Diabetes Treatment Update

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Goals and Objectives

At the conclusion of this session, the learner should be better able to:

• Diagnose Type II Diabetes
• Describe recommended first steps for glycemic control in a patient newly diagnosed with Type II Diabetes
• Compare the pharmacologic classes of diabetic medications
Diabetes Update

https://www.dailysignal.com/2015/06/05/photo-essay-remembering-the-tiananmen-square-protests-26-years-later/
Photo: Stringer/Reuters/Newscom
The Main Reference

https://professional.diabetes.org/content-page/standards-medical-care-diabetes/
Diabetes Care – 15 Sections

1 – Improving Care/ Population Health
2 – Classification/ Dx
3 – Comprehensive Medical Evaluation and Assessment of Comorbidities
4 – Lifestyle Management
5 – Prevention or Delay of Type 2 DM
Diabetes Care – 15 Sections

6 – Glycemic Targets
7 – Obesity Mgt for Tx of Type 2 DM
8 – Pharmacologic Approaches to Glycemic Treatment
9 – Cardiovascular Disease and Risk Management
10 – Microvascular Complications and Foot Care
Diabetes Care – 15 Sections

11 - Older Adults
12 - Children and Adolescents
13 - Management of DM in Pregnancy
14 - DM Care in the Hospital
15 - Diabetes Advocacy
ADA Evidence Grading

A → Strongest (clear evidence, compelling non-experimental or supportive evidence)
B → Supportive Evidence, stronger
C → Supportive Evidence, weaker

E → Expert Consensus or Clinical Experience
Case 1

Which one of the following, when confirmed with a repeat tests, meets the diagnostic criteria for diabetes mellitus (values in mg/ dL)?

– A fasting blood glucose level of 120
– A 2- hour value of 180 on an oral glucose tolerance test
– A random glucose level of 180 in a patient with symptoms of diabetes mellitus
– A positive urine dipstick for glucose
– A hemoglobin A1c of 7.0%
Section 2

Classification and Diagnosis of Diabetes
Classification and Diagnosis of Diabetes

4 General Categories

• Type 1
• Type 2
• Gestational
• Other Causes
Table 2.2—Criteria for the diagnosis of diabetes

- FPG $\geq 126$ mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*

- **OR**

- 2-h PG $\geq 200$ mg/dL (11.1 mmol/L) during OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75-g anhydrous glucose dissolved in water.*

- **OR**

- A1C $\geq 6.5\%$ (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*

- **OR**

- In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose $\geq 200$ mg/dL (11.1 mmol/L).

---

*In the absence of unequivocal hyperglycemia, results should be confirmed by repeat testing.
**Classification and Diagnosis of Diabetes – Type 2**

<table>
<thead>
<tr>
<th>Table 2.2—Criteria for the diagnosis of diabetes</th>
</tr>
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<tbody>
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<td><strong>FPG ≥126 mg/dL (7.0 mmol/L).</strong> Fasting is defined as no caloric intake for at least 8 h.*</td>
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<td><strong>OR</strong></td>
</tr>
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</tr>
</tbody>
</table>

*In the absence of unequivocal hyperglycemia, results should be confirmed by repeat testing.
Diagnosis of Diabetes – HgA1c use

• To avoid misdiagnosis or missed diagnosis, the A1C test should be performed using a method that is certified by the NGSP and standardized to the Diabetes Control and Complications Trial (DCCT) assay. B

• Marked discordance between measured A1C and plasma glucose levels should raise the possibility of A1C assay interference due to hemoglobin variants (i.e., hemoglobinopathies) and consideration of using an assay without interference or plasma blood glucose criteria to diagnose diabetes. B
Diagnosis of Diabetes – HgA1c use

• In conditions associated with increased red blood cell turnover, such as sickle cell disease, pregnancy (second and third trimesters), hemodialysis, recent blood loss or transfusion, or erythropoietin therapy, only plasma blood glucose criteria should be used to diagnose diabetes. B

• Summary of HgA1c recommendation
  – Use a certified lab to measure HgA1c
  – If HgA1c discordance with glucose – consider hemoglobinopathies that interfere with HgA1c and consider using glucose criteria and not the HgA1c
  – If increased RBC turnover, use glucose criteria
Diagnosis of Diabetes – Increased Risk (Prediabetes)

• Screening for prediabetes and risk for future diabetes with an informal assessment of risk factors or validated tools should be considered in asymptomatic adults. B

• Note – the screening for DM and Pre-DM is very similar
Validated Tool
Paper or Online

Are You at Risk for Type 2 Diabetes?

Diabetes Risk Test

1. How old are you?
   - Less than 40 years (0 points)
   - 40–65 years (1 point)
   - 66–74 years (2 points)
   - 75 years or older (3 points)

2. Are you a man or a woman?
   - Man (1 point)
   - Woman (0 points)

3. If you are a woman, have you ever been diagnosed with gestational diabetes?
   - Yes (1 point)
   - No (0 points)

4. Do you have a mother, father, sister, or brother with diabetes?
   - Yes (1 point)
   - No (0 points)

5. Have you ever been diagnosed with high blood pressure?
   - Yes (1 point)
   - No (0 points)

6. Are you physically active?
   - Yes (0 points)
   - No (1 point)

7. What is your weight status?
   - See chart at right

If you scored 3 or higher, you are at increased risk for having type 2 diabetes. However, only your doctor can tell for sure if you do have type 2 diabetes or prediabetes (a condition that precedes type 2 diabetes in which blood glucose levels are higher than normal). Talk to your doctor to see if additional testing is needed.

Type 2 diabetes is more common in African Americans, Hispanics/Latinos, American Indians, and Asian Americans and Pacific Islanders. Higher body weights increase diabetes risk for everyone. Asian Americans are at increased diabetes risk at lower body weights than the rest of the general public (about 15 pounds lower).

For more information, visit us at diabetes.org or call 1-800-DIABETES (1-800-342-2383).

Lower Your Risk

The good news is that you can manage your risk for type 2 diabetes. Small steps make a big difference. If you are at high risk, your first step is to see your doctor to see if additional testing is needed. Visit diabetes.org or call 1-800-DIABETES (1-800-342-2383) for information, tips on getting started, and lower your risk.

Table 2.3—Criteria for testing for diabetes or prediabetes in asymptomatic adults

1. Testing should be considered in overweight or obese (BMI ≥25 kg/m² or ≥23 kg/m² in Asian Americans) adults 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 (≥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 ≥5.7% [39 mmol/mol], IGT, or IFG) 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.
Prediabetes Testing

• In patients with prediabetes, identify and if appropriate, treat other cardiovascular disease risk factors. B

• To test for prediabetes, FBG, 2h plasma glucose test and HgA1c are equally appropriate. B
Testing Criteria (Peds)

Table 2.5—Risk-based screening for type 2 diabetes or prediabetes in asymptomatic children and adolescents in a clinical setting*

<table>
<thead>
<tr>
<th>Criteria</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Overweight (BMI &gt;85th percentile for age and sex, weight for height &gt;85th percentile, or weight &gt;120% of ideal for height) A</td>
<td></td>
</tr>
</tbody>
</table>

Plus one or more additional risk factors based on the strength of their association with diabetes as indicated by evidence grades:

- Maternal history of diabetes or GDM during the child’s gestation A
- Family history of type 2 diabetes in first- or second-degree relative A
- Race/ethnicity (Native American, African American, Latino, Asian American, Pacific Islander) A
- Signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome, or small-for-gestational-age birth weight) B

*Persons aged <18 years.
Diagnosis of Prediabetes

<table>
<thead>
<tr>
<th>Table 2.4—Categories of increased risk for diabetes (prediabetes)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>FPG 100 mg/dL (5.6 mmol/L) to 125 mg/dL (6.9 mmol/L) (IFG)</td>
</tr>
<tr>
<td>OR</td>
</tr>
<tr>
<td>2-h PG during 75-g OGTT 140 mg/dL (7.8 mmol/L) to 199 mg/dL (11.0 mmol/L) (IGT)</td>
</tr>
<tr>
<td>OR</td>
</tr>
<tr>
<td>A1C 5.7–6.4% (39–47 mmol/mol)</td>
</tr>
</tbody>
</table>

*For all three tests, risk is continuous, extending below the lower limit of the range and becoming disproportionately greater at the higher end of the range.
Case 1 – Restate question

Which one of the following, when confirmed with a repeat test, meets the diagnostic criteria for diabetes mellitus?

- A fasting blood glucose level of 120
- A 2-hour value of 180 on an oral glucose tolerance test
- A random glucose level of 180 in a patient with symptoms of diabetes mellitus
- A positive urine dipstick for glucose
- A hemoglobin A1c of 7.0%
Case 1 - Answer

Which one of the following, when confirmed with a repeat test, meets the diagnostic criteria for diabetes mellitus?

<table>
<thead>
<tr>
<th>Correct</th>
<th>Peer Responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>A fasting blood glucose level of 120 mg/dL</td>
<td>9%</td>
</tr>
<tr>
<td>A 2-hour value of 180 mg/dL on an oral glucose tolerance test</td>
<td>9%</td>
</tr>
<tr>
<td>A random glucose level of 180 mg/dL in a patient with symptoms of diabetes mellitus</td>
<td>14%</td>
</tr>
<tr>
<td>A positive urine dipstick for glucose</td>
<td>1%</td>
</tr>
<tr>
<td>✓ A hemoglobin A\textsubscript{1c} of 7.0%</td>
<td>67%</td>
</tr>
</tbody>
</table>

Total Number of Responses: 9,178
Case 1 - Critique

An international expert committee issued a report in 2009 recommending that a hemoglobin A1c level ≥6.5% be used to diagnose diabetes mellitus. This recommendation was later adopted by the American Diabetes Association. Other criteria include a fasting plasma glucose level ≥126 mg/dL, a random glucose level ≥200 mg/dL in a patient with symptoms of diabetes, or a 2-hour oral glucose tolerance test value ≥200 mg/dL. While a urine dipstick may be used to screen for diabetes, it is not a diagnostic test.
A 55-year-old male sees you because of urinary frequency and lightheadedness. His previous history is significant for obesity and hypertension. His hemoglobin A1c level is 8.8% and his glucose level on a nonfasting basic metabolic panel is 221 mg/dL. He also has a serum creatinine level of 1.7 mg/dL (N 0.6–1.2), which is consistent with his baseline, and an estimated glomerular filtration rate of 51 mL/min/1.73 m².

