Author's response to reviews

Title: Self-medication with Antibiotics for the Treatment of Menstrual Symptoms in Southwest Nigeria: A Cross-sectional Study

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Author's response to reviews: see over
BMC Public Health
Melissa Norton, MD
Editor-in-Chief

Re: Revisions to MS: 1790606207373396

Dear Dr. Norton:

Thank you for providing us with the opportunity to revise our manuscript, MS: 1790606207373396, which is now entitled “Self-medication with Antibiotics for the Treatment of Menstrual Symptoms in Southwest Nigeria: A Cross-sectional Study.”

We have carefully gone through each of the reviewers’ comments, accepted all of their suggestions, and completed major revisions to the manuscript. This included completely reworking the methods, results and discussion sections of the manuscript. We feel that the revised manuscript is greatly improved as a result of these major revisions. Please see our point-by-point responses (italicized and highlighted in blue) to each of the reviewer’s comments on the following pages.

In this study, we report for the first time that approximately 1 out of 4 university women surveyed in Southwest Nigeria self-medicate with antibiotics to treat menstrual symptoms. Factors associated with this usage were: lower levels of education; non-science major; usage of analgesics; and mild to extreme heavy bleeding and acne.

We feel that these novel data would be of great interest to readers of *BMC Public Health* who span a diverse array of disciplines involving epidemiology; social and behavioral determinants of health; and community-based interventions; all of which are relevant to the topic and findings of this study.

Thank you for your time and kind consideration. We look forward to hearing from you.

Sincerely yours,

Amy R. Sapkota, Ph.D, M.P.H.
Reviewer 1: Abdelmoneim Awad

Reviewer's report:

General Comments
- This paper describes a cross-sectional study exploring the prevalence of self-medication with antibiotics for the treatment of menstrual symptoms among university students and to identify factors associated with this practice. The aim of the study is interesting but I do have significant concerns about the research methodology and the sampling method used. Moreover, the paper lacks appropriate presentation of the results and discussion of key findings. There are major concerns that should be addressed. I offer the following comments which I hope will improve the manuscript.

Authors' Response to General Comments: We agree with the reviewer that additional details regarding the research methodology and sampling approach used in the study strengthens the manuscript and is helpful to readers. We also agree that 1) providing more details in the results section, and 2) focusing the discussion section greatly improves the manuscript. We have painstakingly gone through all of the reviewers’ specific comments (please see below) and accepted all of the reviewers’ suggestions. This included completely reworking the methods, results and discussion sections of the manuscript. We feel that the revised manuscript is greatly improved as a result of these major revisions.

Major Compulsory Revisions

Title: I would suggest to be changed to “Self-medication with antibiotics for the treatment of menstrual symptoms in Southwest Nigeria”

Authors’ Response: The title has been changed to “Self-medication with Antibiotics for the Treatment of Menstrual Symptoms in Southwest Nigeria: A Cross-sectional Study.” We have kept “A Cross-sectional Study” in the title because the journal’s instructions to authors advise authors to include the study design in the title.

Abstract
- The methods are not adequately described in relation to sampling (convenience or random), data collection (self-administered or structured face-to-face interview). The last sentence to be changed to “Descriptive and logistic regression analysis were used in data analysis.”

Authors’ Response: Thank you for pointing out these omissions in the abstract. The sampling and data collection methods have been included and the last sentence has been changed to include our descriptive methods. The methods section of the abstract (lines 36-41) now reads:
“A cross-sectional survey was administered to female undergraduate and graduate students (n=706) at four universities in Southwest Nigeria in 2008. The study sample was a randomly selected cluster sample, and the survey was self-administered. The survey included questions pertaining to menstrual symptoms, analgesic and antibiotic use patterns, and demographics. Data were analyzed using descriptive statistics and logistic regression.”

- Results: The findings need to be presented more clearly with exact percentages, precision of measures (95% confidence intervals), odds ratio (95% CI) and p-values.

**Authors’ Response:** We agree with the reviewer that the findings should be presented in more detail in the abstract. We have incorporated exact percentages, 95% confidence intervals, odds ratios and their associated 95% CIs and p-values throughout the results section of the abstract. The results section of the abstract (lines 43-58) now reads:

“Forty percent (95% confidence interval (CI): 37-44%) of participants were science, public health or medicine majors, and 55% (95% CI: 53-60%) were non-science majors. Eighty-six percent (95% CI: 83-88%) of participants experienced menstrual symptoms, and 39% (95% CI: 36-43%) reported using analgesics to treat them. Overall, 24% (95% CI: 21-27%) of participants reported self-medicated use of antibiotics to treat the following menstrual symptoms: cramps, bloating, heavy bleeding, headaches, acne, moodiness, tender breasts, backache, joint and muscle pain. Factors associated with this usage were: lower levels of education (Odds Ratio (OR): 2.8, 95% CI: 1.1-7.1, p-value: 0.03); non-science major (OR: 1.58, 95% CI: 1.03-2.50, p-value: 0.04); usage of analgesics (OR: 3.17, 95% CI: 2.07-4.86, p-value: <0.0001); and mild to extreme heavy bleeding (OR: 1.64, 95% CI: 1.01-2.67, p-value: 0.05) and acne (OR: 1.57, 95% CI: 0.98-2.54, p-value: 0.06). Ampicillin, tetracycline, ciprofloxacin and metronidazole were used to treat the most symptoms. Doctors or nurses (6%, 95% CI: 4-7%), friends (6%, 95% CI: 4-7%) and family members (7%, 95% CI: 5-8%) were most likely to recommend the use of antibiotics for menstrual symptoms, while these drugs were most often obtained from local chemists or pharmacists (10.2%, 95% CI: 8-12%).”

- Conclusions: This section needs to be revised to highlight major findings of the study and focus on need for further investigation of impact of self-medication on student health, etc.

**Authors’ Response:** We have revised the conclusions section of the abstract to better highlight the major findings of the study. We have also included a sentence concerning the need for further investigations concerning the impacts of self-medication on student health. However, because the revised results section of the abstract is significantly longer (due to the addition of 95% CIs, ORs and p-values) we had to keep this section short and concise. The revised conclusions section of the abstract (lines 60-64) now reads:
“This is the first formal study to report that 1 out of 4 university women surveyed in Southwest Nigeria self-medicate with antibiotics to treat menstrual symptoms. This practice could provide monthly, low-dose exposures to antibiotics among users. Further studies are necessary to evaluate the impacts of self-medication on student health.”

Introduction

- It is written with information that is relevant to the study. There should be a short paragraph in the introduction on why the certain background factors were studied. It is preferred to include the following reference: A. O. Afolabi. Factors influencing the patterns of self-medication in an adult Nigerian population. Annals of African Medicine Vol. 7, No.3; 2008:120 – 127

Authors’ Response: We agree that a short paragraph regarding the factors that were studied would strengthen the introduction. We have added the following paragraph to the end of the introduction of the revised manuscript (lines 113-122) and included the suggested reference that was erroneously omitted from the first version of the manuscript:

“Therefore, the purpose of the present study was to determine the prevalence of self-medication with antibiotics for the treatment of menstrual symptoms among university women in Southwest Nigeria and to evaluate factors associated with this practice. Our pilot study [6] and a recent study conducted by Afolabi in Lagos State, Nigeria [18], informed the selection of factors evaluated in the present study. Afolabi identified that education and marital status were important factors influencing self-medication, as well as where women obtained medications [18]. We evaluated these factors and other factors that could potentially be associated with the use of antibiotics for the treatment of menstrual symptoms including sexual activity status and childbirth history [6].”

Methods

- In order to help readers understand the context of the study it would be helpful if the authors provide some additional background information on the subject pool. Number of universities in Nigeria and Southwest Nigeria. Percentages of Nigerians go to university. Socioeconomic status of these students compared to the rest of Nigeria.

Authors’ Response: We agree with the reviewer that some additional background information on the universities included in the study, as well as the Nigerian university system, would be helpful to readers. We have included this new information on lines 124-160 of the revised manuscript:

“Survey Setting

This study was carried out in February 2008 at four universities (two public and two private universities) located in Southwest Nigeria. The public universities were the University of Ibadan (>12,000 total students) located in Oyo State and Obafemi Awolowo University (25,000 total students) located in Osun State. The private
universities were Covenant University (6,000 total students) and Babcock University (6,000 total students), which are both located in Ogun State. The proportion of female students is approximately 50% at each of these universities. These universities were included in the study because students attending public versus private universities often represent different socioeconomic groups and we sought to evaluate whether socioeconomic status is one potential factor that influences the use of antibiotics for menstrual symptoms among university women. It is noteworthy that the socioeconomic status of students attending public universities is more or less a direct reflection of Nigerian society since no undergraduate tuition is charged at public universities and on-campus accommodations are heavily subsidized[19]. In comparison, tuition at private Nigerian universities ranges between $2,500 to $4,000 [19]. Thus, enrollment in private institutes seems to be reserved for wealthier citizens since monthly wages can range anywhere from $37 to $760 [20].

The four universities included in the study account for 12% of the 34 operational universities in Southwest Nigeria which are comprised of 6 federally-funded universities, 10 state-funded universities, and 18 privately-owned universities [21]. These 34 universities represent 33% of the total 104 Nigerian universities which are comprised of 27 federally-funded universities, 36 state-funded universities and 41 privately-owned universities throughout the country [22].

Approximately 69% of Nigerians complete primary school [23], and a World Bank report published in 2000 estimated that higher education in Nigeria only enrolls about 4% of the eligible age cohort [24]. However, a recent report described that the proportion of female students attending Nigerian higher institutions is rising, even in programs such as law, medicine, arts, and pharmacy that were previously dominated by males [21]. In addition, a source at the National Universities Commission also indicated that the percentage of female students at Nigerian universities as of the 2008/2009 academic session had risen to about 47% of overall students, while some universities report even higher female populations. For example, Babcock University (one of the private universities included in this study) reported that 51% of their student population was female during the 2007/2008 academic year [21].

Why was n = 706 chosen? Was a sample size calculation done, or was this simply chosen as a round number? The authors did not show any justification for the inclusion of this sample size. The effects of confounders, as opposed to chance effects, are not reduced with increasing the sample size ( Bennan P, Croft P. Interpreting the results of observational research: chance is not such a fine thing. BMJ,309:727-30, 1994). The authors need to indicate how the sample size was calculated, and the power used to determine the difference in population for between different groups at 5% significance level.

Authors’ Response: A sample size calculation was performed using the following equation for the calculation of sample sizes for prevalence studies from Daniel WW (1999). Biostatistics: A Foundation for Analysis in the Health Sciences. 7th edition. New York: John Wiley & Sons:
In our calculation, we used $Z = 1.96$ (corresponding to a 95% level of confidence, which is a conventional level of confidence typically used in epidemiologic studies). For $P$, we used an expected prevalence of 0.3. This expected prevalence was estimated from our pilot study (Ojo, KK and Sapkota AR. Self-prescribed use of antimicrobials during menstrual periods: a disturbing new example of information poverty in Nigeria. J Infect Developing Countries 2007; 1(2):123-124.) where we identified that 2 out of 5 (40%) young female students and nurses interviewed at a market reported using at least one antibiotic to treat menstrual symptoms. We decided to use $P = 0.3$ instead of $P = 0.4$ because we estimated that there may be significant variability around this point estimate and we wanted to use a more conservative estimate of prevalence. For precision, we used $d = 0.05$, which is a typical and appropriate value for precision when the observed prevalence is expected to be between 10% and 90%.

Using these values, we calculated an initial $n = 323$. However, because our sample was a cluster sample and not a simple random sample, a design effect of 2 was assumed. This is a typical design effect value used in cluster sampling. Therefore, $n = 323 \times 2 = 646$. This sample size was then increased by 5% to account for potential non-responses: $646 \times 1.05 = 679$. This sample size was then rounded up to a number that would be easily divided by 4 (the number of universities included in the sample). Hence, we arrived at a targeted $n = 700$. Our ultimate $n$ of 706 met our targeted goal. NOTE: To add even more “cushion” to our numbers we instructed our survey administrators to administer an additional 5% of surveys, resulting in 740 surveys that were actually administered.

To address the reviewer’s concerns we have included the following additional information concerning the sample size calculation in the revised manuscript (lines 162-172):

\[
 n = \frac{Z^2 P(1-P)}{d^2}
\]

where $n$ = sample size,
$Z$ = $Z$ statistic for a level of confidence,
$P$ = expected prevalence or proportion
$d$ = precision

"A sample size calculation was performed using the following equation: $n = (Z^2 \times P(1-P))/(d^2)$, where $n$ = sample size, $Z$ = $Z$ statistic corresponding to a chosen level of confidence, $P$ = expected prevalence, and $d$ = precision [25]. In our calculation, we used $Z = 1.96$ (corresponding to a 95% level of confidence, which is a conventional level of confidence typically used in epidemiologic studies), $P = 0.3$ and $d = 0.05$. After adjusting for the clustered nature of the sampling approach used in this study (multiplying the sample size by two), accounting for potential non-responses (increasing the sample size by 5%) and rounding up to a number that could be easily divided by
four (the number of universities included), these calculations indicated that a sample size of 700 would allow for an estimation of our expected prevalence of 0.3.”

-The authors did not indicate how the universities and the schools were selected? Are these the only universities in Southwest Nigeria?

**Authors’ Response:** These are not the only universities in Southwest Nigeria. They were chosen for inclusion in the study because we wanted to include two public and two private universities in the study. Please see lines 131-141 where we have expanded on our reasoning for including these specific universities:

“These universities were included in the study because students attending public versus private universities often represent different socioeconomic groups and we sought to evaluate whether socioeconomic status is one potential factor that influences the use of antibiotics for menstrual symptoms among university women. It is noteworthy that the socioeconomic status of students attending public universities is more or less a direct reflection of Nigerian society since no undergraduate tuition is charged at public universities and on-campus accommodations are heavily subsidized[19]. In comparison, tuition at private Nigerian universities ranges between $2,500 to $4,000 [19]. Thus, enrollment in private institutes seems to be reserved for wealthier citizens since monthly wages can range anywhere from $37 to $760 [20].”

Please also see our response above on pages 4-5 where we outline the “setting” of these universities in more detail.

-The authors stated that the study participants were recruited from residence halls and from lecture halls, this a classic example of a convenience sampling. Hence, the sample could be biased and not a truly random sample. This is a major limitation that undermines the validity of this study. The findings of such a type of study should be based on data obtained using a multi-stage cluster sample. The use of multi-stage cluster sampling is the most appropriate for studies of this nature. Moreover, the authors did not show how they accounted for selection and information biases.

**Authors’ Response:** We agree with the reviewer that more information is needed in the manuscript to describe our sampling approach. This study employed random sampling, not convenience sampling, at each participating university. To address the reviewer’s concerns, we have provided additional details regarding the specific sampling strategy that was employed in the residence halls and the lecture halls of the participating universities (lines 175-194):

“At the University of Ibadan, Covenant University and Obafemi Awolowo University, study participants were recruited from residence halls. The sampling strategy at these universities was a three-stage cluster sampling plan. Female residence halls that housed both undergraduate and graduate students were randomly selected for inclusion
in the study. Within the residence halls, blocks of rooms were then randomly selected for inclusion in the study. Within the undergraduate blocks, our survey administrators visited every sixth room and invited every resident of those rooms to participate in the survey. Within the graduate blocks, our survey administrators visited every third room (since fewer students live in graduate rooms) and invited every resident of those rooms to participate in the survey.

At Babcock University, study participants were recruited from lecture halls because (to our dismay) we were ultimately not granted access to the residence halls at this university. Instead of eliminating this university from the study, we thought that it would still be valuable and informative to capture study participants at this university through a random sampling of lecture halls. Thus, at Babcock University, a one-stage cluster sampling strategy was employed. Lecture halls that housed both undergraduate and graduate classes were randomly selected for participation in the study and every female student within the randomly selected lecture halls were invited to participate in the study."

The clustered sampling approach employed in this study allowed us to reduce the impacts of selection bias. Selection bias and information bias were then controlled for in our logistic regression analyses. For example, to address information bias, analyses were stratified by education level and by area of study, based on the assumption that higher levels of education, particularly in the health sciences, may result in more informed participants with regard to appropriate antimicrobial uses.

-It seems bizarre, and most unlikely, that all 706 students approached agreed to participate. I find it hard to believe that the response rate was 100%. This needs to be clarified.

Authors’ Response: We agree with the reviewer that the response rate needs to be reported. We have clarified this in the revised manuscript on line 264: “A total of 706 out of 740 administered surveys (95% response rate) were completed and returned…”

-The authors should mention whether or not an incentive was offered for completion of the questionnaire. If there is any information about those who elected to not complete the questionnaire that should be mentioned as well (age, public/private university). Were non self-medicators asked why they didn’t self-medicate?

Authors’ Response: No incentive was offered for completion of the questionnaire. This is clarified in the following sentence that was added to the revised manuscript (line 198): “No incentive was offered for completion of the survey.”

There are no data pertaining to those who elected not to complete the questionnaire. Non self-medicators were not asked why they did not self-medicate (please see the uploaded survey).

-Study Questionnaire
-Please provide a copy of the survey questions for peer review and for inclusion as an Appendix in the event of publication.

**Authors’ Response:** A copy of the survey has been provided along with the revised manuscript.

-Has a pilot study been conducted? If yes, the number of students in whom the questionnaire was pre-tested should be indicated. Also, it whether there were any modifications in the questionnaire after the pilot study or not should be indicated. If any, what was the extent of the modifications?

**Authors’ Response:** A pilot study that is referenced in this manuscript (Ojo, KK and Sapkota AR. Self-prescribed use of antimicrobials during menstrual periods: a disturbing new example of information poverty in Nigeria. J Infect Developing Countries 2007; 1(2):123-124.), as well as a focus group included in the present study, were conducted.

To address the reviewer’s concerns, we have added additional details regarding the conduct and results of the pilot study and focus group in the revised manuscript (lines 201-214):

“Qualitative interviews conducted among twenty-seven young Nigerian women who anecdotally reported using antibiotics to normalize menstrual flow and treat discomfort associated with menstruation [6] informed the initial content and focus of the survey. A preliminary version of the survey was then piloted among a focus group of nine female instructors and students at the University of Ibadan to evaluate language, content, and sensitivity of the instrument [26]. Overall, focus group participants indicated that the survey was “good,” “straight forward,” and “important.” However, focus group participants did suggest that a few minor edits should be incorporated into the final survey. For example, focus group participants indicated that the word “acne” should be accompanied with the word “pimples” in the survey. They also felt that one additional column indicating that “I do not take antibiotics” should be incorporated into all questions regarding the use of antibiotics to treat menstrual symptoms. These edits were incorporated and the revised survey instrument was also visually reformatted to improve flow and conceptual clarity [27].”

-A clearer definition of what self-medication means in the context of local understanding in Nigeria would be helpful, and how was it defined to the study participants.

**Authors’ Response:** In the manuscript, we have referenced the World Health Organization’s definition of self-medication. At the outset of this study, we were not sure whether all uses of antibiotics for the treatment of menstrual symptoms did indeed fall under the “self-medication” paradigm. Our pilot study (Ojo, KK and Sapkota AR. Self-prescribed use of antimicrobials during menstrual periods: a disturbing new example of information poverty in Nigeria. J Infect Developing Countries 2007; 1(2):123-124.)
124.) indicated that this might be so, but we did not want to make any assumptions before embarking on this study. Therefore, self-medication was not explicitly defined to the study participants. As evidenced in the survey, we kept it open, and instead, we wanted to collect information on all types of antimicrobial uses for the treatment of menstrual symptoms. Our ultimate data analyses, however, did indicate that women who used antibiotics to treat menstrual symptoms were “self-medicating.” These data arose from questions 4, 16, 18, and 22 (please see the uploaded survey).

