Reduction of Cardiovascular Events with Icosapent Ethyl–Intervention Trial *Cost-Effectiveness*

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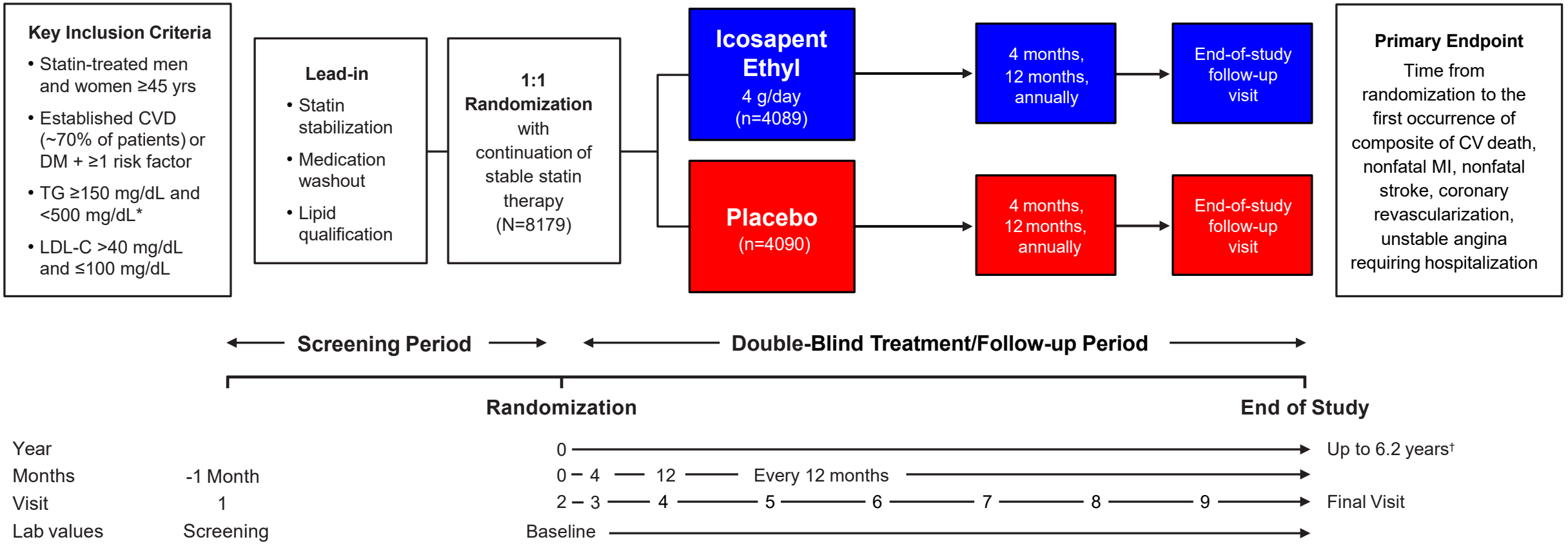
REDUCE-IT Design



*Due to the variability of triglycerides, a 10% allowance existed in the initial protocol, which permitted patients to be enrolled with qualifying triglycerides ≥135 mg/dL. Protocol amendment 1 (May 2013) changed the lower limit of acceptable triglycerides from 150 mg/dL to 200 mg/dL, with no variability allowance.

†Median trial follow-up duration was 4.9 years (minimum 0.0, maximum 6.2 years).

Bhatt DL, Steg PG, Brinton EA, et al; on behalf of the REDUCE-IT Investigators. Rationale and design of REDUCE-IT: Reduction of Cardiovascular Events with Icosapent Ethyl–Intervention Trial. *Clin Cardiol.* 2017;40:138-148.
REDUCE-IT ClinicalTrials.gov number, NCT01492361.

