Empirical investigation of potential bias for the harmful effects in randomized controlled trials

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Research questions

Safety is as important as effectiveness in the assessment of health interventions. As highlighted by the latest Cochrane handbook (version 6.2), all systematic reviews of interventions should investigate the adverse effects of the intervention [1]. Rare adverse events pose a substantial challenge for statistical modelling and inference for safety assessment, for example, low statistical power, biased effect estimation [2]. There are many potential factors that cause events to be rare in single trials. These factors result in either random error or systematic error that may bias the estimation of treatment effects. For example, low incidence, small sample size, and limited treatment duration may lead to large random errors [3-6]; while selective non-reporting or industry funding may lead to large systematic errors that bias estimates of treatment effects [7-10].

One example can illustrate the above bias clearly. Suppose the true incidence rates (per month) of a certain adverse event (AE) are 0.0005 and 0.0001 for treatment A and treatment B, respectively. The expected risk ratio (RR) (A vs. B) is therefore 0.0005/0.0001=5. Now let’s suppose a randomized controlled trial (RCT), with the sample sizes 200 vs. 200, the treatment duration time is 1 month, and therefore the expected events in both arms are 200*0.0005*1=0.1, 200*0.0001*1=0.02; then the observed events could be both 0. Thus, the estimated “pseudo” RR is then 1 that is largely biased. However, if we extend the treatment duration time to 12 months, then the expected events are 0.1*12=1.2, 0.02*12=0.024, and therefore the observed events could be 1 and 0, with an estimated RR of 3 much closer to true effect. Now, if researchers do not report the 1 event as they think this may be unfavorable for their new drug, the “adjusted” RR then back to 1 and showed no difference of the risk.

Considering the substantial impact of these factors on the estimate of treatment effects and conclusions of safety assessment, we plan to employ a large-scale empirical investigation to see the extent of the impact and seek potential solutions to adjust the bias by these factors.

Methods

Database
We will use the database of our recent ongoing project that investigated the preference of systematic review authors in dealing with studies with no events in meta-analyses of adverse events. The database collected systematic reviews of healthcare intervention with safety as exclusive outcome indexed in PubMed from 1 Jan 2015 to 1 Jan 2020.

*Eligibility*

The following systematic reviews will be included:

1) Safety as the exclusive outcome;
2) Includes only clinical trials;
3) Contains meta-analysis which with at least 5 studies;
4) Any drug or biological agent as intervention, with a comparison of any active or non-active drugs drug, biological agent, or placebo;
5) Provided 2 by 2 table data for each study in the table or forest plot;

We plan to limit meta-analyses for at least 5 studies for two reasons. First, the comparison (e.g. for-profit funding vs. not-for-profit funding) will be based on matching (e.g. sample size, treatment duration, incidence), more studies in a meta-analysis mean a higher possibility for successful matching; Second, our simulation suggested that a meta-analysis with less than 5 studies is inconclusive.

We plan to limit intervention to drugs and biological agents since they are more likely to be funded by industry. Our requirement that original 2 by 2 table data for each study be provided is based on the consideration that most of the meta-analyses did not appropriately deal with zero-events studies, leading to further systematic error. Such systematic error will bias our comparison.
**Context**

This study will focus on the potential impact of incidence, sample size, treatment duration time, non-reporting bias, and source of funding on harms reporting in trials, with a special focus on treatment duration time and source of funding. This will be conducted by comparing harms reported in trials with, for example, long treatment duration time/industry funding, to those with short treatment duration time/non-industry funding. Considering the potential impact of the other remaining factors (e.g. sample size, non-reporting bias), we plan to use the matching method whenever possible, say, when comparing the effects of industry-funded trials with non-profit institution funded trials, we will match the trials by baseline incidence, sample size, treatment duration, risk of bias. For risk of bias, the ROB 2.0 tool will be used [11]; for non-reporting bias, the Outcome Reporting Bias in Trials (ORBIT) for harm outcomes will be used [12, 13].

Therefore, thus information (i.e. 2 by 2 table, treatment duration time, risk of bias, source of funding) will be extracted for each trial in each eligible systematic review. In addition, baseline information like year of publication, original data for meta-analysis, related topics (e.g. cancer) will also be extracted.

Considering that some of the trials involve two periods, with different aims for each period, we extract the adverse events, treatment duration for each period separately. The information of whether the study or study period was double-blind, single-blind, or open-label will also be recorded.

**Additional analysis**

Meta-regression analysis for those eligible meta-analyses with 10 or more studies will be conducted for treatment duration time (or other factors is possible).

**Main outcome(s)**

- The proportion of data extraction errors by these systematic reviews.
The main outcome is the relative odds ratio (ROR) of each matched pair of trials. In addition, the topic-specific pooled ROR based on the inverse variance heterogeneous (IVhet) model will be calculated [14]. Considering that the method for dealing with zero-events may impact the pair-specific ROR and further impact the pooled ROR, we only consider trials with 1:1 design or close to 1:1 (i.e., ratio ranges from 0.51 to 1.99). Because under 1:1 design, the continuity correction (add 0.5) works well for both single-arm-zero-events and double-arm-zero-events.

Secondary outcome(s)

- The proportion of single-arm-zero-events studies and double-arm-zero-events studies within a meta-analysis.
- The potential impact of treatment duration time, non-reporting bias, source of funding for the occurrence of zero-events.

The following information will also be of interest for each eligible meta-analysis that reflects what extent the harmful effects were investigated:

1) Whether the meta-analysis investigated the potential impact of different treatment/control on the harmful effects?
2) Whether the meta-analysis investigated the potential impact of treatment duration on the harmful effects?
3) Whether the meta-analysis investigated the potential impact of doses of drug on the harmful effects?
4) Whether the meta-analysis investigated the potential impact of funding sources on the harmful effects?
5) Whether the meta-analysis investigated the potential impact of risk of bias on the harmful effects?
6) Whether the meta-analysis investigated the potential impact of age on the harmful effects?
7) Whether the meta-analysis rank the confidence of the evidence of harmful effects?
Data extraction (selection and coding)

Data extraction will be done by the lead author and several research assistants (see below the table of the records), and further checked by a research assistant. See “context” section for information to be exacted.

Analysis of subgroups or subsets

Year of publication of trials, sample size, incidence.

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Conflicts of interest

We declare no conflict of interest.

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Stage of review

Review Ongoing: Literature screen for the current study has not been done (By 11 April 2021).
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Supplementary Box 1. Search Strategy (PubMed, conducted on 28th-July, 2020)

1. "Systematic Reviews as Topic"[Mesh] OR "Systematic Review" [Publication Type] OR "Meta-Analysis as Topic"[Mesh] OR "Meta-Analysis" [Publication Type] OR "meta-analysis"[Title/Abstract] OR "meta analysis"[Title/Abstract] OR "systematic review"[Title/Abstract]

2. "randomized controlled trials as topic"[MeSH Major Topic] OR "clinical trials as topic"[MeSH Major Topic] OR "controlled clinical trials as topic"[MeSH Major Topic]

3. "randomized controlled trial*"[Title/Abstract] OR "controlled clinical trial*"[Title/Abstract] OR "clinical trial*"[Title/Abstract] OR "controlled trial*"[Title/Abstract] OR "trial*"[Title/Abstract]

4. "safety"[Title/Abstract] OR "harm*"[Title/Abstract] OR safe[Title/Abstract] OR poisoning[Title/Abstract] OR toxicity[Title/Abstract] OR tolerability[Title/Abstract] OR "complication*"[Title/Abstract] OR "adverse event*"[Title/Abstract] OR "adverse outcome*"[Title/Abstract] OR "untoward effect*"[Title/Abstract] OR "side effect*"[Title/Abstract] OR adverse n2 reaction[Title/Abstract]

5. #2 or #3

6. #1 AND #4 AND #5

7. Protocol[Title] OR overview [Title] OR "narrative review" [Title]

8. #6 NOT #7

9. (#8) AND (("2018/01/02"[Date - Publication]: "2020/01/01"[Date - Publication])) AND (humans[Filter]) Filters: Humans

10. (#8) AND (("2015/01/01"[Date - Publication]: "2018/01/01"[Date - Publication])) AND (humans[Filter]) Filters: Humans

11. #9 or # 10
### Supplementary Table 1. Records and amendments

| Date          | Description                                                                 |
|---------------|-----------------------------------------------------------------------------|
| 11-April, 2021| Draft the protocol                                                          |
| 14-April, 2021| Changing “follow-up time” to “treatment time” after consulting experts of clinical trials.  
**Reason:** Any treatment has wash-out period, after the period, any adverse events may not be caused by intervention. |
| 17-April, 2021| Send for collaborators for reviewing, no context changes                      |
| 22-April, 2021| Distinguishing the treatment duration and control duration in data extraction form based on extraction training |
| 25-April, 2021| Adding more information in secondary outcome, say, the seven “Whether…” as an effort to see how well the harmful effects were investigated |
| 4-May, 2021   | Change inclusion criteria: meta-analysis of RCTs to meta-analysis of clinical trials.  
**Reason:** Some meta-analyses claimed they included phase II or II trials, and did not mention whether these were RCTs or not. Based on our experience, the majority were RCTs. Therefore, we expand the inclusion criteria from RCTs to clinical trials. |
| 15-May, 2021  | During the data extraction, we noticed many of the systematic reviews failed to report or conduct the risk of bias of each trial. After an online meeting, we decided to assess the risk of bias by our research team. |
| 17-May, 2021  | Two assistants added in the research, with background of evidence-based medicine. They take charges of the assessment of risk of bias. Since the assessment of ROB is of some subjective, the two assistants are blinded, they were not and will not informed the aim of the project and the potential comparisons. And the assessment of risk of bias will be started after the finish of the data extraction (possibly at July). |
| 28-May, 2021  | Change in analysis of the main outcomes: We primarily plan to limit RCTs with 1:1 design to facilitate the estimation of the ORs in the case of zero-events. But then after our recent simulation study, we found continuity |
correction works well even when the ratio ranges from 0.51 to 1.99, therefore we “relaxed” the limits to 0.51 to 1.99.

| Date       | Description                                                                                                                                                                                                 |
|------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1-June, 2021 | We primarily collected data of the clinical trials from the systematic reviews, while for the sample we finished (accounted for 1/3 of the total), we found that many of the data were incorrectly recorded by these systematic reviews. Based on an urgent online meeting (CX and TQ), we decided to re-do the data extraction, directly from the original studies. |
| 5-June, 2021 | Online meeting with a pharmacist about the definition of different treatments/controls.                                                                                                                                 |
| 10-June, 2021 | Some clinical trials may have a flexible treatment schedule, for example, they use A drug with 5 mg at week 1, and 10 mg at week 2, and 20 mg at week 3, and then continue 20 mg for the following 11 weeks. Makes it difficult to extract the dose. After a discussion (CX and TQ), we decided to use the maximum dose in our study. |
| 14-June, 2021 | Add the tools that will be used for ROB assessment.                                                                                                                                                        |
| 15-June, 2021 | Add information for extraction: whether the trials involve two periods, and the design (double/single blind, open label) of each period.                                                                                                                  |
| 26-June, 2021 | Two assistants (WJ, FY) are ready to start the assessment of the ROB. An online meeting is held discussing the use of ROB 2 (XC, TQ, WJ, FY). A prior training for the two assistants based on 5 trials is prepared and will start tomorrow. The second online meeting will be held after the training for a further discussion of any issues during the preliminary assessment. Note: We finished about 50% of the systematic reviews for the intended data collection, and the included trials of these systematic reviews are ready for the ROB assessment. For the rest 50%, we may finish it 3 weeks later, and as long as we finish, we will prepare the trials included in these reviews for WJ and FY for the ROB assessment. |
| 30-June, 2021 | The two assistants finished the first period training of 2 RCTs; there are many disagreements between them on the judgement of each item. Thus, an online                                                                 |
meeting is held to discuss the issues of the assessment of each domain, each item, by reading the explanation of the ROB 2. After 1 hour’s discussion, an agreement is achieved of the assessment criteria. And the two assistants will continue to assess the remaining 3 RCTs for training.

| Date       | Event Description                                                                                                                                                                                                 |
|------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 2-July, 2021 | The two assistants finished the remaining 3 RCTs, and an online meeting is held to discuss further issues they met during the assessment. There is a high agreement of the judgement of the items this time and only 3 minor points involved. The training is now finished, and they are ready to formally start the assessment of the ROB. |
| 15-July, 2021 | During the data extraction of the meta-analysis data from original RCTs, we recorded many pieces of incorrect information of these meta-analyses. We then decided to treat this as an additional project that investigated how many meta-analyses with the data were incorrect. In this additional project, we will add systematic reviews other than drug/biologics treatment in order to increase the representativeness of the dataset. Both the data obtained from the meta-analyses and the data obtained from original RCTs will be recorded. We will first investigate the proportions that systematic reviews failed to extract the correct 2 x 2 table data; we will also record the type of incorrectness; we will further compare the meta-analysis based on correct data to the incorrect one to see how the incorrectness impact the results. Another assistant (Z.XQ) will take charge of the data extraction for systematic reviews other than drug/biologics treatments. The data will then be double-checked by the assistant after she finishes it. |
| 15-July, 2021 | XC and DMH finished the data extraction of SRs assigned to them, and started double-checking the data they extracted.                                                                                                                                                      |
| 17-July, 2021 | Until now, XC checked for 571 rows of 2 by 2 table data he extracted from RCTs (with 28 meta-analyses), and found 21 rows were incorrect by himself. The main reason is that RCTs present the same outcome for several times, thus leading to confusion (e.g. study by List et al. Diabetes Care. 2009) |
| Date               | Description                                                                                                                                                                                                                                                                                                                                 |
|--------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Apr;32(4):650-7    | Table 2. Urinary tract infection). The estimated proportion of mis-extraction by himself is then 21/571=3.7%. Suggests a high accuracy of the data extraction. However, the mis-extraction also suggests the importance of double-checking process. Therefore, an online meeting (XC, YTQ, and DMH) is then held by XC, and everybody is required to check each cell of the 2 by 2 table very carefully to ensure 0% error. In addition, YTQ and DMH are required to report their own accuracy to XC during their double-checking process. |
| 18-July, 2021      | Until now, XC checked for 696 rows of 2 by 2 table data he extracted from RCTs (with 43 meta-analyses), and found 24 rows were incorrect by himself. The estimated proportion of mis-extraction by himself is then 24/696=3.4%. The accuracy is better for the data extracted more recently (3.7% vs. 2.4% [3/125]).                                                                 |
| 20-July, 2021      | Until now, XC checked for 850 rows of 2 by 2 table data he extracted from RCTs (with 54 meta-analyses), and found 24 rows (no errors from 697-850) were incorrect by himself. The accuracy is 24/850=2.8%. Again, the accuracy is much better for the data extracted more recently (3.7% vs. 2.4% vs. 0%).                                                                 |
| 20-July, 2021      | Z.XQ finished the meta-analytic data (2 by 2 table for each included study) extraction from the forest plot/tables of the meta-analyses other than drug/biologics. She will start the 2 by 2 table data extraction from original RCTs thereafter, and she was required to double-check the data she extracted from meta-analysis and report her accuracy to XC. |
| 20-July, 2021      | Report by DHM: From rows 2 to 519 and row 1068 to 1310, there were 5 to 10 errors (she estimated) in the data extracted by DHM. The proportion ranges from 5/760 (0.66%) to 10/760 (1.32%).                                                                                                                |
| 21-July, 2021      | Report by XC: From rows 850 to 1073, there were 12 errors in the data extracted by XC, with a proportion of 12/223=5.38%. This is because he put the data of “any infection” into “serious infection” while the data of “serious infection” into “any infection” in Silvia 2016’s review.                                                                 |
| Date       | Event Description                                                                 |
|------------|-----------------------------------------------------------------------------------|
| 22-July, 2021 | Report by XC: From rows 1073 to 1678, there were 4 typo errors in the data extracted by XC, with a proportion of 4/605=0.66%. |
| 22-July, 2021 | XC starts to extract the data of the remaining 25 systematic reviews assigned to him. |
| 27-July, 2021 | DHM starts to extract the data of the remaining 15 systematic reviews assigned to her. |
| 30-July, 2021 | Report by XQ: From rows 1 to 145, there was 1 typo error in the data extracted by her, with a proportion of 1/145=0.69%. |
| 30-July, 2021 | TQ starts double-checking for the data she extracted.                               |
| 5-Aug, 2021  | XC has finished the data extraction of the remaining 25 systematic reviews with 86 meta-analyses assigned to him. He plans to check the data thereafter. |
| 7-Aug, 2021  | DHM has finished the data extraction of the remaining 14 systematic reviews assigned to her. And she plans to check the data thereafter. |
| 7-Aug, 2021  | Report by TQ: Until now, by checking the data she extracted, the proportion of errors were 4 from rows 1 to 373 (4/373=1.07%), 6 from rows 374 to 799 (6/425=1.41%), 4 from rows 800 to 1151 (4/351=1.14%), 5 from rows 1151 to 2351 (5/1200=0.42%), and 1 from rows 2352 to 3435 (1/1083=0.093%). |
| 7-Aug, 2021  | TQ starts to extract the data of the remaining 16 systematic reviews assigned to her. |
| 23-Aug, 2021 | DHM finished all the SRs assigned to her.                                           |
| 23-Aug, 2021 | Report by DHM: For the remaining 14 SRs with 68 meta-analyses, there were about 1-5 errors by herself based on her double-checking. The proportion of errors ranged from 1/1023=0.08% to 5/1203=0.49%. |
| 26-Aug, 2021 | Report by XC: For 14 SRs of 39 meta-analyses he double-checked until today, there were 4 errors from 647 rows, with a proportion of 4/647=0.62%. There remains 11 SRs to be double-checked. |
| 27-Aug, 2021 | TQ finished the data extraction of the 16 SRs assigned to her, and she will start the double-checking process thereafter. |
| 30-Aug, 2021 | Report by XC: For the remaining 11 SRs with 47 meta-analyses, there were               |
| Date           | Description                                                                                           |
|----------------|--------------------------------------------------------------------------------------------------------|
| 2-Sep, 2021    | Report by TQ: For the remaining 16 SRs with 59 meta-analyses, there were 6 errors by herself among 1325 rows, with a proportion of self-error of 6/1325=0.45%, mainly due to typo errors as well as failing to find the outcomes in the first time. |
| 19-Sep, 2021   | ZXQ finished the data extraction for the 40 SRs based on the original RCTs.                            |
| 19-Sep, 2021   | Report by ZXQ: From the 40 SRs with 2495 rows, there were 22 errors in total by herself, with a proportion of self-error of 22/2495 = 0.88%.                                             |
| 26-Sep, 2021   | Data cleaning and checking were finished by the principal author, assisted by the three assistants.   |
| 7-Oct, 2021    | A fourth-round checking finished by the principal author, focus on the information of subgroup analysis, those identified with data extraction errors, type of errors classification, and those without full-text recorded by the four assistants. A few minor typos/confusions were addressed. |
| 16-Oct, 2021   | A fifth-round checking by TQ finished, which mainly focused on the coding of the ID of systematic review, ID of each meta-analysis, information of subgroups, and eligibility of all systematic reviews. TQ found that 9 systematic reviews should not be excluded and need further data extraction. |
| 17-Oct, 2021   | An online meeting by XC and TQ for the 9 additional systematic reviews, and decide to extract the data by one of the assistants that do not know the summarized results.       |
| 18-Oct, 2021   | Hanmin started data extraction for the 9 additional systematic reviews.                               |
| 22-Oct, 2021   | Hanmin finished the data extraction of the addition systematic reviews. And XC started double-checking for the data.                                          |
| 25-Oct, 2021   | XC finished the double-checking of the data. And such all the data were finished.                     |
Representativity for searching PubMed only

In our previous study conducted in 2011, we searched Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE) for published systematic reviews of adverse events from 1st-Jan, 2008 to 25th-Apr, 2011, with the same inclusion criteria (current one limit the reviews based on RCTs). The CDSR database covers all the Cochrane reviews and the DARE database collected systematic reviews of health care and social intervention from a board range of health science databases (e.g. PubMed, MEDLINE, Embase, CINAHL, PsycINFO). In the study, 309 systematic reviews were finally included. There were 17 systematic reviews with the files lost as it passed 10 years. The remaining 292 systematic reviews are available to verify our assumption of representativity of our “sample”.

