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Great Plains
Quality Innovation Network

Know Your Diabetes by Heart: Diabetes and Cardiovascular Disease

Eric L. Johnson, MD

February 19, 2019

Welcome and Reminders

- Use chat for questions and comments
- Slides and recording will be available on the GPQIN website in 7-10 days

  http://greatplainsqin.org

Know Your Diabetes By Heart: Diabetes and Cardiovascular Disease

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Disclosures

- Speaker’s Bureau Novo Nordisk, Medtronic
- Advisory Panel Sanofi, Novo Nordisk

AHA, ADA and Industry Leaders Unite

Know Diabetes by Heart™

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SANOFI

Leading organizations collaborate on new initiative to combat growing diabetes and cardiovascular disease threat.

Know Diabetes by Heart™

Initiative Purpose

Reducing CV deaths
and incidence of heart attacks and strokes
in people living with type 2 diabetes.

Objectives

1. Describe pathophysiology of the diabetes connection to cardiovascular disease
2. Discuss risk factors that increase risk for heart attack and stroke
3. Discuss techniques that can be employed to educate and engage patients to decrease risk of heart attack and stroke in the context of diabetes
4. State recommended blood pressure targets (AHA and ADA), blood glucose targets (ADA), and A1C (ADA)
5. Discuss how to use data to drive change and avoid clinical inertia

American Heart Association Get With the Guidelines®
American Diabetes AssociationDiabetes INSIDE®

- Using Data to Drive Change

- Using data effectively is critical to improve care quality. As technology continues to advance, our ability to generate data evolves at a rapid pace. However, many healthcare organizations struggle to access, analyze and meaningfully use their data to inform and drive change.

- AHA's Get With the Guidelines® programs and ADA's Diabetes INSIDE® initiative are designed to help healthcare organizations better apply clinical guidelines and use their data to continually measure and monitor care processes over time, and to use these insights to inform constant and deliberate change to improve the lives of the patients they serve.

Diabetes

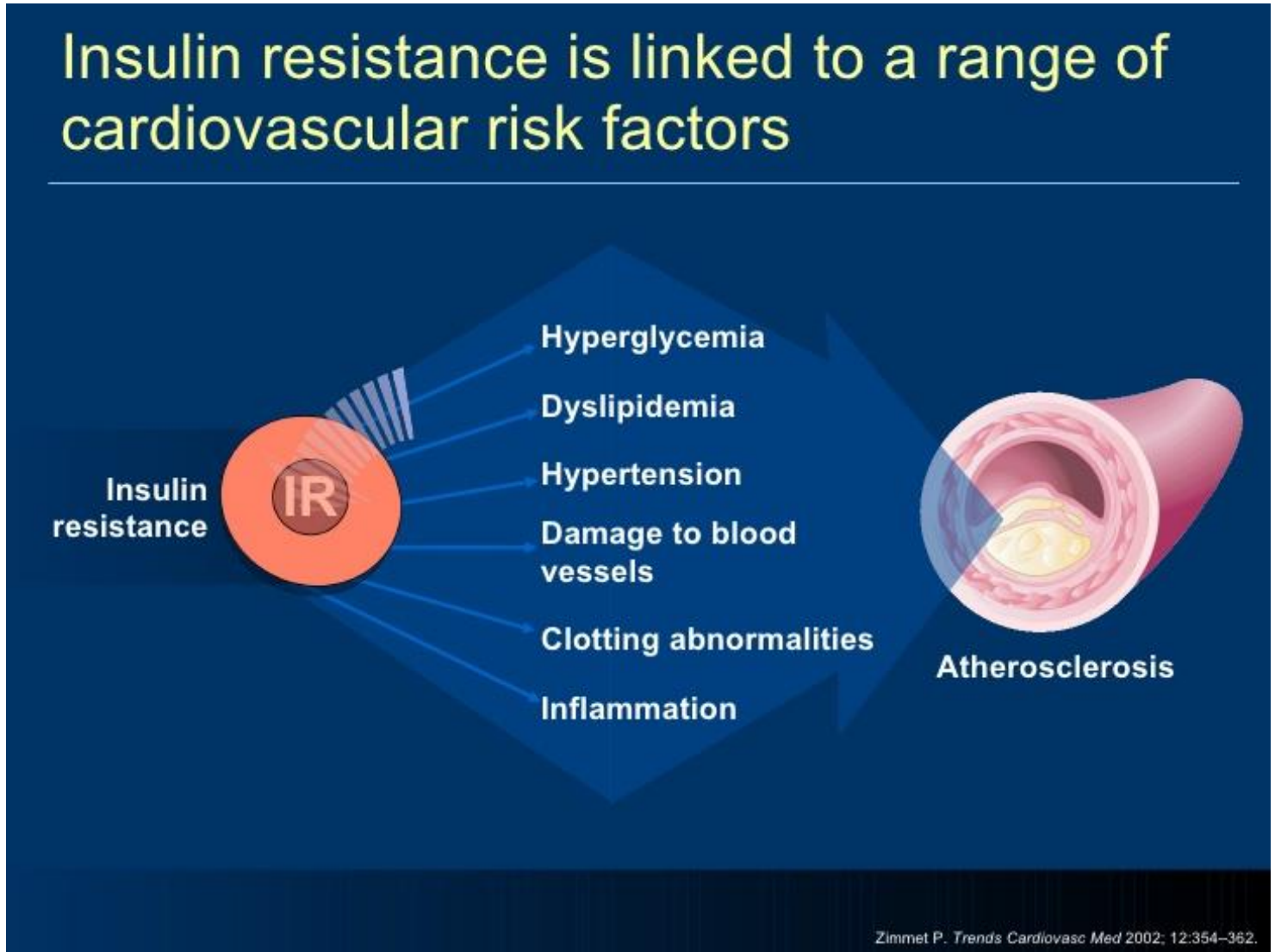
- About 30.3 million people have diabetes in the U.S.
- About 83 million people have prediabetes in the U.S.

