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| **Reference** | **Main Outcome Measures and Results** |
| **1a. Compares number of studies reporting AEs information in matched published and unpublished articles** |
| Hughes 2014 | **Number of studies that report number of SAEs**85/142 (60%) published trials vs 125/142 (88%) associated registry reports vs (95/102 (93%) unrelated registry reports) |
| Kohler 2015 | **Rates of complete information in HTA reports of which 42 publications from 21 matched studies available****Any AEs**Total study population: Publications 6/15 (40%) vs 14/15 (93%) AMNOGSubpopulation of approved indication: Publications 0/13 (0%) vs 11/13 (85%) AMNOG**Any SAEs** Total study population: Publications 5/15 (33%) vs 14/15 (93%) AMNOGSubpopulation of approved indication: Publications 0/13 (0%) vs 10/13 (77%) AMNOG**Any Withdrawals due to AEs**Total study population: Publications 7/15 (47%) vs 14/15 (93%) AMNOGSubpopulation of approved indication: Publications 0/13 (0%) vs 10/15 (77%) AMNOG |
| Mattila 2011 | Safety information missing in 8/15 (53%) publications compared to unpublished trials from EPARs, with one publication lacking any safety data. |
| Maund 2014 | **Reporting in full for 9 trials****Death reported in full**Published trials 3/9 (33%) vs CSRs 9/9 (100%) vs registry reports 6/9 (67%)**SAEs reported in full (number of patients)**Published trials 3/9 (33%) vs CSRs 9/9 (100%) vs registry reports 3/9 (33%)**SAEs reported in full (number of events)**Published trials 3/9 (33%) vs CSRs 9/9 (100%) vs registry reports 3/9 (33%)**Withdrawals due to AEs reported in full (number of patients)**Published trials 7/9 (78%) vs CSRs 9/9 (100%) vs registry reports 7/9 (78%)**Withdrawals due to AEs reported in full (number of events)**Published trials 1/9 (11%) vs CSRs 9/9 (100%) vs registry reports 1/9 (11%)**Treatment emergent AEs reported in full (number of patients)**Published trials 0/9 (0%) vs CSRs 9/9 vs registry reports 9/9 (100%)**Treatment emergent AEs (number of events)**Published trials 0/9 (0%) vs CSRs 9/9 (100%) vs registry reports 0/9 (0%)**Discontinuation emergent AEs reported in full (number of patients)**Published trials 0/9 (0%) vs CSRs 9/9 (100%) vs registry reports 0/9 (0%)**Discontinuation emergent AEs reported in full (number of events)**Published trials 0/9 (0%) vs CSRs 9/9 (100%) vs registry reports 0/9 (0%)**Suicide reported in full**Published trials 2/2 (100%) vs CSRs 2/2 (100%) vs registry reports 2/2 (100%)**Attempted suicide reported in full (number of patients)**Published trial 0/1 (0%) vs CSR 1/1 (100%) vs registry report 0/1 (0%)**Attempted suicide reported in full (number of events)**Published trial 0/1 (0%) vs CSR 1/1 (100%) vs registry report 0/1 (0%) |
| Pranić 2015 | **Number of trials reporting SAEs (“81 trials with 21 corresponding publications”)**Published trials 7/21 (33%) vs unpublished trials from trial registry 38/81 (47%)**Number of trials reporting other AEs**Published trials 15/21 (71%) vs unpublished trials from trial registry 55/81 (68%) |
| Riveros 2013 | **Number of trials reporting total number of AEs** Published trials 128/202 (63%) vs registry reports 194/202 (96%)**Number of trials reporting details of all AEs per arm**Published trials 128/202 (63%) vs registry reports 194/202 (96%)**Number of trials reporting number of withdrawals due to AEs**Published trials 153/202 (76%) vs registry reports 161/202 (80%)**Number of trials reporting total number of SAEs**Publications 144/202 (71%) vs registry reports 200/202 (99%)**Number of trials reporting details of all SAEs per arm**Publications 127/202 (63%) vs registry reports 199/202 (99%)**Number of trials with complete reporting of AEs**Publications 91/202 (45%) vs registry reports 147/202 (73%)**AEs**More information in ClinicalTrials.gov than published article 80/202Similar information in ClinicalTrials.gov and published article 98/202More information in publication than ClinicalTrials.gov 24/202**SAEs**More information in ClinicalTrials.gov than published article 73/202Similar information in ClinicalTrials.gov and published article 128/202More information in publication than ClinicalTrials.gov 1/202 |
| Tang 2015 | **Number of trials reporting SAEs per treatment group**Publications 139/202 (69%) vs registry reports 202/202 (100%) |
| Wieseler 2012/2013 | **Information provided in registry reports vs journal publications (matched sample of 47 studies)****AEs (number of patients)**More information in registry report than publication 23/47 (49%)Similar information in registry report and publication 16/47 (34%)Less information in registry report than publication 8/47 (17%)**SAEs (number of patients)**More information in registry report than publication 18/47 (38%)Similar information in registry report and publication 22/47 (47%)Less information in registry report than publication 7/47 (15%)**Withdrawals due to AEs**More information in registry report than publication 5/47 (10%)Similar information in registry report and publication 32/47 (68%)Less information in registry report than publication 10/47 (21%)**Information provided in registry reports vs CSRs (matched sample of 50 studies)****AEs (number of patients)**More information in registry report than CSR 0/50 (0%)Similar information in registry report and CSR 41/50 (82%)Less information in registry report than CSR 9/50 (18%)**SAEs (number of patients)**More information in registry report than CSR 1/50 (2%)Similar information in registry report and CSR 38/50 (76%)Less information in registry report than CSR 11/50 (22%)**Withdrawals due to AEs**More information in registry report than CSR 0/50 (0%)Similar information in registry report and CSR 43/50 (86%)Less information in registry report than CSR 7/50 (14%)**Completeness of information in CSRs vs journal publications (matched sample of CSRs and journal publication N = 65)**Full information on patients with AEs: CSR: 61/65 (94 %) vs publication: 21/65 (32%)Full information on patients with SAEs: CSR: 60/65 (92%) vs publication: 24/65 (37%)Full information on patients withdrawn due to AEs: CSR 61/65 (94%) vs publication 51/65 (78%)Full information on patients with specific AEs: CSR 183/209 (88%) vs publication 66/209 (32%)**Completeness of information in CSRs vs registry reports (matched sample of CSRs and registry reports N = 50)**Full information on patients with AEs: CSRs: 50/50 (100 %) vs registry reports: 41/50 (82%)Full information on patients with SAEs: CSR: 43/50 (86%) vs registry reports 37/50 (74%)Full information on patients withdrawn due to AEs: CSR 49/50 (98%) vs registry reports 42/50 (84%)Full information on patients with specific AEs: CSR 129/155 (83%) vs registry reports 34/155 (22%) |
| **1b. Compares number of studies reporting AEs information in unmatched published and unpublished articles** |
| Hemminki 1980 | **% of controlled trials giving information on adverse effects;** Published vs unpublished applications for licensing*Finland*:Psychotrophic drugs 56% vs 77% Non Psychotrophics 43% vs 83%*Sweden*:Psychotrophic drugs 73% vs 83%  |
| Wieseler 2012/2013 | **Studies with complete information (identified from 16 HTAs)****AEs**65/192 (34%) publications vs 93/101 (92%) CSR vs 57/78 (73%) registry reports**SAEs**67/192 (35%) publications vs 89/101 (88%) CSR vs 57/78 (73%) registry reports**Withdrawals due to AEs**144/192 (75%) publications vs 92/101 (91%) CSR vs 57/78 (73%) registry reports**Outcomes with complete information (only trials with full CSR available from 16 HTAs)****AEs**21/101 (21%) in 65 publications vs 93/101 (92%) in 101 CSRs vs 41/101 (41%) in 50 registry reports**SAEs**24/101 (24%) in 65 publications vs 89/101 (88%) in 101 CSRs vs37/101 (37%) in 50 registry reports**Withdrawals due to AEs**51/101 (50%) in 65 publications vs 92/101 (91%) in 101 CSRs vs 42/101 (42%) in 50 registry reports**Special AEs**66/321 (21%) in 65 publications vs 271/321 (84%) in 101 CSRs vs34/321 (11%) in 50 registry reports |
