Reviewer’s report

Title: Differential sexual network connectivity offers a parsimonious explanation for population-level variations in the prevalence of bacterial vaginosis: a data-driven, model-supported hypothesis

Version: 1 Date: 04 Sep 2018

Reviewer: Ashley Hazel

Reviewer's report:

I think the general goal of this paper and its insights are intriguing and important. Understanding more about the transmitted nature of BV and BV-associated microbiota is critical for a comprehensive understanding of STI risk and burden, especially among undertreated populations. I think this paper is on its way to being published, but I recommend a few important changes first.

Major issues:

--A big issue as I read this paper is that I do not understand the fundamental structure of it. Is this a review or an original study? The authors present a single new model of the relationship between concurrency and BV transmission, but the rest of the paper reads like a synthesis of previously reported studies and data, i.e., a review paper. In isolation, both approaches are worthwhile but are rather thin. I suggest reworking the manuscript to have a standard original research paper structure (Introduction, Methods, Results, Discussion, etc.) that focuses on the model and the hypothesis it is testing. The review material can be reframed in Introduction and Discussion sections to motivate the model and expand upon its utility to public health.

--I have a few concerns about how the model is parameterized. As is, I think it is overly simplistic and not reliable to use to understand the likely complex process of BV-VMB transmission. However, the changes I suggest are very doable and would yield much more meaningful results.

First, the high-connectivity model basically allows individuals to choose any new eligible partner at each time step, and any eligible partner is someone of the opposite sex. While it is perfectly sensible when modeling some populations to assume total heterosexuality in sexual partner selection, that choice should be explicitly stated and an argument should be made for this. If the model is kept very simple in order to be more generalizable, than the decision to restrict it to opposite sex partnerships needs to be justified. On the other hand, the total lack of any other kind
of sorting beyond heterosexuality constructs a very unrealistic partner-selection landscape and biases the model in favor of stark transmission differences in comparison with the low-connectivity population. If people choose their partners with the same probability across the population, then you essentially have random-mating conditions, which is both unrealistic and well established to lead to much higher transmission rates of STIs. Some type of sorting behavior should be included. I know you mentioned the potential to add such complexities at the end of the manuscript, but I think this is too fundamental to the nature of sex-partner choice to leave it as a hypothetically nice addition down the road.

Also, I think it is unrealistic to assume 100% transmission of BV-VMB after having sex with a partner with a BV-associated microbiota. Surely, there are many factors, including a person's native CST, that would lead to variation in transmission. I realize that you probably do not have enough evidence to confidently estimate the transmission probability, but I would either choose a more conservative value (even somewhat arbitrarily), or run the model over a distribution of probabilities. Using 100% transmission biases your model to producing positive results for the comparison between high- and low-connectivity populations.

Minor issues:

--In the abstract (p3, l5), the authors state that vaginal microbiome types "vary dramatically between different populations around the world." Given that the field is generally in agreement that there are five community state types among women across many populations, I don't understand the characterization "varies dramatically."

--Early in the background section (p4, l31-37), the authors state that "Several longitudinal VMB studies have concluded that the VMB can be relatively stable over time, as well as be quite dynamic in a minority of women." What do you mean? These sound like opposite characterizations of the VMB, so can you explain how they can both be true? Are you saying that in most women, the VMB is stable, but in some it is very dynamic? Or are you saying that it can occasionally become very dynamic for short periods of time in some women? Is there any understanding about why or under what conditions stability varies?

--p12, l31-42, "These considerations leave us to conclude that the most parsimonious explanation for why the prevalence of BV and various STIs is higher in certain populations than other is that these populations have more densely connected sexual networks." I would say "predict" rather than "conclude" because you do not have the ethnographic evidence from a range of high-risk populations to make this conclusion. Rather you are hypothesizing that this is what you would find, if the data were available.

--p13, l12: What does "genetically promiscuous" mean?
--p14, l46: Is enough known about penile microbiota to say that they too should be classified into 5 CSTs?


--Figure 2: I cannot tell what is happening in the low-connectivity graph over time. Has individual B taken on a new partner? In which case, who is now attached to A? Or, rather, is B representing both nodes now? Please make this graph and its labeling of nodes more clear.

Typos and corrections:

p6, l12: "Consistent condom use has been shown in a meta-analysis to BE[insert] associated..."

p8, l7: Sentence needs comma immediately after references and before the word "studies."

p12, l18-22: Sentence needs a comma or colon after phrase "This explanation begs the question...." I also recommend moving "however" to the beginning of the sentence (with a comma following it).

p12, l27: Remove word "explanation" from sentence. It is unnecessary and sounds redundant with later use of "explain."

p13, l12: "...P. maniculatus had a greater vaginal microbiome diversity...." Delete "a."

p14, l29: "...rapid spread of BVAB and the various other STIs...." Delete "the."

p15, l41: "...could translate inTO[insert] large declines...."

p18, l5: "...study of Zozaya et al...." Should be "by" Zozaya, not "of."

--Also, I found several typos in the supplemental material file, "Network Model Description." Please look that over and fix.

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

Yes

**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.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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I am able to assess the statistics

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