# PRISMA 2009 Checklist

<table>
<thead>
<tr>
<th>Section/Topic</th>
<th>#</th>
<th>Checklist Item</th>
<th>Reported on Page #</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TITLE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Title</td>
<td>1</td>
<td>Identify the report as a systematic review, meta-analysis, or both.</td>
<td>Title 1#</td>
</tr>
<tr>
<td><strong>ABSTRACT</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Structured summary</td>
<td>2</td>
<td>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.</td>
<td>Abstract 2-3#</td>
</tr>
<tr>
<td><strong>INTRODUCTION</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rationale</td>
<td>3</td>
<td>Describe the rationale for the review in the context of what is already known.</td>
<td>Introduction 3-4#</td>
</tr>
<tr>
<td>Objectives</td>
<td>4</td>
<td>Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).</td>
<td>Introduction 3-4#</td>
</tr>
<tr>
<td><strong>METHODS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protocol and registration</td>
<td>5</td>
<td>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.</td>
<td>Methods 4#</td>
</tr>
<tr>
<td>Eligibility criteria</td>
<td>6</td>
<td>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.</td>
<td>Selection criteria and Data extraction 4-5#</td>
</tr>
<tr>
<td>Information sources</td>
<td>7</td>
<td>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.</td>
<td>Search strategy 4#</td>
</tr>
<tr>
<td>Search</td>
<td>8</td>
<td>Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.</td>
<td>Appendix: PubMed and Embase</td>
</tr>
</tbody>
</table>
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<tbody>
<tr>
<td>Study selection</td>
<td>9</td>
<td>State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).</td>
<td>Selection criteria 4-5#</td>
</tr>
<tr>
<td>Data collection process</td>
<td>10</td>
<td>Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.</td>
<td>Data extraction 5#</td>
</tr>
<tr>
<td>Data items</td>
<td>11</td>
<td>List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.</td>
<td>Selection criteria and Data extraction 4-5#</td>
</tr>
<tr>
<td>Risk of bias in individual studies</td>
<td>12</td>
<td>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.</td>
<td>Assessment for Risk 5#</td>
</tr>
<tr>
<td>Summary measures</td>
<td>13</td>
<td>State the principal summary measures (e.g., risk ratio, difference in means).</td>
<td>Selection criteria and Data extraction 4-5#</td>
</tr>
<tr>
<td>Synthesis of results</td>
<td>14</td>
<td>Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I²) for each meta-analysis.</td>
<td>Statistical methods 5-6#</td>
</tr>
<tr>
<td>Risk of bias across studies</td>
<td>15</td>
<td>Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).</td>
<td>Publication bias 9#</td>
</tr>
</tbody>
</table>
# PRISMA 2009 Checklist

## RESULTS

<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Study selection</strong></td>
<td>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.</td>
</tr>
<tr>
<td><strong>Study characteristics</strong></td>
<td>18 For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.</td>
</tr>
<tr>
<td><strong>Risk of bias within studies</strong></td>
<td>19 Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).</td>
</tr>
<tr>
<td><strong>Results of individual studies</strong></td>
<td>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.</td>
</tr>
<tr>
<td><strong>Synthesis of results</strong></td>
<td>21 Present the main results of the review. If meta-analyses done, include for each, confidence intervals and measures of consistency.</td>
</tr>
<tr>
<td><strong>Risk of bias across studies</strong></td>
<td>22 Present results of any assessment of risk of bias across studies (see Item 15).</td>
</tr>
<tr>
<td><strong>Additional analysis</strong></td>
<td>23 Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).</td>
</tr>
</tbody>
</table>

## DISCUSSION

<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Summary of evidence</strong></td>
<td>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).</td>
</tr>
<tr>
<td><strong>Limitations</strong></td>
<td>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).</td>
</tr>
<tr>
<td><strong>Conclusions</strong></td>
<td>26 Provide a general interpretation of the results in the context of other evidence, and implications for future research.</td>
</tr>
</tbody>
</table>

## 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. |


For more information, visit: [www.prisma-statement.org](http://www.prisma-statement.org).

Page 2 of 2
The Adverse Events of Oxycodone in Cancer-Related Pain: A Systematic Review and Meta-Analysis of randomised controlled trials

Hu Ma MD, Ph.D, Yuan Liu MM, Su-Han Jin MM, Xian-Tao Zeng Ph.D, Joey S.W.Kwong Ph.D, Yu-Ju Bai MD, Xu Tian MN, RN, Jian-Guo Zhou MD*

Supplemental Data 2. The Search Strategy of PubMed and Embase

**PubMed Search terms**
#1 Search ("Oxycodone"[Mesh]) OR (((((((((Oxycone[Title/Abstract]) OR Dinarkon[Title/Abstract]) OR Oxycodeinon[Title/Abstract]) OR Dihydrohydroxycodeinone[Title/Abstract]) OR Dihydrone[Title/Abstract]) OR Oxiconum[Title/Abstract]) OR Theocodin[Title/Abstract]) OR Oxycontin[Title/Abstract]) OR Purdue Frederick Brand of Oxycodone[Title/Abstract]) OR Pancodine[Title/Abstract]) OR Eucodal[Title/Abstract]) OR Oxycodone Hydrochloride [Title/Abstract])
#2 Search (cancer[MeSH Terms]) OR ((((((((((Neoplasm[Title/Abstract]) OR Tumors[Title/Abstract]) OR Tumor[Title/Abstract]) OR Neoplasia[Title/Abstract]) OR Benign Neoplasms[Title/Abstract]) OR Neoplasms, Benign[Title/Abstract]) OR Benign Neoplasm[Title/Abstract]) OR Neoplasm, Benign[Title/Abstract]) OR Cancer[Title/Abstract]) OR Cancers[Title/Abstract])
#3 Search (((pain[Title/Abstract]) OR Pain Measurement[MeSH Major Topic]) OR Pain Management[MeSH Major Topic]) OR pain[MeSH Terms]
#4 Search ("Controlled Clinical Trial"[Publication Type]) OR ("Randomized Controlled Trials as Topic"[Mesh] OR "Randomized Controlled Trial"[Publication Type] OR "Controlled Clinical Trials as Topic"[Mesh]))) OR (((((Controlled Clinical Trial[Title/Abstract]) OR Controlled Clinical Trials, Randomized[Title/Abstract]) OR Clinical Trials, Randomized[Title/Abstract]) OR Trials, Randomized Clinical[Title/Abstract]) OR Controlled Clinical Trials[Title/Abstract]) OR random*[Title/Abstract])
#5 #1 AND #2 AND #3 AND #4

**Embase Search terms**
#1 ‘oxycodone’ OR ‘Oxycone’ OR ‘Dinarkon’ OR ‘Oxycodeinon’ OR ‘Oxycodone Hydrochloride’ OR ‘Dihydrone’ OR ‘Oxiconum’ OR ‘Theocodin’ OR ‘Oxycontin’ OR ‘Purdue Frederick Brand of Oxycodone’ OR ‘Pancodine’ OR ‘Eucodal’ OR ‘Oxycodone Hydrochloride’
#2 ‘controlled clinical trial'/exp OR ‘controlled clinical trial' OR 'randomized controlled trials'/exp OR 'randomized controlled trials' OR 'controlled clinical trials' OR 'controlled clinical trials, randomized' OR 'clinical trials, randomized' OR 'trials, randomized clinical' OR 'random'
#3 ‘Pain’ OR ‘Pain Management’ OR ‘Pain Measurement’
#4 ‘cancer’ OR ‘Neoplasm’ OR ‘Tumors’ OR ‘Tumor’ OR ‘Neoplasia’ OR ‘Cancer’ OR ‘Cancers’
#5 #1 AND #2 AND #3 AND #4
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Supplemental Data 2. The Result of SAS Meta Power Analysis

```sas
data constipation;
input es v;
cards;
-2.1776161 2.2026125
0.04546237 0.03357327
0.64435702 0.46746032
0.37320425 0.38440021
0 0.31292517
-0.06499214 0.0651521
0.06669137 0.16662959
0.15822401 0.08037166
-0.24116206 0.2474026
-0.48550782 0.12019231
0.54654371 0.65191388;
run;
%metapower (test='M', model='fixed', raw_data='yes', alpha=.05, tau2=99, heterogeneity=99, n1=99, n2=99, k=99, eff_type='or', T=-0.005243, Dataset= constipation, B=NA, v=v, x=NA, es=es, p=NA, weight=NA);
run;
```

---

Output - (Untitled)

The SAS Session

Test of Mean Effect Size

Model = Fixed
Effect Size Metric = or

Run data provided: Yes

Mean Effect Size = 0.005243
Number of Studies = 99
Sampling Variance = 0.016463
Alpha = 0.05

Estimated Power of Test (One-Tailed) = 0.0401802
Estimated Power of Test (Two-Tailed) = 0.0502704

```sas
data Nausea;
input es v;
cards;
-0.78249228  0.34214993
  0.04546237  0.03357327
-0.25299651  0.12898099
-0.19798988  0.13354727
  0.48972545  0.20647408
-0.08742281  0.08774091
-0.18232156  0.25648148
-0.08590334  0.08628251
-0.63252256  1.3786765
-0.19415601  0.39201681
-1.1631508  0.535
;
run;
```

%metapower (test='M', model='fixed', raw_data='yes', alpha=.05, tau2=99,heterogeneity=99,
n1=99, n2=99, k=99, eff_type='or', T= -0.04769, Dataset= Nausea, B=NA, v=v, x=NA, es=es, p=NA,
weight=NA);
run;

Test of Mean Effect Size

Model = fixed

Effect Size Metric = or
Raw data provided: Yes

Mean Effect Size = -0.04769

Number of Studies = 11

Sampling Variance = 0.0117891

Alpha = 0.05

Estimated Power of Test (One-Tailed) = 0.0185765

Estimated Power of Test (Two-Tailed) = 0.0723783

data Vomiting;
input es v;
cards;
-2.5261095 2.1344214
0.07711303 0.03269768
-0.61558895 0.26894559
-0.16632122 0.33466462
-0.17206506 0.34615331
0.28995222 0.29632035
0.23638878 0.33060429
Test of Mean Effect Size

Model = fixed

Effect Size Metric = or

Raw data provided= Yes
Mean Effect Size = -0.04866

Number of Studies = 10

Sampling Variance = 0.018354

Alpha = 0.05

Estimated Power of Test (One-Tailed) = 0.0225335
Estimated Power of Test (Two-Tailed) = 0.0649056

```sas
data Pruritus;
input es v;
cards;
-0.3801473 0.15970085
-0.131336 0.41322537
-0.34830669 0.71895425
0.19237189 0.48787879;
run;
%metapower (test='M', model='fixed', raw_data='yes', alpha=.05, tau2=99, heterogeneity=99, n1=99, n2=99, k=99, eff_type='or', T=-0.097997, Dataset= Pruritus, v=v, x=NA, es=es, p=NA, weight=NA);
run;
```

Estimated Power of Test (Two-Tailed) = 0.06344
data Sleepiness;
input es v;
cards;
-0.78495473 0.15982531
-0.23687374 0.20854629
0 0.88235294
-0.63252256 0.68933824
-0.04879016 0.56904762;
run;
%metapower (test='M', model='fixed', raw_data='yes', alpha=.05, tau2=99, heterogeneity=99, n1=99, n2=99, k=99, eff_type='or', T=-0.20691, Dataset= Sleepiness, B=NA, v=v, x=NA, es=es, p=NA, weight=NA);
run;
data dizziness;
input es v;
cards;
-0.55004634   0.37371795
0.05339289    0.07932773
-0.38865799   0.79971751
-0.65981076   0.71665740
0.20686267    0.20950185
-0.43332206   0.35667722
0.00000000    0.27272727
0.17185026    0.34736842
-0.66139848   1.43649190
0.27193372    0.32738095
;
run;
%metapower (test='M', model='fixed', raw_data='yes', alpha=.05, tau2=99, heterogeneity=99, n1=99, n2=99, k=99, eff_type='or', T= -0.02872, Dataset= dizziness, B=NA, v=v, x=NA, es=es, p=NA, weight=NA);
run;
data anorexia;
input es v;
cards;
0.05571061 0.08377805
-1.063521 2.5964696
-0.34830669 0.71895425
-0.05406722 1.8918129;
run;
%metapower (test='M', model='fixed', raw_data='yes', alpha=.05, tau2=99,heterogeneity=99, n1=99, n2=99, k=99, eff_type='or', T= -0.01278, Dataset= anorexia, B=NA, v=v, x=NA, es=es, p=NA, weight=NA);
run;
data Dysuia;
input es v;
cards;
-1.5755364 2.366092
-1.0815179 2.6324761
-0.66139848 1.4364919
;
run;
%metapower (test='M', model='fixed', raw_data='yes', alpha=.05, tau2=99, heterogeneity=99, n1=99, n2=99, k=99, eff_type='or', T= -0.464705879957229, Dataset= Dysuia, B=NA, v=v, x=NA, es=es, p=NA, weight=NA);
run;
Test of Mean Effect Size

Model = fixed
Effect Size Metric = or

Raw data provided: Yes

Mean Effect Size = -0.41423
Number of Studies = 8
Sampling Variance = 0.663978
Alpha = 0.05

Estimated Power of Test (One-Tailed) = 0.1104282

Estimated Power of Test (Two-Tailed) = 0.0870232

------------------------------------------------------------------------
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Supplemental Data 4. The Result of Publication Bias by Egger’ and Begg’ Regression

The publication bias of our meta-analysis was assessed using funnel Begg’s and Egger’s regression. There was no evidence of significant publication bias by inspection of the formal statistical tests [(1) dysuria: Begg’s test, \( P = 1.00 \); Egger’s test, \( P = 0.41 \)); (2) constipation: Begg’s test, \( P = 0.64 \); Egger’s test, \( P = 0.78 \)); nausea: Begg’s test, \( P = 0.06 \); Egger’s test, \( P = 0.06 \)); vomiting: Begg’s test, \( P = 0.16 \); Egger’s test, \( P = 0.09 \)); pruritus: Begg’s test, \( P = 0.73 \); Egger’s test, \( P = 0.43 \)); sleepiness: Begg’s test, \( P = 1.00 \); Egger’s test, \( P = 0.34 \)); dizziness: Begg’s test, \( P = 0.05 \); Egger’s test, \( P = 0.07 \)); anorexia: Begg’s test, \( P = 0.31 \); Egger’s test, \( P = 0.17 \)].

1. Dysuria:

Note: default data input format (theta, se_theta) assumed.

Tests for Publication Bias

Begg’s Test

adj. Kendall’s Score \( (P-Q) = -1 \)

Std. Dev. of Score = 1.91

Number of Studies = 3

\[ z = -0.52 \]

\[ Pr > |z| = 0.602 \]

\[ z = 0.00 \text{ (continuity corrected)} \]

\[ Pr > |z| = 1.000 \text{ (continuity corrected)} \]

Egger’s test

| Std_Eff | Coef. | Std. Err. | t | P>|t| | [95% Conf. Interval] |
|---------|-------|-----------|---|-----|-----------------|
| (Continues) |
---

<table>
<thead>
<tr>
<th>slope</th>
<th>1.210149</th>
<th>1.716098</th>
<th>0.71</th>
<th>0.609</th>
<th>-20.59495</th>
<th>23.01525</th>
</tr>
</thead>
<tbody>
<tr>
<td>bias</td>
<td>-1.594985</td>
<td>1.212918</td>
<td>-1.31</td>
<td>0.414</td>
<td>-17.00657</td>
<td>13.8166</td>
</tr>
</tbody>
</table>

2. Constipation

Note: default data input format (theta, se_theta) assumed.

Tests for Publication Bias

Begg’s Test

adj. Kendall’s Score (P-Q) = 7
Std. Dev. of Score = 12.85
Number of Studies = 11
z = 0.54
Pr > |z| = 0.586

z = 0.47 (continuity corrected)
Pr > |z| = 0.640 (continuity corrected)

Egger’s test

| Std_Eff | Coef.  | Std. Err. | t    | P>|t| | [95% Conf. Interval] |
|---------|--------|-----------|------|-----|----------------------|
|         | slope  | .0478924  | .19199 | 0.25 | 0.809 | -0.3864192 | .4822041 |
|         | bias   | -.1554965 | .5363993 | -0.29 | 0.778 | -1.368916 | 1.057923 |

3. Nausea

Note: default data input format (theta, se_theta) assumed.

Tests for Publication Bias

Begg’s Test

adj. Kendall’s Score (P-Q) = -25
Std. Dev. of Score = 12.85
Number of Studies = 11
z = -1.95
Pr > |z| = 0.052

z = 1.87 (continuity corrected)
Pr > |z| = 0.062 (continuity corrected)

Egger’s test
| Std_Eff | Coef.   | Std. Err. | t    | P>|t| | [95% Conf. Interval] |
|---------|---------|-----------|------|------|----------------------|
| slope   | .2309468| .1691424  | 1.37 | 0.205| -.1516799 to .6135735|
| bias    | -.9987682| .4696943  | -2.13| 0.062| -2.061291 to .0637542|

4. Vomiting

Note: default data input format (theta, se_theta) assumed.

Tests for Publication Bias

Begg's Test

adj. Kendall's Score (P-Q) = -19
Std. Dev. of Score = 12.85
Number of Studies = 11
z = -1.48
Pr > |z| = 0.139

z = 1.40 (continuity corrected)
Pr > |z| = 0.161 (continuity corrected)

Egger's test

| Std_Eff | Coef.   | Std. Err. | t    | P>|t| | [95% Conf. Interval] |
|---------|---------|-----------|------|------|----------------------|
| slope   | .2297391| .1821207  | 1.26 | 0.239| -.1822466 to .6417248|
| bias    | -.7686158| .4103623  | -1.87| 0.094| -1.69692 to .1596883|

5. Pruritus

Note: default data input format (theta, se_theta) assumed.

Tests for Publication Bias

Begg's Test

adj. Kendall's Score (P-Q) = 2
Std. Dev. of Score = 2.94
Number of Studies = 4
z = 0.68
Pr > |z| = 0.497
z = 0.34 (continuity corrected)
\[ Pr > |z| = 0.734 \text{ (continuity corrected)} \]

Egger's test

| Std_Eff | Coef.   | Std. Err. | t    | P>|t|   | [95% Conf. Interval] |
|---------|---------|-----------|------|--------|----------------------|
| slope   | -.6339154 | .4302076  | -1.47 | 0.279  | -2.484949 1.217119   |
| bias    | .7341634  | .7489287  | 0.98 | 0.430  | -2.488217 3.956544   |

6. Sleepiness

Note: default data input format (theta, se_theta) assumed.

Tests for Publication Bias

Begg's Test

\[ \text{adj. Kendall's Score } (P-Q) = 0 \]

\[ \text{Std. Dev. of Score} = 4.08 \]

\[ \text{Number of Studies} = 5 \]

\[ z = 0.00 \]

\[ Pr > |z| = 1.000 \]

Egger's test

| Std_Eff | Coef.   | Std. Err. | t    | P>|t|   | [95% Conf. Interval] |
|---------|---------|-----------|------|--------|----------------------|
| slope   | -.9429237 | .4569466  | -2.06 | 0.131  | -2.397132 0.5112842  |
| bias    | .9008406  | .8017623  | 1.12 | 0.343  | -1.650725 3.452406   |

7. Dizziness

Note: default data input format (theta, se_theta) assumed.

Tests for Publication Bias

Begg's Test

\[ \text{adj. Kendall's Score } (P-Q) = -23 \]

\[ \text{Std. Dev. of Score} = 11.18 \]

\[ \text{Number of Studies} = 10 \]

\[ z = -2.06 \]
\[ Pr > |z| = 0.040 \]
\[ z = 1.97 \text{ (continuity corrected)} \]
\[ Pr > |z| = 0.049 \text{ (continuity corrected)} \]

**Egger's test**

| Std_Eff | Coef. | Std. Err. | t    | P>|t| | [95% Conf. Interval] |
|---------|-------|-----------|------|-----|----------------------|
| slope   | .3788555 | .2154277  | 1.76 | 0.117 | -1.1179216  .8756325 |
| bias    | -.8627398 | .4076116  | -2.12| 0.167 | -1.802694  .0772142 |

**8. Anorexia**

Note: default data input format (theta, se_theta) assumed.

Tests for Publication Bias

**Begg's Test**

adj. Kendall's Score (P-Q) = -4  
Std. Dev. of Score = 2.94  
Number of Studies = 4  
\[ z = -1.36 \]
\[ Pr > |z| = 0.174 \]
\[ z = 1.02 \text{ (continuity corrected)} \]
\[ Pr > |z| = 0.308 \text{ (continuity corrected)} \]

**Egger's test**

| Std_Eff | Coef. | Std. Err. | t    | P>|t| | [95% Conf. Interval] |
|---------|-------|-----------|------|-----|----------------------|
| slope   | .2105003 | .1366696  | 1.54 | 0.263 | -0.3775416  .7985421 |
| bias    | -.5442062 | .2578762  | -2.11| 0.019 | -1.653758  .5653456 |
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Supplemental Data 5 The GRADE profile evidence of the included studies

Date: 2015-10-24
Question: Should Oxycodone vs Other opioid agents be used in Cancer-Related Pain?
Settings: The Adverse Events of Oxycodone in Cancer-Related Pain

<table>
<thead>
<tr>
<th>Quality assessment</th>
<th>No of patients</th>
<th>Effect</th>
<th>Quality</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of studies</td>
<td>Design</td>
<td>Risk of bias</td>
<td>Inconsistency</td>
<td>Indirectness</td>
</tr>
</tbody>
</table>

Bibliography:
<table>
<thead>
<tr>
<th>Condition</th>
<th>Randomised Trials</th>
<th>Risk of Bias</th>
<th>Consistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Event Count 1</th>
<th>Event Count 2</th>
<th>Relative Risk (95% CI)</th>
<th>Adjusted Incidence Rate (per 1000) (95% CI)</th>
<th>GRADE of Evidence</th>
<th>Important?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysuria</td>
<td>3</td>
<td>no serious</td>
<td>no serious</td>
<td>no serious</td>
<td>none</td>
<td>1/144 (0.69%)</td>
<td>5/144 (3.5%)</td>
<td>RR 0.343 (0.071 to 1.667)</td>
<td>23 fewer per 1000 (from 32 fewer to 23 more)</td>
<td>⊕⊕⊕⊕ HIGH</td>
<td>IMPORTANT</td>
</tr>
<tr>
<td>Constipation</td>
<td>11</td>
<td>no serious</td>
<td>no serious</td>
<td>no serious</td>
<td>none</td>
<td>128/604 (21.2%)</td>
<td>132/607 (21.7%)</td>
<td>RR 0.988 (0.800 to 1.220)</td>
<td>3 fewer per 1000 (from 43 fewer to 48 more)</td>
<td>⊕⊕⊕⊕ HIGH</td>
<td>IMPORTANT</td>
</tr>
<tr>
<td>Anorexia</td>
<td>4</td>
<td>no serious</td>
<td>no serious</td>
<td>no serious</td>
<td>none</td>
<td>24/183 (13.1%)</td>
<td>25/184 (13.6%)</td>
<td>RR 0.971 (0.579 to 1.628)</td>
<td>4 fewer per 1000 (from 57 fewer to 85 more)</td>
<td>⊕⊕⊕⊕ HIGH</td>
<td>IMPORTANT</td>
</tr>
<tr>
<td>Pruritus</td>
<td>4</td>
<td>no serious</td>
<td>no serious</td>
<td>no serious</td>
<td>none</td>
<td>18/118 (15.3%)</td>
<td>24/121 (19.8%)</td>
<td>RR 0.798 (0.456 to 1.398)</td>
<td>40 fewer per 1000 (from 108 fewer to 79 more)</td>
<td>⊕⊕⊕⊕ HIGH</td>
<td>NOT IMPORTANT</td>
</tr>
<tr>
<td>Sleepiness</td>
<td>5</td>
<td>no serious</td>
<td>no serious</td>
<td>no serious</td>
<td>none</td>
<td>22/211 (10.4%)</td>
<td>38/212 (17.9%)</td>
<td>RR 0.621 (0.379 to 1.018)</td>
<td>68 fewer per 1000 (from 111 fewer to 3 more)</td>
<td>⊕⊕⊕⊕ HIGH</td>
<td>IMPORTANT</td>
</tr>
</tbody>
</table>
### Vomiting

<table>
<thead>
<tr>
<th>11 randomised trials</th>
<th>no serious risk of bias</th>
<th>no serious inconsistency</th>
<th>no serious indirectness</th>
<th>no serious imprecision</th>
<th>none</th>
<th>88/604 (14.6%)</th>
<th>100/607 (16.5%)</th>
<th>RR 0 (0.690 to 1.158)</th>
<th>165 fewer per 1000 (from 51 fewer to 26 more)</th>
<th>⊕⊕⊕⊕ HIGH</th>
<th>IMPORTANT</th>
</tr>
</thead>
</table>

### Nausea

<table>
<thead>
<tr>
<th>11 randomised trials</th>
<th>no serious risk of bias</th>
<th>no serious inconsistency</th>
<th>no serious indirectness</th>
<th>no serious imprecision</th>
<th>none</th>
<th>125/604 (20.7%)</th>
<th>144/607 (23.7%)</th>
<th>RR 0.896 (0.725 to 1.108)</th>
<th>25 fewer per 1000 (from 65 fewer to 26 more)</th>
<th>⊕⊕⊕⊕ HIGH</th>
<th>IMPORTANT</th>
</tr>
</thead>
</table>

### Dizziness

<table>
<thead>
<tr>
<th>10 randomised trials</th>
<th>no serious risk of bias</th>
<th>no serious inconsistency</th>
<th>no serious indirectness</th>
<th>no serious imprecision</th>
<th>none</th>
<th>61/512 (11.9%)</th>
<th>65/515 (12.6%)</th>
<th>RR 0.936 (0.676 to 1.295)</th>
<th>8 fewer per 1000 (from 41 fewer to 37 more)</th>
<th>⊕⊕⊕⊕ HIGH</th>
<th>IMPORTANT</th>
</tr>
</thead>
</table>