Stata 統計軟體教育訓練課程

Network Meta-analysis

醫學研究部 基礎醫學科 生統小組：陳韻伃 博士

授課日期：112年4月27日

安裝Network Meta-analysis相關套件

***從以下開始安裝**

*** MA/NMA**

net from "http://www.homepages.ucl.ac.uk/~rmjwiww/stata/meta/"
net install network.pkg, replace
net install mvmeta.pkg, replace

***Network plot**

ssc install netplot
net from "https://clinicalepidemio.fr/Stata"
net install network_graphs.pkg, replace
net install metamiss2.pkg, replace

help network graph

```
SJ-15-4 st0411  . Visualizing assumptions and results in network meta-analysis
        . . . . . . . . . . . . . . . . . . . . . . . . A. Chaimani and G. Salanti
        (help network graphs, clusterank, ifplot, intervalplot, mdsrank,
        netfunnel, netleague, netweight, networkplot, sucra if installed)
        Q4/15   SJ 15(4):905--950
        provides a suite of commands with graphical tools to facilitate
        the understanding of data, the evaluation of assumptions, and
        the interpretation of findings from network meta-analysis
```

*** SE code**

net from "http://www.stata-journal.com/software/sj10-4/"
net install st0043_2.pkg, replace

Preparing for Analysis: 先設定長檔案

use “D:\助理研究員\中榮醫研部-生統小組\全院教育課程規劃-2022oct\112年生統課程規劃\護理部-Stata\Stata-Network meta_new\long_data.dta"

network setup d n, studyvar (study) trtvar(trt) ref(A)

Data Editor (Browse) - [long_data]

File Edit View Data Tools

study[1] Alshryda2013

	study	d	n	trt
1	Alshryda2013	10	80	C
2	Alshryda2013	26	81	A
3	Barrachina2016	8	35	E
4	Barrachina2016	4	36	B
5	Barrachina2016	14	37	A
6	Benoni2000	9	20	B
7	Benoni2000	15	19	A
8	Benoni2001	4	18	E

d: number of events
n: total sample size
studyvar → study: variable of study title
trtvar → trt: variable of treatment
ref: A or Placebo

先設定檔案 for Network Meta-analysis

network setup d n, studyvar (study) trtvar(trt) ref(A)

A	B	C	D	E
Placebo	IV_single use	IV_double use	Topical_use	Combination_IV_and_topical

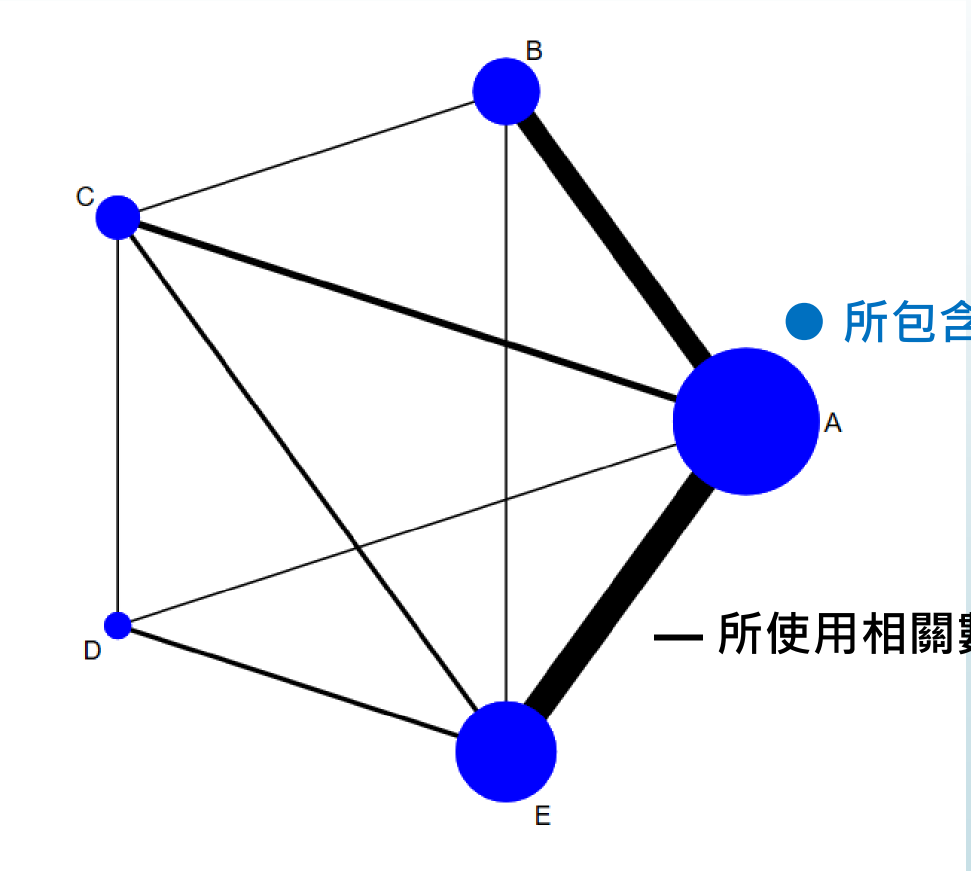
```
. network setup d n, studyvar (study) trtvar(trt) ref(A)
Treatments used
   A (reference):                        A
   B:                                    B
   C:                                    C
   D:                                    D
   E:                                    E

Measure                                  Log odds ratio

Studies
   ID variable:                          study
   Number dropped:                       1
   Number used:                          24
   IDs with zero cells:                  `"Xie2016"' `"Yamasaki2004"'
   - count added to all their cells:     .5
   IDs with augmented reference arm:     `"North2016"' `"Xie2016"'
   - observations added:                 0.00001
   - mean in augmented observations:     study-specific mean

Network information
   Components:                           1 (connected)
   D.f. for inconsistency:               8
   D.f. for heterogeneity:               16

Current data
   Data format:                          augmented
   Design variable:                      _design
   Estimate variables:                   _y*
   Variance variables:                   _S*
   Command to list the data:             list study _y* _S*, noo sepby(_design)
```

