Costs of Screening for Pre-diabetes Among U.S. Adults

A comparison of different screening strategies

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OBJECTIVE — We evaluated various strategies to identify individuals aged 45–74 years with pre-diabetes (either impaired glucose tolerance or impaired fasting glucose).

RESEARCH DESIGN AND METHODS — We conducted a cost analysis to evaluate the effectiveness (proportion of cases identified), total costs, and efficiency (cost per case identified) of five detection strategies: an oral glucose tolerance test (OGTT), a fasting plasma glucose (FPG) test, an HbA1c test, a capillary blood glucose (CBG) test, and a risk assessment questionnaire. For the first strategy, all individuals received an OGTT. For the last four strategies, only those with a positive screening test received an OGTT. Data were from the Third U.S. National Health and Nutrition Examination Survey, 2000 census, Medicare, and published literature. One-time screening costs were estimated from both a single-payer perspective and a societal perspective.

RESULTS — The proportion of pre-diabetes and undiagnosed diabetes identified ranged from 69% to 100% (12.1–17.5 million). The cost per case identified ranged from $176 to $332 from a societal perspective.

CONCLUSIONS — There is a tradeoff between effectiveness and efficiency in choosing a strategy. The most favorable strategy depends on if the goal of the screening program is to identify more cases or to pursue the lowest cost per case. The expected percentage of the population willing to take an OGTT is also a consideration.

Type 2 diabetes is a serious and costly disease and a growing public health problem (1, 2). Despite the availability and use of a number of effective treatments to prevent diabetes complications, the disease pursues a degenerative path. Results of recent clinical trials indicate that the progression to diabetes from impaired glucose tolerance (IGT) can be delayed or prevented substantially by lifestyle modification or medications (3–5).

Responding to the results of the Diabetes Prevention Program (DPP) and other prevention trials, the American Diabetes Association (ADA) has recommended that diabetes prevention efforts target people with pre-diabetes (either IGT or impaired fasting glucose [IFG]) (6). To identify people with pre-diabetes, the ADA has recommended screening during a health care office visit for men and women who are age ≥45 years, particularly those with a BMI ≥25 kg/m². The purpose of this study was to examine the effectiveness, costs, and efficiency of five strategies to identify people with pre-diabetes based on a one-time screening of the U.S. population.

Study population
Our study population included individuals age 45–74 years who visited a health care provider at least once in the past year and did not report a previous diagnosis of diabetes. To estimate the number in the U.S. population who were eligible, we first obtained the number of civilian people age 45–74 years from the 2000 census (80.3 million) (7). Second, using estimates from the Third U.S. National Health and Nutrition Examination Survey (8), we excluded 7.7 million (9.6%) people who had previously been diagnosed with diabetes. Finally, we excluded 18.2 million individuals (25%) who did not visit a health provider in the year 2000 (9). Therefore, the total number of people eligible for pre-diabetes screening in our study was 54.4 million. An estimated 70.9% of the population age 45–74 years had a BMI ≥25 kg/m² (8). If screening was restricted to those with a BMI ≥25 kg/m² in the targeted age-group, the eligible population would be further reduced to 37.4 million.

Analytical procedures
Detection strategies and evaluation measurements. Our selection of strategies to detect pre-diabetes was based on information available on screening tests and the feasibility of large-scale screening in clinicians’ offices. We examined five screening strategies: 1) testing all with an oral glucose tolerance test (OGTT), in which all individuals in the study popu-
Table 1—Sensitivity and specificity of various tests for identifying prediabetes (IGT or IFG) or undiagnosed diabetes

<table>
<thead>
<tr>
<th>Identification test</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-h OGTT with cutoff value $\geq 140$ mg/dl in the testing all with OGTT strategy</td>
<td>100</td>
<td>100</td>
<td>—</td>
</tr>
<tr>
<td>FPG test with cutoff values $\geq 110$ mg/dl in the testing all with OGTT strategy</td>
<td>100</td>
<td>100</td>
<td>—</td>
</tr>
<tr>
<td>$\geq 95$ mg/dl in the FPG testing strategy</td>
<td>91</td>
<td>19</td>
<td>8</td>
</tr>
<tr>
<td>A1C test with cutoff values of $\geq 5.0%$</td>
<td>70</td>
<td>67</td>
<td>17</td>
</tr>
<tr>
<td>CBG test with a cutoff value of $\geq 100$ mg/dl</td>
<td>69</td>
<td>54</td>
<td>17</td>
</tr>
</tbody>
</table>

Different cutoff values can be used to define positive cases for three of the strategies (FPG testing, HbA$_{1c}$ screening, and CBG screening). To assess the impact of different definitions of a positive case on our results, we examined multiple cutoff values used in clinical trials (5) or suggested in the literature (10–13). Three cutoff values were assessed for FPG testing (90, 95, and 110 mg/dl), three cutoff values for HbA$_{1c}$ screening (5.0%, 5.5%, and 6.0%), and five cutoff values for CBG screening (90, 100, 110, 120, and 140 mg/dl). The following cutoff values (a glucose level 95 mg/dl for FPG testing, an HbA$_{1c}$ level 5.0%, and a glucose value 100 mg/dl for CBG screening) yielded the lowest cost per case identified for each strategy and, thus, were selected for this study.

We measured the effectiveness of a detection strategy by the proportion of pre-diabetes and undiagnosed diabetes cases identified. We defined IGT, IFG, and undiagnosed diabetes using ADA or World Health Organization criteria (14,15). We included the number of undiagnosed diabetes identified in measuring the effectiveness because identification of undiagnosed diabetes is an unintentional but beneficial by-product of screening for pre-diabetes. We measured the total cost of a strategy by estimating the direct economic cost associated with screening everyone in our study population. We evaluated the efficiency of each strategy using the cost of detecting each case of pre-diabetes or undiagnosed diabetes. We also evaluated the effectiveness, cost, and efficiency of each detection strategy when screening for pre-diabetes was restricted to those age 45–74 years with a BMI $\geq 25$ kg/m$^2$.

**Estimating the effectiveness of each detection strategy.** The effectiveness of each detection strategy was measured by the proportion of cases identified, which by definition is equal to the sensitivity of the strategy. Information on the sensitivity and specificity of individual tests is presented in Table 1. For the purpose of this study, we assumed that the OGTT and FPG were both 100% sensitive and specific for identifying IGT, IFG, and undiagnosed diabetes.

**Estimating the total cost and efficiency of each detection strategy.** We included both medical and nonmedical costs in estimating the direct cost of each strategy. Medical costs included laboratory tests, personnel time, and other material costs (e.g., costs of copying and mailing). Non-medical costs included transportation to a health care provider and patient’s time spent traveling and receiving tests. The total direct cost for each strategy was calculated as a sum of the cost associated with various resources (e.g., physician time, laboratory tests) used. The cost of each resource was the product of the following three components: number of physical units used to screen one person, the unit value of the resource, and the number of individuals screened. The resources used and their unit values by detection strategy are presented in Table 2.

The cost of a laboratory test was based on Medicare reimbursement rates (16). Physician fees were estimated from HealthCare Consultants of America (17). Transportation costs to a health provider were obtained from the literature (18,19). The time cost of medical office staffs other than physicians and patients was obtained from the Bureau of Labor Statistics (20). All costs were expressed in U.S. dollars for the year 2000.

The cost of identifying one case was calculated as the total cost of a detection strategy divided by the total number of cases identified. We estimated the unit cost from two perspectives: a single-payer health care system perspective, which included only the direct medical cost, and a societal perspective, which included both the direct medical and nonmedical costs.

