Reviewer's report

Title: A retrospective claims analysis of combination therapy in the treatment of adult attention-deficit/hyperactivity disorder (ADHD)

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Reviewer: Michael C Monuteaux

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Re: A retrospective claims analysis of combination therapy in the treatment of adult attention-deficit/hyperactivity disorder (ADHD)

This was in insurance claims study that examined patterns of pharmacotherapy for ADHD among adults. The authors found that long-acting stimulants (LAS) and atomoxetine (ATX) were the least likely medications to be used in combination with other drugs. Also, several factors were identified that predicted combination therapy within persons taking LAS and ATX.

The strengths of this study include the use of a large, national database with information about specific prescription uses. However, several concerns were also noted, as follows:

Major Compulsory Revisions

1. The most important issue with this study is that the findings do not seem to represent a contribution to the scientific literature. The authors need to develop and present a compelling argument for why this information is important to the field and how it advances the state of knowledge about adult ADHD.

2. According to information on page 6, among all the patients with at least one claim for ADHD, only 3.7% were treated during the study period. So, 96% of patients diagnosed with ADHD by a health care professional are not given any pharmacotherapy? This does not seem plausible. Can the authors clarify?

3. The authors should discuss the rationale for restricting the testing of predictors for combination therapy to only LAS and ATX. Why are the predictors for combination therapy for SAS, for example, not of interest?

4. Since it cannot be determined from these data why each medication was prescribed, it would seem a more prudent approach to only consider medications in the various analyses looking at combination treatment that are primarily prescribed for ADHD. For example, given the high rates of comorbid disorders in this sample, it is not surprising that bupropion was given to patients on an ADHD drug. Also, it is not surprising to see that comorbid depression predicted combination treatment in both models, since one of the drugs that could designate an observation as “combination treatment” was a depression drug.

5. On page 12 (and elsewhere), the authors state that LAS and ATX are least
likely to be associated with combination therapy. While this is true, the rates of monotherapy for LAS and ATX, 21% and 19.7%, are very close to that of SAS, 23.1%. Why designate only LAS and ATX as those least likely to be associated with combination therapy? Was this cut-off made a priori? What was the rationale for this decision?

Minor Essential Revisions
1. The figure is difficult to interpret. Can the authors present two figures, one for each model?

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests