Options for Treating Prediabetes and Diabetes: Get Your Patient to Goal

Celia Levesque MSN, RN, CNS-BC, NP-C, CDE, BC-ADM
clevesqu@mdanderson.org

Objectives
- Differentiate types of diabetes and prediabetes
- Describe various treatment options for managing diabetes and prediabetes
- Describe various treatment options for managing diabetes and prediabetes

CDC Diabetes Statistics Report 20171
- Diabetes 30.3 million (9.4%)
- Diabetes: 25% in age 65+
- Highest in Asians, non-Hispanic blacks, and Hispanics
- Children: in 2012: 17,900 w T1DM, 5,300 w T2DM
- Prediabetes: 84.1 million (33.9%)
- Prediabetes: 48% in age 65+

Screening for Prediabetes & Diabetes2
- Overweight/obese who have 1+ risk factors
  - 1st degree relative with DM
  - High-risk ethnic group
  - Hx CVD, HTN, HDL < 35, Triglyceride > 250
  - PCOS
  - Sedentary lifestyle
  - Other: Acanthus nigricans
    - If normal: test at least every 3 years or more often
- GDM lifelong testing every 3 years

Secreted by Adipose Tissue3

![Diagram showing secreted substances by adipose tissue](image-url)
| Lept = Leptin | Signals to brain about body fat stores, regulates appetite and energy expenditure |
| Adipo = Adiponectin | Plays role in protection in patho of T2DM and CVD |
| Resi = Resistin | May contribute to insulin resistance |
| TNF = TNF-α | Affects insulin signaling may cause insulin resistance in obesity |
| IL6 = Interleukin-6 | Pro-inflammatory, plays role in lipid and glucose metabolism, and weight regulation |
| PAI = Plasminogen activator inhibitor 1 | Inhibitor of fibrinolytic system by inhibition of activation of plasminogen |
| Angi = Angiotensinogen | Precursor of angiotensin II, regulator of BP and electrolyte homeostasis |
| FFA = Free fatty acids | Oxidized in tissues to produce local energy, substrate for triglyceride and structural molecular synthesis, involved in development of insulin resistance |
| ASP = acylation stimulating protein | Influences rate of triacylglycerol synthesis in adipose tissue |
| VEGF = vascular endothelial growth factor | Stimulates angiogenesis |
| Adip = Adipsin | Potential relation between complement pathway and adipose tissue metabolism |
| Glyc=Glycerol | Structural component of major classes of biological lipids and gluconeogenic precursor |
| IGF1= insulin-like growth factor 1 | Stimulates proliferation of wide variety of cells and mediates many cells and many of the effects of growth hormone |

### Diagnosis of Prediabetes/Diabetes

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Prediabetes</th>
<th>Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting</td>
<td>&lt; 100</td>
<td>100-125</td>
<td>126+</td>
</tr>
<tr>
<td>2 h PG</td>
<td>&lt;140</td>
<td>140-199</td>
<td>200+</td>
</tr>
<tr>
<td>HbA1c</td>
<td>&lt;5.7</td>
<td>5.7-6.4</td>
<td>6.5+</td>
</tr>
</tbody>
</table>

In absence of unequivocal hyperglycemia, dx requires 2 abnormal tests from 1 or 2 separate test sample(s)

### Estimated Average Glucose

\[ \text{Estimated Average Glucose} = \text{AG mg/dL} = 28.7 \times \text{A1c} - 46.7^4 \]

### Causes of Inaccurate HbA1c

- Hemoglobin variants
- Sickle cell disease
- Pregnancy 2nd or 3rd trimester, Postpartum
- Glucos-6 phosphate dehydrogenase deficiency
- HIV
- Hemodialysis
- Recent blood loss, Blood transfusion
- Erythropoietin therapy
Prediabetes$^5$

- Impaired Fasting Glucose
  - Normal insulin sensitivity in skeletal muscle
  - Impaired 1$^{st}$ phase insulin
  - Decreased liver glucose uptake
  - Impaired suppression of endogenous glucose production