Diabetes Complications

Macrovascular Complications

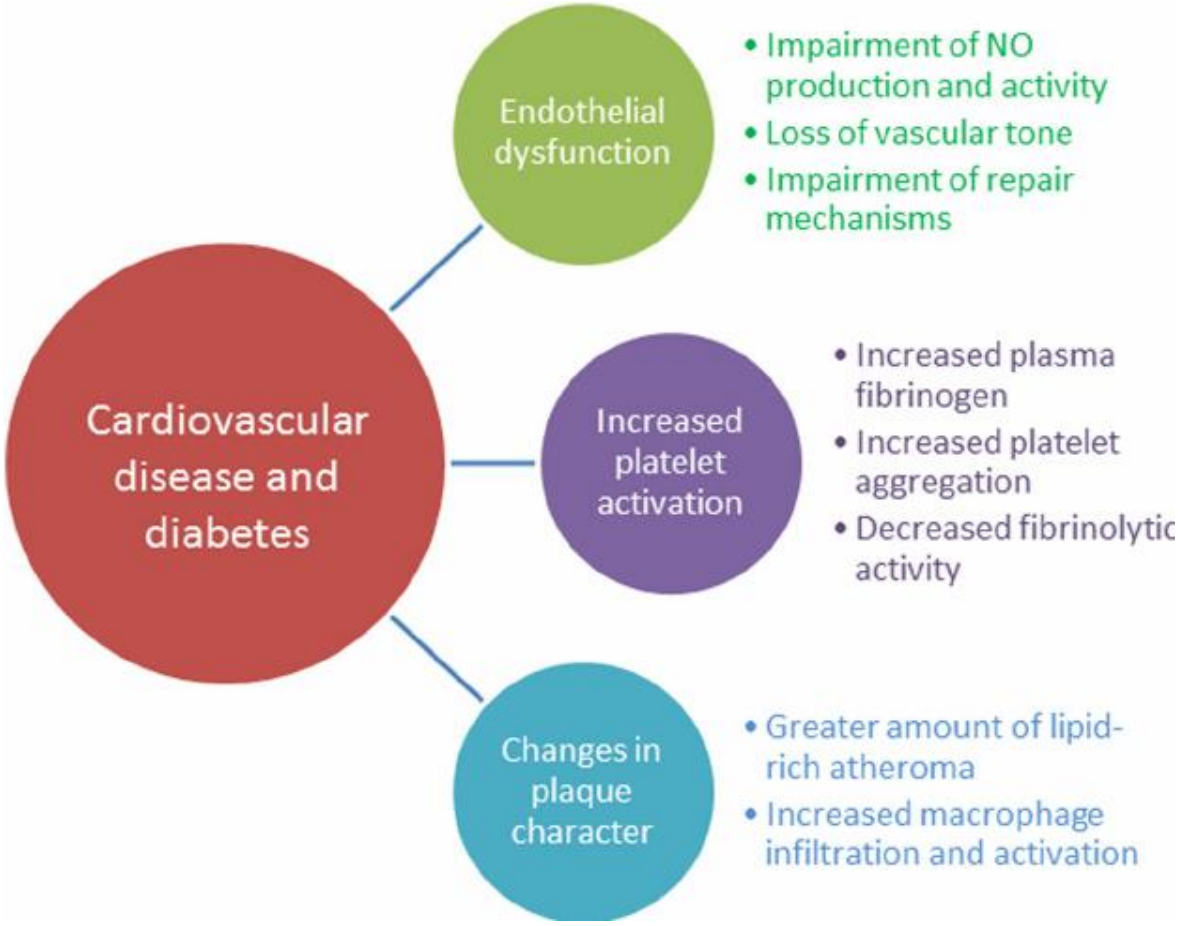
- Cardiovascular disease
  - Coronary Heart disease (CHD)
  - Stroke
  - Peripheral arterial disease (PAD)/amputation

