Prevention of MACROvascular Complications of Diabetes

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Conflicts of Interest

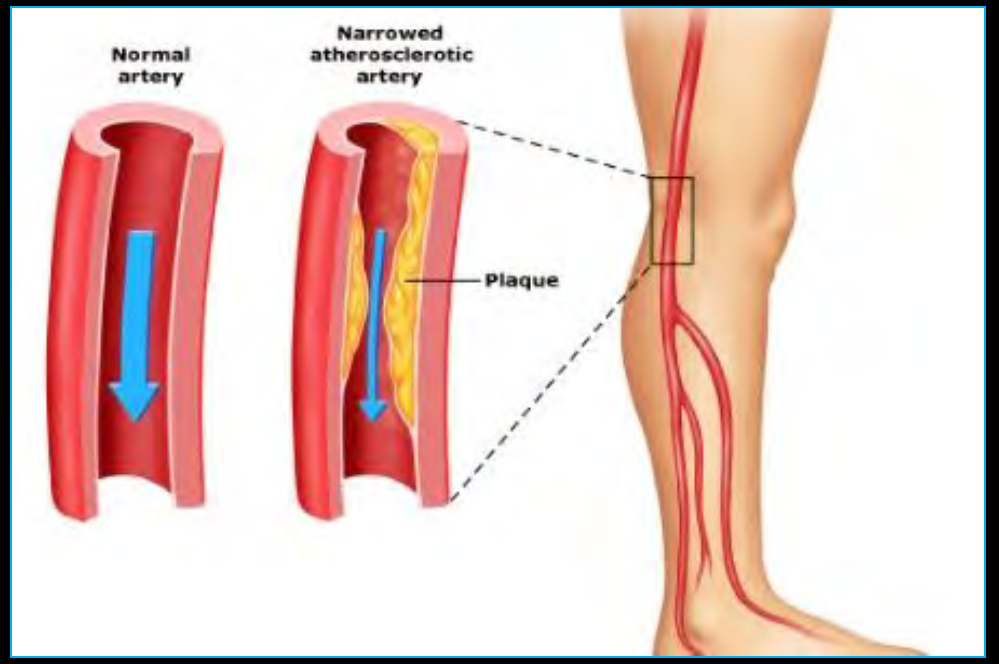
None

Objectives

1. To recognize macrovascular complications as the leading cause of death in people with diabetes
2. To be familiar with risk factors for macrovascular complications of diabetes
3. To understand the impact of multifactorial risk reduction on outcomes in patients with diabetes

