Cost-Effectiveness of Alternative Thresholds of the Fasting Plasma Glucose Test to Identify the Target Population for Type 2 Diabetes Prevention in Adults Aged ≥45 Years

XIAOHUI ZHUO, PHD
PING ZHANG, PHD

HENRY S. KAHN, MD
EDWARD W. GREGG, PHD

OBJECTIVE—The study objective was to evaluate the cost-effectiveness of alternative fasting plasma glucose (FPG) thresholds to identify adults at high risk for type 2 diabetes for diabetes preventive intervention.

RESEARCH DESIGN AND METHODS—We used a validated simulation model to examine the change in lifetime quality-adjusted life years (QALYs) and medical costs when the FPG threshold was progressively lowered in 5-mg/dL decrements from 120 to 90 mg/dL. The study sample includes nondiabetic adults aged ≥45 years in the United States using 2006–2010 data from the National Health and Nutritional Examination Survey. High-risk individuals were assumed to receive a lifestyle intervention, as that used in the Diabetes Prevention Program. We calculated cost per QALY by dividing the incremental cost by incremental QALY when lowering the threshold to the next consecutive level. Medical costs were assessed from a health care system perspective. We conducted univariate and probabilistic sensitivity analyses to assess the robustness of the results using different simulation scenarios and parameters.

RESULTS—Progressively lowering the FPG threshold would monotonically increase QALYs, cost, and cost per QALY. Reducing (in-5 mg/dL decrements) the threshold from 120 to 90 mg/dL cost $30,100, $32,900, $42,300, $60,700, $81,800, and $115,800 per QALY gained, respectively. The costs per QALY gained were lower for all thresholds under a lower-cost and less-effective intervention scenario.

CONCLUSIONS—Lowering the FPG threshold leads to a greater health benefit of diabetes prevention but reduces the cost-effectiveness. Using the conventional benchmark of $50,000 per QALY, a threshold of 105 mg/dL or higher would be cost effective. A lower threshold could be selected if the intervention cost could be lowered.

Impaired fasting glucose (IFG) is an intermediate state of hyperglycemia in which fasting plasma glucose (FPG) levels do not meet the criteria for diabetes but are consistently elevated above what is considered normal (1). The concept of IFG has been endorsed by leading professional organizations (2,3) and adopted as one measure for identifying the high-risk population for type 2 diabetes preventive interventions in clinical settings and large-scale, community-based prevention programs (4,5).

Despite the increasing use of FPG testing to identify the high-risk state, the appropriate threshold for the lower limit of IFG remains unclear. The American Diabetes Association (ADA) currently uses 100 mg/dL (5.6 mmol/L) as the threshold to define IFG (6), while the World Health Organization and the European Diabetes Epidemiology Group recommends using 110 mg/dL (6.1 mmol/L) (7). Varying standards exist in large part because there is no clear threshold at which an FPG value can be associated with a sharp increase in the risk of future diabetes and its complications (7–10). Recent ADA guidelines also recommend glycated hemoglobin (A1C) as a blood test to identify people at high risk for type 2 diabetes and such a continuous relationship with the incidence of diabetes and its complications also has been observed for A1C (6).

When FPG is used to identify the target population for type 2 diabetes prevention, the choice of the IFG-defining FPG threshold ultimately affects the intervention's cost-effectiveness. A lower FPG threshold would result in more people being eligible for intervention, which would likely lead to more cases of diabetes being prevented or delayed. However, a lower threshold might be less cost-effective because it incurs costs for intervening in a population with a lower risk of developing type 2 diabetes. To better understand the potential cost implications, major clinical and public health organizations called for systematic economic analyses of the FPG thresholds (3). Our study sought to estimate and compare the long-term cost-effectiveness of alternative FPG thresholds for identifying high-risk adults for inclusion in type 2 diabetes prevention programs.

RESEARCH DESIGN AND METHODS—Using the model described below, we simulated average lifetime costs and quality-adjusted life years (QALYs) for U.S. adults aged ≥45 years who had no diabetes at baseline under scenarios using alternative FPG thresholds. For each scenario, the FPG threshold

Diabetes Care Publish Ahead of Print, published online October 17, 2013

was lowered by 5 mg/dL from that in the previous scenario. We calculated results for seven scenarios with FPG thresholds ranging from 120 to 90 mg/dL. Thresholds <90 mg/dL were not considered because such a standard would identify a vast majority of the U.S. population as high risk. Lifetime cost and QALY estimates from each scenario were used to estimate the cost-effectiveness associated with each threshold.

