Diabetes
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Diabetes Evidence-Based Summary and Supporting Research

The Diabetes Evidence Review Team reviewed evidence from the national guidelines provided by the American Association of Clinical Endocrinologists, the American Diabetes Association, Joslin Diabetes Center, and the American Dietetic Association. Additionally, the team consulted the AHRQ Comparative Effectiveness Review Number 27: Oral Diabetes Medications for Adults with Type 2 Diabetes: An Update. These resources may be found in full at:

1. American Diabetes Association (ADA). (2014). Standards of Medical Care in Diabetes. *Diabetes Care, 37*(Supp. 1), S1-S80. [http://care.diabetesjournals.org/content/37/Supplement_1](http://care.diabetesjournals.org/content/37/Supplement_1)

This summary highlights only those items the review committee deemed important to emphasize. Levels of evidence vary dependent upon the source. Please see the levels guide at the end of this document.

**Treatment Goal**

The AACE target of <6.5%. Hb A1C is an appropriate treatment goal.

- Therapy should target an A1C level of 6.5% or less for most non pregnant adults, if it can be achieved safely (Grade D). In certain patients, a less stringent goal may be considered (A1C 7-8%) (Grade A). Such individuals as those with history of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, extensive comorbid conditions, or long-standing DM in which the general goal has been difficult to attain despite intensive efforts (Grade A). This goal of 6.5% may be too stringent for some elderly patients. (AACE)

While a team approach is understood to be usual care in diabetes, it is important to emphasize self care/patient as a critical member of the team.
Pre-Diabetes

- ADA statements for identifying pre-diabetes, i.e. an A1C of 5.7-6.4%, are recommended.
- Testing to detect type 2 diabetes and prediabetes in asymptomatic people should be considered in adults of any age who are overweight or obese (BMI ≥25 kg/m2) and who have one or more additional risk factors for diabetes. In those without these risk factors, testing should begin at age 45 years. (ADA, B). These additional risk factors include:
  - Physical inactivity
  - First-degree relative with diabetes
  - High-risk race /ethnicity: African American, Latino, Native American, Asian American, Pacific Islander
  - Women who delivered a baby > 9 lbs. or were diagnosed with GDM
  - Hypertension, BP over 140/90
  - HDL cholesterol level under 35 mg/dL and /or a triglyceride level over 250 mg/dL
  - Women with polycystic ovary syndrome
  - Clinical conditions associated with insulin resistance
  - History of CVD
- If tests are normal, repeat testing at least at 3-year intervals is reasonable. (ADA, E)
- Follow up counseling appears to be important for success. (ADA, B)
- Lifestyle changes for patients determined at A1C of 5.7-6.4% are supported and include:
  - Medical nutrition therapy (MNT)
  - Moderate physical activity ≥ 150 minutes.
  - Weight loss of 7% of body weight when appropriate.

Individuals at high risk for type 2 diabetes should be encouraged to achieve the U.S. Department of Agriculture (USDA) recommendation for dietary fiber (14 g fiber/1,000 kcal) and foods containing whole grains (one-half of grain intake). (ADA, B)

After 6 months of lifestyle Rx, or with evidence of continued A1C levels in unacceptable range, adopt the following ADA Level B recommendation: Metformin therapy for prevention of type 2 diabetes may be considered in those with IGT (ADA, A), IFG (ADA, E), or an A1C 5.7–6.4% E, especially for those with BMI >35 kg/m2, aged <60 years, and women with prior GDM. (ADA, A)

At least annual monitoring for the development of diabetes in those with prediabetes is suggested. (ADA, E)

Screening for and treatment of modifiable risk factors for CVD is suggested. (ADA, B)
**Diabetes Diagnosis** (ADA specifications) is based upon:

a) One time A1C ≥ 6.5% **OR**  
b) Fasting glucose ≥ 126 mg/dl on 2 different days **OR**  
c) Any random glucose reading ≥ 200 mg/dl.  
d) Two hour plasma glucose ≥ 200mg/dL (11.1 mmol/L) during an oral glucose tolerance test (OGTT).

**Frequency of Hgb A1C Monitoring** (ADA)

- Perform the A1C test at least two times a year in patients who are meeting treatment goals (and who have stable glycemic control) (ADA, E).
- Perform the A1C test quarterly in patients whose therapy has changed or who are not meeting glycemic goals. (ADA, E)  
- Use point of care testing to provide the opportunity for more timely treatment changes (ADA, E)

**Blood Glucose Monitoring Goals** (ADA):  
- Goals for glycemic control for people with diabetes are:  
  Fasting: 70-130mg/dl; 2 hr. postprandial: <180 mg/dl (this was supported in Joslin and ADA Guidelines).

**Self Monitoring per ADA Recommendations:**

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 (A). The 2014 guidelines suggest: prior to meals and snacks and occasionally postprandially, at bedtime, prior to exercise, when they suspect low blood glucose, after treating low blood glucose until they are normoglycemic and prior to critical tasks such as driving (ADA, B)

For patients using less-frequent insulin injections, non-insulin therapies, or MNT alone, SMBG may be useful as a guide to success of therapy.

**Continuous Glucose Monitoring**

When used properly, continuous glucose monitoring (CGM) in conjunction with intensive insulin regimens is a useful tool to lower A1C in selected adults (aged ≥25 years) with type 1 diabetes. (ADA, A)
Although the evidence for A1C lowering is less strong in children, teens, and younger adults, CGM may be helpful in these groups. Success correlates with adherence to ongoing use of the device. (ADA, C)

CGM may be a supplemental tool to SMBG in those with hypoglycemia unawareness and/or frequent hypoglycemic episodes. ADA, E)

**Type 1 Diabetes Insulin Therapy**

Most people with type 1 diabetes should be treated with MDI injections (three to four injections per day of basal and prandial insulin) or continuous subcutaneous insulin infusion (CSII). (ADA, A). Basal insulin should not be discontinued so to prevent DKA.

Most people with type 1 diabetes should be educated in how to match prandial insulin dose to carbohydrate intake, premeal blood glucose, and anticipated activity. (ADA, E)

Most people with type 1 diabetes should use insulin analogs to reduce hypoglycemia risk. (ADA, A)

**Screening for Type 1 Diabetes**

Consider screening those with type 1 diabetes for other autoimmune diseases (thyroid, vitamin B12 deficiency, celiac) as appropriate. B

**Pharmacologic Management of Diabetes Type 2** is summarized in the accompanying document containing a grid comparing effects, side effects, costs, ease of use, and safety. This document was derived from a combination of resources from the ADA and the AACE. Note: In newly diagnosed type 2 patients with markedly symptomatic and/or elevated blood glucose levels or A1C, consider insulin therapy, with or without additional agents, from the outset. (ADA, E) Use the algorithm below to address the patient in a step-wise framework.
Algorithm for Treating Type 2 Diabetes Mellitus—adapted from the AACE, 2013.

