Weekend Update: New Recommendations in Diabetes Management

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Recent Drug Developments
March 2019
Objectives

- Compare and Contrast guideline recommendations to effectively management patients with diabetes.
  - American Diabetes Association (ADA)
  - American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE)

- Apply current ADA and AACE/ACE guidelines to guide choice of pharmacotherapy in diabetes management.

- Apply current ADA and AACE/ACE guidelines to guide prevention and/or management of complications of diabetes.
How I spent my weekend …..
A 56-year old male is newly diagnosed with Type 2 Diabetes. PMH is negative for ASCVD and positive for 1 ppd smoker, HTN, and GERD. You calculate his 10-year ASCVD risk to be 6.4%. Your choice of statin therapy is based on which of the following:

A. A desired LDL of < 100 mg/dL based on ADA 2019 Guidelines.
B. A desired LDL of < 70 mg/dL based on AACE/ACE 2019 Guidelines.
C. Low-intensity statin, such as pravastatin 10mg daily, because patient does not have ASCVD.
D. No statin therapy necessary due to ASCVD risk < 10%.
A 42-year female is here for follow up on her new diagnosis of Type 2 Diabetes. She asks if she needs to start a medication called an “ARB”. She read on the internet that it is supposed to help protect her kidneys. Her BP at her last 3 office visits was 126/78, 132/80, and 130/72 mmHg. Her recent labs indicate SCr 0.8 mg/dL, CrCl 88 mL/min; eGFR 92 mL/min/1.73m2; and albumin/creatinine ratio 18mg/g.

- Losartan should be started due to presence of BP > 130/80 and presence of albuminuria.
- Candesartan should be started to prevent chronic kidney disease and to maintain normal blood pressure.
- Irbesartan should be started to achieve and maintain goal BP < 130/80 mmHg per ADA 2019 guidelines.
- No ARB is necessary at this time because patient does not have hypertension and albumin/creatinine ratio is normal. Continue monitoring.
Patient Case

- 47yo Latina female here to establish care – unknown medical history
  - Last visit to a provider was over 2 years ago.

- S/sx nausea, 30# weight loss in 2 months; recurrent UTIs (having current symptoms); ↑ joint pain self-treated with ibuprofen; occasional episodes of vomiting bile; poor taste in mouth

- ROS: (+) appetite Δ, fatigue, unexpected weight Δ, (+) abdominal distention, abdominal pain, constipation, N/V, arthralgias, sleep disturbances

- NKDA
Patient Case

➤ **PE**: oriented to PPP, well developed
  ➤ CV – RRR, normal heart sounds
  ➤ Abdomen/GI – soft, normal appearance, bowel sounds normal, no shifting/dullness/distension, no abdominal bruit, no mass, no hepatosplenomegaly
    ➤ (+) for RUQ tenderness and guarding, (+) Murphy’s sign, No rigidity or rebound, No tenderness @ McBurney’s point
  ➤ Skin warm, dry, and intact
  ➤ Cognition, memory, mood, and affect normal
Patient Case

- Height 60.25"; Weight 51.8kg, BMI 22 kg/m²

- Urine Culture (+) *E. coli*
  - Resistant to Ampicillin, Amp/Sulbactam, Cipro/Levo-floxacin, Gentamicin
  - Sensitive to Nitrofurantoin, Ceftriaxone, Ceftazidime

- Medications – OTC Ibuprofen 600mg every 4-6h PRN

- Immunizations – HepB x 2 doses at appropriate interval
Patient Case

- **Labs**
  - CMP normal
  - K+ on lower end @ 3.9
  - SCr 0.6 mg/dL
  - Glucose 251 mg/dL
  - Alk Phos 126, AST 10, ALT 14
  - A1C 12.7%
  - C-peptide 2.4 ng/mL (range 1.1 – 4.4)
  - TSH 0.711
  - Amylase & Lipase normal
Screening for Pre-Diabetes

- Adults with BMI ≥ 25 kg/m² (≥ 23 kg/m² in Asian Americans) & 1 or more of the following:
  - 1ˢᵗ degree relative with diabetes
  - High risk ethnicity (e.g. African, Asian, or Native American, Latino, Pacific Islander)
  - History of CVD
  - HTN (≥ 140/90 mmHg or taking Rx for HTN)
  - HDL < 35mg/dL &/or TG > 250mg/dL
  - PCOS
  - Sedentary lifestyle
  - Other clinical conditions associated with diabetes (e.g. severe obesity, acanthosis nigricans)
Screening for Diabetes

- Test for diabetes in Adults:
  - Yearly in patients with Pre-Diabetes
  - Every 3 years for women with history of Gestational Diabetes
  - Begin at Age 45 for everyone else
    - Test in 3 year intervals if results are normal
    - Change test interval as necessary with changes in risk factors

- Test for diabetes in adolescents:
  - After puberty or age 10 years (whichever occurs first)
  - For those who are overweight (≥ 85% percentile) or obese (≥ 95% percentile) & have 1 or more risk factors:
    - Maternal diabetes or gestational diabetes with child in utero
    - Family history of Type 2 diabetes in 1st or 2nd degree relative
    - Race/ethnicity
    - Signs of insulin resistance or conditions associated with insulin resistance
Diagnosing Diabetes in Adults & Adolescents

- Must have 2 abnormal tests
  - From same sample or from 2 separate samples

- If 2 separate samples, can:
  - Repeat same test
  - Perform a different test

- A1C issues
  - Race, ethnicity, and hemoglobinopathies can affect A1C
    - Most assays in US okay
  - Check [www.ngsp.org/interf.asp](http://www.ngsp.org/interf.asp) for a list of A1C assays that have interferences

- What if A1C and glucose results are contradictory?
  - Example A1C x 2 tests > 7% but FPG is < 120 → patient considered to have diabetes
  - Results still too close for comfort?
Our Patient

- A1C = 12.7%
- Random plasma Glucose = 251mg/dL

- Patient states she is surprised by diabetes diagnosis – “I did not have any symptoms!”
  - 30# weight loss over 2 months
  - Very tired all the time
  - Recurrent UTIs
  - Mom had diabetes and was on dialysis
  - Father had diabetes
Let’s Talk C-Peptide

- Our Patient
  - C-peptide = 2.4 ng/mL (range 1.1 – 4.4 ng/mL)
  - Did we need to measure it?

- C-peptide is commonly used to assess β-cell function
  - Measures patient’s current status of insulin production
  - Does not take into account insulin resistance

- Produced in equimolar amounts to insulin when Pro-Insulin is cleaved

- C-peptide T1/2 = 20 to 30 min where Insulin T1/2 = 3 to 5 min
  - Systemic concentrations of C-peptide are 5x higher than insulin
C-Peptide

▶ Why check C-peptide?
  ▶ Differentiate between Type 1 and Type 2 diabetes
  ▶ May help to determine if insulin or oral therapy is more appropriate

▶ Not recommended for routine use per ADA 2011 guidelines
▶ Not addressed in ADA or AACE/ACE 2019 guidelines

▶ What did the C-peptide measurement tell us for our patient?
  ▶ She is still producing insulin!
  ▶ Ranges vary
    ▶ < 0.6ng/mL → likely absolute insulin deficiency (can confirm with auto-antibody test)
    ▶ < 1.2 ng/mL → likely Type 1 diabetes
Diabetes Prevention

Could I have prevented this?
- May consider metformin for prevention of T2DM for those with pre-diabetes if:
  - BMI $\geq$ 35 kg/m2
  - age < 60 yrs
  - history of gestational diabetes
  - per ADA and AACE/ACE guidelines

Diabetes Prevention Program (DPP)
- Intensive lifestyle management interventions
I have Diabetes... Now What?