Simulation model
Our model is a validated Markov-based model in which the progression of type 2 diabetes was simulated based on annual transition probabilities from a person's diagnosis to death. In the model, separate modules simulated incidence of and progression through each of five types of diabetes complication (nephropathy, neuropathy, retinopathy, stroke, and coronary heart diseases) that people with diabetes could possibly develop. Details of the model appear in the Supplementary Material. The model has been validated (11) and used for assessing the long-term cost-effectiveness of various interventions for preventing type 2 diabetes and its complications (12–15).

A nationally representative sample of nondiabetic U.S. adults aged ≥45 years, based on the 2006–2010 data from the National Health and Nutrition Examination Survey, was used for the simulations. We did not include people younger than 45 years because data concerning diabetes incidence by FPG level in this population are limited and relatively few people are diagnosed with type 2 diabetes before age 45 (16). We identified people with diabetes by self-report or by test results: FPG ≥126 mg/dL, 2-h glucose value ≥200 mg/dL, or A1C ≥6.5% (6).

For each decremental 5 mg/dL FPG value (threshold $_i$, e.g., threshold$_{115}$) evaluated in our simulations, the nondiabetic sample was divided into two groups: those at high risk for type 2 diabetes (threshold $_i$ < FPG < 126 mg/dL) and those with "normal" FPG (FPG < threshold$_i$). The population size, baseline characteristics, and diabetes incidence rate in the two groups were all dependent on the FPG threshold selected (i.e., the value of i.)

Rates of diabetes incidence in both the high-risk group and the normal FPG group were estimated using data from the Atherosclerosis Risk in Communities (ARIC) study, a prospective study including 15,792 adults aged 45 years or older at baseline in 1987 to 1989 (17). In the

study, diabetes incidence was defined by subsequent plasma measurements (fasting glucose ≥126 mg/dL or nonfasting glucose ≥200 mg/dL), a self-reported diagnosis of diabetes, or use of antidiabetic medications during 6 years of follow-up (18). The estimates of annual risk for developing type 2 diabetes used in the simulation are presented in Table 1. We found that increments in the level of FPG were associated with a continuum of increasing risk for diabetes, which is consistent with previous studies (18–22).

In the model, disease progression subsequent to a diagnosis of diabetes was simulated based on data primarily obtained from the United Kingdom Prospective Diabetic Study (UKPDS) (23). Risk of developing hypertension, hyperlipidemia, coronary heart disease, or stroke, all of which are associated with diabetes, before the clinical diagnosis of diabetes also was incorporated in the model (9,24–26). Technical details are provided in the Supplementary Material.

Diabetes prevention interventions
In the simulation, we assumed that 50% of individuals identified as high risk started the lifestyle intervention and 50% of those completed the program (27,28). Attrition was assumed to occur evenly through the years of participation. After 1 year of the lifestyle intervention, participants received a test for diabetes. The intervention and testing continued annually until an individual was diagnosed with diabetes (by the definition of diabetes used in the ARIC study), died, or dropped out. The intervention was modeled based on the intensive lifestyle intervention program implemented in the Diabetes Prevention Program (DPP) study (4). The DPP study was a 3-year randomized trial with a 16-lesson core curriculum covering diet, exercise, and behavior modification that was taught by case managers. Lessons were delivered one-on-one for the first 6 months, followed by individual and group sessions over the subsequent 6 months (4). The costs and effectiveness measures associated with the intervention are summarized in Table 2.

Among people who developed diabetes while receiving intervention, we assumed diabetes was diagnosed during the year of onset. After diagnosis, these individuals would continue to receive the lifestyle intervention and additionally receive a metformin therapy (850 mg twice per day) (29). This treatment would last until the person's A1C level reached

Table 1—Annual risk of developing type 2 diabetes by FPG level

FPG level (mg/dL)	Mean follow-up (years)	Annual risk of developing type 2 diabetes*
<90	9.97	0.006
90–<94	9.92	0.008
95–<99	9.99	0.012
100–<104	9.97	0.018
105–<109	9.98	0.031
110–<114	9.99	0.053
115–<119	9.95	0.080
120–<126	9.93	0.126

Data from the Atherosclerosis Risk in Communities study. *The annual risks of developing type 2 diabetes were calculated from a 10-years survival function using the Kaplan-Meier method.

7.0%, at which point the person would receive intensive treatment for glycemic control, as implemented in the UKPDS (15). Patients in the UKPDS were treated intensively, with a goal of maintaining an A1C level below 7.0% using metformin, sulfonylureas, and dietary advice from a dietitian.

The group with an FPG value below a threshold (i.e., the low-risk group) was assumed to receive no lifestyle intervention. People in this group, as well as those who were identified as high-risk individuals but did not participate in the lifestyle intervention, were assumed to develop type 2 diabetes based on the incidence rates observed in the ARIC study. When their diabetes was clinically diagnosed, the mean A1C level was assumed to be 7.1%, the level observed among UKPDS subjects after the dietary run-in period (23). After diagnosis, they were assumed to receive the same intensive treatment for glycemic control as those in the UKPDS.

Cost and health utility
The study was conducted from a health care system perspective, and thus only the following costs were considered: 1) the cost of a one-time fasting glucose screening test for all participants; 2) the annual cost for the lifestyle program and the screening test for high-risk adults who took up the intervention; and 3) treatment costs for diabetes and diabetes-related complications (details appear in the Supplementary Table 18). All costs are expressed in 2012 U.S. dollars. Future costs were discounted at 3% annually. Calculations were performed in full precision and costs were rounded to the nearest $100.

Table 2—*Cost of FPG testing and costs and effectiveness of a hypothetical lifestyle intervention program based on the DPP*

	Base-case value	Probabilistic sensitivity analysis		Univariate sensitivity analysis
		Distribution assumption*	Data source	
Cost of FPG test ($)	5.01	Not varied	Medicare fee schedule (2011)	
Cost of the additional time in physician office visit ($)	53.20	Not varied	Medicare fee schedule (2011)	
Patients participating in lifestyle intervention (%)	50	Not varied	Gans et al. (27); Burke et al. (28)	
Patients completing the lifestyle intervention (%)	50	Triangle (0.4, 0.5, 0.6)	Assumed	
DPP-based lifestyle intervention (%)				
Diabetes risk reduction	55.3†	Normal (45, 63)	DPP data†	27.5 after year 3
Hypertension risk reduction	26.0	Normal (10, 50)	DPP data	19.0 Stevens et al. (43)
Hypercholesterolemia risk reduction	0.0	Not varied	Assumed	22.6 Ratner et al. (44)
Cost of lifestyle intervention ($)				
Year 1	1,803	Lognormal (1,803, 1,532)	Herman et al. (14)	
Year 2	875	Lognormal (875, 743)	Herman et al. (14)	
Year 3 and after	905	Lognormal (905, 769)	Herman et al. (14)	
Reduction of medical cost due to intervention (year 1 to year 3) ($)‡				
Women	43	Lognormal (43, 36)	Herman et al. (14)	
Men	135	Lognormal (135, 114)	Herman et al. (14)	

*Normal (*a, b*) = normal distribution (95% CI with a lower 2.5th percentile of *a* and an upper 97.5th percentile of *b*); lognormal (*a, b*) = lognormal distribution with mean (not median) *a* and a lower bound of 95% confidence interval *b*. †The 55.3% estimate of risk reduction used here is based on all DPP data through the end of July 2001[14]. A slightly higher estimate of 58% was reported earlier based on DPP data collected only through March 2001 [4]. ‡The reduction in the normal medical cost per year due to the lifestyle intervention in the first 3 years of the intervention (zero in subsequent years).

The health utility values of individuals with elevated FPG and type 2 diabetes were based on data from the DPP study (30) and a health utility model developed by Coffey and colleagues (31), who estimated health utility values associated with diabetes treatment mode and diabetes-related complications and adjusting for socioeconomic and demographic variables. Their estimated baseline utility score of 0.69 represents the utility value for a nonobese man with type 2 diabetes who is treated with diet and exercise, has no cardiovascular risk factors, and has no microvascular, neuropathic, or cardiovascular complications. Additional treatments, cardiovascular risk factors, or complications would lead to reductions from the baseline utility score. Detailed specifications on the health utilities appear in the Supplementary Material (Supplementary Table 19). QALYs were discounted at 3% annually.

Incremental cost-effectiveness ratio
The cost-effectiveness associated with a threshold was measured by the incremental cost-effectiveness ratio (ICER), which was calculated by dividing the incremental cost by the incremental effectiveness between that threshold (e.g.,115 mg/dL)

and its next higher threshold (e.g.,120 mg/dL) (32). This differs from conventional cost-effectiveness analyses, in which ICERs are calculated by comparing cost and effectiveness of new interventions with those of existing interventions or with doing nothing. The objectives of conventional analyses are to compare cost-effectiveness of different intervention options in a fixed intervention population. Conversely, the objective here was to assess how the cost-effectiveness of a fixed intervention would change when the intervention population (people with IFG) is progressively expanded by lowering the FPG value used to define IFG.

Sensitivity analyses
We conducted both univariate and probabilistic sensitivity analyses. First we tested whether using a different preventive intervention might change the ICERs of the FPG thresholds. We considered a program implemented in the Promoting a Lifestyle of Activity and Nutrition for Working to Alter the Risk of Diabetes (PLAN4WARD) study (33). PLAN4WARD is a community-based program designed to deliver at a lower cost the key elements of the lifestyle intervention used in the DPP study (33). Compared with the DPP

intervention, PLAN4WARD costs about 75% less and was 60% as effective in reducing risk of diabetes (34). Details of the cost and effectiveness of the intervention appear in the Supplementary Material.

