JOINING EPIDEMIOLOGY WITH ECONOMICS

An approach to person-level cost-effectiveness analysis (PLCEA)

Hojoon Sohn

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dhjsohn@gmail.com

Revisit of CE plane

	Less Effective	More Effective
More Cost	Do not adopt	Is the increased in effect worth the cost?
Less Cost	Is decreased in effect wo rth the savings?	Definitely Choose

Cost-Effectiveness Analysis

- **Cost $ / Effectiveness**

- What does it cost to get a given health ou tcome (or diagnostic performance)?:
  - **To gain a year of life**
  - **To prevent treatment with wrong regimen**
  - **To prevent secondary TB infection**
  - **To increase case detection**
  - **Etc.**

Cost Effectiveness Analysis

- Most common type of analysis
- Incremental Cost Effectiveness Ratio (ICER) most informative for competing intervention
- Examples:
  - Drug-eluting stents: prevention of revascularization interventions (angioplasty & CABG) =+/- 20K$
  - Screening for breast cancer 50-69: $5700/ life year gained (LYG)
  - Screening for prostate cancer (CETS) or down syndrome (AETMIS, 2004)
  - Prevention of vaccine-preventable diseases, STDs, HIV and AIDS
- Limitation : one indicator at a time in analysis

Cost Utility Analysis

- Cost per health utility measure (QALY or DALY)
- QALY vs. DALY, which one to choose?

Solutions to the limitations

- Increase in transparency
  - Ingredients approach for models and clinical path ways explicit
  - Direct combination of epi analysis as an essential t ool for CEA
    - Person-level economic evaluations
    - Empirical data and real cohort of patients
- Test of the robustness of the model/analysis
  - Sensitivity analysis: impact of variation of input pa rameters on results
  - Test for uncertainty – true statistical meaning of 'u ncertainty'

A need for multi-disciplinary approach

- Decision making process in public health must be a multi-disciplinary process
- Epidemiology is an essential component of cost and cost effectiveness study – Link Epidemiology and Economics
- Modeling in cost effectiveness analysis that co mbines epidemiological, economical, and social factors allows complete evaluation of a public health problem

Epidemiology and Economics
they come hand-in-hand

- Person-level economic evaluation or person-level cost effectiveness analysis (PLCEA)

Getting started with PLCEA

- You have
  - 2 Comparators
  - Want to do a CUA or CEA
  - Individual person-level data (from RCT, clinical trial, cohort study, etc.)
    - Patient receiving new intervention (TX = 1)
      - Each person's cost and effect
    - Patient receiving routine intervention (Tx = 0)
      - Each person's cost and effect

Incremental Cost Effectiveness Ratio (ICER)

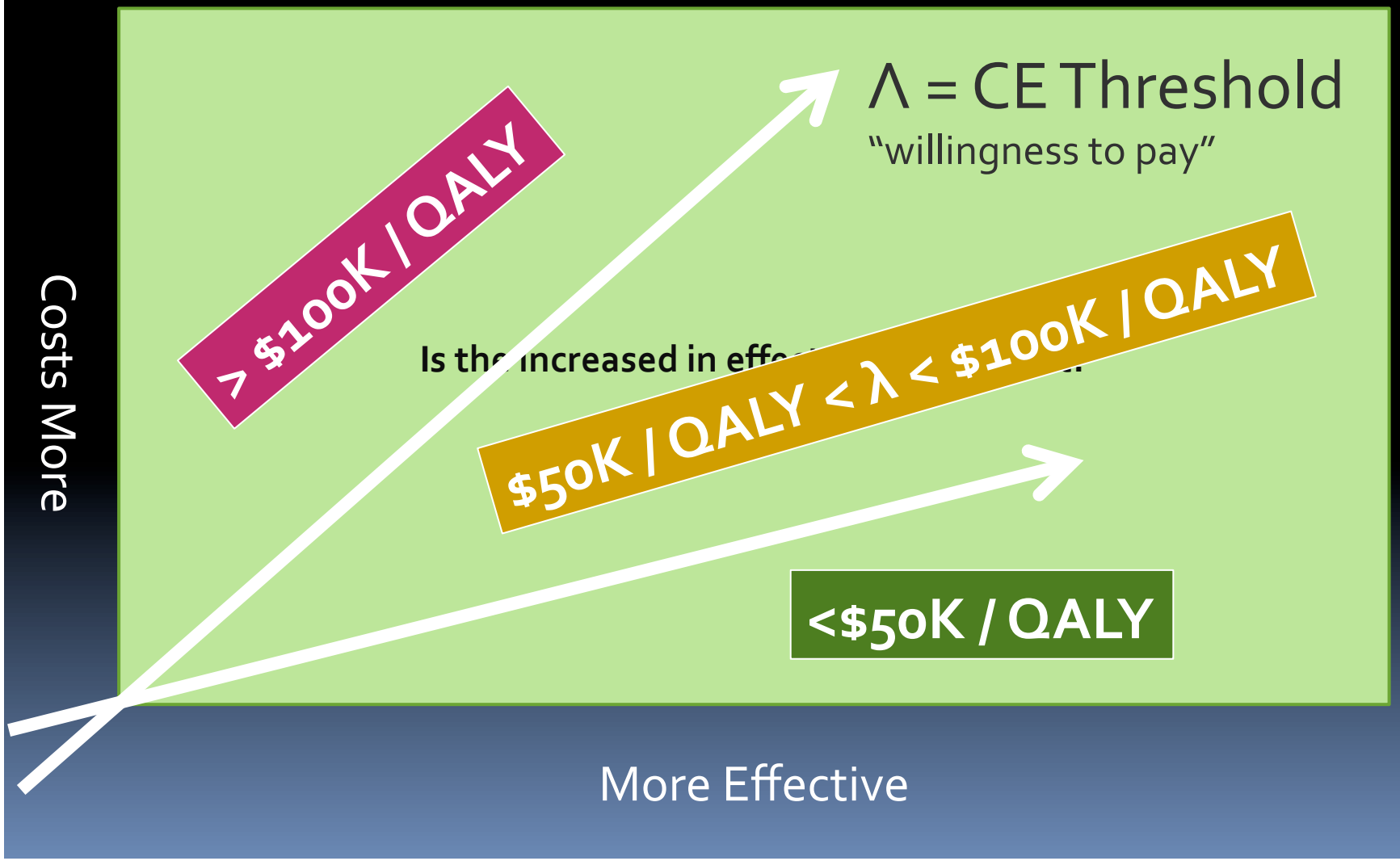
$$\frac{\text{Cost (New Intervention)} - \text{Cost (Compared / Routine Intervention)}}{\text{Effectiveness (New Intervention)} - \text{Effectiveness (Routine)}}$$

ICER challenges

- The ICER yields a 'price tag' for one more unit of effect
- Key issues
  - Is the decision maker willing to pay this?
  - How precise is your estimate of the price tag?

Making decisions based on ICER

Depends on the "willingness to pay"



Confidence in your ICER estimate

- The change in Cost estimate is made from a difference in means

- The means are made from sample data

- The sample data I draw may differ from the sample data drawn by another person

This is essentially same for the change in 'effectiveness'

Thus, ICER varies

Main issues in CEA

- How to know if ICER < " Willingness to Pay" gi ven ICER varies and "Willingness to Pay" is no t certain/unknown?

95% Confidence Interval (Ellipse)

Sensitivity Analysis (Change "Willingness to Pay"

The idea of Net Benefit

Introducing WTP to ICER estimate

- It is easier to make a confidence interval of $\Delta C / \Delta E < \lambda$ (WTP) than that of ICER
- A confidence interval to answer "Is $\Delta C / \Delta E < \lambda$ (WTP) ?" can be made from "Is $\Delta C < \Delta E \times \lambda$?"

- $\Delta E \times \lambda - \Delta C =$

Incremental Net Benefit (ΔNB)

Estimating ΔNB – NB Regression

- $\Delta E \times \lambda - \Delta C = NB$
- $NB = \beta_0 + \beta_1 TX$
- $\beta_1 TX = \Delta E \times \lambda = \Delta NB$

- IF $\beta_1 > 0$ → New Tx. is Cost-Effective!

Steps for NB regression

- Collect cost and effect data
- Create NB = Effect x λ – Cost
- Create a dummy variable
  - TX = 1 if receiving new Tx
  - TX = 0 if receiving usual care
- Run the regression → NB = $\beta_0 + \beta_1 TX$
- Repeat with few different WTP (i.e. sensitivity anal ysis)

  - LET's RUN a NB Regression as an example!!!