**Sensitivity analysis.** We examined several factors that may have important effects on study outcomes. These factors included: <100% adherence to each screening strategy, changes in the prevalence of pre-diabetes and undiagnosed diabetes, and the need for an OGTT test to confirm identified cases. In our base case analysis, we assumed 100% adherence for each detection strategy. This is unlikely if testing is carried out in a normal clinical setting. There are many reasons why patients may not desire to be screened, such as a lack of perceived benefit and cost of the visit. Health care providers may not follow the recommended guidelines due to lack of time and financial incentive. In addition, adherence would likely vary by detection strategy. For example, adher-
en for an OGTT may be lower than a FPG test alone because of the time needed and inconvenience of the OGTT. We examined how the results of our base case analysis changed when adherence to the FPG test was 75% and that to the OGTT was 50%.

Further, the prevalence of pre-diabetes and undiagnosed diabetes differs by subpopulations and changes over time. For example, the prevalence of pre-diabetes and undiagnosed diabetes is higher for African Americans (21). Prevalence may also decrease if screening was performed every 3 years, as the ADA recommends (6). Thus, we examined how a 25% change in the prevalence of pre-diabetes and undiagnosed diabetes would affect the study results.

Finally, we assumed FPG and OGTT were 100% sensitive and specific for identifying pre-diabetes and undiagnosed diabetes. This is a reasonable assumption considering FPG and OGTT are the current “gold standards” for defining pre-diabetes and diabetes (14,15). However, there are reasons, such as intraindividual reproducibility, to believe these tests are “less than perfect.” Additionally, confirmation tests may be needed before treatments are initiated. In fact, the ADA recommends retesting anyone with an abnormal test to confirm the result (6). Thus, we examined the effect of adding a confirmatory OGTT to each strategy. We assumed that this additional OGTT would result in a 10% rate of false-positive cases.

RESULTS

Effectiveness of the detection strategy

Among the 54.4 million people who met our inclusion criteria for the year 2000, we estimated that 12.1 million people would have pre-diabetes and 5.4 million would have undiagnosed diabetes. If screening was restricted to those with BMI ≥25 kg/m², 37.4 million people would be screened, 9.6 million of whom would have pre-diabetes and 4.7 million undiagnosed diabetes. The proportion of pre-diabetes and undiagnosed diabetes cases identified ranged from 69% to 100% (12.1–17.5 million). If the screening was carried out among those with BMI ≥25 kg/m², the proportion of pre-diabetes and undiagnosed diabetes cases identified remained the same as for screening all individuals, but the numbers of cases reduced to a range from 9.8 to 14.3 million. The number of pre-diabetes or undiagnosed diabetes cases identified per 1,000 people screened ranged from 153 to 222 with no BMI restriction and from 175 to 259 with the BMI restriction. Testing all with OGTT was the most effective, followed by HbA1c screening and FPG testing.

Efficiency of the detection strategy

The total costs (direct medical and direct nonmedical costs) for screening 54.4 million individuals age 45–74 years who visited a health care provider in the U.S. during the previous year ranged from $3.03 to $5.30 billion (Table 3), whereas the direct medical costs alone ranged from $2.16 to $3.76 billion. The total cost per 1,000 people screened ranged from $55,300 to $96,000, and the direct medical costs alone ranged from $39,500 to $68,700. HbA1c screening had the highest cost, followed by testing all with OGTT and FPG testing. CBG screening had the lowest cost. The total cost (medical and nonmedical costs) was lower when screening was restricted to the 37.4 million individuals who had a BMI ≥25 kg/m² (Table 3).

The cost per case of pre-diabetes or undiagnosed diabetes identified varied by detection strategy (Table 3). From a single payer perspective, the costs per case identified ranged from $176 to $236, with HbA1c screening being the highest cost strategy and CBG screening being the lowest cost strategy. All strategies, with the exception of HbA1c screening, cost <$200 per case identified. From a societal perspective, the cost per case of pre-diabetes or undiagnosed diabetes identified ranged from $247 to $332 (Table 3). Again, HbA1c screening was the most expensive strategy, and CBG screening was the least expensive strategy.

