ACC Latin America Conference 2017

MEXICO CITY

JUNE 22 – 24, 2017

GLOBAL EXPERTS, LOCAL LEARNING

ACC Latin America Conference 2017

Women's Heart Health: Holistic Approaches Throughout the Lifetime - Key Differences in Heart Failure in Women

C. Noel Bairey Merz MD
Medical Director and
Barbra Streisand Women's Heart Center
Preventive Cardiac Center
Cedars-Sinai Heart Institute
Los Angeles, California USA
merz@cshs.org

Presenter Disclosure Information

Key Differences in Heart Failure in Women (Bairey Merz)

DISCLOSURE INFORMATION:

The following relationships exist related to this presentation (*paid to CSMC):

Grant support*: NHLBI, FAMRI, SWHR, Gilead, NIH-CTSI

Consulting*: Abbott-Diagnostics, Sanofi

Honorarium*: Gilead, Pri-Med

Stocks: None

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55 year old woman with history of hypertension, angina, abnormal exercise treadmill test, invasive coronary angiogram with “normal” coronary arteries, abnormal microvascular blood flow to acetylcholine treated with carvedilol, lisinopril, eplenerone, pravastatin and aspirin. At 10 year followup, she presents to the emergency department for heart failure, after her antihypertensive medications were temporarily discontinued by her surgeon post-shoulder surgery.
EXAM: BP 184/85, lower extremity edema.
LABS: BNP 343 mg/dL. ECHO: LVEF 68%
She was treated medically with lasix, lisinopril, eplerenone, carvedilol, pravastatin, and aspirin. Her BP, SOB improved and BNP fell to 40 mg/DL.

How should she be chronically treated?

1. Current treatment is fine
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Key Differences in Heart Failure in Women

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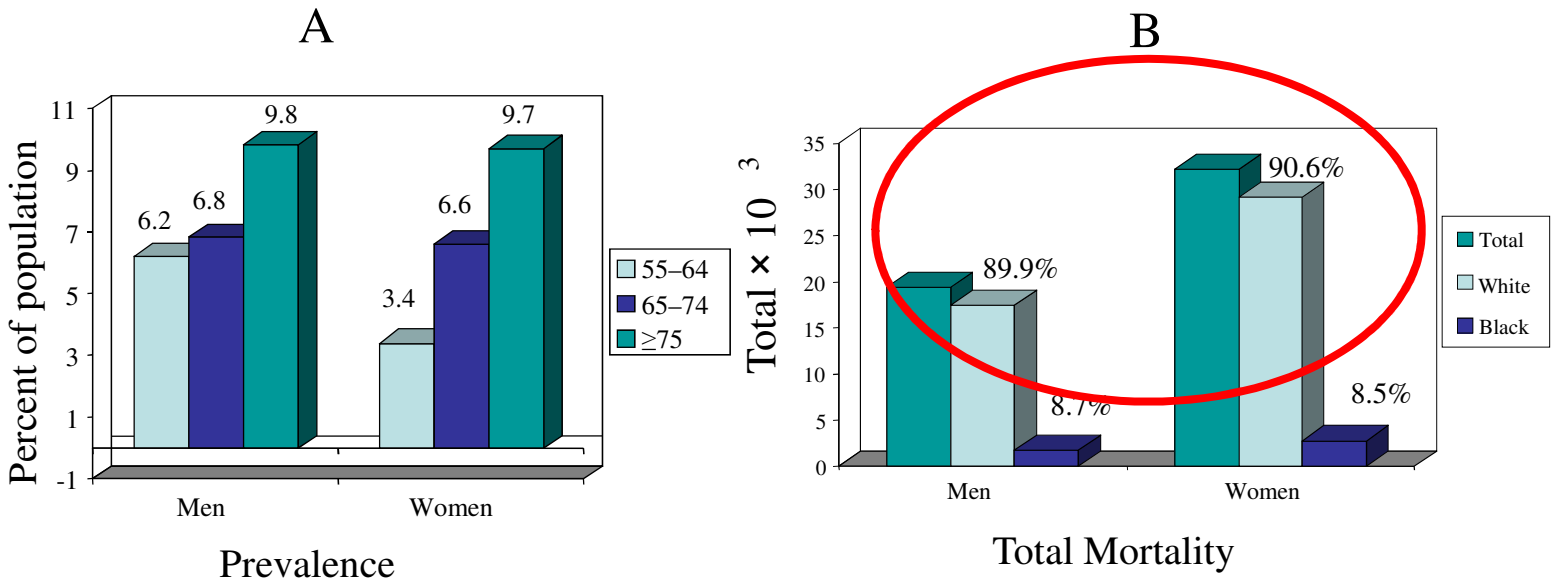
1. **Prevalence – Heart Failure in Women**
2. **Diastolic Heart Failure (Heart Failure with Preserved Ejection Fraction – HFpEF)**
3. **Management and Knowledge Gaps**

