Screening Adults for Pre-Diabetes and Diabetes May Be Cost-Saving

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OBJECTIVE — The economic costs of hyperglycemia are substantial. Early detection would allow management to prevent or delay development of diabetes and diabetes-related complications. We investigated the economic justification for screening for pre-diabetes/diabetes.

RESEARCH DESIGN AND METHODS — We projected health system and societal costs over 3 years for 1,259 adults, comparing costs associated with five opportunistic screening tests. All subjects had measurements taken of random plasma and capillary glucose (RPG and RCG), A1C, and plasma and capillary glucose 1 h after a 50 g oral glucose challenge test without prior fasting (GCT-pl and GCT-cap), and a subsequent diagnostic 75 g oral glucose tolerance test (OGTT).

RESULTS — Assuming 70% specificity screening cutoffs, Medicare costs for testing, retail costs for generic metformin, and costs for false negatives as 10% of reported costs associated with pre-diabetes/diabetes, health system costs over 3 years for the different screening tests would be GCT-pl $180,635; GCT-cap $182,980; RPG $182,780; RCG $186,090; and A1C $192,261; all lower than costs for no screening, which would be $205,966. Under varying assumptions, projected health system costs for screening and treatment with metformin or lifestyle modification would be less than costs for no screening as long as disease prevalence is at least 70% of that of our population and false-negative costs are at least 10% of disease costs. Societal costs would equal or exceed costs of no screening depending on treatment type.

CONCLUSIONS — Screening appears to be cost-saving compared to no screening from a health system perspective, and potentially cost-neutral from a societal perspective. These data suggest that strong consideration should be given to screening—with preventive management—and that use of GCTs may be cost-effective.

The prevalence and costs associated with diabetes and pre-diabetes challenge the financial integrity of our healthcare systems. However, screening would allow management aimed at preventing or delaying development of diabetes and complications and could possibly reduce costs. Recommendations regarding screening for pre-diabetes and diabetes have been made by the American Diabetes Association (ADA) (1), but formal screening is infrequent (2). Screening options include fasting plasma glucose (FPG) and oral glucose tolerance tests (OGTTs), but both require fasting samples that patients find inconvenient (3), and it is not clear what the best screening strategy is—another reason screening is under-performed (4). There is also controversy as to whether screening for diabetes is cost-effective (5). Previous analyses of the costs of screening have often focused only on diabetes, have not compared different screening strategies, or have examined screening in only limited ways, e.g., have not included the downstream implications of detecting diabetes as well as pre-diabetes or have ignored the costs of false-negative and false-positive screening results (6–12).

We evaluated the economic justification for screening for diabetes and pre-diabetes. We estimated the costs of screening with random plasma or capillary glucose (RPG or RCG) and A1C tests, informal screening tests frequently used in routine practice, and a glucose challenge test (GCT) approach similar to that used to screen for gestational diabetes, along with the costs of management. Our objectives were to determine whether screening coupled with 3 years of preventive management is likely to be cost-effective compared with no screening, and if there is an optimal screening strategy from an economic perspective.

RESEARCH DESIGN AND METHODS

The study was approved by the Emory University Institutional Review Board and utilized data from 1,259 adults in the Screening for Impaired Glucose Tolerance (SIGT) study, described previously (13). Briefly, this study recruited participants without known diabetes between January 2005 and March 2008. The subjects' first visit was at different times of the day, without an overnight fast. Random capillary and plasma glucose (RCG and RPG) were measured, a 50 g glucose drink was given, and capillary and plasma glucose 1 h after a 50 g oral glucose challenge test (GCT-cap and GCT-pl) were measured. At a second visit, after an overnight fast, A1C was drawn and a 75 g OGTT was begun before 11:00 A.M.

Case definitions

Based on glucose levels that confer increased mortality, pre-diabetes included: *1)* impaired fasting glucose_{110} (IFG_{110}), fasting glucose 110–125 mg/dl and 2-h OGTT glucose <140 mg/dl; *2)* impaired glucose tolerance (IGT), fasting glucose <110 mg/dl and 2-h OGTT glucose 140–199 mg/dl; and *3)* IFG_{110} with IGT (IFG+IGT), fasting glucose 110–125 mg/dl and 2-h OGTT glucose 140–199 mg/dl (14). Diabetes included fasting glu-

cose $\geq$126 mg/dl and/or 2-h OGTT glucose $\geq$200 mg/dl.

Screening test characteristics

Sensitivities and specificities were calculated at different cutoffs, and receiver operating characteristic (ROC) curves were generated using logistic regression. All statistical analyses were performed using SAS, version 9.1 (SAS Institute, Cary, NC).

Screening test cutoffs

Cutoffs were based on sensitivity and specificity, as well as the optimality criterion (where ROC curve slope = [marginal cost of false positives/marginal cost of false negatives] $\times$ [prevalence of no disease/prevalence of disease]) (15). Our base case analyses utilized 70% specificity cutoffs, as higher-specificity cutoffs are thought to be cost-effective (5).

Cost assessment

Costs were expressed in 2007 U.S. dollars. Health system costs were assessed from a Centers for Medicare and Medicaid Services (CMS)-as-payer perspective—thus reflecting the types and levels of costs that would be incurred in the Medicare fee for service program—and compared with Veterans Administration (VA) costs, to provide a single-payer perspective. Included were the direct medical costs associated with screening, the costs of false negatives, and the costs for true positive cases of pre-diabetes and diabetes. Societal costs included both the direct medical and direct nonmedical costs of testing, direct and indirect (lost labor productivity) costs of false negatives, and direct medical, direct nonmedical, and indirect costs of true positives. Base case assumptions are outlined below. Cost components for these analyses are provided in more detail in the online appendix available at http://care.diabetesjournals.org/cgi/content/full/dc10-0054/DC1.

Costs of testing

CMS-based direct costs of testing included costs for laboratory tests, cost of the GCT glucose drink, and staff costs. It was assumed that blood for GCT-pl, RPG, and OGTT would be drawn at an on-site laboratory. The direct nonmedical costs of testing reflected excess time spent by the patient. Since screening was assumed to be opportunistic (during a visit), the visit time was not included.

Costs of false negatives

For the base case analyses, the cost of a false negative (pre-diabetes or diabetes that was undetected) was evaluated as 10% of the projected marginal 3-year medical costs for that condition, assuming that marginal costs could be decreased by appropriate management, as they were in the Diabetes Prevention Program (DPP) (16,17). The cost of a false negative was assumed to include the 3-year direct medical cost of diabetes, pre-diabetes, and/or pre-diabetes that progressed to diabetes. Direct medical costs for diabetes were based on Medical Expenditure Panel Survey costs from 2000–2004, which came to $4,174/year in 2005 U.S. dollars for a 50-year-old person with new-onset diabetes (18). Patients with IFG_{110} in Kaiser Permanente Northwest had marginal direct medical costs of $1,316/year (19), used for all patients with pre-diabetes (although IGT might incur higher costs [14,20]). In the DPP, treatment with metformin and lifestyle changes reduced medical costs outside of the study by 5–9% (16). Since the DPP participants were all receiving medical follow-up through the study, the cost impact would likely be greater in the general population, in which close medical care for missed diagnoses would be lacking; 10% of projected costs was assigned as a reasonable amount that might be reduced by detection of the condition. A 3-year time period for the estimation of cost was chosen, because this is the period over which DPP costs were calculated and is also the time between ADA-recommended screenings.

Indirect costs for false negatives (absenteeism, reduced productivity at work, and unemployment) were derived from the ADA 2007 economic assessment and were attributed only to those with diabetes or whose pre-diabetes progressed to diabetes during the 3 years (21).

