

# **DIABETES AND CARDIOVASCULAR DISEASE: *DATA YOU SHOULD KNOW BY HEART***

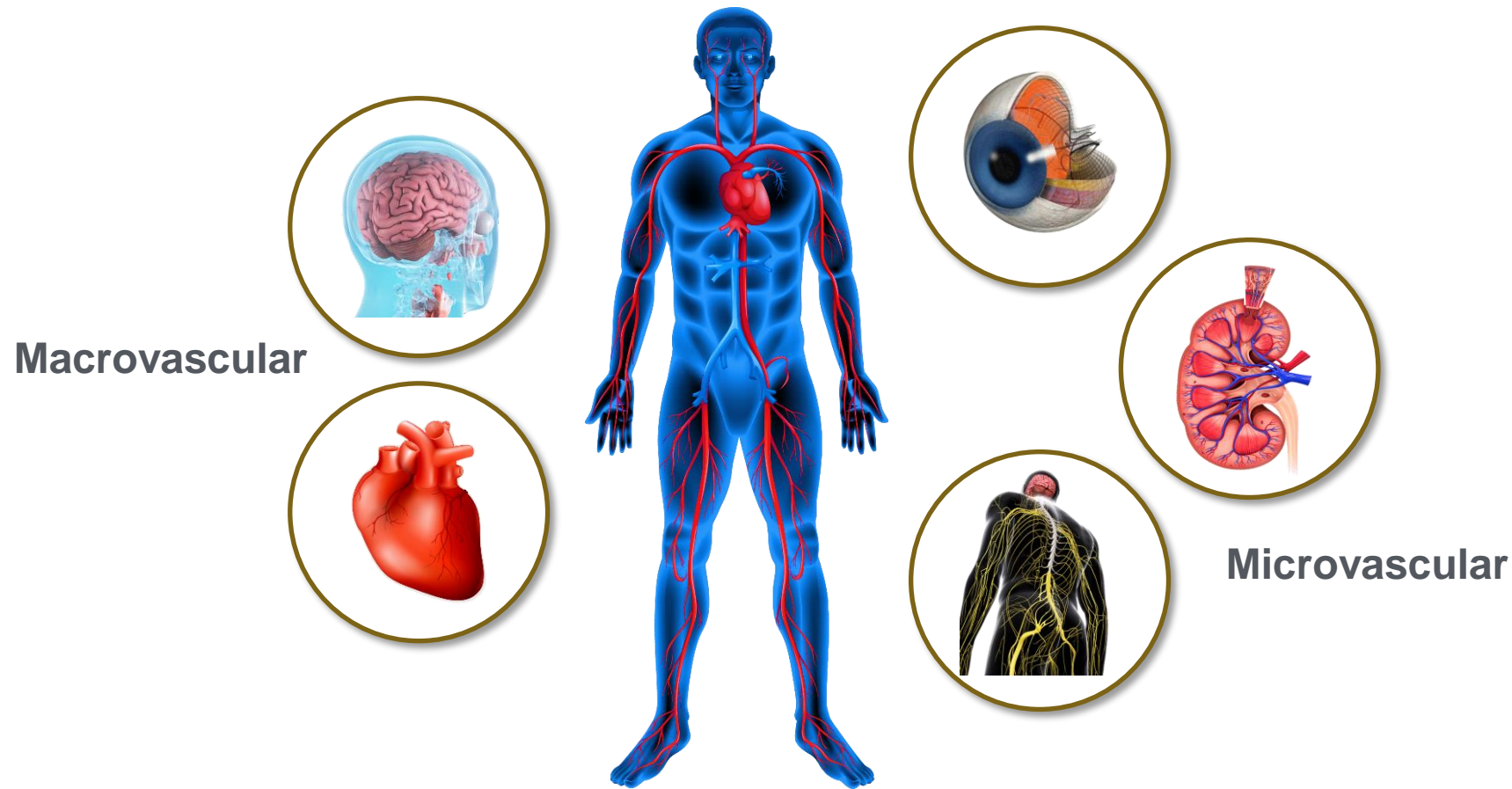
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# SPEAKER DISCLOSURES

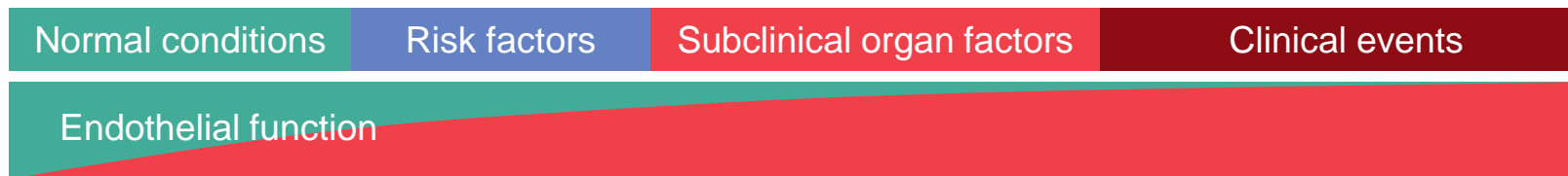
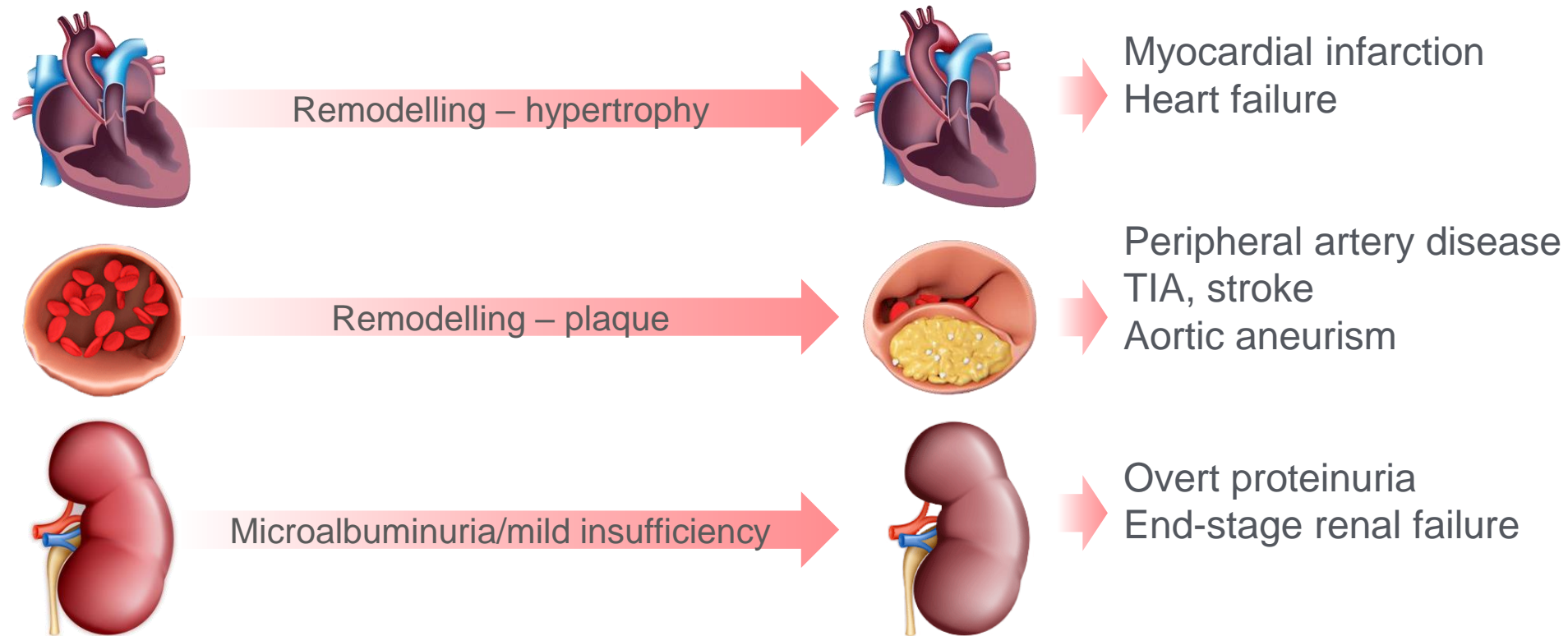
Research support from Bayer, Kestra, Eli Lilly, Sanofi.

