

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

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Background: No randomized, controlled trial of screening for diabetes has been conducted. In the absence of direct evidence, cost-effectiveness models may provide guidance about preferred screening strategies.

Objective: To estimate the incremental cost-effectiveness of 2 diabetes screening strategies: screening targeted to people with hypertension and universal screening.

Design: Markov model.

Data Sources: United Kingdom Prospective Diabetes Study, Hypertension Optimal Treatment trial, and recent cost data.

Target Population: General primary care population in the United States.

Time Horizon: Lifetime.

Perspective: Health care system.

Interventions: Diabetes screening targeted to people with hypertension and universal screening.

Outcome Measures: Cost per quality-adjusted life-year (QALY) gained. Costs (in 1997 U.S. dollars) and QALYs discounted at a 3% annual rate.

Results of Base-Case Analysis: At all ages, incremental cost-effectiveness ratios were more favorable for screening targeted to people with hypertension than for universal screening. For example, at age 55 years, the cost per QALY for targeted screening compared with no screening was \$34 375, whereas the cost per QALY for universal screening compared with targeted screening was \$360 966. Screening was more cost-effective for ages 55 to 75 years than for younger ages.

Results of Sensitivity Analysis: In single-way and probabilistic sensitivity analyses, findings were robust to therapy costs, screening costs, screening lead time, reduced effectiveness of intensive antihypertensive therapy, and increased relative risk reduction for stroke attributable to intensive hypertension control.

Limitations: We did not consider screening targeted to persons with dyslipidemia, and we used studies of people whose diabetes was detected clinically to estimate screening benefits.

Conclusions: Diabetes screening targeted to people with hypertension is more cost-effective than universal screening. The most cost-effective strategy is targeted screening at age 55 to 75 years.

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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).

In the absence of direct evidence, researchers have applied mathematical models of diabetes progression to the issue of screening. One 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 age 25 to 34 years, increasing to \$116 908 at age 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) trial 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). Be-

cause the benefit may be greater for older people (at greater risk for CVD), the conclusion of the previous analysis, that diabetes 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 one-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, available at www.annals.org). 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

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 gained. Expanding screening to all adults regardless of the presence of hypertension would cost an additional \$360 966 per quality-adjusted life-year.

