Safety of lumbar interbody fusion procedures for degenerative disc disease:

a network meta-analysis of prospective study

(Appendix)

Appendix

Appendix 1
Database and Search Strategy

Appendix 1
Database and search strategy

EMBASE:
('degenerative spinal disease' OR 'degenerative spine disease'/exp OR 'degenerative spine disease' OR 'degenerative disc disease'/exp OR 'degenerative disc disease' OR 'degenerative disc disorder' OR 'degenerative spine disorder' OR 'degenerative spine disorders' OR 'degenerative spinal disorder' OR 'degenerative spinal disorders' OR 'degenerative disc disorders' OR 'degenerative lumbar') AND (('posterior lumbar interbody fusion'/exp OR 'posterior lumbar interbody fusion' OR plif) AND ('transforaminal lumbar interbody fusion'/exp OR 'transforaminal lumbar interbody fusion' OR tlif) OR (('posterior lumbar interbody fusion'/exp OR 'posterior lumbar interbody fusion' OR plif) AND ('anterior lumbar interbody fusion'/exp OR 'anterior lumbar interbody fusion' OR alif)) OR (('transforaminal lumbar interbody fusion'/exp OR 'transforaminal lumbar interbody fusion' OR tlif) AND ('anterior lumbar interbody fusion'/exp OR 'anterior lumbar interbody fusion' OR alif)))

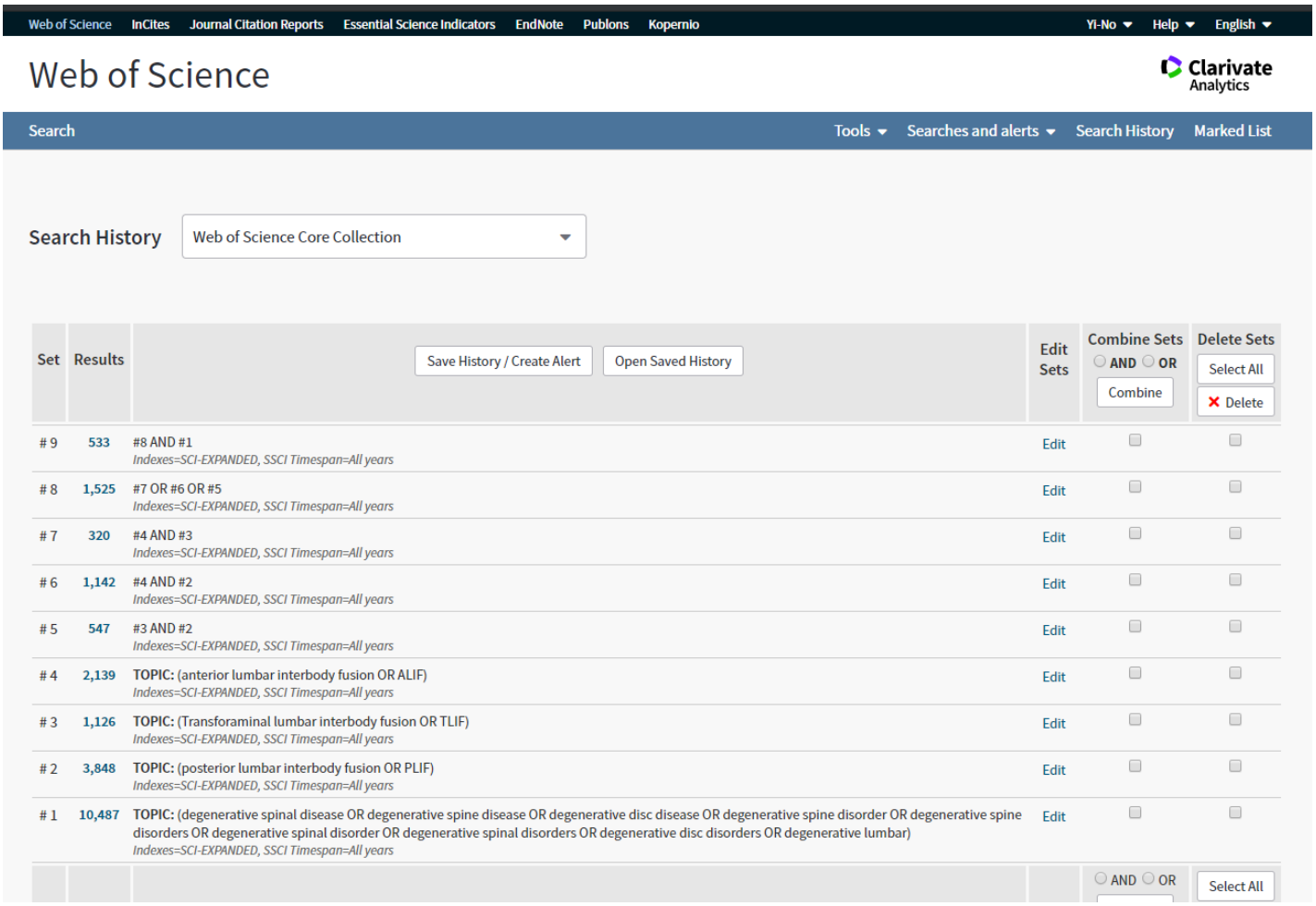
PubMed (including MEDLINE):
(((((((((degenerative spinal disease) OR degenerative spine disease) OR degenerative disc disease) OR degenerative spine disorder) OR degenerative spine disorders) OR degenerative spinal disorder) OR degenerative spinal disorders) OR degenerative disc disorders OR degenerative lumbar)) AND (((((((posterior lumbar interbody fusion) OR PLIF)) AND ((Transforaminal lumbar interbody fusion) OR TLIF))) OR ((((posterior lumbar interbody fusion) OR PLIF)) AND ((anterior lumbar interbody fusion) OR ALIF))) OR ((((Transforaminal lumbar interbody fusion) OR TLIF)) AND ((anterior lumbar interbody fusion) OR ALIF)))

Ovid Medline:

# ▲	Searches
1	degenerative spinal disease. af
2	degenerative spine disease. af
3	degenerative disc disease. af
4	degenerative disc disorder. af
5	degenerative spine disorder. af
6	degenerative spine disorders. af
7	degenerative spinal disorder. af
8	degenerative spinal disorders. af
9	degenerative disc disorders. af
10	degenerative lumbar. af
11	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 11
12	posterior lumbar interbody fusion. af
13	PLIF. af
14	12 or 13
15	Transforaminal lumbar interbody fusion. af
16	TLIF. af
17	15 or 16
18	anterior lumbar interbody fusion. af
19	ALIF. af
20	18 or 19
21	14 and 17
22	14 and 20
23	17 and 20
24	21 or 22 or 23
25	11 and 24

Appendix 1

Database and search strategy



Web of Science InCites Journal Citation Reports Essential Science Indicators EndNote Publons Kopernio — Yi-No — Help — English

Web of Science — Clarivate Analytics

Search — Tools — Searches and alerts — Search History — Marked List

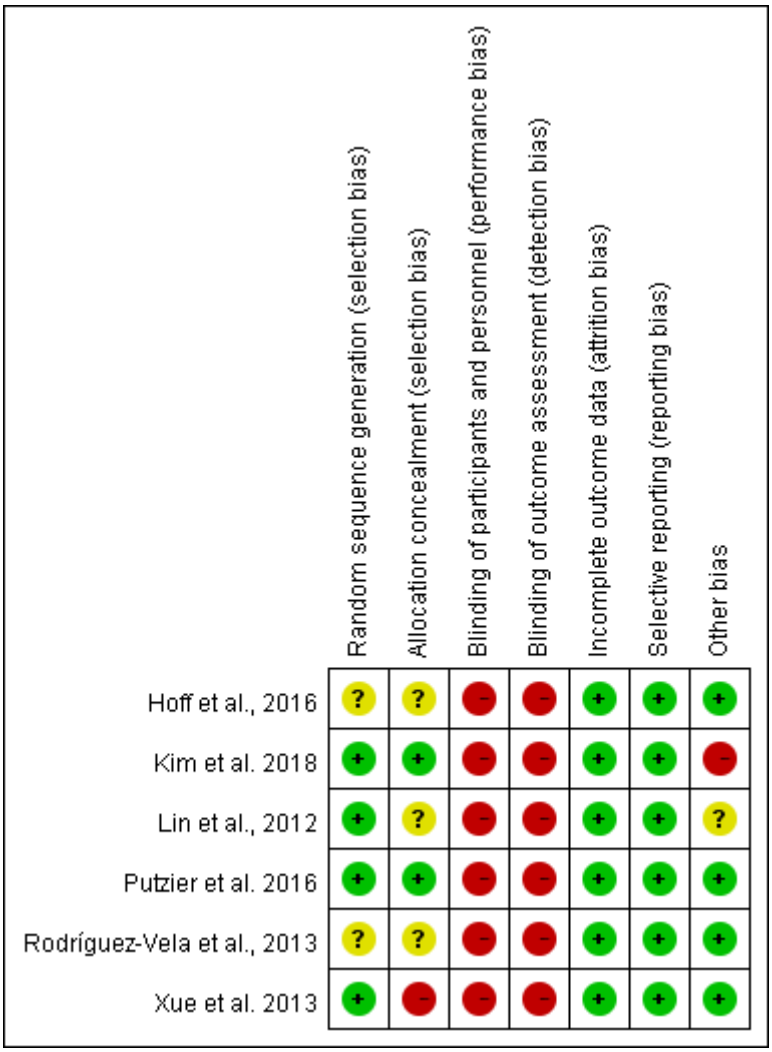
Search History — Web of Science Core Collection

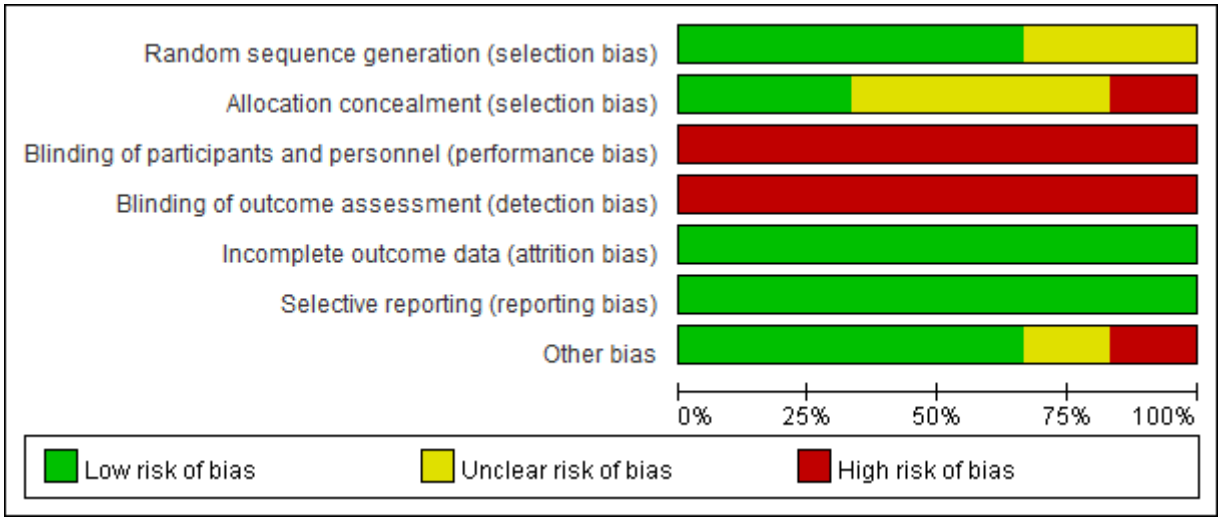
Set	Results	Save History / Create Alert / Open Saved History	Edit Sets	Combine Sets (AND / OR, Combine)	Delete Sets (Select All, Delete)
# 9	533	#8 AND #1 *Indexes=SCI-EXPANDED, SSCI Timespan=All years*	Edit		
# 8	1,525	#7 OR #6 OR #5 *Indexes=SCI-EXPANDED, SSCI Timespan=All years*	Edit		
# 7	320	#4 AND #3 *Indexes=SCI-EXPANDED, SSCI Timespan=All years*	Edit		
# 6	1,142	#4 AND #2 *Indexes=SCI-EXPANDED, SSCI Timespan=All years*	Edit		
# 5	547	#3 AND #2 *Indexes=SCI-EXPANDED, SSCI Timespan=All years*	Edit		
# 4	2,139	**TOPIC:** (anterior lumbar interbody fusion OR ALIF) *Indexes=SCI-EXPANDED, SSCI Timespan=All years*	Edit		
# 3	1,126	**TOPIC:** (Transforaminal lumbar interbody fusion OR TLIF) *Indexes=SCI-EXPANDED, SSCI Timespan=All years*	Edit		
# 2	3,848	**TOPIC:** (posterior lumbar interbody fusion OR PLIF) *Indexes=SCI-EXPANDED, SSCI Timespan=All years*	Edit		
# 1	10,487	**TOPIC:** (degenerative spinal disease OR degenerative spine disease OR degenerative disc disease OR degenerative spine disorder OR degenerative spine disorders OR degenerative spinal disorder OR degenerative spinal disorders OR degenerative disc disorders OR degenerative lumbar) *Indexes=SCI-EXPANDED, SSCI Timespan=All years*	Edit		
				AND / OR	Select All

Appendix 2
Risk of Bias Assessment

Appendix 2

Risk of bias assessment (randomized clinical trials)





Appendix 2

Risk of bias assessment (ROBINS-I)

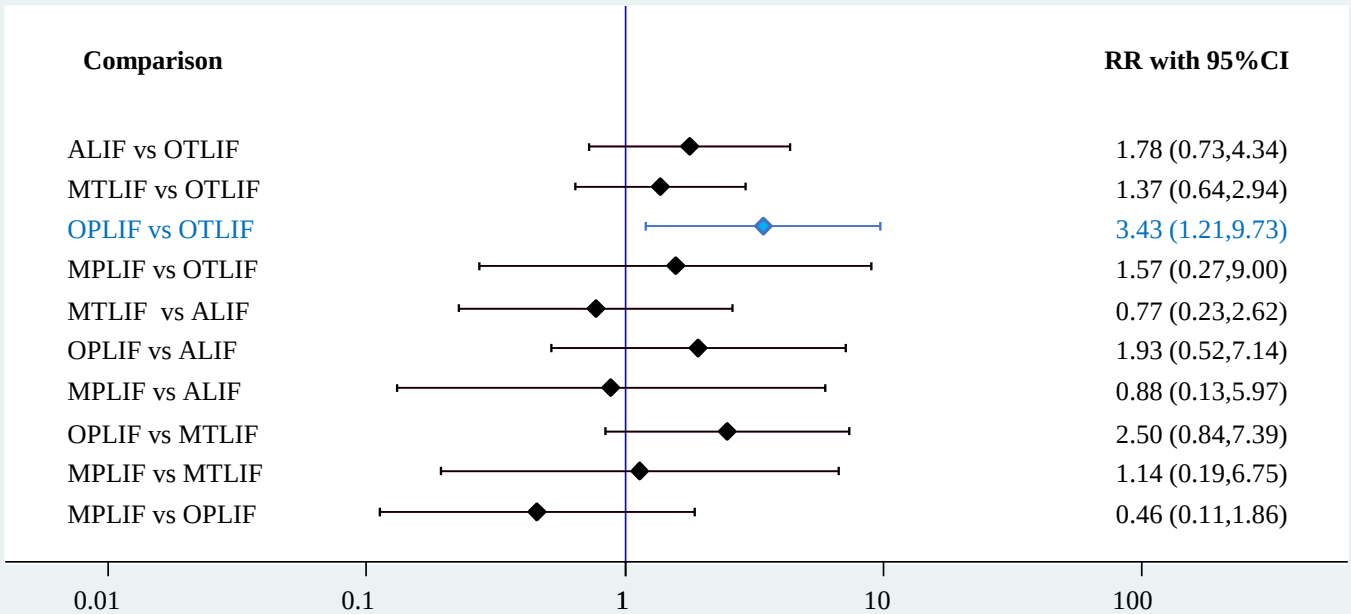
Study	Chen 2017	Lee 2017	Kulkarni 2016	Parker 2014	Fen 2010	Crandall 2009	Klara 2003
Bias due to confounding	Low	Moderate	Moderate	Low	Low	Moderate	Low
Bias in selection of participants into the study	Low	Low	Low	Low	Low	Moderate	Low
Bias in classification of interventions	Low	Low	Low	Low	Low	Low	Low
Bias due to deviations from intended intervetnions	Low	Low	Low	Low	Low	Low	Low
Bias due to missing data	Low	Low	Moderate	Low	Moderate	Low	Low
Bias in measurements of outcomes	Low	Low	Low	Low	Low	Low	Low
Bias in selection of reported results	Low	Low	Low	Low	Low	Moderate	Low
Overall	Low	Moderate	Moderate	Low	Moderate	Moderate	Low

