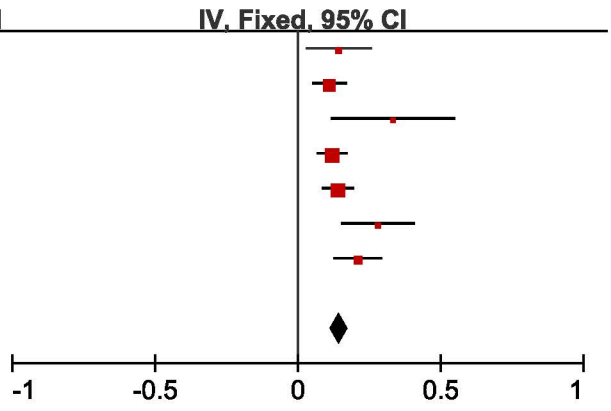
## A Aspartate Aminotransferase Increase

| Study or Subgroup | event rate | SE | Weight | IV, Fixed, 95% CI |
|---|---|---|---|---|
| Hida 2016 | 0.143 | 0.0592 | 6.0% | 0.14 [0.03, 0.26] |
| Hida 2017 | 0.11 | 0.0308 | 22.2% | 0.11 [0.05, 0.17] |
| Iwama 2017 | 0.333 | 0.1111 | 1.7% | 0.33 [0.12, 0.55] |
| Ou 2016 | 0.12 | 0.0277 | 27.5% | 0.12 [0.07, 0.17] |
| Peters 2017 | 0.14 | 0.0281 | 26.7% | 0.14 [0.08, 0.20] |
| Seto 2013 | 0.28 | 0.0662 | 4.8% | 0.28 [0.15, 0.41] |
| Shaw 2016 | 0.21 | 0.0437 | 11.0% | 0.21 [0.12, 0.30] |
| **Total (95% CI)** | | | **100.0%** | **0.15 [0.12, 0.17]** |

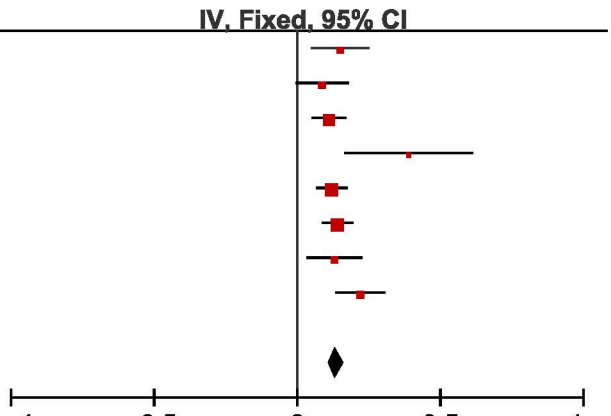
Heterogeneity: Chi² = 11.37, df = 6 (P = 0.08); I² = 47%
Test for overall effect: Z = 10.04 (P < 0.00001)




## B Nausea

| Study or Subgroup | event rate | SE | Weight | IV, Fixed, 95% CI |
|---|---|---|---|---|
| Gadgeel 2014 | 0.15 | 0.0521 | 6.8% | 0.15 [0.05, 0.25] |
| Hida 2016 | 0.086 | 0.0474 | 8.2% | 0.09 [-0.01, 0.18] |
| Hida 2017 | 0.11 | 0.0308 | 19.4% | 0.11 [0.05, 0.17] |
| Iwama 2017 | 0.389 | 0.1149 | 1.4% | 0.39 [0.16, 0.61] |
| Ou 2016 | 0.12 | 0.0277 | 24.0% | 0.12 [0.07, 0.17] |
| Peters 2017 | 0.14 | 0.0281 | 23.3% | 0.14 [0.08, 0.20] |
| Seto 2013 | 0.13 | 0.0496 | 7.5% | 0.13 [0.03, 0.23] |
| Shaw 2016 | 0.22 | 0.0444 | 9.3% | 0.22 [0.13, 0.31] |
| **Total (95% CI)** | | | **100.0%** | **0.14 [0.11, 0.16]** |

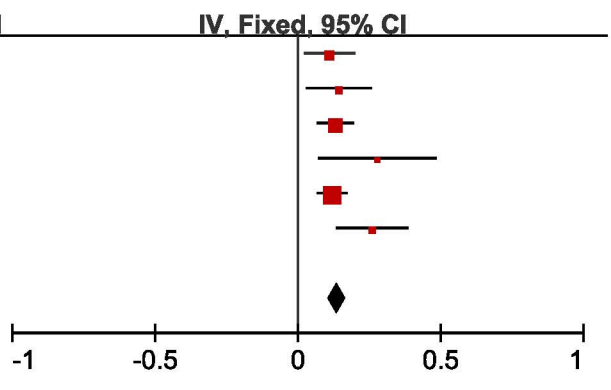
Heterogeneity: Chi² = 10.69, df = 7 (P = 0.15); I² = 35%
Test for overall effect: Z = 10.01 (P < 0.00001)




## C Rash

| Study or Subgroup | event rate | SE | Weight | IV, Fixed, 95% CI |
|---|---|---|---|---|
| Gadgeel 2014 | 0.11 | 0.0456 | 14.5% | 0.11 [0.02, 0.20] |
| Hida 2016 | 0.143 | 0.0592 | 8.6% | 0.14 [0.03, 0.26] |
| Hida 2017 | 0.13 | 0.0331 | 27.6% | 0.13 [0.07, 0.19] |
| Iwama 2017 | 0.278 | 0.1056 | 2.7% | 0.28 [0.07, 0.48] |
| Ou 2016 | 0.12 | 0.0277 | 39.4% | 0.12 [0.07, 0.17] |
| Seto 2013 | 0.26 | 0.0647 | 7.2% | 0.26 [0.13, 0.39] |
| **Total (95% CI)** | | | **100.0%** | **0.14 [0.10, 0.17]** |

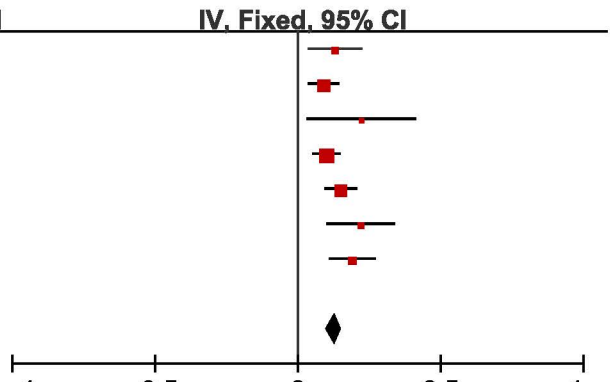
Heterogeneity: Chi² = 6.18, df = 5 (P = 0.29); I² = 19%
Test for overall effect: Z = 7.92 (P < 0.00001)




## D Alanine Aminotransferase Increase

| Study or Subgroup | event rate | SE | Weight | IV, Fixed, 95% CI |
|---|---|---|---|---|
| Gadgeel 2014 | 0.13 | 0.0491 | 7.8% | 0.13 [0.03, 0.23] |
| Hida 2017 | 0.09 | 0.0282 | 23.6% | 0.09 [0.03, 0.15] |
| Iwama 2017 | 0.222 | 0.098 | 2.0% | 0.22 [0.03, 0.41] |
| Ou 2016 | 0.1 | 0.0255 | 28.8% | 0.10 [0.05, 0.15] |
| Peters 2017 | 0.15 | 0.029 | 22.3% | 0.15 [0.09, 0.21] |
| Seto 2013 | 0.22 | 0.0611 | 5.0% | 0.22 [0.10, 0.34] |
| Shaw 2016 | 0.19 | 0.0421 | 10.6% | 0.19 [0.11, 0.27] |
| **Total (95% CI)** | | | **100.0%** | **0.13 [0.10, 0.16]** |

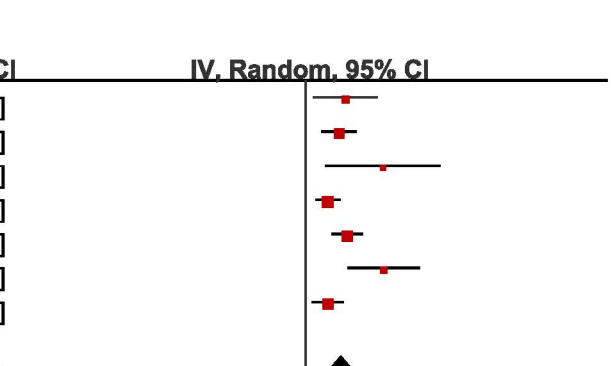
Heterogeneity: Chi² = 8.95, df = 6 (P = 0.18); I² = 33%
Test for overall effect: Z = 9.43 (P < 0.00001)




## E Blood Bilirubin Increase

| Study or Subgroup | event rate | SE | Weight | IV, Random, 95% CI |
|---|---|---|---|---|
| Hida 2016 | 0.143 | 0.0592 | 9.5% | 0.14 [0.03, 0.26] |
| Hida 2017 | 0.12 | 0.032 | 18.0% | 0.12 [0.06, 0.18] |
| Iwama 2017 | 0.278 | 0.1056 | 3.9% | 0.28 [0.07, 0.48] |
| Ou 2016 | 0.08 | 0.0231 | 21.9% | 0.08 [0.03, 0.13] |
| Peters 2017 | 0.15 | 0.029 | 19.3% | 0.15 [0.09, 0.21] |
| Seto 2013 | 0.28 | 0.0662 | 8.2% | 0.28 [0.15, 0.41] |
| Shaw 2016 | 0.08 | 0.0291 | 19.2% | 0.08 [0.02, 0.14] |
| **Total (95% CI)** | | | **100.0%** | **0.13 [0.09, 0.17]** |

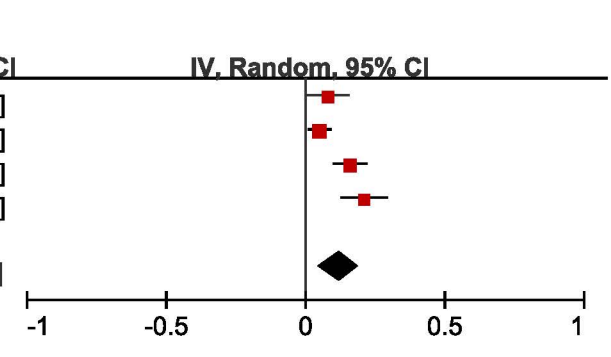
Heterogeneity: Tau² = 0.00; Chi² = 14.04, df = 6 (P = 0.03); I² = 57%
Test for overall effect: Z = 5.83 (P < 0.00001)




## F Headache

| Study or Subgroup | event rate | SE | Weight | IV, Random, 95% CI |
|---|---|---|---|---|
| Gadgeel 2014 | 0.08 | 0.0396 | 23.3% | 0.08 [0.00, 0.16] |
| Hida 2017 | 0.05 | 0.0215 | 28.6% | 0.05 [0.01, 0.09] |
| Ou 2016 | 0.16 | 0.0312 | 25.9% | 0.16 [0.10, 0.22] |
| Shaw 2016 | 0.21 | 0.0437 | 22.1% | 0.21 [0.12, 0.30] |
| **Total (95% CI)** | | | **100.0%** | **0.12 [0.05, 0.19]** |

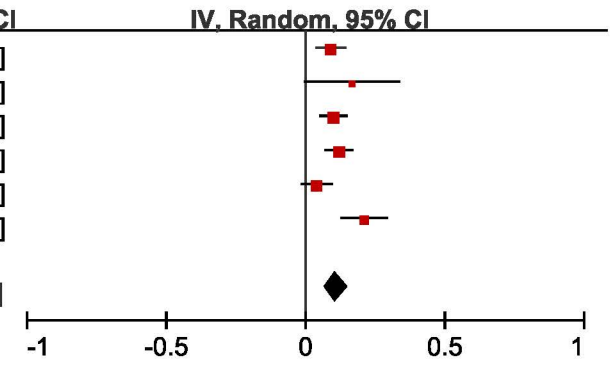
Heterogeneity: Tau² = 0.00; Chi² = 15.70, df = 3 (P = 0.001); I² = 81%
Test for overall effect: Z = 3.23 (P = 0.001)




