Management of Type 2 Diabetes: 2021 ADA Recommendations

Natalie Levy, MD
Associate Professor, NYU School of Medicine
Director, Bellevue Primary Care Diabetes Program

2_5_21
Type 2 Diabetes: ADA management recommendations

- Blood Glucose
- Blood Pressure
- LDL
- If time allows
  - Pre Diabetes
  - DM Outreach in the Time of Covid
Standards of Medical Care in Diabetes—2021 Abridged for Primary Care Providers

American Diabetes Association

The American Diabetes Association (ADA) Standards of Medical Care in Diabetes is updated and published annually in a supplement to the January issue of Diabetes Care. The Standards are developed by the ADA’s multidisciplinary Professional Practice Committee, which comprises physicians, diabetes educators, and other expert diabetes health care professionals. The Standards include the most current evidence-based recommendations for diagnosing and treating adults and children with all forms of diabetes. ADA's grading system uses A, B, C, or E to show the evidence level that supports each recommendation.

- **A**—Clear evidence from well-conducted, generalizable randomized controlled trials that are adequately powered
- **B**—Supportive evidence from well-conducted cohort studies
- **C**—Supportive evidence from poorly controlled or uncontrolled studies
- **E**—Expert consensus or clinical experience

Thus, efforts to improve population health will require a combination of policy-level, system-level, and patient-level approaches. Patient-centered care is defined as care that considers individual patient comorbidities and prognoses; is respectful of and responsive to patient preferences, needs, and values; and ensures that patient values guide all clinical decisions. Further, social determinants of health (SDOH)—often out of direct control of the individual and potentially representing lifelong risk—contribute to medical and psychosocial outcomes and must be addressed to improve all health outcomes.

**Recommendations**

1. Align approaches to diabetes management with the Chronic Care Model (CCM). This model emphasizes person-centered team care, integrated long-term treatment approaches to diabetes and comorbidities, and ongoing collaborative communication and goal setting between all team members.
Blood Glucose

• Blood Glucose-lowering Medication Framework: ADA 2021
• Review GLP1-RA
• Review SGLT2i
• Operationalize This
• Pop-Quiz Questions
GLP1-RA

• Glucagon-like Peptide 1 Receptor Agonist
• GLP1: Secreted by the L cells in the small intestine
  • Increase Insulin
  • Decrease Glucagon
  • Slow gastric emptying
  • Increase satiety
  • Improved Blood Glucose Control
Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes

Steven P. Marso, M.D., Gilbert H. Daniels, M.D., Kirstine Brown-Brandes, M.D., Peter Kristensen, M.D., E.M.B.A.,

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Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): a double-blind, randomised placebo-controlled trial

Hertzl C Gerstein, Helen M Colhoun, Gilles R Dagenais, Rafael Diaz, Mark Lakshmanan, Prem Pais, Jeffrey Probstfield, Jeffrey S Riesmeyer, Matthew C Riddle, Lars Ryden, Denis Xavier, Charles Messer Alisso, Leanne Dyal, Stephanie Hall, Pomima Rau-Melanie, Gloria Wong, Alvaro Aviles, Jon Basile, Namtik Chung, Ignacio Conget, William C Cushman, Edward Frank, Nicolee Hanco, Markoff Hantfeld, Shaun Holt, Petz Jankny, Mikel Izabal, Fernando Lanas, Lawrence A Letter, Patricia Lopez-Jaramillo, Ernesto German Cardona Munoz, Valdis Pirags, Nana Pogosova, Peter J RauBenheimer, Jonathan F Shaw, Wayne H-H Sheu, Theodore Temelkova-Kircktschev, for the REWIND investigators*

Summary
Background Three different glucagon-like peptide-1 (GLP-1) receptor agonists reduce cardiovascular outcomes in

Lancet 2019, 394: 321-30
<table>
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GLP1-RA and MACE: Mechanism of Action

• GLP1-RA...
  • Lower Blood Glucose
  • Lower Weight
  • Lower Blood pressure

• MACE
  • Effects on Blood Glucose, Weight, Blood Pressure: Certainly contribute
  • However, the overall effect on MACE is out of proportion to the Blood Glucose, Weight, BP effects seen w these medications
  • There are felt to be Direct Mechanisms that are cardioprotective
GLP-1

↓ Inflammation
↑ Glucose uptake
↓ Ischemic injury
↑ LV Function
↑ Heart rate

↓ Inflammation
↑ Endothelial Function
↓ Smooth muscle proliferation
↓ Platelet Aggregation

↑ Vasodilation
↑ Plaque Stability
↑ Blood Flow

GLP-1R

Daniel J. Drucker¹,*
Cell Metabolism 24, July 12, 2016
GLP1-RA- Patient Selection

