

Optimizing Cardiovascular Health in People with Diabetes

May 28, 2025 – Presented by Mark Benson, MD PhD

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Conflicts of Interest / Relationships with Industry

Amgen: Grant/Research Support

Boehringer Ingelheim/Lilly: Grant/Research Support/Lecture Honoraria

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Objectives

1. Understand CVD risk in diabetes
2. Review guideline-based targets for glycemia, BP, and lipids
3. Discuss evidence-based pharmacologic and non-pharmacologic strategies
4. Apply recommendations to patients with and without ASCVD

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Insulin Resistance is a Potent Risk Factor for ASCVD

- 2–4x higher risk of CVD death

TABLE 3

Average annual age-adjusted incidence/1000 of specified cardiovascular events, according to sex and diabetic status (Framingham cohort; men and women ages 45–74 yr)

	Men		Women	
	Diabetic	Non-diabetic	Diabetic	Non-diabetic
Cardiovascular disease	39.1	19.1	27.2	10.2
Cardiovascular disease death	17.4	8.5	17.0	3.6
Congestive heart failure	7.6	3.5	11.4	2.2
Intermittent claudication	12.6	3.3	8.4	1.3
Atherothrombotic brain infarction	4.7	1.9	6.2	1.7
Coronary heart disease	24.8	14.9	17.8	6.9

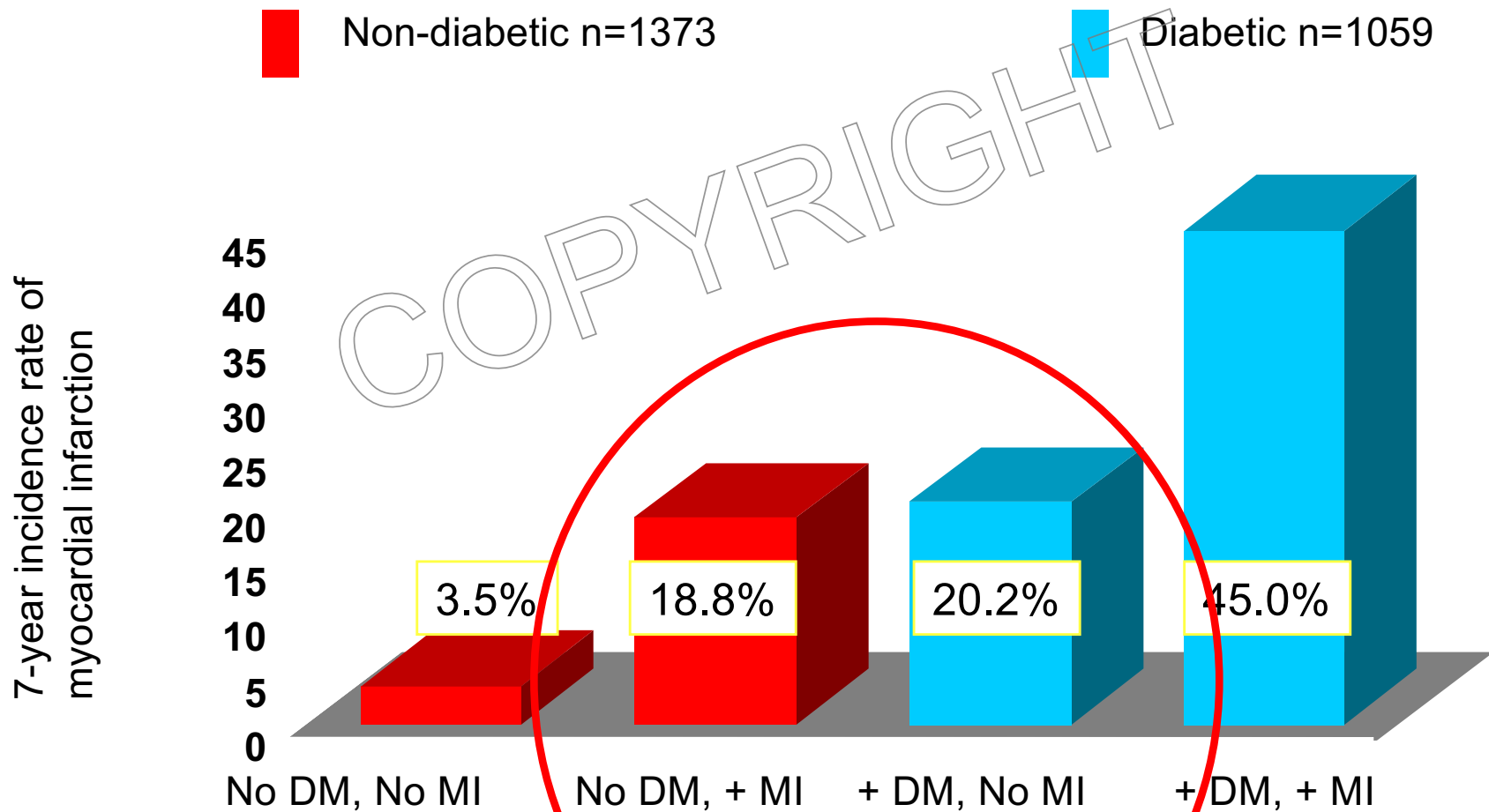
Insulin Resistance is a Potent Risk Factor for ASCVD

- 2–4x higher risk of CVD death
- ASCVD remains primary cause of death and disability in T2D
- ~2/3 deaths in T2D due to ASCVD

HRs (95% CI) for MI in type 2 diabetes compared with no diabetes stratified by sex and attained age-group, adjusted for smoking habit, BMI, hypertension and abnormal lipids

	All	Men	Women
Diabetes (n)	40,727	21,165	19,562
No diabetes (n)	194,913	99,658	95,255
Age 35–54 years	3.07 (2.43–3.88)	2.69 (2.07–3.49)	4.86 (2.78–8.51)
Age 55–64 years	2.83 (2.51–3.19)	2.21 (1.92–2.54)	5.25 (4.11–6.69)
Age 65–74 years	2.59 (2.40–2.81)	2.17 (1.97–2.39)	3.45 (3.01–3.95)
Age ≥75 years	2.21 (2.07–2.36)	1.96 (1.78–2.15)	2.45 (2.24–2.69)
All ages	2.47 (2.36–2.59)	2.13 (2.01–2.26)	2.95 (2.75–3.17)

T2D as a ASCVD “Risk Equivalent”



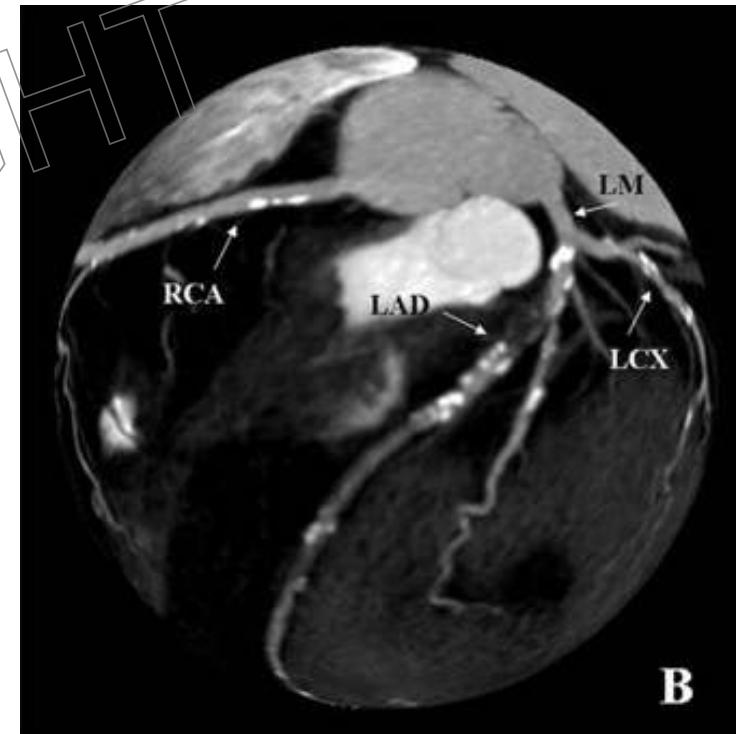
Haffner et al. *N Engl J Med.* 1998;339:229-234.

Patients with T2D have more extensive CHD

Table 3. Cardiac Catheterization Data

	Diabetes (n = 148)	No Diabetes (n = 923)	p Value
LV ejection fraction (%)	48.8 ± 12.3	51.3 ± 11.8	
Regional function (SD/chord)			
Infarct zone	-2.7 ± 1.8	-2.5 ± 1.1	0.15
Noninfarct zone	-0.13 ± 1.8	0.32 ± 1.7	0.02
Patients with 0 or 1-vessel disease	34	54	
Patients with multivessel disease	16	46	< 0.0001
2-vessel disease	40	27	
3-vessel disease	36	18	
Segments with ≥25% stenosis (no./patient)	3.4 ± 2.0	2.9 ± 1.8	< 0.002
Infarct-related artery patency (%)			
90 min after start of thrombolytic therapy	71	70	
At the end of acute catheterization (after attempted PTCA if occluded)	92	93	

Unless otherwise stated values are presented as mean value ± SD or percent of patients. LV = left ventricular; PTCA = percutaneous transluminal coronary angioplasty.



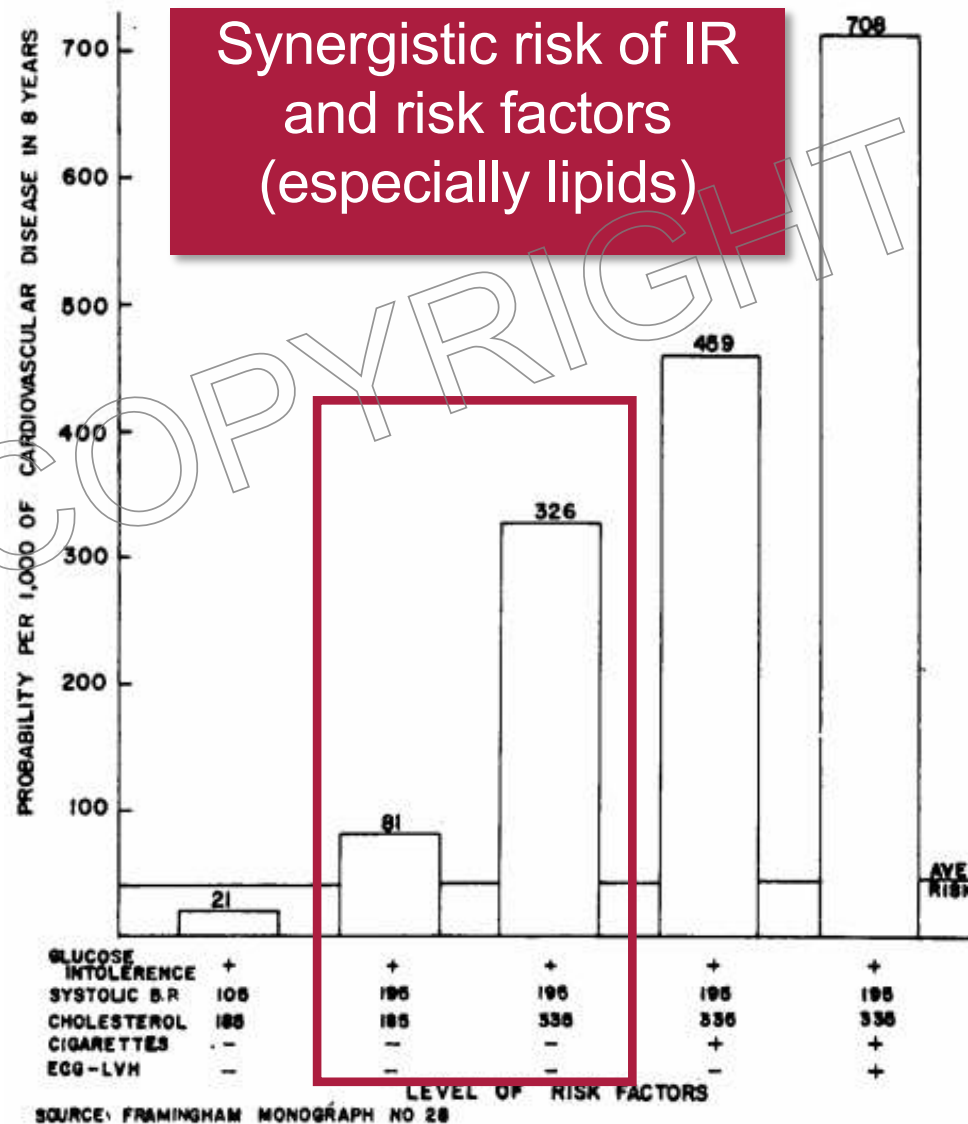
Diabetes

Increases Multiple Mechanisms of CAD Risk

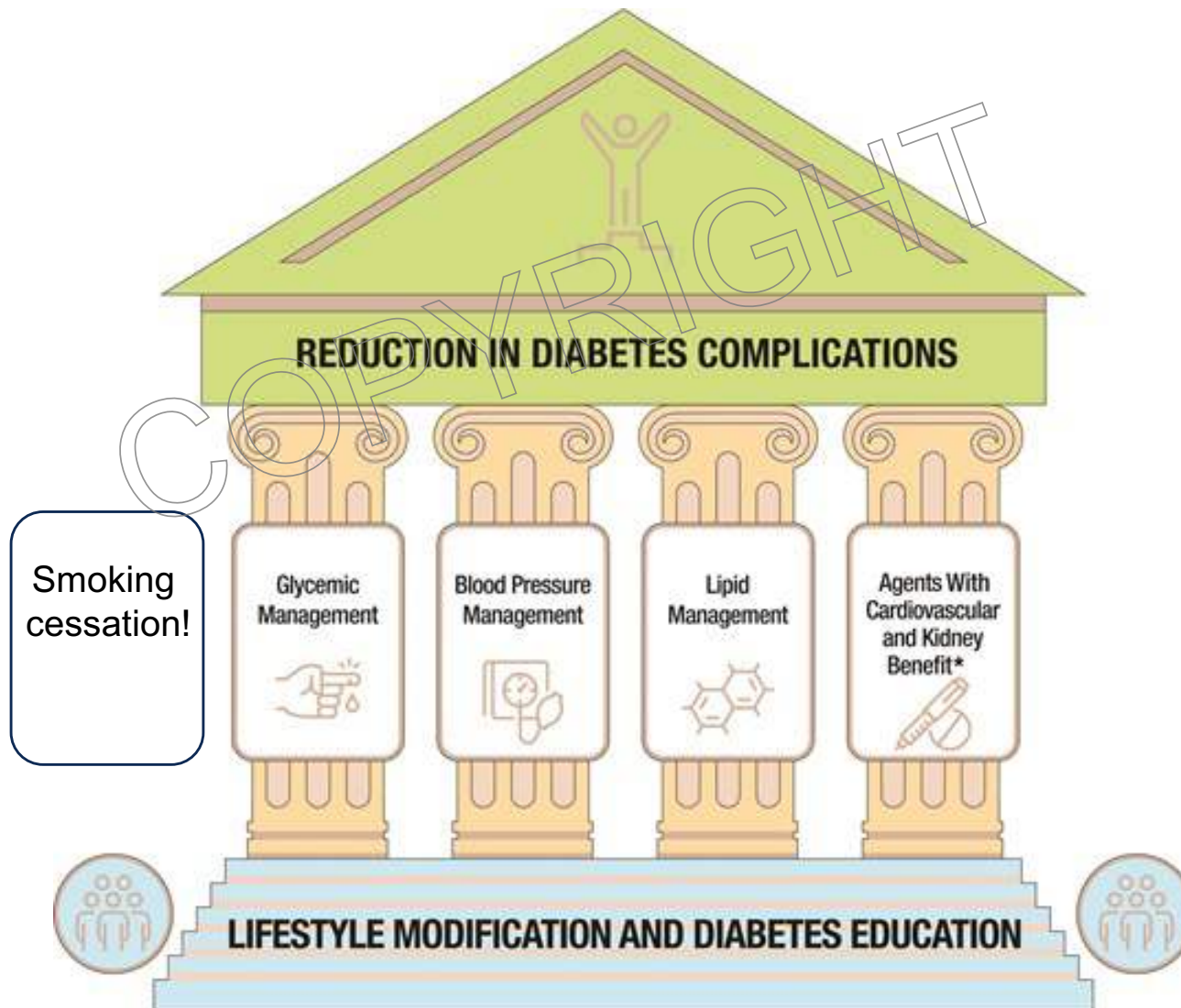
- Endothelial dysfunction
- Platelet Activation
- Coagulation Abnormalities
- Plaque Composition

Insulin Resistance

Associated with additional ASCVD risk factors



Multifactorial Approach to ASCVD Risk Reduction in T2D



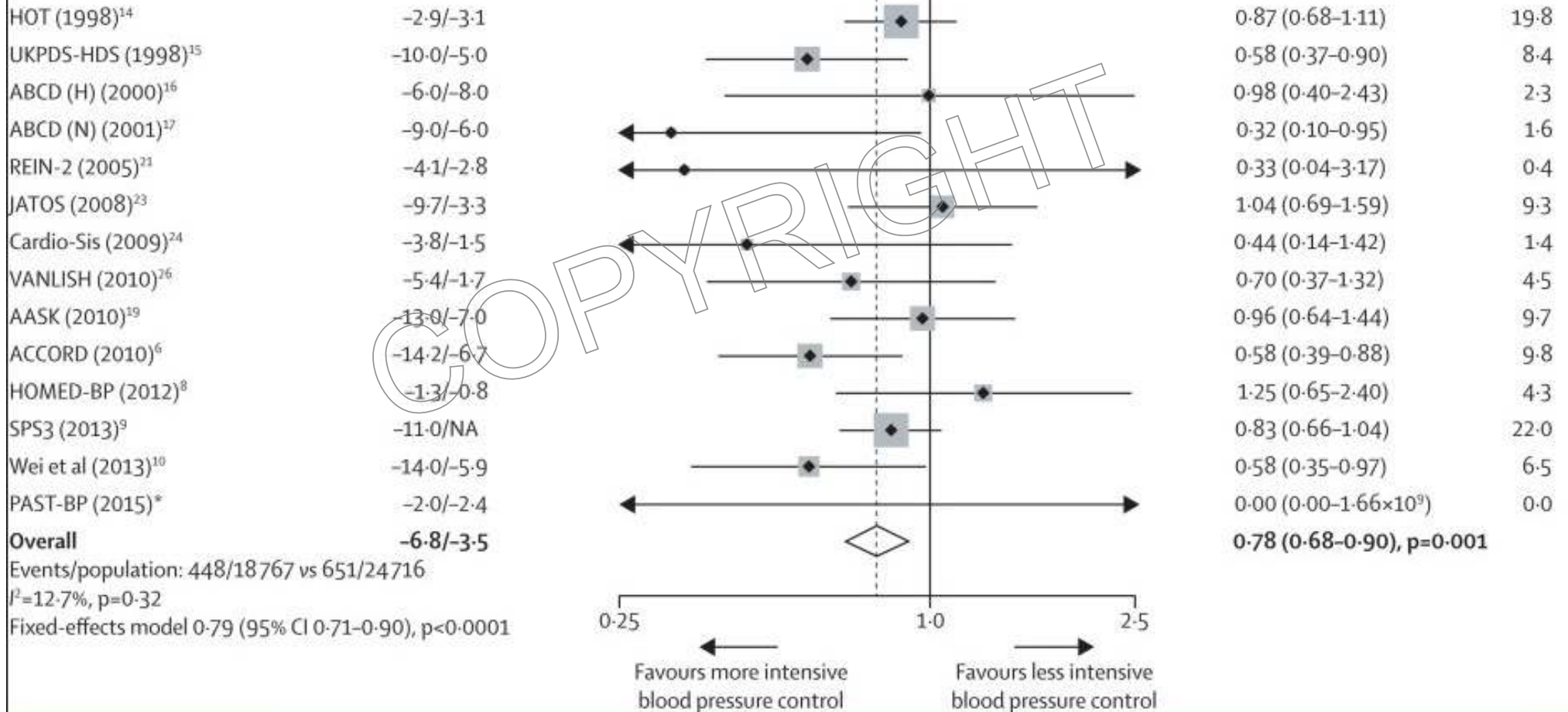
Primary Prevention: Blood Pressure

- BP should be measured every routine clinical visit
- BP goal is <130/80
- All people with HTN and T2D should monitor their BPs at home

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Primary Prevention: Blood Pressure

Major CV Events

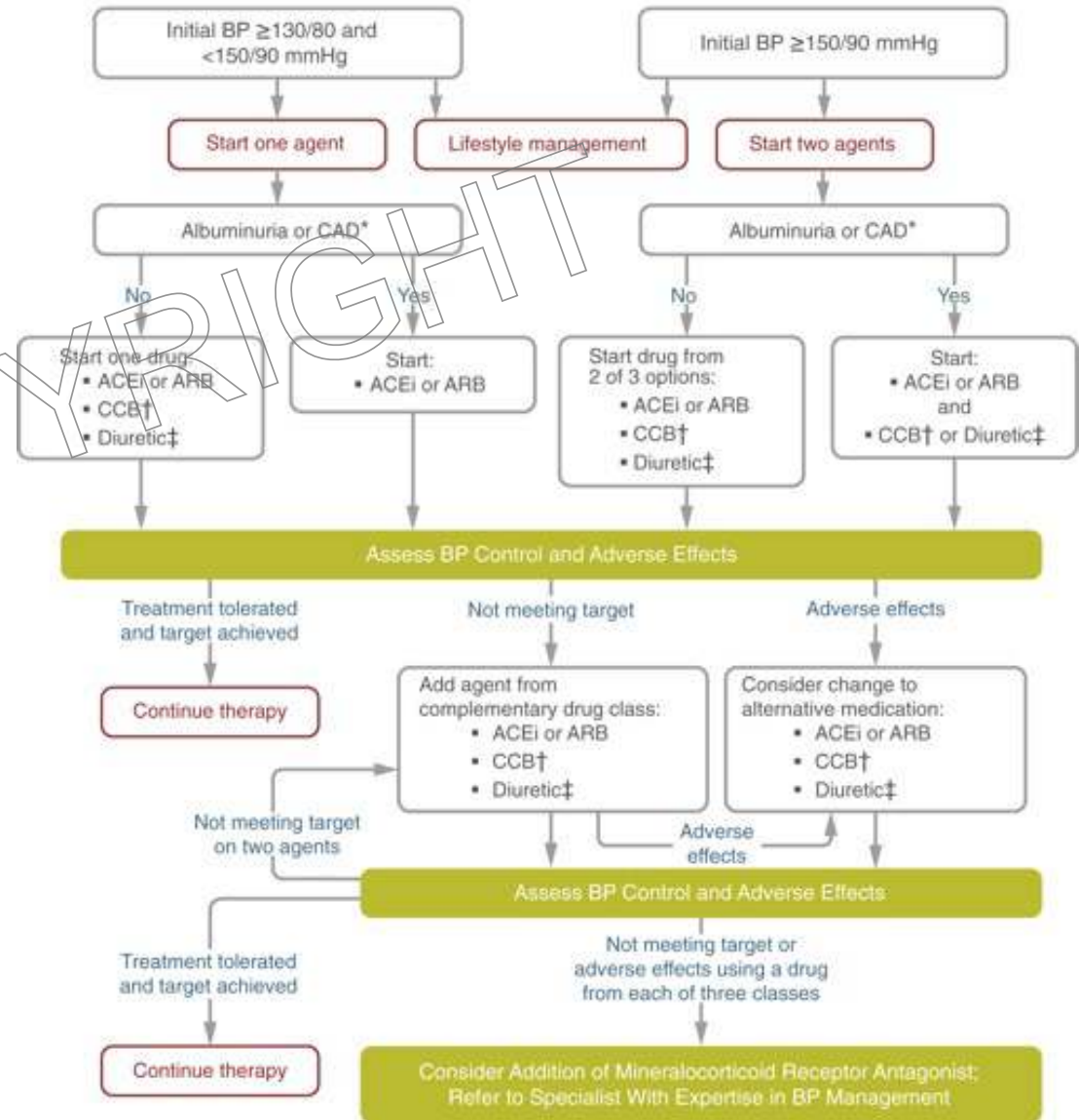


N= 44,989

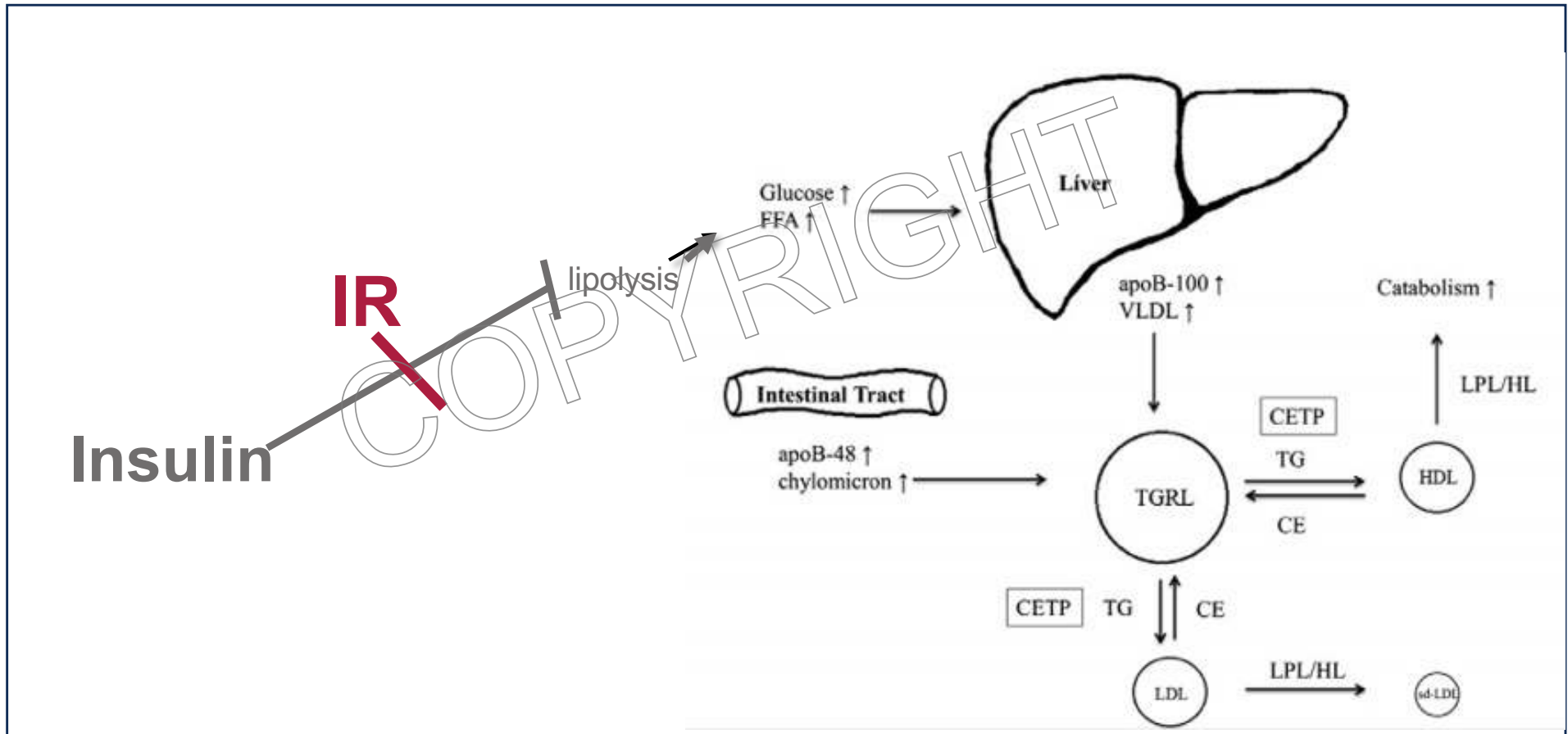
Primary Prevention: Blood Pressure

**First-line:
ACEi or ARB;
add thiazide or CCB if needed**

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Insulin Resistance: Disrupts lipid metabolism at multiple levels



Lipid Profiles: Atherogenic in T2D

Lipid abnormalities present in
60-70% of people with T2DM

Particularly
atherogenic profiles

Occur years before
hyperglycemia

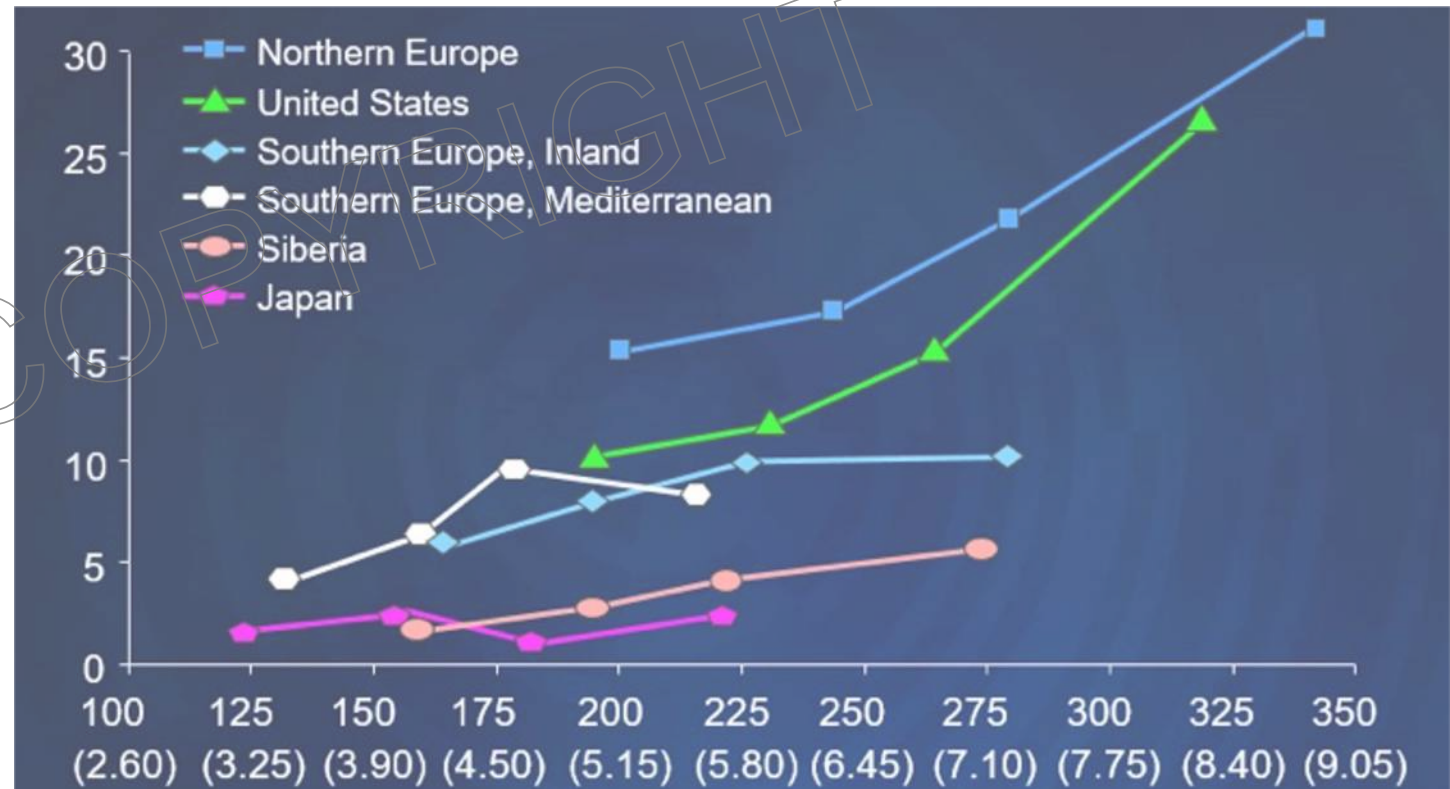
Tied to insulin
resistance

Lipid	T2DM
HDL-C	↓ ↓
LDL-C	← →
sdLDL	↑ ↑
Triglycerides	↑ ↑
apoB	↑ ↑

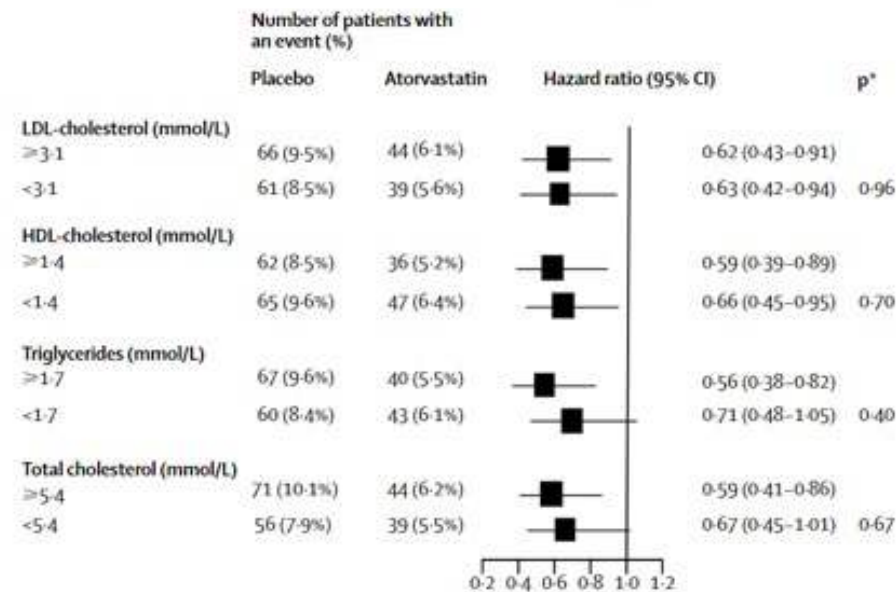
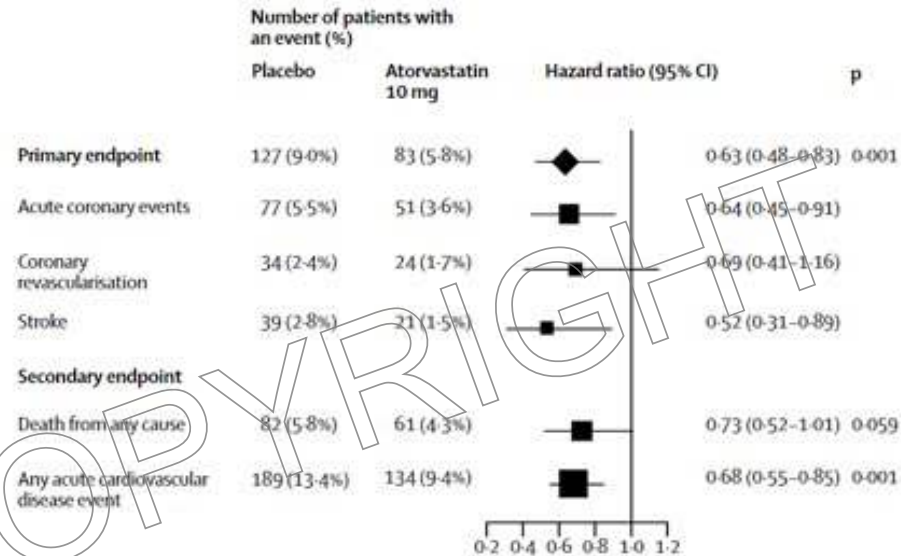
Cholesterol and CHD Seven Countries Study

%CHD
mortality rates

Total
Cholesterol
mg/dL
(mmol/L)



Primary Prevention: Lipid Management



Primary Prevention: Lipid Management

Diabetes (age 40-75): Moderate intensity statin

Diabetics (age 40-75)

+ ASCVD Risk Enhancers: Consider high intensity statin

Goal: Reduce LDL \geq 50% (w/ ezetimibe, if needed)

Risk Enhancers

- Long duration (\geq 10 years for type 2 diabetes mellitus (S4.3-20) or \geq 20 years for type 1 diabetes mellitus (S4.3-6))
- Albuminuria \geq 30 mcg of albumin/mg creatinine (S4.3-25)
- eGFR $<$ 60 mL/min/1.73 m² (S4.3-25)
- Retinopathy (S4.3-19)
- Neuropathy (S4.3-16)
- ABI $<$ 0.9 (S4.3-22, S4.3-24)

Primary Prevention: Lipid Management

Diabetes (age 40-75): Moderate intensity statin

Diabetics (age 40-75)

+ ASCVD Risk Enhancers: Consider high intensity statin

Goal: Reduce LDL \geq 50% (w/ ezetimibe, if needed)

• Add ezetimibe or PCSK9i if needed

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Primary Prevention: Lipid Management

Diabetes (age 20-39):

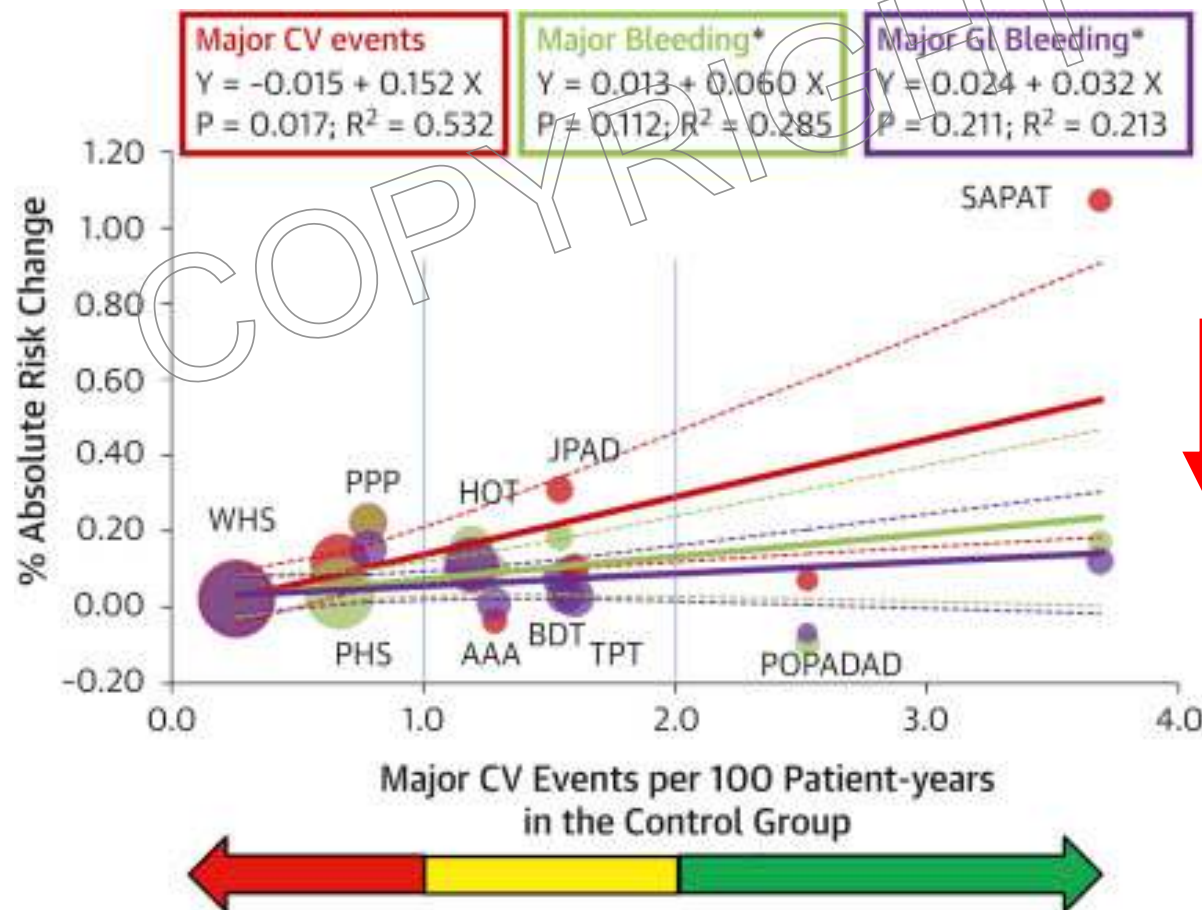
+ ASCVD Risk Enhancers: Consider moderate intensity statin

Risk Enhancers

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- eGFR < 60 mL/min/1.73 m² (S4.3-25)
- Retinopathy (S4.3-19)
- Neuropathy (S4.3-16)
- ABI < 0.9 (S4.3-22, S4.3-24)

Primary Prevention: Antiplatelet Therapy

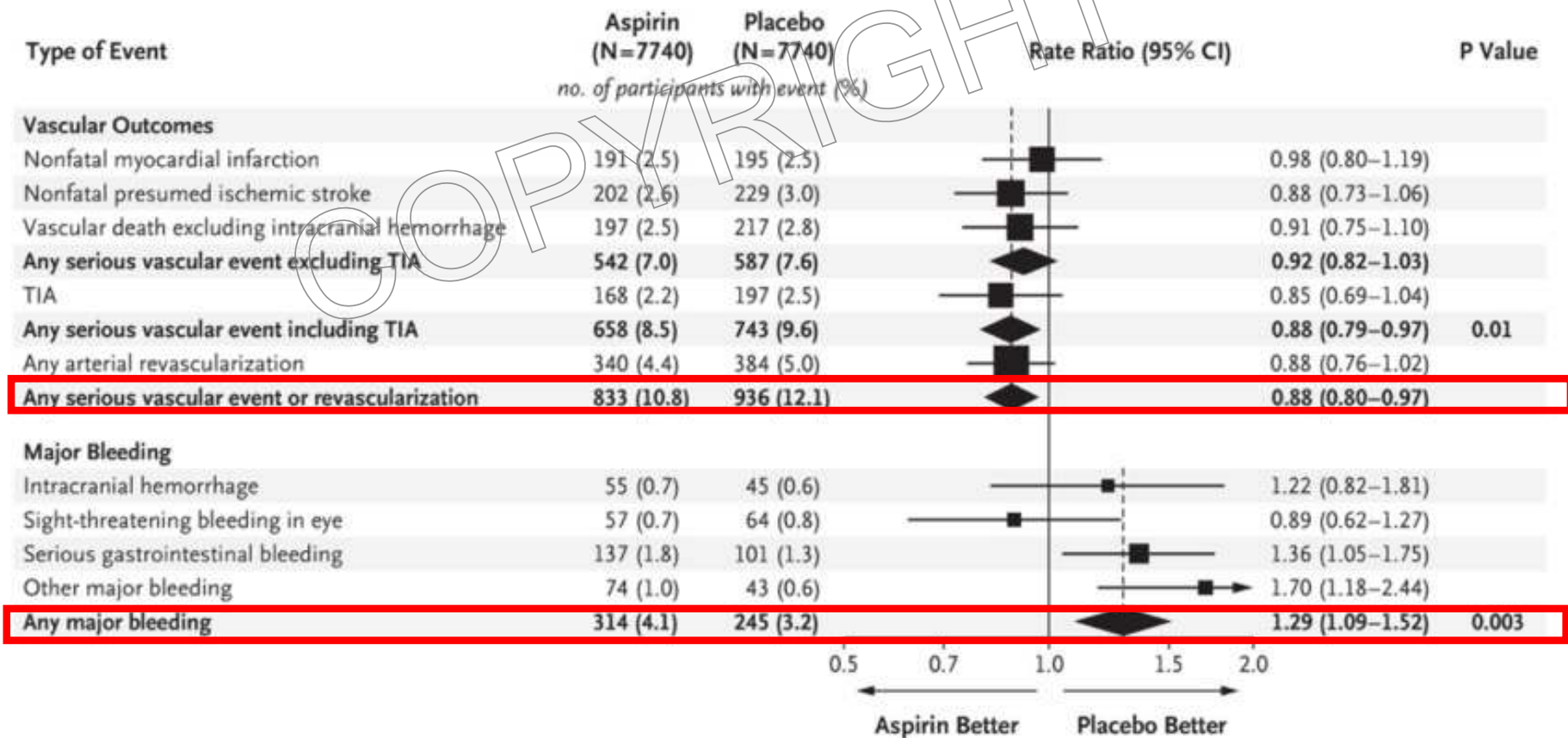
- NOT routine in primary prevention
- Consider ASA only if very high risk + low bleeding risk



ASPREE (2018)
ARRIVE (2018)
ASCEND (2018)