- Could the authors explain why they did not include questions about inappropriate use of antibiotics (i.e. incorrect dosing, duration)?

Authors’ Response: We are unclear about the meaning of this question/comment. Please clarify. In our open ended question (Question #22), we made the following statements and asked the following questions of participants: “This survey contains a lot of questions about different types of medication that women may take to treat menstrual symptoms. Several questions are about ANTIBIOTICS. What do you know about ANTIBIOTICS? Have you heard about using specific antibiotics or other medication as treatment for menstrual symptoms? From whom did you hear this? Have you participated in any other survey on menstrual symptom treatments and/or antibiotics use before?” Is this what the reviewer is alluding to in this comment?

-Did the authors evaluate financial status of students? If so, should include that valuable information, and could help in discussing the results of comparison between public and private universities that should be conducted.

Authors’ Response: The reviewer brings up an important issue that was discussed extensively while we were formulating the survey. After much discussion, questions regarding financial status were dropped from the initial survey instrument (even before the conduct of the focus groups) because our Nigerian collaborators felt that these types of questions were too invasive and would likely go unanswered.

-Description of the data collection should be included before the data analysis section.

Authors’ Response: We agree with the reviewer that a description of the data collection methods would be helpful to readers. We have included such a description on lines 238-252:

“At each university, the surveys were administered by our Nigerian collaborators, who are instructors or lecturers at the participating universities. Survey administrators introduced themselves to potential study participants (in residence or lecture halls) and invited them to participate in the study using the same script that was uniformly used across all universities. If a potential study participant indicated that she wanted to participate, then the survey administrator would hand out the consent form and deliver additional scripted instructions regarding the consent form. If a potential study participant then agreed to participate, and signed the consent form, then the survey
administrator would provide the participant with the survey instrument, deliver additional scripted instructions regarding the completion of the survey, and then step out of the room such that the participant could complete this self-administered survey without the influence of the survey administrator. After 20 minutes, the survey administrator would re-enter the room, deliver additional scripted instructions regarding the collection of the survey instrument and thank the participant for her time.”

-The authors performed simple descriptive analysis that does not allow the calculations of the precision of their estimates (i.e., 95% confidence intervals). A better approach for data analysis and interpretation of the present results should involve calculations of the precision.

Authors’ Response: We agree with the reviewer that calculating and reporting the precision of our estimates would improve our results section. This has been completed. Please see the following new text in the revised manuscript:

(lines 268-273), “Forty percent (95% CI: 37% to 44%) of the study participants were lab science, public health, or medicine majors, and 55% (95% CI: 53% to 60%) of the participants were non-science majors. Eighty-two percent (95% CI: 79% to 85%) of the study participants were between the ages of 17 and 24, and 86% (95% CI: 84% to 89%) of the participants were single.”;

(lines 276-281), “The majority of study participants (88%: 95% CI, 86% to 91%) reported experiencing three or four menstrual periods during the three-month time period that served as the focus for this study. Eighty-six percent (95% CI: 83% to 88%) of participants reported experiencing pain or discomfort associated with their menstrual periods during this time frame. Yet, only 21% (95% CI: 18% to 24%) of study participants reported ever having seen a doctor or nurse…”;

(lines 288-296), “When asked about the self-medicated use of analgesics and other pain-relieving medications, such as aspirin and ibuprofen, 39% (95% CI: 36% to 43%) of respondents reported that they had used these types of medications to treat menstrual symptoms in the past three months. The usage prevalence for these drugs was as follows: aspirin, 2% (95% CI: 1% to 3%); Panadol (paracetamol), 29% (95% CI: 26% to 33%); Panadol Extra (paracetamol and caffeine), 7% (95% CI: 5% to 9%); ibuprofen, 9% (95% CI: 7% to 12%); buscopan (butylscopolamine), 10% (95% CI: 8% to 12%); Feldene (piroxicam), 11% (95% CI: 8% to 13%); and other drugs, 11% (95% CI: 8% to 13%). These other drugs included, but were not limited to, codeine, Midol, Tylenol and Advil.”;

(lines 298-299), “Overall, 24% (95% CI: 21% to 27%) of the study population reported using antibiotics to treat menstrual symptoms in the past three months.”;

(lines 301-312), “Interestingly, the prevalence of self-medicated antibiotic use for menstrual symptoms varied depending on education level (Table 2, Figure 1, Panel A). Graduate level students were 64% less likely to use antibiotics to treat menstrual
symptoms compared with preliminary and undergraduate level students (Odds Ratio (OR) = 0.36, 95% CI = (0.14 to 0.91), p-value = 0.03) (Table 2). In addition, individuals who were non-science majors were 1.58 times more likely to use antibiotics for menstrual symptoms compared with lab science, public health or medicine majors (OR = 1.58, 95% CI = (1.03 to 2.50), p-value = 0.04) (Table 2, Figure 1, Panel B). Study participants who used any pain-relieving medications (e.g. aspirin, ibuprofen) to treat menstrual symptoms were 3.17 times more likely to use antibiotics to treat menstrual symptoms than those who did not use any pain relievers (OR = 3.17, 95% CI = (2.07 to 4.86), p-value = <0.0001) (Table 2)."

"In terms of specific symptoms, those study participants who reported mild to extreme heavy flow/heavy bleeding and mild to extreme pimples/acne associated with menstruation were 1.64 times more likely (OR = 1.64, 95% CI = (1.01 to 2.67), p-value = 0.05) and 1.57 times more likely (OR = 1.57, 95% CI = (0.98 to 2.54), p-value = 0.06), respectively, to use antibiotics to treat these symptoms compared to individuals who reported experiencing no heavy flow/heavy bleeding or pimples/acne (Table 2). Surprisingly, women who reported mild to extreme cramps were 43% less likely (OR = 0.57, 95% CI = (0.36 to 0.91), p-value = 0.02) to use antibiotics…"

"If a preferred antibiotic was not available, 8% (95% CI: 6% to 10%) of study participants reported that they would use another type of antibiotic…";

"When asked whether these antibiotics were effective in relieving symptoms, a number of participants reported that the drugs relieved each of the symptoms, of which the largest proportions indicated that antibiotics relieved backache, joint or muscle pain (10%, 95% CI: 8% to 12%), headaches (10%, 95% CI: 8% to 12%), and cramps (9%, 95% CI: 6% to 11%)…";

"Doctors or nurses (6%, 95% CI: 4% to 7%), friends (6%, 95% CI: 4% to 7%) and family members (7%, 95% CI: 5% to 8%) were the individuals who were most often cited as recommending antibiotics for these symptoms (Figure 2). However, the antibiotics used to treat menstrual symptoms were most often obtained from local chemists or pharmacists (10.2%, 95% CI: 8% to 12%) (Figure 2)."