study[1] Alshryda2013

	study	dA	nA	dB	nB	dC	nC	dD	nD	dE	nE	_design	_y_B	_y_C	_y_D	_y_E	_S_B_B
1	Alshryda2013	26	81	.	.	10	80	.	.	.	.	A C	.	-1.1966735	.	.	.
2	Barrachina2016	14	37	4	36	.	.	.	.	8	35	A B E	-1.5830047	.	.	-.71995844	.39615683
3	Benoni2000	15	19	9	20	.	.	.	.	.	.	A B	-1.5224265	.	.	.	.51868687
4	Benoni2001	8	20	.	.	.	.	.	.	4	18	A E	.	.	.	-.84729786	.
5	Claeys2007	6	20	.	.	.	.	.	.	1	20	A E	.	.	.	-2.0971411	.
6	Ekb2000	1	20	1	20	.	.	.	.	.	.	A B	0	.	.	.	2.1052632
7	Fraval2017	6	51	1	50	.	.	.	.	.	.	A B	-1.8769173	.	.	.	1.2092971
8	Garneti2004	14	25	.	.	.	.	.	.	16	25	A E	.	.	.	.33420209	.
9	Hsu2015	9	30	2	30	.	.	.	.	.	.	A B	-1.7917595	.	.	.	.69444444
10	Husted2003	7	20	2	20	.	.	.	.	.	.	A B	-1.5781854	.	.	.	.77533578
11	Johansson2005	23	53	.	.	.	.	.	.	8	47	A E	.	.	.	-1.3184169	.

Step 1: Generating Network Geometry

- Network plot: 輸入指令 **network map**



● 所包含研究的數量

— 所使用相關數據的數量

Step 2: Testing for Inconsistency

- Global inconsistency Test 輸入指令 **network meta inconsistency**

```
Multivariate meta-analysis
Variance-covariance matrix = proportional .5*I(4)+.5*J(4,4,1)
Method = reml                                Number of dimensions    =     4
Restricted log likelihood = -34.684006       Number of observations  =    24
```

	Coefficient	Std. err.	z	P>|z|	[95% conf. interval]	
_y_B						
des_ABE	-.2177834	.6846	-0.32	0.750	-1.559575	1.124008
_cons	-1.365221	.269296	-5.07	0.000	-1.893032	-.8374108
_y_C						
des_ACE	-.6561662	.6028711	-1.09	0.276	-1.837772	.5254395
des_BC	.1947812	.6700162	0.29	0.771	-1.118426	1.507989
des_CDE	.6167358	.974232	0.63	0.527	-1.292724	2.526195
_cons	-1.070454	.3665995	-2.92	0.004	-1.788976	-.3519321
_y_D						
des_CDE	.6929186	1.922747	0.36	0.719	-3.075596	4.461433
_cons	-3.402272	1.051331	-3.24	0.001	-5.462844	-1.3417
_y_E						
des_ACE	-.9961905	.7114154	-1.40	0.161	-2.390539	.3981581
des_ADE	-.4487215	.7145929	-0.63	0.530	-1.849298	.9518549
des_AE	-.2528214	.5704532	-0.44	0.658	-1.370889	.8652463
_cons	-.7199583	.5262546	-1.37	0.171	-1.751398	.3114817

Estimated between-studies SDs and correlation matrix

	SD	_y_B	_y_C	_y_D	_y_E
_y_B	3.083e-07	1	.	.	.
_y_C	3.083e-07	.5	1	.	.
_y_D	3.083e-07	.5	.5	1	.
_y_E	3.083e-07	.5	.5	.5	1

Estimated between-studies SDs and correlation matrix

	SD	_y_B	_y_C	_y_D	_y_E
_y_B	3.083e-07	1	.	.	.
_y_C	3.083e-07	.5	1	.	.
_y_D	3.083e-07	.5	.5	1	.
_y_E	3.083e-07	.5	.5	.5	1

```
Testing for inconsistency:
 ( 1)  [_y_B]des_ABE = 0
 ( 2)  [_y_E]des_ACE = 0
 ( 3)  [_y_C]des_ACE = 0
 ( 4)  [_y_E]des_ADE = 0
 ( 5)  [_y_E]des_AE = 0
 ( 6)  [_y_C]des_BC = 0
 ( 7)  [_y_C]des_CDE = 0
 ( 8)  [_y_D]des_CDE = 0

           chi2(  8) =    4.09
         Prob > chi2 =    0.8492
```

無法拒絕虛無假說

一致性 consistency 的水準可接受

Step 2: Testing for Inconsistency

- Local inconsistency Test 輸入指令 **network sidesplit all**

```
. network sidesplit all
```

無法拒絕虛無假說
一致性 consistency 的水準可

Side	Direct Coef.	Direct Std. Err.	Indirect Coef.	Indirect Std. Err.	Difference Coef.	Difference Std. Err.	P>|z|
A B	-1.387832	.246631	-1.834588	.5000808	.4467555	.5475861	0.415
A C	-1.346768	.2878734	-.7355726	.4132222	-.6111958	.4901931	0.212
A D	-3.420298	.939617	-3.203182	1.005883	-.2171159	.9367965	0.817
A E	-1.08404	.1738511	-.7891631	.6352852	-.2948771	.6513169	0.651
B C	.4895483	.4919413	.2233391	.3632928	.2662092	.6115455	0.663
B E	.8919491	.655003	.3065194	.2968191	.5854297	.7146861	0.413
C D	-2.534345	1.25485	-2.009367	.9639263	-.5249778	1.320922	0.691
C E	-.0989284	.4620928	.1914716	.3474008	-.2904	.5783735	0.616
D E *	2.152297	.8813737	2.593058	1.087671	-.4407617	.8966076	0.623

Because inconsistency was found to be absent in both global and local tests, the consistency assumption was accepted