Which one of the following is the preferred first-line agent to treat this patient’s new onset of diabetes mellitus?

- Exenatide (Byetta)
- Glipizide (Glucotrol)
- Metformin (Glucophage)
- Rosiglitazone (Avandia)
- Sitagliptin (Januvia)
Section 8

Pharmacologic Approaches to Glycemic Treatment

Focus on Type 2 Diabetes
Pharmacologic Therapy
Recommendations – General Principles

• Metformin is preferred and should be the preferred first line medication and should be continued unless contraindicated or not tolerated. A.

• Metformin (long term) may be associated with Vitamin B12 Deficiency, check periodically, especially in patients with anemia or neuropathy. B.
Pharmacologic Therapy Recommendations – Newly Dx Patients

General Principles

• When HgA1c ≥10 and/ or BG ≥300 (with or without other agents) consider insulin. E

• HgA1c ≥9 consider dual therapy when. E
### Pharmacologic Therapy Recommendations – CVD?

#### General Principles

<table>
<thead>
<tr>
<th><strong>No CVD</strong></th>
<th><strong>CVD</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• If on mono or dual therapy and not at goal over 3 months, add another agent. A</td>
<td>• Start with lifestyle management and metformin; later introduce agent(s) proven to reduce CV events and mortality (empagliflozin, liraglutide). A</td>
</tr>
<tr>
<td></td>
<td>• Consider use of canagliflozin. C</td>
</tr>
</tbody>
</table>
Pharmacologic Therapy
Recommendations – Not at Goal
– General Principles

• Don’t delay drug intensification if not at glycemic goals, including considering insulin therapy. B
Antihyperglycemic Therapy in Adults with Type 2 Diabetes

At diagnosis, initiate lifestyle management, set A1C target, and initiate pharmacologic therapy based on A1C.

1. A1C is less than 9%, consider Monotherapy.
2. A1C is greater than or equal to 9%, consider Dual Therapy.
3. A1C is greater than or equal to 10%, blood glucose is greater than or equal to 300 mg/dL, or patient is markedly symptomatic, consider Combination Injectable Therapy (See Figure 8.2).

**Monotherapy**

<table>
<thead>
<tr>
<th>Lifestyle Management + Metformin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initiate metformin therapy if no contraindications* (See Table 8.1)</td>
</tr>
</tbody>
</table>

**Dual Therapy**

<table>
<thead>
<tr>
<th>Lifestyle Management + Metformin + Additional Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASCVD? Yes: Add agent proven to reduce major adverse cardiovascular events and/or cardiovascular mortality (see recommendations with * on p. 575 and Table 8.1) No: Add second agent after consideration of drug-specific effects and patient factors (See Table 8.1)</td>
</tr>
</tbody>
</table>

**Triple Therapy**

<table>
<thead>
<tr>
<th>Lifestyle Management + Metformin + Two Additional Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Add third agent based on drug-specific effects and patient factors (Table 8.1)</td>
</tr>
</tbody>
</table>

**Combination Injectable Therapy**

(See Figure 8.2)
Basal Insulin Therapy

Initiate Basal Insulin
Usually with metformin +/- other noninsulin agent
- Start: 10 U/day or 0.1-0.2 U/kg/day
- Adjust: 10-15% or 2-4 units once or twice weekly to reach FBG target
- For hypo: Determine & address cause; if no clear reason for hypo, ↓ dose by 4 units or 10-20%

If A1C not controlled, consider combination injectable therapy

Add 1 rapid-acting insulin injection before largest meal
- Start: 4 units, 0.1 U/kg, or 10% basal dose. If A1C <7%, consider ↓ basal by same amount
- Adjust: ↑ dose by 1-2 units or 10-15% once or twice weekly until SMBG target reached
- For hypo: Determine and address cause; if no clear reason for hypo, ↓ corresponding dose by 2-4 units or 10-20%

If A1C not controlled, advance to basal-bolus

Add ≥2 rapid-acting insulin injections before meals ('basal-bolus')
- Start: 4 units, 0.1 U/kg, or 10% basal dose/meal. If A1C <7%, consider ↓ basal by same amount
- Adjust: ↑ dose(s) by 1-2 units or 10-15% once or twice weekly to achieve SMBG target
- For hypo: Determine and address cause; if no clear reason for hypo, ↓ corresponding dose by 2-4 units or 10-20%

If A1C not controlled, advance to 3rd injection

Add GLP-1 RA
- If not tolerated or A1C target not reached, change to 2 injection insulin regimen
- If goals not met, consider changing to alternative insulin regimen

Change to premixed insulin twice daily (before breakfast and supper)
- Start: Divide current basal dose into ½ AM, ½ PM or ⅛ AM, ⅛ PM
- Adjust: ↑ dose by 1-2 units or 10-15% once or twice weekly until SMBG target reached
- For hypo: Determine and address cause; if no clear reason for hypo, ↓ corresponding dose by 2-4 units or 10-20%

Change to premixed analog insulin 3 times daily (breakfast, lunch, supper)
- Start: Add additional injection before lunch
- Adjust: ↑ doses by 1-2 units or 10-15% once or twice weekly to achieve SMBG target
- For hypo: Determine and address cause; if no clear reason for hypo, ↓ corresponding dose by 2-4 units or 10-20%
Meds! 12 Classes

- Biguanide(s) – 1st Line
- Sulfonylureas*
- Meglitinides
- Thiazolidinediones*
- Alpha-Glucosidase inhibitors
- DPP-4 inhibitors*
- Bile acid sequestrants
- Dopamine-2 agonists
- SGLT2 inhibitors*
- GLP-1 receptor agonists*
- Amylin mimetic(s)
- Insulin/ analog(s)*
## Drug and Patient Factors Table

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Efficacy</th>
<th>Hypoglycemia</th>
<th>Weight Change</th>
<th>CV Effects</th>
<th>Cost</th>
<th>Dial/SQ</th>
<th>Renal Effects</th>
<th>Additional Considerations</th>
</tr>
</thead>
</table>
| Metformin        | High     | No           | Neutral (Potentially Medial Loss) | Neutral Benefit | Low   | Oral    | Neutral        | - Gastrointestinal side effects common (diarrhea, nausea)  
|                  |          |              |               |            |       |         |               | - Potential for S12 deficiency |
| SGL-2 Inhibitors | Intermediate | No       | Less | Neutral | High | Oral | Benefit canagliflozin, empagliflozin | - FDA Black Box: Risk of amputation (canagliflozin)  
|                  |          |              |               |            |       |         |               | - Risk of bone fracture (canagliflozin)  
|                  |          |              |               |            |       |         |               | - DKA risk (all agents, rare in T2DM)  
|                  |          |              |               |            |       |         |               | - Genitourinary infections  
|                  |          |              |               |            |       |         |               | - Risk of volume depletion, hypertension  
|                  |          |              |               |            |       |         |               | - Not indicated |
| GLP-1 RAs        | High     | No           | Less | Neutral | High | SQ     | Benefit | - FDA Black Box: Risk of hypoglycemia  
|                  |          |              |               |            |       |         |               | - Contraindication (no evidence of extended release)  
|                  |          |              |               |            |       |         |               | - Gastrointestinal side effects common (nausea, vomiting, diarrhea)  
|                  |          |              |               |            |       |         |               | - Injection site reactions  
|                  |          |              |               |            |       |         |               | - None prescribed |
| DPP-4 Inhibitors | Intermediate | No       | Neutral | Neutral | High | Oral | Neutral | - Renal dose adjustment required can be used in renal impairment  
|                  |          |              |               |            |       |         |               | - Potential risk of acute pancreatitis  
|                  |          |              |               |            |       |         |               | - Arthritis |
| Thiazolidinediones | High     | No           | Gain | Neutral | High | Oral | Neutral | - No dose adjustment required  
|                  |          |              |               |            |       |         |               | - Contraindication (no evidence of extended release)  
|                  |          |              |               |            |       |         |               | - FDA Black Box: Congestive heart failure (rosiglitazone, pioglitazone)  
|                  |          |              |               |            |       |         |               | - Fluid retention (edema, heart failure)  
|                  |          |              |               |            |       |         |               | - Benefit in NASH  
|                  |          |              |               |            |       |         |               | - Risk of bone fractures  
|                  |          |              |               |            |       |         |               | - Nodular onset (rosiglitazone)  
|                  |          |              |               |            |       |         |               | - Not indicated (rosiglitazone) |
| Sulfonylureas (Third Generation) | High | Yes | Gain | Neutral | High | Oral | Neutral | - Glyburide: increased risk of cardiovascular mortality based on studies of an older sulfonylurea (tolbutamide)  
|                  |          |              |               |            |       |         |               | - FDA Special Warning an increased risk of cardiovascular mortality  
|                  |          |              |               |            |       |         |               | - Injection site reactions  
|                  |          |              |               |            |       |         |               | - Higher risk of hypoglycemia with human insulin  
| Insulin Analogs  | Highest | No | Gain | Neutral | High | SQ | Neutral | - Less insulin doses required with a decrease in mGluR10 per clinical response  
|                  |          |              |               |            |       |         |               | - Injection site reactions  
|                  |          |              |               |            |       |         |               | - Higher risk of hypoglycemia with human insulin (NPH) or premixed formulations vs. analogues |
Biguanides (Metformin)

- Decreased hepatic glucose production
- High efficacy, generally first line therapy
- Low risk of hypoglycemia
- Weight neutral to weight loss
- Potentially beneficial with CVD
- Low cost
- Oral
- CI with GFR <30 (care if 30-45)
# Biguanides (Metformin)