Consulting/Advisory Board for Janssen, Bayer, Kestra, Sana.

# T2D: INDEPENDENT RISK FACTOR FOR MICROVASCULAR AND MACROVASCULAR COMPLICATIONS

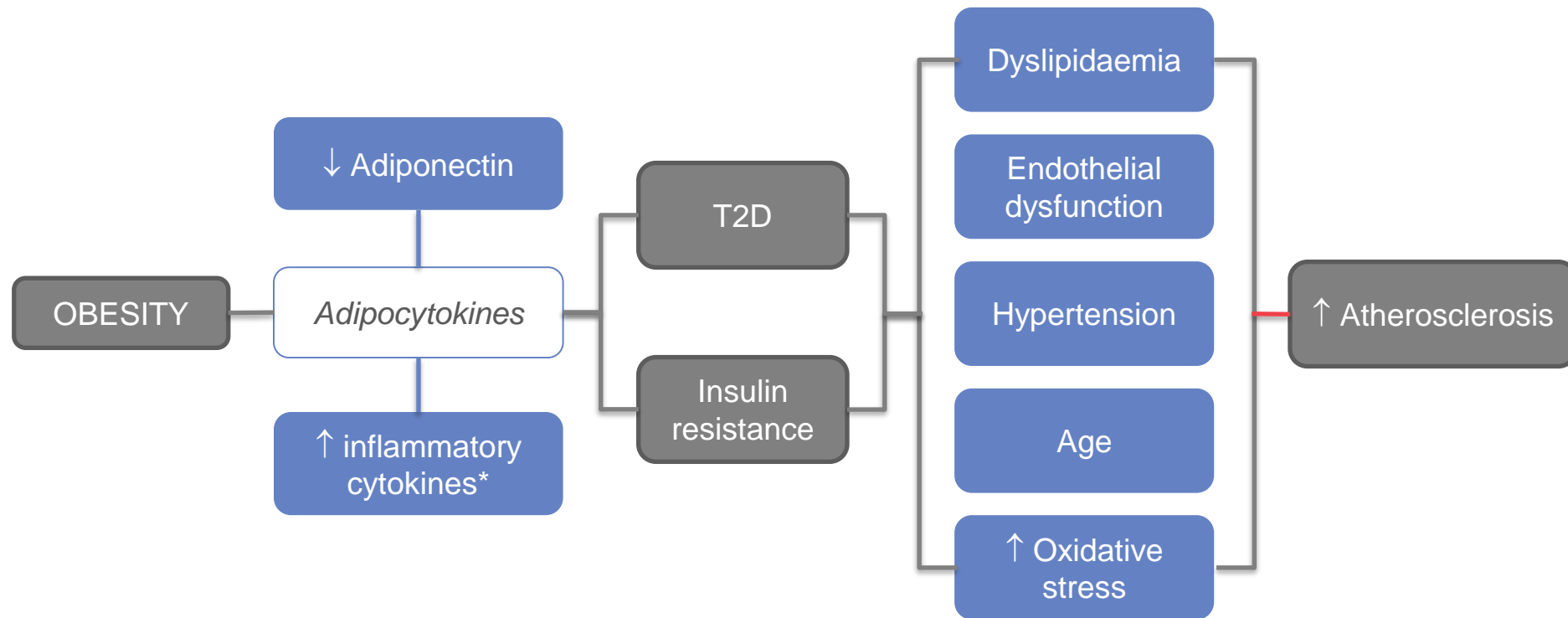


# ENDOTHELIAL DYSFUNCTION COMMON TO MICROVASCULAR AND MACROVASCULAR EVENTS



# VISCERAL ADIPOSITY AND ATHEROSCLEROSIS

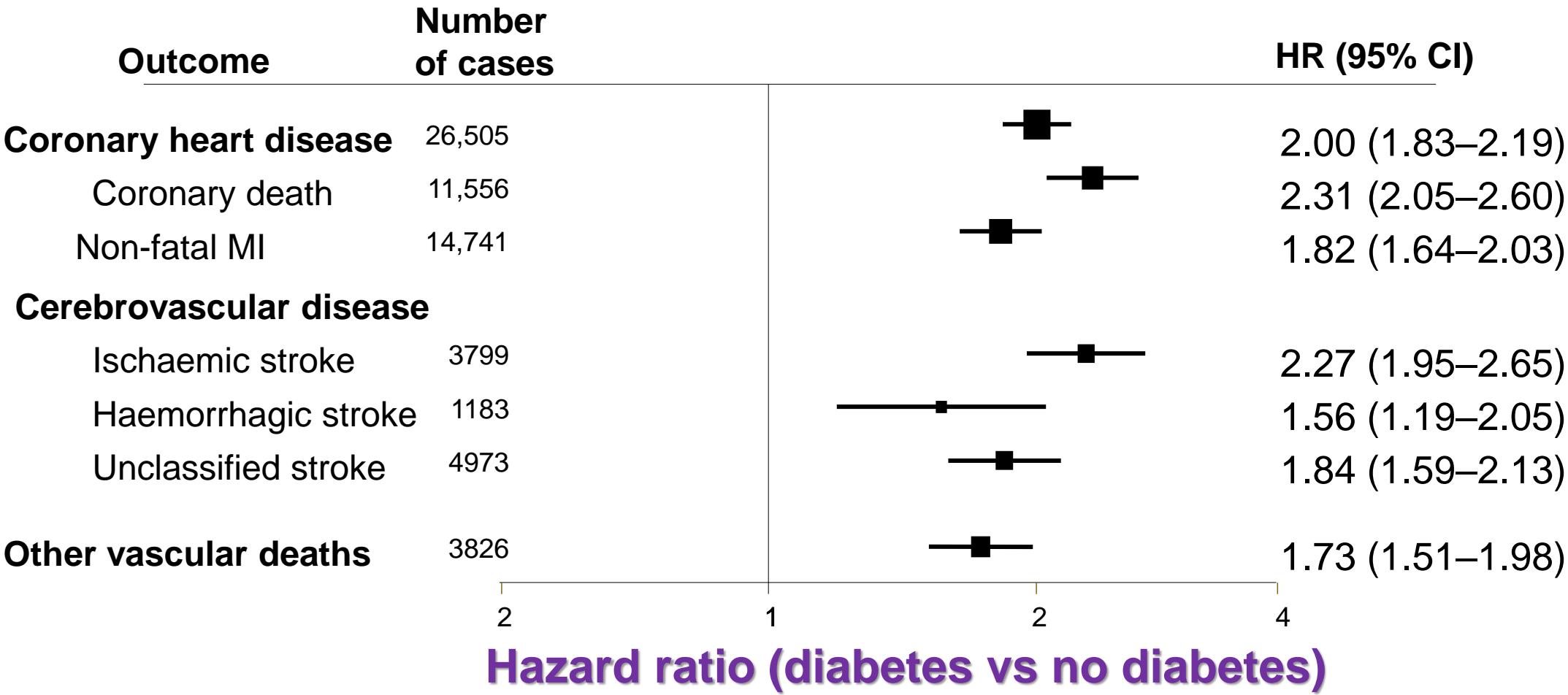
Interactions are complex, inter-related and not necessarily causal



\*including: TNF $\alpha$ , IL-6, resistin, PAI-1, angiotensinogen

*Lau et al. Am J Physiol Heart Circ Physiol 2005;288:H2031–41.*

# DIABETES DOUBLES THE RISK OF VASCULAR EVENTS



# CARDIOVASCULAR RISK FACTORS WITH EXISTING ATHEROSCLEROTIC DISEASE: THE REACH REGISTRY

**Table 2.** Multivariable Predictors of Cardiovascular Death, Myocardial Infarction, or Stroke From the Cox Regression Model

Variable	HR (95% CI)	Estimate	P Value
Polyvascular disease vs risk factors only	1.99 (1.78-2.24)	0.69	<.001
Congestive heart failure, yes vs no	1.71 (1.60-1.83)	0.54	<.001
Ischemic event $\leq 1$ y vs no ischemic event	1.71 (1.57-1.85)	0.53	<.001
History of diabetes, yes vs no	1.44 (1.36-1.53)	0.37	<.001
Ischemic event $> 1$ y vs no ischemic event	1.41 (1.32-1.51)	0.34	<.001
Single vascular territory disease vs risk factors only	1.39 (1.25-1.54)	0.33	<.001
Atrial fibrillation/flutter, yes vs no	1.28 (1.18-1.38)	0.25	<.001
Sex, male vs female	1.14 (1.07-1.21)	0.13	<.001
Age, per 1-year increase	1.04 (1.03-1.04)	0.03	<.001
Aspirin, yes vs no	0.93 (0.87-0.98)	-0.08	.01
Statins, yes vs no	0.73 (0.69-0.77)	-0.31	<.001
Japan vs other regions <sup>b</sup>	0.70 (0.63-0.77)	-0.36	<.001

Abbreviations: CI, confidence interval; HR, hazard ratio.

