SUPPLEMENTAL MATERIAL

Cost effectiveness of smoking-cessation interventions in patients with ischemic stroke and transient ischemic attack

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Supplemental Methods

Design

We performed a cost effectiveness analysis using decision tree models combined with Markov models to evaluate several strategies for smoking cessation in the secondary stroke prevention setting. In this Supplemental Materials document, we provide results of an analysis that used input parameters and a target population similar to patients included in the Insulin Resistance Intervention After Stroke (IRIS) trial. The IRIS trial population consisted of non-diabetic patients with a mean age of 58 years, 44% women, and mean smoking duration of 40 years.[1] An analysis with this population is provided because the beneficial impact of smoking cessation (on recurrent stroke, myocardial infarction, and death rates) was originally described in the IRIS study cohort.

Comparators

As in the primary analysis, three evidence-based smoking-cessation interventions, delivered in addition to brief counseling, were compared to brief smoking-cessation counseling alone: (1) varenicline, (2) any pharmacotherapy with intensive counseling, and (3) monetary incentives.[7-9]

Model Parameters and Costs

All parameter inputs are found in Supplementary Table 1.[1, 7-9, 15-32] We constructed our model from the payer and societal perspectives with a lifetime horizon. Cost inputs were the same as for the primary analysis (Table 2).

Statistical Analysis and Sensitivity Analyses

As in the primary analysis, effectiveness was measured in QALYs, and costs were measured in US dollars. We used the incremental cost-effectiveness ratio (ICER) and the incremental net monetary benefit (NMB) to evaluate cost effectiveness. Interventions could be cost effective in three ways: (1) an intervention was considered cost-effective if the ICER was < $100,000 per QALY gained, a commonly used willingness-to-pay (WTP) threshold for the United States;[44] (2) interventions with a negative ICER were both less expensive and more effective as compared to brief counseling alone and thus considered the dominant strategy; (3) an intervention was considered cost effective with a positive incremental NMB. We performed probabilistic sensitivity analyses for each of the three interventions using Monte Carlo simulations to evaluate the impact of parameter uncertainty.

Supplemental Table 1. Decision model input parameters for the IRIS trial population

Variable	Base Case Value	Distribution type, uncertainty	Reference
Probability of smoking cessation			
Brief counseling alone	0.42	β, 0.39-0.45	1
Varenicline	0.62	β, 0.58-0.94	7, 20,26
Pharmacotherapy + intensive counseling	0.72	β, 0.48-1	9
Monetary incentives	0.63	β, 0.54-0.73	8,24
Risk of events in patients who quit smoking			
Recurrent ischemic stroke	8.6%	β, 6.0%-11.2%	1
Myocardial infarction	4.8%	β, 2.8%-6.7%	1
Death	7.9%	β, 5.4%-10.3%	1
Recurrent stroke after MI	4.4%	β, 2.6% - 4.4%	28,31
MI after MI	13.8%	β, 6.3%-13.8%	28, 30
Death after MI	9.7%	β, 5.0%-17.0%	27
Risk of events in patients who continue smoking			
Recurrent ischemic stroke	10.9%	β, 8.5%-13.3%	1
Myocardial infarction	5.9%	β, 4.0%-7.8%	1
Death	13.1%	β, 10.4%-15.8%	1
Recurrent stroke after MI	5.9%	β, 3.4%-5.9%	1, 28
MI after MI	16.7%	β, 9.5%-20.8%	29
Death after MI	15.4%	β, 8%-27%	27, 32
Discharge destination after stroke			
Home	58.3%	β, 49.0%-58.0%	15
Skilled nursing facility	16.5%	β, 16.5%-19.9%	15
Rehabilitation facility	18.2%	β, 17.9%-18.3%	15
In-hospital death	6.5%	β, 6.1%-8.0%	15
mRS distribution after recurrent stroke			
mRS 0	0.21	NA	16
mRS 1	0.23	NA	16
mRS 2	0.09	NA	16
mRS 3	0.09	NA	16
mRS 4	0.07	NA	16
mRS 5	0.06	NA	16
mRS 6	0.23	NA	16
Outcome QALYs			
mRS 0	0.85	NA	17,18,19
mRS 1	0.80	NA	17,18,19
mRS 2	0.70	NA	17,18,19
mRS 3	0.51	NA	17,18,19
mRS 4	0.30	NA	17,18,19
mRS 5	0.15	NA	17,18,19
Myocardial infarction	0.84	NA	25
Death	0	NA	25