• Ideal patient
  • Hx ASCVD
  • Overweight
  • Important to avoid hypoglycemia
  • Needs significant A1c lowering
  • Liraglutide, Dulaglutide, Semaglutide- not cleared by the kidney, can use w low GFR

• Avoid if History of
  • Gastroparesis
  • Pancreatitits
  • Medullary Thyroid Cancer or MEN2

• Side Effects / Warnings
  • N/V/D. Stop if anything more than mild
  • Severe abdominal pain: Acute Gallstone Disease, Pancreatititis
  • Retinopathy (Semaglutide, likely because it is the strongest)
GLP1-RA- Prescribing

• Liraglutide SQ
  • 0.6mg daily for 2 weeks => 1.2mg daily automatically; 1.8mg if needed
  • Small pen needle, 32 gauge 4mm
  • Significant GI effects possible

• Dulaglutide SQ
  • Less GI side effects
  • Weekly instead of daily
  • 0.75 mg once weekly; 1.5 mg if needed
  • Device is great: single use
  • Needle is embedded: patient never has to handle or see the needle
  • Dispense #4 for one month

• Semaglutide SQ (or po)
  • 0.25mg weekly for 4 weeks => 0.5mg weekly automatically; 1.0 mg weekly if needed
  • Oral
    • 3mg => 7mg at 4 weeks; 14mg daily if needed
    • ≥ 30 min before the first meal, solo, daily
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SGLT2i

• Sodium Glucose Co-Transporter 2 Inhibitor
  • SGLT2 is in the proximal tube
    • Responsible for the majority of reabsorption of filtered glucose
    • Blocking SGLT2 => Excretion of more glucose in the urine
  • Increases Glycosuria
    • Leads to Weight Loss
    • Lowers Blood Glucose
Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes
Bernard Zinman, M.D., Christoph Wanner, M.D., John M. Lachin, Sc.D.,

Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes
Bruce Neal, M.B., Ch.B., Ph.D., Vlado Perkovic, M.B., B.S., Ph.D.,

Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes
S.D. Wiviott, I. Raz, M.P. Bonaca, O. Mosenzon, E.T. Kato, A. Cahn, M.G. Silverman,
<table>
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<td>0.53 (0.43-0.66) 0.4GFR, ESRD, RD</td>
<td>0.81 (0.63-1.04) 2Cr,RRT,RD</td>
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SGLT2i and ↓ CKD, hHF: Mechanism of Action

• Like with GLP1-RA, SGLT2i:
  • Lower Blood Glucose
  • Lower Weight
  • Lower Blood Pressure

• Also, like GLP1-RA, the ↓ in CKD and hHF
  • Are out of proportion to SGLT2i’s effect on Blood Glucose, Weight, Blood Pressure
  • There are felt to be direct effects that are Cardio and Renal Protective
Glycosuria
Blood sugar goes down
Insulin levels go down
Weight loss

Natriuresis
Reduced intraglomerular pressure, proteinuria
Lower Blood Pressure

hHF MOA?
Decrease Insulin / Glucagon Ratio =>
Increase Ketone Bodies
SGLT2i- Patient Selection

• Ideal patient
  • Hx ASCVD
  • Hx CKD (of note, GFR can’t be too low)
  • Hx CHF
  • Overweight
  • Important to avoid hypoglycemia

• Avoid if
  • A1c >9%
  • Hx of GU infections; At risk for GU infections
  • Have or at risk for foot infections

• Side Effects / Warnings
  • GU infections: Yeast infections, UTIs, Fournier’s gangrene
  • eDKA: sick day warnings
  • Lower Limb amputation: only w canagliflozin
Empaglifozin CVOT

**Table 2. Adverse Events.**

<table>
<thead>
<tr>
<th>Event</th>
<th>Placebo (N = 2333)</th>
<th>Empaglifozin, 10 mg (N = 2345)</th>
<th>Empaglifozin, 25 mg (N = 2342)</th>
<th>Pooled Empaglifozin (N = 4687)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic ketoacidosis</td>
<td>1 (&lt;0.1)</td>
<td>3 (0.1)</td>
<td>1 (&lt;0.1)</td>
<td>4 (0.1)</td>
</tr>
</tbody>
</table>

**CANAGLIFLOZIN AND CARDIOVASCULAR EVENTS IN TYPE 2 DIABETES**

**Table 2. Adverse Events.**

<table>
<thead>
<tr>
<th>Event</th>
<th>Canagliflozin event rate per 1000 patient-yr</th>
<th>Placebo event rate per 1000 patient-yr</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic ketoacidosis (adjudicated)</td>
<td>0.6</td>
<td>0.3</td>
<td>0.14</td>
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</table>