Implications

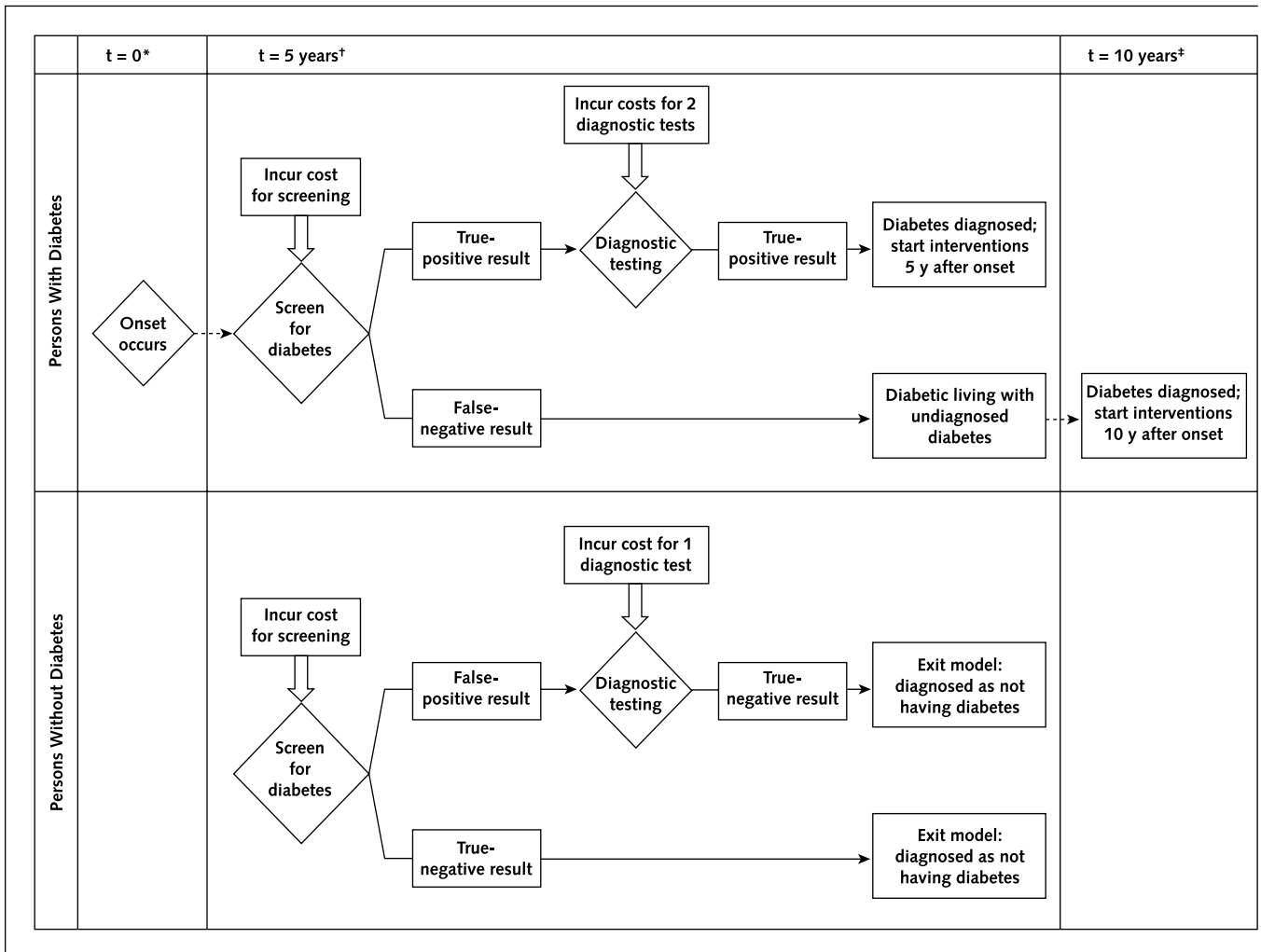
The cost-effectiveness of targeting diabetes screening to hypertensive adults older than 55 years of age is similar to the cost-effectiveness of many accepted health care interventions. Universal diabetes screening is far more costly.

—The Editors

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 of 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 the **Appendix Tables 1 to 10** (available at www.annals.org).

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.

Figure. Progression of persons screened for diabetes.



*Diabetes onset; †Diabetes diagnosis by screening; ‡Diabetes diagnosed clinically.

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§	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

* CBG = capillary blood glucose.

† Data from National Health and Nutrition Examination Survey III (1).

‡ Sensitivity and specificity of CBG screening test is based on test results of ≤ 120 mg/dL and ≥ 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) = 2 + number needed to screen (1 - diabetes prevalence)(1 - CBG test specificity).

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 one-time opportunistic screening, diabetes would be diagnosed on average 5 years after onset 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 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 age 25 to 44 years, 47% of people age 45 to 64 years, and 60% of people age 65 to 74 years had hypertension and therefore were included in targeted screening (20).

Treatment of hypertension is modeled as standard (with a 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 inten-