- Impaired Glucose Tolerance
  - Severe skeletal muscle insulin resistance
  - Impaired 2$^{nd}$ phase insulin
  - The 1-hour PP BG is strongest predictor of T2DM
  - If IFG and 1 hr PP > 155 had 4 fold increased risk of T2DM

Treatment of Prediabetes$^2,6$

- Intensive Lifestyle Therapy
  - Weight loss ~7%
  - Nutrition: mostly plant based polyunsaturated/monounsaturated fat, avoid trans and saturated fat
  - Exercise: moderate intensity 150 min week + strength training
  - Moderate alcohol consumption
  - Sleep 7 hours per night
  - No tobacco products

- Dyslipidemia management
- Hypertension management
- Consider Diabetes Medications:

Classifications of Diabetes Mellitus$^2$

- Type 1 DM autoimmune B-cell destruction
- Type 2 DM progressive insulin resistance / B-cell failure
- Gestational DM diagnosed 2$^{nd}$ or 3$^{rd}$ trimester
- Specific types due to other causes
  - Monogenic diabetes syndromes: neonatal, MODY
  - Medications: steroids
  - Cystic fibrosis
  - Pancreatitis
Type 1 Diabetes

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Stage 1</th>
<th>Stage 2</th>
<th>Stage 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autoimmunity</td>
<td>Autoimmunity</td>
<td>Autoimmunity</td>
<td>Hyperglycemia</td>
</tr>
<tr>
<td>Normoglycemia</td>
<td>Normoglycemia</td>
<td>Normoglycemia</td>
<td>Symptomatic</td>
</tr>
<tr>
<td>Presymptomatic</td>
<td>Presymptomatic</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diagnostic Criteria</th>
<th>Stage 1</th>
<th>Stage 2</th>
<th>Stage 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple autoantibodies</td>
<td>No IGT or IFG</td>
<td>Multiple autoantibodies</td>
<td>Clinical symptoms</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dysglycemia IGT and/or IGT</td>
<td>Diabetes by standard criteria</td>
</tr>
</tbody>
</table>

Type 1 Diabetes

- Antibodies:
  - GAD65
  - Insulin
  - Tyrosine phosphatases IA-2, IA-2B, and ZnT8

- HLA associations
  - DQA and DQB

- Prone to other autoimmune disorders
  - Hashimoto thyroiditis
  - Graves disease
  - Addison disease
  - Celiac disease
  - Vitiligo
  - Autoimmune hepatitis
  - Myasthenia gravis
  - Pernicious anemia
Type 2 Diabetes

Treatment of Diabetes\(^2\)
- Uses person-centered and strength-based language
  - Active listening
  - Elicit patient preferences and beliefs
  - Assesses literacy, numeracy, barriers
- Multidisciplinary team

Patient Centered Approach
- Assess key patient characteristics
- Consider factors that impact care
- Shared decision making
- Agree on management plan
- Implement management plan
- Ongoing monitoring / adjust plan as needed

Initial Diabetes Evaluation
- DM hx including hx of DM education
- Family hx
- Hx of DM complications and medical
- Lifestyle assessment
- Current medication/vaccines
- Psychosocial assessment

Physical exam
- Ht, wt, BMI, growth & development in children
- BP, orthostatic BP if indicated
- Fundoscopic exam by eye specialist
- Thyroid palpation
- Skin exam (acanthosis, injection sites)
- Foot exam
Lab evaluation
- A1c
- Lipid profile
- Liver function
- Spot urinary albumin-to-creatinine ratio
- Serum creatinine and eGFR
- TSH if autoimmune T1DM
- Vitamin B12 if on metformin
- Serum K+ if on ACEI, ARB, or diuretics