Insulin Resistance



Pathophysiology of the connection between diabetes and cardiovascular disease

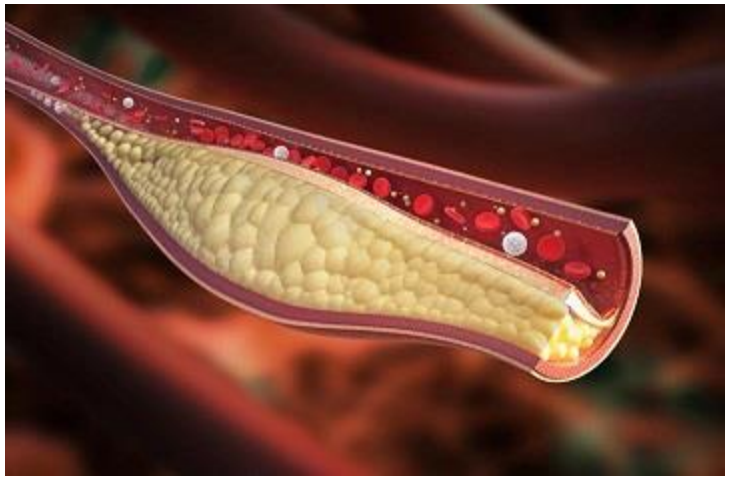
- Hyperglycemia
  - A1C? Variability, postprandial
- Chronic inflammation and thrombosis
- Dyslipidemia and atherogenesis
- Hypertension
- Inflammatory cytokines
- Endothelial dysfunction
- Oxidative stress



Adv Exp Med Biol. 2012;771:139-54
Current Cardiology Reports 17(3):566 · March 2015
Cardiovascular Endocrinology & Metabolism 7(1) 4-9: March 2018

Risk Factors for Atherosclerotic Cardiovascular Disease (ASCVD)

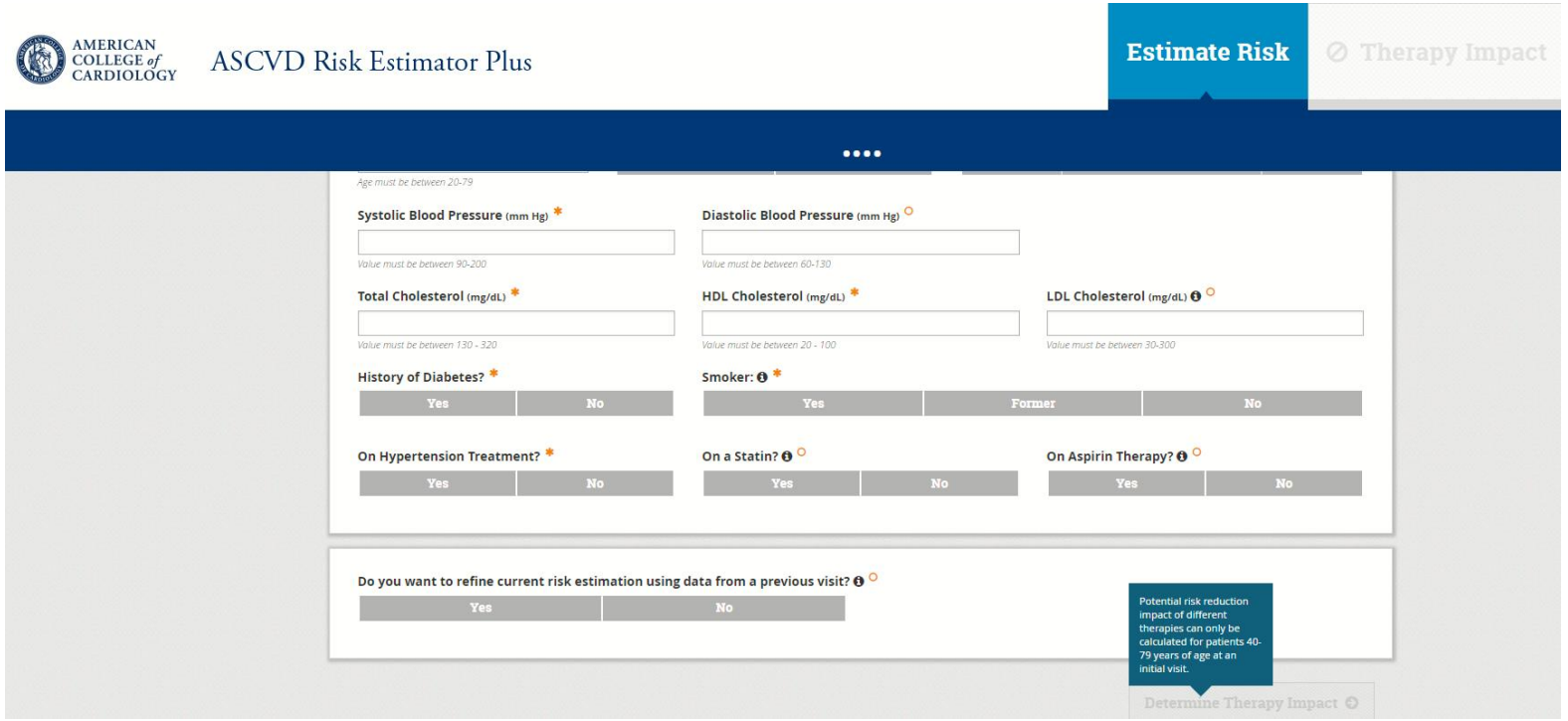
- Diabetes/Insulin resistance
- Hypertension
- Hypercholesterolemia/dyslipidemia
- Cigarette smoking
- Family history
- Sedentary lifestyle/obesity
- Post-menopausal-women
- Over 45- men



AHA CDC

Risk Calculator

The American College of Cardiology/ American Heart Association ASCVD risk calculator (Risk Estimator Plus) is generally a useful tool to estimate 10-year ASCVD risk



tools.acc.org/ASCVD-Risk-Estimator-Plus

Blood Pressure and Lipids

Cardiovascular Disease

Cardiovascular Disease

Risk:

- Stroke 2 to 4 times higher
- Heart Disease 2 to 4 times higher
- ~70% of diabetes patients have high blood pressure (hypertension)
- ~70% of people with diabetes have a dyslipidemia (cholesterol disease)
- Diabetes confers risk about the same as pre-existing CVD in persons without diabetes
- Patients with diabetes have a reduction in life expectancy of about 4–8 years, compared with individuals without diabetes
- At least 68% of adults with diabetes die from some form of heart disease, 16% die of stroke

WHO ADA AHA

Cardiovascular Disease

- **Routine screening of asymptomatic not recommended**
- Treat risk factors (lipids, BP, smoking, etc)
- Those with diabetes are high risk

American Diabetes Association. Diabetes Care. 2019;42(suppl 1)

Blood Pressure

- Done at every visit (x2?)
- Target is <140/<90 (<130/<80)
- Consider weight loss if BP >120/>80

American Diabetes Association. *Diabetes Care.* 2019;42(suppl 1)

Hypertension Treatment in Diabetes

Lifestyle management for all

- Initial BP between 140/90 and 160/100
- Start one agent
  - ACE
  - ARB
  - Calcium channel blocker
  - Thiazide diuretic

- Initial BP greater than 160/100
- Start two agents
  - ACE or ARB
  - Calcium channel blocker
  - Thiazide diuretic

- **If albuminuria, should have ACE or ARB**

- **Consider mineralocorticoid receptor agonist (i.e., spironolactone) if not meeting target on 3 agents**
- **Consider specialty referral if not meeting targets**

American Diabetes Association. Diabetes Care. 2019;42(suppl 1)

Hypertension Treatment

- Lowering blood pressure reduces CVD and kidney disease
- Caveat: worsening renal function on ACEI or ARB warrants imaging of kidneys/renal arteries or nephrology referral
- If on more than one anti-hypertensive, consider giving one at bedtime

American Diabetes Association. Diabetes Care. 2019;42(suppl 1)

Lipids (Cholesterol)

- Increased cardiovascular risk (e.g., LDL cholesterol ≥100mg/dL [2.6 mmol/L], high blood pressure, smoking, albuminuria, and family history of premature ASCVD) and with ASCVD
- Obtain a lipid profile at initiation of statin therapy and periodically thereafter because doing so may help monitor the response to therapy and inform about adherence

American Diabetes Association. Diabetes Care. 2019;42(suppl 1)

Lipids and Cardiovascular Complications:

"target normal"

- Total cholesterol <200
- Triglycerides <150
- HDL ("good") >40 men, >50 women
- LDL ("bad") <100, <70 high risk

These are no longer "targets", but abnormals represent "at risk"

American Diabetes Association. Diabetes Care. 2019;42(suppl 1)

Anti-Lipid Therapy

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.

ASCVD risk factors include:

- **LDL cholesterol ≥ 100**
- **high blood pressure,**
- **smoking,**
- **overweight or obesity,**
- **family history of premature ASCVD**

*In addition to lifestyle therapy.

American Diabetes Association. Diabetes Care. 2019;42(suppl 1)

Statin Intensity

High–intensity statin therapy	Moderate–intensity statin therapy
Lowers LDL by ≥ 50: Atorvastatin 40–80 mg Rosuvastatin 20–40 mg	Lowers LDL by 30% to <50%: Atorvastatin 10–20 mg Rosuvastatin 5–10 mg Simvastatin 20–40 mg Pravastatin 40–80 mg Lovastatin 40 mg Fluvastatin XL 80 mg Pitavastatin 2–4 mg

American Diabetes Association. Diabetes Care. 2019;42(suppl 1)

Commonly Used Anti-Lipid Medications

- Statins
  - Potent
  - Lower total cholesterol, LDL most effectively
  - Cut CVD risk by ~30%

- Ezetimibe (add if not meeting target on maximally targeted statin)
- PCSK-9 inhibitor

  - Obtain a lipid profile at initiation of statins or other lipid-lowering therapy, 4–12 weeks after initiation or a change in dose, and annually thereafter as it may help to monitor the response to therapy and inform adherence.

Anti-Lipid Medications

Caveats:

- Use with caution in known liver disease
  (but may improve fatty liver-NAFLD)
- Use with caution in more advanced kidney disease (usually dose reduction)
- Increasing muscle aches- rare complication of rhabdomyolysis

Package inserts

Summary:
Blood Pressure and Lipids Treatment

BP:

ACEI or ARB if albuminuria or proteinuria

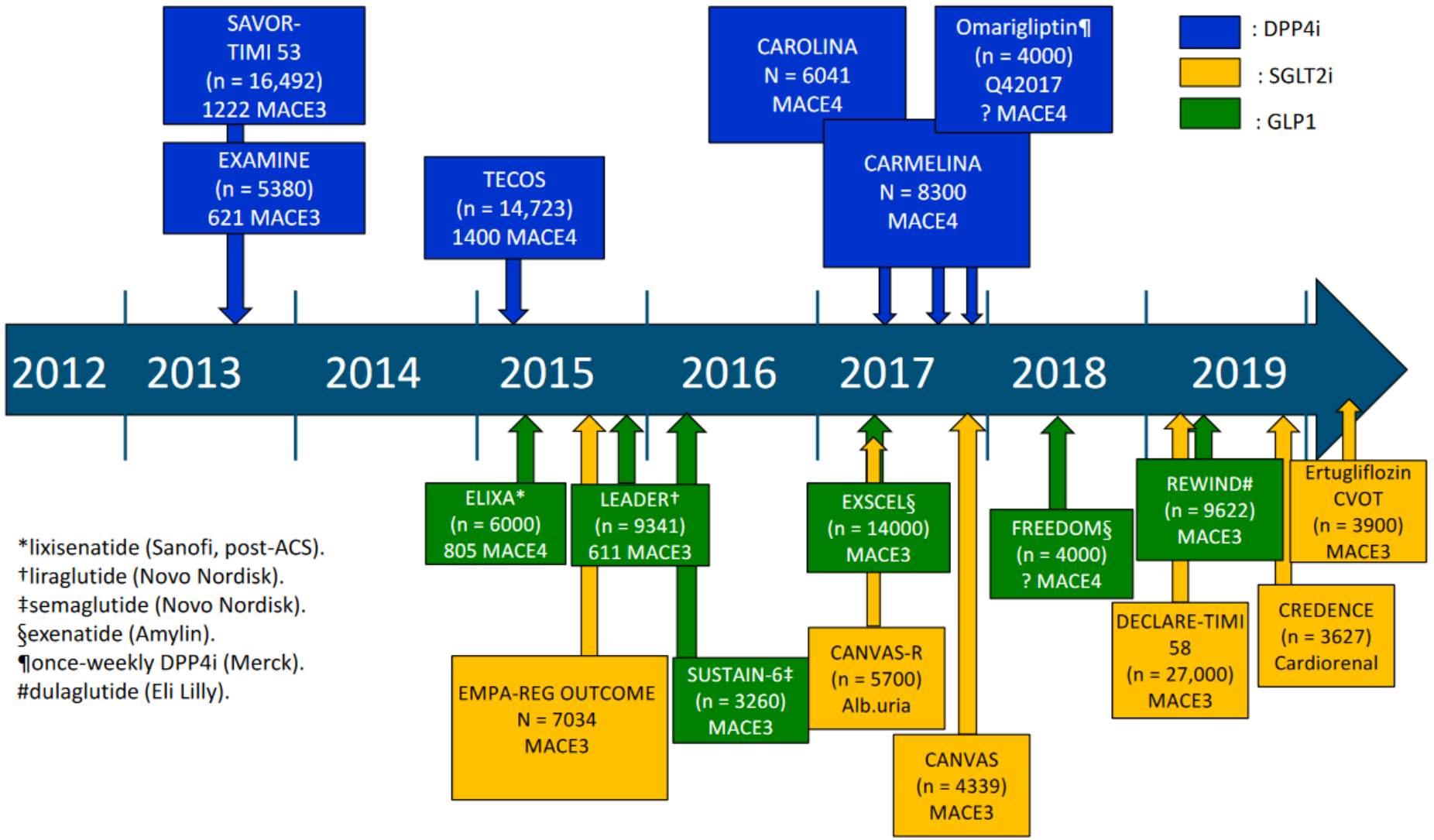
Lipids:

