Not another correlation coefficient: A method to adjust cost-effectiveness acceptability curves in economic evaluations

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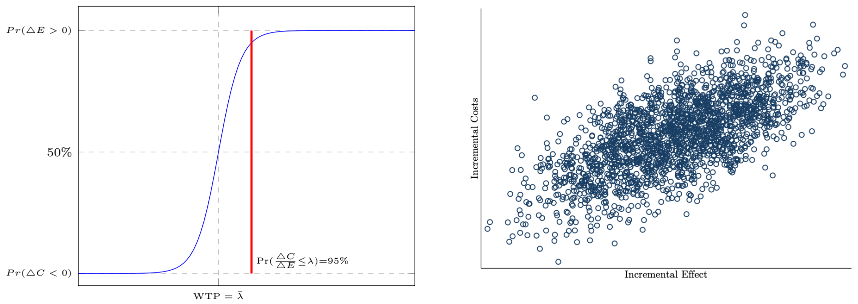
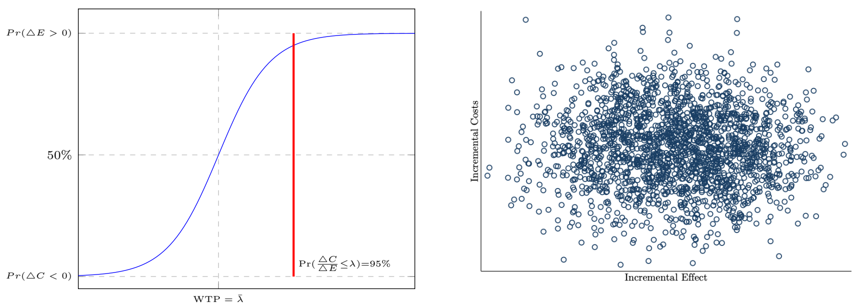
Objectives

- Illustrate the sensitivity of cost-effectiveness acceptability curves (CEACs) to the correlation between estimated incremental cost ($\triangle C_i$) and effectiveness ($\triangle E_i$) outcomes (hereafter ρ) in health economic evaluations.
- Introduce a method to adjust the empirical joint distribution of incremental cost and effect data in order to vary ρ, while holding first-order estimates constant (e.g., incremental cost-effectiveness ratio, ICER).
- Provide a Stata program which can be used to:
  1. Transform data generated in probabilistic sensitivity analysis (PSA) or resampling procedure to adjust $\rho \longrightarrow \rho'$, for $\rho' \in [-1, 1]$
  2. Generate *ex-post* confidence intervals for CEACs.
  3. Assess the robustness of willingness-to-pay (WTP)-type statistical claims used to inform stakeholder decision-making.

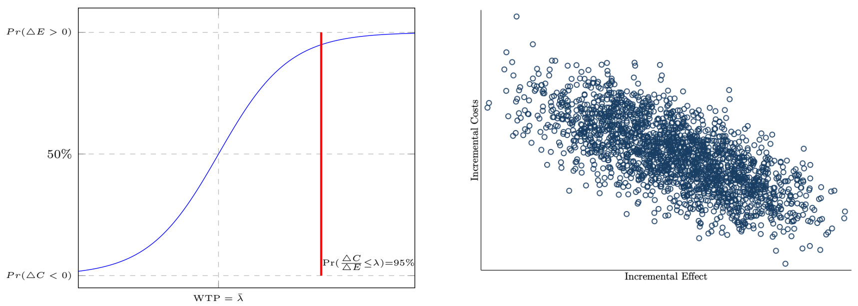
Figure 1: The relationship between the shape of cost-effectiveness acceptability curves (left panel) and the correlation between $\triangle E_i$ and $\triangle C_i$ (right panel).



Case 1: ρ is positively correlated



Case 2: $\rho = 0$, or uncorrelated



Case 3: ρ is negatively correlated

Notice in the left panel of Fig. 1 that the WTP value above which we are 95% *confident a new health intervention is cost-effective compared to control* (vertical red line) shifts left as $\rho \longrightarrow 1$, and likewise shifts right as $\rho \longrightarrow -1$.

