

Investing in Real World Comparative Trials

Anirban Basu, Ph.D.
University of Chicago &
The National Bureau of Economic Research

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Introduction

- 2009 ARRA dedicated \$1.1 billion for head-to-head research
- Renewed interest in comparative effectiveness research among different stakeholders
- IOM committee appointed by the Federal Coordinating Council on CER
 - Produced a priority list of CER topics
 - Was ambiguous about who should invest in such research
- Current administration is averse to link CER to coverage policies
 - But such a link may be unavoidable after all

Goal

- Understand economic incentives for different stakeholders to invest in CER
 - Public versus private
 - Cost/duration of trials

Outline

- Understand role of comparative effectiveness information
- The value of CE information to patients, payers and manufacturers and their incentives to invest
- Lay out a framework for understanding the role of trial durations on private investments
- Discuss future work

Role of comparative effectiveness information

- Focus on drugs & head-to-head trials
- FDA approves drug based on placebo control trials, direct head to head comparison are seldom available
- Uncertainty exist about the which drug is more efficacious (will ignore all issues regarding heterogeneity)
- Resolving this uncertainty will allow patients to receive the more efficacious treatment thereby enhancing welfare

Role of comparative effectiveness information

- Question: When is evidence sufficient?
- Claxton et al. (2005)
 - used value of information arguments
 - Invest if $E(\text{value of information}) > E(\text{costs of investment})$
- However, who appropriates this value has implications for understanding who has the incentive to invest in CER.

Value of CE information to Stakeholders & Incentives to Invest

(Meltzer, Basu and Conti, IOM White Paper)

- Consider two drugs, A & B, on which CE study is required
- The truth can be any of these three possibilities: $A > B$, $A < B$ & $A = B$
- Prior belief about the likelihood of these possibilities :
 - Is not degenerate -> representing uncertainty about the truth.
 - would be partly reflected in the utilization of these drugs and therefore their market shares and their prices

Values & Incentives (contd..)

- Assume, both drugs are on patent → market is split but prices remain high.
- A perfect CER reveals $A > B$, $B > A$ or $A=B$
- *Ex-post* value of CER come from
 - $A > B$: welfare gain among those who were consuming B before.
 - $B > A$: welfare gain among those who were consuming A before.
 - $A=B$: welfare driven by reduction in prices

Values & Incentives (contd..)

- Expected social value of CE information is the weighted average of these values that is often very high
- Public investments in CER
 - High social value on average
 - If such spending will only crowd-out private investments, then at the margin value is less

Values & Incentives (contd..)

