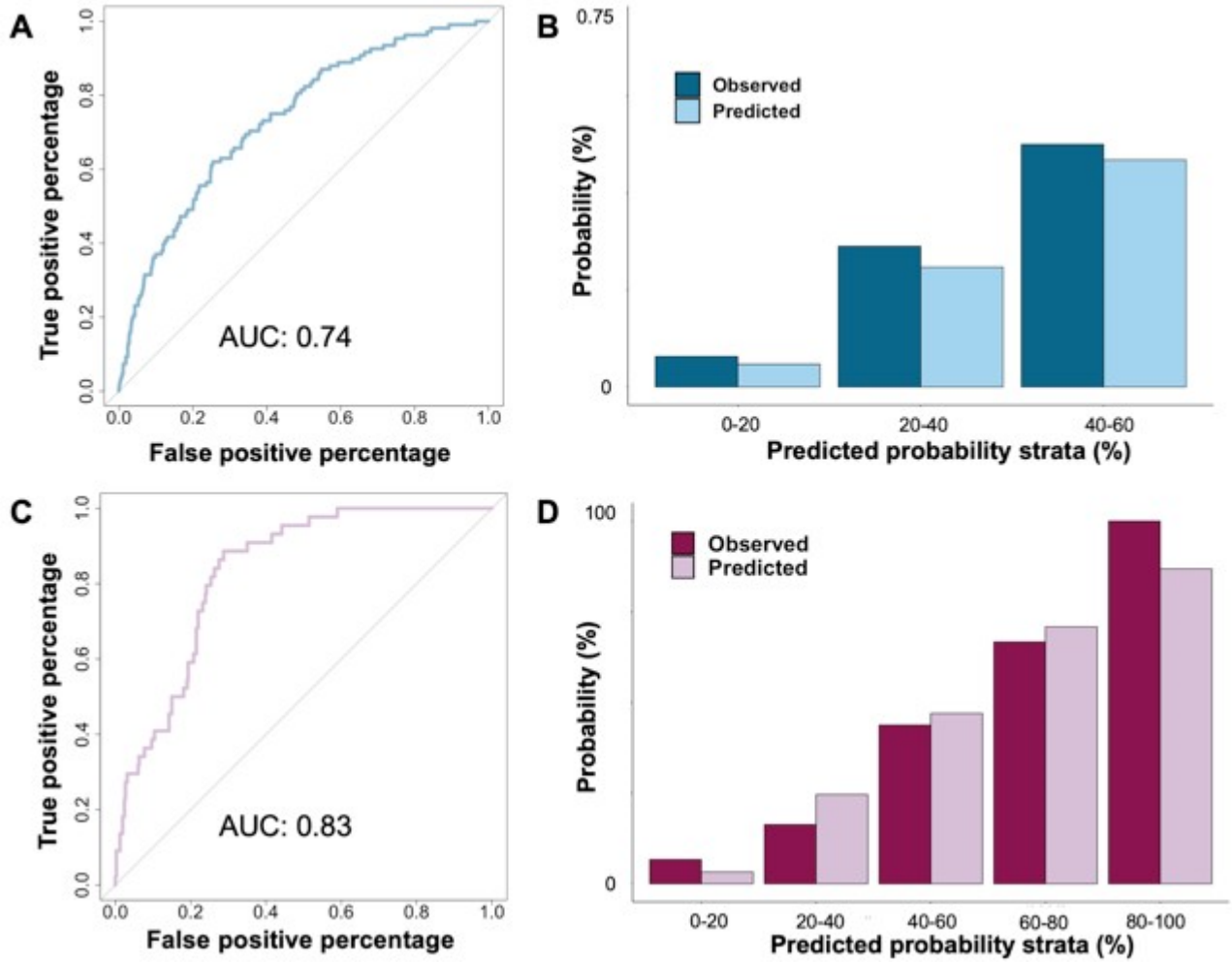
Hypothesis

- *expensive*
- *more difficult to control*
- *science is disconnected from EBM*

IRCCS Ospedale Policlinico San Martino

- 1,920 patients who underwent non-contrast abdominal CT upon admission to the ED between Jan. 2019 and Jan. 2020
- mean age 65±19 years, 46% women
- all-cause death by 30 days from admission in 7.9%