-The authors performed a multivariate logistic regression analysis that would strengthen the study by providing a more thorough explanation of the relationships between predictive variables, however, no information is provided about the categories of the predictive variable used. Table (1) shows 7 groups of age; 7 groups of level of education; 5 areas of concentration; 7 groups of year of study. The authors need to show how do they classify these groups in the multivariate regression analysis. It is preferred to classify your data of each predictive variable to 2 or 3 groups after that you can compare between the groups to predict factors associated with self-medication. The groups should be defined in the data analysis section.

Authors’ Response: We agree with the reviewer that it would be helpful for readers to see how we categorized each of our predictive variables. We have added a new Table 2
(page 33) to the revised manuscript that indicates 1) the way the variables were
categorized; and 2) the Odds Ratios (ORs), 95% confidence intervals, and p-values
associated with each variable in the model. In this model, we collapsed the “education
level” variable to only 2 groups (compared to all 8 groups that were used for the model
in the original manuscript); therefore, the ORs, CIs and p-values have changed slightly
compared to the original manuscript. These changes appear in the revised manuscript
(Results section and Table 2).

This sentence “Continuous data are presented as mean # 95% CI” should be
included in the data analysis section

Authors' Response: We have included this statement in the statistical analysis section
(lines 260-261): “Continuous data are presented as means, along with their 95%
confidence intervals (CIs).”

Results
- In general, the presentation of the results is poor. A better approach for
presentation of the results is needed.
- The results should be indicated in the text with numbers, prevalence (%) (95%
confidence intervals). The differences in responses according to predictive
variables should be presented in the tables and expressed as odds ratio (95%
confidence interval) and p-value.

Authors’ Response: We agree with the reviewer that the presentation of results could be
improved. We have included the point estimates along with their 95% CIs in the text of
the revised manuscript (please see our response above, pages 11-12), and we have
included odds ratios, 95% CIs and p-values in the new Table 2 (page 33)and results
section of the revised manuscript ((please see our response above, pages 11-12).

- The authors should make sure that results (i.e. numbers, percentages) are
reported in a consistent method.

Authors' Response: We agree with the reviewer and have made sure that the results
are reported consistently in the revised manuscript. Please see our responses noted
above on this page and pages 11-12).

- Table (1) The first three levels of education should be defined at the legend of
the table. I would suggest its presentation with 2 or 3 groups for each predictive
variable. 95% CI should also be included. The numbers and percentages need to
be recalculated, since the total for some the variables is not 706 (100%) for e.g.,
the level of education (697; 95.9%), area of concentration (671; 95%), age (705;
97.1%), marital status (683, 96.8%). An explanation should be provided for these
discrepancies.

Authors’ Response: The first levels of education have been defined in the revised Table
1 (page 32) of the revised manuscript. Preliminary = (Pre-college), Freshman = 100
level, Sophomore = 200 level, Junior = 300 level, and Senior = 400 level. We feel that presenting > 2 groups for each predictive variable provides the readers with a better picture of the study population. Therefore, we have left the original categories of the original Table 1. We also feel that it is not necessary to include 95% CIs in a table that is describing study characteristics. This is very typical of epidemiologic studies that have been published in peer-reviewed journals; thus, we have kept the original format of the original Table 1 where we reported numbers and percentages for each category. We have, however, double-checked our calculations and recalculated numbers and percentages where necessary. The reason for the discrepancies is that some of the questions went unanswered by some participants and therefore we have missing data (as is the case with all survey-based studies). We have explicitly indicated the numbers and percentages of missing data for each category in the revised Table 1 of the revised manuscript.

- Table (2) needs to be replaced with a table showing the percentages (95% CI) of use of the different antibiotics in the treatment of menstrual symptoms.

Authors’ Response: To address the reviewer’s concern, Table 2 has been replaced with a new Table 3 (page 34) in the revised manuscript. The new Table 3 shows the number of study participants (percentages and 95% CIs) who reported using different antibiotics to treat specific menstrual symptoms.

- Figures 1 (A) and (B) to be replaced with tables showing the results of the multivariate regression analysis with odds ratio (95% CI) and p-values.

Authors’ Response: To address the reviewer’s concern, we have added a new Table 2 (page 33) in the revised manuscript that shows the results of the multivariate regression analysis with ORs, 95% CIs and p-values. However, we feel that many readers are more visually (versus quantitatively) oriented; therefore, we would also like to keep Figure 1 (Panels A and B) in the manuscript. In addition, Panel B of this figure offers additional information that does not appear in the text. This type of visual figure in a published manuscript is also useful if readers would like to incorporate the data into future powerpoint presentations.

- Figure 2 to be deleted and the information should be provided in the text with percentages (95% CI).

Authors’ Response: To address the reviewer’s concern, we have included percentages and 95% confidence intervals in the text (lines 340-346):

“Study participants also reported that a variety of individuals first recommended that they take antibiotics to treat menstrual symptoms. Doctors or nurses (6%, 95% CI: 4% to 7%), friends (6%, 95% CI: 4% to 7%) and family members (7%, 95% CI: 5% to 8%) were the individuals who were most often cited as recommending antibiotics for these symptoms (Figure 2). However, the antibiotics used to treat menstrual symptoms were
most often obtained from local chemists or pharmacists (10.2%, 95% CI: 8% to 12%) (Figure 2).”

However, as noted above, we also feel that leaving Figure 2 in the manuscript would be helpful to readers who are more visually oriented (please see our response above). Therefore, if the editors agree, we would like to keep Figure 2 in the revised manuscript.

Discussion
- It should be written considering the aforementioned suggested changes in the results and discussing key findings. It should be strengthened to highlight what is most important, and what is the value added by the present study compared to the previous published reports from developed and developing countries.

Authors’ Response: To address the reviewer’s concerns, we have completely re-written the discussion section in accordance with previous changes noted above. We have emphasized the key findings and clarified the value of the present study compared with previous reports. The sub-sections of the revised discussion are now entitled: key findings; public health implications; comparison with similar peer-reviewed research; future interventions; limitations; and conclusions. Please see lines 348-484 of the revised manuscript which contain the new discussion.

- The acknowledgement of the weak study design and the recommendation that a further trial with a more robust design to be undertaken should be discussed.

