

Predicting Risk for Diabetes: Choosing (or Building) the Right Model

Whether to screen for type 2 diabetes mellitus in asymptomatic adults is controversial (1). No trial has established that systematic screening for diabetes and early treatment improve health outcomes more than treatment after routine clinical diagnosis (2). The U.S. Preventive Services Task Force (USPSTF) recently recommended testing adults for diabetes if they have symptoms of diabetes or evidence of diabetic complications, including vascular disease (2). It also recommended screening adults for diabetes if they have sustained blood pressure greater than 135/80 mm Hg, because lowering blood pressure below conventional target values in patients with diabetes reduces the incidence of cardiovascular events and mortality (2). Although the ongoing ADDITION (Anglo-Danish-Dutch Study of Intensive Treatment in People with Screen Detected Diabetes in Primary Care) (3) may settle the benefits of screening and early treatment, the USPSTF currently recommends against screening asymptomatic adults for diabetes, largely because evidence of benefit is lacking (2).

If we do not screen asymptomatic adults for diabetes, we miss an opportunity to identify those who are at increased risk for diabetes because they have dysglycemia (impaired glucose tolerance [IGT] or impaired fasting glucose [IFG]). Randomized, controlled clinical trials from Asia, Europe, and North America have conclusively shown that treating people who have dysglycemia with lifestyle interventions (4–6) or medication (6–8) can delay or prevent type 2 diabetes. The USPSTF recognized that intensive lifestyle modification programs can reduce the incidence of diabetes (2). It concluded, however, that the recommendation to eat a healthful diet, be active, and maintain a healthy weight applies to everyone, not just those at high risk for diabetes (2). To reduce the burden of diabetes, the USPSTF would target entire populations of healthy people rather than persons at especially high risk (2).

Either approach benefits from accurate prediction of risk for diabetes. Intensive lifestyle modification programs may entail substantial costs (9), and medication interventions incur costs and may cause harm. Therefore, potential harms may outweigh benefits when these interventions are applied to persons at relatively low risk for diabetes. Clinicians need simple, sensitive, and specific methods to identify persons who are at increased risk for diabetes and are therefore most likely to benefit from intensive diabetes prevention interventions.

Simple self-assessment questionnaires and more complex scoring systems can identify persons at high risk. Some investigators have used cross-sectional data to develop models to detect prevalent IGT, IFG, and diabetes (10–13). These models have a substantial advantage because efficacy trial results apply directly to the patients these models detect; all such trials have enrolled patients with diagnosed IGT, IFG, or both (4–8). Other investigators

have used longitudinal data from cohorts who are free of diabetes at baseline. These models predict the development of diabetes in 8 to 10 years (14–17) and identify persons who may respond to interventions to prevent diabetes. Both types of models have included readily available demographic, anthropometric, and clinical risk factors and diagnostic tests (10–17).

Models to identify patients with dysglycemia or to predict future risk for type 2 diabetes should be simple, parsimonious, and accurate. The choice of predictors depends in part on how the model will be implemented. A clinician could use the model during an office visit, or a health plan could search an electronic database to find patients who are at increased risk. Demographic risk factors, such as race or ethnicity; anthropometric risk factors, such as waist circumference; and clinical risk factors, such as family history of diabetes, are easily obtained at face-to-face encounters but may not be available in electronic databases. Similarly, test results that help to define risk, such as fasting glucose, high-density lipoprotein cholesterol, and triglyceride levels, may be obtained from electronic databases but may not be readily available during an office visit. Finally, knowing whether a patient has clinical risk factors, such as a history of glucose intolerance, gestational diabetes, or polycystic ovary disease, depends on the patient's access to care and local standards of care, which may vary by socioeconomic status and other factors. The feasibility of implementing any screening model will depend on the context in which it is used and the availability and completeness of the requisite risk factor data.

In developing a screening strategy, one must accept a trade-off between sensitivity and specificity (1), which depend on the threshold value (or cut-point) used to define a positive test result. For example, if one chooses a lower glucose cut-point to define a positive result for dysglycemia, sensitivity increases but specificity decreases. A lower cut-point results in more complete ascertainment of persons with dysglycemia but will identify substantially more persons who do not have dysglycemia on further diagnostic testing (18). To set the cut-point, one must first decide the desired level of sensitivity and specificity, which means weighing the consequences of leaving cases undetected (false-negative results) against those of classifying healthy persons as abnormal (false-positive results). Highly sensitive tests are preferable if screening is performed infrequently, the disease is relatively common, and serious health consequences result from failure to diagnose and treat early. Highly specific tests are preferred if false-positive results can harm the person emotionally, physically, or financially; the target disease is uncommon; screening will be repeated over time; and delayed diagnosis has few adverse consequences. It has been suggested (18) that in diabetes screening, tests with moderate sensitivity

(about 60%) but high specificity (about 90%), repeated every 3 years, optimize the trade-off between disease detection and avoiding false-positive results.

Kahn and colleagues (19) present 2 models to predict the future risk for diabetes in patients who do not have diabetes at baseline. Their basic model includes demographic, anthropometric, and clinical risk factors. Their enhanced model includes these risk factors plus fasting laboratory test results (19). Kahn and colleagues developed this model by using data from the ARIC (Atherosclerosis Risk in Communities) study, the same research database Schmidt and colleagues used (16) to develop a model to predict future diabetes. Unlike the earlier study, Kahn and colleagues included data from additional patients and had longer follow-up, and their models are simple enough to calculate with pencil and paper. The investigators validated the models in a separate ARIC study population.

The proposed models have several limitations. The most predictive variables in the basic model include waist circumference, family history of diabetes, history of hypertension, and height, which are easily obtained during an office visit but are often not available in an electronic database. Although fasting glucose and waist circumference were the strongest predictors in the enhanced model, they also are often unavailable in electronic medical records. In 1 large managed care organization, we found that fewer than 5% of nondiabetic patients older than 45 years had received a fasting glucose test in the previous 2 years (20).

A second limitation relates to the cut-point used to define a positive test. The “optimal” cut-point for the basic model resulted in a sensitivity of 69%, which is good, but a specificity of only 64%, which is quite low for a screening test and yielded many false-positive results. Indeed, the probability of developing diabetes over 10 years for persons with positive screening test results was only 29%; 71% of those identified by the basic model did not develop diabetes over 10 years. Although lifestyle interventions for persons with positive results would be safe, the resources might be better used for other purposes. The risk–benefit ratio of drugs to prevent diabetes could be disadvantageous for those with positive screening test results because relatively few would develop diabetes without the intervention, whereas everyone who received treatment would be at risk for harms.

A third limitation relates to the number of variables included in the proposed models. Screening tools must be parsimonious. Most of the previously published models (10–17) have included only 5 to 8 risk factors. The inclusion of 11 risk factors in the basic model and 13 in the enhanced model improved Kahn and colleagues’ models relative to earlier models with fewer predictors. However, when comparing alternative models, performance must be weighed against simplicity, and model fit should be assessed as a function of the number of terms in the model, with a penalty for additional variables. Furthermore, when the model is implemented, missing data for individual risk

factor variables will predictably decrease model performance relative to that observed in the derivation data set. With many variables in the model, missing data are more likely, particularly for infrequently measured analytes, such as uric acid.

The models Kahn and colleagues propose clearly advance the cause of identifying persons at risk for diabetes who are likely to benefit from focused clinical interventions. Their models should be applicable to both white and African-American persons in the United States who are 45 to 64 years of age. Factors to consider when choosing a model for screening include the availability of risk factor data in the clinical setting, the optimal cut-point to define a positive test, and the simplicity of the model. Experience indicates that applying strategies to populations with different demographic, socioeconomic, and clinical characteristics yields substantially different sensitivities, specificities, positive predictive values, and numbers needing further testing (1). Ideally, health care systems should generate their own population-specific screening models.

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