Reviewer’s report

Title: Trends in antimicrobial management of gonorrhoea by general practitioners in Amsterdam, the Netherlands, between 2010 and 2016: A cross-sectional study

Version: 0 Date: 08 Aug 2018

Reviewer: Lisa McCarthy

Reviewer’s report:

General Comments:

This cross-sectional study reports the 5-year patterns toward guideline concordance in gonorrhoea treatment with first-line intramuscular ceftriaxone between 2010 and 2015 in Amsterdam, The Netherlands. This manuscript would be strengthened by the addition of more context regarding the rationale for the 2013 Dutch Guidelines update (i.e., susceptibility data that supported the removal of cefotaxime as a first-line treatment option) and by including details regarding the development and administration of the survey in the Methods. Other opportunities to improve the manuscript include clarifying the consistency of the reported Results between the text and figures and discussing additional limitations.

Title:

1. Please add the study design to the title per the submission guidelines. (i.e., Trends in antimicrobial management of gonorrhoea by general practitioners in Amsterdam, the Netherlands, between 2010 and 2015: A Cross-sectional study)

Abstract:

1. Throughout the manuscript, both 2013 and 2014 are cited as the year of the guideline update. (e.g. 2013 in lines 23 and 64 and 2014 in lines 119 and 150). Please reconcile.

2. The Results provided in the abstract may not accurately capture the article's content. The overall aim is to "investigate trends in the antimicrobial management for the treatment of gonorrhoea". It is unclear however, whether the aim was to investigate prescribing concordance with the 2013 guideline update or if it was to simply convey the change in the rate of ceftriaxone prescribing. It is presumed by the reader that the authors intended to demonstrate guideline concordance as the data analysis method chosen was "the annual percentage of administered first choice treatment according to the guidelines was reported" (lines 116-117). From this data the authors conclude that "The results demonstrate a successful shift in the antimicrobial management of gonorrhoea infections to ceftriaxone monotherapy according to the national guideline." (lines 38-39). For this reason, reporting the change in the rate of ceftriaxone monotherapy between 2010 and
2015 is potentially misleading as cefotaxime was also an equally appropriate, recommended option from 2010 to 2013. It may be more appropriate to report the difference in the rate of ceftriaxone monotherapy prescribing between 2013 and 2015.

3. The results and conclusions from the survey require support from an expanded discussion on the methods used to create and administer the questionnaire. Please see Methods below.

Background:

1. Dividing the first paragraph into smaller sections would help the readability of this section. Suggested natural breaks would be in line 55 before "In the Netherlands…", line 59 before "It has recently been shown in Estonia…", and line 63 before "Since 2013…".

2. The manuscript would be greatly enhanced by expansion on two particular concepts introduced in this section.

   i. Impetus for this study: Lines 56-59 briefly mention a previous report that appears to be the inciting factor for this investigation. Lines 185-189 address this, but it is unclear why this is relevant. Since the reference is not available in English, the reader would greatly benefit from understanding who the "64% of general practitioners" represent since it is understood that these GPs are not the same as the group included in the present study.

   ii. The Dutch Guidelines: The comment regarding the guideline update in lines 64-65 does not provide the reader with enough context for the rationale of recommending only ceftriaxone monotherapy. Please provide a reference to these guidelines and clarify: (1) which author(s)/organization wrote and published the guidelines (if available, could also speak to the methods used to develop the guidelines e.g., was GRADE used? http://www.gradeworkinggroup.org/), (2) which third generation cephalosporins are available in the Netherlands, (3) why cefotaxime was taken out of the guidelines, and (4) what susceptibility patterns were used to narrow the WHO guidelines?

3. Suggest removing lines 60-63 regarding international rates.

4. The last sentence describing objectives of the study should be revisited to ensure that each aim can be matched to a method and a result. For the reader to interpret the results of the investigation of preferences and potential barriers, more context needs to be provided in the methods regarding the survey. Please see Methods below.

