

Ohio-ACC FIT Grand Round Series

Disparities in Cardiology

Cleveland Clinic

11/17/2022



Ohio-ACC FIT Grand Round Series

Disparities in Cardiology

- Noon session approximately every two months highlighting the extraordinary work being done to mitigate disparities in cardiology.
- Rotate between different Ohio fellowship programs.

Ohio-ACC FIT Grand Round Series

Disparities in Cardiology

- Goals
 - Awareness of current disparities present in the cardiology field
 - Expanded understanding of the root causes of particular disparities and future directions to mitigate the disparity
 - Inspire fellows through speaker's career journey and niche in the field.
 - Build community among Ohio Cardiology programs
 - Open doors for future networking and collaborations

Cleveland Clinic HVTI

Yearly

- 786,871 patient visits
- 14,344 admissions

Capacity

- 440 total beds
- 24 CICU beds
- 12 HF-ICU beds
- 95 CTS-ICU beds



Cleveland Clinic Ohio-ACC FIT Reps



2022 - 2023 Cardiovascular Medicine Fellows

Third Year Fellows



Bryan Abadie



Ambreen Ali



Beka Bakhtadze



Jeremy Brooksbank



Tiffany Dong



Zackary Goff



Nicholas Kamp



Andrew LaCombe



Gregory Ogunnowo



Gary Parizher



Sameer Prasada



*Rohan Shah



Ramya Vajapey



*Weili Zheng



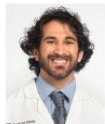
Radi Zinoviev

Second Year Fellows

Venugopal Menon, MD



Mohammad Abbasi



Thomas Das



Arsalan Derakhshan



Eunice Dugan



Robert Dunn



Evan Harmon



David Katziarier



Simrat Kaur



Christopher Massad



Nandini Mehra



*Julia Simkowski



Abhayjit Singh



*Trent Wei



Mohammad Zmaili

First Year Fellows



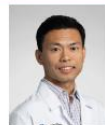
Andrew Abboud



Agam Bansal



Brittany Chapman



Vincent Chen



Megan Covington



Alejandro Duran



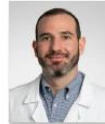
Medhat Farwati



Alice Haouzi



Ryan Keane



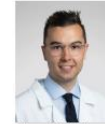
Samuel Kelly



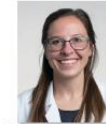
Aditya Mantha



Anirudh Nandan



Evan Whitehead



Tessa Benanzer-Zeis

*Chief Fellow

Ohio-ACC FIT Grand Round Series

Sex Differences in Heart Failure



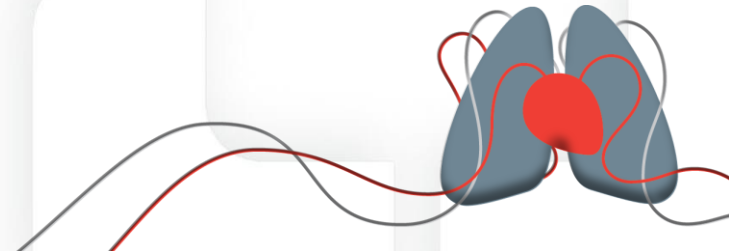
- Eileen Hsich, MD
- Medical Director for Heart Transplant | HVTI
Associate Professor of Medicine
Cleveland Clinic

FIT Disparity Grand Round Series: Sex Differences in Heart Failure

Eileen Hsich, MD

Medical Director for Heart Transplant | HVTI
Associate Professor of Medicine
Cleveland Clinic

Disclosure: Supported by NHLBI Award Number R01HL141892



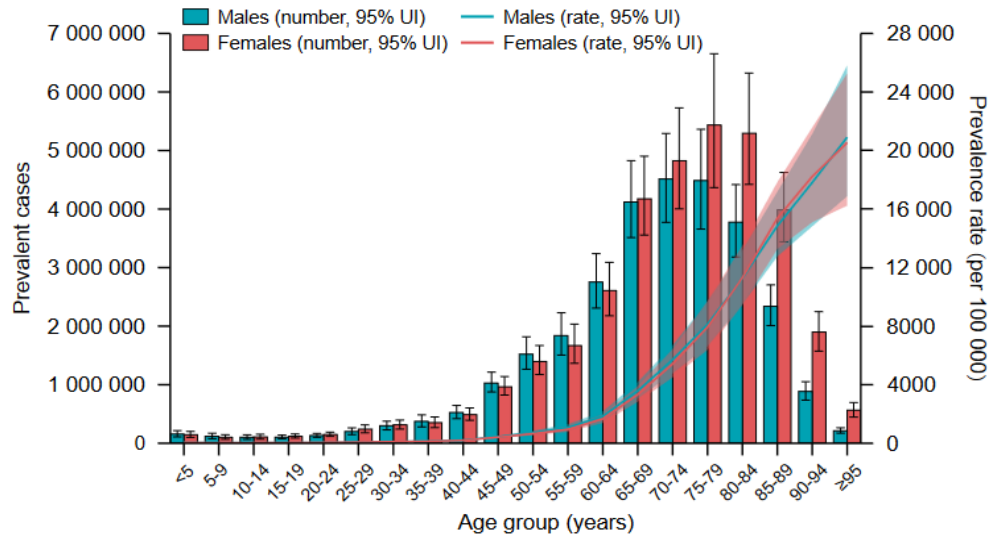
Sex Differences in HF

- **Overview**
 - Epidemiology
 - Risk Factors
 - Biomarkers
 - Treatment
 - Limitations
 - Outcomes
- **Career Pathway**



Epidemiology: Global

Sex Differences in Global HF Prevalence



In 2017, based on data from 195 countries, the global prevalence of HF increased with age peaking at ages 70-74 years in men and 75-79 years in women.

Epidemiology: U.S.



Population Group	Prevalence 2015-2018 Age \geq 20 yo	Incidence 2014 Age \geq 55 yo
Total Population	6,000,000	1,000,000
Total Males	3,400,000	495,000
Total Females	2,600,000	505,000

Risk Factors

	Women sHR (95% CI)	Men sHR (95% CI)
Myocardial Infarction	1.69 (1.28-2.22)	2.19 (1.85-2.60)
★ Hypertension	1.98 (1.68-2.34)	1.67 (1.45-1.93)
★ Diabetes mellitus	1.76 (1.49-2.09)	1.49 (1.28-1.72)
★ Atrial Fibrillation	2.58 (1.62-4.13)	1.83 (1.37-2.44)
★ LBBB	3.14 (2.13-4.64)	2.43 (1.62-3.63)

Sex differences in HF risk factors are based on 4 cohorts with 22,756 participants followed for 12.5 years: Framingham Heart Study, PREVEND, MESA, and the Cardiovascular Health Study.

BNP Biomarker in ADHF

	EF <40% Female <i>N=17,447</i>	EF <40% Male <i>N=29,578</i>	EF 40-49% Female <i>N=6,752</i>	EF 40-49% Male <i>N=7,198</i>	EF ≥50% Female <i>N=25,244</i>	EF ≥50% Male <i>N=13,711</i>
Age yo (IQR)	74 (62-83)	69 (57-79)	78 (67-85)	74 (63-83)	79 (69-86)	74 (63-83)
BNP (pg/mL)	1259 (606-2413)	1113 (535-2130)	821 (421-1574)	732 (366-1420)	559 (279-1075)	540 (253-1064)
EF % (IQR)	25 (20-31)	25 (19-30)	44 (40-45)	43 (40-45)	60 (55-65)	56 (53-60)

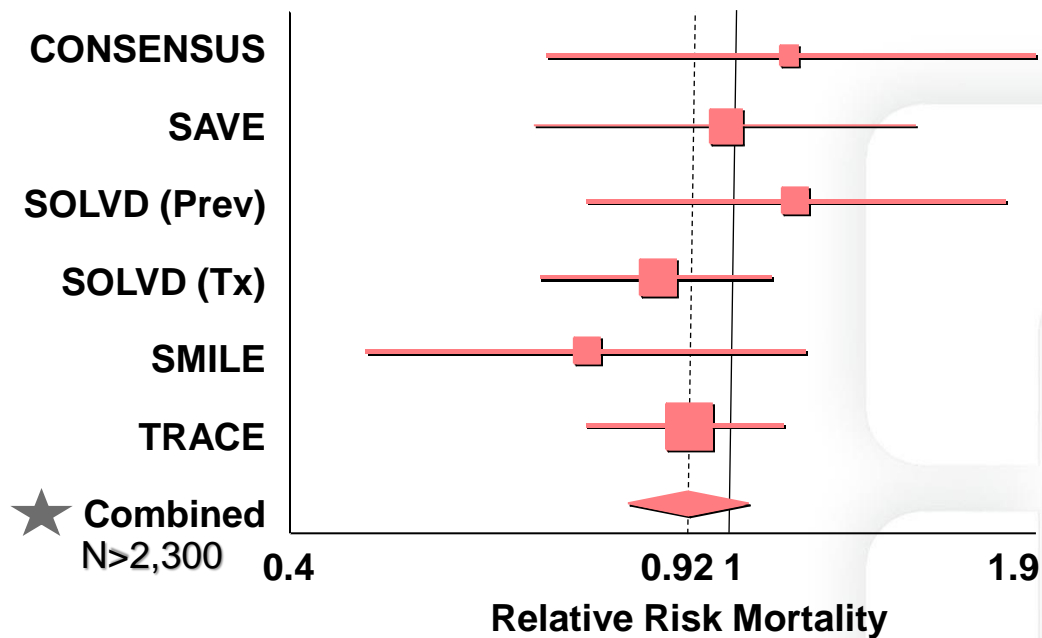
In a large GWTG-HF registry (N=99,930), we found that despite sex/EF differences in BNP values (levels higher F > M, HF_rEF > HF_mEF > HF_pEF), there was no significant difference in the ability of BNP to predict in-hospital mortality among these subgroups.

