Reviewer’s report

Title: Fluoroquinolone consumption and Escherichia coli resistance in Japan: An ecological study

Version: 0 Date: 25 Oct 2018

Reviewer: Željko VOJVODIĆ

Reviewer's report:

Major objections

Any analysis between antibiotic consumption and resistance without inclusion of disease prevalence (in this case urinary tract infections, and possibly respiratory infections) does not provide a meaningful interpretation.

The authors should include this important factor in the analysis (if available) or at least emphasize it adequately in the Limitations.

The authors should clearly separate outpatient and inpatient pharmaceutical sales, as well as proportions of outpatient and inpatient microbiological samples in the Methods. If that was not possible, they should elaborate that in the Limitations.

Other remarks

Page 5 lines 85-87

For fluoroquinolone consumption, we used pharmaceutical sales data from wholesalers, representing the total amount of drug sold [22] by prefecture in 2015-2016, which has been publicly shared by the AMR Clinical Reference Centre, the National Centre for Global Health and Medicine.

What are the proportions of outpatient and inpatient sales?

Methods

Among „the number of physicians per 100 000 individuals” the authors did not specify the number of hospital and primary care physicians separately. If that was not possible, the authors should address that in the Limitations.

The main confounders should actually be data on prevalence of urinary tract infections and (perhaps to a lesser extent) respiratory infections.
The information was retrieved from the clinical laboratory section of the Japan Nosocomial Infections Surveillance (JANIS) system [21] that encompasses the microbiological testing results of all registered medical facilities.

What proportion of sample came from outpatient and what from inpatient setting?

Second, the JANIS data that we mined were not accompanied by information on the type of clinical specimen or sensitivity to other antimicrobial agents. More detailed insights into levofloxacin resistance by clinical and biological classifications could be gained by incorporating this information into the analysis.

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.

No

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

No

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.

I am able to assess the statistics

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