From the Table

<table>
<thead>
<tr>
<th>Efficacy</th>
<th>Hypoglycemia</th>
<th>Weight Change</th>
<th>CV Effects</th>
<th>Cost</th>
<th>Oral/SQ</th>
<th>Renal Effects</th>
<th>Additional Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>ASCVD</td>
<td>GFR</td>
<td>Low</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metformin</td>
<td>High</td>
<td>No</td>
<td>Neutral (Potential for Modest Loss)</td>
<td>Neutral</td>
<td>Low</td>
<td>Oral</td>
<td>Neutral</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Potential Benefit</td>
<td>Neutral</td>
<td>Low</td>
<td>Oral</td>
<td>Neutral</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Potential for B12 deficiency</td>
</tr>
</tbody>
</table>
Metformin

• Comes in IR and ER
• Depending on formulation, maximum dose between 2,000 – 2,550 mg
• GI side effects are common
• B12 deficiency is a possibility
Sulfonureas – 2\textsuperscript{nd} generation

- Glyburide (regular and micronized, [not bioequivalent], qD or BID)
- Glipizide (IR and XL, qD or BID)
- Glimepiride (qD)

- Glyburide and Glipizide + Metformin
- Glimepiride + Thiazolidinediones
## Sulfonureas – From the Table

<table>
<thead>
<tr>
<th>Sulfonureas (2nd Generation)</th>
<th>Efficacy</th>
<th>Hypoglycemia</th>
<th>Weight Change</th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>High</td>
<td>Yes</td>
<td>Gain</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Oral</td>
<td>FDA Special Warning on increased risk of cardiovascular mortality based on studies of an older sulfonylurea (tolbutamide)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Glyburide: not recommended</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Glipizide &amp; olmesapide; initiate conservatively to avoid hypoglycemia</td>
</tr>
</tbody>
</table>
Sulfonureas – 2\textsuperscript{nd} generation

- Increases insulin secretion
- High efficacy
- **Risk of hypoglycemia**
- **Potential weight gain**
- Cardiac neutral
- Low cost
- Oral
Sulfonureas – 2\textsuperscript{nd} generation

- Glyburide – avoid if CrCl <50
- Start the other 2 slowly to avoid hypoglycemia if RI

- Old studies showed increased risk of CV mortality with an older sulfonurea
Meglitinides (glinides)

- Repaglinide (Prandin)
- Nateglinide (Starlix)

- Repaglinide also with metformin
Meglitinides (glinides)

- Increases insulin secretion (same mechanism as Sulfonureas)
- Oral
- Care with CrCl <30
- Best for patients with
  - Sulfa allergies
  - Irregular schedules
  - Late post-prandial hypoglycemia on Sulfonureas
Thiazolidinediones

- Pioglitazone (Actos)
- Rosiglitazone (Avandia)

- Both with metformin or glimepiride
- Pioglitazone with alogliptin (DPP-4 inhibitor)
## Thiazolidinediones – From the Table

<table>
<thead>
<tr>
<th>Efficacy</th>
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<tbody>
<tr>
<td>Thiazolidinediones</td>
<td>High</td>
<td>No</td>
<td>Gain</td>
<td>Potential Benefit: pioglitazone</td>
<td>Increased Risk</td>
<td>Low</td>
<td>Oral</td>
</tr>
</tbody>
</table>
| | | | | | | | | - No dose adjustment required
- Generally not recommended in renal impairment due to potential for fluid retention
- FDA Black Box: Congestive heart failure (pioglitazone, rosiglitazone)
- Fluid retention (edema; heart failure)
- Benefit in NASH
- Risk of bone fractures
- Bladder cancer (pioglitazone)
- ↑ LDL cholesterol (rosiglitazone) |
Thiazolidinediones

- Increases insulin sensitivity
- High Efficacy
- *No risk of hypoglycemia*
- **Potential weight gain**
- Pioglitazone may be beneficial in CVD
- Increased risk of CHF (fluid retention)
- Low cost
- Oral
Thiazolidinediones

- Neutral for kidneys, avoid use in RI due to fluid retention risk
- BLACK BOX WARNING for both → CHF
- Risks
  - Fluid retention
  - May be beneficial in NASH
  - Risk of bone fracture
  - Pioglitazone → bladder cancer
  - Rosiglitazone → increased LDL cholesterol
DPP-4 Inhibitors

- Sitagliptin (Januvia)
- Saxagliptin (Onglyza)
- Linagliptin (Tradjenta)
- Alogliptin (Nesina)

DPP-4 $\rightarrow$ Dipeptidyl peptidase-4
DPP-4 Inhibitors

- Sitagliptin → Ertugliflozin (SGLT-2i); simvastatin
- Saxagliptin → Dapagliflozin (SGLT-2i)
- Linagliptin → Empagliflozin (SGLT-2i)
- Alogliptin → Pioglitazone (TDZ)

- All 4 with metformin
# DPP-4 Inhibitors – From the Table

<table>
<thead>
<tr>
<th>Efficacy*</th>
<th>Hypoglycemia</th>
<th>Weight Change</th>
<th>CV Effects</th>
<th>Cost</th>
<th>Oral/SQ</th>
<th>Renal Effects</th>
<th>Additional Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>DPP-4 Inhibitors</td>
<td>Intermediate</td>
<td>No</td>
<td>Neutral</td>
<td>Neutral</td>
<td>High</td>
<td>Oral</td>
<td>Neutral</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ASCVD</td>
<td>C/I/F</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Risk: saxagliptin, alogliptin</td>
<td></td>
<td></td>
<td></td>
<td>▪ Joint pain</td>
</tr>
</tbody>
</table>

* Insulin

* Glucagon
DPP-4 Inhibitors

• Increase insulin secretion and decreases glucagon secretion
• Intermediate efficacy
• *No risk of hypoglycemia*
• *Neutral for weight gain*
• CVD neutral; CHF potential with Saxagliptin and Alogliptin
DPP-4 Inhibitors

• High cost
• Oral, once daily
• May need renal dose adjustment
• Can use in RF
• Potential risk of pancreatitis/ joint pain
SGLT-2 Inhibitors

- Canagliflozin (Invokana)
- Dapagliflozin (Farxiga)
- Empagliflozin (Jardiance)
- Ertugliflozin* (Steglatro)

SGLT-2 $\rightarrow$ Sodium GLucose co-Transporter 2
SGLT-2 Inhibitor Combos

- Canagliflozin $\rightarrow$ Metformin
- Dapagliflozin $\rightarrow$ Metformin; Saxagliptin (DPP-4i)
- Empagliflozin $\rightarrow$ Metformin; Linagliptin (DPP-4i)
### SGLT-2 Inhibitor – From the Table

#### Glucose

<table>
<thead>
<tr>
<th>SGLT-2 inhibitors</th>
<th>Efficacy</th>
<th>Hypoglycemia</th>
<th>Weight Change</th>
<th>CV Effects</th>
<th>Cost</th>
<th>Oral/SQ</th>
<th>Renal Effects</th>
<th>Additional Considerations</th>
</tr>
</thead>
</table>
|                   | Intermediate | No | Loss | Benefit: canagliflozin, empagliflozin<sup>1</sup> | Benefit: canagliflozin, empagliflozin | High | Oral | Benefit: canagliflozin, empagliflozin | Canagliflozin: not recommended with eGFR <60  
Dapagliflozin: not recommended with eGFR <60; contraindicated with eGFR <30  
Empagliflozin: contraindicated with eGFR <30 | FDA Black Box: Risk of amputation (canagliflozin)  
Risk of bone fractures (canagliflozin)  
DKA risk (all agents, rare in T2DM)  
Genitourinary infections  
Risk of volume depletion, hypotension  
↑LDL cholesterol |
SGLT-2 Inhibitors

- Blocks glucose reabsorption by the kidney → increases glucosuria
- Intermediate effectiveness
- No risk of hypoglycemia
- Promotes weight loss
- Canagliflozin and Empagliflozin may benefit CVD and CHF
- High cost
SGLT-2 Inhibitors

• **Oral**

• Canagliflozin and Empagliflozin may help avert diabetic renal disease

• Care with decreased GFR

• Reference table as each has different recommendations for renal insufficiency
SGLT-2 Inhibitors

- Canagliflozin - **Black box warning**
  - Risk of amputation
- Canagliflozin – risk of bone fractures
- DKA risk (all) – rare
- GU infections (all)
- Risk of hypovolemic; hypotension
- Elevated LDL

Glucose
GLP-1 Receptor Agonists

- Exenatide (Byetta)
- Lixisenatide (Adlyxin)
- Liraglutide (Victoza, Saxenda)
- Exenatide (extended release - weekly) (Bydureon)
- Albiglutide (Tanzeum)
- Dulaglutide (Trulicity)
- Semaglutide (Ozempic)

GLP-1 → Glucagon Like Peptide 1 (Incretin Mimetic)
GLP-1 RAs – From the Table

<table>
<thead>
<tr>
<th>GLP-1 RAs</th>
<th>Efficacy</th>
<th>Hypoglycemia</th>
<th>Weight Change</th>
<th>CV Effects</th>
<th>Cost</th>
<th>Oral/SQ</th>
<th>Renal Effects</th>
<th>Additional Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>High</td>
<td>No</td>
<td>Loss</td>
<td>Neutral</td>
<td>High</td>
<td>SQ</td>
<td>Benefit: Exenatide</td>
<td>FDA Black Box: Risk of thyroid C-cell tumors</td>
</tr>
</tbody>
</table>

- Exenatide not indicated with eGFR <30
- Lisinamide caution with eGFR <30
- Increased risk of side effects in patients with renal impairment

*Insulin*
*Glucagon*
GLP-1 RAs and Combos

• With Basal Insulins:
  – Liraglutide → Degludec
  – Lixisenatide → Glargine

• Mechanism of Action – 4
  – Increased insulin secretion (glucose dependent)
  – Decreased glucagon secretion (glucose dependent)
  – Slows gastric emptying
  – Increased satiety
GLP-1 RAs

• High efficacy
• *No risk of hypoglycemia*
• *Promotes weight loss*
• Liraglutide (regular not XR) may benefit CVD
• No CHF effect
GLP-1 RAs

• High cost
• **Subcutaneous**
• Liraglutide may help with renal disease
• Increased risk of Side Effects with RI (check prescribing information)
• GFR<30
  – CI for Exenatide (both)
  – Caution with Lixisenatide
GLP-1 RAs Side Effects