**DAPAGLIFLOZIN IN TYPE 2 DIABETES**

**Table 2. Safety Events.**

<table>
<thead>
<tr>
<th>Event</th>
<th>Dapagliflozin (N = 8374)</th>
<th>Placebo (N = 8369)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. (%)</td>
<td>no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetic ketoacidosis</td>
<td>27 (0.3)</td>
<td>12 (0.1)</td>
<td>2.18 (1.10–4.30)</td>
<td>0.02</td>
</tr>
</tbody>
</table>
SGLT2i- Patient Selection

• Ideal patient
  • Hx ASCVD
  • Hx CKD (but GFR can’t be too low, CKD 3a is a sweet spot, GFR 45-59)
  • Hx CHF
  • Overweight
  • Important to avoid hypoglycemia

• Avoid if
  • A1c >9%
  • Hx of GU infections; At risk for GU infections
  • Have or at risk for foot infections

• Side Effects / Warnings
  • GU infections: Yeast infections, UTIs, Fournier’s gangrene
  • DKA: sick day warnings
  • Lower Limb amputation: only w canagliflozin
During the trial, an increased risk of lower limb amputation was identified in another trial of canagliflozin. A protocol amendment for the present trial in May 2016 asked investigators to examine patients’ feet at each trial visit and temporarily interrupt the assigned treatment in patients with any active condition that might lead to amputation.

### Table 2. Adverse Events.*

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<tr>
<td>Amputation</td>
<td>6.3</td>
<td>3.4</td>
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### Table 2. Efficacy and Safety.*

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<th>Variable</th>
<th>Canagliflozin</th>
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<tr>
<td>Amputation</td>
<td>70/2200</td>
<td>63/2197</td>
<td>12.3</td>
<td>11.2</td>
<td>1.11 (0.79–1.56)</td>
<td>NA</td>
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SGLT2i- Prescribing

• Empagliflozin
  • 10mg daily
  • Sometimes I increase to 25mg
  • May notice increased UOP, Stay hydrated, Take it in the morning
  • Can lower BP a few points (usually good, but if borderline BP to begin with use w caution)
  • LMK if you have a GU infection
  • Sick day precautions
    • I don’t prescribe unless A1c <10% and on its way to 9%

• Dapagliflozin
  • 5mg daily
  • Can go to 10mg if needed

• Canagliflozin
  • 100mg daily before the first meal of the day
  • 300mg if needed
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ASCVD:
Either one GLP1-RA -or- SGLT2i

HF:
SGLT2i
(GLP1-RA while cardioprotective in other ways do not specifically have protection against CHF)

CKD:
SGLT2i
If patient cannot be on an SGLT2i, then use a GLP1-RA
COMPELLING NEED TO MINIMIZE HYPOGLYCEMIA

1. DPP-4i
   - If A1C above target
     - SGLT2i OR TZD

2. GLP-1 RA
   - If A1C above target
     - SGLT2i OR TZD

3. SGLT2i
   - If A1C above target
     - GLP-1 RA OR DPP-4i OR SGLT2i OR TZD

4. TZD
   - If A1C above target
     - GLP-1 RA

If A1C above target

Continue with addition of other agents as outlined above

If A1C above target

Consider the addition of SU* OR basal insulin:
- Choose later generation SU with lower risk of hypoglycemia
- Consider basal insulin with lower risk of hypoglycemia*
COMPELLING NEED TO MINIMIZE WEIGHT GAIN OR PROMOTE WEIGHT LOSS

- GLP-1 RA with good efficacy for weight loss
- SGLT2i

If A1C above target

- SGLT2i
- GLP-1 RA with good efficacy for weight loss

If A1C above target

If quadruple therapy required, or SGLT2i and/or GLP-1 RA not tolerated or contraindicated, use regimen with lowest risk of weight gain

PREFERABLY
- DPP-4i (if not on GLP-1 RA) based on weight neutrality

If DPP-4i not tolerated or contraindicated or patient already on GLP-1 RA, cautious addition of:
- SU
- TZD
- Basal insulin
COST IS A MAJOR ISSUE\textsuperscript{11,12}

SU\textsuperscript{11} \quad Tzanidiclofenac\textsuperscript{12}

If A1C above target

TZD\textsuperscript{12} \quad SU

If A1C above target

Insulin therapy basel insulin with lowest acquisition cost

OR

Consider other therapies based on cost
To select the best anti-glycemic medications..... We have to know: Co-Morbidities

• Epic
  • T2DM
  • Overview

• Overview
  • BMI
  • CKD (gfr 54, uacr 15)
  • CAD (NSTEMI, PCI, CABG)
  • CHF (HFpEF, HFrEF)
  • Hypoglycemia unawareness
  • Cost is an issue
  • Retinopathy
  • 10 year ASCVD risk score
FIRST-LINE Therapy is Metformin and Comprehensive Lifestyle (including weight management and physical activity)

INDICATORS OF HIGH-RISK OR ESTABLISHED ASCVD, CKD, OR HF^®

CONSIDER INDEPENDENTLY OF BASELINE A1C, INDIVIDUALIZED A1C TARGET, OR METFORMIN USE^®

+ASCVD/Indicators of High Risk
- Established ASCVD
- Indicators of high ASCVD risk (age ≥55 years with coronary, carotid, or lower-extremity artery stenosis ≥50%, or LVH)

+HF
- Particularly HFREF (LVEF <45%)

+CKD
- DKD and Albuminuria^*

SGLT2i with proven benefit in this population^9,10

NO

IF A1C ABOVE INDIVIDUALIZED TARGET PROCEED AS BELOW

COMPELLING NEED TO MINIMIZE HYPOGLYCEMIA

- SGLT2i
- GLP-1 RA
- DPP-4
- TZD

PREFERABLY

SGLT2i with primary evidence of reducing CVD progression
OR
SGLT2i with evidence of reducing CKD progression in CVOTs^11,12

GLP-1 RA with good efficacy for weight loss^10

OR
GLP-1 RA with proven CVD benefit^* If SGLT2i not tolerated or contraindicated

If A1C above target

IF A1C above target

Continue with addition of other agents as outlined above

IF A1C above target

COMPELLING NEED TO MINIMIZE WEIGHT GAIN OR PROMOTE WEIGHT LOSS

- SGLT2i
- GLP-1 RA or
dPP-4i
- TZD

GLP-1 RA with good efficacy for weight loss^10

IF A1C above target

IF A1C above target

IF A1C above target

COST IS A MAJOR ISSUE^11,12

- SU^*
- TZD^®

IF A1C above target

ESOMEP OR

Su

If A1C above target

Insulin therapy basal insulin with lowest acquisition cost

OR

- TZD^12
- SU^*

IF A1C above target

IF A1C above target

For patients on a GLP-1 RA, consider adding SGLT2i with

EITHER

OR

GLP-1 RA with proven CVD benefit^*
SGLT2i

If further intensification is required or patient is unable to tolerate GLP-1 RA and/or SGLT2i, choose agents demonstrating CV benefit and/or safety:

- For patients on a GLP-1 RA, consider adding SGLT2i with

- Particularly HFREF (LVEF <45%)

- DKD and Albuminuria^*

- SGLT2i with proven benefit in this population^9,10

- Established ASCVD
- Indicators of high ASCVD risk (age ≥55 years with coronary, carotid, or lower-extremity artery stenosis ≥50%, or LVH)
Pop Quiz

• 47 T2DM, metformin, BMI 42
  • GLP1-RA > SGLT2i (add both with time)

• 65, T2DM, Metformin, A1c 10%, Cost is a big issue
  • SU and TZD

• 59 w T2DM on Metformin w hx STEMI, PCI, No CHF, A1c 9%
  • GLP1-RA or SGLT2i

• 59 w T2DM on Metformin w hx STEMI, PCI, w resultant ICM 35%, A1c 9%
  • Which one first? SGLT2i but then GLP1-RA

• 59 w T2DM on Metformin and GFR 58 w UACR 110, A1c of
  • 12%: GLP1-RA first and once A1c closer to 9% add on an SGLT2i
  • 8.5%: SGLT2i first and later on consider a GLP1-RA
The numbers 19 and 20 got into a fight.
Blood Glucose -> Blood Pressure

• Goals
• Medications
• Pop Quiz Questions
Blood Pressure: Goals

• What 2 blood pressure goals do we hear about:
  • <140/90
  • <130/80

• Which is the goal?
  • Both
    • IT DEPENDS ON THE RISK OF THE PATIENT...
Blood Pressure: Goals

Treatment Goals

10.3 For patients with diabetes and hypertension, blood pressure targets should be individualized through a shared decision-making process that addresses CV risk, potential adverse effects of antihypertensive medications, and patient preferences. C

10.4 For individuals with diabetes and hypertension at higher CV risk (existing ASCVD or 10-year ASCVD risk ≥15%), a blood pressure target of <130/80 mmHg may be appropriate, if it can be safely attained. C

10.5 For individuals with diabetes and hypertension at lower risk for CVD (10-year ASCVD risk <15%), treat to a blood pressure target of <140/90 mmHg. A
Blood Pressure: Goals

Treatment Goals

10.3 For patients with diabetes and hypertension, blood pressure targets should be individualized through a shared decision-making process that addresses CV risk, potential adverse effects of antihypertensive medications, and patient preferences.

10.4 For individuals with diabetes and hypertension at higher CV risk (existing ASCVD or 10-year ASCVD risk ≥15%), a blood pressure target of <130/80 mmHg may be appropriate, if it can be safely attained.

10.5 For individuals with diabetes and hypertension at lower risk for CVD (10-year ASCVD risk <15%), treat to a blood pressure target of <140/90 mmHg.
Blood Pressure: Goals

POP QUIZ

• Q1: re- The blood pressure goal in lower risk patients with diabetes
  • What 10 year ASCVD risk score is considered lower risk?
    • <15%
  • What is the blood pressure goal for lower risk patients
    • <140/90

• Q2: re- The blood pressure goal in higher risk patients with diabetes
  • What defines higher risk?
    • 10 year ASCVD score >15%
    • Known ASCVD
  • What is the blood pressure goal – to be considered- for higher risk patients?
    • <130/80 MAY be appropriate IF it can be done safely

• General agreement that <140/90 is Grade A evidence
• Where does the debate re <130/80 stem from?
Eligible:
HIGH RISK pts w T2DM
>40 + ASCVD
>55 + ASCVD Risk Factors
RESULTS
After 1 year, the mean systolic blood pressure was 119.3 mm Hg in the intensive-therapy group and 133.5 mm Hg in the standard-therapy group. The annual rate of the primary outcome was 1.87% in the intensive-therapy group and 2.09% in the standard-therapy group (hazard ratio with intensive therapy, 0.88; 95% confidence interval [CI], 0.73 to 1.06; P=0.20). The annual rates of death from any cause were 1.28% and 1.19% in the two groups, respectively (hazard ratio, 1.07; 95% CI, 0.85 to 1.35; P=0.55). The annual rates of stroke, a prespecified secondary outcome, were 0.32% and 0.53% in the two groups, respectively (hazard ratio, 0.59; 95% CI, 0.39 to 0.89; P=0.01). Serious adverse events attributed to antihypertensive treatment occurred in 77 of the 2362 participants in the intensive-therapy group (3.3%) and 30 of the 2371 participants in the standard-therapy group (1.3%) (P<0.001).

CONCLUSIONS
In patients with type 2 diabetes at high risk for cardiovascular events, targeting a systolic blood pressure of less than 120 mm Hg, as compared with less than 140 mm Hg, did not reduce the rate of a composite outcome of fatal and nonfatal major cardiovascular events. (ClinicalTrials.gov number, NCT00000620.)
Accord: 2 Items to point out...

• SBP <120 vs SBP <130
  • SBP 120 mm Hg in a study = ~ 130 mm Hg in real life

• Everyone in ACCORD was high risk
  • >40 years old with ASCVD
  • >55 years old with ASCVD Risk Factors
    • 10 year ASCVD risk probably high
Blood Pressure: Goals

Treatment Goals

10.3 For patients with diabetes and hypertension, blood pressure targets should be individualized through a shared decision-making process that addresses CV risk, potential adverse effects of antihypertensive medications, and patient preferences.

10.4 For individuals with diabetes and hypertension at higher CV risk (existing ASCVD or 10-year ASCVD risk $\geq 15\%$), a blood pressure target of $<130/80$ mmHg may be appropriate, if it can be safely attained.

10.5 For individuals with diabetes and hypertension at lower risk for CVD (10-year ASCVD risk $<15\%$), treat to a blood pressure target of $<140/90$ mmHg.

To select the correct BP goal...

The 10 Year ASCVD Risk must be calculated
Blood Pressure: Goals

**Treatment Goals**

10.3 For patients with diabetes and hypertension, blood pressure targets should be individualized through a shared decision-making process that addresses CV risk, potential adverse effects of antihypertensive medications, and patient preferences. C

10.4 For individuals with diabetes and hypertension at higher CV risk (existing ASCVD or 10-year ASCVD risk ≥15%), a blood pressure target of <130/80 mmHg may be appropriate, if it can be safely attained. C

10.5 For individuals with diabetes and hypertension at lower risk for CVD (10-year ASCVD risk <15%), treat to a blood pressure target of <140/90 mmHg. A

You have to know the 10 year ASCVD Risk Score
### Highlights from the 2017 Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults

**New blood pressure targets and treatment recommendations:** For years, hypertension was classified as a blood pressure (BP) reading of 140/90 mm Hg or higher, but the updated guideline classifies hypertension as a BP reading of 130/80 mm Hg or higher. The updated guideline also provides new treatment recommendations, which include lifestyle changes as well as BP-lowering medications, as shown in Table 1.