Second, data from the DPP study suggest a greater reduction in diabetes incidence in adults aged ≥60 years than in those aged <60 years (71% vs. 59%) (4). To test the difference of the ICERs among different age groups, we ran the simulation for individuals aged 45–59 years and those aged ≥60 years, using DPP estimates of effectiveness for the two groups. In addition, we ran a separate analysis for persons aged 18 to 44, assuming that, given the same FPG value, they had the same level of risk of developing diabetes as persons aged 45 or older.

We performed four additional univariate sensitivity analyses to address uncertainty associated with the magnitude of the intervention effects. For the first, we replaced our base-case estimate for diabetes risk reduction (55.3%) with the estimate of 38.0% from the 10-year DPP follow-up (35). The lower risk reduction figure may be considered conservative because the intensive lifestyle intervention was discontinued at the end of the 3-year trial period and all participants,

including those in the control group, received a group-based lifestyle intervention afterward. For the second analysis, to account for participants' possibly diminished adherence to the practices of the lifestyle change intervention over time, we assumed that the effectiveness of the intervention declined by 50% after the third year of the intervention. For the third analysis, we varied the effectiveness of the intervention on reducing the risk of hypertension. For the fourth analysis, we varied the effectiveness of the intervention on reducing the risk of hypercholesterolemia (Table 2).

In addition, we conducted a probabilistic sensitivity analysis in which a set of 85 model parameters were simultaneously varied based on the associated probability in 500 iterations of the simulation. The probabilities of each FPG threshold being cost-effective, given a range of the monetary value of QALYs gained, were plotted to form cost-effectiveness acceptability curves (36). Details appear in the Supplementary Material. In addition, we tested the statistical difference of the ICER associated with one threshold versus the next level using the random sample (N = 500 × 7 = 3,500) generated from the probabilistic sensitivity analysis.

RESULTS

Base-case analysis
Table 3 shows the average lifetime cost and QALY estimates when using different FPG thresholds to define IFG. When 120 mg/dL was used as the initial threshold for intervention, the lifetime cost was $59,100 and achieved 10.69 QALYs. Progressively lowering the FPG threshold led

to a monotonic increase in both QALYs and costs. Lowering the threshold from 120 to 90 mg/dL increased QALYs from 10.69 to 10.80 and increased lifetime costs from $59,100 to $65,800. Decreasing the FPG threshold—and thereby increasing the number of people eligible for the intervention and the health benefit—also increased the cost per QALY gained. Because of the monotonic relationship between the FPG threshold and QALYs, the next higher threshold always yielded a larger QALY than the current one. Lowering the threshold from 120 to 115 mg/dL cost $30,100 per additional QALY gained. The cost per QALY gained of moving the threshold from 115 to 110 mg/dL was $32,900; from 110 to 105 mg/dL was $42,300; from 105 to 100 mg/dL was $60,700; from 100 to 95 mg/dL was $81,800; and from 95 to 90 mg/dL was $115,800.

Univariate sensitivity analyses
Table 4 shows that, regardless of model parameters or assumptions, the ICER consistently increased as the FPG threshold was lowered. However, referring individuals to a less costly and less effective intervention, such as PLAN4WARD, in the first sensitivity analysis (SA1 in Table 4) considerably reduced ICERs at all threshold levels; these reductions were greater at lower thresholds. The cost per QALY gained associated with 115 mg/dL was $21,500, compared with $30,100 in the base-case. The cost per QALY gained was $22,600 when lowering the threshold from 115 to 110 mg/dL; $27,900 from 110 to 105 mg/dL; $40,800 from 105 to 100 mg/dL; was $71,500 from 100 to 95 mg/dL; and $96,000 from 95 to 90 mg/dL.

When the analysis was restricted to persons aged 45–59 years (SA2), the

Table 3—Lifetime cost and QALY per person and incremental cost per QALY gain under seven FPG threshold scenarios

FPG threshold (mg/dL)	Cost (SD), $	QALYs (SD)	Incremental cost per QALY gained (SD), $*
120	59,100 (1,500)	10.69 (0.12)	—
115	59,400 (1,500)	10.70 (0.12)	30,100 (3,700)
110	60,000 (1,500)	10.72 (0.10)	32,900 (3,900)
105	60,900 (1,700)	10.74 (0.09)	42,300 (4,400)†
100	62,300 (1,800)	10.77 (0.06)	60,700 (4,200)†
95	64,100 (1,700)	10.79 (0.07)	81,800 (4,200)†
90	65,800 (1,700)	10.80 (0.07)	115,800 (3,900)†

The SDs are derived from the sample produced by the probabilistic sensitivity analysis. *Calculated by comparing the cost and QALY of one threshold with the next most effective threshold (i.e., the threshold with the next highest QALY). For example, the cost per QALY of the FPG threshold of 110 mg/dL is calculated by comparing it with 115 mg/dL. Calculations were performed in full precision and costs were rounded to the nearest $100. †The ICER of the FPG threshold is statistically different from that of the next higher threshold (P < 0.05).

Table 4—Incremental cost per QALY ($) of FPG threshold in the univariate sensitivity analyses

FPG threshold (mg/dL)	Base case	Sensitivity analyses*									
		SA1	SA2	SA3	SA4	SA5	SA6	SA7	SA8	SA9	SA10
120	—	—	—	—	—	—	—	—	—	—	—
115	30,100	21,500	13,900	31,700	32,400	62,000	58,000	28,700	30,000	22,000	37,100
110	32,900	22,600	18,100	31,100	34,800	62,800	61,500	31,200	38,500	22,800	41,700
105	42,300	27,900	29,100	34,500	53,600	72,300	76,000	39,900	58,400	28,400	55,300
100	60,700	40,800	46,900	45,500	84,800	92,900	104,600	56,500	90,900	40,100	80,400
95	81,800	71,500	68,500	61,200	123,100	118,300	138,800	74,900	129,400	53,300	109,600
90	115,800	96,000	101,400	84,500	172,700	159,300	193,900	104,100	188,600	74,600	156,700

* SA1: used a lower-cost, lower-effectiveness lifestyle intervention based on PLAN4WARD (Promoting a Lifestyle of Activity and Nutrition for Working to Alter the Risk of Diabetes); SA2: participants aged 45–59 years only; SA3: among persons aged 25–44, assuming that, given a same FPG value, they had a same level of the risk of developing diabetes as persons aged 45 or older; SA4: aged ≥60 years only; SA5: used 10-year data from the DPP follow-up study for cost and effectiveness assumptions; SA6: intervention was assumed to be 50% less effective after year 3; SA7: in addition to diabetes risk reduction, a 19% reduction in the risk of hypertension was assumed; SA8: in addition to diabetes risk reduction, a 22.6% reduction of the risk of hypercholesterolemia was assumed; SA9: cost and QALY were discounted at 0% per year; SA10: cost and QALY were discounted at 5% per year.Calculations were performed in full precision and costs were rounded to the nearest $100.

ICERs were lower at all FPG thresholds, ranging from $13,900 to $101,400 per QALY gained. For persons aged 25–44 (SA3), the ICERs for most of the thresholds evaluated were also lower than those in persons aged 45 or older. In comparison, the ICER for individuals aged ≥60 years were higher, ranging from $32,400 to $172,700 per QALY gained (SA4). Using data from the 10-year DPP risk reduction estimate (SA5) resulted in higher ICERs, as did assuming a long-term diminishing effect of the intervention (SA6). However, assuming that lifestyle intervention also reduced the risk of developing hypertension (SA7) or hypercholesterolemia (SA8) resulted in lower ICERs.

Probabilistic sensitivity analysis

Figure 1 shows the cost effectiveness acceptability curves of seven FPG thresholds. Each curve represents the probability that the given threshold is cost-effective by the monetary value of a QALY, or willingness to pay. One FPG threshold would be more likely to be cost-effective if the willingness to pay for QALY gain is higher. For instance, in a scenario in which the monetary value of $50,000 per QALY (a conventional benchmark figure for a society's willingness to pay [37]) is assigned, the probability of the 105-mg/dL IFG

threshold will be cost-effective was 0.92. The probability would increase to 0.99 if the value of a QALY was increased to $60,000. However, the probability that an IFG threshold of 100 mg/dL is cost effective is 0.29 and 0.65 at the willingness-to-pay benchmarks of the $50,000 and $60,000 per QALY, respectively. Each FPG threshold was statistically significantly different from its next higher threshold, except the level of 110 mg/dL. Details about the results of the probabilistic sensitivity analysis appear in section VII of the Supplementary Material.

CONCLUSIONS—FPG tests have been increasingly used to identify individuals at high risk of developing type 2 diabetes and refer them for diabetes prevention interventions (38). The selection of the threshold of the FPG test determines the target population for preventive intervention and thus ultimately affects the efficiency of the interventions. The economic implications need to be well understood so scarce health care resources can be used in an efficient manner. In this study we examined the cost-effectiveness of seven possible FPG test thresholds when they were used for referral to a diabetes prevention intervention. We found that as the FPG threshold was

lowered the population-level health benefit increased but cost-effectiveness was reduced.

