Reviewer's report

Title: Comorbidities in ADHD children treated with methylphenidate: a database study

Version: 1 Date: 15 October 2012

Reviewer: Guilherme Polanczyk

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Discretionary Revisions

1) Given how the Results are presented, I understand the evaluation of prevalence/incidence of MPH use is also a primary aim of the study. I suggest the ms is re-written based on this.

Major Compulsory Revisions

1) I'm curious to understand why is it not possible to disentangle ADHD diagnosis and prescription of MPH. If ADHD diagnosis is not coded validly, I would also assume that all other diagnosis (at least psychiatric diagnosis) would also not be coded validly.

2) Prevalence/incidence of MPH use is based on "at least one MPH prescription filled in the year". This is an overestimation of MPH treatment, which means continuous use. It is necessary to make this distinction very clear in the ms. Would be relevant to conduct secondary analysis restricted to individuals on adequate treatment for ADHD.

3) Is it possible to understand the temporal ordering between comorbid diagnosis and MPH prescription? It would be very relevant to understand whether comorbid diagnosis where made before of after MPH prescription. Also, because MPH use is defined as at least one MPH prescription, is it possible that those with comorbidities where more likely to be on MPH for a reduced period of time.

4) Would be extremely relevant to have an ADHD group treated with non-stimulants as a second comparison group, or even a group with a similar condition that also would prompt clinicians' attention to investigate comorbid conditions. It is very likely that those with ADHD, to whom stimulants might be prescribed, would receive additional medical attention and consequently, would have more diagnosis (some of them with unknown clinical meaning). This is a major potential bias in this study and might be true not only in regard to hyperthyroidism, but also in regard to all other conditions.

Minor Essential Revisions

1) On page 16, authors state that "Our study focussed on description of pre-existing comorbidities among children receiving MPH to investigate the
impact of new contraindications implemented by the EMA.

However, on page 17, authors state that "...at the time the analysis was conducted, only data for the years 2004 to 2006 were available. For that reason, we were not able to ascertain the impact of the contraindications introduced by the EMA in the beginning of 2009 on prescribing behaviour." I suggest authors explicitly state since the beginning of the ms that this study analyze data that precedes the EMA.

2) Page 11 - "MPH is known to be used more commonly in the US than in Germany [2] which corresponds to the markedly higher prevalence of ADHD in the US." There is no evidence that indicate that ADHD prevalence is higher in the US or even vary according to country.

3) I suggest authors revise Table 1, Figures and text to not present the same data.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

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

Declaration of competing interests:

Guilherme Polanczyk has served as a speaker and/or consultant to Eli-Lilly, Novartis, Janssen-Cilag, and Shire Pharmaceuticals, developed educational material to Janssen-Cilag, and receives unrestricted research support from Novartis and from the National Council for Scientific and Technological Development (CNPq, Brazil).