#### Table 1. Classification of BP

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<th>Diastolic BP</th>
<th>Treatment or Follow-up</th>
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<tr>
<td>Normal</td>
<td>&lt;120 mm Hg</td>
<td>&lt;80 mm Hg</td>
<td>Evaluate yearly; encourage healthy lifestyle changes to maintain normal BP</td>
</tr>
<tr>
<td>Elevated</td>
<td>120-129 mm Hg and &lt;80 mm Hg</td>
<td>Recommend healthy lifestyle changes and reassess in 3-6 months</td>
<td></td>
</tr>
<tr>
<td>Hypertension: stage 1</td>
<td>130-139 mm Hg or 80-89 mm Hg</td>
<td>Assess the 10-year risk for heart disease and stroke using the atherosclerotic cardiovascular disease (ASCVD) risk calculator. If risk is less than 10%, start with healthy lifestyle recommendations and reassess in 3-6 months. If risk is greater than 10% or the patient has known clinical cardiovascular disease (CVD), diabetes mellitus, or chronic kidney disease, recommend lifestyle changes and BP-lowering medication (1 medication); reassess in 1 month for effectiveness of medication therapy. If goal is met after 1 month, reassess in 3-6 months. If goal is not met after 1 month, consider different medication or titration. Continue monthly follow-up until control is achieved.</td>
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<td>≥140 mm Hg or ≥90 mm Hg</td>
<td>Recommend healthy lifestyle changes and BP-lowering medication (2 medications of different classes); reassess in 1 month for effectiveness. If goal is met after 1 month, reassess in 3-6 months. If goal is not met after 1 month, consider different medications or titration. Continue monthly follow-up until control is achieved.</td>
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ADA 2021 Standards

Treatment Goals

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Highlights
FROM THE 2017 GUIDELINE FOR THE PREVENTION, DETECTION, EVALUATION AND MANAGEMENT OF HIGH BLOOD PRESSURE IN ADULTS

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

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Blood Pressure

• Goals
• Medications
• Pop Quiz
Blood Pressure: Medications

BP Meds that reduce risk of CV events in patient w diabetes
- ACE/ARB
- Calcium Channel Blockers (Dihydropyridine, ex amlodipine)
- Thiazide Diuretics

ACE / ARB are recommended First Line if
- DM + HTN and
  - a history of CAD
  - or
  - UACR ≥30
- Don’t use them together
Blood Pressure: Medications

Recommendations for the Treatment of Confirmed Hypertension in People With Diabetes

Initial BP >140/90 and <160/100 mmHg
Start one agent
  Albuminuria or CAD*
  No
  Start one drug:
  - ACEI
  - ARB
  - CCB***
  - Diuretic**
  Yes
  Start:
  - ACEI or ARB

Initial BP ≥160/100 mmHg
Start two agents
  Albuminuria or CAD*
  No
  Start drug from 2 of 3 options:
  - ACEI or ARB
  - CCB***
  - Diuretic**
  Yes
  Start:
  - ACEI or ARB
  - CCB*** or Diuretic**

Assess BP Control and Adverse Effects

Treatment tolerated and target achieved
Not meeting target
Adverse effects
Blood Pressure
Pop Quiz

• The ADA recommends consideration of a goal of <130/80 if
  • ASCVD 10 year risk score >15%
  • The person has a hx of ASCVD

• What are the categories of meds shown to have CV benefit in patients with diabetes?
  • Dihydropyridine Calcium Channel Blockers, ACE/ARB, Thiazide Diuretics

• ACE/ARB should be first line for a person w DM and HTN and what additional conditions
  • Albuminuria >30 mg/g
  • Hx CAD
What’s the best thing about Switzerland?

I don’t know, but the flag is a big plus.
Blood Pressure => LDL
LDL: 2021 ADA Recommendations

• Goals
• Treatments
• Pop Quiz Questions
LDL: 2021 ADA Recommendations

• **Goals:** It is all about risk
• **Treatments:** Statins, Statins, Statins; but also Ezetimibe and PCSK9i
• **Pop Quiz Questions**
LDL: 2021 ADA Recommendations

• Goals
• IT IS ALL ABOUT RISK
  • What you prescribe/What you aim for: It is all about risk of the patient
  • Primary Prevention
    • All patients w T2DM 40-75 A
    • Patients at ‘Higher Risk’ B
    • Patients with a 10 year ASCVD >20% C
  • Secondary Prevention
    • T2DM, All Ages, with ASCVD A
    • ASCVD at ‘Very High Risk Using Specific Criteria’ A
LDL: ADA 2021 Statin Rec, Primary Prevention

Statin Treatment

*Primary Prevention Recommendations*

10.19 For patients with diabetes aged 40–75 years without ASCVD, use moderate-intensity statin therapy in addition to lifestyle therapy. A

10.20 For patients with diabetes aged 20–39 years with additional ASCVD risk factors, it may be reasonable to initiate statin therapy in addition to lifestyle therapy. C

10.21 In patients with diabetes at higher risk, especially those with multiple ASCVD risk factors or aged 50–70 years, it is reasonable to use high-intensity statin therapy. B

10.22 In adults with diabetes and 10-year ASCVD risk of 20% or higher, it may be reasonable to add ezetimibe to maximally tolerated statin therapy to reduce LDL cholesterol levels by 50% or more. C

---

Everyone w T2DM 40-75 yo

Higher Risk

10 year ≥ 20%

ASCVD: 30%
Starting LDL 150
Goal: LDL 75
Achieved: LDL 90
10.21 In patients with diabetes at higher risk, especially those with multiple ASCVD risk factors or aged 50–70 years, it is reasonable to use high-intensity statin therapy. 

