Screening for Type 2 Diabetes Mellitus in Adults: Recommendations and Rationale
U.S. Preventive Services Task Force

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This statement summarizes the U.S. Preventive Services Task Force (USPSTF) recommendations on screening for type 2 diabetes in adults and the supporting evidence, and it updates the 1996 recommendations contained in the *Guide to Clinical Preventive Services,* second edition.(1) Explanations of the ratings and of the strength of overall evidence are given in Appendix A and Appendix B, respectively. The complete information on which this statement is based, including evidence tables and references, is available in the summary of the evidence (2) and the systematic evidence review(3) on this topic, which can be obtained through the USPSTF web site (www.preventiveservices.ahrq.gov) and through the National Guideline Clearinghouse™ www.guideline.gov). The summary of the evidence and the recommendation statement are also available in print through the AHRQ Publications Clearinghouse (call 1-800-358-9295 or e-mail ahrqpubs@ahrq.gov).

SUMMARY OF RECOMMENDATIONS

The USPSTF concludes that the evidence is insufficient to recommend for or against routinely screening asymptomatic adults for type 2 diabetes, impaired glucose tolerance, or impaired fasting glucose. **I recommendation.**

The USPSTF found good evidence that available screening tests can accurately detect type 2 diabetes during an early, asymptomatic phase. The USPSTF also found good evidence that intensive glycemic control in patients with clinically detected (not screening detected) diabetes can reduce the progression of microvascular disease. However, the benefits of tight glycemic control on microvascular clinical outcomes take years to become apparent. It has not been demonstrated that beginning diabetes control early as a result of screening provides an incremental benefit compared with initiating treatment after clinical diagnosis. Existing studies have not shown that tight glycemic control significantly reduces macrovascular complications including myocardial infarction and stroke. The USPSTF found poor evidence to assess possible harms of screening. As a result, the USPSTF could not determine the balance of benefits and harms of routine screening for type 2 diabetes.

The USPSTF recommends screening for type 2 diabetes in adults with hypertension or hyperlipidemia. **B recommendation.**

The USPSTF found good evidence that, in adults who have hypertension and clinically detected diabetes, lowering blood pressure below conventional target blood pressure values reduces the incidence of cardiovascular events and cardiovascular mortality; this evidence is considered fair when extrapolated to cases of diabetes detected by screening. Among patients with hyperlipidemia, there is good evidence that detecting diabetes substantially improves estimates

of individual risk for coronary heart disease, which is an integral part of decisions about lipid-lowering therapy.

CLINICAL CONSIDERATIONS

- In the absence of evidence of direct benefits of routine screening for type 2 diabetes, the decision to screen individual patients is a matter of clinical judgment. Patients at increased risk for cardiovascular disease may benefit most from screening for type 2 diabetes, since management of cardiovascular risk factors leads to reductions in major cardiovascular events. Clinicians should assist patients in making that choice. In addition, clinicians should be alert to symptoms suggestive of diabetes (ie, polydipsia and polyuria) and test anyone with these symptoms.

- Screening for diabetes in patients with hypertension or hyperlipidemia should be part of an integrated approach to reduce cardiovascular risk. Lower targets for blood pressure (ie, diastolic blood pressure ≤80 mm Hg) are beneficial for patients with diabetes and high blood pressure. The report of the Adult Treatment Panel III of the National Cholesterol Education Program recommends lower targets for low-density lipoprotein cholesterol for patients with diabetes. Attention to other risk factors such as physical inactivity, diet, and overweight, is also important, both to decrease risk for heart disease and to improve glucose control.

- Three tests have been used to screen for diabetes: fasting plasma glucose (FPG), 2-hour post-load plasma glucose (2 hr PG), and hemoglobin A1c (HbA1c). The American

Diabetes Association (ADA) has recommended the FPG test (≥126 mg/dL) for screening because it is easier and faster to perform, more convenient and acceptable to patients, and less expensive than other screening tests. The FPG test is more reproducible than the 2-hr PG test, has less intraindividual variation, and has similar predictive value for development of microvascular complications of diabetes. Compared with the FPG test, the 2-hr PG test may lead to more individuals being diagnosed as diabetic. HbA1c is more closely related to FPG than to 2-hr PG, but at the usual cut-points it is less sensitive in detecting lower levels of hyperglycemia. The random capillary blood glucose (CBG) test has been shown to have reasonable sensitivity (75% at a cut-point of ≥ 120 mg/dL) in detecting persons who have either an FPG level ≥126 mg/dL or a 2-hr PG level ≥ 200 mg/dL, if results are interpreted according to age and time since last meal; however, the random blood glucose test is less well standardized for screening for diabetes.

- The ADA recommends confirmation of a diagnosis of diabetes with a repeated FPG test on a separate day, especially for patients with borderline FPG results and patients with normal FPG levels for whom suspicion of diabetes is high. The optimal screening interval is not known. The ADA, on the basis of expert opinion, recommends an interval of every three years but shorter intervals in high-risk persons.

- Regardless of whether the clinician and patient decide to screen for diabetes, patients should be encouraged to exercise, eat a healthy diet, and maintain a healthy weight, choices that may prevent or forestall the development of type 2 diabetes. More aggressive interventions to establish and maintain these behaviors should be considered for patients at increased risk for developing diabetes, such as those who are overweight,

have a family history of diabetes, or have a racial or ethnic background associated with an increased risk (eg, American Indians). Intensive programs of lifestyle modification (diet, exercise, and behavior) should also be considered for patients who have impaired fasting glucose or impaired glucose tolerance, since several large trials have demonstrated that these programs can significantly reduce the incidence of diabetes in these patients. Evidence and recommendations regarding counseling about diet, physical activity, and obesity are provided in the USPSTF evidence summaries "Counseling to Promote a Healthy Diet," "Counseling to Promote Physical Activity," and "Screening and Treatment for Obesity in Adults," available on the Agency for Healthcare Research and Quality Web site at www.preventiveservices.ahrq.gov.

SCIENTIFIC EVIDENCE

Epidemiology and Clinical Consequences

The burden of suffering caused by type 2 diabetes is enormous. Among individuals aged 40-74, the prevalence increased from 8.9% for the period 1976-80, to 12.3% for the period 1988-94.(4) Current prevalence in the United States is likely even higher due to the increasing prevalence of obesity.(5) Patients with type 2 diabetes are at increased risk for both microvascular and macrovascular disease. Microvascular disease contributes to high rates of blindness, end stage renal disease, and lower extremity amputations; macrovascular disease accounts for a 2 to 4-fold increased risk for heart disease and stroke. In addition, a substantial number of people who have elevations in blood glucose not meeting criteria for diabetes (impaired fasting glucose or impaired glucose tolerance) are at increased risk for progression to diabetes and for cardiovascular disease.

The 10-year incidence of blindness among those with type 2 diabetes of 20-25 years' duration is between 5-15%, and the 10-year incidence of visual deterioration (doubling of the visual angle) is between 35-45%, with the higher rates for those requiring insulin.(6) The highest risk is among those who have a longer time to develop visual complications because of onset of diabetes at a younger age.(7)(8)

Some patients with diabetes manifest diabetic nephropathy, a condition that can progress to chronic renal failure (CRF). The incidence of CRF among those without macroalbuminuria at diagnosis of type 2 diabetes is about 0.5% after 15 years of diabetes duration and 10% after 30 years. The incidence of CRF is substantially higher (about 12% after 15 years) among those with macroalbuminuria at time of diagnosis of diabetes.(9)

Two cohort studies found that the 20-25-year cumulative incidence of lower extremity amputation (LEA) in patients with type 2 diabetes is between 3-11%.(10)(11) In the United Kingdom Prospective Diabetes Study (UKPDS) cohort, between 1-2% of participants had had an amputation within 10 years (12); in the Wisconsin Epidemiologic Study of Diabetic Retinopathy population-based cohort, about 7% of those with type 2 diabetes of short duration had had an amputation within 14 years.(13)

Elevated blood glucose is an independent risk factor for cardiovascular disease (CVD). The risk increases with the level of glucose. The absolute prevalence of established CVD at diagnosis of type 2 diabetes ranges from 8-23% (depending on the presence of other CVD risk factors) and at least 14 prospective cohort studies have found that the risk for CVD events in diabetic men is about twice that in nondiabetics, even after adjusting for age, hypertension, dyslipidemia, and smoking.(3) For women, the adjusted CVD risk among diabetics is elevated as much as fourfold compared with nondiabetics. In the UKPDS cohort of diabetic patients undergoing conventional treatment, there were 17 events of myocardial infarction (MI), 5 events of stroke, and 12 events of diabetes-related deaths, respectively, per 1000 patient-years.(12)

Diabetes also imposes a significant economic burden. In 1997, the U.S. health care system spent some $98 billion on medical care and lost productivity for people with type 2 diabetes.(14) Many individuals who satisfy the criteria for type 2 diabetes have not been diagnosed. Data from the third National Health and Nutrition Examination Survey (NHANES III) showed that 3% of the adult population aged 20 and older had not been diagnosed and yet met the diagnostic criteria for diabetes.(4)

Accuracy and Reliability of Screening Tests

Determining the accuracy of screening tests for type 2 diabetes is complicated by uncertainty of what is the most appropriate gold standard for comparison. Definitions of diabetes were originally developed using results of 2 hr PG to identify a population at substantially increased risk for retinopathy. The criterion for an abnormal FPG level was developed based on 2 hr PG, and recently revised downward (from 140 mg/dL to 126 mg/dL) to make the sensitivity of FPG comparable with that of 2 hr PG. Additional criteria – impaired fasting glucose (110 to 125 mg/dL) and impaired glucose tolerance (140 to 199 mg/dL for 2 hr PG) – have been developed to define persons who have less severe elevations of blood glucose. A study using NHANES III data demonstrated that, compared with FPG, the 2 hr PG as a screening test leads to more individuals being diagnosed as diabetic.(4)

Large population-based studies have examined the sensitivity of 2 hr PG, FPG, and HbA1c for identifying patients with retinopathy. Sensitivity and specificity for detecting retinopathy were in the range of 75-80% for all three tests using the following thresholds: FPG $\geq$ 126 mg/dL, 2 hr PG$\geq$ 200 mg/dL, or HbA1c $\geq$ 6.4%. (15)(16)(17) Other studies have examined whether these tests predict future cardiovascular disease (CVD) events. A recent meta-regression analysis of 20 observational studies found that both FPG and 2 hr PG were significantly associated with future CVD events in a continuous graded fashion, beginning at levels consistent with impaired glucose tolerance (IGT) and impaired fasting glucose (IFG) and increasing more steeply at the highest glucose levels.(18) Among those with previously undiagnosed type 2 diabetes who are in the low range of "diabetic level" FPG (ie, FPG between 126-140 mg/dL), HbA1c was normal

in about 60% of those tested, indicating it may be less sensitive for detecting lower levels of hyperglycemia.

In clinical practice, the requirement for a screening test to be fasting (as with the FPG) or post-glucose load (as with 2 hr PG) presents logistical problems. A well-conducted, population-based study found that random CBG had sensitivity and specificity in the 75-80% range for detecting type 2 diabetes defined by older criteria (ie, FPG $\geq$140 mg/dL or 2 hr PG greater than or equal to 200 mg/dL), but only if results were interpreted according to age and time since last meal.(19)

Effectiveness of Early Treatment

No trial has been conducted to establish whether systematic screening for diabetes improves health outcomes compared with usual care. Establishing the health benefits of screening for type 2 diabetes is complex because under current practice many patients with diabetes are detected through haphazard screening: about 50% of adults over 45 may have been screened for diabetes in a 3 year period.(20) The USPSTF attempted to compare the expected health outcomes from a strategy of systematic screening to those from existing care. In the absence of direct evidence from a trial of screening, the USPSTF examined indirect evidence to estimate whether screening, early diagnosis, and treatment of type 2 diabetes were likely to improve four health outcomes compared with usual care/clinical detection: visual impairment, chronic renal failure, lower extremity amputations, and CVD events.

Additionally, the results from recent RCTs demonstrate the effectiveness of intensive lifestyle interventions in reducing the incidence of diabetes in individuals with impaired fasting glucose or impaired glucose tolerance. Three large trials in the United States, Finland, and China have demonstrated that intensive programs of lifestyle modification (diet, exercise, and behavior modification) can reduce incidence of diabetes by up to 58% in these patients.(21-23)

Visual Impairment

Although early retinopathy is present in a substantial portion of patients with diabetes at the time of initial diagnosis, severe retinopathy (ie, that requiring treatment) and visual problems usually develop later in the course of disease. Two well-performed RCTs have shown that tight glycemic control reduces the relative risk for development or progression of retinopathy by 29-40%.(12)(24) After 10 years of follow-up in the UKPDS, 7.6% of those in the tight control group required laser photocoagulation compared with 10.3% of patients in the conventional treatment arm; however, no difference in visual outcomes was detected.(25)(26) One large well-performed RCT found that tighter control of systolic blood pressure (improvement of approximately 10 mm Hg) among hypertensive diabetics decreased the need for retinal photocoagulation by an absolute 4.1% and reduced deterioration in visual acuity by an absolute 9.2% over 7.5 years.(27) The incidence of blindness, however, was similar in both groups (3.3% vs. 2.4%) in this study.

The USPSTF concluded that, although retinal photocoagulation is effective in reducing the incidence of visual impairment among those with severe retinopathy or macular edema, most patients detected by routine screening will not require this intervention. Further, although tight glycemic control reduces the development and progression of retinopathy, its effects on serious visual impairment are less clear and probably occur 10 years or more after the diagnosis of

diabetes. The degree to which tight glycemic control during the preclinical period between screening and clinical detection (when glucose levels are lower compared with later stages of the disease) reduces retinopathy and later visual impairment is even less certain.

Chronic Renal Failure

Three treatments have been examined to reduce the incidence of CRF among diabetics: tight glycemic control, tight blood pressure control, and medications that interrupt the angiotensin-renin system (angiotensin converting enzyme [ACE] inhibitors and angiotensin receptor blockers [ARBs]).

Evidence from several RCTs shows that tight glycemic control, and tight blood pressure control, reduce the development and progression of albuminuria in those with type 2 diabetes, but neither intervention had a statistically significant effect on the incidence of CRF.(12)(24)(27) Good evidence shows that ACE inhibitors or ARBs, or both, reduce the development and progression of albuminuria and CRF among those with type 2 diabetes. (28-37) Two of these studies, both involving diabetics with macroalbuminuria, found a reduction in CRF in patients taking ARBs compared with placebo.(32)(33) Evidence is mixed as to whether ACE inhibitors are more effective than beta–blockers in reducing development and progression of albuminuria.

Between 3% and 8% of individuals with diabetes (detected clinically or by screening) have macroalbuminuria. As a result, most patients detected by screening will be at low risk (< 1%) for developing CRF over the next 15 years.

The USPSTF concluded that, although tight glycemic and blood pressure control and use of ACE inhibitors and ARBs reduce the development and progression of albuminuria, it could not determine whether initiating these treatments earlier as a result of screening would have an important impact on CRF.

Lower Extremity Amputations

Three types of treatment have been tested to reduce LEA: tight glycemic control, tight blood pressure control, and foot care programs. The UKPDS reported a trend toward a lower incidence of amputations with both tight glycemic control (12) and tight blood pressure control (27), but the differences did not attain statistical significance. A recent well-conducted systematic review examined the efficacy of foot care programs on the incidence of foot ulcers and amputations, and its findings were inconclusive.(38) Well-conducted trials of diabetics at high risk for foot ulcers found that intensive programs including patient education, special shoes, and health care interventions can reduce the incidence of both foot ulcers and LEAs by as much as 60%. (39)(40)

The USPSTF concluded that LEA in diabetics occurs primarily as a late complication related to the development of distal sensory neuropathy and peripheral vascular disease**,** both of which take time to develop. Although foot care programs, and perhaps tight glycemic and blood pressure control, may reduce LEA over the long term, the Task Force found no evidence that early implementation of these interventions during the time between screening and clinical detection would have an impact on the later development of LEA.

Cardiovascular Disease

Four treatments to reduce the incidence of CVD events among patients with diabetes have been studied in high-quality RCTs: tight glycemic control, tight blood pressure control, treatment of dyslipidemia, and aspirin. No RCT has demonstrated a statistically significant reduction in total CVD events from tight glycemic control. The UKPDS trial (after 10 years of follow-up) showed a trend towards reduced CVD events in patients randomized to tight glycemic control.(12) These patients had lower rates of myocardial infarction (14.7 vs. 17.4 events per 1000 patient-years) and sudden death (0.9 vs. 1.6 events per 1000 patient-years) than those receiving conventional management. Further, there were no reductions in stroke (Relative Risk [RR], 1.11), heart failure (RR, 0.91), angina (RR, 1.02), or all-cause mortality (RR, 0.94).

A number of recent RCTs have examined various aspects of the treatment of hypertension among patients with type 2 diabetes. Principal findings are that an aggressive approach to blood pressure control among patients with diabetes reduces CVD events by a relative 50% (27)(41); treatment of isolated systolic hypertension among older patients with diabetes reduces CVD events by a relative 34-69% (42)(43); treatment of those with diabetes and at least 1 other CVD risk factor with ramipril (regardless of whether they have hypertension) reduces CVD events by a relative 22% and all-cause mortality by a relative 16% (37); and ACE inhibitors and ARBs are useful antihypertensive agents for diabetics.(41)(44)

Several secondary prevention trials of treatments for patients with lipid abnormalities had enough patients with diabetes to permit subgroup analyses. Lipid treatment reduced the incidence of coronary heart disease (CHD) events by about the same relative percentage among those with diabetes as among those without diabetes (relative risk reduction between 19-42%).(45-47) No primary prevention trial of lipid therapy has included sufficient numbers of patients with diabetes to perform reliable analyses, although trends in these trials are also in the direction of benefit. The Heart Protection Study (HPS) found that including simvastatin in the treatment regimen of diabetic patients reduces major vascular events (myocardial infarction, stroke, and revascularization) from 25% to 20%, i.e. prevents one major vascular event in 20 patients, over a five-year period.(48) Aspirin reduces CHD in both diabetics and nondiabetics, with a comparable relative risk reduction (about 30%) in both groups.(49-51)

Potential Harms of Screening and Treatment

Screening for type 2 diabetes could cause harm in several ways. A diagnosis of diabetes could potentially cause "labeling" in asymptomatic individuals (ie, anxiety or a negative change in self-perception, or both) and could lead to social consequences (eg, loss of insurability). However, there is little evidence that patients found to have diabetes at screening experience any adverse effect of labeling.(52) Early detection could subject individuals to the potential risks of treatment for longer than if the diagnosis was made clinically, with uncertain benefits. Finally, screening could produce false-positive results, especially since there is not yet complete consensus on criteria for diagnosing diabetes in asymptomatic persons. Further complicating the issue are natural history data that show that between 30-50% of persons labeled as having impaired glucose tolerance or impaired fasting glucose will revert to normal glycemia without developing type 2 diabetes.(53-59) False-positive screening tests could contribute to psychological distress, a problem known to exist for other conditions.

Treatments for diabetes are relatively safe. Tight glycemic control at a time when glycemic levels are relatively low (ie, the time between screening and clinical diagnosis) can induce hypoglycemia. In the UKPDS, 2.3% of people on insulin suffered a major hypoglycemic episode each year, as did 0.4-0.6% of those on oral hypoglycemic agents.(12) ACE inhibitors(60) and statins (61)(62) have reasonably low levels of serious adverse effects. Finally, although the impact of diabetes treatment on quality of life has been a concern, data from RCTs indicate that better glycemic control among symptomatic patients improves quality of life, although these findings may not apply to patients detected by screening during the preclinical phase.(12)(63-65)

The USPSTF concluded that, despite the potential for harm in patients whose diabetes is detected by screening, the magnitude of the problem is unknown. The potential harm for patients is an important consideration because, even if early detection is assumed to be beneficial, several thousand people in the general population may need to be screened to prevent a single diabetes-related complication over a 5-year period.(3) When screening is targeted to patients with hypertension or hyperlipidemia, however, the number needed to screen to prevent a cardiovascular event is substantially lower.(3)

RECOMMENDATIONS OF OTHERS

The ADA acknowledged that data from prospective studies were insufficient to determine the benefits of diabetes screening and thus concluded that the decision to test for diabetes should be based on clinical judgment and patient preference.(66) On the basis of expert consensus, the ADA recommends clinicians consider screening for diabetes with the FPG test beginning at age 45 years and at a younger age for individuals with such risk factors as family history, overweight, and hypertension, among others. The American College of Obstetricians and Gynecologists endorses the ADA recommendations.(67) The American Heart Association recommends measuring fasting blood glucose in persons 20 years of age and older according to patient's risk for diabetes, as part of overall risk assessment for cardiovascular disease.(68) The Canadian Task Force on Preventive Health Care is currently updating its recommendations on diabetes screening.

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APPENDIX A

U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS AND RATINGS

The Task Force grades its recommendations according to one of 5 classifications (A, B, C, D, I) reflecting the strength of evidence and magnitude of net benefit (benefits minus harms):

A. The USPSTF strongly recommends that clinicians routinely provide [the service] to eligible patients. *The USPSTF found good evidence that [the service] improves important health outcomes and concludes that benefits substantially outweigh harms.*

B. The USPSTF recommends that clinicians routinely provide [this service] to eligible patients. *The USPSTF found at least fair evidence that [the service] improves important health outcomes and concludes that benefits outweigh harms.*

C. The USPSTF makes no recommendation for or against routine provision of [the service]. *The USPSTF found at least fair evidence that [the service] can improve health outcomes but concludes that the balance of benefits and harms is too close to justify a general recommendation.*

D. The USPSTF recommends against routinely providing [the service] to asymptomatic patients. *The USPSTF found at least fair evidence that [the service] is ineffective or that harms outweigh benefits.*

I. The USPSTF concludes that the evidence is insufficient to recommend for or against routinely providing [the service]. *Evidence that [the service] is effective is lacking, of poor quality, or conflicting and the balance of benefits and harms cannot be determined.*

APPENDIX B

U.S. PREVENTIVE SERVICES TASK FORCE
STRENGTH OF OVERALL EVIDENCE

The USPSTF grades the quality of the overall evidence for a service on a 3-point scale (good, fair, poor):

Good: Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes.

Fair: Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies, generalizability to routine practice, or indirect nature of the evidence on health outcomes.

Poor: Evidence is insufficient to assess the effects on health outcomes because of limited number or power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.