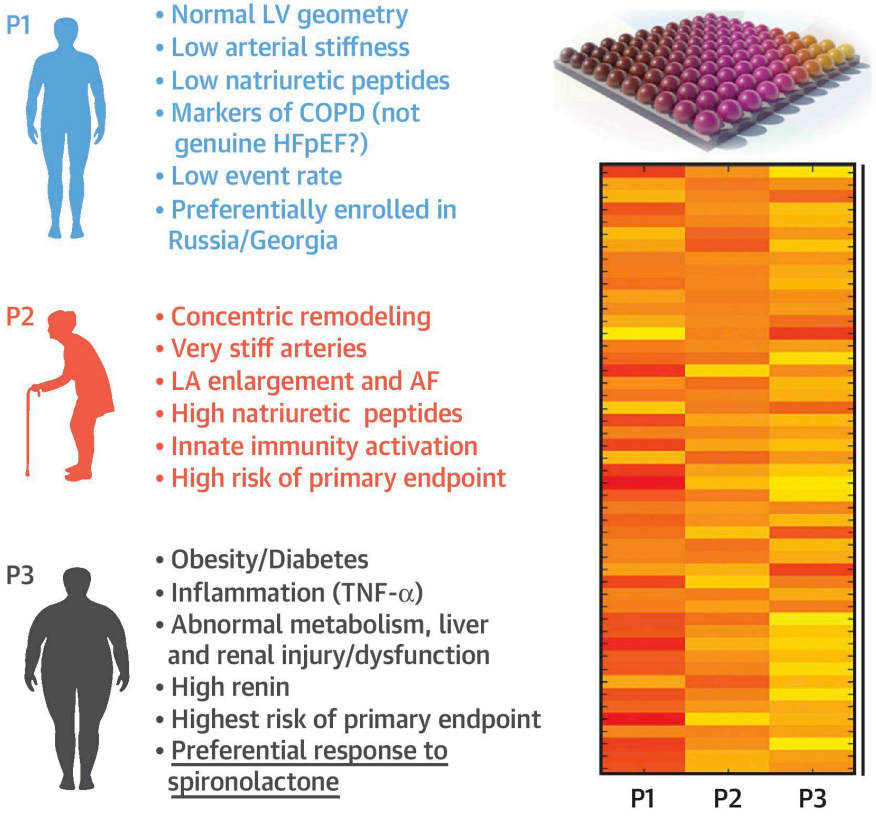
- ✓ age
- ✓ sex
- ✓ history of cancer
- ✓ dilated infrarenal aorta: no / yes
- ✓ bone density at the first lumbar vertebra
- ✓ cross-sectional area (mm2) and density (HU) of the psoas muscle at the third lumbar vertebra



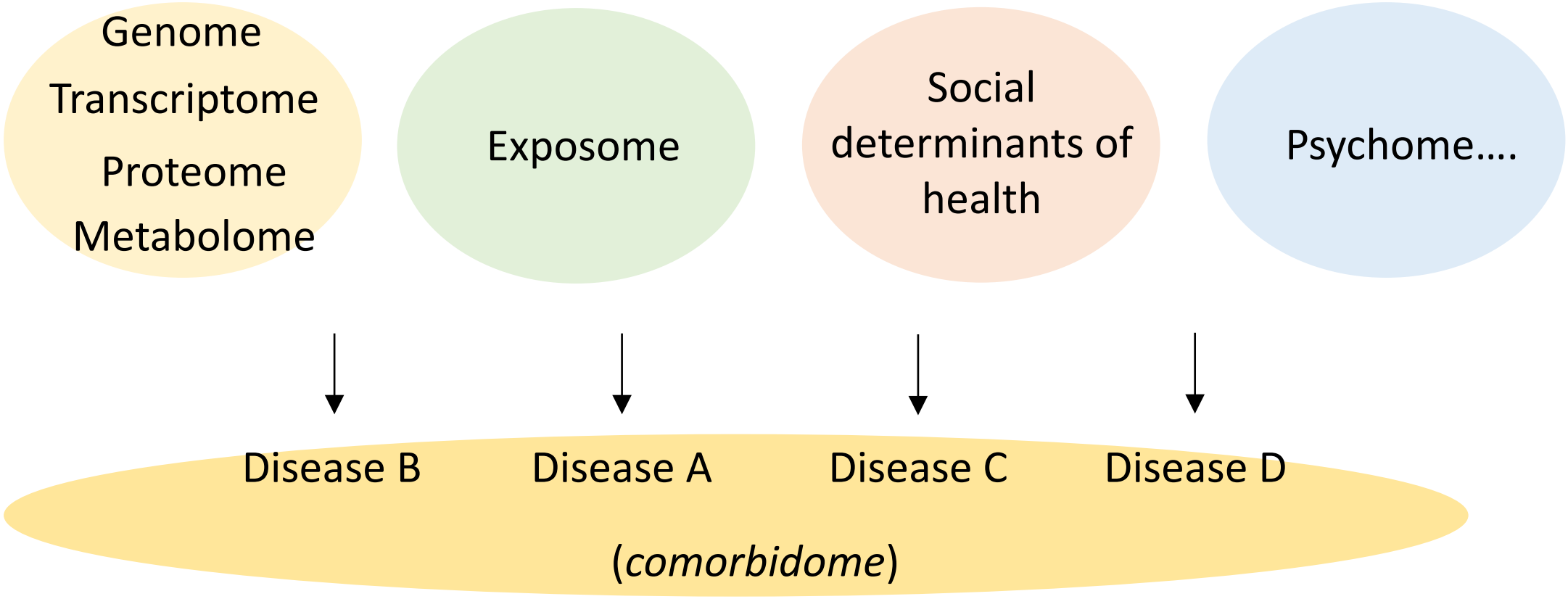
Tagliafico A, Benenati S, …, Ameri P. Submitted

TOPCAT

CENTRAL ILLUSTRATION: Clinical Phenogroups in HFpEF



Cohen, J.B. et al. J Am Coll Cardiol HF. 2020;8(3):172-84.


Genome
Transcriptome
Proteome
Metabolome
Exposome
Social determinants of health
Psychome….
Disease B
Disease A
Disease C
Disease D
(*comorbidome*)

“All our knowledge brings us nearer to our ignorance”

T.S. Eliot, The Rock