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

Illustrative Case in the Model	Age at Diagnosis	Results per True Diabetes Case						
		Lifetime Cumulative Incidence					Life-Years†	QALYs‡
		ESRD	LEA	Blindness	Stroke	CHD		
	y	← % →						
Screening at 35 y	(onset at 30 y)							
Without screening	40	25.3	40.18	12.32	13.08	21.86	33.27	19.73
With 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
Screening at 45 y	(onset at 40 y)							
Without screening	50	14.9	27.64	8.72	15.12	26.13	26.20	16.84
With screening	45	14.57	27.92	8.87	15.4	24.67	26.49	17.00
Screening effect		-0.33	0.28	0.15	0.28	-1.46	0.30	0.16
Screening at 55 y	(onset at 50 y)							
Without screening	60	6.5	15.1	5.15	15.38	29.93	18.90	13.23
With screening	55	6.39	15.4	5.29	15.76	27.4	19.24	13.44
Screening effect		-0.11	0.3	0.14	0.38	-2.53	0.35	0.22
Screening at 65 y	(onset at 60 y)							
Without screening	70	1.82	6.04	2.45	15.58	28.87	12.30	9.34
With screening	65	1.79	6.2	2.56	16.06	25.57	12.63	9.57
Screening effect		-0.03	0.16	0.11	0.48	-3.3	0.33	0.23
Screening at 75 y	(onset at 70 y)							
Without screening	80	0.23	1.69	0.84	14.97	24.42	7.28	5.93
With screening	75	0.22	1.72	0.88	15.4	21.09	7.51	6.11
Screening effect		-0.01	0.03	0.04	0.43	-3.33	0.23	0.18

* 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.
 † Undiscounted.
 ‡ Discounted at 3%.

sive 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 (17, 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 A_{1c} 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 \$1100 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.

Screening Tests

We assume a one-time opportunistic screening during a regularly scheduled physician office visit. The model as-

sumes 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 (Rolka DB, 18 January 2002), and the number needed to screen to detect one previously undiagnosed person with diabetes by sex, hypertension status, and age.

Diagnostic Tests

All people who screen (true or false) positive receive a diagnostic test, the fasting plasma glucose test, which is repeated if the result is positive. Because 2 consecutive elevated fasting plasma glucose test results 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

Table 2—Continued

Screening and Diagnostic Testing	Results per Person Screened				Life-Years Gained†	QALYs Gained‡	Cost/QALY
	Lifetime Costs‡						
	Diabetes Treatment	Diabetes Intervention	Diabetes Complications	Total			
	←————— \$ —————→						\$
0	1012	920	2619	4551			
25	1174	1149	2569	4917			
25	162	229	−50	366	0.010	0.004	87 096
0	830	758	1827	3415			
25	999	999	1798	3820			
25	169	241	−29	405	0.016	0.008	46 881
0	941	858	1884	3682			
25	1187	1221	1859	4292			
25	246	363	−25	610	0.029	0.018	34 375
0	249	223	526	998			
23	336	361	522	1242			
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

needed to identify one 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 to 10, available at www.annals.org).

To examine the variability of the cost-effectiveness ratios associated with screening, we conducted one-way sensitivity analyses for people screened at age 55 years 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 when appropriate (Appendix Tables 1 to 10, available at www.annals.org).

.org). We computed cost-effectiveness results for each of 1000 iterations for both targeted and universal screening of people age 55 years by using @Risk software (Palisade Corp., 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. Development of the cost-effectiveness model was supported by the Centers for Disease Control and Prevention. Staff of the Agency for Healthcare Research and Quality 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

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

Illustrative Case in the Model	Age at Diagnosis	Results per True Diabetes Case						
		Lifetime Cumulative Incidence					Life-Year [†]	QALYs Gained [‡]
		ESRD	LEA	Blindness	Stroke	CHD		
	y	←————— % —————→						
Screening at 35 y	(onset at 30 y)							
Without screening	40	24.28	41.05	12.89	12.41	26.87	34.05	20.08
With 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
Screening at 45 y	(onset at 40 y)							
Without screening	50	14.54	28.36	9.18	14.25	31.05	26.92	17.26
With 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
Screening at 55 y	(onset at 50 y)							
Without screening	60	6.25	14.89	5.23	14.47	32.76	18.96	13.32
With 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
Screening at 65 y	(onset at 60 y)							
Without screening	70	1.74	5.91	2.47	14.83	30.95	12.33	9.40
With 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
Screening at 75 y	(onset at 70 y)							
Without screening	80	0.21	1.59	0.81	14.06	25.12	7.11	5.82
With 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

* Screening effects for cumulative incidence are expressed as percentage points. CHD = coronary heart disease events; ESRD = end-stage renal disease; LEA = lower-extremity amputation; QALY = quality-adjusted life-year.

