Screening for Type 2 Diabetes Mellitus: A Cost-effectiveness Analysis

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Although many adults who meet criteria for type 2 diabetes (hereafter, diabetes) have not been identified,[1] screening for diabetes remains controversial.[2–11] Direct evidence indicates that various treatments to reduce complications are effective among people with clinically detected diabetes,[12–14] but no direct evidence tells us the magnitude of any further benefit from starting these treatments earlier, after detection by screening.[15]

Context. In 2003, the U.S. Preventive Services Task Force recommended screening for type 2 diabetes in adults with hypertension or hyperlipidemia. The economic implications of this recommendation are unclear.

Contribution. Diabetes screening for 55-year-old hypertensive persons would cost the U.S. health care system $34,375 per quality-adjusted life-year.

Implications. The cost-effectiveness of targeting diabetes screening to hypertensive adults older than 55 years of age is similar to the cost-effectiveness of many accepted health care interventions. Universal diabetes screening is far more costly.

In the absence of direct evidence, researchers have applied mathematical models of diabetes progression to the issue of screening. One important analysis found that the cost per quality-adjusted life-year (QALY) gained by universal diabetes screening was lower for younger than for older people: $13,376 at ages 25 to 34 years, increasing to $116,908 at ages 55 to 64 years.[16] This conclusion followed from the model's focus on the provision of glycemic control after screening to prevent microvascular complications. The analysis did not consider treatments to reduce the risks for complications of cardiovascular disease (CVD).

More recent research suggests that the benefits of CVD risk reduction may be substantial for people with diabetes. The Hypertension Optimal Treatment (HOT) Study found that the optimal blood pressure target is lower for people with hypertension and diabetes than for people with hypertension without diabetes.[14] Other research supports the finding that intensive control of hypertension is beneficial among people with diabetes.[15,17–19] Because the benefit may be greater for older people (at greater risk for CVD), the conclusion of the previous analysis, that diabetes

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This study was conducted by RTI International under contract to the Agency for Healthcare Research and Quality Contract #290-97. Development of the cost-effectiveness model was supported by Centers for Disease Control and Prevention Contract 200-97-0621.

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This first appeared in *Ann Intern Med*. 2004;140:689–699.

screening is most cost-effective among younger people, needs to be reconsidered.

We performed a new cost-effectiveness analysis to compare universal diabetes screening (universal screening) and diabetes screening targeted to patients with hypertension (targeted screening). When an updated version of the model used in the previous analysis that includes benefits from intensive treatment of hypertension was applied, we estimated the incremental cost-effectiveness of these 2 strategies for people in different age groups. Our analysis considers a 1-time opportunistic screening for men and women of all races and ethnicities.

Methods

The Model

We used a Markov model of diabetes disease progression to simulate lifetime diabetes-related health care costs and QALYs for people with diabetes (Appendix Figure 1). Demographic characteristics of the simulated cohort are based on 1997 population estimates projected from the 1990 U.S. Census and data on the distribution of people with diabetes by hypertension, cholesterol level, and smoking status.[20] As people progress through the simulation model from the onset of diabetes to death, they can develop 5 types of complications: nephropathy, neuropathy, retinopathy, coronary heart disease (CHD), and stroke. People can die of some of these complications or from other causes. The model includes transition probabilities between disease stages on each of the 5 complication paths. The basic model structure has been described previously.[16–21] Key model parameters are presented in Appendix Tables 1 to 10.

To incorporate screening into the model, we first added a screening module in which some patients with diabetes are identified earlier than they would usually have been in the absence of screening. Second, we made assumptions about the transition probabilities between disease stages from the onset of diabetes to the time of usual clinical diagnosis of diabetes on the basis of the knowledge that progression is relatively slow during this period.[15] After clinical diagnosis, disease progression depends on the number of years after normal diagnosis.

Screening allows for earlier diagnosis, which in turn allows for earlier treatment interventions, such as intensive glycemic control and intensive hypertension control. These interventions decrease the transition probabilities, thereby delaying or preventing progression to diabetes complications.

Costs are incurred for screening and diagnostic testing; standard glycemic control and, if the person is hypertensive, standard hypertension control; interventions (intensive glycemic control and, if the person is hypertensive, intensive hypertension control); and complications over the remaining lifetime of each person with diabetes. The sum of these costs and the model's estimate of the expected QALYs for each screening strategy are used to calculate the incremental cost-effectiveness ratio of screening relative to no screening. We discounted future costs and QALYs at a 3% annual rate. Costs are measured in 1997 U.S. dollars.

Interventions

We assumed that, in the absence of screening, diabetes would be diagnosed 10 years after its onset.[15] With 1-time opportunistic screening, people would be diagnosed with diabetes on average 5 years after the onset of diabetes and therefore patients would begin treatment 5 years earlier. After diabetes diagnosis, all patients are treated with intensive glycemic control and, if they have hypertension, with intensive hypertension control.

With targeted screening, only people with hypertension are screened. Those who screen positive and who receive a diagnosis of diabetes begin intensive glycemic control and intensive hypertensive control 5 years earlier than they would in the absence of screening. With universal screening, all people, regardless of hypertension status, are screened. Those who screen positive and receive a diagnosis of diabetes begin intensive glycemic control 5 years earlier than in the absence of screening and begin intensive hypertension control 5 years earlier if they have hypertension.

We defined hypertension as a blood pressure of 140/90 mm Hg or higher. We assumed that 19% of people aged 25 to 44 years, 47% of people aged 45 to 64 years, and 60% of people aged 65 to 74

years had hypertension and therefore were included in targeted screening.[20]

Treatment of hypertension is modeled as standard (with target diastolic blood pressure of 90 mm Hg) or intensive (with a target diastolic blood pressure of 80 mm Hg), as in the HOT trial.[14] All persons with hypertension receive standard hypertension treatment until they receive a diagnosis of diabetes, after which they receive intensive hypertension treatment. The incremental cost of intensive hypertension control relative to standard control is $149 per year.

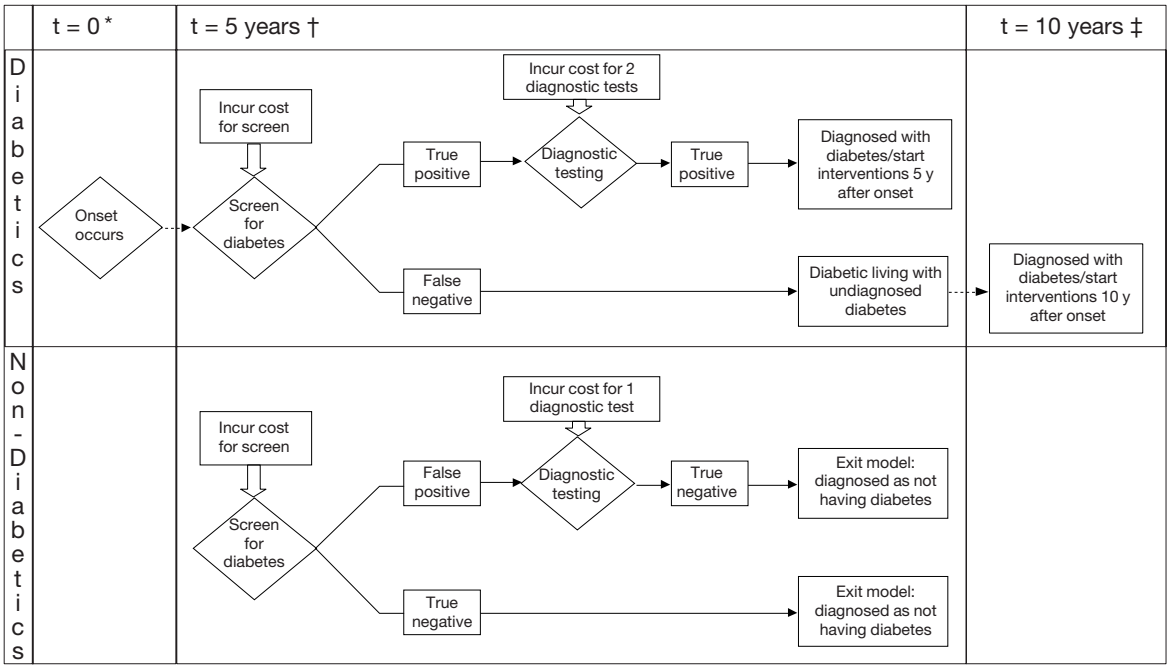
In the HOT trial, the relative risk reduction for CHD events (fatal and nonfatal myocardial infarction) was 51%, and the relative risk reduction for stroke was about 30%. Although neither of these separate relative risk reductions was statistically significant, the relative risk reduction (51%) for the aggregate outcome of major CVD events was statistically significant (P = 0.005). We initially modeled the relative risk reduction for CHD events for intensive hypertension control to be 51% with no risk reduction for stroke. We conducted a sensitivity analysis that included a 30% relative risk reduction for stroke on the basis of other studies showing that intensive hypertension control reduces risk among people with diabetes.[7,19]

Model estimates of the effects of glycemic control are based on the United Kingdom Prospective Diabetes Study (UKPDS), a 10-year randomized controlled trial of intensive versus conventional glycemic control.[12] On the basis of the UKPDS, the reduction in hemoglobin A1c from intensive glycemic treatment is modeled as slowing the progression of microvascular complications.[12] The incremental cost of intensive glycemic control (relative to standard control) ranges from $900 to $1,100 per year, depending on the number of years since diagnosis.