- Statins first line +/- ezitimibe
- Fibrates, Fish Oil, Niacin, Colsevelam not a lot of good outcome data
- PCSK-9 (add data here)

Treating these appropriately aggressively reduces CVD and renal disease

Anti-hyperglycemic Medications and ASCVD

Major CV Outcome Trials in Type 2 Diabetes



*lixisenatide (Sanofi, post-ACS).
†liraglutide (Novo Nordisk).
‡semaglutide (Novo Nordisk).
§exenatide (Amylin).
¶once-weekly DPP4i (Merck).
#dulaglutide (Eli Lilly).

A1C and CVD Outcomes

- DCCT: Trend toward lower risk of CVD events with intensive control (T1D)
- EDIC: 57% reduction in risk of nonfatal MI, stroke, or CVD death (T1D)
- UKPDS: nonsignificant reduction in CVD events (T2D).
- ACCORD, ADVANCE, VADT suggested no significant reduction in CVD outcomes with intensive glycemic control. (T2D)
- Post-prandial glucose and glucose variablility may be related to CVD

American Diabetes Association. Diabetes Care. 2019;42(suppl 1)

Glycemic Recommendations: Individualized Treatment

A1C

- **<7.0%***

Preprandial capillary plasma glucose

- **80–130 mg/dL***
  (4.4–7.2 mmol/L)

Peak postprandial capillary plasma glucose†

- **<180 mg/dL***
  (<10.0 mmol/L)

More or less stringent glycemic goals may be appropriate for individual patients. Goals should be individualized based on duration of diabetes, age/life expectancy, comorbid conditions, known CVD or advanced microvascular complications, hypoglycemia unawareness, and individual patient considerations.

† Postprandial glucose measurements should be made 1–2 h after the beginning of the meal, generally peak levels in patients with diabetes

American Diabetes Association. 8. Pharmacologic approaches to glycemic treatment: Standards of Medical Care in Diabetes. *Diabetes Care* 2019; 42 (Suppl. 1)

October 2018 ADA/EASD Consensus Statement
Antihyperglycemic Medication in T2D: Overall Approach

First-line therapy is Metformin and comprehensive lifestyle (including weight management and physical activity)

Established ASCVD or Chronic Kidney Disease (CKD)

NO

Without Established ASCVD or CKD:
Individualize based on need to minimize hypoglycemia, address weight loss, or costs

ASCVD Predominates

GLP-1 agonist with proven CVD benefit

EITHER/OR

SGLT-2 inhibitor with proven CVD benefit if eGFR adequate

If HbA_{1c} above target

If further intensification is required or patient is now unable to tolerate GLP-1 agonist and/or SGLT-2 inhibitor,
Consider adding the other class with proven CVD benefit

- DPP-4 inhibitor if not on GLP-1 agonist
- Basal insulin, TZD, SU

Heart Failure or CKD Predominates

PREFERABLY: SGLT-2 inhibitor with evidence of reducing HF and/or CKD in cardiovascular outcome trials if eGFR adequate

OR

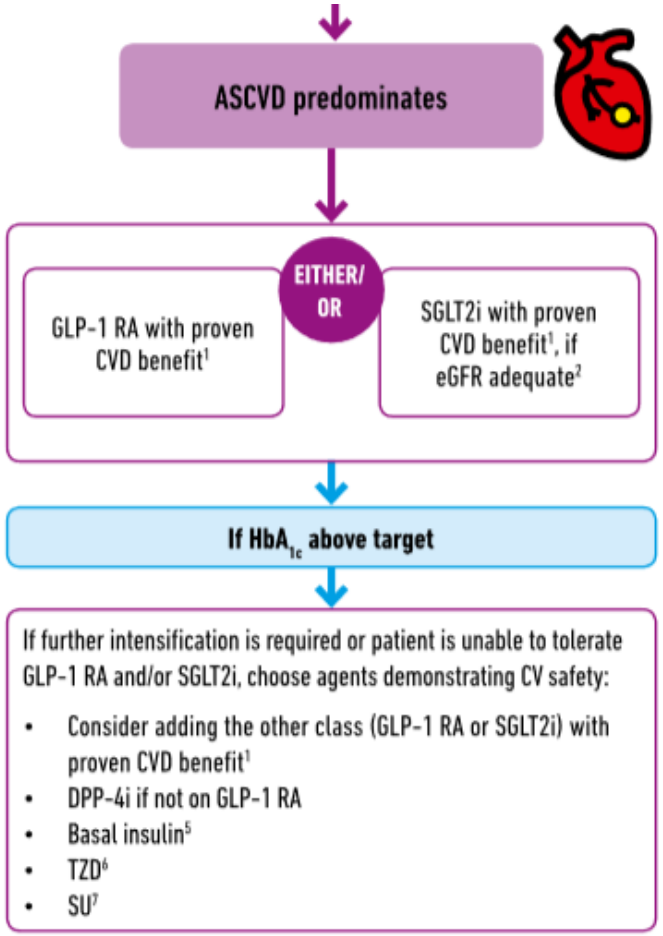
If SLGT-2 inhibitor not tolerated or contraindicated, GLP-1 agonist with proven CVD benefit if eGFR less than adequate