The cost per case identified for each strategy was lower when screening was restricted to those individuals with a BMI of ≥25 kg/m². It ranged from $153 to $200 from a single payer perspective and from $215 to $282 from a societal perspective (Table 3).

Comparisons of effectiveness and efficiency of different strategies

The proportion of cases missed and the cost per case identified by each strategy are presented in Fig. 1. The vertical axis represents the percent of cases missed, and the horizontal axis represents the cost per case identified. The closer a point is to the origin, the more efficient the strategy represented by that point. This curve (sometimes referred to as an “efficiency frontier”) represents the “best” combination of effectiveness and efficiency that could be achieved based on the five screening strategies evaluated. The points off the curve represent an inferior strategy because the same proportion of cases could be identified at a lower cost or a high proportion of the cases could be identified at the same cost. HbA1c screening was an inferior strategy compared with testing all with OGTT. There was a tradeoff between the proportion identi-
Table 3—Total and unit costs of prevalence-based screening for prediabetes (IGT or IFG) or undiagnosed diabetes, individuals age 45–74 years by payers’ perspective and detection strategy

<table>
<thead>
<tr>
<th>Case detection strategies</th>
<th>Societal perspective</th>
<th>Single payer perspective</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total direct medical and nonmedical costs (billion U.S.$)</td>
<td>Costs per case identified (U.S.$/case)</td>
</tr>
<tr>
<td>All individuals</td>
<td>Individuals with BMI ≥25 kg/m²</td>
<td>All individuals</td>
</tr>
<tr>
<td>Testing all with OGTT</td>
<td>5.23</td>
<td>3.59</td>
</tr>
<tr>
<td>FPG testing with a cutoff values of ≥95 mg/dl</td>
<td>4.86</td>
<td>3.56</td>
</tr>
<tr>
<td>A1C screening with cutoff values of ≥5.0%</td>
<td>5.30</td>
<td>3.70</td>
</tr>
<tr>
<td>CBG screening with cutoff values of ≥100 mg/dl</td>
<td>3.03</td>
<td>2.15</td>
</tr>
<tr>
<td>Risk assessment questionnaire screening</td>
<td>3.17</td>
<td>2.22</td>
</tr>
</tbody>
</table>

Figure 1—Proportions of pre-diabetes (either IGT or IFG) and undiagnosed diabetes missed and cost per case identified for individuals age 45–74 years by detection strategy. OGTT, all eligible individuals received a 2-h OGTT. A1C, all people received an HbA1c test, and those who had a value of 5.0% or more would be given an OGTT. FPG, all individuals received a fasting plasma glucose test, and those who had a value between 95 and 110 mg/dl would be given an OGTT. CBG, all individuals received a CBG test, and those who scored ≥10 points were given an OGTT. Questions, all individuals responded to the risk assessment questionnaire, and those who scored ≥10 points were given an OGTT. CBG screening was off the efficiency frontier curve, the difference in both the proportion of cases missed and cost per case identified was small compared with the CBG screening strategy.

Sensitivity analysis
Reducing adherence by 25% for the FPG test and by 50% for the OGTT lowered the number of cases detected and thus the effectiveness (Table 4). Compared with a 100% adherence, total medical costs of implementing each strategy decreased, but costs per case identified increased (Tables 3 and 4). In addition, lower adherence made FPG testing the most effective strategy and changed the efficiency rankings of the strategies. A higher or lower prevalence of pre-diabetes and undiagnosed diabetes cases identified but would not change the effectiveness. Additionally, a higher or lower prevalence would affect the total cost for all detection strategies (except testing all with OGTT), as well as the efficiency for all detection strategies. Finally, a higher prevalence of pre-diabetes and undiagnosed diabetes would affect the efficiency ranking of each strategy, which favors high-sensitivity strategies. However, with either a 25% increase or a 25% decrease in the prevalence of pre-diabetes and undiagnosed diabetes, the CBG screening strategy remained the most efficient strategy.