We (XC) searched these 292 systematic reviews in PubMed with the title, the DOI number, or the citation (journal name, year of publish, volume, pages) on 26th-Jan, 2022, and we identified that 290 (99.3%) of them were indexed in PubMed (see Supplementary Table 2 below). For a more conservative estimation, suppose the lost 17 systematic reviews were all not indexed in PubMed; there were still 290/309= 93.85% systematic reviews indexed in PubMed. Based on this prior probability, for the 201 systematic reviews of RCTs in the current study out of 511 systematic reviews of adverse events during 2015 to 2020 we collected from PubMed, we expect there would be, at most, 12 (201*17-290) systematic reviews that were not included in our study. This suggested that searching for PubMed is sufficient to reach a representative sample.
Supplementary Table 2. Index situation for 292 previous systematic reviews of adverse events of our previous study (BMJ. 2014;348: f7668.).

| SR name            | Indexed in PubMed | Citation                                                                 |
|--------------------|-------------------|--------------------------------------------------------------------------|
| Aasheim 2008       | Y                 | Ann Surg. 2008 Nov;248(5):714-20.                                         |
| Abad 2010          | Y                 | J Hosp Infect. 2010 Oct;76(2):97-102.                                     |
| Agbalka 2009       | Y                 | Drug Saf. 2009;32(8):637-47.                                              |
| Agrafiotis 2009    | Y                 | Respiration. 2009;78(1):69-74.                                            |
| Aksoy 2009         | Y                 | Leukemia & Lymphoma.2009; 50(3): 357–365                                 |
| Albavera-Harnandez 2009 | Y       | Clinical Rehabilitation 2009; 23: 394–407                                  |
| Alvarez-Jimenez 2008 | Y             | CNS Drugs 2008; 22 (7): 547-562                                          |
| An 2010            | Y                 | Eur J Clin Pharmacol (2010) 66:813–821                                     |
| Aprili 2008        | Y                 | Anesthesiology 2009; 111:1346–55                                         |
| Arbyn 2008         | Y                 | BMJ 2008;337:a1284                                                        |
| Bacha 2009         | Y                 | Int J Gynecol Cancer 2009;19: 202Y207                                    |
| Bager 2008         | Y                 | Clinical and Experimental Allergy, 38, 634-642                            |
| Banach 2010        | Y                 | Drug Saf 2010; 33 (1): 73-79                                             |
| Bangalore 2 2011   | Y                 | Lancet Oncol 2011; 12: 65–82                                             |
| Bangalore 2011     | Y                 | BMJ 2011;342;d2234                                                       |
| Bani-Hani 2008     | Y                 | Eur J Vasc Endovasc Surg (2008) 36, 565e573                               |
| Bar-Oz 2009        | Y                 | European Journal of Obstetrics & Gynecology and Reproductive Biology 143 (2009) 75–78 |
| Bennet2008         | Y                 | JAMA. 2008;299(8):914-924                                               |
| Bergendal 2009     | Y                 | Acta Obstetricia et Gynecologica. 2009; 88: 261 266                      |
| Bhuriya 2010       | Y                 | International Journal of Cardiology 142 (2010) 213–217                  |
| Bloch 2010         | Y                 | Drugs Aging 2010; 27 (11): 895-901                                       |
| Bolland 2010       | Y                 | BMJ 2010;341:c3691                                                       |
| Bongartz 2009      | Y                 | Ann Rheum Dis 2009;68:1177–1183.                                         |
| Bonzetti 2009      | Y                 | Clinical Nutrition 28 (2009) 226–230                                     |
| Brettun 2008       | Y                 | Respiratory Medicine (2008) 102, 862–875                                 |
| Brunelli 2009      | Y                 | Am J Kidney Dis 53:448-456.                                              |
| Campbell 2009      | Y                 | Clinical Interventions in Aging 2009;4 225–233                          |
| Canonico 2008      | Y                 | BMJ. 2008 May 31;336(7655):1227-31.                                       |
| Cao 2 2010         | Y                 | Chemotherapy 2010;56:459–465.                                            |
| Cao 2010           | Y                 | Cancer Chemother Pharmaco (2010) 66;37–42                                |
| Carnes 2010        | Y                 | Manual Therapy 15 (2010) 355–363                                         |
| Carwell 2008       | Y                 | Diabetologia (2008) 51:726–735                                           |
| Castillo 2010      | Y                 | Blood 2010 116: 2897-2907                                                |
| Chakhtoura 2009    | Y                 | Stroke 2009, 40:1059-1062                                               |
| Chamot 2010        | Y                 | BMC Women’s Health 2010, 10:11                                          |
| Chan 2009          | Y                 | Journal of Hypertension 2009, 27:2332–2341                               |
| Charles 2008       | Y                 | Contraception 78 (2008) 436–450                                          |
| Author                  | Year | Journal/Title                                      |
|------------------------|------|---------------------------------------------------|
| Charlson 2009          | Y    | Pharmacoepidemiology and drug safety 2009; 18: 93–103 |
| Chavez-Tapia 2009      | Y    | BMC Gastroenterology 2009, 9:75                   |
| Chilshon 2009          | Y    | Laryngoscope, 119:1135–1139, 2009                 |
| Choueiri 2010          | Y    | J Clin Oncol 28:2280-2285                         |
| Chu 2008               | Y    | Acta Oncologica, 2008; 47: 176 186                 |
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### Supplementary Table 3. List of excluded studies (with reasons)

| Exclusion lists | Reasons for exclusion |
|-----------------|-----------------------|
| 1. Aires FT, Dedivitis RA, Petrarolha SM, Bernardo WM, Cernea CR, Brandão LG. Early oral feeding after total laryngectomy: A systematic review. Head Neck. 2015;37(10):1532-1535. doi:10.1002/hed.23755 | NRSIs included, less than 5 studies |
| 2. Alfageh BH, Wang Z, Mongkhon P, et al. Safety and Tolerability of Antipsychotic Medication in Individuals with Autism Spectrum Disorder: A Systematic Review and Meta-Analysis. Paediatr Drugs. 2019;21(3):153-167. doi:10.1007/s40272-019-00333-x | NRSIs included |
| 3. Aljebab F, Choonara I, Conroy S. Systematic review of the toxicity of short-course oral corticosteroids in children. Arch Dis Child. 2016;101(4):365-370. doi:10.1136/archdischild-2015-309522 | NRSIs included |
| 4. Aljebab F, Choonara I, Conroy S. Systematic Review of the Toxicity of Long-Course Oral Corticosteroids in Children. PLoS One. 2017;12(1):e0170259. Published 2017 Jan 26. doi:10.1371/journal.pone.0170259 | NRSIs included |
| 5. Almpani K, Papageorgiou SN, Papadopoulos MA. Autotransplantation of teeth in humans: a systematic review and meta-analysis. Clin Oral Investig. 2015;19(6):1157-1179. doi:10.1007/s00784-015-1473-9 | NRSIs included |
| 6. Ando T, Briasoulis A, Holmes AA, Takagi H, Slovut DP. Percutaneous versus surgical cut-down access in transfemoral transcatheter aortic valve replacement: A meta-analysis. J Card Surg. 2016;31(12):710-717. doi:10.1111/jocs.12842 | NRSIs included |
| 7. Azoulay L, Suisse S. Sulfonylureas and the Risks of Cardiovascular Events and Death: A Methodological Meta-Regression Analysis of the Observational Studies. Diabetes Care. 2017;40(5):706-714. doi:10.2337/dc16-1943 | NRSIs included |
| 8. Bai Y, Chen H, Yang Y, et al. Safety of antithrombotic drugs in patients with atrial fibrillation and non-end-stage chronic kidney disease: Meta-analysis and systematic review. Thromb Res. 2016;137:46-52. doi:10.1016/j.thromres.2015.11.020 | NRSIs included |
| 9. Balasubramanian I, Fleming C, Mohan HM, Schmidt K, Haglind E, Winter DC. Out-Patient Management of Mild or Uncomplicated Diverticulitis: A Systematic Review. Dig Surg. 2017;34(2):151-160. doi:10.1159/000450865 | NRSIs included |
| 10. Balk EM, Earley A, Avendano EA, Raman G. Long-Term Health Outcomes in Women With Silicone Gel Breast Implants: A Systematic Review. Ann Intern Med. 2016;164(3):164-175. doi:10.7326/M15-1169 | NRSIs included |
| 11. Barzilay E, Gadot Y, Koren G. Safety of vaginal delivery in very low birthweight vertex singletons: a meta-analysis. J Matern Fetal Neonatal Med. 2016;29(22):3724-3729. doi:10.3109/14767058.2016.1141889 | NRSIs included |
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NRSIs included
Less than 5 studies
NMA, without pairwise MA
Continuous outcomes
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| No. | Reference                                                                                           | Title                                                                                           | J.                                                                 | doi                                                                 | Notes                           |
|-----|-----------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|------------------------------------------------------------------|----------------------------------------------------------------------|---------------------|
| 222 | Tang HL, Li DD, Zhang JJ, et al. Lack of evidence for a harmful effect of sodium-glucose co-transporter 2 (SGLT2) inhibitors on fracture risk among type 2 diabetes patients: a network and cumulative meta-analysis of randomized controlled trials. Diabetes Obes Metab. 2016;18(12):1199-1206. doi:10.1111/dom.12742 | Lack of evidence for a harmful effect of sodium-glucose co-transporter 2 (SGLT2) inhibitors on fracture risk among type 2 diabetes patients: a network and cumulative meta-analysis of randomized controlled trials. | No 2 by 2 table data | NMA, without pairwise MA                                             |                     |
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| 225 | Thomopoulos C, Parati G, Zanchetti A. Effects of blood-pressure-lowering treatment in hypertension: 9. Discontinuations for adverse events attributed to different classes of antihypertensive drugs: meta-analyses of randomized trials. J Hypertens. 2016;34(10):1921-1932. doi:10.1097/HJH.0000000000001052 | Effects of blood-pressure-lowering treatment in hypertension: 9. Discontinuations for adverse events attributed to different classes of antihypertensive drugs: meta-analyses of randomized trials. | No 2 by 2 table data | NMA, without pairwise MA                                             |                     |
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| 228 | Verrotti A, Prezioso G, Di Sabatino F, Franco V, Chiarelli F, Zaccara G. The adverse event profile of levetiracetam: A meta-analysis on children and adults. Seizure. 2015;31:49-55. doi:10.1016/j.seizure.2015.07.004 | The adverse event profile of levetiracetam: A meta-analysis on children and adults. | No 2 by 2 table data | NMA, without pairwise MA                                             |                     |
| 229 | Vouri SM, Kebodeaux CD, Stranges PM, Teshome BF. Adverse events and treatment discontinuations of antimuscarinics for the treatment of overactive bladder in older adults: A systematic review and meta-analysis. Arch Gerontol Geriatr. 2017;69:77-96. doi:10.1016/j.archger.2016.11.006 | Adverse events and treatment discontinuations of antimuscarinics for the treatment of overactive bladder in older adults: A systematic review and meta-analysis. | No 2 by 2 table data | NMA, without pairwise MA                                             |                     |
| 230 | Wang C, Wang F, Min X, et al. Toxicties of chemoradiotherapy and radiotherapy in nasopharyngeal carcinoma: an updated meta-analysis. J Int Med Res. 2019;47(7):2832-2847. doi:10.1177/0300060519858031 | Toxicties of chemoradiotherapy and radiotherapy in nasopharyngeal carcinoma: an updated meta-analysis. | No 2 by 2 table data | NMA, without pairwise MA                                             |                     |
| 231 | Wang XF, Huang WF, Nie J, Zhou Y, Tan DW, Jiang JH. Toxicity of chemotherapy regimens in advanced and metastatic pancreatic cancer therapy: A network meta-analysis. J Cell Biochem. 2018;119(7):5082-5103. doi:10.1002/jcb.26266 | Toxicity of chemotherapy regimens in advanced and metastatic pancreatic cancer therapy: A network meta-analysis. | No reference for included studies | NMA, without pairwise MA                                             |                     |
| 232 | Wang Z, Yang X, Wang J, et al. Risk of serious adverse event and fatal adverse event with molecular target anticancer drugs in cancer patients: A meta-analysis. J Cancer Res Ther. 2019;15(7):1435-1449. doi:10.4103/jcrt.JCRT_577_18 | Risk of serious adverse event and fatal adverse event with molecular target anticancer drugs in cancer patients: A meta-analysis. | No reference for included studies | NMA, without pairwise MA                                             |                     |
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## Supplementary table 4. Impacts of data extraction errors on the results based on 288 meta-analyses.