- New text in ADA 2019 guidelines focusing on patient-centered collaborative care.

- Evaluate:
  - PMH
  - Lifestyle – eating patterns, physical activity, sleep behavior, tobacco, EtOH, & substance use
  - Medications
  - Vaccinations
  - Technology Use
  - Behavior and DSME Skills
  - Physical Exam
  - Labs
DECISION CYCLE FOR PATIENT-CENTERED GLYCEMIC MANAGEMENT IN TYPE 2 DIABETES

REVIEW AND AGREE ON MANAGEMENT PLAN
- Review management plan
- Mutual agreement on changes
- Ensure agreed modification of therapy is implemented in a timely fashion to avoid clinical inertia
- Decision cycle undertaken regularly (at least once/twice a year)

ASSESS KEY PATIENT CHARACTERISTICS
- Current lifestyle
- Comorbidities, i.e., ASCVD, CKD, HF
- Clinical characteristics, i.e., age, HbA1c, weight
- Issues such as motivation and depression
- Cultural and socioeconomic context

ONGOING MONITORING AND SUPPORT INCLUDING:
- Emotional well-being
- Check tolerability of medication
- Monitor glycemic status
- Biofeedback including SMBG, weight, step count, HbA1c, blood pressure, lipids

GOALS OF CARE
- Prevent complications
- Optimize quality of life

CONSIDER SPECIFIC FACTORS THAT IMPACT CHOICE OF TREATMENT
- Individualized HbA1c target
- Impact on weight and hypoglycemia
- Side effect profile of medication
- Complexity of regimen, i.e., frequency, mode of administration
- Choose regimen to optimize adherence and persistence
- Access, cost, and availability of medication

IMPLEMENT MANAGEMENT PLAN
- Patients not meeting goals generally should be seen at least every 3 months as long as progress is being made; more frequent contact initially is often desirable for DSMES

AGREE ON MANAGEMENT PLAN
- Specify SMART goals:
  - Specific
  - Measurable
  - Achievable
  - Realistic
  - Time limited

UPDATED DECISION MAKING TO CREATE A MANAGEMENT PLAN
- Involves an educated and informed patient (and their family/caregiver)
- Seeks patient preferences
- Effective consultation includes motivational interviewing, goal setting, and shared decision making
- Empowers the patient
- Ensures access to DSMES

ASCVD = Atherosclerotic Cardiovascular Disease
CKD = Chronic Kidney Disease
HF = Heart Failure
DSMES = Diabetes Self-Management Education and Support
SMBG = Self-Monitored Blood Glucose
Comprehensive Diabetes Evaluation

- **Medications**
  - Current Rx
  - OTC/herbal and alternative medications
  - Medication-taking behavior
  - Intolerance or side-effects

- **Technology**
  - How tech savvy is your patient?
    - Health apps, online education, and patient portals
  - Glucose meter use and/or CGM
    - Patient should bring meter to every visit for result review
  - Insulin pump settings & use
    - Evaluate at every visit
Comprehensive Diabetes Evaluation

- **Psychosocial**
  - PHQ-2/9, GAD-7
  - Eating habits? --check for disordered eating
  - What social/family support do they have?
  - Is there concern for cognitive impairment?

- **Behavioral**
  - DSME
  - Family planning
Pieces of your Assessment & Treatment Plan

- **Risk of diabetes complication**
  - History of ASCVD and/or CHF?
  - 10-yr ASCVD risk assessment + ASCVD risk factors
  - CKD evaluation and staging
  - Risk of hypoglycemia?

- **Set some goals**
  - What is your A1C target?
  - What is your BP target?
  - How often should your patient check their sugars?

- **What is your treatment plan?**
  - Lifestyle management
  - Drug therapy – sugars, ASCVD prevention/treatment, renal
  - Glucose meters
  - Insulin devices
  - Referrals!
Mood Assessment

- Anxiety disorders are prevalent in patients with diabetes.
  - BRFSS estimates 19.5% prevalence of GAD, regardless of type of diabetes.
  - What are they worried about?
    - It is not just needles, injections, or lancets....
    - I am not making my A1C targets....
    - What if I get a low blood sugar?
    - Implementing lifestyle changes

- Depression
  - Women > men

- Eating Disorders
  - Type 1 Diabetes – higher frequency of insulin omission to lose weight
  - Type 2 Diabetes – binge eating + feeling out of control; omitting insulin
Mood Assessment

- What should I check?
  - GAD-7 for anxiety
  - PHQ-2 or PHQ-9 for depression
  - Validated screening measures for eating disorders

- Frequency of assessment?
  - At first visit
  - Periodically thereafter
  - Any changes to disease, treatment, or life circumstances
  - Include caregivers and family where possible
    - Do they notice anything different?
Lifestyle Management

- Diabetes Self-Management Education (DSME)
- Medical Nutrition Therapy (MNT)
- Physical activity
- Tobacco cessation
  - No role for e-cigarettes
- Psychosocial care
Diabetes Distress

- Recommend routine monitoring –
  - Especially when treatment goals are not being met or complications occur

- New section in ADA 2019
  - Diabetes is a chronic, worrisome, burdensome health condition
  - Constant behavior demands
    - Nutrition, physical activity, medication use, cost of therapy, glucose monitoring
  - Reported prevalence of 18-45%
    - Yet only ~24% report diabetes distress being discussed with their healthcare team
Diabetes Distress

- DSME helps
  - Group education – Support system?

- Talk to your patients!
  - Set realistic expectations
  - Discuss potential occurrence for changes in mood/behavior as diabetes progresses
Targets of Therapy
## Targets of Therapy

<table>
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<tr>
<th>Measure</th>
<th>When to Check</th>
<th>Goal</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1C</td>
<td>2x yearly – pts meeting goals</td>
<td>&lt; 7% for non-pregnant adults</td>
<td>• Does not identify sugar variability or periods of hypoglycemia</td>
</tr>
<tr>
<td></td>
<td>4x yearly – pts not meeting goals or therapy Δ</td>
<td>&lt; 6.5% for select pts (no hypoglycemia or adverse effects)</td>
<td>• Can help determine if home glucose monitor is accurate</td>
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<tr>
<td></td>
<td></td>
<td>&lt; 8% for elderly, h/o severe hypoglycemia; advanced macro/micro-vascular complications; extensive co-morbidities</td>
<td>• Conditions affecting RBC turnover can affect A1C</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• Anemias, G6PD deficiency, blood transfusion, ESRD, pregnancy</td>
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# A1C correlation to Glucose

