Efficacy of Polyunsaturated Fatty Acids on Inflammatory Markers in Patients Undergoing Dialysis:

a Systematic Review with Network Meta-Analysis of Randomized Clinical Trials

(Supplementary Files)

Supplementary File

Supplementary File 1. Head-to-head comparisons of CRP

Supplementary File 2. Ranking probability and SUCRA of CRP

Supplementary File 3. Small study bias in network meta-analysis of CRP

Supplementary File 4. Head-to-head comparisons of hs-CRP

Supplementary File 5. Ranking probability and SUCRA of hs-CRP

Supplementary File 6. Inconsistency test for network meta-analysis of hs-CRP

Supplementary File 7. Small study bias in network meta-analysis of hs-CRP

Supplementary File 8. Head-to-head comparisons of IL-6

Supplementary File 9. Ranking probability and SUCRA of IL-6

Supplementary File 10. Small study bias in network meta-analysis of IL-6

Supplementary File 11. Head-to-head comparisons of albumin

Supplementary File 12. Ranking probability and SUCRA of albumin

Supplementary File 13. Inconsistency test for network meta-analysis of hs-CRP

Supplementary File 14. Small study bias in network meta-analysis of albumin

Supplementary File 15. Detection of Regions on the outcomes of CRP

Supplementary File 16. Detection of Regions on the outcomes of hs-CRP

Supplementary File 17. Cluster plot of SUCRA for CRP and hs-CRP
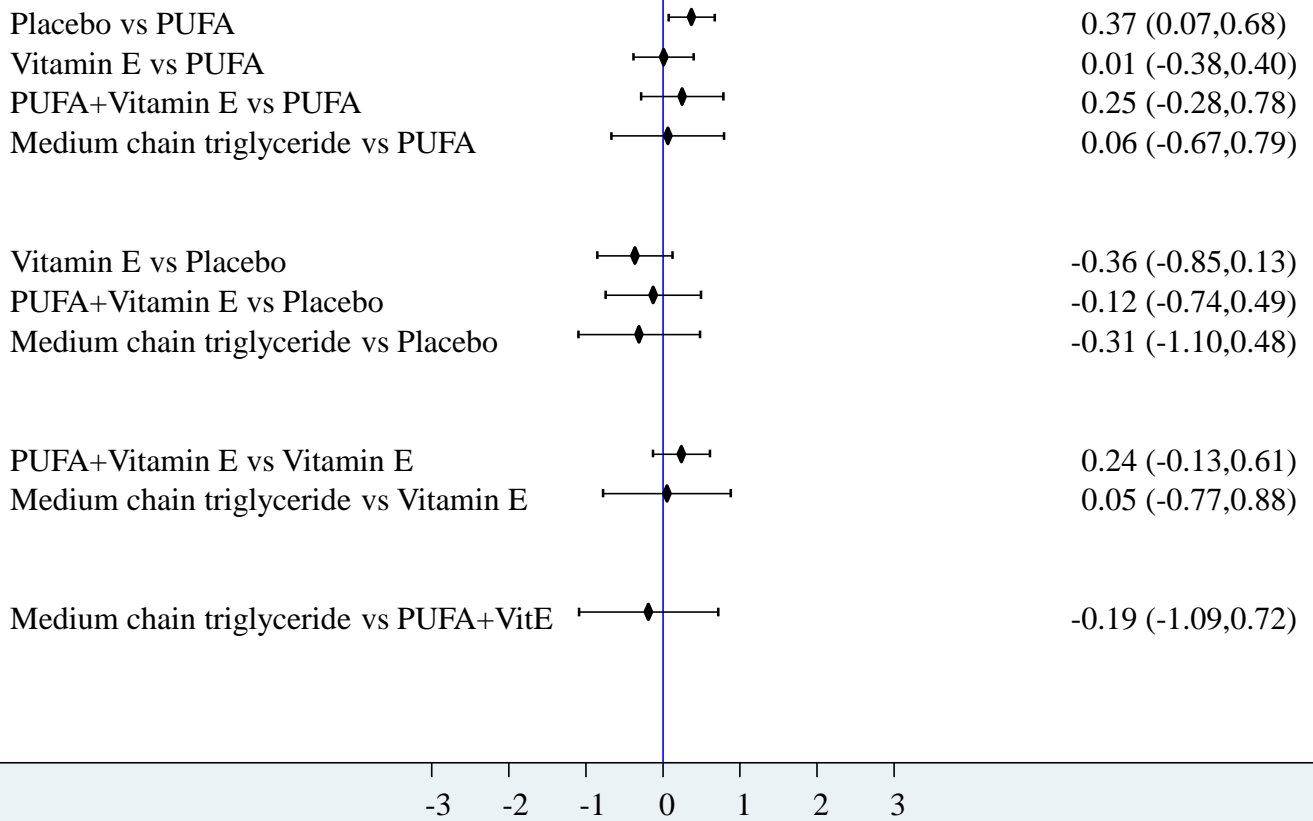
Supplementary File 18. Search strategy

Supplementary File 1 to 3
Outcome of C-reactive protein

Head-to-head comparisons

Mean with 95%CI
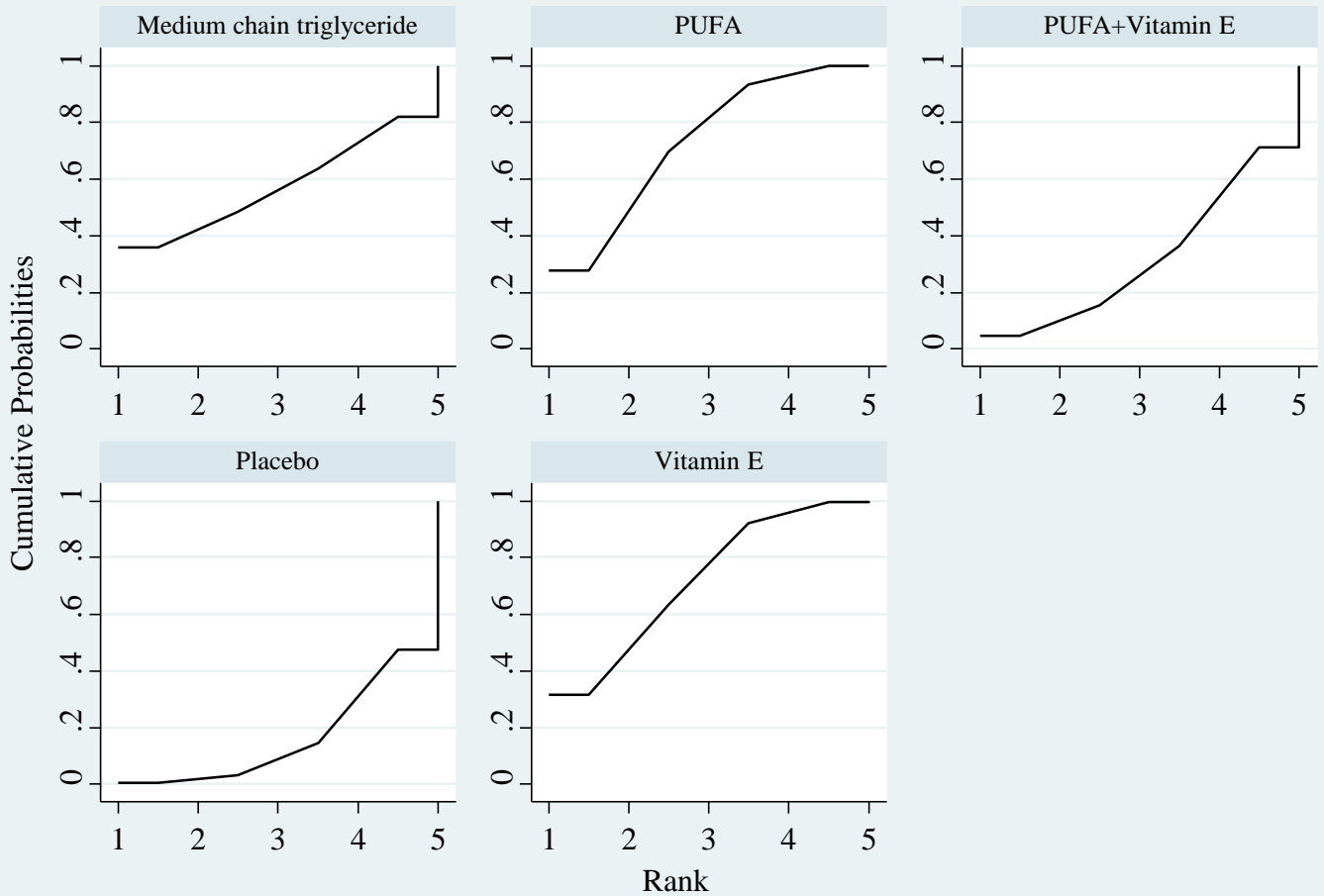
Placebo vs PUFA — 0.37 (0.07,0.68)
Vitamin E vs PUFA — 0.01 (-0.38,0.40)
PUFA+Vitamin E vs PUFA — 0.25 (-0.28,0.78)
Medium chain triglyceride vs PUFA — 0.06 (-0.67,0.79)

