Diabetes Updates

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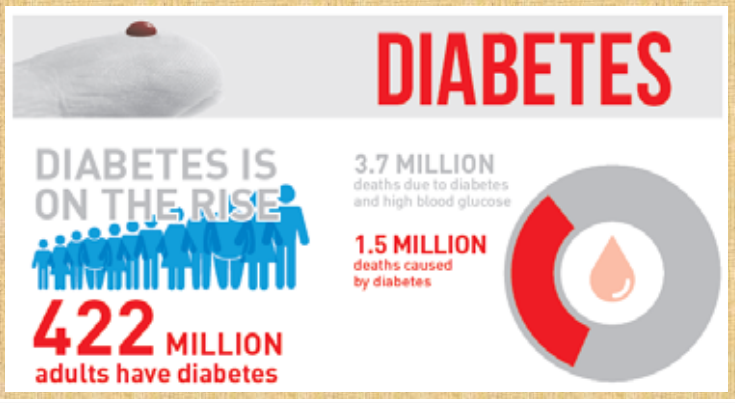
Disclosures

- I have no relevant financial relationships with any commercial interests that may be mentioned in this CME activity offering.
- The views expressed herein are those of the author and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, nor the U.S. Government

Objectives

- Epidemiology of Diabetes
- Synopsis of the 2018 American Diabetes Association Clinical Practice Recommendations
- Appropriate referral to Endocrinology

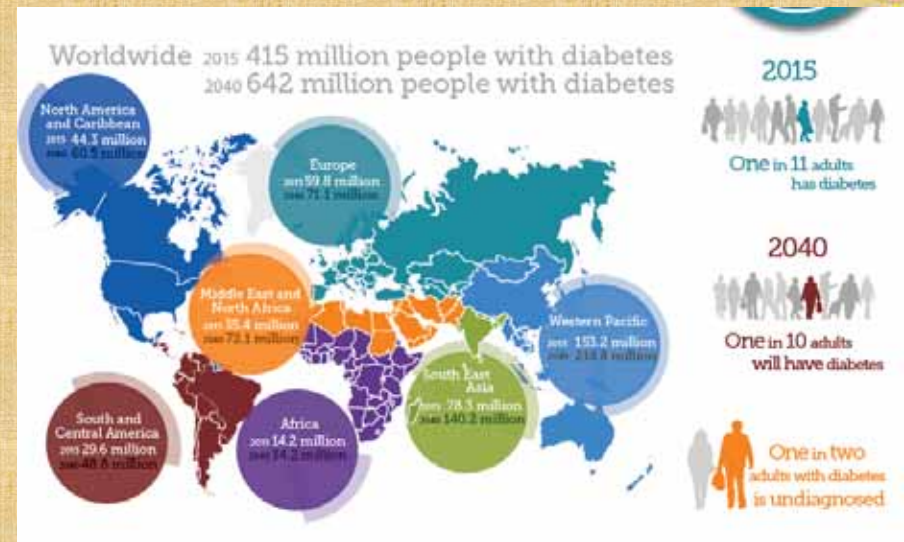
Epidemiology of Diabetes



More than 80% live in low- and middle-income countries
The greatest number of people with diabetes 40-59 yrs old
46.5% adults with diabetes are undiagnosed

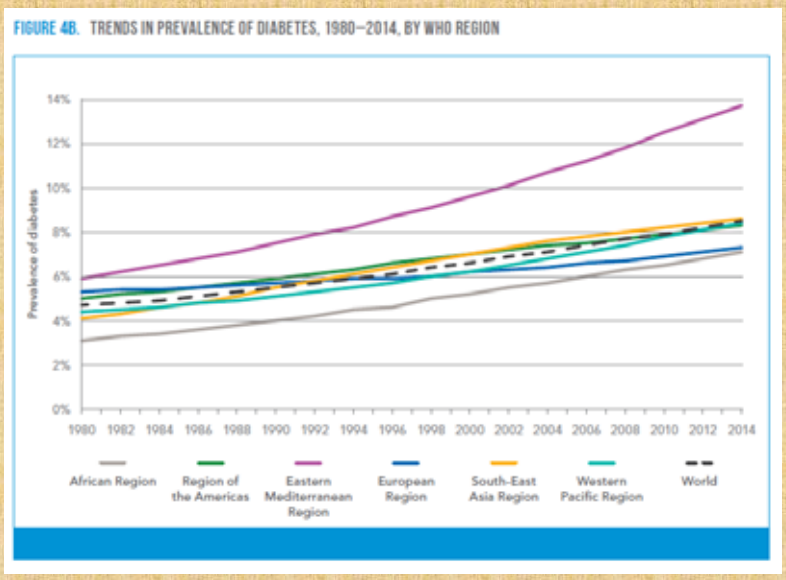
WHO 2016
IDF Diabetes Atlas

Epidemiology of Diabetes



IDF 2015

Epidemiology of Diabetes



Global report on Diabetes 2016

Epidemiology of Diabetes – in USA

Fast Facts on Diabetes

30.3 million people have diabetes

(9.4% of the U.S. population)

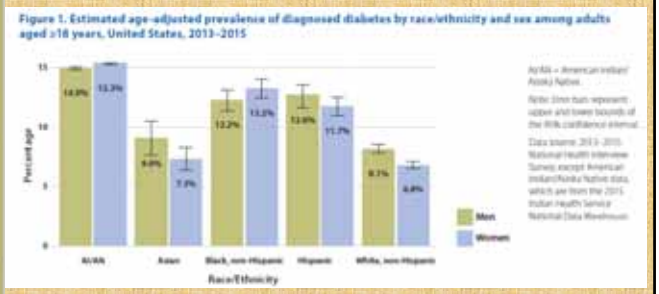
Diagnosed

23.1 million people

Undiagnosed

7.2 million

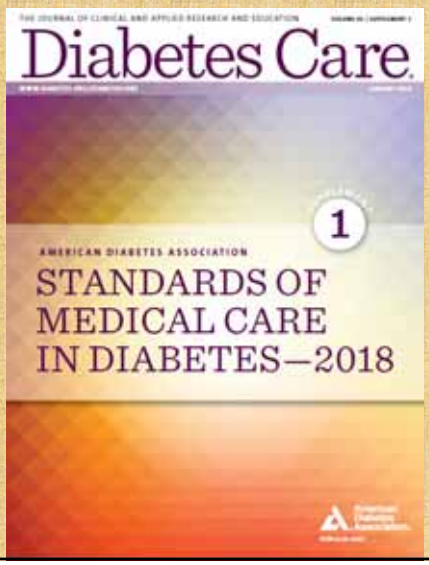
(23.8% of people with diabetes are undiagnosed)



National Diabetes Statistic Report 2017

Clinical Practice Guidelines

- American Diabetes Association
  - Updated annually in Diabetes Care; released every January
  - Available at http://care.diabetesjournals.org



2018 ADA Clinical Practice Recommendations

Classification of Diabetes:

- Type 1 diabetes (autoimmune β-cell destruction)
- Type 2 diabetes (insulin secretion deficiency/resistance)
- Gestational diabetes mellitus (GDM) (dx'ed 2nd/3rd trimester)
- Other specific causes
  - Monogenic diabetes syndromes (neonatal, MODY)
  - Disease of exocrine pancreas (cystic fibrosis)
  - Drug or chemical-induced diabetes (glucocorticoid, HIV/AIDS treatment, post organ transplant)

2018 ADA Clinical Practice Recommendations

Table 2.1—Staging of type 1 diabetes (4,5)

	Stage 1	Stage 2	Stage 3
Stage	• Autoimmunity • Normoglycemia • Presymptomatic	• Autoimmunity • Dysglycemia • Presymptomatic	• New-onset hyperglycemia • Symptomatic
Diagnostic criteria	• Multiple autoantibodies • No IGT or IFG	• Multiple autoantibodies • Dysglycemia: IFG and/or IGT • FPG 100–125 mg/dL (5.6–6.9 mmol/L) • 2-h PG 140–199 mg/dL (7.8–11.0 mmol/L) • A1C 5.7–6.4% (39–47 mmol/mol) or ≥10% increase in A1C	• Clinical symptoms • Diabetes by standard criteria

2018 ADA Clinical Practice Recommendations

Table 2.7—Most common causes of monogenic diabetes (82)

		Gene	Inheritance	Clinical features
MODY				
	2	*GCK*	AD	GCK-MODY: stable, nonprogressive elevated fasting blood glucose; typically does not require treatment; microvascular complications are rare; small rise in 2-h PG level on OGTT (<54 mg/dL [3 mmol/L])
	3	*HNF1A*	AD	HNF1A-MODY: progressive insulin secretory defect with presentation in adolescence or early adulthood; lowered renal threshold for glucosuria; large rise in 2-h PG level on OGTT (>90 mg/dL [5 mmol/L]); sensitive to sulfonylureas
	1	*HNF4A*	AD	HNF4A-MODY: progressive insulin secretory defect with presentation in adolescence or early adulthood; may have large birth weight and transient neonatal hypoglycemia; sensitive to sulfonylureas
	5	*HNF1B*	AD	HNF1B-MODY: developmental renal disease (typically cystic); genitourinary abnormalities; atrophy of the pancreas; hyperuricemia; gout
Neonatal diabetes				
		KCNJ11	AD	Permanent or transient: IUGR; possible developmental delay and seizures; responsive to sulfonylureas
		INS	AD	Permanent: IUGR; insulin requiring
		ABCC8	AD	Transient or permanent: IUGR; rarely developmental delay; responsive to sulfonylureas
		6q24 (*PLAGL1, HYMAI*)	AD for paternal duplications	Transient: IUGR; macroglossia; umbilical hernia; mechanisms include UPD6, paternal duplication or maternal methylation defect; may be treatable with medications other than insulin
		GATA6	AD	Permanent: pancreatic hypoplasia; cardiac malformations; pancreatic exocrine insufficiency; insulin requiring
		EIF2AK3	AR	Permanent: Wolcott-Rallison syndrome: epiphyseal dysplasia; pancreatic exocrine insufficiency; insulin requiring
		FOXP3	X-linked	Permanent: immunodysregulation, polyendocrinopathy, enteropathy X-linked (IPEX) syndrome: autoimmune diabetes; autoimmune thyroid disease; exfoliative dermatitis; insulin requiring

AD, autosomal dominant; AR, autosomal recessive; IUGR, intrauterine growth restriction.