Appendix 3 to 6

Outcome of Overall Adverse Event

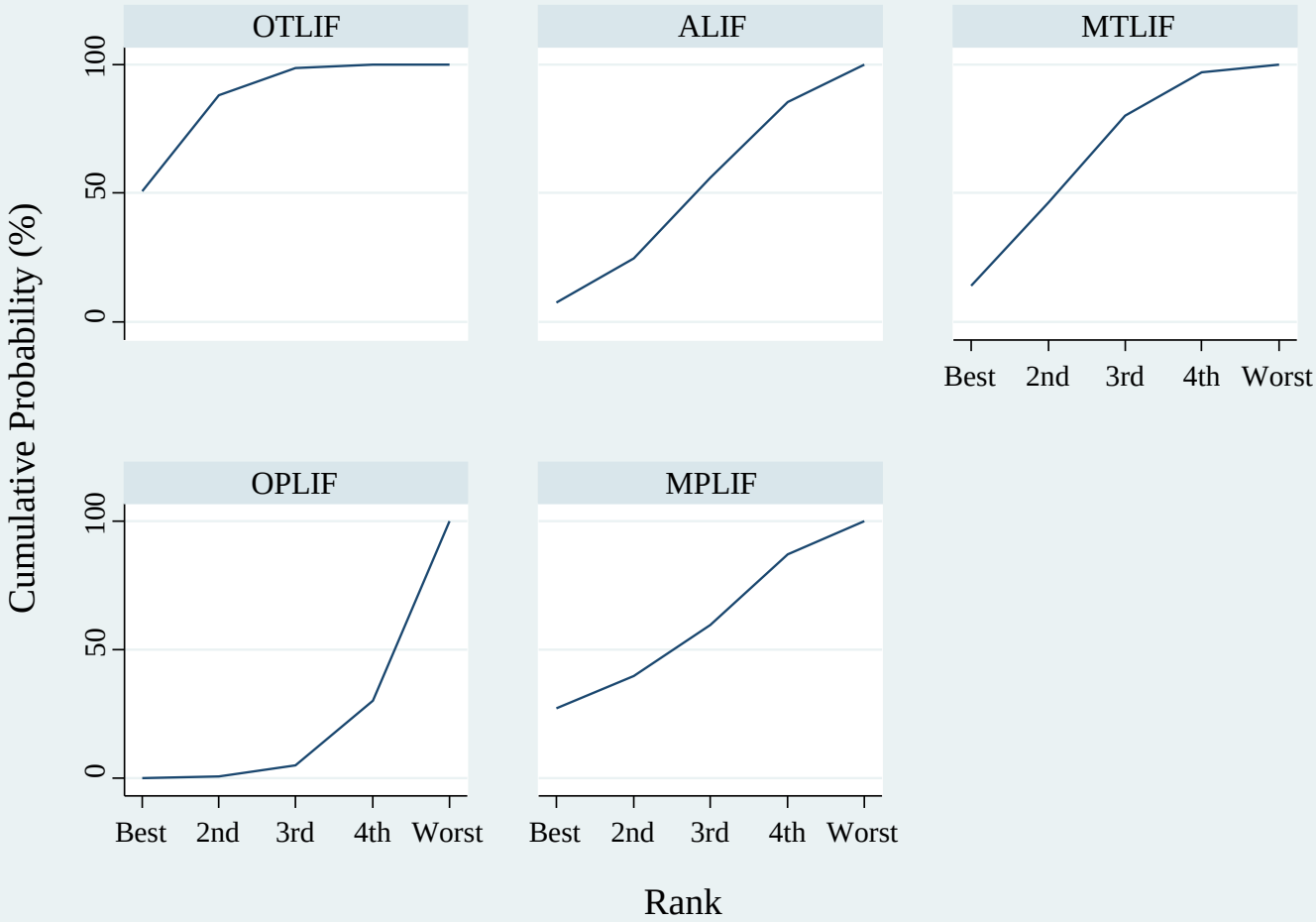
Appendix 3

Pairwise meta-analysis of overall adverse event



Appendix 4

Cumulative rank probability and SUCRA of overall adverse event



. sucra prob*, labels("OTLIF" "ALIF" "MTLIF" "OPLIF" "MPLIF")

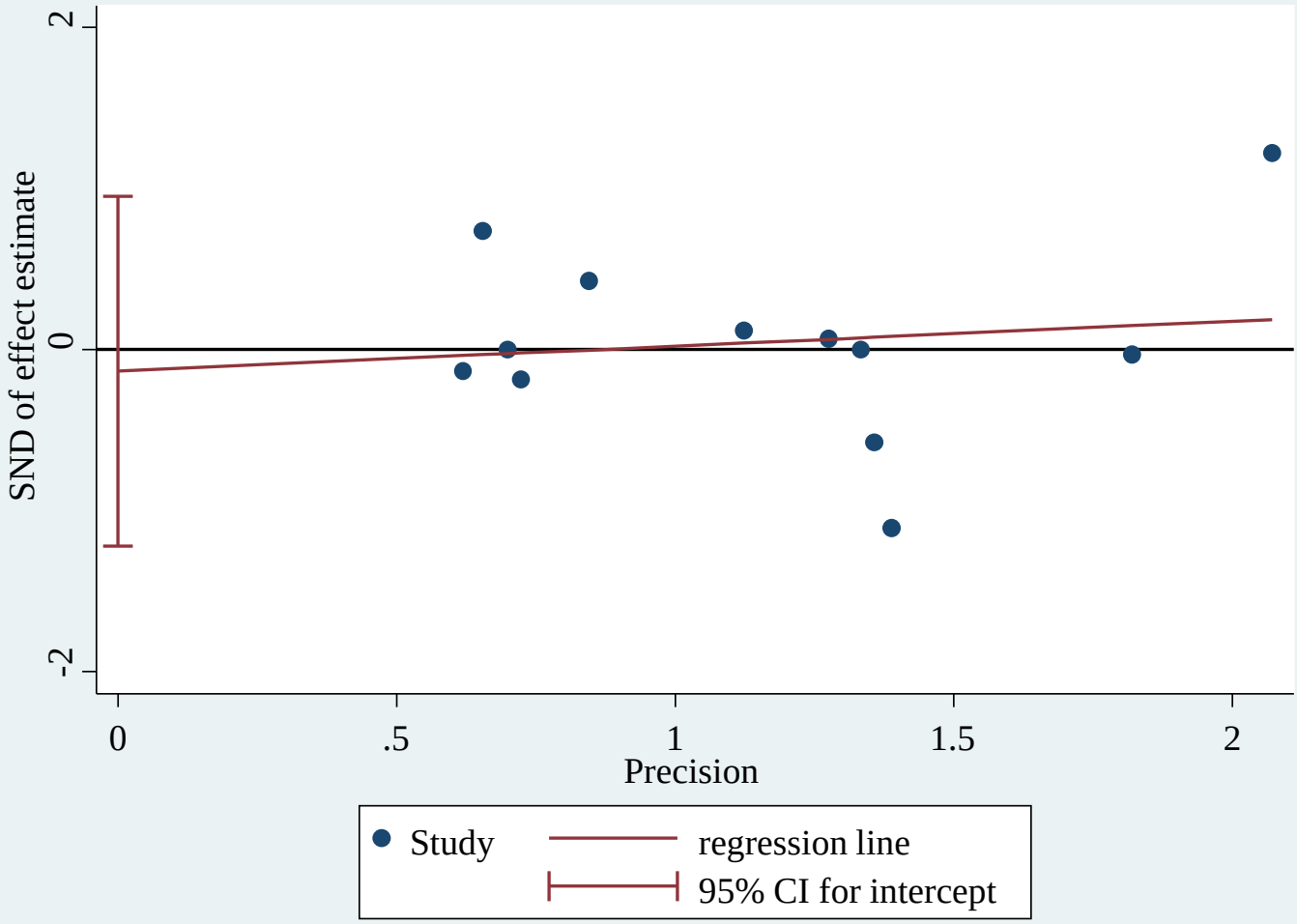
Treatment	SUCRA	PrBest	MeanRank
OTLIF	84.4	50.8	1.6
ALIF	43.5	7.5	3.3
MTLIF	59.5	14.3	2.6
OPLIF	9.1	0.1	4.6
MPLIF	53.4	27.3	2.9