Chronic Kidney Disease Stages

<table>
<thead>
<tr>
<th>Stage</th>
<th>eGFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>No clinical evidence</td>
<td>&gt; 60</td>
</tr>
<tr>
<td>1</td>
<td>&gt; 90</td>
</tr>
<tr>
<td>2</td>
<td>60-89</td>
</tr>
<tr>
<td>3</td>
<td>30-59</td>
</tr>
<tr>
<td>4</td>
<td>15-29</td>
</tr>
<tr>
<td>5</td>
<td>&lt;15</td>
</tr>
</tbody>
</table>

Refer to nephrologist if uncertain about etiology, difficulty in managing complications of CKD including anemia, secondary hyperparathyroidism, metabolic bone disease, resistant hypertension, electrolyte disturbances, eGFR < 30

Diabetic Retinopathy
- Initial exam
  - Type 1 after 5 years duration
  - Type 2 at time of dx
- Retinal photography with remote reading by an ophthalmologist or optometrist can be screening tool until comprehensive eye exam can be done
- Pregnant or planning pregnancy: eye exam before or in 1st trimester
- Optimize blood glucose, blood pressure, and lipids

Treatment of Diabetic Retinopathy
- If any DR, refer to a specialist experienced with management of DR
- Treatment
  - Laser photocoagulation
  - Intravitreous injections of antivascular endothelial growth factor ranibizumab
  - Intravitreous injections of antivascular endothelial growth factor

Goal setting
- A1c / Blood glucose / BP / lipid goals
- Self management goals

A1c / Blood Glucose Goals

<table>
<thead>
<tr>
<th></th>
<th>Less Stringent</th>
<th>More stringent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoglycemia risk</td>
<td>High risk</td>
<td>Low risk</td>
</tr>
<tr>
<td>Disease duration</td>
<td>Long duration</td>
<td>Short duration</td>
</tr>
<tr>
<td>Life expectancy</td>
<td>Short</td>
<td>Long</td>
</tr>
</tbody>
</table>
Comorbidities | Severe | None  
---|---|---  
Vascular disease | Severe | None  
Patient preference | Wants less burden | Highly motivated  
Resources/support | Limited | Readily available  

### ADA General Recommendations for A1c, Glucose, BP and Lipids

<table>
<thead>
<tr>
<th>Health status</th>
<th>Rationale</th>
<th>A1c goal</th>
<th>FBS/ac</th>
<th>Bedtime BG</th>
<th>BP</th>
<th>Lipids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy, few complications, good cognition</td>
<td>Long life</td>
<td>&lt;7.5%</td>
<td>90-130</td>
<td>90-150</td>
<td>&lt;140/90</td>
<td>Statin if possible</td>
</tr>
<tr>
<td>Intermed, multiple complications, impaired cognition</td>
<td>Less life exp, high hypo risk</td>
<td>&lt;8%</td>
<td>90-150</td>
<td>100-180</td>
<td>&lt;140/90</td>
<td>Statin if possible</td>
</tr>
<tr>
<td>Very complex limited life, severe cognitive impairment</td>
<td>Benefit of tight control uncertain</td>
<td>&lt;8.5%</td>
<td>100-180</td>
<td>110-200</td>
<td>&lt;150/90</td>
<td>Consider benefit of statin?</td>
</tr>
</tbody>
</table>

**Nutrition**
- No such thing as a “diabetic diet”
- No recommendations for macronutrients
- Mostly plant based, healthy fats, high fiber, low sugar
- Limit alcohol, sodium, sugar sweetened beverages
- Individualized meal planning with registered dietitian
- Promote healthy eating pattern to achieve weight, BP, lipid goals

**Dyslipidemia Management**
- Intensive lifestyle
- Assess ASCVD Risk: American College of Cardiology/American Heart Association ASCVD risk calculator
- Does not account for duration of diabetes or presence of diabetes complications
- Risk factors: DM, HTN, Fam Hx, low HDL-C, smoking, CKD 3-4

