NOTICE: This document contains correspondence generated during peer review and subsequent revisions but before transmittal to production for composition and copyediting:

- Comments from the reviewers and editors (email to author requesting revisions)
- Response from the author (cover letter submitted with revised manuscript)*

**The corresponding author has opted to make this information publicly available.*

Personal or nonessential information may be redacted at the editor's discretion.

Questions about these materials may be directed to the *Obstetrics & Gynecology* editorial office: obgyn@greenjournal.org.

Date: Jun 10, 2022
To: "Ganesa Wegienka" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-22-798

RE: Manuscript Number ONG-22-798

Ultrasound Confirmed Age-Specific Uterine Fibroid Incidence in a Cohort of Black Individuals

Dear Dr. Wegienka:

Thank you for sending us your work for consideration for publication in Obstetrics & Gynecology. Your manuscript has been reviewed by the Editorial Board and by special expert referees. The Editors would like to invite you to submit a revised version for further consideration.

If you wish to revise your manuscript, please read the following comments submitted by the reviewers and Editors. Each point raised requires a response, by either revising your manuscript or making a clear argument as to why no revision is needed in the cover letter.

To facilitate our review, we prefer that the cover letter you submit with your revised manuscript include each reviewer and Editor comment below, followed by your response. That is, a point-by-point response is required to each of the EDITOR COMMENTS (if applicable), REVIEWER COMMENTS, STATISTICAL EDITOR COMMENTS (if applicable), and EDITORIAL OFFICE COMMENTS below. Your manuscript will be returned to you if a point-by-point response to each of these sections is not included.

The revised manuscript should indicate the position of all changes made. Please use the "track changes" feature in your document (do not use strikethrough or underline formatting).

Your submission will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Jul 01, 2022, we will assume you wish to withdraw the manuscript from further consideration.

EDITOR COMMENTS:

Please better align the findings of your results (especially in the abstract) with the conclusion so that results of the study support the conclusion. The conclusion leaves the impression that this is a study focused on screening rather than disease incidence.

REVIEWER COMMENTS:

Reviewer #1: The findings from this study support research conducted by leaders in the field. One major concern is the age of the data. Perhaps, it should be stated that this manuscript examines a historical dataset. Overall, the paper is suited for publication with 2 minor edits:

- For race data please use the term self-reported in front of Black. Since participants had to identify their race at time of care. If this is not accurate and the race data was obtained in the medical record please add this detail.
- The description is given provided to determine actual and observed agreement is lacking. Was data collected to determine agreement between the lead sonographer and the study songrapher. If this was not done then this should be added as a limitation to the study.

The findings from the study are important to assist Black women in receiving proper screening for fibroids.

Reviewer #2: Thank you for your submission. I have reviewed this manuscript in detail and provide the following points that may assist with any requested revision. I very much appreciate the work of the authors.

1) Introduction, Lines 40-44: Both sentences have one reference mid-sentence, but some to point to more information after the reference. Please look at these sentences to see if more references are needed ("Ultrasound…fibroids,3 but…")

2) Introduction, Lines 50 and following: The introduction could be greatly improved by providing a paragraph about the impact of underestimation of fibroid incidence. Does this increase infertility, expose more Black women to hysterectomy, etc?

3) Methods, Lines 73-76: The authors do well at the end of the introduction to establish this as a longitudinal study. In the methods, the word cohort is used to describe SELF and the group of patients studied in this project. Please re-introduce the term longitudinal study in the methods to clearly state the study design, possibly best stated in the second sentence.

4) Methods, Lines 117-118: It is not clear how patients with a "questionable fibroid" were accounted for in the analysis. Please indicate if these were counted as fibroid cases, if they were reviewed by an expert sonographer, or if not counted.

Reviewer #3: In this prospective observational cohort study of Black women aged 23-35 years, authors sought to determine the incidence of uterine fibroids identified by transvaginal US over a 10-year period. Overall incidence of 54 cases per 1000 person-years is higher than that from previous reports; age specific data showed doubled incidence of fibroids in those aged <30 years compared to past reports.

This is important work with sound methodology and unique findings.

1. How were "questionable fibroid" images resolved? Was there additional imaging or were they included or excluded without further investigation? Lack of additional imaging (MR) may have led to under/over estimation of fibroids diagnoses.

2. What was the age distribution of those excluded from the study on the basis of having fibroid diagnosis at baseline? Exclusion likely led to under-estimation of disease burden at specific age intervals.

3. How were participants recruited into the study? Convenient sampling? Advertisements? Payments to subjects??

4. Lines 226-7; surely authors are not advocating for routine screening for fibroids?

STATISTICAL EDITOR COMMENTS:

Table 2: Need to include more information in this Table. For each age stratum: how many persons, median (range) of follow-up times, median (range) for number of follow-up ultrasound exams, median (range) for intervals between ultrasound exams. If there is a systematic difference between age groups in terms of number of follow-up visits, intervals between follow-up exams, then the comparison across age groups may be biased.

Also, should point out for reader that the differences among the age strata are nominally, but not statistically different from one another. Using the < 30 yo as the referent, the incident rate ratios are ~ 1.11 and 1.17, both with CIs that include the referent. That the rates do not increase with age seems counterintuitive. Is there something different about how frequently the age strata were sampled?

General: Should include in supplemental material the analysis of timing for incident cases based on mid-point, rather than random assignment. Should include in Results section and discuss.

As stated by the Authors, these incidence rate estimates differ from self-reported data, since this study followed-up all women with ultrasound exams. Therefore, one cannot compare these incidence rates with other estimates that did not include systematic ultrasound examinations for all women.

EDITORIAL OFFICE COMMENTS:

1. If your article is accepted, the journal will publish a copy of this revision letter and your point-by-point responses as supplemental digital content to the published article online. You may opt out by writing separately to the Editorial Office at em@greenjournal.org, and only the revision letter will be posted.

2. When you submit your revised manuscript, please make the following edits to ensure your submission contains the required information that was previously omitted for the initial double-blind peer review:
* Funding information (ie, grant numbers or industry support statements) should be disclosed on the title page and at the end of the abstract. For industry-sponsored studies, describe on the title page how the funder was or was not involved in the study.
* Include clinical trial registration numbers, PROSPERO registration numbers, or URLs at the end of the abstract (if applicable).
* Name the IRB or Ethics Committee institution in the Methods section (if applicable).
* Add any information about the specific location of the study (ie, city, state, or country), if necessary for context.

3. Obstetrics & Gynecology's Copyright Transfer Agreement (CTA) must be completed by all authors. When you uploaded your manuscript, each coauthor received an email with the subject, "Please verify your authorship for a submission to Obstetrics & Gynecology." Please ask your coauthor(s) to complete this form, and confirm the disclosures listed in their CTA are included on the manuscript's title page. If they did not receive the email, they should check their spam/junk folder. Requests to resend the CTA may be sent to em@greenjournal.org.

4. For studies that report on the topic of race or include it as a variable, authors must provide an explanation in the manuscript of who classified individuals' race, ethnicity, or both, the classifications used, and whether the options were defined by the investigator or the participant. In addition, describe the reasons that race and ethnicity were assessed in the Methods section and/or in table footnotes. Race and ethnicity must have been collected in a formal or validated way. If it was not, it should be omitted. Authors must enumerate all missing data regarding race and ethnicity as in some cases missing data may comprise a high enough proportion that it compromises statistical precision and bias of analyses by race.

Use "Black" and "White" (capitalized) when used to refer to racial categories.

List racial and ethnic categories in tables in alphabetic order. Do not use "Other" as a category; use "None of the above" instead.

Please refer to "Reporting Race and Ethnicity in Obstetrics & Gynecology" at https://edmgr.ovid.com/ong/accounts/Race_and_Ethnicity.pdf.

5. ACOG uses person-first language. Please review your submission to make sure to center the person before anything else. Examples include: "Patients with obesity" instead of "obese patients," "Women with disabilities" instead of "disabled women," "women with HIV" instead of "HIV-positive women," "women who are blind" instead of "blind women."