Abbreviations: mRS, modified rankin scale; MI, myocardial infarction; QALY, quality-adjusted life year

Supplemental Table 2. Results of cost effectiveness analysis of smoking-cessation interventions in stroke secondary prevention with a lifetime horizon in the IRIS trial population

|	Brief counseling alone	Varenicline	Pharmacotherapy with intensive counseling	Monetary Incentives
Payer perspective				
Total Cost, $	215,014	214,698	211,659	214,790
Total Effectiveness, QALY	15.48	16.36	16.80	16.41
ICER, $/QALY	-	-358*	-2,535*	-242*
Incremental NMB, $	-	88,547	135,701	92,867
Cost effective Monte Carlo runs %	-	97%	97%	99%
Societal perspective				
Total Cost, $	690,019	670,006	660,194	669,421
Total Effectiveness, QALY	15.48	16.36	16.80	16.41
ICER, $/QALY	-	-22,682*	-22,535*	-22,233*
Incremental NMB, $	-	108,244	162,171	113,241
Cost effective Monte Carlo runs %	-	98%	97%	99%

Total costs, total effectiveness, incremental cost-effective ratios, incremental net monetary benefits, and Monte Carlo results. Monte Carlo results are probabilistic sensitivity analyses.

Abbreviations: QALY, quality adjusted life year; ICER, incremental cost-effective ratio; NMB, net monetary benefit.
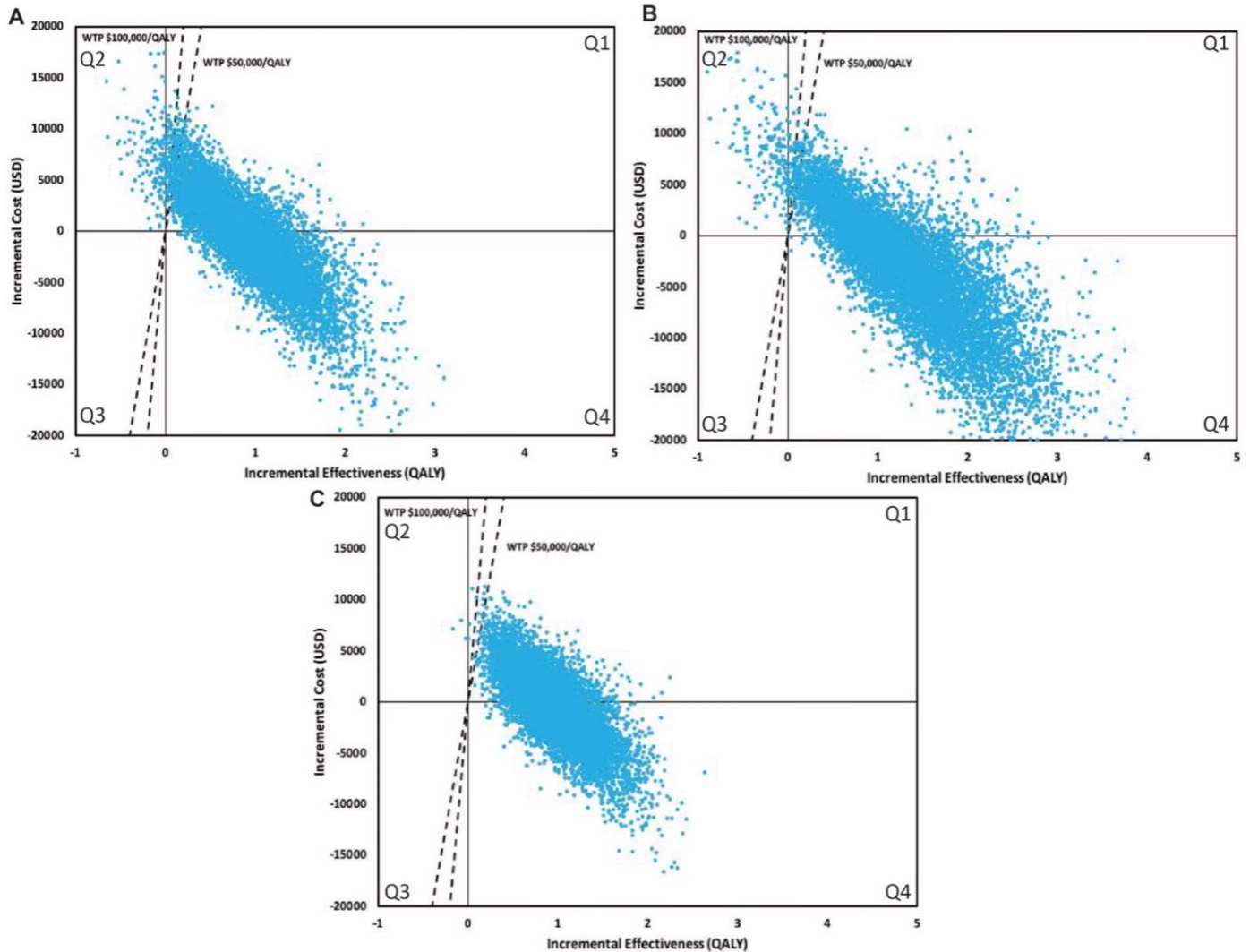
*Negative ICER indicates intervention was the dominant strategy (less costly, more effective) compared to brief counseling alone. Interventions with a positive ICER less than the Willingness to Pay threshold are also cost-effective.
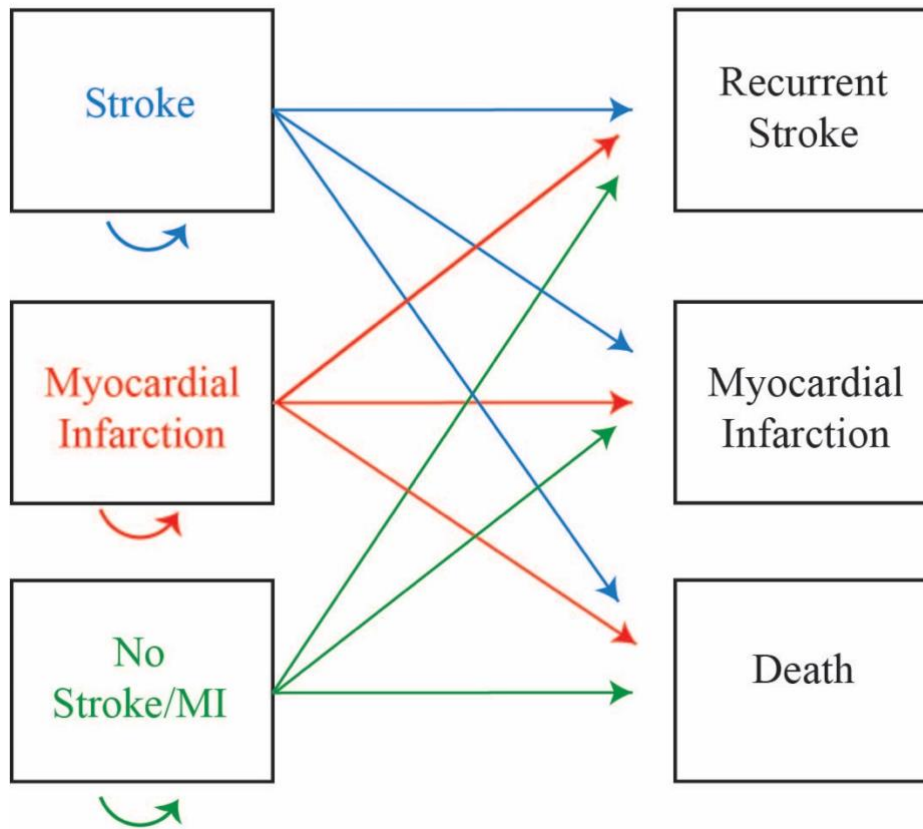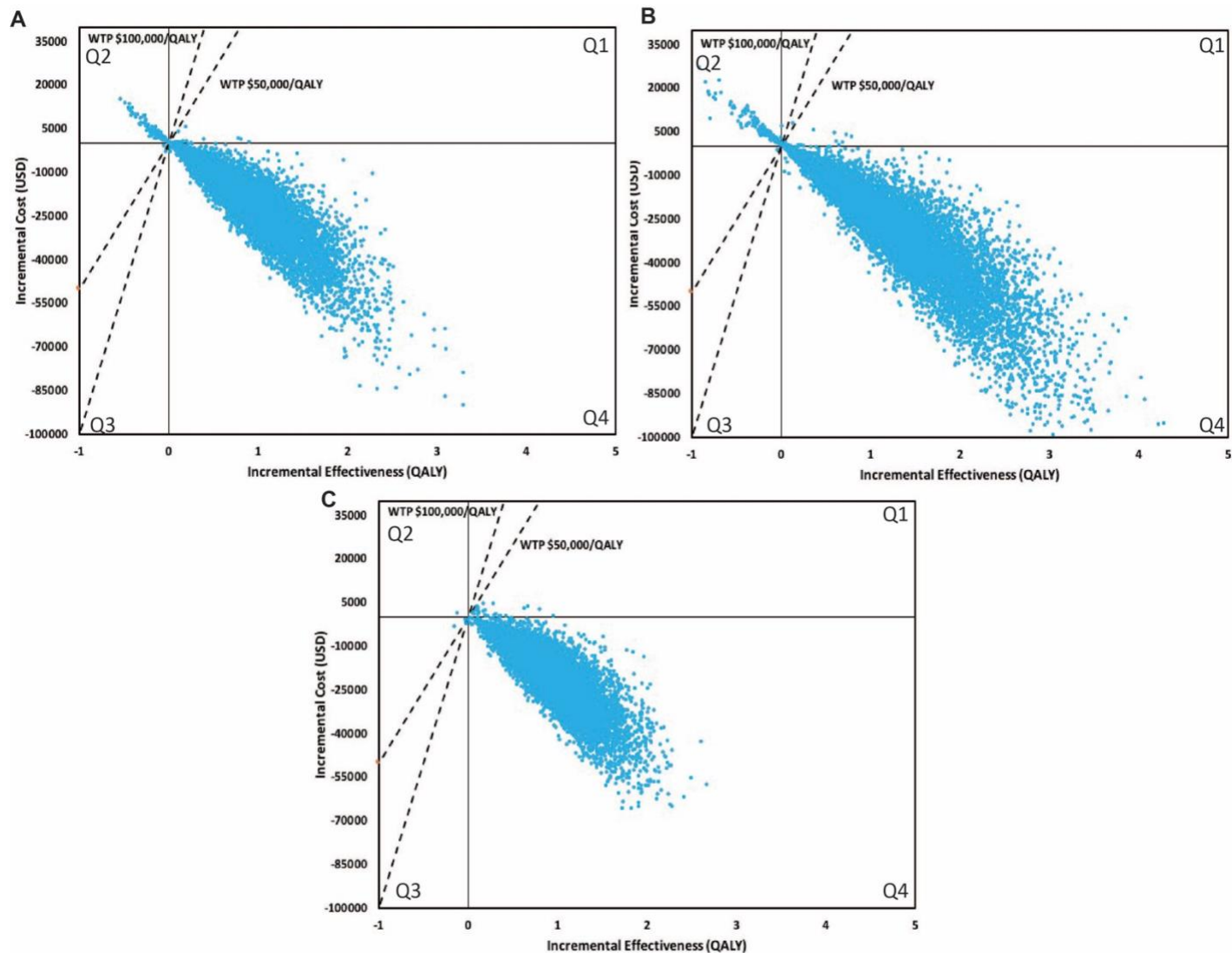