Primary and Key Secondary Composite Endpoints

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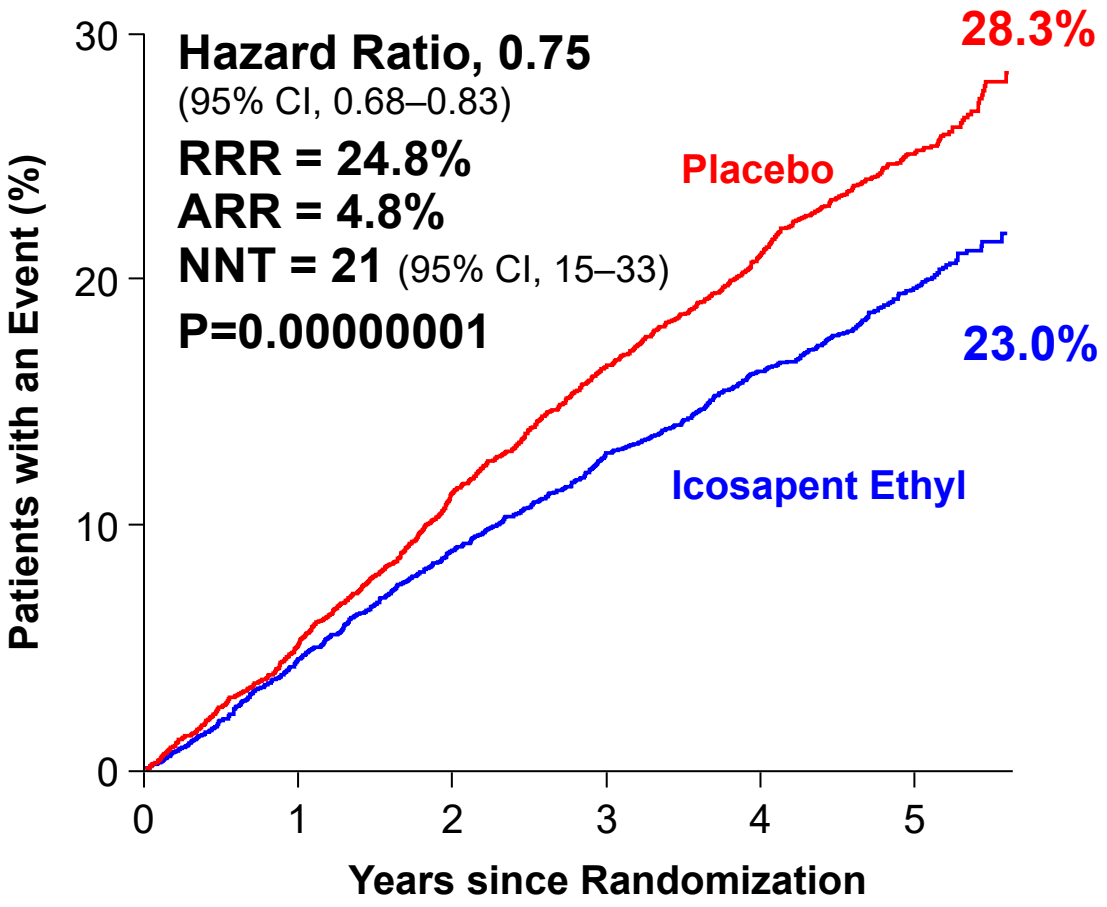
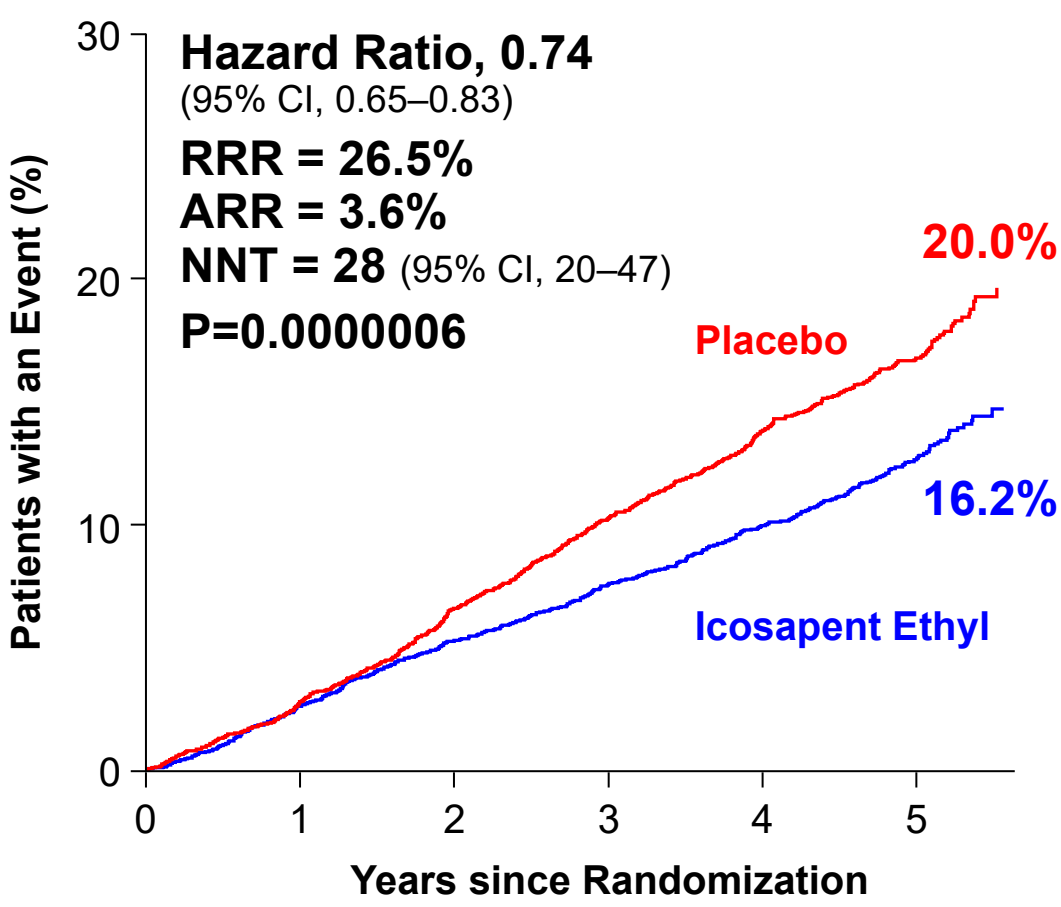
Primary Composite Endpoint:

CV Death, MI, Stroke, Coronary Revasc, Unstable Angina



Key Secondary Composite Endpoint:

CV Death, MI, Stroke



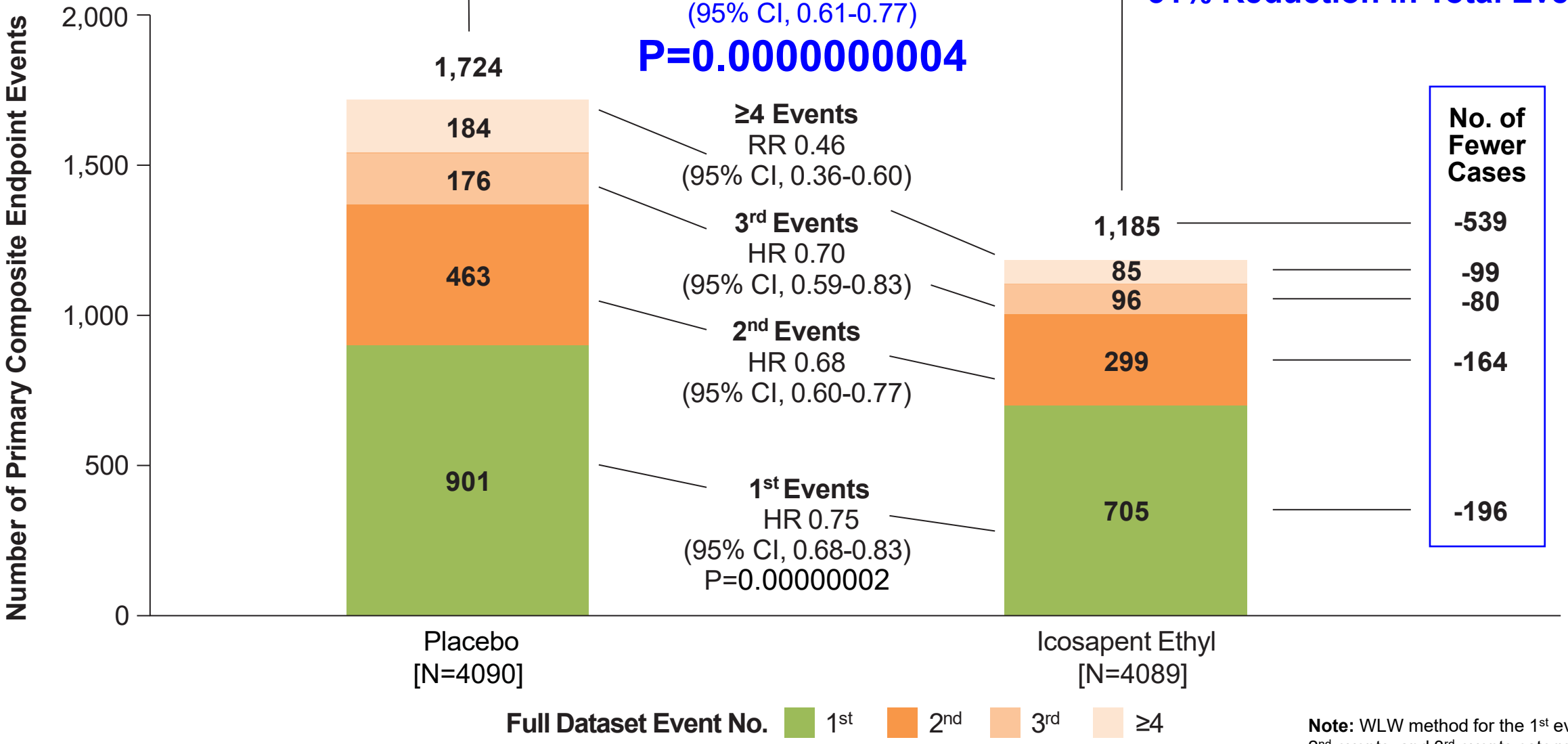
Bhatt DL, Steg PG, Miller M, et al. *N Engl J Med.* 2019; 380:11-22. Bhatt DL. AHA 2018, Chicago.

