Does screening for diabetes in at-risk patients improve long-term outcomes?

EVIDENCE-BASED ANSWER

No randomized clinical trials or prospective studies have demonstrated adequate evidence to screen individuals for diabetes mellitus. A recently published meta-analysis for the United States Preventative Services Task Force (USPSTF) stated that "until we have better evidence about its benefits, harms, and costs, the role of screening as a strategy to reduce the burden of suffering of diabetes will remain uncertain" (strength of recommendation [SOR]: **B**, based on inconclusive studies).

The group of patients most likely to benefit from diabetes screening are patients with hypertension (SOR: **B**), or those whose risk for coronary heart disease is such that a diagnosis of diabetes would mandate addition of aspirin or lipid-lowering agents (SOR: **C**).

EVIDENCE SUMMARY

It is estimated that by the year 2010 approximately 216 million individuals worldwide will be affected with diabetes; 90% of these people will have type 2.[1] In addition, it is well documented that diabetes significantly increases the risk of morbidity and mortality, especially due to retinopathy, nephropathy, neuropathy, and coronary artery disease.[2]

For screening to be effective, the disease of interest must have an easily detectable asymptomatic state, and a treatment that improves outcomes by intervening before symptoms develop. Diabetes does have an asymptomatic state, which is of uncertain duration (likely years), and is detectable with simple, inexpensive tests: specifically, either a fasting blood glucose or a 2-hour post-glucose-load blood glucose. In order to be useful, a screening program must also lead to an intervention that reduces morbidity or mortality. The data are much less clear whether any interventions during the presymptomatic period improve patient outcomes.

No randomized trials have tested whether screening provides any benefits.[3] In a thorough systematic review using USPSTF methodologies, several potential postscreening interventions were evaluated.[3] While tight glycemic control reduces progression of albuminuria and retinopathy, it is unclear how large the long-term clinical benefit would be, or at what cost. Reasonable evidence supports more aggressive control of blood pressure for patients with diabetes to reduce adverse cardiovascular outcomes. It is

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What are Clinical Inquiries?

Clinical Inquiries answer real questions that family physicians submit to the Family Practice Inquiries Network (FPIN), a national, not-for-profit consortium of family practice departments, residency programs, academic health sciences libraries, primary care practice-based research networks, and other specialists.

Questions chosen for Clinical Inquiries are those that family physicians vote as most important through a web-based voting system.

Answers are developed by a specific method:

- FPIN medical librarians conduct systematic and standardized literature searches in collaboration with an FPIN clinician or clinicians.
- FPIN clinician authors select the research articles to include, critically appraise the research evidence, review the authoritative sources, and write the answers.
- Each Clinical Inquiry is reviewed by 4 or more peers and editors before publication in *JFP*.
- FPIN medical librarians coauthor Type I Clinical Inquiries that have required a systematic search.
- Finally, a practicing family physician writes an accompanying commentary.

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Evidence supports more aggessive control of blood pressure for patients with diabetes

important to note that the data for these interventions (aggressive blood sugar and blood pressure control) were derived in studies of patients with established diabetes; no studies have tested these interventions for patients who had early diagnosis by screening.

Since undiagnosed diabetes doubles the risk of coronary artery disease, there is the potential that intervention with prophylactic aspirin and lipid-lowering agents could reduce coronary artery disease, although this has not been tested. There is no evidence that the diagnosis of diabetes per se alters individual patients' behavior in response to lifestyle counseling, particularly about smoking cessation, diet, and exercise. It is unlikely that screening for foot ulcers would provide any benefit in those with an early diagnosis of diabetes.

There is reasonable evidence that aggressive counseling and behavioral interventions can postpone the diagnosis of diabetes for patients with glucose intolerance. The studies were too small and short to detect any meaningful difference in morbidity or mortality. In addition, it is unknown if this postponing of the onset of diabetes is cost-effective.

The risks of screening include false-positive diagnosis, labeling effect, and subjecting patients to potentially harmful medications. There is little data to estimate the size of these effects.

Using a best-case scenario, the number needed to screen (NNS) is 500 to prevent cardiovascular outcomes by aggressive hypertension therapy. This assumes a baseline rate of 6% undetected diabetes, with a 5-year lead-time benefit to screening, and 50% increase in the rate of aggressive hypertension control. Assuming the baseline rate is 3% and the lead time is 2.5 years, the NNS is 3600.

The NNS for preventing monocular blindness is higher, even using best-case assumptions. The calculations for blindness rely on greater extrapolations of the data; the other potential interventions described above had inadequate data even to make such calculations.

RECOMMENDATIONS FROM OTHERS

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. The USPSTF recommends screening for type 2 diabetes in adults with hypertension or hyperlipidemia. They report that it is likely that more aggressive treatment of hypertension, hyperlipidemia, and other cardiovascular risk factors could reduce cardiovascular morbidity and mortality.[4]

The American Diabetes Association (ADA) recommends that health care providers consider screening patients at age 45 years and continue screening in 3-year intervals. The ADA also notes that individuals who are overweight or considered to be at higher risk should be screened at a younger age and more frequently.

The ADA recommends routine screening in "high-risk" patients, defined as those with a positive family history of type 2 diabetes (in first- and second-degree relatives), or who are Native Americans, African-Americans, Hispanic Americans, or Asians/South Pacific Islanders.

The ADA also recommends screening for patients who have signs of insulin resistance or conditions associated with insulin resistance, such acanthosis nigricans, hypertension, dyslipidemia, and polycystic ovary syndrome. They note that this advice is based on expert opinion and should be carried out at the discretion of the health care provider.[5]

Danielle S. Nordone, DO, Dyanne Westerberg, DO, Diane Wolf, MLS, Department of Family Medicine, Christiana Care Health System, Wilmington, Del

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CLINICAL COMMENTARY: Evidence for universal screening is not there

Many of my patients lead unhealthy lifestyles; they become obese and often develop hypertension, diabetes, dyslipidemia, and heart disease. Further, the incidence of diabetes in the United States has grown by one third in the last decade, and the urge to screen is great. However, the evidence for a significant benefit from screening for diabetes is not there. In fact, the meta-analysis by Harris et al suggests that the number needed to screen in the most favorable group, hypertensives, would still be 900 to prevent 1 cardiovascular event. Furthermore, that estimate results from extrapolation and conjecture; no randomized controlled trial of screening for diabetes has been done. Accordingly, the recommendations by the ADA and USPSTF to screen high-risk patients are likely as aggressive as can be supported at this time—regardless of the drive to do something.

Jim Holt, MD, East Tennessee State University, Johnson City

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APPLIED EVIDENCE
"Strategies to reduce complications of type 2 diabetes," *page 366*

What is the best treatment for diabetic neuropathy?

EVIDENCE-BASED ANSWER

Tricyclic antidepressants, anticonvulsants, and capsaicin reduce the pain of diabetic neuropathy; limited data suggests that lidocaine patches may also be efficacious. Both tricyclic antidepressants and anticonvulsants are superior to placebo in relieving painful diabetic neuropathy. Compared with placebo, patients taking tricyclic antidepressants report reduced pain (number needed to treat [NNT] for at least 50% reduction= 3.5) (strength of recommendation [SOR]: **A**). Similarly, patients taking anticonvulsants report reduced pain (NNT for at least 50% reduction in pain=2.7) (SOR: **A**).

Limited evidence suggests that selective serotonin reuptake inhibitors (SSRIs) are no more efficacious than placebo (SOR: **C**). Both antidepressants and anticonvulsants have a high rate of minor adverse effects (number needed to harm [NNH]=2.7 for both). Tricyclic antidepressants have an NNH of 17 for side effects severe enough that patients withdrew from the study.

Compared with placebo, topical capsaicin also reduces pain (NNT=4) (SOR: **A**); however, there are no systematically collected data on side effects for capsaicin. A single case series demonstrates that lidocaine patches are efficacious for neuropathic pain, though expensive (SOR: **B**). Almost no trials comparing different classes of treatments have been performed.

EVIDENCE SUMMARY

A recent well-done meta-analysis[1] summarized available randomized placebo-controlled trials of antidepressants (including tricyclics and SSRIs) and anticonvulsants (including phenytoin, carbamazepine, and gabapentin). Almost all trials compare individual agents against placebo, and there have been no head-to-head trials that address functional outcomes, quality of life, patient

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