Vitamin E vs Placebo — -0.36 (-0.85,0.13)
PUFA+Vitamin E vs Placebo — -0.12 (-0.74,0.49)
Medium chain triglyceride vs Placebo — -0.31 (-1.10,0.48)

PUFA+Vitamin E vs Vitamin E — 0.24 (-0.13,0.61)
Medium chain triglyceride vs Vitamin E — 0.05 (-0.77,0.88)

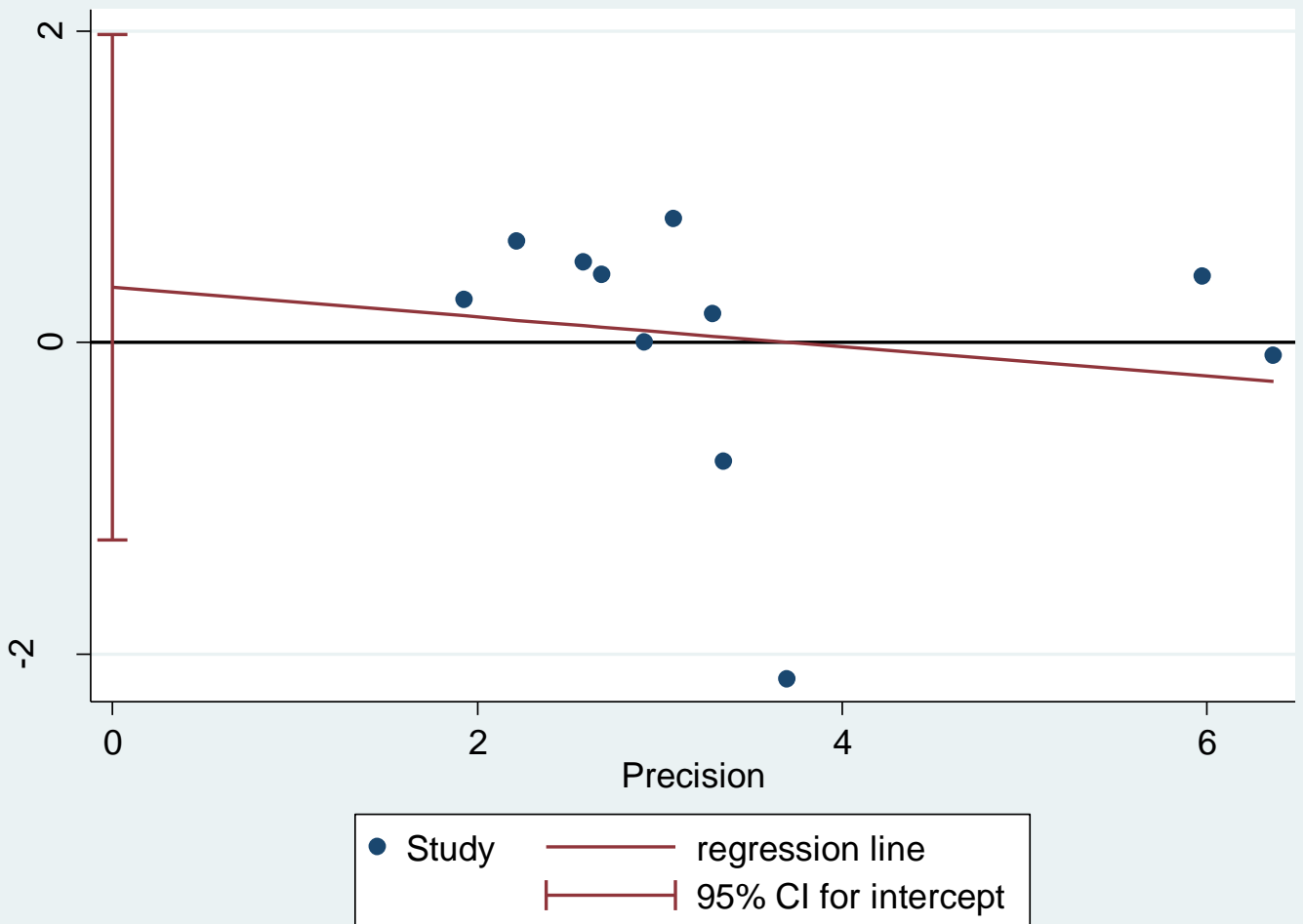Medium chain triglyceride vs PUFA+VitE — -0.19 (-1.09,0.72)

-3 -2 -1 0 1 2 3

. sucra prob*, labels("PUFA" "Placebo" "Vitamin E" "PUFA+Vitamin E" "Medium chain triglyceride")

Treatment	SUCRA	PrBest	MeanRank
PUFA	72.7	27.7	2.1
Placebo	16.3	0.3	4.3
Vitamin E	71.6	31.6	2.1
PUFA+Vitamin E	31.9	4.7	3.7
Medium chain triglyceride	57.4	35.7	2.7

. metabias _ES_CEN seES , egger graph

Number of studies = 11   Root MSE   = .875

   Std_Eff | Coef.   Std. Err.   t   P>|t| [95% Conf. Interval]
-----------+---
     slope | -.0953048 .1930426   -0.49 0.633   -.5319974   .3413878
      bias | .3555706 .7185349   0.49 0.633   -1.269868   1.981009
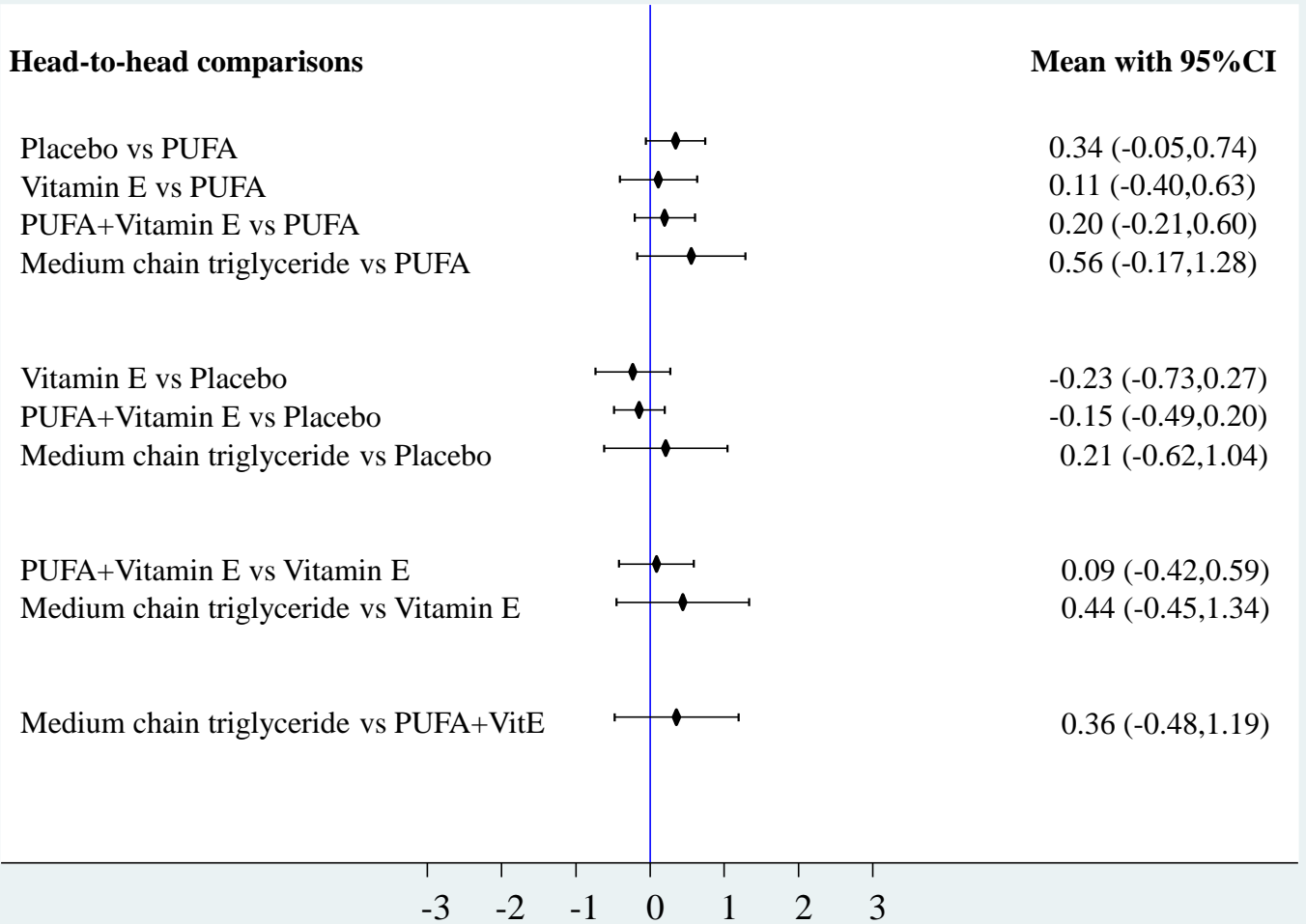---

Test of H0: no small-study effects   P = 0.633

Supplementary File 4 to 7
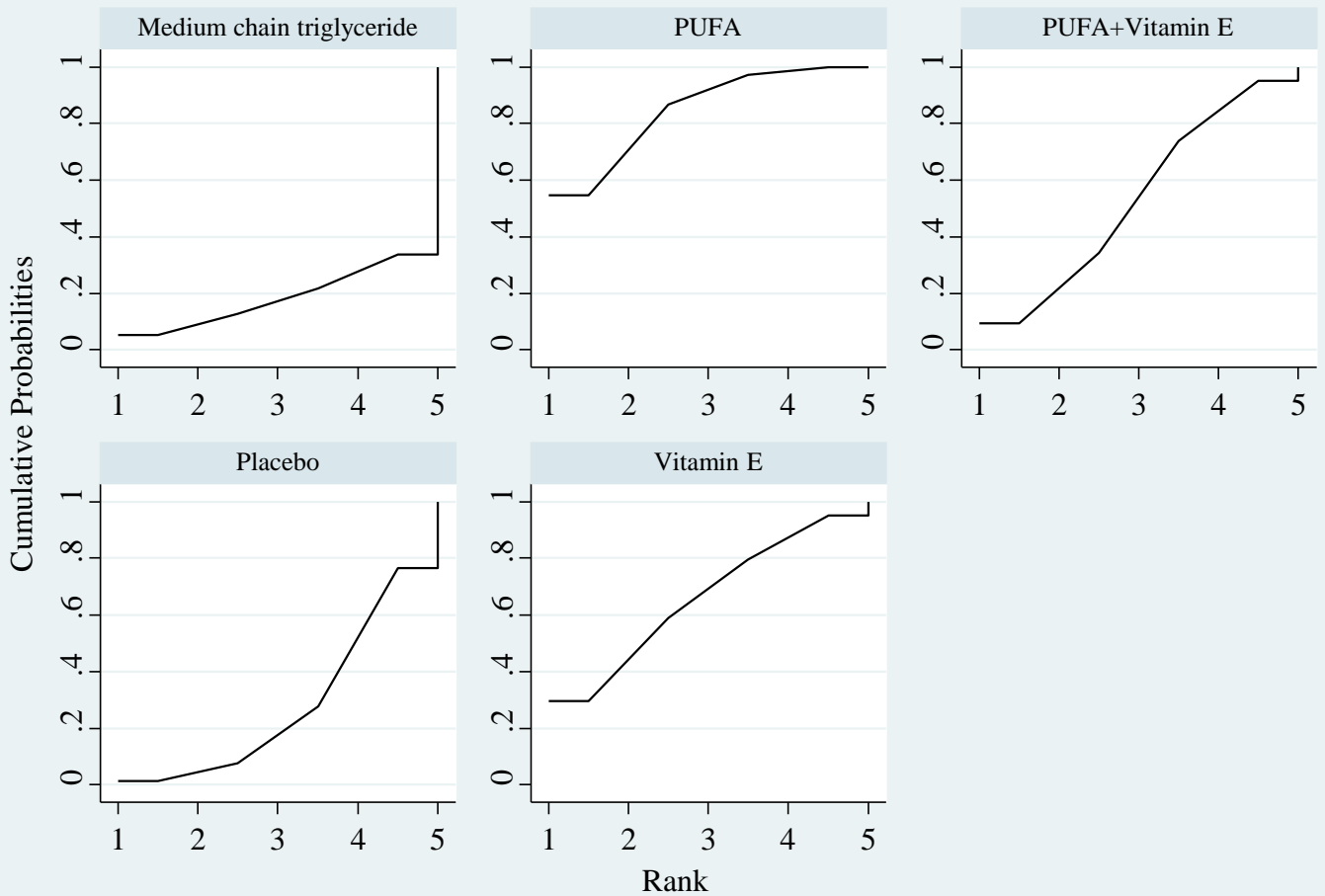**Outcomes of high sensitive C-reactive protein**

Head-to-head comparisons	Mean with 95%CI
Placebo vs PUFA	0.34 (-0.05,0.74)
Vitamin E vs PUFA	0.11 (-0.40,0.63)
PUFA+Vitamin E vs PUFA	0.20 (-0.21,0.60)
Medium chain triglyceride vs PUFA	0.56 (-0.17,1.28)
Vitamin E vs Placebo	-0.23 (-0.73,0.27)
PUFA+Vitamin E vs Placebo	-0.15 (-0.49,0.20)
Medium chain triglyceride vs Placebo	0.21 (-0.62,1.04)
PUFA+Vitamin E vs Vitamin E	0.09 (-0.42,0.59)
Medium chain triglyceride vs Vitamin E	0.44 (-0.45,1.34)
Medium chain triglyceride vs PUFA+VitE	0.36 (-0.48,1.19)

-3 -2 -1 0 1 2 3

. sucra prob*, labels("PUFA" "Placebo" "Vitamin E" "PUFA+Vitamin E" "Medium chain triglyceride")

Treatment	SUCRA	PrBest	MeanRank
PUFA	84.6	54.7	1.6
Placebo	28.2	1.2	3.9
Vitamin E	65.7	29.4	2.4
PUFA+Vitamin E	53.1	9.4	2.9
Medium chain triglyceride	18.4	5.3	4.3

. network meta i, luades

```
initial:      log likelihood = -12.736872
rescale:      log likelihood = -11.490398
rescale eq:   log likelihood = -10.661025
Iteration 0:  log likelihood = -10.661025
Iteration 1:  log likelihood = -10.368251  (not concave)
Iteration 2:  log likelihood = -10.021288
Iteration 3:  log likelihood = -9.9930264
Iteration 4:  log likelihood = -9.9924889
Iteration 5:  log likelihood = -9.9924888
```

Multivariate meta-analysis
Variance-covariance matrix = proportional .5*I(4)+.5*J(4,4,1)
Method = reml   Number of dimensions   =   4
Restricted log likelihood = -9.9924888   Number of observations =   6
```
-----------------------------------------------------------------------------
          |   Coef.   Std. Err.    z    P>|z|    [95% Conf. Interval]
----------+------------------------------------------------------------------
_y_B      |
    _cons |  .4690762  .2054935   2.28  0.022    .0663163   .871836
----------+------------------------------------------------------------------
_y_C      |
    _cons |  .1090441  .2387646   0.46  0.648   -.358926   .5770142
----------+------------------------------------------------------------------
_y_D      |
   groupB |  .4761785  .3177915   1.50  0.134   -.1466813  1.099038
    _cons |  .0624081  .2030203   0.31  0.759   -.3355044   .4603206
----------+------------------------------------------------------------------
_y_E      |
    _cons |  .5561661  .3503694   1.59  0.112   -.1305454  1.242877
-----------------------------------------------------------------------------
```