Supplemental Figure 1. Representation of the Markov model. Patients enter into the Markov model after experiencing a stroke, MI, or no event occurs (health states). They cycle between health states in 5-year cycles until death. Arrows emanating from each initial health state represent the different health states they can transition to over the cycle. The arrows pointing back to each initial health state indicate no event occurs during that cycle and the patient stays in their initial health state. Abbreviations: MI, myocardial infarction.
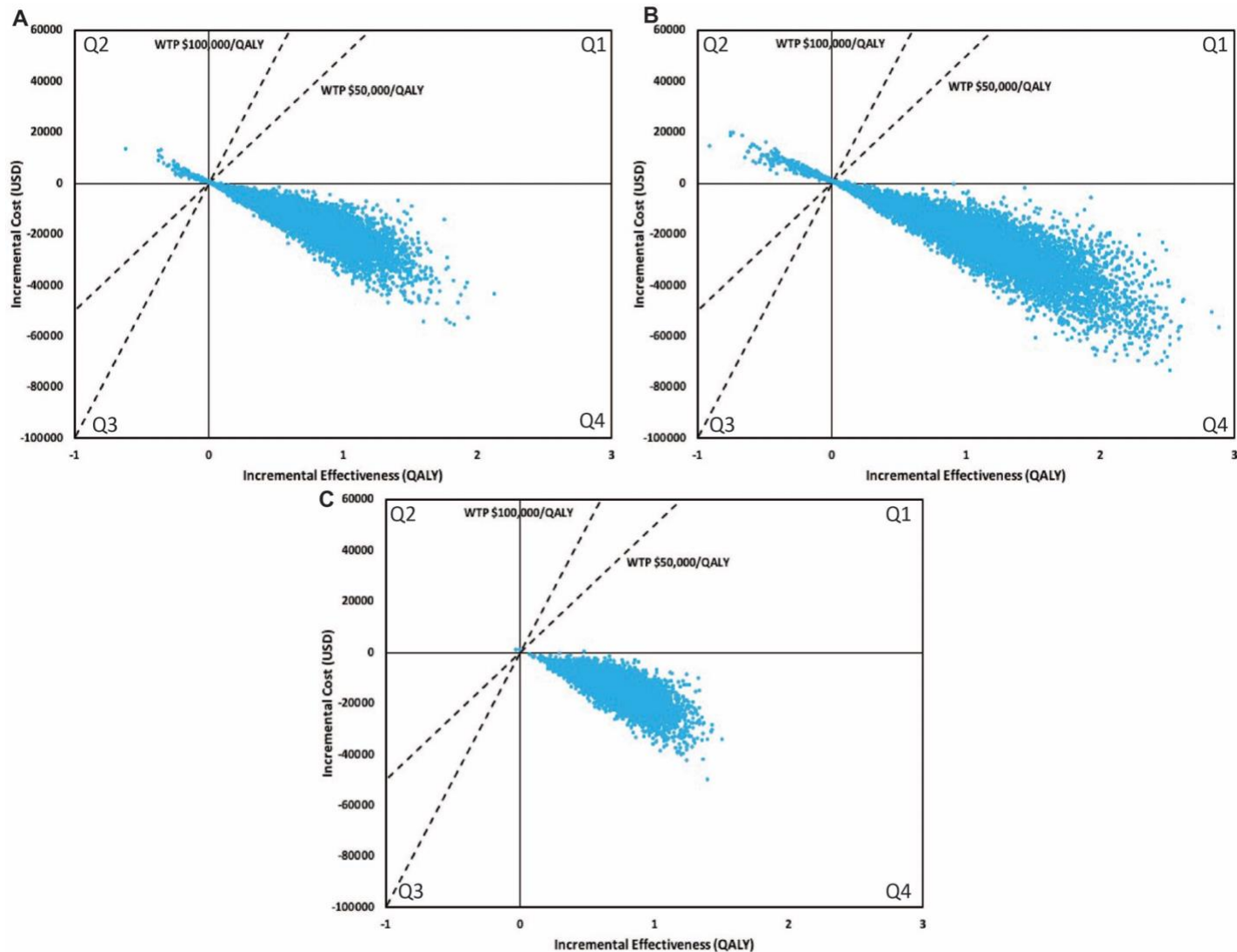
Supplemental Figure 2. Incremental cost-effectiveness scatterplot of smoking-cessation intervention with brief counseling versus brief counseling alone for the societal perspective in the primary analysis population. Each scatterplot includes a set of points representing pairs of incremental cost and effectiveness values from the simulation results (n=10,000). The comparator is brief counseling alone. The dashed line is the willingness-to-pay threshold. Each scatterplot is divided into four quadrants. Points in Q1 indicate the intervention is more costly and more effective. Points in this quadrant below the willingness-to-pay threshold are cost-effective and points above the willingness-to-pay threshold are not cost-effective. Points in Q2 indicate the intervention is more costly and less effective. Points in Q3 indicate the intervention is less costly and less effective. Points in Q4 indicate the intervention is less costly and more effective (dominant strategy). **A.** Varenicline **B.** Any pharmacotherapy with intensive counseling **C.** Monetary incentives