Treatment

- ACE/ARB/ARNI
- Aldosterone antagonists
- B-blockers
- SGLT2i
- ICD
- CRT
- LVAD



Effect in Women: ACE I



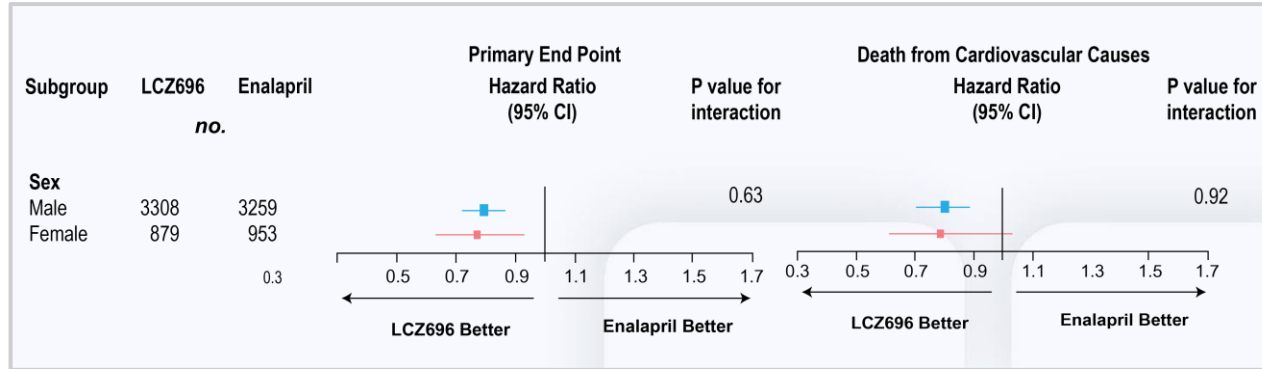
Sex Differences: ARBS

Study	Drugs	Endpoint	Women HR (95%CI)	Men HR (95%CI)
Val-HeFT	Valsartan	Mortality	0.93 (0.68-1.27)	1.04 (0.90-1.19)
★ Val-HeFT	Valsartan	HF hospitalization	0.74 (0.55-0.98)	0.73 (0.62-0.86)
ELITE II	Losartan	Mortality	1.14 (0.8-1.8)	1.12 (0.9-1.4)
★ CHARM	Candesartan	CV Mortality	0.78 (0.69-0.88)	1.0 (ref)
★ CHARM	Candesartan	HF hospitalization	0.87 (0.78-0.97)	1.0 (ref)

