Reviewer's report

Title: Incidence of pelvic inflammatory disease in a large cohort of women tested for Chlamydia trachomatis: a historical follow-up study

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Reviewer: Deborah Dean

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The manuscript is a historical review of the incidence of pelvic inflammatory disease requiring hospitalization among women who tested positive for Chlamydia trachomatis in the past. This is an important study and the evaluation of a large population of young women is a distinct advantage. The authors found a significant association between prior infection and hospitalization for pelvic inflammatory disease. The manuscript is well written but requires some major clarifications and additional analyses.

Major Compulsory Revision:

Abstract: Since the authors conclude that pelvic inflammatory disease was a rare event, the results should include the numbers that resulted in the elevated hazard ratio. Also, since age would likely impact the results, a stratification by age and recalculation of the hazard ratio would be important to perform and include in the abstract.

Background: Abbreviations should be defined first before use (e.g., CT). The rate of one in six Norwegian women being positive for CT by the age of 25 is important data. It would be equally important to further breakdown these data and determine the number with only one infection versus those with more than one infection in terms of timeframe for occurrence of recurrent infection. Multiple infections will have a greater impact on the outcome of pelvic inflammatory disease. Also, how do these data compare with other countries? This should be discussed in the background.

Methods and Results: The different tests used for diagnosis would affect the sensitivity and specificity of detection, and thus the data used for analysis. Some discussion of this should be included — certainly in the discussion section.

It is not clear why data collected at 60 days after the previous test were not used. If there is documentation of treatment, these data would provide important information on recurrent infection which would be more likely to impact outcome.

Why were data on pelvic inflammatory disease not collected from 1990 onwards? This might give more information on pelvic inflammatory disease that occurred temporally closer to the CT infection. Please state the temporal occurrence of pelvic inflammatory disease in relation to testing positive for CT.

For data analyses, it is not clear how many women were at each age under 20
years and what the youngest age was. Why was 20 years of age selected as the cut off? High rates of CT infections occur throughout the 20 to 30 year age group. This would also allow for more occurrences of the outcome as a first time event. A stratification of the analyses for very young adolescents versus older adolescents and young adults would be important to do to better understand the risk across the adolescent to young adult age span. Use of hospitalized pelvic inflammatory disease captures only the most severe form of disease while mildly symptomatic infection treated as an outpatient would still be a risk for infertility and ectopic pregnancy. Obviously, asymptomatic pelvic inflammatory disease would be missed, likely has a significant impact on the complications listed above and could not be measured by the present study design. Thus, the conclusion that “pelvic inflammatory disease is a rare event irrespective of C. trachomatis status” is unfounded based on the current study design and should be changed.

The authors should state if the Declaration of Helsinki was followed.

Discussion: It is not clear from the methods that the authors identified all cases of pelvic inflammatory disease from hospital in and outpatient registries. This should be clarified. Also, while the authors start to mention use of less sensitive tests in the Swedish study, this is really essential to discuss in more detail for their own study as a limitation because earlier less sensitive tests were used. Perhaps evaluating data for women who were tested with the more sensitive nucleic amplification tests would provide a more robust analysis and greater confidence in the results. Again, the conclusion is faulty because the study did not assess rates of outpatient treated pelvic inflammatory disease and asymptomatic pelvic inflammatory disease both of which will contribute to the severe sequelae of C. trachomatis infections.

Level of interest: An article of importance 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.