Reviewer's report

Title: Is it time to switch to doxycycline from azithromycin for treating genital chlamydial infections? Modelling the impact of autoinoculation from the gastrointestinal tract to the genital tract

Version: 1

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Reviewer: Matthew Beymer

Reviewer's report:

Overall Feedback

The authors explore a question which definitely deserves greater attention in the age of increasing antibiotic resistance and waning treatment efficacy. The authors present a cogent narrative and the mathematical equations given are easily verifiable by a non-statistically minded audience. However, the article would benefit from an expanded introduction and greater clarification on the target population.

Major Compulsory Revisions

1. The second paragraph of the Background section seems to emphasize that the change from azithromycin to doxycycline should be made due to the probability for autoinoculation in women, but there is no discussion about this probability in men. Based on this background as well as the Study Objective listed in Line 69, it appears that the recommendations in this article are solely intended for women. If that is the case, the authors should explicitly outline this population in both the title of the manuscript as well as the abstract to ensure that the reader is clear who the recommendation is intended to target. For example, this could be done simply by adding “in women” so that the title appears as follows: “Is it time to switch to doxycycline from azithromycin for treating genital chlamydial infections in women? Modelling the impact of autoinoculation from the gastrointestinal tract to the genital tract.” As stated previously, similar edits would be needed for the abstract.

Minor Compulsory Revisions

2. The authors cite the Bachmann study in Lines 48-49 to indicate that the use-effectiveness with doxycycline seems to be high. However, it would be useful to explicitly indicate what percentage of patients cleared their initial chlamydia infection as is the case for lines 49-51. While the authors are correct in their assessment, the current wording does not allow the reader to judge for themselves what constitutes “high” without referencing the cited article.

3. There is a lot of white space in Figure 1 that may be unnecessary. It may be useful to revise the y-axis to 80% to 100% so that the confidence interval is a bit more explicit for the doxycycline group.
Discretionary Revisions

Introduction

4. The authors may want to also include the meta-analysis by Lau and Qureshi entitled, “Azithromycin versus doxycycline for genital chlamydial infections - A meta-analysis of randomized clinical trials.” The Kong article is an important recent contribution, but the Lau/Qureshi article from 2002 shows how the conversation has evolved from equal efficacy of each drug in 2002 to potentially superior efficacy of doxycycline in the current treatment environment.

5. Although the focus of the article is among women, there is another important study by Khosropour et al. called “Comparing Azithromycin and Doxycycline for the Treatment of Rectal Chlamydial Infection: A Retrospective Cohort Study” which would also add important information to the rectal discussion in the first paragraph. Similarly, work by Hathorn et al. “What is the appropriate treatment for the management of rectal Chlamydia trachomatis in men and women?” would bolster this section a bit.

6. Autoinoculation is defined in lines 56-57 implicitly, it would be useful to explicitly define this term in the text for individuals who may be external to the field but hold a cursory interest.

Discussion

7. In the Discussion section, the manuscript may benefit from a greater discussion of medication reminders as 5 of the 81 individuals tested positive for chlamydia at follow-up in the Bachmann study. While the use effectiveness is high, it may be useful to discuss the need for providers to emphasize medication adherence given the fact that doxycycline is multiple doses instead of just one dose with azithromycin. This may be placed in the "common sense" bin, but I think it bears reiteration given the sub-optimal adherence levels.

Level of interest: An article of outstanding merit and interest in its field

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.