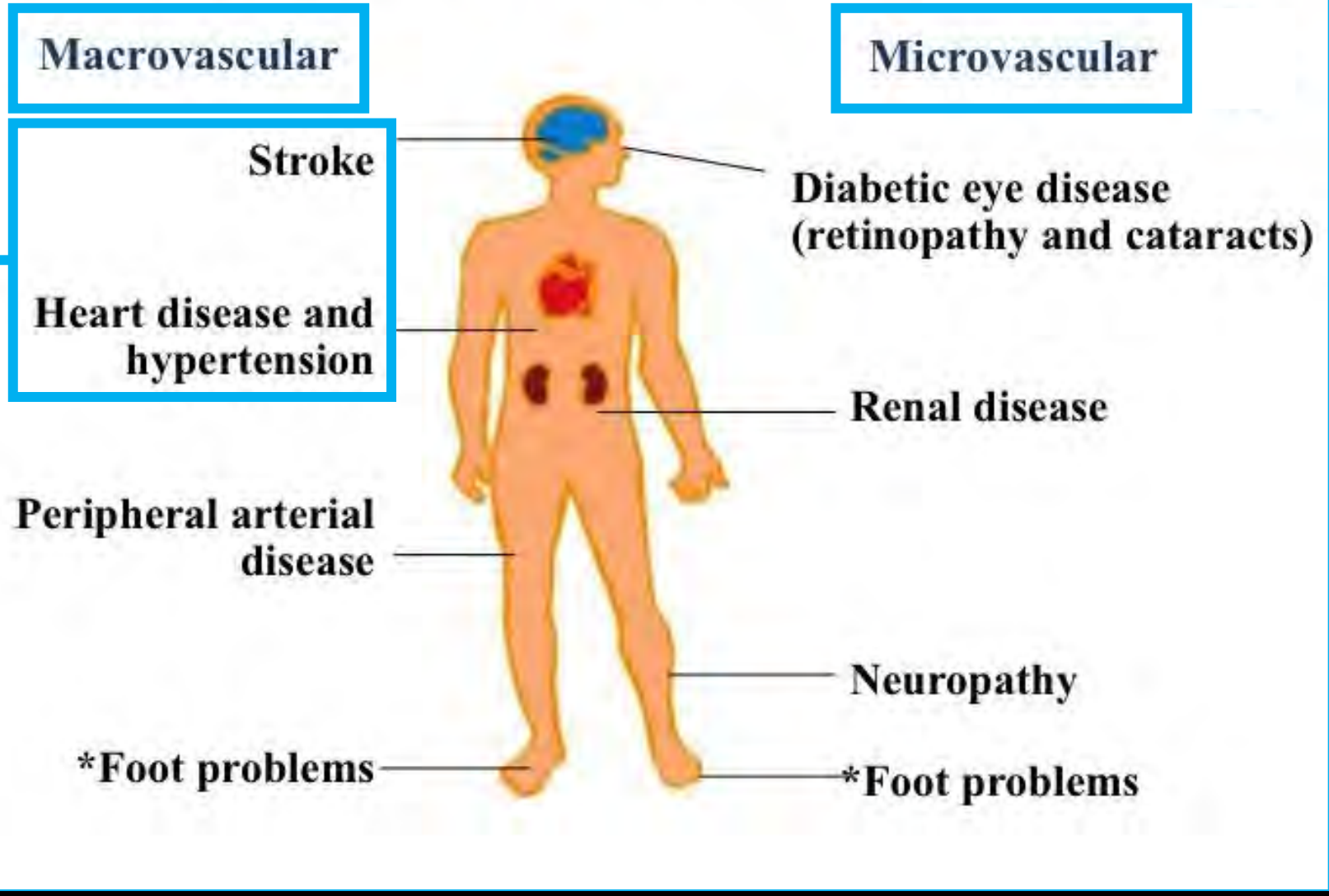
Microvascular =
small vessel disease

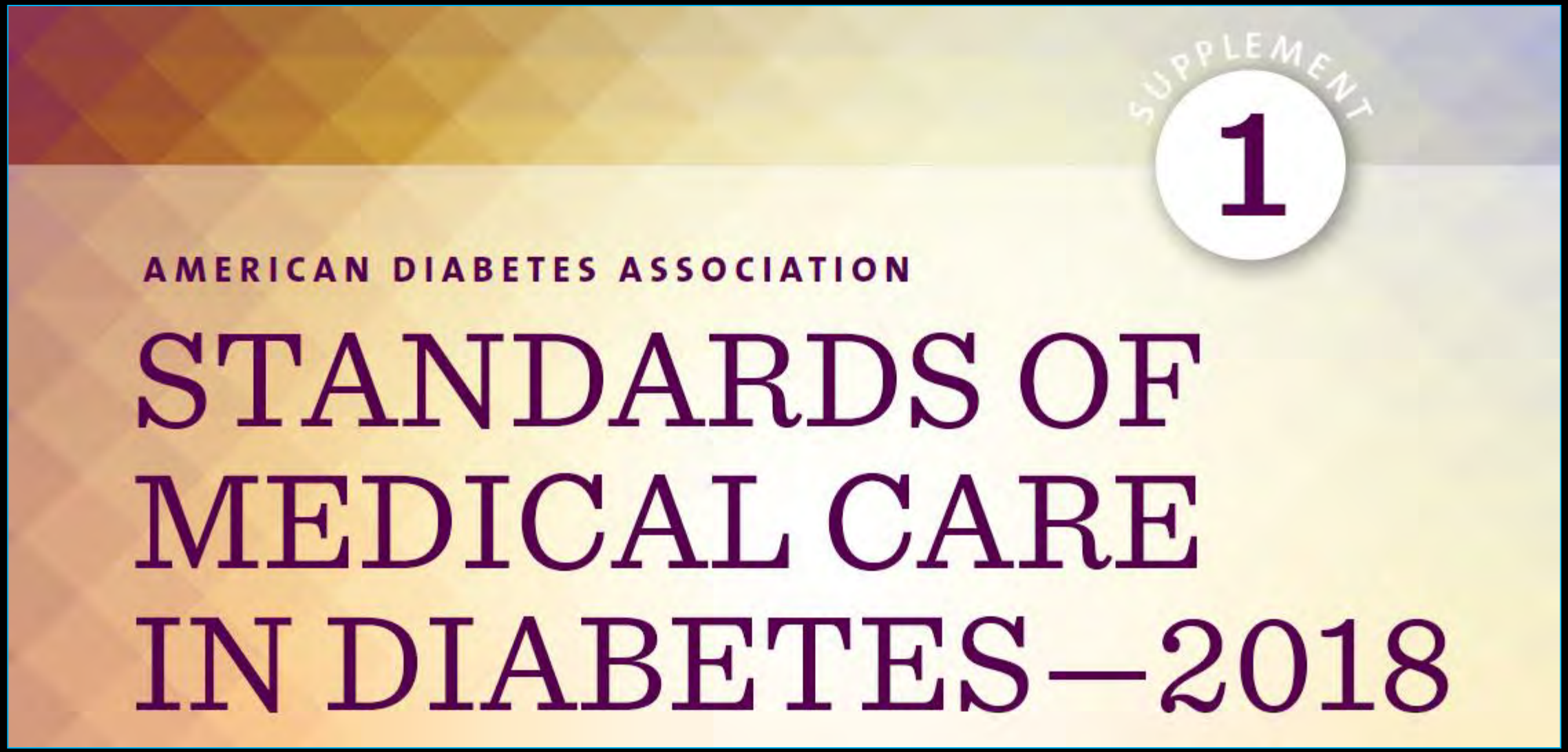
Macrovascular =
large vessel disease



Overview of Diabetic Complications

Leading cause of death in people with diabetes





Diabetes Care 2018;41(S1).

Screening for Coronary Artery Disease (CAD)

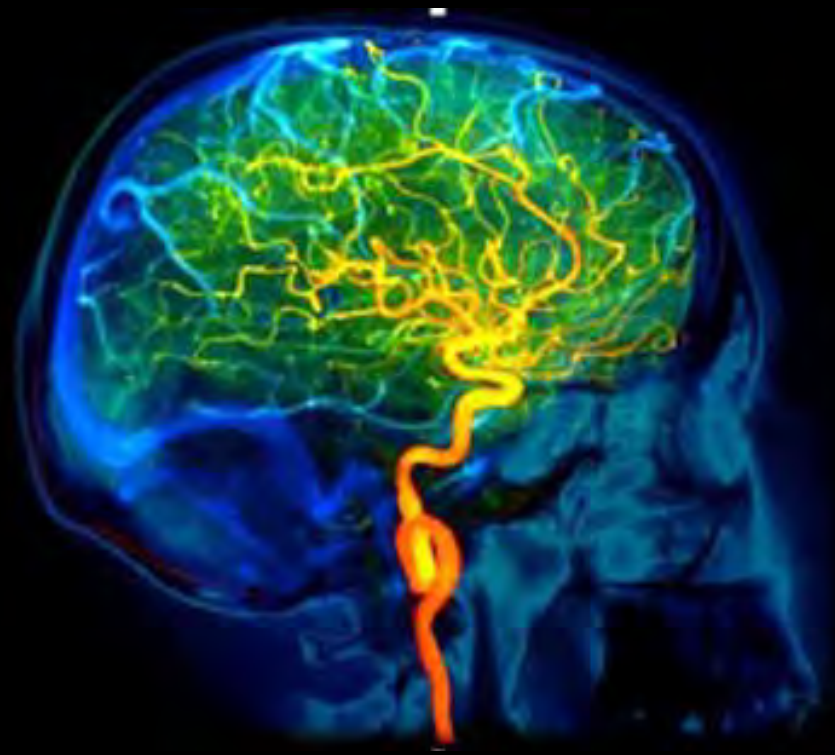
Screening

- In asymptomatic patients, routine screening for coronary artery disease is not recommended as it does not improve outcomes as long as atherosclerotic cardiovascular disease risk factors are treated. **A**

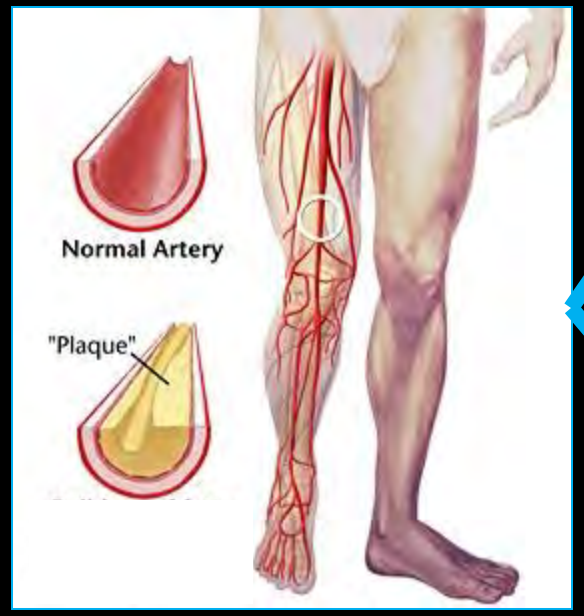
Diabetes Care 2018;41(S1).