Goals for Glycemic Control:
- Target A1C ≤ 6.5% for most patients
- Target less stringent A1C goal > 6.5% for patients with significant illness and at risk for hypoglycemia and the elderly

Lifestyle Modification
Including medical nutrition therapy, exercise, and surgery when indicated to promote weight loss

Entry A1C < 7.5%
- Monotherapy
  - Metformin is the drug of choice
  - Alternatives:
    1. GLP-1 receptor agonists (GLP-1 RA)
    2. DPP4 inhibitors (DPP4-I)
    3. Sodium-glucose co-transporter-2 (SGLT-2) inhibitor
    4. Thiazolidinediones (TZD)**
    5. Alpha-glucosidase inhibitors (AG-I)
    6. Sulfonamides/other (SU/GLI)**
- Evaluate after 3 months, if A1C > 6.5%
  - Add a 2nd agent (Dual Therapy)

Entry A1C ≥ 7.5%
- Dual Therapy
  - Metformin or other first-line agent
  - Alternatives:
    1. GLP-1 RA
    2. DPP4-I
    3. SGLT-2 inhibitor
    4. TZD
    5. AG-I
    6. SU/GLI
    7. Basal insulin
    8. Colesevelam
    9. Bromocriptine Mesylate
- Evaluate after 3 months, if not at goal
  - Add a 3rd agent (Triple Therapy)

Entry A1C > 9.0%
- Therapy Duplication Warning:
  Do NOT use GLP-1 RA and DPP4-inhibitor concurrently due to duplicate therapeutic effect

No Symptoms
- Dual Therapy OR Insulin ± Other Agents

Symptoms
- Triple Therapy
  - Add or Intensify Insulin
Helpful Information on Titration of Metformin from the ADA

1. Begin with low-dose metformin (500 mg) taken once or twice per day with meals (breakfast and/or dinner) or 850 mg once per day.
2. After 5–7 days, if gastrointestinal side effects have not occurred, advance dose to 850, or two 500 mg tablets, twice per day (medication to be taken before breakfast and/or dinner).
3. If gastrointestinal side effects appear as doses advanced, decrease to previous lower dose and try to advance the dose at a later time.
4. The maximum effective dose can be up to 1,000 mg twice per day but is often 850 mg twice per day. Modestly greater effectiveness has been observed with doses up to about 2,500 mg/day. Gastrointestinal side effects may limit the dose that can be used.
5. Based on cost considerations, generic metformin is the first choice of therapy. A longer-acting formulation is available in some countries and can be given once per day.

Nutritional Management (All guidelines from ADA, 2014)

Nutrition interventions should emphasize a variety of minimally processed nutrient dense foods in appropriate portion sizes as part of a healthful eating plan and provide the individual with diabetes practical tools for day – to –day food plan and behavior change that can be maintained over the long-term.

<table>
<thead>
<tr>
<th>CARBOHYDRATES</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>The amount of carbohydrates and available insulin may be the most important factor influencing glycemic response after eating and should be considered when developing an eating plan.</td>
<td>A</td>
</tr>
<tr>
<td>To promote good health, carbohydrate intake from vegetables, fruits whole grains, legumes and low-fat dairy products are recommended over intake from other carbohydrate sources, especially from those that contain added fats, sugars or sodium.</td>
<td>B</td>
</tr>
<tr>
<td>While substituting sucrose-containing foods for isocaloric amounts of other carbohydrates may have similar blood glucose effects, consumption should be minimized to avoid displacing nutrient-dense food choices.</td>
<td>A</td>
</tr>
<tr>
<td>People with diabetes should consume at least the amount of fiber and whole grains recommended for the general public.</td>
<td>C</td>
</tr>
<tr>
<td>People with diabetes should limit or avoid intake of SSB’s (Sugar Sweetened Beverages) to reduce risk for weight gain and worsening of cardiometabolic risk profile.</td>
<td>B,C</td>
</tr>
</tbody>
</table>
Use of NNS’s (Non Nutritive Sweeteners) has the potential to reduce overall calorie intake if substituted for caloric sweeteners without compensation by intake of additional calories from other food sources.

**PROTEIN**

In individuals with type 2 diabetes, ingested protein appears to increase insulin response without increasing plasma glucose concentrations. Therefore, carbohydrate sources high in protein should not be used to treat or prevent hypoglycemia.

For people with diabetes and no evidence of diabetic kidney disease, evidence is inconclusive to recommend an ideal amount of protein intake for optimizing glycemic control or improving one or more CVD risk measures, goals should be individualized.

For people with diabetes and diabetic kidney disease, reducing the amount of dietary protein below the usual intake (15%-20% of total daily energy) is not recommended because it does not alter glycemic measures, cardiovascular risk measures, or the course of the GFR decline.

**FAT**

Evidence is inconclusive for an ideal amount of total fat intake for people with diabetes, therefore goals should be individualized.

Fat quality appears to be far more important than fat quantity. For people with type 2 diabetes, a Mediterranean-style, MUFA-rich eating pattern may benefit glycemic control and CVD risk factors. Therefore it can be recommended as an effective alternative to a lower-fat, higher-carbohydrate eating pattern.

Evidence does not support recommending omega-3 (EPA and DHA) supplements for people with diabetes.

The recommendation for the general public is to eat fatty fish at least two times a week, this is also appropriate for people who have diabetes.

The amount of dietary saturated fat, cholesterol, and trans fat recommended for people with diabetes is the same that is recommended for the general population.

**ALCOHOL**

If adults with diabetes choose to drink alcohol, they should be advised to do so in moderation (one drink per day or less for adult women and two drinks per day or less for adult men).

Alcohol consumption may place people with diabetes at increased risk for delayed hypoglycemia, especially if taking insulin or insulin secretagogues. Education and awareness regarding the recognition and management of delayed hypoglycemia is warranted.

**MICRONUTRIENTS**
Routine supplementation with antioxidants, such as vitamins E and C and carotene, is not advised because of lack of efficacy and concern related to long term safety. **A**

The recommendation for the general population to reduce sodium to less than 2,300 mg/day is also appropriate for people with diabetes. For individuals with both diabetes and hypertension, further reduction in sodium intake should be individualized. **B**

There is insufficient evidence to support the routine use of micronutrients such as chromium, magnesium, and vitamin D to improve glycemic control in people with diabetes. There is insufficient evidence to support the use of cinnamon or other herbs/supplements for the treatment of diabetes. **C**

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**Initial Diabetes MNT for Newly Diagnosed Patients**

- Consume 3 meals per day at regular times, and do not skip meals. This will help prevent hypoglycemia and reduce the incidence of overeating.
- Separate meals by no more than 4 to 5 hours, otherwise a small snack will be needed.
- Carbohydrate foods affect blood glucose the most, so set a maximum limit per meal to keep blood glucose from going too high.
- Intake from vegetables, fruits, whole grains, legumes and low-fat or fat-free dairy products should be advised over intake from other carbohydrate sources, especially those that contain added fats, sugar, or sodium.
- Choose carbohydrate-free beverages only. Avoid regular soda, fruit juice, and regular sports drinks. Instead, choose water, diet sodas, drinks made with sugar substitutes and sports drinks without carbohydrates.
- Focus on serving size and total amount of carbohydrate per serving on the food label, to prevent weight gain.
- Evidence is inconclusive for an ideal amount of carbohydrate intake for people with diabetes. Most men need 60-75 grams of carbohydrate per meal, and most women need 45-60 grams of carbohydrate per meal to provide adequate energy, vitamins, minerals and fiber. Individual goals should be developed for each person with diabetes whenever possible.
- Additional alterations in the quality of fat consumed are contingent upon current lipid panel, individual risk factors for heart disease and stroke, as well as the need to prevent weight gain.
- Individuals with a diagnosis of diabetes should reduce sodium intake to <2300 mg/day, as recommended for the general population. For individuals with diabetes and hypertension, further restrictions in sodium intake should be individualized.