Screening and Diagnostic Tests

The figure illustrates the screening and diagnostic testing process and shows where costs are incurred.

Figure. Progression of Persons Screened for Diabetes



*t = 0: diabetes onset.
†t = 5 y: diabetes diagnosis by screening.
‡t = 10 y: diabetes diagnosed clinically.

Screening Tests

We assume a 1-time opportunistic screening during a regularly scheduled physician office visit. The model assumes screening by a fasting capillary blood glucose (CBG) test[22] and an extra 10 minutes over the usual 15 minutes for the physician visit, incurring a cost of $24.40 per person screened. Costs for the CBG test are derived from the Medicare Clinical Diagnostic Laboratory Fee Schedule[23]; physician visit costs are derived from *Relative Values for Physicians*.[24] Table 1 shows prevalence (from the National Health and Nutrition Examination Survey III data tape), CBG sensitivity and specificity values[22] with exact data points clarified via personal communication (Rola DB, January 18 2002), and the number needed to screen to detect 1 previously undiagnosed person with diabetes (NNS) by sex, hypertension status, and age.

Diagnostic Tests

All people who screen (true or false) positive receive a diagnostic test, the fasting plasma glucose (FPG) test, which is repeated if it is positive. Because 2 consecutive elevated FPG tests define diabetes,[11] we assume that this strategy has 100% sensitivity and 100% specificity. Diagnostic testing costs $8.32 per test ($5.32 for test processing plus $3.00 for blood drawing[23]). Table 1 reports the number of diagnostic tests needed to identify 1 previously undiagnosed diabetes case.

Analyses

Diabetes complications, life-years, and QALYs are calculated for each true case of undiagnosed diabetes in the given population. We calculated change in life-years, change in QALYs, and change in costs for diabetes-related care for people with diabetes, as well as costs for screening per person screened. Future medical costs are not calculated for those without diabetes because their care does not change with screening. However, the analysis does include the cost of screening them. "Base Case" analyses are performed by using the model's standard parameter values (Appendix Tables 1–10).

To examine the variability of the cost-effectiveness ratios associated with screening, we conducted one-way sensitivity analyses for people screened at age 55 to investigate the effect of key parameter values and assumptions. We also conducted a probabilistic sensitivity analysis in which 129 critical parameters were simultaneously varied over probability distributions on the basis of published 95% CIs or other reasonable ranges. We used the logistic normal distribution for most parameters[25] but used uniform and triangular distributions where appropriate (Appendix Tables 1–10). We computed cost-effectiveness results for each of 1,000 iterations for both targeted and universal screening of people aged 55 years using @Risk software (Palisade Corporation, Newfield, New York) and examined the distribution of cost-effectiveness ratios across iterations.

Role of the Funding Sources

This study was supported by the Agency for Healthcare Research and Quality (AHRQ). Development of the cost-effectiveness model was supported by the Centers for Disease Control and Prevention. AHRQ staff reviewed the study and provided comments on drafts of the manuscript. Staff of the Centers for Disease Control and Prevention participated in the development of the model and contributed to the manuscript. The authors were responsible for deciding to submit the manuscript for publication.

Results

Targeted Screening

Table 2 shows the cost-effectiveness analysis comparing targeted screening with no screening for people of different ages. Diabetes complication incidence, life-years, and QALYs are reported for each case of diabetes in the population screened. Change in life-years, change in QALYs, and costs of diabetes-related care for those with diabetes, as well as costs of screening, are reported per person eligible for screening. Compared with no screening, targeted screening leads to earlier initiation of intensive glycemic and hypertension treatment and a longer lifetime. It also increases costs. The

Table 1. Number of Screenings and Diagnostic Tests Needed to Identify One Undiagnosed Diabetes Case

Category of Cases	Age at Screening, y	Prevalence of Undiagnosed Diabetes at Screening*	Sensitivity of CBG Screening Test†	Specificity of CBG Screening Test†	Number Needed to Screen‡	Number of Diagnostic Tests Needed, n§
Men with hypertension	35	0.05302	0.912	0.961	20.7	2.8
	45	0.05302	0.938	0.905	20.1	3.8
	55	0.08178	0.938	0.905	13.0	3.1
	65	0.03403	0.938	0.905	31.3	4.9
	75	0.04047	0.938	0.905	26.3	4.4
Women with hypertension	35	0.05302	0.74	0.973	25.5	2.7
	45	0.05302	0.796	0.928	23.7	3.6
	55	0.08178	0.796	0.928	15.4	3.0
	65	0.03403	0.796	0.928	36.9	4.6
	75	0.04047	0.796	0.928	31.0	4.1
Men without hypertension	35	0.05534	0.912	0.961	19.8	2.7
	45	0.05534	0.938	0.905	19.3	3.7
	55	0.05742	0.938	0.905	18.6	3.7
	65	0.02606	0.938	0.905	40.9	5.8
	75	0.04779	0.938	0.905	22.3	4.0
Women without hypertension	35	0.05534	0.74	0.973	24.4	2.6
	45	0.05534	0.796	0.928	22.7	3.5
	55	0.05742	0.796	0.928	21.9	3.5
	65	0.02606	0.796	0.928	48.2	5.4
	75	0.04779	0.796	0.928	26.3	3.8

*Data from National Health and Nutrition Examination Survey III.[1]

†Sensitivity and specificity of CBG screen based on test results of ≤120 mg/dL, ≥8 h postprandial time, as reported in Figure 2 of Rolka 2001.[22]

‡Number needed to screen to identify one undiagnosed diabetes case = [(prevalence of undiagnosed diabetes)(CBG sensitivity)].[1]

§Number of diagnostic tests to identify one undiagnosed diabetes case = 2 (1 true positive) + (number of false positive screening results undiagnosed diabetes case per undiagnosed diabetes case) = 2 + number needed to screen (1 - diabetes prevalence) (1 - CBG test specificity).

CBG = capillary blood glucose.

Table 2. Targeted Screening for People with Hypertension Only, with Intensive Glycemic Control and Intensified Hypertension Control after Diagnosis

		Results per True Diabetes Case						
		Lifetime Cumulative Incidence (%)						
Illustrative Case in the Model	Age at Diagnosis	ESRD	LEA	Blind	Stroke	CHD	Life-Years*	QALYs†
	—y—	—%—						
Screen at 35 y	**(onset at 30 y)**							
W/o screening	40	25.30	40.18	12.32	13.08	21.86	33.27	19.73
W/ screening	35	24.68	40.27	12.41	13.24	21.51	33.45	19.81
Screening effect		–0.62	0.09	0.09	0.16	–0.35	0.18	0.08
Screen at 45 y	**(onset at 40 y)**							
W/o screening	50	14.90	27.64	8.72	15.12	26.13	26.20	16.84
W/ screening	45	14.57	27.92	8.87	15.40	24.67	26.49	17.00
Screening effect		–0.33	0.28	0.15	0.28	–1.46	0.30	0.16
Screen at 55 y	**(onset at 50 y)**							
W/o screening	60	6.50	15.10	5.15	15.38	29.93	18.90	13.23
W/ screening	55	6.39	15.40	5.29	15.76	27.40	19.24	13.44
Screening effect		–0.11	0.30	0.14	0.38	–2.53	0.35	0.22
Screen at 65 y	**(onset at 60 y)**							
W/o screening	70	1.82	6.04	2.45	15.58	28.87	12.30	9.34
W/ screening	65	1.79	6.20	2.56	16.06	25.57	12.63	9.57
Screening effect		–0.03	0.16	0.11	0.48	–3.30	0.33	0.23
Screen at 75 y	**(onset at 70 y)**							
W/o screening	80	0.23	1.69	0.84	14.97	24.42	7.28	5.93
W/ screening	75	0.22	1.72	0.88	15.40	21.09	7.51	6.11
Screening effect		–0.01	0.03	0.04	0.43	–3.33	0.23	0.18

*Undiscounted.
†Discounted at 3%.
Note: Screening effects are expressed as percentage points.
CHD = Coronary heart disease events; ESRD = End-stage renal disease; LEA = Lower-extremity amputation; QALY = Quality-adjusted life year.

Table 2. Targeted Screening for People with Hypertension Only, with Intensive Glycemic Control and Intensified Hypertension Control after Diagnosis (cont)

Results per Person Screened							
Lifetime Costs ($)*							Cost/QALY
Screen & Diagnostic Testing	Diabetes Treatment	Diabetes Intervention	Diabetes Compli-cations	Total	Life Years Gained*	QALYs Gained†	
—$—							—$—
0	1,012	920	2,619	4,551			
25	1,174	1,149	2,569	4,917			
25	162	229	–50	366	0.010	0.004	87,096
0	830	758	1,827	3,415			
25	999	999	1,798	3,820			
25	169	241	–29	405	0.016	0.008	46,881
0	941	858	1,884	3,682			
25	1,187	1,221	1,859	4,292			
25	246	363	–25	610	0.029	0.018	34,375
0	249	223	526	998			
23	336	361	522	1,242			
23	88	138	–4	245	0.011	0.008	31,228
0	162	136	422	720			
21	238	270	423	952			
21	76	134	1	231	0.009	0.007	32,106

increase in total incremental costs per person screened is somewhat greater for those who are younger than for those who are older. Incremental QALYs for persons with diabetes generally increase with age, primarily because of a reduction in CHD incidence. The cost-effectiveness ratios for targeted screening are lower in older people.

Universal Screening

Compared with no screening, universal screening increases lifetime costs at all ages (Table 3). The increased costs are attributable primarily to increased treatment and intervention (including earlier intensive glycemic and hypertension control) for those who are diagnosed through screening. The incremental total costs increase slightly from $331 per person eligible for screening at age 35 years to $479 per person eligible at age 55 years, before declining to $92 per person eligible at age 75 years.

Universal screening also adds QALYs over the lifetime of previously undiagnosed people with diabetes. The incremental cost-effectiveness ratios for universal screening compared with no screening are generally quite high and decrease with age.

Universal vs Targeted Screening

The cost-effectiveness ratios in Tables 2 and 3 show that targeted screening is more cost-effective than universal screening at every age when each alternative is compared with no screening. This finding suggests that policymakers would want to adopt targeted screening before universal screening. Then, the next relevant question is, given targeted screening, how cost-effective is it to move to universal screening by adding screening of people without hypertension to the people with hypertension already included in targeted screening? Table 4 shows the cost-effectiveness ratios for targeted vs no screening and for universal vs targeted screening. Relative to targeted screening, universal screening has very high cost-effectiveness ratios, which increase with age. This implies that screening people without hypertension is much less cost effective than screening those with hypertension.

Sensitivity Analyses

We performed sensitivity analyses for 55-year-old people (Table 5); the same pattern of results holds for other ages. In the base-case analysis, the cost-effectiveness ratio was calculated as $34,375/QALY for targeted screening vs no screening and $360,966/QALY for universal screening vs targeted screening. If intensive hypertension control costs $300 per year more than standard hypertension control (instead of $149 more in the base case), then the cost-effectiveness ratio increases to $37,153/QALY for targeted screening and $362,079/QALY for universal screening. If screening costs are twice as much as in the initial analysis, the cost-effectiveness ratios increase by only a small amount, approximately 5%, for both targeted and universal screening.

In the base-case analysis, people receive intensive glycemic control after receiving a diagnosis of diabetes. Intensive glycemic control is expensive, costing from $900 to $1,100 per year more than standard glycemic control. In a sensitivity analysis, we assumed that people 55 years of age at screening receive lifetime standard glycemic control after diagnosis, where standard control is based on the conventional treatment arm of the UKPDS.[12] The incremental cost-effectiveness ratios for both targeted and universal screening are cut in half. In another sensitivity analysis, we assumed that those screened with diabetes incurred no extra cost for intensive glycemic control during their first 5 years of treatment. This reduced the cost-effectiveness ratio for targeted screening by more than 50%, even more than the reduction associated with lifetime standard glycemic control.

If screening were to lead to diagnosis 2 or 8 years earlier than no screening (i.e., 8 or 2 years after onset), the incremental cost-effectiveness ratios would be modestly different from what they are in the base-case analysis, in which screening leads to diagnosis 5 years earlier.

We found that if the sensitivity and specificity of the CBG screen test were based on values associated with random (<8 hour postprandial time) rather than fasting (≥8 hours postprandial time) testing, the incremental cost-effectiveness ratios would be only slightly higher (<1%).

The base-case analysis assumed that intensive hypertension control reduces the relative risk for CHD by 51% relative to standard hypertension control, on the basis of HOT trial findings. If medication adherence is lower or if the effects of intensive hypertension control are more moderate than they were in the HOT trial, resulting in only a 25% risk reduction, the incremental cost-effectiveness ratios would increase substantially for both targeted and universal screening, to $119,262 and $411,623, respectively. As expected, the cost-effectiveness of screening is highly sensitive to the effects of intensive hypertension control.

Previous research suggests that intensive hypertension control reduces the risk for stroke.[7,19] In a sensitivity analysis, we assumed that intensive hypertension control leads to a 30% relative risk reduction for stroke (the not-statistically-significant relative risk reduction for stroke reported for the HOT trial), in addition to the risk reduction for CHD. The incremental cost-effectiveness ratios decline modestly.

The prevalence of undiagnosed diabetes may have changed since the National Health and Nutrition Examination Survey III. We reduced and increased all prevalence values by 1 standard deviation; these analyses produced only negligible differences from the base-case cost-effectiveness ratios.

We prepared histograms of cost-effectiveness ratios resulting from the probabilistic sensitivity analyses (Appendix Figure 2). Targeted screening analysis resulted in cost-effectiveness ratios with a median of $34,229 per QALY. Ninety-five percent of cost-effectiveness ratios were between $21,594 and $76,099 per QALY. The universal screening analysis resulted in a median cost-effectiveness ratio of $371,324/QALY when compared with targeted screening. Ninety-five percent of cost-effectiveness ratios were between $275,518 and $541,216 per QALY.

Discussion

We found that, at every age, diabetes screening targeted to people with hypertension is more cost-effective than universal screening. We further found that, taking into consideration a reduction in CHD events from earlier treatment of hypertension, both universal and targeted screening are more cost-effective for people at 55, 65, and 75 years of age than for people 35 and 45 years of age. The most cost-effective approach to one-time diabetes screening is to target people with hypertension between ages 55 and 75 years.

In this analysis, the benefit of screening comes predominantly from reducing CHD events by intensive control of hypertension rather than from reducing microvascular complications such as end-stage renal disease or blindness by intensive glycemic control. Among people at low risk for CHD events (eg, people in their thirties), the benefit of screening derives predominantly from decreasing end-stage renal disease, but it must be purchased at the high cost of intensive glycemic control. Among people at higher risk for CHD events (eg, people in their fifties and sixties), the benefit of intensive control of hypertension is larger and can be purchased less expensively. The benefits of intensive control of hypertension are also realized sooner than the benefits of intensive glycemic control.[15]

Our findings differ dramatically from those of a previous cost-effectiveness analysis.[16] Our model modifies the previous model in several ways. First, we allow people with hypertension and diabetes to receive intensive hypertension control. Second, intensive glycemic control produces smaller reductions in diabetes complications in our model. Our assumptions about risk reduction from intensive glycemic control are based on UKPDS results[12] that were not available at the time of the previous analysis. Because intensive glycemic control leads to smaller effects on diabetes complications in our model, cost-effectiveness ratios for universal screening are higher than those in the previous report. Third, the earlier model assumed that people with diabetes would receive standard glycemic control after diagnosis. In our analysis, we assumed that people with diabetes would receive intensive glycemic control after diagnosis. Our sensitivity analyses show that cost-effectiveness ratios are substantially higher with intensive glycemic control than with standard control; the previous model produced similar results.

Table 3. Universal Screening with Intensive Glycemic Control and Intensive Hypertension Control after Diagnosis

		Results per True Diabetes Case						
		Lifetime Cumulative Incidence (%)						
Illustrative Case in the Model	Age at Diagnosis	ESRD	LEA	Blind	Stroke	CHD	Life-Years*	QALYs†
	—y—	—%—						
Screen at 35 y	**(onset at 30 y)**							
w/o screening	40	24.28	41.05	12.89	12.41	26.87	34.05	20.08
w/ screening	35	23.53	41.03	12.96	12.50	27.01	34.16	20.13
Screening effect		–0.75	–0.02	0.07	0.09	0.14	0.12	0.05
Screen at 45 y	**(onset at 40 y)**							
w/o screening	50	14.54	28.36	9.18	14.25	31.05	26.92	17.26
w/ screening	45	13.99	28.32	9.25	14.34	30.91	27.02	17.32
Screening effect		–0.55	–0.04	0.07	0.09	–0.14	0.10	0.05
Screen at 55 y	**(onset at 50 y)**							
w/o screening	60	6.25	14.89	5.23	14.47	32.76	18.96	13.32
w/ screening	55	6.02	14.96	5.31	14.65	31.61	19.14	13.43
Screening effect		–0.23	0.07	0.08	0.18	–1.15	0.18	0.11
Screen at 65 y	**(onset at 60 y)**							
w/o screening	70	1.74	5.91	2.47	14.83	30.95	12.33	9.40
w/ screening	65	1.67	5.94	2.53	15.05	29.38	12.50	9.51
Screening effect		–0.07	0.03	0.06	0.22	–1.57	0.16	0.11
Screen at 75 y	**(onset at 70 y)**							
w/o screening	80	0.21	1.59	0.81	14.06	25.12	7.11	5.82
w/ screening	75	0.20	1.59	0.84	14.32	23.05	7.26	5.94
Screening effect		–0.01	0.00	0.03	0.26	–2.07	0.15	0.11

*Undiscounted.
†Discounted at 3%.
Note: Screening effects are expressed as percentage points.
CHD = Coronary heart disease events; ESRD = End-stage renal disease; LEA = Lower-extremity amputation; QALY = Quality-adjusted life year.

Table 3. Universal Screening with Intensive Glycemic Control and Intensive Hypertension Control after Diagnosis (cont)

Results per Person Eligible for Screening							
Lifetime Costs ($)†							Cost/QALY
Screen & Diagnostic Testing	Diabetes Treatment	Diabetes Intervention	Diabetes Compli-cations	Total	Life Years Gained*	QALYs Gained†	
——————————$——————————							—$—
0	794	897	2,677	4,369			
25	952	1,103	2,620	4,700			
25	158	206	–58	331	0.007	0.003	126,238
0	639	742	1,882	3,263			
25	800	957	1,844	3,627			
25	162	214	–38	364	0.005	0.003	121,965
0	633	687	1,552	2,872			
25	830	966	1,529	3,351			
25	197	279	–23	479	0.012	0.008	62,934
0	167	185	453	805			
23	239	295	449	1,007			
23	72	110	–4	202	0.005	0.003	59,183
0	53	54	175	282			
8	84	107	175	374			
8	31	53	0	92	0.003	0.002	48,146

Table 4. Incremental Cost-effectiveness Ratios for Diabetes Screening

Age at Screening (Age at Onset)	Targeted Screening vs No Screening	Universal Screening vs Targeted Screening
y (y)	$/QALY	
35 (30)	87,096	143,839
45 (40)	46,881	215,701
55 (50)	34,375	360,966
65 (60)	31,228	466,942
75 (70)	32,106	443,433

QALY = Quality-adjusted life year.

Our findings are consistent with modeling studies showing that people with diabetes are at highest risk for eventually developing microvascular complications if they are relatively young or have highly elevated glycemic levels.[26,27] People with diabetes identified by screening usually have mildly to moderately elevated glycemic levels; intensive glycemic control to reduce hyperglycemia may be less beneficial for these people than for those with higher glycemic levels.[27] Our findings also are consistent with studies showing that much of the cost and burden of diabetes is attributable to CVD complications, outcomes affected by intensive hypertension control.[21,28–33]

Our conclusions could change if future research provides better and different evidence on model parameters. If, for example, intensive glycemic control during the preclinical phase of diabetes was shown to have a large effect on subsequent diabetes complications, then all of the cost-effectiveness ratios would become more favorable. The HOT trial was a subgroup analysis; if other research shows that treatment of hypertension among people with diabetes should not differ from treatment of those without diabetes, the cost-effectiveness ratios for targeted screening would be too favorable. Similarly, if poor adherence to antihypertensive medications reduces the effectiveness of intensive hypertension treatment, the cost-effectiveness ratios will be less favorable. Further evidence can be incorporated within the model by changing model parameters.

We did not consider screening people without hypertension but with other CHD risk factors for diabetes such as dyslipidemia or tobacco use. Compared with evidence on treatment for hypertension, there is less evidence that treatment for these risk factors should be different in people with and without diabetes.[15] If future research shows that knowing a patient has diabetes affects treatment for lipid and tobacco disorders, then our analysis would need amending. People with dyslipidemia whose cardiovascular risk crosses a lipid treatment threshold with the diagnosis of diabetes might especially benefit from earlier diabetes diagnosis and earlier lipid treatment. Future models could examine the cost-effectiveness of diabetes screening for people in this group.

Our results do not contradict other analyses of the beneficial effects or cost-effectiveness of intensive glycemic control or intensive hypertension control after clinical diagnosis.[21,29,30] This issue is distinct from the issue of screening. For screening, we assumed that everyone would receive intensive glycemic control and intensive hypertension control after diagnosis. The screening comparison is between starting these treatments a few years earlier and starting them after clinical diagnosis.

We did not examine the cost-effectiveness of screening to detect and treat impaired glucose tolerance or impaired fasting glucose levels. Although new research shows that intensive treatment can reduce the development of

Table 5. Sensitivity Analyses		
Sensitivity Analysis Scenario	**Cost-effectiveness Ratio ($/QALY)**	
	Targeted vs No Screening	**Universal vs Targeted Screening**
Base-case analysis	34,375	360,966
Incremental cost of tight hypertension control, $149		
Screening test cost, $24.40		
Diagnostic test cost, $8.32		
People identified with diabetes receive intensive glycemic control		
5 y detection benefit from screening		
Screening sensitivity based on ≥8 h postprandial time*		
Intensive hypertension control results in a 51% relative risk reduction for CHD		
Intensive hypertension control has no effects on relative risk for stroke		
Diabetes prevalence = mean prevalence reported in NHANES III		
Incremental cost of tight hypertension control, $300	37,153	362,079
Screening, diagnostic test costs doubled	35,783	384,503
Screening test cost, $48.80		
Diagnostic test cost, $16.64		
People identified with diabetes receive standard glycemic control	17,472	164,850
No extra cost for intensive glycemic control for persons screened with diabetes during first 5 y of treatment	14,497	190,454
2-y detection benefit from screening	35,875	308,525
8-y detection benefit from screening	33,850	474,121
Screening sensitivity, specificity based on <8 hrs postprandial time*	34,551	364,465
Intensive hypertension control results in a 25% relative risk reduction for CHD	68,448	411,623
Intensive hypertension control results in a 30% relative risk reduction for stroke	28,122	352,186
Diabetes prevalence (mean – 1 standard deviation) reported prevalence in NHANES III	34,696	367,371
Diabetes prevalence (mean + 1 standard deviation) reported prevalence in NHANES III	34,157	356,866

*Sensitivity and specificity of capillary blood glucose test screening is based on test results ≤ 120 mg/dL and both ≥8 and <8 hours postprandial time based on CBG as reported in Figure 2 of Rolka 2001.[22]

Note: All incremental cost-effectiveness ratios are calculated for persons age 50 years at diabetes onset and 55 years at screening.

CHD = coronary heart disease events; NHANES III = National Health and Nutrition Examination Survey III; QALY = Quality adjusted life-year.

diabetes,[34,35] cost-effectiveness models examining this question will need to make assumptions about the effect of reductions in diabetes incidence on various diabetes complications. We also did not examine the impact of periodic, rather than 1-time, screening. For longer time intervals between screenings, the cost-effectiveness would be similar to 1-time screening. For shorter intervals, the cost-effectiveness ratios would be higher.

As we had no randomized controlled trial of screening for diabetes, we extrapolated much of the input data on various benefits of screening from studies of people whose diabetes was detected clinically. The longest follow-up is 10 years.[12]

The study's strengths are that our model used the most recent and highest quality data on benefits and costs and our ability to carry out several sensitivity analyses, all of which gave similar results. Unlike researchers using previous models, we could model the macrovascular benefits of screening.

This study has important implications for screening for diabetes. Although universal screening achieves greater overall benefit than targeted screening, the cost of the additional benefit is high. A more efficient strategy is targeted screening of people with hypertension between the ages of 55 and 75 years, with intensive hypertension control for people detected with diabetes. This strategy provides most of the benefits of universal screening at much less cost.

Acknowledgments

The authors thank David Atkins, MD, MPH, and Jean Slutsky, PA, MSPH, at the Agency for Healthcare Research and Quality, who helped us obtain funding and provided useful feedback. Also at AHRQ, Eve Shapiro, Amy Pfeiffer and Margi Grady provided editing help and Nilam Patel provided general organizational assistance. At RTI International, Kathleen N. Lohr, PhD, Director of the RTI-UNC Evidence-based Practice Center, provided many suggestions and essential editorial help. Also at RTI, Sonya Sutton and Loraine Monroe developed the manuscript, managed the reference database, and created tables from our description. At the UNC Cecil G. Sheps Center for Health Services Research, Audrina Bunton assisted us with manuscript and reference preparation. The Director of the Sheps Center, Timothy Carey, MD, MPH, created an environment in which this work could be conducted.

The authors also thank the reviewers, including U.S. Preventive Services Task Force members Steven Teutsch, MD, MPH; Steven H. Woolf, MD, MPH; and Paul Frame, MD, who gave excellent suggestions.

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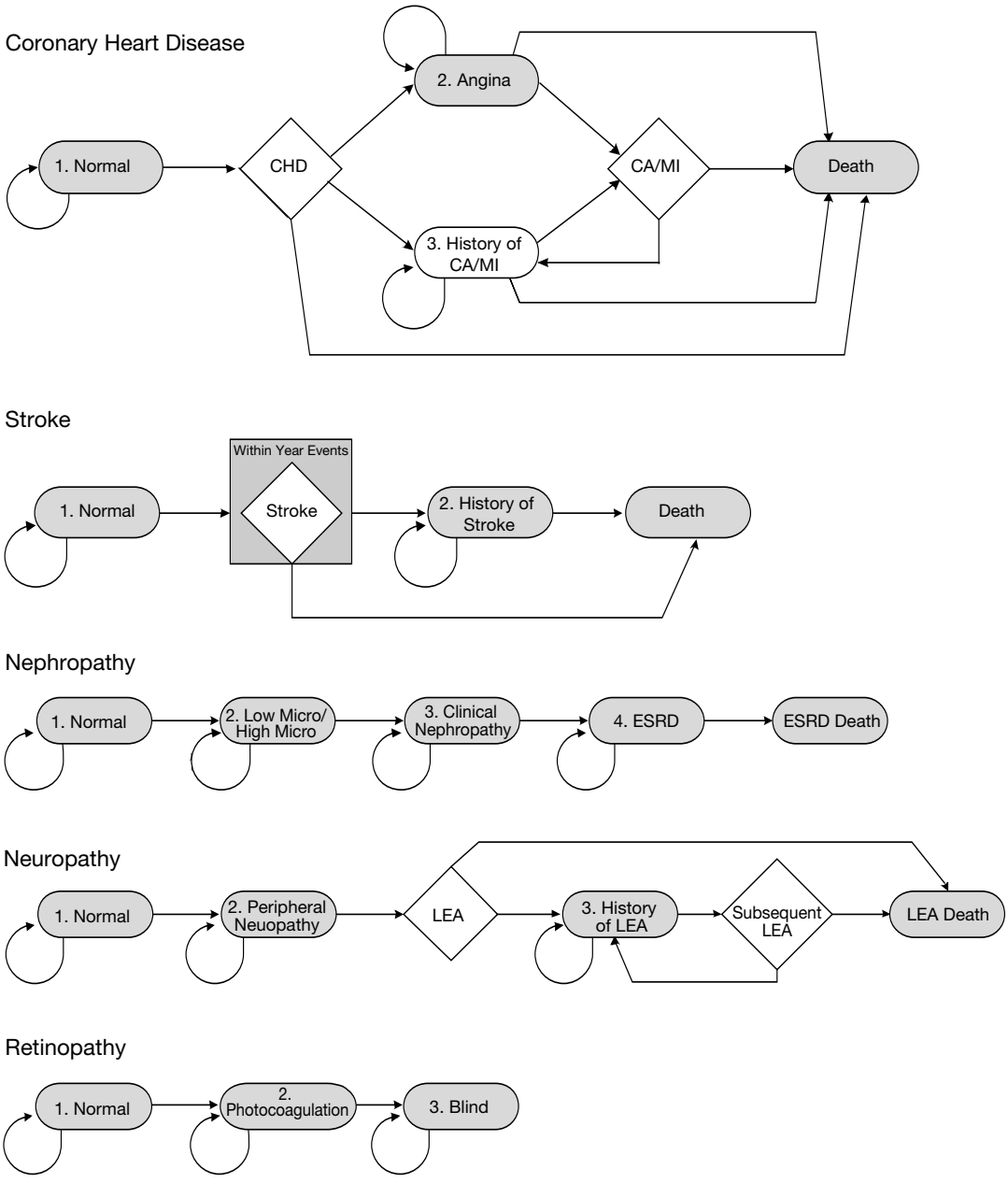
Appendix

Appendix Figure 1. Markov Model of Diabetes Disease Progression

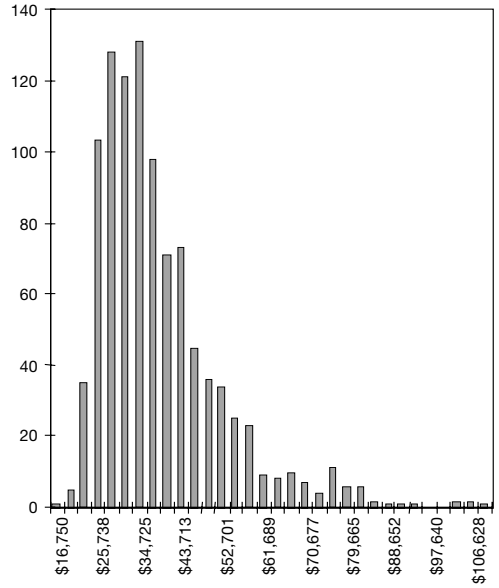


The model is used to follow the disease progression of all members of a cohort simultaneously on 5 different disease paths. For the simulation, transitions between states take place at discrete time intervals 1 year apart. Thus, at the end of each 1-year period, portions of the cohort can move from one disease state to another or stay in the same disease state. The simulation program determines what proportion of the cohort will move from one state to another based on the transition probability. In several cases, an individual can experience a complication event that the patient either dies of or survives during the period. The Markov model keeps track of the number of patients who are in each state in each period. It also keeps track of the cumulative incidence of patients who have undergone complication events such as lower extremity amputation (LEA), angina, cardiac arrest (CA) or myocardial infarction (MI), and stroke. In the diagrams, complication events are represented by diamonds; states are numbered and represented by ovals.

Appendix Figure 2. Histograms of Cost-effectiveness Ratios Resulting from Probabilistic Sensitivity Analyses Based on Universal and Targeted Screening

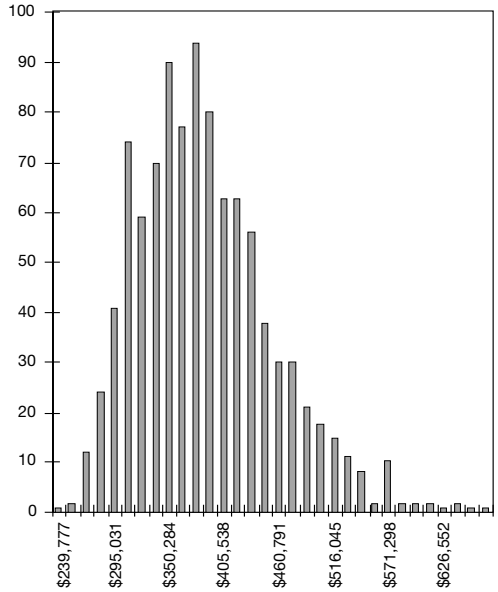
A probabilistic sensitivity analysis was conducted in which 129 critical parameters were simultaneously varied over probability distributions based on published 95% confidence intervals or other reasonable ranges. A cost-effectiveness ratio was computed for each of 1,000 iterations for both targeted and universal screening of people aged 55 years. The histograms below present the distribution of those ratios.

Targeted Screening



Cost-effectiveness ratios resulting from 1000 targeted screening trials

Universal vs. Targeted Screening



Cost-effectiveness ratios resulting from 1000 universal screening trials, when compared to targeted screening

Note: QALY = Quality-adjusted life-year.

Appendix Table 1. Base-Case Values and Distributions Applied in Probabilistic Sensitivity Analysis for Selected Parameters: Diabetes Screening

Parameter				Parameter Value		Base-Case Source
				Base-Case Analysis*	Probabilistic Sensitivity Analysis Distribution†	
Prevalence of undiagnosed diabetes, %	Non-hypertensive		Ages 0 to 49 y	5.534	Logn(5.53, 3.61)	36
			50 to 59 y	5.742	Logn(5.74, 3.26)	36
			60 to 69 y	2.606	Logn(2.61, 0.96)	36
			70 to 94 y	4.779	Logn(4.78, 3.07)	36
	Hypertensive		Ages 0 to 49 y	5.302	Logn(5.30, 2.71)	36
			50 to 59 y	8.178	Logn(8.18, 5.09)	36
			60 to 69 y	3.403	Logn(3.40, 1.70)	36
			70 to 94 y	4.047	Logn(4.05, 2.55)	36
Sensitivity and specificity of capillary blood glucose (CBG) test for identifying diabetes	Sensitivity	Female	Ages 0 to 44 y	0.973	Logn(0.973, 0.954)	22
			45 to 94 y	0.796	Logn(0.796, 0.780)	22
		Male	Ages 0 to 44 y	0.961	Logn(0.961, 0.942)	22
			45 to 94 y	0.938	Logn(0.938, 0.919)	22
	Specificity	Female	Ages 0 to 44 y	0.740	Logn(0.740, 0.725)	22
			45 to 94 y	0.928	Logn(0.928, 0.909)	22
		Male	Ages 0 to 44 y	0.912	Logn(0.912, 0.894)	22
			45 to 94 y	0.905	Logn(0.905, 0.887)	22
Transition probabilities	Normal to microalbuminuria			0.0113	Not varied	37
	Normal to peripheral neuropathy			0.0036	Not varied	37
Costs	Screening test (CBG)			$4.37	Triang(3.28, 4.37, 5.46)	23
	Diagnostic test (Fasting Plasma Glucose)			$5.32	Triang(3.99, 5.32, 6.65)	23
	Blood draw (for diagnostic test)			$3.00	Triang(2.25, 3.00, 3.75)	23
	15-min physician visit			38.63	Triang(29, 39, 48)	23
	25-min physician visit (extra 10 mins for screen)			58.66	Triang(44, 59, 73)	23
Other	Time from diabetes onset to screening, y			5	Unif(4.00, 6.00)	Assumed
	Time from diabetes onset to diagnosis, y			10	Unif(9, 12)	15

*These values were applied in all model runs unless otherwise specified (in one-way and probabilistic sensitivity analyses).

†The distributions from which parameter values were randomly sampled in the probabilistic sensitivity analyses. The ranges for parameters without published variability data followed these guidelines: screening sensitivity and specificity values vary by +/– 2%; costs more than $300 vary by +/–15%; costs less than $300, time durations, transition probabilities, hazard rates, and quality-of-life values vary by +/–25%; and the discounting factor varies from 2% to 5%. Relevant limits were applied to all ranges (eg, quality of life and probabilities must be between 0 and 1).

Logn(*a,b*) = Lognormal distribution with mean *a*, lower bound of 95% confidence interval *b;* Triang(*a,b,c*) = Triangular distribution with minimum *a*, mode *b*, maximum *c*. Unif(*a,b*) = Uniform distribution with minimum *a,* maximum *b.*

Appendix Table 2. Discount Rates

Parameter	Parameter Value		Base-Case Source
	Base-Case Analysis*	Probabilistic Sensitivity Analysis Distribution†	
Discount rate applied to costs	3.00	Triang(2.00, 3.33, 5.00)	Assumed
Discount rate applied to life years, QALYs	3.00	Triang(2.00, 3.33, 5.00)	Assumed

*These values were applied in all model runs unless otherwise specified (in one-way and probabilistic sensitivity analyses).

†The distributions from which parameter values were randomly sampled in the probabilistic sensitivity analyses. The ranges for parameters without published variability data followed these guidelines: screening sensitivity and specificity values vary by +/–2%; costs more than $300 vary by +/–15%; costs less than $300, time durations, transition probabilities, hazard rates, and quality-of-life values vary by +/–25%; and the discounting factor varies from 2% to 5%. Relevant limits were applied to all ranges (eg, quality of life and probabilities must be between 0 and 1).

QALY = quality-adjusted life-year; Triang(*a,b,c*) = Triangular distribution with minimum *a*, mode *b*, maximum *c*.

Appendix Table 3. Base-Case Values and Distributions Applied in Probabilistic Sensitivity Analysis for Selected Parameters: Nephropathy

Parameter*			Parameter Value		Base-Case Source
			Base-Case Analysis†	Probabilistic Sensitivity Analysis Distribution‡	
Costs, QALYs	Normal	One-time cost, $	0.00	Not varied	Assumed
		Annual treatment cost, $	0.00	Not varied	Assumed
		QALY	1.00	Unif(0.75, 1.00)	Assumed
	Microalbuminuria	One-time cost, $	0.00	Not varied	Assumed
		Annual treatment cost, $	0.00	Not varied	Assumed
		QALY	1.00	Unif(0.75, 1.00)	Assumed
	Nephropathy	One-time cost (renal evaluation), $	1201	Logn(1,201, 1,021)	38
		Annual treatment cost, $	0.00	Not varied	Assumed
		QALY	1.00	Unif(0.75, 1.00)	Assumed
	End stage renal disease (ESRD)	One-time cost, $	0.00	Not varied	Assumed
		Annual treatment cost, $	72,488	Logn(72,488, 61,615)	38
		QALY	0.610	Unif(0.458, 0.763)	38, 39
Transition probabilities	Normal to Microalbuminuria	Baseline	0.033	Logn(0.033, 0.024)	17
		Hypertensive w/moderate control	0.056	Logn(0.056, 0.042)	39
		Hypertensive w/tight control	0.038	Logn(0.038, 0.028)	39
	Microalbuminuria to nephropathy	Baseline	0.075	Logn(0.075, 0.056)	17
		Hypertensive w/moderate control	0.151	Logn(0.151, 0.113)	39
		Hypertensive w/tight control	0.128	Logn(0.128, 0.096)	39
	Nephropathy to end-stage renal disease. Y since diagnosis	0 to 11	0.004	Logn(0.004, 0.003)	37, 40
		12 to 19	0.039	Logn(0.039, 0.029)	37, 40
		20 to 94	0.074	Logn(0.074, 0.056)	37, 40

*One-time cost refers to costs incurred only one time, at the time of diagnosis of a state or complication event. Annual treatment cost refers to costs incurred every year after diagnosis of a state or complication event.

†These values were applied in all model runs unless otherwise specified (in one-way and probabilistic sensitivity analyses).

‡The distributions from which parameter values were randomly sampled in the probabilistic sensitivity analyses. The ranges for parameters without published variability data followed these guidelines: screening sensitivity and specificity values vary by +/– 2%; costs more than $300 vary by +/–15%; costs less than $300, time durations, transition probabilities, hazard rates, and quality-of-life values vary by +/–25%; and the discounting factor varies from 2% to 5%. Relevant limits were applied to all ranges (eg, quality of life and probabilities must be between 0 and 1). Because QALY values with a value of 1.0 in the base case were varied between 0.75 and 1.0 (averaging around 0.9 rather than 1.0, the base-case value), we expect that mean cost-effectiveness ratios from the probabilistic analyses will be slightly higher than the base case in both analyses. The results were consistent with this expectation.

Logn(*a,b*) = Lognormal distribution with mean *a*, lower bound of 95% confidence interval *b;* QALY = Quality-adjusted life-year; Unif(*a,b*) = Uniform distribution with minimum *a,* maximum *b*.