2018 ADA Clinical Practice Recommendations

- **Post-transplantation Diabetes Mellitus**
- Screen after organ transplantation for hyperglycemia
  - stable on immunosuppressive regimen and no acute infection
- OGTT is preferred to make a diagnosis.
- Immunosuppresive regimens shown to provide the best outcomes for patient and graft survival should be used (irrespective to posttransplantation DM risk)

2018 ADA Clinical Practice Recommendations

Table 2.2—Criteria for the diagnosis of diabetes

FPG ≥126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*
OR
2-h PG ≥200 mg/dL (11.1 mmol/L) during OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75-g anhydrous glucose dissolved in water.*
OR
A1C ≥6.5% (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*
OR
In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L).

*In the absence of unequivocal hyperglycemia, results should be confirmed by repeat testing.

- In the absence of unequivocal hyperglycemia, repeat testing REQUIRED
- If tests discordant, repeat test that classifies patient as diabetic

2018 ADA Clinical Practice Recommendations

- Potential limitations in A1c due to Hb variants, assay interference, & conditions assoc with RBC turnover

- Age (unclear cut points in children/adolescents)
- Race/ethnicity (higher A1c/ fructosamine in African Americans)
- Anemia/ hemoglobinopathies
- Increased RBC turnover – Sickle cell disease, pregnancy, HD, recent blood loss/ transfusion, erythropoietin therapy

2018 ADA Clinical Practice Recommendations

Table 2.6—Screening for and diagnosis of GDM

One-step strategy

Perform a 75-g OGTT, with plasma glucose measurement when patient is fasting and at 1 and 2 h, at 24–28 weeks of gestation in women not previously diagnosed with overt diabetes.

The OGTT should be performed in the morning after an overnight fast of at least 8 h.

The diagnosis of GDM is made when any of the following plasma glucose values are met or exceeded:

- Fasting: 92 mg/dL (5.1 mmol/L)
- 1 h: 180 mg/dL (10.0 mmol/L)
- 2 h: 153 mg/dL (8.5 mmol/L)

Two-step strategy

Step 1: Perform a 50-g GLT (nonfasting), with plasma glucose measurement at 1 h, at 24–28 weeks of gestation in women not previously diagnosed with overt diabetes.

If the plasma glucose level measured 1 h after the load is ≥130 mg/dL, 135 mg/dL, or 140 mg/dL (7.2 mmol/L, 7.5 mmol/L, or 7.8 mmol/L), proceed to a 100-g OGTT.

Step 2: The 100-g OGTT should be performed when the patient is fasting.

The diagnosis of GDM is made if at least two* of the following four plasma glucose levels (measured fasting and 1 h, 2 h, 3 h during OGTT) are met or exceeded:

	Carpenter-Coustan (73)	or	NDDG (74)
• Fasting	95 mg/dL (5.3 mmol/L)		105 mg/dL (5.8 mmol/L)
• 1 h	180 mg/dL (10.0 mmol/L)		190 mg/dL (10.6 mmol/L)
• 2 h	155 mg/dL (8.6 mmol/L)		165 mg/dL (9.2 mmol/L)
• 3 h	140 mg/dL (7.8 mmol/L)		145 mg/dL (8.0 mmol/L)

NDDG, National Diabetes Data Group. *ACOG recently noted that alternatively one elevated value can be used for diagnosis.

2018 ADA Clinical Practice Recommendations

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

1. Testing should be considered in overweight or obese (BMI ≥25 kg/m^2 or ≥23 kg/m^2 in Asian Americans) adults who have one or more of the following risk factors:
   - First-degree relative with diabetes
   - High-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
   - History of CVD
   - Hypertension (≥140/90 mmHg or on therapy for hypertension)
   - HDL cholesterol level <35 mg/dL (0.90 mmol/L) and/or a triglyceride level >250 mg (2.82 mmol/L)
   - Women with polycystic ovary syndrome
   - Physical inactivity
   - Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)

2. Patients with prediabetes (A1C ≥5.7% [39 mmol/mol], IGT, or IFG) should be tested yearly.
3. Women who were diagnosed with GDM should have lifelong testing at least every 3 years.
4. For all other patients, testing should begin at age 45 years.
5. If results are normal, testing should be repeated at a minimum of 3-year intervals, with consideration of more frequent testing depending on initial results and risk status.

2018 ADA Clinical Practice Recommendations

- Pre Diabetes (increased risk for diabetes):
  - FPG 100-125 mg/dL (5.6-6.9 mmol/L); fasting >8h
  - 2-h post oral 75 g glucose 140-199 mg/dL (7.8-11.0 mmol/L)
  - A1C 5.7-6.4% (39-47 mmol/mol)
  - Prevention or Delay of type 2 Diabetes:
    - Weight loss target of 7% baseline
    - Exercise >150 minutes/week
    - Metformin for those at highest risk
    - Surveillance Q 1 yr
  - Rate of Progression of Pre Diabetes:
    - A1C over 5.6 years:
      - A1C (5.5-6.0%) → 9-25% will be diabetic
      - A1C (6.0-6.5%) → 25-50% will be diabetic
    - Fasting Plasma Glucose:
      - FPG (100-109 mg/dL): 1.3%/year will be diabetic
      - FPG (110-125 mg/dL): 5.6%/year will be diabetic

2018 ADA Clinical Practice Recommendations

- **Comprehensive Medical Evaluation of Comorbidities**
- Patient-centered collaborative care
- Confirm diagnosis and classify diabetes
- Detect diabetes complications/ comorbid conditions
- Review previous treatment & risk factor control
- Begin patient engagement for care plan
- Develop a plan for continuing care

- Assess sleep pattern & duration
- Diabetes comorbidities:
  - Autoimmune diseases (autoimmune thyroid dz, celiac dz)
  - HIV (screen for DM/ preDM q6-12 mos before ART and 3 mos after ART)
  - Anxiety disorders & depression
  - Eating disorders
  - Serious mental illness
  - Periodontal disease

Table 3.1 – Components of the comprehensive diabetes medical evaluation at initial and follow-up visits

		INITIAL VISIT	EVERY FOLLOW-UP VISIT	ANNUAL VISIT
PAST MEDICAL AND FAMILY HISTORY	**Diabetes history** ▪ Characteristics at onset (e.g., age, symptoms) ▪ Review of previous treatment regimens and response ▪ Assess frequency/cause/severity of past hospitalizations	✓ ✓ ✓		
	Family history ▪ Family history of diabetes in a first-degree relative ▪ Family history of autoimmune disorder	✓ ✓		
	Personal history of complications and common comorbidities ▪ Macrovascular and microvascular ▪ Common comorbidities ▪ Presence of hemoglobinopathies or anemias ▪ High blood pressure or abnormal lipids ▪ Last dental visit ▪ Last dilated eye exam ▪ Visits to specialists	✓ ✓ ✓ ✓ ✓ ✓ ✓	✓	✓ ✓ ✓
	Interval history ▪ Changes in medical/family history since last visit		✓	✓
SOCIAL HISTORY	**Assess lifestyle and behavior patterns** ▪ Eating patterns and weight history ▪ Sleep behaviors and physical activity ▪ Familiarity with carbohydrate counting in type 1 diabetes ▪ Tobacco, alcohol, and substance use ▪ Identify existing social supports	✓ ✓ ✓ ✓ ✓	✓ ✓	✓ ✓
	Interval history ▪ Changes in social history since last visit		✓	✓
MEDICATIONS AND VACCINATIONS	▪ Medication-taking behavior ▪ Medication intolerance or side effects ▪ Complementary and alternative medicine use ▪ Vaccination history and needs	✓ ✓ ✓ ✓	✓ ✓ ✓	✓ ✓ ✓ ✓
TECHNOLOGY USE	▪ Assess use of health apps, online education, patient portals, etc. ▪ Glucose monitoring (meter/CGM): results and data use ▪ Review insulin pump settings	✓ ✓ ✓	✓ ✓	✓ ✓ ✓
SCREENING	**Psychosocial conditions** ▪ Screen for depression, anxiety, and disordered eating; refer for further assessment or intervention if warranted ▪ Consider assessment for cognitive impairment*	✓ ✓		✓ ✓
	Diabetes self-management education and support ▪ History of dietitian/diabetes educator visits ▪ Screen for barriers to diabetes self-management ▪ Refer or offer local resources and support as needed	✓ ✓ ✓	✓ ✓	✓ ✓ ✓
	Hypoglycemia ▪ Timing of episodes, awareness, frequency and causes	✓	✓	✓
	Pregnancy planning ▪ For women with childbearing capacity, review contraceptive needs and preconception planning	✓	✓	✓