See appendix for MNT Resources.
Physical Activity

The current recommendation of ≥ 150 minutes per week of moderate – intensity exercise, such as brisk walking or its equivalent, is recommended. (Endorsed by all three sources).

The 2014 ADA guidelines added some specificity to this:

Adults with diabetes should be advised 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/week with no more than 2 consecutive days without exercise. A

In the absence of contraindications, adults with type 2 diabetes should be encouraged to perform resistance training at least twice per week. A

For overweight or obese adults with type 2 diabetes or at risk for diabetes, reducing energy intake while maintaining a healthful eating pattern is recommended to promote weight loss. A

Modest weight loss may provide clinical benefits (improved glycemia, blood pressure, and/or lipids) in some individuals with diabetes, especially those early in the disease process. To achieve modest weight loss, intensive lifestyle interventions (counseling about nutrition therapy, physical activity, and behavior change) with ongoing support are recommended. A

Management of Hypoglycemia (sourced mostly from Joslin)

Individuals at risk for hypoglycemia should be asked about symptomatic and asymptomatic hypoglycemia at each encounter (ADA, C)

Hypoglycemia unawareness or one or more episodes of severe hypoglycemia should trigger re-evaluation of the treatment regimen (ADA, E)

All patients with type 1 diabetes should ensure a family member/companion can administer glucagon.

- With mild-moderate hypoglycemia (a blood glucose level of around 70 and/or symptoms of hypoglycemia):
  - Glucose (rapidly absorbed) is preferred for conscious individual with hypoglycemia (1/2 cup juice, one cup of low fat milk, 4 ounces of regular soft drink, 3-4 glucose tabs or 6-7 hard candies like Life Savers). If the patient remains hypoglycemic
15 minutes after initial treatment, the treatment should be repeated. If the patient remains hypoglycemic after 2 treatments, the patient should seek medical assistance

- For severe hypoglycemia:
  - Glucagon should be prescribed for all individuals who use insulin; caregivers/family should be instructed on its use.
- Hypoglycemia patient education should include:
  - Instruct patient to obtain and wear/carry diabetes identification (a medical alert for diabetes).
  - Inform patient of the need to check blood glucose before driving and/or periodically during a long drive and when operating heavy machinery.
  - Monitor blood glucose level prior to exercise.
  - Instruct patient to carry treatment for hypoglycemia at all times.

Hypoglycemia symptoms may occur at lower blood glucose levels in the elderly and may be harder to recognize.

**Cardiovascular Health (ADA) The 2014 emphasis is on lifestyle management**

In patients with known CVD:

- Angiotensin converting enzyme (ACE) inhibitor (C) or angiotensin II receptor blocker (ARB) and aspirin and statin therapy (A) (if not contraindicated) should be used to reduce the risk of cardiovascular events.
- In patients with a prior myocardial infarction, beta-blockers should be continued for at least 2 years after the event. (B).
- Longer-term use of beta-blockers in the absence of hypertension is reasonable if well tolerated, but data are lacking. (E) Avoid thiazolidinedione (TZD) treatment in patients with symptomatic heart failure (C).
- Metformin may be used in patients with stable congestive heart failure (CHF) if renal function is normal. It should be avoided in unstable or hospitalized patients with CHF. (C)

**Antiplatelet Therapy**

Consider aspirin therapy (75–162mg/day) as a primary prevention strategy in those with type 1 or type 2 diabetes at increased cardiovascular risk (10-year risk >10%). This includes most men aged >50 years or women aged >60 years who have at least one additional major risk factor (family history of CVD, hypertension, smoking, dyslipidemia, or albuminuria). (ADA, C)

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

Use aspirin therapy (75–162 mg/day) as a secondary prevention strategy in those with diabetes with a history of CVD. (ADA, A)

For patients with CVD and documented aspirin allergy, clopidogrel (75 mg/day) should be used. (ADA, B)

Dual antiplatelet therapy is reasonable for up to a year after an acute coronary syndrome. (ADA, B)

**Stress Testing**

Indications for stress testing for DM patient include (Joslin 1B):
- Complaint of chest pain
- Abnormal EKG
- Diagnosis of peripheral artery disease or carotid disease
- >35 years of age with a sedentary lifestyle about to start a rigorous exercise program

**Sleep Apnea**

- Obstructive sleep apnea is common and should be screened for in adult diabetic patients. In decisions for ordering sleep studies, clinician judgment plays a significant role (Grade D; BEL 1 AACE)
- The STOP BANG tool (attached) should be used for screening all populations.


**Lipids Management**

The 2014 emphasis is on lifestyle management to improve lipid profile.

- Lipid measurement (fasting) should be done *annually* with targets (ADA) at:
  - LDL cholesterol <100mg/dl
  - HDL cholesterol >50 mg/dl
  - Triglycerides <150 mg /dl
If lifestyle modification dietary management fails after 4 months (LDL cholesterol greater than 100mg/dl), statin therapy should be considered (Level A- ADA). Refer to dietician for intensive dietary modification and therapeutic lifestyle changes (Joslin 1A).

- In patients with overt CVD, a lower LDL cholesterol goal of <70 mg/dl is necessary. Lipids should be re-evaluated every 12 weeks.
- In patients with fasting triglycerides levels of 500 mg/dl, endocrinology consultation is warranted.

**Blood Pressure**

- Address patients with BP ≥ 130/80 (all sources). The 2014 ADA guidance emphasizes lifestyle changes for those with BP over 120/80 and initiates pharmacologic therapy at 140/80 (ADA, B)
- Lifestyle therapy for elevated blood pressure consists of weight loss, if overweight; Dietary Approaches to Stop Hypertension (DASH)-style dietary pattern including reducing sodium and increasing potassium intake; moderation of alcohol intake; and increased physical activity. (ADA,B)
- Pharmacologic therapy for patients with diabetes and hypertension should be with a regimen that includes either an ACE inhibitor or an ARB (ADA, C).
- Multiple-drug therapy (two or more agents at maximal doses) is generally required to achieve blood pressure targets. B
- If ACE inhibitors, ARBs or diuretics are used, serum creatinine/estimated glomerular filtration rate (eGFR) and serum potassium levels should be monitored. (ADA, E)
- Advise all patients not to smoke. Use the 5A’s to address tobacco use – Level A evidence (see attached).