First and Subsequent Events – Full Data

reduce-it TOTAL EVENTS

RR 0.69
(95% CI, 0.61-0.77)
P=0.0000000004

31% Reduction in Total Events



Note: WLW method for the 1st events, 2nd events, and 3rd events categories; Negative binomial model for ≥4th events and overall treatment comparison.

Bhatt DL, Steg PG, Miller M, et al. *J Am Coll Cardiol*. 2019;73:2791-2802. Bhatt DL. ACC 2019, New Orleans.

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Cost-effectiveness of Icosapent Ethyl for High-risk Patients With Hypertriglyceridemia Despite Statin Treatment

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Methods

Objective: Estimate the cost-effectiveness of IPE compared with standard care.

Design: In-trial cost-effectiveness analysis using patient-level study data from REDUCE-IT and a lifetime analysis using a microsimulation model and data from published literature.

Setting: Analyses performed from a US healthcare sector perspective.

Participants: 8179 patients w/ hypertriglyceridemia despite stable statin therapy recruited between 2011-16.

Intervention: Patients were randomized to IPE 4 g/day or placebo and followed a median of 4.9 years. Cost of IPE was $4.16 per day after rebates using SSR Health net cost (SSR), and $9.28 per day with wholesale acquisition cost (WAC).

Outcome Measures: Incremental quality-adjusted life-years (QALYs), total direct healthcare costs (2019 USD), and cost-effectiveness.

Weintraub WS, Bhatt DL, Zhang Z, et al. *JAMA Netw Open*. 2022;5(2):e2148172.

Baseline Characteristics of REDUCE-IT (N=8179)

	Icosapent Ethyl (N=4089)	Standard Care (N=4090)
Age (years), Median (Q1-Q3)	64.0 (57.0-69.0)	64.0 (57.0-69.0)
Female, n (%)	1162 (28.4%)	1195 (29.2%)
Non-White, n (%)	398 (9.7%)	401 (9.8%)
Westernized Region*, n (%)	2906 (71.1%)	2905 (71.0%)
Cardiovascular Risk Category, n (%)		
Secondary Prevention Cohort	2892 (70.7%)	2893 (70.7%)
Primary Prevention Cohort	1197 (29.3%)	1197 (29.3%)
Ezetimibe, n (%)	262 (6.4%)	262 (6.4%)
Statin Intensity, n (%)		
Low	254 (6.2%)	267 (6.5%)
Moderate	2533 (61.9%)	2575 (63.0%)
High	1290 (31.5%)	1226 (30.0%)
Type 2 Diabetes, n (%)	2367 (57.9%)	2363 (57.8%)
HDL-C (mg/dL), Median (Q1-Q3)	40.0 (34.5-46.0)	40.0 (35.0-46.0)
LDL-C (mg/dL), Median (Q1-Q3)	74.0 (61.5-88.0)	76.0 (63.0-89.0)
Triglycerides (mg/dL), Median (Q1-Q3)	216.5 (176.5-272.0)	216.0 (175.5-274.0)
Triglycerides, n (%)		
<150 mg/dL	412 (10.1%)	429 (10.5%)
150 to <200 mg/dL	1193 (29.2%)	1191 (29.1%)
≥200 mg/dL	2481 (60.7%)	2469 (60.4%)

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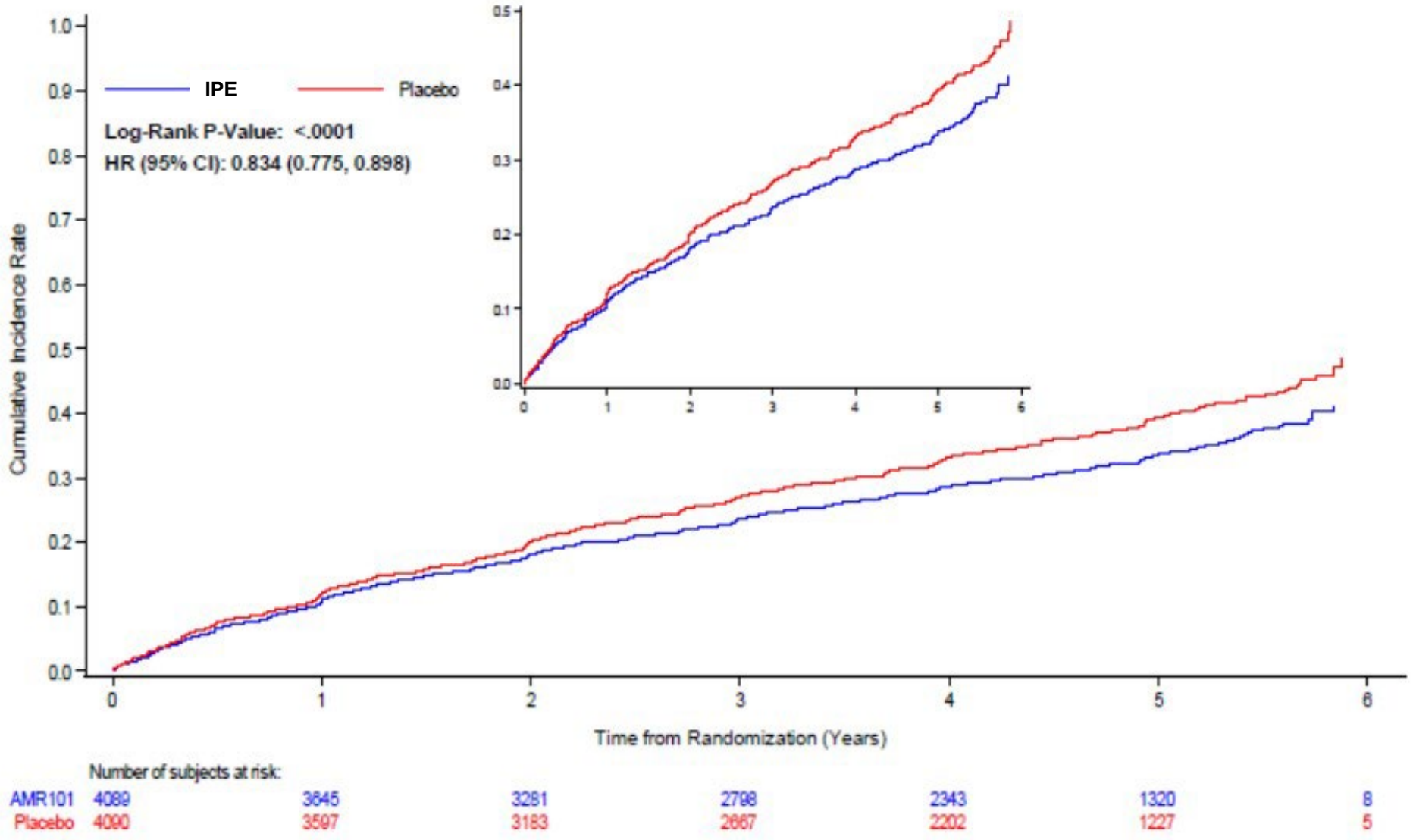
Time to Permanent Study Drug Discontinuation for Icosapent Ethyl and Placebo