<table>
<thead>
<tr>
<th>A1C %</th>
<th>Mean Plasma Glucose (mg/dL)</th>
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<tbody>
<tr>
<td>6</td>
<td>126</td>
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<tr>
<td>7</td>
<td>154</td>
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<tr>
<td>8</td>
<td>183</td>
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<td>9</td>
<td>212</td>
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<tr>
<td>10</td>
<td>240</td>
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<tr>
<td>11</td>
<td>269</td>
</tr>
<tr>
<td>12</td>
<td>298</td>
</tr>
</tbody>
</table>

**Calculation**  
\[ eAG = (28.7 \times A1C) - 46.7 \]  
eAG (estimated average glucose)
<table>
<thead>
<tr>
<th>Measure</th>
<th>When to Check</th>
<th>Goal</th>
<th>Notes</th>
</tr>
</thead>
</table>
| SMBG      | **Basal/Bolus Insulin Regimens:** Check fasting, prior to meals/snacks, before exercise, s/sx hypoglycemia, & more frequently as needed  

**Basal Insulin + Oral Agents:** Fasting AM; Need for additional checks unclear  

**Oral Agents only:** Unclear benefit based on several RCTs; Consider 1x daily | **Pre-Prandial:** 80-130 mg/dL  
**Post-Prandial:** < 180 mg/dL | • Post-prandial testing recommended for patients with pre-prandial sugars within target range but A1C is > target. |
More or Less Stringent Goal Setting?

Approach to Individualization of Glycemic Targets

- **Patient / Disease Features**
  - Risks potentially associated with hypoglycemia and other drug adverse effects:
    - More stringent: low
    - Less stringent: high
  - Disease duration:
    - Newly diagnosed
    - Long-standing
  - Life expectancy:
    - Long
    - Short
  - Important comorbidities:
    - Absent
    - Few/mild
    - Severe
  - Established vascular complications:
    - Absent
    - Few/mild
    - Severe
- **Patient preference**:
  - Highly motivated, excellent self-care capabilities
  - Preference for less burdensome therapy
- **Resources and support system**:
  - Readily available
  - Limited

Diabetes Care 2019; 42(Suppl): S64
Technology Use in Diabetes Management
Diabetes Technology

- New section in ADA 2019 Standards

- Previous definition:
  - Insulin delivery devices – syringe, pen, pump
  - Monitoring – SMBG & CGM

- New definition:
  - Insulin delivery devices
  - Monitoring
  - Hybrid devices – deliver insulin & monitor sugars
  - Software serving as a medical device & providing DSME & support
Diabetes Technology

- Future foci:
  - Software as a medical device
  - Privacy
  - Cost
  - Technology-enabled diabetes education/support
  - Telemedicine
  - Other technology related issues
Glucose Meters

- Many different types of meters available
- Meters follow accuracy standards put forth by FDA and by the International Organization for Standardization (ISO).
- Accuracy is monitored by manufacturer & not routinely checked

| Table 7.1—Comparison of ISO 15197 and FDA blood glucose meter accuracy standards |
|-----------------------------------|-----------------------------------|
| **Setting**                      | **FDA**                           | **ISO 15197-2013**                  |
| Home use                         | 95% within 15% for all BG in the usable BG range† | 95% within 15% for BG ≥100 mg/dL |
|                                  | 99% within 20% for all BG in the usable BG range† | 95% within 15 mg/dL for BG <100 mg/dL |
| Hospital use                     | 95% within 12% for BG ≥75 mg/dL | 95% within 12 mg/dL for BG <75 mg/dL |
|                                  | 95% within 12 mg/dL for BG <75 mg/dL | 98% within 15 mg/dL for BG ≥75 mg/dL |
|                                  | 98% within 15 mg/dL for BG <75 mg/dL | 98% in A or B region of Consensus Error Grid‡ |

BG, blood glucose. To convert mg/dL to mmol/L, see http://www.endmemo.com/medical/unitconvert/Glucose.php. †The range of BG values for which the meter has been proven accurate and will provide readings (other than low, high, or error). ‡Values outside of the “clinically acceptable” A and B regions are considered “outlier” readings and may be dangerous to use for therapeutic decisions.
Glucose Meter Accuracy

- Diabetes Technology Society Blood Glucose Monitor System Surveillance Program established to assess accuracy of SMBG monitors

- Triple blind trial
  - Subjects were ≥ 18 years and had T1DM, T2DM, pre-diabetes or no diabetes
  - 18 BG monitors were assessed for accuracy across 3 clinical sites

- Protocol
  - Fingerstick blood sample
  - Did 18 BG monitors meet the following criteria?
    - BG within 15% of reference plasma value for BG > 100 mg/dL
    - BG within 15 mg/dL reference plasma value for BG < 100 mg/dL
  - Each monitor was assessed at each site. For a monitor to “pass” it must have met criteria at each of the 3 sites.
<table>
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<th>Brand</th>
<th>Blood Glucose Monitor</th>
<th>Test Strip</th>
<th>Study 1</th>
<th>Study 2</th>
<th>Study 3</th>
<th>Passes out of 3 Studies</th>
<th>Seal of Approval</th>
<th>Valid Trials</th>
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<th>Compliant %</th>
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<td>Contour Next</td>
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## Results

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<td>Philosys, Inc.</td>
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Total Data Pairs: 5584

https://www.diabetestechology.org/surveillance.shtml
Insulin Delivery

- No recommendation for insulin syringe versus pen
  - Choice is based on patient preference, cost, insulin type, & dose regimen
  - Evaluate dexterity & vision deficits
    - Pens may be more accurate
- Insulin injection aids available

- Needle gauge and length
  - Gauge range 22 – 33
    - Thicker needle = faster administration
    - Thinner needle = less discomfort
  - Length 4 – 12.7mm
    - Shorter needle may ↓ risk of IM injection
Obesity Management

- BMI should be measured & documented at each encounter.
- Our Patient
  - BMI 22 kg/m²; Height 60.25”; Weight 51.8kg

Table 8.1—Treatment options for overweight and obesity in type 2 diabetes

<table>
<thead>
<tr>
<th>Treatment</th>
<th>25.0–26.9 (or 23.0–26.9*)</th>
<th>27.0–29.9 (or 27.5–32.4*)</th>
<th>30.0–34.9 (or 32.5–37.4*)</th>
<th>35.0–39.9 (or ≥37.5*)</th>
<th>≥40 (or ≥37.5*)</th>
</tr>
</thead>
<tbody>
<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.

