The Growing Importance of Diabetes Screening

Editorials

A classic report by T. Franklin Williams et al. (1) in 1967 documented glaring deficiencies in diabetes care that went largely uncorrected for the next 30 years. It is only in the last 10 years that we have seen substantial and sustained improvement in basic aspects of care such as glycemic control, blood pressure control, and lipid control (2). Since 1995, there have been substantial and sustained improvements in glucose, blood pressure, and lipid control in adults with diabetes, and in some reports from medical groups, A1C is now <7.0%, mean SBP <128 mmHg, and mean LDL <90 mg/dl (3). The increased likelihood that those with diabetes will receive adequate treatment increases the importance of early detection of diabetes through screening for diabetes and pre-diabetes.

However, in the last decade sobering data have also emerged that indicate that more intensive control is not necessarily better. The hope that normalization of glucose in those with diabetes would virtually abolish the increased cardiovascular risk associated with type 2 diabetes is vanishing. Rather than confirm expected benefits, recent trials instead provide a most unwelcome quantification of the risks of intensive glycemic control, including high treatment costs, increased risk of severe hypoglycemia, substantial weight gain, and even, in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial, an increased risk of death (4–6). These sobering and unexpected data have far reaching implications that will take years to appreciate. However, it is immediately apparent that more attention needs to be devoted to primary prevention of type 2 diabetes and to early identification of cases of diabetes and its insidious progenitor, pre-diabetes.

Our recent success in achieving reasonable levels of glycemic control, and emerging data that more intensive control is not necessarily better, clearly indicate the need for more effective screening for and primary prevention of diabetes. Those identified with pre-diabetes may benefit from lifestyle or pharmacological intervention that prevents or delays the onset of diabetes.

Critique of Chatterjee et al.

In this issue of Diabetes Care, Chatterjee et al. (7) report that population-based diabetes screening may be cost saving. This seems like very good news, and one imagines that data such as these might create some momentum for health plans to endorse a policy of more widespread diabetes screening. But before acting on these data, we must carefully examine the design and conduct of the study, and the assumptions that underlie the model’s cost-saving conclusion.

In the analysis presented, volunteer participants aged 40–74 years without a prior diagnosis of diabetes were recruited for diabetes screening. Participants averaged 48 years of age with a BMI of 30 kg/m²; 55% were African American. Multiple nonfasting testing strategies were investigated at an initial visit. Nonfasting tests were chosen due to convenience and the ability to administer tests without prior planning. At a second visit, participants had a diagnostic 75-g oral glucose tolerance test. Pre-diabetes (impaired glucose tolerance [IGT] and/or impaired fasting glucose [IFG]) was identified in 19.5% of participants and diabetes in 4.9%. Thus, combining diabetes and pre-diabetes, nearly one-quarter of the population was identified for possible intervention. Costs for screening are tallied, and cost savings resulting from early detection are proposed. Screening is found to be cost saving from a health system perspective and nearly cost neutral from a societal perspective.

Unfortunately, several considerations make it unlikely that these findings can be replicated in primary care settings. First, the age, racial composition, and BMI of the sample indicate that the population was at high risk for diabetes and pre-diabetes. Moreover, the use of volunteers, rather than a well-defined practice-based population, inflates the rate of diabetes and pre-diabetes detected, because those who volunteer for screening are likely to do so due to personal concerns of higher diabetes risk. Previous efforts at practice-based screening for diabetes have found fewer candidates for intervention (8).

The authors provide a well-detailed derivation of screening costs, and treatment costs are derived from nationally representative sources. However, their projected cost savings rely on an assumed 10% cost reduction from early detection and treatment. This assumption is largely speculative, and the authors demonstrate that their results are highly sensitive to this assumption. This finding is also inconsistent with the literature examining the costs of diabetes care, which has documented increased costs associated with diabetes care management (9,10). Several cost-effectiveness analyses have shown that while cost-effective, more intensive diabetes care is not typically cost saving (11–13).