| **2a. Compares numbers of AEs reported in matched published and unpublished studies** |
| Carragee 2011 | **Number of early infections (number of rhBMP-2 patients, n=277)**3 published trials 0 vs 1 FDA data summary 26**Number of delayed infection (n=277)**3 published trials 0 vs 1 FDA data summary 12**Number of implant malposition, displacement and loosening (n=277)**3 published trials 9 vs 1 FDA data summary 10**Number of subsidence (n=277)**3 published trials 7 vs 1 FDA data summary 7**Number of reoperation for device-related AE (n=277)**3 published trials 7 vs 1 FDA data summary 22**Number of retrograde ejaculation (n=277)**3 published trials 0 vs 1 FDA data summary 12**Number of other urogenital AE (n=277)**3 published trials 0 vs 1 FDA data summary 36 |
| Hartung 2014 | **Number of SAEs**38 published trials 4784 vs 38 registry reports 9366 |
| Hodkinson 2016 | **Number of AEs**5 published trials 42 vs 5 CSRs 118**Number of SAEs**5 published trials 15 vs 5 CSRs 375 |
| Hughes 2014 | **Number of SAEs in drug-treated participants**142 published trials 914 vs 142 registry reports 1,608 **Number of SAEs per patient treated**142 published trials 0.03 vs 142 registry reports 0.05 **Number of deaths in drug-treated participants**142 published trials 57 vs 142 registry reports 151 **Number of completed suicides in drug-treated participants**142 published trials 7 vs 142 registry reports 15 **Number of suicidal ideations, attempts or injury in drug-treated participants**142 published trials 47 vs 142 registry reports 87 **Number of homicidal ideations in drug-treated participants**142 published trials 1 vs 142 registry reports 1 **Number of new or worsened psychiatric symptoms in drug-treated participants**142 published trials 115 vs 142 registry reports 238  |
| Jefferson 2011 | **Number of SAEs**2 published trials 0 vs 2 CSRs 10 (9 subjects) |
| Le Noury 2015 | **Paroxetine****Number of all AEs**1 published trial 265 vs 1 CSR 338 (vs RIAT 481)**Number of cardiovascular AEs**1 published trial 5 vs 1 CSR 7 (vs RIAT 44)**Number of gastrointestinal/digestive AEs**1 published trial 84 vs 1 CSR 80 (vs RIAT 112)**Number of respiratory AEs** 1 published trial 33 vs 1 CSR 39 (vs RIAT 42)**Number of neurological/nervous system**1 published trial 115 vs 1 CSR 106 (vs RIAT 101)**Number of other AEs**1 published trial 28 vs 1 CSR 121 (vs RIAT 79)**Number of suicidal and self injurious behaviours**1 published trial 5 vs 1 CSR 7 (vs RIAT 11)**Imipramine****Number of all AEs**1 published trial 340 vs 1 CSR 493 (vs RIAT 552)**Number of cardiovascular AEs**1 published trial 42 vs 1 CSR 60 (vs RIAT 130)**Number of gastrointestinal/digestive**1 published trial 106 vs 1 CSR 108 (vs RIAT 147)**Number of respiratory AEs** 1 published trial 27 vs 1 CSR 32 (vs RIAT 22)**Number of neurological/nervous system**1 published trial 135 vs 1 CSR 117 vs (RIAT 114)**Number of other AEs**1 published trial 30 vs 1 CSR 51 vs RIAT 76**Number of suicidal and self injurious behaviours**1 published trial 3 vs 1 CSR 3 (vs RIAT 4) |
| Maund 2014 | **Number of treatment emergent AEs**9 published trials 1558 vs 9 CSRs 6087 vs 9 registry reports 4629 |
| Pranić 2015 | **Number of SAEs (21 publications)**Higher number and /or frequency in publication 0 (0%)Higher number and /or frequency in registry reports 1 (5%)**Number of other AEs (21 publications)**Higher number and /or frequency in publication 11 (52%)Higher number and /or frequency in registry reports 2 (10%) |
| Rodgers 2013 | **Number of AEs** Publications 533 vs data from manufacturer 2302 |
| Scharf 2006 | **Number of AEs**AEs =>grade 322 publications 413 vs Clinical Data Update System (CDUS) 423**Number of AEs grade 1 to 5 (all AEs)**22 publications 1910 vs Clinical Data Update System (CDUS) 2995 |
| Tang 2015  | **Number of SAEs**Number of SAEs greater in registry reports than published article 31Matching number of SAEs in published and registry reports 95Number of SAEs greater in published than registry reports 13 |
