Reference	Type of study	Intervention comparisons	Source comparison	Take home message
Eyding et al. 2010	Systematic review of 13 trials. 76% of patient data unpublished: 86% (1946 of 2256 patients) for reboxetine vs placebo and 67% (1760 of 2641 patients) for reboxetine vs SSRIs	Reboxetine for depression vs placebo or vs other SSRIs included in IQWIG HTA report	CSRs vs publications	The addition of unpublished data changed the direction and conclusions of the efficacy and harms analyses. Published data vs full dataset overestimate benefits by 99-115% vs placebo and 19-23% vs other SSRIs.
Jefferson et al. 2012	Cochrane review of 25 trials (15 oseltamivir, 60% unpublished, those published had been ghostwritten and corresponding "authors" had no access to study data)	Neuraminidase inhibitors for influenza vs placebo	CSRs vs publications	Lack of detail in publication and unexplained discrepancies when compared to CSRs led the authors to change methods compared to previous version of the review and include only regulatory data, significantly changing the conclusions of the review.
Coyne 2012	Review of the Normal Hematocrit Trial (NHT) run in the 1990s on 1265 hemodialysis patients with cardiac disease	Epoetin lower (9–11 g/dl) vs higher (13–15 g/dl) doses to increase haematocrit to reduce mortality and improve survival and QoL.	CSR vs publication	"Disclosure of these [CSR] results in the 1998 publication or access to the FDA filed report on the NHT in the late 1990s would likely have led to earlier concerns about epoetin safety and greater doubts about its benefits."
Wieseler et al. 2012	Systematic review of 29 studies included in 16 HTA reports prepared by IQWIG during 2006-2011	16 different pharmaceuticals mainly for depression and type I and II diabetes	CSRs vs publications vs register entries	CSR consistently reported more information than registers or journal publications.
Wieseler et al. 2013	Systematic review of 101 trials with full CSR available included in 16 HTA reports prepared by IQWIG. The study population is the same as Wieseler 2012 but in this study the authors quantified information gain for patient-relevant outcomes graded from 1 to 4	16 different pharmaceuticals mainly for depression, asthma and type I and II diabetes	CSRs vs publications vs register entries (unclear which trials have been registered where. Also some trials were conducted in the late 1980s)	CSRs reported complete information on 78%-100% of benefit outcomes vs 20% - 53% in combined publicly available sources. The authors estimated 13% publication bias. CSRs reported complete information on 84% - 92% of harm outcomes vs 27% to 72% of combined publicly available sources. 15% NR by publicly available sources for both general harms and withdrawals due to possible harms.

Rodgers 2013 et al. & Fu et al. 2013	Systematic review of 13 trials and 4 single arms studies (10 and 1 journal published)	Recombinant human bone morphogenetic protein 2 (rhBMP-2) for spinal fusion vs iliac crest bone graft	IPD vs CSRs vs journal publications	Wealth of extra detail from CSRs provided by manufacturer. "Early journal publications misrepresented the effectiveness and harms through selective reporting, duplicate publication, and underreporting." Fu et al. conclude that "Early journal publications misrepresented the effectiveness and harms through selective reporting, duplicate publication, and underreporting."
Doshi and Jefferson 2013	Descriptive review of 78 CSRs	14 different pharmaceuticals and biologics	CSRs vs publications (comparison in size)	The ratio of CSR pages to publication pages for available full CSRs with a corresponding publication ("compression factor") ranged from 379 to 8805.
Vedula et al. 2013	Review of transparency and accuracy of reporting of the numbers of participants, description of types of analyses, and criteria for including participants in the analysis in 11 published trials	Gabapentin vs placebo for four off-label uses (migraine prophylaxis, treatment of bipolar disorders, neuropathic pain, and nociceptive pain)	CSRs accessed from litigation with their published counterparts (21 trials identified, 11 assessed, 8 trials excluded because unpublished, 1 not randomised, 1 no CSR available)	Probably biggest discrepancies occurred between protocol and publication. Authors conclude "we found that the trial publication was not a transparent, or accurate (presuming that the research report truly describes the facts) record for the numbers of participants randomized and analyzed for efficacy".
Maund et al. 2014	Review of nine trials in 1999-2001 (7 journal-published)	Duloxetine vs placebo	CSR vs publications vs register entries. 1/9 R1 and 9/9 R2	7 S published 2 NS unpublished 1 NS published as S after post hoc analysis not mentioned in the paper Harms 50% and 25% participant reporting inconsistency in 2 trials, 1 death in active arm in unpublished trial; lack of clarity on phase of deaths Suicide NR < 2% in register reports.