Diabetes Care 2019; 42(Supp1): S82
Obesity Management

- Assess readiness for weight loss

- Goal is > 5% weight loss for overweight/obese patients with T2DM

- High intensity interventions are recommended
  - focus on diet, physical activity, & behavior strategies
  - Achieve 500-750 kcal/day deficit
  - ≥ 16 sessions in 6 months

- No specific diet recommended

- Long-term comprehensive maintenance programs are recommended for those that achieve goals quickly or require strict intervention (≤ 800 kcal/day) to achieve goals
Pharmacotherapy and Weight Loss

- Minimize concomitant medications that contribute to weight gain
  - Examples
    - Antipsychotics, antidepressants, glucocorticoids, injectable medroxyprogesterone, gabapentin, anticholinergic medications
  - Antihyperglycemics that can ↑ weight gain
    - Insulin, sulfonylureas, thiazolidinediones
Pharmacotherapy for Weight Loss

- Rx may be used in conjunction to lifestyle management for select patients
  - Short- & long-term options available

- Evaluate use monthly x 3 months then every 3 months thereafter

- When to stop?
  - If weight loss < 5% after 3 months
  - Safety or tolerability issues arise
## Pharmacotherapy for Weight Loss

<table>
<thead>
<tr>
<th>Rx</th>
<th>MOA</th>
<th>Dose</th>
<th>Side Effects</th>
<th>Short or Long Term</th>
<th>Watch For</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phentermine</td>
<td>MOA: RECEPTOR</td>
<td>8-37.5mg daily</td>
<td>Dry mouth, Dizzy, Insomnia, irritability</td>
<td>Short</td>
<td>HTN Contraindicated with MAOIs</td>
</tr>
<tr>
<td>Orlistat</td>
<td>Lipase inhibitor</td>
<td>Rx: 120mg TID OTC: 60mg TID</td>
<td>Gas, fecal urgency, abdominal pain, back pain, HA</td>
<td>Long</td>
<td>Fat soluble vitamin malabsorption Malabsorption of some Rx (thyroid hormone, some anticonvulsants) Liver injury (rare) Cholelithiasis Nephrolithiasis</td>
</tr>
<tr>
<td>Lorcaserin</td>
<td>5-HT2C Receptor Antagonist</td>
<td>10mg BID or 20mg daily</td>
<td>HA, Nausea, fatigue, dizzy, nasopharyngitis</td>
<td>Long</td>
<td>Serotonin Syndrome Depression Suicidal thoughts HTN worsening Avoid in liver/renal failure</td>
</tr>
</tbody>
</table>
# Pharmacotherapy for Weight Loss

<table>
<thead>
<tr>
<th>Rx</th>
<th>MOA</th>
<th>Dose</th>
<th>Side Effects</th>
<th>Short or Long Term</th>
<th>Watch For</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phentermine/Topiramate</td>
<td>Sympathomimetic Amine anorectic + antiepileptic</td>
<td>7.5mg/46mg</td>
<td>Constipation, paresthesia, insomnia, dry mouth, nasopharyngitis</td>
<td>Long</td>
<td>Acute angle glaucoma Birth defects Cognitive impairment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 tablet daily</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Natrexone/Bupropion ER</td>
<td>Opioid antagonist + Antidepressant</td>
<td>8mg/90mg</td>
<td>Dry mouth, insomnia, constipation, nausea, HA</td>
<td>Long</td>
<td>Acute angle glaucoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 tablets daily</td>
<td></td>
<td></td>
<td>Contraindicated in: Uncontrolled HTN Seizure disorders Chronic opioid therapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>BBB:</strong> suicidal ideation</td>
</tr>
</tbody>
</table>
## Pharmacotherapy for Weight Loss

<table>
<thead>
<tr>
<th>Rx</th>
<th>MOA</th>
<th>Dose</th>
<th>Side Effects</th>
<th>Short or Long Term</th>
<th>Watch For</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liraglutide</td>
<td>GLP-1 agonist</td>
<td>3mg SQ daily</td>
<td>Hypoglycemia, Constipation, Upset stomach, Nausea, HA</td>
<td>Long</td>
<td>Acute Pancreatitis, Do not use with DPP-4 inhibitors</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>BBW: Thyroid C-cell Tumor Risk MTC or MEN2 personal or family Hx</td>
</tr>
</tbody>
</table>
Metabolic Surgery

- Recommended option for BMI ≥ 40 kg/m²
- Recommended option for BMI 35-39.9 kg/m² without durable weight loss and improved co-morbidities when non-surgical methods used.
- May consider for BMI 30-34.9 kg/m² if no improvement with non-surgical methods.
- Must focus on long-term lifestyle support
- Comprehensive readiness & mental health assessment needed
**Metabolic Surgery**

- **Roux-en-Y bypass surgery**
  - 30-60% patients have documented diabetes remission for T2DM
  - 35-50% have been found to eventually experience recurrence
  - Mean remission period ~ 8 years
  - Substantial glycemic control improvement found to last 5 to 15 years regardless of relapse

- **Predictors of success**
  - Age
  - Prior use of insulin
  - Ability to maintain weight loss
  - Better glycemic control
  - Baseline visceral fat area (Asian American > Caucasian w/ same BMI)
Metabolic Surgery

- **Added health benefits**
  - ASCVD risk reduction
  - Microvascular disease reduction
  - enhanced QOL

- **Adverse Effects**
  - Major Complications ➔ 2-6% (e.g. VTE, operative re-intervention)
  - Minor Complications ➔ up to 15%
  - Complications include staple line leaks, GI bleed, intestinal obstruction
  - Proficiency of operating surgeon is important in reduction of complications.
Metabolic Surgery

- **Adverse effects**
  - Dumping syndrome
    - N/V, colic, diarrhea
  - Vitamin & mineral deficiencies due to malabsorption
    - Variable with procedure – require lifelong supplementation
  - anemia
  - osteoporosis
  - severe hypoglycemia
  - ↑ risk of substance use – alcohol, tobacco, drugs
  - ↑ risk of new onset or worsening depression &/or anxiety & suicidal ideation
Obesity Management – AACE/ACE

- Complications-Centric model for therapy (versus BMI-centric)
  - 3 obesity stages
    - Stage 0 = ↑ BMI without obesity complications
    - Stage 1 = 1 or 2 mild to moderate obesity complications
    - Stage 3 = > 2 mild to moderate obesity complications or ≥ 1 severe complication
  - Obesity complications in 2 categories:
    - insulin resistance and/or cardiometabolic disease
    - Biomechanical consequences of excess body weight
  - Lifestyle change is key
  - Pharmacotherapy
    - May be considered when BMI ≥ 27 kg/m2 when complications present
    - May be considered when BMI ≥ 30 kg/m2 without complications
  - Bariatric surgery
    - For adults with BMI ≥ 35 kg/m2 and comorbidities present
Pharmacologic Therapy – Key Points

- Metformin!
  - Consider checking B12 levels with long-term use – especially if anemia or peripheral neuropathy present

- Should I start insulin?
  - Consider if:
    - Ongoing weight loss present
    - S/sx hyperglycemia present
    - BG $\geq$ 300 mg/dL
    - A1C $\geq$ 10%
  - GLP-1 agonists preferred to insulin in most patients

- Re-evaluate Pharmacotherapy every 3 to 6 months & adjust PRN
Our Patient

- A1C 12.7%
- BG 251 mg/dL
- BP 127/86 mmHg
- 30# weight loss over 2 months
- Alk Phos 126, AST 10, ALT 14
- CrCl = 88.4 mL/min; eGFR = 113.9 mL/min/1.73m2
- Albumin/Creatinine Ratio = 178 mg/g
- No current medications beyond OTC pain relievers
- Much later in a follow-up visit patient states she had tried metformin “many years ago” but stopped it due to severe GI side effects
FIRST-LINE therapy is metformin and comprehensive lifestyle (including weight management and physical activity). If HbA1c above target proceed as below.

