

Preventing **Heart Failure in Diabetics** via Contemporary  
Glucose-Lowering  
Pharmacotherapies

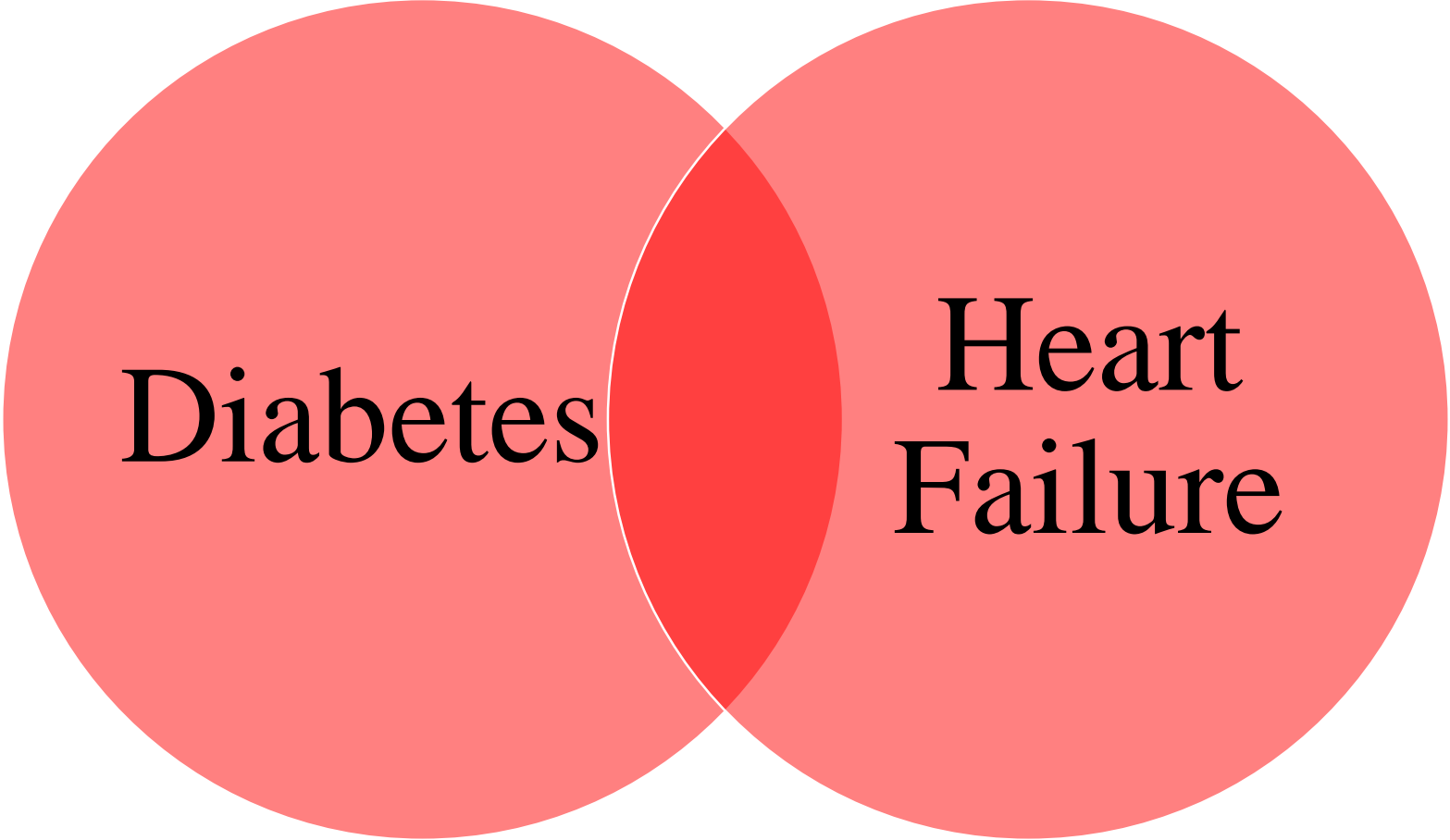
*Aditya Mandawat, MD, FACC*

# Disclosures

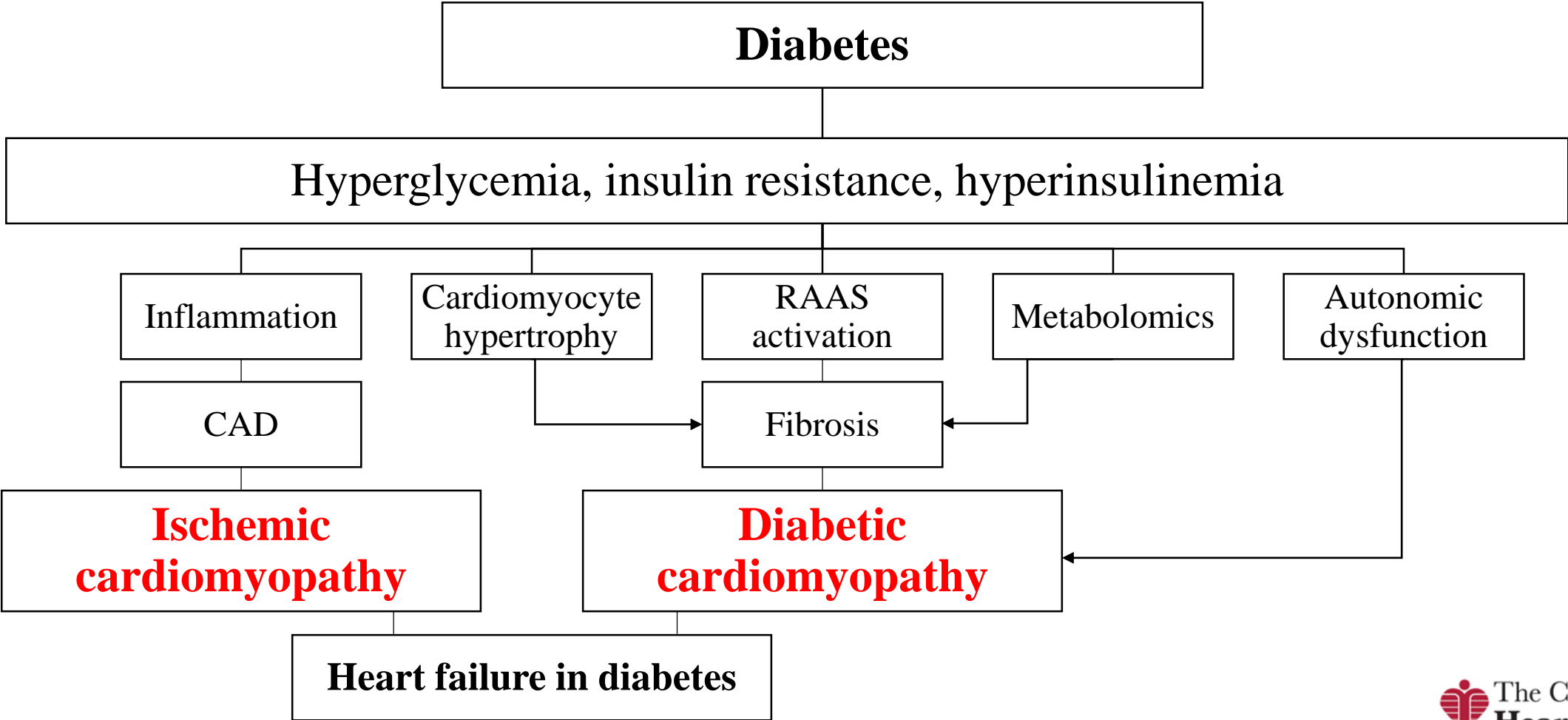
- None

# Objectives

- Describe the **epidemiology** of heart failure and diabetes
- Describe the **risks and benefits** of contemporary glucose-lowering pharmacotherapies in patients with diabetes and heart failure.