Appendix Table 4. Base-Case Values and Distributions Applied in Probabilistic Sensitivity Analysis for Selected Parameters: Neuropathy

Parameter*			Parameter Value		Base-Case Source
			Base-Case Analysis†	Probabilistic Sensitivity Analysis Distribution‡	
Costs, QALYs	Normal	One-time cost, $	0.00	Not varied	Assumed
		Annual treatment cost, $	0.00	Not varied	Assumed
		QALY	1.00	Unif(0.75, 1.00)	Assumed
	Peripheral neuropathy	One-time cost (neurologic exam), $	357	Logn(357, 303)	38
		Annual treatment cost, $	0.00	Not varied	Assumed
		QALY	1.00	Unif(0.75, 1.00)	Assumed
	Lower extremity amputation (LEA)	One-time cost, $	33,131	Logn(33, 131, 28, 161)	41
		Annual treatment cost, $	0.00	Not varied	Assumed
		QALY	0.800	Unif(0.600, 1.000)	39
	Cost of fatal LEA		67,635	Logn(67,635, 57,490)	41
Transition Probabilities	Normal to peripheral neuropathy		0.036	Logn(0.036, 0.027)	12
	Peripheral neuropathy to LEA	Y since diagnosis: 0 to 7	0.028	Logn(0.028, 0.021)	42
		8 to 12	0.046	Logn(0.046, 0.034)	42
		13 to 18	0.056	Logn(0.056, 0.042)	42
		19 to 94	0.140	Logn(0.140, 0.105)	42
Other	Probability of additional amputations, %		11	Logn(11, 8)	43
	Probability of diabetes foot ulcer, %		4.00	Logn(4.00, 3.00)	43, 44
	Probability of death from amputation, %		10.50	Logn(10.5, 8)	43
	Cost of diabetes foot ulcer, $		2800	Logn(2,100, 2,800, 3,500)	45

*One-time cost refers to costs incurred only one time, at the time of diagnosis of a state or complication event. Annual treatment cost refers to costs incurred every year after diagnosis of a state or complication event.

†These values were applied in all model runs unless otherwise specified (in one-way and probabilistic sensitivity analyses).

‡The distributions from which parameter values were randomly sampled in the probabilistic sensitivity analyses. The ranges for parameters without published variability data followed these guidelines: screening sensitivity and specificity values vary by +/–2%; costs more than $300 vary by +/–15%; costs less than $300, time durations, transition probabilities, hazard rates, and quality-of-life values vary by +/–25%; and the discounting factor varies from 2% to 5%. Relevant limits were applied to all ranges (eg, quality of life and probabilities must be between 0 and 1). Because QALY values with a value of 1.0 in the base case were varied between 0.75 and 1.0 (averaging around 0.9 rather than 1.0, the base-case value), we expect that mean cost-effectiveness ratios from the probabilistic analyses will be slightly higher than the base case in both analyses. The results were consistent with this expectation.

Logn(*a*,*b*) = Lognormal distribution with mean *a*, lower bound of 95% confidence interval *b*; QALY = Quality-adjusted life-year; Triang(*a*,*b*,*c*) = Triangular distribution with minimum *a*, mode *b*, maximum *c*. Unif(*a*,*b*) = Uniform distribution with minimum *a*, maximum *b*.

Appendix Table 5. Base-Case Values and Distributions Applied in Probabilistic Sensitivity Analysis for Selected Parameters: Retinopathy

Parameter*			Parameter Value		Base-Case Source
			Base-Case Analysis†	Probabilistic Sensitivity Analysis Distribution‡	
Costs, QALYs	Normal	One-time cost, $	0.00	Not varied	Assumed
		Annual treatment cost, $	0.00	Not varied	Assumed
		QALY	1.00	Unif(0.75, 1.00)	Assumed
	Photocoagulation	One-time cost, $	2,943	Logn(2,943; 2,502)	38
		Annual treatment cost, $	0.00	Not varied	Assumed
		QALY	1.00	Unif(0.75, 1.00)	Assumed
	Blindness	One-time cost, $	0.00	Not varied	Assumed
		Annual treatment cost, $	2,125	Logn(2,125; 1,806)	38
		QALY	0.690	Unif(0.518, 0.863)	39
Transition probabilities	Normal to Photocoagulation	Baseline	0.011	Logn(0.011, 0.008)	12
		Hypertensive w/moderate control	0.017	Logn(0.017, 0.012)	17
		Hypertensive w/tight control	0.010	Logn(0.010, 0.008)	17
	Photocoagulation to blindness	Baseline	0.107	Logn(0.107, 0.080)	17
		Hypertensive w/moderate control	0.107	Logn(0.107, 0.080)	17
		Hypertensive w/tight control	0.107	Logn(0.107, 0.080)	17

*One-time cost refers to costs incurred only one time, at the time of diagnosis of a state or complication event. Annual treatment cost refers to costs incurred every year after diagnosis of a state or complication event.

†These values were applied in all model runs unless otherwise specified (in one-way and probabilistic sensitivity analyses).

‡The distributions from which parameter values were randomly sampled in the probabilistic sensitivity analyses. The ranges for parameters without published variability data followed these guidelines: screening sensitivity and specificity values vary by +/– 2%; costs more than $300 vary by +/–15%; costs less than $300, time durations, transition probabilities, hazard rates, and quality-of-life values vary by +/– 25%; and the discounting factor varies from 2% to 5%. Relevant limits were applied to all ranges (eg, quality of life and probabilities must be between 0 and 1). Because QALY values with a value of 1.0 in the base case were varied between 0.75 and 1.0 (averaging around 0.9 rather than 1.0, the base-case value), we expect that mean cost-effectiveness ratios from the probabilistic analyses will be slightly higher than the base case in both analyses. The results were consistent with this expectation.

Logn(*a,b*) = Lognormal distribution with mean *a*, lower bound of 95% confidence interval *b;* QALY = Quality-adjusted life-year; Unif(*a,b*) = Uniform distribution with minimum *a,* maximum *b*.

Appendix Table 6. Base-Case Values and Distributions Applied in Probabilistic Sensitivity Analysis for Selected Parameters: Coronary Heart Disease

Parameter*			Parameter Value		Base-Case Source
			Base-Case Analysis†	Probabilistic Sensitivity Analysis Distribution‡	
Costs, QALYs	Normal	One-time cost, $	0	Not varied	Assumed
		Annual treatment cost, $	0	Not varied	Assumed
		QALY	1.00	Unif(0.75, 1.00)	Assumed
	Angina	One-time cost, $	2,733	Logn(2,733; 2,323)	46
		Annual treatment cost, $	1,118	Logn(1,118; 950)	46
		QALY	0.947	Unif(0.710, 1.000)	47
	History of CA or MI	One-time cost, $	0	Not varied	Assumed
		Annual treatment cost, $	1,118	Logn(1,118; 950)	46
		QALY	0.880	Unif(0.660, 1.000)	48
	Other one-time costs	Angina death (extra over normal death), $	0	Not varied	Assumed
		Before admission CA or MI death, $	759	Logn(759, 645)	46
		With hospitalization CA or MI death, $	18,653	Logn(18,653; 15,855)	46
		Death from chronic MI, $	0	Not varied	Assumed
		CA or MI survivors, $	16,534	Logn(16,534; 14,054)	46

*One-time cost refers to costs incurred only one time, at the time of diagnosis of a state or complication event. Annual treatment cost refers to costs incurred every year after diagnosis of a state or complication event.

†These values were applied in all model runs unless otherwise specified (in one-way and probabilistic sensitivity analyses).

‡The distributions from which parameter values were randomly sampled in the probabilistic sensitivity analyses. The ranges for parameters without published variability data followed these guidelines: screening sensitivity and specificity values vary by +/–2%; costs more than $300 vary by +/–15%; costs less than $300, time durations, transition probabilities, hazard rates, and quality-of-life values vary by +/–25%; and the discounting factor varies from 2% to 5%. Relevant limits were applied to all ranges (eg, quality of life and probabilities must be between 0 and 1). Because QALY values with a value of 1.0 in the base case were varied between 0.75 and 1.0 (averaging around 0.9 rather than 1.0, the base-case value), we expect that mean cost-effectiveness ratios from the probabilistic analyses will be slightly higher than the base case in both analyses. The results were consistent with this expectation.

CA=cardiac arrest; Logn(*a,b*) = Lognormal distribution with mean *a*, lower bound of 95% confidence interval *b;* MI = myocardial infarction; QALY = Quality-adjusted life-year; Unif(*a,b*) = Uniform distribution with minimum *a,* maximum *b*.