<sup>a</sup>Calculated as weight in kilograms divided by height in meters squared.

<sup>b</sup>Other regions were North America, Latin America, Western Europe, and Asia.

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# INTERHEART:

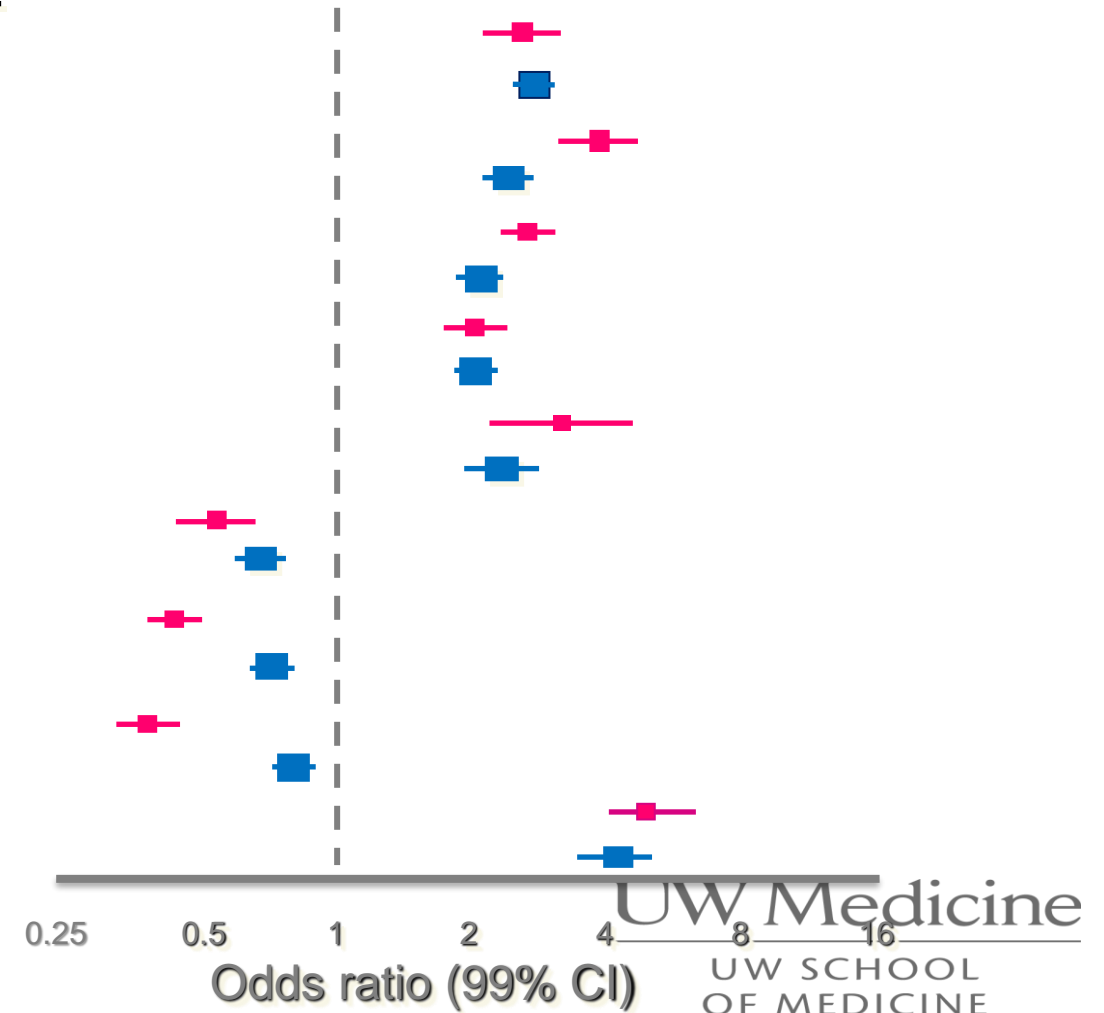
## Association Of Risk Factors With Acute MI In Women And Men

N=27,098

**\*80% of AMI\***

**9 Risk Factors:**  
*Accounts for  
90% of all  
AMI*

Risk factor	Gender
Current smoking	F
	M
Diabetes	F
	M
Hypertension	F
	M
Abdominal obesity	F
	M
Psychosocial index	F
	M
Fruits/Vegetables	F
	M
Exercise	F
	M
Alcohol	F
	M
ApoB-ApoA1 ratio (~LDL/HDL)	F
	M



Adjusted for age, sex, geographic region  
Note: odds ratio plotted on a doubling scale



# AUDIENCE QUESTION:

Which is the correct statement about preventative atherosclerotic therapies?

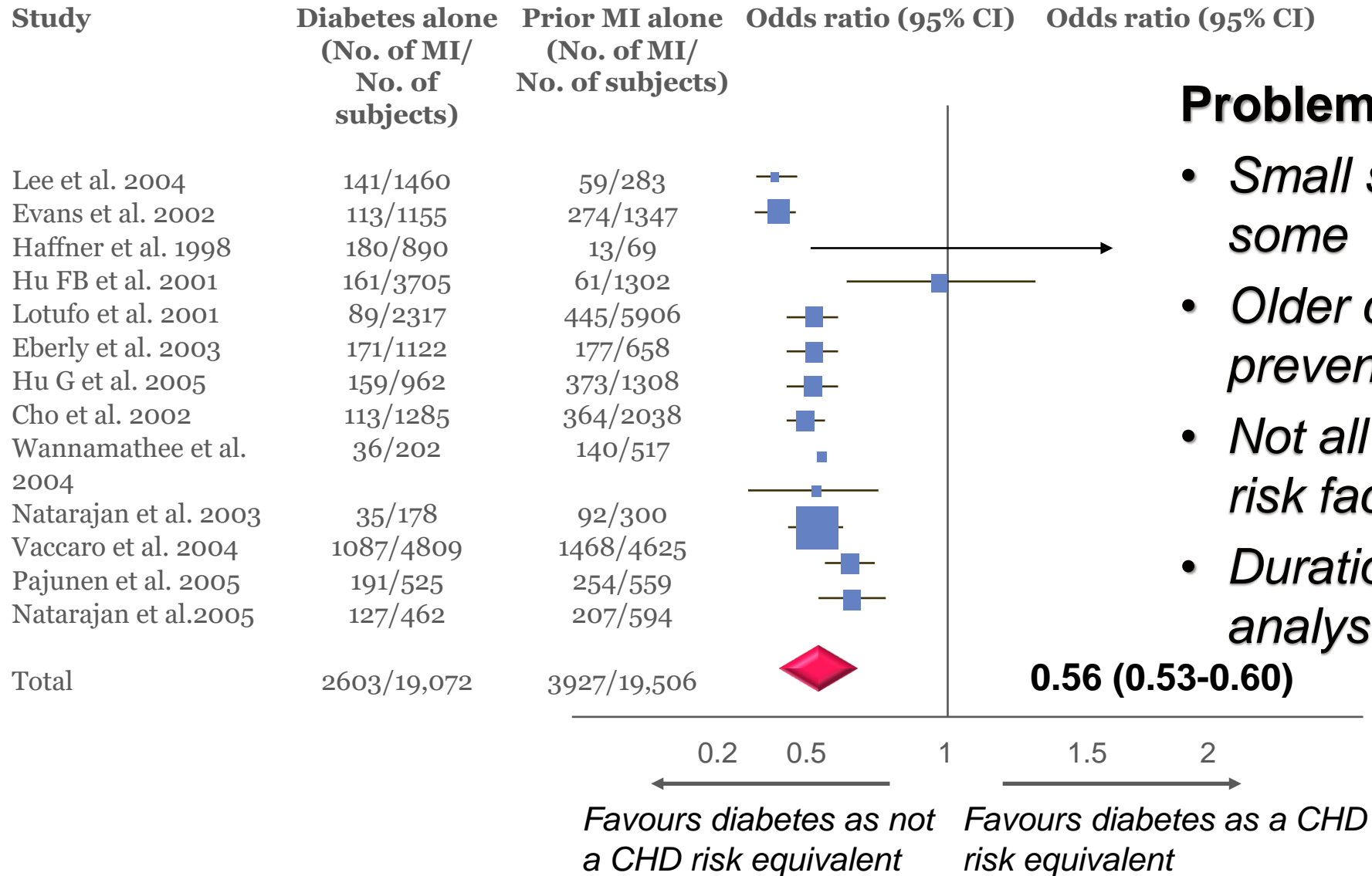
- A. All patients with diabetes should start secondary prevention treatment because DM is a coronary artery disease equivalent.
- B. Risk scores (e.g., ASCVD) are needed to accurately risk stratify prior to any therapy.
- C. Further cardiovascular stress testing is required in patients with new onset diabetes.
- D. I will refer my patient to a cardiologist if the pituitary is OK