Methods:
1. Suggested enhancements under each subheading include:

a. Design:
   i. Please specify what type of gonorrhoea cases were analyzed. (i.e., were oropharngeal, anorectal, or treatment-resistant cases of gonorrhoea included?)

b. Setting:
   i. Please clarify whether gender or sex (or both) are available in the database. Physiological sex is recorded in most databases as opposed to gender.
   ii. Lines 82-84 regarding ethics would ideally be presented at the end of the Methods section.

c. Data Collection:
   i. Please clarify what data was collected from the research database in addition to the ICPC-1 code (i.e., sex, date of birth, antibiotic, diagnostic rationale, etc.).
   ii. Please discuss how the 6-year period from 2010 to 2016 was chosen. Was this to present data 3 years before and 3 years following release of the guideline?
   iii. The reader requires more context regarding the choice of ICPC-1 codes to use in case identification. Please discuss how additional related conditions were excluded (e.g. cervicitis, pharyngitis, etc.). Please also address how the cases identified as urethritis or epididymitis were determined appropriate for inclusion if the gonorrhoea code was not used.
   iv. Please specify in line 97 if the treatment indications are derived from the WHO guidelines or the Dutch guidelines.

d. Suggest adding a subheading called 'Survey Design' between Data Collection and Data Analysis:
   i. The paragraph in lines 103-110 could be contained under its own subheading as greater detail is required regarding the development and administration of the questionnaire. This section would ideally address the following questions:

1. Who designed the questions?/How was consensus obtained?
2. How were statements actually phrased on the questionnaire? (Taking into account possible non-direct translations, of course.)

3. How many times were the GPs reminded to complete the questionnaire?

e. Data Analysis:

   i. Please clarify what is meant by "characteristics of diagnosed gonorrhoea".

   ii. Annual report GAZO in line 116 requires a reference if publically available.

   iii. Consider removing lines 122-124 as they are not necessary in this section.

Results:

1. It would be beneficial to add a statement about the excluded cases being outlined in Figure 1 to direct the reader to the graphic for these details.

2. This section would greatly be strengthened by clarification of the term "microbiologically confirmed" as this term is not used in the WHO Guidelines. It is presumed the authors intend for this term to encompass culture, NAAT, and gram-stain confirmed cases.

   a. Line 140 states that 36% (98/276) of cases were confirmed via culture. Please include the proportion of cases confirmed via NAAT and gram-stain.

   b. In line 139, n=24 whereas in Figure 1, partner management (n=16) and syndrome management (n=18) add up to n=34. Please reconcile.

3. In line 147, the rate of cefotaxime and ceftriaxone prescribing in 2010 is given as 77% whereas it appears closer to 81% in Figure 3. Please reconcile.

4. The results provided under 'Antibiotic treatment preferences' are difficult to interpret without knowing how the statements were actually phrased on the questionnaire. It may be more reader-friendly to provide the results in a table, as opposed to the graph in Figure 4. The graph is incomplete since it does not acknowledge that two bars are missing ('strongly agree' in question 1 and 'strongly disagree' in question 2). When grouping responses on a Likert scale, it is optimal to specify what categories are being combined (e.g. to rephrase lines 163-164, "Sixty per cent (n=9) of GPs disagreed or strongly disagreed that intramuscular administration of ceftriaxone is experienced as a cumbersome procedure".

Discussion:
1. For consistency, suggest specifying the dates in line 177 (e.g. from January 1, 2010 to January 1, 2016).

2. Again, providing more details in the methods may validate the conclusions drawn from the responses. As of right now however, it appears inaccurate to say that "GPs did not experience barriers" (lines 40, 180, 210). Since the questions were posed on a Likert scale, the respondents presumably did not have an opportunity to provide their perceptions of perceived barriers in an open-ended question and thus, there is no way to definitively rule out that the GPs did not perceive any barriers.

3. The rationale for comparing the results of the referenced study [8] to the results of this investigation does not translate particularly well for the reader, as stated in Background above. Report [8] appears to have assessed the proportion of practitioners adhering to guidelines while this study examined the proportion of cases treated per guidelines.

4. Please support the statement in lines 186-189 with a reference. Who is expecting the GPs in the AMC to be earlier adopters of guidelines?

5. It is unclear why the comparison to other jurisdictions is particularly relevant in this manuscript as the objective was to characterize the trends in gonorrhoea management in GPs offices in Amsterdam. Some of the discourse is contradictory to the conclusions of this study and the overall message is unclear.

Limitations:

1. Please consider including a statement about limitations associated with the survey (e.g. response rate of less than 50%, non-direct translations of the questionnaire statements, etc.).

Conclusions:

1. As per BMC guidelines, consider providing a brief explanation of the importance and relevance of the study reported.

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

No

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.

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

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons
CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal