

JOSLIN DIABETES CENTER & JOSLIN CLINIC CLINICAL GUIDELINE FOR ADULTS WITH DIABETES 10/23/2014

The *Joslin Clinical Guideline for Adults with Diabetes* is designed to assist primary care physicians and specialists individualize the care of, and set goals for non-pregnant adults with diabetes. This Guideline focuses on the unique needs of the patient with diabetes. It is not intended to replace sound medical judgment or clinical decision-making and may need to be adapted for certain patient care situations where more or less stringent interventions are necessary.

The objectives of the Joslin Clinical Diabetes Guidelines are to support clinical practice and to influence clinical behaviors in order to improve clinical outcomes and assure that patient expectations are reasonable and informed. Guidelines are developed and approved through the Clinical Oversight Committee that reports to the Medical Director of Joslin Diabetes Center. The Clinical Guidelines are established after careful review of current evidence, medical literature and sound clinical practice. This Guideline will be reviewed periodically and modified as clinical practice evolves and medical evidence suggests.

Joslin's Guidelines are evidence-based. In order to allow the user to evaluate the quality of the evidence used to support each standard of care, a modification of the GRADE system has been adopted. The table provided on page 13 describes the categories in which methodological quality and strength of recommendations have been classified. Evidence levels are graded 1A through 2C, as indicated in brackets. Where evidence is not graded, recommendations are made based on the expertise of the Clinical Oversight Committee

APPROACH TO CARE

Team care: Diabetes is best managed by a team including medical specialists and diabetes educators. The patient needs to be informed of the roles of the various team members. If access to a team is not possible within the office practice, identify community resources. Clear communication between all providers is critical to ensure patients' needs are being met.

Patient centric: Diabetes is a condition that requires self-management. A collaborative counseling model (where the patient is involved in decisions and goal setting) helps promote behavior change. Whenever appropriate, with the patient's consent, involve family members and caregivers in medical visits and education.

Individualized treatment plan: Develop a treatment plan based on a thorough assessment which includes an understanding of not only the patient's medical needs, but also other factors that may influence the treatment plan such as social history, race, cultural issues, ethnicity, education needs (including literacy and numeracy), comorbidities and barriers to care. The plan identifies medical treatment, educational interventions and follow-up. Consider use of a flow sheet to track care parameters and identify areas for intervention.

Regular medical visits: The frequency of visits for ongoing care should be individualized, but usually includes at least 2-4 visits/year. Special attention should be given to patients who do not keep scheduled appointments, have frequent hospitalizations or missed days of work/school. Since many factors contribute to the patient's ability to manage their care, the provider should:

- Engage patients in identifying and resolving contributing factors or barriers to under-utilization or over-utilization of healthcare services
- Consider referral to a diabetes educator (DE), social service or behavioral health professional to address possible barriers and/or psychosocial issues
- Establish a process of follow-up communication regarding progress of the treatment plan and sustaining behaviors.

DIAGNOSIS OF DIABETES MELLITUS

The diagnosis of diabetes mellitus can be made based upon:

- Random plasma glucose ≥ 200 mg/dl and symptoms of diabetes (polyuria, polydipsia, ketoacidosis, or unexplained weight loss) **OR**
- Fasting plasma glucose (FPG)* ≥ 126 mg/dl **OR**
- Results of a 2-hour 75-g Oral Glucose Tolerance Test (OGTT)* ≥ 200 mg/dl **OR**
- Glycated hemoglobin* (A1C) $\geq 6.5\%$ **

* *These tests should be confirmed by a repeat test, on a different day, unless unequivocally high*

**A glycated hemoglobin A1C (A1C) level of 6.5% or higher on 2 separate days is acceptable for diagnosis of diabetes. [1B]. However, some individuals may have an A1C $< 6.5\%$ with diabetes diagnosed by previously established blood glucose criteria. Therefore, presence of either criterion is acceptable for diagnosis. Those with an A1C of 5.7-6.4% are considered to have pre-diabetes and are at increased risk for diabetes, and should be treated with lifestyle changes and followed more frequently. *The A1C should be performed in a laboratory using a method that is National Glycohemoglobin Standardization*

Program (NGSP) certified and standardized to the Diabetes Control and Complications Trial (DCCT) assay. A point of care (POC) A1C is not acceptable for diagnosis of diabetes.

A1C

Diagnosis:

See above section on Diagnosis of Diabetes Mellitus

Note: The A1C may not be accurate in several settings, including pediatric and geriatric populations, patients with anemia or other blood disorders resulting in rapid turnover of red blood cells, in chronic liver and renal disease, following recent transfusions, or in the hospital setting. Interpret A1C results accordingly when determining treatment plans and goals.

Follow-up visits:

Check the A1C 2-4 times a year as part of the scheduled medical visit, with frequency dependent upon revision of the treatment program and the need to reinforce behavior changes. Increase frequency when therapy has changed and/or when glycemic goals are not met. Having the A1C result at the time of the visit can be useful in making timely treatment decisions. [1C] The A1C can be done pre-visit by using a POC method.

Goal:

A1C target goal should be individualized for each patient. A goal of < 7% is chosen as a practical level for most patients to reduce the risk of complications. Achieving normal blood glucose and A1C is recommended if it can be done practically and safely. [1B]

The A1C goal may be modified based upon presence or absence of microvascular and/or cardiovascular complications, hypoglycemic unawareness, cognitive status and life expectancy. [1A] For patients with longstanding type 2 diabetes with pre-existing CVD, or high CAD risk (diabetes plus two or more additional risk factors), consider revising A1C goals to maintain safety. [1A]

Some clinicians may translate patients' A1C level into their estimated average glucose level (eAG), based upon the work of the A1C Derived Average Glucose Study (ADAG). This is also a valid metric to use in following diabetes treatments. [1C]

Joslin's A1C goal is consistent with that of the ADA. Other expert panels such as AACE suggest that the goal of treatment should be $\leq 6.5\%$ in those newly diagnosed with diabetes and without co-morbidities.

