Piedmont WellStar HealthPlans, Inc.
ADULT DIABETES CLINICAL GUIDELINE

Relevance to Population

Diabetes is a serious, costly disease with rapidly rising prevalence. It remains the 7th leading cause of death for U.S. Residents. In 2012, an American Diabetes Association (ADA) scientific statement estimated there were 22.3 million people in the U.S. with a diagnosis of diabetes (7% of the population).[1] This was higher than the U.S. Department of Health and Human Services (HHS) estimate in 2010, which reported 18.8 million people diagnosed with diabetes and another 7 million undiagnosed. A total of 1.9 million new cases of diabetes were diagnosed in people aged 20 years or older in 2010. The incidence is rising disproportionately in children, particularly in the high-risk ethnic populations. Under the age of 20, approximately 215,000 children and adolescents have type 1 or type 2 diabetes representing 0.26% of the population in this age group. Diabetes is the leading cause of kidney failure, lower-limb amputations and new cases of blindness among adults in the United States. It is also a major contributor to heart disease and stroke. After adjusting for age and sex, medical expenses for people with diabetes are 2.3 times higher than for people without diabetes.[1] Uncontrolled diabetes or diabetes with complications especially increases costs, estimated at 2 – 8 times more than people with controlled diabetes and those without advanced end-organ disease.2,3 ADA research estimates that the total costs of diagnosed diabetes have risen 41% in five years, from $174 billion in 2007 to $245 billion in 2012.1

The Coach on Call Program focuses on education for providers and members to empower them to take control of their disease and improve their quality of life. People with diabetes should receive medical care from a physician-coordinated team that may include, but is not limited to, physicians, nurses, dietitians, pharmacists, and behavioral health professionals.

Population Covered by Guideline

All adult members age 18 and over with Diabetes Mellitus.

Clinical Indicators Measured by Piedmont WellStar HealthPlans, Inc.

- Screening for diabetic retinal eye disease with a dilated retinal eye exam in the measurement year HEDIS®
- Screening for diabetic nephropathy in the measurement year -HEDIS®
- Screening for HbA1c during the measurement year - HEDIS®
- Screening for LDL-C during the measurement year -HEDIS®
- Screening for blood pressure control during the measurement year -HEDIS®

Definition

Diabetes mellitus is a group of metabolic diseases characterized by high blood glucose levels, which result from defects in insulin secretion, insulin action, or both.

Classification of Diabetes Mellitus

- Type 1 diabetes – results from β-cell destruction, usually leading to absolute insulin deficiency*
- Type 2 diabetes – results from progressive defects in insulin secretion and insulin resistance*
- Gestational diabetes (GDM) – any degree of glucose intolerance with onset or first recognition during pregnancy
- Other specific type of diabetes – due to other causes, e.g., genetic defects in β-cell function or insulin action, exocrine pancreatic diseases, endocrinopathies, drug- or chemical-induced (such as drugs for HIV/AIDS or post-organ transplant), certain viruses, other genetic syndromes [4]

**Occasionally diagnosis of type 1 or 2 is not clear. Type 1 can progress slowly; type 2 can present with ketoacidosis. Absence of metabolic syndrome, low C-peptide, & presence of pancreatic autoantibodies*

suggest type 1 diabetes.

Diabetes Management

The current American Diabetes Association (ADA) Clinical Practice Recommendations 2103 is available at http://care.diabetesjournals.org/content/36/Supplement_1.toc

Goals of Diabetes Management

Maintain laboratory and clinical targets and prevent complications of diabetes.

Blood glucose levels:

- Non-pregnant adults:
  - Preprandial: 70-130 mg/dL
  - Peak postprandial (1-2 hours after beginning a meal): 180 mg/dL
  - Bedtime: 100–140 mg/dL
- Pregnant women with type 1 or type 2 diabetes:
  - Preprandial, bedtime and overnight glucose: 60-99 mg/dL
  - Peak postprandial: 100-129 mg/dL

HbA1c (A1C):

- Non-pregnant adults: < 7.0% (the goal may be individualized to meet a Patient's needs)
- Women who are pregnant with type 1 or type 2 diabetes: <

- 6.0% LDL: < 100 mg/dl
- HDL: > 40 mg/dl in men and > 50 mg/dl in women
- Triglycerides: < 150 mg/dl
- Urinary albumin excretion: < 30µg/mg creatinine for spot collection or 24-hr collection; <20µg/min timed collection
- Serum creatinine: 0.6–1.2 mg/dl (values are laboratory
- dependent) Blood pressure:
  - Non-pregnant adults: <140/80 - Lower systolic targets (such as <130 mmHg) may be appropriate for certain individuals, if it can be achieved without undue treatment burden.[5,6,7]
  - Pregnant adults: Target goals 110-129 mmHg systolic and 65-79 mmHg diastolic

Recommended Screening Tests for Diabetes

- A1C testing by a laboratory using a method that is NGSP certified and standardized to the DCCT assay:
  - Advantages include no fasting and more stability with less day-to-day variation from stress and illness
  - Point of care A1C assays not sufficiently accurate at this time to use for diagnostic purposes

