

# The importance of understanding pelvic inflammatory disease as a polymicrobial infection - authors' reply



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We thank Prof. Kenyon for their suggestion<sup>1</sup> to also consider a possible role of interactions between Chlamydia trachomatis (CT), Neisseria gonorrhoeae (NG), and bacterial vaginosis (BV) on reproductive tract complications.<sup>2</sup> While our cohort study design limits our ability to assess potential mediating or direct effects of non-CT infections,<sup>3</sup> it offers some considerations. NG was reported by only 2.1% (n = 120) of people and of those who were NG positive a majority (75%) also had a history of CT (in people without NG that was 36%). Adjusting for exposure time and covariates, NG was not associated with pelvic inflammatory disease nor did NG mediate the association between CT and pelvic inflammatory disease.<sup>2</sup> We did not analyze microbiota. However, in case BV would be more prevalent in people with symptomatic CT than in those with asymptomatic CT, co-occurring BV symptoms could possibly be mistaken for CT symptoms or partly explain observed risk differences. In our analysis of 797 persons with symptomatic CT, we found just 35% reported having abnormal/malodorous discharge as their only symptom

(a common symptom of both chlamydia and BV).<sup>4</sup> The majority reported additional symptoms, such as bleeding between periods or pain by urination or during sex. We conducted additional statistical analyses and found the CT-associated risk of pelvic inflammatory disease for people with only abnormal/malodorous discharge to be much lower (adjusted hazard ratio (aHR) 1.20 95% confidence interval (CI) 0.61–2.34) than for symptoms other than discharge (aHR 2.74 95% CI 1.88–3.98). These findings support our assumption that the reported symptoms are directly related to CT and the subsequent pelvic inflammatory disease. Finally, it should be noted that our reported estimates of symptomatic CT were corrected for BV-related factors, such as ethnicity, intrauterine device use, number of sex partners.<sup>5</sup> Hence, we expect our findings and conclusions relating to symptomatic CT to be robust, even if we cannot rule out a potential polymicrobial genesis of pelvic inflammatory disease.<sup>2</sup> Early pelvic inflammatory disease detection and treatment remain crucial, regardless whether microbial causes are singular or

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multimicrobial, supporting a low-threshold approach to STI testing for individuals with symptoms.

#### Contributors

ZWA conducted the analyses and drafted the manuscript. NHTMD-M and MABvdS provided revisions. The final manuscript was reviewed and approved by NHTMD-M, MABvdS, BHBvB, SAM, CJPAH, HMG, HJcDv, JEdH and BMH, all of whom accept responsibility for its submission for publication.

#### Declaration of interests

We declare no competing interests.

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