Authors’ Response: We have clarified in our responses above (and in the abstract and the text of the revised manuscript) that the study design involved a randomly selected cluster sample and not a convenience sample. However, to address the reviewer’s concern we have emphasized that one additional limitation (beyond those discussed in the original manuscript) was that the survey was self-administered. Please see lines 461-468 of the revised manuscript that layout our limitations:

“This is a cross-sectional study that utilized a self-administered survey to estimate the prevalence of self-medicated antibiotic use in the past. Therefore, by design, recall bias cannot be ruled out. In addition, since the survey was self-administered, respondents may have skipped questions that they did not understand. Moreover, respondents may have underreported antibiotic usage because issues related with menses are culturally sensitive and often viewed as a taboo subject. Furthermore, respondents also might not have known what an antibiotic is; although this may be less of an issue particularly among our survey respondents since they were all university students.”

Minor Essential Revisions
- The manuscript contains grammatical errors and the quality of the written English needs attention.

Authors’ Response: The first and corresponding author is a native English speaker who has strong grammatical skills. To address the reviewer’s concerns, we have had
another native English speaker from the University of Maryland, College Park review the revised manuscript.

**Level of interest:** An article whose findings are important to those with closely related research interests

*Author’s Response:* We agree with the reviewer that the findings of this study are important to those with closely related research interests.

**Quality of written English:** Needs some language corrections before being Published

*Author’s Response:* Please see the response noted above on page 15.

**Statistical review:** Yes, and I have assessed the statistics in my report.

*Author’s Response:* We have taken into account all of the reviewer’s suggestions and we have incorporated major changes concerning the presentation of data in the revised manuscript (please see our detailed responses above).

**Declaration of competing interests:**
I declare that I have no competing interests
Reviewer 2: Inge Gyssens

Reviewer's report:

The manuscript describes a cross sectional study on self-medication with antibiotics for menstrual symptoms among university students in Southwest Nigeria. The idea for the study emerged following a pilot study conducted by the first and last author (reference 15). In-depth interviews of 27 subjects revealed that students and young nurses were taking antibiotics for menstrual symptoms. The present study is conducted as a written survey on a large number of students in four universities. According to the abstract, the aim of the study was to determine the prevalence of self-medication with antibiotics for menstrual symptoms among university women in Southwest Nigeria and to understand the characteristics of women most likely to report this practice. The authors found that in this population, 74% of participants experienced menstrual symptoms, 39% reported using analgesics to treat these, and over 24% of participants reported self-medicated use of antibiotics. Up to 12 different antibiotics are cited. Ampicillin, tetracycline, ciprofloxacin and metronidazole were used to treat most symptoms. The authors conclude that this type of practice could provide monthly, low-dose exposures to antibiotics among users, and could partially explain the high rates of antibiotic resistant urinary tract infections previously described in Nigeria.

General/major comments

The design of this study was appropriate to reach a large population of the target group of university students. Some prevalence data and characteristics of young women were recorded. However, important epidemiological information to interpret the findings are missing. In particular, data are needed to estimate the size of the problem in the area. Also, no response rates are given. Very little information is provided on some crucial methodological aspects of the survey, e.g. type and formulation of questions on antibiotics. The survey instrument should be uploaded as additional material to clarify the responses. Regarding the third aim of the study (cited in the background section, not in the abstract), i.e. to identify the reasons for self-medication, the study does not provide a real clue. It seems that the in-depth interviews of the pilot study (reference 15) revealed more on this issue. However, the authors do not discuss their findings in the present manuscript.

Authors' Response: We agree with the reviewer that more detailed information concerning the study methodology improves the manuscript and is helpful to readers. We also agree that it is necessary to include the response rates, as well as our uploaded survey instrument, and we have done this in the revised manuscript submittal. As noted above in our response to reviewer 1’s overall comments, we have painstakingly gone through both reviewers’ comments and made major revisions to the methods, results and discussion sections of the manuscript. Please see our specific
responses (above) to reviewer 1, as well as our specific responses to reviewer 2 (noted below).

In response to this particular comment, we have also clarified the aims of the study in the background section. The overall objectives were 1) to determine the prevalence of self-medication with antibiotics for the treatment of menstrual symptoms, and 2) to evaluate factors associated with this usage. We apologize that our use of the phrase “to identify reasons for self-medication” was unclear in the original manuscript. We had intended to get across the point that we were evaluating factors associated with this practice. This has been clarified in the background section (lines 113-116):

“Therefore, the purpose of the present study was to determine the prevalence of self-medication with antibiotics for the treatment of menstrual symptoms among university women in Southwest Nigeria and to evaluate factors associated with this practice.”

We are unable to include the phrase “and to evaluate factors associated with this practice” in the abstract because reviewer 1 felt very strongly that we should include all Odds Ratios, 95% confidence intervals, and p-values in the abstract. This has taken up a tremendous amount of room and we are now up to the word-limit for the abstract.

In terms of describing factors associated with self-medication, the inclusion of our new Table 2 (page 33), that details the results of our multivariate analysis, offers a very transparent report of our findings (please see our response to reviewer 1 above, page 14).

Specific comments
- Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)

Background
First paragraph.
1. There is too much text on antimicrobial resistance, in particular in non-African regions. Information on resistance should be focused on Nigeria/the area, UTI pathogens. I suggest to remove some text and references 3-11, 13, 16 on children or/and other developing countries and to keep references 1,2,12.

Authors’ Response: We agree with the reviewer that this paragraph should be shortened and focused, and we have incorporated her/his specific suggestions. Please see lines 69-74 of the revised introduction:

“For example, rates of multiple antibiotic resistance among urinary tract infection (UTI) bacterial isolates in Southwest Nigeria are significantly higher than that of any other country [3]. In addition, rates of other life-threatening bacterial infections, such as community-acquired methicillin-resistant Staphylococcus aureus (MRSA), continue to rise in African countries including Nigeria [4] and Botswana [5].”
Second paragraph
2. This paragraph should also be shortened and focused on Nigeria. A more recent reference should replace reference 14 (dating from 1980!) to describe the (lack of) drug regulation in Nigeria.

Authors’ Response: We agree with the reviewer that this paragraph also should be shortened, more focused and updated with more recent references. We have incorporated the reviewer’s suggestions on lines 81-86 of the revised manuscript:

“In Nigeria, there are limited controls on the sale or advertisement of antimicrobials, creating opportunities for misinformation, misperceptions and sociocultural beliefs that can exacerbate improper and excessive use of antibiotics [1,6]. In addition, counterfeit drugs and poor pharmaceutical qualities of available antimicrobials (containing no or substandard active ingredients) have been widely reported [7-9].”

Also, in order to give an overall picture, the problem of counterfeit drugs (containing no or substandard active ingredient) in Nigeria should be briefly mentioned and referenced.

Authors’ Response: We agree with the reviewer and have briefly mentioned this problem. Please see our response directly above.