† Undiscounted.

‡ Discounted at 3%.

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 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 identified 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 unidentified people with diabetes. The incremental cost-effectiveness ratios for universal screening

compared with no screening are generally high and decrease with age.

Universal versus 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 versus no screening and for universal versus 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 persons (Table 5); the same pattern of results holds for other ages. In the base-case analysis, the cost-effectiveness ratio

Table 3—Continued

Results per Person Eligible for Screening					Cost/QALY		
Screening and Diagnostic Testing	Lifetime Costs‡				Life-Years Gained†	QALYs Gained‡	
	Diabetes Treatment	Diabetes Intervention	Diabetes Complications	Total			
←————— \$ —————→							
0	794	897	2677	4369			
25	952	1103	2620	4700			
25	158	206	-58	331	0.007	0.003	126 238
0	639	742	1882	3263			
25	800	957	1844	3627			
25	162	214	-38	364	0.005	0.003	121 965
0	633	687	1552	2872			
25	830	966	1529	3351			
25	197	279	-23	479	0.012	0.008	62 934
0	167	185	453	805			
23	239	295	449	1007			
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

was calculated as \$34 375/QALY for targeted screening versus no screening and \$360 966/QALY for universal screening versus 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 \$900 to \$1100 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, when 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 (that is, 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

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.

Table 5. Sensitivity Analyses*

Sensitivity Analysis Scenario	Cost-Effectiveness Ratio	
	Targeted vs. No Screening	Universal vs. Targeted Screening
	\$/QALY	
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 and specificity 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 and diagnostic test costs doubled		
Screening test cost, \$48.80	35 783	384 503
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
Detection benefit from screening		
2 y	35 875	308 525
8 y	33 850	474 121
Screening sensitivity and specificity based on < 8 h 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 SD) reported prevalence in NHANES III	34 696	367 371
(mean + 1 SD) reported prevalence in NHANES III	34 157	356 866

*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.

† 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, as reported in Figure 2 of Rolka 2001 (22).

25% risk reduction, the incremental cost-effectiveness ratios would increase substantially for both targeted (\$119 262) and universal (\$411 623) screening. 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 (17, 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 SD; these analyses produced only negligible differences from the base-case cost-effectiveness ratios.

We prepared histograms of cost-effectiveness ratios re-

sulting from the probabilistic sensitivity analyses (Appendix Figure 2, available at www.annals.org). 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 per 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. In addition, we 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 at 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 (for example, 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 (for example, people in their fifties and sixties), the benefit of intensive control of hypertension is greater and can be purchased less expensively. The benefits of intensive control of hypertension are also realized sooner than are 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.

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 pre-clinical 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, our 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 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 effect of periodic, rather than one-time, screening. For longer time intervals between screenings, the cost-effectiveness would be similar to one-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 the model's use of 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.

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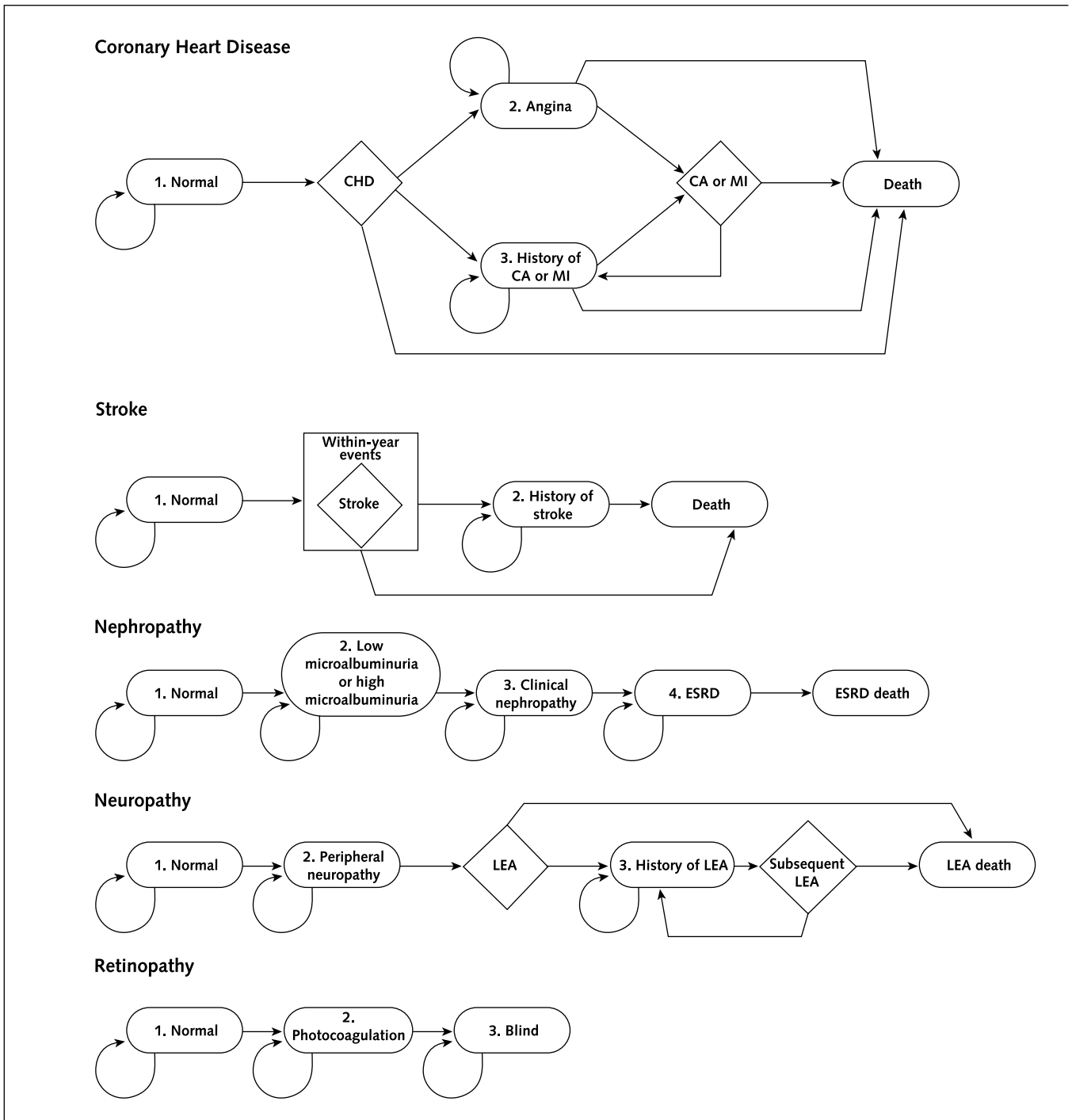
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Appendix Figure 1. Markov model of diabetes disease progression.



The model is used to follow the disease progression of all members of a cohort simultaneously on 5 different disease paths. At the end of any period, the cohort occupies one state on each of the 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 on the basis of 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 tracks 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. CHD = coronary heart disease. ESRD = end-stage renal disease.

