Reviewer’s report

Title: Consecutive antibiotic use in the outpatient setting: an extensive, longitudinal descriptive analysis of antibiotic dispensing data in the Netherlands

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Reviewer: Nick Daneman

Reviewer's report:

The authors present a descriptive study of outpatient antibiotics dispensed in the Netherlands between 2006-2014. The analysis includes 43,179,867 prescriptions, but focuses on the 5% which involve antibiotic prolongations and/or switches (two antibiotic prescriptions for the same patient with \(\leq 3\) days between the calculated end date of the first prescribed antibiotic and the start date of the next), and especially the 2% which involve antibiotic switches (to a different agent). Although primarily descriptive, the analysis yields novel insights into the frequency of switches, and the variability by class of drug (both in terms of the initial drug leading to switches, and the subsequent drugs to which people are switched). Note: I was able to see the manuscript with tracked changes and the authors' summary responses, but did not see the full reviewers' comments. It is my impression that the manuscript is already improved from the original version and in near publishable form. The current study is limited by the lack of linked clinical and microbiologic characteristics for the treatment episodes, but I believe it to be an important literature contribution. In particular it will inspire numerous threads of follow-up research globally, including work to understand the drivers of antibiotic switches, as well as work to understand the clinical impact of switches.

Minor comments:

- Background: the material in the first three paragraphs could be condensed

- Methods: "A consecutive prescription was defined as two antibiotic prescriptions for the same patient with \(\leq 3\) days in between the calculated end date of the first prescribed antibiotic and the start date of the next". It may be too late at this point, but it would be interesting to see how variations in this definition would impact the main results. For example, if the switch was defined as another agent being prescribed anywhere from \(>1\)d after the initial dispensation date to \(>3\)d after the end date, how much would the frequency of switches increase? Would there be a different spectrum of drugs involved in these switches? 
- Methods: Would it be possible to exclude patients admitted to hospital prior to completion of their first dispensed antibiotic? They should not be part of the denominator of patients at risk of switches.

- Methods: Please add a sentence justifying why patients with >8wks of annual antibiotic exposure were excluded.

- Table 1: could consider adding percentages to table 1?

- Figures: could consider adding a display related to time trends of 'prolongations'?

- Discussion: "The evidence linking antibiotic treatment failure and antibiotic resistance is considered to be weak (20, 21). Therefore, we cannot expect that bacterial resistance is the major cause of treatment failure and antibiotic switches". But couldn't some of the switches relate to the arrival of culture and susceptibility results, such as urine culture data, prompting switch to an agent with documented in vitro resistance to one with in vitro susceptibility?

- Discussion: Future challenges: as per prior comment, I think future challenges should involve linking to clinical patient data with antibiotic indication, but also to microbiology data, and to clinical outcome data.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

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