				SAE 3 articles failed to report, register entries unclear.
Le Noury et al. 2015	RIAT publication, restoring GSK's trial 329 run in the 1990s and journal published in 2001	Paroxetine vs placebo & imipramine vs placebo	IPD with CRFs for 34% (93/275) participants and CSR vs publication	Paroxetine was reported as safe and effective in company sponsored ghost written publications. Access to CSR data led the restoration authors to conclude that the drug was no more effective than placebo and was toxic in adolescents. The authors identified 4 outcomes cited in the protocol but not reported in the CSR and publication.
Köhler et al. 2015	Systematic review of 15 dossier assessments by AMNOG submitted to IQWIG between 2011 and 2015. The authors assessed completeness of reporting in each document category	15 different drugs including anti HIV and oncology	AMNOG documents: IQWiG dossier assessments and publicly available modules of company dossiers vs non-AMNOG documents: EPARs vs journal publications vs register entries available at market entry datepoint	"At the time of market entry of a new drug, a substantial amount of information needed for assessment of the corresponding clinical studies and for understanding of the drug's benefits and harms is missing in publicly available European public assessment reports, journal publications, and registry reports (non-AMNOG documents)".
Lawrence et al. 2015	Cochrane review update of 4 CSR (3 journal-published in 4 publications)	Olanzepine vs placebo	CSRs vs publications	Dilution due to different coding of similar events (e.g. – "nervousness", "anxiety" and "agitation"). Long term harms not reported in publications.1 suicide in active arm NR in publication; 1 death in active arm from CV causes identified from DAP not reported in either CSR or publication. 2 suicide attempts not reported in active arm in publication and S

				dose-response with metabolic syndrome NR in a journal publication.
Cosgrove et al. 2016	Review of data considered by regulators for registration vs other data available to them vs publications and comparison of regulatory vs SR process	Vortioxetine vs placebo (4 RCTs) or active comparator (6 studies) for depression	FDA DAP (based on 10 short term RCTs) and EMA EPAR (12 RCTs) vs publications. At least 3 studies were unpublished (38% of randomised participants). All unpublished studies showed no difference with comparator*	"Published literature gives the impression that vortioxetine is efficacious, safe, and well tolerated, when in fact the data were not collected or analyzed in a way that provides sound empirical support for this conclusion." Authors note extensive sponsor ties of 8/10 authors of published studies and comment on regulatory practice which focuses on an in-depth analysis of "positive" trials rather than the whole evidence base.
Hodkinson et al. 2016	Exploratory review to assess the reporting of harms in Orlistat trials	Orlistat vs placebo	5 Roche CSRs vs 5 journal publications	Journal publications provided insufficient information on harms outcomes compared to CSRs. Serious adverse events were not reported or mentioned in the journal publications. Overall, CSRs provide extensive information about harms for study methods, including design, conduct, and analysis of the trial.
Jureidini et al. 2016	Litigation documents vs publication	Citolapram vs placebo	Comparison of 750 documents from the Celexa and Lexapro Marketing and Sales Practices Litigation and publication.	"The published article contained efficacy and safety data inconsistent with the protocol criteria. Procedural deviations went unreported imparting statistical significance to the primary outcome, and an implausible effect size was claimed; positive post hoc measures were introduced and negative secondary outcomes were not reported; and adverse events were misleadingly analysed. Manuscript drafts were prepared by company employees and outside

				ghostwriters with academic researchers solicited as 'authors".
Schroll et al. 2016	Descriptive review of 7 RCTs to assess the reporting of AEs	Orlistat vs placebo	7 CSRs from Roche vs. Protocols vs. Journal publications	"Study identified important disparities in the reporting of adverse events between protocols, clinical study reports, and published papers. Reports of the trials systematically understated adverse events. Based on the study findings, systematic reviews of drugs might be improved by including protocols and CSRs in addition to published articles".
Mayo-Wilson et al. 2017	Impact assessment to determine whether disagreements among multiple data sources of the same trials affected meta-analytic effect estimates, statistical significance and interpretation	Gabapentin and quetiapine	21 gabapentin RCTs (74 reports, 6 IPDs) and 7 quetiapine RCTs (50 reports, 1 IPD	"Disagreements across data sources affect the effect size, statistical significance and interpretation of trials and meta-analyses".

Table 1. Examples of studies comparing different sources of data for the same trials. Key: CSR = clinical study reports; DAP = FDA drug approval package; IQWIG = Institute for Quality and Efficiency in Health Care, Germany; AMNOG = Arzneimittelmarktneuordnungsgesetz (Germany's Act on reform of the market for medicinal products); R1 (Registration 1) = in public register; R2 (Registration 2) = in manufacturer register); SAE = serious adverse events; AE= Adverse event; S = statistically significantly different; NS = statistically not significantly different; NR = Not reported (by the authors); NK = Not known; NA = Not applicable; CV = cardiovascular; QoL = quality of life. The table is based on Jefferson et al. 2018.