		Initial	f/u	annual
PAST MEDICAL AND FAMILY HISTORY	**Diabetes history** ▪ Characteristics at onset (e.g., age, symptoms) ▪ Review of previous treatment regimens and response ▪ Assess frequency/cause/severity of past hospitalizations	✓ ✓ ✓		
	Family history ▪ Family history of diabetes in a first-degree relative ▪ Family history of autoimmune disorder	✓ ✓		
	Personal history of complications and common comorbidities ▪ Macrovascular and microvascular ▪ Common comorbidities ▪ Presence of hemoglobinopathies or anemias ▪ High blood pressure or abnormal lipids ▪ Last dental visit ▪ Last dilated eye exam ▪ Visits to specialists	✓ ✓ ✓ ✓ ✓ ✓ ✓	 ✓	 ✓ ✓ ✓
	Interval history ▪ Changes in medical/family history since last visit		✓	✓
SOCIAL HISTORY	**Assess lifestyle and behavior patterns** ▪ Eating patterns and weight history ▪ Sleep behaviors and physical activity ▪ Familiarity with carbohydrate counting in type 1 diabetes ▪ Tobacco, alcohol, and substance use ▪ Identify existing social supports	✓ ✓ ✓ ✓ ✓	✓ ✓	✓ ✓
	Interval history ▪ Changes in social history since last visit		✓	✓

		Initial	f/u	annual
MEDICATIONS AND VACCINATIONS	▪ Medication-taking behavior ▪ Medication intolerance or side effects ▪ Complementary and alternative medicine use ▪ Vaccination history and needs	✓ ✓ ✓ ✓	✓ ✓ ✓	✓ ✓ ✓ ✓
TECHNOLOGY USE	▪ Assess use of health apps, online education, patient portals, etc. ▪ Glucose monitoring (meter/CGM): results and data use ▪ Review insulin pump settings	✓ ✓ ✓	 ✓ ✓	✓ ✓ ✓
SCREENING	**Psychosocial conditions** ▪ Screen for depression, anxiety, and disordered eating; refer for further assessment or intervention if warranted ▪ Consider assessment for cognitive impairment*	✓ ✓		✓ ✓
	Diabetes self-management education and support ▪ History of dietitian/diabetes educator visits ▪ Screen for barriers to diabetes self-management ▪ Refer or offer local resources and support as needed	✓ ✓ ✓	✓ ✓	✓ ✓ ✓
	Hypoglycemia ▪ Timing of episodes, awareness, frequency and causes	✓	✓	✓
	Pregnancy planning ▪ For women with childbearing capacity, review contraceptive needs and preconception planning	✓	✓	✓

		INITIAL VISIT	EVERY FOLLOW-UP VISIT	ANNUAL VISIT
PHYSICAL EXAMINATION	▪ Height, weight, and BMI; growth/pubertal development in children and adolescents	✓	✓	✓
	▪ Blood pressure determination	✓	✓	✓
	▪ Orthostatic blood pressure measures (when indicated)	✓		
	▪ Fundoscopic examination (refer to eye specialist)	✓		✓
	▪ Thyroid palpation	✓		✓
	▪ Skin examination (e.g., acanthosis nigricans, insulin injection or insertion sites, lipodystrophy)	✓	✓	✓
	▪ Comprehensive foot examination			
	• Visual inspection (e.g., skin integrity, callous formation, foot deformity or ulcer, toenails)	✓	✓	✓
	• Screen for PAD (pedal pulses; refer for ABI if diminished)	✓		✓
	• Determination of temperature, vibration or pinprick sensation, and 10-g monofilament exam	✓		✓
LABORATORY EVALUATION	▪ A1C, if the results are not available within the past 3 months	✓	✓	✓
	▪ If not performed/available within the past year			
	• Lipid profile, including total, LDL, and HDL cholesterol and triglycerides#	✓		✓^
	• Liver function tests#	✓		✓
	• Spot urinary albumin-to-creatinine ratio	✓		✓
	• Serum creatinine and estimated glomerular filtration rate†	✓		✓
	• Thyroid-stimulating hormone in patients with type 1 diabetes#	✓		✓
	• Vitamin B12 if on metformin (when indicated)	✓		
	• Serum potassium levels in patients on ACE inhibitors, ARBs, or diuretics†	✓		✓

		Initial	f/u	annual
ASSESSMENT AND PLAN	**Goal setting**			
	▪ Set A1C/blood glucose target and monitoring frequency	✓	✓	✓
	▪ If hypertension diagnosed, establish blood pressure goal	✓		✓
	▪ Incorporate new members to the care team as needed	✓	✓	✓
	▪ Diabetes education and self-management support needs	✓	✓	✓
	Cardiovascular risk assessment and staging of CKD			
	▪ History of ASCVD	✓	✓	✓
	▪ Presence of ASCVD risk factors (see Table 9.2)	✓	✓	✓
	▪ Staging of CKD (see Table 10.1)†	✓	✓	✓
	Therapeutic treatment plan			
	▪ Lifestyle management	✓	✓	✓
	▪ Pharmacologic therapy	✓	✓	✓
	▪ Referrals to specialists (including dietitian and diabetes educator) as needed	✓	✓	✓
	▪ Use of glucose monitoring and insulin delivery devices	✓	✓	✓

ABI, ankle-brachial pressure index; ARBs, angiotensin receptor blockers; ASCVD, atherosclerotic cardiovascular disease; CGM, continuous glucose monitoring; CKD, chronic kidney disease; PAD, peripheral arterial disease.

*≥65 years;

†may be needed more frequently in patients with known chronic kidney disease or with changes in medications that affect kidney function and serum potassium (see Table 10.2);

#may also need to be checked after initiation or dose changes of medications that affect these laboratory values (i.e., diabetes medications, blood pressure medications, cholesterol medications, or thyroid medications);

^in people without dyslipidemia and not on cholesterol-lowering therapy, testing may be less frequent.

Comprehensive Medical Evaluation and Assessment of Comorbidities

Table 3.2—Referrals for initial care management

- Eye care professional for annual dilated eye exam
- Family planning for women of reproductive age
- Registered dietitian for MNT
- DSMES
- Dentist for comprehensive dental and periodontal examination
- Mental health professional, if indicated

2018 ADA Clinical Practice Recommendations

- Prevention or delay of type 2 Diabetes:
- At least annual monitoring for those with prediabetes
- Referral to an intensive lifestyle program
  - 7% body weight loss, 150 min/week physical activity
- Consider Metformin if BMI ≥ 35 kg/m^2, aged <60 yrs, prior GDM
- measure vitamin B12 in metformin-treated patients (anemia or peripheral neuropathy)
- Diabetes self-management education and support for patients with diabetes and prediabetes.

2018 ADA Clinical Practice Recommendations

- A1C:
  - At least 2 times per year in patients meeting targets and stable
  - Quarterly if not at target and/or unstable
  - Overall target of <7% in most non-pregnant adults remains.
    - More stringent (<6.5%): if no hypoglycemia or adverse effects of tx
    - Less stringent (<8%): history of hypoglycemia, limited life expectancy, advanced complications….
  - Premeal blood glucose target 80-130 mg/dL (4.4 – 7.2 mmol/L) rather than 70-130 mg/dL
  - Peak postprandial capillary plasma glucose < 180 mg/dL (<10.0 mmol/L)

2018 ADA Glycemic Control Targets

- Outpatient:
  - Targets for capillary plasma glucose (nonpregnant):
    - A1C: <7.0% (53 mmol/mol)
    - Before Meals: 80-130 mg/dL
    - Peak post prandial: <180 mg/dL
  - Targets for capillary plasma glucose (pregnant):
    - Preprandial: = or <95
    - 1h post meal:= or <140
    - 2h post meal:= or <120
- Inpatient:
  - Critically ill patients:
    - Plasma glucose 140-180 mg/dL
    - Plasma glucose 110-140 mg/dL in selected patients
  - Non critically ill patients:
    - Premeal < 140 mg/dL.
    - All random glucose <180 mg/dL
- IV preparations: No advantage of Lispro/Aspart over Regular insulin
- Hypoglycemia: ≤70 mg/dL (hypoglycemia alert value); < 54 mg/dL (clinically significant hypoglycemia)
- CGM recommendation

Glycated Hemoglobin Range

Most Intensive Level, Approximately 6.0%	Factors	Least Intensive Level, Approximately 8.0%
Highly motivated, adherent, knowledgeable, strong self-care capability	Psychosocial considerations	Less motivated, nonadherent, less knowledge, weak self-care capability
Adequate	Resources or support systems	Inadequate
Low	Risk of hypoglycemia	High
Short	Duration of type 2 diabetes	Long
Long	Life expectancy	Short
None	Microvascular disease	Advanced
None	Cardiovascular disease	Established
None	Coexisting conditions	Multiple, severe, or both

Faramarz IB. *Glycemic Management of Type 2 Diabetes Mellitus.* NEJM 2012;366(14)1319-1327

Approach to the Management of Hyperglycemia

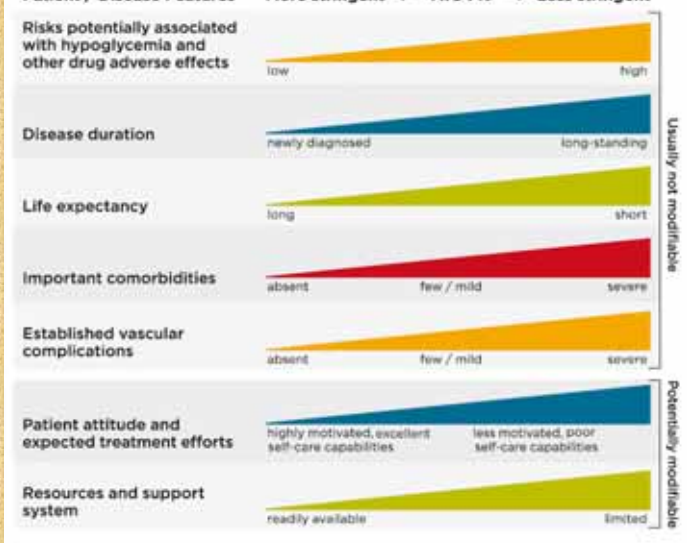


Figure 6.1—Depicted are patient and disease factors used to determine optimal A1C targets. Characteristics and predicaments toward the left justify more stringent efforts to lower A1C; those toward the right suggest less stringent efforts. Adapted with permission from Inzucchi et al. (72).

Standards of Diabetes Care 2018

2018 ADA Glycemic Control Targets

- Hypoglycemia: ≤70 mg/dL (hypoglycemia alert value); < 54 mg/dL (clinically significant hypoglycemia)

Table 6.3—Classification of hypoglycemia*

Level	Glycemic criteria	Description
Hypoglycemia alert value (level 1)	≤70 mg/dL (3.9 mmol/L)	Sufficiently low for treatment with fast-acting carbohydrate and dose adjustment of glucose-lowering therapy
Clinically significant hypoglycemia (level 2)	<54 mg/dL (3.0 mmol/L)	Sufficiently low to indicate serious, clinically important hypoglycemia
Severe hypoglycemia (level 3)	No specific glucose threshold	Hypoglycemia associated with severe cognitive impairment requiring external assistance for recovery

*Adapted from ref. 75.

2018 Obesity Management for T2DM treatment

- Obesity Management for Treatment of Type 2 Diabetes
- Weight loss > 5 %
- 500-750 kcal/day energy deficit
- Metabolic surgery :
- BMI ≥40 kg/m^2 (BMI ≥ 37.5 kg/m^2 in Asian Americans)
- BMI 35.0-39.9 kg/m^2 (32.5-37.4 kg/m^2 in Asian Americans)
- Consider in DM2, BMI 30-34.9 kg/m^2 (27.5-32.4 kg/m^2 in Asian Americans)

Table 7.1—Treatment options for overweight and obesity in type 2 diabetes

	BMI category (kg/m^2)				
Treatment	25.0–26.9 (or 23.0–26.9*)	27.0–29.9	30.0–34.9 (or 27.5–32.4*)	35.0–39.9 (or 32.5–37.4*)	≥40 (or ≥37.5*)
Diet, physical activity, and behavioral therapy	†	†	†	†	†
Pharmacotherapy		†	†	†	†
Metabolic surgery			†	†	†

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

2018 Obesity Management for T2DM treatment

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

Generic drug name (proprietary name(s)), dosage, strength, and form	Usual adult dosing frequency	Average wholesale price (per month)[a]	National Average Drug Acquisition Cost (per month)[a]	1-Year weight change status[b,c]		Adverse effects[d,e]	
				Average weight loss relative to placebo	% Patients with ≥5% loss of baseline weight	Common[f]	Serious[g]
Short-term treatment (a few weeks)							
Phentermine (Lomaira)	37.5 mg q.d. or 8 mg t.i.d.	$5–$76 (37.5 mg); $52 (8 mg)	$3–$60 (37.5 mg); Unavailable (8 mg)	N/A*	N/A*	Headache, elevated blood pressure, elevated heart rate, insomnia, dry mouth, constipation, anxiety, palpitations	Dyspnea, angina pectoris, syncope, severe hypertension
Long-term treatment (more than a few weeks)							
Lipase inhibitor							
Orlistat (AB) 60 mg caps or orlistat (Xenical) 120 mg caps	60 mg or 120 mg t.i.d. (during or up to 1 h after a low-fat meal)	$41–$2 (60 mg); $703 (120 mg)	$42 (60 mg); $556 (120 mg)	2.5 kg (60 mg); 3.4 kg (120 mg)	35–73%	Abdominal pain/ discomfort, oily spotting/ stool, fecal urgency, flatulence, malabsorption of fat soluble vitamins (A, D, E, K) and medications (e.g., cyclosporine, thyroid hormone replacement, or anticonvulsants), potentiation of the effects of warfarin	Liver failure and oxalate nephropathy
Selective serotonin (5-HT) 5-HT$_2$C receptor agonist							
Lorcaserin (Belviq) 10 mg tabs	10 mg b.i.d.	$289	$230	3.2 kg	38–48%	Hypoglycemia, headache, fatigue	Serotonin syndrome or NMS-like reactions, suicidal ideation, heart valve disorder (<2.4%), bradycardia
Lorcaserin (Belviq XR) 20 mg extended-release tabs	20 mg q.d.	$289	$231	3.2 kg	38–48%	Hypoglycemia, headache, fatigue	Serotonin syndrome or NMS-like reactions, suicidal ideation, heart valve disorder (<2.4%), bradycardia
Sympathomimetic amine anorectic/antiepileptic combination							
Phentermine/topiramate ER (Qsymia) 3.75 mg/ 23 mg caps, 7.5 mg/ 46 mg caps, 11.25 mg/ 69 mg caps, 15 mg/ 92 mg caps	Recommended dose: 3.75 mg/23 mg q.d. for 14 days, then increase to 7.5 mg/ 46 mg q.d. Maximum dose: 15 mg/92 mg q.d.	$239 (maximum dose using the highest strength)	$192 (maximum dose using the highest strength)	6.7 kg (7.5 mg/46 mg); 8.9 kg (15 mg/92 mg)	45–70%	Paresthesia, xerostomia, constipation, headache	Topiramate is teratogenic and has been associated with cleft lip/palate

2018 Obesity Management for T2DM treatment

Table 7.2—Continued

Generic drug name (proprietary name(s)), dosage, strength, and form	Usual adult dosing frequency	Average wholesale price (per month)[a]	National Average Drug Acquisition Cost (per month)[a]	1-Year weight change status[b,c]		Adverse effects[d,e]	
				Average weight loss relative to placebo	% Patients with ≥5% loss of baseline weight	Common[f]	Serious[g]
Opioid antagonist/aminoketone antidepressant combination							
Naltrexone/bupropion (Contrave) 8 mg/90 mg tabs	Maximum dose: two tablets of Contrave b.i.d. for a total daily dosage of naltrexone 32 mg/bupropion 360 mg	$290 (maximum dose)	$231 (maximum dose)	2.0–4.1 kg (32 mg/360 mg)	36–57%	Nausea, constipation, headache, vomiting	Depression, precipitation of mania, contraindicated in patients with a seizure disorder
Glucagon-like peptide 1 receptor agonist							
Liraglutide (Saxenda) 6 mg/mL prefilled pen	Maintenance dose: 3 mg s.c. q.d.	$1,385	$1,105	5.8–6.4 kg	51–73%	Hypoglycemia, nausea, vomiting, diarrhea, constipation, headache	Pancreatitis, thyroid C-cell tumors in rodents, contraindicated in patients with personal/ family history of MTC or MENE, acute renal failure

All medications are contraindicated in women who are or may become pregnant. Women in their reproductive years must be cautioned to use a reliable method of contraception. Caps, capsules; ER, extended release; MENE, multiple endocrine neoplasia type 2; MTC, medullary thyroid carcinoma; N/A, not applicable; NMS, neuroleptic malignant syndrome; s.c., subcutaneous; tabs, tablets. *Phentermine is FDA-approved as a short-term adjunct (a few weeks) in a regimen of weight reduction based on exercise, behavioral modification, and caloric restriction.