# Pathophysiology of heart failure in diabetes



# DM & HF = Poor Outcomes



# Anti-glycemics in DM & HF

Biguanides

Sulfonylureas

Thiazolidinediones

Insulin

GLP-1 agonists

DDP-4 inhibitors

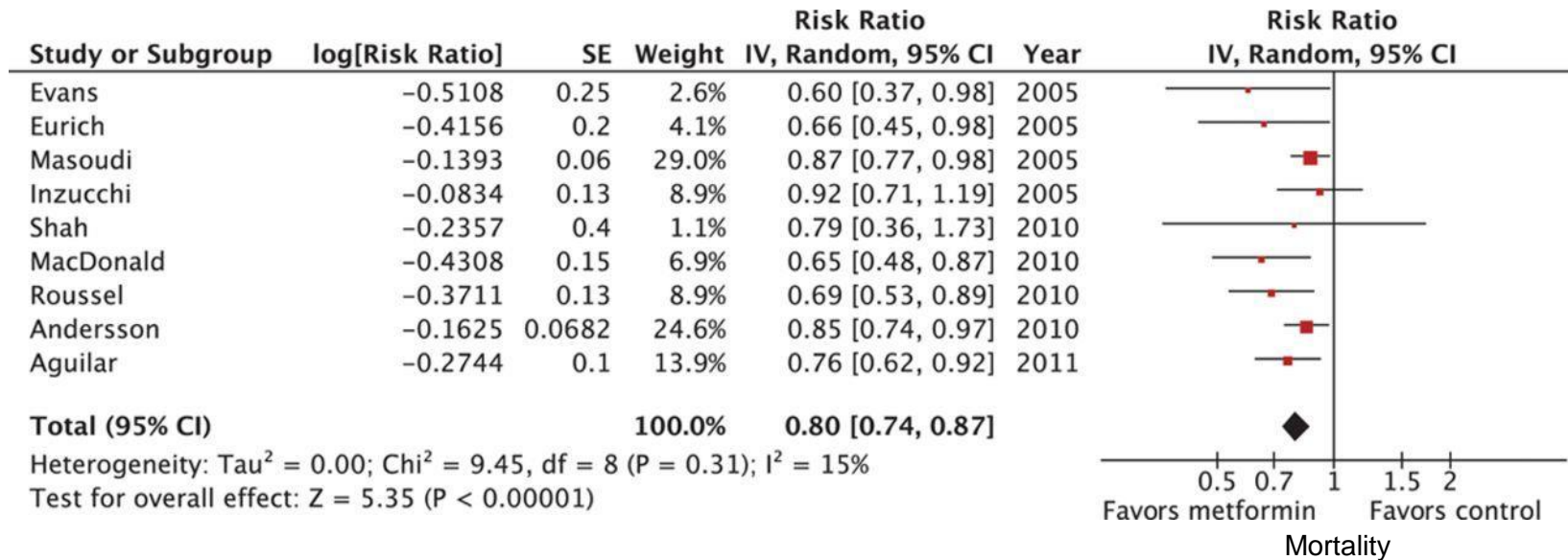
SGLT-2 inhibitors

# Anti-glycemics in DM & HF

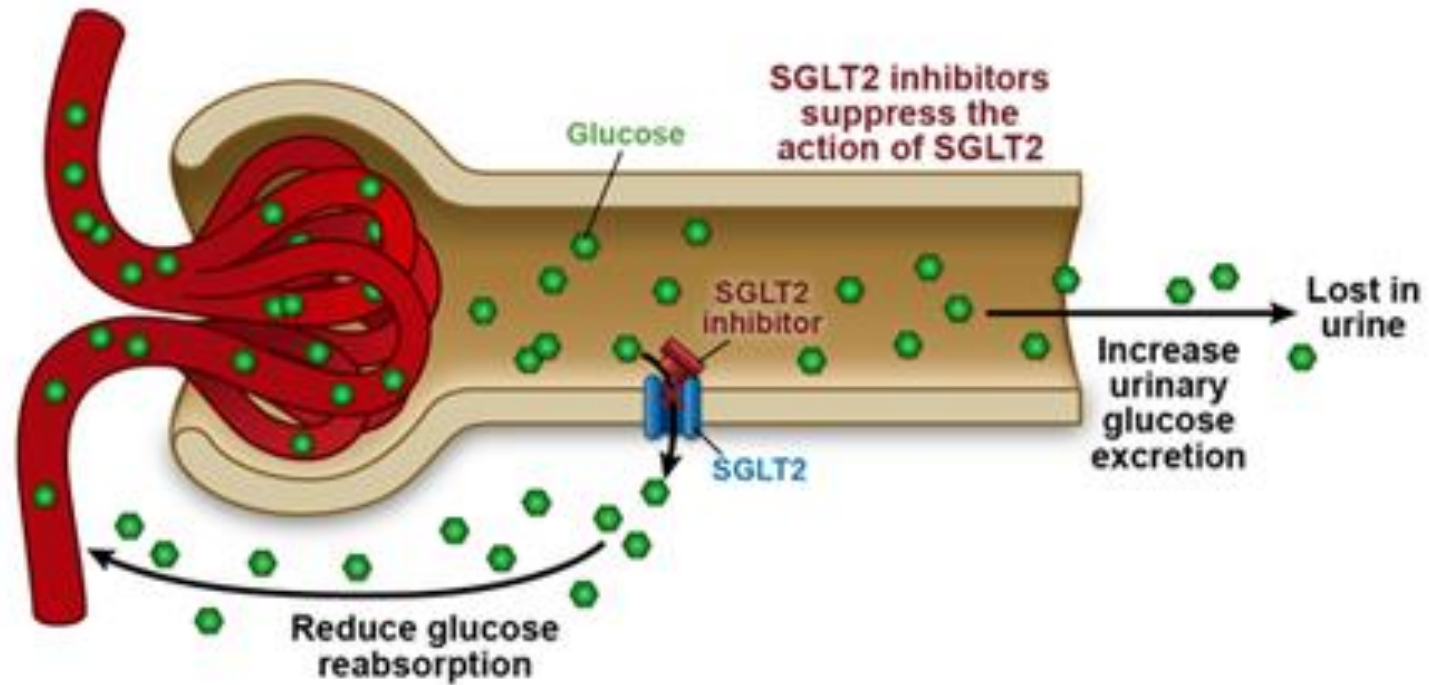




# Biguanides remain the preferred initial anti-glycemic therapy in HF



# SGLT-2 inhibitors



# SLT-2 inhibitors - Early trials hinted at ↓ HF hospitalizations

- Secondary endpoint
- Majority of patients (~85%) did not have HF