6. Responsible reporting of research studies, which includes a complete, transparent, accurate and timely account of what was done and what was found during a research study, is an integral part of good research and publication practice and not an optional extra. Obstetrics & Gynecology supports initiatives aimed at improving the reporting of health research, and we ask authors to follow specific guidelines:

STROBE: observational studies

Include the appropriate checklist for your manuscript type upon submission, if applicable, and indicate in your cover letter which guideline you have followed. Please write or insert the page numbers where each item appears in the margin of the checklist. Further information and links to the checklists are available at www.equator-network.org/.

7. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. Please access the obstetric data definitions at https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-obstetrics-data-definitions and the gynecology data definitions at https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-gynecology-data-definitions. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

8. Make sure your manuscript meets the following word limit. The word limit includes the manuscript body text only (for example, the Introduction through the Discussion in Original Research manuscripts), and excludes the title page, précis, abstract, tables, boxes, and figure legends, reference list, and supplemental digital content. Figures are not included in the word count.

Original Research: 3,000 words

9. Specific rules govern the use of acknowledgments in the journal. Please review the following guidelines and edit your title page as needed:

* All financial support of the study must be acknowledged.
* Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.
* All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your response in the journal's electronic author form verifies that permission has been obtained from all named persons.
* If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting or indicate whether the meeting was held virtually).
* If your manuscript was uploaded to a preprint server prior to submitting your manuscript to Obstetrics & Gynecology, add the following statement to your title page: "Before submission to Obstetrics & Gynecology, this article was posted to a preprint server at: [URL]."
* Do not use only authors' initials in the acknowledgement or Financial Disclosure; spell out their names the way they appear in the byline.

10. Be sure that each statement and any data in the abstract are also stated in the body of your manuscript, tables, or figures. Statements and data that appear in the abstract must also appear in the body text for consistency. Make sure there are no inconsistencies between the abstract and the manuscript, and that the abstract has a clear conclusion statement based on the results found in the manuscript.

In addition, the abstract length should follow journal guidelines. Please provide a word count.

Original Research: 300 words

11. Only standard abbreviations and acronyms are allowed. A selected list is available online at http://edmgr.ovid.com /ong/accounts/abbreviations.pdf. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

12. The journal does not use the virgule symbol (/) in sentences with words, except with ratios. Please rephrase your text to avoid using "and/or," or similar constructions throughout the text. You may retain this symbol if you are using it to express data or a measurement.

13. ACOG avoids using "provider." Please replace "provider" throughout your paper with either a specific term that defines the group to which are referring (for example, "physicians," "nurses," etc.), or use "health care professional" if a specific term is not applicable.

14. In your abstract, manuscript Results sections, and tables, the preferred citation should be in terms of an effect size, such as odds ratio or relative risk or the mean difference of a variable between two groups, expressed with appropriate confidence intervals. When such syntax is used, the P value has only secondary importance and often can be omitted or noted as footnotes in a Table format. Putting the results in the form of an effect size makes the result of the statistical test more clinically relevant and gives better context than citing P values alone.

Please standardize the presentation of your data throughout the manuscript submission. For P values, do not exceed three decimal places (for example, "P = .001").

Express all percentages to one decimal place (for example, 11.1%"). Do not use whole numbers for percentages.

15. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available at http://edmgr.ovid.com/ong/accounts/table_checklist.pdf.

16. Please review examples of our current reference style at https://edmgr.ovid.com/ong/accounts/ifa_suppl_refstyle.pdf. Include the digital object identifier (DOI) with any journal article references and an accessed date with website references.

Unpublished data, in-press items, personal communications, letters to the editor, theses, package inserts, submissions, meeting presentations, and abstracts may be included in the text but not in the formal reference list. Please cite them on the line in parentheses.

If you cite ACOG documents in your manuscript, be sure the references you are citing are still current and available. Check the Clinical Guidance page at https://www.acog.org/clinical (click on "Clinical Guidance" at the top). If the reference is still available on the site and isn't listed as "Withdrawn," it's still a current document. In most cases, if an ACOG document has been withdrawn, it should not be referenced in your manuscript.

Please make sure your references are numbered in order of appearance in the text.

17. Figures

Figure 1: Please upload as a figure file on Editorial Manager.

Figure 2: Please replace bars with solid colors and upload as a figure file on Editorial Manager.

18. Authors whose manuscripts have been accepted for publication have the option to pay an article processing charge and publish open access. With this choice, articles are made freely available online immediately upon publication. An information sheet is available at http://links.lww.com/LWW-ES/A48. The cost for publishing an article as open access can be found at https://wkauthorservices.editage.com/open-access/hybrid.html.

If your article is accepted, you will receive an email from the Editorial Office asking you to choose a publication route (traditional or open access). Please keep an eye out for that future email and be sure to respond to it promptly.

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If you choose to revise your manuscript, please submit your revision through Editorial Manager at http://ong.editorialmanager.com. Your manuscript should be uploaded as a Microsoft Word document. Your revision's cover letter should include a point-by-point response to each of the received comments in this letter. Do not omit your responses to the EDITOR COMMENTS (if applicable), the REVIEWER COMMENTS, the STATISTICAL EDITOR COMMENTS (if applicable), or the EDITORIAL OFFICE COMMENTS.

If you submit a revision, we will assume that it has been developed in consultation with your coauthors and that each author has given approval to the final form of the revision.

Again, your manuscript will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Jul 01, 2022, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Ebony B. Carter, MD, MPH
Associate Editor, Equity

2020 IMPACT FACTOR: 7.661
2020 IMPACT FACTOR RANKING: 3rd out of 83 ob/gyn journals

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In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Use the following URL: https://www.editorialmanager.com/ong/login.asp?a=r). Please contact the publication office if you have any questions.

2 August 2022

Jason D. Wright, MD
Editor-in-Chief
Obstetrics and Gynecology

Dear Dr. Wright:

On behalf of my co-authors, I am pleased to submit the enclosed revised manuscript, "Ultrasound Confirmed Age-Specific Uterine Fibroid Incidence in a Cohort of Black Individuals," to *Obstetrics and Gynecology* for review.

All authors have fulfilled the requirements for authorship of this manuscript (meaningful participation in the conception and design of the research, analysis of the data, and writing and approval of the manuscript, to a degree sufficient that they can take public responsibility for the work). None has any conflict of interest, either financially or otherwise, that would bias the presentation of the results. The human subject review board at all clinical sites (Henry Ford Health System Institutional Review Board, the NIEHS Institutional Review Board, the Bostone University Institutional Review Board) approved this research, and all participants provided written informed consent. This manuscript has not been published at any length elsewhere, is not under consideration for publication elsewhere, and will not be submitted elsewhere while under review with *Obstetrics and Gynecology*.

We think the results are novel. We have estimated age-specific fibroid incidence rates in a cohort of Black individuals. Ultrasound screening was performed up to 5 times over a period of up to 10 years.

As lead author and manuscript guarantor, I affirm that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained. NIH funded this research and was not involved in study design, execution, analysis, or reporting.

Reviewer Responses follow this letter. We have completed the STROBE document.

Thank you for your consideration of this manuscript.

Ganesa Wegienka

Corresponding Author

Henry Ford Health System

Department of Public Health Sciences

[redacted] [redacted]

Response to Reviewers:

Thank you for the thoughtful comments. We have added new text, revised previous text and added Supplemental tables to address these important concerns. We look forward to any additional feedback from Reviewers to improve this manuscript.

Please note line numbers correspond to the version with highlighted changes.

EDITOR COMMENTS:

Please better align the findings of your results (especially in the abstract) with the conclusion so that results of the study support the conclusion. The conclusion leaves the impression that this is a study focused on screening rather than disease incidence.

Author's response: The text has been revised to clarify that young Black women with fibroid symptoms may benefit from having ultrasound as part of their clinical care because fibroids are more common in these young women than was previously reported.

REVIEWER COMMENTS:

Reviewer #1: The findings from this study support research conducted by leaders in the field. One major concern is the age of the data. Perhaps, it should be stated that this manuscript examines a historical dataset. Overall, the paper is suited for publication with 2 minor edits:

Author's response: The data for these analyses were collected from 2010-2021. This has been added to the Introduction. Line 61.

- For race data please use the term self-reported in front of Black. Since participants had to identify their race at time of care. If this is not accurate and the race data was obtained in the medical record please add this detail.

Author's response: The study participants identified themselves as Black/African American at time of study enrollment. Please see lines 59 and 73 which now include "self-identified."

- The description is given provided to determine actual and observed agreement is lacking. Was data collected to determine agreement between the lead sonographer and the study songrapher. If this was not done then this should be added as a limitation to the study.

Author's response: The review by the lead sonographer was to maintain high quality ultrasound data by keeping all sonographers consistently following the study protocol. There was no systematic recording of the outcome of each review.

"We did not record the agreement of each review (e.g., agreement, recommended revision, etc.)." Lines 128-129.

The findings from the study are important to assist Black women in receiving proper screening for fibroids.

Author's response: We agree with this statement and greatly appreciate the recognition of this idea.

Reviewer #2: Thank you for your submission. I have reviewed this manuscript in detail and provide the following points that may assist with any requested revision. I very much appreciate the work of the authors.

1) Introduction, Lines 40-44: Both sentences have one reference mid-sentence, but some to point to more information after the reference. Please look at these sentences to see if more references are needed ("Ultrasound…fibroids,3 but…")

Author's response: Thank you for asking us to review this. We have moved one of the references to the end of the sentence. Both sentences have only one reference.

2) Introduction, Lines 50 and following: The introduction could be greatly improved by providing a paragraph about the impact of underestimation of fibroid incidence. Does this increase infertility, expose more Black women to hysterectomy, etc?

Author's response: We have added the following sentence to the first paragraph of the Introduction:
"If it is appreciated that fibroids often develop at young ages, individuals could have earlier intervention with minimally invasive treatments that could delay or eliminate the need for interventions such as hysterectomy." Lines 44-46.

3) Methods, Lines 73-76: The authors do well at the end of the introduction to establish this as a longitudinal study. In the methods, the word cohort is used to describe SELF and the group of patients studied in this project. Please re-introduce the term longitudinal study in the methods to clearly state the study design, possibly best stated in the second sentence.

Author's response: The following are the first sentences of the Methods section (Lines 71-74):
"SELF is an ongoing longitudinal cohort study specifically designed to study incidence and growth of uterine fibroids with standardized ultrasound assessments.[1,2] Briefly, in 2010-2012, 1,693 individuals who self-identified as Black/African American, were ages 23-35 years, had a uterus and did not report a prior diagnosis of uterine fibroids were enrolled."

4) Methods, Lines 117-118: It is not clear how patients with a "questionable fibroid" were accounted for in the analysis. Please indicate if these were counted as fibroid cases, if they were reviewed by an expert sonographer, or if not counted.

Author's response: We apologize for failing to clarify this in the text. This text has been added:
"All "questionable" fibroids were reviewed by the lead sonographer. After this additional review, there were three participants with a questionable fibroid that were considered incident fibroid cases." Lines 129-131

Reviewer #3: In this prospective observational cohort study of Black women aged 23-35 years, authors sought to determine the incidence of uterine fibroids identified by transvaginal US over a 10-year period. Overall incidence of 54 cases per 1000 person-years is higher than that from previous reports; age specific data showed doubled incidence of fibroids in those aged <30 years compared to past reports.

This is important work with sound methodology and unique findings.

1. How were "questionable fibroid" images resolved? Was there additional imaging or were they included or excluded without further investigation? Lack of additional imaging (MR) may have led to under/over estimation of fibroids diagnoses.

Author's response: We apologize for failing to clarify this in the text. This text has been added:

"All "questionable" fibroids were reviewed by the lead sonographer. After this additional review, there were three participants with a questionable fibroid that were considered incident fibroid cases." Lines 129-131.

"Additional imaging was not performed." Lines 121-122.

These three incident cases did not create an overestimation of incidence rates.

2. What was the age distribution of those excluded from the study on the basis of having fibroid diagnosis at baseline? Exclusion likely led to under-estimation of disease burden at specific age intervals.

Author's response: The focus of our analyses is on age-specific incidence rather than the overall burden of disease which would be determined by both the incident and prevalent cases in our cohort. We have added a Supplemental Table 1 that includes the age distribution of those who had a fibroid detected at baseline. The Methods text has also been revised: "The 385 (22.7%) participants who had a fibroid detected during the baseline ultrasound were excluded from these analyses of incident fibroids and their age distribution is presented in Supplemental Table 1." Lines 100-101.

Supplemental Table 1. Age distribution at the baseline study visit among 385 reproductive-aged Black participants in the Study Environment Lifestyle and Fibroids (SELF) who had a fibroid detected at the baseline visit

	Number (%)
Sociodemographic variables	
Age (years)	
23-25	38 (9.9)
26-28	89 (23.1)
29-31	118 (30.6)
32-35	140 (36.4)

3. How were participants recruited into the study? Convenient sampling? Advertisements? Payments to subjects??

Author's response: Details have been previously published and we have added additional text to this paper.
"We have previously published detail of participant recruitment; briefly, we mailed letters to Henry Ford Health System patients who were ages 23-34 years to invite study participation and patients 35-65 to ask them to share study information with those who may be eligible. Media advertisements and information booths at community events were also used to recruit possible participants. Participants were provided stipends for research activities." Lines 74-79.

4. Lines 226-7; surely authors are not advocating for routine screening for fibroids?

Author's response:
We are not advocating for routine ultrasound screening of fibroids. We suggest that Black individuals with symptoms consistent with fibroids, however, could benefit from ultrasound screening given the incidence findings of this study and the prevalence findings that others have shown in young Black individuals.
The last paragraph includes the following text:
"It can also raise awareness of the elevated risk for young Black individuals who may benefit from ultrasound screening when symptoms (heavy menstrual bleeding, anemia, pelvic pain) are compatible with fibroids as part of their clinical care." Lines 273-275.

STATISTICAL EDITOR COMMENTS: (We requested more information from the Reviewer about the specific concerns which are addressed in the last section of these Responses.)

Table 2: Need to include more information in this Table. For each age stratum: how many persons, median (range) of follow-up times, median (range) for number of follow-up ultrasound exams, median (range) for intervals between ultrasound exams. If there is a systematic difference between age groups in terms of number of follow-up visits, intervals between follow-up exams, then the comparison across age groups may be biased.

Also, should point out for reader that the differences among the age strata are nominally, but not statistically different from one another. Using the < 30 yo as the referent, the incident rate ratios are ~ 1.11 and 1.17, both with CIs that include the referent. That the rates do not increase with age seems counterintuitive. Is there something different about how frequently the age strata were sampled?

Author's response: To clarify, in the manuscript we state, "The age-specific incidence rates (cases per 1,000 person-years) increased with age…" and do not report that the age-specific incidence rates are statistically significantly different. Based on the incident rates increasing from 49.7 per 1000 person-years for individuals ages <30 to 58.2 per 1000 person-years for individuals ages 35-39, the incidence rates do appear to increase with age in this population.

General: Should include in supplemental material the analysis of timing for incident cases based on mid-point, rather than random assignment. Should include in Results section and discuss.

As stated by the Authors, these incidence rate estimates differ from self-reported data, since this study followed-up all women with ultrasound exams. Therefore, one cannot compare these incidence rates with other estimates that did not include systematic ultrasound examinations for all women.

Author's response: There is only one other small study that has conducted longitudinal screening for fibroids with ultrasound and it was conducted in a cohort of n=64 White women. A baseline ultrasound was performed and was repeated approximately 2.5 years later.[3] The single prior image-based, prospective study of fibroid incidence reported 13% per 31 months among 53 fibroid-free White women.

Given that the only available age-specific incidence rates for fibroids that is available in the literature are based on clinical diagnoses, we think it is important to provide these comparisons. We acknowledge that the fibroid identification methods are different across studies and think the

results and text highlight the misclassification of fibroid status that have existed for decades in research.

Additional Statistical Reviewer Comments per email:

The imputed timing of fibroid detection (whether by mid-point between previous visit without fibroid detection or by random assignment during that interval) depends on similar intervals between detection and previous visits for the various age subsets. That is, if one age stratum were to have more frequent visits as compared to another age stratum, then the imputed detection would, on average, be later for the group with less frequent examinations.

So, it is not that I object to random vs mid-point as the imputation method, but rather that the Authors need to demonstrate that the various groups are comparable in terms of number and frequency of examinations. If there is a systematic difference in terms of examination frequency for various ages, then the estimation of incidence is biased, since the denominators would not be comparable. Hence my queries re: Table 2.