Adding a confirmatory OGTT for all identified cases (assuming a 10% false-positive rate) would increase both the total cost and cost per case identified for each strategy. The cost per case identified would range from $252 to $318 from a single payer perspective and from $365 to $459 from a societal perspective. These costs represented a range of increase between 35% and 43% from a single payer perspective and an increase of between 38% and 48% from a societal perspective, compared with the efficiency estimates from our base case analysis. However, efficiency rankings of the five strategies remained the same.

CONCLUSIONS—We selected five strategies that can be used for detecting people with pre-diabetes or undiagnosed diabetes and evaluated their effectiveness, total cost of screening all eligible individuals, and their efficiency. Evaluations were performed under two scenarios: screening all individuals age 45–74 years...
Cost of screening for prediabetes

Table 4—Percentage of cases identified, total and unit cost from a single payer perspective of a prevalence-based screening for pre-diabetes (IGT or IFG) or undiagnosed diabetes among individuals aged 45–74 years old, assumed lower adherence*

<table>
<thead>
<tr>
<th>Case detection strategies</th>
<th>Cases identified (%)</th>
<th>Total medical cost (U.S.$ billion)</th>
<th>Medical costs per case identified (U.S.$/case)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All individuals</td>
<td>All individuals</td>
<td>All individuals with BMI ≥25 kg/m²</td>
</tr>
<tr>
<td>Testing all with OGTT</td>
<td>50</td>
<td>2.07</td>
<td>1.42</td>
</tr>
<tr>
<td>FPG testing with a cutoff values ≥95 mg/dl</td>
<td>63</td>
<td>2.09</td>
<td>1.19</td>
</tr>
<tr>
<td>A1C screening with cutoff values of ≥5.0%</td>
<td>46</td>
<td>2.61</td>
<td>1.81</td>
</tr>
<tr>
<td>CBG screening with cutoff values of ≥100 mg/dl</td>
<td>35</td>
<td>1.55</td>
<td>1.08</td>
</tr>
<tr>
<td>Risk assessment questionnaire screening</td>
<td>35</td>
<td>1.43</td>
<td>1.00</td>
</tr>
</tbody>
</table>

*Assuming adherence of 75% for FPG and 50% for 2-h OGTT.

and screening only individuals age 45–74 years with a BMI ≥25 kg/m².

To select the most favorable strategy for detecting pre-diabetes and undiagnosed diabetes, both the effectiveness and efficiency of each strategy need to be considered. From Fig. 1, we concluded testing all with OGTT identifies more cases at a lower cost than HbA₁c screening. Thus, testing all with OGTT was a better detection strategy than HbA₁c screening. However, the choices among the three screening strategies that were on the efficacy frontier (testing all with OGTT, CBG screening, and FPG testing) were less clear because of the tradeoff between effectiveness and efficiency. Thus, the choice would depend on if the goal of the screening program was to identify more cases or to pursue the lowest cost per case identified. CBG screening and the risk assessment questionnaire were similar with respect to effectiveness and efficiency for detecting pre-diabetes and undiagnosed diabetes.

Screening for pre-diabetes and undiagnosed diabetes among overweight individuals had a lower cost per case identified compared with screening all individuals. This is primarily due to the higher prevalence of pre-diabetes and undiagnosed diabetes in those individuals. Because the relative efficiency of the different strategies did not change, the choice for a favorable screening strategy remains the same whether the screening was conducted among all individuals age 45–74 years or among those with a BMI ≥25 kg/m².

Taking nonadherence into account, FPG testing would be the best detection strategy. A 75% adherence for FPG alone and 50% adherence for OGTT may be more realistic in the clinical setting. Changing the prevalence of pre-diabetes and undiagnosed diabetes did not affect the proportion of the cases identified but had a moderate impact on the cost per case identified. An additional OGTT to confirm positive cases would increase the cost per case identified but would not affect the relative effectiveness and efficiency of the five strategies.

