Reviewer's report

Title: Influence of mandatory generic substitution on pharmaceutical sales patterns: a national study over five years

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Reviewer: Michael A Fischer

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General

This manuscript evaluates the impact of a mandatory generic substitution policy in Sweden. The information here is of potential interest to policy-makers and prescribers but, as currently presented, the data do not speak to the most relevant policy question. The key question is how implementation of a mandatory generics policy will change sales patterns relative to the baseline seen in the absence of the policy. The authors have the information to do this type of analysis since they include medications that went off patent before the policy was implemented. The manuscript would be greatly strengthened by making this comparison explicit.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Page 4 top and page 5, full paragraph: A clear definition of what is meant by generic substitution should be provided. The papers cited at the top of page 4 cover several topics, including generic substitution and reference pricing. This is relevant because when the policy is described on page 5, it is not immediately clear if it is a true generic substitution policy or more of a reference pricing scheme. It becomes clear as one reads on, but being more explicit here would be helpful for setting up the rest of the analysis.

The paragraph on the bottom of page 4/top of page 5 is extraneous.

Page 10, top: The point made here about ACE inhibitors is critical. Since there were already two substitutable drugs in this class, it gives a better indication of what was happening in the absence of a generic substitution policy. A comparison between the changes in the use patterns of ACE inhibitors when generic versions became available without a mandatory substitution policy and the use patterns of the other classes presented would be very useful information.

Page 10 bottom and page 11 top: Not sure what to make of the various subgroup data by age and gender. Do the authors have a hypothesis about drug use across different demographic groups that they would propose to test here? Otherwise this is a bit of a distraction from the main point.
Again, calling attention to my central concern, one would expect the most dramatic changes to occur when a patent expires and a generic substitute becomes available, but one would expect this regardless of the policies in place; we are really interested in the impact of the policy itself, controlling for the underlying prescribing habits of Swedish physicians.

The point about stable sales patterns for ACE inhibitors and antiretrovirals again begs the question of the true impact of reform, especially in a region where prescribers may start prescribing generic medications relatively quickly after they are introduced.

Question the statement about differences in patient failure to redeem prescriptions between substitutable and non-substitutable drugs. There is evidence that increased patient cost-sharing leads to decreased medication adherence. If I understand the policy correctly, patients prescribed some drugs may arrive at the pharmacy and find that they are required to pay additional amounts to cover a non-substituted product. This could lead to prescriptions not being filled, either due to the immediate cost faced by the patient or due to the administrative hurdles of needing to call the prescriber back. I don’t see this as a fatal flaw, but this point needs to be considered more carefully and consideration of unintended consequences on adherence is one of the downsides of this type of policy intervention.

The data presented in the figures are interesting, but as currently presented the figures are difficult to read and presenting 18 separate graphs is a little much. It would be best to present the raw data with the 5 parts of figure 1 shown in more legible fashion and then focus on a couple of key highlight points for any additional figures.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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

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