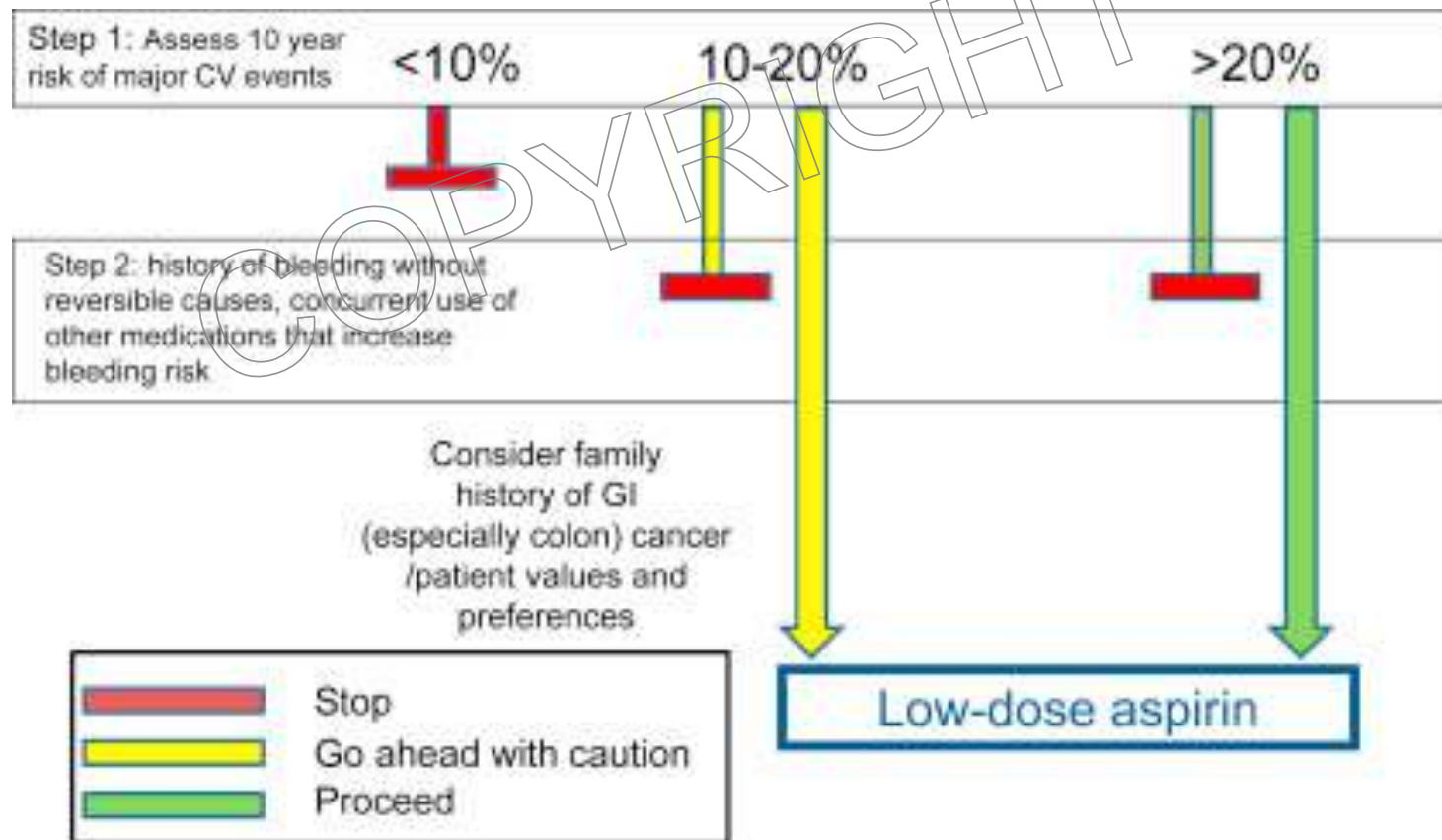
ASCEND: 1.1% ARR ASCVD vs 0.9% AR Major Bleed

- NOT routine in primary prevention
- Consider ASA only if very high risk + low bleeding risk



Primary Prevention: Antiplatelet Therapy

- NOT routine in primary prevention
- Consider ASA only if very high risk + low bleeding risk



The Complicated History of Targeting T2D in CVD

Rosiglitazone and the Thiazolidinediones

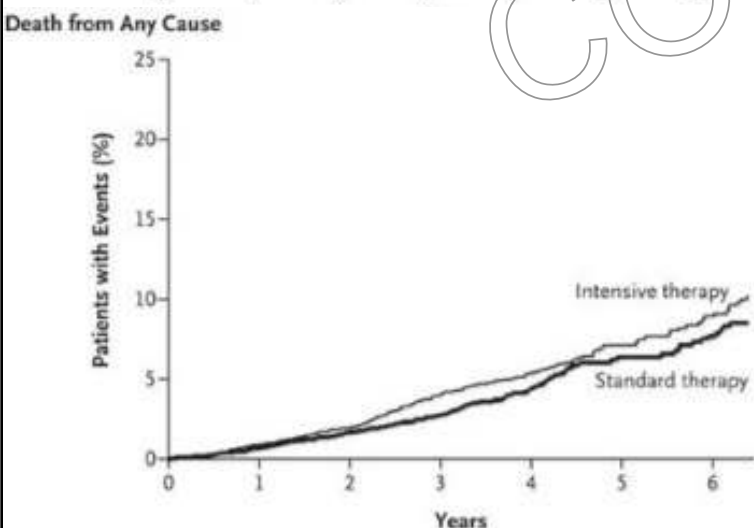
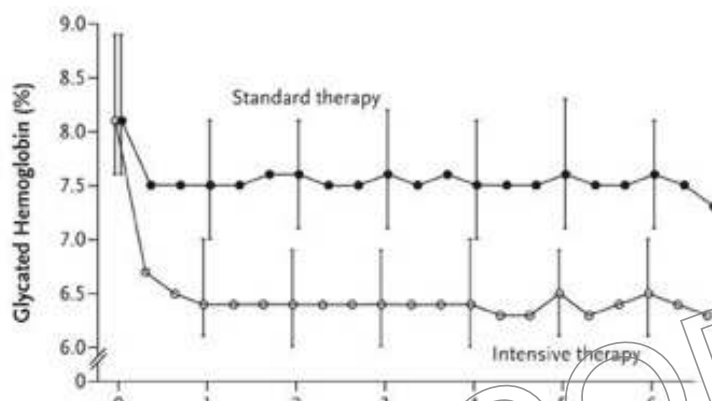


Table 4. Rates of Myocardial Infarction and Death from Cardiovascular Causes.

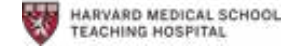
Study	Rosiglitazone Group <i>no. of events/total no. (%)</i>	Control Group <i>no. of events/total no. (%)</i>	Odds Ratio (95% CI)	P Value
Myocardial infarction				
Small trials combined	44/10,285 (0.43)	22/6106 (0.36)	1.45 (0.88–2.39)	0.15
DREAM	15/2,635 (0.57)	9/2634 (0.34)	1.65 (0.74–3.68)	0.22
ADOPT	27/1,456 (1.85)	41/2895 (1.42)	1.33 (0.80–2.21)	0.27
Overall			1.43 (1.03–1.98)	0.03
Death from cardiovascular causes				
Small trials combined	25/6,845 (0.36)	7/3980 (0.18)	2.40 (1.17–4.91)	0.02
DREAM	12/2,635 (0.46)	10/2634 (0.38)	1.20 (0.52–2.78)	0.67
ADOPT	2/1,456 (0.14)	5/2895 (0.17)	0.80 (0.17–3.86)	0.78
Overall			1.64 (0.98–2.74)	0.06

N Engl J Med 2008; 358:2545-2559

N Engl J Med 2007; 356:2457-2471

FDA Requires Demonstration of CVD Safety For All New Anti-Hyperglycemic Medications for T2D

Beth Israel Deaconess
Medical Center



Guidance for Industry

Diabetes Mellitus — Evaluating Cardiovascular Risk in New Antidiabetic Therapies to Treat Type 2 Diabetes