Stroke

No ADA guidelines for screening for cerebrovascular disease in asymptomatic patients



Peripheral Arterial Disease (PAD)



Cholesterol (plaque) embolization

Severe ischemia in setting of infection

Screening for Peripheral Arterial Disease (PAD)

- **PAD**
  - Routine foot examination (including pulses)
  - Ankle brachial index (ABI)
    - Symptomatic patients (claudication)
    - Asymptomatic
      - Not specifically addressed in 2018 ADA guidelines

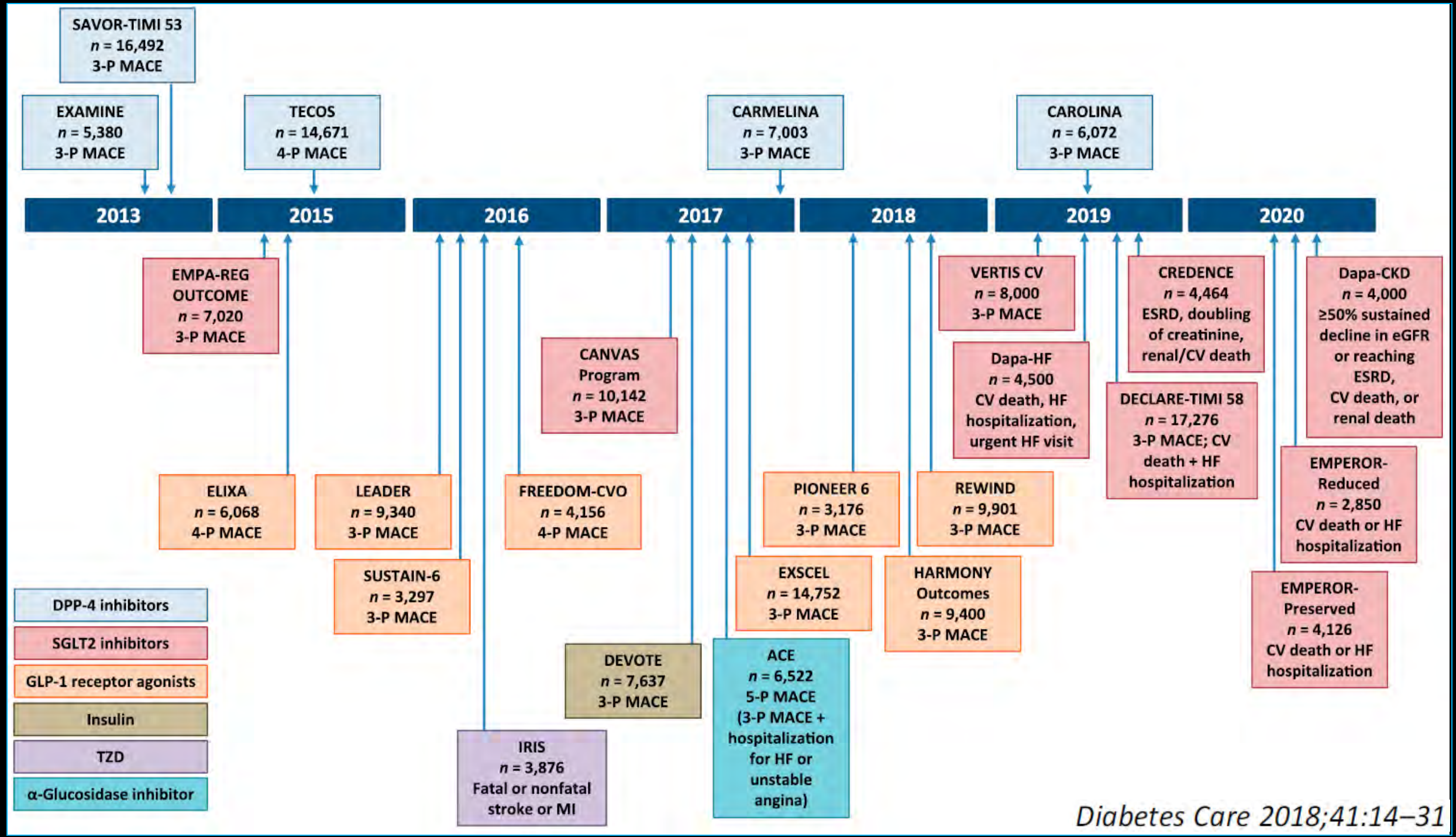
Why isn’t there greater emphasis on screening for these macrovascular complications?

A1c target: < 7-8%

Blood pressure target: < 140/90

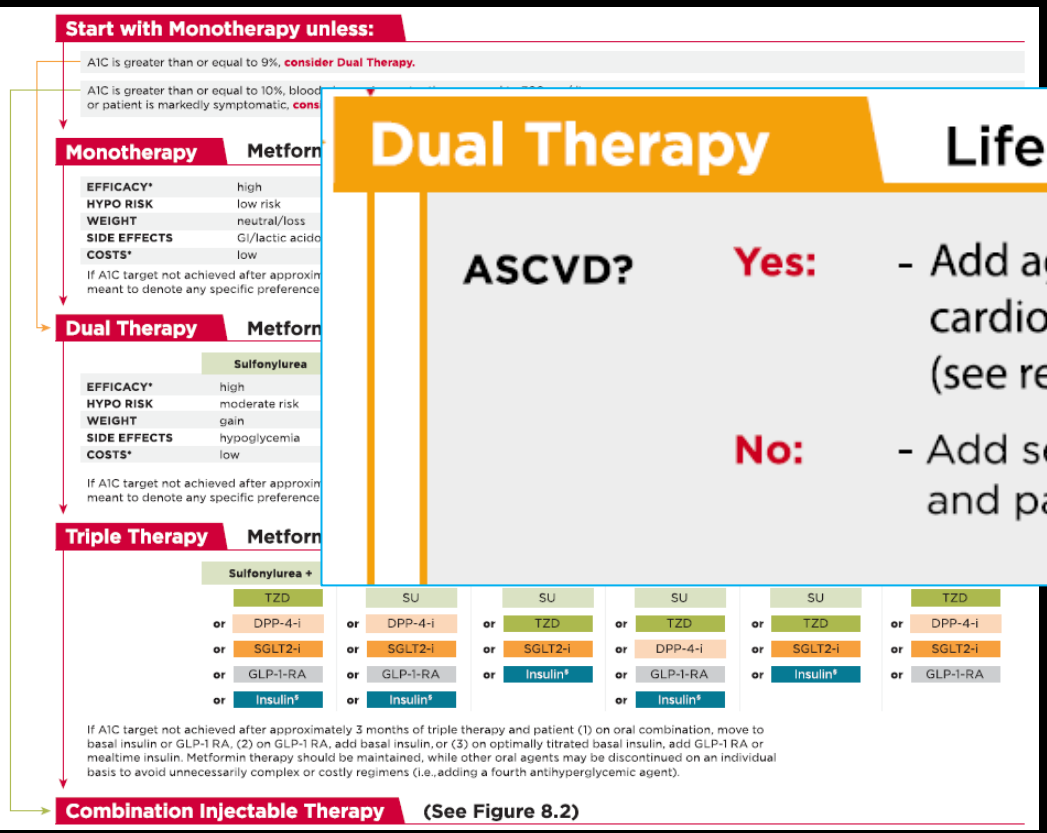
Cholesterol treatment: Statins

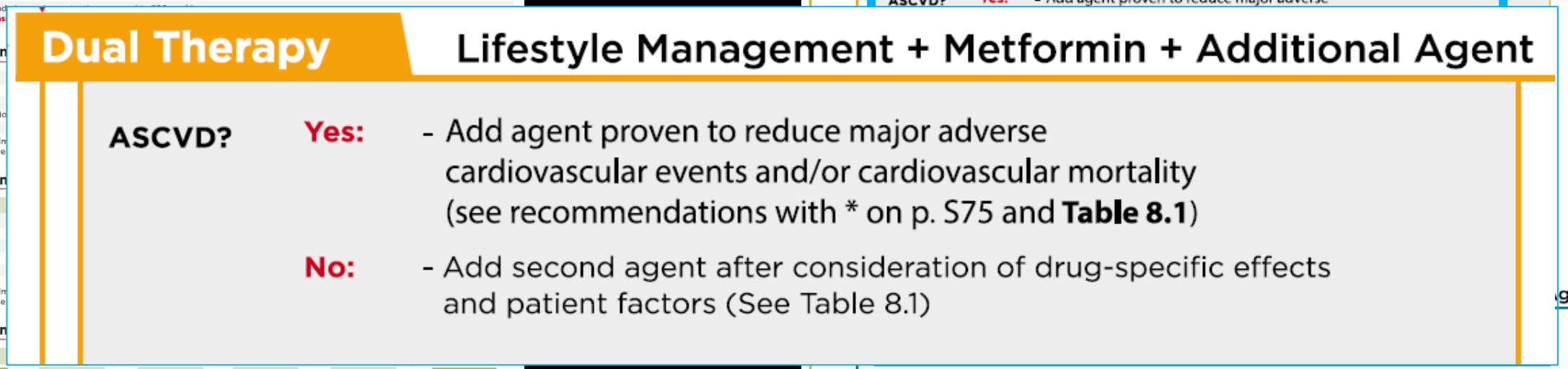
018;41(S1).

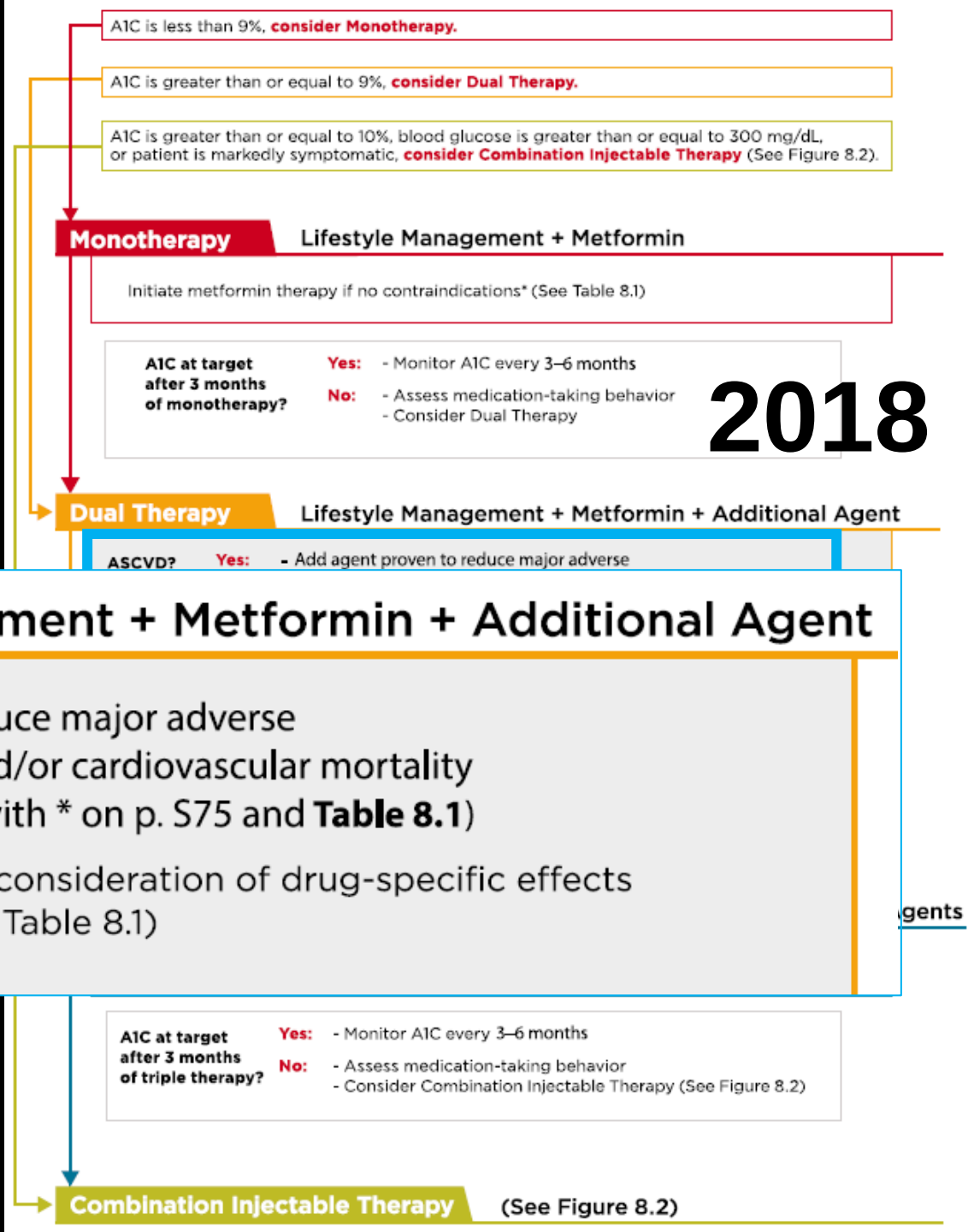


Diabetes Care 2018;41:14–31

Therapies added to metformin should be based on presence or absence of CVD







See Table 8.1 for a helpful comparison of CV/renal effects of available hyperglycemic agents

Efficacy*	Hypoglycemia	Weight Change	CV Effects		Cost	Oral/SQ	Renal Effects	
			ASCVD	CHF			Progression of DKD	Dosing/Use considerations

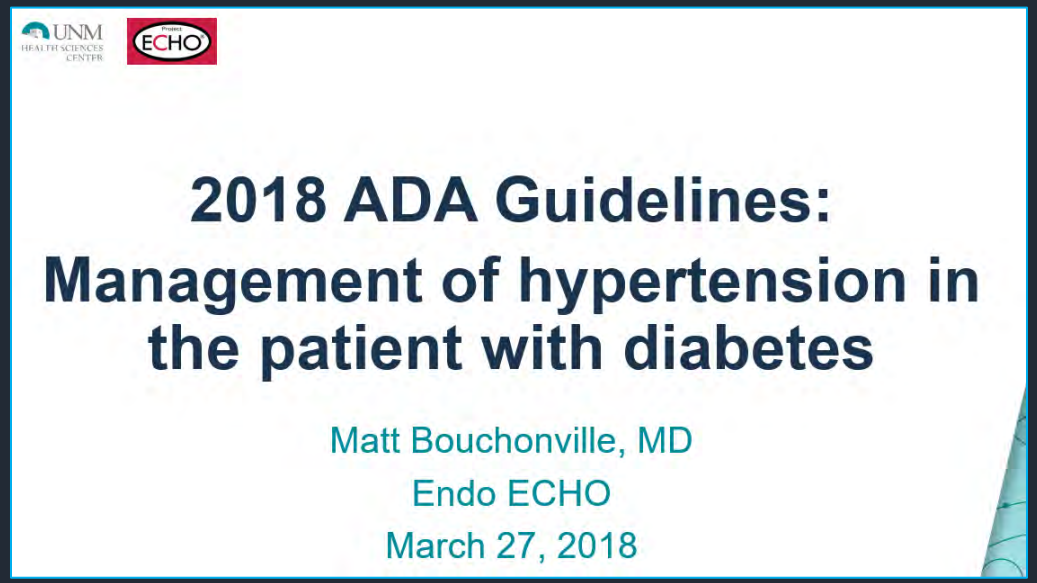
Diabetes Care 2018;41(S1).