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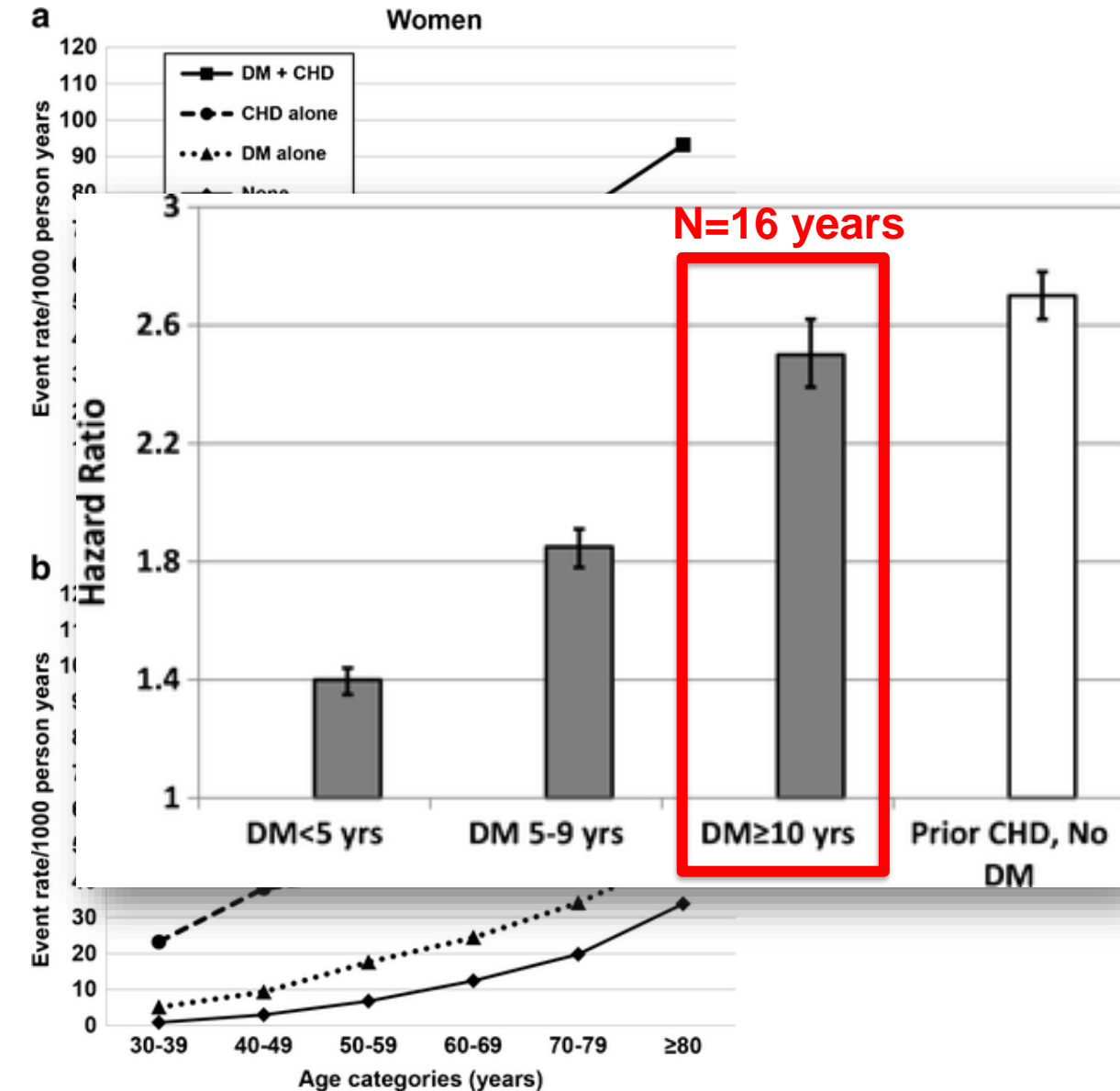
# DOES DM = MI RISK? META-ANALYSIS



## Problems with Analyses:

- *Small sample sizes for some*
- *Older cohorts (less primary prevention)*
- *Not all adjusted for other risk factors/confounders*
- *Duration of DM not in all analyses*

# DM, CORONARY HEART DISEASE (CHD) AND CV RISK: CONTEMPORARY DATA



Kaiser Permanente

( $N=1,586,061$ , 30-90 years old)

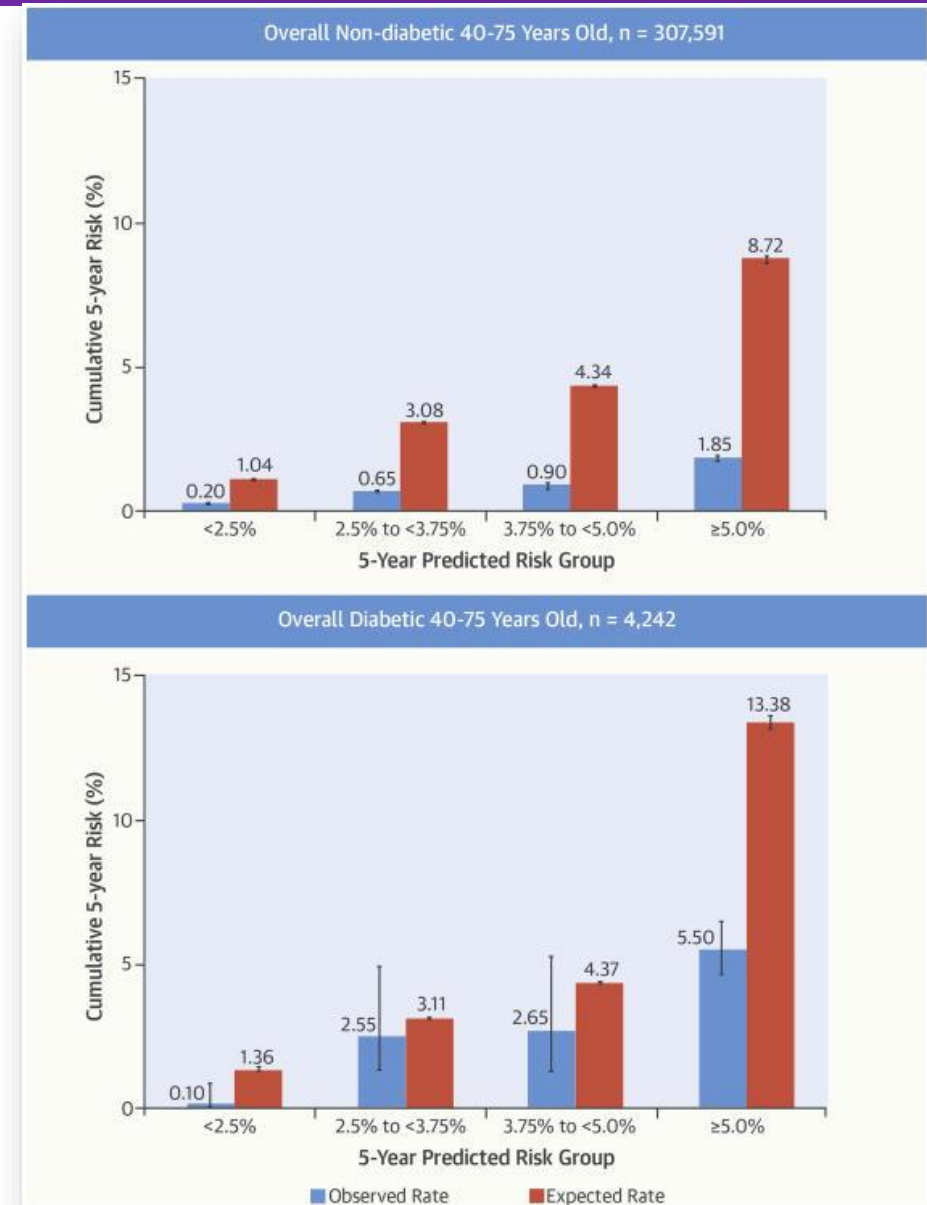
- 80,012 CV events
- Adjusted hazard ratios for CV event:
  - *Diabetes* 1.7 (95% CI 1.66-1.74)
  - *CHD* 2.8 (95% CI 2.7-2.85)
  - *DM+CHD* 3.9 (95% CI 3.8-4.0)