If HbA_{1c} above target

- Avoid TZD in the setting of heart failure
- Consider adding the other class with proven CVD benefit
- DPP-4 inhibitor (not saxagliptin) if not on GLP-1 agonist
- Basal insulin, SU

Davies MJ et al. *Diabetes Care*. [published online October 5, 2018].

Choosing an anti-hyperglycemic agent

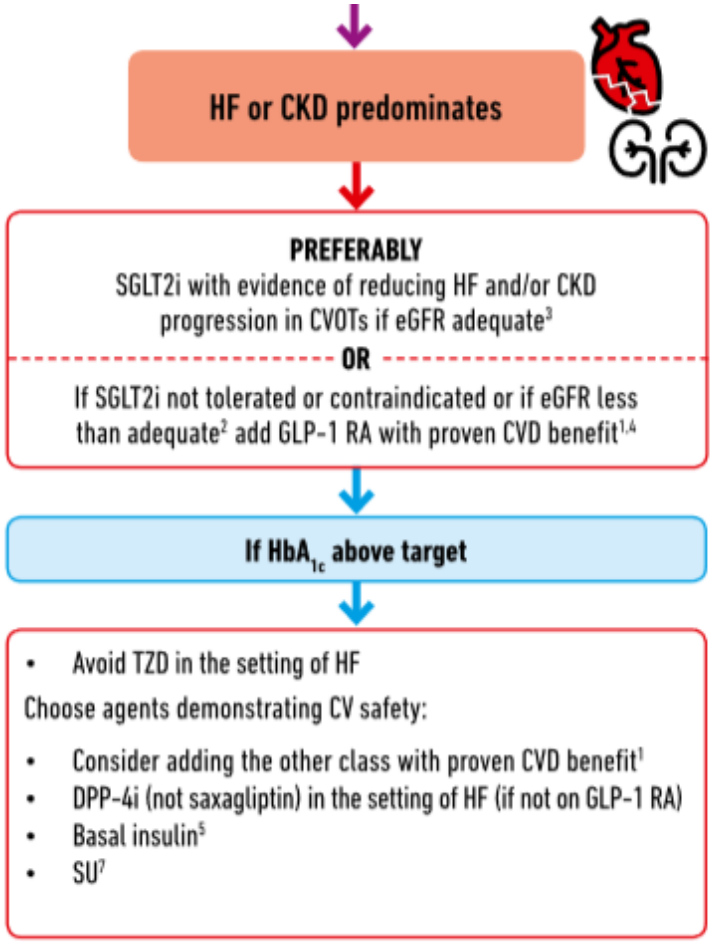


SGLT-2 with CVD Benefit:
Canagliflozin (CVD Death)
Empaglifolozin

GLP-1 with CVD Benefit:
Liraglutide
Semaglutide (stroke?, short study)

Diabetes Care 2018 Sep; dci180033.

Choosing an anti-hyperglycemic agent



Diabetes Care 2018 Sep; dci180033.

Case 1: MT

- MT is a 58-year-old Hispanic female
- T2DM x 11 years with dyslipidemia, HTN, albuminuria, non-painful peripheral neuropathy, obesity, non-alcoholic fatty liver disease (NAFLD), history of myocardial infarction (MI) 3 years ago
- Current medications:
  - Metformin 1000 mg orally twice a day
  - Glipizide 10 mg orally once daily
  - Pioglitazone 30 mg orally once daily
  - Lisinopril 20 mg orally once daily
  - Metoprolol XL 25 mg orally once daily
  - Atorvastatin 80 mg orally once daily
  - Aspirin 81 mg orally once daily

Case 1: MT

- **Physical exam**
  - Nonproliferative retinopathy, normal heart and lung sounds, obese, decreased vibratory and filament sensation in otherwise healthy appearing feet
- **Concerns**
  - Many blood sugars in 200-300s mg/dL , but occasionally less than 70 mg/dL
  - Fatigue
  - Difficulty losing weight
  - Urinary frequency
- **Labs**
  - A1C 10.2%
  - Lipids in target range (on high intensity statin), serum creatinine 0.9 mg/dL, GFR 54 mL/minute/1.73 m^2, hepatic function revealing minor transaminase elevation, urine albumin 110 mg/24 hr (normal <30 mg/24 hr)

What next?