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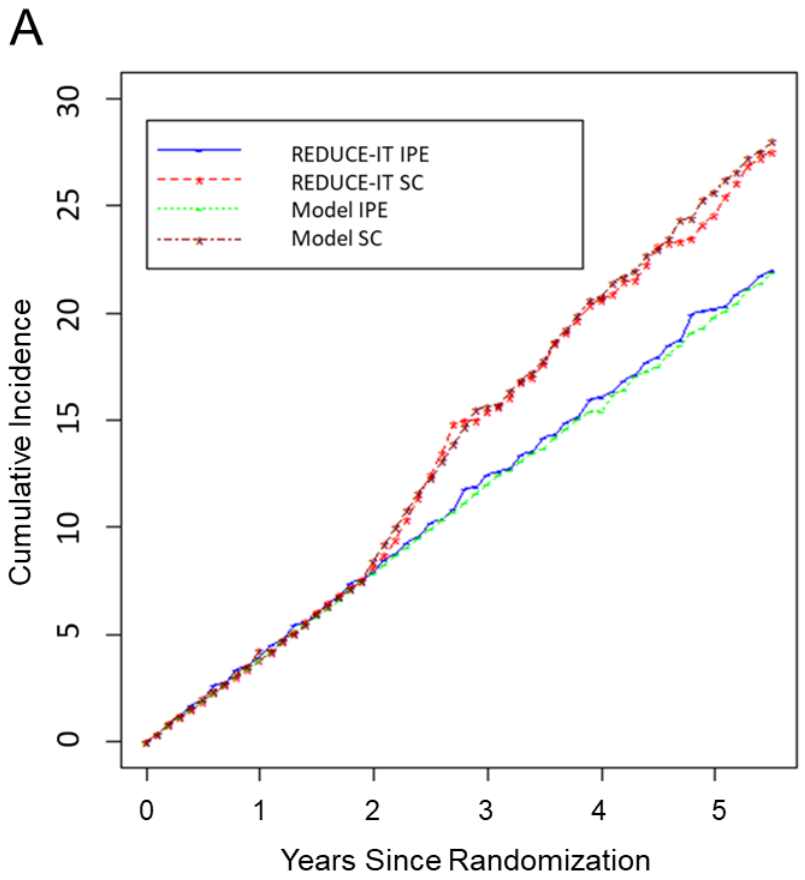
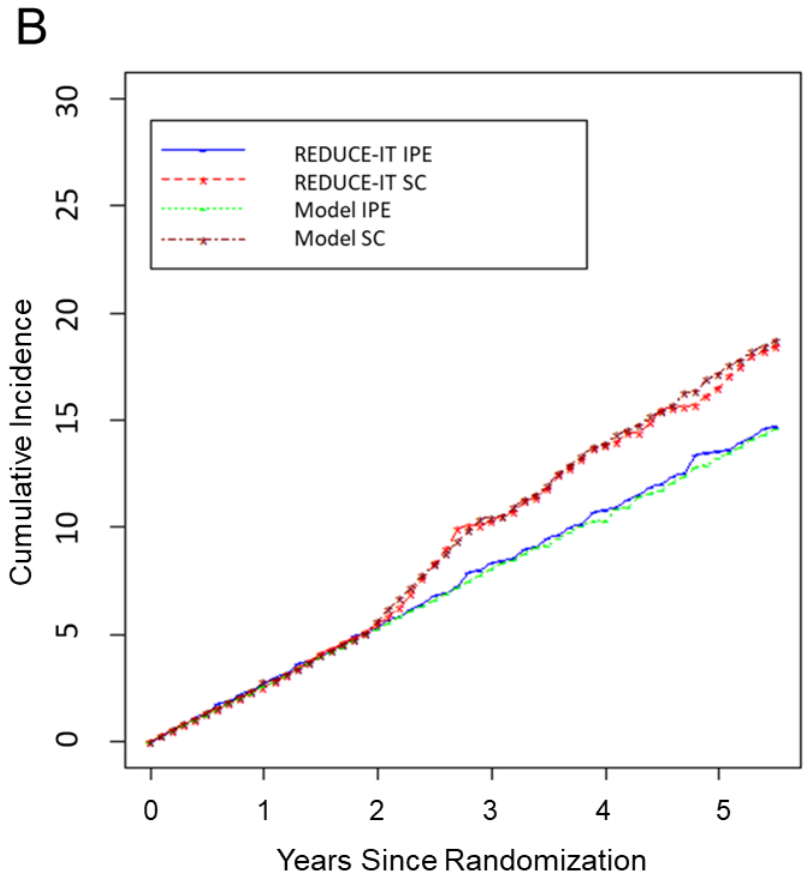
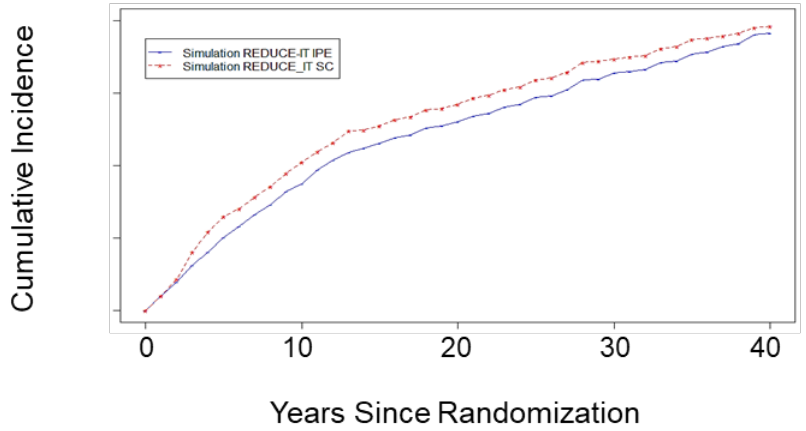
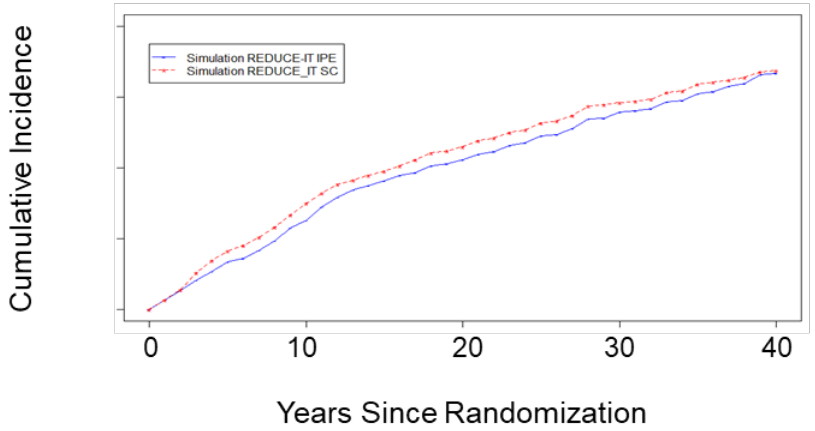