Appendix 5
Inconsistency test of overall adverse event

```
. network meta i, luades
Command is: mvmeta _y _S  , bscovariance(exch 0.5) longparm suppress(uv mm)
eq(_y_D: groupB groupC) vars(_y_B _y_C _y_D _y_E)

Multivariate meta-analysis
Variance-covariance matrix = proportional .5*I(4)+.5*J(4,4,1)
Method = reml                              Number of dimensions    =     4
Restricted log likelihood = -37.714535     Number of observations  =    12
------------------------------------------------------------------------------
             |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
_y_B         |
       _cons |   .6684841   .4011767     1.67   0.096    -.1178078    1.454776
-------------+----------------------------------------------------------------
_y_C         |
       _cons |   .1363817   .3986513     0.34   0.732    -.6449605    .9177239
-------------+----------------------------------------------------------------
_y_D         |
      groupB |   .7516184   1.664417     0.45   0.652    -2.51058     4.013817
      groupC |  -1.140805   1.132547    -1.01   0.314    -3.360557    1.078947
       _cons |   1.576334   .7502161     2.10   0.036     .1059374    3.046731
-------------+----------------------------------------------------------------
_y_E         |
       _cons |   .7975606   1.030094     0.77   0.439    -1.221387    2.816508
------------------------------------------------------------------------------

Estimated between-studies SDs and correlation matrix:
           SD       _y_B       _y_C       _y_D       _y_E
_y_B  9.577e-07          1          .          .          .
_y_C  9.577e-07         .5          1          .          .
_y_D  9.577e-07         .5         .5          1          .
_y_E  9.577e-07         .5         .5         .5          1

Testing for inconsistency:
 ( 1)  [_y_D]groupB = 0
 ( 2)  [_y_D]groupC = 0

           chi2(  2) =    1.64
         Prob > chi2 =    0.4413
```

Appendix 6

Publication bias in network meta-analysis of overall adverse event



. metabias _ES_CEN seES , egger graph

Number of studies = 5 Root MSE = .1784

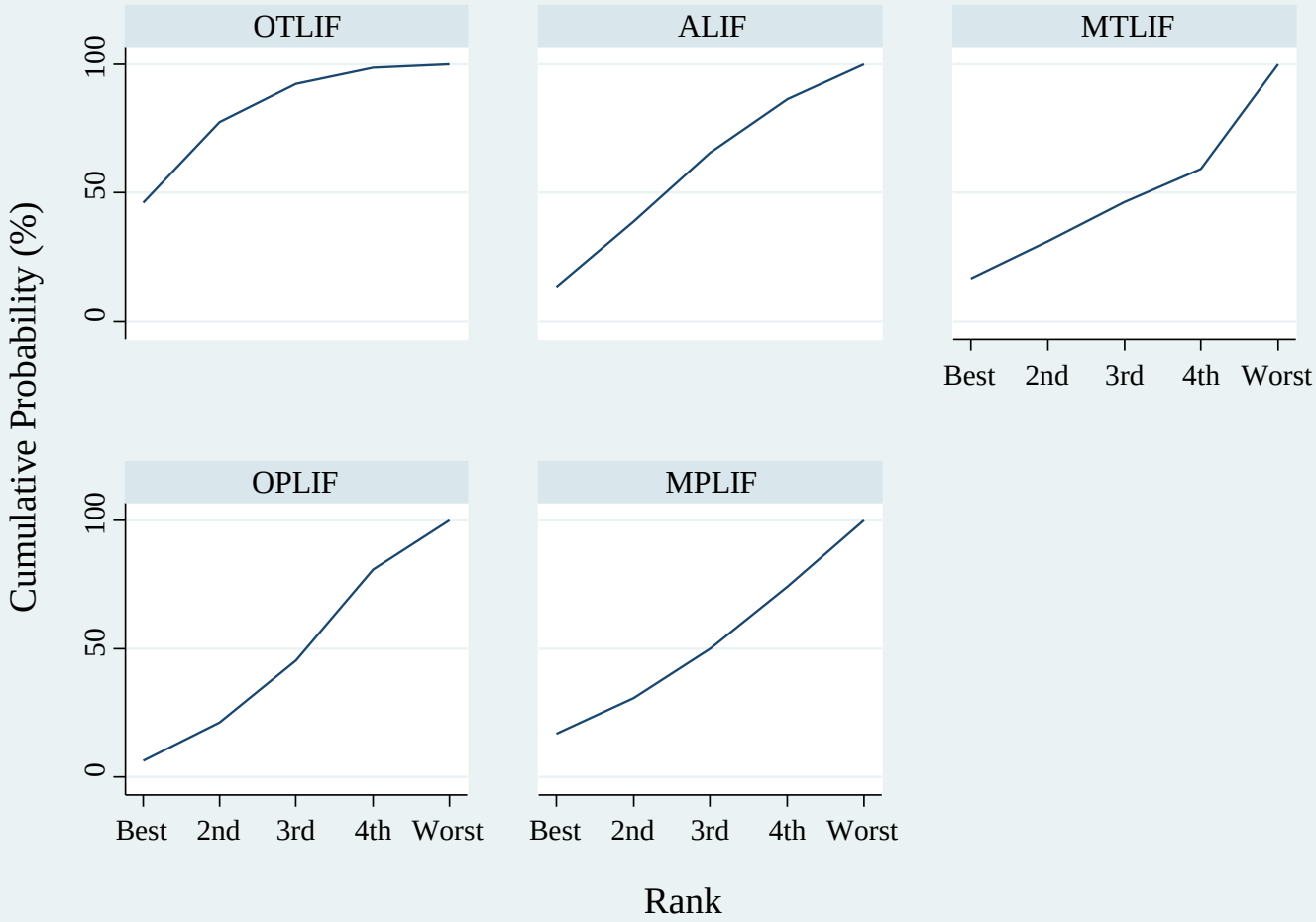
Std_Eff	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
slope	.1537296	.3915531	0.39	0.703	-.718705	1.026164
bias	-.1336616	.4869563	-0.27	0.789	-1.218668	.9513445

Test of H0: no small-study effects P = 0.789

Appendix 7 to 9
Outcomes of Neural Event

Appendix 7

Cumulative rank probability and SUCRA of neural event



. sucra prob*, labels("OTLIF" "ALIF" "MTLIF" "OPLIF" "MPLIF")

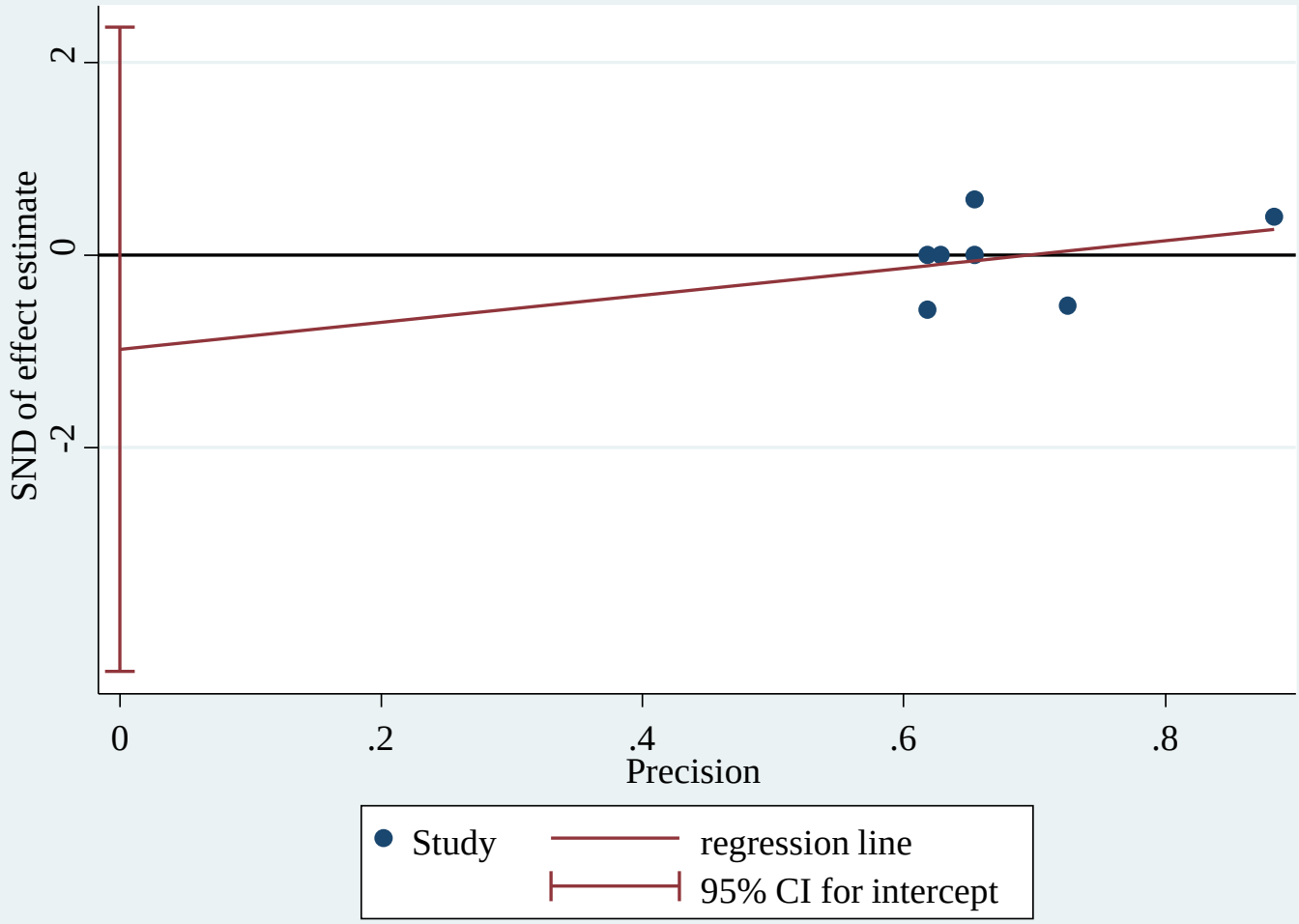
Treatment	SUCRA	PrBest	MeanRank
OTLIF	78.7	46.3	1.9
ALIF	51.2	13.5	3.0
MTLIF	38.6	16.8	3.5
OPLIF	38.4	6.3	3.5
MPLIF	43.1	17.1	3.3