Which of the following antihyperglycemic therapies has NOT been linked to a reduction in cardiovascular events or mortality?

A. Liraglutide
B. Pioglitazone
C. Empagliflozin
D. Sitagliptin

A1c target: < 7-8%

Blood pressure target: < 140/90



(Happy to share these slides with you!)

Cholesterol treatment: Statins

Diabetes Care 2018;41(S1).

A1c target: < 7-8%

Blood pressure target: < 140/90

Cholesterol treatment: Statins

018;41(S1).

Table 9.2—Recommendations for statin and combination treatment in adults with diabetes

Age	ASCVD	Recommended statin intensity^ and combination treatment*
<40 years	No	None†
	Yes	High • If LDL cholesterol ≥70 mg/dL despite maximally tolerated statin dose, consider adding additional LDL-lowering therapy (such as ezetimibe or PCSK9 inhibitor)#
≥40 years	No	Moderate‡
	Yes	High • If LDL cholesterol ≥70 mg/dL despite maximally tolerated statin dose, consider adding additional LDL-lowering therapy (such as ezetimibe or PCSK9 inhibitor)

*In addition to lifestyle therapy. ^For patients who do not tolerate the intended intensity of statin, the maximally tolerated statin dose should be used. †Moderate-intensity statin may be considered based on risk-benefit profile and presence of ASCVD risk factors. ASCVD risk factors include LDL cholesterol ≥100 mg/dL (2.6 mmol/L), high blood pressure, smoking, chronic kidney disease, albuminuria, and family history of premature ASCVD. ‡High-intensity statin may be considered based on risk-benefit profile and presence of ASCVD risk factors. #Adults aged <40 years with prevalent ASCVD were not well represented in clinical trials of non-statin–based LDL reduction. Before initiating combination lipid-lowering therapy, consider the potential for further ASCVD risk reduction, drug-specific adverse effects, and patient preferences.

Revised statin guidelines for 2018

- Consolidated middle and older ages
- Less aggressive recommendations for younger patients
- Increased emphasis on LDL targets

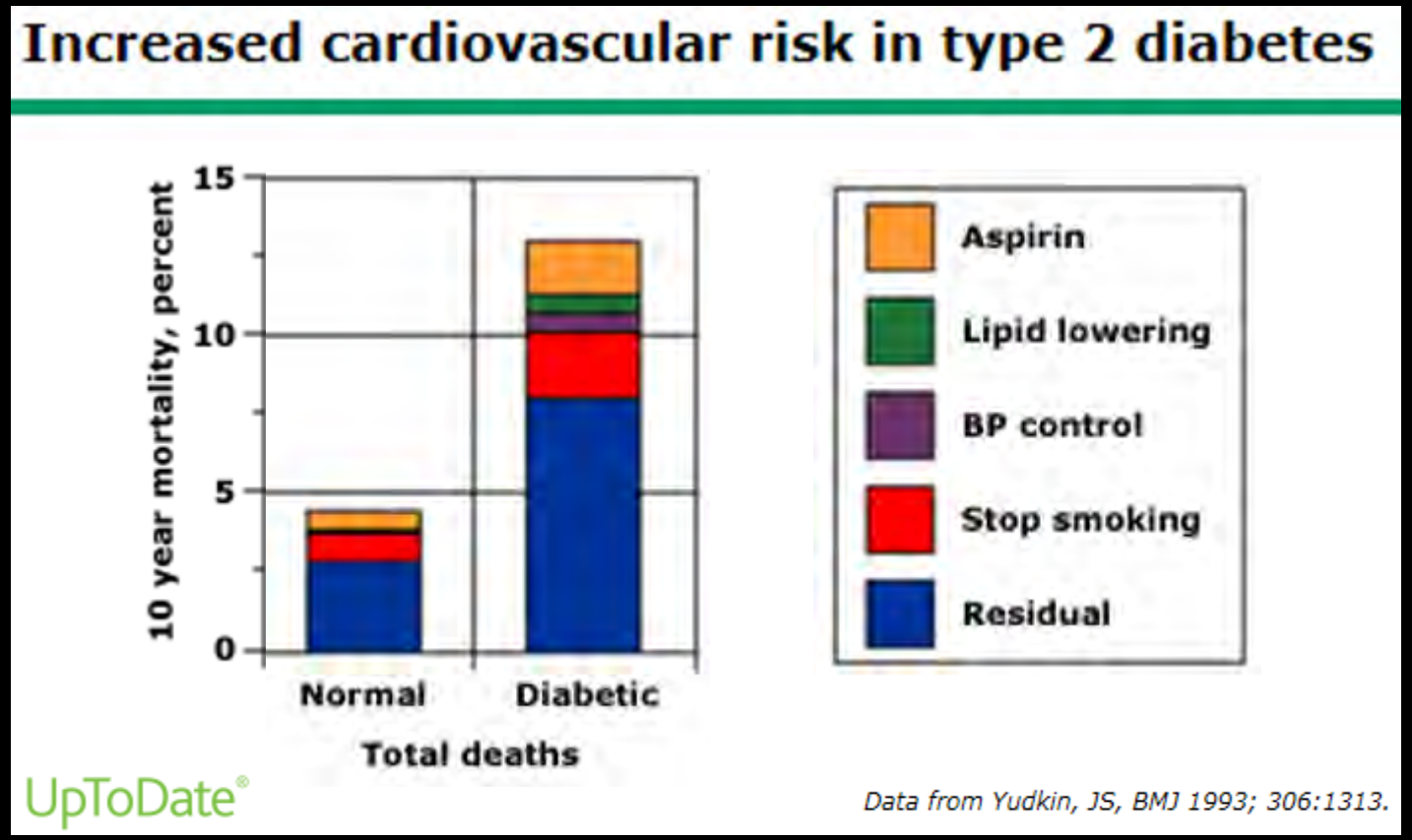
Diabetes Care 2018;41(S1).

How about other interventions besides blood glucose, blood pressure, and cholesterol lowering?

Which of the following interventions has the greatest impact on survival in patients with diabetes?

A. Blood pressure control
B. Lipid lowering
C. Aspirin
D. Smoking cessation

Smoking cessation



Meta-analysis: Smoking cessation has greater impact on survival than several other interventions

Aspirin

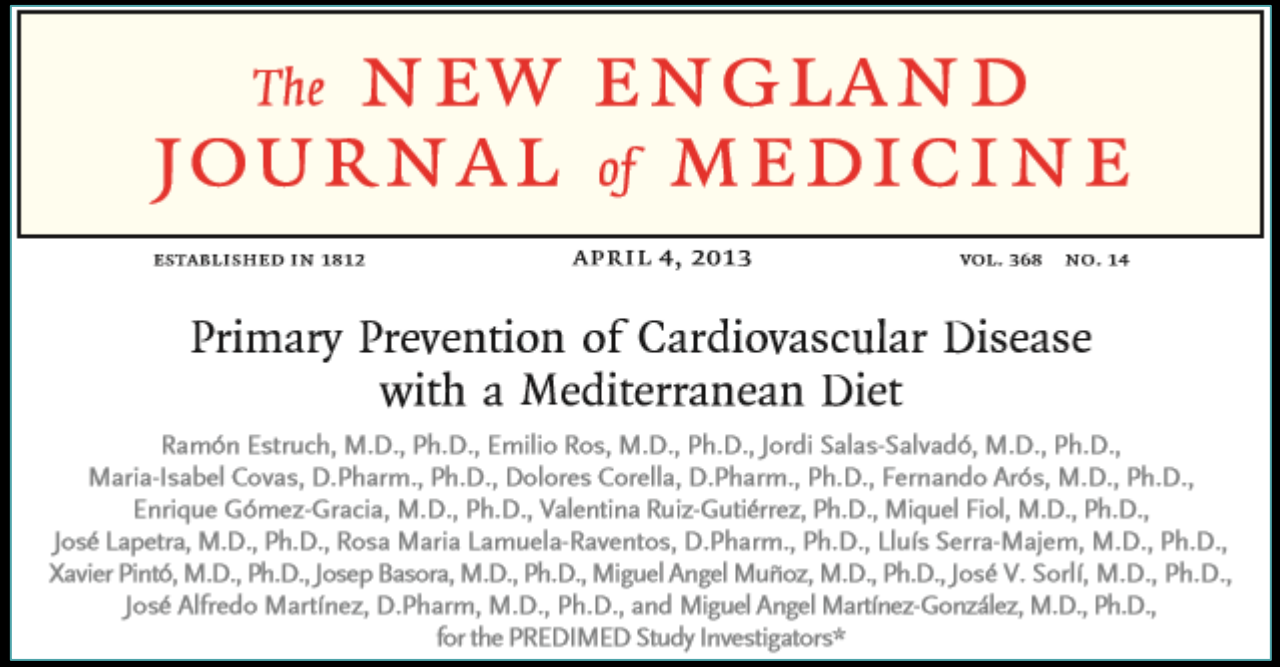
Secondary prevention

- Use aspirin therapy (75–162 mg/day) as a secondary prevention strategy in those with diabetes and a history of atherosclerotic cardiovascular disease. **A**

Primary prevention

- Aspirin therapy (75–162 mg/day) may be considered as a primary prevention strategy in those with type 1 or type 2 diabetes who are at increased cardiovascular risk. This includes most men and women with diabetes aged ≥50 years who have at least one additional major risk factor (family history of premature atherosclerotic cardiovascular disease, hypertension, dyslipidemia, smoking, or albuminuria) and are not at increased risk of bleeding. **C**

Diabetes Care 2018;41(S1).



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 4, 2013 VOL. 368 NO. 14

Primary Prevention of Cardiovascular Disease with a Mediterranean Diet

Ramón Estruch, M.D., Ph.D., Emilio Ros, M.D., Ph.D., Jordi Salas-Salvadó, M.D., Ph.D., Maria-Isabel Covas, D.Pharm., Ph.D., Dolores Corella, D.Pharm., Ph.D., Fernando Arós, M.D., Ph.D., Enrique Gómez-Gracia, M.D., Ph.D., Valentina Ruiz-Gutiérrez, Ph.D., Miquel Fiol, M.D., Ph.D., José Lapetra, M.D., Ph.D., Rosa Maria Lamuela-Raventos, D.Pharm., Ph.D., Lluís Serra-Majem, M.D., Ph.D., Xavier Pintó, M.D., Ph.D., Josep Basora, M.D., Ph.D., Miguel Angel Muñoz, M.D., Ph.D., José V. Sorlí, M.D., Ph.D., José Alfredo Martínez, D.Pharm, M.D., Ph.D., and Miguel Angel Martínez-González, M.D., Ph.D., for the PREDIMED Study Investigators*

(PREDIMED Study)

- ~7500 participants with high CV risk but NO known CVD (~50% with diabetes)
- Mediterranean diet vs low fat diet; no caloric restriction

Mediterranean diet	
Recommended	
Olive oil*	≥4 tbsp/day
Tree nuts and peanuts†	≥3 servings/wk
Fresh fruits	≥3 servings/day
Vegetables	≥2 servings/day
Fish (especially fatty fish), seafood	≥3 servings/wk
Legumes	≥3 servings/wk
Sofrito‡	≥2 servings/wk
White meat	Instead of red meat
Wine with meals (optionally, only for habitual drinkers)	≥7 glasses/wk
Discouraged	
Soda drinks	<1 drink/day
Commercial bakery goods, sweets, and pastries§	<3 servings/wk
Spread fats	<1 serving/day
Red and processed meats	<1 serving/day

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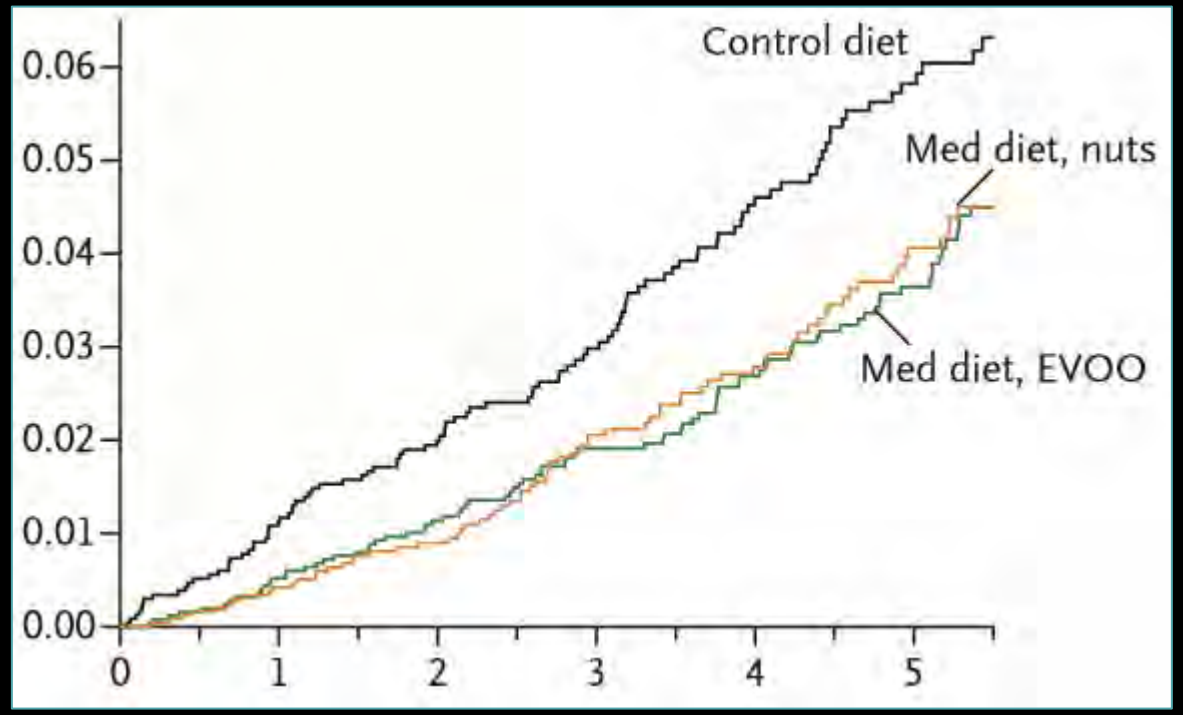
Trial stopped early at median of 4.8 yrs based on interim analysis