**Renal Disease**

- Serum creatinine and estimated GFR should be measured every six months in diabetic patients.
- Perform an annual test to quantitate urine albumin excretion in type 1 diabetic patients with diabetes duration of ≥5 years and in all type 2 diabetic patients starting at diagnosis. (ADA, B)

Refer to a Nephrologist: (ADA, B)

- Creatine 1.5 mg/dl or GFR <60 ml/min or
- Urine microalbuminuria >300 or urine protein >30 mg /dl
- MNT consult is needed annually and upon diagnosis of renal disease
Retinal Health

- At time of diagnosis patients with diabetes should be referred to an ophthalmologist (AACE grade D; BEL 4).
- Frequency of follow-up should be annually at minimum and then determined by the ophthalmologist.

Neuropathy

- All diabetic patients should be screened initially and every four to six months for neuropathy using:
  - Vibration with 128-Hz tuning fork
  - Pinprick (monofilament) sensation for fine point discrimination assessment

Foot Care

Foot exam should be done every routine visit. Referral to podiatrist per clinician judgment.

Food care patient education should include (Joslin):

- Avoidance of foot trauma
- Daily foot inspection
- Nail care
- Proper footwear; no bare feet
- Impact of loss of protective sensation on morbidity
- Need for smoking cessation
- Action to take when problems arise
- Importance of glucose control on disease progression

Smoking Cessation

Patients should be advised to stop smoking using the 5A’s algorithm found in this document Level A).

Immunizations

- Influenza vaccine: yearly for all adult patients with diabetes (1B).
- Pneumococcal vaccine: once for all patients with diabetes. (1B-Joslin).
• Patients ≥ 65 years of age should receive a second dose of pneumococcal vaccine if they received the previous dose ≥ 5 years earlier and they were <65 years of age when they received the previous dose.
• Consider vaccines for other disease prevention such as for herpes zoster.
• Administer hepatitis B vaccination to unvaccinated adults with diabetes who are aged 19-59 years (ADA, C) Consider administering hepatitis B vaccination to unvaccinated adults with diabetes who are aged 60 or older (ADA, C)

**Mental Health**

Depression screening is recommended. (all sources)

It is reasonable to include assessment of the patient’s psychological and social situation as an ongoing part of the medical management of diabetes. (ADA, B)

Psychosocial screening and follow-up may include, but are not limited to, attitudes about the illness, expectations for medical management and outcomes, affect/mood, general and diabetes-related quality of life, resources (financial, social, and emotional), and psychiatric history. (ADA, E)

**Bariatric Surgery**

Bariatric surgery may be considered for adults with BMI >35 kg/m2 and type 2 diabetes, especially if diabetes or associated comorbidities are difficult to control with lifestyle and pharmacological therapy. (ADA, B)

Patients with type 2 diabetes who have undergone bariatric surgery need lifelong lifestyle support and medical monitoring. (ADA, B)

Although small trials have shown glycemic benefit of bariatric surgery in patients with type 2 diabetes and BMI 30–35 kg/m2, there is currently insufficient evidence to generally recommend surgery in patients with BMI <35 kg/m2 outside of a research protocol. (ADA, E)

**Dental Health**

At initial visit and annually, discuss need for dental exams at least every six months. (Joslin)
**Pregnancy**

Pregnant woman with diabetes should be referred to an endocrinologist.

**Diabetes Self Management Education**

- Every person with a diagnosis of diabetes and their care partner should have diabetes self management education (Grade A) with focus on supporting behaviors related to:
  - Healthy eating
  - Being active
  - Monitoring
  - Medication adherence
  - Problem solving
  - Healthy coping
  - Risk reduction (Grade B)
- Assessment, goal setting, planning, implementation and evaluation should occur.
- Such programming should be delivered by individuals who are prepared and competent (Grade A).

**SUMMARY OF KEY BENEFITS AND RISKS OF MEDICATIONS**

Benefits are classified according to major effect on fasting glucose, postprandial glucose, and nonalcoholic fatty liver disease (NAFLD). Eight broad categories of risks are summarized. The intensity of the background shading of the cells reflects relative importance of the benefit of risk.*

<table>
<thead>
<tr>
<th>Generic names</th>
<th>Metformin</th>
<th>DPP-4 Inhibitors</th>
<th>GLP-1 Agonist (Incretin mimetic)</th>
<th>Sulfonylureas (SU)</th>
<th>Glinides</th>
<th>Thiazolidinedione (TZD)</th>
<th>Sodium-glucose cotransporter-2 (SGLT-2) inhibitor</th>
<th>Bile acid sequestrant</th>
<th>Alpha-glucosidase inhibitor (AG-i)</th>
<th>Insulin</th>
<th>Pramlintide</th>
<th>Bromocriptine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brand names</td>
<td>Glucophage</td>
<td>Tradjenta</td>
<td>Byetta</td>
<td>Bydureon</td>
<td>Victoza</td>
<td>Prandin</td>
<td>Starlix</td>
<td>Invokana</td>
<td>Farxiga</td>
<td>Welchol</td>
<td>Precose Glyset</td>
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<td></td>
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<td>Onglyza Januvia</td>
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<tr>
<td>A1C % Reduction</td>
<td>1.0-1.5</td>
<td>0.5-0.9</td>
<td>0.8-2.0</td>
<td>0.5-1.5</td>
<td>1.0-1.5</td>
<td>0.7-1.2</td>
<td>0.7-1.03</td>
<td>0.4-0.6</td>
<td>0.4-0.7</td>
<td>1.5-3.5 or more</td>
<td>0.5-1.0</td>
<td>0.4-0.6</td>
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<td>Post-Prandial Glucose (PPG) – Lowering</td>
<td>Mild</td>
<td>Moderate</td>
<td>Moderate to Marked</td>
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<td>Mild</td>
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<td>Mild</td>
<td>Moderate</td>
<td>Moderate to Marked</td>
<td>Moderate to Marked</td>
<td>Mild</td>
</tr>
<tr>
<td>Fasting Glucose (FPG) – Lowering</td>
<td>Moderate</td>
<td>Mild</td>
<td>Mild</td>
<td>Moderate</td>
<td>Mild</td>
<td>Moderate</td>
<td>Mild</td>
<td>Mild</td>
<td>Neutral</td>
<td>Moderate to Marked</td>
<td>Mild</td>
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<tr>
<td>Non-alcoholic fatty liver disease (NAFLD)</td>
<td>Metformin</td>
<td>DPP-4 Inhibitors</td>
<td>GLP-1 Agonist (Incretin mimetic)</td>
<td>Sulfonylureas (SU)</td>
<td>Glinides</td>
<td>Thiazolidinedione (TZD)</td>
<td>Sodium-glucose cotransporter-2 (SGLT-2) inhibitor</td>
<td>Bile acid sequestrant</td>
<td>Alpha-glucosidase inhibitor (AG-i)</td>
<td>Insulin</td>
<td>Pramlintide</td>
<td>Bromocriptine</td>
</tr>
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<td>-----------------------------------------</td>
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</tr>
<tr>
<td>Effect on LDL</td>
<td>↓↓</td>
<td>↓</td>
<td>---</td>
<td>↓</td>
<td>---</td>
<td>↑</td>
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<td>---</td>
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</tr>
<tr>
<td>Effect on HDL</td>
<td>↑</td>
<td>---</td>
<td>---</td>
<td>↑</td>
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<td>---</td>
<td>---</td>
<td>↑</td>
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</tr>
<tr>
<td>Effect on Triglycerides</td>
<td>↓</td>
<td>---</td>
<td>---</td>
<td>Minimal</td>
<td>↓</td>
<td>---</td>
<td>---</td>
<td>rosiglitazone</td>
<td>↑</td>
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**RISKS**