• EMPA-REG	NNT 71
• CANVAS	NNT 32
• DECLARE-TIMI-58	NNT 125



RENEW TODAY →



## REVIEW ARTICLE

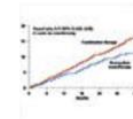
Anemia of Inflammation

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## PERSPECTIVE

Why Is a Cow? Curiosity,  
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Why

## ORIGINAL ARTICLE

Antithrombotic Therapy for  
Atrial Fibrillation with Stable  
Coronary Disease

## ORIGINAL ARTICLE

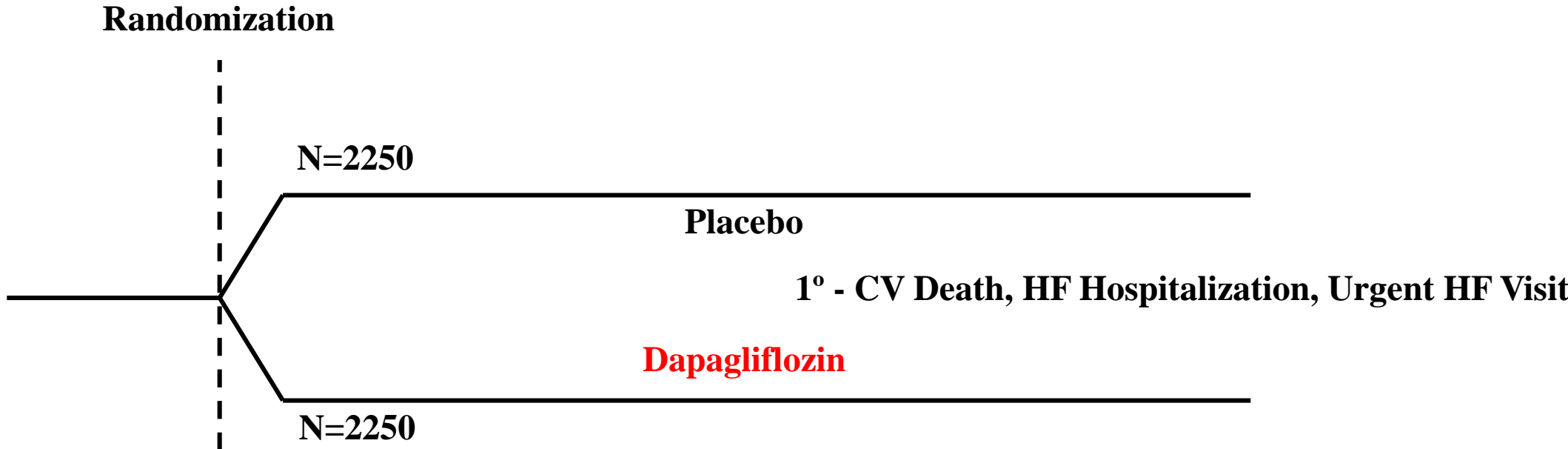
Polypill for Cardiovascular  
Disease Prevention in an  
Underserved Population