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, %			
Nonhypertensive			
Age 0–49 y	5.534	Logn(5.53, 3.61)	36
50–59 y	5.742	Logn(5.74, 3.26)	36
60–69 y	2.606	Logn(2.61, 0.96)	36
70–94 y	4.779	Logn(4.78, 3.07)	36
Hypertensive			
Age 0–49 y	5.302	Logn(5.30, 2.71)	36
50–59 y	8.178	Logn(8.18, 5.09)	36
60–69 y	3.403	Logn(3.40, 1.70)	36
70–94 y	4.047	Logn(4.05, 2.55)	36
Sensitivity and specificity of capillary blood glucose test for identifying diabetes			
Sensitivity			
Female			
Age 0–44 y	0.973	Logn(0.973, 0.954)	22
45–94 y	0.796	Logn(0.796, 0.780)	22
Male			
Age 0–44 y	0.961	Logn(0.961, 0.942)	22
45–94 y	0.938	Logn(0.938, 0.919)	22
Specificity			
Female			
Age 0–40 y	0.740	Logn(0.740, 0.725)	22
45–94 y	0.928	Logn(0.928, 0.909)	22
Male			
Age 0–44 y	0.912	Logn(0.912, 0.894)	22
45–94 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 (capillary blood glucose)	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)	24
25-min physician visit (extra 10 min for screening)	58.66	Triang(44, 59, 73)	24
Other			
Time from diabetes onset to screening, y	5	Unif(4.00, 6.00)	Assumed
Time from onset to diabetes diagnosis, y	10	Unif(9, 12)	15

* Logn(*a,b*) = lognormal distribution with mean *a*, lower bound of 95 CI *b*; Triang(*a, b, c*) = triangular distribution with minimum *a*, mode *b*, maximum *c*; Unif(*a,b*) = uniform distribution with minimum *a*, maximum *b*.

† 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 (e.g., quality of life and probabilities must be between 0 and 1).

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

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

† 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 the following 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 (e.g., quality of life and probabilities must be between 0 and 1).

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	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	Not varied	Assumed
Annual treatment cost, \$	0	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	Not varied	Assumed
QALY	1.00	Unif(0.75, 1.00)	Assumed
End-stage renal disease			
One-time cost, \$	0	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 with moderate control	0.056	Logn(0.056, 0.042)	39
Hypertensive with tight control	0.038	Logn(0.038, 0.028)	39
Microalbuminuria to nephropathy			
Baseline	0.075	Logn(0.075, 0.056)	17
Hypertensive with moderate control	0.151	Logn(0.151, 0.113)	39
Hypertensive with tight control	0.128	Logn(0.128, 0.096)	39
Nephropathy to end-stage renal disease			
Time since diabetes diagnosis			
0–11 y	0.004	Logn(0.004, 0.003)	37, 40
12–19 y	0.039	Logn(0.039, 0.029)	37, 40
20–94 y	0.074	Logn(0.074, 0.056)	37, 40

* 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*.

† 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 the following 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 (e.g., 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 sensitivity analyses will be slightly higher than the base case in both analyses. The results were consistent with this expectation.

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 Distributions§	
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
Peripheral neuropathy			
One-time cost (neurologic examination), \$	357	Logn(357, 303)	38
Annual treatment cost, \$	0	Not varied	Assumed
QALY	1.00	Unif(0.75, 1.00)	Assumed
Lower-extremity amputation			
One-time cost, \$	33 131	Logn(33 131, 28 161)	41
Annual treatment cost, \$	0	Not varied	Assumed
QALY	0.800	Unif(0.600, 1.000)	39
Cost of fatal lower-extremity amputation, \$	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 lower-extremity amputation			
Time since diabetes diagnosis			
0–7 y	0.028	Logn(0.028, 0.021)	42
8–12 y	0.046	Logn(0.046, 0.034)	42
13–18 y	0.056	Logn(0.056, 0.042)	42
19–94 y	0.140	Logn(0.140, 0.105)	
Other			
Probability of additional amputations, %	11	Logn(11, 8)	43
Probability of diabetes-related foot ulcer, %	4.00	Logn(4.00, 3.00)	43, 44
Probability of death from amputation, %	10.5	Logn(10.5, 8)	43
Cost of diabetes-related foot ulcer, \$	2800	Triang(2100; 2800, 3500)	45

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

† One-time cost refers to costs incurred only one time, at the time of diagnosis of a state or complication event. Annual 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 the following 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 (e.g., 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 sensitivity analyses will be slightly higher than the base case in both analyses. The results were consistent with this expectation.

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	Not varied	Assumed
Annual treatment cost, \$	0	Not varied	Assumed
QALY	1.00	Unif(0.75, 1.00)	Assumed
Photocoagulation			
One-time cost, \$	2943	Logn(2943; 2502)	38
Annual treatment cost, \$	0	Not varied	Assumed
QALY	1.00	Unif(0.75, 1.00)	Assumed
Blindness			
One-time cost, \$	0	Not varied	Assumed
Annual treatment cost, \$	2125	Logn(2125; 1806)	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 with moderate control	0.017	Logn(0.017, 0.012)	17
Hypertensive with tight control	0.010	Logn(0.010, 0.008)	17
Photocoagulation to blindness			
Baseline	0.107	Logn(0.107, 0.080)	17
Hypertensive with moderate control	0.107	Logn(0.107, 0.080)	17
Hypertensive with tight control	0.107	Logn(0.107, 0.080)	17

* 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*.

† One-time cost refers to costs incurred only one time, at the time of diagnosis of a state or complication event. Annual 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 the following 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 (e.g., 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 sensitivity analyses will be slightly higher than the base case in both analyses. The results were consistent with this expectation.

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, \$	2733	Logn(2733; 2323)	46
Annual treatment cost, \$	1118	Logn(1118; 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, \$	1118	Logn(1118; 950)	46
QALY	0.880	Unif(0.660, 1.000)	48
Other one-time costs, \$			
Death from angina (extra over normal death)	0	Not varied	Assumed
Death from CA or MI before admission	759	Logn(759, 645)	46
Death from CA or MI with hospitalization	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

* CA = cardiac arrest; Logn(*a*, *b*) = lognormal distribution with mean *a*, lower bound of 95% CI *b*; MI = myocardial infarction; QALY = quality-adjusted life-year; Unif(*a*, *b*) = uniform distribution with minimum *a*, maximum *b*.

† One-time cost refers to costs incurred only one time, at the time of diagnosis of a state or complication event. Annual 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 the following 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 (e.g., 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 sensitivity analyses will be slightly higher than the base case in both analyses. The results were consistent with this expectation.

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			
Age 0–64 y	27 914	Logn(27 14; 23 727)	51
65–74 y	21 613	Logn(21 613; 18 371)	51
75–84 y	20 530	Logn(20 530; 17 451)	51
85–94 y	15 974	Logn(15 974; 13 578)	51
Immediate death due to stroke			
Age 0–64 y	27 914	Logn(27 914; 23 727)	51
65–74 y	21 613	Logn(21 613; 18 371)	51
75–84 y	20 530	Logn(20 530; 17 451)	51
85–94 y	15 974	Logn(15 974; 13 578)	51
Stroke, annual treatment			
Age 0–44 y	5150	Logn(5150; 4378)	51
45–54 y	2940	Logn(2940; 2499)	51
55–64 y	9505	Logn(9505; 8079)	51
65–74 y	7599	Logn(7599; 6459)	51
75–84 y	6596	Logn(6596; 5607)	51
85–94 y	2886	Logn(2886; 2453)	51

* 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*.

† 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 the following 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 (e.g., 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 sensitivity analyses will be slightly higher than the base case in both analyses. The results were consistent with this expectation.

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
	Base-Case Analysis†	Probabilistic Sensitivity Analysis Distribution‡	
Annual costs (includes drugs, physician office visits, self-testing, case management), \$			
Time since diabetes diagnosis			
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
13–94 y	870	Logn(870, 740)	52
Treatment effect: Reduction in hemoglobin A_{1c} level, percentage points	2.0	Not varied	12

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

† 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 the following 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 (e.g., quality of life and probabilities must be between 0 and 1).

