Harms reporting in trials of orlistat

August 16 2016

The reporting of trials of orlistat in the 1990s appears to have understated harms, both in the summarized results submitted to the European Medicines Agency for drug approval, and in the published papers, according to a document analysis conducted by Jeppe Schroll and colleagues of the Nordic Cochrane Centre, Rigshospitalet, Copenhagen, Denmark, and published in *PLOS Medicine*.

Pharmaceutical companies seeking to market a new drug must report adverse effects observed in trial participants in Clinical Study Reports (CSRs), which they provide to regulatory authorities. Additionally, investigators may report harms in published reports of their trials. In an analysis of CSRs and published reports of seven trials, Schroll and colleagues sought to understand the accuracy, and potential bias, in harms reporting for trials of orlistat, a slimming drug from Roche approved in Europe in 1998 and still marketed in Europe today. They found various ways in which protocol instructions to trial investigators had the potential to dilute the appearance of drug-associated harms. Additionally, in these trials, only 3% to 33% of the total adverse effects from CSR summaries were described in published papers. Finally, in one trial, Schroll and colleagues counted adverse events individually and found that both the number of adverse effects and the number of days with adverse effects in participants taking the drug were understated in the corresponding publication.

The reporting accuracy of these trials may not reflect broad practice, and reporting practice may have changed substantially over the two decades since these trials were conducted. However, the analysis indicates that

important disparities can occur in the reporting of adverse events between protocols, clinical study reports, and published papers, and can result in understatement of adverse events. The authors state, "(b)ased on these findings, systematic reviews of drugs might be improved by including protocols and CSRs in addition to published articles."

More information: Schroll JB, Penninga EI, Gøtzsche PC (2016) Assessment of Adverse Events in Protocols, Clinical Study Reports, and Published Papers of Trials of Orlistat: A Document Analysis. *PLoS Med* 13(8): e1002101. DOI: 10.1371/journal.pmed.1002101