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So It Begins

Real-world studies are a great source of evidence
Reflect true consumption of ressources
More feasible and less costly

However, these studies are prone to confounding bias

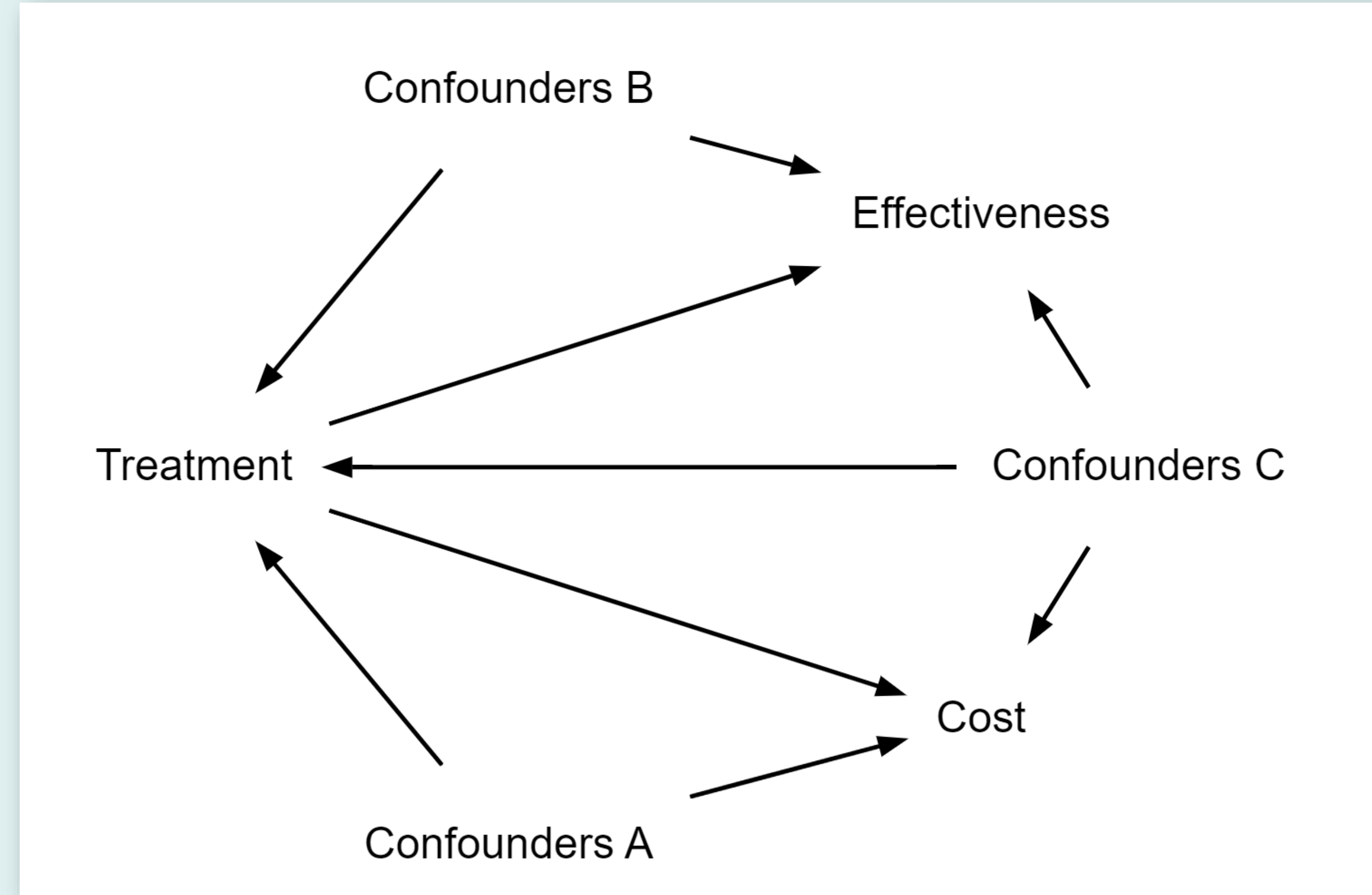
Failure to account for confounders may result in an incorrect assessment of economic value of treatment

Correction of this bias is well studied when facing single outcome

Economic evaluation are confronted with the fact that they must account for two outcomes simultaneously; cost and effectiveness

Here we want to show what happens when confounders influence these outcomes;
How cost-effectiveness analysis (CEA) are affected by this bias
How these biases affect uncertainty evaluation
What impact do these biases have on final decision on cost-effectiveness

Figure 1 : DAG of confounding variables in cost-effectiveness studies



Why Do I Care

Uncertainty analysis of a CEA fuels decision making

Therefore, we consider the impact of confounders on cost-effectiveness acceptability curve (CEAC) on expected value of perfect information (EVPI)

These two methods are not designed to account for confounders

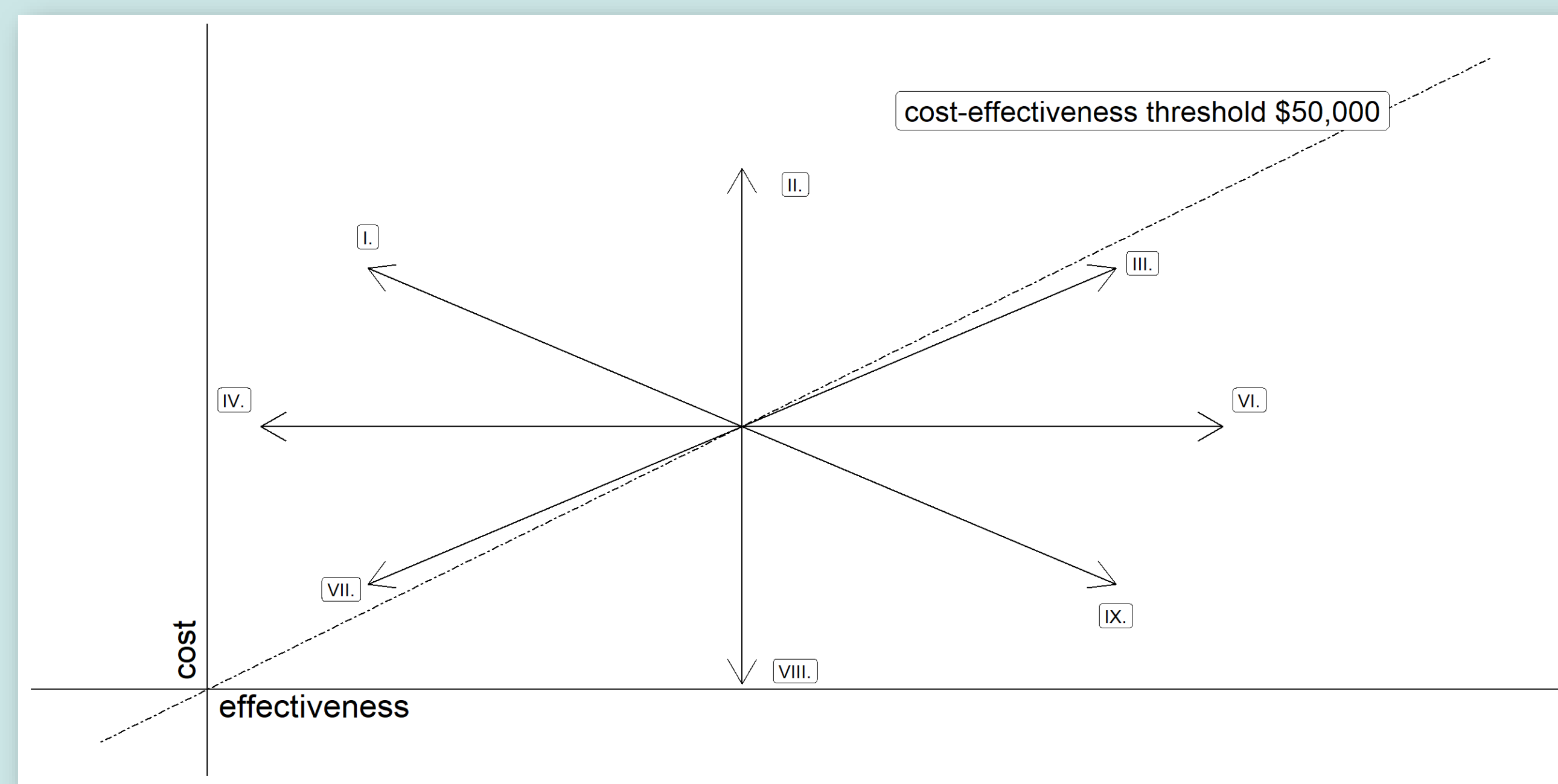
We expected confounder to modify uncertainty around treatment cost-effectiveness
Increase uncertainty → Complexify decision-making
Decrease uncertainty → Mislead our confidence in our conclusions

Show It To Me Please

We simulated a two-arm non-randomised trial with varying patterns of confounders.

Illustrates nine possible situations that arise in an economic evaluation: eight radial direction of the cost-effectiveness plane scenario with no confounding bias as reference

Figure 2 : Illustration of potential effect of confounders in CE plane



What does this all mean

- I. Increase incremental cost estimates and decrease incremental effectiveness estimates
- II. Increase incremental cost estimates
- III. Increase incremental cost estimates and increase incremental effectiveness estimates
- IV. Decrease incremental effectiveness estimates
- V. Reference scenario
- VI. Increase incremental effectiveness estimates
- VII. Decrease incremental cost estimates and decrease incremental effectiveness estimates
- VIII. Decrease incremental cost estimates
- IX. Decrease incremental cost estimates and increase incremental effectiveness estimates

But Wait There Is More

True ICER of 50,000 with incremental cost of 5,000 and incremental effectiveness of 0.1

At willingness-to-pay threshold of 50,000; we expect the treatment to be cost-effective in 50% of the cases in absence of confounding effect

Assess uncertainty with CEAC et EVPI graphs for multiple willingness-to-pay threshold

We also did the work in a setting where there is little to no difference in treatments.

Figure 3 : Estimates Cost-effectiveness of Treatment Influenced by Confounders in Each Scenarios

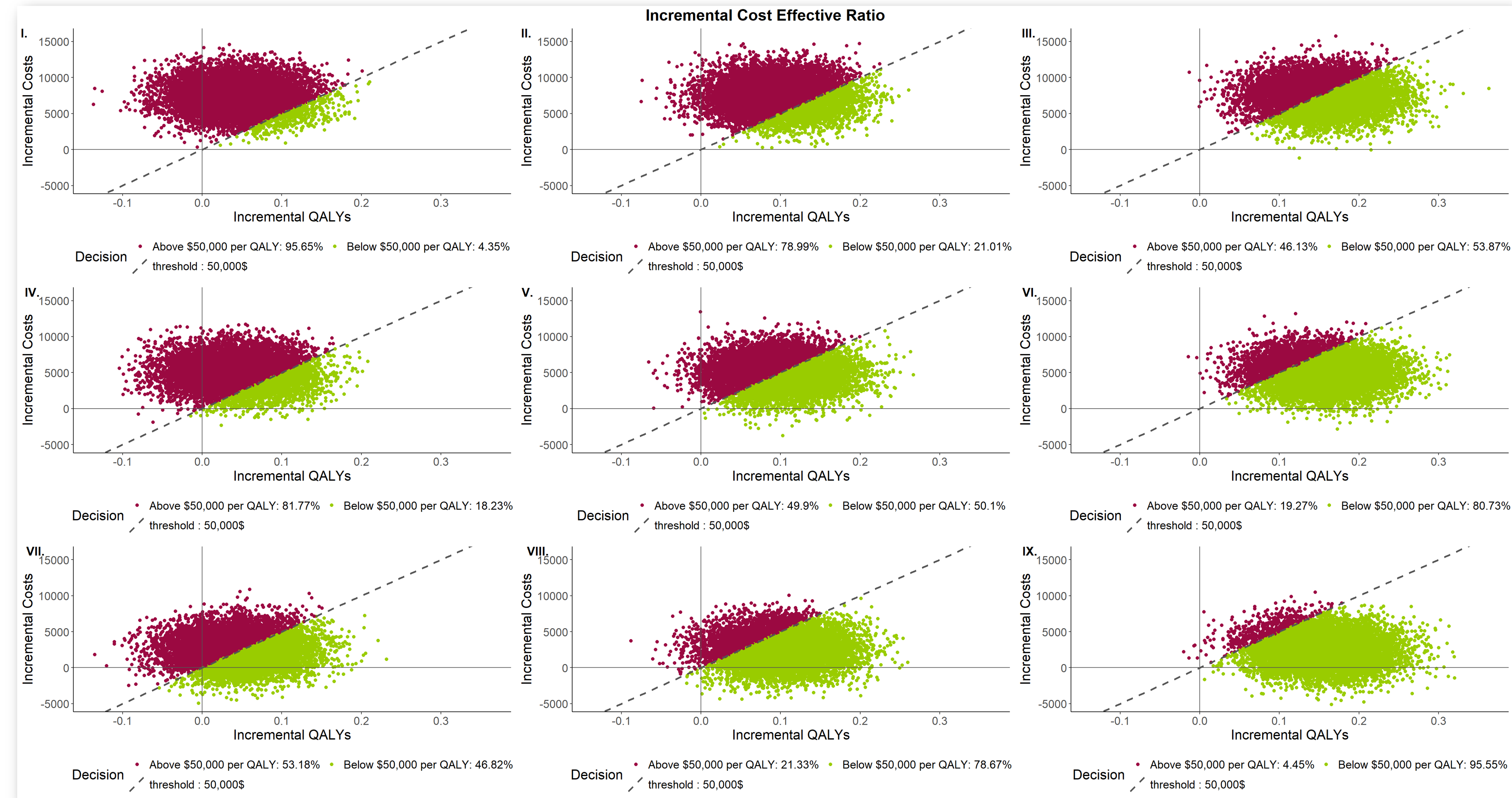
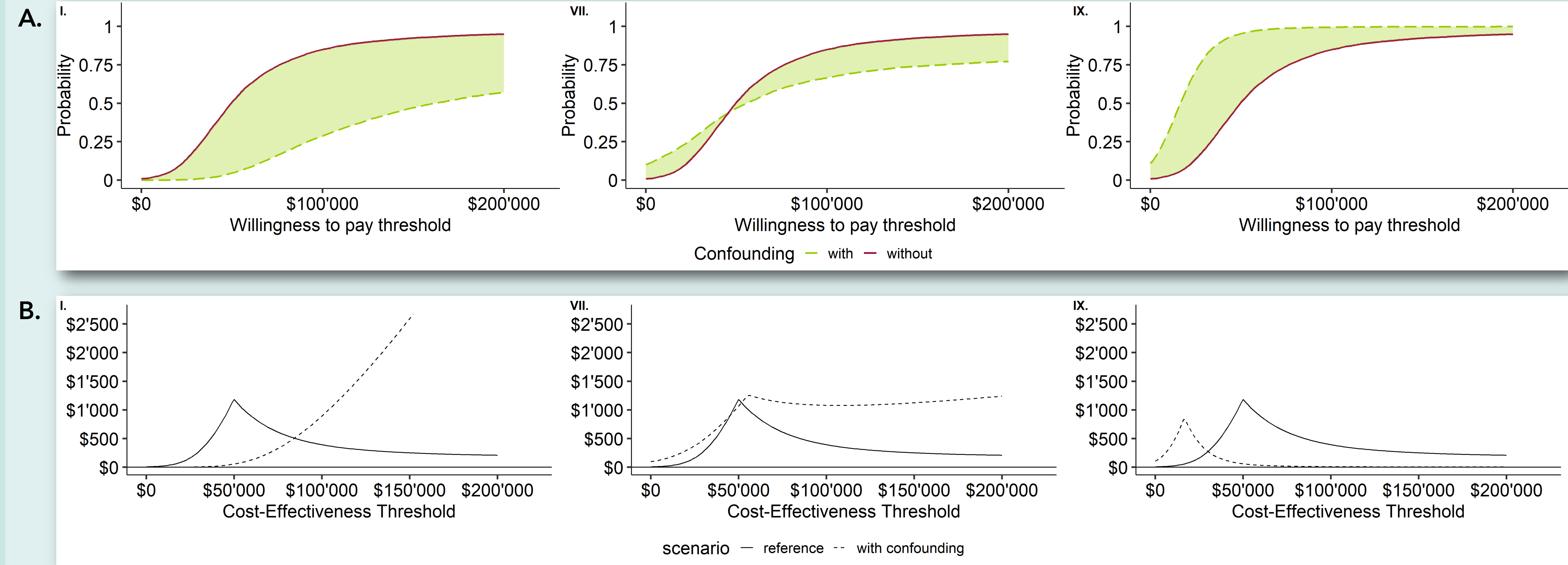


Figure 4 : Effect of confounders on A) CEAC B) EVPI curves for scenarios I, VII and IX



Oh That Is Why

We see how ignoring confounders withing real-world studies can influence conclusions

Scenarios in which confounding increases costs estimates and reduces effectiveness estimates (or vice versa) are the most likely to distort the resulting ICERs

Can significantly shift the distribution of incremental cost and incremental effectiveness within the CE planes
Can incorrectly lower or incorrectly raise CEAC
Can increase or decrease EVPI in certain scenarios

In some instances it is harder to ascertain the impact of confounders on CEAC and EVPI

Now What

Several studies have suggested different promising methods to control confounding variables

However confounding adjusment is still poorly reported; No large scale report has been made to suggest a « best » approach

A more skewed distribution of cost could be interesting to look at