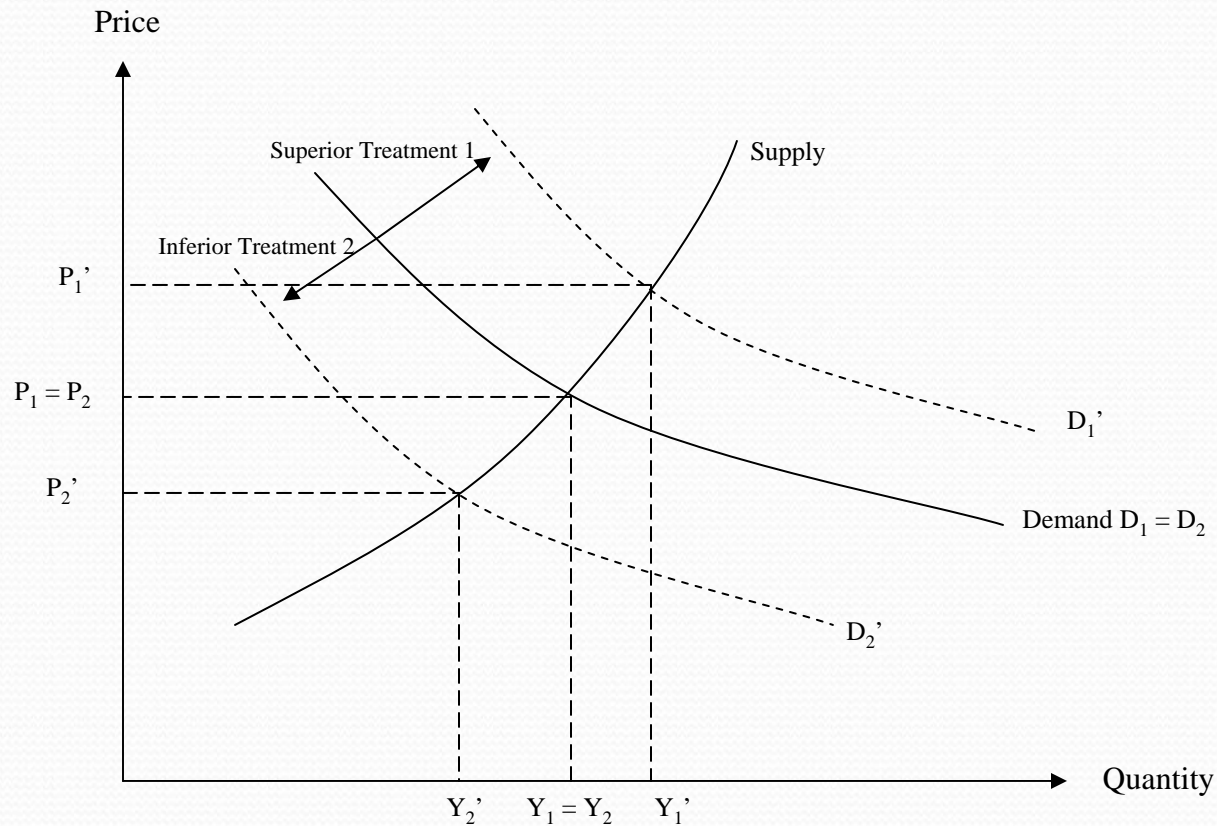
- Private investments in CER
- Value to the private payer is small as CER information will be public
- Value to manufacturer
 - reduces if they are risk averse -portfolio of investments helps to spread risk
 - increases with appropriation of value through prices and market share

Manufacturer's Value & Incentive

- Consider manufacturer's value and incentives to invest assuming they are risk neutral
- Use a revenue maximizing model
 - Equilibrium quantity
 - Equilibrium price
 - Time to patent expiry
- Effects of CER
 - Changes equilibrium price and quantity
 - Changes time to patent expiry under new price & quantity

Private Market Effects of CER

(Basu & Philipson, 2009)



Effects are multiplied in a subsidized market

Manufacturer's Value & Incentives

- The manufacturer will invest in a CE trial of length T :

$$\Delta(T) = E\{R_A^1\} - E\{R_A^0\} > 0$$

- Manipulating parameters in a comparative -static analysis will help us understand thresholds to invest
- Incentives to invest for a manufacturer will depend on
 - Prior belief about success of CER
 - Competition in CER investment

Conclusions

- Prior distribution matters!!
- A manufacturer is less likely to invest if prior information “ambiguously” shows equivalence between its own and competitor’s drugs
- A manufacturer is more likely to invest if prior information either “ambiguously” favors or opposes the superiority of its drug
 - If manufacturer’s competitor has incentives to invest, then manufacturer might as well invest to control design points
- Interesting implications for public investments

Future Directions

- Our current work lays out a normative model to study incentives to invest
- Also interested in a positive model – understand how decisions on CER are made in private firms.
- Three approaches
 - Revealed preference approach
 - Stated preference approach
 - Qualitative interviewing

Revealed preference approach

- Disease-specific approach
- Identify relevant stakeholders for CER research on alternative drugs in a clinical area
- Set up disease specific panel data based on clinical trial registries
- Model investment in a CE trial as an annual firm-specific decision.
- Collect information on equilibrium prices, quantity and time to patent expiry for each drug
- Run probit models predicting decision to invest.

Stated preference approach

- Create vignettes asking whether to invest in CER comparing two competing products
- Vary parameter levels across vignettes
- Recruit senior managers/directors from industry and randomly assign vignettes to study their decision to invest in CER.

Qualitative interviewing

- Develop questionnaire containing both close-ended and open-ended questions
- Understand factors that play in to the decisions to invest in CER
- Recruit senior managers/directors from industry

Conclusions

- Positive approach will help us understand the nuances of decision making in practice that may not be captured by a theoretical model.
- It will also help us understand the key parameters on which decision making hinges on
- This in turn may help us to better inform the roles that pragmatic trials such as adaptive designs can play to improve decision making