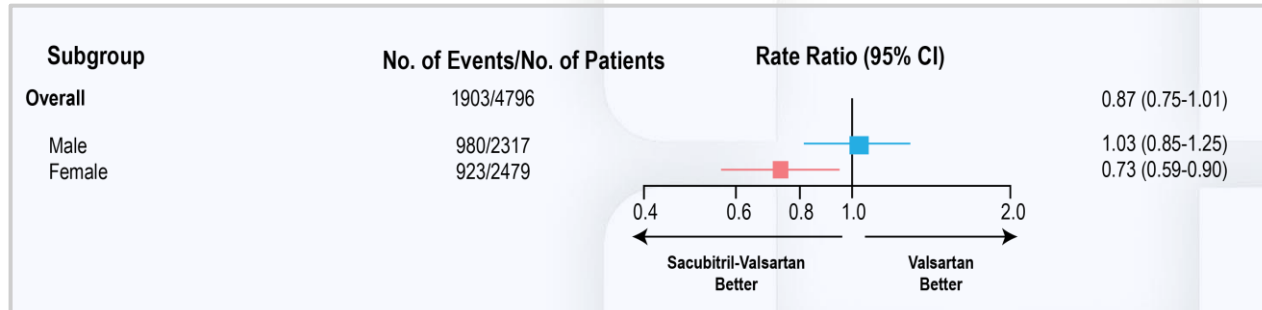


ARNI

PARADIGM-HF*



PARAGON-HF**

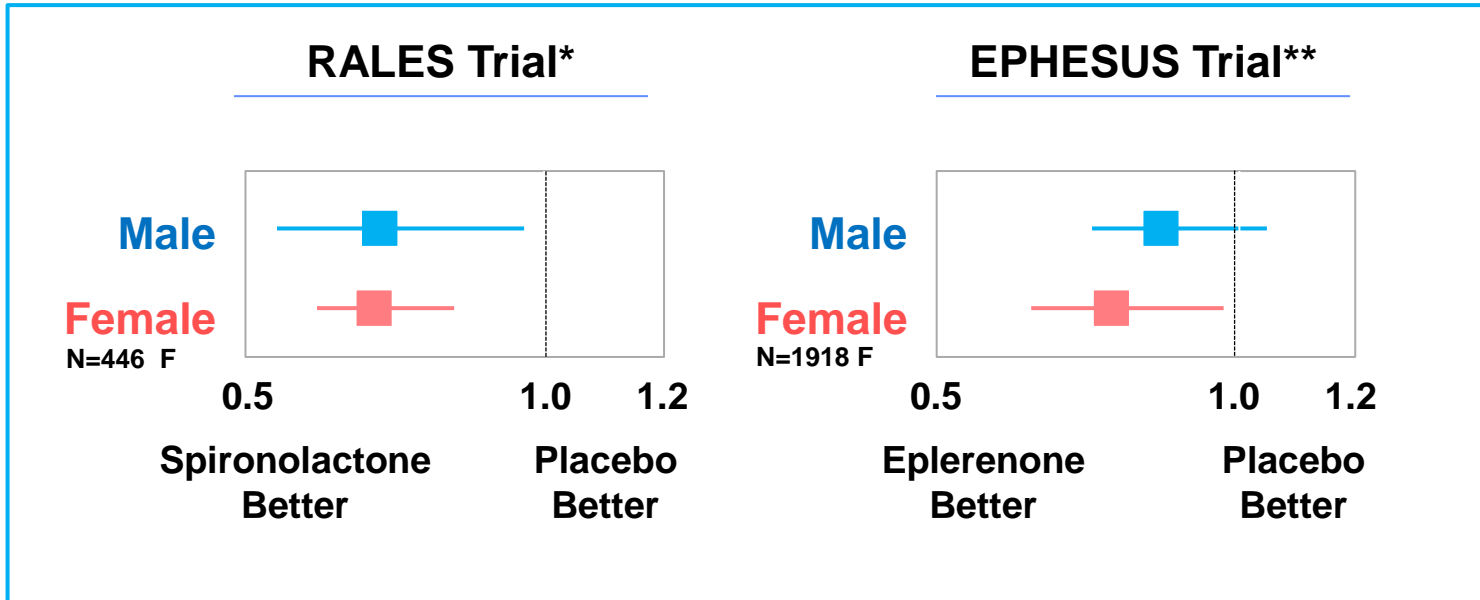


*NEJM 2014; 371:993-1004

**N Engl J Med 2019;381:1609-20

Aldosterone Blockers

Relative Risk of Death from All Causes



*Pitt B, et al. NEJM. 1999;341:709-17

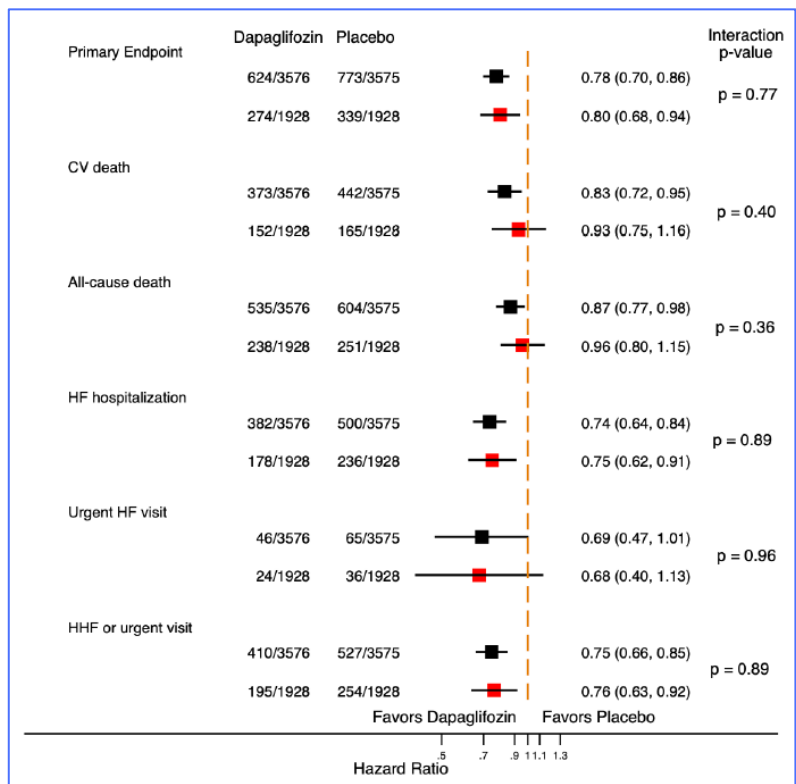
**Pitt B, et al. NEJM. 2003;348:1309-21

β-Blockers and Mortality Risk

Study	Male, N	Female, N	RR Male (95%CI)	RR Female (95% CI)
★ CIBIS-II	2,132	515	0.71 (0.58-0.87)	0.52 (0.30-0.89)
COPERNICUS	1,822	465	0.68 (0.54-0.86)	0.63 (0.39-1.04)
★ MERIT-HF	3,093	898	0.63 (0.50-0.78)	0.93 (0.58-1.49)
★ US Carvedilol HF	838	256	0.44 (0.24-0.82)	0.32 (0.11-0.93)
Random Effects pooled estimate	7,885	2,134	0.66 (0.59-0.75)	0.63 (0.44-0.91)

Carvedilol studies: Copernicus, US carvedilol HF
Metoprolol studies: MERIT-HF
Bisoprolol study: CIBIS-II

SGLT2i: Sex Differences



Cohort:

DAPA-HF: EF \leq 40%
 DELIVER: EF > 40%

Primary Outcome: composite of worsening HF or CV death

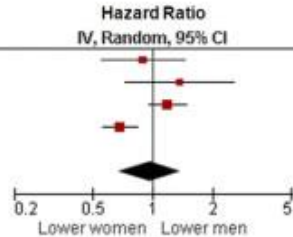
■ Male
 ■ Female

ICD

A. Overall Mortality

Study or Subgroup	Weight	IV, Random, 95% CI
DEFINITE	21.2%	0.89 [0.54, 1.46]
MADIT-II	16.9%	1.37 [0.72, 2.59]
MUSTT	30.8%	1.19 [0.95, 1.48]
SCD-HeFT	31.2%	0.68 [0.55, 0.84]
Total (95% CI)	100.0%	0.96 [0.67, 1.39]

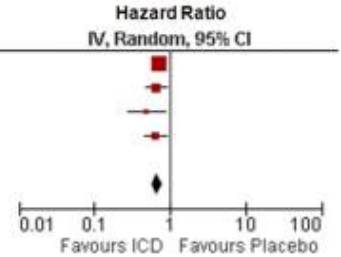
Heterogeneity: Tau² = 0.10; Chi² = 14.85, df = 3 (P = 0.002); I² = 80%
 Test for overall effect: Z = 0.21 (P = 0.84)



A. ICD survival benefit among men

Study or Subgroup	Weight	IV, Random, 95% CI
SCD-HeFT	51.0%	0.71 [0.57, 0.88]
MADIT-II	23.5%	0.66 [0.48, 0.90]
DEFINITE	6.6%	0.49 [0.27, 0.88]
COMPANION	18.8%	0.65 [0.46, 0.92]
Total (95% CI)	100.0%	0.67 [0.58, 0.78]

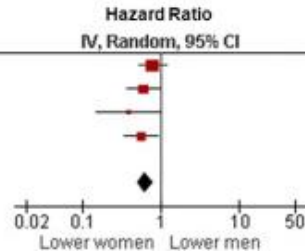
Heterogeneity: Tau² = 0.00; Chi² = 1.40, df = 3 (P = 0.70); I² = 0%
 Test for overall effect: Z = 5.17 (P < 0.00001)



B. Appropriate ICD Intervention

Study or Subgroup	Weight	IV, Random, 95% CI
SCD-HeFT	39.4%	0.78 [0.52, 1.17]
MADIT-II	27.9%	0.60 [0.37, 0.97]
DEFINITE	7.1%	0.39 [0.15, 1.01]
COMPANION	25.6%	0.56 [0.34, 0.92]
Total (95% CI)	100.0%	0.63 [0.49, 0.82]

