Dear Editor,

The study by Balci et al.\textsuperscript{1}, published in the 3\textsuperscript{rd} issue of this year's Bulletin of Clinical Psychopharmacology, is deeply appreciated for emphasizing the possible drug-drug interactions (DDIs) and adverse effects (AE) that patients may experience while receiving antipsychotic polytherapy. This subject is of vital importance for patient safety, given that 5-20\% of all hospitalizations for AE are reported to be caused by DDIs. Considering the frequency of serious adverse effects, this means that one in 200 hospitalized patients experienced a serious adverse effect as a consequence of DDIs\textsuperscript{2}.

However, with all due respect to the authors' approach and interpretation, I would like to mention some important points regarding the use of DDI information sources that should have been taken into account while devising the methodology of the study and included in the discussion section.

First of all, there is no full agreement on how DDIs should be classified, as different information sources use different classifications. Additionally, a “major” DDI according to one source can be classified as “moderate” in another one. Therefore, I believe it would have been more comprehensive if the DDI of interest had been checked by using another DDI database, e.g. medscape.com, or DDI textbooks.

Secondly, an important part of the information included in DDI information sources is derived from drug labels which lack clarity as to whether the data originated from animal or human studies and whether it is pharmacokinetic or pharmacodynamic, which makes clinical interpretation very difficult\textsuperscript{3,4}. Given the vast amount of DDIs in all known drugs, any suggested interaction should always be examined for clinical relevance\textsuperscript{2-4}. In an observational, prospective study, Smithburger et al. demonstrated that proprietary databases and clinicians’ assessments regarding the severity of DDIs did not agree and suggested that clinical opinion should be considered in databases\textsuperscript{5}. Customization of automatized DDI clinical decision support systems (CDS) is suggested so as not to expose clinicians to trivial or irrelevant alerts, which lead to alert overload and alert fatigue\textsuperscript{3,4}. It has been demonstrated that a proprietary CDS database used in a 900-bed hospital could generate nearly 25,000 alerts per day. After customization and reclassification, this number could be reduced to 500 alarms of high quality in terms of clinical significance\textsuperscript{4}.

Therefore, the risk percentage calculated by using drugs.com as information source for a particular DDI in this study may be an overestimation. The only available solution for this problem is designing epidemiological studies in order to observe if the patients really experience the DDI with a frequency comparable to that suggested by the database.

Finally, as the authors themselves mentioned to some extent, raising the awareness for DDIs among clinicians, patients and regulatory authorities very important in the context of patient safety and avoidance of malpractice.

Keywords: Drug-drug interactions, sources on drug-drug interaction, computerized decision support systems, adverse effects, antipsychotics
The clinical relevance of information sources on drug-drug interaction

References:


4. Horn JR, Hansten PD. Careful scrutiny of the evidence for drug-drug interactions in clinical decision support systems is necessary. J Manag Care Pharm 2011;17(9):713.


1 Visiting Researcher, The Motherisk Program, Division of Clinical Pharmacology and Toxicology, The Hospital for Sick Children, Toronto, Canada
2 Assoc. Prof., Izmir Katip Celebi University, School of Medicine, Department of Pharmacology, İzmir - Turkey

Correspondence Address: Dr. Yusuf Cem Kaplan
İzmir Kâtip Çelebi Üniversitesi Atatürk Eğitim ve Araştırma Hastanesi, Klinik Farmakoloji ve Toksikoloji Birimi, 35360, Karabağlar, İzmir - Türkiye
Email address: seawise@gmail.com

This letter was accepted for publication in December 10, 2014.

Declaration of interest:
Y.C.K.: The author reported no conflict of interest related to this letter.