<table>
<thead>
<tr>
<th>Hypoglycemia</th>
<th>Neutral</th>
<th>Neutral</th>
<th>Neutral</th>
<th>Moderate</th>
<th>Mild</th>
<th>Mild</th>
<th>Neutral</th>
<th>Neutral</th>
<th>Neutral</th>
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<tbody>
<tr>
<td>Gl Symptoms</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Neutral</td>
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<td>Neutral</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Moderate</td>
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<tr>
<td>Renal insufficiency</td>
<td>Contra-indicated in stage 3B, 4, 5</td>
<td>Dosage reduction (except linagliptin)</td>
<td>Exenatide contra-indicated in CrCr &lt; 30</td>
<td>Dosage reduction</td>
<td>More hypoglycaemia</td>
<td>May worsen fluid retention</td>
<td>Dosage reduction</td>
<td>Contra-indicated in CrCr &lt; 30</td>
<td>Neutral</td>
<td>Neutral</td>
<td>More hypoglycemia &amp; fluid retention</td>
<td>Neutral</td>
</tr>
<tr>
<td></td>
<td>Metformin</td>
<td>DPP-4 Inhibitors</td>
<td>GLP-1 Agonist (Incretin mimetic)</td>
<td>Sulfonylureas (SU)</td>
<td>Glinides</td>
<td>Thiazolidine-dione (TZD)</td>
<td>Sodium-glucose cotransporter-2 (SGLT-2) inhibitor</td>
<td>Bile acid sequestrant</td>
<td>Alpha-glucosidase inhibitor (AG-i)</td>
<td>Insulin</td>
<td>Pramlintide</td>
<td>Bromocriptine</td>
</tr>
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<td>---------------</td>
</tr>
<tr>
<td>Liver Failure</td>
<td>Avoid use</td>
<td>---</td>
<td>Use with caution</td>
<td>Use with caution</td>
<td>Avoid use in active liver disease</td>
<td>Avoid use in severe disease</td>
<td>---</td>
<td>---</td>
<td>Contraindicated in cirrhosis</td>
<td>---</td>
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</tr>
<tr>
<td>Heart failure/Edema</td>
<td>Use with caution in CHF</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>Mild - Moderate (2x risk CHF) Contraindicated in Class 3,4 CHF</td>
<td>---</td>
<td>---</td>
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<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Weight</td>
<td>↓</td>
<td>Neutral</td>
<td>↓ (1-4 kg)</td>
<td>↑</td>
<td>↑↑</td>
<td>↓↓ (0.7-3.5 kg)</td>
<td>Neutral</td>
<td>Neutral</td>
<td>↑↑</td>
<td>(1-3 kg)</td>
<td>↑</td>
<td></td>
</tr>
<tr>
<td>Fractures</td>
<td>Moderate bone loss risk with thiazolidinedione (TZD)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**CONSIDERATIONS**

<table>
<thead>
<tr>
<th>Usual frequency of dosing</th>
<th>1-2 times daily with food</th>
<th>Daily</th>
<th>1-2 injections daily Bydureon-1 injection per week</th>
<th>1-2 times daily with meals</th>
<th>3 times daily (15-30 min before meals)</th>
<th>Daily</th>
<th>Daily</th>
<th>1-2 times daily with meals and liquid</th>
<th>3 times daily with food</th>
<th>1-4 injection daily</th>
<th>3 injections daily prior to meals; dosage differs for type 2 or type 1 diabetes</th>
<th>Daily, within 2h of waking</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to achieve max response per dose</td>
<td>2 – 3 hours</td>
<td>1 – 4 hours</td>
<td>exenatide 2 hours</td>
<td>2 – 3 hours</td>
<td>&lt; 4 hours</td>
<td>1 – 2 hours</td>
<td>1-2 hours</td>
<td>N/A</td>
<td>1 – 3 hours</td>
<td>varies 0.5 – 12 hours</td>
<td>20 minutes</td>
<td>1 – 2 hours</td>
</tr>
<tr>
<td>Cost</td>
<td>$</td>
<td>$$$</td>
<td>$$$$$$</td>
<td>$</td>
<td>$</td>
<td>$-$</td>
<td>$$$$$$</td>
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<td>$$$$$$</td>
<td>$</td>
</tr>
</tbody>
</table>
Insulin Tips

**Only Regular may be administered IV**

- When mixing insulin in a syringe, draw up (immediately before administration) the quickest acting insulin first. (Example: Draw up Regular before NPH).
- Do NOT use “U” for Units due to potential misinterpretation. (Example: 2U → can be confused as 20 Units).
- Use 50 Unit syringes whenever feasible (if larger syringe required, verify the high dose is accurate).

<table>
<thead>
<tr>
<th>Type: Insulin Brand® (Generic Name/Active Ingredient)</th>
<th>Timing With Meals (N/A = Not Applicable)</th>
<th>Onset</th>
<th>Peak (hours)</th>
<th>Duration (hours)</th>
<th>Compatible Mixed With</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid-Acting:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>☯ Novolog® (Aspart)</td>
<td>Give with meal</td>
<td>15 minutes</td>
<td>1 – 3 hours</td>
<td>3 – 5 hours</td>
<td>NPH</td>
</tr>
<tr>
<td>Rapid-Acting:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>☯ Humalog® (Lispro)</td>
<td>Give with meal</td>
<td>15- 30 minutes</td>
<td>0.5 – 2.5 hours</td>
<td>3 – 5 hours</td>
<td>NPH</td>
</tr>
<tr>
<td>Rapid-Acting:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>☯ Apidra® (Glulisine)</td>
<td>Give with meal</td>
<td>15- 30 minutes</td>
<td>1.6 – 2.8 hours</td>
<td>3 – 4 hours</td>
<td>Nothing!</td>
</tr>
<tr>
<td>Short-Acting:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>☯ Novolin® R/Humulin® R (Regular)</td>
<td>Give ½ hour before meal</td>
<td>30 minutes</td>
<td>2.5 – 5 hours</td>
<td>4 – 12 hours</td>
<td>NPH</td>
</tr>
<tr>
<td>Intermediate-Acting:</td>
<td>N/A</td>
<td>1 – 2 hours</td>
<td>4 – 12 hours</td>
<td>14 – 24 hours</td>
<td>Regular, Aspart</td>
</tr>
<tr>
<td>----------------------</td>
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</tr>
<tr>
<td>Novolin® N/ Humulin® N (NPH)</td>
<td>N/A</td>
<td>1 – 2 hours</td>
<td>4 – 12 hours</td>
<td>14 – 24 hours</td>
<td>Regular, Aspart</td>
</tr>
<tr>
<td>Levemir® (Insulin Detemir)</td>
<td>N/A</td>
<td>3 – 4 hours</td>
<td>No pronounced peak</td>
<td>6 – 23 hours (dose dependent)</td>
<td>Nothing!</td>
</tr>
<tr>
<td>Lantus ® (Glargine)</td>
<td>N/A</td>
<td>1 – 3 hours</td>
<td>No pronounced peak</td>
<td>24 hours</td>
<td>Nothing!</td>
</tr>
<tr>
<td>Combination:</td>
<td>Give with meal</td>
<td>10-20 minutes</td>
<td>1 – 4 hours</td>
<td>18 – 24 hours</td>
<td>Nothing! Already a Mix</td>
</tr>
<tr>
<td>Novolog® Mix 70/30 (70 % Aspart Protamine &amp; 30 % Aspart)</td>
<td>Give with meal</td>
<td>15-30 minutes</td>
<td>1 – 6.5 hours</td>
<td>14 – 24 hours</td>
<td>Nothing! Already a Mix</td>
</tr>
<tr>
<td>Humalog® Mix 75/25 (Insulin Lispro &amp; Insulin Lispro Protamine)</td>
<td>Give with meal</td>
<td>15 – 30 minutes</td>
<td>0.8 – 4.8 hours</td>
<td>14 – 24 hours</td>
<td>Nothing! Already a Mix</td>
</tr>
<tr>
<td>Humalog® Mix 50/50 (Insulin Lispro &amp; Insulin Lispro Protamine)</td>
<td>Give ½ hour before meal</td>
<td>30 minutes</td>
<td>2 – 12 hours</td>
<td>18-24 hours</td>
<td>Nothing!</td>
</tr>
<tr>
<td>Novolin®/Humulin® 70/30 (NPH &amp; Regular)</td>
<td>Give ½ hour before meal</td>
<td>30 minutes</td>
<td>2 – 12 hours</td>
<td>18-24 hours</td>
<td>Nothing!</td>
</tr>
</tbody>
</table>
WARNINGS

**Thiazolidinediones (TZDs)**

**CLASS EFFECTS:**
Closely monitor for signs and symptoms of heart failure (e.g. rapid weight gain, dyspnea, edema), particularly after initiation or dose increases; if heart failure develops, treat accordingly and consider dose reduction or discontinuation. Not recommended for use in any patient with symptomatic heart failure. Initiation of therapy is contraindicated in patients with NYHA class III or IV heart failure.

**Pioglitazone (Actos®):**
Clinical trial data suggest an increased risk of bladder cancer in patients exposed to pioglitazone; risk may be increased with duration of use. Avoid use in patients with active bladder cancer and consider risks vs. benefits prior to initiating therapy in patients with a history of bladder cancer. In Canada, use is contraindicated in patients with active or a history of bladder cancer.

**Rosiglitazone (Avandia®): UPDATED 2014**
The FDA announced that the readjudicated results of the RECORD trial confirm that rosiglitazone does NOT increase the risk of myocardial infarction (MI) as compared with standard-of-care diabetes drugs, metformin and a sulfonylurea. In the RECORD trial, patients treated with rosiglitazone experienced fewer cardiovascular-related, stroke-related and MI-related deaths; fewer nonfatal strokes; and fewer deaths from any cause compared to patients treated with metformin and a sulfonylurea. Patients treated with metformin and a sulfonylurea experienced fewer nonfatal MIs compared to patients treated with rosiglitazone. None of the differences between treatment groups reached statistical significance. In light of the readjudicated findings of the RECORD trial, the FDA has removed the requirements for restricted distribution of rosiglitazone.

**DPP-4 Inhibitors**

**CLASS EFFECTS:**
Cases of acute pancreatitis, including fatalities, have been reported with use. Monitor for signs/symptoms of pancreatitis; discontinue use immediately if pancreatitis is suspected and initiate appropriate management. If patients have a history of pancreatitis, other agents should be used.

**Saxagliptin (Onglyza®):**
Recent FDA alert- possible association between use of the drug and heart failure.
GLP-1 Receptor Agonists

Exenatide (Byetta®):
In post marketing reports Byetta has been associated with cases of acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis.

Exenatide extended release (Bydureon®):
Cases of acute pancreatitis (including hemorrhagic and necrotizing with some fatalities) have been reported; monitor for unexplained severe abdominal pain, and if pancreatitis is suspected, discontinue use. Due to the class effect of a potential for pancreatitis, if patients have a history of pancreatitis, other agents should be used.

**Box Warning:** Exenatide extended-release causes thyroid C-cell tumors at clinically relevant exposures in rats. It is unknown whether it causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as human relevance could not be determined by clinical or nonclinical studies. Contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2).

Liraglutide (Victoza®):
Cases of acute and chronic pancreatitis (including one case of fatal necrotizing pancreatitis) have been reported although conclusive evidence linking pancreatitis to liraglutide therapy has not been established; monitor for signs and symptoms of pancreatitis (eg, persistent severe abdominal pain which may radiate to the back and which may or may not be accompanied by vomiting).

**Box Warning:** Dose- and duration- dependent thyroid C-cell tumors have developed in animal studies with liraglutide therapy; relevance in humans unknown. Due to the finding in animal studies, patients were monitored with serum calcitonin or thyroid ultrasound during clinical trials; however, it is unknown if this is beneficial in decreasing the risk of thyroid tumors. Patients should be counseled on the risk and symptoms (eg, neck mass, dysphagia, dyspnea, persistent hoarseness) of thyroid tumors. Use is contraindicated in patients with or a family history of medullary thyroid cancer and in patients with multiple endocrine neoplasia syndrome type 2 (MEN2).
Algorithm for Adding/Intensifying Insulin

I. Start with Basal Insulin:

- A1C < 8.0% → Total daily dose (TDD) = 0.1 - 0.2 units/kg of body weight
- A1C > 8.0% → TDD = 0.2 - 0.3 units/kg of body weight

Insulin titration: titrate every 2-3 days to glycemic goal

1. Fixed regimen: increase TDD by 2 units every 2-3 days until FBG at goal
2. Adjustable regimen:
   - FBG > 180 mg/dL → add 4 units
   - FGB 140-180 mg/dL → add 2 units
   - FGB 110-139 mg/dL → add 1 unit