2018 Pharmacologic Approaches to Glycemic Treatment

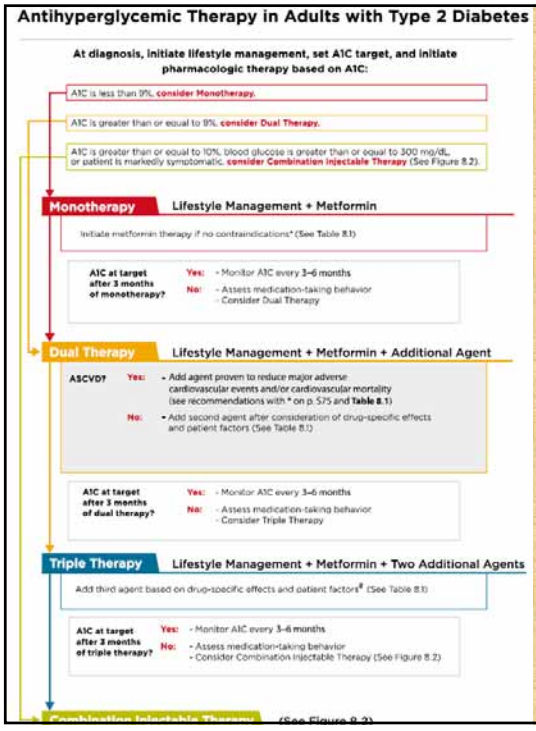


Figure 8.1—Antihyperglycemic therapy in type 2 diabetes: general recommendations. *If patient does not tolerate or has contraindications to metformin, consider agents from another class in Table 8.1.

GLP-1 receptor agonists and DPP-4 inhibitors should not be prescribed in combination. If a patient with ASCVD is not yet on an agent with evidence of cardiovascular risk reduction, consider adding.

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Table 8.1—Drug-specific and patient factors to consider when selecting antihyperglycemic treatment in adults with type 2 diabetes

		Efficacy*	Hypoglycemia	Weight Change	CV Effects		Cost	Oral/SQ	Renal Effects		Additional Considerations
					ASCVD	CHF			Progression of DKD	Dosing/Use considerations	
Metformin		High	No	Neutral (Potential for Modest Loss)	Potential Benefit	Neutral	Low	Oral	Neutral	• Contraindicated with eGFR <30	• Gastrointestinal side effects common (diarrhea, nausea) • Potential for B12 deficiency
SGLT-2 Inhibitors		Intermediate	No	Loss	Benefit: canagliflozin, empagliflozin[†]	Benefit: canagliflozin, empagliflozin	High	Oral	Benefit: canagliflozin, empagliflozin	[illegible]	[illegible]
GLP-1 RAs		High	No	Loss	Neutral: lixisenatide, exenatide extended release / Benefit: liraglutide[†]	Neutral	High	SQ	Benefit: liraglutide	[illegible]	[illegible]
DPP-4 Inhibitors		Intermediate	No	Neutral	Neutral	Potential Risk: saxagliptin, alogliptin	High	Oral	Neutral	[illegible]	• Potential risk of acute pancreatitis • Joint pain
Thiazolidinediones		High	No	Gain	Potential Benefit: pioglitazone	Increased Risk	Low	Oral	Neutral	[illegible]	[illegible]
Sulfonylureas (2nd Generation)		High	Yes	Gain	Neutral	Neutral	Low	Oral	Neutral	[illegible]	[illegible]
Insulin	Human Insulin	Highest	Yes	Gain	Neutral	Neutral	Low	SQ	Neutral	[illegible]	• Injection site reactions • [illegible]
	Analogs						High	SQ			

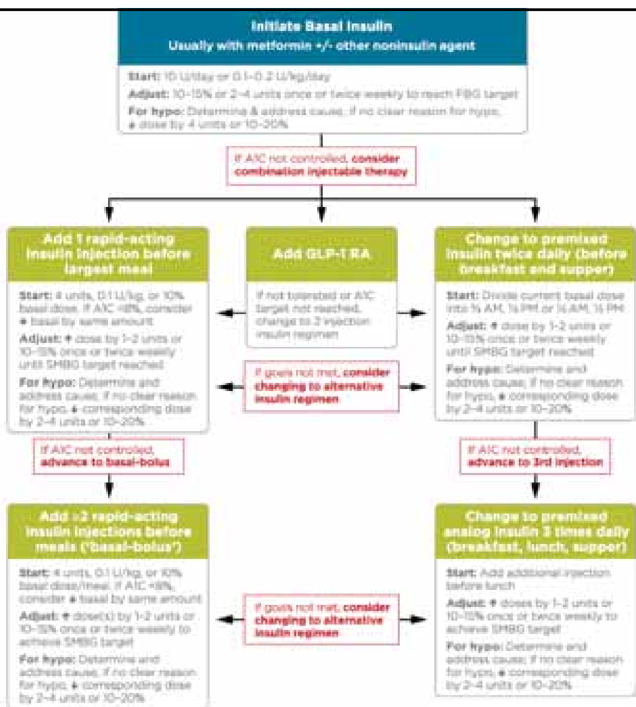
Initiate Basal Insulin
Usually with metformin +/- other noninsulin agent
Start: 10 U/day or 0.1–0.2 U/kg/day
Adjust: 10–15% or 2–4 units once or twice weekly to reach FBG target
For hypo: Determine & address cause; if no clear reason for hypo, ↓ dose by 4 units or 10–20%
If A1C not controlled, consider combination injectable therapy
Add 1 rapid-acting insulin injection before largest meal
Start: 4 units, 0.1 U/kg, or 10% basal dose. If A1C <8%, consider ↓ basal by same amount
Adjust: ↑ dose by 1–2 units or 10–15% once or twice weekly until SMBG target reached
For hypo: Determine and address cause; if no clear reason for hypo, ↓ corresponding dose by 2–4 units or 10–20%
Add GLP-1 RA
If not tolerated or A1C target not reached, change to 2 injection insulin regimen
If goals not met, consider changing to alternative insulin regimen
Change to premixed insulin twice daily (before breakfast and supper)
Start: Divide current basal dose into ⅔ AM, ⅓ PM or ½ AM, ½ PM
Adjust: ↑ dose by 1–2 units or 10–15% once or twice weekly until SMBG target reached
For hypo: Determine and address cause; if no clear reason for hypo, ↓ corresponding dose by 2–4 units or 10–20%
If A1C not controlled, advance to basal-bolus
If A1C not controlled, advance to 3rd injection
Add ≥2 rapid-acting insulin injections before meals ('basal-bolus')
Start: 4 units, 0.1 U/kg, or 10% basal dose/meal. If A1C <8%, consider ↓ basal by same amount
Adjust: ↑ dose(s) by 1–2 units or 10–15% once or twice weekly to achieve SMBG target
For hypo: Determine and address cause; if no clear reason for hypo, ↓ corresponding dose by 2–4 units or 10–20%
If goals not met, consider changing to alternative insulin regimen
Change to premixed analog insulin 3 times daily (breakfast, lunch, supper)
Start: Add additional injection before lunch
Adjust: ↑ doses by 1–2 units or 10–15% once or twice weekly to achieve SMBG target
For hypo: Determine and address cause; if no clear reason for hypo, ↓ corresponding dose by 2–4 units or 10–20%

Figure 8.2—Combination injectable therapy for type 2 diabetes. FBG, fasting blood glucose; hypo, hypoglycemia. Adapted with permission from Inzucchi et al. (31).

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2018 Pharmacologic Approaches to Glycemic Treatment

Table 8.2—Pharmacology of available glucose-lowering agents in the U.S. for the treatment of type 2 diabetes

Class	Compound(s)	Cellular mechanism(s)	Primary physiological action(s)	Renal dosing recommendations (63-66)*
Biguanides	• Metformin	Activates AMP kinase (? other)	↓ Hepatic glucose production	• No dose adjustment if eGFR >45; do not initiate OR assess risk/benefit if currently on metformin if eGFR 30–45; discontinue if eGFR <30
Sulfonylureas (2nd generation)	• Glyburide • Glipizide • Glimepiride	Closes K_{ATP} channels on β-cell plasma membranes	↑ Insulin secretion	• Avoid use in patients with renal impairment • Initiate conservatively at 2.5 mg daily to avoid hypoglycemia • Initiate conservatively at 1 mg daily to avoid hypoglycemia
Meglitinides (glinides)	• Repaglinide • Nateglinide	Closes K_{ATP} channels on β-cell plasma membranes	↑ Insulin secretion	• Initiate conservatively at 0.5 mg with meals if eGFR <30 • Initiate conservatively at 60 mg with meals if eGFR <30
Thiazolidinediones	• Pioglitazone • Rosiglitazone‖	Activates the nuclear transcription factor PPAR-γ	↑ Insulin sensitivity	• No dose adjustment required • No dose adjustment required
α-Glucosidase inhibitors	• Acarbose • Miglitol	Inhibits intestinal α-glucosidase	Slows intestinal carbohydrate digestion/absorption	• Avoid if eGFR <30 • Avoid if eGFR <25
DPP-4 inhibitors	• Sitagliptin	Inhibits DPP-4 activity, increasing postprandial incretin (GLP-1, GIP) concentrations	↑ Insulin secretion (glucose dependent); ↓ Glucagon secretion (glucose dependent)	• 100 mg daily if eGFR >50; 50 mg daily if eGFR 30–50; 25 mg daily if eGFR <30
	• Saxagliptin			• 5 mg daily if eGFR >50; 2.5 mg daily if eGFR ≤50
	• Linagliptin			• No dose adjustment required
	• Alogliptin			• 25 mg daily if eGFR >60; 12.5 mg daily if eGFR 30–60; 6.25 mg daily if eGFR <30
Bile acid sequestrants	• Colesevelam	Binds bile acids in intestinal tract, increasing hepatic bile acid production	? ↓ Hepatic glucose production; ? ↑ Incretin levels	• No specific dose adjustment recommended by manufacturer
Dopamine-2 agonists	• Bromocriptine (quick release)‖	Activates dopaminergic receptors	Modulates hypothalamic regulation of metabolism; ↑ Insulin sensitivity	• No specific dose adjustment recommended by manufacturer
SGLT2 inhibitors	• Canagliflozin	Inhibits SGLT2 in the proximal nephron	Blocks glucose reabsorption by the kidney, increasing glucosuria	• No dose adjustment required if eGFR ≥60; 100 mg daily if eGFR 45–59; avoid use and discontinue in patients with eGFR persistently <45
	• Dapagliflozin			• Avoid initiating if eGFR <60; not recommended with eGFR 30–60; contraindicated with eGFR <30
	• Empagliflozin			• Contraindicated with eGFR <30
GLP-1 receptor agonists	• Exenatide • Exenatide extended release	Activates GLP-1 receptors	↑ Insulin secretion (glucose dependent)	• Not recommended with eGFR <30 • Not recommended with eGFR <30