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
	Base-Case Analysis†	Probabilistic Sensitivity Analysis Distribution‡	
Annual costs (includes drugs, physician office visits, self-testing, case management), \$			
Time since diabetes diagnosis			
0 y	1118	Logn(1118; 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
15–94 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

* Logn(*a,b*) = lognormal distribution with mean *a*, lower bound of 95% CI *b*; Triang(*a,b,c*) = triangular distribution with minimum *a*, mode *b*, maximum *c*.

† 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 the following 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 (e.g., quality of life and probabilities must be between 0 and 1).

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

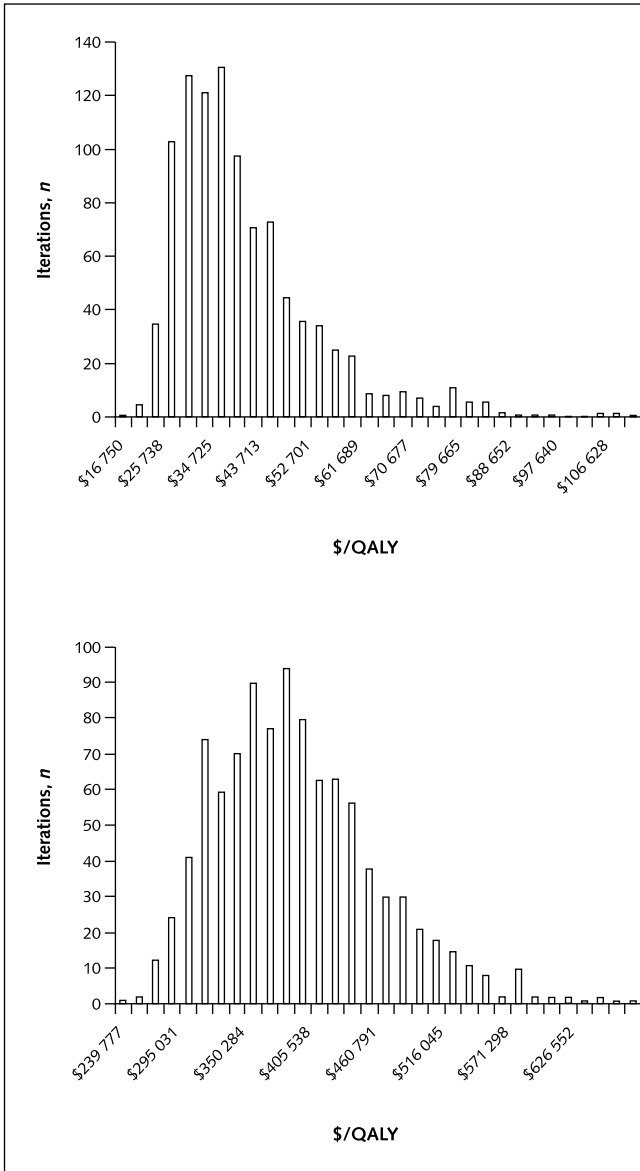
Parameter	Parameter Value		Base-Case Source
	Base-Case Analysis†	Probabilistic Sensitivity Analysis Distribution‡	
Annual drug costs, \$			
Moderate			
5-mg felodipine, 100-mg captopril, 50-mg atenolol, 25-mg hydrochlorothiazide	297	Triang(223, 297, 371)	52
Tight (given to 100% of patients)			
5-mg felodipine, 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

* CHD = coronary heart disease; Logn(*a*,*b*) = lognormal distribution with mean *a*, lower bound of 95% CI *b*; Triang(*a*,*b*,*c*) = triangular distribution with minimum, *a*, mode *b*, maximum *c*.

† 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 the following 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).

Appendix Figure 2. Histograms of cost-effectiveness ratios resulting from probabilistic sensitivity analyses based on targeted (top) and universal (bottom) screening.



A probabilistic sensitivity analysis was conducted in which 129 critical parameters were simultaneously varied over probability distributions on the basis of published 95% CIs or other reasonable ranges. A cost-effectiveness ratio was computed for each of 1000 iterations for both targeted and universal screening of people age 55 years. QALY = quality-adjusted life-year.