<table>
<thead>
<tr>
<th></th>
<th>HIGH RISK DM but no other major risk and/or age &lt;40</th>
<th>VERY HIGH RISK DM + major ASCVD risk</th>
<th>EXTREME RISK DM plus dx CVD</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-C</td>
<td>&lt;100</td>
<td>&lt;70</td>
<td>&lt;55</td>
</tr>
<tr>
<td>Non HDL-C</td>
<td>&lt;130</td>
<td>&lt;100</td>
<td>&lt;80</td>
</tr>
<tr>
<td>TG</td>
<td>&lt;150</td>
<td>&lt;150</td>
<td>&lt;150</td>
</tr>
<tr>
<td>Apo B</td>
<td>&lt;90</td>
<td>&lt;80</td>
<td>&lt;70</td>
</tr>
</tbody>
</table>
**Lipid Management**

<table>
<thead>
<tr>
<th>No statin</th>
<th>Moderate statin</th>
<th>High statin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy</td>
<td>&lt; age 40 with ASCVD risk factors</td>
<td>All ages with ASCVD or 10 yr CVD risk &gt; 20%</td>
</tr>
<tr>
<td>&lt; 40 no ASCVD risk fx</td>
<td>Age &gt;40 without ASCVD</td>
<td>Consider in those with multiple ASCVD risk fx</td>
</tr>
</tbody>
</table>

If don’t tolerate statin dose, try alternate statin, decrease dose or frequency
If not at goal with statin: Intensify statin, add ezetimibe, PCSK9i, coleselam or niacin
If triglycerides over 500: add fibrate, Rx-grade omega-3 fatty acids, niacin

**Statin Therapy**

<table>
<thead>
<tr>
<th>High intensity statin 🍒 ≥ 50%</th>
<th>Moderate intensity 🍒 ≥ 30-50%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atorvastatin 40-80 mg</td>
<td>Atorvastatin 10-20 mg</td>
</tr>
<tr>
<td>Rosuvastatin 20-40 mg</td>
<td>Rosuvastatin 5-10 mg</td>
</tr>
<tr>
<td>Simvastatin 20-40 mg</td>
<td>Simvastatin 20-40 mg</td>
</tr>
<tr>
<td>Pravastatin 40-80 mg</td>
<td>Pravastatin 40-80 mg</td>
</tr>
<tr>
<td>Lovastatin 40 mg</td>
<td>Lovastatin 40 mg</td>
</tr>
<tr>
<td>Fluvastatin XL 80 mg</td>
<td>Fluvastatin XL 80 mg</td>
</tr>
<tr>
<td>Pitavastatin 2-4 mg</td>
<td>Pitavastatin 2-4 mg</td>
</tr>
</tbody>
</table>

**Blood Pressure**

- Measure at each visit
- Measured by a trained professional
- Seated position, feet on floor, arm supported at level of the heart after 5 minutes of rest
- Cuff size appropriate
- Elevated values confirmed on another day

**Blood Pressure Goals**

- If DM + HTN and ASCVD or 10-year risk > 15% may choose target of <130/80 if can safely do so
- Lower risk individuals < 140/90

**HTN TX: Initial BP < 160/100**

- Start with 1 agent + intensive lifestyle
- No albuminuria: ACEI or ARB or β-blocker or CCB or thiazide diuretic
- Albuminuria: ACEI or ARB
- Not meeting target: add different drug class from ACEI/ARB, β-blocker, CCB, thiazide diuretic (don’t combine ACEI and ARB).
- If not meeting goal with above agents consider adding mineralocorticoid receptor antagonist, α-blocker, central agents, vasodilator, aldosterone antagonist or refer to specialist

**HTN TX: Initial BP < 160/100**

- No albuminuria: Start with 2 agents: ACEI/ARB or β-blocker, or CCB, or thiazide diuretic
- Albuminuria: ACEI or ARB AND β-blocker, or CCB or thiazide diuretic
- Not meeting target: add different drug class from ACEI/ARB, β-blocker, CCB, thiazide diuretic (don’t combine ACEI and ARB).
- If not meeting goal with above agents consider adding mineralocorticoid receptor antagonist, α-blocker, central agents, vasodilator, or aldosterone antagonist or refer to specialist