**ESTABLISHED ASCVD OR CKD**

- **Either**
  - GLP-1 RA with proven CV benefit
  - SGLT2i with proven CV benefit

**IF HbA1c above target**

- If further intensification is required or patient is now unable to tolerate GLP-1 RA and/or SGLT2i, choose agents demonstrating CV safety:
  - Consider adding the other class (GLP-1 RA or SGLT2i) with proven CV benefit
  - DPP-4 if not on GLP-1 RA
  - Basal insulin
  - SGLT2i

**PREFERRABLY**

- SGLT2i with evidence of reducing HF and/or CKD progression in CVOTs if GLP-1 RA adequate
- If SGLT2i not tolerated or contraindicated or if GLP-1 RA less than adequate, add GLP-1 RA with proven CV benefit

- If HbA1c above target
- If HbA1c above target
- If HbA1c above target
- If HbA1c above target
- If HbA1c above target
- If HbA1c above target
- If HbA1c above target
- If HbA1c above target
- If HbA1c above target
- If HbA1c above target

**COMPPELLING NEED TO MINIMIZE HYPOGLYCEMIA**

- **GLP-1 RA with good efficacy for weight loss**
  - DPP-4i
  - GLP-1 RA
  - SGLT2i

**COMPPELLING NEED TO MINIMIZE WEIGHT GAIN OR PROMOTE WEIGHT LOSS**

- **SGLT2i with good efficacy for weight loss**
  - GLP-1 RA
  - DPP-4i
  - T2D

**COST IS A MAJOR ISSUE**

- **SGLT2i with lowest acquisition cost**
- **T2D with lowest acquisition cost**
- **Insulin therapy basal insulin with lowest acquisition cost**
  - SLR
  - TZR

1. Proven CV benefit means it has label indication of reducing CV events. For GLP-1 RA strongest evidence for lixisenatide > semaglutide > exenatide extended release. For SGLT2i evidence modestly stronger for empagliflozin > canagliflozin.
2. Be aware that SGLT2i vary by region and individual agent with regard to indicated level of CVG for initiation and continued use.
3. Both empagliflozin and canagliflozin have shown reduction in HF and reduction in CKD progression in CVOTs.
4. Dipeptidyl peptidase-4 inhibitors have demonstrated CV safety.
5. Low-dose may be better tolerated though less well studied for CV effects.
6. Choose later generation SU with lower risk of hypoglycemia.
7. Dipeptidyl peptidase-4 inhibitors < glucagon-like peptide 1 receptor > metformin insulin.
8. Semaglutide > lixisenatide > exenatide > insulin degludec > insulin glargine.
9. If no specific comorbidities (e.g., established CV risk, risk of hypoglycemia, and lower priority to avoid weight gain or other weight-related comorbidities).
10. Consider sensitivity and regional-specific cost of drugs, in some countries T2D relatively more expensive and DPP-4i relatively cheaper.
1. Proven CVD benefit means it has label indication of reducing CVD events. For GLP-1 RA strongest evidence for lixisatide > semaglutide > exenatide extended release. For SGLT2i evidence modestly stronger for emagliflozin > canagliflozin.

2. Be aware that SGLT2i vary by region and individual agent with regard to indicated level of eGFR for initiation and continued use.

3. Both emagliflozin and canagliflozin have shown reduction in HF and reduction in CKD progression in CVOTs.

4. Degludec or U100 glargine have demonstrated CVD safety.

5. Low dose may be better tolerated than less well studied for CVD effects.

6. Choose later generation SU with lower risk of hypoglycemia.

7. Degludec / glargine U300 < glargine U100 / detemir < NPH insulin.

8. Semaglutide > lixisatide > dulaglutide > exenatide > lixisenatide.

9. If no specific comorbidities (i.e., no established CVD, low risk of hypoglycemia, and lower priority to avoid weight gain or no weight-related comorbidities).

10. Consider country- and region-specific cost of drugs. In some countries TZDs relatively more expensive and DPP-4i relatively cheaper.
Pharmacotherapy

**Diabetes Care 2019; 42(Suppl): S94**

**Compelling Need to Minimize Hypoglycemia**
- DPP-4i
  - If HbA1c above target
- GLP-1 RA
  - If HbA1c above target
- SGLT2i
  - If HbA1c above target
- TZD
  - If HbA1c above target

If HbA1c above target
- SGLT2i
  - OR TZD

Continue with addition of other agents as outlined above

If HbA1c above target
- Consider the addition of SU or basal insulin:
  - Choose later generation SU with lower risk of hypoglycemia
  - Consider basal insulin with lower risk of hypoglycemia

---

**Without Established ASCVD or CKD**

**Compelling Need to Minimize Weight Gain or Promote Weight Loss**
- GLP-1 RA with good efficacy for weight loss
  - SGLT2i

If HbA1c above target
- GLP-1 RA
  - OR DPP-4i
  - OR TZD

If HbA1c above target
- SGLT2i

If triple therapy required or SGLT2i and/or GLP-1 RA not tolerated or contraindicated use regimen with lowest risk of weight gain
- PREFERABLY
  - DPP-4i (if not on GLP-1 RA)
  - Based on weight neutrality

If DPP-4i not tolerated or contraindicated or patient already on GLP-1 RA, cautious addition of:
- SU
- TZD
- Basal insulin

---

**Cost is a Major Issue**

- SU
- TZD

If HbA1c above target

---

1. Choose later generation SU with lower risk of hypoglycemia
2. Degludec / glargine U300 < glargine U100 / detemir < NPH insulin
3. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
4. If no specific comorbidities (i.e., no established CVD, low risk of hypoglycemia, and lower priority to avoid weight gain or no weight-related comorbidities)
Simplify Insulin Regimens for Elderly

Simplification of Complex Insulin Therapy

Patient on basal (long- or intermediate-acting) and/or mealtime (short- or rapid-acting) insulins**

- Basal insulin
- Change timing from bedtime to morning
- Titrate dose of basal insulin based on fasting fingerstick glucose test results over a week
  - Fasting goal: 90–150 mg/dL (4.9–8.3 mmol/L)
  - May change goal based on overall health and goals of care**
- If 50% of fasting fingerstick glucose values are over the goal:
  - ↑ dose by 2 units
- If ≥2 fasting fingerstick values/week are <80 mg/dL (4.4 mmol/L):
  - ↓ dose by 2 units
- If mealtime insulin ≥10 units/dose:
  - ↓ dose by 50% and add noninsulin agent
- Titrate mealtime insulin doses down as noninsulin agent doses are increased with aim to discontinue mealtime insulin

Patient on premixed insulin§

- Mealtime insulin
- Use 70% of total dose as basal only in the morning
- If mealtime insulin ≤10 units/dose:
  - Discontinue mealtime insulin and add noninsulin agent(s)
- Add noninsulin agents:
  - If eGFR is >45 mg/dL, start metformin 500 mg daily and increase dose every 2 weeks, as tolerated
  - If eGFR is <45 mg/dL, patient is already taking metformin, or metformin isn’t tolerated, proceed to second-line agent