- **Black Box Warning** → Risk of thyroid C-cell tumors for 5 in class (see prescribing information)
  - End in ‘-TIDE’ think about ‘TIroiDE’
- GI side effects common
- Injection site reactions
- ? Pancreatitis risk

http://togotv.dbcls.jp/ja/togopic.2014.4.html
Alpha-Glucosidase Inhibitors

- Acarbose (Preconse)
- Miglitol (Glyset)
Alpha-Glucosidase Inhibitors

• Slows intestinal carbohydrate digestion and absorption

• Oral

• Avoid use if Cr <30 (Acarbose) or <25 (Miglitol)
Bile Acid Sequestrants

• Colesevelam (Welchol)
Bile Acid Sequestrants

• Unsure mechanism of action – think decreased hepatic glucose production and increased incretin levels

• Used for both DM and high cholesterol (same doses)

• Oral

• No adjustment for renal or liver issues
Dopamine-2 Agonists

- Bromocriptine quick release (0.8 mg)
- Oral, first thing in the morning
- Modulates hypothalamic regulation of metabolism; may increase insulin sensitivity
- Lower doses (up to 4.8 mg daily)
- Main side effect – Nausea
- CI – Type I DM, syncope, psychosis

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3152192/
Dopamine-2 Agonists

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3152192/
Amylin Mimetics

- Pramlintide (Symlin)
  - Decreased glucagon secretion
  - Slows gastric emptying
  - Increased satiety
  - No renal dosing changes
  - Risk of hypoglycemia
  - Subcutaneous
  - Expensive
Specific Recommendation from Section 8

A patient-centered approach should be used to guide the choice of pharmacologic agents. Considerations include efficacy, hypoglycemia risk, history of atherosclerotic cardiovascular disease, impact on weight, potential side effects, renal effects, delivery method (oral versus subcutaneous), cost, and patient preferences. E
Insulin

- Rapid acting analogs
- Short-acting analogs
- Intermediate acting analogs
- Concentrated Regular
- Basal analogs
- Premixed
- Premixed insulin/ GLP-1 RA (2)
Case 2

A 55-year-old male sees you because of urinary frequency and lightheadedness. His previous history is significant for obesity and hypertension. His hemoglobin A\textsubscript{1c} level is 8.8% and his glucose level on a nonfasting basic metabolic panel is 221 mg/dL. He also has a serum creatinine level of 1.7 mg/dL (N 0.6–1.2), which is consistent with his baseline, and an estimated glomerular filtration rate of 51 mL/min/1.73 m\textsuperscript{2}.

Which one of the following is the preferred first-line agent to treat this patient’s new onset of diabetes mellitus?

- Exenatide (Byetta)
- Glipizide (Glucotrol)
- Metformin (Glucophage)
- Rosiglitazone (Avandia)
- Sitagliptin (Januvia)
Case 2 - Answer

A 55-year-old male sees you because of urinary frequency and lightheadedness. His previous history is significant for obesity and hypertension. His hemoglobin A1c level is 8.8% and his glucose level on a nonfasting basic metabolic panel is 221 mg/dL. He also has a serum creatinine level of 1.7 mg/dL (N 0.6–1.2), which is consistent with his baseline, and an estimated glomerular filtration rate of 51 mL/min/1.73 m².

Which one of the following is the preferred first-line agent to treat this patient’s new onset of diabetes mellitus?

- **Correct**
- Exenatide (Byetta) 10%
- Glipizide (Glucotrol) 17%
- **Metformin (Glucophage)** 65%
- Rosiglitazone (Avandia) 1%
- Sitagliptin (Januvia) 9%

Total Number of Responses 2,171
Case 2 - Critique

Metformin is the preferred first-line agent for this patient’s new-onset diabetes mellitus, and may be tried as monotherapy if the hemoglobin A1c level is <9%. Metformin is effective, and there is mortality data to support its use. There is a low risk of hypoglycemia and a neutral to beneficial effect on weight for patients who are overweight or obese. Metformin is available as a generic drug and has a low cost with an excellent safety record. Concerns about lactic acidosis in patients with renal dysfunction have been largely unfounded. The FDA has changed the labeling regarding the use of metformin in patients with kidney impairment, shifting from a focus on creatinine to a focus on estimated glomerular filtration rate (eGFR) and being less restrictive about use in these patients. Metformin is contraindicated in patients with an eGFR <30 mL/min/1.73 m², can be safely used with an eGFR >45 mL/min/1.73 m², and merits consideration for those with an eGFR between these two values.

A sulfonylurea is not the preferred first-line treatment for this patient, partly due to the risks of hypoglycemia and weight gain. A thiazoladinedione would increase his risk of weight gain and possibly of renal cancer and heart failure, and a DPP-4 inhibitor has a high cost and low efficacy. A GLP-1 receptor agonist is not preferred because of its high cost, gastrointestinal side effects, and administration via injection.
References/ Additional Information


• Summary of Revisions: Standards of Medical Care in Diabetes – 2018 Diabetes Care 2018; 41(Suppl. 1):54-56
There’s an App for That!

Search for → ADA Standards of Care app in app store or Google play

• Available from: https://www.ncbi.nlm.nih.gov/books/NBK425702/
References/ Additional Information

- http://resources.aace.com/
- http://outpatient.aace.com/slide-library
- www.diabetes.org/socrisktest
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3152192/
Educational Podcast

Description

If you've ever wanted to know about champagne, satanism, the Stonewall Uprising, chaos theory, LSD, El Nino, crime and Rosa Parks then look no further. Josh and Chuck have you covered.

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
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<tr>
<td>1 How the Stanford Prison ...</td>
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<tr>
<td>2 How Diabetes Works</td>
<td>Type 2 diabetes is on ...</td>
<td>7/3/2018</td>
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How Diabetes Works

July 3, 2018

Type 2 diabetes is one of the biggest killers of people on the planet. And yet, it also seems to be tied to diet and exercise, which makes it preventable. Learn about the fascinating mechanisms that can make your body go haywire and lead to this disease.
Section 3

Comprehensive Medical Evaluation and Assessment of Comorbidities
Patient-Centered Collaborative Care

• A patient-centered communication style that uses person-centered and strength-based language, active listening, elicits patient preferences and beliefs, and assesses literacy, numeracy, and potential barriers to care should be used to optimize patient health outcomes and health-related quality of life. B
Overarching Themes

- Patient centered
- Active listening
- Patient preferences / beliefs
- Barrier identification
  - Literacy
  - Numeracy
  - Others
- Optimizing outcomes/ QOL
Comprehensive Medical Evaluation 1/3

• Confirm the diagnosis and classify diabetes (section 2). B
• Evaluate for diabetes complications and potential comorbid conditions. E
• Review previous treatment and risk factor control in patients with established diabetes. E
Comprehensive Medical Evaluation 2/3

• Begin patient engagement in the formulation of a care management plan. B

• Develop a plan for continuing care. B
Comprehensive Medical Evaluation – Follow up 3/3

• Interval medical history
• Medication
• Physical examination
• Labs (A1C and metabolic targets)
• Assessment:
  – Complications risk
  – Self-management
  – Behaviors, nutrition, psychosocial health
  – Referral need
  – Immunizations and other routine health maintenance screening. B
# History Review

<table>
<thead>
<tr>
<th>Past Medical and Family History</th>
<th>1 – Initial</th>
<th>2 – Follow up</th>
<th>3 – Annual visit</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diabetes history</strong></td>
<td>✓</td>
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<tr>
<td>Characteristics at onset (e.g., age, symptoms)</td>
<td>✓</td>
<td>✓</td>
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<td>✓</td>
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</tr>
<tr>
<td>Assess frequency/cause/severity of past hospitalizations</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td><strong>Family history</strong></td>
<td></td>
<td>✓</td>
<td></td>
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<tr>
<td>Family history of diabetes in a first-degree relative</td>
<td>✓</td>
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<tr>
<td>Family history of autoimmune disorder</td>
<td>✓</td>
<td>✓</td>
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</tr>
<tr>
<td><strong>Personal history of complications and common comorbidities</strong></td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>Macrovascular and microvascular</td>
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<tr>
<td>Common comorbidities</td>
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<tr>
<td>Presence of hemoglobinopathies or anemias</td>
<td>✓</td>
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<tr>
<td>High blood pressure or abnormal lipids</td>
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<td>✓</td>
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<tr>
<td>Last dental visit</td>
<td>✓</td>
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<tr>
<td>Last dilated eye exam</td>
<td>✓</td>
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<tr>
<td>Visits to specialists</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td><strong>Interval history</strong></td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Changes in medical/family history since last visit</td>
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<table>
<thead>
<tr>
<th>Social History</th>
<th>1 – Initial</th>
<th>2 – Follow up</th>
<th>3 – Annual visit</th>
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</thead>
<tbody>
<tr>
<td><strong>Assess lifestyle and behavior patterns</strong></td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>Eating patterns and weight history</td>
<td>✓</td>
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<td></td>
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<tr>
<td>Sleep behaviors and physical activity</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>Familiarity with carbohydrate counting in type 1 diabetes</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Tobacco, alcohol, and substance use</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Identify existing social supports</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td><strong>Interval history</strong></td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Changes in social history since last visit</td>
<td>✓</td>
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<td>✓</td>
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</table>