## G Diarrhea

| Study or Subgroup | event rate | SE | Weight | IV, Random, 95% CI |
|---|---|---|---|---|
| Hida 2017 | 0.09 | 0.0282 | 20.0% | 0.09 [0.03, 0.15] |
| Iwama 2017 | 0.167 | 0.0879 | 4.9% | 0.17 [-0.01, 0.34] |
| Ou 2016 | 0.1 | 0.0255 | 21.4% | 0.10 [0.05, 0.15] |
| Peters 2017 | 0.12 | 0.0264 | 20.9% | 0.12 [0.07, 0.17] |
| Seto 2013 | 0.04 | 0.0289 | 19.6% | 0.04 [-0.02, 0.10] |
| Shaw 2016 | 0.21 | 0.0437 | 13.3% | 0.21 [0.12, 0.30] |
| **Total (95% CI)** | | | **100.0%** | **0.11 [0.07, 0.15]** |

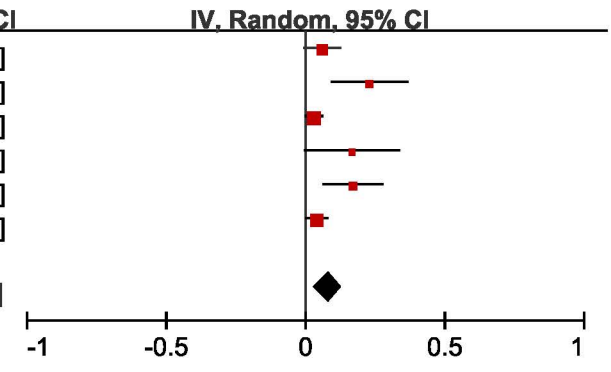
Heterogeneity: Tau² = 0.00; Chi² = 11.91, df = 5 (P = 0.04); I² = 58%
Test for overall effect: Z = 5.13 (P < 0.00001)




## H Neutropenia

| Study or Subgroup | event rate | SE | Weight | IV, Random, 95% CI |
|---|---|---|---|---|
| Gadgeel 2014 | 0.06 | 0.0346 | 19.5% | 0.06 [-0.01, 0.13] |
| Hida 2016 | 0.229 | 0.071 | 8.9% | 0.23 [0.09, 0.37] |
| Hida 2017 | 0.03 | 0.0168 | 27.3% | 0.03 [-0.00, 0.06] |
| Iwama 2017 | 0.167 | 0.0879 | 6.4% | 0.17 [-0.01, 0.34] |
| Seto 2013 | 0.17 | 0.0554 | 12.3% | 0.17 [0.06, 0.28] |
| Shaw 2016 | 0.04 | 0.021 | 25.5% | 0.04 [-0.00, 0.08] |
| **Total (95% CI)** | | | **100.0%** | **0.08 [0.03, 0.13]** |

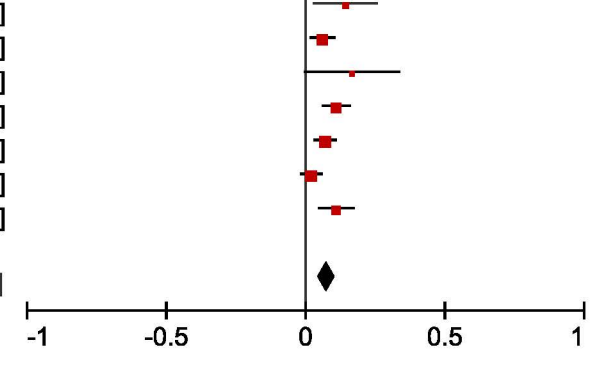
Heterogeneity: Tau² = 0.00; Chi² = 14.54, df = 5 (P = 0.01); I² = 66%
Test for overall effect: Z = 3.28 (P = 0.001)



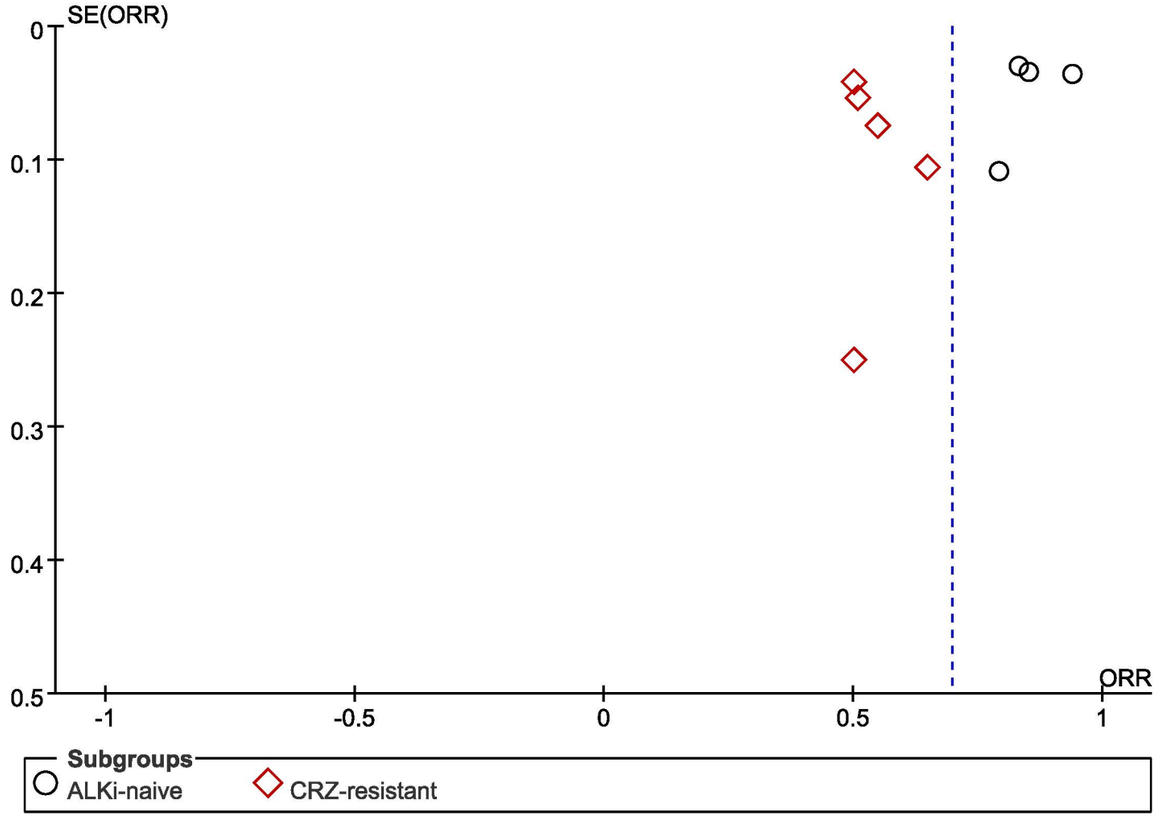

## I Vomiting

| Study or Subgroup | event rate | SE | Weight | IV, Random, 95% CI |
|---|---|---|---|---|
| Hida 2016 | 0.143 | 0.0592 | 6.2% | 0.14 [0.03, 0.26] |
| Hida 2017 | 0.06 | 0.0234 | 18.9% | 0.06 [0.01, 0.11] |
| Iwama 2017 | 0.167 | 0.0879 | 3.1% | 0.17 [-0.01, 0.34] |
| Ou 2016 | 0.11 | 0.0266 | 17.0% | 0.11 [0.06, 0.16] |
| Peters 2017 | 0.07 | 0.0207 | 20.6% | 0.07 [0.03, 0.11] |
| Seto 2013 | 0.02 | 0.0206 | 20.7% | 0.02 [-0.02, 0.06] |
| Shaw 2016 | 0.11 | 0.0335 | 13.5% | 0.11 [0.04, 0.18] |
| **Total (95% CI)** | | | **100.0%** | **0.08 [0.05, 0.11]** |

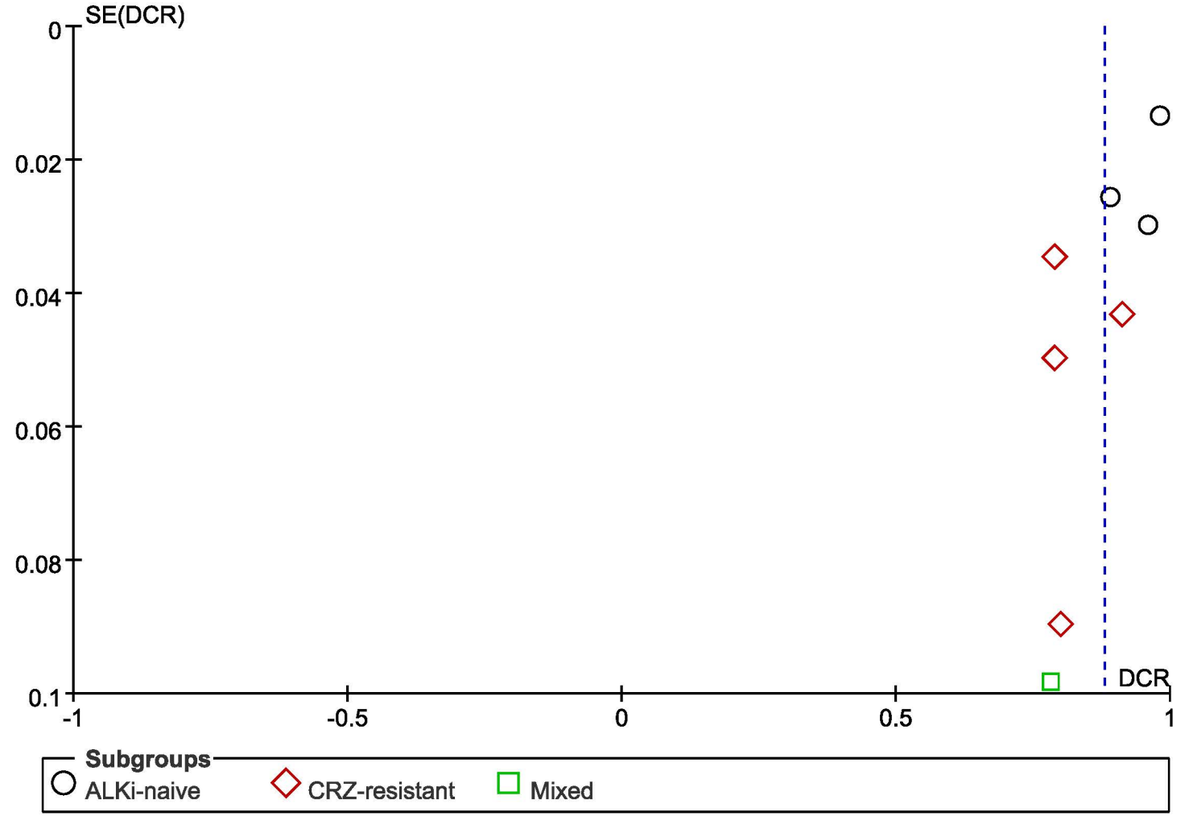
Heterogeneity: Tau² = 0.00; Chi² = 12.49, df = 6 (P = 0.05); I² = 52%
Test for overall effect: Z = 4.72 (P < 0.00001)



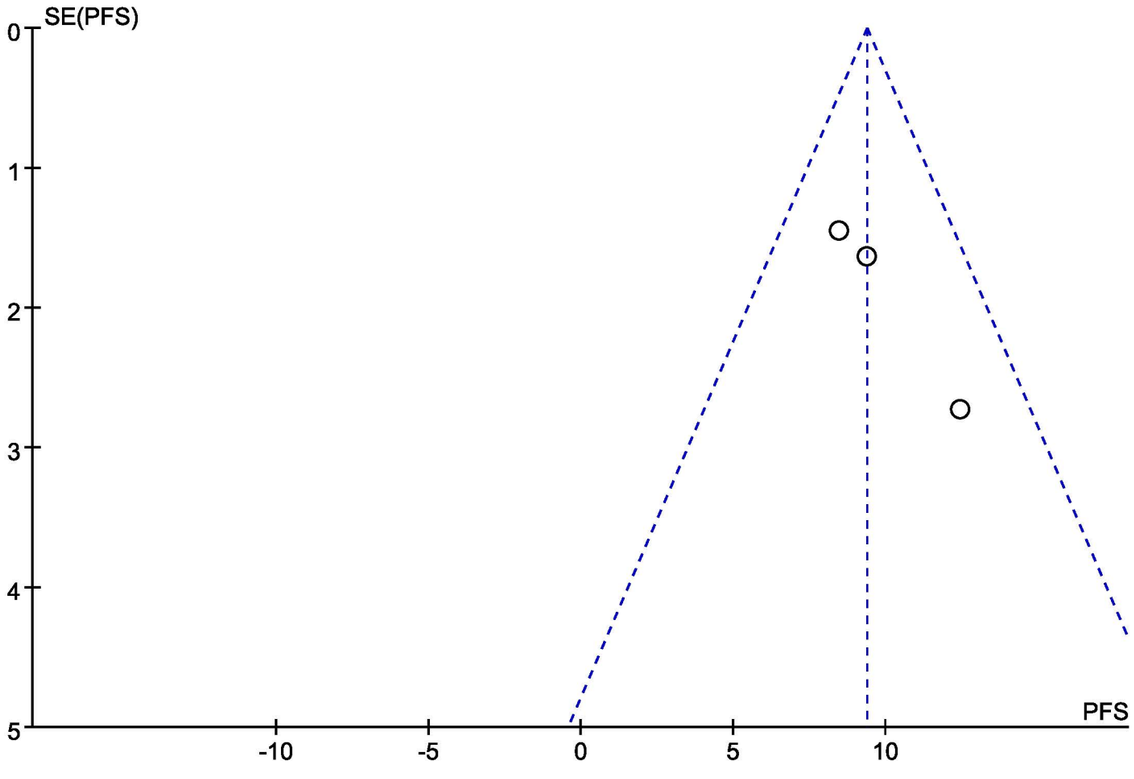
**A** ORR



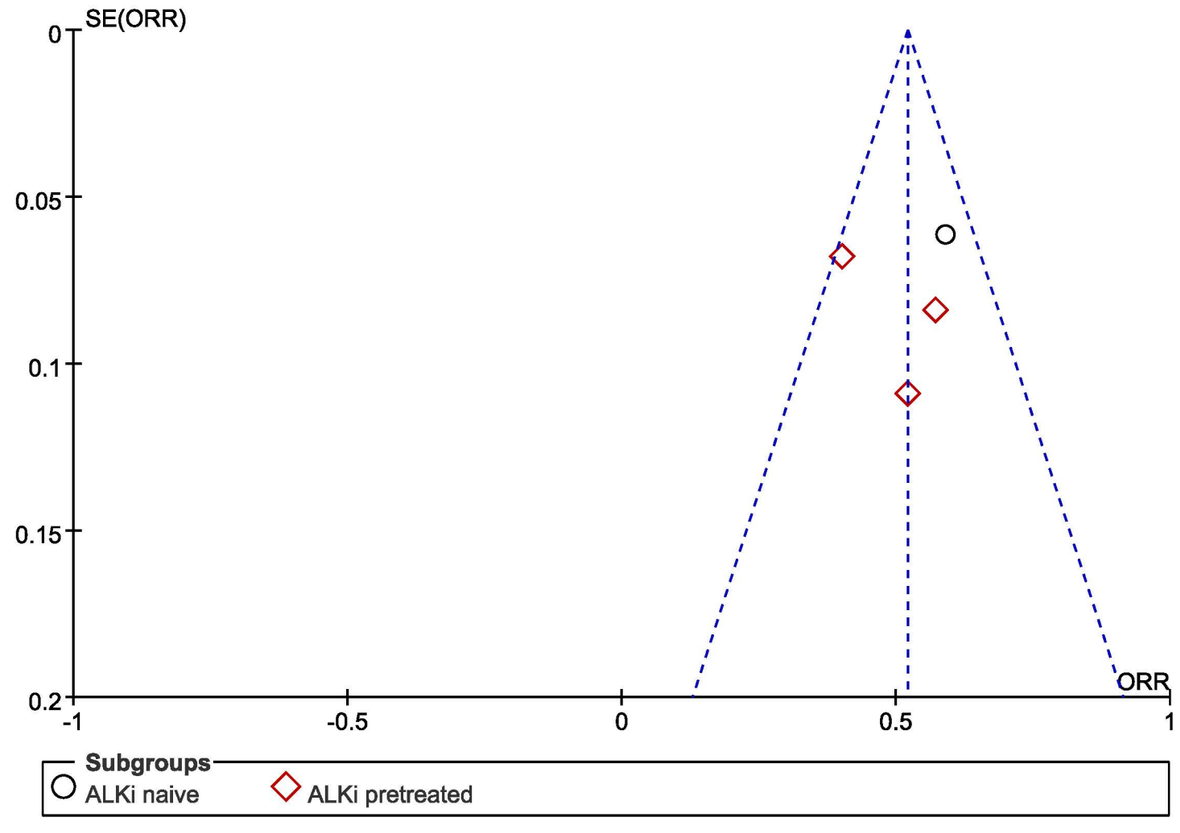

**B** DCR

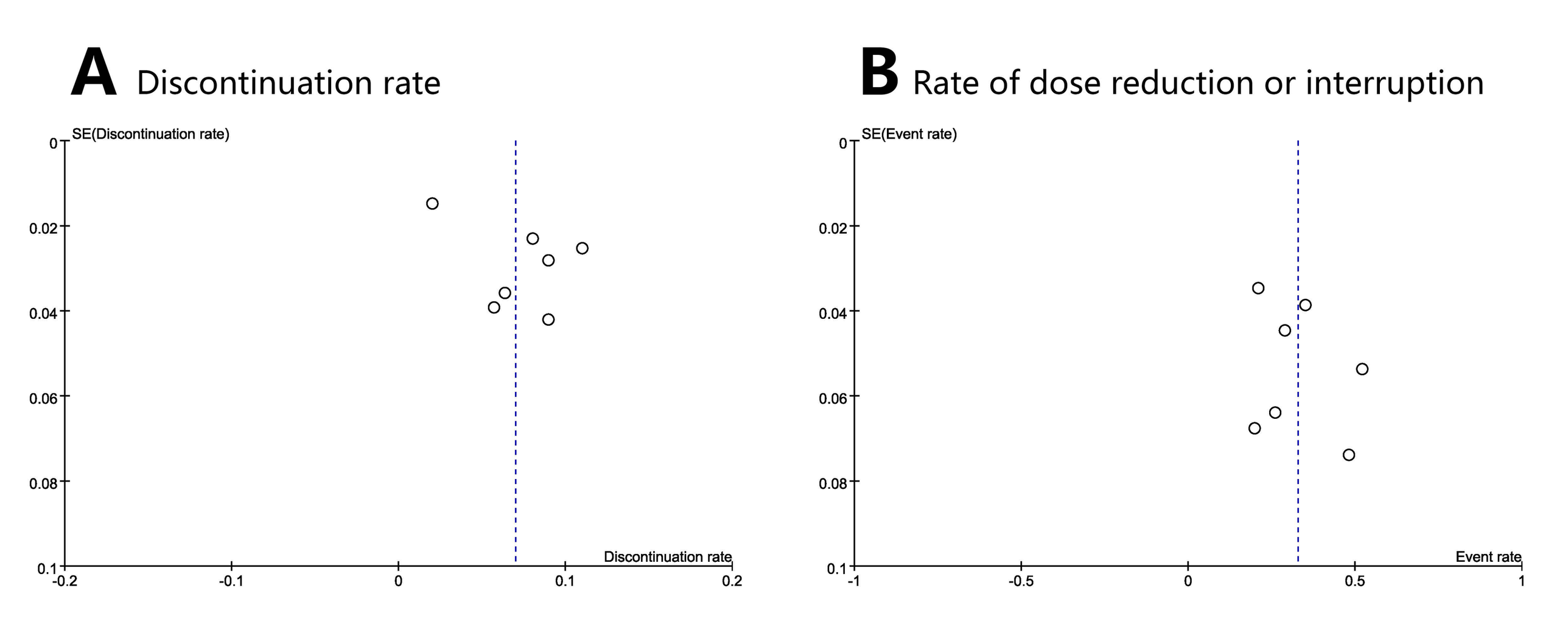



**C** PFS

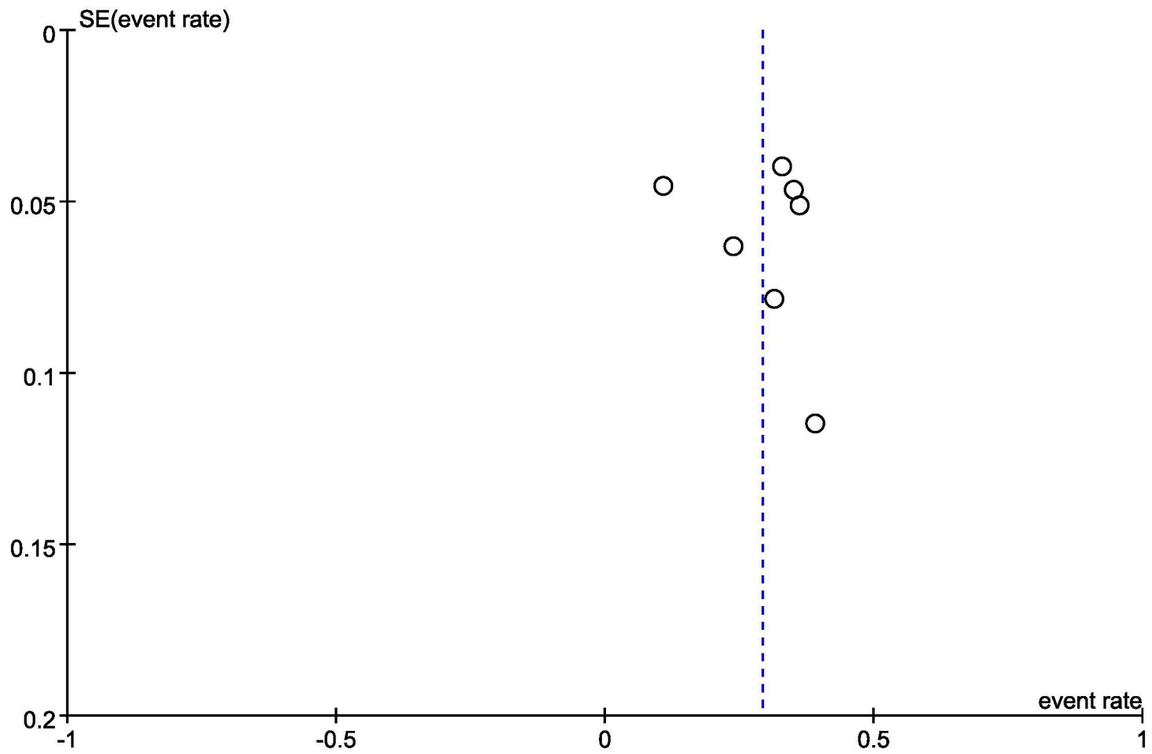



**D** Intracranial ORR

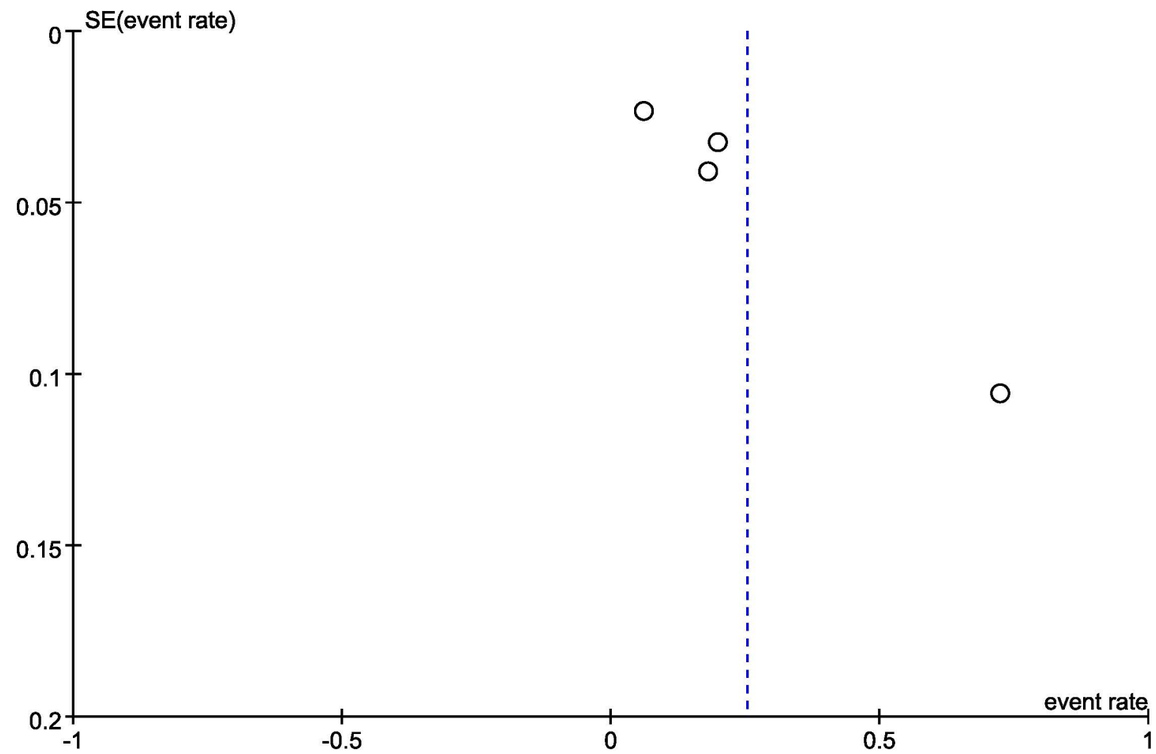



A Discontinuation rate
SE(Discontinuation rate)
0
0.02
0.04
0.06
0.08
0.1
-0.2
-0.1
0
0.1
0.2
Discontinuation rate
B Rate of dose reduction or interruption
SE(Event rate)
0
0.02
0.04
0.06
0.08
0.1
-1
-0.5
0
0.5
1
Event rate

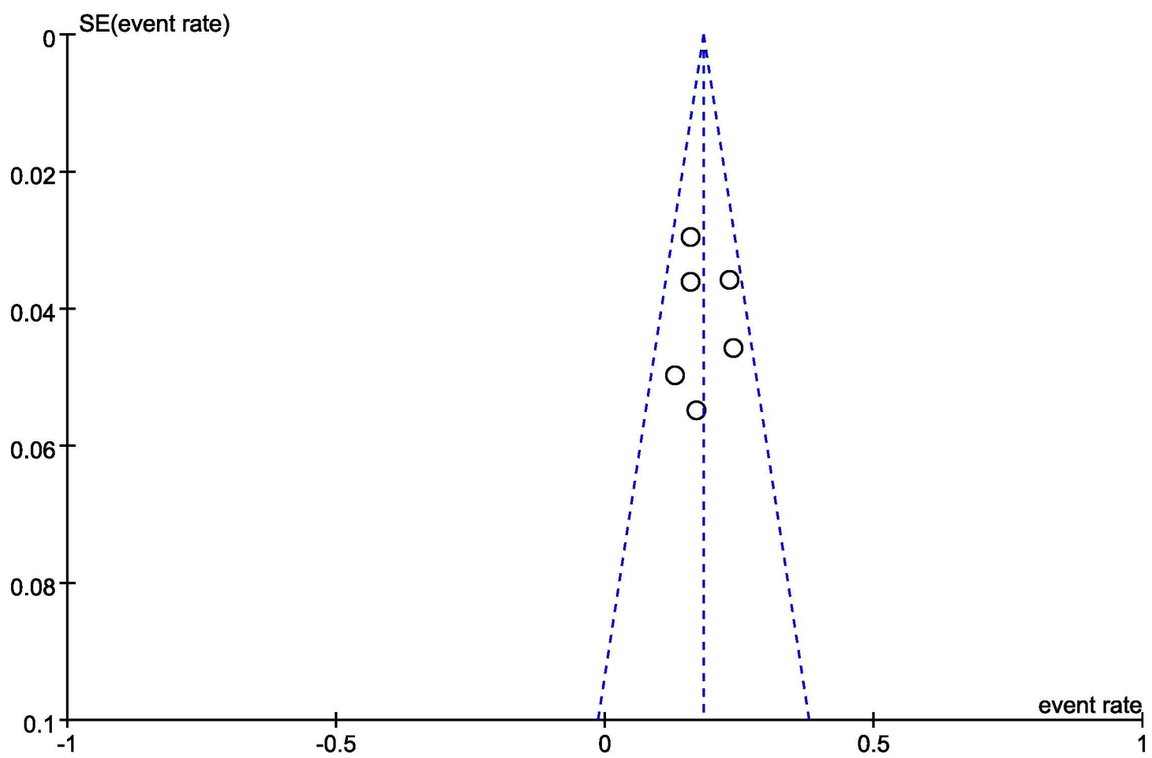
**A** Constipation



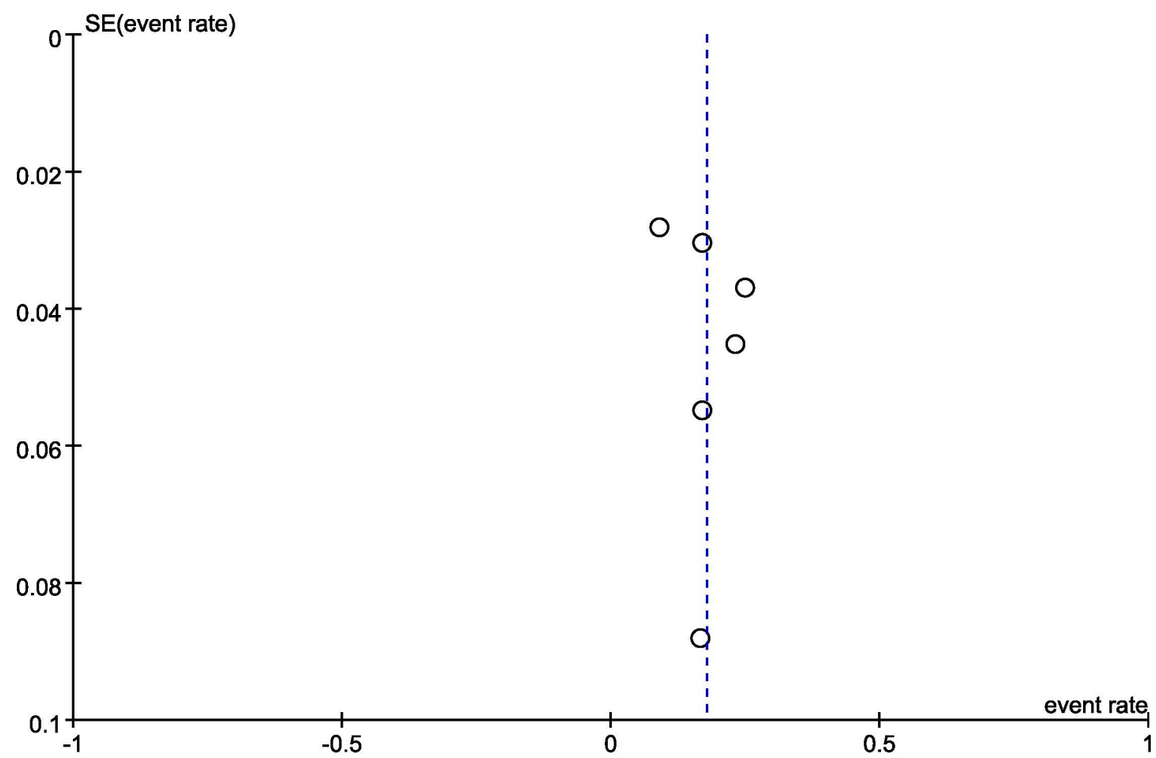

**B** Anemia



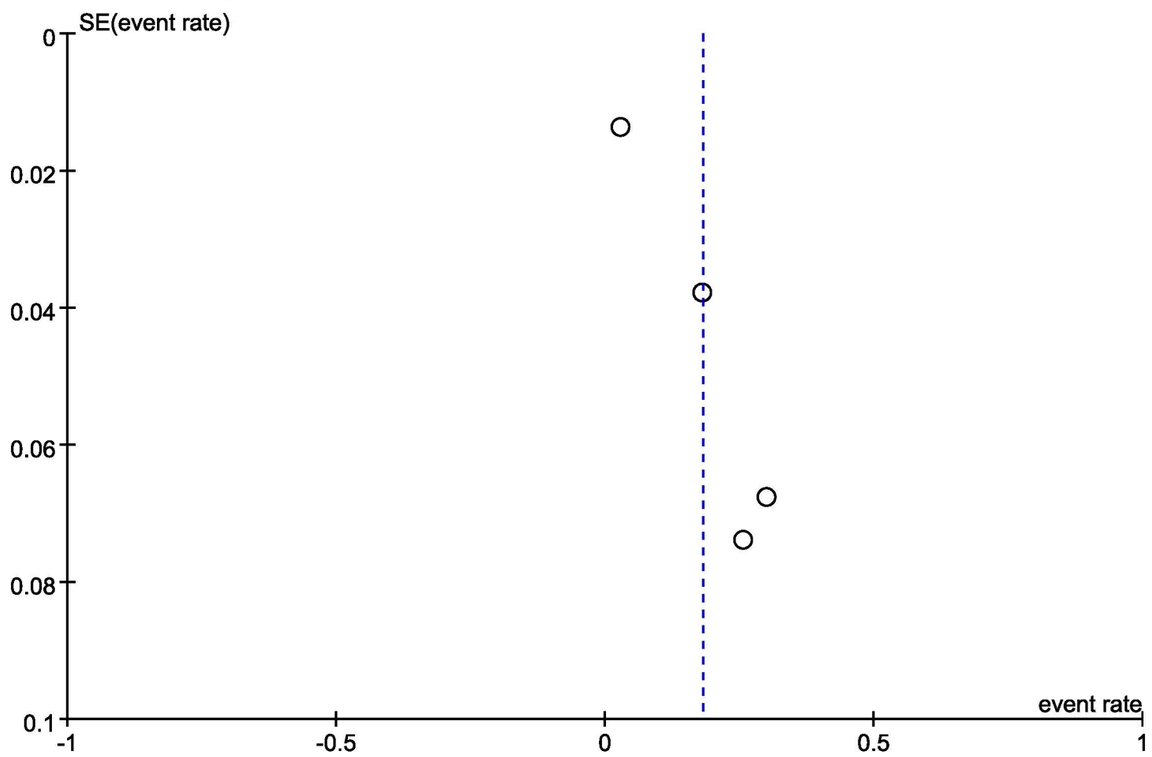

**C** Myalgia



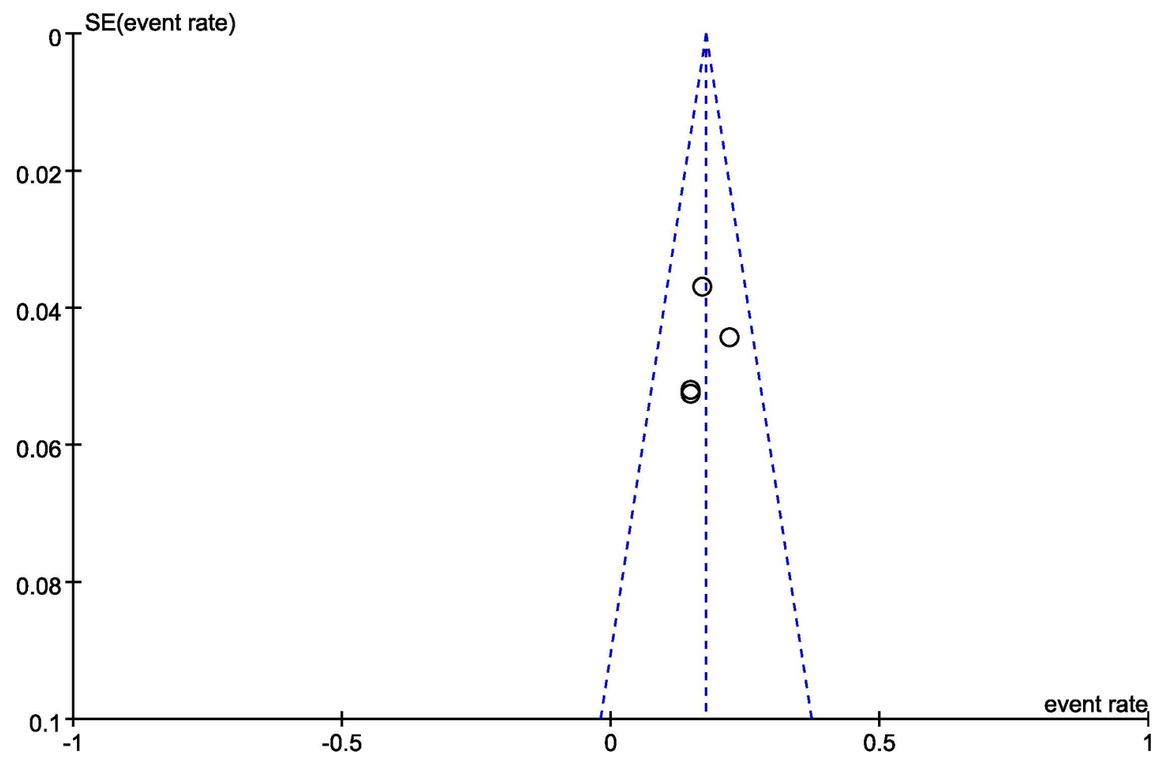

**D** Peripheral Edema



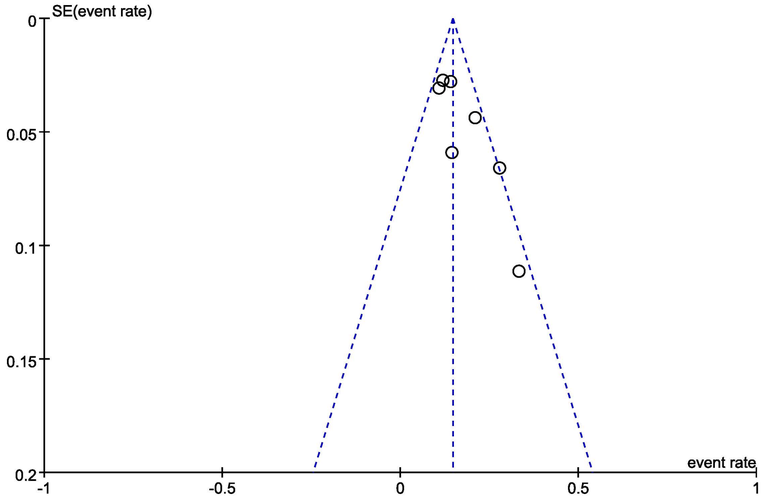

**E** Dysgeusia



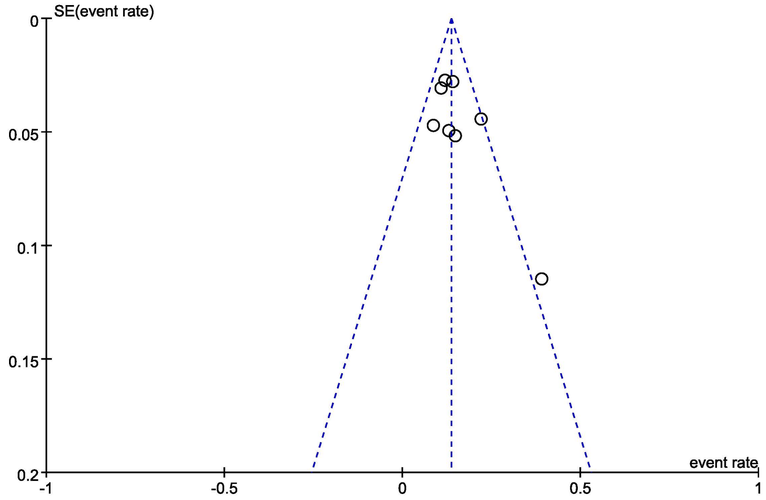

**F** Blood CPK Increase



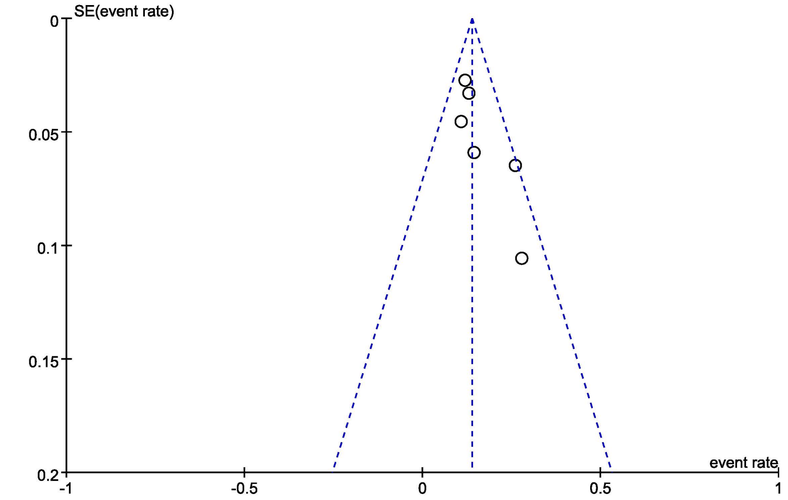
**A** Aspartate Aminotransferase Increase



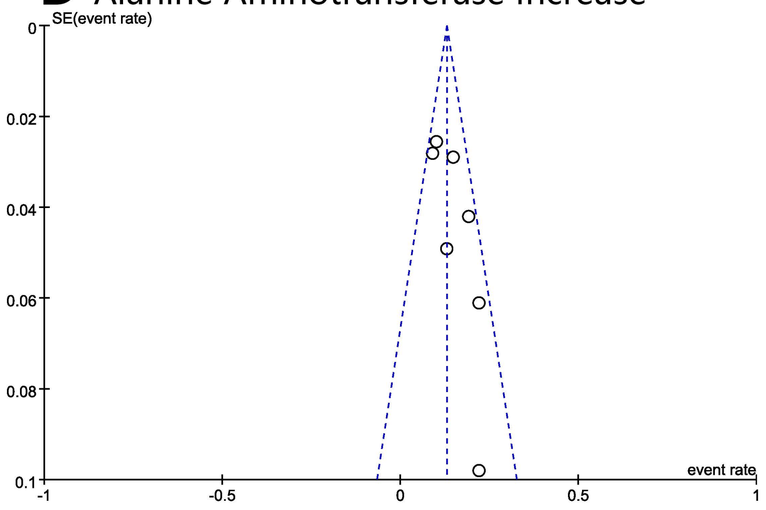

**B** Nausea



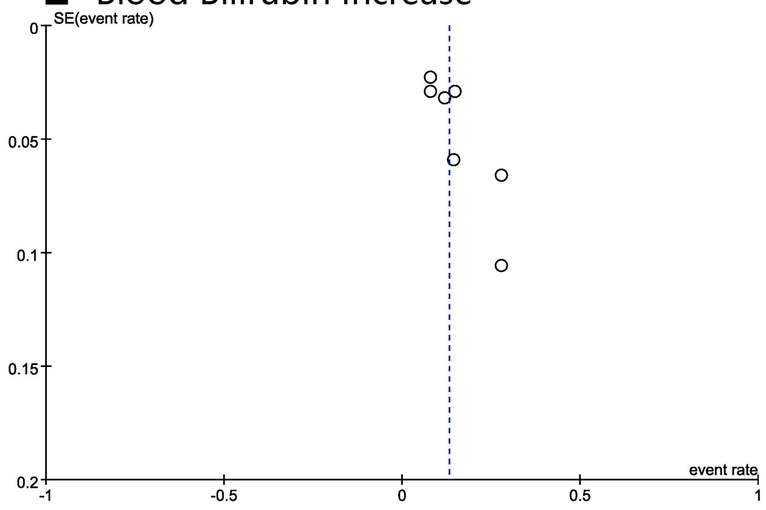

**C** Rash



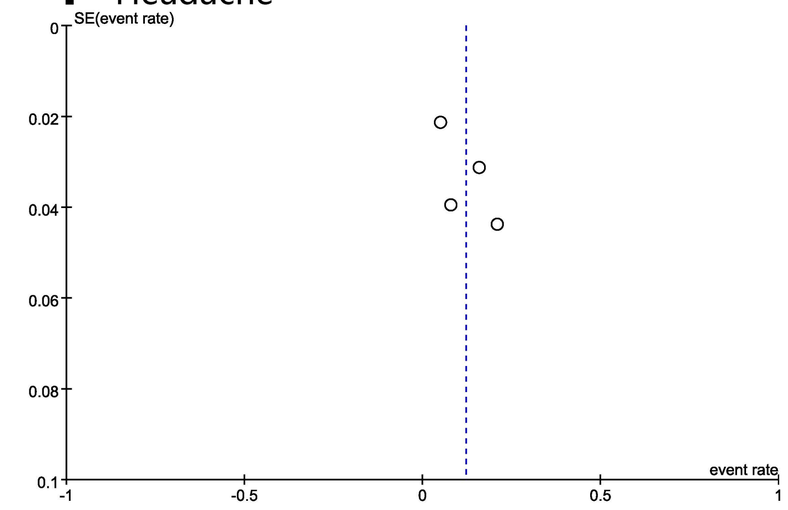

**D** Alanine Aminotransferase Increase



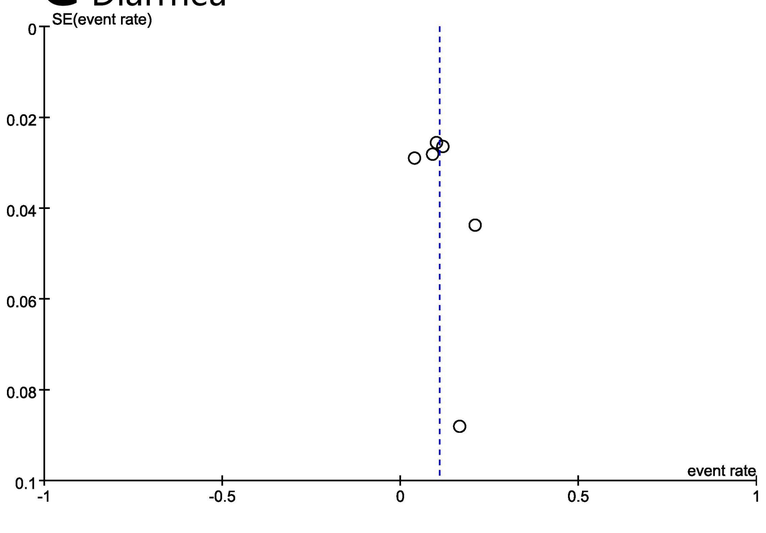

**E** Blood Bilirubin Increase



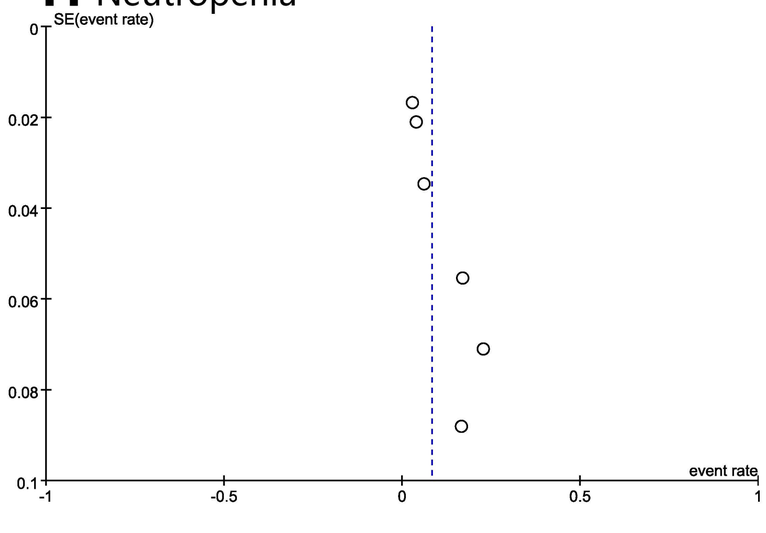

**F** Headache



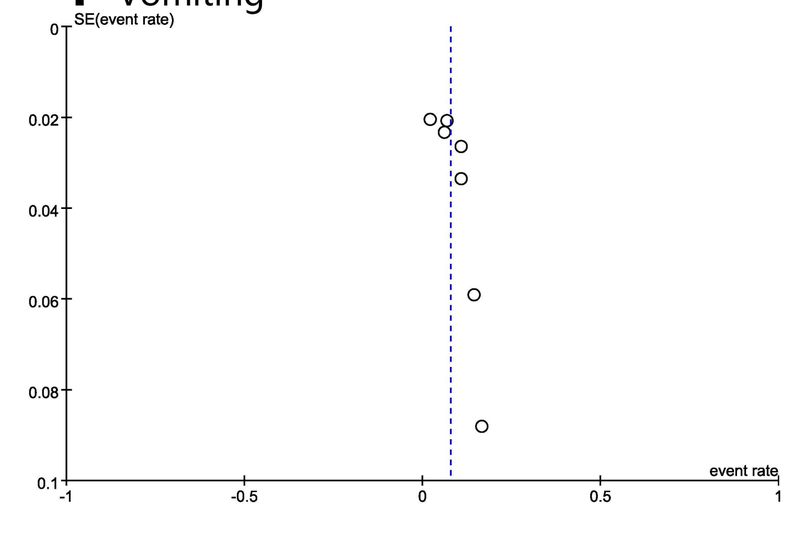

**G** Diarrhea

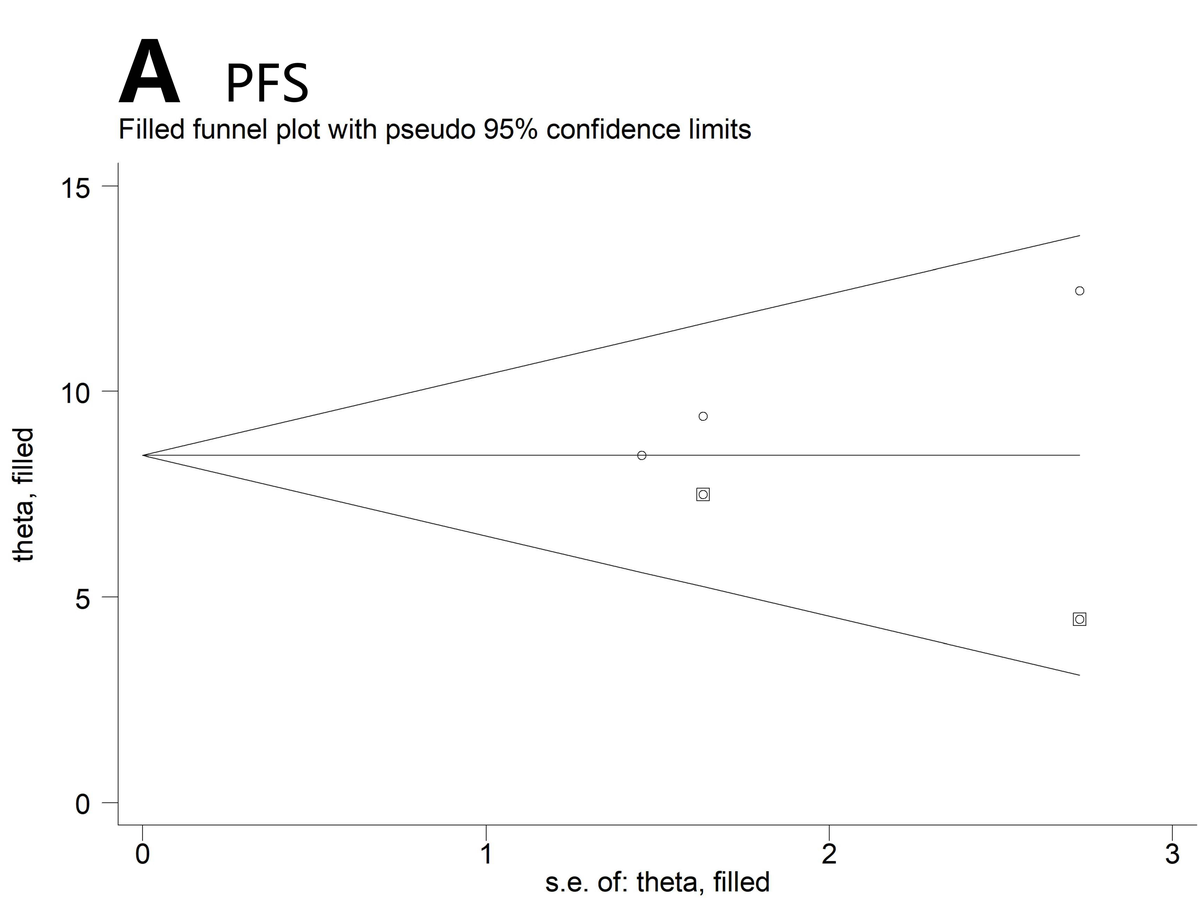


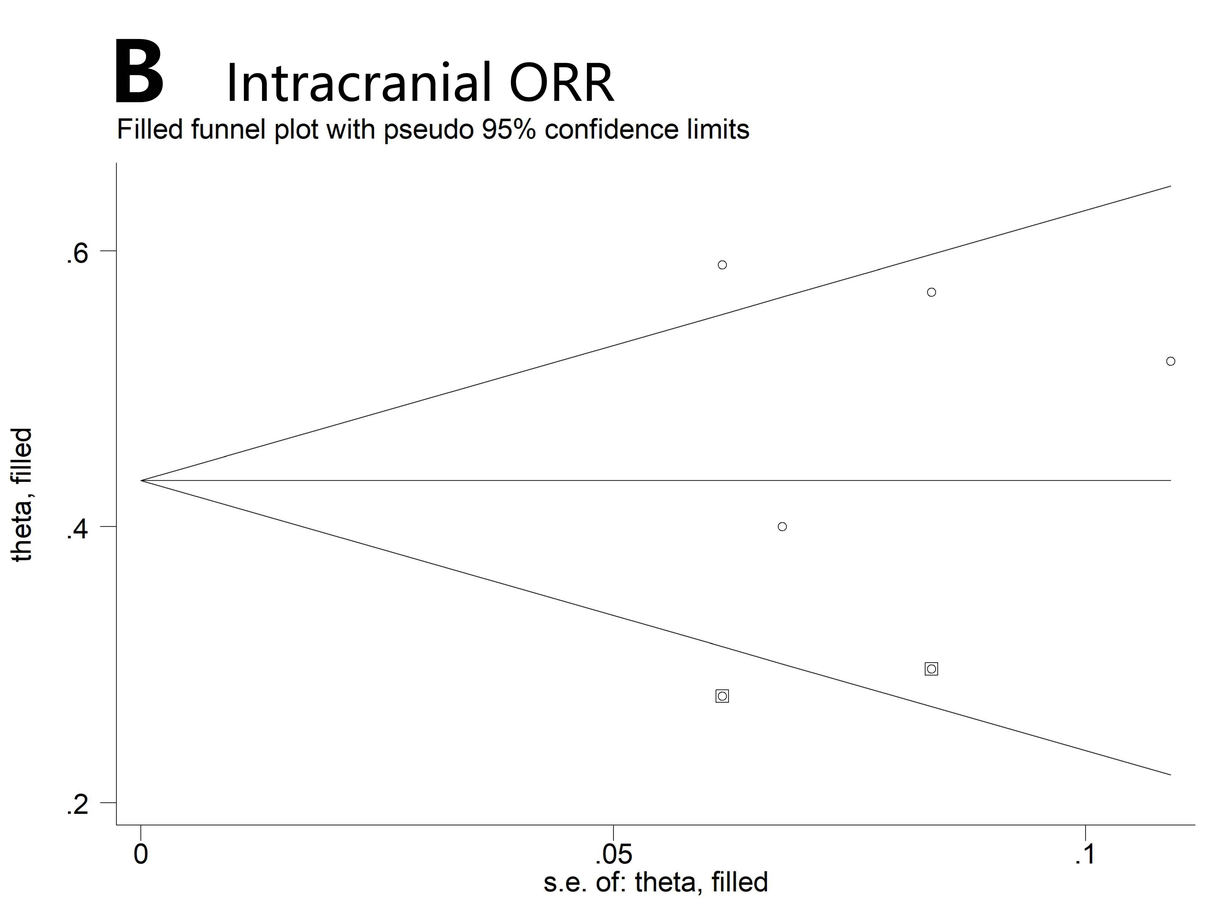

**H** Neutropenia



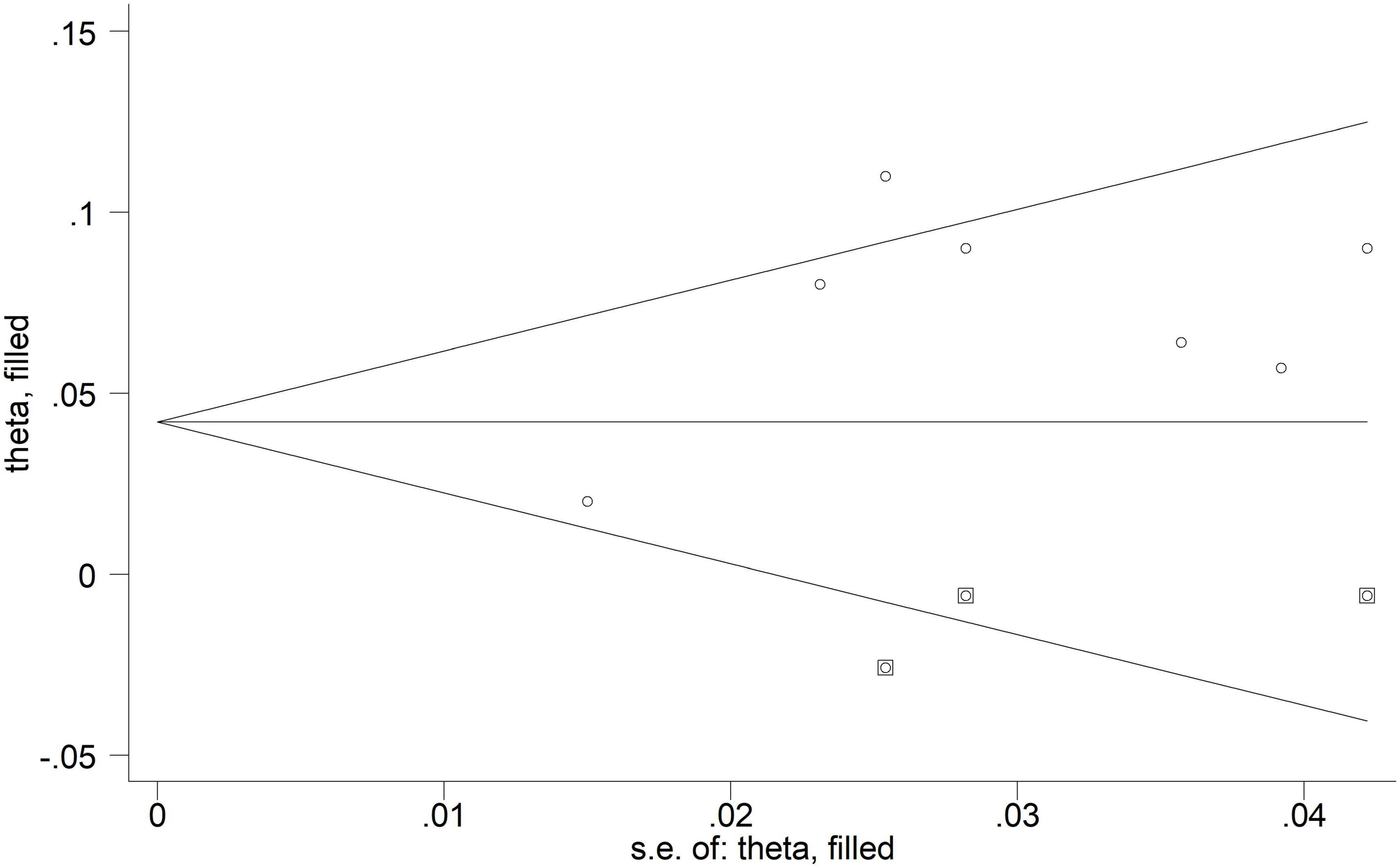

**I** Vomiting



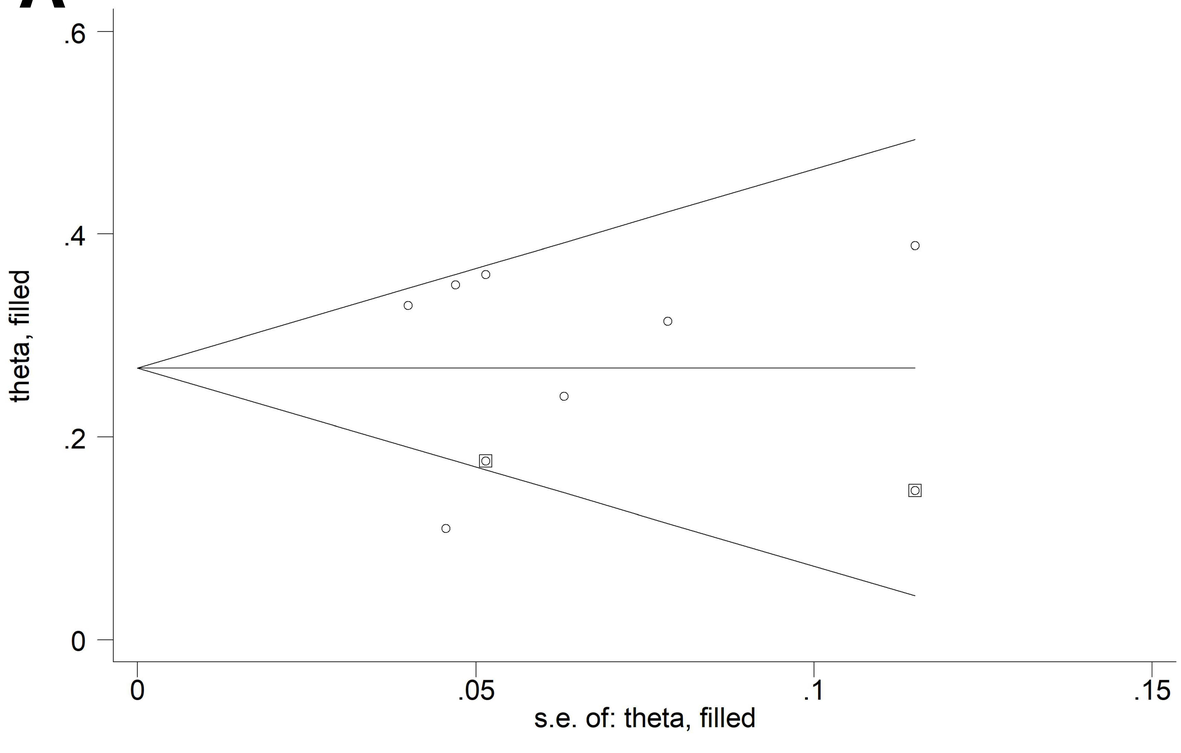

A PFS
Filled funnel plot with pseudo 95% confidence limits
theta, filled
15
10
5
0
0
1
2
3
s.e. of: theta, filled


B Intracranial ORR
Filled funnel plot with pseudo 95% confidence limits
theta, filled
.6
.4
.2
0
.05
.1
s.e. of: theta, filled

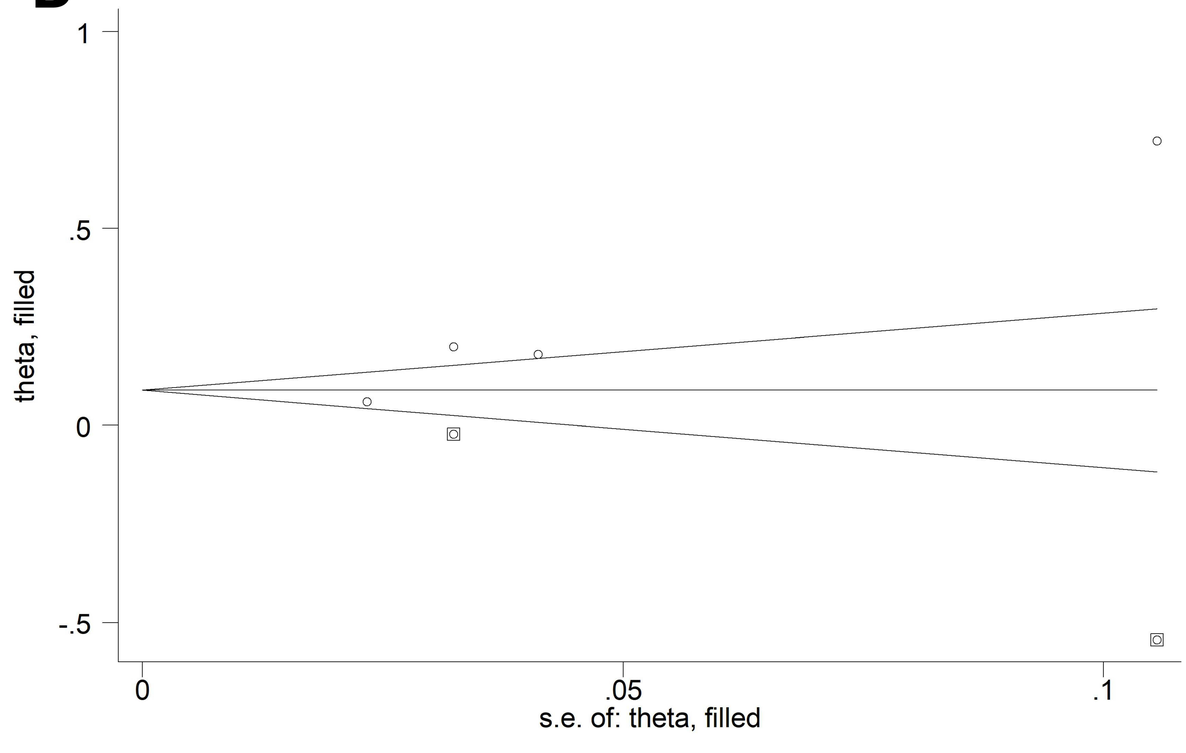
Filled funnel plot with pseudo 95% confidence limits



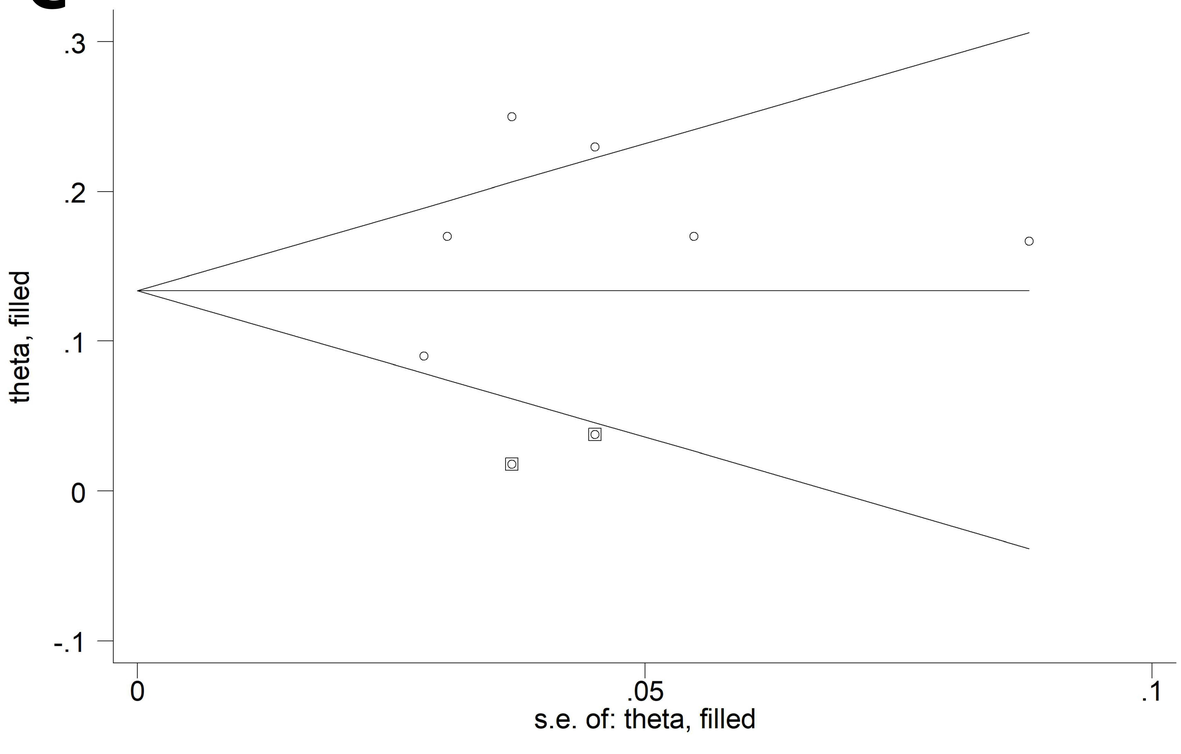
A


Constipation
Filled funnel plot with pseudo 95% confidence limits
theta, filled
.6