Cumulative incidence of primary endpoint (A) and key secondary endpoint (B) in trial and primary endpoint (C) and key secondary endpoint (D) observed in the lifetime simulation model.

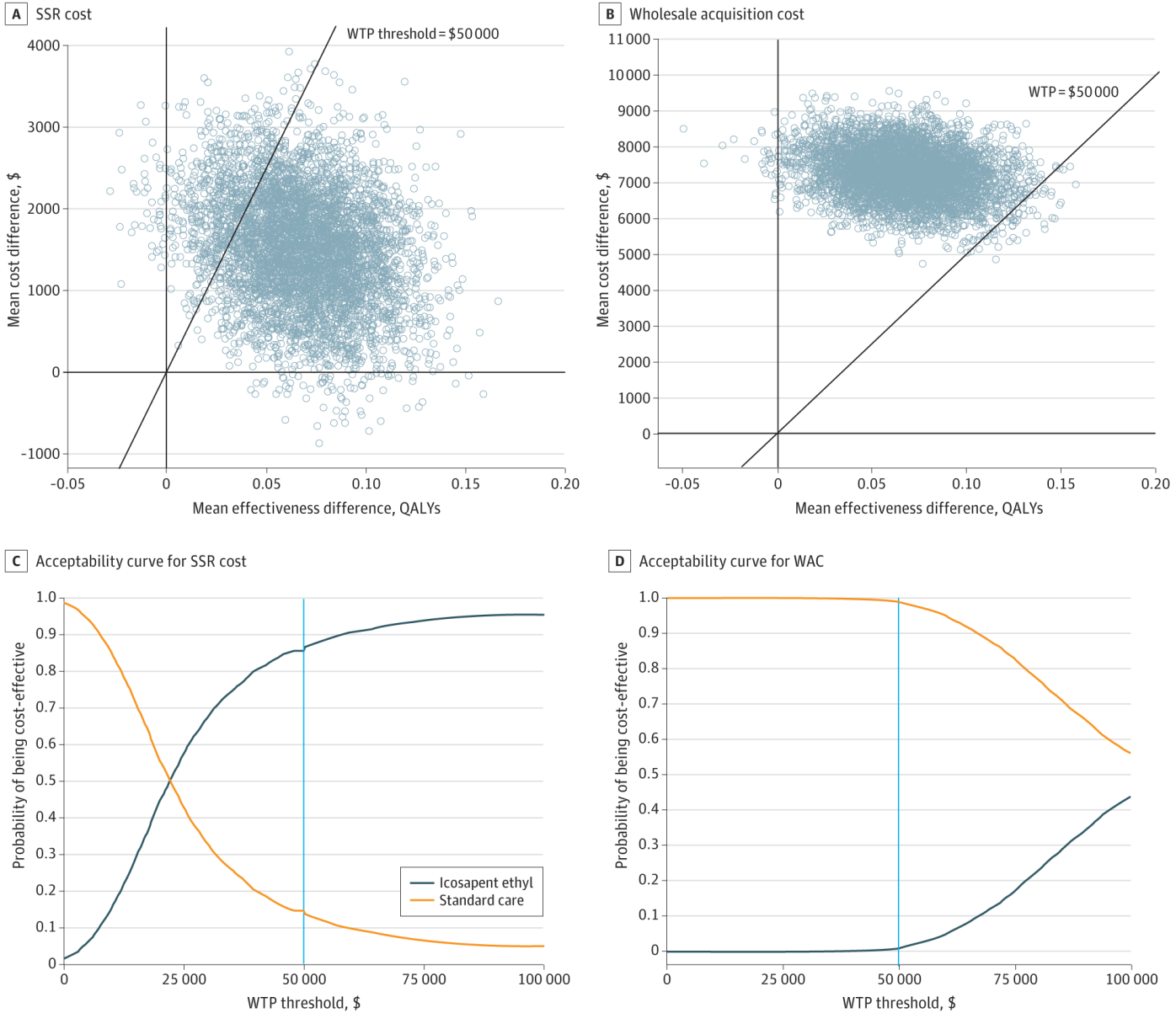
Weintraub WS, Bhatt DL, Zhang Z, et al. *JAMA Netw Open*. 2022;5(2):e2148172.

Cost-effectiveness of Icosapent Ethyl vs Standard Care Using National Inpatient Sample Costs

	Mean Total Cost (2019 USD)			Mean LYs/QALYs			ICER, USD/LY or USD/ QALY	IPE Dominant	IPE Dominated	Probability of Cost-Effectiveness		
	IPE	SC	Δ (95% CI)	IPE	SC	Δ (95% CI)				< $50,000	< $100,000	< $150,000
In-Trial Analysis (LYs; SSR)	18,786	17,273	1513 (155; 2870)	4.31	4.25	0.06 (0.00; 0.12)	26,328	1.2%	3.1%	77.7%	89.2%	92.1%
In-Trial Analysis (LYs; WAC)	24,544	17,273	7271 (5911; 8630)	4.31	4.25	0.06 (0.00; 0.12)	126,524	0.0%	2.7%	0.0%	31.1%	60.3%
In-Trial Analysis (QALYs; SSR)	18,786	17,273	1513 (155; 2870)	3.34	3.27	0.07 (0.01; 0.12)	22,311	1.5%	0.9%	85.4%	95.2%	97.1%
In-Trial Analysis (QALYs; WAC)	24,544	17,273	7271 (5911; 8630)	3.34	3.27	0.07 (0.01; 0.12)	107,218	0.0%	0.6%	1.0%	42.7%	74.5%
Lifetime Model (LYs; SSR)	195,276	197,064	-1788 (-9735; 6159)	14.08	13.94	0.16 (0.08, 0.24)	Dominant	69.7%	<0.1%	92.5%	99.9%	99.9%
Lifetime Model (LYs; WAC)	202,830	197,064	5766 (1094; 10,438)	14.08	13.94	0.16 (0.08, 0.24)	36,042	1.8%	1.5%	58.9%	78.2%	85.7%
Lifetime Model (QALYs; SSR)	195,276	197,064	-1788 (-9735; 6159)	10.59	10.35	0.24 (0.15; 0.33)	Dominant	58.4%	<0.1%	89.4%	98.9%	99.9%
Lifetime Model (QALYs; WAC)	202,830	197,064	5766 (1094; 10,438)	10.59	10.35	0.24 (0.15; 0.33)	23,866	1.2%	0.6%	72.5%	94.8%	96.4%
PSA (LYs; SSR)	208,148	209,407	-1259 (-5136; 3618)	14.10	13.96	0.14 (0.10, 0.18)	Dominant	42.5%	0.2%	83.4%	91.3%	98.5%
PSA (LYs; WAC)	214,675	209,407	5268 (2784; 7752)	14.10	13.96	0.14 (0.10, 0.18)	37,751	1.9%	2.2%	56.1%	76.8%	91.7%
PSA (QALYs; SSR)	208,148	209,407	-1259 (-5136; 3618)	10.64	10.43	0.20 (0.18; 0.22)	Dominant	47.6%	0.1%	86.2%	96.9%	99.6%

Weintraub WS, Bhatt DL, Zhang Z, et al. *JAMA Netw Open*. 2022;5(2):e2148172.

Cost-effectiveness Planes During the Trial Period Using National Inpatient Sample Costs for Events



A, Cost-effectiveness plane for SSR cost.

B, Cost-effectiveness plane for wholesale acquisition cost (WAC).

C, Acceptability curve for SSR cost.

D, Acceptability curve for WAC. QALY indicates quality-adjusted life-year; and WTP, willingness-to-pay.

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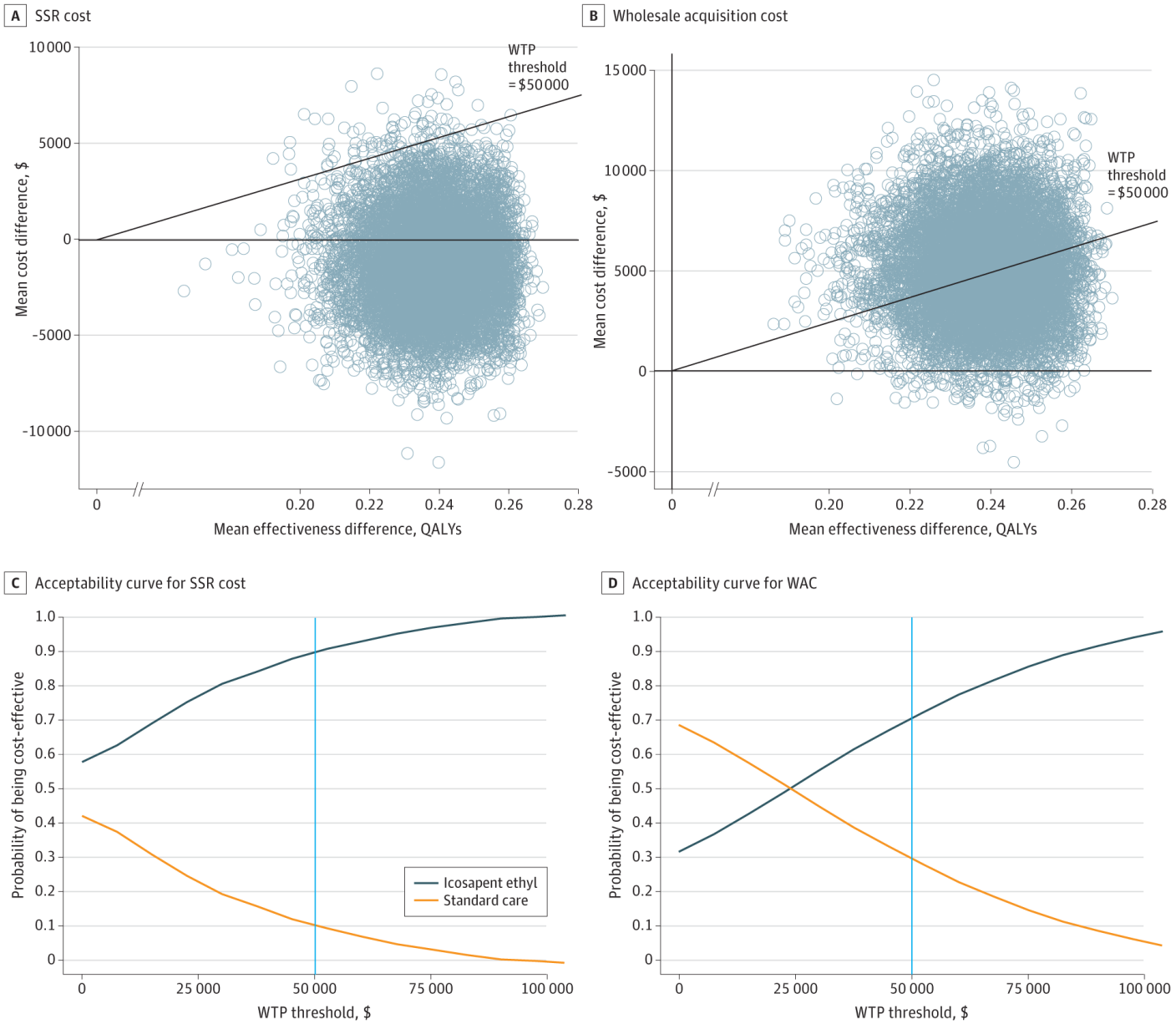
Cost-effectiveness Planes Over the Lifetime Using National Inpatient Sample Costs for Events



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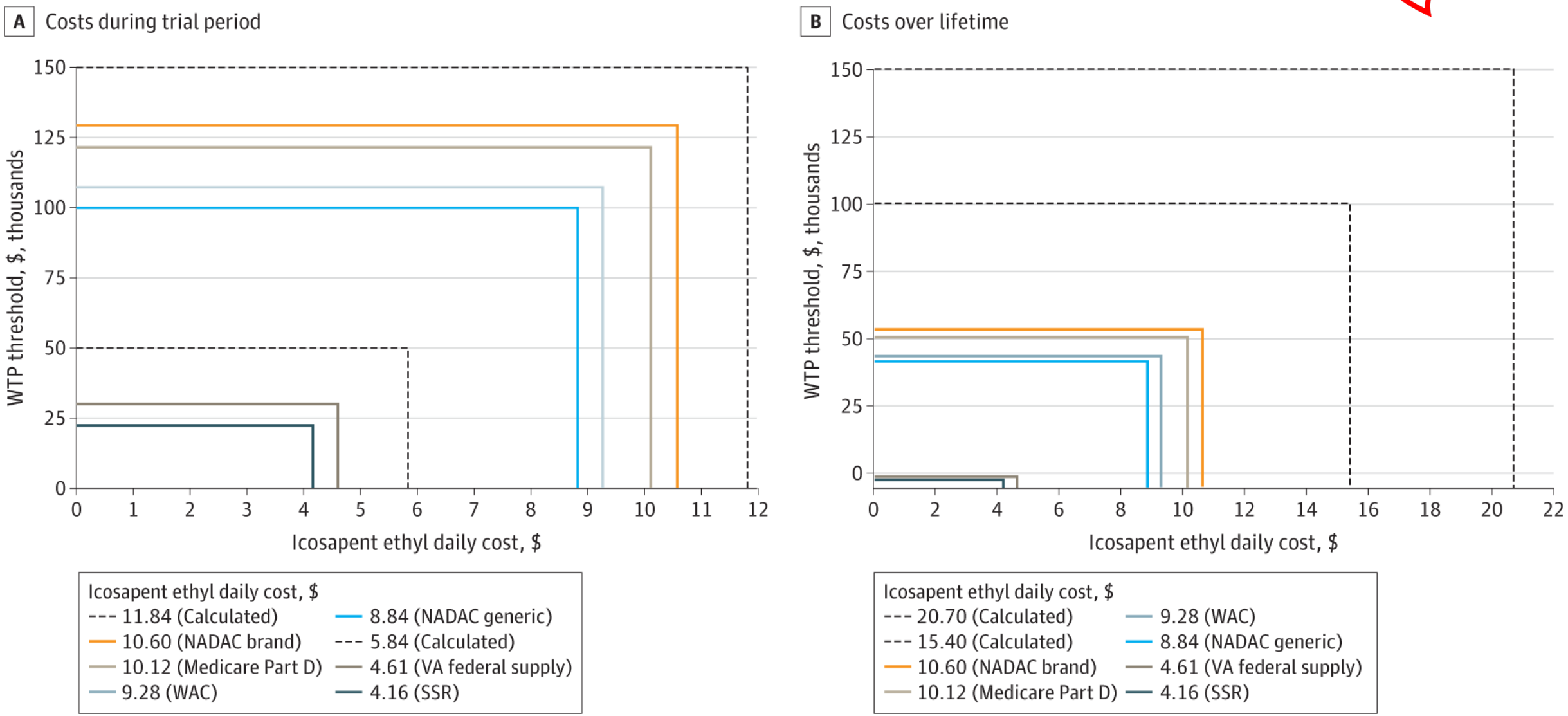
Icosapent Ethyl Daily Costs for Various WTP Thresholds



A, Costs during the trial period. B, Costs over the lifetime. NADAC indicates National Average Drug Acquisition Cost; VA, Veterans Administration; and WAC, wholesale acquisition cost.