-OR-

- Fasting plasma glucose (FPG) *fasting is defined as no caloric intake for at least 8 hours*

-OR-

- Two hour Oral Glucose Tolerance Test (OGTT): using a glucose load containing the equivalent of 75g anhydrous glucose dissolved in water

Screening Criteria for Diabetes

- Screening for diabetes should begin routinely at the age of 45
- Screening should be considered, at any age, in overweight adults, i.e., body mass index (BMI) ≥ 25 kg/m^2 with one or more of the following risk factors:
  - Physically inactive
  - First degree relative with diabetes

- High-risk ethnicity (*e.g., African-American, Latino, Native American, Asian American, Pacific Islander*)
- Women who were diagnosed with GDM or delivered a baby weighing > 9 lbs
- Women with polycystic ovary syndrome (PCOS)
- Hypertension: ≥ 140/90 or on therapy for hypertension
- HDL < 35mg/dL and/or triglyceride level > 250 mg/dl
- Previous A1C ≥ 5.7%, impaired glucose tolerance (IGT) or impaired fasting glucose (IFG)
- Insulin resistance associated conditions (e.g., severe obesity, acanthosis nigricans)
- History of CVD

- If screening results are normal, testing should be repeated at a minimum of 3-year intervals
- Screening in people with pre-diabetes should be repeated yearly (for the ADA definition of pre-diabetes, refer below under "Criteria for Diagnosis of diabetes and pre-diabetes")
- Screening for GDM in pregnant women:
  - Screen at first prenatal visit in those with risk factors using standard diagnostic criteria (two abnormal tests confirm overt diabetes, not GDM)
  - Screen routinely for GDM at 24-28 weeks using the 75gm 2hr-OGTT using modified criteria for pregnancy (one abnormal test confirms GDM):
    - Fasting glucose: ≥ 92 mg/dL
    - 1 hour post 75 gm glucose: ≥ 180 mg/dL
    - 2 hour post 75 gm glucose: ≥ 153 mg/dL
  - Women diagnosed with GDM should be screened 6-12 weeks post-partum using the 75gm 2-hr OGTT and standard diagnostic criteria; if negative, they should have conventional screening every 3 years

Criteria for Diagnosis of Diabetes and Pre-diabetes

- Diagnosis of Diabetes*
  - A1C:** ≥ 6.5%
  - FPG: ≥ 126 mg/dl (7 mmol/l)
  - Two hour glucose during an oral OGTT: ≥ 200 mg/dl (11.1 mmol/l)
  - Random plasma glucose (PG): ≥ 200 mg/dl (11.1 mmol/l) with classic symptoms of hyperglycemia (polyuria, polydipsia, unexplained weight loss) or hyperglycemic crisis

  **Confirm abnormal results with repeat testing on a different day, unless there is symptomatic hyperglycemia*

  ***A1C is inaccurate with certain anemias and hemoglobinopathies. A1C assays without hemoglobin interference may be requested for Sickle Cell trait. For hemoglobinopathies and anemias with high RBC turnover, or following blood transfusions, it may be necessary to use glucose criteria exclusively for diagnosis and treatment.*
- Diagnosis of Pre-diabetes (ADA criteria)
  - A1C: 5.7–6.4%
  - FPG: 100–125 mg/dl (5.6–6.9 mmol/l) [Impaired Fasting Glucose (IFG)]
  - Two hour PG: 140–199 mg/dl (7.8–11.0 mmol/l) [Impaired Glucose Tolerance (IGT)]

  For pre-diabetes treatment recommendations refer below to "Recommended Therapy to Prevent or Delay Type 2 Diabetes in Persons With Pre-diabetes"

General Management

Office visits

- Frequency
  - For patients meeting goals: semiannual
  - Uncontrolled (goals not met): quarterly
  - Initiation of oral hypoglycemics: weekly
  - Initiation of insulin: daily until stable glucose control and patient is capable of self-management

- **Assessment: Medical History and Physical Exam**
  - At every visit: along with an interim history, evaluate the following:
    - Height, weight, BMI, pulse, blood pressure
    - Cardiac assessment
    - Neurological evaluation, including presence/absence of patellar and Achilles reflexes
    - Thyroid palpation
    - Fundoscopic exam
    - Oral/Periodontal assessment: (inflamed, bleeding gums, caries, xerostomia, candida, oral lesions)
      - Diabetes is a risk factor for severe, progressive periodontal disease
      - Periodontal disease can cause systemic inflammation that promotes atherogenesis and may contribute to poor A1C control[8]
      - Encourage regular dental exams and an annual visit with a periodontist
    - Skin examination (for acanthosis nigricans and complications of, assess insulin injection sites)
    - Tobacco use status
    - Nutrition and exercise
    - Home glucose levels
    - Assessment for hypoglycemic episodes and hypoglycemia unawareness

  - Annually: Comprehensive foot exams should be performed at least annually to identify risk factors predictive of ulcers, infections and amputations, including the presence/absence of the following:
    - Inspection: redness, blisters, skin lesions, ulcerations, signs of infection
    - Palpation: dorsalis pedis and posterior tibial pulses to detect evidence of peripheral vascular disease
    - Neurological:
      - Reflexes: patellar and Achilles
      - Sensory: 10g monofilament to detect loss of protective sensation, plus any of the following: vibration (*using a 128 Hz tuning fork*), proprioception, pin prick

  - Frequency as specified: Evaluate at diabetic visits with frequency specified as follows:
    - Autonomic neuropathy assessment[9,10]
      - Frequency:
        - ◊ Type 1 diabetes – 5 years after diagnosis and then annually
        - ◊ Type 2 diabetes – at the time of diagnosis and then annually thereafter
      - Goal: Early recognition and management of autonomic neuropathy (may be asymptomatic) to prevent/reduce cardiovascular morbidity/mortality, GI (gastroparesis, constipation, or diarrhea) and GU dysfunction (erectile/bladder

dysfunction, incontinence, UTI, or pyelonephritis)
- Cardiovascular Autonomic Neuropathy (CAN) may present with:
  - ◊ Resting tachycardia (> 100 bpm) or orthostasis (*systolic BP drop >20 mmHg upon standing without compensatory increase in heart rate*)
- Sudden death and silent myocardial ischemia have been attributed to CAN [11]
- Recommendation: optimize glycemic and metabolic control; consider other management according to symptoms and organ systems affected

▪ Retinopathy screening - performed by an ophthalmologist or optometrist
- Frequency:
  - ◊ Type 1 diabetes – within 5 years after the onset of diabetes, then
  - ◊ annually Type 2 diabetes – shortly after the diagnosis, then annually
- Less frequent exams may be considered after one or more normal eye exam; q2 years for ages 18-75 years; q2-3 years for ages >75years
- More frequent exams may be required if retinopathy is active and progressing
- Screening may include high quality fundus photography, but this test is not a substitute for a comprehensive eye exam by an ophthalmologist or optometrist
- Goal: To prevent, slow the progression, or reverse diabetic retinopathy
- Recommendation: optimize glycemic and blood pressure control

- **Assessment: Laboratory and Diagnostic Testing/Screening**
  - **HbA1c**
    - Frequency: Every 3–4 months if not meeting treatment goals or if therapy has changed; at least every 6 months if treatment goals have been met
    - Treatment goal: HbA1c < 7.0% (*The goal may be individualized to meet patient needs*); in pregnant women with type 1 or type 2 diabetes the recommended A1C goal is < 6.0%
  - **Lipid Profile (fasting)**
    - Frequency:
      - At least annually and more often if needed to achieve goals
      - In adults with low-risk lipid values, repeat lipid assessment every 2 years if >75years of age.
    - Goals for patients with diabetes:
      - LDL goal < 100 mg/dL in individuals without overt CVD
      - Optional LDL goal < 70 mg/dL in diabetes with overt coronary/peripheral vascular disease
      - HDL cholesterol > 40 mg/dL in men and > 50 mg/dl in women
      - Triglycerides < 150 mg/dL
  - **Liver Function Tests (LFTs)** (*People with type 2 diabetes have a higher incidence of hepatic steatosis and other liver function abnormalities than those without diabetes*)[12]
    - Frequency: Routine monitoring of LFTs in patients with type 2 diabetes should occur:
      - At the start of drug therapy
      - If symptoms of hepatic impairment develop
      - Periodically based on clinical judgment
    - Goal: Reduce the risk of chronic liver disease in patients with type 2 diabetes
      - Chronic low-grade transaminase elevations are not uncommon in type 2 diabetes
      - People with mild chronic transaminase elevation (AST/ALT $\leq$ 250 units/L) for > 6 months should be evaluated for treatable causes of chronic liver disease
  - **Urinalysis**

- Frequency: Annually, and with acute illness
- Goal: Negative for protein and ketones; negative urinary sediment

- **Albuminuria Status**
  - Frequency:
    - Type 1 diabetes: annually starting 5 years after diagnosis
    - Type 2 diabetes: annually from the time of diagnosis
  - Goals for patients with diabetes:
    - < 30 micrograms/mg creatinine in a random spot urine collection (preferred method)
    - < 20 micrograms/min in a timed collection
  - Definitions by level of proteinuria (*random spot urine collection in micrograms/mg creatinine*):
    - Normal: < 30 µg/mg creatinine
    - Increased urinary albumin excretion: ≥30 µg/mg creatinine
- **Serum Creatinine** Used to estimate the glomerular filtration rate (GFR) and stage of chronic kidney disease (CKD) in all adults with diabetes
  - Frequency: Annually
  - Goal: 0.6–1.2 mg/dL (*normal values may be laboratory dependent*)
  - Estimate GFR and stage of CKD using the Modification of Diet in Renal Disease (MDRD) Study equation and not serum creatinine alone

    (*Online MDRD GFR equation*: http://www.kidney.org/professionals/kdoqi/gfr_calculator.cfm)
- **Thyroid-stimulating hormone (TSH)**
  - Frequency:
    - Type 1 diabetes (*prevalence of thyroid disease 17-30%*) : TSH and anti-thyroid antibodies soon after diagnosis, then TSH every 1-2 years
    - Type 2 diabetes (*prevalence of thyroid disease 10-31%*):[13] no ADA recommendation, but expert opinions are to evaluate with TSH initially then every 1-2 years[13] to every 5 years[14]
  - Goal: Serum TSH level 0.5–5.0 mIU/L
  - Hypothyroidism in type 2 diabetes is often subclinical, but can still increase CV risk[13]
  - Risk is higher in women, age > 50 years, family history, positive anti-thyroid antibodies, high- normal TSH, and in those with another autoimmune disease
- Screening for other autoimmune diseases in type 1 diabetes should be considered based on patients' signs and symptoms (e.g., Pernicious Anemia, Celiac Disease)
- Screening for vitamin B-12 deficiency should be considered in patients with type 2 diabetes on long- term metformin therapy (≥ 4 years)
- **Electrocardiogram**
  - Frequency: Baseline for all adults with diabetes, then PRN (*stress test based on risk factors*)

Treatment of Diabetes

- **Recommended Therapy for Type 1 Diabetes**
  - Use of multiple dose insulin injections (3-4+ injections per day of basal and bolus insulin) or Continuous Subcutaneous Insulin Infusion (CSII) administered via insulin pump therapy
  - Calculate pre-prandial bolus insulin dose according to carbohydrate intake in grams
  - Apply correction factors for pre-prandial insulin dose according to pre-meal blood glucose level, physical activity, and alcohol intake (*exercise and alcohol increase the effect of insulin*)

- **Recommended Therapy for Type 2 Diabetes**[5,15]
  - Glycemic targets and glucose-lowering therapies must be individualized, however, all treatment should include lifestyle changes including Medical Nutrition Therapy (MNT), and exercise.
  - For baseline A1c ≥ 9.0%, consider initial treatment with 2 noninsulin anti-hyperglycemic agents
  - For baseline A1c ≥ 10.0-12.0%, strongly consider initial treatment with insulin
    - After resolution of symptoms and glucose toxicity, it may be possible to taper and/or completely discontinue insulin, with transfer to oral anti-hyperglycemic agents
  - Metformin, if not contraindicated, is the preferred and most cost-effective first-line oral agent
    - Titrate Metformin gradually to minimize potential gastrointestinal side effects
    - Long-term Metformin use, i.e., >4 years, is linked to progressive Vitamin B-12 deficiency[16]
    - Monitor B-12 levels with long-term Metformin use, especially when there is neuropathy
  - If maximal noninsulin monotherapy does not achieve glycemic goals after 3-6 months, then add:
    - A second oral agent - Options: meglitinides, sulfonylureas, dipeptidyl peptidases 4 inhibitor (DPP-4 I), thiazolidinediones, and alpha-glucosidase inhibitors
      - Meglitinides and sulfonylureas are associated with hypoglycemia and weight gain
      - DPP-4 I agents are nearly as effective as sulfonylureas, are not associated with hypoglycemia, are weight neutral, and have a side effect profile similar to placebo[17]
        - Thiazolidinediones (TZD) are associated with increased risk of osteoporosis, fractures, diabetic macular edema, increased fluid retention, and heart failure.[16,18,19,20]
          - ◊ Rosiglitazone has been associated with increased myocardial ischemia, CV events, and CV deaths [21]
          - ◊ Pioglitazone has been linked to a higher risk of bladder cancer with highest rates after taking the drug > 24 months and with a cumulative dose > 28,000mg. (Note: absolute risk remains relatively low with up to 137 additional cases per 100,000 person years).[22]
      - Alpha-glucosidase inhibitors (AG-I) – used alone or in combination; well-established efficacy, safety, and tolerability (mild-moderate GI complaints tend to subside with continued use); improve impaired glucose tolerance and improve CV risk profile[23]

    -OR-

    - Glucagon-like peptide-1 receptor agonist (GLP-1 RA)[24]
      - Long-acting GLP-1 agents appear superior to short-acting agents and are associated with:
        - ◊ Decrease in A1c by 0.87 –
        - ◊ 1.9% Weight loss
        - ◊ Less hypoglycemia
        - ◊ Decrease in systolic BP by 4.7 – 6.7 mmHg

    -OR-

    - Insulin

Due to the progressive nature of type 2 diabetes, many patients will eventually require insulin therapy

NOTE: The 2013 American Association of Clinical Endocrinology (AACE) Diabetes Management Algorithm recommends pharmacotherapy for type 2 diabetes according to the initial and 3 month post- treatment A1c levels in order of preference, as follows: [25]