• Higher risk =
  • Age 50-70
  • Multiple ASCVD Risk Factors
    • What risk factors?

HTN
Dyslipidemia
Smoking

Family History of Premature ASCVD
Obesity / Overweight
Low GFR
Albuminuria
Statin Treatment

Primary Prevention Recommendations

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Everyone w T2DM 40-75

Specific Target: No # Target. ‘Moderate-intensity’ is the Target

Higher Risk

Specific Target: No # Target. ‘High-intensity’ is the Target

10 year > 20%

Specific Target:Lower LDL by >50%
LDL Primary Prevention Pop Quiz Q#1 & 2

• 48 yo woman with T2DM. No Hx ASCVD. Relatively fit. No other ASCVD risk factors. You check an ASCVD (because action is required if the 10 year ASCVD >20%) and it is 6%. What type of statin do you start?
  • Moderate-intensity statin Grade A
  • (contraindicated in pregnancy)

• Same 48 yo woman with T2DM. No Hx ASCVD. 10 year risk is still 6%, but this time, her dad had an MI at 51, she herself has a BMI of 32, a GFR of 58, and a UACR of 76. Her ASCVD risk score is the same 6%. What type of statin would you start?
  • Certainly at least moderate-intensity statin
  • ‘Consider’ a high-intensity statin Grade B
Statin Treatment

Primary Prevention

Recommendations

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48 yo woman, no ASCVD hx, 10 yr ASCVD risk 6%

Scenario 1: otherwise healthy.

Scenario 2: Family Hx, Obesity, GFR 58, UACR 76
LDL Primary Prevention
Pop Quiz Q#3

• 68 yo woman, T2DM, No Hx ASCVD, but this time she has HTN, low HDL, high LDL 160, smokes and her ASCVD score is 28%
  • ASCVD is above the threshold of \( >20\% \)
  • Guidance to add maximally tolerated statin AND...
  • Follow to see if the LDL drops by \( >50\% \)
  • A \( >50\% \) drop would be a follow up LDL of 80 or less

• 3 months later- LDL dropped to 95
  • You ask yourself:
    • Did the LDL drop by \( >50\% \)? No
  • Now what
    • Consider adding ezetimibe 10mg
**Statin Treatment**

**Primary Prevention Recommendations**

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---

68 yo woman
10 year ASCVD risk score is: 28%

Step 1: You started a high-intensity statin

Step 2: You remembered to look for a >50% LDL reduction
LDL Primary Prevention: Take home points

- Everyone 40-75 gets (at least) a moderate-intensity statin
- But, they need an evaluation for being high risk
  - Calculate a 10 year ASCVD risk score
  - Remember the list of ‘high risk’ characteristics
  - Discuss if a high-intensity statin should be tried
- If you started a high intensity statin due to
  - A 10 year ASCVD risk score >20%
  - Note the starting LDL
  - Look to see if it drops by >50%
  - If not, it may be reasonable to add ezetimibe

- HTN
- Dyslipidemia
- Smoking

Family History of Premature ASCVD
Obesity / Overweight
GFR <60
Albuminuria
Why did the farmer win an award?

He was outstanding in his field.
Simpler

Primary prevention had 3 risk groups

Second prevention has only 2 risk groups
  • High potency statin for all
  • In some, aim for an LDL <70 mg/dL
Secondary Prevention

Recommendations

10.23 For patients of all ages with diabetes and ASCVD, high-intensity statin therapy should be added to lifestyle therapy. A

10.24 For patients with diabetes and ASCVD considered very high risk using specific criteria, if LDL cholesterol is \( \geq 70 \) mg/dL on maximally tolerated statin dose, consider adding additional LDL-lowering therapy (such as ezetimibe or PCSK9 inhibitor). A Ezetimibe may be preferred due to lower cost.

10.25 For patients who do not tolerate the intended intensity, the maximally tolerated statin dose should be used. E
Primary Prevention: Multiple ASCVD Risk Factors

HTN
Dyslipidemia
Smoking

Family History of Premature ASCVD
Obesity / Overweight
CKD
Albuminuria

Secondary Prevention: It’s a different list.....
Statin- 2’ Prevention: Definition of Very High Risk

**CHOLESTEROL CLINICAL PRACTICE GUIDELINES**


A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines
### Table 4. Very High-Risk* of Future ASCVD Events

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*Very high-risk includes a history of multiple major ASCVD events or one major ASCVD event and multiple high-risk conditions.

ABI indicates ankle-brachial index; ACS, acute coronary syndrome; ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HF, heart failure; LDL, low-density lipoprotein cholesterol; and MI, myocardial infarction.
• What should my LDL goal be?
  • 75 yo man w T2DM had an MI 3 years ago
  • Already getting a high-potency statin
  • Am I ‘very high risk’?