| **2b. Compares different types of AEs in matched published and unpublished trials** |
| Pang 2011 | **Description of specific types of ‘Fatal’ AEs**198 specific fatal events described in GSK trial register; 29 (14.6%) were reported in published version**Description of specific types of SAEs**1147 specific types of serious events described in GSK trial register, 76 (6.7%) were reported in published version **Description of specific types of ‘most frequent’ adverse events** 281 types of frequent events described in GSK trial register, 91(32.4%) were reported in published version**Total number of types of AEs reported**1626 types of adverse events described in GSK trial register, 196 (12.1%) were reported in published version |
| Kohler 2015 | **Description of specific AE** (54 different types in CSR for total study population, and 52 different types for subpopulation)Total study population: 18 (33%) types of AE described in publications vs 49 (91%) types of AE in AMNOG**Subpopulation with approved indication:** 0 (0%) types of AE described in publications vs 29 (56%) types of AE in AMNOG  |
| **2c. Compares numbers of AEs reported in unmatched published and unpublished studies** |
| Hughes 2014 | **Number of SAEs in drug-treated participants**142 published trials 914 vs 102 registry reports 1423**Number of SAEs per patient treated**142 published trials 0.03 vs 102 registry reports 0.07**Number of deaths in drug-treated participants**142 published trials 57 vs 102 registry reports 45**Number of completed suicides in drug-treated participants**142 published trials 7 5 vs 102 registry reports 5**Number of suicidal ideations, attempts or injury in drug-treated participants**142 published trials 47 vs 102 registry reports 79**Number of homicidal ideations in drug-treated participants**142 published trials 1 vs 102 registry reports 5**Number of new or worsened psychiatric symptoms in drug-treated participants**142 published trials 115 vs 102 registry reports 357 |
| **3. Compares pooled effect estimates in published and unpublished studies** |
| Connolly 2013 | **Subdural hematoma**4 published trials (N=6565) OR 2.2 (0.6-7.8) vs 5 unpublished trials (from contacting investigators) (N=90689) OR 1.3 (0.5-3.5) vs 9 published and unpublished trials (N=97254) OR 1.6 (0.8-3.5) |
| Eyding 2010 | **Reboxetine vs placebo****AEs**2 published trials (N=310) OR 2.67 (0.52-13.79) vs 6 unpublished trials (from manufacturer) (N=1938) OR 2.15 (1.66-2.80) vs 8 published and unpublished trials (N=2248) OR 2.14 (1.59-2.88)**Withdrawals due to AEs**2 published trials (N=310) OR 0.95 (0.45-1.99) vs 6 unpublished trials (from manufacturer) (N=1938) OR 2.61 (1.79-3.80) vs 7 published and unpublished (N=2248)2.21 (95% CI 1.45–3.37)**Reboxetine vs SSRIs****AES**2 published trials (N=421) OR 1.07 (0.72-1.61) vs 5 unpublished trials (from manufacturer) (N=1752) OR 1.08 (0.74-1.58) vs 7 published and unpublished trials (N=2173) OR 1.06 (0.82-1.36)**Withdrawals due to AEs**2 published trials (N=421) OR 1.58 (0.81-3.08) vs 2 unpublished trials (from manufacturer) (N=385) OR 1.72 (0.46-6.42) vs 4 published and unpublished (N=806) 1.79 (95% CI 1.06–3.05) |
| Hart 2012 | **Any AEs**Published trials RR 0.85 (0.71-1.03) vs unpublished trials (from FDA) RR 0.96 (0.84-1.1) vs 4 published and unpublished trials (N=827) RR 0.92 (0.82-1.02) |
| Hemminki and McPherson 2000 | **Cardiovascular events**22 published trials OR 1.39 (0.48-3.95) vs 28 unpublished and published trials OR 1.78 (0.70-4.52)**Cardiovascular and thrombotic events**22 published trials OR 1.64 (0.65-4.21) vs 28 unpublished and published trials OR 1.97 (0.84-4.58) |
| MacLean et al 2003 | **Dyspepsia**15 published trials (N=1455), RR 1.21; (0.81 – 1.81) vs 11 unpublished trials (from FDA) (N=2368), RR 1.07; (0.70-1.63) vs 26 published and unpublished trials (N=3823) RR 1.14 (0.85-1.53) |
| Moja 2014 | **SAE\***6 published trials 1.21 (1.06-1.37) vs 3 unpublished trials 0.94 (0.58 – 1.50) vs 9 published and unpublished trials (from authors and internet) (N=3665) 1.08 (0.90-1.31)**Death\***6 published trials 1.12 (0.78-1.62) vs 2 unpublished trials 0.85 (0.22 – 3.38) vs 8 published and unpublished trials (from authors and internet) (N=3338) 1.10 (0.78-1.57)  |
| Potthast 2014 | **AE (Schwarz 2009)**1 published trial (N=249) RR 1.11 (0.98-1.26) vs 1 unpublished trial (from registries) OR 1.6 (0.8-3.5) vs 2 published and unpublished trials RR 1.08 (1.00-1.16)**Withdrawals due to AE (Cipriani 2009)**1 published trial (N=361) RR 21.22 (1.29-349.99) vs unpublished data (from registries) RR 1.55 (0.82-2.92) vs published and unpublished data RR 1.76 (0.95-3.28)There were also three systematic reviews where unpublished additional trial data were available; inclusion of unpublished data did not change significance of results in these instances; but the unpublished data led to additional trials/data for a new comparison not reported in the systematic reviews (Nakagawa 2009 and Cipriani 2009\_sertraline) or to additional safety data for a comparison already reported in the systematic review (Ara 2008) |
| Ross 1997 | **Major adverse events in trials**2 published trials (N=414) OR 0.92 (0.49-1.72) vs 8 unpublished trials (from manufacturer) (N=1988) OR 1.04 (0.64-1.71) vs 10 published and unpublished trials (N=2402) OR 0.99 (0.67-1.46)**Angina**2 published trials (from manufacturer) (N=414) OR 0.92 (0.49-1.72) vs 8 unpublished (N=1105) OR 0.99 (0.50-1.97) vs 10 published and unpublished trials (N=1519) OR 1.08 (0.42-2.73) |
| Singh-Franco 2012 | **Any AEs**5 published trials (N=2784) RR 1.00 (0.91-1.10) vs 4 unpublished trials (from registries) (N=1106) RR 0.84 (0.39-1.81)**Withdrawals**5 published trials (N=2784) RR 0.89 (0.50-1.59) vs 4 unpublished trials (from registries) (N=1106) RR 0.58 (0.29-1.18)**SAEs**5 published trials (N=2784) RR 0.96 (0.60-1.53) vs 3 unpublished trials (from registries) (N=984) RR 2.85 (0.86-9.43)**Medication-related AEs**4 published trials (N=2647) RR 1.24 (0.66-2.32) vs 2 unpublished trials (from registries) (N=336) RR 0.70 (0.39-1.28)**Hyperglycaemia**3 published trials (N=2258) RR 0.44 (0.30-0.64) vs 4 unpublished trials (from registries) (N=1106) RR 0.39 (0.19-0.78) vs 7 published and unpublished (N=3364) 0.42 (95% CI 0.31–0.58)**Musculoskeletal**4 published trials (N=2395) RR 1.32 (0.98-1.78) vs 2 unpublished trials (from registries) (N=739) RR 2.33 (0.69-7.84) vs 6 published and unpublished (N=3134) RR 1.38 (95% CI 1.03–1.84)**Gastrointestinal**3 published trials (N=2281) RR 0.76 (0.58-1.00) vs 3 unpublished trials (from registries) (N=861) RR 2.02 (1.15-3.54)**Central nervous system**3 published trials (N=2258) RR 0.90 (0.63-1.28) vs None provided**Respiratory** 4 published trials (N=2395) RR 0.87 (0.71-1.08) vs 3 unpublished trials (from registries) (N=861) RR 2.22 (0.61-8.03)**Renal** 2 published trials (N=1755) RR 0.67 (0.40-1.11) vs 2 unpublished trials (from registries) (N=739) RR 0.75 (0.33-1.66)**Vascular**4 published trials (N=2647) RR 1.72 (0.98-3.05) vs 1 unpublished trial (from registries) (N=500) RR 0.59 (0.20-1.74) |
| Wallace 2006 | **SAEs for SSRIs**7 published trials (N=1303); Treated 56/657 vs Placebo 28/646, RR 2.0 (1.3-3.0) vs 11 published and unpublished trials (N=2145) RR 1.97 (1.42-2.75) |
| Whittington 2004  | **SAEs**1 published trial (N=180); Treated 11/93 - Placebo 2/87, RR 5.15 (1.17-22.56), vs 1 unpublished trial (from UK regulatory agency) (N=275); Treated; 22/182 - Placebo 6/93 RR 1.87 (0.79-4.46) vs 2 published and unpublished trials RR 2.55 (1.23-5.3)**Suicide attempt or ideation**1 published trial (N=180); Treated 5/93 - Placebo 0/87, RR 10.30 (0.58 – 183.53) vs published and unpublished from UK regulatory agency(N=663), RR 1.51 (0.62 -3.69) |

\*calculated values using the same meta-analytic approach as described by the authors