## Conclusions:

- **Diabetes alone is less risky than CHD**
- **Diabetes >10 years = CHD risk**
- **Combination of CHD and DM confer additive risk**

# HOW WELL DOES THE ASCVD CALCULATOR WORK FOR DM?

- If DM is present, ~ 65% risk increase in Pooled Risk equation
- ASCVD slightly overestimates risk in DM
  - Worse discrimination in non-DM



# INTERHEART:

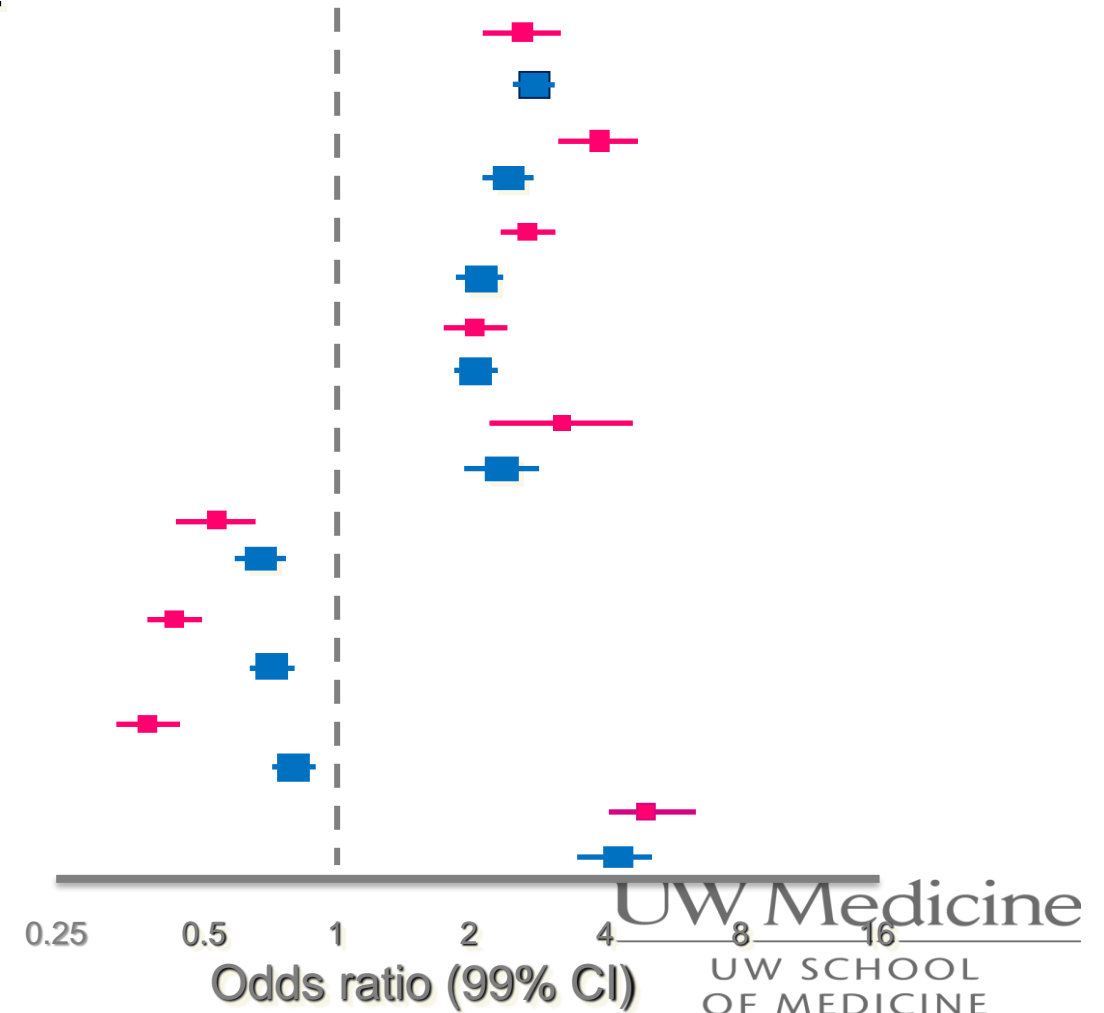
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**\*80% of AMI\***

**9 Risk Factors:**  
*Accounts for  
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Risk factor	Gender
Current smoking	F
	M
Diabetes	F
	M
Hypertension	F
	M
Abdominal obesity	F
	M
Psychosocial index	F
	M
Fruits/Vegetables	F
	M
Exercise	F
	M
Alcohol	F
	M
ApoB-ApoA1 ratio (~LDL/HDL)	F
	M



Adjusted for age, sex, geographic region  
Note: odds ratio plotted on a doubling scale



# GUIDELINES FOR DM AND PRIMARY PREVENTION

## AHA/ACC Primary Prevention - 2019

T2DM and age 40-75 years:

### STATIN

- Moderate-intensity statin (*Class I*)
  - Risk estimate for high-intensity statin
    - ≥10 years for T2DM, >20 years T1DM,
    - ≥30 mcg albumin/mg creatinine
    - eGFR <60 ml/min/1.73 m<sup>2</sup>
    - Retinopathy
    - Neuropathy
    - ABI <0.9
- **Goals:** >50% lowering with higher risk (*Class IIa*)

### ASPIRIN

- Low dose aspirin only with high risk (>20% over 10 years)

## ESC CVD Prevention - 2019

Any DM and age > 40 years:

### STATIN

- Very High Risk (*Class I*)
  - DM with end-organ damage (proteinuria, eGFR < 30, LVH, retinopathy) or >3 major risk factor (smoking, significant lipids or HTN)
  - **Goals:** LDL <55 or 50% decrease for LDL
- High Risk
  - DM>10 years or additional risk factors.
  - Exception: Young T1DM, no major risk factors
  - **Goals:** LDL <70 or 50% decrease for LDL 100-200

### ASPIRIN

- Aspirin is NOT recommended without CVD (*Class III*)



# LIPID MANAGEMENT: MAKE IT EASY

Rosuvastatin 20 or 40 mg daily

Atorvastatin 80 or 40 mg daily

The rest...

# LIPID MANAGEMENT

Not at goal?

- Rosuvastatin or atorvastatin
- Add ezetimibe or bempedoic acid

Low HDL?

- Rosuvastatin

Intolerance of statin (*less common than you think!*)

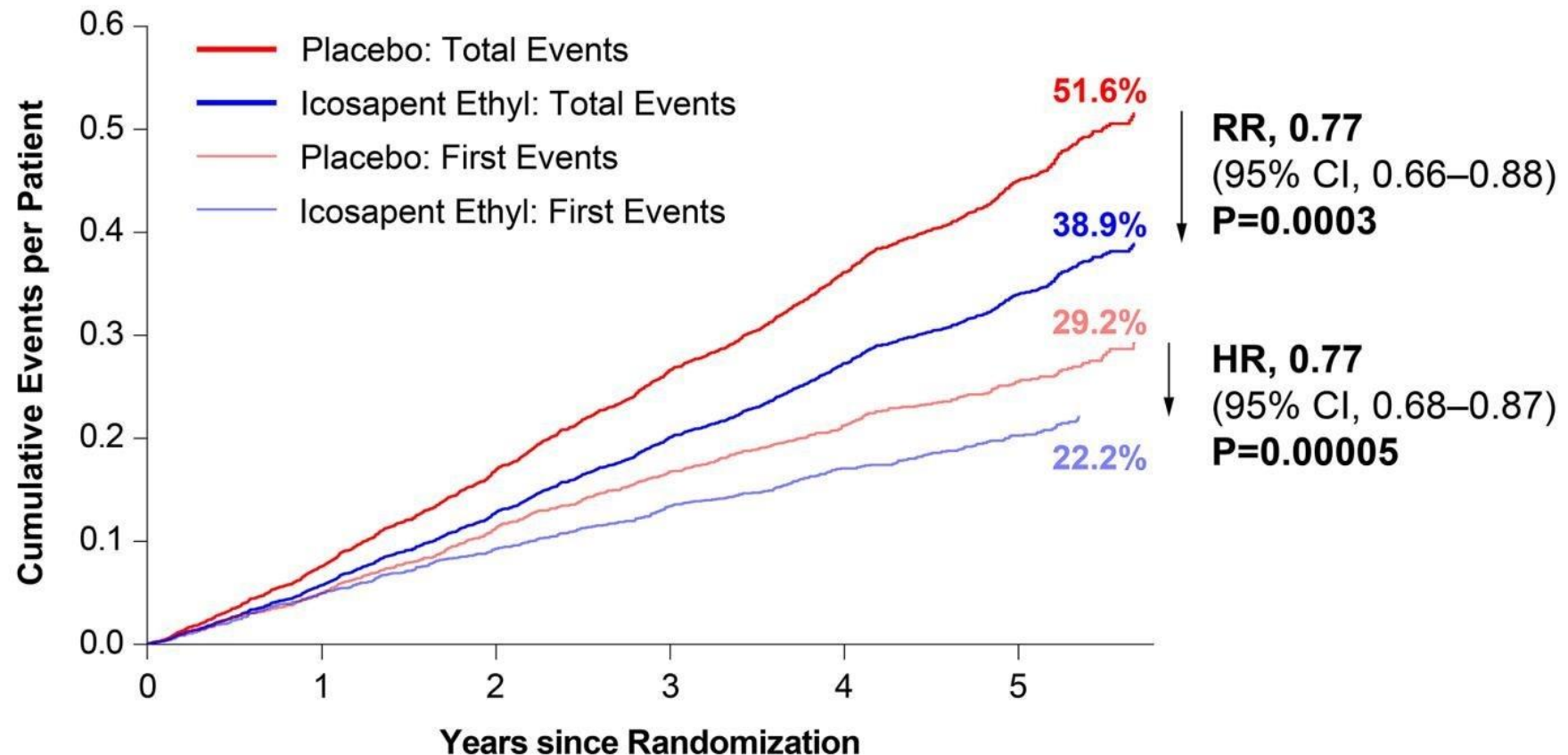
- ½ dose
- Ezetimibe + moderate intensity statin therapy
- PCSK9 if statin intolerant, inadequate LDL lowering

High triglyceride?

- Icosapent ethyl

# ICOSAPENT ETHYL IN PATIENTS WITH DIABETES: REDUCE-IT DIABETES

Primary Composite Endpoint

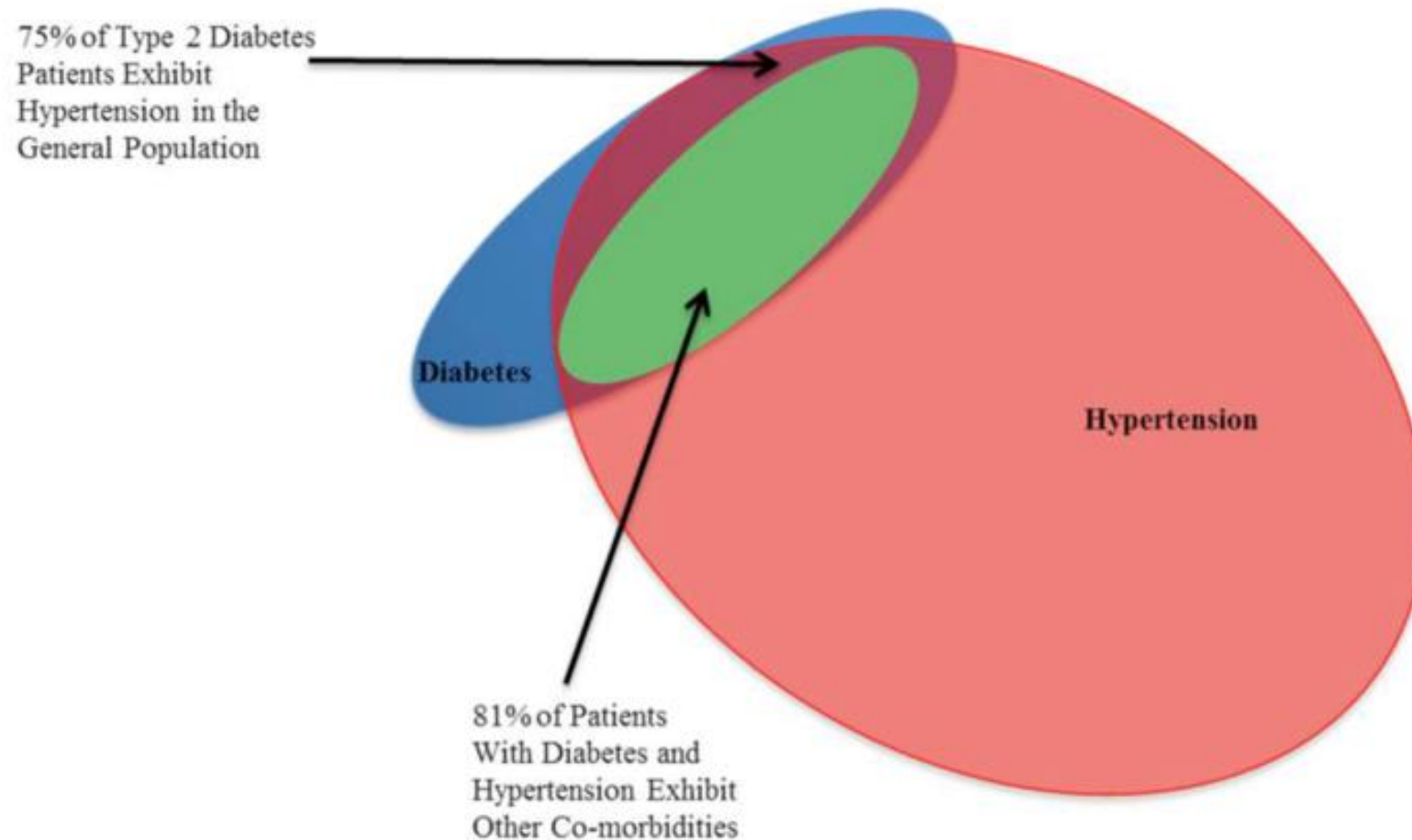


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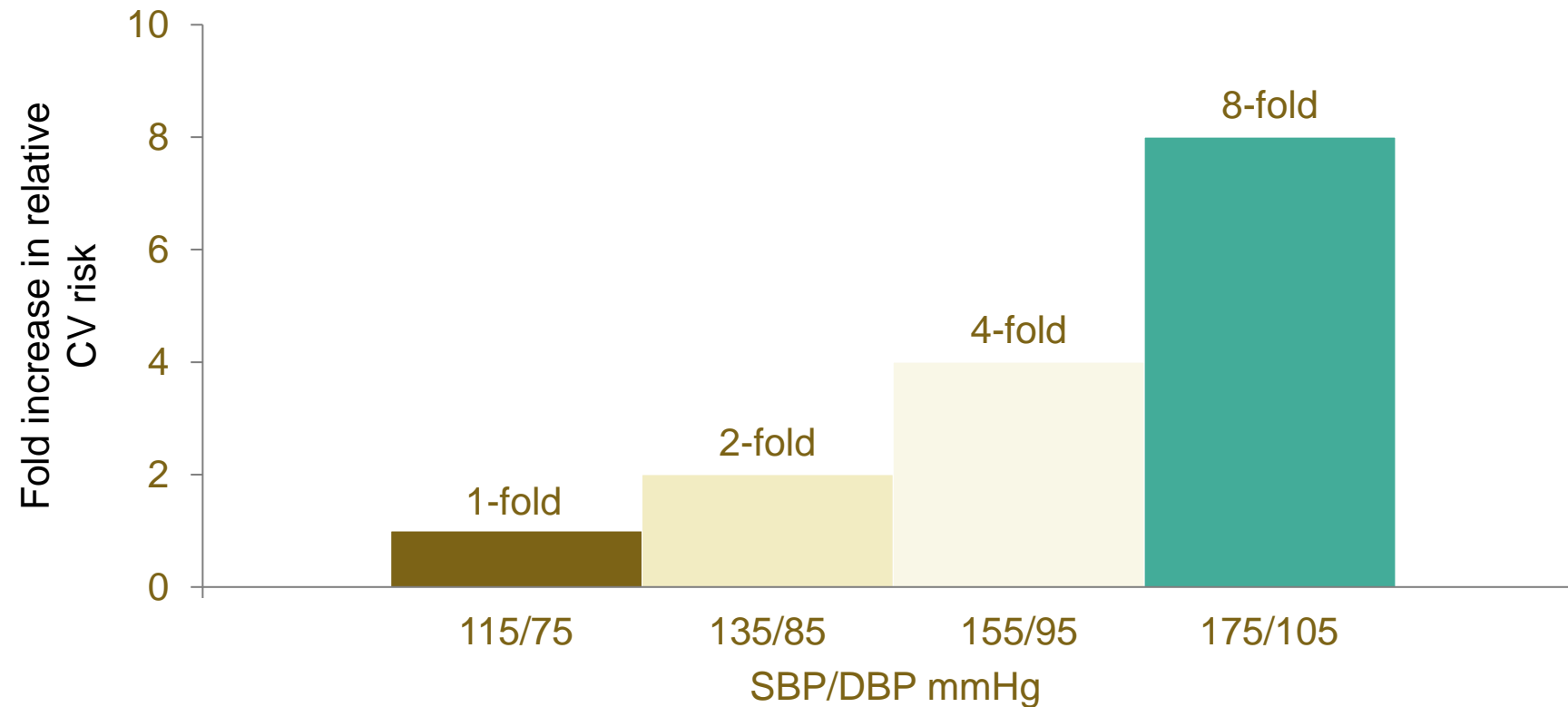
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# DM AND HYPERTENSION

Global Burden of Type 2 Diabetes and Hypertension (2014)



# HYPERTENSION: EACH 20/10 MMHG BP INCREASE DOUBLES THE RISK OF CV MORTALITY



Population of 1 million adults with no previous vascular disease recorded at baseline in 61 prospective observational studies of blood pressure and mortality

# ADA BLOOD PRESSURE RECOMMENDATIONS 2021

- Individuals with diabetes and **higher cardiovascular risk** — **existing ASCVD, 10-year ASCVD risk  $\geq 15\%$** 
  - **blood pressure target of  $<130/80$  mmHg, if safe**
- **Lower cardiovascular risk** = blood pressure target of  **$<140/90$  mm Hg**

# Antihypertensive Agents

## (Cheat Sheet)

Formulation	Minimum dose	Maximum dose	Remarks
Diuretics			
Chlorothiazide	250mg OD	500mg OD	• Potassium should be closely monitored.
Hydrochlorothiazide	25mg OD	200mg OD	
Amiloride/hydrochlorothiazide	1 tablet OD	4 tablet OD	• Used with care in patient with gout.
5mg/50mg			• Potassium sparing diuretics may cause hyperkalemia if given with ACEIs/ARBs/renal insufficiency.
Indapamide SR	1.5mg OD	1.5mg OD	
Indapamide	2.5mg OD	2.5mg OD	
Triamterene/hydrochlorothiazide	1 tablet BD	2 tablet BD	
50mg/25mg			
Beta Blockers			
Atenolol	50mg OD	100mg OD	• Contraindicated in patient with COAD, severe Peripheral Vascular Disease and heart block.
Bisoprolol	5mg OD	10mg OD	
Metoprolol	50mg BD	200mg BD	
Propranolol	40mg BD	320mg BD	
Calcium Channel Blockers (CCBs)			
Amlodipine	5mg OD	10mg OD	• Verapamil may reduce heart rate and use with care with Beta Blockers.
Diltiazem	30mg TDS	60mg TDS	
Diltiazem SR	90mg BD	90mg BD	
Felodipine	2.5mg OD	10mg OD	
Lercanidipine	10mg OD	20mg OD	
Nifedipine	10mg TDS	30mg TDS	
Nifedipine SR	30mg OD	120mg OD	
Verapamil	80mg BD	240mg TDS	
Verapamil CR	200mg OD	200mg BD	
ACE Inhibitors (ACEIs)			
Captopril	25mg BD	50mg TDS	• Contraindicated in pregnancy and bilateral renal artery stenosis.
Enalapril	2.5mg OD	20mg BD	
Lisinopril	5mg OD	80mg OD	
Perindopril	2mg OD	8mg OD	
Ramipril	2.5mg OD	10mg OD	
Quinapril	2.5mg OD	40mg BD	
Angiotensin Receptor Blockers (ARBs)			
Candesartan	8mg OD	16mg OD	• Contraindicated in pregnancy and bilateral renal artery stenosis.
Irbesartan	150mg OD	300mg OD	
Losartan	50mg OD	100mg OD	
Telmisartan	20mg OD	80mg OD	
Valsartan	80mg OD	160mg OD	
Olmesartan	20mg OD	40mg OD	
Miscellaneous			
Prazosin (Alpha Blocker)	0.5mg BD	10mg BD	• Doxazosin is useful in patient with benign prostatic hypertrophy.
Doxazosin	1mg OD	16mg OD	
Labetalol	100mg BD	800mg TDS	
Carvedilol	12.5mg OD	50mg OD	
			• In elderly, start Labetalol with 50mg BD.