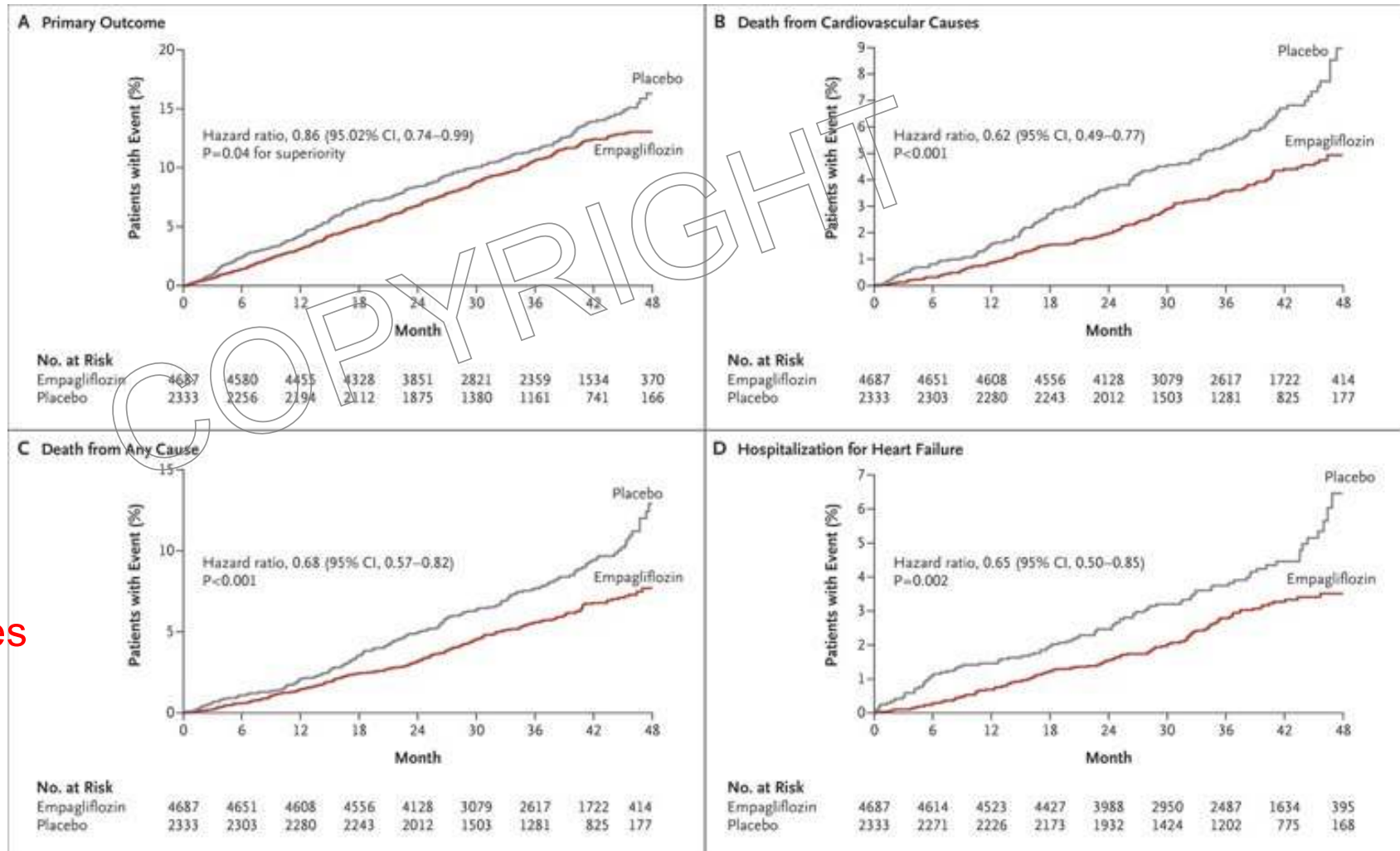
U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

December 2008
Clinical/Medical

EMPA-REG OUTCOMES

Empagliflozin Reduces CVD Events

N=7020
63 yo
+T2D
+ASCVD
(10% HF)



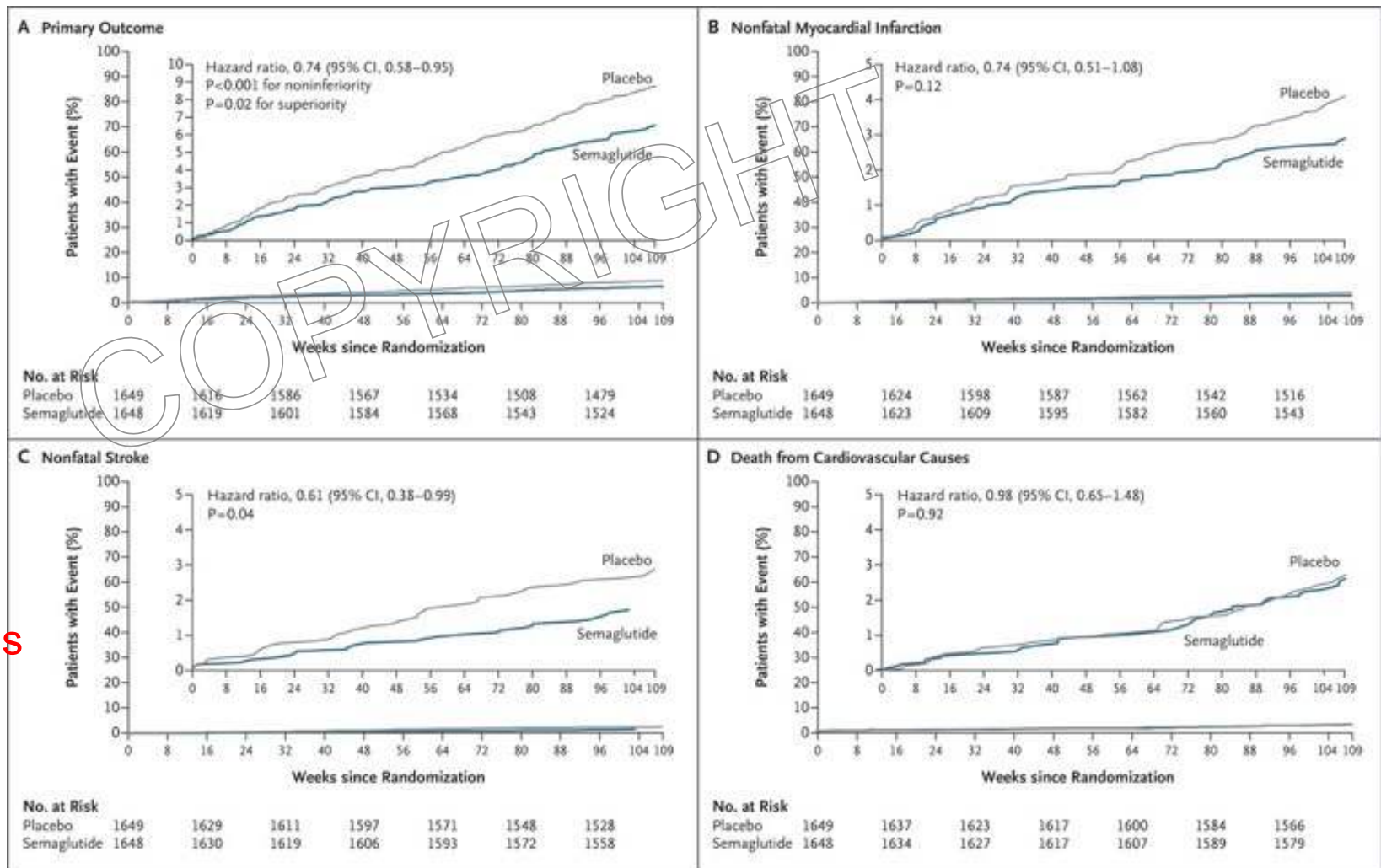
+Meta-analyses
Across 5 trials

SUSTAIN-6

Semaglutide Reduces CVD Events

N=3297
 65 yo
 +T2D
 +ASCVD
 (25% HF)

+Meta-analyses
 Across 8 trials



Cardioprotective Medications: Trial Evidence

- Empagliflozin (EMPA-REG): ↓ CV death, ↓ HF hosp
- Liraglutide (LEADER): ↓ MACE
- Canagliflozin (CANVAS): ↓ MACE, ↓ HF hosp

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Lifestyle Modifications

- Mediterranean/DASH diet
- ≥ 150 min/week aerobic exercise
- Smoking cessation
- Weight loss 5-10% improves multiple risk factors

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Secondary Prevention: ASCVD Present

- High-intensity statin ± ezetimibe/PCSK9i
- BP <130/80 mmHg
- GLP-1RA or SGLT2i with CV benefit

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Summary

Algorithm

1. All ≥ 40 y: start statin; higher intensity if ASCVD or high risk
2. BP $< 130/80$. screen at every visit and monitor home BPs
3. GLP-1RA or SGLT2i if ASCVD or multiple risk factors
4. Lifestyle at every step

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Summary

Key Takeaways

- ✓ Diabetes doubles CV risk
- ✓ BP & lipids & smoking cessation = high-impact targets
- ✓ GLP-1RA/SGLT2i reduce CV/renal events
- ✓ Lifestyle foundational
- ✓ Guidelines provide clear roadmap

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Thank you!

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