• Answer:
  • Yes, very high risk
  • Goal LDL <70mg/ dL
  • If on: Maximally tolerated statin
  • And: LDL is not < 70mg/ dL
    • Add on ezetimibe first (lower cost)
    • And then a PCSK9i if still not <70


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**Secondary Prevention**

**Recommendations**

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10.25 For patients who do not tolerate the intended intensity, the maximally tolerated statin dose should be used. E
**LDL Secondary Prevention. Pop Quiz Q#2**

- **What should my LDL goal be?**
  - 55 yo man w T2DM had an MI 3 years ago
  - No other ‘very high risk’ characteristics

- **Answer**
  - Trick question. No LDL Goal
  - Goal is a High-Intensity statin

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Statins

• High Intensity
  • Rosuvastatin 20mg and 40mg
  • Atorvastatin 40mg and 80mg

• Medium Intensity
  • Rosuvastatin 5mg or 10mg
  • Atorvastatin 10mg or 20mg
  • Simvastatin 20mg or 40mg
Lowering LDL: Beyond Statins

• Ezetimibe
  • Decreases intestinal absorption of cholesterol
    • Dietary Cholesterol + Biliary Cholesterol
Lowering LDL: Beyond Statins

- PCSK9
  - PCSK9 =>
  - Decreased LDL-r =>
  - Increased LDL-c

- PCSK9i
  - Less PCSK9
  - More LDL-r
  - Less LDL-c
  - 2 PCSK9i available
    - Evolocumab and Alirocumab
**Statin Treatment**

**Primary Prevention**

**Recommendations**

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**Secondary Prevention**

**Recommendations**

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10.25 For patients who do not tolerate the intended intensity, the maximally tolerated statin dose should be used. E
What did the buffalo say when his son left for college?

Bison.
Pre Diabetes

• It is important to screen for DM and Pre Diabetes
  • ~30 million Americans with Diabetes
  • ~90 million Americans with Pre Diabetes

• A1c 5.7 – 6.4%

• Patients that should be screened .... BMI 25 (23 in Asian Americans),
  Plus an additional risk factor....(next slide)
## TABLE 2.3 Criteria for Testing for Diabetes or Prediabetes in Asymptomatic Adults

1. Testing should be considered in adults with overweight or obesity (BMI $\geq 25$ kg/m$^2$ or $\geq 23$ kg/m$^2$ in Asian Americans) who have one or more of the following risk factors:
   - First-degree relative with diabetes
   - High-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
   - History of CVD
   - Hypertension ($\geq 140/90$ mmHg or on therapy for hypertension)
   - HDL cholesterol level $< 35$ mg/dL (0.90 mmol/L) and/or a triglyceride level $> 250$ mg/dL (2.82 mmol/L)
   - Women with polycystic ovary syndrome
   - Physical inactivity
   - Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)

2. Patients with prediabetes (A1C $\geq 5.7$% [39 mmol/mol], impaired glucose tolerance, or impaired fasting glucose) should be tested yearly.

3. Women who were diagnosed with GDM should have lifelong testing at least every 3 years.

4. For all other patients, testing should begin at age 45 years.

5. If results are normal, testing should be repeated at a minimum of 3-year intervals, with consideration of more frequent testing depending on initial results and risk status.

6. HIV
Pre Diabetes

• It is important to screen for DM
  • ~30 million Americans with Diabetes
  • ~90 million Americans with Pre Diabetes

• A1c 5.7 – 6.4% = Pre Diabetes
  • A1c 6.5% and up = Diabetes

• Patients that should be screened: “BMI >25 + one other risk factor”

• Do something with the results
  • Counsel the patient yourself
  • Refer to an education class
  • Add Pre Diabetes as a problem on the problem list
  • Talk to patient about lifestyle at each visit
  • Follow the A1c at least annually
You Just Realized...

If tomatoes are a fruit that makes ketchup a smoothie.
Diabetes In the Time of Covid

• The main effects of Covid were terrible

• A main side effect of Covid was it’s awful impact on chronic disease management, in particular patients with diabetes
  • Patients were afraid to leave the house to get their prescriptions
  • Patients were afraid to leave the house to exercise
  • Many people no longer stuck to their diets
    • Loss of job = inability to pay for healthy food
    • Stress eating
  • So many people were lost to follow-up

• We are trying to be innovative in terms of Diabetes Outreach
  • People are still afraid to come to the hospital
  • If we bring them in it needs to be for a quick visit w minimal waiting room time
  • Monthly outreach letters still being sent
  • One long in-person visit => 2 visits: a short Fast Check (vitals, labs, retinal scan), and then a televisit for analysis and the plan
Last Intellectual Break

What did the ocean say to the shore?

Nothing...
It just waved.
Thank you!

Management of Type 2 Diabetes:
2021 ADA Recommendations

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