Step 3: Creating Plots and League Table of Effect Size by Treatment

➨先設定 network meta consistency

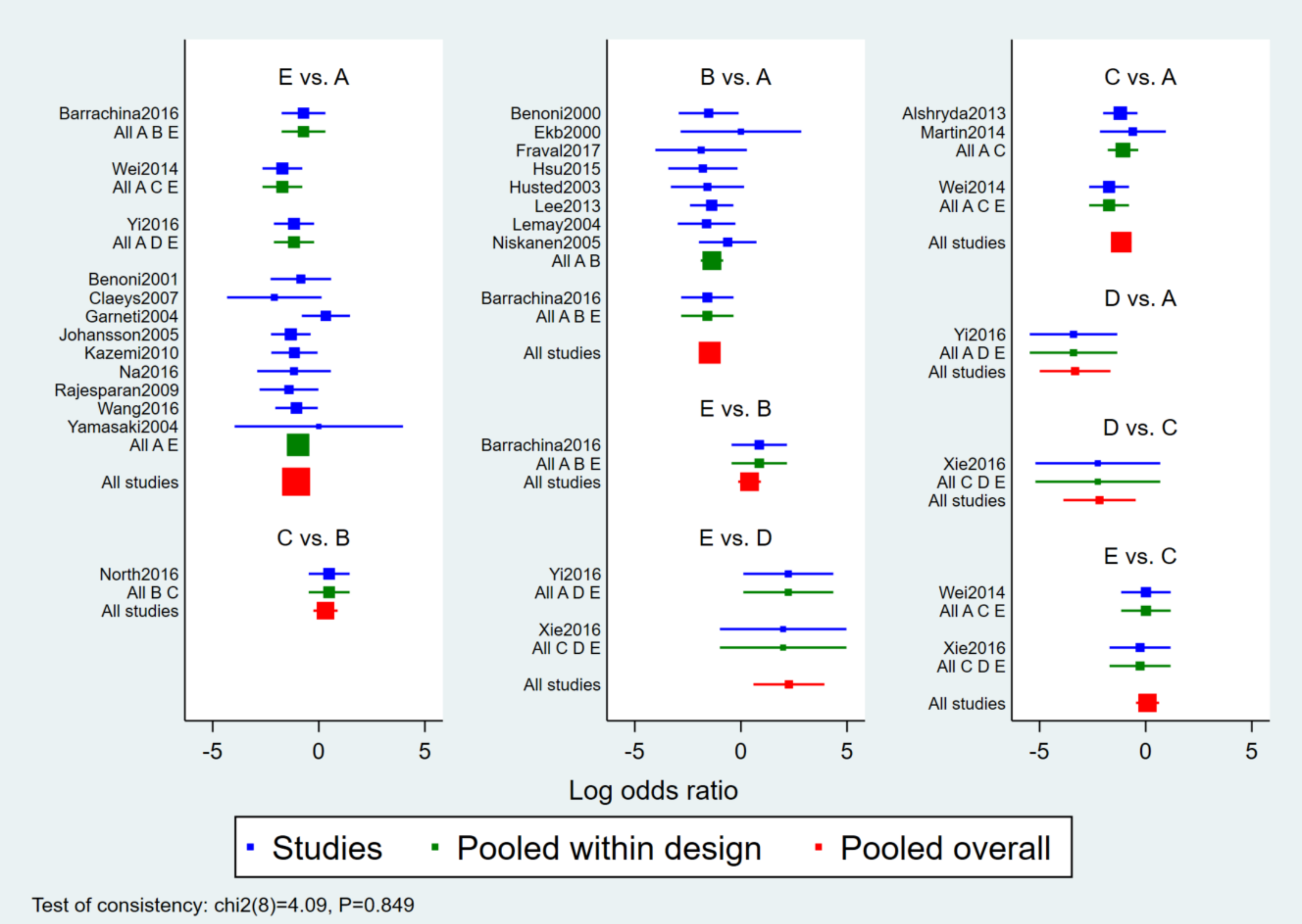
For network forest

```
. network meta consistency
Command is: mvmeta _y _S  , bscovariance(exch 0.5) longparm suppress(uv mm)  vars(_y_B _y_C _y_D _y_E)
Note: using method reml
Note: using variables _y_B _y_C _y_D _y_E
Note: 24 observations on 4 variables
Note: variance-covariance matrix is proportional to .5*I(4)+.5*J(4,4,1)

initial:       log likelihood = -49.494181
rescale:       log likelihood = -49.494181
rescale eq:    log likelihood = -41.242314
Iteration 0:   log likelihood = -41.242314
Iteration 1:   log likelihood = -41.138072
Iteration 2:   log likelihood =  -41.13807

Multivariate meta-analysis
Variance-covariance matrix = proportional .5*I(4)+.5*J(4,4,1)
Method = reml                                   Number of dimensions     =      4
Restricted log likelihood = -41.13807           Number of observations   =     24

------------------------------------------------------------------------------
             | Coefficient  Std. err.      z    P>|z|     [95% conf. interval]
-------------+----------------------------------------------------------------
_y_B         |
       _cons |  -1.470223   .2250083    -6.53   0.000    -1.911231   -1.029215
-------------+----------------------------------------------------------------
_y_C         |
       _cons |  -1.152938   .2422897    -4.76   0.000    -1.627817   -.6780585
-------------+----------------------------------------------------------------
_y_D         |
       _cons |  -3.327687   .8504168    -3.91   0.000    -4.994473   -1.660901
-------------+----------------------------------------------------------------
_y_E         |
       _cons |  -1.066367   .1694118    -6.29   0.000    -1.398408   -.7343258
------------------------------------------------------------------------------

Estimated between-studies SDs and correlation matrix
----------------------------------------------------

             SD         _y_B        _y_C        _y_D        _y_E
_y_B  2.246e-07            1           .           .           .
_y_C  2.246e-07           .5           1           .           .
_y_D  2.246e-07           .5          .5           1           .
_y_E  2.246e-07           .5          .5          .5           1
----------------------------------------------------
```