Our results have two important implications for detecting pre-diabetes or undiagnosed diabetes. First, they can be used for selecting the best strategy for detecting pre-diabetes and undiagnosed diabetes. Second, they indicate that the most favorable cutoff points for screening tests were lower than those recommended in the literature (10–13). Our results indicate that for CBG screening, a random glucose value of ≳100 mg/dl was a better cutoff value than the usually recommended value of ≳140 mg/dl (10). For FPG testing, a glucose value of ≳95 mg/dl was the most favorable cutoff point rather than a value of ≳100 mg/dl that has been used in screening for undiagnosed diabetes (11). For HbA₁c screening, our favorable cutoff value of ≥5.0% was lower than the recommended value of ≥5.6% (12), and the value of ≥6.0% used for screening undiagnosed diabetes (13).

Three factors may have contributed to the difference between our results and those of previous studies. First, our selection of a favorable cutoff point and best strategy were based on both performance (sensitivity and specificity) and the cost of the strategy, whereas previous studies were based only on performance of the screening test. Second, previous studies might have given too much weight to the specificity of a screening test in determining the best cutoff value and the best detection strategy (10,18). In screening for either pre-diabetes or undiagnosed diabetes, true positive cases would ultimately be determined by either the OGTT or the FPG test. A highly specific screening test reduces the number of false-positive cases, thus reducing the number of people who need the OGTT and FPG test and the total cost of screening. If the cost saving resulting from high specificity were outweighed by other cost factors, the unit cost per case identified for that test would be greater than that of a low specificity test. Raising the cutoff value of a test would increase its specificity, but would diminish its sensitivity, thus a lower number of cases would be identified. If the screening cost that was lowered by a higher specificity were outweighed by a reduction in the number of cases identified, the cost per case identified would increase.

Finally, the cutoff value of a screening test for the best detection strategy for pre-diabetes and undiagnosed diabetes may differ from that for detecting undiagnosed diabetes alone. We also calculated the cost per case identified if detecting undiagnosed diabetes was the sole purpose. It appeared that the best cutoff value would
be higher if the purpose of screening changed from identifying both pre-diabetes and undiagnosed diabetes to detecting undiagnosed diabetes only. For example, the cost per case of undiagnosed diabetes identified was $758 if the cutoff value was ≥110 mg/dl and $950 if the cutoff value was ≥95 mg/dl for FPG testing. Similarly, the cost per case of undiagnosed diabetes identified was $498 if the cutoff value was ≥120 mg/dl and $692 if the cutoff value was ≥100 mg/dl for CBG screening.

Our study has limitations. First, we were not able to include part of the population, such as individuals who were >74 years or <45 years with a family history of diabetes. This population is recommended for pre-diabetes screening. However, information is not available on the national prevalence of pre-diabetes or the specificity and sensitivity of various detection strategies for identifying pre-diabetes cases in this group. The number of people who need to be screened and the number of pre-diabetes cases in the U.S. population would be larger than our estimates if these other groups were included. Second, we did not impose any cost for pre-diabetes or undiagnosed diabetes cases missed under each detection strategy. For clinicians, the cost of a case of diabetes is a worthwhile public health investment. A more important and costly task is ensuring appropriate treatment for the identified individuals. Regarding the question whether screening for pre-diabetes is a worthwhile public health investment, the cost of detection and appropriate treatments is only a part of the equation. The answer to the question is perhaps largely determined by the long-term health benefit of treating pre-diabetes. Unfortunately, we currently have little information on this issue. The ongoing DPP follow-up study will provide an answer for this question in the future. If the benefit of preventing or delaying diabetes can be translated into long-term health benefits by preventing diabetes complications, screening and treating pre-diabetes are likely to be good public health investments. Future studies should evaluate the entire costs and benefits of screening programs, including the cost of both detection and treatment as information becomes available.

Primary prevention is a new and visible means to combat the growing epidemic of diabetes. While several strategies can be used for screening individuals with pre-diabetes, not all of the strategies are the same in terms of effectiveness and efficiency. Information provided here can be used by physicians and public policymakers in choosing a strategy if pre-diabetes screening is carried out as currently recommended.

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