If hypoglycemia occurs:

- BG < 70 mg/dL → reduce TDD by 10% - 20%
- BG < 40 mg/dL → reduce TDD by 20% - 40%

Evaluate after 3 months, if not at goal → intensify treatment

- Add GLP-1 RA or DPP4-I to Basal Insulin regimen (if A1C is not far from goal)
- Add Prandial Insulin to Basal Insulin regimen (basal-bolus regimen)

II. Transition from basal to basal-bolus regimen:

- Cover the largest meal with a prandial injection. Consider additional mealtime injections later if needed
- Mealtime insulin: start with ~ 5 units/meal or ~ 10% daily basal insulin dose

III. Initiation of a basal-bolus regimen:

- Calculate TDD = 0.3 - 0.5 units/kg of body weight
• Divide TDD into 2 parts:
  o 50% Basal Analog (insulin glargine or detemir)
  o 50% Prandial Analog

**Note:** *NPH and regular insulin or premixed insulin are less desirable*

**Insulin titration:** titrate every 2-3 days to glycemic goal

• Titrare basal insulin as follow:
  1. **Fixed regimen:** increase TDD by 2 units every 2-3 days until FBG at goal
  2. **Adjustable regimen:**
     o FBG > 180 mg/dL → add 4 units
     o FGB 140-180 mg/dL → add 2 units
     o FGB 110-139 mg/dL → add 1 unit

• Titrare prandial insulin as follow:
  o 2-hour postprandial or next premeal glucose > 80 mg/dL → Increase prandial dose by 10% for that meal time

• Titrare premixed insulin: increase TDD by 10% if fasting/premeal BG > 180 mg/dL

**If hypoglycemia occurs:**

  o Fasting AM hypoglycemia → reduce basal insulin
  o Nighttime hypoglycemia → reduce basal insulin +/- reduce short/rapid-acting insulin at pre-supper or pre-evening snack
  o Between meal daytime hypoglycemia → reduce the previous premeal short/rapid-acting insulin

---

**Abbreviations:**

GLP-1 RA = GLP-1 receptor agonists, **DPP4-i** = DPP4 inhibitors, **AG-i** = Alpha glucosidase inhibitors, **SGLT-2** = Sodium-glucose cotransporter-2, **TZD** = Thiazolidinediones, **SU/GLN** = Sulfonylureas/glinides, **TDD** = Total daily dose, **FBG** = Fasting blood glucose
# Stability of Insulin Vials/Pens

<table>
<thead>
<tr>
<th>DRUG</th>
<th>For unopened product kept at room temperature</th>
<th>For opened product *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Novolog vials</td>
<td>28 days</td>
<td>28 days refrigerated OR room temperature</td>
</tr>
<tr>
<td>Novolog pens/cartridges</td>
<td>28 days</td>
<td>28 days at room temperature</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Do NOT refrigerate open pens</td>
</tr>
<tr>
<td>Humalog vials</td>
<td>28 days</td>
<td>28 days refrigerated OR room temperature</td>
</tr>
<tr>
<td>Humalog pens/cartridges</td>
<td>28 days</td>
<td>28 days at room temperature</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Do NOT refrigerate open pens</td>
</tr>
<tr>
<td>Apidra vials</td>
<td>28 days</td>
<td>28 days refrigerated OR room temperature</td>
</tr>
<tr>
<td>Apidra pens/cartridges</td>
<td>28 days</td>
<td>28 days at room temperature</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Do NOT refrigerate open pens</td>
</tr>
<tr>
<td>Novolin R vials</td>
<td>42 days</td>
<td>42 days at room temperature</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Refrigeration of opened vials is NOT recommended</td>
</tr>
<tr>
<td>Humulin R vials</td>
<td>31 days</td>
<td>31 days refrigerated OR room temperature</td>
</tr>
<tr>
<td>Novolin N vials</td>
<td>42 days</td>
<td>42 days at room temperature</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Refrigeration of opened vials is NOT recommended</td>
</tr>
<tr>
<td>Humulin N vials</td>
<td>Should be stored in refrigerator; 31 days if left unrefrigerated.</td>
<td>31 days refrigerated OR room temperature</td>
</tr>
<tr>
<td>Humulin N pens/cartridges</td>
<td>Should be stored in refrigerator; 14 days if left unrefrigerated.</td>
<td>14 days at room temperature</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Refrigeration of opened pens/cartridges is NOT recommended</td>
</tr>
<tr>
<td>Lantus vials</td>
<td>28 days</td>
<td>28 days refrigerated OR room temperature</td>
</tr>
<tr>
<td>Lantus pens/cartridges</td>
<td>28 days</td>
<td>28 days at room temperature</td>
</tr>
<tr>
<td>Medication</td>
<td>Storage Duration</td>
<td>Storage Condition</td>
</tr>
<tr>
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<td>------------------</td>
<td>------------------------------------</td>
</tr>
<tr>
<td>Novolog mix 70/30 vials</td>
<td>28 days</td>
<td></td>
</tr>
<tr>
<td>Novolog mix 70/30 pens</td>
<td>14 days</td>
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<tr>
<td>Humalog Mix 75/25 vials</td>
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<tr>
<td>Humalog Mix 75/25 KwikPen</td>
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<tr>
<td>Humalog Mix 50/50 vials</td>
<td>28 days</td>
<td></td>
</tr>
<tr>
<td>Humalog Mix 50/50 Kwikpen</td>
<td>10 days</td>
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<tr>
<td>Humulin 70/30 vials</td>
<td>31 days</td>
<td></td>
</tr>
<tr>
<td>Humulin 70/30 Pens and Cartridges</td>
<td>10 days</td>
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</tr>
<tr>
<td>Novolin 70/30 vials</td>
<td>42 days</td>
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<td></td>
</tr>
<tr>
<td>Byetta (exenatide)</td>
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<tr>
<td>Bydureon (exenatide extended release)</td>
<td>4 weeks</td>
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</tr>
<tr>
<td>Victoza (liraglutide)</td>
<td>30 days</td>
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</tr>
<tr>
<td>SymlinPen (pramlintide)</td>
<td>30 days</td>
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</tbody>
</table>

*For all medication, do NOT freeze. Keep medications away from heat and sunlight.

* This includes any days that product is stored at room temperature prior to opening

*Created by: Christopher Ullo and David Dalton, PharmD Candidates 2014. Tien Van, PharmD, PGY-1 Pharmacy Practice Resident*
Figure 1. The “5 A’s”: Treating Tobacco Dependence as a Chronic Disease

ASK
Do you currently use tobacco?

YES

NO

ADVISE
to quit

ASSESS
Are you willing to quit now?

YES

NO

ASK
Have you ever used tobacco?

YES

NO

ASSESS
Have you recently quit? Any challenges?