Additional Tips
- Do not use short-acting insulin at bedtime
- While adjusting mealtime insulin, may use simplified sliding scale, for example:
  - Premeal glucose >250 mg/dL (13.9 mmol/L): give 2 units of short- or rapid-acting insulin
  - Premeal glucose <250 mg/dL (13.9–180 mg/dL): give 4 units of short- or rapid-acting insulin
  - Stop sliding scale when not needed daily

Using patient and drug characteristics to guide decision making, as depicted in Fig. 9.1 and Table 9.1, select additional agent(s) as needed:
- Every 2 weeks, adjust insulin dose and/or add glucose-lowering agents based on fingerstick glucose testing performed before lunch and before dinner
- Goal: 90–150 mg/dL (4.9–8.3 mmol/L) before meals; may change goal based on overall health and goals of care**
- If 50% of premeal fingerstick values over 2 weeks are above goal, increase the dose or add another agent
- If ≥2 premeal fingerstick values/week are <90 mg/dL (4.9 mmol/L), decrease the dose of medication

Diabetes Care 2019; 42(Suppl.): S143
<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>Keep using metformin!</td>
</tr>
<tr>
<td>Thiazolidinediones</td>
<td>If starting insulin: Stop TZD or ↓ dose</td>
</tr>
<tr>
<td>Sulfonylureas</td>
<td>Starting basal insulin?</td>
</tr>
<tr>
<td></td>
<td>• Stop sulfonylurea or ↓ dose by 50%</td>
</tr>
<tr>
<td></td>
<td>Starting prandial insulin or premix?</td>
</tr>
<tr>
<td></td>
<td>* Consider stopping sulfonylurea</td>
</tr>
<tr>
<td>SGLT2 Inhibitors</td>
<td>Add if: Established ASCVD</td>
</tr>
<tr>
<td></td>
<td>A1C above target</td>
</tr>
<tr>
<td></td>
<td>Watch for: DKA (euglycemic)</td>
</tr>
<tr>
<td>DPP-4 Inhibitors</td>
<td>Stop DPP-4 Inhibitor if GLP-1 Agonist started</td>
</tr>
</tbody>
</table>
Blood Pressure Management

- BP should be checked at every visit.
  - HTN diagnosis based on multiple BP readings ≥ 140/90 mmHg on separate days.

- Home BP monitors recommended for all patients with HTN & diabetes.

- BP Targets (ADA)
  - < 140/90 mmHg for HTN/diabetes patients with ASCVD risk < 15%
  - < 130/80 mmHg for HTN/diabetes patients with existing ASCVD or risk > 15%
  - Pregnancy?
    - SBP goal 120-160 mmHg
    - DBP goal 80-105 mmHg
Blood Pressure Management

- AACE/ACE goal BP < 130/80 mmHg for most
  - Less stringent goal okay for frail patients, those with comorbidities, or those with medication side effects
  - More stringent goal BP < 120/80 mmHg may be indicated if tolerated and without adverse Rx effects
Blood Pressure Management

- If BP > 120/80 mmHg – Lifestyle interventions!
  - DASH diet, adjust Na & K intake, moderate EtOH, ↑ Physical activity

- ACE-I or ARB for urinary albumin-to-creatinine ratio ≥ 300mg/g creatinine or if 30-299 mg/g creatinine
  - Monitor SCr, eGFR, and K+ levels at least annually

- Limited data indicates taking at least 1 anti-HTN medication @ bedtime reduced CV events

- Pregnancy
  - No need to treat mild to moderate gestational HTN (SBP < 160mmHg, DBP < 110 mmHg) per ACOG
  - ACE-I, ARBs, Spironolactone contraindicated due to potential for fetal harm
  - Methyldopa, labetalol, long-acting Nifedipine have been shown to be effective and safe
  - Hydralazine for acute management
Blood Pressure Management

**Initial BP <160/100 mmHg**
- **Start one agent**
  - Albuminuria*
    - No: **Start one drug:**
      - ACEi
      - ARB
      - CCB***
      - Diuretic**
    - Yes: **Start:**
      - ACEi or ARB

**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
      - CCB***
      - Diuretic**

Assess BP Control and Adverse Effects

*Diabetes Care 2019; 42(Supp1): S108*
Blood Pressure Management

Assess BP Control and Adverse Effects

- Treatment tolerated and target achieved
  - Continue therapy

- Not meeting target
  - Add agent from complementary drug class:
    - ACEi or ARB
    - CCB
    - Diuretic
  - Adverse effects

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

Assess BP Control and Adverse Effects

- Treatment tolerated and target achieved
  - Continue therapy

- Not meeting target on two agents
  - Not meeting target or adverse effects using a drug from each of three classes

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

- ADA Standards of Medical Care now align with ACC/AHA ASCVD Management Guidelines

- Assess 10-year ASCVD risk using tool
  - Tool does not account for duration of diabetes or presence of complications
  - Risk prediction with this tool does not differ between those with diabetes & those without.
Our Patient

Current Age 1 *
47
Age must be between 20-79

Sex *
Male  Female

Race *
White  African American  Other

Note: These estimates may underestimate the 10-year and lifetime risk for persons from some race/ethnic groups, especially American Indians, some Asian Americans (e.g., of south Asian ancestry), and some Hispanics (e.g., Puerto Ricans), and may overestimate the risk for others, including some Asian Americans (e.g., of east Asian ancestry) and some Hispanics (e.g., Mexican Americans). Because the primary use of these risk estimates is to facilitate the very important discussion regarding risk reduction through lifestyle change, the imprecision introduced is small enough to justify proceeding with lifestyle change counseling informed by these results.

Systolic Blood Pressure (mm Hg) *
127
Value must be between 90-200

Diastolic Blood Pressure (mm Hg) ○
68
Value must be between 60-130

Total Cholesterol (mg/dL) *
233
Value must be between 130 - 320

HDL Cholesterol (mg/dL) *
47
Value must be between 20 - 100

LDL Cholesterol (mg/dL) ○
152
Value must be between 30-100

History of Diabetes? *
Yes  No

Smoker: *
Yes  Former  No

On Hypertension Treatment? *
Yes  No

On a Statin? ○
Yes  No

On Aspirin Therapy? ○
Yes  No
Lipid Management

- Lifestyle modifications and interventions

- Check lipid panel
  - At time of diagnosis
  - Every 5 years if < 40 yo
  - More frequently PRN

- Starting a statin or other lipid lowering Rx?
  - Check lipid panel at baseline, 4-12 wks after drug therapy start or dose change, and then annually.
# Statin Recommendations

<table>
<thead>
<tr>
<th>Age</th>
<th>Existing ASCVD or 10-yr Risk &gt; 20%?</th>
<th>Statin Intensity &amp; Combo Therapy Recommendations</th>
<th>Comments</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 40 years</td>
<td>No</td>
<td>None</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 40 years</td>
<td>Yes</td>
<td>High</td>
<td>If LDL ≥ 70 mg/dL and on max tolerated statin – consider adding LDL-lowering Rx like ezetimibe or PCSK9 inhibitor</td>
<td></td>
</tr>
<tr>
<td>≥ 40 years</td>
<td>No</td>
<td>Moderate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 40 years</td>
<td>Yes</td>
<td>High</td>
<td>If LDL ≥ 70 mg/dL and on max tolerated statin – consider adding LDL-lowering Rx like ezetimibe or PCSK9 inhibitor</td>
<td></td>
</tr>
</tbody>
</table>
2018 Cholesterol Management Guidelines

