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<th>Section</th>
<th>Slide No.</th>
</tr>
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<tr>
<td>Level of Evidence</td>
<td>Description</td>
</tr>
<tr>
<td>-------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>A</td>
<td>Clear or supportive evidence from adequately powered well-conducted, generalizable, randomized controlled trials</td>
</tr>
<tr>
<td></td>
<td>Compelling nonexperimental evidence</td>
</tr>
<tr>
<td>B</td>
<td>Supportive evidence from well-conducted cohort studies or case-control study</td>
</tr>
<tr>
<td>C</td>
<td>Supportive evidence from poorly controlled or uncontrolled studies</td>
</tr>
<tr>
<td></td>
<td>Conflicting evidence with the weight of evidence supporting the recommendation</td>
</tr>
<tr>
<td>E</td>
<td>Expert consensus or clinical experience</td>
</tr>
</tbody>
</table>
I. CLASSIFICATION AND DIAGNOSIS
Classification of Diabetes

- Type 1 diabetes
  - β-cell destruction
- Type 2 diabetes
  - Progressive insulin secretory defect
- Other specific types of diabetes
  - Genetic defects in β-cell function, insulin action
  - Diseases of the exocrine pancreas
  - Drug- or chemical-induced
- Gestational diabetes mellitus
Criteria for the Diagnosis of Diabetes

A1C ≥6.5%  

OR  

Fasting plasma glucose (FPG) ≥126 mg/dL (7.0 mmol/L)  

OR  

2-h plasma glucose ≥200 mg/dL (11.1 mmol/L) during an OGTT  

OR  

A random plasma glucose ≥200 mg/dL (11.1 mmol/L)

ADA. I. Classification and Diagnosis. Diabetes Care 2012;35(suppl 1):S12. Table 2.
Criteria for the Diagnosis of Diabetes

A1C $\geq 6.5\%$

The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay*

*In the absence of unequivocal hyperglycemia, result should be confirmed by repeat testing.
Fasting plasma glucose (FPG) ≥126 mg/dL (7.0 mmol/L)

Fasting is defined as no caloric intake for at least 8 h*

*In the absence of unequivocal hyperglycemia, result should be confirmed by repeat testing.
Criteria for the Diagnosis of Diabetes

2-h plasma glucose $\geq 200 \text{ mg/dL (11.1 mmol/L)}$ during an 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*

*In the absence of unequivocal hyperglycemia, result should be confirmed by repeat testing.
In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose $\geq 200$ mg/dL (11.1 mmol/L)
Prediabetes: IFG, IGT, Increased A1C

Categories of increased risk for diabetes (prediabetes)*

FPG 100–125 mg/dL (5.6–6.9 mmol/L): IFG

OR

2-h plasma glucose in the 75-g OGTT
140–199 mg/dL (7.8–11.0 mmol/L): IGT

OR

A1C 5.7–6.4%

*For all three tests, risk is continuous, extending below the lower limit of a range and becoming disproportionately greater at higher ends of the range.
II. TESTING FOR DIABETES IN ASYMPTOMATIC PATIENTS
Recommendations: Testing for Diabetes in Asymptomatic Patients

- Consider testing overweight/obese adults (BMI $\geq 25$ kg/m$^2$) with one or more additional risk factors
  - In those without risk factors, begin testing at age 45 years (B)
- If tests are normal
  - Repeat testing at least at 3-year intervals (E)
- Use A1C, FPG, or 2-h 75-g OGTT (B)
- In those with increased risk for future diabetes
  - Identify and, if appropriate, treat other CVD risk factors (B)
### Criteria for Testing for Diabetes in Asymptomatic Adult Individuals (1)

1. Testing should be considered in all adults who are overweight (BMI ≥25 kg/m²) and who have one or more additional risk factors:

- Physical inactivity
- First-degree relative with diabetes
- High-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
- Women who delivered a baby weighing >9 lb or were diagnosed with GDM
- 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 ovarian syndrome (PCOS)
- A1C ≥5.7%, IGT, or IFG on previous testing
- Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)
- History of CVD

*At-risk BMI may be lower in some ethnic groups.*

**ADA. Testing in Asymptomatic Patients. *Diabetes Care* 2012;35(suppl 1):S14. Table 4.**
2. In the absence of criteria (risk factors on previous slide), testing for diabetes should begin at age 45 years.

3. If results are normal, testing should be repeated at least at 3-year intervals, with consideration of more frequent testing depending on initial results (e.g., those with prediabetes should be tested yearly), and risk status.
III. DETECTION AND DIAGNOSIS OF GESTATIONAL DIABETES MELLITUS (GDM)
Recommendations: Detection and Diagnosis of GDM (1)

- Screen for undiagnosed type 2 diabetes at the first prenatal visit in those with risk factors, using standard diagnostic criteria (B)

- In pregnant women not previously known to have diabetes, screen for GDM at 24–28 weeks’ gestation, using a 75-g OGTT and specific diagnostic cut points (B)

ADA. III. Detection and Diagnosis of GDM. *Diabetes Care* 2012;35(suppl 1):S15.
Recommendations: Detection and Diagnosis of GDM (2)

- Screen women with GDM for persistent diabetes at 6–12 weeks’ postpartum, using a test other than A1C (E)
- Women with a history of GDM should have lifelong screening for the development of diabetes or prediabetes at least every 3 years (B)
- Women with a history of GDM found to have prediabetes should receive lifestyle interventions or metformin to prevent diabetes (A)
Screening for and Diagnosis of GDM

- Perform a 75-g OGTT, with plasma glucose measurement fasting and at 1 and 2 h, at 24–28 weeks’ gestation in women not previously diagnosed with overt diabetes.
- Perform OGTT in the morning after an overnight fast of at least 8 h.
- GDM diagnosis: when any of the following plasma glucose values are exceeded:
  - Fasting ≥92 mg/dL (5.1 mmol/L)
  - 1 h ≥180 mg/dL (10.0 mmol/L)
  - 2 h ≥153 mg/dL (8.5 mmol/L)
IV. PREVENTION/DELAY OF TYPE 2 DIABETES
Recommendations: Prevention/Delay of Type 2 Diabetes

- Refer patients with IGT (A), IFG (E), or A1C 5.7–6.4% (E) to ongoing support program
  - Targeting weight loss of 7% of body weight
  - At least 150 min/week moderate physical activity
- Follow-up counseling important for success (B)
- Based on cost-effectiveness of diabetes prevention, third-party payers should cover such programs (E)
- Consider metformin for prevention of type 2 diabetes if IGT (A), IFG (E), or A1C 5.7–6.4% (E)
  - Especially for those with BMI >35 kg/m², age <60 years, and women with prior GDM (A)
- In those with prediabetes, monitor for development of diabetes annually (E)
V. DIABETES CARE
Diabetes Care: Initial Evaluation

• A complete medical evaluation should be performed to
  – Classify the diabetes
  – Detect presence of diabetes complications
  – Review previous treatment, glycemic control in patients with established diabetes
  – Assist in formulating a management plan
  – Provide a basis for continuing care

• Perform laboratory tests necessary to evaluate each patient’s medical condition
Components of the Comprehensive Diabetes Evaluation (1)

Medical history (1)

- Age and characteristics of onset of diabetes (e.g., DKA, asymptomatic laboratory finding)
- Eating patterns, physical activity habits, nutritional status, and weight history; growth and development in children and adolescents
- Diabetes education history
- Review of previous treatment regimens and response to therapy (A1C records)
Medical history (2)

- Current treatment of diabetes, including medications and medication adherence, meal plan, physical activity patterns, and readiness for behavior change
- Results of glucose monitoring and patient’s use of data
- DKA frequency, severity, and cause
- Hypoglycemic episodes
  - Hypoglycemia awareness
  - Any severe hypoglycemia: frequency and cause
Medical history (3)

- History of diabetes-related complications
  - Microvascular: retinopathy, nephropathy, neuropathy
  - Sensory neuropathy, including history of foot lesions
  - Autonomic neuropathy, including sexual dysfunction and gastroparesis
  - Macrovascular: CHD, cerebrovascular disease, PAD
  - Other: psychosocial problems*, dental disease*

*See appropriate referrals for these categories.
Components of the Comprehensive Diabetes Evaluation (4)

Physical examination (1)

- Height, weight, BMI
- Blood pressure determination, including orthostatic measurements when indicated
- Fundoscopic examination*
- Thyroid palpation
- Skin examination (for acanthosis nigricans and insulin injection sites)

*See appropriate referrals for these categories.
Components of the Comprehensive Diabetes Evaluation (5)

Physical examination (2)

- Comprehensive foot examination
  - Inspection
  - Palpation of dorsalis pedis and posterior tibial pulses
  - Presence/absence of patellar and Achilles reflexes
  - Determination of proprioception, vibration, and monofilament sensation
Components of the Comprehensive Diabetes Evaluation (6)

Laboratory evaluation

- A1C, if results not available within past 2–3 months
- If not performed/available within past year
  - Fasting lipid profile, including total, LDL, and HDL cholesterol and triglycerides
  - Liver function tests
  - Test for urine albumin excretion with spot urine albumin-to-creatinine ratio
  - Serum creatinine and calculated GFR
  - Thyroid-stimulating hormone in type 1 diabetes, dyslipidemia, or women over age 50 years
Components of the Comprehensive Diabetes Evaluation (7)

Referrals

• Eye care professional for annual dilated eye exam
• Family planning for women of reproductive age
• Registered dietitian for MNT
• Diabetes self-management education
• Dentist for comprehensive periodontal examination
• Mental health professional, if needed
People with diabetes should receive medical care from a physician-coordinated team

- Physicians, nurse practitioners, physician’s assistants, nurses, dietitians, pharmacists, mental health professionals
- In this collaborative and integrated team approach, essential that individuals with diabetes assume an active role in their care

Management plan should recognize diabetes self-management education (DSME) and on-going diabetes support
Diabetes Care: Glycemic Control

• Two primary techniques available for health providers and patients to assess effectiveness of management plan on glycemic control
  – Patient self-monitoring of blood glucose (SMBG), or interstitial glucose
  – A1C
Recommendations: Glucose Monitoring (1)

- Self-monitoring of blood glucose (SMBG) should be carried out three or more times daily for patients using multiple insulin injections or insulin pump therapy (B)
- For patients using less frequent insulin injections, noninsulin therapies, or medical nutrition therapy (MNT) alone, SMBG may be useful as a guide to management (E)
Recommendations: Glucose Monitoring (2)

• To achieve postprandial glucose targets, postprandial SMBG may be appropriate (E)
• When prescribing SMBG, ensure patients receive initial instruction in, and routine follow-up evaluation of, SMBG technique and their ability to use data to adjust therapy (E)
Recommendations: Glucose Monitoring (3)

- Continuous glucose monitoring (CGM) with intensive insulin regimens useful tool to lower A1C in selected adults (age ≥ 25 years) with type 1 diabetes (A)
- Evidence for A1C-lowering less strong in children, teens, and younger adults; however, CGM may be helpful; success correlates with adherence to device use (C)
- CGM may be a supplemental tool to SMBG in those with hypoglycemia unawareness and/or frequent hypoglycemic episodes (E)
Recommendations: A1C

- Perform A1C test at least twice yearly in patients meeting treatment goals (and have stable glycemic control) (E)
- Perform A1C test quarterly in patients whose therapy has changed or who are not meeting glycemic goals (E)
- Use of point-of-care (POC) testing for A1C provides the opportunity for more timely treatment changes (E)
## Correlation of A1C with Average Glucose (AG)

<table>
<thead>
<tr>
<th>A1C (%)</th>
<th>Mean plasma glucose (mg/dL)</th>
<th>Mean plasma glucose (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>126</td>
<td>7.0</td>
</tr>
<tr>
<td>7</td>
<td>154</td>
<td>8.6</td>
</tr>
<tr>
<td>8</td>
<td>183</td>
<td>10.2</td>
</tr>
<tr>
<td>9</td>
<td>212</td>
<td>11.8</td>
</tr>
<tr>
<td>10</td>
<td>240</td>
<td>13.4</td>
</tr>
<tr>
<td>11</td>
<td>269</td>
<td>14.9</td>
</tr>
<tr>
<td>12</td>
<td>298</td>
<td>16.5</td>
</tr>
</tbody>
</table>

These estimates are based on ADAG data of ~2,700 glucose measurements over 3 months per A1C measurement in 507 adults with type 1, type 2, and no diabetes. The correlation between A1C and average glucose was 0.92. A calculator for converting A1C results into estimated average glucose (eAG), in either mg/dL or mmol/L, is available at http://professional.diabetes.org/GlucoseCalculator.aspx.
Lowering A1C to below or around 7% has been shown to reduce microvascular complications and, if implemented soon after the diagnosis of diabetes, is associated with long-term reduction in macrovascular disease.

Therefore, a reasonable A1C goal for many nonpregnant adults is <7% (B).
Providers might reasonably suggest more stringent A1C goals (such as <6.5%) for selected individual patients, if this can be achieved without significant hypoglycemia or other adverse effects of treatment.

Appropriate patients might include those with short duration of diabetes, long life expectancy, and no significant CVD (C).

Recommendations: Glycemic Goals in Adults (2)
Recommendations: Glycemic Goals in Adults (3)

• Less stringent A1C goals (such as <8%) may be appropriate for patients with (B)
  – History of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, extensive comorbid conditions
  – Those with longstanding diabetes in whom the general goal is difficult to attain despite diabetes self-management education, appropriate glucose monitoring, and effective doses of multiple glucose lowering agents including insulin
Intensive Glycemic Control and Cardiovascular Outcomes: ACCORD

Primary Outcome: Nonfatal MI, nonfatal stroke, CVD death

HR = 0.90 (0.78-1.04)

Primary Outcome: Microvascular plus macrovascular (nonfatal MI, nonfatal stroke, CVD death)

HR = 0.90 (0.82-0.98)

No. at Risk

Intensive: 5570 5457 5369 5256 5100 4957 4867 4756 4599 4044 1883 447
Standard: 5569 5448 5342 5240 5065 4903 4808 4703 4545 3992 1921 470


Intensive Glycemic Control and Cardiovascular Outcomes: VADT

Primary Outcome: Nonfatal MI, nonfatal stroke, CVD death, hospitalization for heart failure, revascularization

HR = 0.88 (0.74-1.05)


Glycemic Recommendations for Nonpregnant Adults with Diabetes (1)

<table>
<thead>
<tr>
<th></th>
<th>A1C</th>
<th>Preprandial capillary plasma glucose</th>
<th>Peak postprandial capillary plasma glucose†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;7.0%*</td>
<td>70–130 mg/dL* (3.9–7.2 mmol/L)</td>
<td>&lt;180 mg/dL* (&lt;10.0 mmol/L)</td>
</tr>
</tbody>
</table>

*Individualize goals based on these values.
†Postprandial glucose measurements should be made 1–2 h after the beginning of the meal, generally peak levels in patients with diabetes.
Glycemic Recommendations for Nonpregnant Adults with Diabetes (2)

- Goals should be individualized based on
  - Duration of diabetes
  - Age/life expectancy
  - Comorbid conditions
  - Known CVD or advanced microvascular complications
  - Hypoglycemia unawareness
  - Individual patient considerations
Glycemic Recommendations for Nonpregnant Adults with Diabetes (3)

- More- or less-stringent glycemic goals may be appropriate for individual patients
- Postprandial glucose may be targeted if A1C goals are not met despite reaching preprandial glucose goals
Recommended Therapy for Type 1 Diabetes: Three Components

- Use of multiple-dose insulin injections (3–4 injections/day of basal and prandial insulin) or continuous subcutaneous insulin infusion (CSII)
- Matching prandial insulin to carbohydrate intake, premeal blood glucose, and anticipated activity
- For many patients (especially if hypoglycemia is a problem), use of insulin analogs

Recommendations: Therapy for Type 2 Diabetes (1)

- At the time of type 2 diabetes diagnosis, initiate metformin therapy along with lifestyle interventions, unless metformin is contraindicated (A)
- In newly diagnosed type 2 diabetes patients with markedly symptomatic and/or elevated blood glucose levels or A1C, consider insulin therapy, with or without additional agents, from the outset (E)

Recommendations: Therapy for Type 2 Diabetes (2)

- If noninsulin monotherapy at maximal tolerated dose does not achieve or maintain the A1C target over 3–6 months, add a second oral agent, a GLP-1 receptor agonist, or insulin (E)

## Noninsulin Therapies for Hyperglycemia in Type 2 Diabetes (1)

<table>
<thead>
<tr>
<th>Class</th>
<th>Biguanides</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compound</td>
<td>Metformin</td>
</tr>
<tr>
<td>Mechanism</td>
<td>Activates AMP-kinase</td>
</tr>
<tr>
<td>Action(s)</td>
<td>• Hepatic glucose production ↓</td>
</tr>
<tr>
<td></td>
<td>• Intestinal glucose absorption ↓</td>
</tr>
<tr>
<td></td>
<td>• Insulin action ↑</td>
</tr>
<tr>
<td>Advantages</td>
<td>• No weight gain</td>
</tr>
<tr>
<td></td>
<td>• No hypoglycemia</td>
</tr>
<tr>
<td></td>
<td>• Reduction in cardiovascular events and mortality (UKPDS f/u)</td>
</tr>
<tr>
<td>Disadvantages</td>
<td>• Gastrointestinal side effects (diarrhea, abdominal cramping)</td>
</tr>
<tr>
<td></td>
<td>• Lactic acidosis (rare)</td>
</tr>
<tr>
<td></td>
<td>• Vitamin B₁₂ deficiency</td>
</tr>
<tr>
<td></td>
<td>• Contraindications: reduced kidney function</td>
</tr>
<tr>
<td>Cost</td>
<td>Low</td>
</tr>
</tbody>
</table>
Noninsulin Therapies for Hyperglycemia in Type 2 Diabetes (2)

<table>
<thead>
<tr>
<th>Class</th>
<th>Sulfonylureas (2\textsuperscript{nd} generation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compound</td>
<td>• Glibenclamide/Glyburide&lt;br&gt;• Glipizide&lt;br&gt;• Gliclazide&lt;br&gt;• Glimepiride</td>
</tr>
<tr>
<td>Mechanism</td>
<td>Closes $K_{\text{ATP}}$ channels on $\beta$-cell plasma membranes</td>
</tr>
<tr>
<td>Action(s)</td>
<td>↑ Insulin secretion</td>
</tr>
<tr>
<td>Advantages</td>
<td>• Generally well tolerated&lt;br&gt;• Reduction in cardiovascular events and mortality (UKPDS f/u)</td>
</tr>
<tr>
<td>Disadvantages</td>
<td>• Relatively glucose-independent stimulation of insulin secretion: Hypoglycemia, including episodes necessitating hospital admission and causing death&lt;br&gt;• Weight gain&lt;br&gt;• May blunt myocardial ischemic preconditioning&lt;br&gt;• Low “durability”</td>
</tr>
<tr>
<td>Cost</td>
<td>Low</td>
</tr>
</tbody>
</table>

ADA. V. Diabetes Care. *Diabetes Care* 2012;35(suppl 1):S22. Adapted with permission from Silvio Inzucchi, Yale University.
### Noninsulin Therapies for Hyperglycemia in Type 2 Diabetes (3)

<table>
<thead>
<tr>
<th>Class</th>
<th>Meglitinides</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Compound</strong></td>
<td>• Repaglinide</td>
</tr>
<tr>
<td></td>
<td>• Nateglinide</td>
</tr>
<tr>
<td><strong>Mechanism</strong></td>
<td>Closes $K_{\text{ATP}}$ channels on β-cell plasma membranes</td>
</tr>
<tr>
<td><strong>Action(s)</strong></td>
<td>Insulin secretion ↑</td>
</tr>
<tr>
<td><strong>Advantages</strong></td>
<td>Accentuated effects around meal ingestion</td>
</tr>
<tr>
<td><strong>Disadvantages</strong></td>
<td>• Hypoglycemia, weight gain</td>
</tr>
<tr>
<td></td>
<td>• May blunt myocardial ischemic preconditioning</td>
</tr>
<tr>
<td></td>
<td>• Dosing frequency</td>
</tr>
<tr>
<td><strong>Cost</strong></td>
<td>Medium</td>
</tr>
</tbody>
</table>
### Noninsulin Therapies for Hyperglycemia in Type 2 Diabetes (4a)

<table>
<thead>
<tr>
<th>Class</th>
<th>Thiazolidinediones (Glitazones)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Compound</strong></td>
<td>Pioglitazone</td>
</tr>
<tr>
<td><strong>Mechanism</strong></td>
<td>Activates the nuclear transcription factor PPAR-γ</td>
</tr>
<tr>
<td><strong>Action(s)</strong></td>
<td>Peripheral insulin sensitivity ↑</td>
</tr>
</tbody>
</table>
| **Advantages**         | • No hypoglycemia  
                        | • HDL cholesterol ↑  
                        | • Triglycerides ↓ |
| **Disadvantages**      | • Weight gain  
                        | • Edema  
                        | • Heart failure  
                        | • Bone fractures |
| **Cost**               | High                             |
Noninsulin Therapies for Hyperglycemia in Type 2 Diabetes (4b)

<table>
<thead>
<tr>
<th>Class</th>
<th>Thiazolidinediones (Glitazones)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compound</td>
<td>Rosiglitazone</td>
</tr>
<tr>
<td>Mechanism</td>
<td>Activates the nuclear transcription factor PPAR-γ</td>
</tr>
<tr>
<td>Action(s)</td>
<td>Peripheral insulin sensitivity ↑</td>
</tr>
<tr>
<td>Advantages</td>
<td>No hypoglycemia</td>
</tr>
<tr>
<td>Disadvantages</td>
<td>• LDL cholesterol ↑</td>
</tr>
<tr>
<td></td>
<td>• Weight gain</td>
</tr>
<tr>
<td></td>
<td>• Edema</td>
</tr>
<tr>
<td></td>
<td>• Heart failure</td>
</tr>
<tr>
<td></td>
<td>• Bone fractures</td>
</tr>
<tr>
<td></td>
<td>• Increased cardiovascular events (mixed evidence)</td>
</tr>
<tr>
<td></td>
<td>• FDA warnings on cardiovascular safety</td>
</tr>
<tr>
<td></td>
<td>• Contraindicated in patients with heart disease</td>
</tr>
<tr>
<td>Cost</td>
<td>High</td>
</tr>
</tbody>
</table>

ADA. V. Diabetes Care. *Diabetes Care* 2012;35(suppl 1):S22. Adapted with permission from Silvio Inzucchi, Yale University.
Noninsulin Therapies for Hyperglycemia in Type 2 Diabetes (5)

<table>
<thead>
<tr>
<th>Class</th>
<th>α-Glucosidase inhibitors</th>
</tr>
</thead>
</table>
| Compound       | • Acarbose
                | • Miglitol                |
| Mechanism      | Inhibits intestinal α-glucosidase |
| Action(s)      | Intestinal carbohydrate digestion (and consecutively, absorption) slowed |
| Advantages     | • Nonsystemic medication
                | • Postprandial glucose ↓ |
| Disadvantages  | • Gastrointestinal side effects (gas, flatulence, diarrhea)
                | • Dosing frequency       |
| Cost           | Medium                    |

Adapted with permission from Silvio Inzucchi, Yale University.