The query re: mid-point imputation was merely for completeness and would be in supplemental digital content (an online Appendix).

The main issue is to assure the reader that we are comparing groups with similar survey frequency when incidences based on right-censored data are compared.

Author's response: We appreciate the Reviewer highlighting the potential for bias due to varying levels of visit completion and interval length between age groups. We have examined our data in multiple ways to ensure this bias in unlikely in our analyses.

First, we have added the following Supplemental Table 2 to the manuscript which shows similar visit frequency across age groups (age at time of enrollment). The following text was added:

"The number of follow-up clinic visits completed over time did not vary by age at enrollment (Supplemental Table 2)." Lines 190-191.

Supplemental Table 2. Number of completed follow-up visits in the Study Environment Lifestyle and Fibroids (SELF) by age at baseline visit

	Number of participants by total follow-up visits completed (% of all participants n=1241)			
Sociodemographic variables	1	2	3	4
Age (years)				
23-25	21 (1.7)	29 (2.3)	65 (5.2)	200 (16.1)
26-28	9 (0.7)	24 (1.9)	67 (5.4)	221 (17.8)
29-31	13 (1.0)	21 (1.7)	54 (4.4)	239 (19.3)
32-35	9 (0.7)	11 (0.9)	47 (3.8)	211 (17.0)

Second, the data from this closed cohort do not suggest that age groups differ by follow-up time and number of visits (indicating similar interval lengths between visits). We also share an additional table only with the Reviewers. The table shows the events within that age group. The N should be interpreted to mean that those are the number of unique individuals that contributed person time to that age group and participants can contribute to more than one age group. The number of exams should be interpreted similarly. We are not including this table in the

manuscript and we think it would be confusing for the reader who may easily confuse the n=1241 with the sum of the n in the table which are not comparable. The data do not suggest there is a disproportionate number of visits or incident fibroids by age group in this closed cohort.

Table for Reviewers. Age-specific incidence rates among 1,241 reproductive-aged Black participants in the Study Environment Lifestyle and Fibroids using random date imputation

Age	Person-years of follow-up	N	Follow-up, Median (range), in years	Number of US exams, Median (range)	Number of Incident Fibroids	Age-specific Incidence Rate* (IR), (95% CI)
<30	2212	736	2.9 (0.1–6.9)	1 (0-3)	110	49.7 (40.9 , 59.9)
30 – 34	2937	1052	2.8 (0.1-5.0)	2 (0-3)	162	55.2 (47.0 , 64.3)
35 - 39	1791	571	3.2 (0.1-5.0)	2 (0-3)	99	58.2 (47.3 , 70.9)

We provided justification for our choice of analytical approach in the Methods (Lines 144-149) as follows: “Because fibroids were observed at irregular intervals (study visits), a random date imputation method was used rather than mid-point imputation, which has been shown to create biased estimates when participants begin to miss study visits, which is expected in a longitudinal cohort study.[4] Incidence dates were randomly imputed between the last ultrasound date in which no fibroids were detected and the date of the ultrasound in which fibroids were first detected.”

Prior to conducting any analyses, the analytical approach was selected due to potential bias from midpoint analyses (based on published research). For this reason, analyses using the midpoint were not conducted.

References cited in the Responses:

1. Baird DD, Harmon QE, Upson K, et al. A Prospective, Ultrasound-Based Study to Evaluate Risk Factors for Uterine Fibroid Incidence and Growth: Methods and Results of Recruitment. J Womens Health (Larchmt) 2015;24:907-15.
2. Baird DD, Patchel SA, Saldana TM, et al. Uterine fibroid incidence and growth in an ultrasound-based, prospective study of young African-Americans. Am J Obstet Gynecol 2020.
3. DeWaay DJ, Syrop CH, Nygaard IE, Davis WA, Van Voorhis BJ. Natural history of uterine polyps and leiomyomata. Obstet Gynecol 2002;100:3-7.
4. Vandormael A, Dobra A, Barnighausen T, de Oliveira T, Tanser F. Incidence rate estimation, periodic testing and the limitations of the mid-point imputation approach. Int J Epidemiol 2018;47:236-45.

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Use "Black" and "White" (capitalized) when used to refer to racial categories.

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