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.

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Questions about these materials may be directed to the Obstetrics & Gynecology editorial office: obgyn@greenjournal.org.
RE: Manuscript Number ONG-22-310

Screening Has Meaning: Evaluating Expanded Non-invasive Prenatal Testing

Dear Dr. Bayefsky:

Your manuscript has been reviewed by the Editorial Board and by special expert referees. Although it is judged not acceptable for publication in Obstetrics & Gynecology in its present form, we would be willing to give further consideration to a revised version.

If you wish to consider revising your manuscript, you will first need to study carefully the enclosed reports submitted by the referees and editors. Each point raised requires a response, by either revising your manuscript or making a clear and convincing argument as to why no revision is needed. To facilitate our review, we prefer that the cover letter include the comments made by the reviewers and the editor followed by your response. The revised manuscript should indicate the position of all changes made. We suggest that you use the "track changes" feature in your word processing software to do so (rather than strikethrough or underline formatting).

Please be sure to address the Editor comments (see "EDITOR COMMENTS" below) in your point-by-point response.

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

REVIEWER COMMENTS:

Reviewer #1:

1. The title is somewhat demeaning, and possibly sarcastic. What screening does not have meaning ?!

2. The author(s) as others, repeatedly and incorrectly refer to "non-invasive prenatal testing". The correct terminology is cell-free DNA (cfDNA) screening, or alternatively non-invasive prenatal screening (NIPS). This comment is not simply nomenclature, as the former may infer incorrect clinical assumptions (testing). cfDNA screening has been renamed for now several years to separate this entity from the incorrect assumption of testing.

3. Lines # 36-64: I/we remain unconvinced regarding the comparison of cfDNA screening to overall Public Health Screening.

4. Line # 27: "Some have focused on the fact that NIPT should only be used as a screening test". This statement is unclear as the inherent nature of cfDNA screening is screening(!), and not testing (see above). cfDNA screening is not utilized with the intent of replacing diagnostic testing.

5. The author(s) do not recognize, nor have the commented that cfDNA screening has literally changed the face of prenatal care. cfDNA in fact has improved prenatal screening accuracy and offers additional insight into conditions, which could not be screened for previously.

Accordingly, I/we draw their attention to the following:

A. cfDNA screening has negated invasive (read: diagnostic) testing, for a multitude of sonographic "soft markers" including (but not limited to), absent or hypoplastic nasal bone, choroid plexus cysts, thickened nuchal fold, intracardiac echogenic focus, pyelectasis, echogenic bowel and possibly others. In addition, patient anxiety in the face of sonographic soft markers (with negative cfDNA screening) has been reduced / negated.

B. cfDNA screening does not entail by any means an "opportunity to decrease the incidence of disease and disability in the general population" (see lines # 61-62). This concept / comment is inherently wrong.

C. Lines # 73-74: cfDNA screening decreases invasive testing. All other prenatal screening tools entail a calculated 5% false positive rate. cfDNA screening bypasses this widely accepted clinical management paradigm, which knowingly entails
unwarranted invasive testing (for a calculated 5% false positive rate).

D. The author(s) have not discussed cfDNA screening upon the notation of sonographically depicted structural fetal anomalies.

E. In our inner-city teaching hospital, cfDNA screening has enabled prenatal diagnosis of two cases of Prader-Willi syndrome (third-trimester fetal growth restriction in the presence of polyhydraminos), one case of Angelman syndrome and others with microdeletions and microduplications of concern. cfDNA screening for Prader-Willi syndrome a life-long condition is noted to carry a PPV rate of approximately 15%. Our two cases demonstrate that the calculated PPV rate upon the diagnosis of structural concerns is likely considerably higher.

F. Lines # 82-86: None of the microdeletions/microduplications conditions are of adult onset nature. All of these conditions are congenital, chronic, syndromic disorders without other reliable means of screening.

G. Lines 84-86: Regarding the definition of the author(s) "reasonable level of accuracy". Expanded cfDNA screening (as described above, see points 5A, 5C-5E) is already changing prenatal care.

6. Newly developed technologies should be embraced and utilized appropriately, not withheld from the public. Developing technologies drive scientific development.

7. In our view it is likely unethical to deny public insured patients access to cfDNA technology.

8. The time for appropriate utilization of expanded cfDNA screening has arrived, is being implemented and as mentioned above, is undoubtedly improving prenatal care.

9. In general, I/we believe that cfDNA screening is a rapidly evolving technology, which will continue to enhance prenatal care.