Noninsulin Therapies for Hyperglycemia in Type 2 Diabetes (6)

<table>
<thead>
<tr>
<th>Class</th>
<th>GLP-1 receptor agonists (incretin mimetics)</th>
</tr>
</thead>
</table>
| Compound                      | • Exenatide  
• Liraglutide                            |
| Mechanism                     | Activates GLP-1 receptors (β-cells/endocrine pancreas; brain/autonomous nervous system) |
| Action(s)                     | • Insulin secretion ↑ (glucose-dependent)  
• Glucagon secretion ↓ (glucose-dependent)  
• Slows gastric emptying  
• Satiety ↑ |
| Advantages                    | • Weight reduction  
• Potential for improved β-cell mass/function |
| Disadvantages                 | • Gastrointestinal side effects (nausea, vomiting, diarrhea)  
• Cases of acute pancreatitis observed  
• C-cell hyperplasia/medullary thyroid tumors in animals (liraglutide)  
• Injectable  
• Long-term safety unknown |
| Cost                          | High |

ADA. V. Diabetes Care. *Diabetes Care* 2012;35(suppl 1):S23. Adapted with permission from Silvio Inzucchi, Yale University.
# Noninsulin Therapies for Hyperglycemia in Type 2 Diabetes

## Class
DPP-4 inhibitors (incretin enhancers)

## Compound
- Sitagliptin
- Vildagliptin
- Saxagliptin
- Linagliptin

## Mechanism
Inhibits DPP-4 activity, prolongs survival of endogenously released incretin hormones

## Action(s)
- Active GLP-1 concentration $\uparrow$
- Active GIP concentration $\uparrow$
- Insulin secretion $\uparrow$
- Glucagon secretion $\downarrow$

## Advantages
- No hypoglycemia
- Weight “neutrality”

## Disadvantages
- Occasional reports of urticaria/angioedema
- Cases of pancreatitis observed
- Long-term safety unknown

## Cost
High

---

ADA. V. Diabetes Care. *Diabetes Care* 2012;35(suppl 1):S23. Adapted with permission from Silvio Inzucchi, Yale University.
Noninsulin Therapies for Hyperglycemia in Type 2 Diabetes (8)

<table>
<thead>
<tr>
<th>Class</th>
<th>Bile acid sequestrants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compound</td>
<td>Colesevelam</td>
</tr>
<tr>
<td>Mechanism</td>
<td>Binds bile acids/cholesterol</td>
</tr>
<tr>
<td>Action(s)</td>
<td>Unknown</td>
</tr>
<tr>
<td>Advantages</td>
<td>• No hypoglycemia</td>
</tr>
<tr>
<td></td>
<td>• LDL cholesterol ↓</td>
</tr>
<tr>
<td>Disadvantages</td>
<td>• Constipation</td>
</tr>
<tr>
<td></td>
<td>• Triglycerides ↑</td>
</tr>
<tr>
<td></td>
<td>• May interfere with absorption of other medications</td>
</tr>
<tr>
<td>Cost</td>
<td>High</td>
</tr>
</tbody>
</table>
Noninsulin Therapies for Hyperglycemia in Type 2 Diabetes (9)

<table>
<thead>
<tr>
<th>Class</th>
<th>Dopamine-2 agonists</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compound</td>
<td>Bromocriptine</td>
</tr>
<tr>
<td>Mechanism</td>
<td>Activates dopaminergic receptors</td>
</tr>
</tbody>
</table>
| Action(s)              | • Alters hypothalamic regulation of metabolism  
                        | • Insulin sensitivity ↑ |
| Advantages             | No hypoglycemia     |
| Disadvantages          | • Dizziness/syncope  
                        | • Nausea            
                        | • Fatigue           
                        | • Rhinitis          
                        | • Long-term safety unknown |
| Cost                   | Medium              |

ADA. V. Diabetes Care. *Diabetes Care* 2012;35(suppl 1):S23. Adapted with permission from Silvio Inzucchi, Yale University.
Recommendations: Medical Nutrition Therapy (MNT)

- Individuals who have prediabetes or diabetes should receive individualized MNT as needed to achieve treatment goals, preferably provided by a registered dietitian familiar with the components of diabetes MNT (A)
- Because MNT can result in cost-savings and improved outcomes (B), MNT should be adequately covered by insurance and other payers (E)
Look AHEAD (Action for Health in Diabetes): One-Year Results

- Intensive lifestyle intervention resulted in:
  - Average 8.6% weight loss
  - Significant reduction of A1C
  - Reduction in several CVD risk factors
- Benefits sustained at 4 years
- Final results of Look AHEAD to provide insight into effects of long-term weight loss on important clinical outcomes

Recommendations: Diabetes Self-Management Education (DSME)

- People with diabetes should receive DSME according to national standards and diabetes self-management support at diagnosis and as needed thereafter (B)
- Effective self-management, quality of life are key outcomes of DSME; should be measured, monitored as part of care (C)
- DSME should address psychosocial issues, since emotional well-being is associated with positive outcomes (C)
- Because DSME can result in cost-savings and improved outcomes (B), DSME should be reimbursed by third-party payers (E)
Recommendations: Physical Activity

- Advise people with diabetes to perform at least 150 min/week of moderate-intensity aerobic physical activity (50–70% of maximum heart rate), spread over at least 3 days per week with no more than 2 consecutive days without exercise (A)

- In absence of contraindications, people with type 2 diabetes should be encouraged to perform resistance training at least twice per week (A)
Recommendations: Psychosocial Assessment and Care

- Ongoing part of medical management of diabetes (E)
- Psychosocial screening/follow-up: attitudes about diabetes, medical management/outcomes expectations, affect/mood, quality of life, resources, psychiatric history (E)
- When self-management is poor, screen for psychosocial problems: depression, diabetes-related anxiety, eating disorders, cognitive impairment (C)

Recommendations: Hypoglycemia

- Glucose (15–20 g) preferred treatment for conscious individual with hypoglycemia (E)
- Glucagon should be prescribed for all individuals at significant risk of severe hypoglycemia and caregivers/family members instructed in administration (E)
- Those with hypoglycemia unawareness or one or more episodes of severe hypoglycemia should raise glycemic targets to reduce risk of future episodes (B)

ADA. V. Diabetes Care. *Diabetes Care* 2012;35(suppl 1):S27.
Recommendations: Bariatric Surgery

- Consider bariatric surgery for adults with BMI >35 kg/m² and type 2 diabetes (B)
- After surgery, life-long lifestyle support and medical monitoring is necessary (B)
- Insufficient evidence to recommend surgery in patients with BMI <35 kg/m² outside of a research protocol (E)
- Well-designed, randomized controlled trials comparing optimal medical/lifestyle therapy needed to determine long-term benefits, cost-effectiveness, risks (E)
Recommendations: Immunization

• Provide influenza vaccine annually to all diabetic patients ≥6 months of age (C)
• Administer pneumococcal polysaccharide vaccine to all diabetic patients ≥2 years (C)
  – One-time revaccination recommended for those >64 years previously immunized at <65 years if administered >5 years ago
  – Other indications for repeat vaccination: nephrotic syndrome, chronic renal disease, immunocompromised states
• Administer hepatitis B vaccination per CDC recommendations (C)
VI. PREVENTION AND MANAGEMENT OF DIABETES COMPLICATIONS
Cardiovascular Disease (CVD) in Individuals with Diabetes

- CVD is the major cause of morbidity, mortality for those with diabetes
- Common conditions coexisting with type 2 diabetes (e.g., hypertension, dyslipidemia) are clear risk factors for CVD
- Diabetes itself confers independent risk
- Benefits observed when individual cardiovascular risk factors are controlled to prevent/slow CVD in people with diabetes
Screening and diagnosis

- Measure blood pressure at every routine diabetes visit (C)
- If patients have systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg (C)
  - Confirm blood pressure on a separate day
  - Repeat systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg confirms a diagnosis of hypertension
Recommendations: Hypertension/Blood Pressure Control

Goals

• A goal systolic blood pressure <130 mmHg is appropriate for most patients with diabetes (C)

• Based on patient characteristics and response to therapy, higher or lower systolic blood pressure targets may be appropriate (B)

• Patients with diabetes should be treated to a diastolic blood pressure <80 mmHg (B)
Recommendations: Hypertension/Blood Pressure Control

Treatment (1)

- Patients with a systolic blood pressure 130–139 mmHg or a diastolic blood pressure 80–89 mmHg (E)
  - May be given lifestyle therapy alone for a maximum of 3 months
  - If targets are not achieved, patients should be treated with the addition of pharmacological agents

Recommendations: Hypertension/Blood Pressure Control

Treatment (2)

• Patients with more severe hypertension (systolic blood pressure \( \geq 140 \) mmHg or diastolic blood pressure \( \geq 90 \) mmHg) at diagnosis or follow-up (A)
  – Should receive pharmacologic therapy in addition to lifestyle therapy
Recommendations: Hypertension/Blood Pressure Control

Treatment (3)

- Lifestyle therapy for hypertension (B)
  - Weight loss if overweight
  - DASH-style dietary pattern including reducing sodium, increasing potassium intake
  - Moderation of alcohol intake
  - Increased physical activity
Recommendations: Hypertension/Blood Pressure Control

Treatment (4)

- Pharmacologic therapy for patients with diabetes and hypertension
  - A regimen that includes either an ACE inhibitor or angiotensin II receptor blocker
  - If one class is not tolerated, the other should be substituted

- Multiple drug therapy (two or more agents at maximal doses) is generally required to achieve blood pressure targets (B)

Recommendations: Hypertension/Blood Pressure Control

Treatment (5)

- If ACE inhibitors, ARBs, or diuretics are used, kidney function, serum potassium levels should be monitored (E)
- In pregnant patients with diabetes and chronic hypertension, blood pressure target goals of 110–129/65–79 mmHg are suggested in interest of long-term maternal health and minimizing impaired fetal growth; ACE inhibitors, ARBs, contraindicated during pregnancy (E)
Recommendations: Dyslipidemia/Lipid Management

Screening

- In most adult patients, measure fasting lipid profile at least annually (E)
- In adults with low-risk lipid values (LDL cholesterol <100 mg/dL, HDL cholesterol >50 mg/dL, and triglycerides <150 mg/dL), lipid assessments may be repeated every 2 years (E)
Recommendations: Dyslipidemia/Lipid Management

Treatment recommendations and goals (1)

• To improve lipid profile in patients with diabetes, recommend lifestyle modification (A), focusing on
  – Reduction of saturated fat, *trans* fat, cholesterol intake
  – Increased n-3 fatty acids, viscous fiber, plant stanols/sterols
  – Weight loss (if indicated)
  – Increased physical activity
**Recommendations: Dyslipidemia/Lipid Management**

**Treatment recommendations and goals (2)**

- Statin therapy should be added to lifestyle therapy, regardless of baseline lipid levels
  - with overt CVD (A)
  - without CVD >40 years of age who have one or more other CVD risk factors (A)
- For patients at lower risk (e.g., without overt CVD, <40 years of age) (E)
  - Consider statin therapy in addition to lifestyle therapy if LDL cholesterol remains >100 mg/dL
  - In those with multiple CVD risk factors
Recommendations: Dyslipidemia/Lipid Management

Treatment recommendations and goals (3)

• In individuals without overt CVD
  – Primary goal is an LDL cholesterol <100 mg/dL (2.6 mmol/L) (A)

• In individuals with overt CVD
  – Lower LDL cholesterol goal of <70 mg/dL (1.8 mmol/L), using a high dose of a statin, is an option (B)
Recommendations: Dyslipidemia/Lipid Management

Treatment recommendations and goals (4)

• If targets not reached on maximal tolerated statin therapy
  – Alternative therapeutic goal: reduce LDL cholesterol ~30–40% from baseline (A)

• Triglyceride levels <150 mg/dL (1.7 mmol/L), HDL cholesterol >40 mg/dL (1.0 mmol/L) in men and >50 mg/dL (1.3 mmol/L) in women, are desirable
  – However, LDL cholesterol–targeted statin therapy remains the preferred strategy (C)
Recommendations: Dyslipidemia/Lipid Management

Treatment recommendations and goals (5)

- If targets are not reached on maximally tolerated doses of statins (E)
  - Combination therapy using statins and other lipid lowering agents may be considered to achieve lipid targets
  - Has not been evaluated in outcome studies for either CVD outcomes or safety

- Statin therapy is contraindicated in pregnancy (B)
Recommendations: Glycemic, Blood Pressure, Lipid Control in Adults

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1C</td>
<td>&lt;7.0%*</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>&lt;130/80 mmHg†</td>
</tr>
<tr>
<td>Lipids</td>
<td></td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>&lt;100 mg/dL (&lt;2.6 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.

†Based on patient characteristics and response to therapy, higher or lower systolic blood pressure targets may be appropriate.

‡In individuals with overt CVD, a lower LDL cholesterol goal of <70 mg/dL (1.8 mmol/L), using a high dose of statin, is an option.
Recommendations: Antiplatelet Agents (1)

• Consider aspirin therapy (75–162 mg/day) (C)
  – As a primary prevention strategy in those with type 1 or type 2 diabetes at increased cardiovascular risk (10-year risk >10%)
  – Includes most men >50 years of age or women >60 years of age who have at least one additional major risk factor
    • Family history of CVD
    • Hypertension
    • Smoking
    • Dyslipidemia
    • Albuminuria
Recommendations: Antiplatelet Agents (2)

- Aspirin should not be recommended for CVD prevention for adults with diabetes at low CVD risk, since potential adverse effects from bleeding likely offset potential benefits (C)
  - 10-year CVD risk <5%: men <50 and women <60 years of age with no major additional CVD risk factors
- In patients in these age groups with multiple other risk factors (10-year risk 5–10%), clinical judgment is required (E)
Recommendations: Antiplatelet Agents (3)

- Use aspirin therapy (75–162 mg/day)
  - Secondary prevention strategy in those with diabetes with a history of CVD (A)
- For patients with CVD and documented aspirin allergy
  - Clopidogrel (75 mg/day) should be used (B)
- Combination therapy with ASA (75–162 mg/day) and clopidogrel (75 mg/day)
  - Reasonable for up to a year after an acute coronary syndrome (B)
Recommendations: Smoking Cessation

- Advise all patients not to smoke (A)
- Include smoking cessation counseling and other forms of treatment as a routine component of diabetes care (B)
Recommendations: Coronary Heart Disease Screening

- In asymptomatic patients, routine screening for CAD is not recommended, as it does not improve outcomes as long as CVD risk factors are treated (A)

Recommendations: Coronary Heart Disease Treatment (1)

- To reduce risk of cardiovascular events in patients with known CVD, use
  - ACE inhibitor* (C)
  - Aspirin* (A)
  - Statin therapy* (A)
- In patients with a prior MI
  - Beta-blockers should be continued for at least 2 years after the event (B)

*If not contraindicated.
Recommendations: Coronary Heart Disease Treatment (2)

- Longer-term use of beta-blockers in the absence of hypertension
  - Reasonable if well tolerated, but data are lacking (E)
- Avoid TZD treatment
  - In patients with symptomatic heart failure (C)
- Metformin use in patients with stable CHF
  - Indicated if renal function is normal
  - Should be avoided in unstable or hospitalized patients with CHF (C)
Recommendations: Nephropathy

• To reduce risk or slow the progression of nephropathy
  – Optimize glucose control (A)
  – Optimize blood pressure control (A)
**Recommendations: Nephropathy Screening**

- **Assess urine albumin excretion annually (B)**
  - In type 1 diabetic patients with diabetes duration of $\geq 5$ years
  - In all type 2 diabetic patients at diagnosis

- **Measure serum creatinine at least annually (E)**
  - In all adults with diabetes regardless of degree of urine albumin excretion
  - Serum creatinine should be used to estimate GFR and stage level of chronic kidney disease, if present

ADA. VI. Prevention, Management of Complications. *Diabetes Care* 2012;35(suppl 1):S34.
Recommendations: Nephropathy Treatment (1)

- Nonpregnant patient with micro- or macroalbuminuria
  - Use either ACE inhibitors or ARBs (A)
  - If one class is not tolerated, the other should be substituted (E)

- Reduction of protein intake may improve measures of renal function (urine albumin excretion rate, GFR) (B)
  - To 0.8–1.0 g x kg body wt\(^{-1}\) x day\(^{-1}\) in those with diabetes, earlier stages of CKD
  - To 0.8 g x kg body wt\(^{-1}\) x day\(^{-1}\) in later stages of CKD
Recommendations: Nephropathy Treatment (2)

- When ACE inhibitors, ARBs, or diuretics are used, monitor serum creatinine and potassium levels for the development of increased creatinine and hyperkalemia (E)
- Continued monitoring of urine albumin excretion to assess both response to therapy and progression of disease is reasonable (E)
- When estimated GFR is <60 mL x min/1.73 m², evaluate and manage potential complications of CKD (E)
Recommendations: Nephropathy Treatment (3)

- Consider referral to a physician experienced in care of kidney disease (B)
  - Uncertainty about etiology of kidney disease
  - Difficult management issues
  - Advanced kidney disease
### Definitions of Abnormalities in Albumin Excretion

<table>
<thead>
<tr>
<th>Category</th>
<th>Spot collection (µg/mg creatinine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;30</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>30-299</td>
</tr>
<tr>
<td>Macroalbuminuria (clinical)</td>
<td>≥300</td>
</tr>
</tbody>
</table>
Stages of Chronic Kidney Disease

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR (mL/min per 1.73 m² body surface area)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney damage* with normal or increased GFR</td>
<td>≥90</td>
</tr>
<tr>
<td>2</td>
<td>Kidney damage* with mildly decreased GFR</td>
<td>60–89</td>
</tr>
<tr>
<td>3</td>
<td>Moderately decreased GFR</td>
<td>30–59</td>
</tr>
<tr>
<td>4</td>
<td>Severely decreased GFR</td>
<td>15–29</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure</td>
<td>&lt;15 or dialysis</td>
</tr>
</tbody>
</table>

GFR = glomerular filtration rate

*Kidney damage defined as abnormalities on pathologic, urine, blood, or imaging tests.
### Management of CKD in Diabetes (1)

<table>
<thead>
<tr>
<th>GFR (mL/min/1.73 m²)</th>
<th>Recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All patients</strong></td>
<td>Yearly measurement of creatinine, urinary albumin excretion, potassium</td>
</tr>
<tr>
<td><strong>45-60</strong></td>
<td>Referral to nephrology if possibility for nondiabetic kidney disease exists</td>
</tr>
<tr>
<td></td>
<td>Consider dose adjustment of medications</td>
</tr>
<tr>
<td></td>
<td>Monitor eGFR every 6 months</td>
</tr>
<tr>
<td></td>
<td>Monitor electrolytes, bicarbonate, hemoglobin, calcium, phosphorus, parathyroid hormone at least yearly</td>
</tr>
<tr>
<td></td>
<td>Assure vitamin D sufficiency</td>
</tr>
<tr>
<td></td>
<td>Consider bone density testing</td>
</tr>
<tr>
<td></td>
<td>Referral for dietary counselling</td>
</tr>
</tbody>
</table>

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## Management of CKD in Diabetes (2)

<table>
<thead>
<tr>
<th>GFR (ml/min/1.73 m²)</th>
<th>Recommended</th>
</tr>
</thead>
</table>
| 30-44                | Monitor eGFR every 3 months  
Monitor electrolytes, bicarbonate, calcium, phosphorus, parathyroid hormone, hemoglobin, albumin, weight every 3–6 months  
Consider need for dose adjustment of medications |
| <30                  | Referral to nephrologists |
Recommendations: Retinopathy

• To reduce risk or slow progression of retinopathy
  – Optimize glycemic control (A)
  – Optimize blood pressure control (A)
Recommendations: Retinopathy Screening (1)

- Initial dilated and comprehensive eye examination by an ophthalmologist or optometrist
  - Adults and children aged 10 years or older with type 1 diabetes
    - Within 5 years after diabetes onset (B)
  - Patients with type 2 diabetes
    - Shortly after diagnosis of diabetes (B)
Recommendations: Retinopathy Screening (2)

- Subsequent examinations for type 1 and type 2 diabetic patients
  - Should be repeated annually by an ophthalmologist or optometrist
- Less frequent exams (every 2–3 years)
  - May be considered following one or more normal eye exams
- More frequent examinations required if retinopathy is progressing (B)

Recommendations: Retinopathy Screening (3)

• High-quality fundus photographs
  – Can detect most clinically significant diabetic retinopathy (E)

• Interpretation of the images
  – Performed by a trained eye care provider (E)

• While retinal photography may serve as a screening tool for retinopathy, it is not a substitute for a comprehensive eye exam
  – Perform comprehensive eye exam at least initially and at intervals thereafter as recommended by an eye care professional (E)
Recommendations: Retinopathy Screening (4)

- Women with preexisting diabetes who are planning pregnancy or who have become pregnant (B)
  - Comprehensive eye examination
  - Counseled on risk of development and/or progression of diabetic retinopathy
- Eye examination should occur in the first trimester (B)
  - Close follow-up throughout pregnancy
  - For 1 year postpartum
Recommendations: Retinopathy Treatment (1)

- Promptly refer patients with any level of macular edema, severe NPDR, or any PDR
  - To an ophthalmologist knowledgeable and experienced in management, treatment of diabetic retinopathy (A)