Supplemental Figure 3. Incremental cost-effectiveness scatterplot of smoking-cessation intervention with brief counseling versus brief counseling alone for the payer perspective in the IRIS trial population. Each scatterplot includes a set of points representing pairs of incremental cost and effectiveness values from the simulation results (n=10,000). The comparator is brief counseling alone. The dashed line is the willingness-to-pay threshold. Each scatterplot is divided into four quadrants. Points in Q1 indicate the intervention is more costly and more effective. Points in this quadrant below the willingness-to-pay threshold are cost-effective and points above the willingness-to-pay threshold are not cost-effective. Points in Q2 indicate the intervention is more costly and less effective. Points in Q3 indicate the intervention is less costly and less effective. Points in Q4 indicate the intervention is less costly and more effective (dominant strategy). **A.** Varenicline **B.** Any pharmacotherapy with intensive counseling **C.** Monetary incentives

Supplemental Figure 4. Incremental cost-effectiveness scatterplot of smoking-cessation intervention with brief counseling versus brief counseling alone for the societal perspective in the IRIS trial population. Each scatterplot includes a set of points representing pairs of incremental cost and effectiveness values from the simulation results (n=10,000). The comparator is brief counseling alone. The dashed line is the willingness-to-pay threshold. Each scatterplot is divided into four quadrants. Points in Q1 indicate the intervention is more costly and more effective. Points in this quadrant below the willingness-to-pay threshold are cost-effective and points above the willingness-to-pay threshold are not cost-effective. Points in Q2 indicate the intervention is more costly and less effective. Points in Q3 indicate the intervention is less costly and less effective. Points in Q4 indicate the intervention is less costly and more effective (dominant strategy). **A.** Varenicline **B.** Any pharmacotherapy with intensive counseling **C.** Monetary incentives