Our study results suggest that the selection of the FPG threshold may ultimately depend on the health care resources that are available for diabetes prevention or the willingness to pay to prevent diabetes. A lower IFG threshold might be preferred if more resources are available or the willingness to pay for preventing diabetes is higher. Using $50,000 per QALY as a benchmark for acceptability (37), we are quite certain (with more that 90% certainty) that diabetes prevention would be cost-effective if we used an FPG level of 105 mg/dL as the threshold to identify a high-risk state. However, if a higher willingness to pay per QALY were acceptable, a threshold that is lower than 105 mg/dL is preferred.

Furthermore, our findings suggest that a lower threshold might be preferred if the cost of the diabetes prevention intervention could be reduced. In our sensitivity analysis, under a scenario in which a less costly but less effective intervention was used, cost-effectiveness was improved at all threshold levels. For instance, the ICER associated with the threshold of 100 mg/dL decreased from $60,700 per QALY in the base-case to $40,800 per QALY when the less costly and less effective intervention was used. This indicates that by using the less expensive intervention the FPG threshold could be lowered from 105 to 100 mg/dL, even when the willingness to pay benchmark remained at the same level of $50,000 per QALY. Because the cost of the intervention affects the cost-effectiveness of the FPG threshold, it ultimately affects the selection of an economically preferred threshold of the FPG test for diabetes prevention.

Our study demonstrates a deteriorating cost-effectiveness associated with the decreasing FPG threshold and provides a valuable health economics perspective into the debate over the selection of the optimal FPG threshold. However, our study did not aim to determine the definitive value of a universally optimal threshold because selecting such a threshold may depend on many factors. In particular, the cost-effectiveness of a specified FPG threshold is likely to change by age: the risk of type 2 diabetes indicated by the value may vary depending on age (39,40). To understand how such differences in the population might affect the choice of a threshold, we estimated the ICERs at each FPG threshold by age group. We
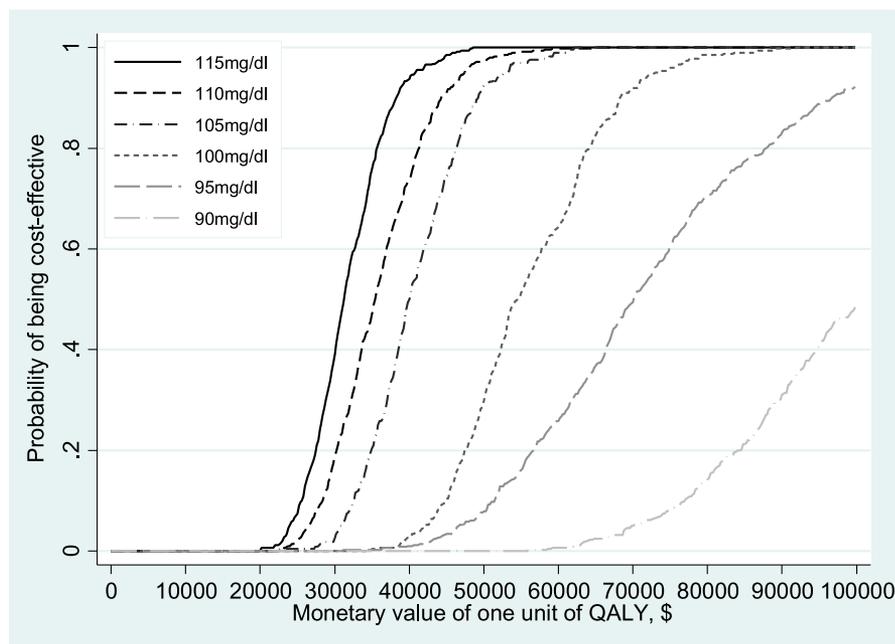

Figure 1—*Cost-effectiveness acceptability curves associated with alternative FPG thresholds. Note that the FPG threshold of 120 mg/dL served as the reference threshold for 115 mg/dL. For each of the other FPG thresholds, the next higher threshold served as the reference threshold. For instance, the comparison threshold for FPG 110 mg/dL was 115 mg/dL. See Table 3 for more details. (A high-quality color representation of this figure is available in the online issue.)*

found lower cost-effectiveness ratios associated with all FPG thresholds in those aged 45–64 years and younger than 45 than in those aged ≥65 years. This is primarily because of the longer life expectancy of the younger populations. Preventing more cases of type 2 diabetes and possibly other risk factors over that time creates a higher likelihood of recouping the cost of the intervention via reduced treatment and complication costs, even though the intervention is more effective in the older group.

Limitations—Our study has several limitations. First, our analysis is based on a single measure of FPG. Since FPG can vary from day to day, multiple measures might give a better definition of IFG. Second, FPG is one of several markers that can be used to identify people at high risk for developing type 2 diabetes. Recent ADA guidelines also recommended A1C as a test to identify people at high risk (6). Other variables such as sex, race/ethnicity, family history, and body weight may affect an individual's future risk of type 2 diabetes (39–41). Future studies should examine the cost-effectiveness of alternative thresholds of FPG testing, stratified by other risk factors, when data on diabetes incidences are available for those stratified subpopulations. Third, our simulation model was developed based on data collected from multiple sources and thus was inevitably subject to the accuracy of the data sources and the assumptions used by the researchers in the source studies.