- Laser photocoagulation therapy is indicated (A)
  - To reduce risk of vision loss in patients with
    - High-risk PDR
    - Clinically significant macular edema
    - Some cases of severe NPDR
Recommendations: Retinopathy Treatment (2)

- Presence of retinopathy
  - Not a contraindication to aspirin therapy for cardioprotection, as this therapy does not increase the risk of retinal hemorrhage (A)

Recommendations: Neuropathy Screening, Treatment (1)

- All patients should be screened for distal symmetric polyneuropathy (DPN) (B)
  - At diagnosis of type 2 diabetes with 5 years after diagnosis of type 1 diabetes
  - At least annually thereafter using simple clinical tests
- Electrophysiological testing rarely needed
  - Except in situations where clinical features are atypical (E)

Recommendations: Neuropathy Screening, Treatment (2)

- Screening for signs and symptoms of cardiovascular autonomic neuropathy
  - Should be instituted at diagnosis of type 2 diabetes and 5 years after the diagnosis of type 1 diabetes
  - Special testing rarely needed; may not affect management or outcomes (E)

- Medications for relief of specific symptoms related to DPN, autonomic neuropathy are recommended
  - Improve quality of life of the patient (E)
Recommendations: Foot Care (1)

• For all patients with diabetes, perform an annual comprehensive foot examination to identify risk factors predictive of ulcers and amputations
  – Inspection
  – Assessment of foot pulses
  – Test for loss of protective sensation: 10-g monofilament plus testing any one of
    • Vibration using 128-Hz tuning fork
    • Pinprick sensation
    • Ankle reflexes
    • Vibration perception threshold (B)
To perform the 10-g monofilament test, place the device perpendicular to the skin, with pressure applied until the monofilament buckles.

Hold in place for 1 second and then release.

The monofilament test should be performed at the highlighted sites while the patient’s eyes are closed.
Recommendations: Foot Care (3)

• Provide general foot self-care education (B)
• Use multidisciplinary approach
  – Individuals with foot ulcers, high-risk feet; especially prior ulcer or amputation (B)
• Refer patients to foot care specialists for ongoing preventive care, life-long surveillance (C)
  – Smokers
  – Loss of protective sensation or structural abnormalities
  – History of prior lower-extremity complications
Recommendations: Foot Care (4)

- Initial screening for peripheral arterial disease (PAD)
  - Include a history for claudication, assessment of pedal pulses
  - Consider obtaining an ankle-brachial index (ABI); many patients with PAD are asymptomatic (C)

- Refer patients with significant claudication or a positive ABI for further vascular assessment
  - Consider exercise, medications, surgical options (C)
VII. ASSESSMENT OF COMMON COMORBID CONDITIONS
**Recommendations: Assessment of Common Comorbid Conditions**

- For patients with risk factors, signs or symptoms, consider assessment and treatment for common diabetes-associated conditions (B)
- Common comorbidities for which increased risk is associated with diabetes

  - Hearing impairment
  - Obstructive sleep apnea
  - Fatty liver disease
  - Low testosterone in men
  - Periodontal disease
  - Certain cancers
  - Fractures
  - Cognitive impairment
VIII. DIABETES CARE IN SPECIFIC POPULATIONS
Recommendations: Pediatric Glycemic Control (Type 1 Diabetes)

- Consider age when setting glycemic goals in children and adolescents with type 1 diabetes (E)
Recommendations: Pediatric Nephropathy (Type 1 Diabetes)

• Annual screening for microalbuminuria, with a random spot urine sample for albumin-to-creatinine (ACR) ratio
  – Consider once child is 10 years of age and has had diabetes for 5 years (E)

• Confirmed, persistently elevated ACR on two additional urine specimens from different days
  – Treat with an ACE inhibitor, titrated to normalization of albumin excretion, if possible (E)
Recommendations: Pediatric Hypertension (Type 1 Diabetes) (1)

• Treat high-normal blood pressure (systolic or diastolic blood pressure consistently above the 90th percentile for age, sex, and height) with
  – Dietary intervention
  – Exercise aimed at weight control and increased physical activity, if appropriate

• If target blood pressure is not reached with 3–6 months of lifestyle intervention
  – Consider pharmacologic treatment (E)
Pharmacologic treatment of hypertension

- Systolic or diastolic blood pressure consistently above the 95th percentile for age, sex, and height

  Or

- Consistently >130/80 mmHg, if 95% exceeds that value

- Initiate treatment as soon as diagnosis is confirmed (E)
Recommendations: Pediatric Hypertension (Type 1 Diabetes) (3)

- ACE inhibitors
  - Consider for initial treatment of hypertension, following appropriate reproductive counseling due to potential teratogenic effects (E)

- Goal of treatment
  - Blood pressure consistently <130/80 mmHg or below the 90th percentile for age, sex, and height, whichever is lower (E)
Recommendations: Pediatric Dyslipidemia (Type 1 Diabetes) (1)

Screening (1)

- If family history of hypercholesterolemia (total cholesterol >240 mg/dL) or a cardiovascular event before age 55 years, or if family history is unknown
  - Perform fasting lipid profile on children >2 years of age soon after diagnosis (after glucose control has been established)
Recommendations: Pediatric Dyslipidemia (Type 1 Diabetes) (2)

Screening (2)

• If family history is not of concern
  – Consider first lipid screening at puberty (≥10 years)

• All children diagnosed with diabetes at or after puberty
  – Perform fasting lipid profile soon after diagnosis (after glucose control has been established) (E)
Screening (3)

- For both age-groups, if lipids are abnormal
  - Annual monitoring is recommended
- If LDL cholesterol values are within accepted risk levels (<100 mg/dL [2.6 mmol/L])
  - Repeat lipid profile every 5 years (E)
Treatment

• Initial therapy: optimize glucose control, MNT using Step II AHA diet aimed at decreasing dietary saturated fat (E)

• > age 10 years, statin reasonable in those (after MNT and lifestyle changes) with
  – LDL cholesterol >160 mg/dL (4.1 mmol/L) or
  – LDL cholesterol >130 mg/dL (3.4 mmol/L) and one or more CVD risk factors (E)

• Goal: LDL cholesterol <100 mg/dL (2.6 mmol/L) (E)
Recommendations: Pediatric Retinopathy (Type 1 Diabetes)

- First ophthalmologic examination
  - Obtain once child is 10 years of age; has had diabetes for 3–5 years (E)
- After initial examination
  - Annual routine follow-up generally recommended
  - Less frequent examinations may be acceptable on advice of an eye care professional (E)
Recommendations: Pediatric Celiac Disease (Type 1 Diabetes) (1)

- Children with type 1 diabetes
  - Screen for celiac disease by measuring tissue transglutaminase or antiendomysial antibodies, with documentation of normal total serum IgA levels, soon after the diagnosis of diabetes (E)

- Repeat testing in children with
  - Growth failure
  - Failure to gain weight, weight loss
  - Diarrhea, flatulence, abdominal pain, or signs of malabsorption
  - Frequent unexplained hypoglycemia or deterioration in glycemic control (E)
Recommendations: Pediatric Celiac Disease (Type 1 Diabetes) (2)

- Children with positive antibodies
  - Refer to a gastroenterologist for evaluation with endoscopy and biopsy (E)
- Children with biopsy-confirmed celiac disease
  - Place on a gluten-free diet
  - Consult with a dietitian experienced in managing both diabetes and celiac disease (E)
**Recommendations: Pediatric Hypothyroidism (Type 1 Diabetes)**

- Children with type 1 diabetes
  - Screen for thyroid peroxidase, thyroglobulin antibodies at diagnosis (E)
- Thyroid-stimulating hormone (TSH) concentrations
  - Measure after metabolic control established
    - If normal, recheck every 1-2 years; or
    - If patient develops symptoms of thyroid dysfunction, thyromegaly, or an abnormal growth rate

Recommendations: Transition from Pediatric to Adult Care

- As teens transition into emerging adulthood, health care providers and families must recognize their many vulnerabilities (B) and prepare the developing teen, beginning in early to mid adolescence and at least 1 year prior to the transition (E).