Appendix Table 7. Base-Case Values and Distributions Applied in Probabilistic Sensitivity Analysis for Selected Parameters: Stroke

Parameter			Parameter Value		Base-Case Source
			Base-Case Analysis*	Probabilistic Sensitivity Analysis Distribution†	
QALYs	Normal		1.00	Unif(0.75, 1.00)	Assumed
	Stroke		0.500	Unif(0.375, 0.625)	49
Transition probabilities	Stroke to death	Immediate	0.142	Logn(0.142, 0.107)	50
		1 y	0.092	Logn(0.092, 0.069)	50
Costs, $	Stroke, one-time	Ages 0 to 64 y	27,914	Logn(27,914; 23,727)	51
		65 to 74 y	21,613	Logn(21,613; 18,371)	51
		75 to 84 y	20,530	Logn(20,530; 17,451)	51
		85 to 94 y	15,974	Logn(15,974; 13,578)	51
	Immediate death due to stroke	Ages 0 to 64 y	27,914	Logn(27,914; 23,727)	51
		65 to 74 y	21,613	Logn(21,613; 18,371)	51
		75 to 84 y	20,530	Logn(20,530; 17,451)	51
		85 to 94 y	15,974	Logn(15,974; 13,578)	51
	Stroke, annual treatment	Ages 0 to 44 y	5,150	Logn(5,150; 4,378)	51
		45 to 54 y	2,940	Logn(2,940; 2,499)	51
		55 to 64 y	9,505	Logn(9,505; 8,079)	51
		65 to 74 y	7,599	Logn(7,599; 6,459)	51
		75 to 84 y	6,596	Logn(6,596; 5,607)	51
		85 to 94 y	2,886	Logn(2,886; 2,453)	51

*These values were applied in all model runs unless otherwise specified (in one-way and probabilistic sensitivity analyses).

†The distributions from which parameter values were randomly sampled in the probabilistic sensitivity analyses. The ranges for parameters without published variability data followed these guidelines: screening sensitivity and specificity values vary by +/– 2%; costs more than $300 vary by +/–15%; costs less than $300, time durations, transition probabilities, hazard rates, and quality-of-life values vary by +/–25%; and the discounting factor varies from 2% to 5%. Relevant limits were applied to all ranges (eg, quality of life and probabilities must be between 0 and 1). Because QALY values with a value of 1.0 in the base case were varied between 0.75 and 1.0 (averaging around 0.9 rather than 1.0, the base-case value), we expect that mean cost-effectiveness ratios from the probabilistic analyses will be slightly higher than the base case in both analyses. The results were consistent with this expectation.

Logn(*a,b*) = Lognormal distribution with mean *a*, lower bound of 95% CI *b;* QALY = Quality-adjusted life-year; Unif(*a,b*) = uniform distribution with minimum *a,* maximum *b*.

Appendix Table 8. Base-Case Values and Distributions Applied in Probabilistic Sensitivity Analysis for Selected Parameters: Standard Glycemic Control

Parameter	Parameter Value		Base-Case Source
Annual costs (includes drugs, physician office visits, self-testing, case management) Time since diabetes diagnosis, $	**Base-Case Analysis***	**Probabilistic Sensitivity Analysis Distribution†**	
0 y	372	Logn(372, 316)	52
1 y	413	Logn(413, 351)	52
2 y	447	Logn(447, 380)	52
3 y	490	Logn(490, 417)	52
4 y	538	Logn(538, 457)	52
5 y	594	Logn(594, 505)	52
6 y	642	Logn(642, 546)	52
7 y	679	Logn(679, 577)	52
8 y	717	Logn(717, 609)	52
9 y	741	Logn(741, 630)	52
10 y	771	Logn(771, 655)	52
11 y	839	Logn(839, 713)	52
12 y	860	Logn(860, 731)	52
13 to 94 y	870	Logn(870, 740)	52
Treatment effect: Reduction in hemoglobin A 1c level, percentage points	2.0	Not varied	12

*These values were applied in all model runs unless otherwise specified (in one-way and probabilistic sensitivity analyses).

†The distributions from which parameter values were randomly sampled in the probabilistic sensitivity analyses. The ranges for parameters without published variability data followed these guidelines: screening sensitivity and specificity values vary by +/–2%; costs more than $300 vary by +/–15%; costs less than $300, time durations, transition probabilities, hazard rates, and quality-of-life values vary by +/–25%; and the discounting factor varies from 2% to 5%. Relevant limits were applied to all ranges (eg, quality of life and probabilities must be between 0 and 1).

Logn(*a,b*) = Lognormal distribution with mean *a*, lower bound of 95% CI *b.*

Appendix Table 9. Base-Case Values and Distributions Applied in Probabilistic Sensitivity Analysis for Selected Parameters: Tight Glycemic Control

Parameter	Parameter Value		Base-Case Source
Annual costs (includes drugs, physician office visits, self-testing, case management) Time since diabetes diagnosis, $	**Base-Case Analysis***	**Probabilistic Sensitivity Analysis Distribution†**	
0 y	1,118	Logn(1,118; 950)	52
1 y	985	Logn(985, 837)	52
2 y	995	Logn(995, 846)	52
3 y	994	Logn(994, 845)	52
4 y	993	Logn(993, 844)	52
5 y	980	Logn(980, 833)	52
6 y	979	Logn(979, 832)	52
7 y	969	Logn(969, 824)	52
8 y	966	Logn(966, 821)	52
9 y	970	Logn(970, 825)	52
10 y	967	Logn(967, 822)	52
11 y	921	Logn(921, 783)	52
12 y	927	Logn(927, 788)	52
13 y	924	Logn(924, 785)	52
14 y	930	Logn(930, 791)	52
15 to 94 y	943	Logn(943, 802)	52
Treatment effect: reduction in hemoglobin A 1c level, percentage points	2.90	Triang(2.00, 2.90, 3.80)	12

*These values were applied in all model runs unless otherwise specified (in one-way and probabilistic sensitivity analyses).

†The distributions from which parameter values were randomly sampled in the probabilistic sensitivity analyses. The ranges for parameters without published variability data followed these guidelines: screening sensitivity and specificity values vary by +/–2%; costs more than $300 vary by +/–15%; costs less than $300, time durations, transition probabilities, hazard rates, and quality-of-life values vary by +/–25%; and the discounting factor varies from 2% to 5%. Relevant limits were applied to all ranges (eg, quality of life and probabilities must be between 0 and 1).

Logn(*a,b*) = Lognormal distribution with mean *a*, lower bound of 95% confidence interval *b;* Triang(*a,b,c*) = Triangular distribution with minimum *a*, mode *b*, maximum *c*.

Appendix Table 10. Base-Case Values and Distributions Applied in Probabilistic Sensitivity Analysis for Selected Parameters: Hypertension Control

Parameter*			Parameter Value		Base-Case Source
			Base-Case Analysis*	Probabilistic Sensitivity Analysis Distribution†	
Annual drug costs, $	Moderate	5 mg felodipine, 100 mg captopril, 50 mg atenolol 25 mg hydrochlorothiazide	297	Triang(223, 297, 371)	52
	Tight (given to 100% of patients)	5 mg felodipine, 100 mg captopril, 50 mg atenolol, 25 mg hydrochlorothiazide	315	Triang(237, 315, 394)	52
	Tight (given to 50% of patients)	5 mg felodipine, 100 mg captopril, 50 mg atenolol	262	Triang(197, 262, 328)	52
Treatment effect, %	Relative risk reduction of CHD for moderate hypertension control		13	Logn(13, 10)	17
	Additional risk reduction of CHD for tight hypertension control		51	Triang(19, 47, 71)	14
	Relative risk reduction of stroke for moderate hypertension control		54	Not varied	17
	Additional risk reduction of stroke for tight hypertension control		0	Triang(–47, –19, 66)	14

*These values were applied in all model runs unless otherwise specified (in one-way and probabilistic sensitivity analyses).

†The distributions from which parameter values were randomly sampled in the probabilistic sensitivity analyses. The ranges for parameters without published variability data followed these guidelines: screening sensitivity and specificity values vary by +/– 2%; costs more than $300 vary by +/–15%; costs less than $300, time durations, transition probabilities, hazard rates, and quality-of-life values vary by +/– 25%; and the discounting factor varies from 2% to 5%. Relevant limits were applied to all ranges (eg, quality of life and probabilities must be between 0 and 1).

CHD = coronary heart disease; Logn(*a*,*b*) = Lognormal distribution with mean *a*, lower bound of 95% confidence interval *b;* Triang(*a*,*b*,*c*) = Triangular distribution with minimum *a*, mode *b*, maximum *c*.

AHRQ Pub. No. 04-0539
May 2004