When FPG testing is used to identify a target population for type 2 diabetes prevention, selecting a lower FPG threshold leads to a greater gain in overall health benefit but also to a deteriorated cost-effectiveness. The selection of an appropriate FPG threshold for any given population ultimately depends on the resources available or the willingness to pay for diabetes prevention. Using the conventional benchmark of $50,000 per QALY, a threshold of 105 mg/dL or higher is highly likely to be cost effective. Furthermore, a lower FPG threshold is preferred if the cost of the intervention can be lowered without compromising too much effectiveness.

References
1. Heianza Y, Hara S, Arase Y, et al. HbA1c 5·7-6·4% and impaired fasting plasma glucose for diagnosis of prediabetes and risk of progression to diabetes in Japan (TOPICS 3): a longitudinal cohort study. Lancet 2011;378:147–155
2. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2013;36(Suppl 1):S67–S74
3. Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia: report of a WHO/IDF consultation [report online], 2006. Geneva, Switzerland, World Health Organization. Available from http://www.who.int/diabetes/publications/Definition%20and%20diagnosis%20of%20diabetes_new.pdf. Accessed 8 August 2013
4. Knowler WC, Barrett-Connor E, Fowler SE, et al.; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002;346:393–403
5. National Diabetes Prevention Program [Internet], 2012. Atlanta, Georgia, Centers for Disease Control and Prevention. Available from http://www.cdc.gov/diabetes/prevention/index.htm. Accessed June 2012
6. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2010;33(Suppl 1):S62–S69
7. Forouhi NG, Balkau B, Borch-Johnsen K, et al; EDEG. The threshold for diagnosing impaired fasting glucose: a position statement by the European Diabetes Epidemiology Group. Diabetologia 2006;49:822–827
8. Lawes CM, Parag V, Bennett DA, et al; Asia Pacific Cohort Studies Collaboration. Blood glucose and risk of cardiovascular disease in the Asia Pacific region. Diabetes Care 2004;27:2836–2842
9. Levitan EB, Song Y, Ford ES, Liu S. Is nondiabetic hyperglycemia a risk factor for cardiovascular disease? A meta-analysis of prospective studies. Arch Intern Med 2004;164:2147–2155
10. Sorkin JD, Muller DC, Fleg JL, Andres R. The relation of fasting and 2-h post-challenge plasma glucose concentrations to mortality: data from the Baltimore Longitudinal Study of Aging with a critical review of the literature. Diabetes Care 2005;28:2626–2632
11. Hoerger TJ, Segel JE, Zhang P, Sorensen SW. Validation of the CDC-RTI diabetes cost-effectiveness model [report online], 2009.. Research Triangle Park, North Carolina, RTI International. Available from https://www.rti.org/pubs/mr-0013-0909-hoerger.pdf. Accessed 8 August 2013
12. Hoerger TJ, Harris R, Hicks KA, Donahue K, Sorensen S, Engelgau M. Screening for type 2 diabetes mellitus: a cost-effectiveness analysis. Ann Intern Med 2004;140:689–699
13. Hoerger TJ, Hicks KA, Sorensen SW, et al. Cost-effectiveness of screening for pre-diabetes among overweight and obese U.S. adults. Diabetes Care 2007;30:2874–2879
14. Herman WH, Hoerger TJ, Brandle M, et al; Diabetes Prevention Program Research Group. The cost-effectiveness of lifestyle modification or metformin in preventing type 2 diabetes in adults with impaired glucose tolerance. Ann Intern Med 2005;142:323–332
15. CDC Diabetes Cost-effectiveness Group. Cost-effectiveness of intensive glycemic control, intensified hypertension control, and serum cholesterol level reduction for type 2 diabetes. JAMA 2002;287:2542–2551
16. Centers for Disease Control and Prevention. N.C.f.H.S., Division of Health Interview Statistics, Distribution of Age at Diagnosis of Diabetes Among Adult Incident Cases Aged 18–79 Years, United States, 2011. Available from http://www.cdc.gov/diabetes/statistics/age/fig1.htm. Accessed 23 September 2013
17. Selvin E, Steffes MW, Zhu H, et al. Glycated hemoglobin, diabetes, and cardiovascular risk in nondiabetic adults. N Engl J Med 2010;362:800–811
18. de Vegt F, Dekker JM, Jager A, et al. Relation of impaired fasting and postload glucose with incident type 2 diabetes in a Dutch population: The Hoorn Study. JAMA 2001;285:2109–2113
19. Balkau B, Hillier T, Vierron E, et al. Comment to: Borch-Johnsen K, Colagiuri S, Balkau B et al. (2004) Creating a pandemic of prediabetes: the proposed new

diagnostic criteria for impaired fasting glycaemia. Diabetologia 47:1396-1402. Diabetologia 2005;48:801–802

20. Tirosh A, Shai I, Tekes-Manova D, et al; Israeli Diabetes Research Group. Normal fasting plasma glucose levels and type 2 diabetes in young men. N Engl J Med 2005;353:1454–1462

21. Qiao Q, Lindström J, Valle TT, Tuomilehto J. Progression to clinically diagnosed and treated diabetes from impaired glucose tolerance and impaired fasting glycaemia. Diabet Med 2003;20: 1027–1033

22. Wareham NJ, Byrne CD, Williams R, Day NE, Hales CN. Fasting proinsulin concentrations predict the development of type 2 diabetes. Diabetes Care 1999;22: 262–270

23. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. Lancet 1998;352: 837–853

24. Levitzky YS, Pencina MJ, D'Agostino RB, et al. Impact of impaired fasting glucose on cardiovascular disease: the Framingham Heart Study. J Am Coll Cardiol 2008; 51:264–270

25. Diabetes Prevention Program Research Group. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. Hypertension 2002; 40:679–686

26. Lee M, Saver JL, Hong KS, Song S, Chang KH, Ovbiagele B. Effect of pre-diabetes on future risk of stroke: meta-analysis. BMJ 2012;344:e3564

27. Gans KM, Lapane KL, Lasater TM, Carleton RA. Effects of intervention on compliance to referral and lifestyle recommendations given at cholesterol screening programs. Am J Prev Med 1994;10:275–282

28. Burke LE, Dunbar-Jacob JM, Hill MN. Compliance with cardiovascular disease prevention strategies: a review of the research. Ann Behav Med 1997;19:239–263

29. Eddy DM, Schlessinger L, Kahn R. Clinical outcomes and cost-effectiveness of strategies for managing people at high risk for diabetes. Ann Intern Med 2005;143: 251–264

30. Diabetes Prevention Program Research Group. Within-trial cost-effectiveness of lifestyle intervention or metformin for the primary prevention of type 2 diabetes. Diabetes Care 2003;26:2518–2523

31. Coffey JT, Brandle M, Zhou H, et al. Valuing health-related quality of life in diabetes. Diabetes Care 2002;25:2238–2243

32. Gold M, Siegel JE, Russell LB, Weinstein MC. *Cost-effectiveness in health and medicine*. New York, Oxford University Press, 1996

33. Ackermann RT, Marrero DG. Adapting the Diabetes Prevention Program lifestyle intervention for delivery in the community: the YMCA model. Diabetes Educ 2007;33:69, 74–75, 77–78

34. Ackermann RT, Finch EA, Brizendine E, Zhou H, Marrero DG. Translating the Diabetes Prevention Program into the community. The DEPLOY Pilot Study. Am J Prev Med 2008;35:357–363

35. Diabetes Prevention Program Research Group; Knowler WC, Fowler SE, Hamman RF, et al. 10-Year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. Lancet 2009;374:1677–1686

36. Fenwick E, Claxton K, Sculpher M. Representing uncertainty: the role of cost-effectiveness acceptability curves. Health Econ 2001;10:779–787

37. Grosse SD. Assessing cost-effectiveness in healthcare: history of the $50,000 per QALY threshold. Expert Rev Pharmacoecon Outcomes Res 2008;8:165–178

38. Cheng C, Kushner H, Falkner BE. The utility of fasting glucose for detection of prediabetes. Metabolism 2006;55:434–438

39. Kahn HS, Cheng YJ, Thompson TJ, Imperatore G, Gregg EW. Two risk-scoring systems for predicting incident diabetes mellitus in U.S. adults age 45 to 64 years. Ann Intern Med 2009;150:741–751

40. Wilson PW, Meigs JB, Sullivan L, Fox CS, Nathan DM, D'Agostino RB Sr. Prediction of incident diabetes mellitus in middle-aged adults: the Framingham Offspring Study. Arch Intern Med 2007;167:1068–1074

41. Kim C, Newton KM, Knopp RH. Gestational diabetes and the incidence of type 2 diabetes: a systematic review. Diabetes Care 2002;25:1862–1868

42. Stevens VJ, Obarzanek E, Cook NR et al. Long-term weight loss and changes in blood pressure: results of the Trials of Hypertension Prevention, phase II. Ann Intern Med 2001;134:1–11

43. Ratner R, Goldberg R, Haffner S et al. Impact of intensive lifestyle and metformin therapy on cardiovascular disease risk factors in the diabetes prevention program. Diabetes Care 2005;28:888–894