<table>
<thead>
<tr>
<th>Medications and Vaccinations</th>
<th>1 – Initial</th>
<th>2 – Follow up</th>
<th>3 – Annual visit</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medications-taking behavior</strong></td>
<td>✓</td>
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<tr>
<td>Medication intolerance or side effects</td>
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<tr>
<td>Complementary and alternative medicine use</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>Vaccination history and needs</td>
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<table>
<thead>
<tr>
<th>Technology Use</th>
<th>1 – Initial</th>
<th>2 – Follow up</th>
<th>3 – Annual visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assess use of health apps, online education, patient portals, etc.</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Glucose monitoring (meter/CGM); results and data use</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Review insulin pump settings</td>
<td>✓</td>
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<table>
<thead>
<tr>
<th>Screening</th>
<th>1 – Initial</th>
<th>2 – Follow up</th>
<th>3 – Annual visit</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Psychosocial conditions</strong></td>
<td></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Screen for depression, anxiety, and disordered eating; refer for further assessment or intervention if warranted</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Consider assessment for cognitive impairment*</td>
<td>✓</td>
<td>✓</td>
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</tr>
<tr>
<td><strong>Diabetes self-management education and support</strong></td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>History of clinical/diabetes educator visits</td>
<td>✓</td>
<td>✓</td>
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</tr>
<tr>
<td>Screen for barriers to diabetes self-management</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Refer or offer local resources and support as needed</td>
<td>✓</td>
<td>✓</td>
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</tr>
<tr>
<td><strong>Hypoglycemia</strong></td>
<td></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Timing of episodes, awareness, frequency and causes</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
</tbody>
</table>

| Pregnancy Planning            |            | ✓            |                  |
| For women with childbearing capacity, review contraception needs and preconception planning | ✓          | ✓            |                 |
# PMHx and FHx Review

**Columns:**
1. Initial
2. Follow up
3. Annual visit

## Past Medical and Family History

<table>
<thead>
<tr>
<th>Diabetes History</th>
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<td>Characteristics at onset (e.g., age, symptoms)</td>
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<tr>
<th>Family History</th>
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<tbody>
<tr>
<td>Family history of diabetes in a first-degree relative</td>
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<table>
<thead>
<tr>
<th>Personal history of complications and common comorbidities</th>
<th>Initial</th>
<th>Follow up</th>
<th>Annual visit</th>
</tr>
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<tbody>
<tr>
<td>Macrovascular and microvascular</td>
<td>✓</td>
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<tr>
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</table>

<table>
<thead>
<tr>
<th>Interval History</th>
<th>Initial</th>
<th>Follow up</th>
<th>Annual visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Changes in medical/family history since last visit</td>
<td>✓</td>
<td></td>
<td>✓</td>
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</tbody>
</table>
# Social History Review

## Assess lifestyle and behavior patterns
- Eating patterns and weight history
- Sleep behaviors and physical activity
- Familiarity with carbohydrate counting in type 1 diabetes
- Tobacco, alcohol, and substance use
- Identify existing social supports

## Interval history
- Changes in social history since last visit

<table>
<thead>
<tr>
<th>Columns:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 – Initial</td>
</tr>
<tr>
<td>2 – Follow up</td>
</tr>
<tr>
<td>3 – Annual visit</td>
</tr>
</tbody>
</table>
# Medication Review

Columns:
1 – Initial
2 – Follow up
3 – Annual visit

<table>
<thead>
<tr>
<th>Medications and Vaccinations</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Medication-taking behavior</td>
</tr>
<tr>
<td>- Medication intolerance or side effects</td>
</tr>
<tr>
<td>- Complementary and alternative medicine use</td>
</tr>
<tr>
<td>- Vaccination history and needs</td>
</tr>
</tbody>
</table>
Immunizations

• Provide routinely recommended vaccinations for children and adults with diabetes by age. C
  – Annual influenza vaccine is recommended for all people ≥6 months of age. C

• Pneumococcal disease
  – PCV13 (13-valent pneumococcal conjugate vaccine) → children before age 2 years. C
  – PPSV23 (23-valent pneumococcal polysaccharide vaccine) for ages 2 through 64 years with diabetes AND ≥65 years. C

• Hepatitis B
  – Unvaccinated adults with diabetes ages 19 through 59 years. C
  – Consider same for unvaccinated adults with diabetes ages ≥60 years. C
## Technology Review

### Columns:
1. Initial
2. Follow up
3. Annual visit

<table>
<thead>
<tr>
<th>TECHNOLOGY USE</th>
<th>Initial</th>
<th>Follow up</th>
<th>Annual visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assess use of health apps, online education, patient portals, etc.</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Glucose monitoring (meter/CGM): results and data use</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Review insulin pump settings</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>
## Screening

**Columns:**
1. Initial
2. Follow up
3. Annual visit

### Psychosocial conditions
- Screen for depression, anxiety, and disordered eating; refer for further assessment or intervention if warranted
- Consider assessment for cognitive impairment*

<table>
<thead>
<tr>
<th>Screening</th>
<th>Initial</th>
<th>Follow up</th>
<th>Annual visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

### Diabetes self-management education and support
- History of dietitian/diabetes educator visits
- Screen for barriers to diabetes self-management
- Refer or offer local resources and support as needed

<table>
<thead>
<tr>
<th>Screening</th>
<th>Initial</th>
<th>Follow up</th>
<th>Annual visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

### Hypoglycemia
- Timing of episodes, awareness, frequency and causes

<table>
<thead>
<tr>
<th>Screening</th>
<th>Initial</th>
<th>Follow up</th>
<th>Annual visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

### Pregnancy planning
- For women with childbearing capacity, review contraceptive needs and preconception planning

<table>
<thead>
<tr>
<th>Screening</th>
<th>Initial</th>
<th>Follow up</th>
<th>Annual visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>
Other Co-Morbidities

• In people with a history of cognitive impairment/dementia, intensive glucose control cannot be expected to remediate deficits. Treatment should be tailored to avoid significant hypoglycemia. B

• Annually screen people who are prescribed atypical antipsychotic medications for prediabetes or diabetes. B
Other Recommendations

• Check morning testosterone in men with DM with signs/ sx of hypogonadism - B
• Patients with HIV screened for DM before treatment, when adjusting and regularly if negative (for DM) - E
• 2\textsuperscript{nd} Generation antipsychotic usage in person with DM, weight, glucose control and lipids should be watched and reassess treatment regimen – C
• DM self-care activities with people with DM and serious mental illness
Other Co-Morbidities

• Fatty liver disease – can be improved with DM and lipid tx
• Fractures – increased hip fx risk
  – Thiazolidinediones; SGLT-2 Inhibitors
• Hearing impairment
  – 2x as common in patients with Diabetes than those without.
• Obstructive Sleep Apnea
  – If present, treatment may improve BP, QOL and some glycemic control
Anxiety/ Depression

• Anxiety – screen those with anxious sx that interfere with their life or tx. B
• Fear of hypoglycemia can be treated with blood glucose awareness training. A
• Depression – Consider annual screening, at diagnosis or significant changes. B
• Depression – Refer to experienced practitioners. A
Disordered Eating

• Providers should consider reevaluating the treatment regimen of people with diabetes who present with symptoms of disordered eating behavior, an eating disorder, or disrupted patterns of eating. B

• Consider screening for disordered or disrupted eating using validated screening measures when hyperglycemia and weight loss are unexplained based on self-reported behaviors related to medication dosing, meal plan, and physical activity. In addition, a review of the medical regimen is recommended to identify potential treatment related effects on hunger/caloric intake. B
<table>
<thead>
<tr>
<th>PHYSICAL EXAMINATION</th>
<th>Columns:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Height, weight, and BMI: growth/ pubertal development in children and adolescents</td>
<td>Initial</td>
<td>✔</td>
</tr>
<tr>
<td>▪ Blood pressure determination</td>
<td>Follow up</td>
<td>✔</td>
</tr>
<tr>
<td>▪ Orthostatic blood pressure measures (when indicated)</td>
<td>Annual visit</td>
<td>✔</td>
</tr>
<tr>
<td>▪ Fundoscopic examination (refer to eye specialist)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ Thyroid palpation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ Skin examination (e.g., acanthosis nigricans, insulin injection or insertion sites, lipodystrophy)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| ▪ Comprehensive foot examination  
  ▪ Visual inspection (e.g., skin integrity, callous formation, foot deformity or ulcer, tears) | Initial | ✔ |
| ▪ Screen for PAD (pedal pulses; refer for ABI if diminished) | Follow up | ✔ |
| ▪ Determination of temperature, vibration or pinprick sensation, and 10-g monofilament exam | Annual visit | ✔ |

<table>
<thead>
<tr>
<th>LABORATORY EVALUATION</th>
<th>Columns:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ A1C, if the results are not available within the past 3 months</td>
<td>Initial</td>
<td>✔</td>
</tr>
</tbody>
</table>
| ▪ If not performed/available within the past year  
  ▪ Lipid profile, including total, LDL, and HDL cholesterol and triglycerides#  
  ▪ Liver function tests#  
  ▪ Spot urinary albumin-to-creatinine ratio  
  ▪ Serum creatinine and estimated glomerular filtration rate†  
  ▪ Thyroid-stimulating hormone in patients with type 1 diabetes‡  
  ▪ Vitamin B12 if on metformin (when indicated)  
  ▪ Serum potassium levels in patients on ACE inhibitors, ARBs, or diuretics§ | Follow up | ✔ |

<table>
<thead>
<tr>
<th>ASSESSMENT AND PLAN</th>
<th>Columns:</th>
<th></th>
</tr>
</thead>
</table>
| ▪ Goal setting  
  ▪ Set A1C/blood glucose target and monitoring frequency  
  ▪ If hypertension diagnosed, establish blood pressure goal  
  ▪ Incorporate new members to the care team as needed  
  ▪ Diabetes education and self-management support needs | Initial | ✔ |

<table>
<thead>
<tr>
<th>Cardiovascular risk assessment and staging of CKD</th>
<th>Columns:</th>
<th></th>
</tr>
</thead>
</table>
| ▪ History of ASCVD  
  ▪ Presence of ASCVD risk factors (see Table 9.2)  
  ▪ Staging of CKD (see Table 10.1)† | Initial | ✔ |

<table>
<thead>
<tr>
<th>Therapeutic treatment plan</th>
<th>Columns:</th>
<th></th>
</tr>
</thead>
</table>
| ▪ Lifestyle management  
  ▪ Pharmacologic therapy  
  ▪ Referrals to specialists (including dietitian and diabetes educator) as needed  
  ▪ Use of glucose monitoring and insulin delivery devices | Initial | ✔ |
# Physical