| MA_id | Methods   | Effect estimator | ES_old | LCI_old | UCI_old | Error_detail   | ES_corrected | LCI_corrected | UCI_corrected | Bias  |
|-------|-----------|------------------|--------|---------|---------|----------------|--------------|--------------|--------------|-------|
| 1     | RE        | RR               | 3.72   | 1.74    | 7.94    | Mismatching    | 3.38         | 1.76         | 6.46         | -9.2% |
| 2     | Fixed     | RR               | 2.79   | 1.36    | 5.73    | Mismatching    | 2.79         | 1.36         | 5.73         | 0.0%  |
| 3     | RE        | RR               | 1.49   | 1.13    | 1.97    | Mismatching    | 1.49         | 1.13         | 1.96         | -0.3% |
| 4     | RE        | RR               | 1.54   | 1.14    | 2.08    | Mismatching    | 1.54         | 1.14         | 2.08         | -0.2% |
| 5     | MH-Fixed  | RR               | 1.16   | 1.05    | 1.27    | Numerical      | 1.16         | 1.06         | 1.27         | 0.1%  |
| 6     | RE        | RR               | 0.88   | 0.81    | 0.96    | Numerical      | 0.87         | 0.81         | 0.94         | -0.6% |
| 7     | RE        | RR               | 0.39   | 0.29    | 0.53    | Numerical      | 0.39         | 0.30         | 0.53         | 0.3%  |
| 18    | DL-RE     | RR               | 1.23   | 1.03    | 1.46    | Numerical      | 1.24         | 1.04         | 1.47         | 0.5%  |
| 20    | DL-RE     | RR               | 0.70   | 0.30    | 1.66    | Zero-assumption| 0.69         | 0.29         | 1.65         | -1.6% |
| 29    | RE        | OR               | 1.07   | 1.02    | 1.13    | Numerical      | 1.07         | 1.05         | 1.09         | -0.5% |
| 30    | RE        | OR               | 2.86   | 2.49    | 3.27    | Numerical      | 2.91         | 2.61         | 3.25         | 1.8%  |
| 34    | RE        | OR               | 33.58  | 14.50   | 77.77   | Numerical      | 48.80        | 20.69        | 115.10       | 45.3% |
| 35    | RE        | OR               | 40.77  | 19.52   | 85.19   | Numerical      | 89.57        | 50.35        | 159.32       | 119.7%|
| 36    | RE        | OR               | 3.99   | 1.09    | 14.64   | Numerical      | 4.28         | 1.16         | 15.75        | 7.2%  |
| 38    | MH-Fixed  | RD               | 0.00   | -0.01   | 0.01    | Numerical      | 0.00         | -0.02        | 0.01         | -300.0%|
| 39    | MH-Fixed  | RD               | 0.00   | -0.01   | 0.01    | Numerical      | 0.00         | -0.01        | 0.01         | 0.0%  |
| 42    | MH-Fixed  | RR               | 2.86   | 1.24    | 5.48    | Misidentification+Numerical| 2.64         | 1.39         | 5.00         | -7.7% |
| 41    | MH-Fixed  | RR               | 4.36   | 2.58    | 7.38    | Numerical      | 3.61         | 2.23         | 5.84         | -17.2%|
| 43    | Peto      | RR               | 2.26   | 1.40    | 3.64    | Numerical      | 2.29         | 1.40         | 3.75         | 1.4%  |
| 44    | RE        | RR               | 2.60   | 1.85    | 3.63    | Numerical      | 2.64         | 1.87         | 3.71         | 1.5%  |
| 47    | IV-Fixed  | OR               | 3.14   | 0.76    | 12.98   | Numerical+Zero-assumption| 3.11         | 0.85         | 11.37        | -1.0% |
| 49    | IV-Fixed  | OR               | 6.92   | 3.25    | 14.75   | Numerical+Zero-assumption| 5.81         | 3.81         | 8.84         | -16.1%|
|   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|
| 50 | IV-Fixed | OR | 1.38 | 1.03 | 11.08 | Numerical+Zero-assumption | 2.27 | 0.68 | 7.64 | 64.7% |
| 46 | IV-Fixed | OR | 2.88 | 1.30 | 6.37 | Numerical | 2.48 | 1.22 | 5.07 | -13.8% |
| 48 | IV-Fixed | OR | 3.82 | 1.27 | 11.45 | Numerical | 0.93 | 0.63 | 1.37 | -75.7% |
| 52 | IV-Fixed | OR | 0.84 | 0.65 | 1.09 | Numerical | 0.80 | 0.72 | 0.88 | -5.2% |
| 53 | IV-Fixed | OR | 0.78 | 0.57 | 1.05 | Numerical | 0.68 | 0.61 | 0.77 | -12.4% |
| 64 | MH-Fixed | OR | 1.18 | 1.03 | 1.37 | Misidentification+Numerical | 1.21 | 1.05 | 1.39 | 2.5% |
| 66 | MH-Fixed(ECC) | OR | 1.17 | 0.93 | 1.47 | Misidentification+Numerical | 0.99 | 0.79 | 1.24 | -15.8% |
| 58 | MH-Fixed(ECC) | OR | 1.83 | 1.00 | 2.62 | Numerical | 1.54 | 1.10 | 2.16 | -15.7% |
| 62 | MH-Fixed(ECC) | OR | 2.84 | 0.70 | 11.56 | Misidentification | 2.84 | 0.70 | 11.56 | 0.0% |
| 65 | MH-Fixed(ECC) | OR | 1.36 | 1.10 | 1.67 | Numerical | 1.46 | 1.19 | 1.79 | 7.1% |
| 69 | MH-Fixed | RR | 4.28 | 1.08 | 17.01 | Numerical+Zero-assumption | 3.33 | 0.83 | 13.36 | -22.1% |
| 70 | MH-Fixed | OR | 2.11 | 0.70 | 6.35 | Misidentification+Numerical | 4.10 | 1.40 | 12.00 | 94.4% |
| 73 | MH-Fixed(ECC) | OR | 1.43 | 0.58 | 3.53 | Misidentification | 1.49 | 0.70 | 3.17 | 3.8% |
| 77 | RE | RR | 4.26 | 2.30 | 7.90 | Misidentification+Numerical | 4.93 | 2.41 | 10.06 | 15.7% |
| 78 | RE | RR | 4.08 | 2.71 | 6.14 | Misidentification+Numerical | 3.92 | 2.72 | 5.65 | -4.0% |
| 79 | RE | RR | 1.88 | 1.10 | 3.20 | Misidentification+Numerical | 1.95 | 1.18 | 3.22 | 3.8% |
| 74 | RE (CC) | RR | 2.49 | 1.83 | 3.36 | Numerical | 2.61 | 1.85 | 3.69 | 5.0% |
| 75 | RE (CC) | RR | 2.97 | 2.25 | 3.92 | Numerical | 2.90 | 2.14 | 3.94 | -2.2% |
| 76 | RE (CC) | RR | 2.22 | 1.70 | 2.89 | Numerical | 2.22 | 1.65 | 2.99 | 0.0% |
| 88 | Peto | OR | 0.93 | 0.79 | 1.10 | Mismatching+Numerical | 0.92 | 0.77 | 1.08 | -1.6% |
|   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|
| 83 | Peto | OR | 1.17 | 0.47 | 2.89 | Numerical | 1.05 | 0.42 | 2.67 | -10.1% |
| 87 | Peto | OR | 0.98 | 0.83 | 1.15 | Numerical | 0.97 | 0.82 | 1.14 | -1.4% |
| 89 | Peto | OR | 0.90 | 0.45 | 1.78 | Numerical | 0.78 | 0.40 | 1.54 | -13.2% |
| 90 | Peto | OR | 1.06 | 0.86 | 1.31 | Mismatching | 1.05 | 0.85 | 1.29 | -1.2% |
| 95 | Peto | OR | 1.12 | 0.90 | 1.40 | Numerical | 1.10 | 0.88 | 1.37 | -2.0% |
| 96 | Peto | OR | 0.49 | 0.24 | 1.00 | Numerical | 0.63 | 0.32 | 1.25 | 28.2% |
| 99 | Peto | OR | 1.06 | 0.33 | 3.37 | Numerical | 0.94 | 0.28 | 3.14 | -11.6% |
| 102 | Peto | OR | 1.87 | 0.84 | 4.15 | Numerical | 1.19 | 0.53 | 2.67 | -36.5% |
| 108 | Peto | OR | 1.58 | 0.52 | 4.76 | Numerical | 1.30 | 0.41 | 4.08 | -17.8% |
| 114 | Peto | OR | 1.14 | 0.47 | 2.78 | Numerical | 1.40 | 0.58 | 3.41 | 23.0% |
| 115 | Peto | OR | 1.47 | 0.64 | 3.42 | Numerical | 1.36 | 0.60 | 3.10 | -7.3% |
| 117 | Peto | OR | 1.92 | 0.72 | 5.11 | Numerical | 2.67 | 0.94 | 7.62 | 39.3% |
| 118 | IV-Fixed (CC) | RR | 1.21 | 1.07 | 1.37 | Numerical | 1.28 | 1.13 | 1.45 | 5.5% |
| 122 | MH-Fixed | OR | 1.00 | 0.88 | 1.15 | Numerical | 0.99 | 0.86 | 1.12 | -1.8% |
| 126 | MH-RE | OR | 0.72 | 0.27 | 1.95 | Numerical | 0.72 | 0.27 | 1.95 | 0.1% |
| 129 | Fixed | RD | 0.00 | 0.00 | 0.00 | Numerical+Zero-assumption | 0.00 | 0.00 | 0.01 | 130.8% |
| 130 | DL-RE | RR | 1.13 | 1.07 | 1.20 | Numerical | 1.16 | 1.09 | 1.23 | 2.2% |
| 131 | DL-RE | RR | 1.74 | 1.24 | 2.45 | Numerical | 1.73 | 1.24 | 2.44 | -0.3% |
| 132 | DL-RE | RR | 2.63 | 1.43 | 4.82 | Numerical | 2.58 | 1.41 | 4.75 | -1.7% |
| 134 | MH-RE | RR | 1.09 | 0.87 | 1.36 | Numerical | 1.09 | 0.87 | 1.36 | 0.1% |
| 135 | MH-RE | RR | 1.04 | 0.64 | 1.71 | Numerical | 1.04 | 0.64 | 1.71 | 0.2% |
| 136 | MH-RE | RR | 1.69 | 0.71 | 4.03 | Numerical | 1.39 | 0.57 | 3.39 | -17.8% |