Transformation Matrix

Let $\bar{\lambda} = \bar{\triangle C}/\bar{\triangle E}$ and $\bar{\lambda}^{-1} = \bar{\triangle E}/\bar{\triangle C}$ be the estimated *ICER* and inverse *ICER* from a health economic evaluation study with a given empirical distribution $\begin{bmatrix}\triangle E_i & \triangle C_i\end{bmatrix}^\top$ generated from PSA or resampling procedure. The following piece-wise transformation, $T(\delta)$ is thus defined as,

$$\begin{bmatrix}\triangle E_i' \\ \triangle C_i'\end{bmatrix} = \begin{cases} \begin{bmatrix}(1-\frac{\delta}{2}) & \frac{\delta}{2}\bar{\lambda}^{-1} \\ \frac{\delta}{2}\bar{\lambda} & (1-\frac{\delta}{2})\end{bmatrix}\begin{bmatrix}\triangle E_i \\ \triangle C_i\end{bmatrix}, & \text{for } \rho \to 1 \\ \begin{bmatrix}(1-\frac{\delta}{2}) & -\frac{\delta}{2}\bar{\lambda}^{-1} \\ -\frac{\delta}{2}\bar{\lambda} & (1-\frac{\delta}{2})\end{bmatrix}\begin{bmatrix}\triangle E_i \\ \triangle C_i\end{bmatrix} + \delta\begin{bmatrix}\bar{\triangle E} \\ \bar{\triangle C}\end{bmatrix}, & \text{for } \rho \to -1 \end{cases}$$

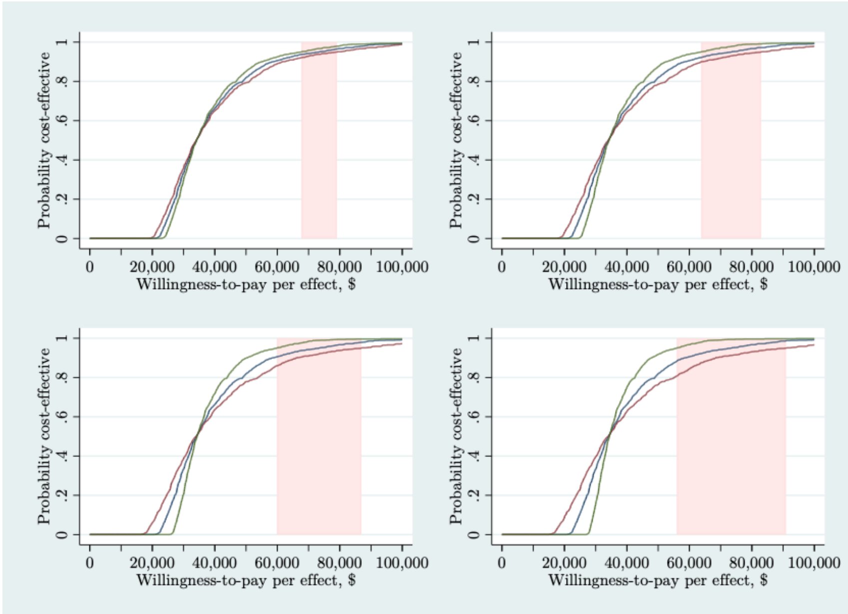
Intuition: The above transformation is based on an analytic tool employed in macroeconomics to study equilibrium processes—i.e., phase diagrams. $T(\delta)$ maps all cost and effect pairs, $(\triangle C_i, \triangle E_i)$ to a convex combination between their original value and that of the nearest point corresponding to nullclines (or stable isoclines) of a system of first-order ordinary differential equations described by the matrices in $T(\delta)$, which can be interpreted as a Jacobian matrix.

The *saddle path* solutions for $\rho \to 1$ and $\rho \to -1$ is given by $\triangle C_i = \bar{\lambda}\triangle E_i$ and $\triangle C_i = -\bar{\lambda}\triangle E_i + 2\bar{\triangle C}$, respectively.

Convergence and linearity: We observe that in both matrix transformations, the determinant of the Jacobian is $-\delta - 1 < 0$, which is strictly less than the squared value of its trace $(2-\delta)$, for all $\delta \in [0, 1]$. Therefore, the matrix transformations in $T(\delta)$ have real (linear) and distinct roots, and there exists a saddle path convergent sequence in the domain of $\begin{bmatrix}\triangle E_i & \triangle C_i\end{bmatrix}^\top$.

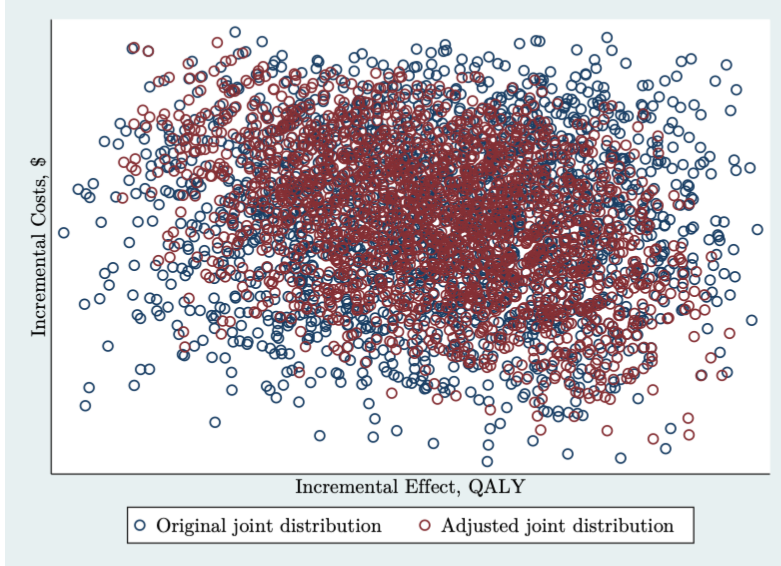
Results: Stata Program Examples

Example 1: Generate *ex-post* confidence intervals for CEACs for varying degrees of uncertainty in estimated $\hat{\rho}$.

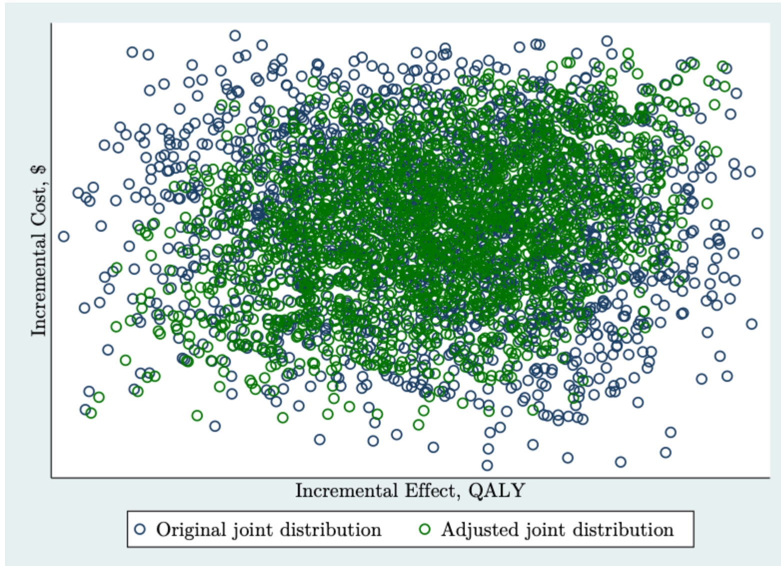


Note: Pink shaded areas display the lower ($\rho \to 1$) and upper ($\rho \to -1$) range of WTP values above which the adjusted empirical distributions, $\begin{bmatrix}\triangle E_i' & \triangle C_i'\end{bmatrix}^\top$ indicate that a health intervention is cost-effective at a 95% confidence level.

Example 2: Adjust the empirical joint distribution of incremental cost and effect estimates to be more negatively correlated ($\rho \longrightarrow -1$).



Example 3: Adjust the empirical joint distribution of incremental cost and effect estimates to be more positively correlated ($\rho \longrightarrow 1$).



Conclusion and Dissemination

- A method to adjust the joint distribution of incremental cost and effect estimates from an economic evaluation study was presented.
- Studies that do not directly observe individual-level cost and effect outcomes, such as decision-analytic or simulation models, may find the Stata program (available via email: alj4004@med.cornell.edu) described in this study useful in addressing uncertainty in $\hat{\rho}$.
- **Recommendation: economic evaluation studies should include the estimated value of $\hat{\rho}$ when reporting results.**

†*the author reports no conflicts of interest.*