Consistency with American Diabetes Association screening recommendations

At first glance, the findings of Chatterjee et al. (7) may appear to contradict current guidelines of the American Diabetes Association (ADA), which recommend screening adults age 45 years and older every 3 years (14). However, with further consideration, it is clear that their approach is consistent with clinical guidelines that recommend periodic screening for high-risk populations.

ADA recommends testing for diabetes and pre-diabetes among all individuals age 45 years and older and also among adults with BMI ≥25 kg/m² who have additional risk factors including physical inactivity, a first-degree relative with diabetes, being a member of a high-risk ethnic population, and having a history of gestational diabetes, polycystic ovary syndrome, or one of several clinical risk factors such as hypertension, HDL <35 mg/dl, triglycerides >250 mg/dl, A1C ≥5.7%, IGT, IFG, or cardiovascular disease. If results are normal, screening should be repeated at 3-year intervals, with consideration of more frequent testing depending on initial results and risk status. Separate testing criteria are proposed for pregnant women and for children.
The ADA guidelines are based largely on expert recommendation, in the absence of definitive randomized clinical trials examining population-based screening. Clearly, diabetes and pre-diabetes are common and costly chronic diseases that are increasing in prevalence and impose a significant public health burden (15). The long presymptomatic phase, the availability of testing, and the ability of interventions to reduce the progression from pre-diabetes to diabetes and to reduce the risk of complication from diabetes, support the clinical recommendations (16). Other advisory groups may require more strict evidence to guide screening for diabetes and pre-diabetes. For example the U.S. Preventive Services Task Force (USPSTF) recommends testing only during hypertension visits (blood pressure >135/80 mmHg) on the basis that strong evidence exists only for increased cardiovascular risk among people with diabetes (17).

A recent cost-effectiveness analysis of alternative sequential screening strategies in a representative U.S. population also supports the ADA’s guidelines. Kahn et al. (18) show that screening adults age 45 years and older every 3 years resulted in a 91% increase in quality of life-years gained compared with annual screening among adults with hypertension (blood pressure >140/90 mmHg). Kahn et al. also identify a main limitation for randomized trials of screening: Even a trial including 650,000 participants followed over 50 years would probably fail to show a difference among strategies. Thus, screening recommendations may need to be based on a variety of study designs including simulation studies.

Summary
The work of Chatterjee et al. (7) and Kahn et al. (18), along with other recent reports, provide important new information on the merits and costs of screening for diabetes. Although the case for type 2 diabetes screening being cost saving is a dubious one, these new data confirm that screening high-risk patients for diabetes is a reasonable clinical strategy and not prohibitively expensive. Thus, these data can be interpreted as providing additional support for the current ADA type 2 diabetes screening recommendations. Conducting a definitive randomized trial to support or refute diabetes screening recommendations is increasingly unfeasible in the U.S. or most of Europe for a variety of reasons. Instead, we will be left with a large number of studies of varied design and conduct, and we must infer from their sometimes incongruent results a reasonable approach to diabetes screening. Several questions come up in this regard. First, to what extent will the recent endorsement of new A1C thresholds for the diagnosis of diabetes and pre-diabetes reshape the diabetes screening landscape (14)? Second will the new emphasis on comparative effectiveness, and the use of sophisticated instrumental variable or propensity score analytic strategies, increase the confidence we have in the results of large observational studies? Third, will revised simulation models that include new information reflecting the recent findings of ACCORD, Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation (ADVANCE), and Veterans Affairs Diabetes Trial (VADT) change the calculus on cost-effectiveness of screening? Fourth, can organizations including ADA and USPSTF reach a common, practical understanding of what constitutes a reasonable approach to diabetes screening, so that primary care providers will have one, instead of multiple guidelines to follow? And finally, how will new genetic and other novel predictors of macrovascular or microvascular complications inform future diabetes screening strategies?

We live in exciting times, and our collaborative effort to develop more effective and efficient diabetes screening strategies in conjunction with the development of improved primary preventive strategies is a signature challenge now faced by the worldwide diabetes community.

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