- Entry A1c < 7.5%:
  - Monotherapy with Metformin, GLP-1 RA, DPP-4 I, OR AG-I
  - 3 month A1c > 6.5%: Add a second agent (Dual Therapy) with Metformin PLUS a GLP-1 RA, DPP-4 I, Colesevelam (bile acid sequestrant – lowers glucose and lipids), Bromocriptine (CNS modulator of glucose/energy metabolism), OR AG-I
- Entry A1c ≥ 7.5%:
  - Begin Dual Therapy with Metformin PLUS GLP-1 RA, DPP-4 I, Colesevelam, Bromocriptine, OR AGI
  - 3 month A1c not at goal: Add a third agent (Triple Therapy) with Metformin PLUS Second Line Agent PLUS GLP-1 RA, DPP-4 I, Colesevelam, Bromocriptine, OR AG-I
- Entry A1c > 9.0%:
  - Symptoms:
    - Insulin with or without other agents
  - No Symptoms:
    - Dual Therapy OR Triple Therapy
  - 3 month A1C not at goal: Add or intensify insulin therapy
- The AACE advises to use the following oral agents with caution: TZD, sulfonylureas, meglitinides and sodium-glucose co-transporter 2 (SGLT2) Inhibitors (new drug class that blocks glucose reabsorption in the proximal tubule of the kidney and increases glucose excretion)

- **Recommended Therapy to Prevent Or Delay Type 2 Diabetes in Persons With Pre-diabetes**
  - Support program for 7% loss of body weight and at least 150 min/week of moderate activity
  - Screening for and treatment of modifiable risk factors for CVD is vital to reduce cardiometabolic risk
  - Consider low risk medication shown to be effective in reducing impaired glucose tolerance:
    - Consider adding Metformin for those at high risk of diabetes *(combined IGT, IFG, A1C 5.7- 6.4%, especially in those with BMI ≥ 35 kg/m^2 , < 60 years old, and women with prior GDM)* (ADA) or if FBG > 100 mg/dL and 2-hour pp glucose > 140 mg/dL (AACE)
    - Consider adding an Alpha-Glucosidase Inhibitor (Acarbose) if FBS > 100 mg/dL and 2-hour pp glucose > 140 mg/dL (AACE)[25]
  - Follow-up counseling is important for success
  - People with pre-diabetes should be monitored each year for development of diabetes

- **Recommended Considerations for Diabetes and Pregnancy**
  - Preconception counseling – begin at puberty and reinforce at follow-up visits in all women of childbearing potential who have diabetes
  - Refer women considering pregnancy to a high risk obstetrician at a center with an established program for diabetes and pregnancy, including a hospital with a neonatal intensive care unit
  - Normalize control first – A1c should be as close to normal as possible (< 7%) before conception
    - Goals: reduced unplanned pregnancies and prevent first trimester fetal malformations
  - Evaluate and adjust medications before conception
    - Stop: statins, ACE/ARBs, diuretics most non-insulin meds, or others unsafe with pregnancy
    - Safe drugs with pregnancy: insulin, methyldopa, labetolol, diltiazem, clonidine, and prazosin
  - Evaluate and treat retinopathy, nephropathy, neuropathy before pregnancy if indicated

- Maintain near-normal control throughout pregnancy (recommended A1c 6.0%)
  - Frequent BG testing, 6-8X per day is required

    Goals: reduce first trimester fetal malformations, late-term macrosomia, improve health of the mother (pregnancy can establish skills/motivation to improve diabetes management for life)

Glucose Monitoring (*two primary methods of glucose monitoring*)

Self-Monitoring of Blood Glucose (SMBG)

- Patients using multiple-dose insulin or insulin pump therapy should perform SMBG at least:
  - Before meals and snacks
  - Occasionally post-prandial
  - At bedtime
  - Prior to exercise
  - When they suspect low blood glucose and after treating low blood glucose until they are normoglycemic
  - Before critical tasks such as driving

- **Continuous Glucose Monitoring (CGM)**
  - May be indicated for people with inadequate glycemic control (HbA1c > 7.0) and type 1 diabetes including those who are pregnant or attempting to become pregnant, and may be useful in conjunction with SBGM in patients with frequent hypoglycemic episodes or hypoglycemia unawareness.
  - CGM should only be considered in people who meet the following criteria:
    - The person is capable of understanding and using the technology
    - The person has demonstrated compliance with therapy
    - The person administers ≥ 3 insulin injections daily or uses continuous insulin pump therapy
    - The person performs ≥ 4 finger stick blood glucose tests daily (CGM should not replace finger stick blood glucose testing and should not be used for calculating insulin dosages*)

**CGM measures interstitial glucose, which has a time lag compared to blood glucose. CGM is useful for providing glucose trends and high/low alerts, but lacks real-time accuracy to support decisions for acute insulin therapy. Finger stick SMBG remains the standard for making acute treatment decisions.*

Note: Insurance coverage of CGM may not apply in all circumstances. Specific indications and limitations of coverage are detailed in Policy MP.034 of the Piedmont WellStar HealthPlans, Inc. Policy and Procedure Manual.

Prevention and Management of Diabetes Complications

Hypertension Management

- Frequency: Measure BP at every routine diabetes visit
- Goal: BP < 140/80 - Lower systolic targets (such as <130 mmHg) may be appropriate for certain individuals, such as younger patients, if it can be achieved without undue treatment burden.[5,7,26]
- Goal BP for pregnant women with diabetes: Systolic BP 110-129 mmHg / Diastolic BP 65–79 mmHg
- Recommendations:
  - For baseline BP >120/80mmHg:
    - Lifestyle/behavioral modification therapy for 3 months, including weight loss,

decrease in dietary sodium and increasing potassium intake , moderation of alcohol, and increased physical activity[5]

- If BP targets are not achieved by 3 months, then begin medication therapy for BP

- For baseline BP ≥140/80 mmHg :
  - Begin therapy with lifestyle/behavioral modification and antihypertensive medication
- Selection of antihypertensive medications in patients with diabetes:
  - ACEI/ARBs: preferred first line initial therapy due to proven renal & vascular protection & favorable metabolic profile[27]
    - ◊ Serum creatinine often rises 25% from baseline in first four weeks of ACEI/ARB Rx
    - ◊ Serum creatinine usually stabilizes after four weeks of ACE/ARB Rx
    - ◊ It is not necessary to discontinue ACE/ARB Rx unless the serum creatinine increases or GFR decreases by > 30% from baseline
  - Low-dose thiazides are excellent second line add-ons agents; loop diuretics are preferred if the GFR is reduced (< 60ml/min)[6]
    - ◊ HCTZ 12.5-25mg daily, has been shown to reduce CV events in elderly patients with HBP and diabetes[28] and have little impact on insulin sensitivity[29]
  - Calcium Channel Blockers (CCBs) are acceptable third line agents:
    - ◊ Dihydropyridine CCBs - optimal for patients with bradycardia, conduction abnormality and/or congestive heart failure (CHF)
    - ◊ Non-Dihydropyridine CCBs – optimal for patients with abnormalities in albumin secretion, proteinuria
  - β-blockers may be considered third or fourth line adjunctive agents for compelling indications, i.e., post-myocardial infarction, coronary artery disease, CHF
    - ◊ Carvedilol has distinct advantages compared to other β-blockers in diabetes[30]
      - $Alpha_1$ blocker effect lowers blood pressure by vasodilation
      - $Beta_1/Beta_2$ blocker effects prevent reflex tachycardia
      - Does not compromise renal blood flow or Na^+ excretion
      - Increases insulin sensitivity, does not increase HbA1c, and has beneficial effects on serum triglycerides and HDL cholesterol
  - α-blockers, central-acting and direct vasodilators are fourth/ last line agents (*the latter two are rarely used in managing hypertension in patients with diabetes*)

- **Lipid Management**
  - Lifestyle modification, i.e., reduction of dietary cholesterol, reduction of saturated fat and *trans* fats, weight loss, and exercise, should be recommended to improve lipids in all patients with diabetes
  - Statin therapy should be added regardless of baseline lipid levels in patients with diabetes as follows:
    - *With* overt coronary artery disease (CAD) or peripheral vascular disease (PVD)

- *With* multiple cardiovascular risk factors.
- *Without* overt CAD or PVD and > 40 years old and with one or more additional CV risk factors
- *Without* overt CAD or PVD and < 40 years old with LDL > 100 mg/dl despite lifestyle changes

- If drug-treated patients do not reach targets on maximal statin therapy, a reduction in LDL cholesterol of ≈30–40% from baseline is an alternative therapeutic goal

- **Coronary Heart Disease (CHD) Management in Patients With Diabetes**
  - Assess CV risk factors annually in all patients with diabetes
  - Patients with increased risk of CHD should receive aspirin and a statin, and ACEI/ARB therapy if hypertensive, unless contraindicated.
  - In patients with known CHD, consider ACEI/ARB therapy, and use aspirin and a statin, if not contraindicated, to reduce risk of CV events In patients with a prior MI, β-blockers should be continued for at least 2 years after the event to reduce mortality
  - Thiazolidinedione use is contraindicated in patients with symptomatic CHF
  - Metformin may be used in patients with stable CHF and normal renal function (it should be avoided in unstable or hospitalized patients)

- **Nephropathy Management**
  - Goals: Reduce the risk of development or progression of nephropathy related to diabetes
  - Recommendations:
    - Optimize BP and glucose control to reduce the risk and/or slow progression of nephropathy
    - ACEI or ARBs should be used in *non-pregnant* patients with abnormalities in albumin excretion
    - Limit protein intake to the Recommended Dietary Allowance (RDA) of 0.8–1.0 g/kg body weight in individuals with diabetes and the earlier stages of CKD and 0.8 g/kg in the later stages of CKD

