

# Proceed With Caution in Generating Evidence in the "Oropharyngeal-Anorectal Chlamydia Hypothesis" in Humans

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## Proceed With Caution in Generating Evidence in the “Oropharyngeal-Anorectal Chlamydia Hypothesis” in Humans

### To the Editor

There is an on-going debate on whether oropharyngeal *Chlamydia trachomatis* (CT) infections can inoculate the human gastrointestinal tract, and subsequently lead to anorectal CT infections.<sup>1–3</sup> Evidence in animals suggests that chlamydia bacteria can undergo gastrointestinal passage.<sup>1,2</sup> However, no evidence exists in humans. We have read the article by Batteiger et al.<sup>4</sup> with great interest and compliment the authors with their attempt to provide answers on this hypothesis in humans. The authors assume that oral sex (cunnilingus) leads to oropharyngeal CT infections, as they look into the relation between oral sex and anorectal infections, without testing for oropharyngeal CT infection. Although there have been speculations,<sup>3</sup> it has not yet been proven that oral sex leads to oropharyngeal CT infections. The authors conclude that anorectal CT infections could result from inoculation via the GI tract after the self-report of oral sex. From an epidemiological point-of-view, the current study does not provide enough evidence to draw this conclusion.<sup>5</sup>

Batteiger et al.<sup>6</sup> used a cross-sectional study design. This design is often chosen to report descriptives or prevalence and lacks the ability to infer causality. In their study, no statistical tests or adjustment for potential confounders were done to assess the relation between cunnilingus and anorectal CT. Additionally, the authors did not describe a control group. Among men who did not report cunnilingus or reported anal behaviors, none had anorectal CT (0%; 95% confidence interval [CI], 0.0–0.7). When we look at men who report cunnilingus and denied anal sex behaviors, 2 (2.4%) men had anorectal CT infection (95% CI, 0.3–8.3). The confidence intervals of both groups are large and overlap. The exact difference between these

groups (2.4%; 95% CI, –0.88 to 5.64) includes zero, and thus, there is no difference between both groups. Moreover, the power of the study is low, as the authors based their findings on a population of 84 men, of which 2 were anorectally CT positive. Because of these small sample numbers, this finding could be based on coincidence. The 2 anorectal CT infections could be acquired through other ways (e.g., underreported anorectal behavior). We compliment the authors in their efforts to maximize the accuracy of the self-reported sexual behaviors. However, as the authors describe in their discussion, when using self-reported data, it cannot be ruled out that these self-identified heterosexual men had engaged in anorectal activities, and thus, information bias could have occurred.<sup>7</sup> This is not unlikely as they showed that men who identify themselves as heterosexual also report anorectal sex or sex with men.

We studied the oropharyngeal-anorectal hypotheses using a large longitudinal data set of MSM and women (n = 21,245) and found no statistically significant independent association between preceding oropharyngeal and subsequent anorectal infections (adjusting for confounders).<sup>8</sup> Although cross-sectional studies do not have the optimal design to infer causality, Batteiger's study contributes to understanding the oropharyngeal-anorectal hypothesis in humans. However, in our view, the scientific evidence from Batteiger et al. is too weak to draw conclusions regarding the oropharyngeal-anorectal hypothesis in humans, and we advise caution for overinterpreting results.

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