Appendix 8
Inconsistency test of neural event

```
. network meta i, luades
Command is: mvmeta _y _S  , bscovariance(exch 0.5) longparm suppress(uv mm)
eq(_y_D: groupB groupC) vars(_y_B _y_C _y_D _y_E)

Multivariate meta-analysis
Variance-covariance matrix = proportional .5*I(4)+.5*J(4,4,1)
Method = reml                              Number of dimensions    =     4
Restricted log likelihood = -21.651553     Number of observations  =     7
------------------------------------------------------------------------------
             |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
_y_B         |
       _cons |    .7215717   1.023726     0.70   0.481    -1.284893    2.728037
-------------+----------------------------------------------------------------
_y_C         |
       _cons |   1.256617    1.527911     0.82   0.411    -1.738034    4.251267
-------------+----------------------------------------------------------------
_y_D         |
      groupB |   -.086557    2.489752    -0.03   0.972    -4.966381    4.793267
       _cons |   1.169025    1.618348     0.72   0.470    -2.002879    4.340929
-------------+----------------------------------------------------------------
_y_E         |
       _cons |   1.089964    1.865302     0.58   0.559     -2.56596    4.745888
------------------------------------------------------------------------------

Estimated between-studies SDs and correlation matrix:
           SD       _y_B       _y_C       _y_D       _y_E
_y_B  2.779e-10          1          .          .          .
_y_C  2.779e-10         .5          1          .          .
_y_D  2.779e-10         .5         .5          1          .
_y_E  2.779e-10         .5         .5         .5          1

Testing for inconsistency:
 ( 1)  [_y_D]groupB = 0

           chi2(  1) =    0.00
         Prob > chi2 =    0.9723
```

Appendix 9

Publication bias in network meta-analysis of neural event



. metabias _ES_CEN seES , egger graph

Number of studies = 7 Root MSE = .4431

Std_Eff	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
slope	1.40986	1.890679	0.75	0.489	-3.450285	6.270006
bias	-.9792592	1.302321	-0.75	0.486	-4.326983	2.368464

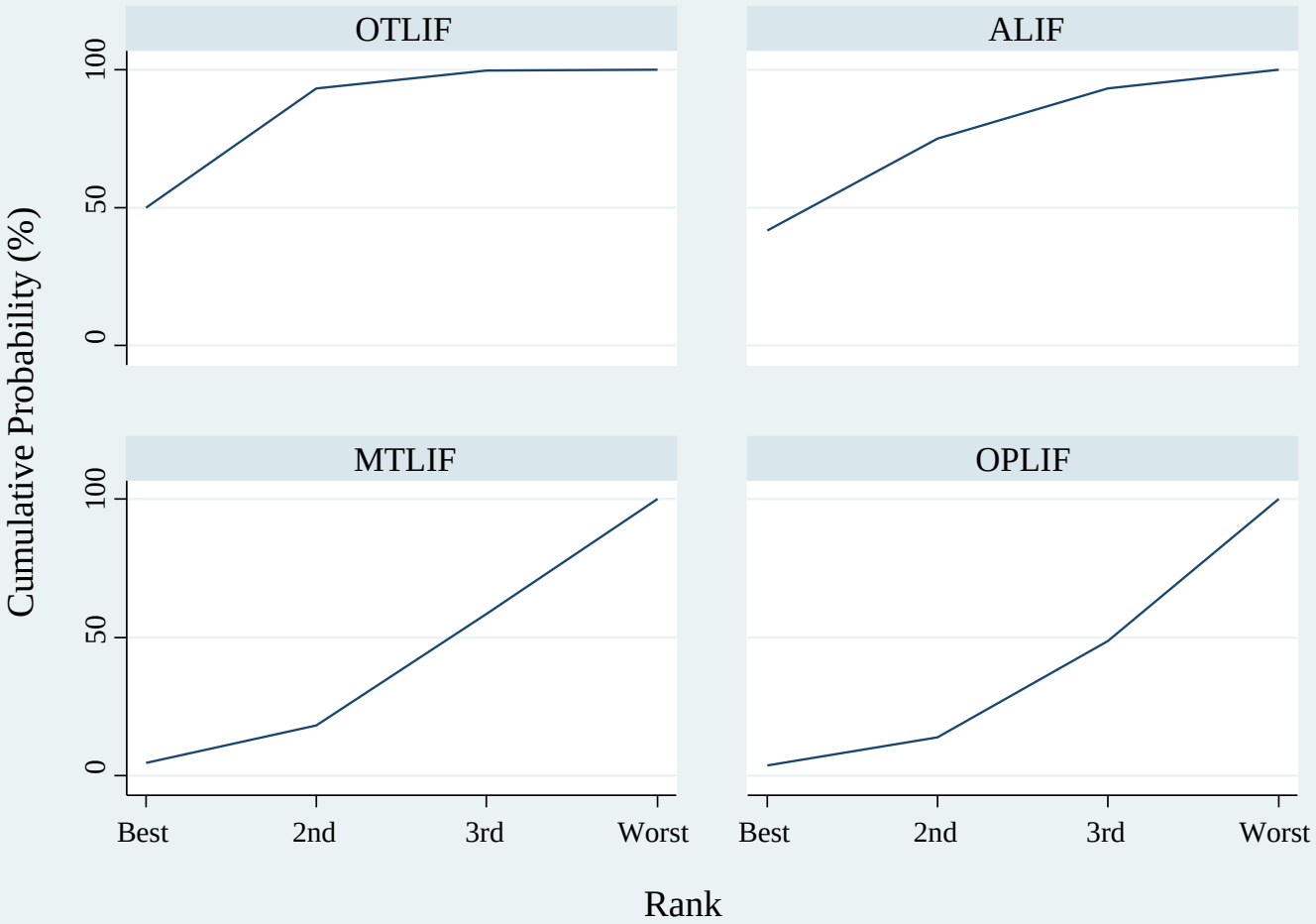
Test of H0: no small-study effects P = 0.486

Appendix 10 to 12

Outcomes of Spinal Event

Appendix 10

Cumulative rank probability and SUCRA of spinal event



. sucra prob*, labels("OTLIF" "ALIF" "MTLIF" "OPLIF")

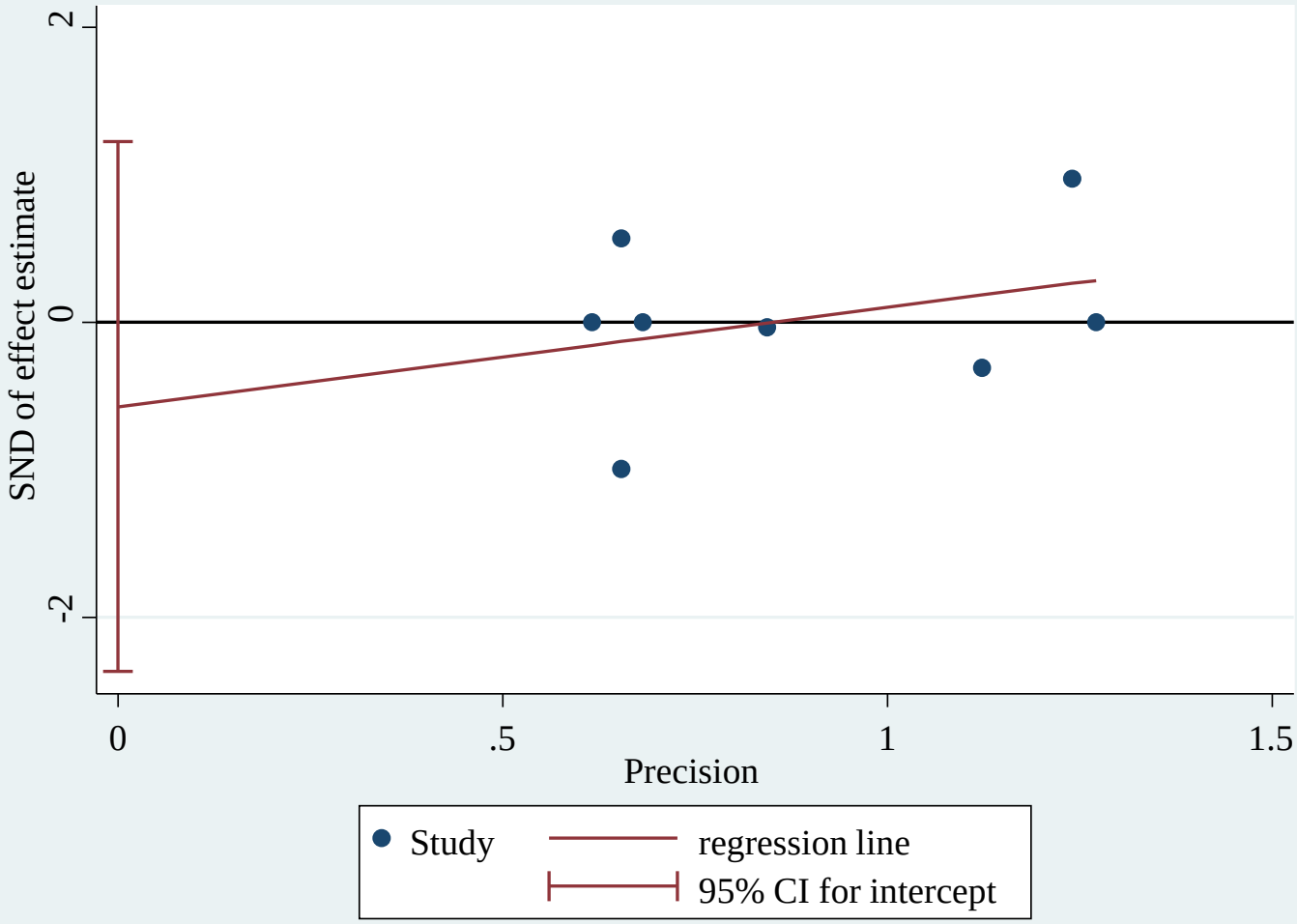
Treatment	SUCRA	PrBest	MeanRank
OTLIF	80.8	49.9	1.6
ALIF	69.9	41.6	1.9
MTLIF	27.2	4.7	3.2
OPLIF	22.1	3.8	3.3

Appendix 11
Inconsistency test of spinal event

```
. network meta i, luades
Command is: mvmeta _y _S  , bscovariance(exch 0.5) longparm suppress(uv mm)
eq(_y_D: groupB groupC) vars(_y_B _y_C _y_D)

Multivariate meta-analysis
Variance-covariance matrix = proportional .5*I(3)+.5*J(3,3,1)
Method = reml                              Number of dimensions    =     3
Restricted log likelihood = -17.025336     Number of observations  =     8
------------------------------------------------------------------------------
             |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
_y_B         |
       _cons |   .1920891    .713122     0.27   0.788    -1.205604    1.589782
-------------+----------------------------------------------------------------
_y_C         |
       _cons |   .6797541   .6453069     1.05   0.292     -.5850242    1.944532
-------------+----------------------------------------------------------------
_y_D         |
     groupB |    .2291764   1.810397     0.13   0.899    -3.319136    3.777489
     groupC |  -1.589795   1.913704    -0.83   0.406    -5.340586    2.160997
       _cons |   1.170933    .786391     1.49   0.136     -.3703652    2.712231
------------------------------------------------------------------------------

Estimated between-studies SDs and correlation matrix:
           SD       _y_B       _y_C       _y_D
_y_B  8.701e-09          1          .          .
_y_C  8.701e-09         .5          1          .
_y_D  8.701e-09         .5         .5          1

Testing for inconsistency:
 ( 1)  [_y_D]groupB = 0
 ( 2)  [_y_D]groupC = 0

           chi2(  2) =    0.77
         Prob > chi2 =    0.6811
```

Appendix 12

Publication bias in network meta-analysis of spinal event



. metabias _ES_CEN seES , egger graph

Number of studies = 8 Root MSE = .5909

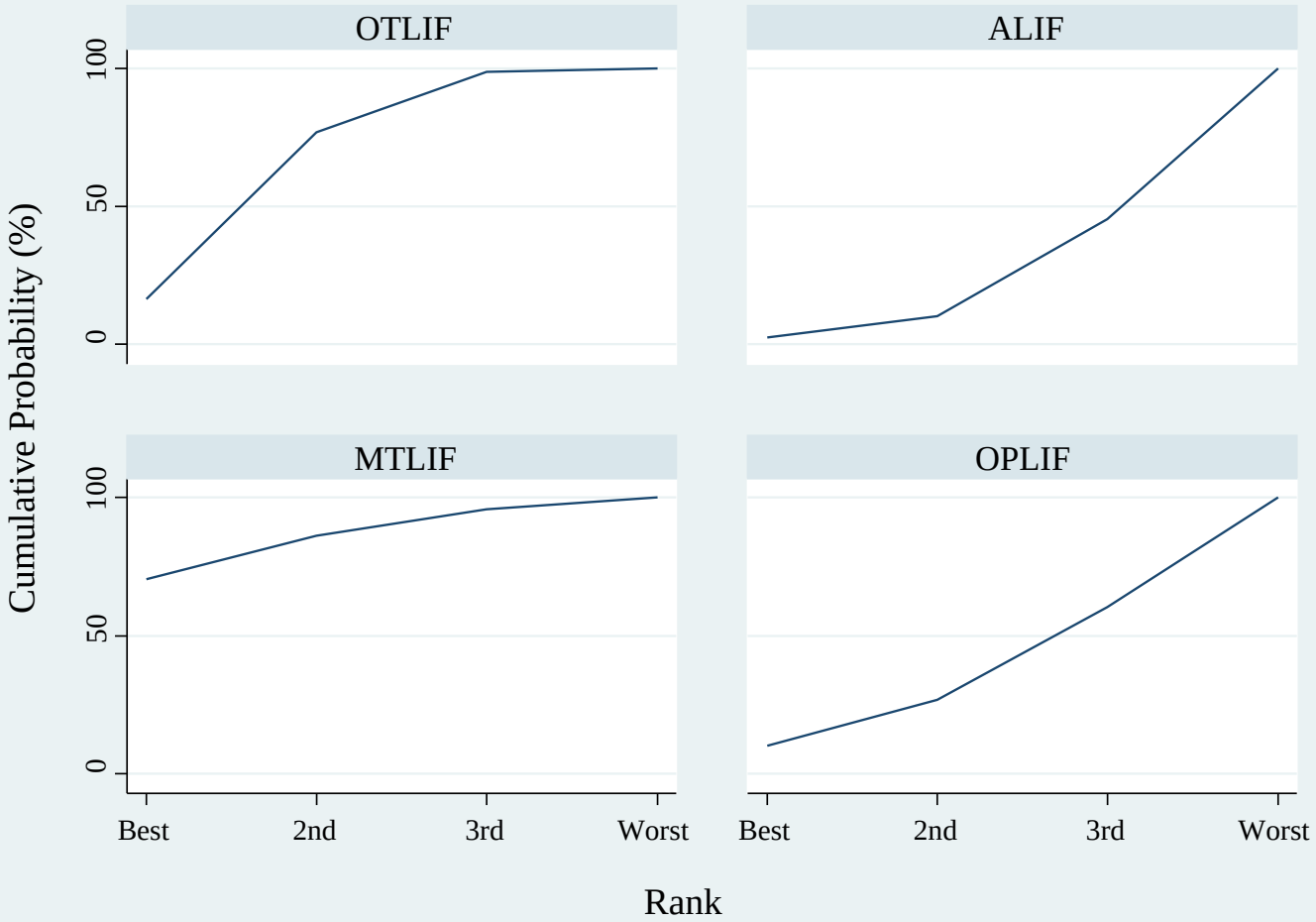
Std_Eff	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
slope	.6718966	.7941071	0.85	0.430	-1.271214	2.615007
bias	-.5688645	.7337513	-0.78	0.468	-2.364289	1.22656