Estimated between-studies SDs and correlation matrix:
```
          SD      _y_B     _y_C     _y_D     _y_E
_y_B  1.681e-08     1       .        .        .
_y_C  1.681e-08    .5       1        .        .
_y_D  1.681e-08    .5      .5        1        .
_y_E  1.681e-08    .5      .5       .5        1
```
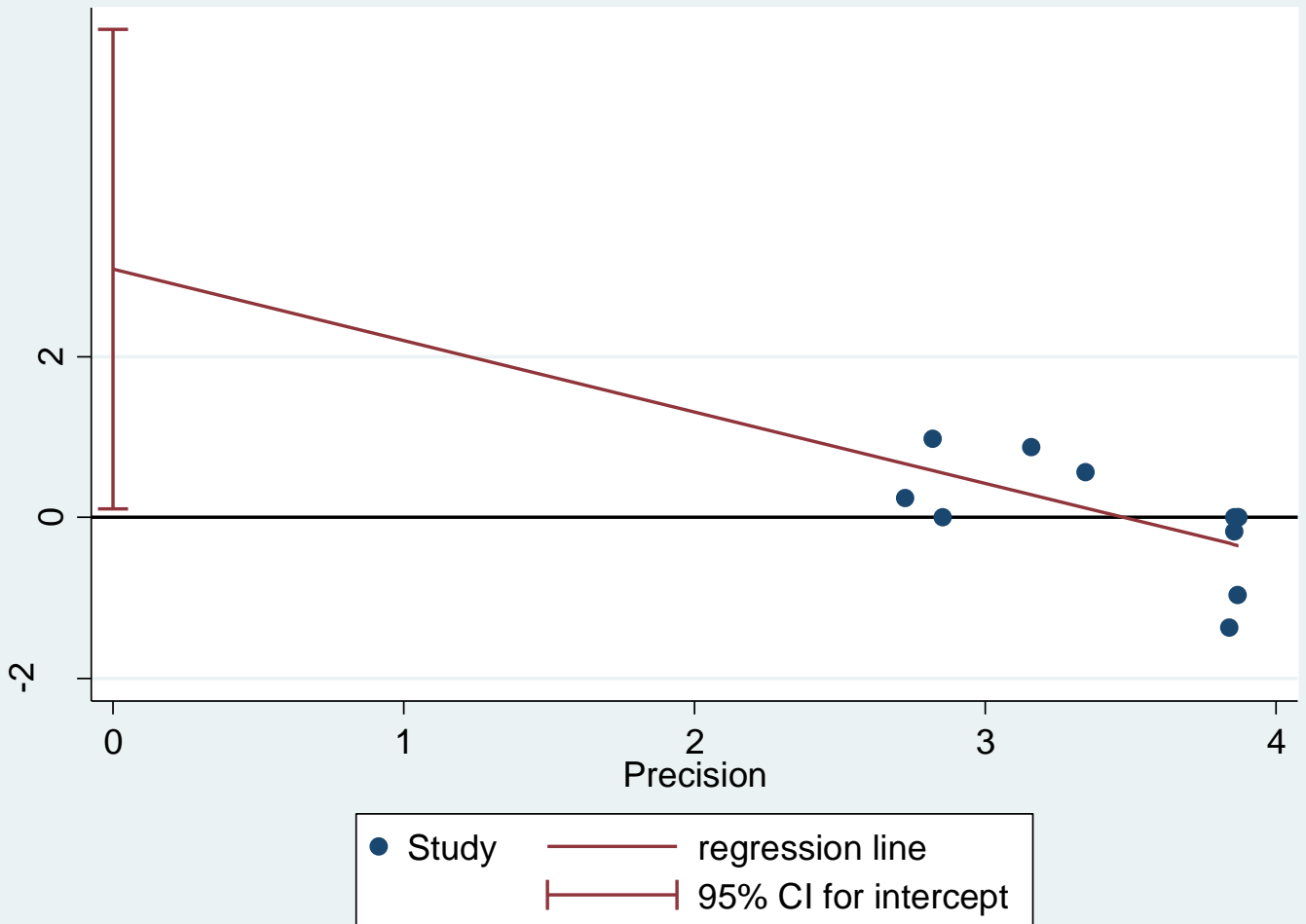
Testing for inconsistency:
 (1) [_y_D]groupB = 0

```
        chi2( 1) =   2.25
      Prob > chi2 =   0.1340
```

. metabias _ES_CEN seES , egger graph

Number of studies = 11   Root MSE   = .582

  Std_Eff | Coef.   Std. Err.   t   P>|t| [95% Conf. Interval]
----------+--
    slope | -.8856047   .3767878   -2.35   0.043 -1.737958   -.0332515
    bias | 3.080732   1.315908   2.34   0.044   .1039413 6.057522

Test of H0: no small-study effects   P = 0.044

Head-to-head comparisons   **Mean with 95%CI**

Placebo vs PUFA   0.18 (-0.23,0.59)

Medium chain triglyceride vs PUFA   -0.49 (-1.24,0.26)

Medium chain triglyceride vs Placebo   -0.67 (-1.52,0.18)