- Adults 40 to 75 years of age
  - Moderate intensity statin indicated regardless of 10-yr ASCVD risk
  - Assess 10-yr ASCVD risk in all patients with diabetes & LDL 70-189 mg/dL
  - High intensity statin recommended for those with multiple ASCVD risk factors

- Adults > 75 years
  - Continue statin if already taking
  - Start statin after risk/benefit discussion
2018 Cholesterol Management Guidelines

- ASCVD risk 20% or higher?
  - Consider adding ezetimibe to max tolerated statin

- Adults 20 – 39 years old
  - Consider statin if:
    - ≥ 10 years T2DM, ≥ 20 years T1DM
    - albuminuria
    - eGFR < 60 mL/min/1.73 m2
    - Retinopathy, neuropathy, or ABI < 0.9
2018 Cholesterol Management Guidelines

- Risk Enhancers Specific to Diabetes
  - > 10 years T2DM, > 20 years T1DM
  - Albuminuria ≥ 30 mcg albumin/mg creatinine
  - eGFR < 60 mL/min/1.73m²
  - Retinopathy
  - Neuropathy
  - ABI < 0.9
# Statin Dosing and Therapy Intensity

<table>
<thead>
<tr>
<th>High Intensity</th>
<th>Moderate-Intensity</th>
<th>Low-Intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily dose ↓ LDL-C by approximately ≥ 50%</td>
<td>Daily dose ↓ LDL-C by approximately 30% to &lt; 50%</td>
<td>Daily dose ↓ LDL-C by &lt; 30%</td>
</tr>
</tbody>
</table>

- **Atorvastatin 40 – 80mg**
  - **Rosuvastatin 20 – 40mg**
  - **Atorvastatin 10 - 20mg**
  - **Rosuvastatin 5 - 10mg**
  - **Simvastatin 20-40mg‡**
  - **Pravastatin 40 - 80mg**
  - **Lovastatin 40mg**
  - **Fluvastatin 40mg BID**
  - **Fluvastatin XL 80mg**
  - **Pitavastatin 2-4mg**

- **Pravastatin 10-20mg**
- **Lovastatin 20mg**
- **Simvastatin 10mg**
- **Fluvastatin 20-40mg**
- **Pitavastatin 1mg**

- **Bold** = evaluated in RCTs and demonstrated a reduction in major cardiovascular events.
- **Italics** = approved by the FDA but not tested in RCTs.
- Individual responses may vary in clinical practice.
- †Evidence from one RCT only (down-titration if unable to tolerate atorvastatin 80mg).
- ‡Although simvastatin 80mg was evaluated in RCTs, initiation of simvastatin 80mg or titration to 80mg is not recommended by the FDA due to increased risk of myopathy, including rhabdomyolysis.
## Table 1

<table>
<thead>
<tr>
<th>Risk category</th>
<th>Risk factors&lt;sup&gt;a&lt;/sup&gt;/10-year risk&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Treatment goals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>LDL-C (mg/dL)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Non-HDL-C (mg/dL)</td>
</tr>
<tr>
<td>Extreme risk</td>
<td>– Progressive ASCVD including unstable angina in patients after achieving an LDL-C &lt; 70 mg/dL</td>
<td>&lt;55</td>
</tr>
<tr>
<td></td>
<td>– Established clinical cardiovascular disease in patients with DM, CKD 3/4, or HeFH</td>
<td></td>
</tr>
<tr>
<td></td>
<td>– History of premature ASCVD (&lt;55 male, &lt;65 female)</td>
<td></td>
</tr>
<tr>
<td>Very high risk</td>
<td>– Established or recent hospitalization for ACS, coronary, carotid, or peripheral vascular disease</td>
<td>&lt;70</td>
</tr>
<tr>
<td></td>
<td>– Diabetes or CKD 3/4 with one or more risk factor(s)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>– HeFH</td>
<td></td>
</tr>
<tr>
<td>High risk</td>
<td>≥2 risk factors and 10-year risk &gt;10% or CHD risk equivalent&lt;sup&gt;c&lt;/sup&gt;, including diabetes or CKD 3/4 with no other risk factors</td>
<td>&lt;100</td>
</tr>
<tr>
<td>Moderate risk</td>
<td>≥2 risk factors and 10-year risk &lt;10%</td>
<td>&lt;130</td>
</tr>
<tr>
<td>Low risk</td>
<td>≤1 risk factor</td>
<td>&lt;160</td>
</tr>
</tbody>
</table>

### Abbreviations:
- AACE = American Association of Clinical Endocrinologists
- ACS = acute coronary syndrome
- Apo = apolipoprotein
- ASCVD = atherosclerotic cardiovascular disease
- CHD = coronary heart disease
- CKD = chronic kidney disease
- DM = diabetes mellitus
- HeFH = heterozygous familial hypercholesterolemia
- HDL-C = high-density-lipoprotein cholesterol
- LDL-C = low-density-lipoprotein cholesterol
- NR = not recommended
- T2D = type 2 diabetes

<sup>a</sup>Major independent risk factors are high LDL-C, polycystic ovary syndrome, cigarette smoking, hypertension (blood pressure >140/90 mm Hg or on antihypertensive medication), low HDL-C (<40 mg/dL), family history of coronary artery disease (in males, first-degree relative younger than 55 years; in females, first-degree relative younger than 65 years), chronic renal disease (CKD) stage 3/4, evidence of coronary artery calcification and age (males ≥45 years; females ≥55 years). Subtract one risk factor if the person has high HDL-C.

<sup>b</sup>Framingham risk scoring is applied to determine 10-year risk.

<sup>c</sup>Coronary artery disease risk equivalents include diabetes and clinical manifestations of noncoronary forms of atherosclerotic disease (peripheral arterial disease, abdominal aortic aneurysm, and carotid artery disease).
<table>
<thead>
<tr>
<th>Lipid Management Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ADA 2019</strong></td>
</tr>
<tr>
<td>- Focus on statin intensity &amp; is 1\textsuperscript{st} line</td>
</tr>
<tr>
<td>- Lifestyle changes</td>
</tr>
<tr>
<td>- Fibrates not generally recommended – not shown to improve ASCVD outcomes</td>
</tr>
<tr>
<td>- Niacin not generally recommended – citing AIM-HIGH trial and not shown additional ASCVD benefit, may ↑ BG transiently, &amp; potential for ↑ risk of stroke</td>
</tr>
<tr>
<td>- Does not address Omega-3 or Bile Acid Sequestrants</td>
</tr>
<tr>
<td><strong>AACE/ACE 2019</strong></td>
</tr>
<tr>
<td>- Focus on lipid level cut-point in addition to statin intensity</td>
</tr>
<tr>
<td>- Lifestyle changes</td>
</tr>
<tr>
<td>- Statins are first line</td>
</tr>
<tr>
<td>- Ezetimibe &amp; PCSK9 inhibitors</td>
</tr>
<tr>
<td>- Bile acid sequestrants an option</td>
</tr>
<tr>
<td>- Fibrates to ↓ TG if indicated</td>
</tr>
<tr>
<td>- Niacin may be used for LDL lowering effects noting that it has no effect on ASCVD outcomes per AIM-HIGH trial.</td>
</tr>
<tr>
<td>- Omega-3 for TG if indicated</td>
</tr>
</tbody>
</table>
Microvascular Complications: CKD