.4
.2
0
0
.05
.1
.15
s.e. of: theta, filled

B


Anemia
Filled funnel plot with pseudo 95% confidence limits
theta, filled
1
.5
0
-.5
0
.05
.1
s.e. of: theta, filled

C


Peripheral Edema
Filled funnel plot with pseudo 95% confidence limits
theta, filled
.3
.2
.1
0
-.1
0
.05
.1
s.e. of: theta, filled

D

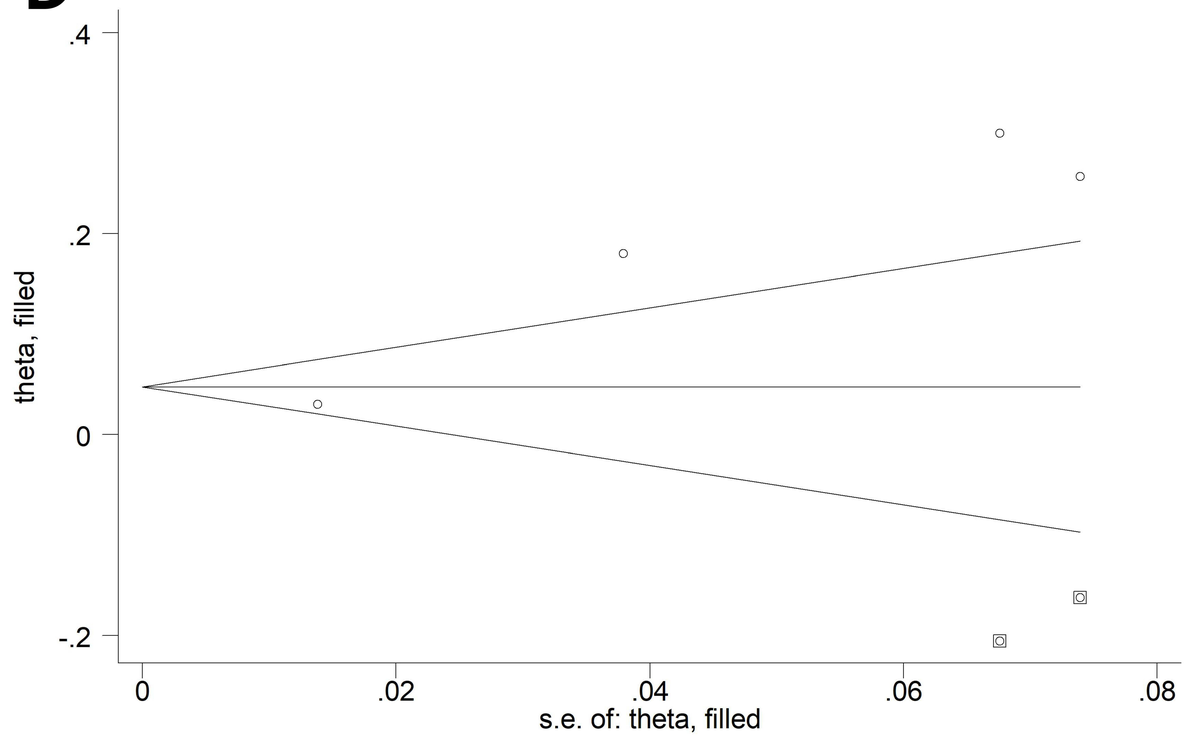

Dysgeusia
Filled funnel plot with pseudo 95% confidence limits
theta, filled
.4
.2
0
-.2
0
.02
.04
.06
.08
s.e. of: theta, filled

Table S1. Quality assessment of the included studies.