-10   -5   0   5   10
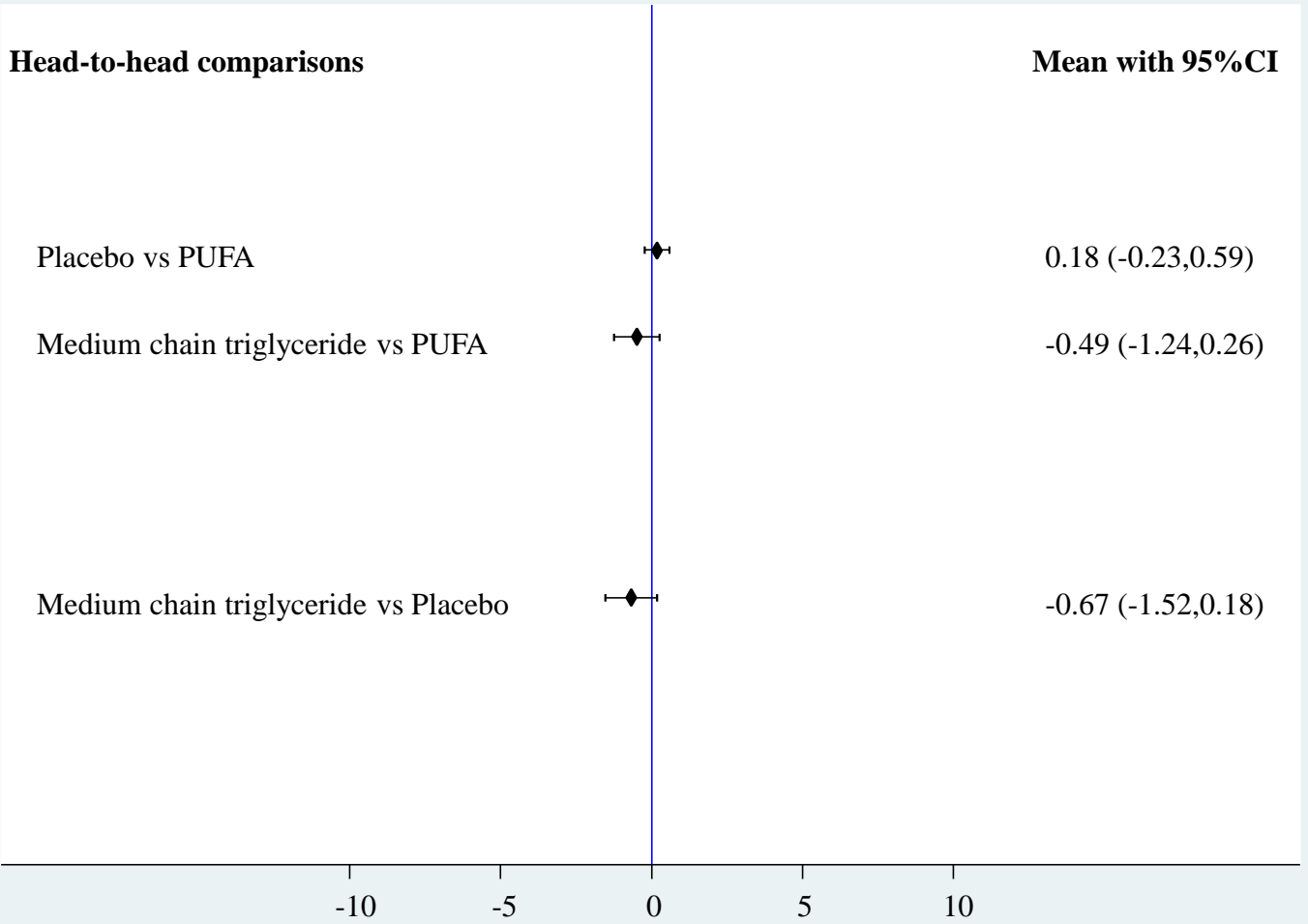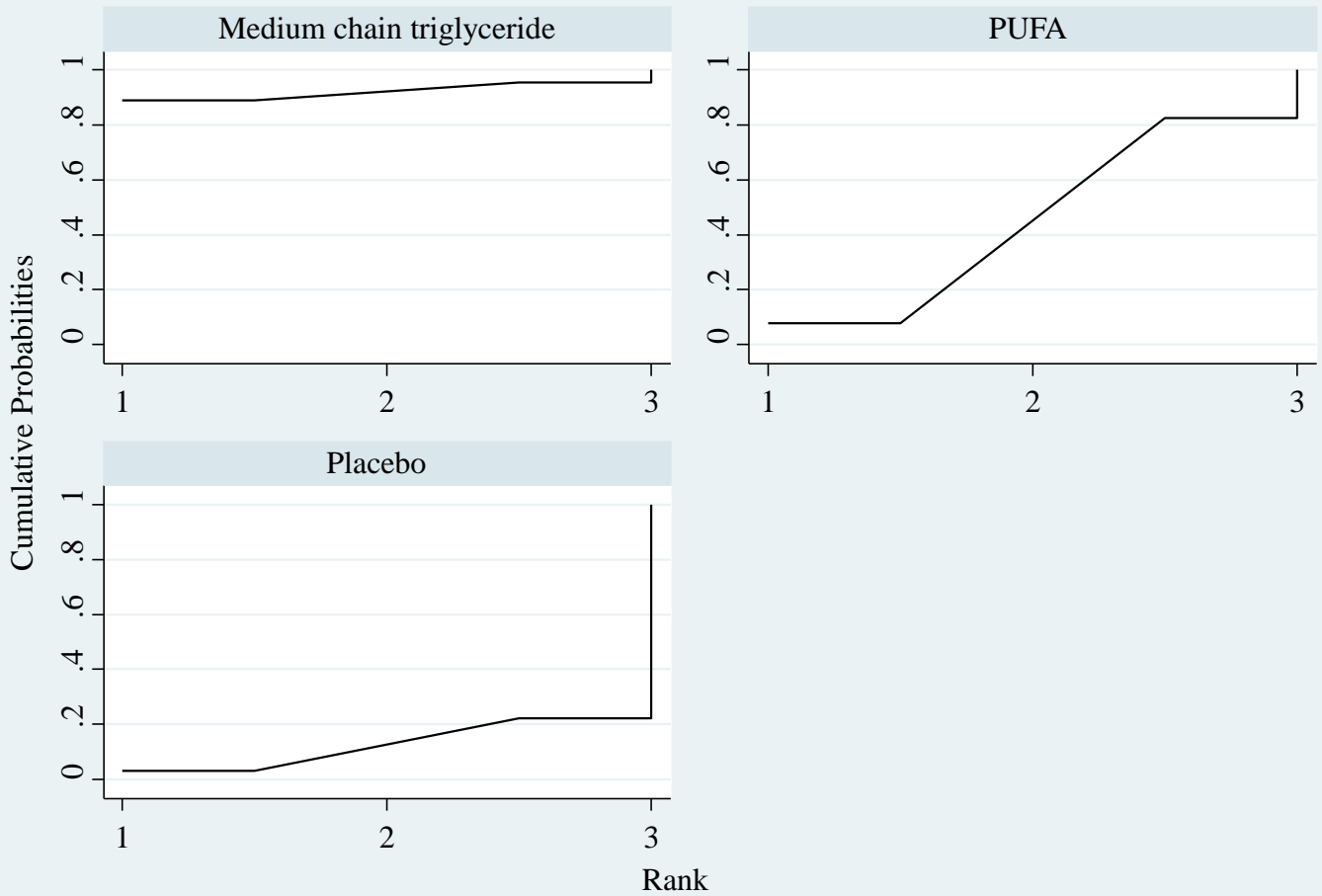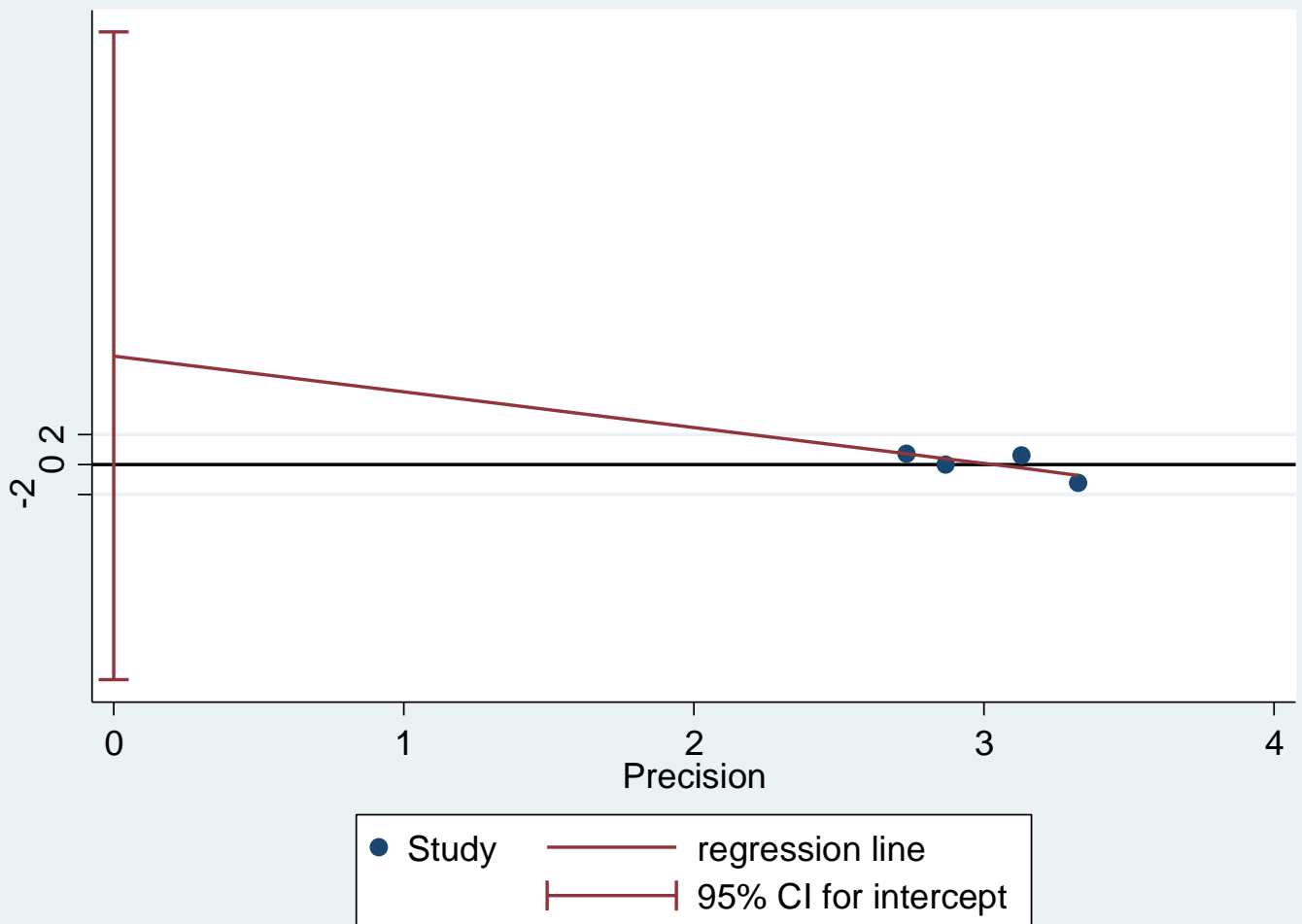
Graphs by Treatment