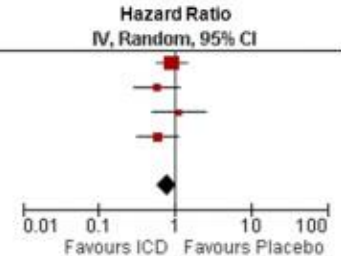
Heterogeneity: Tau² = 0.00; Chi² = 2.32, df = 3 (P = 0.51); I² = 0%
 Test for overall effect: Z = 3.54 (P = 0.0004)



B. ICD survival benefit among women

Study or Subgroup	Weight	IV, Random, 95% CI
SCD-HeFT	44.3%	0.90 [0.57, 1.43]
MADIT-II	18.9%	0.57 [0.28, 1.15]
DEFINITE	14.1%	1.14 [0.50, 2.58]
COMPANION	22.8%	0.59 [0.31, 1.12]
Total (95% CI)	100.0%	0.78 [0.57, 1.05]

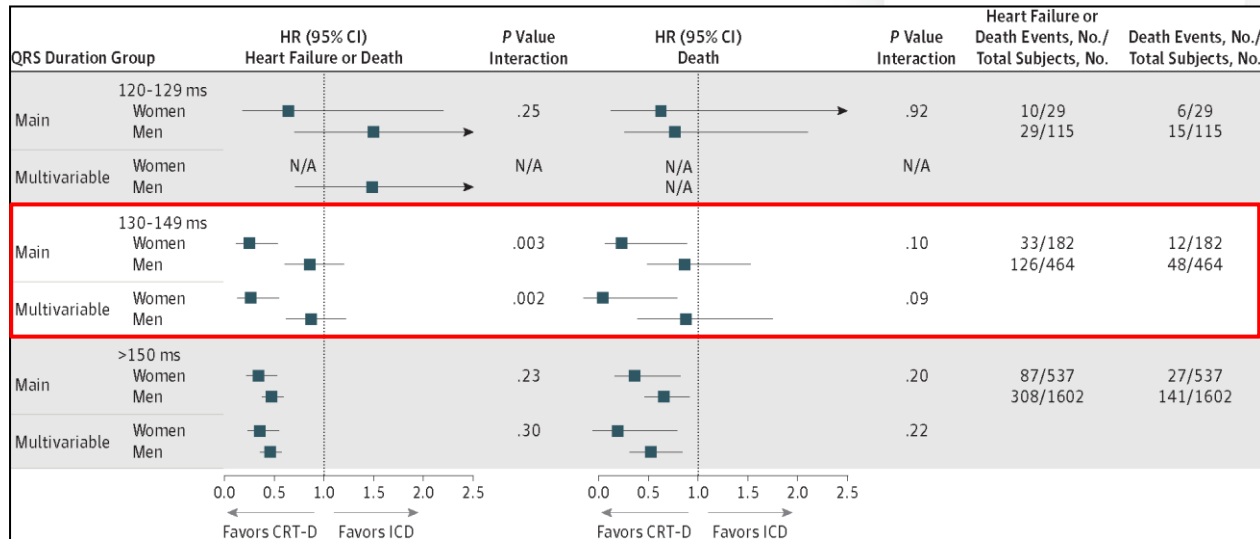
Heterogeneity: Tau² = 0.00; Chi² = 2.69, df = 3 (P = 0.44); I² = 0%
 Test for overall effect: Z = 1.63 (P = 0.10)



Cardiac Resynchronization Therapy

This meta-analysis combined 3 studies:

- **MADIT-CRT:** CRTD vs ICD, NYHA Class I/II, LVEF $\leq 30\%$
- **REVERSE:** CRT on vs off, NYHA Class I/II, LVEF $\leq 40\%$
- **RAFT:** CRTD vs ICD, NYHA Class II/III, LVEF $\leq 30\%$