- Both pediatricians and adult health care providers should assist in providing support and links to resources for the teen and emerging adult (B).
Recommendations: Preconception Care (1)

• A1C levels should be as close to normal as possible (7%) in an individual patient before conception is attempted (B)
• Starting at puberty, incorporate preconception counseling in routine diabetes clinic visit for all women of childbearing potential (C)
• Women with diabetes contemplating pregnancy should be evaluated and, if indicated, treated for diabetic retinopathy, nephropathy, CVD (B)
Medications should be evaluated prior to conception, since drugs commonly used to treat diabetes and its complications may be contraindicated or not recommended in pregnancy, including statins, ACE inhibitors, ARBs, and most noninsulin therapies (E).

Since many pregnancies are unplanned, consider potential risks/benefits of medications contraindicated in pregnancy in all women of childbearing potential; counsel accordingly (E).
Recommendations: Older Adults (1)

• Functional, cognitively intact older adults with significant life expectancies should receive diabetes care using goals developed for younger adults (E)

• Glycemic goals for those not meeting the above criteria may be relaxed using individual criteria, but hyperglycemia leading to symptoms or risk of acute hyperglycemic complications should be avoided in all patients (E)
Recommendations: Older Adults (2)

- Treat other cardiovascular risk factors with consideration of the time frame of benefit and the individual patient.
- Treatment of hypertension is indicated in virtually all older adults; lipid, aspirin therapy may benefit those with life expectancy equal to time frame of primary/secondary prevention trials (E).
- Individualize screening for diabetes complications with attention to those leading to functional impairment (E).

Recommendations: Cystic Fibrosis-Related Diabetes (CFRD)

- Annual screening for CFRD with OGTT should begin by age 10 years in all patients with cystic fibrosis who do not have CFRD (B)
  - Use of A1C as a screening test for CFRD is not recommended (B)
- During a period of stable health, diagnosis of CFRD can be made in patients with cystic fibrosis according to usual diagnostic criteria (E)
Recommendations: Cystic Fibrosis-Related Diabetes (CFRD)

- Patients with CFRD should be treated with insulin to attain individualized glycemic goals (A)
- Annual monitoring for complications of diabetes is recommended, beginning 5 years after the diagnosis of CFRD (E)

IX. DIABETES CARE IN SPECIFIC SETTINGS
Recommendations: Diabetes Care in the Hospital (1)

• All patients with diabetes admitted to the hospital should have their diabetes clearly identified in the medical record (E)

• All patients with diabetes should have an order for blood glucose monitoring, with results available to all members of the health care team (E)
**Recommendations: Diabetes Care in the Hospital (2)**

- **Goals for blood glucose levels**
  - Critically ill patients: 140-180 mg/dL (7.8–10 mmol/L) (A)
  - More stringent goals, such as 110-140 mg/dL (6.1–7.8 mmol/L) may be appropriate for selected patients, if achievable without significant hypoglycemia (C)
  - Critically ill patients require an IV insulin protocol that has demonstrated efficacy and safety in achieving the desired glucose range without increasing risk for severe hypoglycemia (E)
Recommendations: Diabetes Care in the Hospital (3)

- Goals for blood glucose levels
  - **Noncritically ill patients**: No clear evidence for specific blood glucose goals
  - If treated with insulin, premeal blood glucose targets (if safely achieved)
    - Generally <140 mg/dL (7.8 mmol/L) with random blood glucose <180 mg/dL (10.0 mmol/L)
    - More stringent targets may be appropriate in stable patients with previous tight glycemic control
    - Less stringent targets may be appropriate in those with severe comorbidities (E)

Recommendations: Diabetes Care in the Hospital (4)

- Scheduled subcutaneous insulin with basal, nutritional, and correction components is the preferred method for achieving and maintaining glucose control in noncritically ill patients
Recommendations: Diabetes Care in the Hospital (5)

- Initiate glucose monitoring in any patient not known to be diabetic who receives therapy associated with high-risk for hyperglycemia
  - High-dose glucocorticoid therapy, initiation of enteral or parenteral nutrition, or other medications such as octreotide or immunosuppressive medications (B)
- If hyperglycemia is documented and persistent, consider treating such patients to the same glycemic goals as patients with known diabetes (E)

A hypoglycemia management protocol should be adopted and implemented by each hospital or hospital system
- Establish a plan for treating hypoglycemia for each patient; document episodes of hypoglycemia in medical record and track (E)

Obtain A1C for all patients if results within previous 2–3 months unavailable (E)

Patients with hyperglycemia without a diagnosis of diabetes: document plans for follow-up testing and care at discharge (E)
Diabetes Care in the Hospital: NICE-SUGAR Study (1)

- Largest randomized controlled trial to date
- Tested effect of tight glycemic control (target 81–108 mg/dL) on outcomes among 6,104 critically ill participants
- Majority (>95%) required mechanical ventilation
In both surgical/medical patients, 90-day mortality significantly higher in intensively treated vs conventional group (target 144–180 mg/dL)

- 78 more deaths (27.5% vs 24.9%; \( P=0.02 \))
- 76 more deaths from cardiovascular causes (41.6% vs 35.8%; \( P=0.02 \))
- Severe hypoglycemia more common (6.8% vs 0.5%; \( P<0.001 \))
X. STRATEGIES FOR IMPROVING DIABETES CARE
Recommendations: Strategies for Improving Diabetes Care (1)

• Care should be aligned with components of the Chronic Care Model to ensure productive interactions between a prepared proactive practice team and an informed activated patient (A)

• When feasible, care systems should support team-based care, community involvement, patient registries, and embedded decision support tools to meet patient needs (B)
Recommendations: Strategies for Improving Diabetes Care (2)

- Treatment decisions should be timely and based on evidence-based guidelines that are tailored to individual patient preferences, prognoses, and comorbidities (B)
- A patient-centered communication style should be employed that incorporates patient preferences, assesses literacy and numeracy, and addresses cultural barriers to care (B)
Objective 1: Optimize Provider and Team Behavior

- Care team should prioritize timely, appropriate intensification of lifestyle and/or pharmaceutical therapy
  - Patients who have not achieved beneficial levels of blood pressure, lipid, or glucose control
- Strategies include
  - Explicit goal setting with patients
  - Identifying and addressing barriers to care
  - Integrating evidence-based guidelines
  - Incorporating care management teams
Objective 2: Support Patient Behavior Change

- Implement a systematic approach to support patient behavior change efforts
  - a) Healthy lifestyle: physical activity, healthy eating, nonuse of tobacco, weight management, effective coping
  - b) Disease self-management: medication taking and management, self-monitoring of glucose and blood pressure when clinically appropriate
  - c) Prevention of diabetes complications: self-monitoring of foot health, active participation in screening for eye, foot, and renal complications, and immunizations

Objective 3: Change the System of Care

- The most successful practices have an institutional priority for providing high quality of care
  - Basing care on evidence-based guidelines
  - Expanding the role of teams and staff
  - Redesigning the processes of care
  - Implementing electronic health record tools
  - Activating and educating patients
  - Identifying and/or developing community resources and public policy that supports healthy lifestyles
  - Alterations in reimbursement