Columns:
1 – Initial
2 – Follow up
3 – Annual visit

<table>
<thead>
<tr>
<th>Physical Examination</th>
<th>Initial</th>
<th>Follow up</th>
<th>Annual visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height, weight, and BMI; growth/pubertal development in children and adolescents</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Blood pressure determination</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Orthostatic blood pressure measures (when indicated)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Fundoscopic examination (refer to eye specialist)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Thyroid palpation</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Skin examination (e.g., acanthosis nigricans, insulin injection or insertion sites, lipodystrophy)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Comprehensive foot examination</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>- Visual inspection (e.g., skin integrity, callous formation, foot deformity or ulcer, toenails)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>- Screen for PAD (pedal pulses; refer for ABI if diminished)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>- Determination of temperature, vibration or pinprick sensation, and 10-g monofilament exam</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>
## Labs

### Columns:
1. Initial
2. Follow up
3. Annual visit

### Laboratory Evaluation

<table>
<thead>
<tr>
<th>Test</th>
<th>Initial</th>
<th>Follow up</th>
<th>Annual visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1C, if the results are not available within the past 3 months</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>If not performed/available within the past year</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Lipid profile, including total, LDL, and HDL cholesterol and triglycerides#</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>- Liver function tests#</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>- Spot urinary albumin-to-creatinine ratio</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>- Serum creatinine and estimated glomerular filtration rate†</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>- Thyroid-stimulating hormone in patients with type 1 diabetes#</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>- Vitamin B12 if on metformin (when indicated)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>- Serum potassium levels in patients on ACE inhibitors, ARBs, or diuretics†</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>
## Assessment and Plan

**Columns:**
1 – Initial  
2 – Follow up  
3 – Annual visit

### Goal setting
- Set A1C/blood glucose target and monitoring frequency
- If hypertension diagnosed, establish blood pressure goal
- Incorporate new members to the care team as needed
- Diabetes education and self-management support needs

### Cardiovascular risk assessment and staging of CKD
- History of ASCVD
- Presence of ASCVD risk factors (see Table 9.2)
- Staging of CKD (see Table 10.1)

### Therapeutic treatment plan
- Lifestyle management
- Pharmacologic therapy
- Referrals to specialists (including dietitian and diabetes educator) as needed
- Use of glucose monitoring and insulin delivery devices
## Presence of Coronary Artery Disease Risk Factors

<table>
<thead>
<tr>
<th>Age</th>
<th>ASCVD</th>
<th>Recommended statin intensity and combination treatment*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40 years</td>
<td>No</td>
<td>None†</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• If LDL cholesterol $\geq$ 70 mg/dL despite maximally tolerated statin dose, consider adding additional LDL-lowering therapy (such as ezetimibe or PCSK9 inhibitor)#</td>
</tr>
<tr>
<td>≥40 years</td>
<td>No</td>
<td>Moderate‡</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• If LDL cholesterol $\geq$ 70 mg/dL despite maximally tolerated statin dose, consider adding additional LDL-lowering therapy (such as ezetimibe or PCSK9 inhibitor)</td>
</tr>
</tbody>
</table>

*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 $\geq$ 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.
### Staging of Chronic Renal Disease

Table 10.1—CKD stages and corresponding focus of kidney-related care

<table>
<thead>
<tr>
<th>CKD stage†</th>
<th>eGFR (mL/min/1.73 m²)</th>
<th>Evidence of kidney damage*</th>
<th>Diagnose cause of kidney injury</th>
<th>Evaluate and treat CKD progression**</th>
<th>Evaluate and treat CKD complications***</th>
<th>Prepare for renal replacement therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>No clinical evidence of CKD</td>
<td>≥60</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>1</td>
<td>≥90</td>
<td>+</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>—</td>
</tr>
<tr>
<td>2</td>
<td>60–89</td>
<td>+</td>
<td>√</td>
<td>√</td>
<td>—</td>
<td>√</td>
</tr>
<tr>
<td>3</td>
<td>30–59</td>
<td>+/−</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>—</td>
</tr>
<tr>
<td>4</td>
<td>15–29</td>
<td>+/−</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>—</td>
</tr>
<tr>
<td>5</td>
<td>&lt;15</td>
<td>+/−</td>
<td>—</td>
<td>√</td>
<td>√</td>
<td>—</td>
</tr>
</tbody>
</table>

†CKD stages 1 and 2 are defined by evidence of kidney damage (+), while CKD stages 3–5 are defined by reduced eGFR with or without evidence of kidney damage (+/−). *Kidney damage is most often manifest as albuminuria (UACR ≥30 mg/g Cr) but can also include glomerular hematuria, other abnormalities of the urinary sediment, radiographic abnormalities, and other presentations. **Risk factors for CKD progression include elevated blood pressure, glycemia, and albuminuria. ***See Table 10.2.
Section 6

Glycemic Targets
Glycemic Targets

- Intensive insulin regimens should use SMBG (self-monitoring of blood glucose) before meals, snacks and bed and prn. B
- SMBG may help others with DM. E
- Type 1 patients may benefit from CGM (continuous). A
HgA1c Goals

- Non-pregnant adults \(\rightarrow 7\% \text{ or less. A}
- More or less stringent on individual basis. C/ B.

- More stringent?
- Less Stringent?
Factors to Assist HgA1c Goal

- Patient / Disease Features
  - More stringent <-> A1C 7% <-> Less stringent
  - Risks potentially associated with hypoglycemia and other drug adverse effects
    - low to high
  - Disease duration
    - newly diagnosed to long-standing
  - Life expectancy
    - long to short
  - Important comorbidities
    - absent to severe
  - Established vascular complications
    - absent to severe
  - Patient attitude and expected treatment efforts
    - highly motivated, excellent self-care capabilities to less motivated, poor self-care capabilities
  - Resources and support system
    - readily available to limited

- Usually not modifiable
- Potentially modifiable
HgA1c Frequency – How often check?

• If well controlled?
• Not at goal?
• Glycemic therapy changed?
HgA1c Frequency

• Check 2x yearly if well controlled. E
• Check 4x yearly with changed therapy or not at goals. E
• POC testing can be useful. E

• To convert HgA1c to average blood glucose →
  http://professional.diabetes.org/eAG
HgA1c and Microvascular Complications

• Reduced with HgA1c targets <7%
• Suggestion that lower HgA1c further reduces these complications (but at smaller absolute change)
• Have to weigh risks of hypoglycemia vs benefit of reduced microvascular complication

[Eye clipart](http://frpic.com/vectors/eyes-clipart/eyes-clipart.png)
HgA1c and Cardiovascular Complications

• Type I diabetics with intensive glycemic control early in disease course with long term benefit

• Type II diabetics also with intensive glycemic control early had long term CV benefits.
  – Didn’t hold for patients with long standing disease
  – ACCORD halted early
HgA1c and Cardiovascular Complications

- ADVANCE – ESRD was lower in intense group; no benefit or harm for CV events.
- VADT reduced risk in CV events with no benefit in CV or general mortality.
- Hypoglycemia is main risk of intensive therapy
- Risks/ benefits to be discussed for goal setting.
Severe Hypoglycemia risk

• All 3 studies (ACCORD, ADVANCE, VADT) found severe hypoglycemia:
  – Longer duration of diabetes
  – Known h/o hypoglycemia
  – Advanced atherosclerosis
  – Advanced age and/ or fraility
General HgA1c Goal

• Non-pregnant adults → 7% or less. A
• More or less stringent on individual basis. C/ B.

• Individualize
Other Glycemic Goals

<table>
<thead>
<tr>
<th>Table 6.2—Summary of glycemic recommendations for many nonpregnant adults with diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1C</td>
</tr>
<tr>
<td>&lt;7.0% (53 mmol/mol)*</td>
</tr>
<tr>
<td>Preprandial capillary plasma glucose</td>
</tr>
<tr>
<td>80–130 mg/dL* (4.4–7.2 mmol/L)</td>
</tr>
<tr>
<td>Peak postprandial capillary plasma glucose†</td>
</tr>
<tr>
<td>&lt;180 mg/dL* (10.0 mmol/L)</td>
</tr>
</tbody>
</table>

*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 may be targeted if A1C goals are not met despite reaching preprandial glucose goals. Postprandial glucose measurements should be made 1–2 h after the beginning of the meal, generally peak levels in patients with diabetes.
Degrees of Hypoglycemia

- Ask!

- Oral glucose preferred ≤70 and conscious. E

- Glucagon for severe (*Med alert*). E

- Reevaluate regimen if severe/ recurrent. E

<table>
<thead>
<tr>
<th>Table 6.3—Classification of hypoglycemia*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level</td>
</tr>
<tr>
<td>------------------------------------------</td>
</tr>
<tr>
<td>Hypoglycemia alert value (level 1)</td>
</tr>
<tr>
<td>Clinically significant hypoglycemia (level 2)</td>
</tr>
<tr>
<td>Severe hypoglycemia (level 3)</td>
</tr>
</tbody>
</table>
Section 9

Cardiovascular Disease and Risk Management
CVD – Screening and Diagnosis

• Measure BP at each clinical visit, with BP ≥140/90 repeated. B
• All patients with DM and HTN should monitor BP at home. B
CV – Treatment Goals

• What is the goal for most patients with DM? Show of hands:
  • A – Under 150/90
  • B – Under 140/90
  • C – Under 140/80
  • D – Under 130/80
  • E - Other
CV – Treatment Goals

• What is the goal for most patients with DM? Show of hands:
  • A – Under 150/90
  • B – Under 140/90. A
  • C – Under 140/80
  • D – Under 130/80
  • E - Other
CV – Treatment Goals

• What is the goal for most patients with DM? Show of hands:
  • A – Under 150/90
  • B – Under 140/90. A
  • C – Under 140/80
  • D – Under 130/80
  • E – Other – Lower BP goal may be appropriate if high risk for CVD and low risk of treatment. C
## CV Studies