## ORIGINAL ARTICLE

# Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction

John J.V. McMurray, M.D., Scott D. Solomon, M.D., Silvio E. Inzucchi, M.D., Lars Køber, M.D., D.M.Sc., Mikhail N. Kosiborod, M.D., Felipe A. Martinez, M.D., Piotr Ponikowski, M.D., Ph.D., Marc S. Sabatine, M.D., M.P.H., Inder S. Anand, M.D., Jan Bělohávek, M.D., Ph.D., Michael Böhm, M.D., Ph.D., Chern-En Chiang, M.D., Ph.D., *et al.*, for the DAPA-HF Trial Committees and Investigators\*

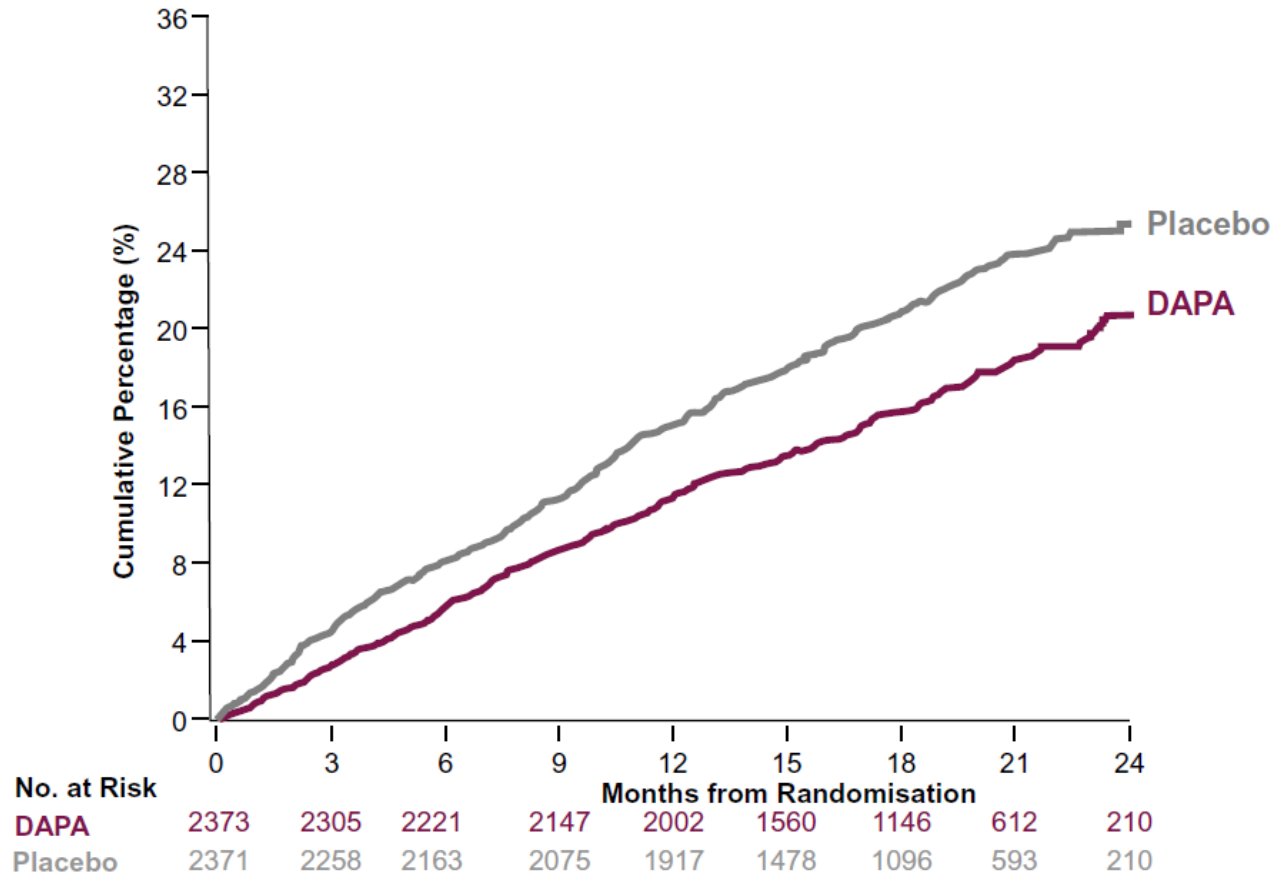
# DAPA-HF



# DAPA-HF I/E Criteria

- **LVEF  $\leq 40\%$**
- **NYHA II-III**
- **GDMT**
- **↑ NTproBNP**
- **SBP  $< 95$  or symptomatic hypotension**
- **eGFR  $< 30$**

# Dapagliflozin ↓ MACE



- 26% RR,  $p < 0.001$
- **NNT = 21**

# Dapagliflozin ↓ Mortality & HF Hospitalizations

- ↓ 2.3% all cause mortality NNT 43
- ↓ 3.7% HF hospitalizations NNT 27
- Improved QoL (KCCQ-12) NNT 14



Subgroup	Dapagliflozin	Placebo	Hazard Ratio (95% CI)	
	(N=2373)	(N=2371)		
	no. of patients/total no.			
All patients	386/2373	502/2371		0.74 (0.65–0.85)
Age				
≤65 yr	162/1032	196/998		0.78 (0.63–0.96)
>65 yr	224/1341	306/1373		0.72 (0.60–0.85)
Sex				
Male	307/1809	406/1826		0.73 (0.63–0.85)
Female	79/564	96/545		0.79 (0.59–1.06)
Race				