MCS and Risk of Stroke

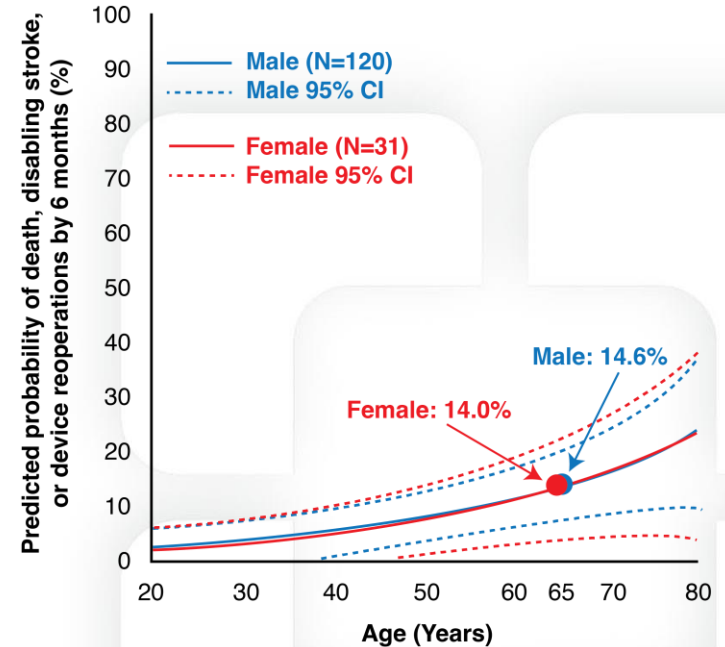
HeartWare: ADVANCE BTT trial*

Adverse events	Women n=96	Men n=236	P value
Ischemic CVA	3 (3%)	5 (11%)	0.86
Hemorrhagic CVA	5 (5%)	7 (17%)	0.97

HM2: BTT and DT trials***

Adverse events	Women n=220	Men n=736	P value
Ischemic CVA	21(10%)	37 (5%)	0.028
Hemorrhagic CVA	31(14%)	45 (6%)	0.001

HM3: Momentum 3 trial **



*Birks E, et al. *J of Heart Lung Transplant*. 2015;34:815-824

**Goldstein, et al. *J Heart Lung Transplant*. 2018 Jan;37(1):7-14

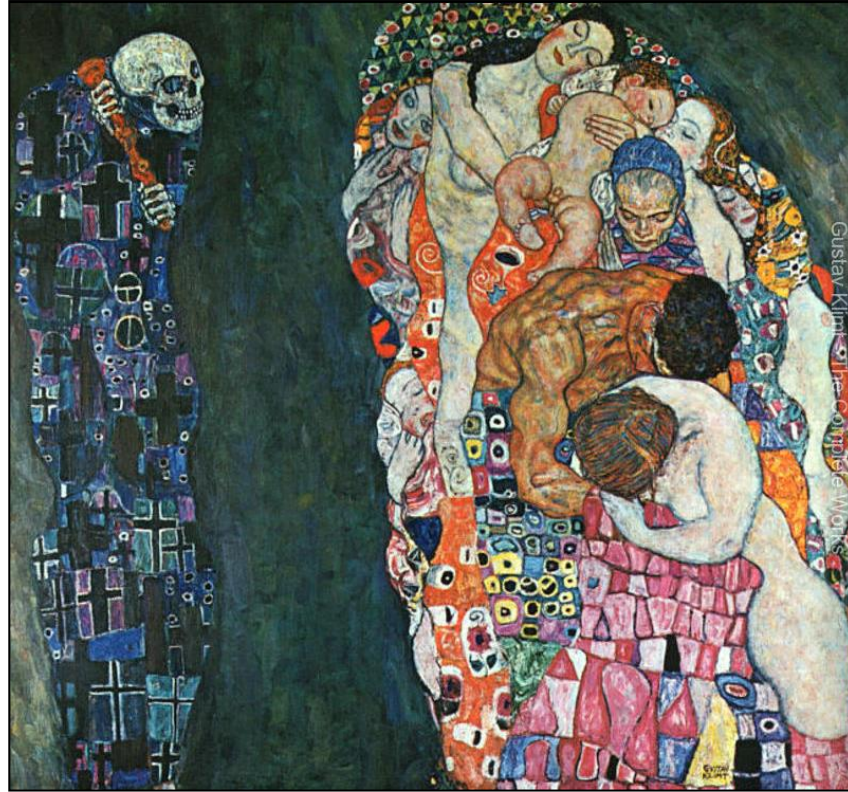
***Boyle A, et al. *J Am Coll Cardiol* 2014;63:880-8

Limitations: Under-representation of Women

Table 1 Female Participants in Chronic Heart Failure Trials

Study (Ref #)	% Women	Number of Women	LVEF
A-HeFT (47)	40	420	≤35%
BEST (12)	22	593	≤35%
CARE-HF (55)	26	215	≤35%
CHARM-low LVEF (37)	26	1,188	≤40%
CIBIS II (41)	19	515	≤35%
COMPANION (52)	32	493	≤35%
CONSENSUS (63)	30	75	Any
COPERNICUS (40)	20	469	<25%
DIG (48)	22	1,520	≤45%
ELITE-II (61)	31	966	≤40%
EPHESUS (45)	29	1,918	≤40%
MADIT II (55)	16	192	≤30%
MERIT-HF (42)	23	898	≤40%
RALES (43)	27	446	≤35%
SCD HeFT (54)	23	588	≤35%
SOLVD prevention (29)	13	548	≤35%
SOLVD treatment (29)	20	514	≤35%
U.S. Carvedilol (40)	23	256	≤35%
Val-HeFT (38)	20	1,003	<40%
V-HeFT I (45)	0	0	<45%
V-HeFT II (46)	0	0	<45%