Some notations

- Cost: individual patient costs
- Effect: individual patient effect estimates
- Tx: Treatment indicator (0: usual | 1: new Tx)
- hisev: indicator for severity of patients (0: low | 1: high severity)

Interpretation

Problem set #2

1) Do regression to confirm the #'s in the graph to the right.
2) What is the best λ to use?
3) With λ = $10, run and explain the parts of the regression:

$$db = \beta_0 + \beta_1 TX + \beta_2 lsav + \beta_3 TX \times lsav$$

Also, separately for black = 0 and black = 1

$$db = \beta_0 + \beta_1 TX$$

From the NB regression results

- Average NB for Tx=0 with low severity = 112
- Average NB for Tx = 1 with low severit= - 517 (112 – 628)
- Difference between these two = - 629
- Average NB for Tx = 0 with high severity = - 84 4 (112 – 957)
- Average NB for Tx = 1 with high severity = 514 (112 – 629 – 957 + 1987)

This sets up nicely with Epi analysis, NO?

- ICER can be estimated from regression analysis (TX = 1 vs. TX = 0)
  - Cost = $a_0 + a_1 TX$
  - Effect = $b_0 + b_0 TX$
  - NB (ICER) = Cost / Effect = $\beta_0 + \beta_1 * TX$
- Parameters included in regression can be variables used in Epi regression analysis!
  - Can include other parameters:
    - NB (ICER) = $\beta_0 + \beta_1 * TX + \beta_2 * Age$
    - NB (ICER) = $\beta_0 + \beta_1 * TX + \beta_2 * Age + \beta_3 Age * Sex$

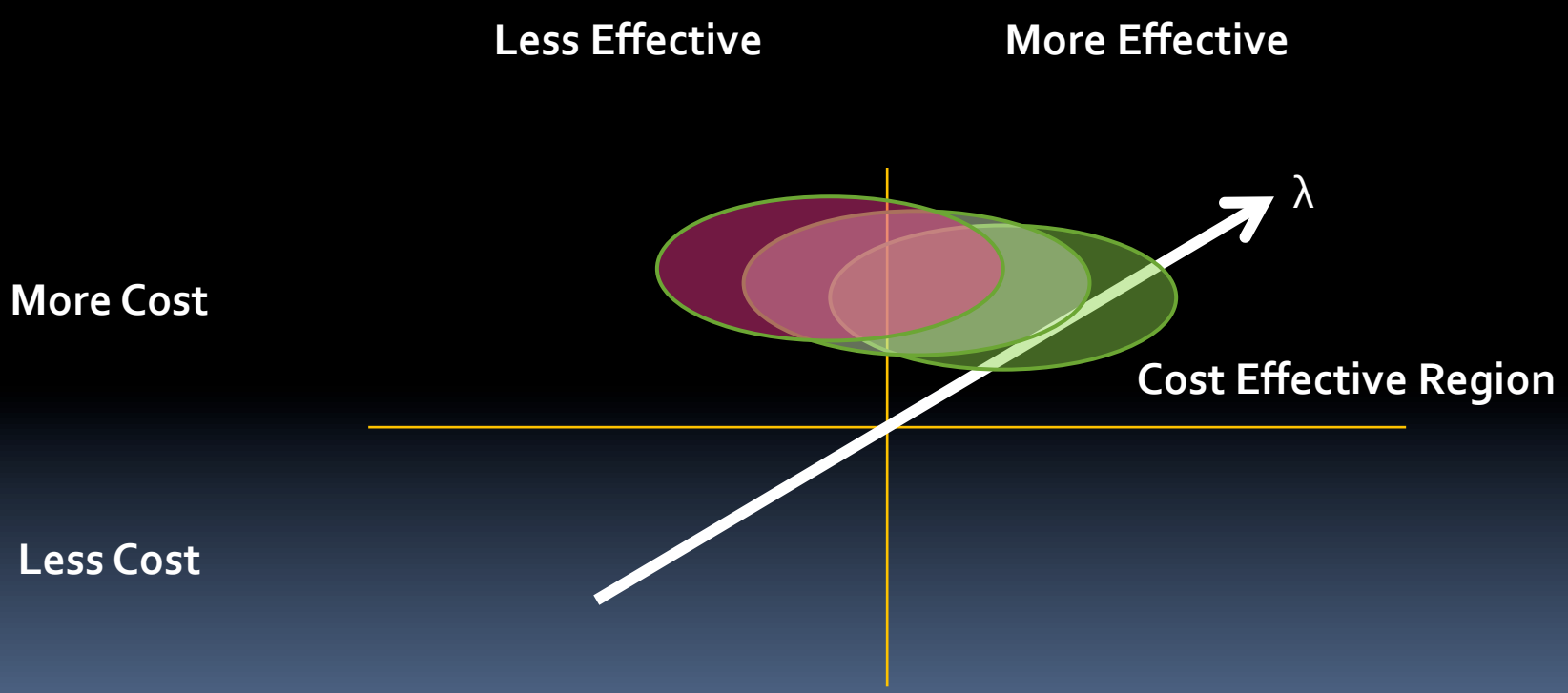
Main issues in CEA

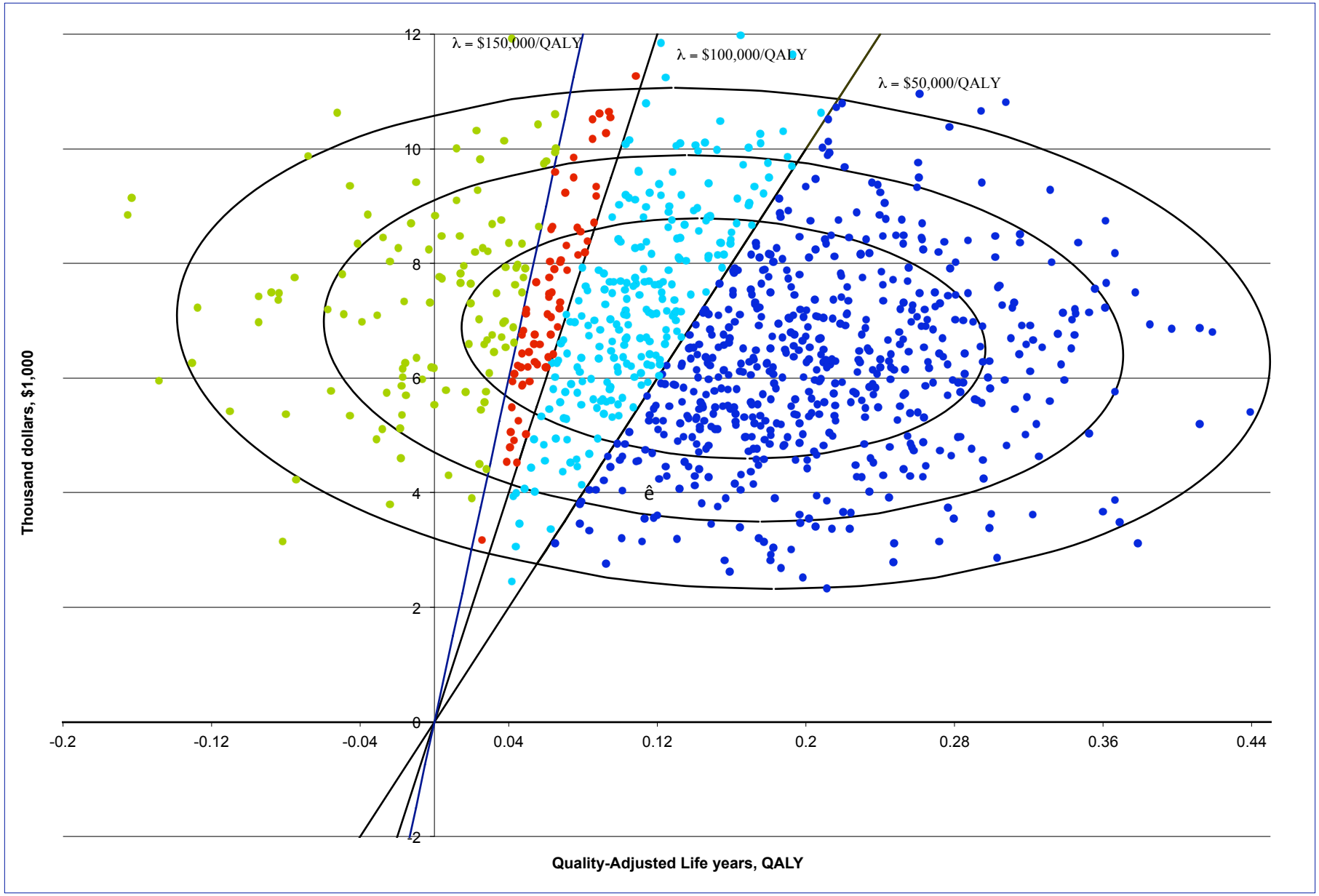
- How to know if ICER < " Willingness to Pay" gi ven ICER varies and "Willingness to Pay" is no t certain/unknown?

95% Confidence Interval (Ellipse)

Sensitivity Analysis (Change "Willingness to Pay"

95% Confidence Intervals - Ellipse




λ = $150,000/QALY
λ = $100,000/QALY
λ = $50,000/QALY
ê
12
10
8
6
4
2
0
-2
-0.2
-0.12
-0.04
0.04
0.12
0.2
0.28
0.36
0.44
Thousand dollars, $1,000
Quality-Adjusted Life years, QALY

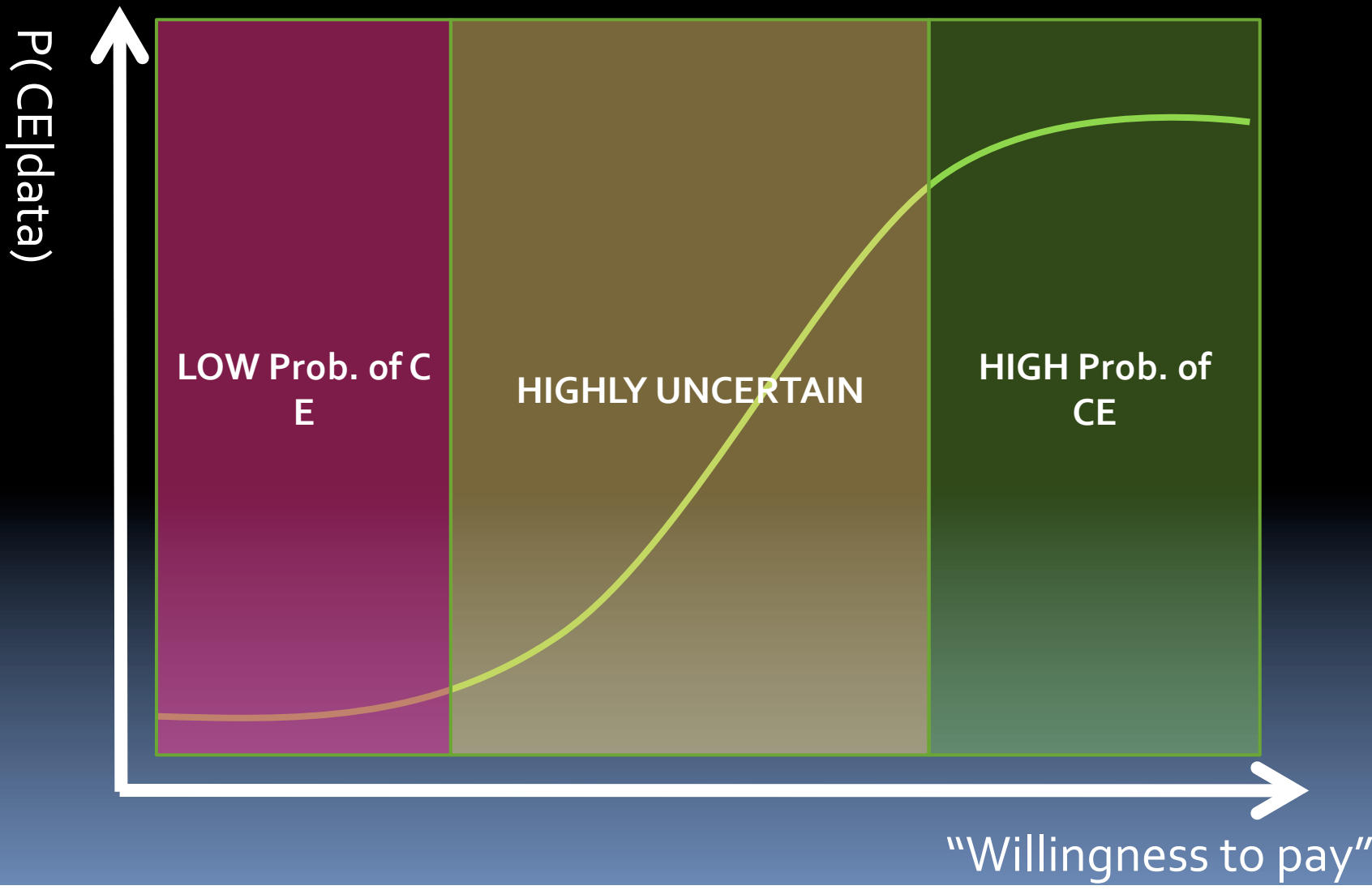
Why an Ellipse?

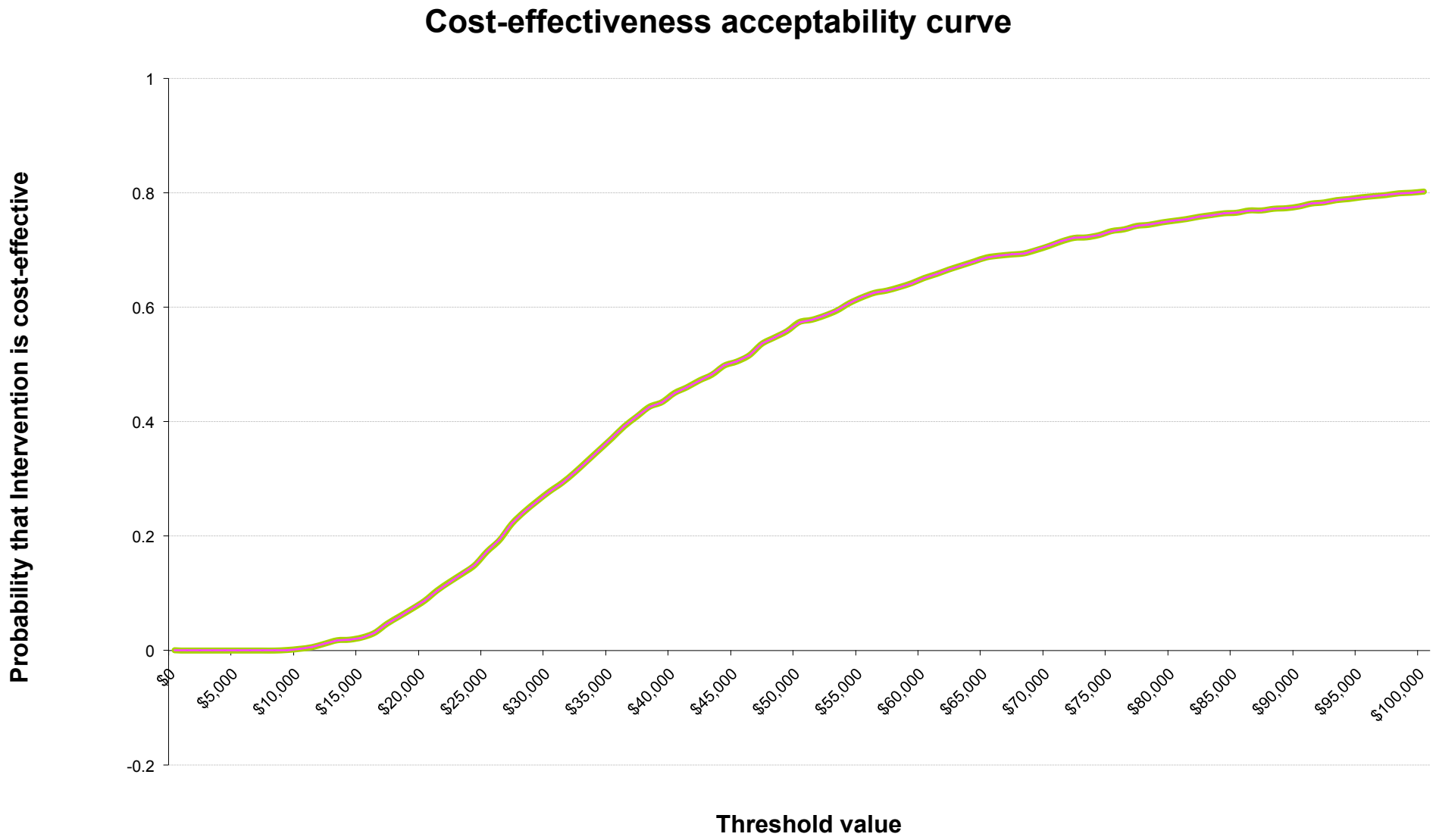
- Outcome of interest (measurement) is a ratio rather than a straight out number
  - Must taken account for:
    - Variances in each cost and effectiveness parameters
    - Covariances of both parameters
    - Correlation between Cost and Effectiveness
      - More correlation, ellipse will be more twisted left (-) or right (+)
- Building one (parabola approach)
  - Use density function and variance covariance matr ix

