Sampling Uncertainty and Economic Outcomes

- Confidence statements about economic outcomes are based on whether or not the confidence interval for the economic outcome includes the decision threshold.
- Methods for assessing confidence:
  - Confidence intervals for cost-effectiveness ratios
  - Confidence intervals for net monetary benefits
  - Acceptability curve
- Decision threshold:
  - FOR CER: Maximum willingness to pay (W) for a unit of health outcome or maximum acceptable cost-effectiveness ratio (e.g., 30,000 GBP or 50-100,000 USD)

Sampling Uncertainty and CI for CER

- Suppose we calculate a point estimate and 95% CI for the incremental cost-effectiveness ratio.
- We determine whether we can be 95% confident a therapy is good value by comparing the confidence interval to our decision threshold (maximum WTP):
  - If maximum willingness to pay is included within the confidence interval, we CANNOT be confident that the two therapies differ in their cost-effectiveness.
  - If it is excluded from / outside the interval, we CAN be 95% confident that one of the therapies is cost-effective compared to the other.
Sampling Uncertainty and NMB
• Suppose we calculate a point estimate for NMB and its 95% CI
  – We determine whether we can be 95% confident that therapy A is good value by comparing the confidence interval to the NMB decision threshold (0)
    • Includes 0, cannot be confident of a difference
    • Excludes 0, can be confident the therapies differ
  – Primary difference between interpretation of CI for CER and CI for NMB is that we compare CER to WTP whereas we build WTP into NMB

Sampling Uncertainty and the Acceptability Curve
• Suppose we calculate a point estimate for fraction of the distribution that is acceptable
  – We determine whether we can be 95% confident that therapy A is good value by comparing the fraction acceptable to the decision threshold (horizontal lines drawn at 0.025 and 0.975)
    • If 0.025 < fraction < 0.975, we cannot be confident that the two therapies differ in their cost-effectiveness
    • If fraction < 0.025 OR fraction > 0.975, we can be 95% confident that one of the therapies is cost-effective compared to the other

Resulting Confidence Statements (I)
• For any given willingness to pay, an experiment ALWAYS allows us to draw one of three conclusions:
  – We can be confident that one therapy is good value compared to the alternative
  – We can be confident that the alternative therapy is good value compared to the first
  – We cannot be confident that the two therapies differ in their economic value
Resulting Confidence Statements (II)

- If our goal is to identify which of these 3 statements holds for a given willingness to pay, confidence intervals for cost-effectiveness ratios, confidence intervals for NMB, and acceptability curves **ALWAYS** provide the same answer:
  - e.g., if our WTP is included within the CI for the CER, then:
    - The CI for the NMB that is calculated by use of our WTP will include 0, and
    - The fraction of the distribution that is acceptable at our WTP will fall between the horizontal lines that define the decision threshold (e.g., between 0.025 and 0.975)

Cost-Effectiveness Plane

- CI for CER, CI for NMB, and the acceptability curve can be estimated parametrically or nonparametrically (by use of a bootstrap)
  - All 3 parametric techniques assume that the difference in costs and effects is distributed bivariate normal (probably not a very strong assumption)
  - Nonparametric bootstrap approach relaxes this assumption
- Stata programs, datasets, and sample calculations for both methods are provided today and are also available at:
  [www.uphs.upenn.edu/dgimhsr/eeinct_cicer.htm](http://www.uphs.upenn.edu/dgimhsr/eeinct_cicer.htm)
**Parametric Methods**

**iprogs.do**
- Contains 4 **PROGRAMS** related to parametric estimates of sampling uncertainty, a (very basic) program for estimation of inputs for use in these programs, and a program that provides documentation for these programs
  - The command `do iprogs` simply loads these programs; it does not calculate anything
- Documentation program: `iprogsdoc`

**iprogs.do (cont.)**
- Programs for calculating sampling uncertainty
  - `fielleri`: Calculates Fieller's theorem method CI for CER
  - `nmbi`: Calculates NMB point estimates, CI, and p-values
  - `accepti`: Calculates % acceptable and p-values
  - `ciboundi`: Calculates t-statistics and p-values defining patterns 1, 2, and 3 for an experiment
- Program for calculating inputs
  - `ipinputs`: Calculates t-test means, SEs, and correlation for use with `fielleri`, etc. Usually want to use regression results, etc., instead
iprogs.do (cont.)