Outcomes



Death and Life 1911 by Gustav Klimt

HF Death

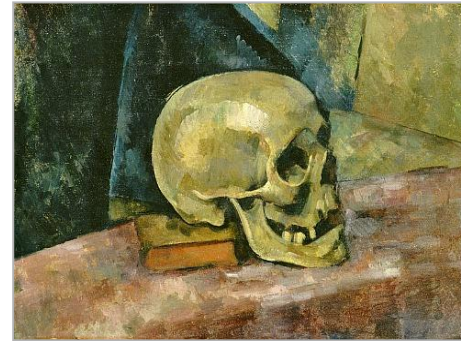
	Female Death (95% UI)	Male Death (95% UI)
Global*		
Total # (millions in 2020)	0.14 (0.12-0.17)	0.23 (0.20-0.25)
Rate per 100,000, age standardized 2020	3.32 (2.73-3.81)	6.20 (5.53-6.85)
US**		
Total # (millions in 2019), all ages	0.046	0.040

* Global Burden of Disease Study 2020

**AHA. Heart Disease and Stroke Stats-2022

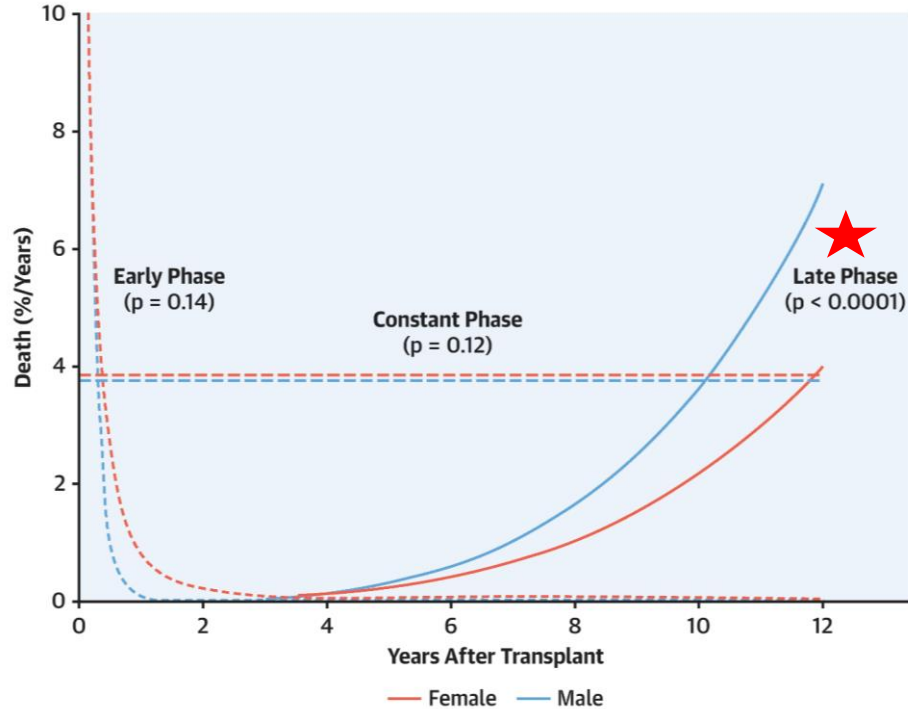
Mode of Death Without ICD

Mortality Rate	N	Total Mortality	Sudden Death	Pump Failure Death	Other Death
Women	1697	9.5%	3.4%	3.4%	2.7%
Men	6640	11.8%	★ 4.8%	3.4%	3.6%



Death by Paul Cezanne

Sex Differences: Heart Transplant



Summary

General Facts

- HF prevalence: ↑ age, **M**>**F** slightly
- HF risk factors: **F** > **M** NICM (HTN)
M > **F** ICM
- HF Survival: **F** > **M**
sudden death **M** > **F**
- Natriuretic pep: HF_rEF > HF_mEF > HF_pEF
F > **M**

Sex Differences in HF therapy

- Valsartan and ARNI: ↓ M: death +HF
F: HF
- Aldosterone antag, β-blocker, SGLT2i
benefit **M** = **F**
- CRT benefit **F** > **M**
- ICD benefit ? **M** > **F**



Closing Thoughts





Cleveland Clinic

Every life deserves world class care.