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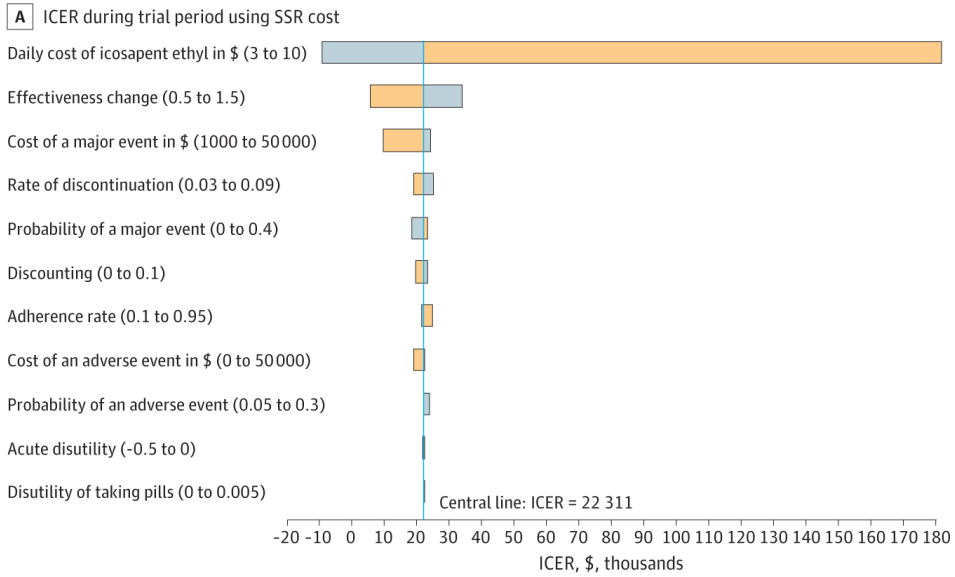
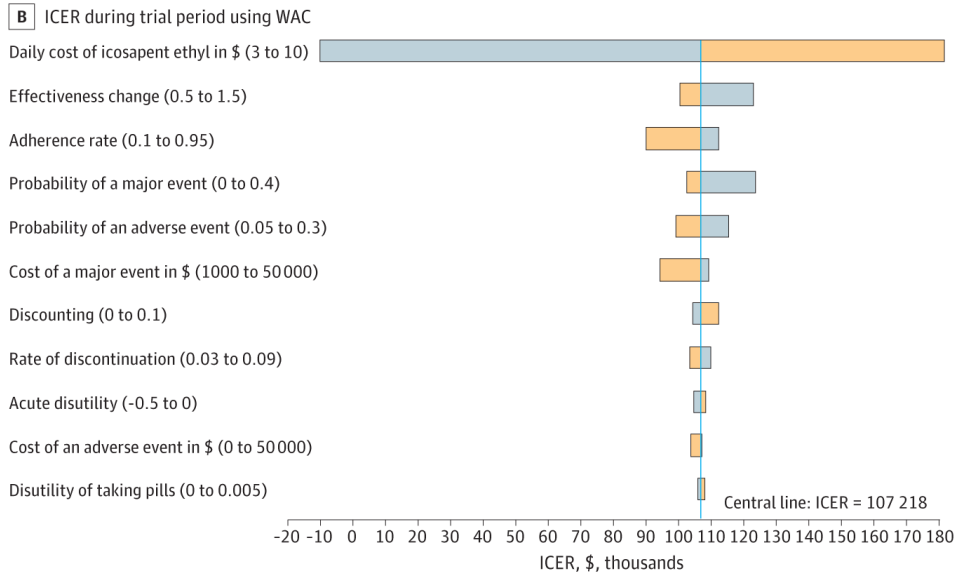
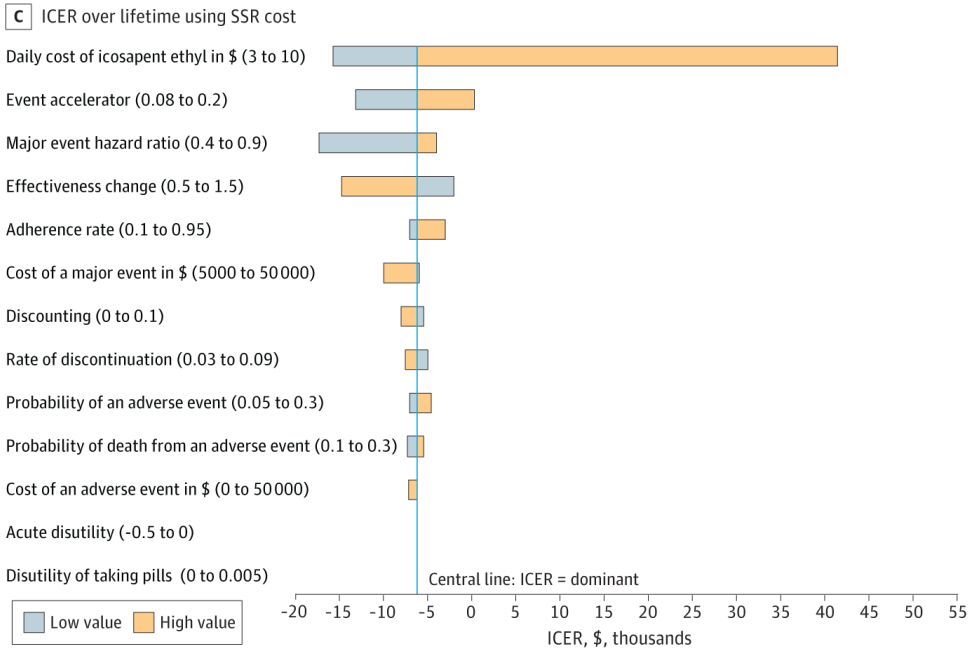
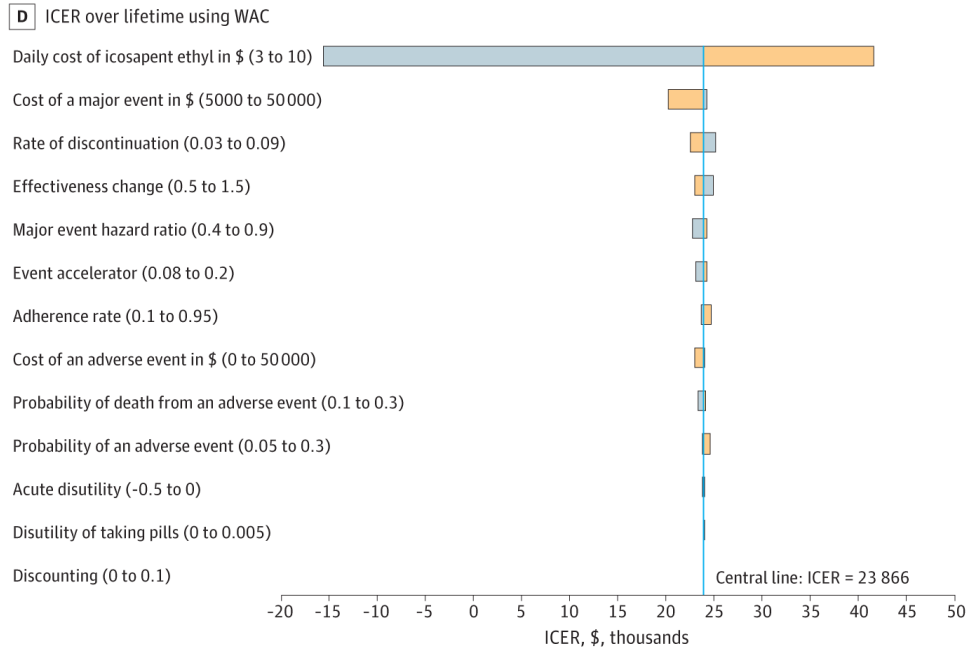
Tornado Diagrams for Incremental Cost-effectiveness Ratio (ICER)









A, ICER during the trial period using SSR Health net cost (SSR cost).

B, ICER during the trial period using wholesale acquisition cost (WAC).

C, ICER over the lifetime using SSR cost.

D, ICER over the lifetime using WAC. Gray bar indicates low value, and orange bar indicates high value, separated by central line (ICER).

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Conclusions

- Both in-trial and lifetime, icosapent ethyl offers better cardiovascular outcomes than standard care in **REDUCE-IT** patients at common willingness-to-pay thresholds.
- Over the lifetime at costs actually paid, icosapent ethyl may improve health care outcomes at no increased cost to society.

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