Reviewer’s report

Title: The epidemiology of pharmacological treatments for attention deficit hyperactivity disorder (ADHD) in children, adolescents and adults in UK primary care.

Version: 1 Date: 6 February 2011

Reviewer: Almut G Winterstein

Reviewer’s report:

Major compulsory revisions

According to the stated objective the authors aimed to describe the prevalence and incidence of ADHD drug use in patients diagnosed with this disorder. Drug utilization studies of this kind are relevant, especially in psychiatric medicine where treatment pattern are oftentimes individualized and show great geographic (and other) variation.

The article introduction is very broad with a quite lengthy review of ADHD presentation and treatment modalities, which might be well-known to interested readers. It is followed by a review of the available body of evidence on ADHD drug utilization, which the authors evaluate as insufficient. However, while the number of previously published utilization studies might be small, the authors might want to clarify the shortcomings of these studies and how their study would contribute additional evidence. In order to position their study properly it would be useful to highlight knowledge deficits that are specifically addressed by the study at hand.

Since the THIN may not be known to all readers it would be important to comment on the generalizability of the physician sample. The methods used to extract specialist prescription from free-text consulting notes and detail on the sensitivity of this approach would furthermore be important to allow the reader to evaluate the accuracy of the presented data.

Most importantly, there appear to be several problems with the definition of the study sample and the two outcomes measures, ADHD drug use prevalence and incidence, which made it impossible for me to interpret the presented results. If all subjects were required to have an ADHD drug prescription for study inclusion how was prevalence calculated? I assume that the inclusion criteria were relaxed to include all patients with some type of ADHD diagnosis but the timing of the presence of such diagnosis is unclear to me. Or did the authors indeed require presence of at least one prescription at some point in time – an approach, which seems counterintuitive? It is furthermore unclear how truncated follow-up was handled. There is reference to a requirement for a minimum of 12 months presence in the database, but it is unclear how incomplete presence in a calendar year was handled.
The definition of prevalence does not specify whether the ADHD diagnosis had to occur in the respective study year or not. Note that annual prevalence estimates in drug utilization studies usually utilize period prevalence estimates where all patients with complete eligibility in a given year are extracted for the denominator. This would allow an appropriate time window to establish presence of ADHD diagnosis.

The incidence definition does need clarification as well – and potentially revision. To accurately measure incidence the denominator can only include patients “at risk” for the outcome, in this case initiation of an ADHD drug. Thus, the denominator should only include patients who have not received ADHD drugs in the past. The look back period that was used to define drug naïve patients needs definition as well.

As for the inferential statistics presented, the comparison of prevalence over time needs to consider lack of independence between denominator populations and adjust standard errors accordingly. See for example our utilization study in Ann Pharmacother 2008 (Winterstein et al). I would also reconsider the presentation of ratios (eg, male/female) to evaluate predictors for ADHD initiation over time. Instead ratio of these ratios can be used to summarize differences between the denominator and the drug use population. Furthermore, any type of point estimate should be accompanied by estimates of precision (ie, confidence intervals).

Since I was not sure about the underlying definitions of prevalence and incidence I deferred my assessment of results and discussion until such clarifications have been made and proper statistical techniques have been employed. However, I did note that the discussion section appears to include more quantitative information than the result section. The authors might want to consider moving some of this information earlier in the manuscript.

Discretionary revisions

It should be noted that ADHD medications are also prescribed for disorders that are closely related to ADHD such as ODD or conduct disorder. These would be more likely indications that made it in the exclusion criteria (rather than narcolepsy or epilepsy).

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

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

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