. sucra prob*, labels("PUFA" "Placebo" "Medium chain triglyceride")

Treatment	SUCRA	PrBest	MeanRank
PUFA	45.2	8.0	2.1
Placebo	12.7	3.2	2.7
Medium chain triglyceride	92.0	88.8	1.2

. metabias _ES_CEN seES , egger graph

Number of studies = 4   Root MSE   = .7567

    Std_Eff | Coef.   Std. Err.   t   P>|t| [95% Conf. Interval]
------------+--
      slope | -2.373224   1.648212   -1.44   0.287   -9.464908   4.718461
       bias | 7.184133   4.983411   1.44   0.286   -14.25776   28.62602

Test of H0: no small-study effects   P = 0.286

Supplementary File 11 to 14
Outcomes of Albumin

Head-to-head comparisons
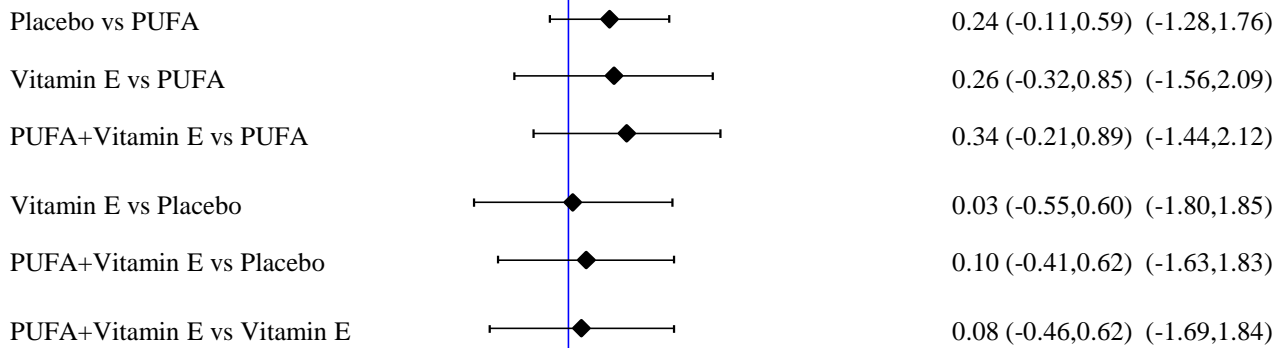
Mean with 95%CI
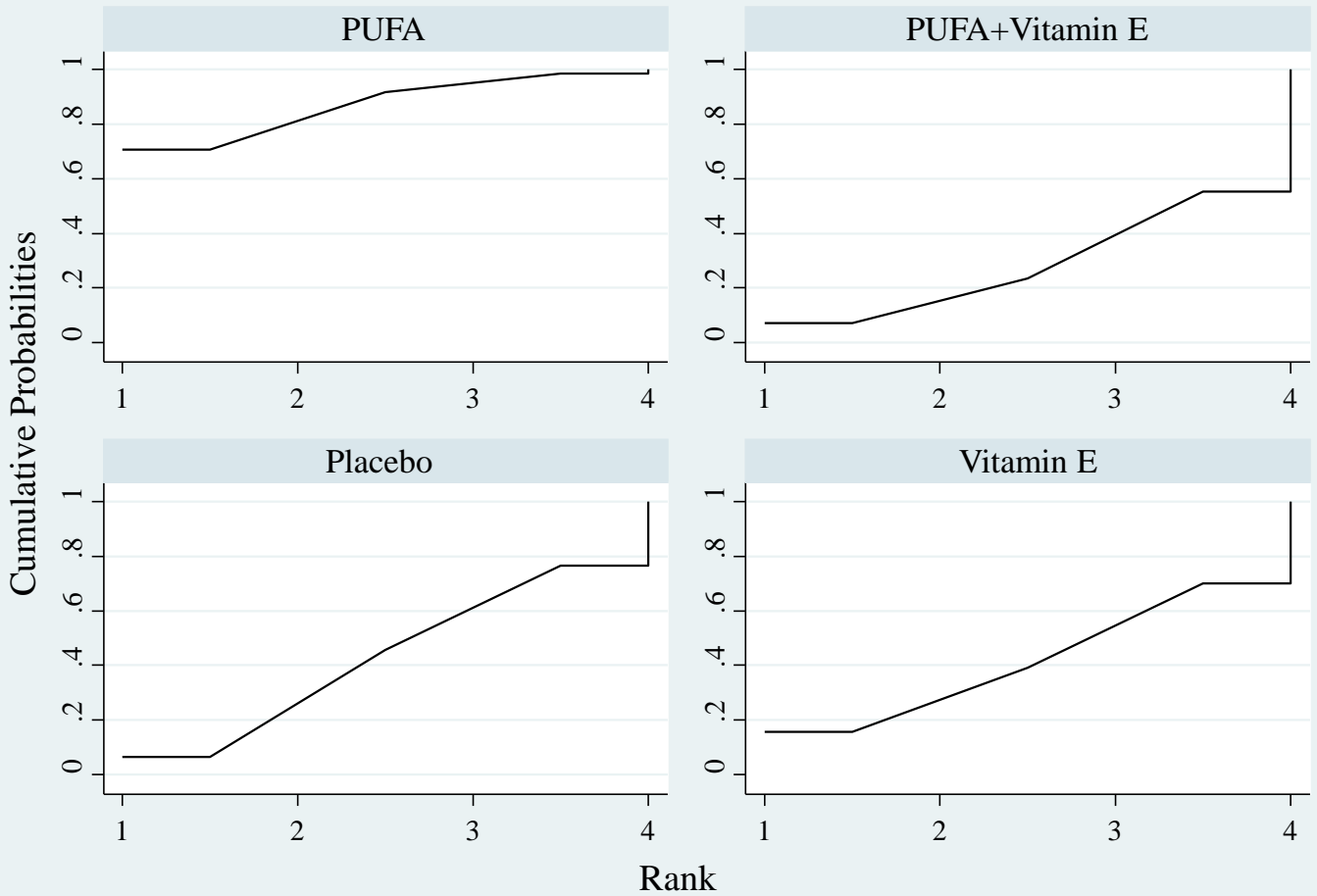
Comparison	Mean with 95%CI
Placebo vs PUFA	0.24 (-0.11,0.59) (-1.28,1.76)
Vitamin E vs PUFA	0.26 (-0.32,0.85) (-1.56,2.09)
PUFA+Vitamin E vs PUFA	0.34 (-0.21,0.89) (-1.44,2.12)
Vitamin E vs Placebo	0.03 (-0.55,0.60) (-1.80,1.85)
PUFA+Vitamin E vs Placebo	0.10 (-0.41,0.62) (-1.63,1.83)
PUFA+Vitamin E vs Vitamin E	0.08 (-0.46,0.62) (-1.69,1.84)

-3   -2   -1   0   1   2   3

Graphs by Treatment

. sucra prob*, labels("PUFA" "Placebo" "Vitamin E" "PUFA+Vitamin E")

Treatment	SUCRA	PrBest	MeanRank
PUFA	86.9	70.6	1.4
Placebo	42.8	6.4	2.7
Vitamin E	41.7	15.7	2.7
PUFA+Vitamin E	28.6	7.2	3.1

. network meta i, luades

```
initial:      log likelihood = -16.443995
rescale:      log likelihood = -14.678721
rescale eq:   log likelihood = -13.884903
Iteration 0:  log likelihood = -13.884903
Iteration 1:  log likelihood = -13.555383
Iteration 2:  log likelihood = -13.546198
Iteration 3:  log likelihood = -13.546175
Iteration 4:  log likelihood = -13.546175
```

Multivariate meta-analysis
Variance-covariance matrix = proportional .5*I(3)+.5*J(3,3,1)
Method = reml   Number of dimensions   =   3
Restricted log likelihood = -13.546175   Number of observations =   9

```
-------------------------------------------------------------------------------
           |    Coef.   Std. Err.     z    P>|z|    [95% Conf. Interval]
-----------+-------------------------------------------------------------------
_y_B       |
     _cons |  .2308547  .1478359    1.56   0.118   -.0588983    .5206077
-----------+-------------------------------------------------------------------
_y_C       |
     _cons |  .4192418  .2803931    1.50   0.135   -.1303187    .9688022
-----------+-------------------------------------------------------------------
_y_D       |
    groupB |  .2329741  .439844     0.53   0.596   -.6291043    1.095052
    groupC |  1.083716  .4673996    2.32   0.020    .1676299    1.999803
     _cons |  .053441   .2740923    0.19   0.845   -.4837701    .5906521
-------------------------------------------------------------------------------
```