Treatment:

If A1C is $\geq 7\%$ and $< 8\%$, or above the individualized goal for 6 or more months:

- Review and clarify the management plan with the patient with attention to:

- nutrition and meal planning
- physical activity
- medication administration, schedule and technique
- self-monitoring blood glucose (SMBG) schedule and technique
- treatment of hypoglycemia and hyperglycemia
- sick day management practices
- Reassess goals and adjust medication as needed [1A]
- Establish and reinforce individualized glycemic goals with patient
- Consider referring patient to diabetes educator (DE) for evaluation, diabetes self-management education (DSME) and support for ongoing consultation. [1C]
- Consider referral to registered dietitian (RD) for medical nutrition therapy (MNT). [1B]
- Schedule follow-up appointment within 3-4 months or more frequently as situation dictates

If A1C is $\geq 8\%$

- Review and clarify the plan as previously noted
- Assess for psychosocial stress [1C]
- Establish and reinforce individualized glycemic goals with the patient
- Intensify therapy
- Refer patient to DE for evaluation, DSME and support for ongoing consultation. Document reason if no referral initiated
- Refer patient to RD for MNT [1C]

If history of severe hypoglycemia or hypoglycemia unawareness (a condition in which the patient is unable to recognize symptoms of hypoglycemia until they become severe):

- Assess for changes in daily routine such as decreased food intake or increased activity [1C]
- Refer to DE for evaluation, DSME and hypoglycemia prevention; encourage family/friend attendance
- Review use of glucagon
- Consider revising A1C goal
- Discuss and reinforce goals with patient
- Adjust medications accordingly [1B]
- If insulin-treated, consider use of a more physiologic insulin replacement program
- Consider and screen for other medical causes
- Consider referral for blood glucose awareness training, if available
- Consider use of continuous glucose monitoring (CGM)
- Schedule follow-up appointment within 1-2 months. If history of recent, severe hypoglycemia or change in pattern of hypoglycemia, recommend increase in frequency of communicating blood glucose levels to provider or diabetes educator.

GLUCOSE MONITORING

Self-monitoring of blood glucose (SMBG) is an important component of the treatment program for all people with diabetes. Its use is to gauge treatment efficacy, help in treatment design, provide feedback on the impact of nutritional intake and activity, provide patterns that assist in medication selection, and for those on insulin, assist in daily dose adjustments. **[1B]**

Goals:

Goals for glycemic control for most people with diabetes are:

- Fasting glucose: 70-130 mg/dl
- 2-hour postprandial glucose: <180 mg/dl
- Bedtime glucose: 90-150 mg/dl

Frequency:

The frequency of SMBG is highly individualized and should be based on such factors as glucose goals, medication changes and patient motivation. Most patients with type 1 diabetes should monitor 4-6 times per day. Some patients may need to monitor even more frequently. For patients with type 2 diabetes, the frequency of monitoring is dependent upon such factors as mode of treatment and level of glycemic control. **[1C]**

Postprandial monitoring:

To obtain meaningful data for treatment decisions, it is helpful for the patient to monitor for several consecutive days (e.g., 2-4 days). In addition to obtaining fasting and preprandial glucose levels, consider obtaining glucose readings 2-3 hours postprandially, as postprandial hyperglycemia has been implicated as an additional cardiovascular risk factor. **[1B]**

Postprandial monitoring is particularly recommended for patients who:

- Have an elevated A1C but fasting glucose is at target
- Are initiating intensive (physiologic) insulin treatment programs
- Are experiencing problems with glycemic control
- Are using glucose-lowering agents targeted at postprandial glucose levels
- Are making meal planning or activity adjustments

One -hour postprandial glucose monitoring should be considered:

- During pregnancy **[1A]**
- For those patients using alpha-glucosidase inhibitors

Encourage the patient to bring SMBG results (written records or meter for downloading) to each visit for review with provider/educator.

Alternate Site Monitoring:

Blood glucose levels from sites such as the upper arm, forearm, and thigh may lag behind samples taken from the fingertips particularly when glucose levels are changing rapidly. Glucose levels may change rapidly with exercise,

eating, after insulin administration or with hypoglycemia. For this reason, alternate site monitoring is not recommended in the following situations:

- When the blood glucose may be changing rapidly
- For patients using intensive insulin treatment programs
- If hypoglycemia is suspected
- In patients with hypoglycemia unawareness

Continuous glucose monitoring:

Real time continuous glucose monitoring (CGM) measures interstitial glucose levels and correlates with plasma glucose levels. It has been shown to decrease A1C and may be helpful in improving blood glucose control for those with general hyperglycemia as well as those with recurrent hypoglycemia. Data from CGM needs to be confirmed with results from self-monitoring of blood glucose.

HYPOGLYCEMIA

Prompt action is recommended for the treatment of hypoglycemia. When possible, the patient should confirm symptoms with SMBG to document hypoglycemia. All patients with type 1 diabetes should ensure that a family member/companion/caregiver knows how to administer a glucagon injection in the event the patient is unable or unwilling to take carbohydrate orally. **[1C]**

Treatment:

- Caution patient to avoid alternate site monitoring with blood glucose meter when hypoglycemic
- Treat as mild-moderate hypoglycemia if patient is symptomatic or unable to confirm hypoglycemia with SMBG, or if blood glucose levels are >50 mg/dl and <70 mg/dl (<90 mg/dl at bedtime or overnight).
- For mild to moderate hypoglycemia (plasma glucose 51-70 mg/dl most times of the day and < 90 mg/dl bedtime or overnight), begin with 15-20 grams of carbohydrate (1/2 cup juice or regular soft drink, 3-4 glucose tabs). **[1C]**
- If glucose level is ≤50 mg/dl, consume 20-30 grams of carbohydrate. **[1C]**
- Recheck blood glucose after 15 minutes. **[1B]**
- Repeat hypoglycemia treatment if blood glucose does not return to normal range after 15 minutes. **[1C]**
- Follow with additional carbohydrates if next meal is more than one hour away. **[1C]**
- If hypoglycemia persists after 2-3 treatments, patient or companion should be instructed to contact their healthcare provider or seek emergency care.
- In event of severe hypoglycemia (altered consciousness, unable to take carbohydrate orally, or requiring the assistance of another person) treat with glucagon and/or intravenous glucose. **[1C]**
- For patients with hypoglycemia unawareness, the threshold for treatment of hypoglycemia needs to be individualized. **[1C]**