Costs of true positives

Direct medical costs for a true positive were based on 3-year costs for the DPP metformin group, in which marginal costs for laboratory tests, physician visits, and follow-up were $703 (17); we substituted current generic costs for metformin 850 mg twice a day. Direct medical costs incurred outside of the study, direct nonmedical costs, and indirect costs for the DPP metformin versus placebo arms were used as other components for the cost of true positives (17); direct medical costs outside the study were −$329 for the metformin versus placebo arms. Societal costs included 3-year direct nonmedical costs (−$11) and indirect costs ($278) in the metformin versus placebo arms.

Sensitivity analyses

Screening cutoffs. We considered alternative cutoffs for a positive screen: 90% sensitivity cutoffs, as well as cutoffs based on the optimality criterion (above).

Testing. We evaluated 5 and 10 min of additional staff time for all tests. Additional patient time was also considered: 10 min for capillary testing and 30 min for plasma testing.

Disease prevalence. We considered prevalences 50% higher and 50% lower than those in the study population.

Rates of progression to diabetes. We considered a higher risk of progression from pre-diabetes to diabetes, 10% per year with IFG_{110} or IGT, and 15% per year for IFG+IGT. False negatives: *1*) We assessed the impact of preventing fractions of direct medical costs ranging from 1–40%; *2*) We examined DPP false-negative costs, which were $329 (the costs incurred by the placebo group outside of the DPP study), using this value (based on IGT with fasting glucose >95 mg/dl) for pre-diabetes, and twice this cost, $658, for diabetes. For alternative societal costs, indirect costs were based on the ADA economic analysis and taken conservatively as $68 over 3 years, which is our estimate of ADA's indirect costs for patients with pre-diabetes (online appendix Table A1) and twice this for patients with diabetes (21).

VA healthcare system. We evaluated VA testing costs. Allowing for costs 50% above those of metformin itself, we evaluated an alternative true positive (VA-TP) cost of $165 per true positive over 3 years (approximately one-third of base case treatment costs). We also considered VA-TP alternative direct nonmedical and indirect costs to be approximately one-third of the direct nonmedical and indirect costs for treatment with metformin in the DPP study, ~$90 combined (online appendix Table A1).

Lifestyle treatment. We evaluated costs of treatment with lifestyle modification using DPP-based costs, assuming group intervention costs and costs for other lifestyle changes as described in the DPP protocol (17).

RESULTS — The subjects had an average age of 48 years and BMI 30 kg/m^2; they were 55% African American and

Table 1—Base case cost assessment in health system and societal costs

	Screen	Cost per screen	Screen cost total	Positives (n)	OGTT costs	Total cost of testing	Testing costs per TP	TP (n)	TP costs	FN (n)	Costs 10% FN	Average cost per FN	Total health system costs	Costs per TP
Health System costs														
					$17.99		$518							
GCT-pl	1,254	$7.77	$9,744	535	$9,625	$19,368	**$78.10**	248	$128,464	61	**$32,803**	**$538**	**$180,635**	**$728**
GCT-cap	1,259	$6.75	$8,498	501	$9,013	$17,511	$81.83	214	$110,852	95	$54,617	$575	$182,980	$855
RPG	1,256	$5.48	$6,883	483	$8,689	$15,572	$79.86	195	$101,010	114	$66,198	$581	$182,780	$937
RCG	1,258	**$3.27**	**$4,114**	451	**$8,113**	**$12,227**	$78.38	156	**$80,808**	153	$93,054	$608	$186,090	$1,193
A1C	1,259	$13.56	$17,072	520	$9,355	$26,427	$130.83	202	$104,636	107	$61,198	$572	$192,261	$952
No screen	0	$0.00	$0.00	0	$0.00	$0.00	$0.00	0	$0.00	309	$205,966	$667	$205,966	NA
Societal costs													Total societal costs	
					$48.61		$785.30							
GCT-pl	1,254	$10.13	$12,703	535	$26,006	$38,709	**$156.09**	248	$194,754	61	**$39,375**	**$645**	$272,839	**$1,100**
GCT-cap	1,259	$7.54	$9,493	501	$24,354	$33,846	$158.16	214	$168,054	95	$67,513	$711	$269,414	$1,259
RPG	1,256	$7.84	$9,847	483	$23,479	$33,326	$170.90	195	$153,134	114	$82,171	$721	$268,630	$1,378
RCG	1,258	**$4.06**	**$5,107**	451	**$21,923**	**$27,031**	$173.27	156	**$122,507**	153	$117,664	$769	**$267,201**	$1,713
A1C	1,259	$15.92	$20,043	520	$25,277	$45,320	$224.36	202	$158,631	107	$75,485	$705	$279,436	$1,383
No screen	0	$0.00	$0.00	0	$0.00	$0.00	$0.00	0	$0.00	309	$269,261	$871	$269,261	NA