White	275/1662	348/1671		0.78 (0.66–0.91)
Black	26/122	32/104		0.62 (0.37–1.04)
Asian	78/552	118/564		0.64 (0.48–0.86)
Other	7/37	4/32		
Geographic region				
Asia	77/543	114/553		0.65 (0.49–0.87)
Europe	193/1094	218/1060		0.84 (0.69–1.01)
North America	54/335	73/342		0.73 (0.51–1.03)
South America	62/401	97/416		0.64 (0.47–0.88)
NYHA class				
II	190/1606	289/1597		0.63 (0.52–0.75)
III or IV	196/767	213/774		0.90 (0.74–1.09)
LVEF				
≤Median	222/1230	307/1239		0.70 (0.59–0.84)
>Median	164/1143	195/1132		0.81 (0.65–0.99)
NT-proBNP				
≤Median	100/1193	155/1179		0.63 (0.49–0.80)
>Median	286/1179	347/1191		0.79 (0.68–0.92)
Hospitalization for heart failure				
Yes	195/1124	279/1127		0.67 (0.56–0.80)
No	191/1249	223/1244		0.84 (0.69–1.01)
MRA at baseline				
Yes	281/1696	361/1674		0.74 (0.63–0.87)
No	105/677	141/697		0.74 (0.57–0.95)
Type 2 diabetes at baseline				
Yes	215/1075	271/1064		0.75 (0.63–0.90)
No	171/1298	231/1307		0.73 (0.60–0.88)
Atrial fibrillation or flutter on enrollment ECG				
Yes	109/569	126/559		0.82 (0.63–1.06)

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# SGLT-2 inhibitor AEs and SAEs

- **\$\$\$ (\$325/month)**
- Genital candidiasis
- Euglycemic diabetic ketoacidosis
  
- Lower limb amputation and fractures (Canagliflozin only)