(1) Quality assessment of the included RCTs.

| Citation | Random sequence generation | Allocation concealment | Blinding of participants and personnel | Blinding of outcome assessment | Incomplete outcome data | Selective reporting | Other bias |
|---|---|---|---|---|---|---|---|
| Hida 2017 | unclear | unclear | unclear | unclear | high | low | low |
| Peters 2017 | unclear | unclear | low | low | low | low | low |

(2) The Newcastle–Ottawa scale (NOS) scores of the included non-RCTs.

| Citation | Representatives of the exposed cohort | Selection of the non-exposed cohort | Ascertainment of exposure | Demonstration that outcome of interest was present at start of study | Comparability of cohorts on the basis of the design or analysis | Assessment of outcome | Was follow-up long enough for outcomes to occur | Adequacy of follow up of cohorts | Total |
|---|---|---|---|---|---|---|---|---|---|
| Seto 2013 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 6 |
| Gadgeel 2014 | 1 | 0 | 1 | 1 | 0 | 1 | 0 | 0 | 4 |
| Hida 2016 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 0 | 5 |
| Ou 2016 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 6 |
| Shaw 2016 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 6 |
| Iwama 2017 | 1 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 3 |

**Table S2. Begg's and Egger's test for all the results.**

| | Begg's test | Egger's test |
|---|---|---|
| Efficacy | | |
| ORR | 0.917 | 0.272 |
| DCR | 0.386 | 0.027 |
| PFS | 0.296 | 0.092 |
| Intracranial ORR | 0.734 | 0.996 |
| Safety | | |
| Discontinuation rate | 1.000 | 0.119 |
| Rate of dose reduction or interruption | 0.764 | 0.431 |
| Adverse effects | | |
| Constipation | 1.000 | 0.350 |
| Anemia | 0.043 | 0.308 |
| Myalgia | 1.000 | 0.100 |
| Peripheral edema | 1.000 | 0.475 |
| Dysgeusia | 0.022 | 0.734 |
| Blood CPK increase | 0.734 | 0.671 |

ORR, overall response rate; DCR, disease control rate; PFS, progression-free survival; CPK, creatine phosphokinase

Table S3. Sensitivity analysis for all the outcome measures.

(1) Sensitivity analysis of the meta-analysis of the overall response rate of ALK-rearranged non-small cell lung cancer treated with alectinib.

| Method | Pooled estimate | 95%CI | | Asymptotic | | Number of studies |
|---|---|---|---|---|---|---|
| | | Lower | Upper | Z value | P value | |
| Before trim and fill analysis | | | | | | |
| Fixed | 0.761 | 0.730 | 0.793 | 47.581 | <0.001 | 9 |
| Random | 0.696 | 0.570 | 0.823 | 10.791 | <0.001 | |
| After trim and fill analysis | | | | | | |
| Fixed | 0.761 | 0.730 | 0.793 | 47.581 | <0.001 | 9 |
| random | 0.696 | 0.570 | 0.823 | 10.791 | <0.001 | |

(2) Sensitivity analysis of the meta-analysis of the disease control rate of ALK-rearranged non-small cell lung cancer treated with alectinib.

| Method | Pooled estimate | 95%CI | | Asymptotic | | Number of studies |
|---|---|---|---|---|---|---|
| | | Lower | Upper | Z value | P value | |
| Before trim and fill analysis | | | | | | |
| Fixed | 0.933 | 0.913 | 0.952 | 93.522 | <0.001 | 8 |
| Random | 0.878 | 0.816 | 0.940 | 27.792 | <0.001 | |
| After trim and fill analysis | | | | | | |
| Fixed | 0.933 | 0.913 | 0.952 | 93.522 | <0.001 | 8 |
| random | 0.878 | 0.816 | 0.940 | 27.792 | <0.001 | |

(3) Sensitivity analysis of the meta-analysis of the progression-free survival of ALK-rearranged non-small cell lung cancer treated with alectinib.

| Method | Pooled estimate | 95%CI | | Asymptotic | | Number of studies |
|---|---|---|---|---|---|---|
| | | Lower | Upper | Z value | P value | |
| Before trim and fill analysis | | | | | | |
| Fixed | 9.359 | 7.382 | 11.337 | 9.276 | <0.001 | 3 |
| Random | 9.359 | 7.382 | 11.337 | 9.276 | <0.001 | |
| After trim and fill analysis | | | | | | |
| Fixed | 8.450 | 6.845 | 10.055 | 10.320 | <0.001 | 5 |
| random | 8.450 | 6.617 | 10.283 | 9.037 | <0.001 | |

(4) Sensitivity analysis of the meta-analysis of the overall response rate of alectinib-treated ALK-rearranged non-small cell lung cancer with brain metastases.

| Method | Pooled estimate | 95%CI | | Asymptotic | | Number of studies |
|---|---|---|---|---|---|---|
| | | Lower | Upper | Z value | P value | |
| Before trim and fill analysis | | | | | | |
| Fixed | 0.519 | 0.446 | 0.593 | 13.824 | <0.001 | 4 |
| Random | 0.519 | 0.423 | 0.615 | 10.634 | <0.001 | |
| After trim and fill analysis | | | | | | |
| Fixed | 0.434 | 0.375 | 0.492 | 14.479 | <0.001 | 6 |
| random | 0.439 | 0.321 | 0.557 | 7.309 | <0.001 | |

(5) Sensitivity analysis of the meta-analysis of discontinuation rate after alectinib treatment.

| Method | Pooled estimate | 95%CI | | Asymptotic | | Number of studies |
|---|---|---|---|---|---|---|
| | | Lower | Upper | Z value | P value | |
| Before trim and fill analysis | | | | | | |
| Fixed | 0.059 | 0.041 | 0.078 | 6.261 | <0.001 | 7 |
| Random | 0.070 | 0.039 | 0.100 | 4.503 | <0.001 | |
| After trim and fill analysis | | | | | | |
| Fixed | 0.042 | 0.026 | 0.058 | 5.063 | <0.001 | 10 |
| random | 0.047 | 0.016 | 0.077 | 2.971 | 0.003 | |

(6) Sensitivity analysis of the meta-analysis of rate of dose reduction or interruption after alectinib treatment.

| Method | Pooled estimate | 95%CI | | Asymptotic | | Number of studies |
|---|---|---|---|---|---|---|
| | | Lower | Upper | Z value | P value | |
| Before trim and fill analysis | | | | | | |
| Fixed | 0.311 | 0.275 | 0.346 | 16.994 | <0.001 | 7 |
| Random | 0.327 | 0.239 | 0.415 | 7.264 | <0.001 | |
| After trim and fill analysis | | | | | | |
| Fixed | 0.311 | 0.275 | 0.346 | 16.994 | <0.001 | 7 |
| random | 0.327 | 0.239 | 0.415 | 7.264 | <0.001 | |

(7) Sensitivity analysis of the meta-analysis of event rate of several adverse effects happened after alectinib treatment.

A. Constipation

| Method | Pooled estimate | 95%CI | | Asymptotic | | Number of studies |
|---|---|---|---|---|---|---|
| | | Lower | Upper | Z value | P value | |
| Before trim and fill analysis | | | | | | |
| Fixed | 0.286 | 0.246 | 0.326 | 14.097 | <0.001 | 7 |
| Random | 0.292 | 0.212 | 0.371 | 7.186 | <0.001 | |
| After trim and fill analysis | | | | | | |
| Fixed | 0.268 | 0.232 | 0.305 | 14.388 | <0.001 | 9 |
| random | 0.268 | 0.197 | 0.338 | 7.416 | <0.001 | |

B. Anemia

| Method | Pooled estimate | 95%CI | | Asymptotic | | Number of studies |
|---|---|---|---|---|---|---|
| | | Lower | Upper | Z value | P value | |
| Before trim and fill analysis | | | | | | |
| Fixed | 0.136 | 0.103 | 0.170 | 8.008 | <0.001 | 4 |
| Random | 0.252 | 0.103 | 0.402 | 3.303 | 0.001 | |
| After trim and fill analysis | | | | | | |
| Fixed | 0.089 | 0.060 | 0.118 | 5.988 | <0.001 | 6 |
| random | 0.100 | -0.046 | 0.246 | 1.342 | 0.180 | |

C. Myalgia

| Method | Pooled estimate | 95%CI | | Asymptotic | | Number of studies |
|---|---|---|---|---|---|---|
| | | Lower | Upper | Z value | P value | |
| Before trim and fill analysis | | | | | | |
| Fixed | 0.182 | 0.150 | 0.213 | 11.333 | <0.001 | 6 |
| Random | 0.182 | 0.149 | 0.215 | 10.756 | <0.001 | |
| After trim and fill analysis | | | | | | |
| Fixed | 0.182 | 0.150 | 0.213 | 11.333 | <0.001 | 6 |
| random | 0.182 | 0.149 | 0.215 | 10.756 | <0.001 | |

D. Peripheral Edema

| Method | Pooled estimate | 95%CI | | Asymptotic | | Number of studies |
|---|---|---|---|---|---|---|
| | | Lower | Upper | Z value | P value | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Before trim and fill analysis | | | | | | |
| Fixed | 0.167 | 0.136 | 0.198 | 10.579 | <0.001 | 6 |
| Random | 0.177 | 0.121 | 0.234 | 6.131 | <0.001 | |
| After trim and fill analysis | | | | | | |
| Fixed | 0.134 | 0.107 | 0.161 | 9.697 | <0.001 | 8 |
| random | 0.139 | 0.077 | 0.201 | 4.397 | <0.001 | |

E. Dysgeusia

| Method | Pooled estimate | 95%CI | | Asymptotic | | Number of studies |
|---|---|---|---|---|---|---|
| | | Lower | Upper | Z value | P value | |
| Before trim and fill analysis | | | | | | |
| Fixed | 0.062 | 0.038 | 0.087 | 4.964 | <0.001 | 4 |
| Random | 0.181 | 0.046 | 0.316 | 2.621 | 0.009 | |
| After trim and fill analysis | | | | | | |
| Fixed | 0.048 | 0.024 | 0.071 | 3.908 | <0.001 | 6 |
| random | 0.068 | -0.056 | 0.192 | 1.080 | 0.280 | |

F. Blood Creatine Phosphokinase Increase

| Method | Pooled estimate | 95%CI | | Asymptotic | | Number of studies |
|---|---|---|---|---|---|---|
| | | Lower | Upper | Z value | P value | |
| Before trim and fill analysis | | | | | | |
| Fixed | 0.175 | 0.131 | 0.220 | 7.783 | <0.001 | 4 |
| Random | 0.175 | 0.131 | 0.220 | 7.783 | <0.001 | |
| After trim and fill analysis | | | | | | |
| Fixed | 0.175 | 0.131 | 0.220 | 7.783 | <0.001 | 4 |
| random | 0.175 | 0.131 | 0.220 | 7.783 | <0.001 | |

Supplementary material legends

Figure S1. Meta-analysis of event rate of several other adverse events happened after alectinib treatment.

Figure S2. Funnel plot of efficacy outcome measures of ALK-rearranged non-small cell lung cancer treated with alectinib.

Figure S3. Funnel plot of safety outcome measures of ALK-rearranged non-small cell lung cancer treated with alectinib.

Figure S4. Funnel plot of several adverse events happened after alectinib treatment.

Figure S5. Funnel plot of event rate of several other adverse events happened after alectinib treatment.

Figure S6. The “trim-and-fill” funnel plot of efficacy outcome measures of ALK-rearranged non-small cell lung cancer treated with alectinib.

Figure S7. The “trim-and-fill” funnel plot of discontinuation rate after alectinib treatment.

Figure S8. The “trim-and-fill” funnel plot of event rate of several adverse events happened after alectinib treatment.

Table S1. Quality assessment of the included studies.

Table S2. Begg’s and Egger’s test for all the results.

Table S3. Sensitivity analysis for all the outcome measures.

SUIVP D#533<#Fkhfnolvw

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 3 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 4 |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 5 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 6 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 5 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 5 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 6 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 7 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 7 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 6 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 7 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | 7 |

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | 7 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | 7 |
| **RESULTS** | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 8, Figure 1 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 8, Table 1 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | 8, Table 1 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 8, Table 1 |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | 8 |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | 10 |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | 10 |
| **DISCUSSION** | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 11 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 13 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 14 |
| **FUNDING** | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 15 |

*From:* Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097