Bold data indicate least expensive cost. TP, true positive; FN, false negative; NA, not applicable.

62% female; 19.5% had pre-diabetes (3.5% IFG_{110} only, 12.5% IGT only, and 3.5% IFG+IGT), and 4.9% had diabetes. Dysglycemia (previously unrecognized pre-diabetes and diabetes) was present in 24.5%, and as reported previously (13) was identified with greatest accuracy by GCT-pl and least well by RCG. For the different tests, 70% specificity cutoffs (true positives, and false negatives), respectively, would be: GCT-pl 138 mg/dl (248, 61); GCT-cap 162 mg/dl (214, 95); RPG 100 mg/dl (195, 114); RCG 106 mg/dl (156, 153); A1C 5.5% (202, 107).

Table 1 shows base case health system and societal cost estimates for screening and 3 years of management in a system with Medicare fee-for-service reimbursement rates, with 70% specificity cutoffs, and assuming that false-negative costs (that could be prevented after detection of dysglycemia) amounted to 10% of 3-year medical costs. Cost components for these cost estimates are described in detail in online appendix Table A1. From both perspectives, total costs for testing (screening test + follow-up OGTT if indicated) were lowest for RCG because it was the least expensive test and had the fewest positive screens. Total true-positive costs were highest for GCT-pl from both perspectives, due to the higher numbers of true positives detected, while the cost of false negatives was highest for RCG because this test had the highest number of false negatives.

Total health system costs for all study subjects using base case assumptions would be GCT-pl $180,635, GCT-cap $182,980, RPG $182,780, RCG $186,090, and A1C $192,261; all were less than the cost of no screening, which was $205,966, with GCT-pl being the least expensive test. Societal costs with the same assumptions were GCT-pl $272,839, GCT-cap $269,414, RPG $268,630, RCG $267,201, and A1C $279,436; all were close to the cost for no screening, which was $269,261, with RCG being the least expensive test and slightly less expensive than no screening. However, GCT-pl was the least expensive test from both perspectives when costs were compared per true positive identified (Table 1).

Sensitivity analyses
Fig. 1 shows varied fractions of false-negative costs from health system and societal perspectives. When false-negative costs were over 10% of 3-year projected marginal costs for pre-diabetes and diabe-
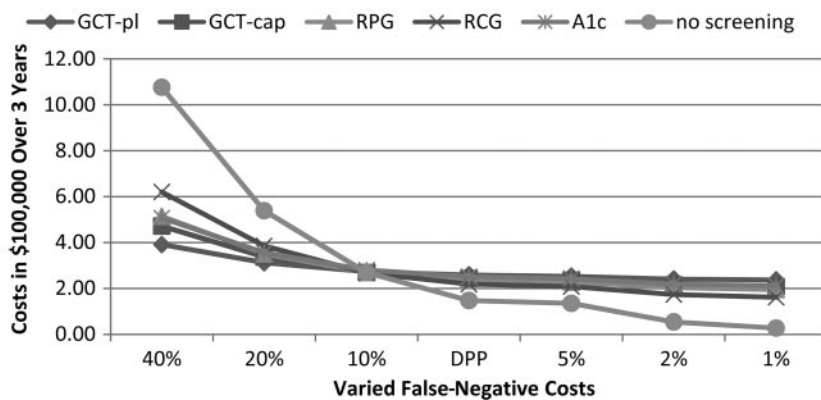
Health system costs
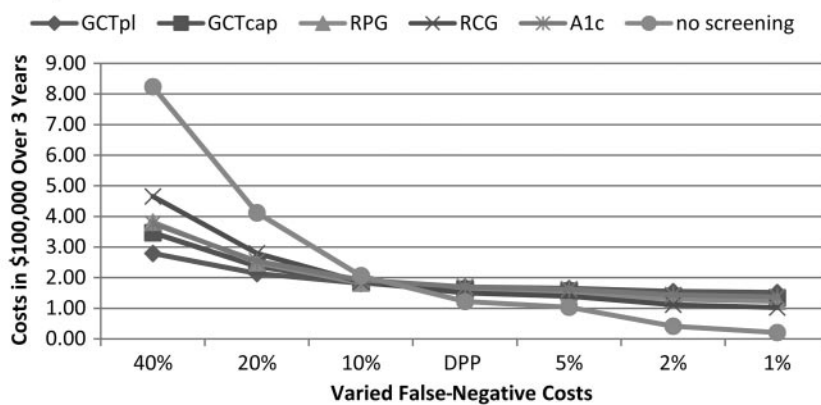
Societal costs

Figure 1—*Health system and societal costs associated with varied fractions of false-negative costs. Total health system and societal costs for each screening test and for no screening, which include costs of testing, false negatives, and treatment of true positives, assuming different fractions of false-negative costs that could be prevented with early detection of conditions.*

tes, both health system and societal projected costs for screening and management would be lower than costs of no screening. When false-negative costs were less than 10% (the DPP false-negative cost was slightly greater than 5%), costs for screening and management would be more than the cost of no screening. For false-negative costs higher than 10%, GCT-pl was the least expensive test from both perspectives, while for fractions less than 10%, RCG was least expensive. False-negative costs contributed most to total costs when higher fractions were used, while true-positive costs contributed more when lower fractions were used (online appendix Figure A1).

In the sensitivity analyses (Table 2), from a health system perspective, GCT-pl screening would be the least expensive test in most of the scenarios described. These scenarios include use of a glucose cutoff for pre-diabetes based on the optimality criterion, longer staff time for administering the screen, higher rates of

progression from pre-diabetes to diabetes, and higher and lower prevalence of disease. From a societal perspective (Table 2), the least expensive test varied more depending on the scenario but tended to be either GCT-pl or RCG.

We examined potential single-payer system costs, using VA-based costs as an example. Using base case assumptions, with VA costs for testing and metformin, health system costs for all tests would be less than costs for no screening, with GCT-pl being the least expensive test. Societal costs for all tests would also be less than no screening, with GCT-cap being least expensive. If VA-TP costs were used, the costs for screening with any of these tests would be substantially less than the cost of no screening, assuming either base case 10% false negative or DPP-false-negative costs, and GCT-pl would be the least expensive test (Table 2 and online appendix Figure A2).

Lifestyle intervention costs, using Medicare testing costs, 10% false-

negative costs, and costs for a group intervention derived from the DPP, were similar from a health system perspective to the costs for treatment with generic metformin: screening with any test was less expensive than no screening, with GCT-pl being the least expensive test. Societal costs were much higher than costs for no screening and higher than costs associated with treatment with metformin due to the significant direct nonmedical costs associated with the lifestyle intervention.

There has been recent interest in using A1C as both a screening and a diagnostic test for diabetes. We calculated the costs of using A1C 6.0–6.4% to diagnose pre-diabetes and A1C ≥6.5% to diagnose diabetes, without confirmatory testing. Health system costs, with our base case assumptions and using metformin and lifestyle modification for management, would be $226,122 and $225,944, respectively—both higher than the costs with GCT or random glucose testing and higher than the cost of no screening, because of a large number of false negatives and treatment of false positives. Societal costs with metformin and lifestyle modification management would be $299,524 and $411,726, again higher than with other screening tests or with no screening.

CONCLUSIONS — This study evaluated the economic justification for a screening program that would detect both pre-diabetes and previously unrecognized diabetes. Over a 3-year horizon (typical of the duration of employer health insurance coverage for many workers), we compared the costs of no screening to the costs of screening with RPG, RCG, or A1C available today as well as novel GCT-pl and GCT-cap tests, and included the costs of management of detected cases. With Medicare-based costs and our base case assumptions, screening would be less expensive than no screening from a health system perspective and cost neutral or only slightly more expensive than no screening from a societal perspective; these results were robust to a variety of sensitivity analyses. GCT-pl screening had the greatest diagnostic accuracy, and, in many scenarios, would provide the lowest health system costs.

The sensitivity analyses performed include a wide range of assumptions and two ends of the spectrum of health system costs for treatment with metformin, Medicare- and VA-based. In both settings, the costs of testing would be only a minor

Table 2—Sensitivity analyses of health system and societal costs

	70% Specificity cutoff	Optimality cutoff	90% Sensitivity cutoff	Higher staff time	Higher patient time	Higher rate of progression	50% Higher prevalence	50% Lower prevalence	VA health system	VA-TP costs	DPP FN + VA-TP costs	Lifestyle costs
Health system costs												
GCT-pl	**$180,635**	**$180,908**	$184,784	**$183,469**	N/A	**$185,483**	**$263,214**	**$98,365**	**$162,639**	**$83,681**	**$71,934**	**$180,139**
GCT-cap	$182,980	$183,171	**$182,714**	$185,825	N/A	$190,173	$266,656	$99,029	$164,718	$96,584	$76,184	$182,552
RPG	$182,780	$181,948	$183,480	$185,619	N/A	$191,335	$267,519	$98,494	$167,212	$105,128	$80,384	$182,390
RCG	$186,090	$185,094	$183,811	$188,933	N/A	$197,180	$273,743	$98,801	$173,334	$123,666	$87,529	$185,778
A1C	$192,261	$191,827	$192,987	$195,106	N/A	$200,388	$276,230	$108,597	$171,985	$91,997	$84,967	$191,857
No screen	$205,966	$205,966	$205,966	$205,966	N/A	$226,555	$309,192	$103,226	$205,966	$205,966	$122,059	$205,966
Societal costs												
GCT-pl	$272,839	$269,253	$288,828	$275,673	$275,798	**$281,342**	$394,237	$151,373	$254,868	**$131,915**	**$117,947**	$585,493
GCT-cap	$269,414	$270,218	$284,990	$272,259	$270,409	$282,031	$389,725	$148,324	**$251,173**	$145,076	$118,851	$539,204
RPG	$268,630	$269,494	$290,917	$271,469	$271,594	$283,635	$389,080	$148,866	$253,081	$156,404	$124,255	$514,467
RCG	**$267,201**	$270,019	$295,126	$270,044	**$268,195**	$286,653	**$388,899**	$145,812	$254,461	$177,119	$128,136	$463,871
A1C	$279,436	**$264,302**	$299,313	$282,281	$282,407	$293,691	$398,958	$159,981	$259,180	$159,032	$129,996	$534,098
No screen	$269,261	$269,261	$269,261	$269,261	$269,261	$305,372	$404,168	**$134,907**	$269,261	$269,261	$147,287	**$269,261**

Bold data indicate least expensive cost. TP, true positive; FN, false negative; DPP-FN, Diabetes Prevention Program false negative; N/A, not applicable. VA-TP, alternative true positive cost; VA-TP, alternative true positive cost in VA system.

portion of total costs, and testing costs with RCG would be least expensive. With more accurate tests (GCT-pl is best, RCG worst), the costs of true positives would rise and the costs of false negatives would fall. Overall, GCT-pl screening would be least expensive in settings with CMS reimbursement rates as well as in VA-based settings.