Cost Effectiveness Acceptability Curve (CESC)

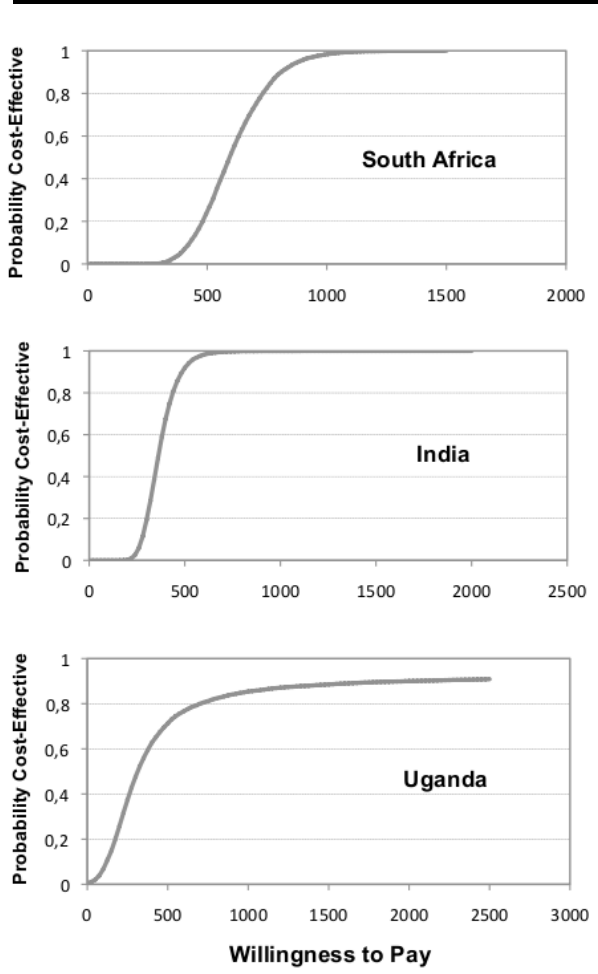
- Main objective – vary "willingness to pay" and test against ICER
- Vertical axis – p (Tx = CE)
  - $P(ICER < \lambda) = P(\Delta E * \lambda - \Delta C > 0) = P(\Delta NB > 0)$
  - A bayseian approach
    - Given the data we have what is the probability of int ervention being CE?
- 2 Options
  - If Bayesian assumption does not hold, use boot-strapping approach

CEAC – what does it look like?




Cost-effectiveness acceptability curve
Probability that Intervention is cost-effective
1
0.8
0.6
0.4
0.2
0
-0.2
$0
$5,000
$10,000
$15,000
$20,000
$25,000
$30,000
$35,000
$40,000
$45,000
$50,000
$55,000
$60,000
$65,000
$70,000
$75,000
$80,000
$85,000
$90,000
$95,000
$100,000
Threshold value

Controversies around CEACs



- Do not distinguish different incremental joint distributions
- CEACs may mislead policy makers regarding the preferred alternative
- CEACs may incorrectly suggest medical urgency or importance
- Interpretation of multiple CEAC – difficult

EPINOMICS anyone?

- Compared to modeling this technique is based on prospective observation of patient important outcomes and their relevant costs according to 'treatment' or 'intervention(s)' assigned
- Regression based allows us to investigate potential confounders and interaction terms that can influence both the treatment/intervention effect and the cost – both of which are very much tied to one another
- While traditionally economic evaluation studies only started AFTER an intervention studies are conducted, this methods engages economists to be part of a health intervention studies early on
- This method has limitations in generalizability of the study findings, but there is not a single study design that is immune to this problem
- This method is not immune to the problem of how we value health
- At the moment, no TB or TB diagnostic studies have used such study d esign – methodologically, we will need to further verify if this techniqu e provides useful unbiased conclusions to cost and cost-effectiveness studies for TB