- Cardiovascular events cut by 30%
- NNT: 61 patients
- No adverse effects



What happens when we combine all of these interventions?

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Effect of a Multifactorial Intervention on Mortality in Type 2 Diabetes

Peter Gæde, M.D., D.M.Sc., Henrik Lund-Andersen, M.D., D.M.Sc., Hans-Henrik Parving, M.D., D.M.Sc., and Oluf Pedersen, M.D., D.M.Sc.

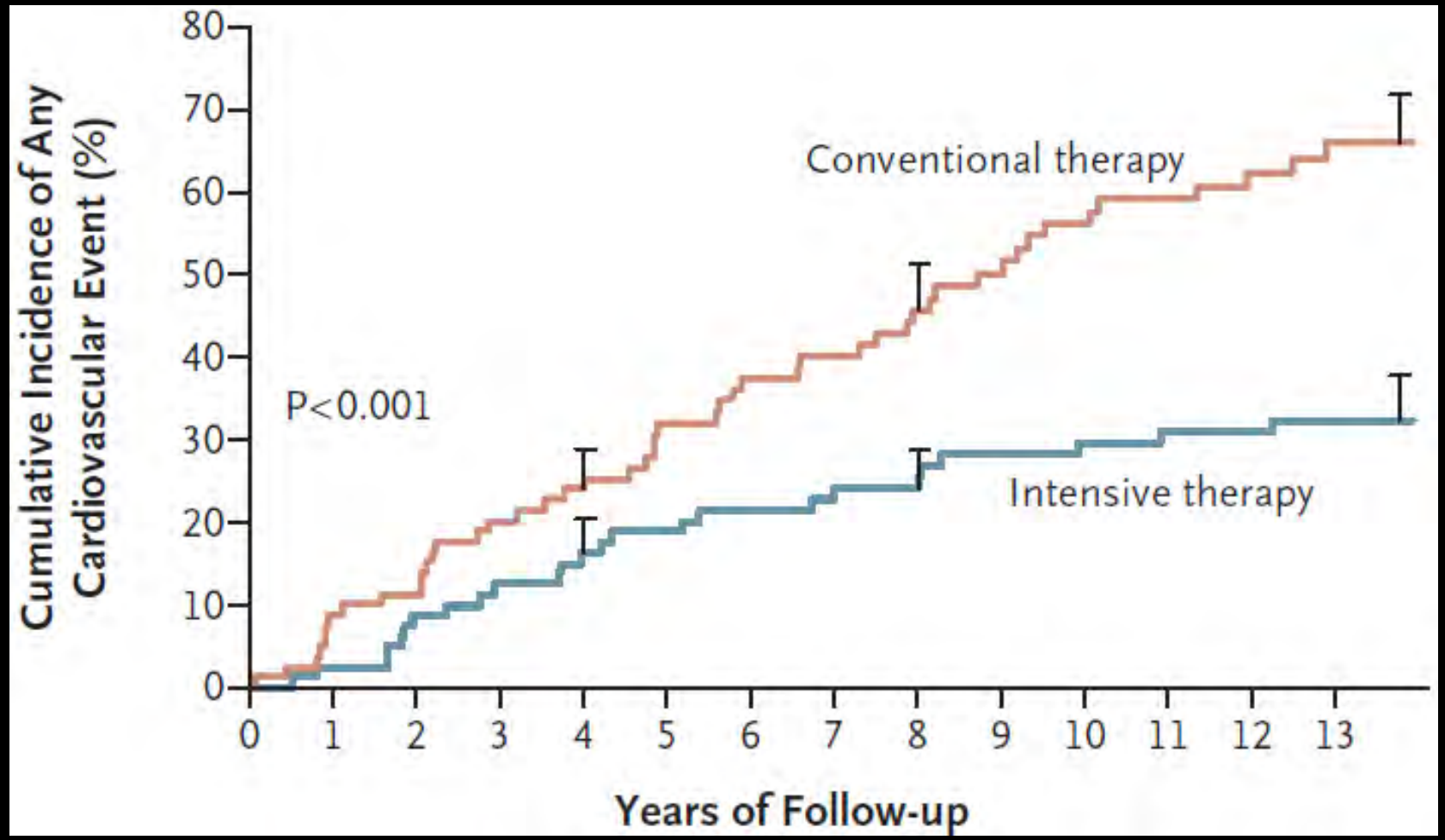
N ENGL J MED 358;6 WWW.NEJM.ORG FEBRUARY 7, 2008

Multifactorial Intervention

- **Subjects**
  - T2D (n=160)
  - Microalbuminuria
  - Mean age 55 yrs
  - Randomized to conventional vs intensive therapy
- **Goals of intervention**
  - A1c < 6.5%
  - Chol < 175 mg/dL
  - Trig < 150 mg/dL
  - SBP < 130 mmHg
  - DBP < 80 mmHg
  - ACE/ARB
  - ASA 81 mg/day