Step 3: Creating Plots and League Table of Effect Size by Treatment

- **Network forest plot (NFP) 輸入：**

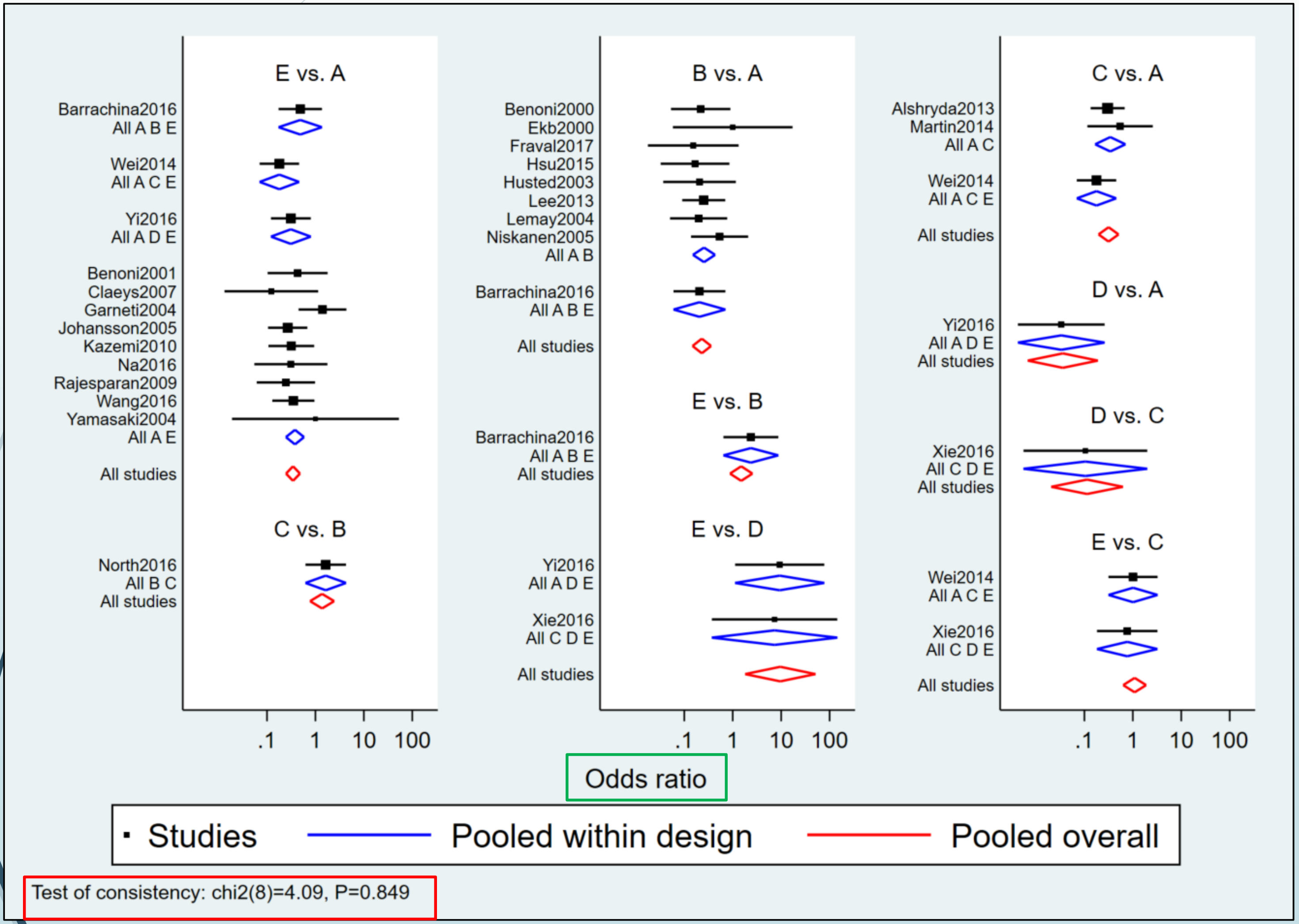
  network forest



Step 3: Creating Plots and League Table of Effect Size by Treatment

- **Network forest plot (NFP)　輸入：**

network forest, msize (*0.15) diamond eform xlabel (0.1 1 10 100) colors (black blue red) list



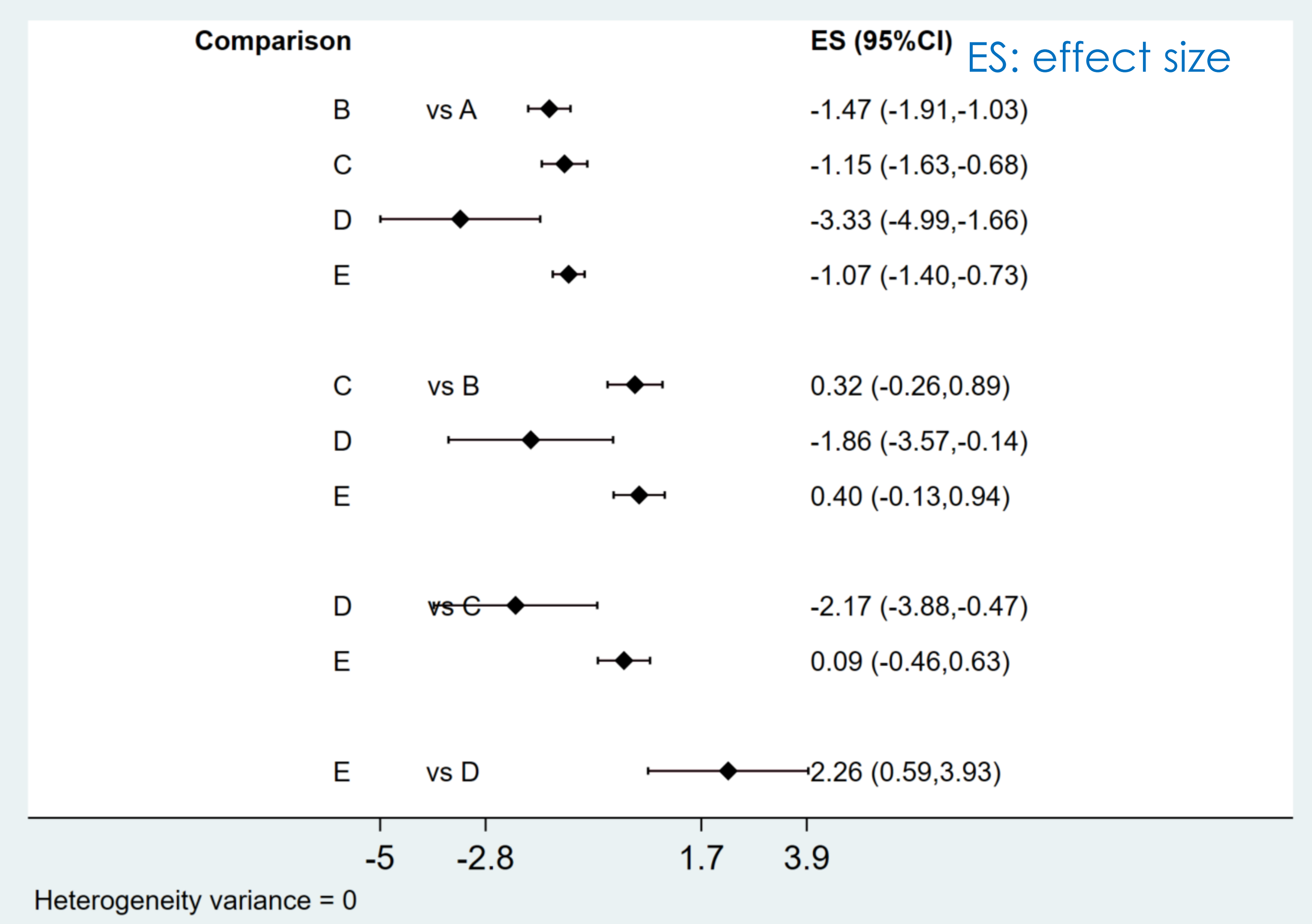
Global test on inconsistency

<diamond> uses a diamond shape to show summary effect sizes

<eform> generates transformed indices to make it easy to interpret the forest plot

Step 3: Creating Plots and League Table of Effect Size by Treatment

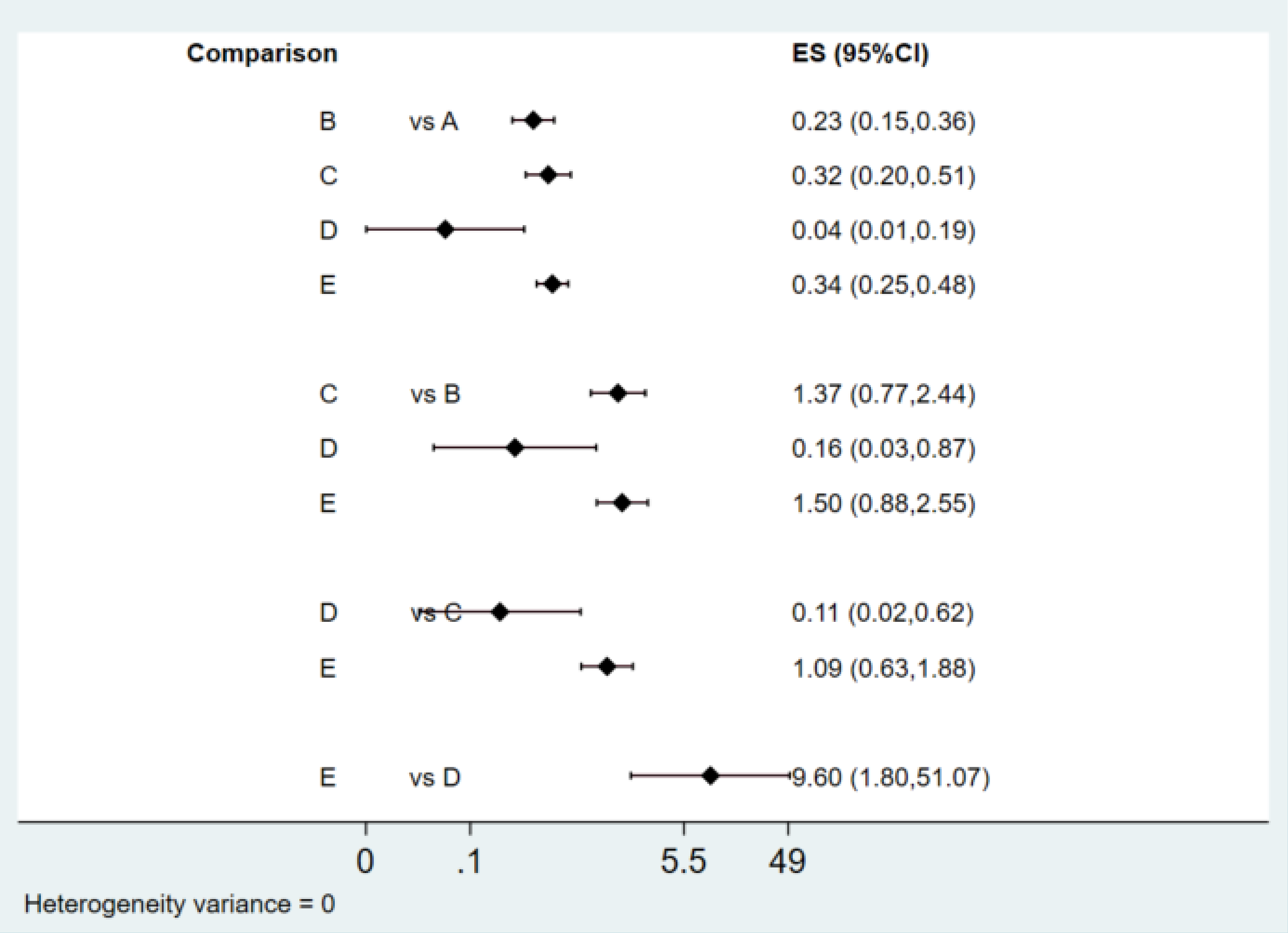
- Network forest plot (NFP) 輸入：
  intervalplot



Step 3: Creating Plots and League Table of Effect Size by Treatment

- Network forest plot (NFP) and interval plot 輸入：

  intervalplot, eform



ES: effect size

<eform> generates transformed indices to make it easy to interpret the forest plot

Step 3: Creating Plots and League Table of Effect Size by Treatment

- Network forest plot (NFP) and interval plot 輸入：

intervalplot, eform null (1) labels (Placebo IV_single IV_double Topical Combination) margin (10 8 5 10) textsize (2) xlabel (0.01 0.1 1 10)

intervalplot, eform null (1) labels (Placebo IV_single IV_double Topical Combination) separate margin (10 8 5 10) textsize (2) xlabel (0.01 0.1 1 10)

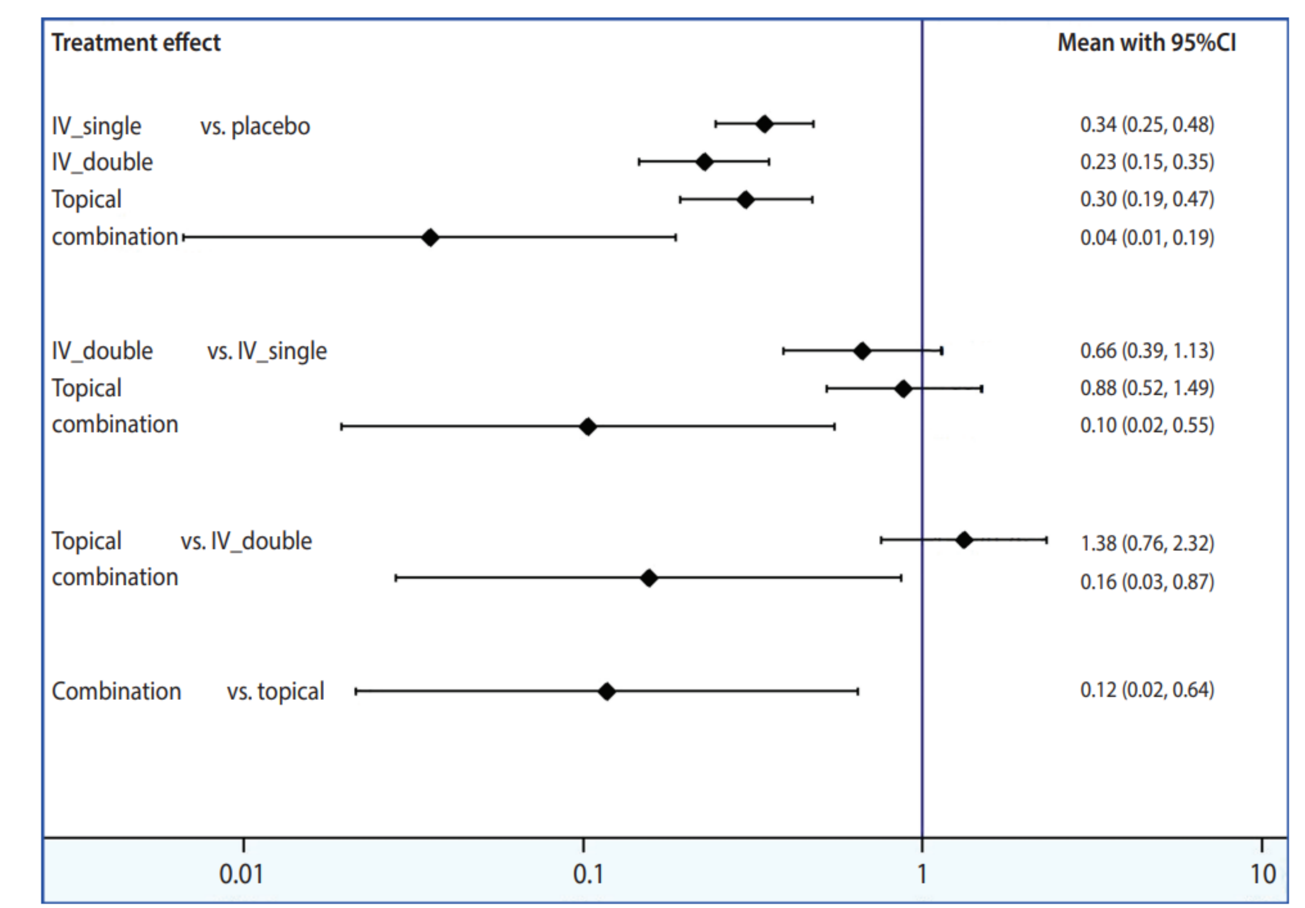


Figure 5. Interval plot. CI, confidence interval.

<eform> generates transformed indices to make it easy to interpret the forest plot

<separate> and < margin> set the ranges to generate easy-to-read plots, the values of which should be appropriately determined by the user

Step 4: Determining Relative Rankings of Treatments

- Identify superiority 輸入：

network rank min

```
. network rank min
Command is: mvmeta, noest pbest(min  in 1, zero id(study)  stripprefix(_y_) zeroname(A) rename(A = A, B = B, C = C, D = D, E = E))

Estimated probabilities (%) of each treatment having each rank
- assuming the minimum parameter is the best
- using 1000 draws
- allowing for parameter uncertainty
```

Rank	Treatment A	B	C	D	E
Best	0.0	1.4	0.4	98.1	0.1
2nd	0.0	81.2	12.5	1.1	5.2
3rd	0.0	13.4	51.3	0.2	35.1
4th	0.0	4.0	35.8	0.6	59.6
Worst	100.0	0.0	0.0	0.0	0.0

network rank max

```
. network rank max
Command is: mvmeta, noest pbest(max  in 1, zero id(study)  stripprefix(_y_) zeroname(A) rename(A = A, B = B, C = C, D = D, E = E))

Estimated probabilities (%) of each treatment having each rank
- assuming the maximum parameter is the best
- using 1000 draws
- allowing for parameter uncertainty
```

Rank	Treatment A	B	C	D	E
Best	100.0	0.0	0.0	0.0	0.0
2nd	0.0	3.0	33.7	0.3	63.0
3rd	0.0	13.3	54.2	0.3	32.2
4th	0.0	82.0	12.0	1.2	4.8
Worst	0.0	1.7	0.1	98.2	0.0

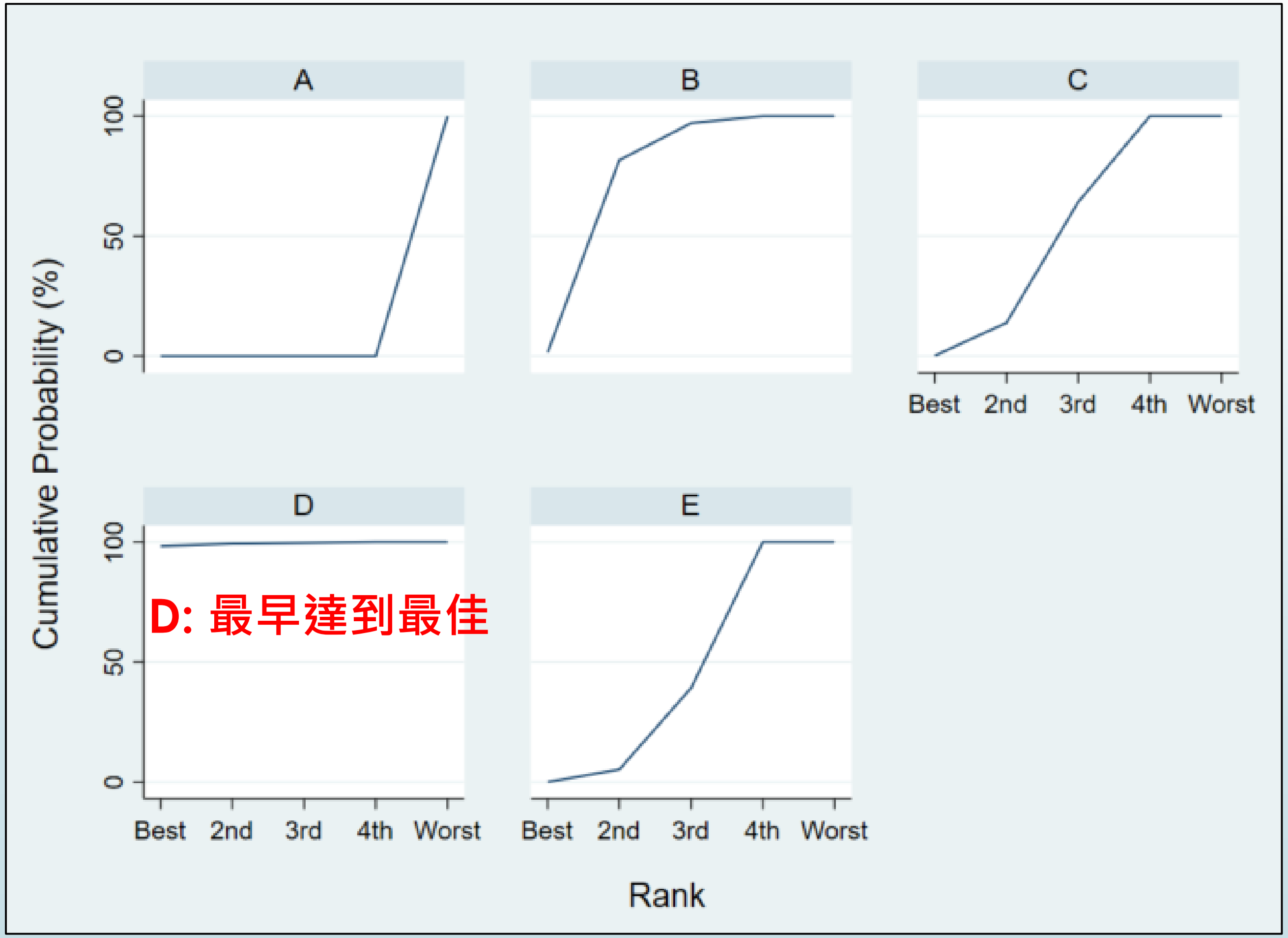
Step 4: Determining Relative Rankings of Treatments

- Identify superiority 輸入：

  network rank min, line cumulative xlabel (1/5) seed (10000) reps (10000) meanrank

```
Estimated probabilities (%) of each treatment hav
- assuming the minimum parameter is the best
- using 10000 draws
- allowing for parameter uncertainty
```

Rank	A	B	C	D	E
	Treatment				
Best	0.0	1.5	0.2	98.3	0.0
2nd	0.0	80.1	13.7	1.0	5.2
3rd	0.0	15.4	50.3	0.3	34.0
4th	0.0	3.0	35.8	0.4	60.8
Worst	100.0	0.0	0.0	0.0	0.0
MEAN RANK	5.0	2.2	3.2	1.0	3.6
SUCRA	0.0	0.7	0.4	1.0	0.4



SUCRA: Surface under the cumulative ranking → more precise estimation of cumulative ranking probabilities

Step 3: Creating Plots and League Table of Effect Size by Treatment
Step 5: Checking for Publication Bias

use "D:\助理研究員\中榮醫研部-生統小組\全院教育課程規劃-2022oct\112年生統課程規劃\護理部-Stata\Stata-Network meta_new\funnel plot.dta ", clear