Reviewer #2:

The authors present a timely commentary on the use of non-invasive prenatal testing (NIPT) for rare chromosomal abnormalities. There are only a few comments/suggestions for the authors:

1. The majority of the readers of this journal are practicing ob/gyns without additional training in either genetics or ethics. The authors should consider explaining the technical terms that they freely use from these disciplines.

2. The authors focus on "commercial companies", but expanded testing has been offered in some academic centers as well. It would be better to state that this commentary applies to "laboratories" offering expanded NIPT.

3. Not all readers of this journal are also readers of the New York Times. A summary of the key points of the Times article would be useful to those who have not read that article and would help the reader understand the practical implications of a false positive test.

4. A more in-depth discussion of the issues around false positive results with a specific example, such as the authors have done with Angelman syndrome, would strengthen their argument. For example, giving specific numbers on positive predictive values for a rare condition gives the reader a clear idea of how unlikely a positive test result is a true positive. That would give the practicing ob/gyn practical information in counseling his/her patient.

5. Do the authors believe that obstetrician gynecologists are well-position to counsel their patients? I would argue that they have limited resources to adequately counsel their patients that isn't provided by the testing laboratories.

6. The final line of the discussion should be changed to "has met accepted scientific and ethical criteria".

Reviewer #3:

This is a beautifully written and well-argued piece. I have two comments for the author to consider.

1. The final conclusion - that patients should be able to purchase commercially available tests out of respect for their autonomy - seems inconsistent with the arguments made about regulation and also reflects a rather thin conception of
autonomy, in that commercial offers of (associated with marketing of) a product that may have profoundly problematic and hidden harms may not if fact respect autonomy in what ethicists call the "thick" sense of the word, and instead undermine it. Perhaps the authors could offer some nuance to this sentence in the conclusion, or delete it. I think in the context of the paper it is confusing and potentially misleading.

2. The authors do a great job of pointing to some of the moral problems associated with NIPT as a public health screening tool, but miss one that seems important which is that treatment where NIPT is concerned is not necessarily amelioration or elimination of the condition, but, where termination is concerned, elimination of the individual (the fetus) who is affected by it. This distinction is often lost in conversations about genetic testing but it seems to me that it should not be glossed over in this piece, where a framework for public health screening is being considered.

EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology have increased transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:

A. OPT-IN: Yes, please publish my point-by-point response letter.
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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:

* Include your title page information in the main manuscript file. The title page should appear as the first page of the document. Add any previously omitted Acknowledgements (ie, meeting presentations, preprint DOIs, assistance from non-byline authors).
* Funding information (ie, grant numbers or industry support statements) should be disclosed on the title page and in the body text. For industry-sponsored studies, the Role of the Funding Source section should be included in the body text of the manuscript.
* 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 uses an "electronic Copyright Transfer Agreement" (eCTA), which must be completed by all authors. When you uploaded your manuscript, each co-author received an email with the subject, "Please verify your authorship for a submission to Obstetrics & Gynecology." Please check with your coauthors to confirm that they received and completed this form, and that the disclosures listed in their eCTA are included on the manuscript’s title page.

4. Our journal requires that all evidence-based research submissions be accompanied by a transparency declaration statement from the manuscript’s lead author. The statement is as follows: "The lead author* affirms 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 (and, if relevant, registered) have been explained." *The manuscript's guarantor.

If you are the lead author, please include this statement in your cover letter. If the lead author is a different person, please ask him/her to submit the signed transparency declaration to you. This document may be uploaded with your submission in Editorial Manager.
5. 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.

6. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Current Commentary articles should not exceed 3,000 words. Stated word limits include the title page, précis, abstract, text, tables, boxes, and figure legends, but exclude references.

7. Specific rules govern the use of acknowledgments in the journal. Please note the following guidelines:
   
   * 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).
   * 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]."

8. Provide a précis on the second page, for use in the Table of Contents. The précis is a single sentence of no more than 25 words that states the conclusion(s) of the report (ie, the bottom line). The précis should be similar to the abstract’s conclusion. Do not use commercial names, abbreviations, or acronyms in the précis. Please avoid phrases like "This paper presents" or "This case presents."

9. The most common deficiency in revised manuscripts involves the abstract. Be 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 paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully.

   In addition, the abstract length should follow journal guidelines. The word limit for Original Research articles is 300 words; Reviews is 300 words; Case Reports is 125 words; Current Commentary articles is 250 words; Executive Summaries, Consensus Statements, and Guidelines are 250 words; Clinical Practice and Quality is 300 words; Procedures and Instruments is 200 words. Please provide a word count.

10. 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.
11. The journal does not use the virgule symbol (/) in sentences with words. 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.

12. Please review examples of our current reference style at http://ong.editorialmanager.com (click on the Home button in the Menu bar and then "Reference Formatting Instructions" document under "Files and Resources"). 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 reference list.