# HYPERTENSION TREATMENT

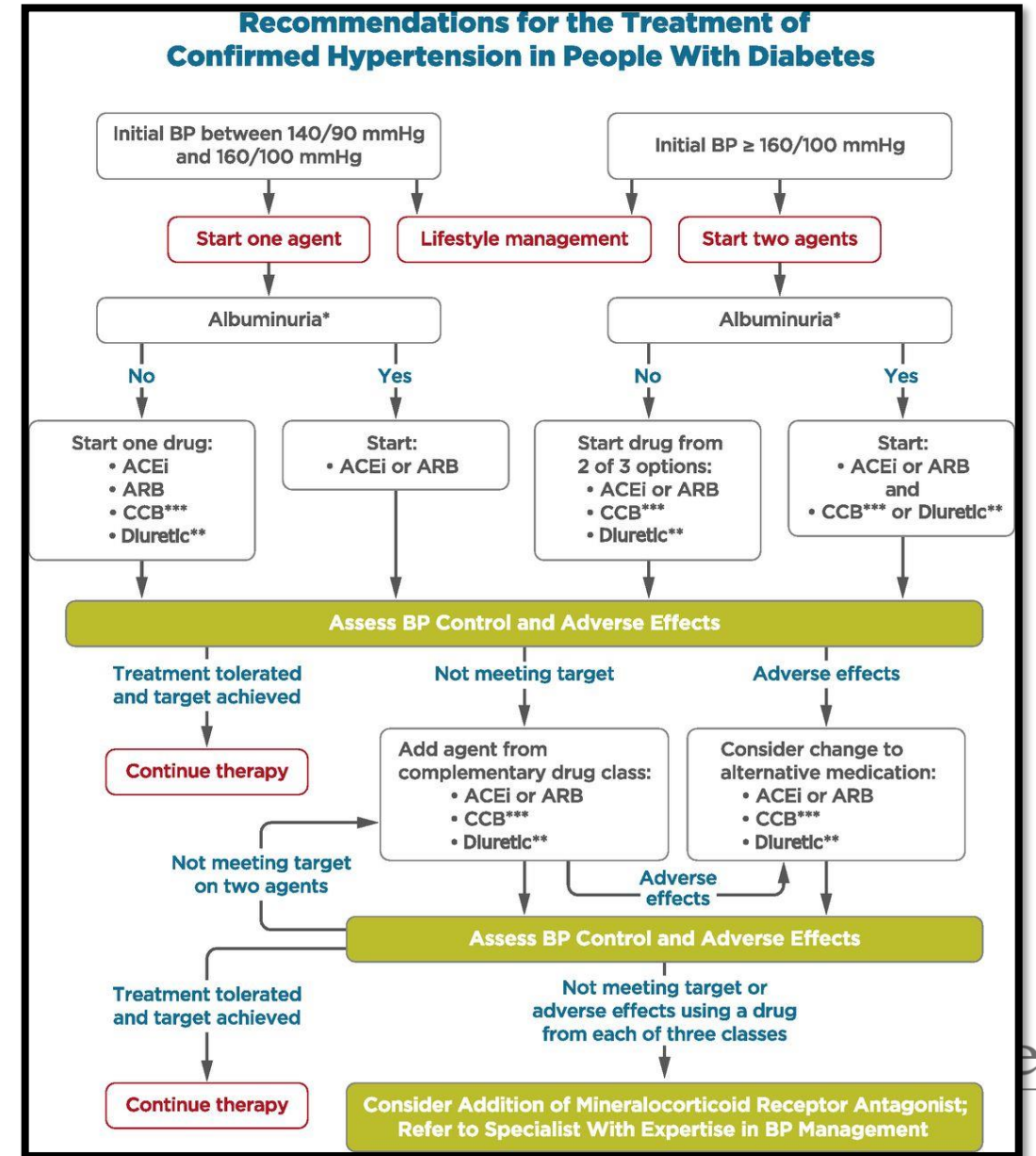
An **ACE inhibitor or ARB**, at the maximum tolerated dose indicated for BP treatment

- HTN in patients with DM and urinary albumin-to-creatinine ratio  $>300$  mg/g creatinine or 30–299 mg/g creatinine

The other class should be substituted if the other is not tolerated

# DM AND HTN

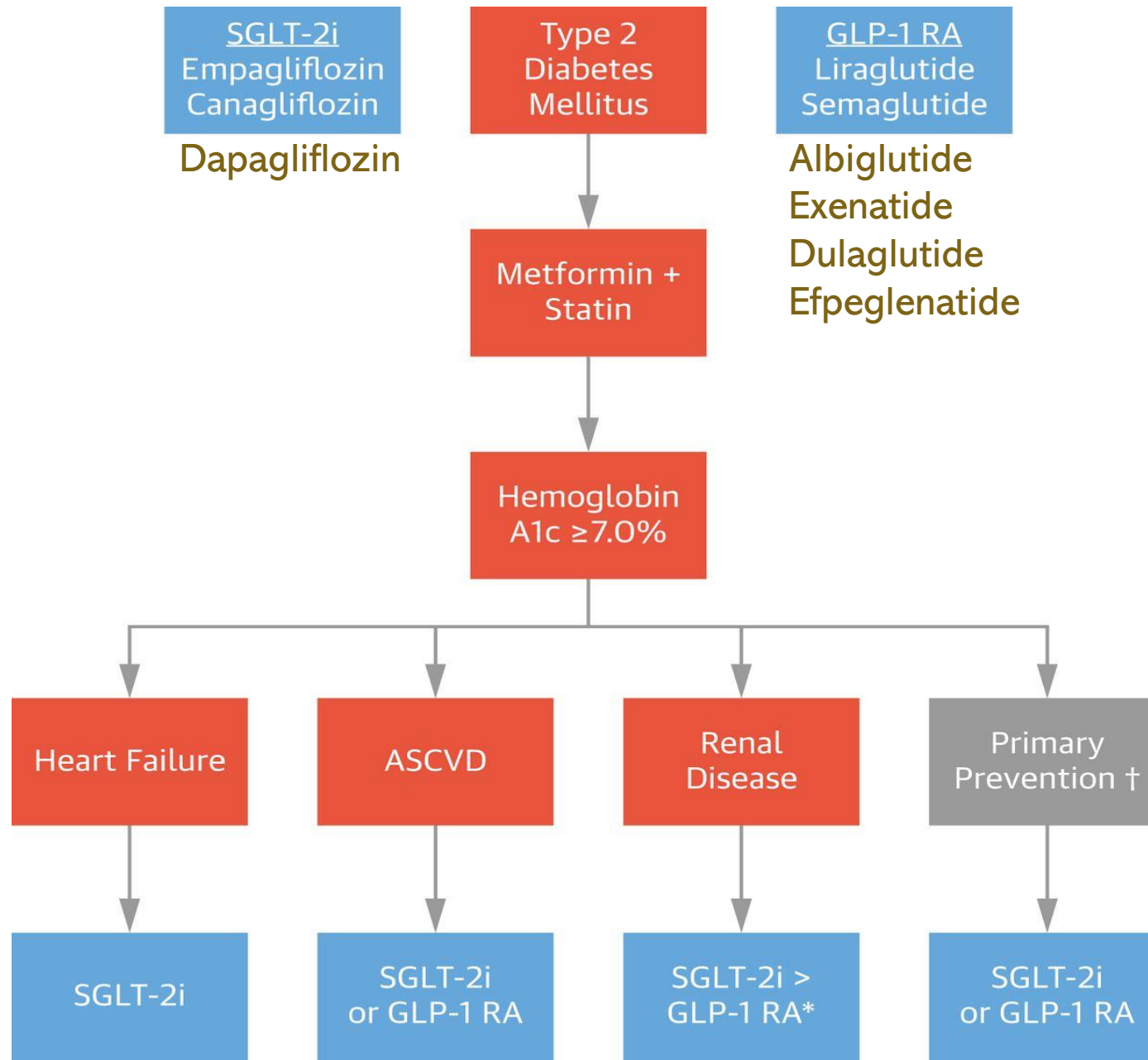
- ACEi/ARB first
- Calcium channel blocker
  - Dihydropyridines preferred (amlodipine, nifedipine)
- Diuretics – thiazides (chlorthalidone > HCTZ)
- Then, get creative...



**REPEAT AFTER ME...**

**BETA BLOCKERS ARE NOT  
ANTIHYPERTENSIVES!**

# A New Algorithm for CVD Risk Reduction in Type 2 Diabetes



# SGLT2 INHIBITORS VERSUS GLP-1RAS WITH DEMONSTRATED CV BENEFIT

## **SGLT2 Inhibitor First When Patient and Clinician Priorities Include:**

- Reducing MACE and CV death
- Preventing heart failure hospitalization
- Reducing blood pressure
- Orally administered therapies
- Consider alternative agents if:
  - Significant CKD\*
  - History of prior amputation, severe peripheral arterial disease, neuropathy, or diabetic foot ulcers (avoid canagliflozin)
  - History of recurrent genital candidiasis
  - History of diabetic ketoacidosis
  - History of osteoporosis (avoid canagliflozin)

## **GLP-1RA First When Patient and Clinician Priorities Include:**

- Reducing MACE and CV death
- Substantial weight loss
- Once weekly (subcutaneous) dosing
- Therapy when eGFR consistently  $<45 \text{ ml/min/1.73 m}^2$ \*
- Consider alternative agents if:
  - Persistent nausea, even at low doses
  - History of pancreatitis
  - History of gastroparesis
  - History of MEN2 or medullary thyroid cancer
  - History of proliferative retinopathy (semaglutide)

# **DIABETES AND CARDIOVASCULAR DISEASE: *DATA YOU SHOULD KNOW BY HEART***

## **THANK YOU!!!**

## ***LET'S SEE WHAT THE PANEL HAS TO SAY...***

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