YES

NO

ASSIST
Provide appropriate tobacco dependence treatments

ASSIST
Intervene to increase motivation to quit

ASSIST
Provide relapse prevention

ASSIST
Encourage continued abstinence

ARRANGE FOLLOWUP
STOP BANG Screening for Obstructive Sleep Apnea

Answer the following questions to find out if you are at risk for Obstructive Sleep Apnea:

**STOP**

S (snore)  Have you been told that you snore? YES / NO
T (tired)  Are you often tired during the day? YES / NO
O (obstruction)  Do you know if you stop breathing or has anyone witnessed you stop breathing while you are asleep? YES / NO
P (pressure)  Do you have high blood pressure or on medication to control high blood pressure? YES / NO

If you answered YES to two or more questions on the STOP portion, you are at risk for Obstructive Sleep Apnea. It is recommended that you contact your primary care provider to discuss a possible sleep disorder.

To find out if you are at moderate to severe risk of Obstructive Sleep Apnea, complete the BANG questions below:

**BANG**

B (BMI)  Is your body mass index greater than 30? YES / NO
A (age)  Are you 50 years old or older? YES / NO
N (neck)  Do you have a neck circumference greater than 40 cm? YES / NO
G (gender)  Are you a male? YES / NO

The more questions you answer YES to on the BANG portion, the greater your risk of having moderate to severe Obstructive Sleep Apnea.


Meridian Health Resources for Medical Nutrition Therapy and Diabetes Self Management Education

Most insurance companies, including Medicare and managed care companies cover MNT counseling with a Registered Dietician and DSME/DSMT

**Jersey Shore University Medical Center**  
*Meridian Medical Associates*  
Diabetes Self Management Education/Training  
Brandywine Commons  
2240 Route 33  
Neptune, NJ  
732-897-3980

*Life Fitness*  
Medical Nutrition Therapy/Nutrition Counseling with Registered Dietician  
732-295-1778

**Ocean Medical Center and Riverview Medical Center**  
*Diabetes Management Center*  
Diabetes Self Management Education Training and Medical Nutrition Therapy/Nutrition Counseling with Registered Dietician  
732-530-2555

**Southern Ocean Medical Center**  
*Diabetes Management Center*  
Diabetes Self Management Education Training and Medical Nutrition Therapy/Nutrition Counseling with Registered Dietician  
1140 Route 72 West  
Manahawkin, NJ  
609-978-3491
Levels of Evidence
ADA Evidence Grading System for Clinical Practice Recommendations

A: Clear evidence from well-conducted, generalizable, randomized controlled trials that are adequately powered, including:
- Evidence from a well-conducted multicenter trial
- Evidence from a meta-analysis that incorporated quality ratings in the analysis
- Compelling nonexperimental evidence, i.e., “all or none” rule developed by Center for Evidence Based Medicine at Oxford
- Supportive evidence from well-conducted randomized controlled trials that are adequately powered, including:
  - Evidence from a well-conducted trial at one or more institutions
  - Evidence from a meta-analysis that incorporated quality ratings in the analysis

B: Supportive evidence from well-conducted cohort studies
- Evidence from a well-conducted prospective cohort study or registry
- Evidence from a well-conducted meta-analysis of cohort studies
- Supportive evidence from a well-conducted case-control study

C: Supportive evidence from poorly controlled or uncontrolled studies
- Evidence from randomized clinical trials with one or more major or three or more minor methodological flaws that could invalidate the results
- Evidence from observational studies with high potential for bias (such as case series with comparison to historical controls)
- Evidence from case series or case reports
- Conflicting evidence with the weight of evidence supporting the recommendation

E: Expert consensus or clinical experience
### AACE Formulation of Level of Evidence

**Table 1**


<table>
<thead>
<tr>
<th>Numerical descriptor (evidence level)</th>
<th>Semantic descriptor (reference methodology)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Meta-analysis of randomized controlled trials (MRCT)</td>
</tr>
<tr>
<td>1</td>
<td>Randomized controlled trials (RCT)</td>
</tr>
<tr>
<td>2</td>
<td>Meta-analysis of nonrandomized prospective or case-controlled trials (MNRCT)</td>
</tr>
<tr>
<td>2</td>
<td>Nonrandomized controlled trial (NRCT)</td>
</tr>
<tr>
<td>2</td>
<td>Prospective cohort study (PCS)</td>
</tr>
<tr>
<td>2</td>
<td>Retrospective case-control study (RCCS)</td>
</tr>
<tr>
<td>3</td>
<td>Cross-sectional study (CSS)</td>
</tr>
<tr>
<td>3</td>
<td>Surveillance study (registries, surveys, epidemiologic study, retrospective chart review, mathematical modeling of database) (SS)</td>
</tr>
<tr>
<td>3</td>
<td>Consecutive case series (CCS)</td>
</tr>
<tr>
<td>3</td>
<td>Single case reports (SCR)</td>
</tr>
<tr>
<td>4</td>
<td>No evidence (theory, opinion, consensus, review, or preclinical study) (NE)</td>
</tr>
</tbody>
</table>
### Table 3

2010 American Association of Clinical Endocrinologists Protocol for Production of Clinical Practice Guidelines—Step III: Grading of Recommendations; How Different Evidence Levels Can Be Mapped to the Same Recommendation Grade

<table>
<thead>
<tr>
<th>Best Evidence Level</th>
<th>Subjective Factor Impact</th>
<th>Two-Thirds Consensus</th>
<th>Mapping</th>
<th>Recommendation Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>None</td>
<td>Yes</td>
<td>Direct</td>
<td>A</td>
</tr>
<tr>
<td>2</td>
<td>Positive</td>
<td>Yes</td>
<td>Adjust up</td>
<td>A</td>
</tr>
<tr>
<td>2</td>
<td>None</td>
<td>Yes</td>
<td>Direct</td>
<td>B</td>
</tr>
<tr>
<td>1</td>
<td>Negative</td>
<td>Yes</td>
<td>Adjust down</td>
<td>B</td>
</tr>
<tr>
<td>3</td>
<td>Positive</td>
<td>Yes</td>
<td>Adjust up</td>
<td>B</td>
</tr>
<tr>
<td>3</td>
<td>None</td>
<td>Yes</td>
<td>Direct</td>
<td>C</td>
</tr>
<tr>
<td>2</td>
<td>Negative</td>
<td>Yes</td>
<td>Adjust down</td>
<td>C</td>
</tr>
<tr>
<td>4</td>
<td>Positive</td>
<td>Yes</td>
<td>Adjust up</td>
<td>C</td>
</tr>
<tr>
<td>4</td>
<td>None</td>
<td>Yes</td>
<td>Direct</td>
<td>D</td>
</tr>
<tr>
<td>3</td>
<td>Negative</td>
<td>Yes</td>
<td>Adjust down</td>
<td>D</td>
</tr>
<tr>
<td>1, 2, 3, 4</td>
<td>NA</td>
<td>No</td>
<td>Adjust down</td>
<td>D</td>
</tr>
</tbody>
</table>

Version 2: February 2014

Diabetes Continuum of Care Evidence Review Team

(Source documents primarily from the AACE and the ADA along with local expert opinion unless otherwise noted)