<table>
<thead>
<tr>
<th>Clinical trial</th>
<th>Population</th>
<th>Intensive</th>
<th>Standard</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACCORD BP (16)</td>
<td>4,733 participants with T2D aged 40–79 years with prior evidence of CVD or multiple cardiovascular risk factors</td>
<td>Systolic blood pressure target: &lt;120 mmHg/Achieved (mean) systolic/diastolic: 119.3/64.4 mmHg</td>
<td>Systolic blood pressure target: 130–140 mmHg/Achieved (mean) systolic/diastolic: 133.5/70.5 mmHg</td>
<td>• No benefit in primary end point: composite of nonfatal MI, nonfatal stroke, and CVD death • Stroke risk reduced 41% with intensive control, not sustained through follow-up beyond the period of active treatment • Adverse events more common in intensive group, particularly elevated serum creatinine and electrolyte abnormalities</td>
</tr>
<tr>
<td>ADVANCE BP (17)</td>
<td>11,140 participants with T2D aged 55 years and older with prior evidence of CVD or multiple cardiovascular risk factors</td>
<td>Intervention: a single-pill, fixed-dose combination of perindopril and indapamide/Achieved (mean) systolic/diastolic: 136/73 mmHg</td>
<td>Control: placebo/Achieved (mean) systolic/diastolic: 141.6/75.2 mmHg</td>
<td>• Intervention reduced risk of primary composite end point of major macrovascular and microvascular events (9%), death from any cause (14%), and death from CVD (18%) • 6-year observational follow-up found reduction in risk of death in intervention group attenuated but still significant (142)</td>
</tr>
<tr>
<td>HOT (143)</td>
<td>18,790 participants, including 1,501 with diabetes</td>
<td>Diastolic blood pressure target: ≤80 mmHg</td>
<td>Diastolic blood pressure target: ≤90 mmHg</td>
<td>• In the overall trial, there was no cardiovascular benefit with more intensive targets • In the subpopulation with diabetes, an intensive diastolic target was associated with a significantly reduced risk (51%) of CVD events</td>
</tr>
<tr>
<td>SPRINT (144)</td>
<td>9,361 participants without diabetes</td>
<td>Systolic blood pressure target: &lt;120 mmHg/Achieved (mean): 121.4 mmHg</td>
<td>Systolic blood pressure target: &lt;140 mmHg/Achieved (mean): 136.2 mmHg</td>
<td>• Intensive systolic blood pressure target lowered risk of the primary composite outcome 25% (MI, ACS, stroke, heart failure, and death due to CVD) • Intensive target reduced risk of death 27% • Intensive therapy increased risks of electrolyte abnormalities and AKI</td>
</tr>
</tbody>
</table>

CVD, cardiovascular disease; T2D, type 2 diabetes. Data from this table can also be found in the ADA position statement “Diabetes and Hypertension” (5).
Lifestyle Recommendations

• BP over 120/80, weight loss (if appropriate, DASH diet, moderation of alcohol, increased physical activity. B
Recommendations for the Treatment of Confirmed Hypertension in People With Diabetes

** TZD preferred (chlorthalidone or indapamide)    *** DHP preferred (-pines, not diltiazem or verapamil)

- Initial BP between 140/90 mmHg and 160/100 mmHg
  - Start one agent
    - Albuminuria*
      - No: Start one drug:
        - ACEi
        - ARB
        - CCB***
        - Diuretic**
      - Yes: Start: ACEi or ARB
  - Lifestyle management

- Initial BP ≥ 160/100 mmHg
  - Start two agents
    - Albuminuria*
      - No: Start drug from 2 of 3 options:
        - ACEi or ARB
        - CCB***
        - Diuretic**
      - Yes: Start: ACEi or ARB and CCB*** or Diuretic**
  - Assess BP Control and Adverse Effects
Assess BP Control and Adverse Effects

1. Treatment tolerated and target achieved
   - **Continue therapy**

2. Not meeting target
   - Add agent from complementary drug class:
     - ACEi or ARB
     - CCB***
     - Diuretic**

3. Adverse effects
   - Consider change to alternative medication:
     - ACEi or ARB
     - CCB***
     - Diuretic**

   - **Adverse effects**

4. Not meeting target on two agents
   - **Assess BP Control and Adverse Effects**

5. Treatment tolerated and target achieved
   - **Continue therapy**

**Consider Addition of Mineralocorticoid Receptor Antagonist; Refer to Specialist With Expertise in BP Management**
Lipids

• Lifestyle modification including reduced saturated and trans fat and cholesterol and increased fiber, plant, exercise and n-3 FA. A

• High trigs (≥150) and/or low HDL (<40 in men, <50 in women) → intensify lifestyle therapy and glycemic control. C
Table 9.2—Recommendations for statin and combination treatment in adults with diabetes

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

*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.
Aspirin

• Good for secondary prevention (75-162 mg/ day). A
• If CVD and ASA Allergy → clopidogrel (75 mg/ day). B
• Dual anti-platet tx (ASA with P2Y12i) for 1 year after ACS (may benefit longer too). A/ B.
• Primary prevention for increased CVD risk (age 50 or older with 1 major CVD RF with no increased bleed risk). C
DM and CVD screening

• Not recommended if ASx. A
• Consider looking of atypical cardiac sx, signs/ symptoms of PVD or EKG abnormalities. E
DM and known CVD

- If known CVD $\rightarrow$ ACEi or ARB to reduce risk of CV events. B
- Prior MI $\rightarrow$ β-blockers for at least 2 years after event. B
- If CHF and GFR over 30, OK to use Metformin. B
- If Type 2 and CVD, use lifestyle, Metformin and drug that reduces CV mortality (empagliflozin, liraglutide) if able. A  Consider Canagliflozin. C
Useful App – Demo

http://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/
Section 10

Microvascular Complications and Foot Care
Microvascular Complications – Kidney Screening

- Screen annually for renal disease with eGFR and urine for microalbumin in all patients with Type 2 DM, Type 1 > 5 years (or sooner if co-morbid HTN). B
Microvascular Complications – Renal Treatment

• Glucose control to reduce risk or progression of DKD. A
• BP control for same. A
• If not on dialysis but have DKD, protein intake should be 0.8 mg/kg. B
• ACEi or ARB for reduced GFR or protein in urine. A, B.
• Check K, Cr if on ACEi, ARB or diuretics. B
Microvascular Complications – Renal Treatment

- Monitor urine protein if on ACEi or ARB to monitor response/progression. E
- If normal BP, no protein in urine and normal BP, ACEi or ARB is not recommended for primary prevention. B
- If GFR <60, evaluate and managed CKD potential complications. E
- If GFR <30, refer for renal replacement. A
Recommendations in Table Form

<table>
<thead>
<tr>
<th>CKD stage†</th>
<th>eGFR (mL/min/1.73 m²)</th>
<th>Evidence of kidney damage*</th>
<th>Diagnose cause of kidney injury</th>
<th>Evaluate and treat risk factors for CKD progression**</th>
<th>Evaluate and treat CKD complications***</th>
<th>Prepare for renal replacement therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>No clinical evidence of CKD</td>
<td>≥60</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>1</td>
<td>≥90</td>
<td>+</td>
<td>—</td>
<td>√</td>
<td>—</td>
<td>√</td>
</tr>
<tr>
<td>2</td>
<td>60–89</td>
<td>+</td>
<td>√</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>3</td>
<td>30–59</td>
<td>+/−</td>
<td>—</td>
<td>√</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>4</td>
<td>15–29</td>
<td>+/−</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>5</td>
<td>&lt;15</td>
<td>+/−</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

†CKD stages 1 and 2 are defined by evidence of kidney damage (+), while CKD stages 3–5 are defined by reduced eGFR with or without evidence of kidney damage (+/−). *Kidney damage is most often manifest as albuminuria (UACR ≥30 mg/g Cr) but can also include glomerular hematuria, other abnormalities of the urinary sediment, radiographic abnormalities, and other presentations. **Risk factors for CKD progression include elevated blood pressure, glycemia, and albuminuria. ***See Table 10.2.
# Complications of CKD

<table>
<thead>
<tr>
<th>Complication</th>
<th>Medical and laboratory evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated blood pressure</td>
<td>Blood pressure, weight</td>
</tr>
<tr>
<td>Volume overload</td>
<td>History, physical examination, weight</td>
</tr>
<tr>
<td>Electrolyte abnormalities</td>
<td>Serum electrolytes</td>
</tr>
<tr>
<td>Metabolic acidosis</td>
<td>Serum electrolytes</td>
</tr>
<tr>
<td>Anemia</td>
<td>Hemoglobin; iron testing if indicated</td>
</tr>
<tr>
<td>Metabolic bone disease</td>
<td>Serum calcium, phosphate, PTH, vitamin 25(OH)D</td>
</tr>
</tbody>
</table>

Complications of CKD generally become prevalent when eGFR falls below 60 mL/min/1.73 m² (stage 3 CKD or greater) and become more common and severe as CKD progresses. Evaluation of elevated blood pressure and volume overload should occur at every possible clinical contact; laboratory evaluations are generally indicated every 6–12 months for stage 3 CKD, every 3–5 months for stage 4 CKD, and every 1–3 months for stage 5 CKD, or as indicated to evaluate symptoms or changes in therapy. PTH, parathyroid hormone; 25(OH)D, 25-hydroxyvitamin D.
Microvascular - Eyes

Same as for kidneys:

• Glucose control to reduce risk or progression of diabetic retinopathy. A
• BP control for same. A
Diabetic Retinopathy

• Screen at diagnosis of Type 2 and 5 years after diagnosis for Type 1. B

• Future screening
  – Well controlled DM and no retinopathy $\rightarrow$ 1-2 years
  – Any retinopathy $\rightarrow$ at least annually
  – If progressive or sight-threatening $\rightarrow$ more frequent

• There is a role for retinal photography, not a substitute for comprehensive exam. E
DR Treatment

- Refer if macular edema, non- or proliferative retinopathy to experienced ophthalmologist. A
- DR is not a CI for aspirin therapy for cardioprotection as ASA does not increase the risk of retinal hemorrhage. A
Neuropathy

• Screen at dx for Type 2 and 5 years after dx for Type 1 for peripheral neuropathy. B

• Assessment of distal symmetric polyneuropathy → history and either temperature or pinprick and vibration with 128 Hz tuning fork. 10gm monofilament done annually. B

• If other microvascular issues – look for autonomonic neuropathy. E
Neuropathy Treatment

• Glycemic and BP control to prevent /delay neuropathy. A, B

• Assess and treat patients to reduce pain of neuropathy and sx of autonomic neuropathy. B, E.

• Neuropathic pain → pregabalin or duloxetine are recommended 1st line therapy. A
Foot Care

• Comprehensive exam annually. B
  – Skin, presence of deformities, neurologic and vascular assessment. B

• Check feet at each visit. C

• Obtain foot history. B

• If sx of claudication or reduced pedal pulses $\rightarrow$ ABI or other assessment. C

• High risk feet and ulcers $\rightarrow$ Multi-disciplinary approach. B
Foot Care

• Refer to foot specialists → smokers, h/o LE complications, loss of sensation, structural abnormalities, PAD. Life-long surveillance. C
• Educate about foot self-care. B
• Specialized therapeutic footwear for high risk patients. B.
Section 1

Improving Care and Promoting Health in Populations
Improving Care and Promoting Health in Populations

• Ensure treatment decisions are timely, rely on evidence-based guidelines, and are made collaboratively with patients based on individual preferences, prognoses, and comorbidities. B

• Align approaches to diabetes management with the Chronic Care Model, emphasizing productive interactions between a prepared proactive care team and an informed activated patient. A
Improving Care and Promoting Health in Populations

• Care systems should facilitate team-based care, patient registries, decision support tools, and community involvement to meet patient needs. B

• Efforts to assess the quality of diabetes care and create quality improvement strategies should incorporate reliable data metrics, to promote improved processes of care and health outcomes, with simultaneous emphasis on costs. E
Improving Care and Promoting Health in Populations

- Providers should assess social context, including potential food insecurity, housing stability, and financial barriers, and apply that information to treatment decisions. A
- Refer patients to local community resources when available. B
- Provide patients with self-management support from lay health coaches, navigators, or community health workers when available. A
Section 4

Lifestyle Management
Self-Management

• All people with DM should participate in DM self-management education. B

• 4 times to evaluate for self-management education and support:
  – At Dx
  – Annually
  – Complicating factors arise
  – Transition in care. E
Exercise

- Children – 60 min/ d aerobic
  – 3x weekly muscle/ bone strengthening
- Most adults – 150 min/ week
- Adults – 2-3 sessions/ week of resistance exercise
- Adults – reduce sedentary time
- Older Adults – 2-3 times/ week of balance and flexibility training
Tobacco

• No tobacco or e-cigarettes. A/ C
• Smoking cessation should be part of routine DM care. B
Mental Health

Table 4.2—Situations that warrant referral of a person with diabetes to a mental health provider for evaluation and treatment

- If self-care remains impaired in a person with DD after tailored diabetes education
- If a person has a positive screen on a validated screening tool for depressive symptoms
- In the presence of symptoms or suspicions of disordered eating behavior, an eating disorder, or disrupted patterns of eating
- If intentional omission of insulin or oral medication to cause weight loss is identified
- If a person has a positive screen for anxiety or fear of hypoglycemia
- If a serious mental illness is suspected
- In youth and families with behavioral self-care difficulties, repeated hospitalizations for diabetic ketoacidosis, or significant distress
- If a person screens positive for cognitive impairment
- Deterioration or impaired ability to perform diabetes self-care behaviors
- Before undergoing bariatric or metabolic surgery and after surgery if assessment reveals an ongoing need for adjustment support
Section 5

Prevention or Delay of Type 2 Diabetes
Prediabetes Recommendations

• Screen annually for DM if a patient has prediabetes.  E

• Refer for intensive behavioral lifestyle intervention program. A
  – 7 ?
  – 150 ?

• Consider technology-assisted tools. B
Prediabetes Medication

• Metformin consideration
  – BMI ≥ 35
  – Age < 60
  – Women with h/o GDM
  – Vitamin B12
Other Prediabetes Issues

• Look for modifiable CV risk factors. B
• Self-Management may be helpful. B
Section 7

Obesity Management for the Treatment of Type 2 Diabetes
Obesity Management for the Treatment of Type 2 Diabetes

- At each encounter, BMI recorded. B

![Table 7.1—Treatment options for overweight and obesity in type 2 diabetes](image)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>25.0–26.9</th>
<th>27.0–29.9</th>
<th>30.0–34.9</th>
<th>35.0–39.9</th>
<th>≥40</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(or 23.0–26.9*)</td>
<td>(or 27.5–32.4*)</td>
<td>(or 32.5–37.4*)</td>
<td>(or ≥37.5*)</td>
<td></td>
</tr>
<tr>
<td>Diet, physical activity, and behavioral therapy</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
</tr>
<tr>
<td>Pharmacotherapy</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
</tr>
<tr>
<td>Metabolic surgery</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
</tr>
</tbody>
</table>

*Cutoff points for Asian American individuals. †Treatment may be indicated for selected motivated patients.

- Be sure to do a readiness assessment, if ready, goal is >5% weight loss. A
Diet, Physical Activity and Behavioral Therapy

• High intensity, 500-750 kcal/d deficit. A
• Individualized diet. A
• If successful, long-term (1+ year) program prescribed. A
• More aggressive short term weight loss program can be done in selected patients by trained clinicians. B
Pharmacotherapy

• Consider medication effect on weight, and minimize where possible. E
• Risk benefit for weight loss medicines as adjunct for patients with type 2 DM and BMI ≥27. A
• Monitor, and if <5% weight loss after 3 months or side effects, stop medication and look at alternatives. A
# Medications Approved for Weight Loss

## Table 7.2—Medications approved by the FDA for the treatment of obesity

<table>
<thead>
<tr>
<th>Generic drug name</th>
<th>Usual adult dosing frequency</th>
<th>Average wholesale price (per month)</th>
<th>National Average Drug Acquisition Cost (per month)</th>
<th>1-Year weight change status</th>
<th>Average weight loss relative to placebo</th>
<th>% Patients with ≤5% loss of baseline weight</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Short-term treatment (a few weeks)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phentermine (Lomaira)</td>
<td>37.5 mg q.d. or 8 mg tid.</td>
<td>$5-$76 ($37.5 mg); $52 ($8 mg)</td>
<td>$3-$60 ($37.5 mg); Unavailable ($8 mg)</td>
<td>N/A*</td>
<td>N/A*</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Long-term treatment (more than a few weeks)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lipase inhibitor</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orlistat (Alli) 60 mg caps or orlistat (Xenical) 120 mg caps</td>
<td>60 mg or 120 mg ti.d. (dosing or up to 1 h after a low-fat meal)</td>
<td>$41-$62 ($60 mg); $70.3 ($120 mg)</td>
<td>$42 ($60 mg); $55.6 ($120 mg)</td>
<td>2.5 kg ($60 mg); 3.4 kg ($120 mg)</td>
<td>3.5–7.9%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Selective serotonin 5-HT₄ receptor agonist</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lorcaserin (Belviq) 10 mg tabs</td>
<td>10 mg b.i.d.</td>
<td>$289*</td>
<td>$2.30</td>
<td>3.2 kg</td>
<td>3.8–8.8%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lorcaserin (Belviq XR) 20 mg q.d. extended-release tabs</td>
<td>$289*</td>
<td>$2.32</td>
<td>3.2 kg</td>
<td>3.8–8.8%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sympathomimetic amine anorectic/antiepileptic combination</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phentermine/topiramate ER (Qsymia) 3.75 mg/23 mg q.d. for 14 days, then increase to 7.5 mg/46 mg q.d.; Maximum dose: 15 mg/92 mg q.d.</td>
<td>$239 (maximum dose using the highest strength)</td>
<td>$192 (maximum dose using the highest strength)</td>
<td>6.7 kg (7.5 mg/46 mg); 8.9 kg (15 mg/92 mg)</td>
<td>45–70%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Adverse effects

- **Common**: Headache, elevated blood pressure, elevated heart rate, insomnia, dry mouth, constipation, anxiety, palpitations
- **Serious**: Dyspnea, angina pectoris, syncope, severe hypertension, abdominal pain, discomfort, oily spotting, stool, fecal urgency, flatulence, malabsorption of fat, soluble vitamins (A, D, E, K) and medications (e.g., cyclosporine, thyroid hormone replacement, or anticonvulsants); potentiation of the effects of warfarin
- **Liver failure and oxalate nephropathy**: Hypoglycemia, headache, fatigue, Serotonin syndrome or NMS-like reactions, suicidal ideation, heart valve disorder (<2.4%), bradycardia
- **Serotonin syndrome or NMS-like reactions, suicidal ideation, heart valve disorder (<2.4%), bradycardia**: Hypoglycemia, headache, fatigue

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*Continued on p. 569*
### Medications Approved for Weight Loss

<table>
<thead>
<tr>
<th>Generic drug name</th>
<th>Usual adult dosing frequency</th>
<th>Average wholesale price (per month)</th>
<th>National Average Drug Acquisition Cost (per month)</th>
<th>1-Year weight change status</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioid antagonist/aminoketone antidepressant combination</td>
<td>Maximum dose: two tablets of Contrave b.i.d. for a total daily dosage of naltrexone 32 mg/buproprion 360 mg</td>
<td>$290 (maximum dose)</td>
<td>$231 (maximum dose)</td>
<td>2.0–4.1 kg (32 mg/360 mg)</td>
<td>36–57% Nausea, constipation, headache, vomiting Depression, predipitation of mania, contraindicated in patients with a seizure disorder</td>
</tr>
<tr>
<td>Glucagon-like peptide 1 receptor agonist</td>
<td>Maintenance dose: 3 mg s.c. q.d.</td>
<td>$1,385</td>
<td>$1,105</td>
<td>5.8–5.9 kg</td>
<td>51–73% Hypoglycemia, nausea, vomiting, diarrhea, constipation, headache Pancreatitis, thyroid C-cell tumors in rodents, contraindicated in patients with personal/family history of MTC or MEN2, acute renal failure</td>
</tr>
</tbody>
</table>
Metabolic Surgery

Should be recommended:
• BMI $\geq 40$ (37.5*)
• BMI 35-39.9 (32.5-37.4*)
  – Inadequate control

Should be considered:
• BMI 30-34.9 (27.5-32.4*)
  – Inadequate control