Estimated between-studies SDs and correlation matrix:
```
       SD       _y_B      _y_C      _y_D
_y_B .16339678     1        .         .
_y_C .16339678    .5        1         .
_y_D .16339678    .5        .5        1
```
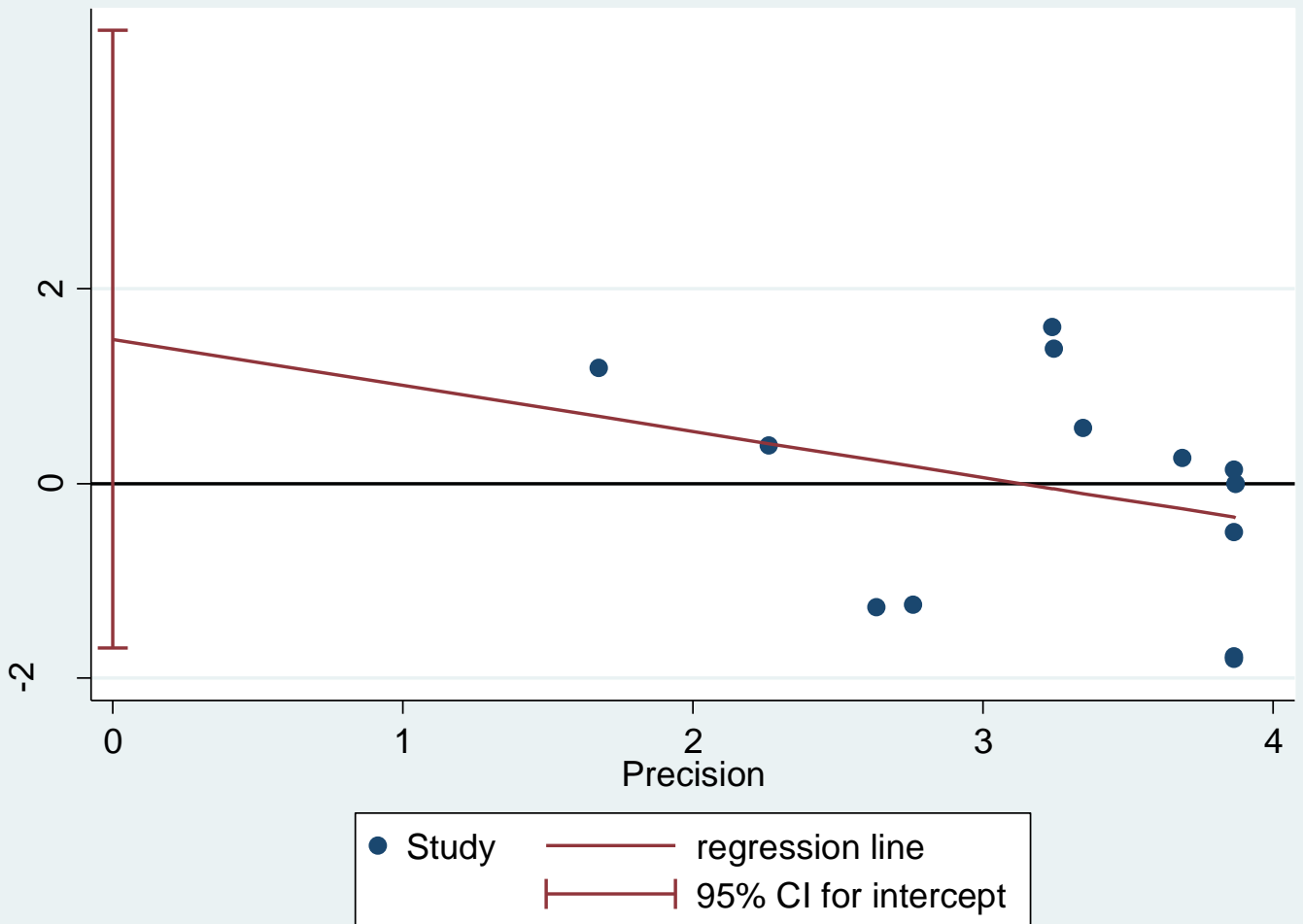
Testing for inconsistency:
(1) [_y_D]groupB = 0
(2) [_y_D]groupC = 0

```
      chi2(  2) =    5.38
    Prob > chi2 =   0.0680
```

```
. metabias _ES_CEN seES , egger graph

Number of studies =  14                          Root MSE    =  1.109
---------------------------------------------------------------------------------
    Std_Eff |    Coef.      Std. Err.      t     P>|t|    [95% Conf. Interval]
------------+--------------------------------------------------------------------
      slope |  -.4728177  .4332609   -1.09  0.297   -1.416812   .4711767
       bias |   1.481466  1.455748    1.02  0.329   -1.690337  4.653269
---------------------------------------------------------------------------------

Test of H0: no small-study effects         P = 0.329
```

Supplementary File 15 to 16
Detection of Regions on the outcomes of C-reactive protein and high sensitive C-reactive protein

. network meta c, regress(Asia America Europe) eform(Mean difference)
Command is: mvmeta _y _S Asia America Europe , eform(Mean difference)
initial: log likelihood = -8.3767857
rescale: log likelihood = -7.529987
rescale eq: log likelihood = -6.5780492
Iteration 0:   log likelihood = -6.5780492 (not concave)
Iteration 1:   log likelihood = -6.3847531 (not concave)
Iteration 2:   log likelihood = -6.382383
Iteration 3:   log likelihood = -6.3445826
Iteration 4:   log likelihood = -6.3435081
Iteration 5:   log likelihood = -6.3434965
Iteration 6:   log likelihood = -6.3434965

Multivariate meta-analysis
Variance-covariance matrix = proportional .5*I(4)+.5*J(4,4,1)
Method = reml   Number of dimensions   =   4
Restricted log likelihood = -6.3434965   Number of observations =   11

          |Mean difference Std. Err.   z   P>|z| [95% Conf. Interval]
------------+---
_y_B |
    Asia | .954335   .411708   -0.11   0.914   .4097184   2.222881
 America | .5749935 .2594293   -1.23   0.220   .237472   1.392238
    _cons | 1.783514 .6901929   1.50   0.135   .8353616   3.807839
------------+---
_y_C |
    Asia | 1.357536 42.95153   0.01   0.992   1.59e-27   1.16e+27
  Europe | 1.1617 36.75095   0.00   0.996   1.37e-27   9.85e+26
    _cons | .8519952 26.95295   -0.01   0.996   1.01e-27   7.22e+26
------------+---
_y_D |
 America | 1.161048 36.73196   0.00   0.996   1.37e-27   9.87e+26
    _cons | 1.022543 .3447171   0.07   0.947   .5281131   1.979869
------------+---
_y_E |
    _cons | 1.06683 .3660272   0.19   0.850   .544565   2.089973

Estimated between-studies SDs and correlation matrix:
         SD   _y_B   _y_C   _y_D   _y_E
_y_B 5.097e-09   1   .   .   .
_y_C 5.097e-09   .5   1   .   .
_y_D 5.097e-09   .5   .5   1   .
_y_E 5.097e-09   .5   .5   .5   1

. network meta c, regress(Asia America Europe) eform(Mean difference)
Command is: mvmeta _y _S Asia America Europe , eform(Mean difference)
initial: log likelihood = -5.7716745
rescale: log likelihood = -5.6813907
rescale eq: log likelihood = -5.3667652
Iteration 0: log likelihood = -5.3667652
Iteration 1: log likelihood = -5.333843 (not concave)
Iteration 2: log likelihood = -5.3337078
Iteration 3: log likelihood = -5.3335849
Iteration 4: log likelihood = -5.3335849

Multivariate meta-analysis
Variance-covariance matrix = proportional .5*I(4)+.5*J(4,4,1)
Method = reml   Number of dimensions   =   4
Restricted log likelihood = -5.3335849   Number of observations =   6

        |Mean difference   Std. Err.   z   P>|z| [95% Conf. Interval]
-------------+---
_y_B |
     Asia | 1.247846   39.45615   0.01   0.994   1.52e-27   1.02e+27
   America | 1.646605   52.06696   0.02   0.987   2.00e-27   1.36e+27
     _cons | .990318   31.31072   -0.00   1.000   1.21e-27   8.09e+26
-------------+---
_y_C |
     _cons | 1.001552   .4278986   0.00   0.997   .4335207   2.31386
-------------+---
_y_D |
     Asia | .9885095   31.25598   -0.00   1.000   1.20e-27   8.12e+26
   America | 1.553719   49.12946   0.01   0.989   1.89e-27   1.28e+27
     _cons | 1.008552   31.88712   0.00   1.000   1.23e-27   8.24e+26
-------------+---
_y_E |
     _cons | 1.743973   .8519281   1.14   0.255   .6694672   4.54308

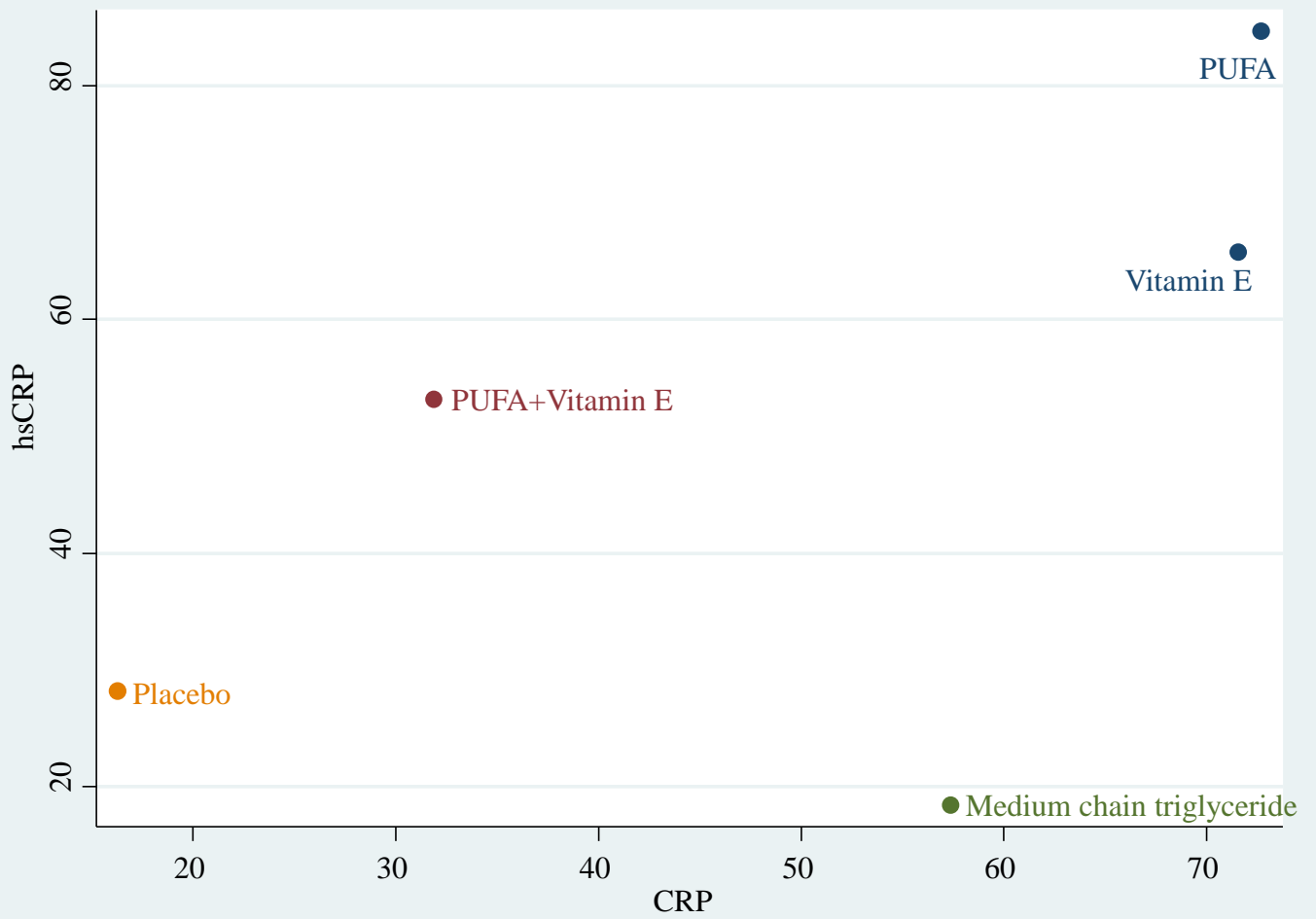Estimated between-studies SDs and correlation matrix:
        SD   _y_B   _y_C   _y_D   _y_E
_y_B .34039961   1   .   .   .
_y_C .34039961   .5   1   .   .
_y_D .34039961   .5   .5   1   .
_y_E .34039961   .5   .5   .5   1

Supplementary File 17
Cluster plot of SUCRA for CRP and hs-CRP

Supplementary File 18
Search strategy

Embase:

('dialysis'/exp OR 'acute dialysis' OR 'coil dialysis' OR 'dialysis' OR 'flow dialysis' OR 'hemodialysis'/exp OR 'blood dialysis' OR 'chronic haemodialysis' OR 'chronic hemodialysis' OR 'chronic intermittent haemodialysis' OR 'chronic intermittent hemodialysis' OR 'dialysis center' OR 'dialysis, blood' OR 'extracorporeal blood cleansing' OR 'extracorporeal dialysis' OR 'haemodialysis' OR 'haemodialysis center' OR 'haemodialysis centre' OR 'haemodialysis department' OR 'haemodialysis unit' OR 'haemodialysis units, hospital' OR 'hemodialyse' OR 'hemodialysis' OR 'hemodialysis center' OR 'hemodialysis department' OR 'hemodialysis unit' OR 'hemodialysis units, hospital' OR 'hemorenodialysis' OR 'hemotrialysate' OR 'intermittent chronic haemodialysis' OR 'intermittent chronic hemodialysis' OR 'intermittent haemodialysis' OR 'intermittent hemodialysis' OR 'renal dialysis') AND ('omega 3' OR omega3 OR 'omega-3 fatty acids' OR 'omega-3 fatty acid' OR 'omega3 fatty acids' OR 'omega3 fatty acid' OR docosahexaenoic OR dha OR eicosapentaenoic OR epa OR polyunsaturated OR 'polyunsaturated fatty acids' OR 'polyunsaturated fatty acid'/exp OR 'fatty acid polyunsaturation' OR 'fatty acid, polyunsaturated' OR 'poly unsaturated fatty acid' OR 'polyunsaturated fat' OR 'polyunsaturated fatty acid' OR lcpufa* OR pufa* OR 'ω 3' OR ω3 OR 'n3 fatty acid' OR 'n3 fatty acids' OR 'n-3 fatty acid' OR 'n-3 fatty acids' OR 'omega-6 fatty acids' OR 'omega-6 fatty acid' OR 'omega6 fatty acids' OR 'omega6 fatty acid')

PubMed:

(dialysis[ti] OR hemodialysis[ti]) AND (omega 3 OR omega3 OR omega-3 fatty acids OR omega-3 fatty acid OR omega3 fatty acids OR omega3 fatty acid OR docosahexaenoic OR dha OR eicosapentaenoic OR epa OR polyunsaturated OR polyunsaturated fatty acids OR polyunsaturated fatty acid OR LCPUFA* OR PUFA* OR ω-3 OR ω3 OR n3 fatty acid OR n3 fatty acids OR n-3 fatty acid OR n-3 fatty acids OR omega-6 fatty acids OR omega-6 fatty acid OR omega6 fatty acids OR omega6 fatty acid)

Web of Science:

TOPIC: (dialysis OR hemodialysis) AND TOPIC: (omega 3 OR omega3 OR omega-3 fatty acids OR omega-3 fatty acid OR omega3 fatty acids OR omega3 fatty acid OR docosahexaenoic OR dha OR eicosapentaenoic OR epa OR polyunsaturated OR polyunsaturated fatty acids OR polyunsaturated fatty acid OR LCPUFA* OR PUFA* OR ω-3 OR ω3 OR n3 fatty acid OR n3 fatty acids OR n-3 fatty acid OR n-3 fatty acids OR omega-6 fatty acids OR omega-6 fatty acid OR omega6 fatty acids OR omega6 fatty acid)