Case 1: MT

- Recall current standards of care recommend a SGLT-2 inhibitor (empagliflozin, canagliflozin) or a GLP-1 agonist (dulaglutide,liraglutide, semaglutide) in the patient with established cardiovascular disease
- One of patient's main complaints is difficulty losing weight, both of these drug classes are weight-neutral or may promote weight loss
- Basal insulin could also be considered here- A1C greater than 10% with symptoms

Case 1: MT

- **Could do any of the following in the patient with established CVD**
  - Add liraglutide, semaglutide, or dulaglutide (drug class: GLP-1 agonist)
  - Add empagliflozin, canagliflozin, or dapagliflozin (drug class: SGLT-2 inhibitor)
  - Using both GLP-1 agonist or SGLT-2 inhibitor for maximal weight loss
- **Would definitely**
  - Continue metformin (renal function is OK)
  - Refer to diabetes educator and dietician for interprofessional team care
  - Review physical activity level/exercise prescription
  - Stop glipizide
  - Stop pioglitazone

Case 1: MT Summary

- What if A1C was not at target in 3 months?
  - If not on insulin yet, would definitely consider
- Advance therapy, avoid clinical inertia
- Remember appropriate interprofessional team-based diabetes self-management education and support

Smoking

- Refer to appropriate resources
- Consider FDA approved medications
- E-cigs are NOT recommended at this time

American Diabetes Assocation
Standards of Care 2016

Aspirin

- If no contraindications
- Men >50 years of age
- Women >50 years of age
- Younger if higher risk

American Diabetes Association. Diabetes Care. 2019;42(suppl 1)

Educate patients about ASCVD Risk In the Context of Diabetes

Risk:

- Stroke 2 to 4 times higher
- Heart Disease 2 to 4 times higher
- ~70% of diabetes patients have high blood pressure (hypertension)
- ~70% of people with diabetes have a dyslipidemia (cholesterol disease)
- Diabetes confers risk about the same as pre-existing CVD in persons without diabetes
- Patients with diabetes have a reduction in life expectancy of about 4–8 years, compared with individuals without diabetes
- At least 68% of adults with diabetes die from some form of heart disease, 16% die of stroke
- Treatment matters!

Heart Disease and Stroke Symptoms

- Educate patients about heart disease and stroke symptoms
- I have seen patients with fairly advanced disease without a lot of symptomotology
- Large knowledge gaps exist with patients

Summary: Cardiovascular Risk in Diabetes

- Assess a patient's cardiovascular risk at least annually in all patients with diabetes
- Individualizing targets for antihypertensive therapy can reduce ASCVD events, heart failure, and microvascular complications
- Statin therapy has beneficial effects on ASCVD outcomes
- Aspirin is effective in reducing CV morbidity and mortality in high-risk patients with previous MI/stroke
- Certain antihyperglycemic therapies can reduce major adverse CV events and mortality

American Diabetes Association. Diabetes Care. 2019;42(suppl 1)

Avoiding Clinical Inertia

- Talking to patients about drug benefits/safety
  - https://www.heart.org/en/news/2018/12/10/safety-of-statins-emphasized-in-new-report
- Translate numbers into something meaningful- we aren't just chasing numbers
- When they should call
- Always include lifestyle counseling/reinforcement
- Meet people where they are at (i.e., motivational interviewing)

QI Systems Improvement- AHA and ADA

Inpatient:

- Get With The Guidelines® Diabetes Measure Improvement (Afib, HF, Stroke and CAD)
- Diabetes INSIDE (ADA Initiative)

Ambulatory:

- Diabetes INSIDE (ADA Initiative)
- •Ambulatory Diabetes Measure and Recognition Program

Core Principles of Get With The Guidelines®

Know Diabetes by Heart™

- Focus is on quality improvement
- Success is in translating guidelines into clinical practice in the hospital setting
- Capitalizing on the 'teachable moment' for both patient and family
- Data drives change- moving from simply collecting data to driving process and system improvements by measuring trends in compliance in real time
- National recognition opportunities celebrating success of improved compliance within one hospital, in a region, and across the country!
- Best Practice sharing within the network of hospitals
- Evaluation through analytics to highlight key insights as well as consider future efforts

In Closing

- Diabetes/prediabetes are very common
- Well established link between CVD and diabetes
- Evidence is strong for risk factor management

Resources

- www.knowdiabetesbyheart.org
- www.knowdiabetebyheart.org/professional

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