- Comparative effect size (diff) and standard error (se) for each pair of treatment 輸入：

network forest, msize (*0.15) diamond eform xlabel (0.1 1 10 100) colors (black blue red) list

```
. network forest, msize (*0.15) diamond eform xlabel (0.1 1 10 100) colors (black blue red) list
Warning: inconsistency matrix of fitted values not found - forest plot will be incomplete
Listing of results extracted from current data and saved network meta-analyses:
```

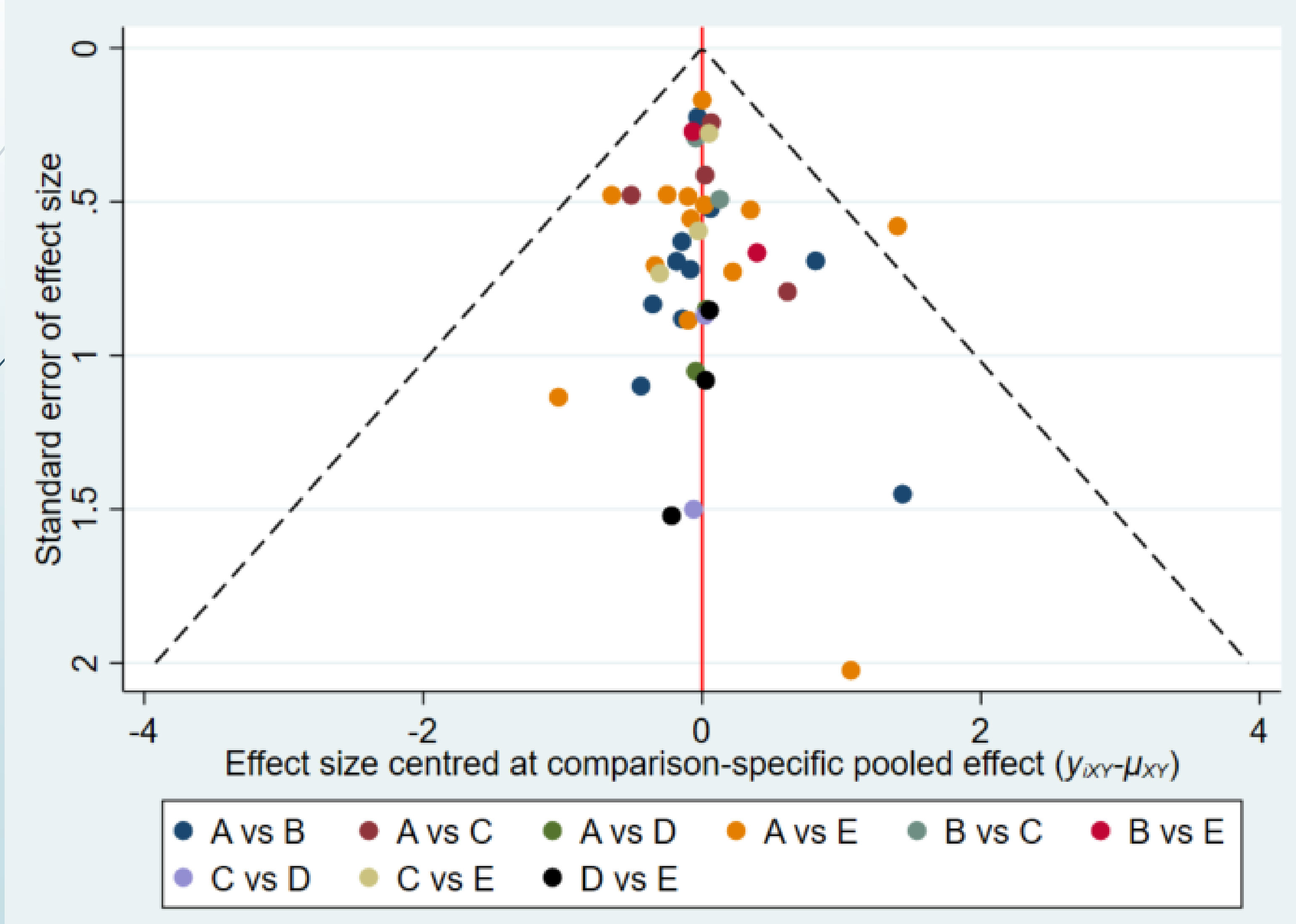
	t1	t2	design	type	studyvar	diff	se
1.	A	B	A B E	study	Barrachina2016	-1.5830047	.62940991
2.	A	B	A B	study	Benoni2000	-1.5224265	.72019919
3.	A	B	A B	study	Ekb2000	0	1.4509525
4.	A	B	A B	study	Fraval2017	-1.8769173	1.0996804
5.	A	B	A B	study	Hsu2015	-1.7917595	.83333333
6.	A	B	A B	study	Husted2003	-1.5781854	.88053153
7.	A	B	A B	study	Lee2013	-1.3783262	.52205333
8.	A	B	A B	study	Lemay2004	-1.6204877	.69403529
9.	A	B	A B	study	Niskanen2005	-.62415431	.69264847
10.	A	B		cons		-1.4702229	.22500835
11.	A	C	A C	study	Alshryda2013	-1.1966735	.41343569
12.	A	C	A C	study	Martin2014	-.6061358	.79296146
13.	A	C	A C E	study	Wei2014	-1.7266202	.47860044
14.	A	C		cons		-1.1529375	.24228968
15.	A	D	A D E	study	Yi2016	-3.4022721	1.0513314
16.	A	D		cons		-3.327687	.85041684
17.	A	E	A B E	study	Barrachina2016	-.71995844	.52625457
18.	A	E	A E	study	Benoni2001	-.84729786	.72784745
19.	A	E	A E	study	Claeys2007	-2.0971411	1.1361016
20.	A	E	A E	study	Garneti2004	.33420209	.57961088

Step 3: Creating Plots and League Table of Effect Size by Treatment

Step 5: Checking for Publication Bias

- **Network Funnel Plot 輸入：**

netfunnel diff se t1 t2, random bycomparison



生統小組：統計方法教育訓練

Thank you for listening