Test of H0: no small-study effects P = 0.486

Appendix 13 to 15
Outcomes of Vascular Event

Appendix 13

Cumulative rank probability and SUCRA of vascular event



. sucra prob*, labels("OTLIF" "ALIF" "MTLIF" "OPLIF")

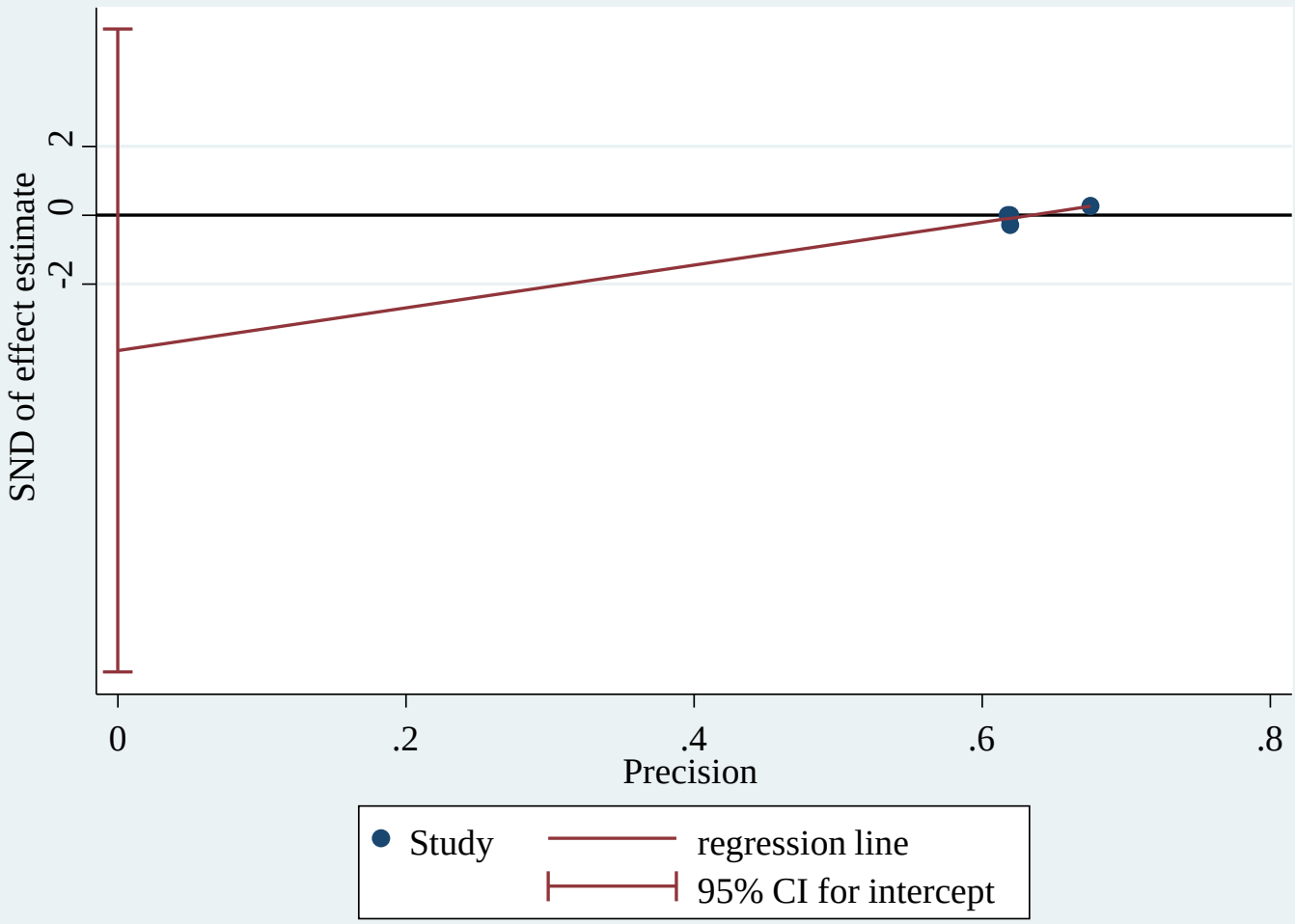
Treatment	SUCRA	PrBest	MeanRank
OTLIF	64.0	16.6	2.1
ALIF	19.4	2.5	3.4
MTLIF	84.2	70.6	1.5
OPLIF	32.5	10.3	3.0

Appendix 14
Inconsistency test of vascular event

```
. network meta i, luades
Command is: mvmeta _y _S  , bscovariance(exch 0.5) longparm suppress(uv mm)
eq(_y_D: groupB groupC) vars(_y_B _y_C _y_D)

Multivariate meta-analysis
Variance-covariance matrix = proportional .5*I(3)+.5*J(3,3,1)
Method = reml                           Number of dimensions    =     3
Restricted log likelihood = -1.7775544        Number of observations  =     4
------------------------------------------------------------------------------
             |      Coef.      Std. Err.        z     P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
_y_B         |
       _cons |   1.558814   1.090751     1.43   0.153    -.5790178    3.696647
-------------+----------------------------------------------------------------
_y_C         |
       _cons |  -1.161133   1.613724    -0.72   0.472    -4.323974    2.001709
-------------+----------------------------------------------------------------
_y_D         |
       _cons |    1.16923   1.618502     0.72   0.470   -2.002976    4.341436
------------------------------------------------------------------------------

Estimated between-studies SDs and correlation matrix:
            SD       _y_B       _y_C       _y_D
_y_B  5.093e-13          1          .          .
_y_C  5.093e-13         .5          1          .
_y_D  5.093e-13         .5         .5          1

Testing for inconsistency:
 ( 1)  [_y_D]_cons = 0

           chi2(  1) =    0.52
         Prob > chi2 =    0.4700
```

Appendix 15

Publication bias in network meta-analysis of vascular event



. metabias _ES_CEN seES , egger graph

Number of studies = 4 Root MSE = .168

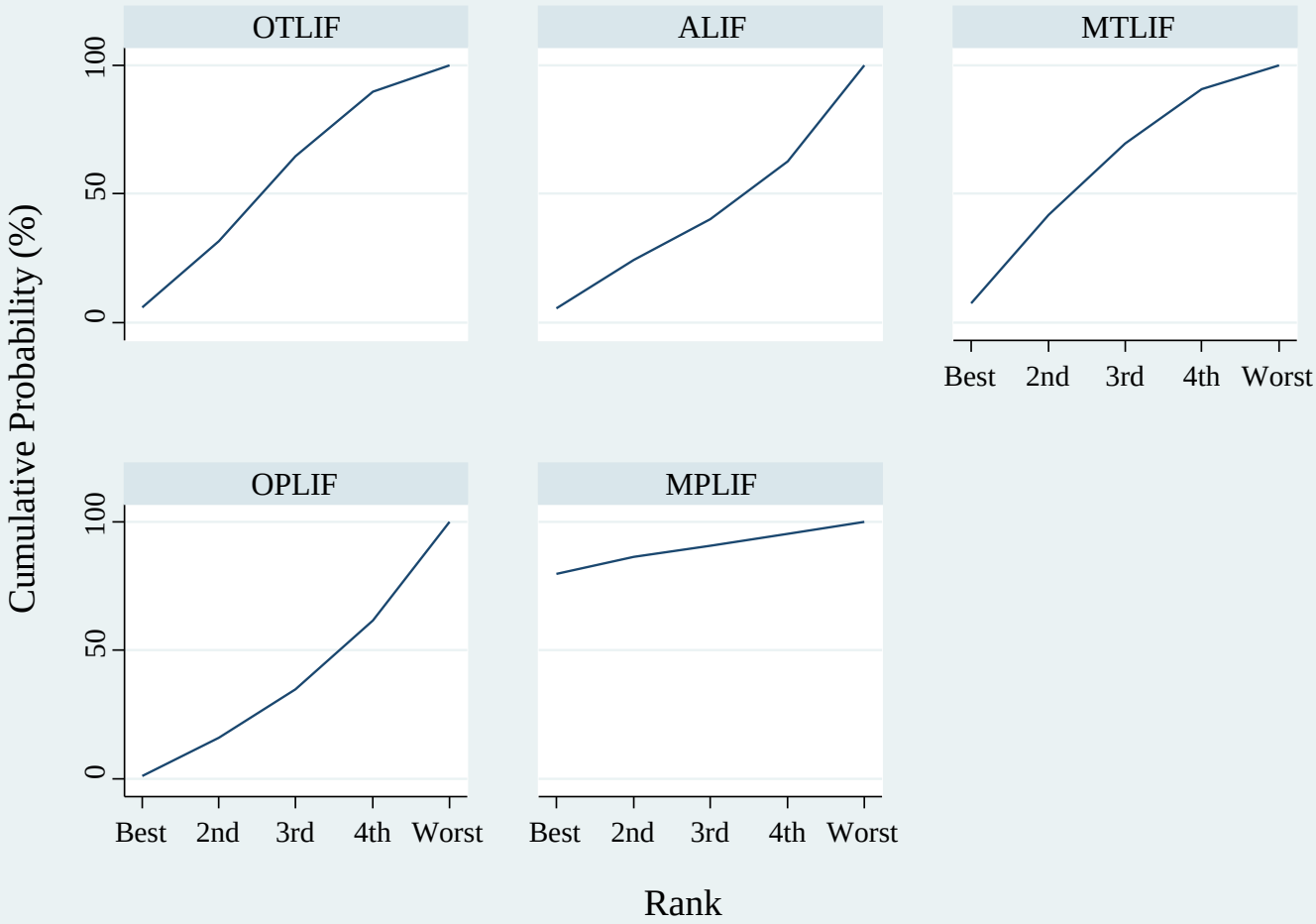
Std_Eff	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
slope	6.223821	3.426827	1.82	0.211	-8.520627	20.96827
bias	-3.946957	2.171562	-1.82	0.211	-13.29044	5.396521

Test of H0: no small-study effects P = 0.486

Appendix 16 to 18
Outcomes of Wound Event

Appendix 16

Cumulative rank probability and SUCRA of wound event



. sucra prob*, labels("OTLIF" "ALIF" "MTLIF" "OPLIF" "MPLIF")

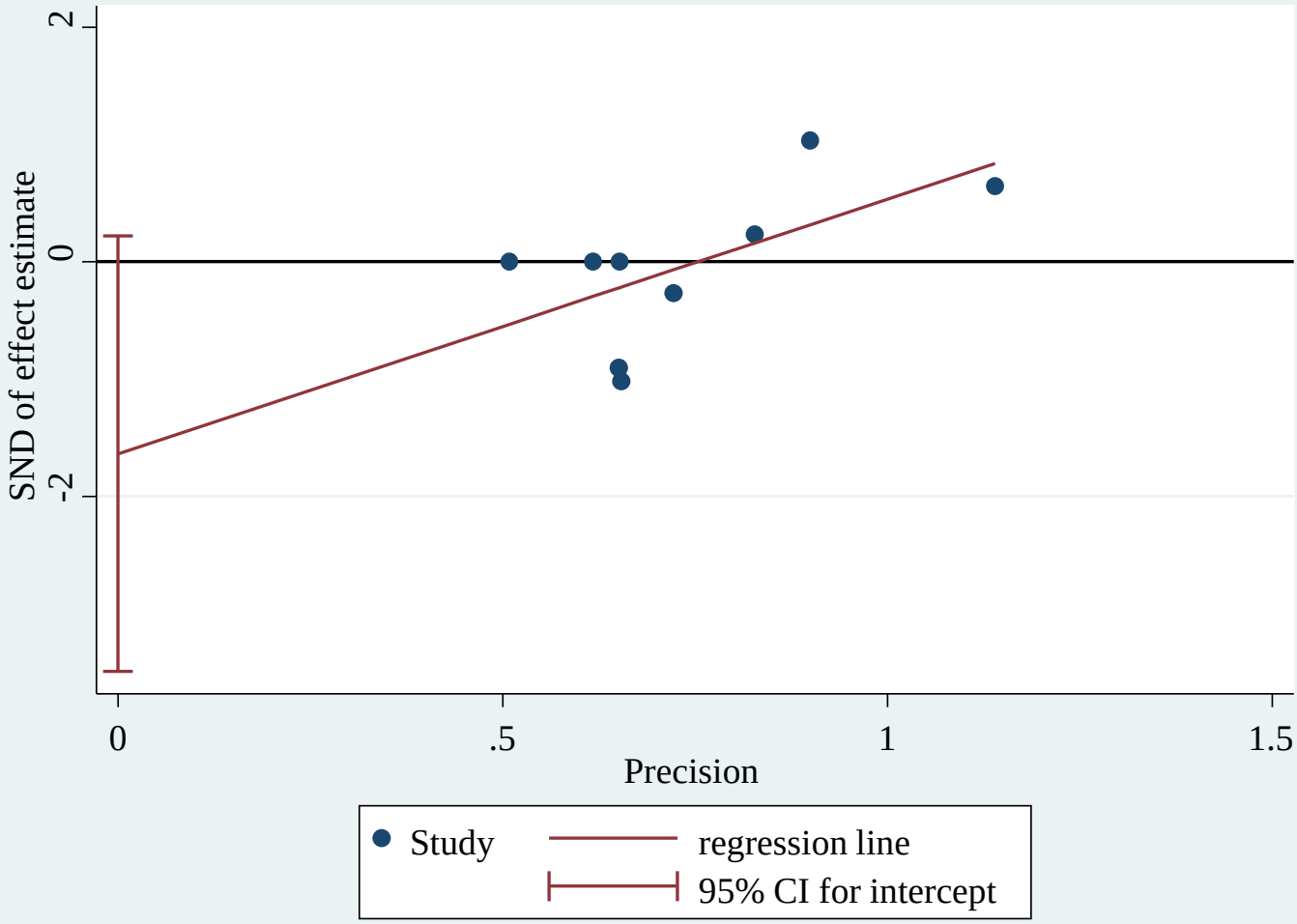
Treatment	SUCRA	PrBest	MeanRank
OTLIF	48.0	5.9	3.1
ALIF	33.2	5.6	3.7
MTLIF	52.4	7.5	2.9
OPLIF	28.3	1.0	3.9
MPLIF	88.1	79.9	1.5

Appendix 17
Inconsistency test of wound event

```
. network meta i, luades
Command is: mvmeta _y _S  , bscovariance(exch 0.5) longparm suppress(uv mm)
eq(_y_D: groupB groupC) vars(_y_B _y_C _y_D _y_E)

Multivariate meta-analysis
Variance-covariance matrix = proportional .5*I(4)+.5*J(4,4,1)
Method = reml                           Number of dimensions    =     4
Restricted log likelihood = -30.48328   Number of observations  =     9
------------------------------------------------------------------------------
             |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
_y_B         |
       _cons |   .1211219   1.000924     0.12   0.904    -1.840654    2.082898
-------------+----------------------------------------------------------------
_y_C         |
       _cons |  -.1943727   .9226487    -0.21   0.833    -2.002731    1.613986
-------------+----------------------------------------------------------------
_y_D         |
      groupB |  -1.785665   2.808264    -0.64   0.525     -7.28976    3.718431
      groupC |  -.9565285   2.150847    -0.44   0.657    -5.172112    3.259055
       _cons |   1.169207   1.67905      0.70   0.486    -2.121671    4.460084
-------------+----------------------------------------------------------------
_y_E         |
       _cons |  -1.149912   2.317178    -0.50   0.620    -5.691498    3.391674
------------------------------------------------------------------------------

Estimated between-studies SDs and correlation matrix:
            SD       _y_B       _y_C       _y_D       _y_E
_y_B  .44713577          1          .          .          .
_y_C  .44713577         .5          1          .          .
_y_D  .44713577         .5         .5          1          .
_y_E  .44713577         .5         .5         .5          1

Testing for inconsistency:
 ( 1)  [_y_D]groupB = 0
 ( 2)  [_y_D]groupC = 0

           chi2(  2) =    0.43
         Prob > chi2 =    0.8073
```

Appendix 18

Publication bias in network meta-analysis of wound event



. metabias _ES_CEN seES , egger graph

Number of studies = 9 Root MSE = .55

Std_Eff	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
slope	2.165664	1.029146	2.10	0.073	-.2678802	4.599208
bias	-1.63626	.7849823	-2.08	0.076	-3.492448	.2199283

Test of H0: no small-study effects P = 0.076