- For patients using real-time CGM, check 15 minutes post treatment using a finger stick and not the sensor reading. Due to the physiologic lag between blood and interstitial glucose, the sensor will yield a lower result and can lead to over-treatment.[1B]
- For patients with gastroparesis, treat hypoglycemia with oral glucose gel.

Education:

- Instruct patient to obtain and wear or carry diabetes identification.
- Instruct patient to carry treatment for hypoglycemia at all times.
- Instruct all patients with type 1 diabetes and patients with type 2 diabetes who are at risk for hypoglycemia to check blood glucose before operating a motor vehicle or other potentially dangerous equipment. In addition, advise them to check blood glucose regularly if driving for one or more hours. Hypoglycemia should be treated immediately, and patients should not drive until blood glucose has reached and stayed at a safe range for at least 30 minutes and/or until cognitive function is restored [1B]
- Identify possible causes of hypoglycemia in order to prevent it. [1C]
- Be clear in communicating modified treatment goals in individuals with hypoglycemia unawareness

DIABETES SELF-MANAGEMENT EDUCATION (DSME) and MEDICAL NUTRITION THERAPY (MNT)

Group education sessions are encouraged for cost effectiveness and efficiency of staff utilization. Group education is a benefit to patients as it allows them to share ideas and concerns and enables them to learn from one another. [1B]

Individuals with diabetes often receive:

- DSME and emotional support through group interactions
 - Individuals who have functioned adequately and appropriately in group settings are generally suitable candidates for group methods
 - Individuals who are severely hearing impaired, cognitively impaired, or psychiatrically impaired may not be appropriate candidates for group methods and should be treated individually

Individuals with newly diagnosed diabetes should receive:

- DSME according to National Standards for Diabetes Self-Management Education and Support [1B]
- Individualized or group Medical Nutrition Therapy (MNT) Education [1A]
- Multiple visits with a diabetes educator (DE) to evaluate progress towards goals [1B]

Individuals with existing diabetes should receive:

- An annual assessment of the need for DSME and MNT, and referral, as appropriate, to a trained DE [1C]
- Initial and ongoing assessment of psychosocial issues [1C]

PHYSICAL ACTIVITY

All adults should consult their healthcare provider and/or see an exercise physiologist to discuss a safe exercise program that is appropriate to their abilities.[1C]

Guidelines for healthy adults:

- Physical activity should be an integral component of the diabetes care plan to optimize glucose control, decrease cardiovascular risk factors, and achieve or maintain optimal body weight. [1A]
- A moderate-intensity aerobic (endurance) physical activity minimum of 30 minutes 5 days per week or vigorous-intensity aerobic physical activity for a minimum of 20 minutes 3 days per week should be achieved unless contraindicated. Activity can be accumulated toward the 30-minute minimum by performing bouts, each lasting 10 or more minutes. [1A]
- A target of 60-90 minutes, 6-7 days per week is encouraged for weight loss if overweight or obese [1A]
- To increase lean body mass, full body resistance training should be incorporated into the activity plan 3-4 days per week, and include upper, core and lower body strengthening exercises using free weights, resistance machines or resistance bands. [1B]
- Stretching exercises should be done when muscles are warm or at the end of the activity plan to loosen muscles and prevent soreness. [1B]

Guidelines for adults with medical or physical limitations:

- A moderate-intensity aerobic (endurance) physical activity minimum of 30 minutes 5 days per week or vigorous-intensity aerobic physical activity for a minimum of 20 minutes 3 days per week should be achieved, as feasible, unless contraindicated. Activity can be accumulated toward the 30- minutes minimum by performing bouts, each lasting 10 or more minutes. [1A]
- To increase lean body mass, resistance training should be incorporated into the activity plan 3-4 days per week, as feasible, and include upper, core and lower body strengthening exercises using free weights, resistance machines or resistance bands. [1B]
- Incorporate balance exercises to prevent falling and injury.
- Functional Fitness Testing is useful to assess patients' functionality and track their progress. Testing such as 6-Minute Walk Test, 2-Minute Step Test, Balance Assessment and Hand strength should be included at baseline and post intervention [1C]
- **See section on EYES**

CARDIOVASCULAR HEALTH

(Also see sections on *Lipids, Blood Pressure, Physical Activity and Smoking*)

Treatment:

A daily enteric-coated ASA (75-162 mg) unless contraindicated * as a **primary** prevention strategy for men ≥ 50 years of age [1C] and for women ≥ 60 years of age [1C] with ONE or more of the following risk factors:

- Family history of premature** CAD or stroke
- HTN
- Current cigarette smoker
- Albuminuria
- Hyperlipidemia

Recommend a daily enteric-coated ASA (75-162 mg) or clopidogrel (75 mg, if aspirin intolerant) or another agent of the class, as a **secondary** prevention strategy for anyone with ONE or more of the following: [1A]

- History of MI, angina, or documented CAD
- Vascular revascularization
- Non-hemorrhagic stroke
- TIA
- PAD

**Possible contraindications for antiplatelet therapy may include allergy, bleeding tendency, anticoagulant therapy, recent gastrointestinal bleeding and clinically active hepatic disease. Eye disease is usually not a contraindication for ASA therapy.*

***Premature – 1st degree male relatives younger than 55 years of age; 1st degree female relatives younger than 65 years of age*