| 139 | MH-RE | RR | 2.38 | 1.36 | 4.18 | Numerical | 2.38 | 1.36 | 4.17 | 0.0% |
| 140 | MH-RE | RR | 1.44 | 1.20 | 1.74 | Numerical | 1.51 | 1.10 | 2.06 | 4.6% |
| 141 | MH-RE | RR | 2.69 | 1.78 | 4.07 | Numerical | 2.19 | 1.13 | 4.23 | -18.6% |
|     | Type       | RR 1     | RR 2     | RR 3     | Misc.     | RR 4     | RR 5     | RR 6     |
|-----|------------|----------|----------|----------|-----------|----------|----------|----------|
| 143 | IV-Fixed   | 1.37     | 0.51     | 3.65     | Numerical | 2.03     | 0.67     | 6.16     | 48.2%    |
| 149 | Fixed      | 1.82     | 1.05     | 3.14     | Zero-assumption | 2.00     | 1.13     | 3.57     | 10.3%    |
| 154 | Fixed      | 1.33     | 1.12     | 1.58     | Mismatching+Numerical+Zero-assumption | 1.33     | 1.12     | 1.58     | 0.2%     |
| 158 | Fixed(CC)  | 2.34     | 1.34     | 4.09     | Numerical+Zero-assumption | 2.31     | 1.27     | 4.20     | -1.5%    |
| 159 | DL-RE      | 3.85     | 3.37     | 4.40     | Zero-assumption | 3.86     | 3.39     | 4.39     | 0.2%     |
| 167 | MH-Fixed   | 4.45     | 3.04     | 6.51     | Misidentification+Numerical | 6.39     | 3.26     | 12.52    | 43.5%    |
| 169 | MH-Fixed   | 1.71     | 1.38     | 2.13     | Misidentification+Numerical | 1.02     | 0.86     | 1.22     | -40.4%   |
| 161 | MH-RE      | 1.73     | 1.39     | 2.16     | Misidentification | 1.73     | 1.39     | 2.16     | 0.1%     |
| 162 | MH-RE      | 5.62     | 2.84     | 11.11    | Misidentification | 4.96     | 2.45     | 10.07    | -11.7%   |
| 163 | MH-RE      | 1.80     | 1.38     | 2.35     | Misidentification | 1.80     | 1.38     | 2.35     | 0.2%     |
| 164 | MH-RE      | 4.98     | 1.67     | 14.87    | Misidentification | 4.30     | 1.36     | 13.58    | -13.7%   |
| 168 | MH-RE      | 6.49     | 3.57     | 11.77    | Misidentification | 5.80     | 3.13     | 10.75    | -10.6%   |
| 170 | MH-RE      | 2.20     | 0.52     | 9.27     | Misidentification | 2.16     | 0.50     | 9.32     | -1.8%    |
| 197 | MH-Fixed   | 0.88     | 0.72     | 1.07     | Numerical | 0.88     | 0.73     | 1.07     | 0.1%     |
| 198 | RE         | 1.08     | 0.85     | 1.56     | Numerical | 0.96     | 0.80     | 1.16     | -10.9%   |
| 226 | MH-Fixed   | 4.17     | 3.11     | 5.58     | Numerical+Zero-assumption | 5.80     | 4.43     | 7.59     | 39.0%    |
| 229 | MH-Fixed   | 0.26     | 0.20     | 0.35     | Numerical | 0.29     | 0.22     | 0.38     | 11.5%    |
| 234 | MH-Fixed   | 2.16     | 1.47     | 3.19     | Numerical | 2.24     | 1.52     | 3.31     | 3.9%     |
| 235 | MH-RE      | 3.15     | 2.54     | 3.92     | Numerical | 3.15     | 2.54     | 3.92     | 0.1%     |
| 237 | MH-RE      | 2.09     | 1.77     | 2.48     | Numerical | 2.03     | 1.69     | 2.43     | -3.1%    |
| 239 | MH-RE      | 3.93     | 3.22     | 4.80     | Numerical | 3.74     | 2.94     | 4.76     | -4.8%    |
| 241 | MH-Fixed   | 0.77     | 0.74     | 0.80     | Numerical | 0.77     | 0.74     | 0.80     | 0.0%     |
| 242 | MH-Fixed   | 0.32     | 0.25     | 0.41     | Numerical | 0.33     | 0.30     | 0.37     | 3.4%     |
| 250 | Fixed      | 1.31     | 0.82     | 2.07     | Mismatching+Numerical | 1.62     | 0.93     | 2.80     | 23.8%    |
|   |   | RR | RR | RR |   |
|---|---|----|----|----|---|
| 251 Fixed |   | 1.87 | 1.52 | 2.30 | Numerical | 1.84 | 1.50 | 2.26 | -1.6% |
| 257-1 MH-Fixed |   | 0.81 | 0.51 | 1.27 | Numerical | 0.84 | 0.54 | 1.31 | 3.7% |
| 257-3 MH-Fixed |   | 1.26 | 0.75 | 2.12 | Numerical | 1.20 | 0.73 | 1.98 | -4.8% |
| 261 RE |   | 2.39 | 1.09 | 7.68 | Mismatching+Numerical | 2.09 | 0.94 | 4.61 | -12.8% |
| 262 RE |   | 1.35 | 0.88 | 2.08 | Mismatching | 1.34 | 0.88 | 2.04 | -0.4% |
| 264-1 Fixed |   | 1.49 | 1.01 | 2.21 | Numerical | 1.35 | 0.90 | 2.03 | -9.7% |
| 264-2 Fixed |   | 1.93 | 1.06 | 3.51 | Numerical | 1.84 | 0.98 | 3.48 | -4.6% |
| 266 MH-RE |   | 0.90 | 0.67 | 1.21 | Numerical | 0.90 | 0.67 | 1.21 | 0.0% |
| 267 MH-RE |   | 0.61 | 0.32 | 1.14 | Numerical | 0.50 | 0.26 | 0.97 | -18.3% |
| 268 MH-RE |   | 0.50 | 0.25 | 1.00 | Numerical | 0.50 | 0.25 | 1.00 | 0.2% |
| 269 MH-RE |   | 1.01 | 0.78 | 1.30 | Numerical | 1.01 | 0.78 | 1.30 | -0.3% |
| 274 MH-RE |   | 3.05 | 1.98 | 4.70 | Numerical | 2.86 | 1.92 | 4.25 | -6.3% |
| 275 MH-RE |   | 1.88 | 0.66 | 5.35 | Numerical | 1.88 | 0.66 | 5.35 | 0.0% |
| 276 MH-RE |   | 2.35 | 1.20 | 4.61 | Numerical | 2.35 | 1.20 | 4.61 | 0.1% |
| 277 MH-RE |   | 4.68 | 1.42 | 15.37 | Numerical | 4.86 | 1.56 | 15.12 | 3.9% |
| 278 MH-RE |   | 1.71 | 1.21 | 2.40 | Numerical | 1.71 | 1.21 | 2.40 | -0.2% |
| 280 MH-RE |   | 6.50 | 2.93 | 14.41 | Numerical | 6.00 | 2.64 | 13.62 | -7.7% |
| 281 MH-RE |   | 1.60 | 1.17 | 2.19 | Numerical | 1.62 | 1.17 | 2.24 | 1.2% |
| 285 MH-RE |   | 1.53 | 1.04 | 2.25 | Numerical | 1.53 | 1.04 | 2.25 | 0.0% |
| 286 MH-RE |   | 1.19 | 0.86 | 1.64 | Numerical | 1.33 | 0.75 | 2.36 | 12.0% |
| 287 MH-RE |   | 1.51 | 1.03 | 2.23 | Numerical | 1.51 | 1.03 | 2.23 | 0.2% |
| 293 MH-RE |   | 0.74 | 0.50 | 1.10 | Numerical | 0.74 | 0.50 | 1.10 | -0.2% |
| 296 RE |   | 0.78 | 0.59 | 1.03 | Numerical | 0.82 | 0.63 | 1.07 | 5.5% |
| 297 RE |   | 2.85 | 2.02 | 4.04 | Numerical | 2.90 | 2.01 | 4.19 | 1.6% |
| 300 RE |   | 3.42 | 2.36 | 4.96 | Numerical | 4.12 | 2.38 | 7.14 | 20.4% |
|   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|
| 301 | RE | OR | 1.85 | 1.13 | 3.02 | Numerical | 1.79 | 1.14 | 2.81 | -3.0% |
| 304 | RE | OR | 1.09 | 0.90 | 1.31 | Numerical | 1.10 | 0.91 | 1.33 | 0.5% |
| 305 | RE | OR | 1.62 | 1.04 | 2.51 | Numerical | 1.64 | 1.06 | 2.55 | 1.3% |
| 306 | MH-RE | RR | 1.27 | 1.13 | 1.43 | Numerical | 1.27 | 1.13 | 1.43 | -0.1% |
| 309 | MH-RE | RR | 0.80 | 0.21 | 2.99 | Numerical | 0.97 | 0.20 | 4.57 | 20.6% |
| 313 | MH-Fixed | RR | 4.59 | 3.26 | 6.48 | Numerical | 4.75 | 3.37 | 6.70 | 3.6% |
| 314 | MH-Fixed | RR | 1.38 | 0.97 | 1.95 | Numerical | 1.40 | 0.99 | 1.99 | 1.7% |
| 335 | MH-RE | OR | 4.95 | 1.64 | 14.93 | Numerical | 4.22 | 1.27 | 14.04 | -14.8% |
| 348 | MH-Fixed | RR | 0.88 | 0.72 | 1.07 | Numerical | 0.94 | 0.77 | 1.15 | 6.8% |
| 349 | MH-Fixed | RR | 0.89 | 0.7 | 1.15 | Numerical | 1.00 | 0.78 | 1.28 | 12.6% |
| 350 | MH-Fixed | RR | 0.86 | 0.38 | 1.96 | Numerical | 0.82 | 0.51 | 1.33 | -4.8% |
| 354 | MH-RE | OR | 1.52 | 1.17 | 1.98 | Numerical | 1.50 | 1.18 | 1.92 | -1.1% |
| 355 | MH-RE | OR | 5.59 | 4.67 | 6.69 | Numerical | 5.59 | 4.67 | 6.69 | 0.0% |
| 356 | MH-RE | OR | 1.66 | 0.84 | 3.3 | Numerical | 1.72 | 0.86 | 3.42 | 3.5% |
| 358 | MH-RE | OR | 1.26 | 0.63 | 2.53 | Numerical | 1.26 | 0.63 | 2.53 | 0.2% |
| 359 | MH-RE | OR | 1.2 | 0.86 | 1.66 | Numerical | 1.20 | 0.86 | 1.66 | -0.2% |
| 360 | MH-RE | OR | 0.94 | 0.58 | 1.52 | Numerical | 0.94 | 0.58 | 1.52 | -0.2% |
| 362 | Peto | OR | 1.11 | 0.99 | 1.25 | Mismatching+Numerical | 1.11 | 0.99 | 1.25 | 0.0% |
| 374 | RE | RR | 0.66 | 0.3 | 1.45 | Numerical | 0.77 | 0.35 | 1.68 | 15.9% |
| 380 | RE | RR | 2.11 | 1.308 | 3.403 | Numerical | 2.48 | 1.41 | 4.36 | 17.3% |
| 381 | IV/RE | RR | 2.418 | 1.227 | 4.762 | Numerical | 2.87 | 1.12 | 7.31 | 18.5% |
| 382 | IV/RE | RR | 2.274 | 1.075 | 4.811 | Numerical | 2.10 | 0.99 | 4.45 | -7.5% |
| 388 | MH-Random | RR | 3.43 | 2.95 | 3.99 | Numerical | 3.35 | 2.82 | 3.98 | -2.3% |
| 402 | MH-Random | RR | 1.56 | 1.22 | 2 | Numerical | 1.56 | 1.22 | 2.00 | 0.1% |
| 403 | MH-Random | RR | 1.87 | 1.22 | 2.87 | Numerical | 1.87 | 1.22 | 2.87 | -0.1% |
|    | Method   | Type   | OR     | SE     | OR     | SE     | P   |
|----|----------|--------|--------|--------|--------|--------|-----|
| 406| MH-Random| RR     | 1.62   | 1.42   | 1.85   | Numerical | 1.59| 1.36| 1.85  |
| 408| MH-Random| RR     | 1.52   | 0.96   | 2.4    | Misidentification | 1.54| 0.98| 2.43  |
| 410| MH-Random| RR     | 1.77   | 1.26   | 2.49   | Numerical | 1.77| 1.26| 2.48  |
| 412| MH-Random| RR     | 1.31   | 0.6    | 2.84   | Misidentification | 1.31| 0.61| 2.84  |
| 414| Peto     | OR     | 0.97   | 0.64   | 1.44   | Numerical | 0.67| 0.44| 1.02  |
| 419| MH-Random| RR     | 1.68   | 1.12   | 2.52   | Numerical | 1.90| 1.27| 2.84  |
| 420| MH-Random| RR     | 3.36   | 2.48   | 4.56   | Numerical | 3.60| 2.36| 5.48  |
| 421| MH-Random| RR     | 3.33   | 2.17   | 5.13   | Numerical | 3.33| 2.17| 5.13  |
| 422| MH-Random| RR     | 2.79   | 1.63   | 4.75   | Numerical | 2.79| 1.63| 4.75  |
| 423| Peto     | OR     | 0.58   | 0.28   | 1.2    | Numerical | 0.44| 0.21| 0.96  |
| 424| Peto     | OR     | 0.96   | 0.75   | 1.22   | Numerical | 0.97| 0.76| 1.23  |
| 426| MH-Fixed | OR     | 1.35   | 0.95   | 1.94   | Numerical | 1.13| 0.90| 1.42  |
| 429| DL-FE    | OR     | 1.7    | 1.17   | 2.46   | Numerical | 2.28| 1.51| 3.43  |
| 430| DL-FE    | OR     | 2.13   | 1.46   | 3.1    | Numerical | 2.04| 1.38| 3.01  |
| 431| DL-FE    | OR     | 15.13  | 5.4    | 42.34  | Numerical | 12.70| 4.53| 35.56 |
| 432| DL-FE    | OR     | 1.54   | 1.15   | 2.05   | Numerical | 1.76| 1.33| 2.35  |
| 439| Peto-Fixed| OR    | 1.24   | 0.96   | 1.6    | Misidentification+Numerical | 1.21| 0.94| 1.55  |
| 436| Peto-Fixed| OR    | 1.14   | 0.95   | 1.35   | Numerical | 0.94| 0.83| 1.06  |
| 445| MH-Fixed | RR     | 1.46   | 1.27   | 1.69   | Numerical | 1.41| 1.20| 1.65  |
| 446| MH-Fixed | RR     | 1.55   | 1.2    | 2      | Numerical | 1.50| 1.15| 1.96  |
| 468| MH-Random| RR     | 1.33   | 1.06   | 1.67   | Numerical | 1.34| 1.07| 1.68  |
| 472| MH-Fixed | RR     | 2.74   | 2.38   | 3.15   | Misidentification | 2.74| 2.39| 3.15  |
| 473| MH-Fixed | RR     | 4.73   | 4.15   | 5.39   | Numerical | 4.77| 4.19| 5.44  |
| 488| MH-Random| RR     | 1.91   | 1.52   | 2.4    | Zero-assumption+Numerical | 1.91| 1.52| 2.40  |
|   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|
| 482 | MH-Fixed | RR | 0.88 | 80 | 0.96 | Numerical | 0.95 | 0.86 | 1.04 | 7.4% |
| 492 | MH-Random | RR | 4.46 | 1.46 | 13.57 | Misidentification | 4.42 | 1.45 | 13.49 | -0.8% |
| 493 | MH-Random | RR | 2.41 | 2.06 | 2.82 | Numerical | 2.41 | 2.06 | 2.82 | 0.2% |
| 496 | MH-Fixed | RR | 10.35 | 5.78 | 18.53 | Misidentification | 10.35 | 5.78 | 18.53 | 0.0% |
| 499 | MH-Random | RR | 1.94 | 1.6 | 2.36 | Zero-assumption+Numerical | 1.94 | 1.60 | 2.36 | 0.2% |
| 505 | MH-Random | RR | 4.45 | 1.15 | 17.19 | Numerical | 4.45 | 1.15 | 17.19 | -0.1% |
| 510 | MH-Fixed | RR | 0.97 | 0.62 | 1.52 | Zero-assumption+Numerical | 0.93 | 0.62 | 1.41 | -3.7% |
| 506 | MH-Fixed | RR | 2.83 | 2.43 | 3.29 | Numerical | 2.86 | 2.45 | 3.33 | 0.9% |
| 513 | MH-Random | RR | 0.78 | 0.2 | 3.13 | Zero-assumption+Numerical | 0.78 | 0.20 | 3.13 | 0.4% |
| 514 | MH-Random | RR | 0.69 | 0.58 | 0.81 | Zero-assumption+Numerical | 0.68 | 0.58 | 0.80 | -1.1% |
| 516 | MH-Random | RR | 0.47 | 0.32 | 0.7 | Misidentification+Numerical+Zero-assumption | 0.47 | 0.32 | 0.70 | 0.9% |
| 512 | MH-Random | RR | 0.27 | 0.16 | 0.46 | Numerical | 0.27 | 0.16 | 0.46 | -0.6% |
| 515 | MH-Random | RR | 0.9 | 0.76 | 1.06 | Numerical | 0.82 | 0.68 | 0.99 | -9.0% |
| 518 | MH-Random | RR | 0.6 | 0.46 | 0.79 | Zero-assumption | 0.70 | 0.49 | 1.00 | 16.0% |
| 519 | MH-Random | RR | 0.9 | 0.75 | 1.09 | Numerical | 0.90 | 0.75 | 1.09 | 0.1% |
| 521 | MH-Fixed | RR | 22.03 | 8.52 | 56.94 | Zero-assumption+Numerical | 18.66 | 7.59 | 45.88 | -15.3% |
| 522 | MH-Fixed | RR | 3.87 | 1.12 | 13.41 | Zero-assumption | 4.05 | 1.16 | 14.08 | 4.6% |
| 523 | MH-Fixed | OR | 0.97 | 0.87 | 1.07 | Numerical | 0.96 | 0.87 | 1.06 | -1.0% |
| 524 | MH-Fixed | OR | 1.03 | 0.81 | 1.31 | Numerical | 1.03 | 0.81 | 1.30 | -0.5% |
| 525 | MH-Random | OR | 1.21 | 1.05 | 1.4 | Zero-assumption+Numerical | 3.24 | 1.24 | 8.43 | 167.5% |
| 527 | MH-Random | OR | 1.41 | 1.05 | 1.9 | Zero-assumption+Numerical | 1.41 | 1.05 | 1.90 | 0.0% |
| 536 | MH-Fixed | RD | 0.11 | 0.09 | 0.13 | Numerical | 0.11 | 0.10 | 0.13 | 0.9% |
| 539 | MH-Fixed | OR | 1.35 | 1.06 | 1.72 | Numerical | 1.43 | 1.10 | 1.88 | 6.2% |
| 542 | MH-Fixed | OR | 0.93 | 0.7 | 1.23 | Numerical | 0.87 | 0.67 | 1.13 | -6.6% |
|   | Method                        | OR   | SE  | RR  | CORR | P   | Method                        | OR   | SE  | RR  | CORR | P   |
|---|-------------------------------|------|-----|-----|------|-----|-------------------------------|------|-----|-----|------|-----|
| 543| MH-Fixed                      | 0.96 | 0.81| 1.13| Numerical | 0.99 | 0.83 | 1.18 | 2.7% |
| 547| RE                            | 2.77 | 1.97| 3.91| Numerical | 2.50 | 1.58 | 3.94 | -9.9%|
| 548| RE                            | 2.55 | 1.11| 5.87| Numerical | 2.17 | 0.63 | 7.54 | -14.9%|
| 549| RE                            | 8.34 | 4.64| 15  | Numerical | 10.53| 5.86 | 18.93| 26.3%|
| 550| RE                            | NA   | NA  | NA  | NA (all double-zero) | NA |
| 551| RE                            | 2.31 | 1.35| 3.93| Numerical | 2.59 | 1.48 | 4.52 | 12.0%|
| 552| RE                            | 4.46 | 0.7 | 28.48| Numerical | 3.82 | 0.39 | 36.96| -14.4%|
| 563| restricted maximum likelihood-RE | 0.016| 0.001 | 0.031 | Numerical | 0.02 | 0.00 | 0.04 | 12.5%|
| 564| restricted maximum likelihood-RE | -0.003| -0.011 | 0.005 | Numerical | 0.00 | -0.01 | 0.01 | 0.0%|
| 567| MH- Random(0.5 correction)    | 0.87 | 0.41| 1.85| Numerical | 0.87 | 0.41 | 1.85 | 0.5% |
| 581| DL-RE(a proportional continuity correction method) | 1.11 | 0.9985 | 1.2339 | Misidentification | 1.11 | 1.01 | 1.22 | 0.1% |
|   | DL-RE(a proportional continuity correction method) | RR | 1.163 | 0.8028 | 1.6849 | Misidentification | 1.12 | 0.79 | 1.59 | -3.9% |
|---|-------------------------------------------------|----|-------|--------|--------|-------------------|------|-----|------|------|
| 584 | MH | RD | 0.0028 | -0.0065 | 0.0121 | Zero-assumption | 0.01 | -0.01 | 0.03 | 292.9% |
| 596 | RE | RR | 0.17 | 0.13 | 0.22 | Misidentification+Numerical+Zero-assumption | 0.09 | 0.04 | 0.17 | -50.0% |
| 591 | RE | RR | 0.9 | 0.86 | 0.94 | Numerical | 0.94 | 0.91 | 0.97 | 4.2% |
| 601 | MH-Fixed | OR | 0.86 | 0.79 | 0.94 | Zero-assumption | 0.86 | 0.79 | 0.94 | 0.1% |
| 602 | MH-Fixed | OR | 0.94 | 0.86 | 1.03 | Zero-assumption | 0.94 | 0.86 | 1.03 | 0.2% |
| 603 | MH-Fixed | OR | 0.9 | 0.82 | 0.98 | Zero-assumption | 0.90 | 0.82 | 0.98 | -0.4% |
| 604 | MH-Fixed | OR | 0.98 | 0.9 | 1.06 | Zero-assumption | 0.98 | 0.90 | 1.06 | -0.3% |
| 606 | MH-Fixed | OR | 0.89 | 0.77 | 1.04 | Zero-assumption | 0.90 | 0.77 | 1.04 | 0.6% |
| 607 | MH-Fixed | OR | 1.07 | 0.88 | 1.3 | Zero-assumption | 1.07 | 0.88 | 1.30 | 0.3% |
| 608 | MH-Fixed | OR | 0.95 | 0.83 | 1.08 | Zero-assumption | 0.95 | 0.83 | 1.08 | 0.0% |
| 609 | MH-Fixed | OR | 1.06 | 0.86 | 1.3 | Zero-assumption | 1.06 | 0.86 | 1.30 | -0.1% |
| 610 | MH-Fixed | OR | 1 | 0.85 | 1.18 | Zero-assumption | 1.00 | 0.85 | 1.18 | -0.1% |
| 612 | DL-RE | RR | 1.163 | 0.887 | 1.524 | Misidentification | 1.14 | 0.89 | 1.47 | -1.9% |
| 614 | DL-RE | RR | 0.613 | 0.177 | 2.128 | Zero-assumption | 0.61 | 0.18 | 2.13 | 0.0% |
| 615 | DL-RE | RR | 1.026 | 0.984 | 1.071 | Numerical | 1.01 | 0.97 | 1.05 | -1.6% |
| 623 | RE? | OR | 0.84 | 0.62 | 1.15 | Numerical | 0.89 | 0.63 | 1.26 | 5.8% |
| 626 | MH-RE | RR | 0.65 | 0.43 | 0.98 | Numerical | 0.85 | 0.44 | 1.67 | 31.3% |
| 633 | MH-Fixed | RR | 1.232 | 0.914 | 1.661 | Numerical | 1.18 | 0.88 | 1.59 | -4.0% |
| 636 | DL-RE | OR | 0.64 | 0.21 | 1.97 | Zero-assumption | 0.59 | 0.17 | 2.01 | -8.0% |
|   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|
| 637 | DL-RE | OR | 0.72 | 0.22 | 2.41 | Zero-assumption | 0.67 | 0.18 | 2.55 | -7.2% |
| 638 | MH-RE | OR | 1.66 | 0.97 | 2.84 | Mismatching+Numerical | 1.66 | 0.97 | 2.84 | 0.2% |
| 640 | MH-Fixed | OR | 2.31 | 1.42 | 3.75 | Numerical | 1.89 | 1.20 | 2.98 | -18.2% |
| 642 | MH-Fixed | OR | 0.94 | 0.5 | 1.77 | Mismatching | 0.97 | 0.62 | 1.50 | 2.7% |
| 643 | MH-Fixed | OR | 1.35 | 0.75 | 2.44 | Numerical | 1.65 | 1.04 | 2.63 | 22.4% |
| 645 | MH-Fixed | OR | 1.57 | 0.82 | 3.03 | Numerical | 1.40 | 1.02 | 1.92 | -10.9% |
| 646 | MH-Fixed | OR | 1.16 | 0.83 | 1.62 | Numerical | 1.18 | 0.85 | 1.64 | 1.6% |
| 648 | MH-Fixed | OR | 1.1 | 0.8 | 1.5 | Numerical | 1.15 | 0.83 | 1.57 | 4.1% |
| 661 | MH-RE | RR | 0.672 | 0.064 | 1.268 | Numerical | 0.67 | 0.36 | 1.27 | 0.0% |
| 662 | MH-RE | RR | 0.243 | 0.356 | 0.922 | Numerical | 0.24 | 0.06 | 0.92 | 0.3% |
| 664 | Peto | OR | 0.28 | 0.202 | 0.439 | Numerical | 0.28 | 0.19 | 0.41 | -1.1% |
| 666 | Exact Fixed | RD | 0.001 | -0.005 | 0.007 | Numerical+Zero-assumption | 0.00 | 0.00 | 0.01 | -7.8% |
| 680 | DL-RE | RR | 0.53 | 0.39 | 0.7 | Numerical | 0.57 | 0.44 | 0.72 | 6.6% |
| 683 | MH-Fixed | OR | 1.24 | 0.85 | 1.79 | Numerical | 1.17 | 0.80 | 1.71 | -6.0% |
| 684 | MH-Fixed | RR | 1.07 | 0.89 | 1.29 | Numerical+Zero-assumption | 1.05 | 0.84 | 1.31 | -2.3% |
| 685 | MH-Fixed | RR | 1.63 | 0.39 | 6.77 | Zero-assumption | 1.63 | 0.39 | 6.77 | -0.2% |
| 686 | MH-Fixed | RR | 0.33 | 0.03 | 3.18 | Zero-assumption | 0.33 | 0.03 | 3.18 | 0.3% |
| 689 | IV-Fixed | RR | 0.64 | 0.18 | 2.24 | Zero-assumption | 0.64 | 0.18 | 2.24 | 0.0% |
| 690 | IV-Fixed | RR | 0.84 | 0.27 | 2.57 | Zero-assumption | 0.84 | 0.27 | 2.57 | 0.0% |
| 691 | IV-Fixed | RR | 1.02 | 0.15 | 6.74 | Zero-assumption | 1.02 | 0.15 | 6.74 | 0.0% |
| 692 | IV-Fixed | RR | 1.61 | 0.63 | 4.12 | Zero-assumption | 1.61 | 0.63 | 4.12 | 0.0% |
| 694 | MH-RE | RR | 0.68 | 0.48 | 0.98 | Mismatching | 0.68 | 0.48 | 0.98 | 0.7% |
| 695 | Peto | OR | 0.93 | 0.69 | 1.26 | Numerical | 0.93 | 0.69 | 1.27 | 0.3% |
| 696 | Peto | OR | 0.96 | 0.75 | 1.22 | Zero-assumption | 0.96 | 0.75 | 1.22 | 0.0% |
| 699 | MH-Fixed | OR | 1.02 | 0.89 | 1.17 | Numerical | 1.02 | 0.89 | 1.17 | 0.0% |
|    | MH-Fixed | OR  |   0.75 |  0.59 |  0.97 | Numerical |  0.77 |  0.60 |  0.99 |   2.5% |
|----|----------|-----|--------|--------|--------|-----------|--------|--------|--------|--------|
| 701| MH-Fixed | OR  |  0.63  |  0.47  |  0.84  | Numerical |  0.63  |  0.47  |  0.85  |   0.2% |
| 703| MH-RE    | RR  |  1.08  |  1.01  |  1.16  | Numerical |  1.08  |  1.01  |  1.16  |   0.2% |
| 705| MH-RE    | RR  |  1.12  |  0.98  |  1.28  | Numerical |  1.12  |  0.98  |  1.28  |  -0.1% |
| 706| MH-RE    | RR  |  1.11  |  1.02  |  1.2   | Numerical |  1.10  |  1.02  |  1.19  |  -0.6% |
| 707| MH-RE    | RR  |  1.09  |  1.02  |  1.17  | Numerical |  1.10  |  1.02  |  1.18  |   0.6% |
| 715| MH-RE    | RR  |  1.05  |  0.96  |  1.14  | Numerical |  1.05  |  0.96  |  1.14  |  -0.3% |
| 716| MH-RE    | RR  |  1.02  |  0.96  |  1.08  | Numerical |  1.02  |  0.96  |  1.08  |  -0.2% |
| 723| MH-RE    | RD  |  0.01  | -0.03  |  0.04  | Numerical |  0.01  | -0.03  |  0.04  | -26.3% |
| 724| MH-RE    | RD  |  0.04  |  0.01  |  0.08  | Numerical |  0.04  |  0.01  |  0.08  |   7.9% |
| 725| MH-RE    | RD  | -0.05  | -0.08  | -0.02  | Numerical | -0.05  | -0.08  | -0.02  |   0.7% |
| 726| MH-RE    | RD  |  0.03  | -0.01  |  0.08  | Numerical |  0.03  | -0.01  |  0.08  |  11.2% |
| 727| MH-RE    | RD  | -0.04  | -0.09  |  0.02  | Numerical | -0.04  | -0.09  |  0.02  | -12.4% |
| 728| MH-RE    | OR  |  0.35  |  0.19  |  0.65  | Numerical |  0.35  |  0.19  |  0.65  |  -1.1% |
| 731| MH-RE    | OR  |  1.18  |  0.06  | 23.92  | Numerical |  1.18  |  0.06  | 23.92  | -0.3%  |
| 733| MH-RE    | OR  |  0.61  |  0.22  |  1.67  | Numerical |  0.61  |  0.22  |  1.67  |  -0.2% |
| 740| MH-RE    | OR  |  0.57  |  0.36  |  0.88  | Numerical |  0.55  |  0.32  |  0.94  |  -4.0% |
| 748| MH-RE    | OR  |  0.32  |  0.13  |  0.75  | Numerical |  0.32  |  0.13  |  0.75  | -1.4%  |
| 751| MH-Fixed | RR  |  1.21  |  0.7   |  2.1   | Numerical |  1.20  |  0.71  |  2.01  | -1.1%  |
| 759| MH-Fixed | RR  |  2.51  |  1.21  |  5.22  | Numerical |  3.19  |  1.34  |  7.59  |  27.2% |
| 762| DL-RE    | RR  |  0.92  |  0.78  |  1.08  | Numerical |  1.11  |  0.93  |  1.32  |  20.4% |
| 768| DL-RE    | RR  |  1.2   |  0.72  |  1.99  | Numerical |  1.41  |  0.96  |  2.07  |  17.7% |
| 773| DL-RE    | RR  |  1.88  |  1.05  |  3.37  | Numerical |  1.78  |  1.18  |  2.69  | -5.2%  |
| 775| MH-Fixed | RR  |  0.81  |  0.62  |  1.04  | Numerical |  0.76  |  0.59  |  0.98  | -6.0%  |
| 779| MH-Fixed | RR  |  1.22  |  0.96  |  1.54  | Numerical |  1.21  |  0.95  |  1.54  | -0.8%  |
| MH     | RR     | RR     | RR     | RR     | RR     | 7.0% |
|--------|--------|--------|--------|--------|--------|------|
| MH-Fixed | RR     | 0.76   | 0.64   | 0.9    | Numerical | 0.81 | 0.69 | 0.96 |
| MH-RE  | RR     | 1.54   | 1.09   | 2.18   | Numerical | 1.54 | 1.09 | 2.18 |
| MH-RE  | RR     | 1.64   | 1.06   | 2.53   | Numerical | 1.64 | 1.06 | 2.53 |
| MH-RE  | RR     | 1.33   | 0.82   | 2.15   | Numerical | 1.33 | 0.82 | 2.15 |
| MH-RE  | RR     | 1.05   | 0.88   | 1.24   | Numerical | 1.05 | 0.88 | 1.24 |
| MH-Fixed | RR     | 1.59   | 0.63   | 4.02   | Numerical | 1.17 | 0.42 | 3.25 |
| MH-Fixed | RR     | 1.91   | 1.33   | 2.75   | Numerical | 1.74 | 1.35 | 2.23 |
| MH-Fixed | RR     | 1.02   | 0.9    | 1.06   | Numerical | 0.98 | 0.88 | 1.10 |
| MH-Fixed | RR     | 1.07   | 0.84   | 1.37   | Numerical | 1.11 | 0.92 | 1.33 |
| MH-Fixed | RR     | 1.35   | 1.17   | 1.56   | Numerical | 1.32 | 1.17 | 1.49 |
| MH-Fixed | RD     | 0.003  | -0.03  | 0.03   | Numerical | 0.01 | -0.03 | 0.04 |
| MH-Fixed | RD     | -0.01  | -0.04  | 0.03   | Numerical | 0.00 | -0.03 | 0.02 |
| MH-Fixed | RD     | 0.06   | 0.02   | 0.1    | Numerical | 0.05 | 0.03 | 0.08 |
| MH-Random | RD     | -0.01  | -0.04  | 0.02   | Numerical | -0.02 | -0.05 | 0.02 |
| MH-Fixed? | OR     | 0.71   | 0.52   | 0.98   | Mismatching+Numerical | 0.71 | 0.52 | 0.98 |
| MH-Fixed  | OR     | 1.08   | 0.7    | 1.66   | Numerical+Zero-assumption | 1.43 | 0.84 | 2.44 |
Supplementary Figure 1. The flowchart for empirically defining the data extraction errors into different types.

1. Literature search and screen to identify eligible systematic reviews for current replication study
2. Metadata collection from eligible meta-analyses of eligible systematic reviews
3. Replication for the metadata from original sources (e.g., publication of the RCTs, supplementary file, ClinicalTrials.gov)
4. Recording and collecting error information, including the “location” of the error and the potential reasons (e.g., calculation errors)
5. Summarizing the reasons of the errors as well as characteristics of these errors (e.g., whether the true numerical value could be obtained)
6. Grouping studies with data extraction errors by reasons and characteristics, then discussed by five authors (CX, YTQ, LFK, LF, SV)
7. Define the type of errors within each group based on the consensus of the same five authors
Supplementary Figure 2. Word cloud analysis of safety outcomes by the type of intervention.
Supplementary Figure 3. Subgroup analysis based on the type of intervention.

**Type of errors**

| Type            | Non-pharmacological interventions | Pharmacological interventions | P value |
|-----------------|-----------------------------------|-------------------------------|---------|
| Zero-assumption | 0.91% (25/2761)                  | 2.57% (196/7625)             | P < 0.001 |
| Numerical       | 5.36% (148/2761)                 | 9.43% (719/7625)             | P < 0.001 |
| Mismatching     | 0.18% (5/2761)                   | 0.37% (28/7625)              | P = 0.0905 |
| Misidentification| 0.07% (2/2761)                   | 1.48% (113/7625)             | P < 0.001 |
| Ambiguous       | 2.35% (65/2761)                  | 6.05% (461/7625)             | P < 0.001 |

**Total errors**

| Type                        | P value |
|-----------------------------|---------|
| Non-pharmacological interventions | P < 0.001 |
| Pharmacological interventions | 19.90% (1517/7625) |