- **Neuropathy Management**[10,11]
  - Neuropathy can improve with optimal glucose control and avoiding extreme glucose fluctuations
  - Neuropathy treatments may improve quality of life, but do not change the underlying disease process
    - Painful neuropathy may respond to pharmacologic treatment, e.g., amitriptyline, gabapentin, topiramate, pregabalin, duloxetine
    - Gastroparesis symptoms may improve with:
      - Dietary changes: e.g., six small meals daily, chewing well, noncarbonated liquids, sitting/standing for 2 hrs. after meals, avoiding high fat and high fiber foods, and liquids or pureed foods for severe symptoms
      - Prokinetic agents: e.g., metoclopramide, erythromycin
    - Erectile dysfunction can be treated with phosphodiesterase type 5 inhibitors, intracorporeal or intraurethral prostaglandins, vacuum devices, or penile implants
    - Cardiac Autonomic Neuropathy with postural hypotension may improve with:
      - Mechanical measures: remove reversible causes of orthostasis (dehydration, drugs); move from supine to standing in stages; encourage physical activity/exercise (avoid isometric exercise); eat small meals to avoid post-prandial hypotension; custom fitted elastic stockings of the lower

extremities extending to the abdomen

- Pharmacologic agents: fludrocortisone;[31] midodrine;[32]; useful supplemental agents may include caffeine, NSAIDs, and other less commonly used agents

- Retinopathy Management
  - Optimize glycemic and blood pressure control to reduce the risk or slow the progression of retinopathy
  - Refer to a retinal specialist

- **Foot Care / Peripheral Vascular Disease (PVD) Management**
  - Provide general foot self-care education to all patients with diabetes
  - Screen for PVD by assessing for claudication, pedal pulses, and ankle-brachial index (ABI)
    - Consider referral to foot care specialist/team: patients who smoke, have loss of protective sensation, structural abnormalities, or previous lower extremity/foot complications
    - Consider referral to vascular surgery: patients with significant claudication or abnormal ABI

- **Anti-platelet Therapy**
  - Aspirin 75–162mg per day should be considered as primary prevention strategy in those with type 1 or type 2 diabetes at increased cardiovascular risk (10 year risk > 10%). This includes most men > 50 years of age or women >60 years of age who have at least one additional major risk factor, i.e., family history of CVD, hypertension, smoking, dyslipidemia, or albuminuria
  - Aspirin therapy is not recommended as primary prevention for men < 50 or women < 60 years of age without other major risk factors. If major risk factors are present, clinical judgment is required
  - Aspirin 75–162mg per day is recommended as secondary prevention in patients with diabetes and a history of CVD
  - Combination therapy with aspirin (75–162 mg/day) and clopidogrel (75 mg/day) is reasonable for up to a year after an acute coronary syndrome
  - Clopidogrel (75 mg/day) should be used if there is allergy or other contraindications to aspirin (clopidrogel has been shown to reduce CV events in people with diabetes)

- **Medical Nutrition Therapy**
  - Frequency: As needed to achieve treatment goals, preferably provided by a registered dietitian familiar with the components of diabetes MNT
  - Goals:
    - Attain/maintain recommended metabolic outcomes, including glucose and A1C levels, LDL-C, HDL-C, triglyceride levels, BP, and ideal body weight
    - Address individual nutritional needs, taking into consideration personal and cultural preferences and lifestyle, while respecting the individual's wishes and willingness to change
  - Recommendations:
    - Integral components of diabetes self-management education include:
      - Monitoring carbohydrates by carbohydrate counting, exchanges, or experience-based estimation remains a key strategy in achieving glycemic control
      - Limit protein intake to recommended dietary allowance of 0.8–1.0 g/kg body

weight per day in early stages and 0.8 g/kg per day in the later stages of CKD
- Saturated fat intake should be <7% of total calories
- Intake of *trans* fat should be minimized
- Weight loss is recommended for all overweight people with or at risk for diabetes
  - ◊ Lifestyle changes are the primary approach, i.e., nutritional education, reduced fat, carbohydrate and calorie intake, and regular physical activity

- **Bariatric Surgery**
  - Bariatric surgery may be considered for adults with a BMI ≥ 35 kg/m^2 and type 2 diabetes, especially if the diabetes is difficult to control with lifestyle and pharmacological therapy
  - Life-long lifestyle support and medical monitoring is needed for patients with type 2 diabetes who have undergone bariatric surgery

- **Tobacco Use Prevention/Cessation**
  - Frequency: Monitor status annually or as indicated
  - Goal: Negative for tobacco use
  - Recommendations:
    - Advise all patients not to smoke or use tobacco products
    - Include smoking cessation counseling and other assistive forms of treatment as a routine component of diabetes care

- **Exercise/Physical Activity**
  - Frequency: Assess at each routine visit as appropriate, or at least annually – assess CV risk factors in patient with diabetes before recommending a program of physical activity
  - Goal: Regular activity improves insulin sensitivity, glycemic control, and selected risk factors for CVD and increased aerobic fitness decreases the risk of coronary artery disease
  - Recommendations: A regular physical activity program, adapted to the presence of complications, is recommended for all patients with diabetes who are capable of participating
    - The U.S. Department of Health and Human Services recommends adults over age 18 do 150 min/week of moderate-intensity or 75 min/week of vigorous-intensity physical activity
      - Vigorous aerobic or resistance exercises may be contraindicated with proliferative retinopathy due to an increased risk of vitreous hemorrhage or retinal detachment
    - Recommend 2 sessions per week of resistance exercises involving the large muscle groups in patients with type 2 diabetes to improve insulin sensitivity, unless contraindicated
    - Insulin/insulin secretagogue dose should be reduced and/or carbohydrate consumption should be increased to prevent hypoglycemia associated with exercise

- **Psychosocial Assessment and Care**
  - Frequency: Screen status at diagnosis, routine visits, during hospitalizations, at discovery of complications, or at the discretion of clinician when problems in glucose control, quality of life, or adherence are identified
  - Goal: To establish emotional well-being as part of diabetes management
  - Recommendations:

- Psychological and social state can impact the patient's ability to manage diabetes; therefore proactive psychological assessment/treatment should be part of routine diabetes care.
- Depression screening with PHQ-2 may be useful; any positive responses to the PHQ-2 may be followed up with the PHQ-9 depression screening tool.
- A sound patient-provider relationship will increase the likelihood the patient will accept referral for other services when necessary.

- **Hypoglycemia Unawareness** (presence of hypoglycemia without usual sympathetic nervous system symptoms and increased risk of loss of consciousness resulting from hypoglycemia):
  - Risk factors for hypoglycemia unawareness include:
    - Diabetes for many years
    - Tight glucose control
    - Presence of diabetes related neuropathy
    - People with diabetes who are on beta-blocker medications
  - Management of hypoglycemia unawareness:
    - More frequent, timed blood glucose monitoring
    - Temporarily increase glycemic treatment goals to restore hypoglycemia awareness
    - Patient should learn to recognize and treat early any subtle symptoms that might represent hypoglycemia, e.g., nausea, visual changes, etc.
    - Avoid alcohol, which potentiates hypoglycemia, especially at night, by increasing insulin sensitivity and reducing hepatic gluconeogenesis
    - Changing insulin delivery from multiple daily injections to continuous subcutaneous insulin infusion (CSII-pump) can result in a marked, sustained reduction in severe hypoglycemia [33,34]
    - Consider CGM for recurrent episodes or complications of undetected hypoglycemia despite the above measures, along with frequent SBGM (at least 4 times daily)
    - Patients with insulin treated diabetes should be prescribed and both patient and caregiver should be educated in the use of a glucagon emergency kit

Preventive Care

Description	Frequency	Recommendation
Influenza Vaccine	Annually	Check status annually and strongly encourage vaccination every year
Hepatitis B Vaccine	Administer to unvaccinated adults with diabetes, aged 19-59 years. Consider Vaccination for those aged ≥60 years	Check status annually and strongly encourage vaccination if needed
Pneumococcal Vaccine	Initially, for all patients with diabetes ≥ 2 y/o. A one-time revaccination is recommended for individuals > 64 y/o, if they were previously immunized < 65 y/o and it has been > 5 years from the previous immunization. Other indications for repeat vaccination include nephrotic syndrome, chronic renal disease, and	Check status annually and strongly encourage vaccination if needed

Action Plan for Patients

Patients with diabetes should be given verbal and written instructions regarding:

- Importance of screening/monitoring for:
  - HbA1c at least twice a year
  - Lipid profile
  - Retinal eye exam
  - Nephropathy
  - Blood pressure control
  - Check feet daily and have complete foot exam annually (check by PCP every visit)
- Hypoglycemia warning signs and action to be taken
- Specific diet recommendations including:
  - How to read food labels for carbohydrate content
    - Limit protein intake to recommended dietary allowance
    - Limit saturated fat intake to recommended dietary allowance
    - Minimize intake of *trans* fats
    - Alcohol limits or abstinence
  - Importance of compliance with medications and diet and behavioral strategies to promote compliance
  - Importance of risk factor modification including:
    - Smoking cessation
    - Blood pressure management to goal
    - Maintain normal HbA1c
    - Control lipids if necessary
    - Maintain specific body weight
- Specific activity/exercise recommendations

Clinical practice guidelines are designed to assist clinicians by providing a framework for the evaluation and treatment of patients. The diabetes management guideline is based on the most current recommendations from the American Diabetes Association: "Clinical Practice Recommendations 2013" in addition to the scientific evidence sources referenced below. The current ADA guideline for the diagnosis and management of diabetes is available at http://care.diabetesjournals.org/content/36/Supplement_1.toc

Additional Resources for Piedmont WellStar HealthPlans, Inc. Members

- ***My*Health Advice Line** is staffed by experienced Registered Nurses and is available 24/7 to provide telephone support to members. Call 855-514-3679.

- **Online** interactive preventive health programs and resources are available in partnership with WebMD by logging in at www.pwplans.org/individuals.

Scientific Evidence Sources

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