N ENGL J MED 358;6 WWW.NEJM.ORG FEBRUARY 7, 2008

Cardiovascular death reduced by 57%

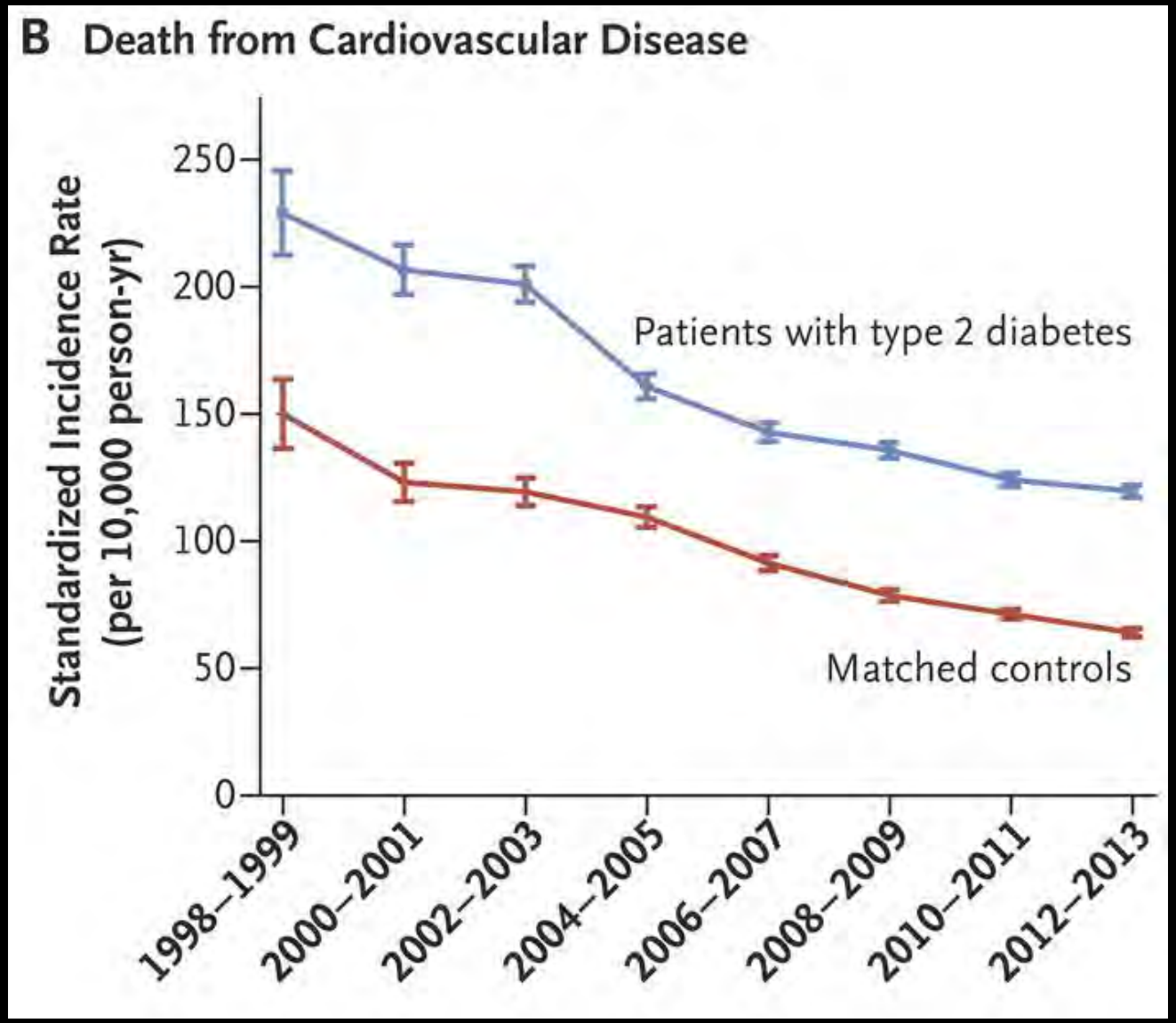


N ENGL J MED 358;6 WWW.NEJM.ORG FEBRUARY 7, 2008

Real world experience:

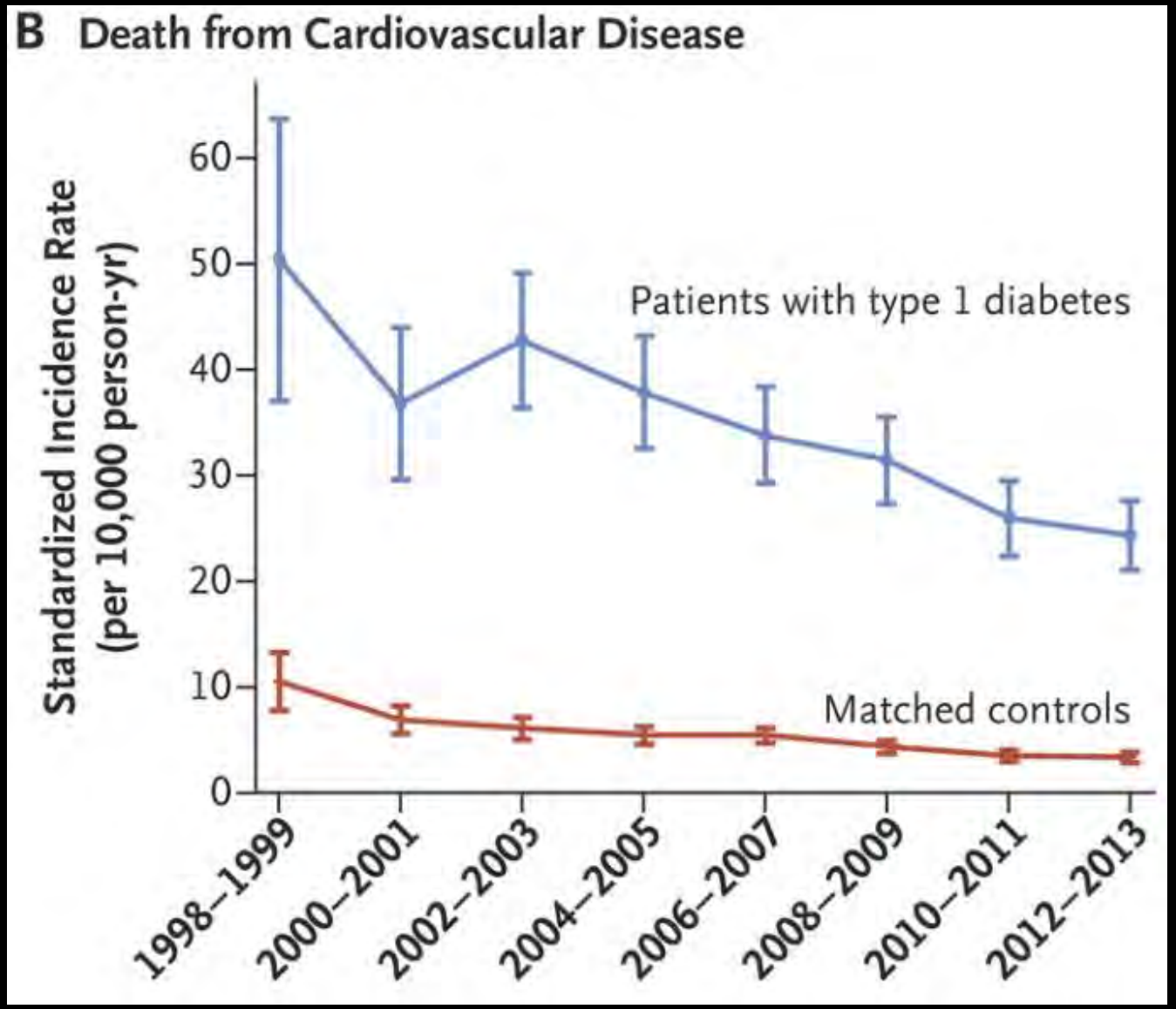
How is greater recognition of the impact of multifactorial intervention affecting cardiovascular outcomes in patients with diabetes?

Fewer patients with type 2 diabetes dying of CVD



N Engl J Med 2017;376:1407-18.

Fewer patients with type 1 diabetes dying of CVD



N Engl J Med 2017;376:1407-18.

Questions?