We estimated costs for treatment of true positives, both with metformin and lifestyle modification, based on the treatment protocol used in the DPP, but substituted drug costs to reflect current prices. However, some have suggested that such involved treatment might be impractical to implement in real-world settings. Recognizing this, we also examined an alternative care system: the VA. Costs in the VA are lower than Medicare testing and retail drug costs and might be representative of costs with a single-payer healthcare system. With these costs (VA-TP costs), screening with any of the tests would be cost-saving from both health system and societal perspectives.

Our analyses also revealed that screening for pre-diabetes and diabetes would involve a high cost for false negatives—a high cost for undetected and untreated pre-diabetes and diabetes. This was not unexpected, since costs attributable to diabetes (before and after diagnosis) are substantial due to a combination of costs of hospitalizations related to complications (particularly cardiovascular disease), pharmacy costs, and other medical visits (18–20,22,23).

The finding that treatment of detected cases might be cost-saving from a health-system perspective is at least partly driven by the findings from the DPP study in which those participants who were treated with metformin or lifestyle changes had reduced medical costs outside of the study compared to those in the placebo arm. We do not have a mechanism through which these cost-savings were obtained, but they may have resulted from improvements in cardiovascular risk factors which have been associated with both types of treatment.

Our study has limitations. The study subjects were volunteers, which may have caused some selection bias. However, the prevalence of pre-diabetes and diabetes in our study is similar to that found in other studies and lower compared to recent National Health and Nutrition Examination Survey (NHANES) estimates (24). We did not consider screening with fasting plasma glucose in this study; however, ac-

curacy should be at least as good and health system costs should be similar to those with RPG testing, so costs should still be favorable compared to no screening. The ADA (25) has recommended that A1C be used for the diagnosis of diabetes and pre-diabetes, so screening with A1C measurements might involve either no follow-up testing or at most a repeat A1C if the first A1C were high, which differs from our main analysis, in which follow-up testing would involve an OGTT. Since A1C is a relatively inaccurate screening test, especially for pre-diabetes (13), an A1C-only screening strategy would increase screening costs but decrease both the projected costs for treatment (because fewer positives would be found), and the costs we attributed to patients who were A1C-negative but OGTT-positive (by defining such patients as true negatives). However, such an approach ignores the empirical findings of increased costs associated with pre-diabetes (above).

Our analysis also assumed that all adults would be screened for pre-diabetes/diabetes. If, however, screening targeted adults with one or more risk factors, the overall screening costs would decrease (due to fewer numbers being screened), and the relative proportion of true positives to false negatives should rise. In this case, the cost-effectiveness of screening should improve (7), and the costs of screening and 3 years of management should become even more favorable relative to no screening, since the cost of treatment of true positives, in our estimation, is less than the average cost of false negatives.

We focused our analysis on costs related to treatment with metformin, but this may not be the best treatment. Lifestyle interventions emphasizing diet and weight loss are a better treatment from a medical and, possibly, also from a cost perspective (12,16). However, metformin is a treatment that can be implemented in a consistent manner by most practitioners with fairly predictable results. Finally, the scope of our study was limited to the costs of one-time screening and did not incorporate the lifetime modeling needed to determine if the cost-savings we project over a 3-year period would continue with a program of repeated screening, as currently recommended by the ADA and the Centers for Disease Control and Prevention. However, a 3-year period might be an ideal representation from the perspective of a payer working with employers whose employees come and go, and who change healthcare plans every few years.

Our analyses indicate that screening programs and 3 years of management for pre-diabetes and previously unrecognized diabetes should be cost-effective, particularly from a health system perspective, and may be cost-saving.

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