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







# AMERICAN DIABETES ASSOCIATION STANDARDS OF MEDICAL CARE IN DIABETES – 2018

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

#### MIDIOAL OALL

**Cholesterol treatment: Statins** 

J18;41(S1)





# 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



#### 2018 ADA Guidelines: Management of hypertension in the patient with diabetes

Matt Bouchonville, MD Endo ECHO March 27, 2018 (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** 

J18;41(S1)

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

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

\*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. ‡High-intensity statin may be considered based on risk-benefit profile and presence of 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

#### Increased cardiovascular risk in type 2 diabetes



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

#### Secondary prevention

# Aspirin



#### Primary prevention

#### Diabetes Care 2018;41(S1).

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

 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  $\geq$  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

#### The NEW ENGLAND JOURNAL of MEDICINE

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#### 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\*

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

# (PREDIMED Study)

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						
Sofritoț	≥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 ENGLJ 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

# Cardiovascular death reduced by 57%



### 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?