# Upcoming trials

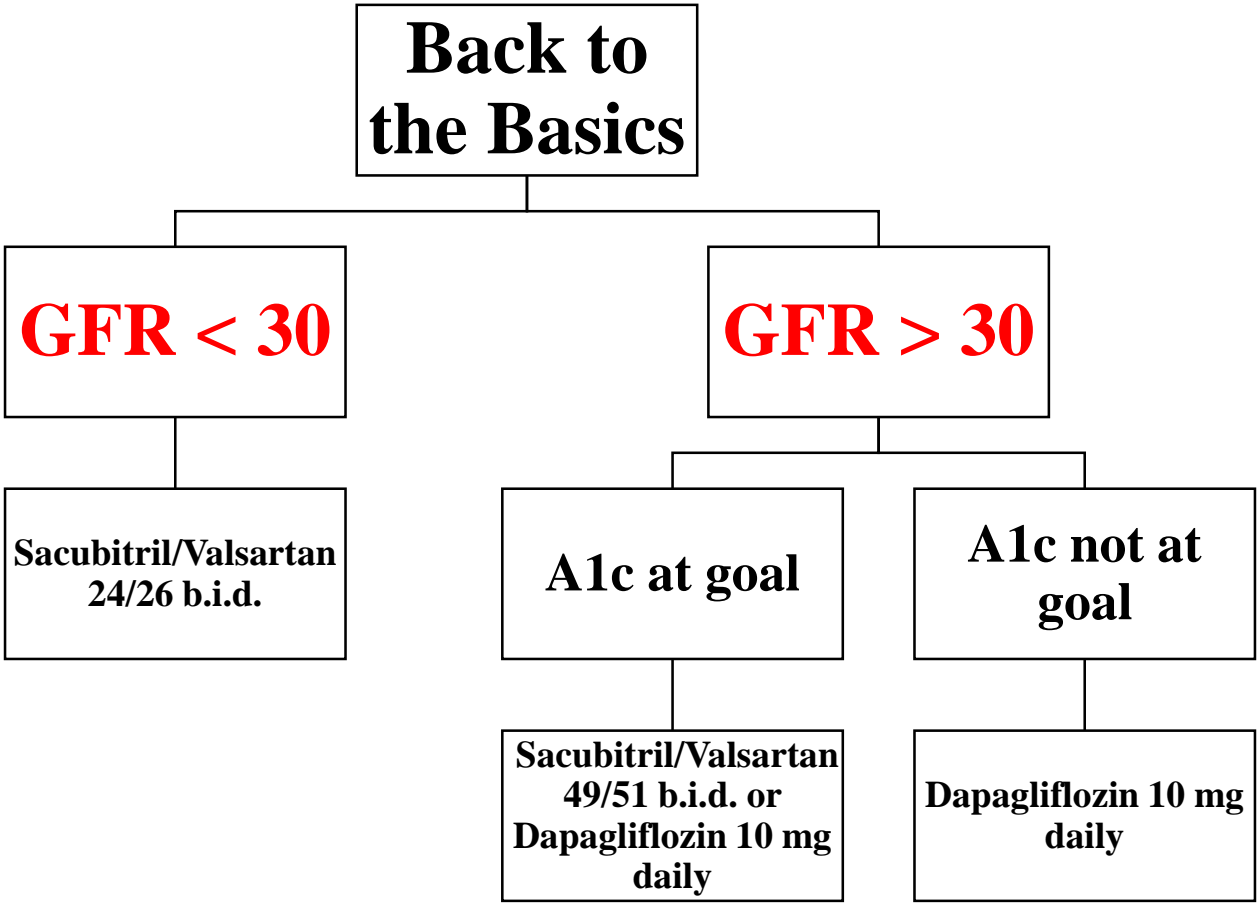
- Reduced ejection fraction
  - Empagliflozin (EMPEROR-Reduced, EMPERIAL-Reduced)
  - Sotagliflozin (WHO)
- Preserved ejection fraction
  - Dapagliflozin (DELIVER)
  - Empagliflozin (EMPEROR-Preserved, EMPERIAL-Preserved)

# Management of HF

- Sodium and fluid restriction
- Goal-directed medical therapy
  - Beta-blockers, ACE/ARB, aldosterone antagonists
- Diuretics
- Cardiac rehabilitation
- Cardiac resynchronization therapy

BACK TO BASICS

# Management of HF & DM



# Questions?

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- 706-589-4086 (cell)

# References

1. Dunlay SM, Givertz MM, Aguilar D et al. Type 2 Diabetes Mellitus and Heart Failure: A Scientific Statement From the American Heart Association and the Heart Failure Society of America: This statement does not represent an update of the 2017 ACC/AHA/HFSA heart failure guideline update. *Circulation* 2019;140:e294-e324.
2. Kramer CK, Ye C, Campbell S, Retnakaran R. Comparison of new glucose-lowering drugs on risk of heart failure in type 2 diabetes: a network meta-analysis. *JACC: Heart Failure* 2018;6:823-830.
3. McMurray JJV, Solomon SD, Inzucchi SE et al. Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction. *New England Journal of Medicine* 2019;381:1995-2008.