Title: Boric Acid, Alternate Solution for Intravaginal Colonization (BASIC) Study: A study protocol for a double blinded, randomized controlled trial comparing intravaginal metronidazole to boric acid and to placebo in symptomatic bacterial vaginosis.

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Reviewer: Ralph D’Agostino

Reviewer’s report:

My comments and issues are as follows:

1. On page 5 it is stated that the objective of the trial is to determine non-inferiority of intravaginal BA to standard treatment metronidazole, for the cure of BV in symptomatic women compared to placebo. This is a strange way to describe a non-inferiority trial. Why is the placebo in the trial? Will there be a test of each drug to placebo and then to each other. The manuscript is never clear on this. The role of the placebo is needed. The comparison of the drugs needs a better explanation.

2. The Design section says nothing about the study design. It reads more like a build up to the sample size determination.

3. From where does the 10% non-inferiority margin come? This needs justification (both in terms of statistics and clinical significance).

4. Should the Participants and Eligibility section make clear which visits (or which time period/days) are on drug, what visit is for the primary outcome and what visit is for the follow up? How many visits if any will be while the participants are on drug?

5. The Randomization section is confusing. It appears routine, but reads as if it is very elaborate. It needs to be made clearer.

6. The Outcomes and Assessment section does not make clear what is the primary outcome visit. It states "at the time of the outcome assessment." Why cannot something simple such as stating again what exactly is the visit for the primary outcome which is the Nugent score.

6.1. The section says the primary outcome is measured at 7 days and 30 days. Are there two primary outcomes or is one time for the primary and one time for the secondary measure? See question 7.2. below.

7. The Statistical Consideration section is very poorly written.

7.1. What is the primary analysis (ITT or Per protocol)? If both are performed
what if they do not agree?

7.2. The Statistical section says analysis will be done at 7 days and 30 days after treatment end for effectiveness. What is primary? The Abstract states that the primary outcome is treatment effectiveness at day 7 but the main manuscript confuses this. Do the authors want both the 7 and 30 day outcomes to be primary? Or is one primary and the other secondary? The use of the Nugent score at day 7 an 30 does not make them both primary outcomes. Clarification is needed.

7.3. How does the placebo fit into the analyses?

7.4. How will multiple testing be controlled? There are 3 treatments, two times when efficacy analyses will be performed and two data set (ITT and PP). How will the error rate be controlled?

8. I believe missing data are covered, but it might be helpful that the authors give that another look.