Consider using beta-blocker in all patients with a history of MI or with documented CAD unless contraindicated. [1A]

Consider using ACE inhibitors (or ARBs if ACE inhibitors not tolerated) in patients with known CAD or cardiovascular risk factors and age 55 yrs or greater. [1B]

Thiazolidinediones (pioglitazone, rosiglitazone) are contraindicated in patients with NYHA classes III and IV and conditions of fluid overload (i.e. CHF). (See Pharmacological Guideline for additional caveats on TZDs) [1A]

Consider recommending aerobic activity if not clinically contraindicated and a weight-loss program if patient is overweight or obese. [1A]

Indications for conducting a stress test:

Based on current research and understanding of coronary artery disease in diabetes, it is reasonable to screen patients with diabetes who: [1C]

- Complain of typical or atypical chest pain
- Have an abnormal ECG

- Have a diagnosis of peripheral artery disease (PAD) or carotid disease
- Are >35 years of age with sedentary lifestyle about to start a rigorous exercise program.

There is currently no strong evidence to support screening asymptomatic patients with type 2 diabetes for silent myocardial ischemia. [1C]

Patients with autonomic neuropathy may have increased risk of asymptomatic ischemia and therefore warrant careful attention. [1B]

If stress testing is performed, either rMPI or echocardiography with ECG monitoring is recommended. Exercise stress is preferred, if resting ECG is normal and patient is able to exercise, as the response to exercise is an important prognostic factor. If the patient cannot adequately exercise, pharmacologic stress testing is warranted.

LIPIDS

Screen:

Adults should be screened annually for lipid disorders with measurements of serum cholesterol, triglycerides, and LDL and HDL cholesterol, preferably fasting. [1B] Cholesterol guidelines from major organizations are under discussion and updates are expected.

Treatment plan:

All patients should receive information about a meal plan designed to improve glycemic and lipid control, physical activity recommendations, and cardio-vascular risk reduction strategies (with an emphasis on smoking cessation and blood pressure control.) Consultation with appropriate education discipline is preferred. [1A]. Institute therapy after abnormal values are confirmed.

- All patients with any form of clinical diagnosis of atherosclerotic cardiovascular disease (ASCVD), or if LDL-C ≥ 190 mg/dl: treat with statin to reduce LDL-C $\geq 50\%$ [1A]
 - Patients, age 40-75 yr, without clinical evidence of ASCVD and LDL-C 100-190 mg/dl: treat with statin to reduce LDL-C by 30-50%. Consider reduction of $> 50\%$ if one or more additional major risk factors* or 10-year risk of ASCVD $> 7.5\%$ by risk equation [1B]
(<http://my.americanheart.org/cvriskcalculator>)
* (family history of premature ASCVD, HBP, smoking, proteinuria)
 - Patients, age 40-75 yr, without clinical evidence of ASCVD and LDL-C 70-100mg/dl: treat with statin to reduce LDL-C by $> 30\%$ [1C]
- In patients < 40 yr of age, consider statin if LDL-C > 100 mg/dl and multiple CVD risk factors [2B]
- In patients > 75 yr of age, there is no clear evidence for benefits of initiating statin therapy in the absence of ASCVD.[2C]

- Re-check lipids after drug initiation or dose escalation in 6-12 week. Thereafter, check lipids every 3-12 months to monitor adherence. May down-titrate statin dose if LDL-C < 40 mg/dl.
- No evidence for benefits of statin therapy in patients on hemodialysis, or those with heart failure (NYHA class II-IV). [1B]
- If achieving adequate reduction in LDL-C as described above, a specific LDL-C goal (< 70 and < 100 mg/dl) or non-HDL-C goal (< 100 and < 130 respectively) for those with or without ASCVD, respectively, is not recommended unless baseline lipid levels not known.
- Statins are contraindicated during pregnancy or if contemplating pregnancy.
- Consider a bile acid sequestrant or cholesterol absorption inhibitor or niacin (alone, or in combination therapy) for patients intolerant to multiple statins, or who have unacceptable adverse events. [2B]

Patients with LDL-C at goal and fasting triglycerides ≥ 150 mg/dl or HDL-C ≤ 40 mg/dl

- Optimize glycemic control [1A]
- Refer to RD for dietary modification and therapeutic lifestyle changes (TLC) [1A]
- Consider referral to exercise specialist for exercise prescription
- Recheck lipids within 6-12 weeks
- In patients with fasting triglyceride levels 200-499 mg/dl and/or HDL-C ≤ 35 mg/dl after optimal statin therapy, consider adding a fibrate. [2B]
- If triglycerides persistently ≥ 500 mg/dl, rule-out other secondary causes. Initiate treatment with very low fat meal plan and with a fibrate for prophylaxis against acute pancreatitis; reassess lipid status when triglycerides < 500 mg/dl [1A]
- If fasting triglycerides remain > 500 mg/dl after initiation of fibrate, consider the addition of fish oil (to provide 2-4 gm omega-3 fatty acids daily), or niacin [2B]

BLOOD PRESSURE

Screen:

- Check BP at all routine visits after patient has been seated for at least 5 minutes. Use proper-size cuff and arm position. Postural BP should be checked initially, and as clinically indicated, and if orthostatic (defined as a fall in systolic BP (SBP) of >20mmHg or diastolic BP (DBP) of ≥ 10 mmHg or the pulse increases by more than 20 beats per minute after 3 minutes of standing up), or if any drop is associated with lightheadedness, syncope or signs of brain hypoperfusion. [1C]
- Initiate lifestyle changes if BP >130/80mm/Hg
- Consider initiating pharmacologic therapy if the average of 3 blood pressure measurements is >140/90mmHg. Schedule for follow up blood pressure check within 1 month [1B]

Goal:

- BP goal for each patient >18 years of age is $\leq 140/90$ mmHg. [1B]
- SBP ≤ 130 mmHg may be appropriate for individuals without CVD or without multiple risk factors. [1B]
- No clear evidence exists for significant benefits to be gained by lowering SBP to < 120mmHg in those with CHD or multiple risk factors. [1B]
- BP goal for patients with albuminuria > 300mcg/mg is <130/80mmHg, if tolerated. [1C]
- Initial goal for patients with isolated systolic HTN (SBP >180 mmHg and DBP <80 mmHg) is a SBP <160 mmHg. [2B]
- Initial goal for patients with SBP 160-179 mmHg is to lower SBP by 20 mmHg. If well tolerated, lower BP goals may be indicated. [1B]

Treatment

If SBP ≥ 140 mmHg or DBP ≥ 90 mmHg, a 3-month trial of lifestyle modification is warranted as follows: [1C]

- Counsel about meal plan, use of DASH and DASH-sodium diet, activity, weight loss, sodium reduction, alcohol and stress reduction
- Consider referral to RD for medical nutrition therapy (MNT)
- Encourage home BP self-monitoring and documenting it in a log to bring to clinic appointments.
- Instruct patient to have BP checked two times a week prior to the next appointment
- Follow-up with healthcare provider within 2-4 weeks
- Initiate or adjust therapy with antihypertensive agents as clinically indicated if BP remains above goals

Studies have shown that aggressive management and control of blood pressure may result in long-term benefits

Drug therapy:

Efficaciousness is the most important consideration in choosing an initial anti-hypertensive drug. In that sense, any available antihypertensive drug can be an appropriate choice; however, other considerations (presence of albuminuria, co-existing CAD, or cost) dictate a preference for ACE inhibitors, ARBs, calcium channel blocker (CCB), and thiazide-type diuretics. [1A] In general, ACEI and ARB should not be used in combination

Consider ACE inhibitors or ARBs for patients with persistent urine albumin/creatinine ratio >30 mcg/mg. These drugs require monitoring of serum creatinine and K⁺ within 1 week of starting therapy and periodically thereafter. [1A] (See section on *Renal Disease and Albuminuria*)

ACEI/ARBs are contraindicated during pregnancy or if contemplating pregnancy

RENAL DISEASE AND ALBUMINURIA

Screen:

Measure serum creatinine at least annually to estimate glomerular filtration rate (GFR) regardless of degree of urine albumin excretion. (See Joslin's *Guideline for Specialty Consultation/Referral* for guidance as to when to refer to a renal specialist.) [1C]

Estimate GFR (eGFR) using CKD-EPI calculation. If eGFR is <60 ml/min, evaluate for complications of kidney disease (anemia, hyperparathyroidism, and vitamin D deficiency).

Screen for albuminuria by checking urine albumin/creatinine (A/C) ratio as follows:

- Type 1 patients within 5 years after diagnosis and then yearly [1C]
- Type 2 patients at diagnosis (after glucose has been stabilized) and then yearly [1C]
- Annually in all patients up to age 70 years [2C]
- As clinically indicated in patients >70 years of age

Albuminuria is recognized as a major independent risk factor for CAD in patients with diabetes. Albuminuria may be measured with a spot or timed urine collection. Spot urine is preferred for simplicity.

Continue use of routine urinalysis as clinically indicated. [2C]

Patients should be advised that BP control, glycemic control and management of albuminuria may slow the progression of CKD.

Treatment:

If A/C ratio < 30 mcg/mg or timed urine albumin < 30 mg/24 hr:

- recheck in 1 year

If A/C ratio 30-300 mcg/mg or timed urine albumin 30-300 mg/24 hr:

- Confirm presence of albuminuria with at least 2 of 3 positive collections done within 3-6 months. In the process, rule out confounding factors that cause a false-positive such as UTI, pregnancy, excessive exercise, menses or severe hypoglycemic event. [1C]
- Consider testing first morning urine
- Consider consult with nephrologist for blood pressure control, successive increases in albumin and other issues (i.e., GFR < 60 ml/min) [2C]

Once confirmed:

- Evaluate BP and initiate/modify aggressive blood pressure treatment to achieve a BP of < 130/80 mmHg [2B]
- Recommend patient self-monitor BP with portable cuff and maintain a record/log. The monitoring schedule should be determined with the healthcare provider and is based on patient circumstance.

- Strive to improve glycemic control with an optimal goal A1C of < 7% or as otherwise clinically indicated [1A]
- Refer to diabetes educator for glucose management
- Initiate/ modify ACE inhibitor or ARB treatment if albuminuria persists. Check K⁺ and creatinine about 1 week after making these medication changes. [1A]
- Repeat A/C ratio at least every 6 months. Consider increase in frequency when changes in medication are made. [2C]

If A/C ratio > 300 mcg/mg (> 300 mg/24 hr) or persistent albuminuria (positive dipstick for protein or ≥30 mg/dl):

- Follow all guidelines as stated for A/C ratio 30-300 mcg/mg
 - Consider BP goal of < 130/80 mmHg [2B]
 - Evaluate for patient adherence, with emphasis on avoidance of high sodium and very high protein intake
 - Consider referral to RD for MNT
- Consider referral to nephrologist to:
- Assess cause(s) of impaired kidney function including assessing for non-diabetes kidney disease
 - Maximize therapies aimed at slowing progression of kidney disease (e.g., blood pressure control and reduction of urine protein level)
 - Treat complications of kidney disease (hyperphosphatemia, anemia, etc)
 - Evaluate a rapid rise in serum creatinine, abnormal sediment, concomitant hematuria or sudden increase in albuminuria.
 - Assess problems with ACE inhibitors use, difficulties in management of high BP or hyperkalemia
 - Manage resistant hypertension (blood pressure that remains above goal in spite of concurrent use of three antihypertensive agents of different classes (one class should be a diuretic and all agents should be prescribed at optimal dose amounts))

EYES

Exam Schedule:

Refer patient for comprehensive dilated eye exam or validated retinal imaging to determine level of retinopathy.

- Type 1 diabetes: initial eye exam at start of puberty or once patient is 10 years of age or older, whichever is earlier, within 3-5 years of diagnosis. Annual eye exam thereafter [1A]
- Type 2 diabetes: at diagnosis and annually thereafter [1A]
- Pregnancy in pre-existing diabetes: prior to conception and during first trimester with follow-up as determined by first trimester exam and 6-12 weeks post-partum. [1B]
- For physiologic insulin therapy (pump therapy or multiple daily injections): consult with patient's eye care provider or evaluate retinal status with validated

retinal imaging to determine level of retinopathy and appropriate follow-up care prior to initiating physiologic insulin therapy. [1A]

Treatment:

Aggressively treat known medical risk factors for retinopathy:

- Strive to improve glycemic control with optimal A1C goal of < 7%. [1A]
- Monitor eye disease carefully when intensifying glycemic control. [1A]
- Strive for BP <130/80 mmHg. [1B]
- Treat albuminuria. [1B]
- Strive to maintain total cholesterol, LDL, HDL and triglyceride levels as per the recommendations outlined in the *Lipids* Section of this Guideline. [1A]
- Treat anemia. [1B]

Activity programs that involve strenuous lifting, harsh, high-impact components, or activities that place the head in an inverted position for extended periods of time may need to be revised depending on the level of retinopathy.

Reinforce follow-up with eye care provider for any level of retinopathy including no apparent retinopathy. The frequency of follow-up is dependent upon the level of retinopathy and presence of risk factors for onset and progression of retinopathy and is determined by the eye care provider.

- For high-risk proliferative diabetic retinopathy, scatter (panretinal) laser photocoagulation is indicated promptly. [1A]
- For clinically significant macular edema (CSME), or center-involved macular edema, focal laser and/or intravitreal anti-vascular endothelial growth factor (VEGF) injection is generally indicated regardless of level of retinopathy. [1A]
- The level of diabetic retinopathy and diabetic macular edema (DME) generally determines follow-up.* [1A] See suggested follow-up below:

If No Diabetic Retinopathy:

12 months

If Mild Nonproliferative Diabetic Retinopathy:

Without DME, 12 months

With DME,** monthly if undergoing (anti-VEGF) treatment, otherwise 3-4 months

If Moderate Nonproliferative Diabetic Retinopathy:

Without DME, 6-9 months

With DME,** monthly if undergoing anti-VEGF treatment, otherwise 3-4 months

If Severe - Very Severe Nonproliferative Diabetic Retinopathy:

Without DME, *** 3-4 months

With DME, ** monthly if undergoing anti-VEGF treatment, otherwise 3-4 months

If Proliferative Diabetic Retinopathy less than High-Risk:

Without DME, *** 1 week – 3-4 months

With DME, ** 1 week – monthly if undergoing anti-VEGF treatment, otherwise 3-4 months

If High-Risk Proliferative Diabetic Retinopathy

With or without DME – scatter laser surgery with follow-up in 3 months, monthly if undergoing anti-VEGF treatment

*The presence of known risk factors for onset and progression of retinopathy may suggest follow-up at shorter intervals for all levels of retinopathy

** Focal laser surgery and/or intravitreal ranibizumab injection is generally indicated for CSME or center-involved macular edema. If receiving anti-VEGF treatment, follow-up is generally monthly

*** Scatter laser surgery may be indicated, especially for type 2 diabetes or type 1 diabetes of long duration

Intravitreal injections of steroids and anti-VEGF agents other than ranibizumab are sometimes used in clinical practice to treat macular edema despite limited studies on their effectiveness or safety to date. These modalities are currently under rigorous investigation to further define their role.

PERIPHERAL NEUROPATHY

Screen:

- Ask patient about loss of sensation in the limbs, symptoms of pain, tingling, paresthesia, weakness or gait instability.
- Evaluate feet for sensation using a 128 hz tuning fork and Semmes-Weinstein 5.07 monofilament. [1B]
- Evaluate reflexes
- Laboratory screening with complete blood count, lipid panel, thyroid panel, B12 level (methylmalonic acid and/or homocysteine if low normal B12), serum and urine protein electrophoresis, as clinically indicated.
- Neurophysiologic testing (EMG, quantitative sensory testing) should be considered in atypical cases.
- Assess for symptoms of autonomic neuropathy such as erectile dysfunction, gastroparesis, or postural hypotension.

Frequency:

- For patients with type 1 and 2 diabetes without complications, conduct symptom and examination screen at time of diagnosis and at least annually. [1C]
- For the “at-risk patients,”* conduct symptom and examination screen at all routine interval visits. [1C]
- Laboratory screening at the time of diagnosis of diabetes or with change in symptoms or examination. [1C]
- Screen for cardiovascular autonomic neuropathy at the time of diagnosis of type 2 diabetes, or 5 years after diagnosis of type 1 diabetes. Screening should be

repeated yearly or with development of symptoms. [1C] If symptoms of autonomic neuropathy are present, refer for evaluation by formal autonomic testing (including heart rate variability testing, blood pressure and heart rate response to a Valsalva maneuver and the blood pressure response to upright tilt table testing or standing.) [1B]

- Neurophysiologic testing only for atypical cases. [1C]

****“At-Risk Patients”** include patients who smoke, have vascular insufficiency, neuropathy, retinopathy, nephropathy, history of ulcers or amputations, structural deformities, infections, skin/nail abnormality, are on anticoagulation therapy or who cannot see, feel or reach their feet.

Treatment:

For patients with acute problems or who are “at risk”:

- Consider referral to neurologist for:
 - atypical neuropathy
 - rapidly progressive symptoms
 - severe pain unresponsive to first line therapy
 - weakness suggestive of diabetic amyotrophy

For patients with symptoms related to diabetic peripheral or autonomic neuropathy:

- Consider medications as they improve quality of life [1A]

FEET

Screen:

Screening should include:

- Questions about loss of sensation in the limbs, or symptoms of pain, including claudication, tingling or other paresthesia
- Foot evaluation for sensorimotor (Semmes-Weinstein 5.07 monofilament.) [1B]
- Evaluate reflexes, skin and soft tissues integrity, nail condition, callous formation, vascular sufficiency (pedal pulses) and biomechanical integrity
- Examination of shoes for wear and appropriateness.

Frequency:

- For patients with type 1 and 2 diabetes without complications, conduct foot screen at time of diagnosis and at least annually thereafter. [1C]
- For the “at-risk patients,”* check feet at all routine interval visits. [1C]

****“At-Risk Patients”** include patients who smoke, have vascular insufficiency, neuropathy, retinopathy, nephropathy, history of ulcers or amputations, structural deformities, infections, skin/nail abnormality, are on anticoagulation therapy or who cannot see, feel or reach their feet.

Treatment:

For patients with acute problems or who are “at risk”:

- Refer to podiatric physician for routine care and evaluation [1B]
- Refer to DE for foot care training** [1C]
- Consider referral to neurologist for:
 - atypical neuropathy
 - rapidly progressive symptoms
 - severe pain unresponsive to first line therapy
 - weakness suggestive of diabetic amyotrophy

****Foot care training: [1C]**

- Foot care training should address:
 - Avoidance of foot trauma
 - Daily foot inspection
 - Nail care
 - Callous formation
 - Proper footwear
 - Impact of loss of protective sensation on morbidity
 - Need for smoking cessation
 - Action to take when problems arise
 - Importance of glucose control on disease progression

For current ulcer or infection: mild* [1C]**

***** Mild Infection or Ulcer**

Superficial (no foul odor)	No significant ischemia
No bone or joint involvement	No systemic toxicity
Minimal or no cellulitis (< 2 cm)	

- Instruct patient in non-weight bearing, if appropriate
- Apply local dressings with topical antiseptic
- Consider baseline x-ray to evaluate for bone integrity and possible osteomyelitis
- Consider systemic antibiotic therapy
- Refer to podiatric physician for evaluation and treatment
- Refer for foot care training
- Ensure follow-up appointments are kept

For limb-threatening** ulcer or infection: [1C]**

******Limb-threatening:**

Deep ulcer	Bone or joint involvement
Gangrene	Lymphangitis
Cellulitis (>2cm)	Systemic toxicity
Significant ischemia	No social support system
Immunocompromised	Foul odor in ulcer

Osteomyelitis is presumed to be present if able to probe through the ulcer to the bone.

- Consider hospitalization
- Refer to a podiatrist and vascular surgeon for immediate evaluation and treatment

BEHAVIORAL HEALTH

A psychosocial evaluation should be an integrated component of the initial assessment and the ongoing care

of all patients with diabetes and should be strongly considered in the following situations:

Newly diagnosed diabetes:

Assess at least the following: [1C]

- Ability to cope with the emotional impact and lifestyle changes of diabetes
- Level of social support
- Type and degree of non-diabetes related stress

Any changes in treatment, self-care, or metabolic stability with established diabetes as evidenced by:

- Initiation of insulin
- Diabetes burnout or lack of adherence with treatment regimen: consider using PAID as a screening tool.
- Symptoms of depression: consider using PHQ-9 or PHQ-2 as a screening tool
- Symptoms of anxiety (e.g., compulsive SMBG)
- A1C >9% and inquiry indicates insulin mismanagement by the patient (omission or under-dosing)
- Exaggerated fear of hypoglycemia
- Recurrent DKA
- Family conflict related to diabetes
- Substance abuse: Consider use of CAGE alcohol screening tool

Newly diagnosed complications from diabetes:

Assess at least the following:

- Ability to cope with the emotional impact and lifestyle changes
- Level of social support
- Type and quantity of non-diabetes related stress

Patients using second generation or atypical antipsychotic medications should be monitored for weight gain with resulting increases in glucose, lipid and blood pressure levels.

SMOKING

Screen:

- Assess patient's smoking status on a routine basis.

Treatment: (If patient smokes)

- Discuss rationale for and strongly recommend smoking cessation. [1A]
- Review options available to assist in smoking cessation, including medications and cessation programs. [1B]

IMMUNIZATIONS

Recommend the following vaccines:

- Influenza vaccine: yearly for all adult patients with diabetes [1B]
- Pneumococcal vaccine: once for all patients with diabetes. [1B]

- Patients ≥ 65 years of age should receive a one-time revaccination if they received the previous dose ≥ 5 years earlier
- Repeat vaccination should be considered for those with nephrotic syndrome, chronic renal disease and other immunocompromised states
- Hepatitis B vaccine for all patients under the age of 60 years [1B]. Consider vaccinating all unvaccinated patients ≥ 60 year of age.
- Consider vaccines for other disease prevention such as for herpes zoster. Zoster vaccination is recommended for those >60 years of age unless severely immunodeficient [1B]

WOMEN'S HEALTH

(Refer to Joslin's *Guideline for Detection and Management of Diabetes in Pregnancy* for more details)

- Counsel women with the potential for conception about contraception use and relationship of blood glucose control to fetal development and pregnancy outcomes. [1C]
- At initial and annual visit, discuss sexual function.
 - Assess for infectious, hormonal, psychological, or structural etiologies if dysfunction exists.
 - Refer to specialist as indicated. [1C]
- Follow appropriate guidelines for pap/pelvic and mammography screening for primary care patients. [1B]
- Individualize approach to bone health for women with risk factors for osteoporosis, including surgical and natural menopause. [1B]
 - Ensure adequate intake of calcium and vitamin D.

MEN'S HEALTH

- At initial and annual visit, discuss sexual function and any fertility concerns.
 - assess for hormonal, psychological, or structural etiologies if dysfunction exists. [1C]
- For men with type 2 diabetes, consider screening for low testosterone: [1B]
 - screen with total testosterone and sex hormone binding globulin
- Refer to specialist as indicated.

DENTAL CARE

- Periodontal disease is associated with suboptimal diabetes control and may be a risk factor for cardiovascular disease.
- At initial visit and annually, discuss need for dental cleaning at *least* every six months. [1C]
- Refer to dental specialist for oral symptoms and findings such as sore, swollen, or bleeding gums, loose teeth or persistent mouth ulcers. [1C]

- If edentulous, refer to dental specialist for restoration of functional dentition.

OBSTRUCTIVE SLEEP APNEA

Obstructive sleep apnea is more frequent in the setting of central obesity and is a risk factor for CVD

- At initial visit and annually, inquire about sleep quality, level of fatigue and symptoms such as snoring and restless sleep [1C]
- Refer for sleep study if indicated

List of Abbreviations

AACE: American Association of Clinical Endocrinologists
 A1C: glycohemoglobin (hemoglobin A1C)
 A/C Ratio: albumin/creatinine ratio
 ACE inhibitor: angiotensin-converting enzyme inhibitor
 ADA: American Diabetes Association
 ADAG: A1c-Derived Average Glucose study
 ARBs: angiotensin receptor blockers
 ASA: aspirin
 ASCVD: arteriosclerotic cardiovascular disease
 BP: blood pressure
 CAD: coronary artery disease
 CAGE: Alcohol screening questionnaire
 CGM: Continuous glucose monitoring
 CHF: Congestive heart failure
 CKD: chronic kidney disease
 CSME: clinically significant macular edema
 CVD: cardiovascular disease
 CVD: cardiovascular disease, including coronary heart disease, peripheral vascular disease, and cerebrovascular disease
 DASH: Dietary approaches to stop hypertension
 DBP: diastolic blood pressure
 DCCT: Diabetes Control and Complication Trial
 DE: diabetes educator
 DKA: diabetic ketoacidosis
 DME: diabetic macular edema
 DSME: diabetes self-management education
 eAG: estimated average blood glucose
 ECG: electrocardiogram
 eGFR: estimated glomerular filtration rate
 EMG: electromyogram
 GFR: glomerular filtration rate
 GRADE: Grading of Recommendations, Assessment, Development and Evaluation
 HDL-C: high-density lipoprotein cholesterol
 HTN: hypertension
 IDF: International Diabetes Federation
 K⁺: potassium
 LDL-C: low-density lipoprotein cholesterol
 MDRD: Modification of diet in renal disease study equation http://nkdep.nih.gov/professionals/gfr_calculators/orig_con.htm
 MI: myocardial infarction
 min: minutes
 MNT: medical nutrition therapy
 NGSP: National Glycohemoglobin Standardization Program
 NYHA: New York Heart Association
 PAD: peripheral artery disease
 PAD: peripheral Arterial Disease
 PAID: Problem Areas in Diabetes
 PHQ-2: Patient Health Questionnaire 2 questions
 PHQ-9: Patient Health Questionnaire, 9 questions
 POC: point of care
 PVD: peripheral vascular disease
 RD: registered dietitian
 RECORD study: Rosiglitazone Evaluated for Cardiac Outcomes and Regulation of Glycaemia in Diabetes
 rMPI: radionuclide myocardial perfusion imaging
 SBP: systolic blood pressure
 SMBG: self-monitoring of blood glucose
 TIA: transient ischemic attack
 TLC: therapeutic lifestyle changes
 UTI: urinary tract infection
 VEGF: vascular endothelial growth factor

Approved by the Joslin Clinical Oversight Committee on June 6, 2014

Working group also included: Dr William Connors, Dr John Giurini and Dr Christopher Gibbons

Joslin Clinical Oversight Committee	
Om Ganda, MD - Chairperson	Medha Munshi, MD
Richard Beaser, MD	Jo- Anne Rizzotto, MEd, RD, CDE
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Lori Laffel, MD, MPH	Robert Gabbay, MD (<i>ex officio</i>)
Melinda Maryniuk, MEd, RD, CDE	

Grading System Used in Guideline

Grade of Recommendation	Clarity of risk/benefit	Quality of supporting evidence
1A Strong recommendation High quality of evidence	Benefits clearly outweigh risk and vice versa.	Consistent evidence from well performed randomized, controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk.
1B Strong recommendation Moderate quality of evidence	Benefits clearly outweigh risk and burdens, or vice versa.	Evidence from randomized, controlled trials with important limitations (inconsistent results, methodological flaws, indirect or imprecise), or very strong evidence of some other research design. Further research is likely to have an impact on our confidence in the estimate of the benefit and risk and may change the estimate.
1C Strong recommendation Low quality of evidence	Benefits outweigh risk and burdens, or vice versa.	Evidence from observational studies, unsystematic clinical experience, or from randomized controlled trials with serious flaws. Any estimate of effect is uncertain.
2A Weak recommendation High quality of evidence	Benefits closely balanced with risks and burdens.	Consistent evidence from well performed randomized controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk.
2B Weak recommendation Moderate quality of evidence	Benefits closely balanced with risks and burdens; some uncertainty in the estimates of benefits, risks and burdens.	Evidence from randomized controlled trials with important limitations (inconsistent results, methodological flaws, indirect or imprecise), or very strong evidence of some other research design. Further research is likely to have an impact on our confidence in the estimate of benefit and risk and may change the estimate.
2C Weak recommendation Low quality of evidence	Uncertainty in the estimates of benefits, risks and burdens; benefits may be closely balanced with risks and burdens.	Evidence from observational studies, unsystematic clinical experience, or from randomized controlled trials with serious flaws. Any estimate of effect is uncertain.

Evidence graded less than “A” is acceptable to support clinical recommendations in a guideline. It is also assumed that for many important clinical recommendations, it would be unlikely that level A evidence be obtained because appropriate studies may never be performed.

¹Guyatt G et al. Grading strength of recommendations and quality of evidence in clinical guidelines: Report from an American College of Physicians Task Force. *Chest* 129:174-181, 2006

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