- Parameter values may be derived from any number of estimation methods, but these programs are particularly useful if one has used multivariable regression to estimate point estimates and SEs.
- While these programs include a program for the derivation of the necessary parameters by use of t-tests (ipinput), if t-tests are sufficient, consider using uprogs.do, which conducts the t-tests as well as assesses sampling uncertainty.

Fieller’s Theorem Method

- A parametric method for calculating CI for CER based on the assumption that the difference in cost and the difference in effect follows a bivariate normal distribution.
  - i.e., the expression \( R \Delta E - \Delta C \) is normally distributed with mean zero (where \( R \) equals \( \Delta C/\Delta E \) and \( \Delta E \) and \( \Delta C \) denote the mean difference in effects and costs, respectively)
  - Standardizing this statistic by its standard error and setting it equal to the critical value from a normal distribution generates a quadratic equation in \( R \)
- The roots of the quadratic equation give the confidence limits.

Fieller’s Theorem Formula

Lower (clockwise) limit: \( \frac{M - [M^2 - NO]^{0.5}}{N} \)
Upper (counterclockwise) limit: \( \frac{M + [M^2 - NO]^{0.5}}{N} \)

Where:

\[
M = \Delta E \Delta C - t_{\nu_2} \rho \ s_E \ s_C \\
N = \Delta E^2 - t_{\nu_2}^2 \ s_E^2 \\
O = \Delta C^2 - t_{\nu_2}^2 \ s_C^2 \\
\]

\( \Delta E \) and \( \Delta C \) denote mean difference in effect and cost; \( s_E \) and \( s_C \) denote estimated standard errors for the difference in effect and cost; \( \rho \) equals the estimated Pearson correlation coefficient between the difference in cost and effect; \( t_{\nu_2} \) is the critical value from the T distribution.
**Program:** FIELLER

*CALCULATES FIELLER INTERVALS. Reports the specified interval as well as the last defined interval, if the specified interval isn't defined, reports the limit of the last defined interval*

**Command Line:**
```
fielleri [COST] [SEcost] [EFFECT] [SEeffect] [CORR] [DOF] [CI]
```

* The 7 arguments are all numbers
  **`1'** difference in costs
  **`2'** SE diff costs
  **`3'** difference in effects
  **`4'** SE diff effects
  **`5'** correlation of differences
  **`6'** degrees of freedom
  **`7'** confidence interval, as decimal (e.g., 0.95 for a 95% interval)

---

**Alternative Command Lines (e.g., for automated calculation):**
```
ipinputs [cost] [effect] [group] [,if]
local a=r(meanc)
local b=r(sec)
local c=r(meanq)
local d=r(seq)
local e=r(rho)
local f=r(dof)
fielleri `a' `b' `c' `d' `e' `f' [CI]
```

* Saved Results
  * `R`
  * `CI`
  * `fll`
  * `ful`
  * `lastCI`

---

**Data Required for Fieller's Theorem Method**

- The data needed to calculate these limits can be obtained from most statistical packages by:
  - Evaluating the difference in costs (and obtaining $\Delta C$ and $s_C$)
  - Evaluating the difference in effects (and obtaining $\Delta E$ and $s_E$)
  - Estimating the correlation between the difference in costs and effects (either from bootstrap or from math in Appendix 1)
Point Estimates and SEs (from Jalpa’s Lecture)

<table>
<thead>
<tr>
<th>Point Estimate</th>
<th>S.E. *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td></td>
</tr>
<tr>
<td>Id/Gau</td>
<td>22</td>
</tr>
<tr>
<td>Id/Pois</td>
<td>113</td>
</tr>
<tr>
<td>Log/Gam</td>
<td>135</td>
</tr>
<tr>
<td>Pow/Pois</td>
<td>88</td>
</tr>
<tr>
<td>QALYs</td>
<td></td>
</tr>
<tr>
<td>Id/Gau</td>
<td>0.0417</td>
</tr>
<tr>
<td>Id/Pois</td>
<td>0.0417</td>
</tr>
<tr>
<td>Pow/Pois</td>
<td>0.0408</td>
</tr>
</tbody>
</table>

* SEs derived from bootstrap

Correlations (from bsmvpred)

drop _all
use bsmvpred
corr pglm?qd pglm?cd
(obs=3000)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
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<td>p.qgd</td>
<td>1.0000</td>
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</tr>
<tr>
<td>p.qgdp</td>
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<tr>
<td>p.pqd</td>
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<td>0.9979</td>
<td>1.0000</td>
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<td></td>
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<td>p.pgcd</td>
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<td>-0.2454</td>
<td>-0.2445</td>
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<td></td>
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<tr>
<td>p.igq</td>
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<td>-0.2523</td>
<td>-0.2504</td>
<td>0.9618</td>
<td>1.0000</td>
<td></td>
</tr>
<tr>
<td>p.ipq</td>
<td>-0.2527</td>
<td>-0.2596</td>
<td>-0.2573</td>
<td>0.9526</td>
<td>0.9914</td>
<td>1.0000</td>
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<td>-0.2563</td>
<td>-0.2545</td>
<td>0.9828</td>
<td>0.9943</td>
<td>0.9906</td>
</tr>
</tbody>
</table>

fielleri

. quietly do iprogs
. fielleri 22 106.85 .0417 .0184 -.2403 494 .95
Cost-Effectiveness Analysis
Point Estimate: 528
Quadrant: NE
Fieller 95 % Confidence Interval
Lower limit: -5536
Upper limit: 18229
Confidence Statements:
For WTP <=18229, we can't be 95% confident that the 2 therapies differ in value;
For WTP > 18229, we can be 95% confident that the therapy with the larger point estimate for effect represents good value compared with the alternative
fielleri (cont.)

.r return list
.scalars:
   r(R) = 528
   r(CI) = 95
   r(fll) = -5536
   r(ful) = 18229
   r(lastCI) = 98.29876824226194

Pick another pair of cost / effect estimates and calculate a 95% CI for the CER

---

**Fieller's Intervals**

<table>
<thead>
<tr>
<th>pglmpqd</th>
<th>pglmppqd</th>
</tr>
</thead>
<tbody>
<tr>
<td>pglmpcqd</td>
<td>pglmppcqd</td>
</tr>
<tr>
<td>528</td>
<td>539</td>
</tr>
<tr>
<td>-5464 to 17,882</td>
<td>-5689 to 19,853</td>
</tr>
<tr>
<td>2710</td>
<td>2770</td>
</tr>
<tr>
<td>-1921 to 31,123</td>
<td>-1970 to 35,076</td>
</tr>
<tr>
<td>3237</td>
<td>3309</td>
</tr>
<tr>
<td>-1643 to 35,707</td>
<td>-1684 to 40,275</td>
</tr>
<tr>
<td>2110</td>
<td>2175</td>
</tr>
<tr>
<td>-2719 to 27,553</td>
<td>2796 to 30,970</td>
</tr>
</tbody>
</table>

---

**NMB Confidence Intervals**

- Uses formula for a difference in two normally distributed continuous variables

\[
\text{NMB CI} = \text{NMB} \pm t_{\alpha/2} \times \text{SE}_{\text{NMB}}
\]

- Standard error for NMB equals:

\[
\text{SE}_{\text{NMB}} = \sqrt{s^2_C + s^2_E - 2 W \rho s_C s_E}
\]

- CI for NMB:

\[
\text{CI}_{\text{NMB}} = (\Delta \text{E} \pm \Delta C) \pm t_{\alpha/2} \times (s^2_C + s^2_E - 2 W \rho s_C s_E)^{0.5}
\]
* PROGRAM: NMBI

* CALCULATES NMB, CI, AND P-VALUE FOR VARYING 
* WILLINGNESSES TO PAY

* COMMAND LINE: nmbi [COST] [SEcost] [EFFECT] [SEeffect] 
[CORR] [DOF] [CI]

* The 7 arguments are all numbers
**``1' difference in costs
**``2' SE diff costs
**``3' difference in effects
**``4' SE diff effects
**``5' correlation of differences
**``6' degrees of freedom
**``7' confidence interval, as decimal (e.g., 0.95 for a 95% interval)

Alternative command lines (e.g., for automated calculation):

ipinputs [cost] [effect] [group] [,if]
local a=r(meanc)
local b=r(sec)
local c=r(meanq)
local d=r(seq)
local e=r(rho)
local f=r(dof)
nmbi `a' `b' `c' `d' `e' `f' [CI]

* Saved Results
* r(CI)
* r(nmbmat)

Stata Programs, nmbi

<table>
<thead>
<tr>
<th>95% Lower</th>
<th>95% Upper</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>W</td>
<td>NMB</td>
<td>Limit</td>
</tr>
<tr>
<td>.</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>-6308</td>
<td>-285</td>
<td>-555</td>
</tr>
<tr>
<td>-5336</td>
<td>-253</td>
<td>-506</td>
</tr>
<tr>
<td>-5118</td>
<td>-235</td>
<td>-480</td>
</tr>
<tr>
<td>-209</td>
<td>-13</td>
<td>-225</td>
</tr>
<tr>
<td>527</td>
<td>0</td>
<td>-215</td>
</tr>
<tr>
<td>857</td>
<td>14</td>
<td>-206</td>
</tr>
<tr>
<td>.</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>15083</td>
<td>607</td>
<td>-23</td>
</tr>
<tr>
<td>18229</td>
<td>738</td>
<td>0</td>
</tr>
<tr>
<td>26931</td>
<td>1101</td>
<td>57</td>
</tr>
<tr>
<td>.</td>
<td>.</td>
<td>.</td>
</tr>
</tbody>
</table>
nmbi Confidence Statements

Confidence Statements:
For WTP <= 18229, we can’t be 95% confident that
the 2 therapies differ in value;
For WTP > 18229, we can be 95% confident that
the therapy with the larger point estimate for
effect represents good value compared with the
alternative

Stata Programs, nmbi (cont.)

. return list
scalars:
r(CI) = 95
matrices:
r(nmbmat) : 104 x 5
To view r(nmbmat): matrix list r(nmbmat)
To access the data in r(nmbmat):
First, create a new matrix: matrix [name]=r(nmbmat)
Second, transform the new matrix into a dataset (svmat)
or assign elements to scalars or localize them (scalar
sname=name[1,1] OR local lname=name[3,4])

NMB Graph
Graphing in Stata

. quietly nmbi 22 106.85 .0417 .0184 -.2403 494 .95
. matrix matrix=r(nmbmat)
. preserve
. drop _all
. svmat matrix
number of observations will be reset to 106
Press any key to continue, or Break to abort
obs was 0, now 106
. ren matrix1 wtp
. ren matrix2 pe
. ren matrix3 ll
. ren matrix4 ul
. twoway line pe ll ul wtp if wtp>=0&wtp<100000,yline(0),xline(0)
. restore

Resulting Stata Graph

Pick another pair of cost / effect estimates and calculate 95% CI for NMB
Parametric Acceptability Curves

• One means of deriving parametric acceptability curves is by estimating the 1-tailed probability that the net monetary benefits, calculated by use of the willingnesses to pay defined on the X-axis, are greater than 0
• Stata commands for the probability of acceptability for a willingness to pay of 20,000

```
scalar w=20000
scalar senmb = ((sec^2) + ((rc^2)*(seq^2)) - (2*w*corrcq*sec*seq))/0.5
scalar acc20=1-ttail(DF,(((mq*rc)-mc)/senmb))
```

iprogscod: accepti

* PROGRAM: ACCEPTI
* CALCULATES CEILING RATIOS (Rc), % ACCEPTABLE, and P-VALUE
* COMMAND LINE: accepti [COST] [SEcost] [EFFECT] [SEeffect] [CORR] [DOF]
  ** The 6 arguments are all numbers
  ** `1' difference in costs
  ** `2' SE diff costs
  ** `3' difference in effects
  ** `4' SE diff effects
  ** `5' correlation of differences
  ** `6' degrees of freedom

Alternative command lines (e.g., for automated calculation):

```
ipinputs [cost] [effect] [group] [,if]
local a=r(meanc)
local b=r(sec)
local c=r(meanq)
local d=r(seq)
local e=r(rho)
local f=r(dof)
accepti `a' `b' `c' `d' `e' `f'
```

* Saved Results
* r(accmat)
Stata Programs, accepti

. accepti 22 106.85 .0417 .0184 -.2403 494

<table>
<thead>
<tr>
<th>W</th>
<th>% Accept</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>-</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>-6308</td>
<td>0.01940</td>
<td>0.0388</td>
</tr>
<tr>
<td>-5536</td>
<td>0.02500</td>
<td>0.0500</td>
</tr>
<tr>
<td>-5118</td>
<td>0.02940</td>
<td>0.0588</td>
</tr>
<tr>
<td>-</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>209</td>
<td>0.45100</td>
<td>0.9020</td>
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<td>527</td>
<td>0.49991</td>
<td>0.9998</td>
</tr>
<tr>
<td>857</td>
<td>0.54892</td>
<td>0.9022</td>
</tr>
<tr>
<td>-</td>
<td>.</td>
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</tr>
<tr>
<td>15083</td>
<td>0.97060</td>
<td>0.0588</td>
</tr>
<tr>
<td>18229</td>
<td>0.97500</td>
<td>0.0500</td>
</tr>
<tr>
<td>26931</td>
<td>0.98060</td>
<td>0.0388</td>
</tr>
<tr>
<td>-</td>
<td>.</td>
<td>.</td>
</tr>
</tbody>
</table>

Stata Programs, accepti (cont.)

. return list

matrices:
  r(accmat) : 104 x 3

To view r(accmat):  matrix list r(accmat)
To access the data in r(accmat):
  First, create a new matrix:  matrix [name]=r(accmat)
  Second, transform the new matrix into a dataset (svmat)
  or assign elements to scalars or localize them (scalar
  sname="name"[1,1] OR local lname="name"[3,4])

Acceptability Curve

[Graph of Acceptability Curve]
Graphing in Stata

```stata
. quietly accepti 22 106.85 .0417 .0184 -.2403 494
. matrix matrix=r(accmat)
. preserve
. drop _all
. svmat matrix
number of observations will be reset to 108
Press any key to continue, or Break to abort
obs was 0, now 108
. ren matrix1 wtp
. ren matrix2 accept
. gen lh=0.025
. gen uh=0.975
. twoway line accept lh uh wtp if wtp>=0&wtp<100000,
yline(0) xline(0)
. restore
```

Resulting Stata Graph

Pick another pair of cost / effect estimates and calculate the acceptability curve
Overview of Patterns of Results

PATTERN 1
One cannot be confident the two therapies differ from one another
One cannot be confident the more effective therapy is not good value
One can be confident the more effective therapy is good value

PATTERN 2
One cannot be confident the two therapies differ from one another
One can be confident that one of the therapies is good value

PATTERN 3
One cannot be confident the two therapies differ from one another

When are the Different Patterns Observed?
• Pattern 1 is observed when the CI for effectiveness ($\Delta E \pm t_{\alpha/2} \frac{s_E}{\sqrt{n}}$) excludes 0 (i.e., the difference in effect is statistically significant)
  – Equivalent to the denominator of the Fieller's theorem equation being positive: $\Delta^2 - t_{\alpha/2}^2 \frac{s_Y}{\sqrt{n}}^2 > 0$
• Pattern 2 is observed when the CI for effectiveness includes 0 (i.e., the denominator of Fieller's theorem is 0 or negative) and when the expression in parentheses in the numerator of Fieller's theorem -- $|M^2 - NO|$ -- is $> 0$
• Pattern 3 is observed when the expression in parentheses in the numerator of Fieller's theorem -- $|M^2 - NO|$ -- is negative

Defining the Boundaries Between the Patterns
• Pattern 1 (denominator $> 0$):
  $\frac{\Delta E}{s_E} > t_{\alpha/2}$
• Pattern 2 (denominator $\leq 0$; rooted term $> 0$):
  $\frac{\Delta E}{s_E} \leq t_{\alpha/2} \leq \frac{\sqrt{\Delta E^2 - \left( \frac{R + y s_Y}{s_E} \frac{1}{\sqrt{1 - s_E^2}} \right)}}{s_E}$
• Pattern 3 (rooted term $< 0$):
  $t_{\alpha/2} < \frac{\sqrt{\Delta E^2 - \left( \frac{R + y s_Y}{s_E} \frac{1}{\sqrt{1 - s_E^2}} \right)}}{s_E}$
ciboundi

- Defines the t-statistics and p-values that form the boundaries between the 3 patterns of results for any experiment

* PROGRAM: CIBOUNDI
* DEFINES T-STATISTICS AND CI THAT FORM BOUNDARIES BETWEEN PATTERNS 1, 2, AND 3
* COMMAND LINE: ciboundi [COST] [SEcost] [EFFECT] [SEeffect] [CORR] [DOF]

** The 6 arguments are all numbers
** '1' difference in costs
** '2' SE diff costs
** '3' difference in effects
** '4' SE diff effects
** '5' correlation of differences
** '6' degrees of freedom

iprogsdoc: ciboundi (cont.)

Alternative command lines (e.g., for automated calculation):
iprops [cost] [effect] [group] [...]
l当地 a=r(meanc)
l当地 b=r(sec)
l当地 c=r(meanq)
l当地 d=r(seq)
l当地 e=r(rho)
l当地 f=r(dof)
ciboundi `a' `b' `c' `d' `e' `f'

* Saved Results
  * tscore1_2
  * tscore2_3
  * tfl1_2
  * tfl2_3
  * tscore1_2
  * tscore2_3
  * lastCI
  * f2

16
Stata Programs, ciboundi

. ciboundi 88 103.26 .0408 .0182 -.2545 494

T-scores and CI that define boundaries between patterns 1, 2, and 3

Pattern 1/2 boundary

T-score for 1/2 boundary: 2.241758
Boundary CI: 97.457987 %
Approximate limits at boundary
    Lower limit: -3819
    Upper limit: 1.199e+17

Pattern 2/3 boundary

T-score for last definable CI: 2.6813937
Last definable CI: 99.242308 %
Upper and lower limits, last definable CI:
    Lower limit: -9805

Boundaries Between the Patterns of Results

<table>
<thead>
<tr>
<th>Confidence Level</th>
<th>Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>97.45% CI</td>
<td>-3818 to 6,593,606</td>
</tr>
<tr>
<td>97.4579% CI</td>
<td>-3824 to 1.916e+14</td>
</tr>
<tr>
<td>97.46% CI</td>
<td>-3825 to -26,109,116</td>
</tr>
<tr>
<td>99.24% CI</td>
<td>-9319 to -10,333</td>
</tr>
<tr>
<td>99.24% CI</td>
<td>-9,805</td>
</tr>
<tr>
<td>99.25% CI</td>
<td>Undefined</td>
</tr>
</tbody>
</table>
Pick another pair of cost/effect estimates and calculate the boundaries between the patterns.

**iprogsdoc: ipinputs**

* PROGRAM: IPINPUTS
* USES T-TESTS TO CALCULATES INPUTS USED WITH
  * CIBOUNDI, FIELLERI, ACCEPTI, AND NMBI
* Calculated inputs include:
  * Difference in cost and SE
  * Difference in effect and SE
  * Correlation of difference in cost and effect
* COMMAND LINE: ipinputs [COST] [EFFECT] [GROUP] [if]
* The 3 arguments are all names of variables
  ** `1` Name of cost variable
  ** `2` Name of effect variable
  ** `3` Name of 0/1 treatment variable

**iprogsdoc: ipinputs (cont.)**

* Saved Results
  * r(mean)
  * r(se)
  * r(meanq)
  * r(seq)
  * r(rho)
  * r(dof)
Summary Statistics

Difference in cost:              25
SE, difference in cost:          124.43806
Difference in effect:            .04245908
SE, difference in effect:        .01889562
Correlation of differences:      -.27811377
Degrees of freedom:              498

scalars:

r(mean_c) =  25
r(sec) =  124.43806
r(mean_q) =  .042459
r(seq) =  .018896
r(rho) =  -.278114
r(dof) =  498

Cost-Effectiveness Analysis

Point Estimate:                  589
Quadrant:                        NE
Fieller 95 % Confidence Interval
  Lower limit :                  -6068
  Upper limit:                   22965
Nonparametric Methods

bsceapros.do
• Contains 4 programs related to sampling uncertainty and a very basic program for estimation of inputs by use of t-tests
  – bscier: Calculates Fieller’s theorem method CI for CER
  – bsnmb: Calculates NMB point estimates, CI, and p-values
  – bsaccept: Calculates % acceptable and p-values

bscier
. quietly do bsceapros
. use bsmvpred
. bscier pglmigcd pglmigqd .95
Bootstrap percentile 95 % Confidence Interval
  Lower limit (quadrant): -5395 ( 4 )
  Upper limit (quadrant): 18391 ( 1 )
  Density omitted by:
    Lower limit: 2.7 %
    Upper limit: 2.6 %
  Fraction of density uniquely excluded: 5 %
  Fraction of density excluded, wedge interpretation: 5 % (cont.)
bscicr (cont.)

Bootstrap acceptability 95% Confidence Interval

Lower limit:    5604
Upper limit:    26390
Density omitted by:
  Lower limit:  2.5 %
  Upper limit:  2.5 %
Fraction of density
  uniquely excluded:  4.7 %

Data for Immediate Form programs

Difference in costs:  22.061692
SE, difference in costs:  106.84924
Difference in effects: .04134237
SE, difference in effects:  .01836383
Correlation of differences: - .24031415

Pick another pair of cost / effect estimates and calculate the bootstrapped confidence interval

Bootstrap Intervals

<table>
<thead>
<tr>
<th></th>
<th>&quot;Percentile&quot;</th>
<th>&quot;Acceptability&quot;</th>
</tr>
</thead>
<tbody>
<tr>
<td>pglmpqcd</td>
<td>-5322 to 16,885</td>
<td>-5501 to 17,420</td>
</tr>
<tr>
<td>pglmpqcd</td>
<td>-2005 to 33,702</td>
<td>-2011 to 35,545</td>
</tr>
<tr>
<td>pglmpqcd</td>
<td>-1556 to 41,054</td>
<td>-1576 to 41,491</td>
</tr>
<tr>
<td>pglmpqcd</td>
<td>-2797 to 29,343</td>
<td>-2803 to 31,546</td>
</tr>
<tr>
<td>pglmpqcd</td>
<td>-5269 to 16,557</td>
<td>-5434 to 17,374</td>
</tr>
<tr>
<td>pglmpqcd</td>
<td>-1990 to 31,186</td>
<td>-2000 to 31,911</td>
</tr>
<tr>
<td>pglmpqcd</td>
<td>-1578 to 35,299</td>
<td>-1583 to 37,553</td>
</tr>
<tr>
<td>pglmpqcd</td>
<td>-2824 to 26,281</td>
<td>-2830 to 26,027</td>
</tr>
</tbody>
</table>
Stata Programs, bsnmb

. bsnmb pglmigcd pglmigqd .95

<table>
<thead>
<tr>
<th>NMB limit</th>
<th>Lower</th>
<th>Upper</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>-6407</td>
<td>-286</td>
<td>-556</td>
<td>0.0386</td>
</tr>
<tr>
<td>-5197</td>
<td>-236</td>
<td>-480</td>
<td>0.0554</td>
</tr>
<tr>
<td>-4526</td>
<td>-208</td>
<td>-442</td>
<td>0.0814</td>
</tr>
<tr>
<td>189</td>
<td>-13</td>
<td>-218</td>
<td>0.9046</td>
</tr>
<tr>
<td>509</td>
<td>0</td>
<td>-212</td>
<td>0.9980</td>
</tr>
<tr>
<td>841</td>
<td>14</td>
<td>-202</td>
<td>0.9020</td>
</tr>
</tbody>
</table>

NMB Graph

Stata Programs, bsaccept

. bsaccept pglmigcd pglmigqd .95

<table>
<thead>
<tr>
<th>% Accept</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>-6407</td>
<td>0.01933</td>
</tr>
<tr>
<td>-5197</td>
<td>0.02767</td>
</tr>
<tr>
<td>-4526</td>
<td>0.04067</td>
</tr>
<tr>
<td>189</td>
<td>0.45233</td>
</tr>
<tr>
<td>509</td>
<td>0.50100</td>
</tr>
<tr>
<td>841</td>
<td>0.54900</td>
</tr>
<tr>
<td>11472</td>
<td>0.96133</td>
</tr>
<tr>
<td>15239</td>
<td>0.97167</td>
</tr>
<tr>
<td>27378</td>
<td>0.97900</td>
</tr>
</tbody>
</table>
Patterns 2 and 3

- Use the fielleri program to calculate the 95% CI for the following 3 sets of experimental results:
  - 35 777.5 0.04 0.0224 0.706 498 0.95
  - 1985 1252.1 0.0001 0.0089 0.976 498 0.95
  - 400 325 0.02 0.02 0.25 498 0.95
- Look at the NMB and acceptability curves
Cost-Effectiveness Analysis

Point Estimate: 875
Quadrant: NE

Fieller 95% Confidence Interval
Lower limit: 245232
Upper limit: 28230

Confidence Statements:
For WTP < 28230 AND for WTP > 245232, we can't be 95% confident that the 2 therapies differ in value;
For WTP >= 28230 and <= 245232:
  IF 875 <= WTP
  We can be 95% confident that the therapy with the larger point estimate for effect represents good value compared with the alternative;
  IF 875 > WTP
  We can be 95% confident that the therapy with the larger point estimate for effect represents bad value compared with the alternative.

Fieller’s Intervals

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Confidence limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>35 777.5 .04 .0224 .706 498 .95</td>
<td>PE: 875</td>
</tr>
<tr>
<td>1985 1252.1 .0001 .0089 .976 498 .95</td>
<td>PE: 1.985e+7</td>
</tr>
<tr>
<td>400 325 .02 .02 .25 498 .95</td>
<td>PE: 20,000</td>
</tr>
</tbody>
</table>

Summary

- We’ve provided you with programs to calculate parametric and nonparametric CI for CER, CI for NMB, and acceptability curves.
- While we often use a bootstrap to estimate SEs (from multiplicative models or when we combine the results from separate models used to predict intervention cost and other medical cost), we usually calculate CI for CER by use of fielleri and not by use of bscicer.
- Once we decide to calculate and report measures of sampling uncertainty, we should use both in our recommendations for adoption (currently many authors report CI or acceptability curves, but then ignore them when they make adoption recommendations).