**Supplementary Table 1 – Examples of decisions made by the CTU group on whether an adverse event description warranted classification as an SAE or not.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Study** | **Event description** | **Classified as SAE by the CTU?** | **Would including these events strengthen the association between SAEs and SSRIs?** |
| Claghorn et. al., 1996 (1) | “Minor non-specific ST-T changes” | Yes | Yes |
| Fabre et. al., 1985 (2) | “Non-specific ST-T change” | No | No |
| Lydiard et. al., 1997 (3) | “Discontinued due to ECG- abnormalities” | No | No |
| Wernicke et. al., 1988 (4) | “Worsening of depression considered clinically significant” | Yes | Yes |
| Norton et. al., 1984 (5) | “Increasing depression throughout study, withdrawal by investigator” | No | No |
| Adamson et. al., 2015 (6) | “Unblinding […] for severe adverse reactions” | Yes | Yes |
| Tollefson et. al., 1995 (7) | “Emergence of substantial suicidal ideation” | No | No |

**Additional errata**

1. While the CTU group chose to include SAEs occurring up to nine months after withdrawal from treatment in the Lundbeck-sponsored protocol 99024 (8), the net result being an increased risk of SAEs for patients treated with an SSRI, they did not include SAEs from the double-blind continuation phase of the study by Detke and co-workers (9) in which one suicide and one SAE occurred in the placebo-group, with no pertinent events in the paroxetine group. Also other studies seem to have been treated differentially with regard to post-therapy SAEs (10, 11).
2. The 1998 report by Fava and colleagues (12) summarizes the results from some of the participating centers in two GlaxoSmithKline sponsored protocols, GSK/115 (13) and GSK/128 (14) (see p. 146, §5). This thus constitutes double inclusion.
3. The efficacy statistics included for the study by Barber and co-workers (15) are slope estimates, not endpoint differences. Apart from the statistic being inaccurate for this analysis, the fact that slope estimates have lower variances than the corresponding endpoint estimates renders this negative study more weight than it should have.
4. Similarly, in the report by Jindal et al. (16) pretreatment values are used instead of posttreatment values. Again, the low variance in the pre-treatment values renders this negative study undue weight.
5. The inclusion of a one week study by Godlewska and co-workers (17) is, if not an error, still questionable, since it likely introduces a bias towards the null as SSRIs are not expected to show any significant effects versus placebo on the HDRS-17 after such short a treatment duration. For the 6-week study by Katz et al. (18), data from the second week of treatment, which finds a nominally worse effect of paroxetine as compared to placebo, is used, even though the report also states numerical superiority for paroxetine at the end of treatment (46% vs 30% responders for paroxetine and placebo, respectively). The CTU group hence has included negative data from an early evaluation while knowing that the trend was towards a positive effect of treatment at study end-point.
6. Regarding the Lundbeck-sponsored study 99024 (8), as in the study by Nyth et al., the CTU included SAEs occurring prior to double-blind treatment in the placebo group.
7. The study by Tyrer and co-workers. (19), which is listed as having a low-risk of for profit bias (figure 3 in the *BMC Psychiatry* paper), *i)* was sponsored by GSK (20) and *ii)* is not placebo-controlled.
8. The study by Feighner and co-workers (21) is listed as not having any SAEs in the placebo group. The relevant passage in the published article states the following: “The serious adverse events that occurred in the citalopram-treated and placebo patients did not appear to be related to study medication or the dose of study medication administered. Serious adverse events occurred in 8 citalopram patients, including 3 suicide attempts, a miscarriage, intestinal flu symptoms, chest pain and dizziness unaccompanied by ECG abnormalities, a severe thinking abnormality, and an allergic reaction.” Thus, while the text alludes to SAEs in placebo-treated patients, such events are not explicitly provided and have thus been missed by the CTU. As we have access to AE data for this particular trial, we can confirm that one case of suicidal ideation, which was classified as an SAE, occurred in a placebo-treated patient.
9. The GSK-sponsored protocol GSK/279 (22) was only placebo-controlled at one of two centers as the independent review board at one of the participating centers refused to administer placebo. As it is impossible to disentangle site-related differences from treatment-related differences in the published report, the inclusion of this partly uncontrolled study is questionable.
10. The odds ratio reported for the trial by Mathews et al. (NCT01473381) was erroneous; this has, however, been corrected without further comment in the response from the CTU group) (23, 24).
11. In table 2 in the response from CTU group (25) it is stated that Kranzler and co-workers (26) did not specify the type of SAEs in their study on co-occuring alcohol dependence and major depression. This is not correct, the type of SAE is explicitly given in the study report: “Among sertraline treated patients, serious adverse events consisted of a worsening of clinical condition because of alcoholic relapse (n = 7; 2 patients required hospitalization), depression (n = 1), suicidal ideation (n =1), or blood in the stool (n = 1). Among placebo-treated patients, serious adverse events consisted of a worsening of clinical condition because of suicidal ideation or attempt (n = 3), alcoholic relapse (n = 2), depression (n = 1), chest pain (n = 1), or syncope (n = 1).” Notably, the numerical overrepresentation of SAEs with sertraline is entirely driven by alcoholic relapses; with these events included the OR is 1.36 (0.52 – 3.53), if excluded the odds ratio drops to 0.53 (0.13 – 2.14).
12. In reference to the study by Schneider and co-workers (27), the CTU group states in their reply that “[w]e do not know if the reported number is a count and one or more of the participants experienced more than one SAE or if it is the number of participants affected by one or more SAEs (proportion).” In fact, we are reasonably certain that it is a count as this is what the manuscript states: “There were 28 serious adverse events in the study: 17 among the patients in the sertraline group and 11 in the placebo group […] Four patients left the study because of serious adverse events; all were receiving sertraline. These events included depression and fecal impaction in one patient and syncope, diverticulitis, and accidental bone fracture in one patient each.”
13. The study by Itil and co-workers (28) concerns fluvoxamine, not fluoxetine.
14. The study by Pettinati and co-workers (29) is not included in the efficacy evaluations.
15. In the *BMC psychiatry* paper, the author state that “[w]hen the four trials with low risk of bias of financial bias were analysed separately then there was no significant difference between the SSRI group and the placebo group (−0.92 points; 95% CI −2.42 to 0.58; I2 26%) (Additional file 4: Figure S1).” However Additional file 4: Figure S1 reveals that that five, not four, trials were included in the analysis; one of these has a duration of merely one week and another erroneously uses pre-treatment values rather than post-treatment ones (see points 4 and 5 above).
16. *The BMC Psychiatry* paper states that “[t]here were no significant differences between participants randomised to SSRIs versus placebo on number of suicides (RR 0.68; 95% CI 0.16 to 2.81; P = 0.59; Trial Sequential Analysis-adjusted CI 0.01 to 226.85; 6 trials [60, 71, 108, 113, 151, 155]).” Table 2, however, shows that suicides occurred in 7 of the tabulated trials. Moreover, there was a suicide in the study by Loo and co-workers (30) which was included in the SAE analysis but not tabulated.

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