Third paragraph
3. The findings of the pilot study (ref 15) leading to the present study should be explained in more detail, now only briefly mentioned in the method section lines 119-121.

Authors’ Response: To address the reviewer’s concern, we have added additional details concerning the findings from our pilot study on lines 104-108 of the revised manuscript:

In particular, participating women reported using antibiotics to reduce cramps, alleviate other menstrual symptoms, and prevent “infections” from feminine sanitary products. Antibiotics were also reportedly used to regulate menstrual flow and to ameliorate perceived abnormalities such as unusual flow qualities including “darker than usual” flow or “heavy odor” [6].”

Method
The study population and recruitment are well described. However, important elements are missing.

4. Please add the following information:
• The total number of students at the 4 universities.
Authors’ Response: The total number of students attending each university has been included in lines 126-130 of the revised manuscript:

“The public universities were the University of Ibadan (>12,000 total students) located in Oyo State and Obafemi Awolowo University (25,000 total students) located in Osun State. The private universities were Covenant University (6,000 total students) and Babcock University (6,000 total students), which are both located in Ogun State.”

• Proportion of female students.

Authors’ Response: The proportion of female students has been included in lines 130-131 and lines 155-160 of the revised manuscript:

“The proportion of female students is approximately 50% at each of these universities.”

“In addition, a source at the National Universities Commission also indicated that the percentage of female students at Nigerian universities as of the 2008/2009 academic session had risen to about 47% of overall students, while some universities report even higher female populations. For example, Babcock University (one of the private universities included in this study) reported that 51% of their student population was female during the 2007/2008 academic year [21].”

• The number of questionnaires distributed.

Authors’ Response: The reviewer’s concern has been clarified on line 264 of the revised manuscript: “A total of 706 out of 740 administered surveys (95% response rate) were completed and returned.”

• The characteristics of study personnel distributing the questionnaires/ the distribution method.

Authors’ Response: We agree with the reviewer that additional details are needed concerning this issue. Please see our response to reviewer 1 that describes our data collection methods in detail (pages 10-11, above).

• Selection of residence/lecture halls?

Authors’ Response: We agree with the reviewer that additional details are needed concerning the selection of residence/lecture halls, as well as our overall sampling strategy. Please see our response to reviewer 1 that describes our sampling methodology in detail (pages 7-8, above).

• The proportion of refusals (allowing to calculate response rates).
Authors’ Response: The response rate has now been reported in the revised manuscript. Please see line 264: “A total of 706 out of 740 administered surveys (95% response rate) were completed and returned.”

- Uploading the survey instrument should inform the reader on type of questions on antibiotics (open or close-ended)

Authors’ Response: We agree that uploading the original survey instrument would be helpful to readers. A copy of the survey has been provided along with the revised manuscript.

- Percentage replies on questions leading to calculation of prevalence and type of antibiotic use. As an example, please check the methodology section of a recent publication on the subject:

Authors’ Response: We agree with the reviewer that the percentages of replies on questions leading to the calculation of prevalence and type of antibiotic use would be helpful to readers. We have included this information in the revised manuscript where we have added details about the questions that were used to calculate prevalence (lines 222-232):

“The first question was a yes/no question: “Have you EVER taken ANY ANTIBIOTICS to treat menses symptoms.” The second question was a grid-formatted question that listed specific menstrual symptoms on the x-axis and specific antibiotics on the y-axis: “In the PAST THREE MONTHS, that is SINCE DECEMBER 1st, 2007, have you taken any of the following SPECIFIC ANTIBIOTICS to treat menses symptoms? (Check all that apply).” The third question was another grid-formatted question that listed specific menstrual symptoms on the y-axis and time frames when antibiotics may have been taken to treat each symptom on the x-axis: “During the PAST THREE MONTHS, have you taken antibiotics to treat symptoms before, during, or after menses? (Check all that apply).” The percentages of replies from study participants on these three questions were 98%, 93%, and 80%, respectively.”

Results
Study population characteristics
5. The first line should give the response rate (% = 706 surveys returned out of xxx distributed). Any difference in response rates between the education levels?

Authors’ Response” The reviewer’s concern has been clarified on line 264 of the revised manuscript: “A total of 706 out of 740 administered surveys (95% response rate) were completed and returned.” We did not observe any significant difference in responses between education levels.
Types of antibiotics used Line 205 and table 2.
I find it hard to believe that non-medical students would cite generic names of antibiotics in such detail. If the names of antibiotics were provided, e.g. a list of these generic names, it is also hard to believe that the students would recognize these products as those passed on by a friend or sister within the previous 3 months. The authors correctly allude to this problem in the limitations section of the discussion lines 300-303.

Authors’ Response: The reviewer points out a very important issue that we had to address when we designed the survey instrument. Instead of merely asking participants to write in the names of antibiotics that they may be using, we decided to both list potential antibiotics that may be used (according to the results of our pilot study: Ojo, KK and Sapkota AR. Self-prescribed use of antimicrobials during menstrual periods: a disturbing new example of information poverty in Nigeria. J Infect Developing Countries 2007; 1(2):123-124,) and allow participants to write in the names of antibiotics that they may be using. In our list of antibiotics, we also described how the antibiotics were recognized in lay terms (ie. “Red and Black Capsule”). Please see survey question #12 for the list of antibiotics that was presented to the study participants. As the reviewer noted, we have alluded to this problem in the limitations section of the discussion.

6. Uploading the survey instrument as additional material would provide this information.

Authors’ Response: We agree with the reviewer. A copy of the survey has been provided along with the revised manuscript.

Importance of the study Lines 230-233
It seems that this survey did not include questions on the frequency (every month?) or the duration of treatment (number of days)
7. Please confirm this. It has important implications, in particular whether the statement on the resistance threat caused by repeated courses is based on speculation or on data collected in the survey.

Authors’ Response: The reviewer is correct. We did not include survey questions on the frequency or duration of treatment. These types of questions were included in original (much longer) drafts of the survey, but were unfortunately eliminated in our attempt to make the survey shorter, such that it could be completed in 15-20 minutes. We have clarified that our statement regarding the resistance threat associated with our findings is speculative. Please see lines 361-365 in the discussion of the revised manuscript:

“While we did not collect data concerning the frequency of self-medication with antibiotics for the treatment of menstrual symptoms, we speculate that the use of antibiotics for menstrual symptoms that may last only a few days every month could possibly provide frequent, low-dose exposures among users.”
There is an important difference in training level of those who recommended the antibiotics: doctors or nurses and the providers (chemists or pharmacists).

8. Please give the numbers (together with percentages of responses to this question) of the different healthcare professionals who recommended the antibiotics and the providers separately.

**Authors’ Response:** We agree with the reviewer that there is a difference in training level between doctors and nurses, and chemists and pharmacists. In hindsight, we would have separated out each of these individuals in the response choices on the survey (question 18). However, instead we grouped them together (question 18); therefore, we are unable to report these individuals separately.

**Discussion**

This section requires a major revision, based on the changes suggested for the introduction, methodology and results.

**Authors’ Response:** As noted above in our response to reviewer 1, page 15, we have completely rewritten the discussion section based on the suggested changes of both reviewers. We have emphasized the key findings and clarified the value of the present study compared with previous reports. The sub-sections of the revised discussion are now entitled: key findings; public health implications; comparison with similar peer-reviewed research; future interventions; limitations; and conclusions. Please see lines 348-484 of the revised manuscript which contain the new discussion.

**Importance of the study/ overall public health implications.**

The young women studied represent only a small proportion (elite) of the female population.


9. Discuss to what extent these female university women are representative for the women in the area, in Nigeria, in Africa? How large would the impact of the ecological pressure by the self-medication of university women be in the area, Nigeria, Africa?

**Authors’ Response:** To address the reviewer’s suggestion, we have added an additional paragraph to the discussion section that addresses these points. Please see lines 385-393 of the revised discussion:

“Moreover, additional studies are necessary to identify whether the antibiotic self-medication practices described here are also prevalent among Nigerian women who do
not attend college. The young women surveyed in this study represent a small, elite proportion of the female, Nigerian population [23]. Thus, it is unclear whether the responses of the surveyed women are representative of other women in Southwest Nigeria (and beyond) who do not attend college. Similarly, at this time, it is difficult to estimate 1) the overall magnitude of the antibiotic selective pressures; and 2) the specific subsequent effects on bacterial antibiotic resistance that are associated with self-medicated antibiotic usage for the treatment of menstrual symptoms in Nigeria.”

Second paragraph
Resistance of UTI pathogens in Nigeria (lines 235-247) and spread (lines 258-272)
10. The sections are too long and contain too many references, as this manuscript does not contain any resistance data.

Authors’ Response: We agree with the reviewer that this paragraph could be shortened. We have deleted sentences and several references. Please see lines 367-371 of the revised manuscript:

“…A previous study in Southwest Nigeria identified a high prevalence of UTIs among women of child-bearing age [28], and other studies have shown that the prevalence of multiple resistance to commonly-used antibiotics among UTI bacterial isolates from Southwest Nigeria is considerably higher than that of any other part of the world [3,29-31].”

-Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)

Results
Menstruation Lines 166-170
1. Why was the question on types of sanitary products included? (Only after reading ref 15, I understand why). The stage should be set in the background section.

Authors’ Response: We agree that including results from this question in the manuscript may be confusing to readers and slightly out of place. Since types of sanitary products used were not associated with self-medicated use of antibiotics for the treatment of menstrual symptoms, we have decided to delete the paragraph concerning these data from the results section (deleted from line 287).

2. The types of analgesics should be grouped according to active ingredient: paracetamol= acetaminophen. Advil = ibuprofen. Provide a uniform formulation, e.g. generic name of ingredient(s) lower case, (BRAND NAME) capitalized
Authors' Response: We agree that this type of grouping makes sense. However, we chose to report these data in a manner consistent with how the survey questions were asked. We would like to maintain the way that we have reported these data in the manuscript.

The article by Ogunfowokan AA and Babatunde OA. Management of primary dysmenorrhea by school adolescents in Ile-Ife, Nigeria. The Journal of School Nursing, vol 26 no 2, April 2010 131-136 DOI: 10.1177/1059840509349723 provides interesting information on the topic in adolescents in the same area. According to this study, only 1% of the girls took only one type of antibiotic (tetracycline), and 63% were advised by their mothers.

Authors' Response: We agree with the reviewer that it is important to include this information in our discussion and we have done so in the revised manuscript. Please see lines 396-409 of the revised manuscript:

“While the present study was the first formal study to assess self-medication with antibiotics for menstrual symptoms among university women in Southwest Nigeria, another recent study identified antibiotic use for menstrual symptoms among secondary school girls in Osun State (the location of one of our participating universities) [32]. In this study, Ogunfowokan and Babatunde (2010) described that 1% of secondary school girls reported using tetracycline for the management of menstrual pain [32]. This is similar to our finding that approximately 1% of our study participants specifically used tetracycline to treat several menstrual symptoms including cramps, and heavy flow (Table 3). Since, Ogunfowokan and Babatunde did not collect data on the usage of other types of antibiotics for the management of menstrual symptoms[32], it is unclear how the overall prevalence rate identified in the present study compares to that of secondary school girls in Southwest Nigeria. Additional, comprehensive, studies concerning self-medicated antibiotic use for menstrual symptoms across all reproductive age groups in Nigeria are warranted.”

Sources of information and antibiotics Lines 217-222.
3. How many times was an antibiotic actually prescribed for this indication?

Authors’ Response: We do not have detailed data concerning the number of times that an antibiotic was recommended by various individuals. The survey questions were “In the PAST THREE MONTHS, where have you obtained the antibiotics that you have used to treat menses symptoms? (Check all that apply)” (question 16), and “Who first recommended that you take antibiotics for menses symptoms?” (question 18).

Discussion Lines 272-282.
4. The authors could discuss the difference in prevalence of antibiotics for menstrual symptoms of their survey and the article on the adolescents. It could well be that antibiotics are fashionable in this group of university students – poorly advised by friends - and that the “fashion trend” has not (yet) spread to younger girls who are primarily advised on management by their mothers.
Conclusion Lines 304-318.

Authors’ Response: We agree with the reviewer, and have included this information in the revised discussion. Please see our response above on page 25.

5. The above cited reference offers some clues for hands-on interventions; for example, information campaigns at the universities

Authors’ Response: We agree with the reviewer that this reference offers good ideas concerning “hands-on interventions.” However, we have already included several paragraphs on intervention possibilities in the discussion section (lines 438-458), and we feel that this section is already getting a little long.

Level of interest: An article whose findings are important to those with closely related research interests

Author’s Response: We agree with the reviewer that the findings of this study are important to those with closely related research interests.

Quality of written English: Acceptable

Author’s Response: We agree with the reviewer that the English is acceptable.

Statistical review: No, the manuscript does not need to be seen by a statistician.

Author’s Response: We agree with Reviewer 2 that our statistical methods in the original manuscript were acceptable. However, Reviewer 1 had concerns/comments regarding the rigor of our statistical methods. We have addressed each of these comments in detail. Please see our responses to Reviewer 1 above.

Declaration of competing interests:
I declare that I have no competing interests