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: 2 Date: 30 April 2011

Reviewer: Almut G Winterstein

Reviewer’s report:

I appreciate the presented revisions and detailed response to my comments but remain concerned about the epidemiologic methods.

I am sorry to say that I remain confused about the inclusion criteria. The authors state in their response to my previous review the following:

With regards to defining the study population, the aim of the study was to ‘investigate the prevalence and incidence of methylphenidate, dexamfetamine and atomoxetine prescribing to children (over 6 years), adolescents and adults with ADHD/HKD in UK primary care’ i.e. the level of drug-treated ADHD in the general primary care population. For this reason, the inclusion required both a prescription for a study drug and a diagnosis of ADHD/HKD. We have aimed to clarify the above point in the manuscript.

Incidence and prevalence are both estimates that result in a proportion or rate. As per the above cited aim this would be the rate or % of patients with ADHD who receive pharmacological treatment. However, the authors continue to require drug treatment in their inclusion criteria.

As for the definition of prevalence, it appears from the results that this was calculated as annual prevalence. This is not reflected in the definition that is provided in the methods section. Likewise, the definition of incidence remains to be flawed. It appears from the first statement that the authors required a 12-months run-in period from index date to define an incident user (not case). However, the definition of “k” in the formula requires being “at risk” in the mid-year population in a particular year. With all due respect, I have no idea what this means and I am still not sure that prevalence and incidence estimates were calculated correctly.

Would the authors please provide the denominator (ie, total number of patients meeting inclusion criteria) for table 1, and denominator values were table 2?

Table 3. If the first set of values shows truly prevalence (ie, the proportion of patients in a certain stratum that received medication) there is no reason to show the ratio (female/male) for the denominator. This is because the definition of prevalence would take care of this. Or did the authors simply report the sum of patients with drug for each gender category and calculated the ratio of this?
Same applies for age. Based on the overlapping confidence intervals there is no statistically significant change of any of the ratios presented in table 3 and no respective conclusions can be drawn. The same concerns to a large extent table 4.

Also, based on what date was age defined for inclusion in the age bands?
 Considering the confusing definitions as well as the presented data I still am not sure what type of data is actually presented.

Abstract

The abstract is still lacking quantitative data and estimates of precision/error or statistical significance.

Further concerns related to the authors response:

As this study sought to examine the prescribing of the study drugs in primary care, only the prescriptions contained on the database within the therapy files were utilised. If a prescription was issued for a study drug by a specialist, it would not be systematically recorded by GPs on the database and thus we did not seek to extract these data from freetext information.

Is there any data on the distribution of ADHD drug prescriptions between GPs and specialists? This seems important. If specialists prescribe a significant amount it would be important to clarify that the database can capture only a proportion of drug utilization and that data is not representative of drug utilization in UK.

As for the calculation of ratios and my respective suggestions the authors state:

It is a method of analysis that we will certainly consider in future studies however we feel that this was not an aim of this study to evaluate predictors for ADHD drug initiation and therefore we have not performed these calculations.

I worry that the authors have misunderstood my suggestions. I was not suggesting a risk model but rather the calculation of the ratios of the ratios that are presented in table 3 and 4. In other words if the ratio between males and females is 1.4 in 2003 and 1.8 in 2008, the ration of 1.4/1.8 along with confidence intervals can provide a direct estimate if the change if these ratio along with statistical significance. Of note, the overlapping confidence intervals suggest that there is not sufficient statistical power to deduce significant changes for most of the presented comparisons. This seems ignored in the write-up of results.

The authors state further:

Response: in the UK, ADHD medications are very rarely prescribed for other behavioural disorders except in a few cases for sleep disorders. In this study, the inclusion criteria required the presence of a diagnosis of ADHD/HKD but did not preclude any comorbidities such as CD or ODD.
I would appreciate a reference for this statement as it conflicts quite significantly from US practice.

**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.