Heart Failure and Gender
Equal HF Prevalance but Higher Mortality in Women

Prevalence of and Mortality From Heart Failure by Gender



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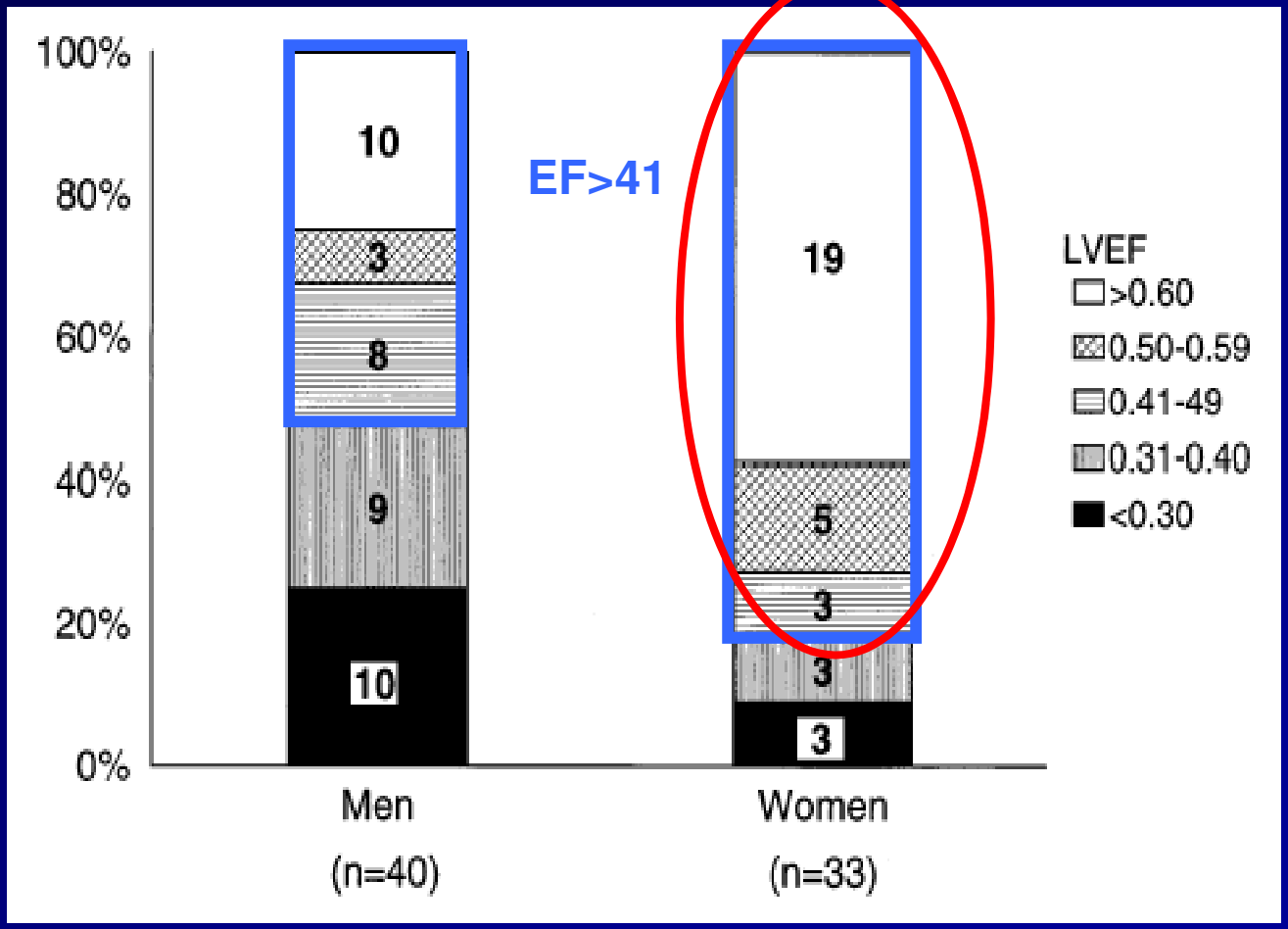
Jessup M et al. *J Thorac Cardiovasc Surg.* 2004;127:1247-1252.

Distribution of EF Among Men and Women With HF: Most HF in Women is HFpEF

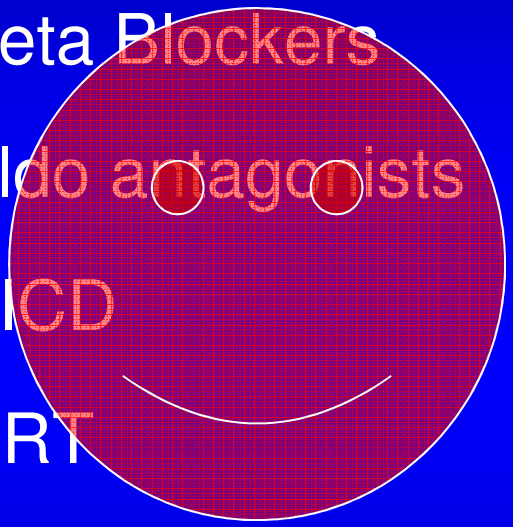


Vasan RS et al. *J Am Coll Cardiol*. 1999;33:1948-1955.

Evidence-based Treatment

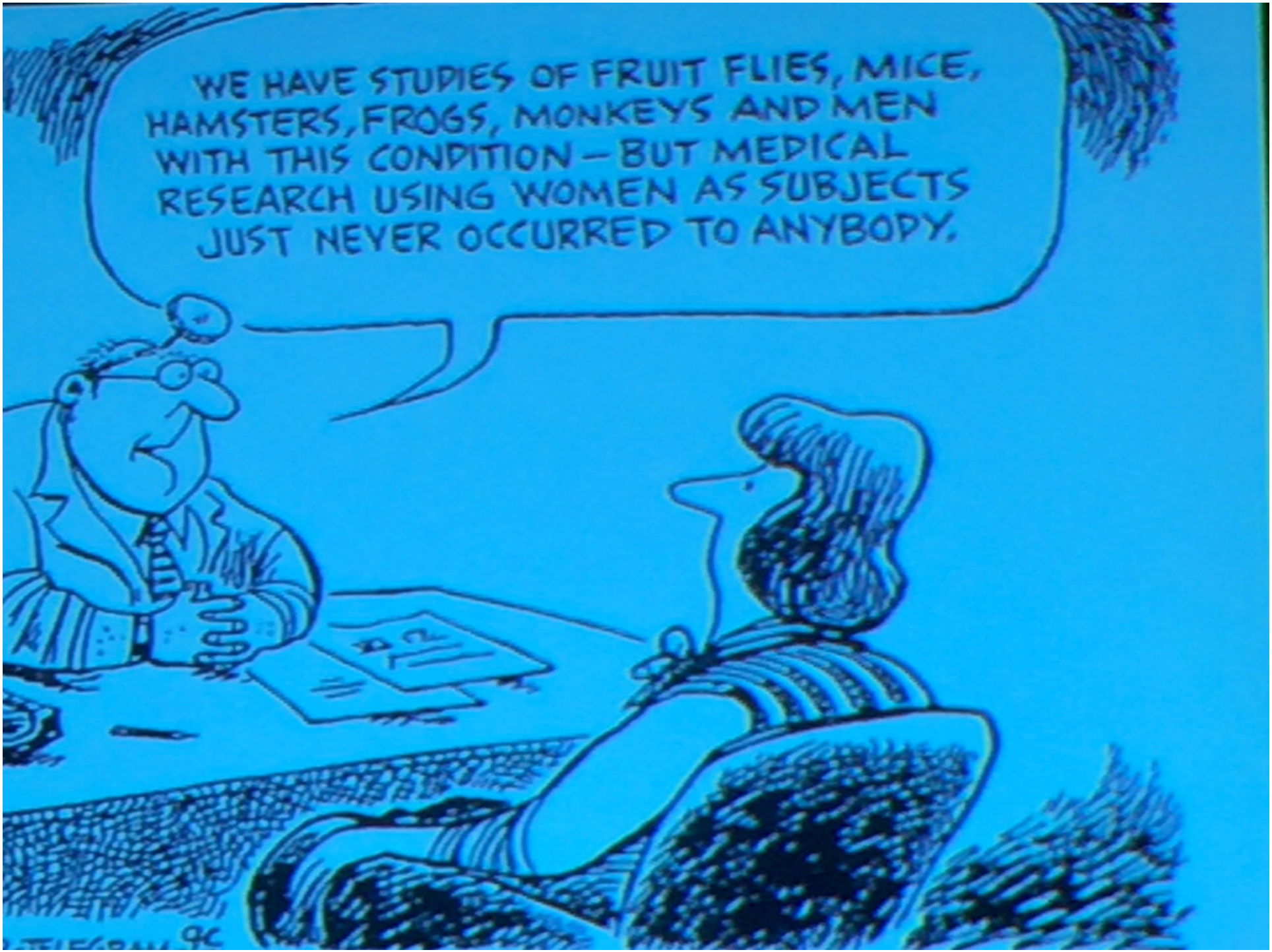
HFrEF

- ACE/ARB
- Beta Blockers
- Aldo antagonists
- AICD
- CRT



HFpEF

- Diuretics
- Verapamil
- Digoxin
- Beta blockers
- Hydralazine/ISDN
- Ace inhibitors/ ARBs
- **Aldo antagonists**
- **PD5 inhibitors**
- **Nitrates**


WE HAVE STUDIES OF FRUIT FLIES, MICE, HAMSTERS, FROGS, MONKEYS AND MEN WITH THIS CONDITION – BUT MEDICAL RESEARCH USING WOMEN AS SUBJECTS JUST NEVER OCCURRED TO ANYBODY.