- Screen yearly for CKD
- Optimize glycemic control and BP to slow down progression
- Consider protein intake
  - 0.8 g/kg body weight daily for non-dialysis dependent CKD
    - ↑ protein intake (> 1.3g/kg/day or >20% daily calories) associated with ↑ albuminuria, ↑ rapid kidney function loss, and CVD mortality.
    - ↓ protein intake (<0.8g/kg/day) not recommended
      - Has not been shown to Δ glycemic control, CVD risk measures, or GFR decline
  - Consider electrolyte intake for those with ↓ eGFR
    - ↓ sodium intake to < 2300 mg/day to ↓ BP and ↓ CVD risk
    - restriction of dietary potassium intake may be needed to control serum K+ levels
    - individualize based on co-morbidities, Rx use, BP, and labs
Microvascular Complications: CKD

- Consider SGLT2 inhibitor or GLP-1 agonist to ↓ risk of CKD and/or CVD progression

- ACE-inhibitor or ARB
  - Recommended if urinary albumin-to-creatinine ratio 30-299 mg/g creatinine
  - Strongly recommended if urinary albumin-to-creatinine ratio ≥ 300 mg/g creatinine and/or eGFR < 60 mL/min/1.73m²
  - NOT recommended for patients with normal BP, urinary albumin-to-creatinine ratio < 30 mg/g creatinine, and normal eGFR.
  - Avoid dual therapy of ACE-I + ARB

- Minimize nephrotoxic medications to ↓ risk of AKI and ↓ progression of CKD
  - NSAIDs
  - Others?
Microvascular Complications: Retinopathy

- Higher risk for cataracts, glaucoma, and other eye disorders
- Optimize sugars, BP, and lipids to delay progression
- Eye exams
  - A time of diagnosis for T2DM
  - Within 5 years of onset for T1DM
  - Yearly to every 2 years thereafter
  - Remote readings of retinal photography as a function of telemedicine can improve screening access
    - Not a substitute for in-person exams
- Treatment of retinopathy
  - Laser photo-coagulation therapy for high-risk proliferative retinopathy
  - Ranibizumab (approved 2017) – anti-vascular endothelial growth factor
    - Intravitreal injection
Microvascular Complications: Neuropathy

- Diabetic neuropathy is a diagnosis of exclusion
  - Patients may experience both diabetic and non-diabetic neuropathy

- Types of neuropathy
  - Diabetic Peripheral Neuropathy (DPN)
    - 50% of Diabetic Peripheral Neuropathy (DPN) has no symptoms
      - Screening, recognition, and prevention are key!
  - Autonomic neuropathy
    - Hypoglycemic unawareness, resting tachycardia, orthostatic hypotension, gastroparesis, constipation, N/V, erectile dysfunction, neurogenic bladder, ↑/↓ sweating
# Pharmacotherapy for Neuropathies

<table>
<thead>
<tr>
<th>Type</th>
<th>Goal of Therapy</th>
<th>Therapeutic Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral Neuropathy</td>
<td>↓ pain, ↓ depression</td>
<td>Gabapentin (not FDA approved)</td>
</tr>
<tr>
<td></td>
<td>Improve mobility</td>
<td>Pregabalin</td>
</tr>
<tr>
<td></td>
<td>Improve Quality of Life</td>
<td>Duloxetine</td>
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<tr>
<td></td>
<td></td>
<td>Tapentadol (3rd line)</td>
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<tr>
<td></td>
<td></td>
<td>TCAs, Venlafaxine, Carbamazepine, &amp; topical capsaicin are options</td>
</tr>
<tr>
<td>Orthostatic Hypotension</td>
<td>Minimize postural symptoms</td>
<td>Rx Measures:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Midodrine</td>
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<tr>
<td></td>
<td></td>
<td>Droxidopa</td>
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<tr>
<td></td>
<td></td>
<td>Non-Rx Measures:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ salt intake</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ meds that can worsen hypotension</td>
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<tr>
<td></td>
<td></td>
<td>Compression stockings</td>
</tr>
<tr>
<td>Type</td>
<td>Goal of Therapy</td>
<td>Treatment Options</td>
</tr>
<tr>
<td>-----------------------</td>
<td>------------------------------------------</td>
<td>-------------------------------------------------------------</td>
</tr>
<tr>
<td>Gastroparesis</td>
<td>Improve food intake &amp; nutrition</td>
<td>Low-fiber/fat diet</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Frequent small meals</td>
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<tr>
<td></td>
<td></td>
<td>Reduce particle size of food</td>
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<tr>
<td></td>
<td></td>
<td>Minimize meds that slow gastric emptying</td>
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<tr>
<td></td>
<td></td>
<td>Prokinetic Agents:</td>
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<tr>
<td></td>
<td></td>
<td>Metoclopramide</td>
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<tr>
<td></td>
<td></td>
<td>Domperidone (not in US)</td>
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<tr>
<td></td>
<td></td>
<td>Erythromycin</td>
</tr>
<tr>
<td>Erectile Dysfunction</td>
<td>Improve quality of life</td>
<td>PDE-5 inhibitors</td>
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<tr>
<td></td>
<td></td>
<td>Intracorporeal or intraurethral prostaglandins</td>
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<td></td>
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<td>Vacuum devices</td>
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<td>Prosthesis</td>
</tr>
</tbody>
</table>
Foot Care!

- Comprehensive foot exam annually
- Evaluate feet at every visit for those with history of lost sensation, amputation, or prior ulceration
- Ankle-Brachial-Index should be performed if pedal pulses absent or symptoms of claudication
- Educate, Educate, Educate!
- Proper footwear & Prescription Shoes
Foot Exam

- **Visual inspection of skin**
  - Foot deformities, blisters, Tinea pedis, maceration, xerosis, interdigital pathology, nail pathology, callus(es), pre-ulcerative lesions, ulcerations

- **Neurologic assessment**
  - Monofilament 10g (5.07) measures loss of protective sensation (LOPS)
  - Vibratory perception – 128 Hz tuning fork
  - Achilles reflex

- **Vascular assessment**
  - Pedal pulses
Our Patient - summary

- Started on Levemir 20 units nights
  - Insulin teaching provided
  - Barriers – Interpreter required (Spanish speaking); Fear of needles

- Started on Atorvastatin 40mg daily

- Started on Lisinopril 2.5mg daily

- PPSV23 indicated due to diabetes diagnosis
  - Don’t forget to assess for additional vaccination status!
    - MMR, Tdap, Flu
Questions
References