Continued on p. S80

2018 Pharmacologic Approaches to Glycemic Treatment

Table 8.2—Continued

Class	Compound(s)	Cellular mechanism(s)	Primary physiological action(s)	Renal dosing recommendations (63-66)*
	• Liraglutide		↓ Glucagon secretion (glucose dependent); Slows gastric emptying; ↑ Satiety	• No specific dose adjustment recommended by the manufacturer; limited experience in patients with severe renal impairment
	• Albiglutide			• No dose adjustment required for eGFR 15–89 per manufacturer; limited experience in patients with severe renal impairment
	• Lixisenatide			• No dose adjustment required for eGFR 60–89; no dose adjustment required for eGFR 30–59, but patients should be monitored for adverse effects and changes in kidney function; clinical experience is limited with eGFR 15–29; patients should be monitored for adverse effects and changes in kidney function; avoid if eGFR <15
	• Dulaglutide			• No specific dose adjustment recommended by the manufacturer; limited experience in patients with severe renal impairment
Amylin mimetics	• Pramlintide‖	Activates amylin receptors	↓ Glucagon secretion; Slows gastric emptying; ↑ Satiety	• No specific dose adjustment recommended by manufacturer
Insulins	• Rapid-acting analogs Lispro Aspart Glulisine Inhaled insulin	Activates insulin receptors	↑ Glucose disposal; ↓ Hepatic glucose production; Suppresses ketogenesis	• Lower insulin doses required with a decrease in eGFR; titrate per clinical response
	• Short-acting analogs Human Regular			
	• Intermediate-acting analogs Human NPH			
	• Basal insulin analogs Glargine Detemir Degludec			
	• Premixed insulin products NPH/Regular 70/30 70/30 aspart mix 75/25 lispro mix 50/50 lispro mix			

*eGFR is given in mL/min/1.73 m^2. ‖Not licensed in Europe for type 2 diabetes. GIP, glucose-dependent insulinotropic peptide; PPAR-γ, peroxisome proliferator–activated receptor γ.

Table 8.3—Median monthly cost of maximum approved daily dose of noninsulin glucose-lowering agents in the U.S.

Class	Compound(s)	Dosage strength/product (if applicable)	Median AWP (min, max)*	Median NADAC (min, max)*	Maximum approved daily dose*
Biguanides	• Metformin	500 mg (IR)	$84 ($4, $93)	$2	2,000 mg
		850 mg (IR)	$108 ($6, $109)	$3	2,550 mg
		1,000 mg (IR)	$87 ($4, $88)	$2	2,000 mg
		500 mg (ER)	$89 ($82, $6,671)	$5 ($5, $3,630)	2,000 mg
		750 mg (ER)	$72 ($65, $92)	$5	1,500 mg
		1,000 mg (ER)	$1,028 ($1,028, $7,214)	$5.39 ($5.39, $5,189)	2,000 mg
Sulfonylureas (2nd generation)	• Glyburide	5 mg	$93 ($63, $103)	$17	20 mg
		6 mg (micronized)	$50 ($48, $71)	$12	12 mg (micronized)
	• Glipizide	10 mg (IR)	$75 ($67, $97)	$4	40 mg (IR)
		10 mg (XL)	$48	$16	20 mg (XL)
	• Glimepiride	4 mg	$71 ($71, $198)	$7	8 mg
Meglitinides (glinides)	• Repaglinide	2 mg	$659 ($122, $673)	$40	16 mg
	• Nateglinide	120 mg	$155	$56	360 mg
Thiazolidinediones	• Pioglitazone	45 mg	$348 ($283, $349)	$5	45 mg
	• Rosiglitazone	4 mg	$387	$314	8 mg
α-Glucosidase inhibitors	• Acarbose	100 mg	$104 ($104, $106)	$25	300 mg
	• Miglitol	100 mg	$241	N/A††	300 mg
DPP-4 inhibitors	• Sitagliptin	100 mg	$477	$382	100 mg
	• Saxagliptin	5 mg	$462	$370	5 mg
	• Linagliptin	5 mg	$457	$367	5 mg
	• Alogliptin	25 mg	$448	$357	25 mg
Bile acid sequestrants	• Colesevelam	625 mg tabs	$713	$570	3.75 g
		1.875 g suspension	$1,426	$572	3.75 g
Dopamine-2 agonists	• Bromocriptine	0.8 mg	$784	$629	4.8 mg
SGLT2 inhibitors	• Canagliflozin	300 mg	$512	$411	300 mg
	• Dapagliflozin	10 mg	$517	$413	10 mg
	• Empagliflozin	25 mg	$517	$415	25 mg
GLP-1 receptor agonists	• Exenatide	10 μg pen	$802	$642	20 μg
	• Lixisenatide	20 μg pen	$669	N/A††	20 μg
	• Liraglutide	18 mg/3 mL pen	$968	$775	1.8 mg
	• Exenatide (extended release)	2 mg powder for suspension or pen	$747	$600	2 mg**
	• Albiglutide	50 mg pen	$626	$500	50 mg**
	• Dulaglutide	1.5/0.5 mL pen	$811	$648	1.5 mg**
Amylin mimetics	• Pramlintide	120 μg pen	$2,336	N/A††	120 μg/injection†††

ER and XL, extended release; IR, immediate release. *Calculated for 30-day supply (AWP or NADAC unit price × number of doses required to provide maximum approved daily dose × 30 days); median AWP or NADAC listed alone when only one product and/or price. †Utilized to calculate median AWP and NADAC (min, max); generic prices used, if available commercially. ††Not applicable; data not available. **Administered once weekly. †††AWP and NADAC calculated based on 120 μg three times daily.

Table 8.4—Median cost of insulin products in the U.S. calculated as AWP (39) and NADAC (40) per 1,000 units of specified dosage form/product

Insulins	Compounds	Dosage form/product	Median AWP (min, max)*	Median NADAC (min, max)*
Rapid-acting analogs	• Lispro	U-100 vial;	$330	$264
		U-100 3 mL cartridges;	$408	$326
		U-100 prefilled pen; U-200 prefilled pen	$424	$339
	• Aspart	U-100 vial;	$331	$265
		U-100 3 mL cartridges;	$410	$330
		U-100 prefilled pen	$426	$341
	• Glulisine	U-100 vial;	$306	$245
		U-100 prefilled pen	$394	$315
	• Inhaled insulin	Inhalation cartridges	$725 ($544, $911)	N/A†
Short-acting analogs	• Human Regular	U-100 vial	$165 ($165, $178)	$135 ($135, $145)
Intermediate-acting analogs	• Human NPH	U-100 vial;	$165 ($165, $178)	$135 ($135, $145)
		U-100 prefilled pen	$377	$305
Concentrated Human Regular insulin	• U-500 Human Regular insulin	U-500 vial;	$178	$143
		U-500 prefilled pen	$230	$184
Basal analogs	• Glargine	U-100 vial; U-100 prefilled pen; U-300 prefilled pen	$298	$239 ($239, $241)
	• Glargine biosimilar	U-100 prefilled pen	$253	$203
	• Detemir	U-100 vial; U-100 prefilled pen	$323	$259
	• Degludec	U-100 prefilled pen; U-200 prefilled pen	$355	$285
Premixed insulin products	• NPH/Regular 70/30	U-100 vial;	$165 ($165, $178)	$134 ($134, $146)
		U-100 prefilled pen	$377	$305
	• Lispro 50/50	U-100 vial;	$342	$278
		U-100 prefilled pen	$424	$339
	• Lispro 75/25	U-100 vial;	$342	$273
		U-100 prefilled pen	$424	$340
	• Aspart 70/30	U-100 vial;	$343	$275
		U-100 prefilled pen	$426	$341
Premixed insulin/GLP-1 receptor agonist products	• Degludec/Liraglutide	100/3.6 prefilled pen	$763	N/A†
	• Glargine/Lixisenatide	100/33 prefilled pen	$508	$404

*AWP or NADAC calculated as in **Table 8.3**; median listed alone when only one product and/or price. †Not applicable; data not available.