HF Studies - Sex Differences in Heart Failure

SciEP Science and Education Publishing
From Scientific Research to Knowledge

Table 1. Percentage of women's population in HF trials

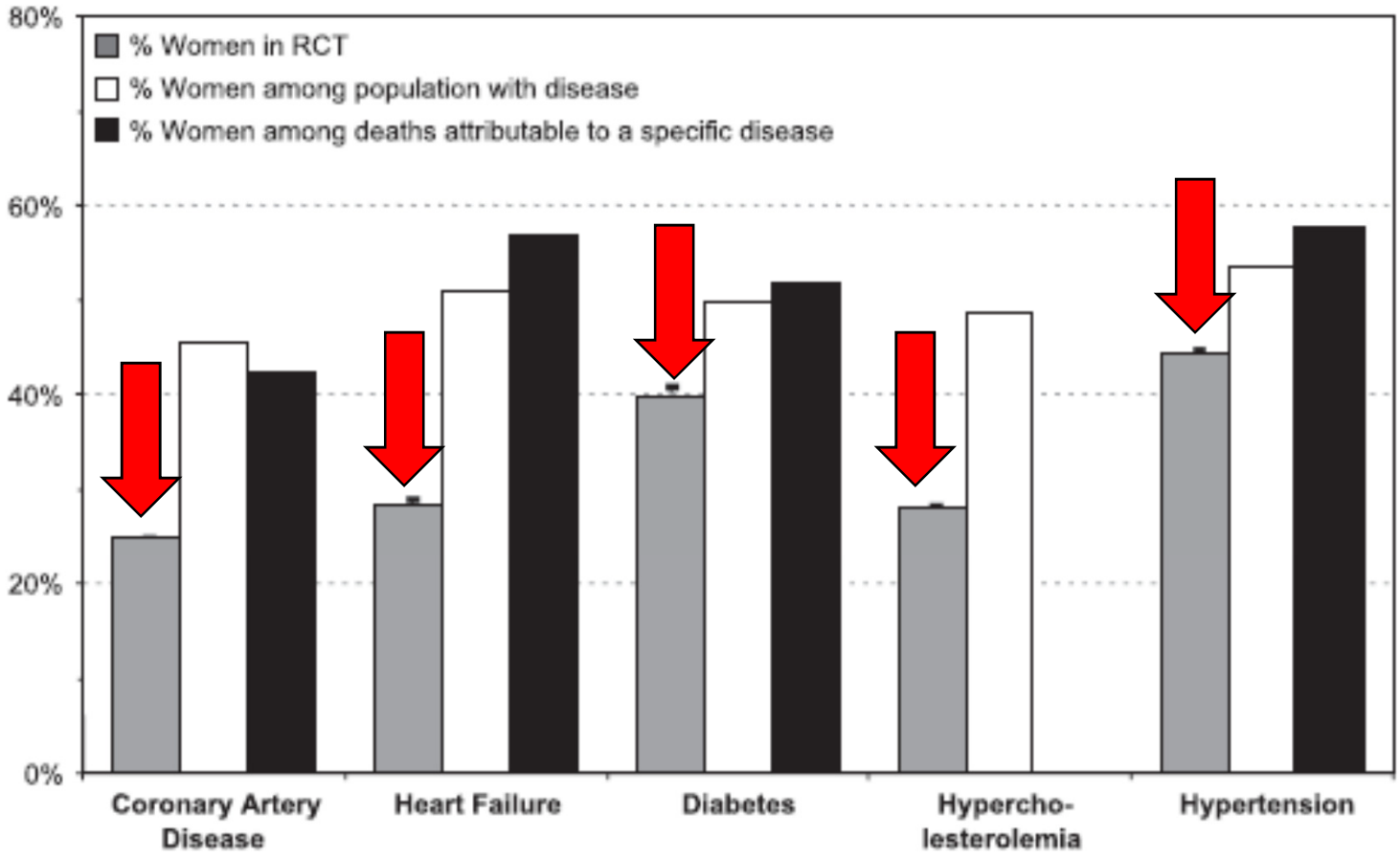
Trial	Total population	Female population	Percentage of females
CONSENSUS [58] (Enalapril)	253	75	30
SOLVD [59] (Ramipril)	4228	486	11.5
ATLAS [60] (Lisinopril)	3164	648	20
COPERNICUS [61] (Carvedilol)	2289	469	20
MERIT HF [62] (Metoprolol)	3991	898	22.5
CIBIS II [63] (Bisoprolol)	2647	515	19
SENIORS [64] (Nebivolol)	2061	785	38
VAL-HeFT [70] (Valsartan)	5010	1003	20
CHARM Added [71] (Valsartan vs Candesartan vs placebo)	2548	542	21.3
ELITE II [72] (Losartan vs Captopril)	3152	966	31
HEEAL [73] (Losartan vs Lisinopril)	3846	1155	29.5
VALIANT [74] (Valsartan)	14703	4570	31.1
OPTIMAAL [75] (Losartan vs Captopril)	20573	5925	28.8
SHIFT [76] (Ivabradine)	6558	1171	17
BEAUTIFUL [77] (Ivabradine)	10917	1870	17
MADIT II [78] (ICD)	720	192	26
SCD- HeFT [79] (ICD)	2521	588	23
COMPANION [80] (CRT)	1520	493	32
CARE HF [81] (CRT)	813	215	26

Women comprise only 6-38% of HF trial participants (most trials are HFrEF and most women are HFpEF)

Giulia D'Agostini et al. Heart Failure in Women: A Disease with Peculiar Pathophysiological Mechanisms and Clinical Presentation. American Journal of Cardiovascular Disease Research, 2013, Vol. 1, No. 1, 1-6. doi:10.12691/ajcdr-1-1-1

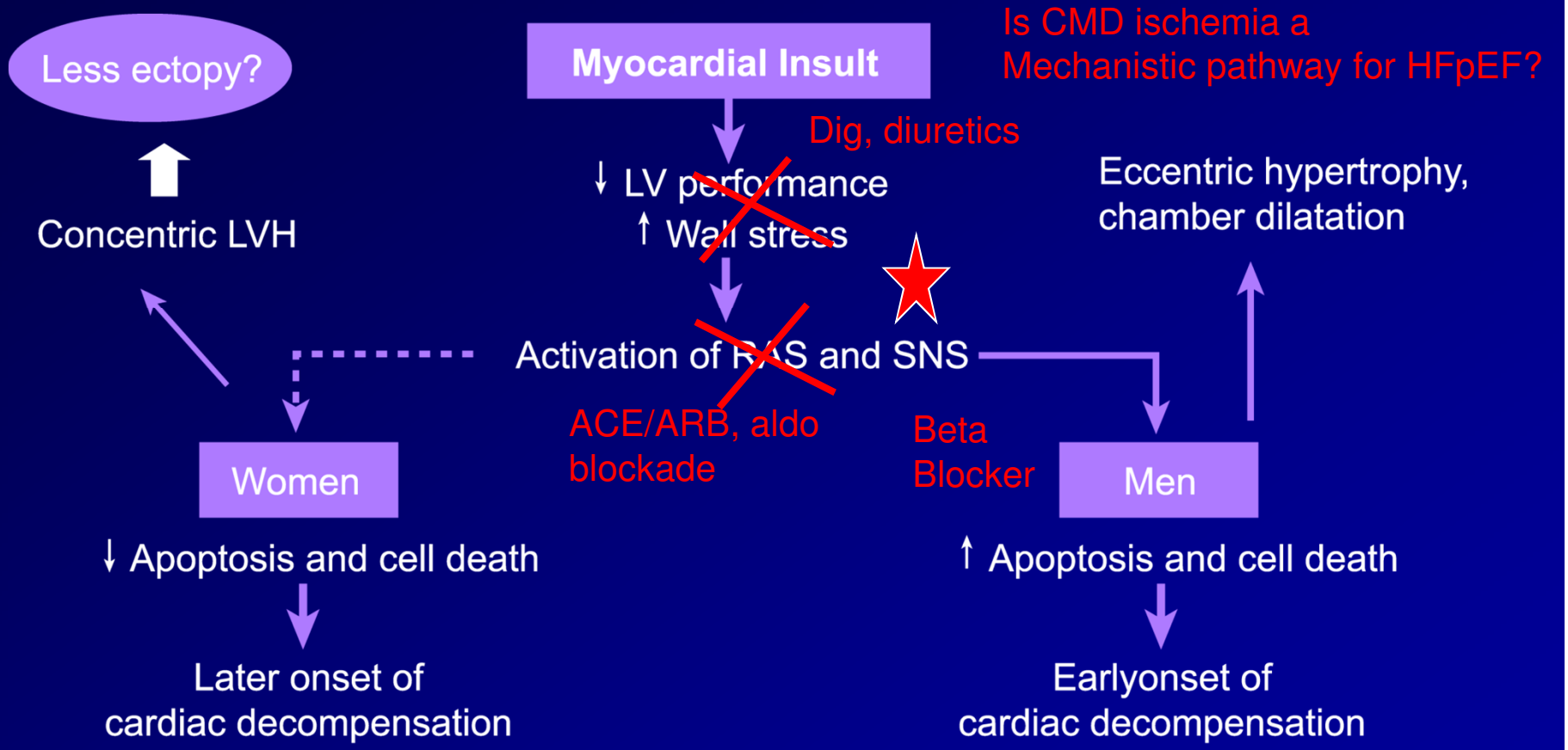
Underrepresentation of Women in Cardiovascular Clinical Trials

Remains low compared to disease prevalence and death rates - Perseverates knowledge gaps which adversely impact women



Melloni, et al, Circ Cardiovasc Qual Outcomes 2010

Gender-Related HFpEF Mechanisms

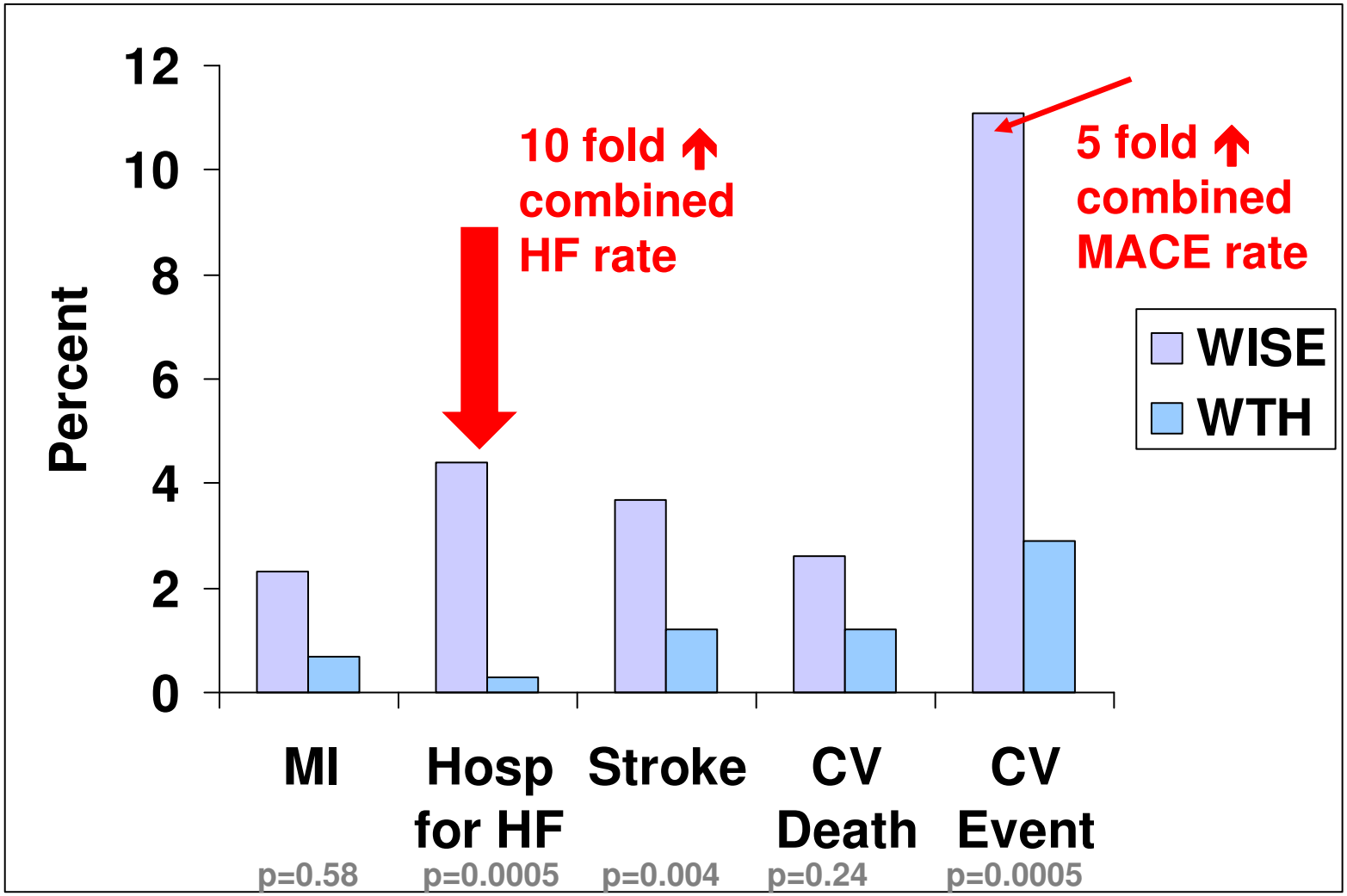


Possible pathophysiologic mechanisms

LVH = left ventricular hypertrophy; RAS = renin-angiotensin system; SNS = sympathetic nervous system.

Jessup M et al. *J Thorac Cardiovasc Surg*. 2004;127:1247-1252.

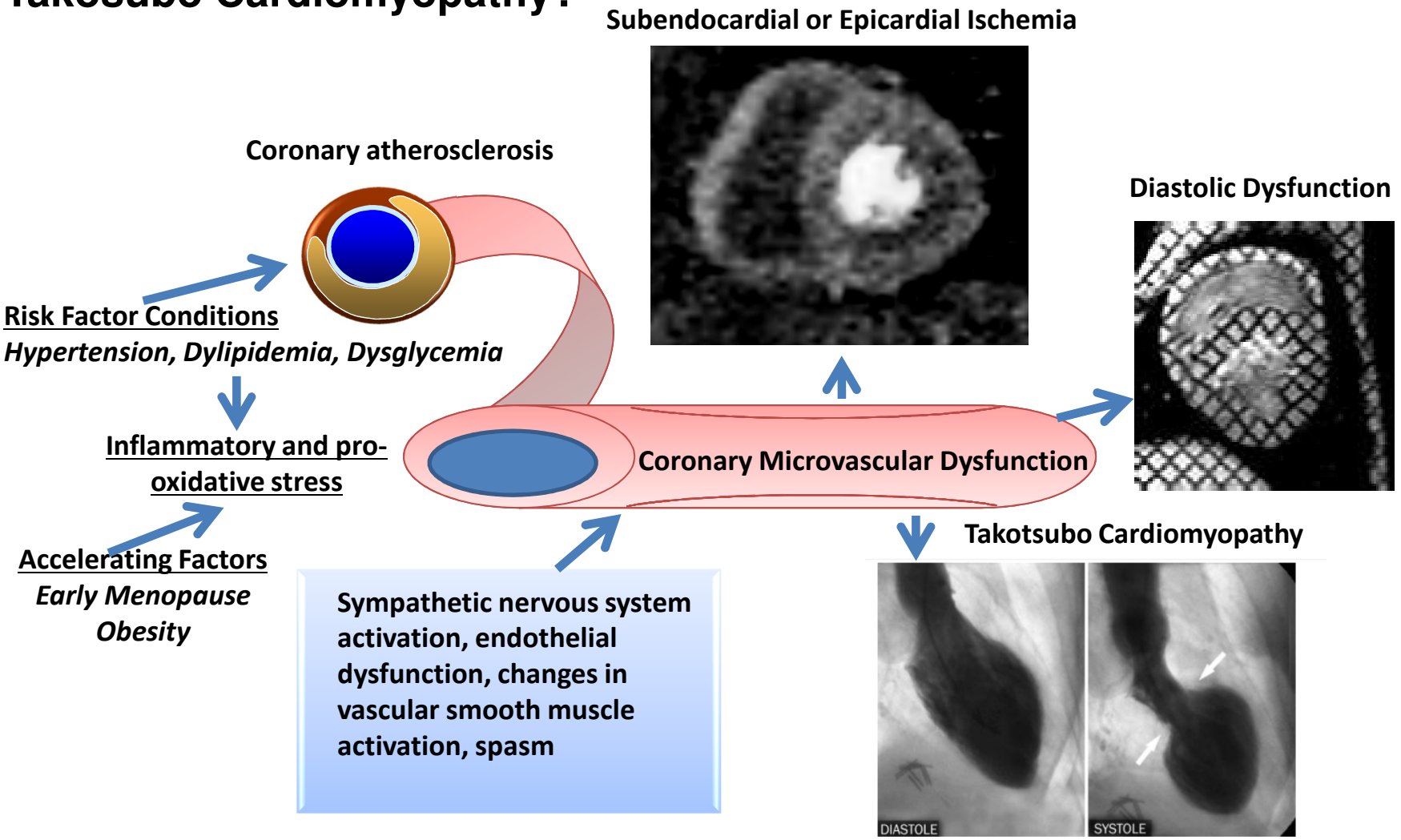
WISE Patients with and without documented ischemia have elevated MACE compared to asymptomatic Women Take Heart (WTH) with no ischemia by Stress Testing



All comparisons adjusted for age, race, BMI, history of hypertension, diabetes, education, employment, family history of CAD, menopausal status, smoking history and metabolic syndrome.

Gulati et al Arch Int Med 2010

Scheme of the potential causes and consequences of coronary microvascular dysfunction – Ischemia, Diastolic Dysfunction and Takosubo Cardiomyopathy?



Crea, Camici, Bairey Merz EHJ 12/13

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?

Conclusions - HFpEF

- HFpEF has become the dominant form of HF and accounts for the majority of HF hospitalization
- HFpEF occurs dominantly in older women
- HFrEF is well understood and effective treatment available in stark contrast to HFpEF which is NOT UNDERSTOOD and a TREATMENT DESERT!
- “Custodial” HFpEF management involves diuretics and BBs and patients remain limited
- Phenotype characterization, mechanistic factors, and intervention trials (stem cells, anti-fibrosis, anti-inflammatory) for HFpEF needed
- Would mandatory female-only studies help?