2018 Cardiovascular Disease and Risk Management

Table 9.1—Randomized controlled trials of intensive versus standard hypertension treatment strategies

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

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

2018 Cardiovascular Disease and Risk Management

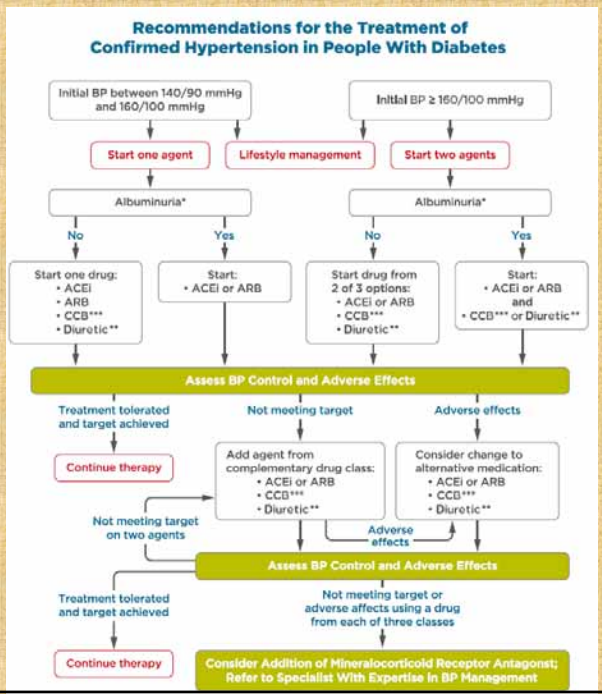

Figure 9.1—Recommendations for the treatment of confirmed hypertension in peoplewith diabetes. *An ACE inhibitor (ACEi) or ARB is suggested to treat hypertension for patients with UACR 30–299 mg/g creatinine and strongly recommended for patients with UACR ≥ 300 mg/g creatinine. **Thiazide-like diuretic; long-acting agents shown to reduce cardiovascular events, such as chlorthalidone and indapamide, are preferred. ***Dihydropyridine calcium channel blocker. BP, blood pressure. This figure can also be found in the ADA position statement "Diabetes and Hypertension" (5).

2018 Cardiovascular Disease and Risk Management

Table 9.2—Recommendations for statin and combination treatment in adults with diabetes

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

*In addition to lifestyle therapy. ^For patients who do not tolerate the intended intensity of statin, the maximally tolerated statin dose should be used. †Moderate-intensity statin may be considered based on risk-benefit profile and presence of ASCVD risk factors. ASCVD risk factors include LDL cholesterol ≥100 mg/dL (2.6 mmol/L), high blood pressure, smoking, chronic kidney disease, albuminuria, and family history of premature ASCVD. ‡High-intensity statin may be considered based on risk-benefit profile and presence of ASCVD risk factors. #Adults aged <40 years with prevalent ASCVD were not well represented in clinical trials of non-statin–based LDL reduction. Before initiating combination lipid-lowering therapy, consider the potential for further ASCVD risk reduction, drug-specific adverse effects, and patient preferences.

2018 Cardiovascular Disease and Risk Management

Table 9.3—High-intensity and moderate-intensity statin therapy*

High-intensity statin therapy (lowers LDL cholesterol by ≥50%)	Moderate-intensity statin therapy (lowers LDL cholesterol by 30% to 50%)
Atorvastatin 40–80 mg	Atorvastatin 10–20 mg
Rosuvastatin 20–40 mg	Rosuvastatin 5–10 mg
	Simvastatin 20–40 mg
	Pravastatin 40–80 mg
	Lovastatin 40 mg
	Fluvastatin XL 80 mg
	Pitavastatin 2–4 mg

*Once-daily dosing. XL, extended release.

2018 Microvascular Complications and Foot Care

- Most frequent cause of amputations in U.S.
- Risk is increased in patients with:
  - Diabetes > 10 yrs and poor control
  - Male
  - CV, retinal, renal, neuropathic, PVD complications
  - Increased pressure under a callus
  - Bone deformity
  - History of ulcer or amputation
  - Severe nail pathology
- Recommendations:
  - Foot inspection at every visit with pedal pulses.
    - Monofilament test, temperature, vibratory senses, ABI
    - At least one test annually; >1 test 87% sensitivity
    - Consider referral to a foot specialist
  - Consider cardiovascular autonomic neuropathy:
    - Resting tachycardia
    - Orthostasis (SBP falls >20 mm w/out appropriate HR response)

2018 Microvascular Complications and Foot Care

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

CKD stage†			Focus of kidney-related care			
Stage	eGFR (mL/min/1.73 m^2)	Evidence of kidney damage*	Diagnose cause of kidney injury	Evaluate and treat risk factors for CKD progression**	Evaluate and treat CKD complications***	Prepare for renal replacement therapy
No clinical evidence of CKD	≥60	—				
1	≥90	+	√	√		
2	60–89	+	√	√		
3	30–59	+/−	√	√	√	
4	15–29	+/−		√	√	√
5	<15	+/−			√	√

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

2018 ADA Screening for Diabetic Retinopathy

- Most frequent cause of blindness age 20-74
- *During pregnancy and 1 year post partum retinopathy may be transiently aggravated*; laser photocoagulation surgery can minimize this risk
- Screening recommendations:
  - DM1: 3-5 years after diagnosis in adults
  - DM2: at diagnosis and annually. Less frequent exams may be considered with the advice of an eye care professional in the setting of a normal examination
  - When planning pregnancy, refer for an exam and counsel on the risk of development/progression of disease
  - Laser photocoagulation surgery is beneficial in reducing the risk of further vision loss but ***not*** for reversal
  - Vascular Endothelial Growth Factor Antibody is effective and should be considered for diabetic macular edema

2018 ADA Screening for Diabetic Nephropathy

Category	Spot Collection (mcg/mg Cr)
Normal	<30
Increased urine albumin excretion	≥30

(1) *2 of 3 specimens within 3-6 month period*
False positives occur with infection, exercise within 24h, fever, CHF, hyperglycemia or marked HTN

(2) Early referral to a nephrologist is cost effective, delays dialysis; always refer if GFR<30

(3) Annual check in DM1 >5 yrs; annually in all DM2 and during gestation

(4) Once albuminuria occurs; ESRD in 50% of DM1 by 10 yrs; 20% of DM2 in 20 yrs (NO TX)

(5) Protein restriction to <0.8-1.0 g/kg/d in CKD

Table 11.1—Framework for considering treatment goals for glycemia, blood pressure, and dyslipidemia in older adults with diabetes (2)

Patient characteristics/health status	Rationale	Reasonable A1C goal§	Fasting or preprandial glucose	Bedtime glucose	Blood pressure	Lipids
Healthy (few coexisting chronic illnesses, intact cognitive and functional status)	Longer remaining life expectancy	<7.5% (58 mmol/mol)	90–130 mg/dL (5.0–7.2 mmol/L)	90–150 mg/dL (5.0–8.3 mmol/L)	<140/90 mmHg	Statin unless contraindicated or not tolerated
Complex/intermediate (multiple coexisting chronic illnesses* or 2+ instrumental ADL impairments or mild-to-moderate cognitive impairment)	Intermediate remaining life expectancy, high treatment burden, hypoglycemia vulnerability, fall risk	<8.0% (64 mmol/mol)	90–150 mg/dL (5.0–8.3 mmol/L)	100–180 mg/dL (5.6–10.0 mmol/L)	<140/90 mmHg	Statin unless contraindicated or not tolerated
Very complex/poor health (LTC or end-stage chronic illnesses** or moderate-to-severe cognitive impairment or 2+ ADL dependencies)	Limited remaining life expectancy makes benefit uncertain	<8.5%† (69 mmol/mol)	100–180 mg/dL (5.6–10.0 mmol/L)	110–200 mg/dL (6.1–11.1 mmol/L)	<150/90 mmHg	Consider likelihood of benefit with statin (secondary prevention more so than primary)

This represents a consensus framework for considering treatment goals for glycemia, blood pressure, and dyslipidemia in older adults with diabetes. The patient characteristic categories are general concepts. Not every patient will clearly fall into a particular category. Consideration of patient and caregiver preferences is an important aspect of treatment individualization. Additionally, a patient's health status and preferences may change over time. ADL, activities of daily living. §A lower A1C goal may be set for an individual if achievable without recurrent or severe hypoglycemia or undue treatment burden. *Coexisting chronic illnesses are conditions serious enough to require medications or lifestyle management and may include arthritis, cancer, congestive heart failure, depression, emphysema, falls, hypertension, incontinence, stage 3 or worse chronic kidney disease, myocardial infarction, and stroke. By "multiple," we mean at least three, but many patients may have five or more (47). **The presence of a single end-stage chronic illness, such as stage 3–4 congestive heart failure or oxygen-dependent lung disease, chronic kidney disease requiring dialysis, or uncontrolled metastatic cancer, may cause significant symptoms or impairment of functional status and significantly reduce life expectancy. †A1C of 8.5% (69 mmol/mol) equates to an estimated average glucose of ~200 mg/dL (11.1 mmol/L). Looser A1C targets above 8.5% (69 mmol/mol) are not recommended as they may expose patients to more frequent higher glucose values and the acute risks from glycosuria, dehydration, hyperglycemic hyperosmolar syndrome, and poor wound healing.

2018 ADA Clinical Practice Recommendations

- Medical Nutrition Therapy:
  - If IGT, IFG, or diabetes, refer
  - Carbohydrate, fat and protein counting
  - Individualized eating plans

- Energy balance, overweight, and obesity:
  - Low carb, high protein, low fat, or Mediterranean diet
  - Saturated fat <7% of overall calories
  - Avoid trans fat intake and increase dietary fiber 14g/Kcal
  - Moderate alcohol (1 drink/d for adult women, no more than 2 drinks/d for adult men)
  - Sodium consumption < 2,300 mg/d
  - Nonnutritional sweeteners are generally safe within limits.

2018 ADA Clinical Practice Recommendations

- Advise no cigarette, or tobacco products, or e-cigarette use.
- Immunization:
  - HBV in ages 19-59yo; consider in those >60yo
  - Annual influenza (patients ≥ 6 months old)
  - Pneumococcal polysaccharide vaccine (PPSV23) age 2-64 yrs
  - > 65 yrs, pneumococcal conjugate vaccine (PCV13), followed by PPSV23
- Hypertension:
  - Lifestyle modification trial (no longer than 3 months)
  - Goal <140/90; <130/80 for certain individuals
  - In pregnant patients: range target 110-129/65-79

2018 ADA Clinical Practice Recommendations

- Antiplatelet agents:
  - Aspirin 75-162 mg/day in DM1 and DM2 with Framingham risk >10% over 10 years (most men and women ≥50)
  - Do not provide ASA to those with Framingham risk <5%
  - 5-10%: clinical judgment
  - Use clopidogrel in lieu of aspirin if allergy exists
- Coronary artery disease screening:
  - In asymptomatic patients routine screening is not recommended.

Table 9.1—Recommendations for statin and combination treatment in people with diabetes

Age	Risk factors	Recommended statin intensity*
<40 years	None	None
	ASCVD risk factor(s)**	Moderate or high
	ASCVD	High
40–75 years	None	Moderate
	ASCVD risk factors	High
	ASCVD	High
	ACS and LDL cholesterol ≥50 mg/dL (1.3 mmol/L) or in patients with a history of ASCVD who cannot tolerate high-dose statins	Moderate plus ezetimibe
>75 years	None	Moderate
	ASCVD risk factors	Moderate or high
	ASCVD	High
	ACS and LDL cholesterol ≥50 mg/dL (1.3 mmol/L) or in patients with a history of ASCVD who cannot tolerate high-dose statins	Moderate plus ezetimibe

*In addition to lifestyle therapy. **ASCVD risk factors include LDL cholesterol ≥100 mg/dL (2.6 mmol/L), high blood pressure, smoking, chronic kidney disease, albuminuria, and family history of premature ASCVD.

Table 9.2—High-intensity and moderate-intensity statin therapy*

High-intensity statin therapy (lowers LDL cholesterol by ≥50%)	Moderate-intensity statin therapy (lowers LDL cholesterol by 30% to <50%)
Atorvastatin 40–80 mg	Atorvastatin 10–20 mg
Rosuvastatin 20–40 mg	Rosuvastatin 5–10 mg
	Simvastatin 20–40 mg
	Pravastatin 40–80 mg
	Lovastatin 40 mg
	Fluvastatin XL 80 mg
	Pitavastatin 2–4 mg

*Once-daily dosing. XL, extended release.

2018 ADA Preconception Care

- 2/3 of pregnancies in diabetics are unplanned
- Risk of malformations increases with increasing hyperglycemia during first 6-8 weeks of gestation
- Risk appears limited to pregnancies in which first trimester A1C > 1% above normal range
- Drug categories:
  - Statins (category X; discontinue if pregnant or planning)
  - ACE/ARB (category C in 1st trimester and D later)
  - Metformin, glyburide, and acarbose (category B)
  - *If in doubt, discontinue all medications (use insulin)*
- Recommendations:
  - A1C as close to normal as possible (< 7%) and treat for complications (retinopathy, nephrop, neurop)
  - Education and family planning (DOCUMENT)
  - Pre prandial glucose 80-110; 2h after meals <155 mg/dL

2018 ADA Glycemic Control: Special Population Considerations

- **Gestational Diabetes**:
  - FDA approved Category B (metformin/acarbose)
  - Targets:
    - Fasting: 70-95 Before meals: 70-105
    - 1h PP 70-140 2h PP 70-120

  - checkup 4-12 weeks postpartum
- **Care of older adults with diabetes**
  - >20% of all diabetics are > 65yo; *No long term studies documenting benefits*
  - Increased risk of hypoglycemia!
  - Life expectancy >10yrs? Use goals for younger adults
- **Care of children and adolescents**
  - Family and daycare provider education!
  - Statins indicated in age>10 if LDL >160 or >130 w/ risk factors

2018 ADA Physical Activity, Exercise and Diabetes

- Exercise recommendations:
  - 150 minutes/week moderate intensity or 75 minutes/week vigorous exercise
  - Resistance training 3 days/week
    - Very effective for insulin resistance in all diabetics
    - May be more effective than aerobic exercise in the elderly
  - No more than 2 days/wk without exercise
- Screening for CVD prior to initiation of Exercise:
  - Not in the asymptomatic patient without other indications
  - No increased risk of an event in asymptomatic patient
  - No evidence that screening asymptomatic patients will result in improved outcomes
  - Monitor glucose before and after activity
  - Carbohydrates should be available before and after

Diabetes Care in the Hospital

- Perform an A1c on all patients with diabetes or hyperglycemia (BG>140 mg/dL) admitted to the hospital if not performed in the prior 3 months.
- Critically ill and noncritically ill patients: target BG 140-180 mg/dL
- More stringent target BG 110-140 mg/dL – for selected patients (w/o hypoglycemia).
- Insulin regimen: basal + bolus correction
- Hypoglycemia management protocol

Diabetes Care in the Hospital

Table 14.1—Insulin dosing for enteral/parenteral feedings

Situation	Basal/nutritional	Correctional
Continuous enteral feedings	Continue prior basal or, if none, calculate from TDD or consider 5 units NPH/detemir every 12 h or 10 units glargine/degludec daily Nutritional: regular insulin every 6 h or rapid-acting insulin every 4 h, starting with 1 unit per 10–15 g of carbohydrate; adjust daily	SQ regular insulin every 6 h or rapid-acting insulin every 4 h for hyperglycemia
Bolus enteral feedings	Continue prior basal or, if none, calculate from TDD or consider 5 units NPH/detemir every 12 h or 10 units glargine/degludec daily Nutritional: give regular insulin or rapid-acting insulin SQ before each feeding, starting with 1 unit per 10–15 g of carbohydrate; adjust daily	SQ regular insulin every 6 h or rapid-acting insulin every 4 h for hyperglycemia
Parenteral feedings	Add regular insulin to TPN IV solution, starting with 1 unit per 10 g of carbohydrate; adjust daily	SQ regular insulin every 6 h or rapid-acting insulin every 4 h for hyperglycemia

IV, intravenous; SQ, subcutaneous; TDD, total daily dose; TPN, total parenteral nutrition.

Common Mistakes in Therapy

- Starting pharmacologic therapy too late
- Not titrating medications aggressively enough
- Hesitation to step-up therapy (clinical inertia)
  - Beta cell failure is the natural progression of type 2 diabetes
- Not initiating insulin therapy early enough
  - Most oral agents decrease A1C by 1.5 – 2%
  - Insulin can decrease A1C by > 2%
  - Insulin is the most effective and most titratable medication
- “Threatening” patient with insulin

When Goals Are Not Met

- Assessment of barriers
  - Income, health literacy, depression, competing demands including family responsibilities and dynamics
- Culturally appropriate diabetes self medication administ
- Co-management with a diabetes team
- Referral to social worker
- Change/simplify therapy
- Revise goals
- Initiate or increase frequency of SMBG
- Frequent contact with the patient
- Referral to mental health
- Provide algorithm for self-titration of insulin doses

Appropriate Referral to Endocrinology

- Type 1 diabetes if PCM is not comfortable with management
- Insulin Pump use or consideration
- Marked insulin resistance
- Contraindications or intolerances to medications typically used in managing diabetes
- Recurrent episodes of incapacitating hypo- and/or hyperglycemia
- Poor recognition of hypoglycemia and who have a history of severe hypoglycemic reactions (including coma, seizures, or frequent need for emergency resuscitation)
- Not achieving glycemic control despite comprehensive treatment with complex regimen of combination pharmacotherapy including insulin
- Require evaluation or management beyond the level of expertise and resource level of the MHP team (consider referral to another provider within your MHP first)

- **Questions** ?!