In addition, the American College of Obstetricians and Gynecologists' (ACOG) documents are frequently updated. These documents may be withdrawn and replaced with newer, revised versions. 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.

If the reference you are citing has been updated and replaced by a newer version, please ensure that the new version supports whatever statement you are making in your manuscript and then update your reference list accordingly (exceptions could include manuscripts that address items of historical interest). If the reference you are citing has been withdrawn with no clear replacement, please contact the editorial office for assistance (obgyn@greenjournal.org). In most cases, if an ACOG document has been withdrawn, it should not be referenced in your manuscript.

13. 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.

If you choose open access, you will receive an Open Access Publication Charge letter from the Journal's Publisher, Wolters Kluwer, and instructions on how to submit any open access charges. The email will be from publicationservices@copyright.com with the subject line, "Please Submit Your Open Access Article Publication Charge(s)." Please complete payment of the Open Access charges within 48 hours of receipt.

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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 the following:

* A confirmation that you have read the Instructions for Authors (http://edmgr.ovid.com/ong/accounts/authors.pdf), and
* A point-by-point response to each of the received comments in this letter. Do not omit your responses to the Editorial Office or Editors’ comments.

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

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

Sincerely,

Dwight J. Rouse, MD
Deputy Editor, Obstetrics
2020 IMPACT FACTOR: 7.661
2020 IMPACT FACTOR RANKING: 3rd out of 83 ob/gyn journals

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.
March 13, 2022

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

Dear Dr. Wright,

We are writing to submit a revision of our Current Commentary article, titled “Evaluating Expanded Non-invasive Prenatal Screening.” We greatly appreciated the reviewers’ questions and comments and have done our best to edit the manuscript accordingly. We believe that the Commentary is timelier than ever, as the national conversation regarding the commercial availability of NIPT for rare chromosomal abnormalities continues in earnest.

The lead author (Dr. Bayefsky) affirms 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 (and, if relevant, registered) have been explained. To the best of our knowledge, the authors have no conflict of interest, financial or otherwise.

Sincerely,

Michelle J. Bayefsky, MD
Resident, Department of Obstetrics & Gynecology
NYU Langone Health

Arthur Caplan, PhD
Director, Division of Medical Ethics
NYU Grossman School of Medicine

Iffath Hoskins, MD
Clinical Professor, Department of Obstetrics & Gynecology
NYU Langone Health
Response to Reviewers

Reviewer #1:

1. The title is somewhat demeaning, and possibly sarcastic. What screening does not have meaning?!

   Thank you for this comment. We certainly did not intend the title to be demeaning or sarcastic and have changed the title accordingly.

2. The author(s) as others, repeatedly and incorrectly refer to "non-invasive prenatal testing". The correct terminology is cell-free DNA (cfDNA) screening, or alternatively non-invasive prenatal screening (NIPS). This comment is not simply nomenclature, as the former may infer incorrect clinical assumptions (testing). cfDNA screening has been renamed for now several years to separate this entity from the incorrect assumption of testing.

   Thank you for this correction. We have edited to “NIPS” throughout the paper.

3. Lines # 36-64: I/we remain unconvinced regarding the comparison of cfDNA screening to overall Public Health Screening.

   Thank you for this comment. We have added another sentence (lines 48-48) to explain why we believe public health screening criteria should apply to NIPS.

4. Line # 27: "Some have focused on the fact that NIPT should only be used as a screening test". This statement is unclear as the inherent nature of cfDNA screening is screening(!), and not testing (see above). cfDNA screening is not utilized with the intent of replacing diagnostic testing.

   Thank you for this clarifying question – we have changed to “cffDNA” so there is no confusion between NIPS and NIPT.

5. The author(s) do not recognize, nor have the commented that cfDNA screening has literally changed the face of prenatal care. cfDNA in fact has improved prenatal screening accuracy and offers additional insight into conditions, which could not be screened for previously.

   Accordingly, I/we draw their attention to the following:

   A. cfDNA screening has negated invasive (read: diagnostic) testing, for a multitude of sonographic "soft markers" including (but not limited to), absent or hypoplastic nasal bone, choroid plexus cysts, thickened nuchal fold, intracardiac echogenic focus, pyelectasis, echogenic bowel and possibly others. In addition, patient anxiety in the face of sonographic soft markers (with negative cfDNA screening) has been reduced / negated.

   Thank you for this point. We have added a comment to this effect in lines 86-87.
B. cfDNA screening does not entail by any means an "opportunity to decrease the incidence of disease and disability in the general population" (see lines # 61-62). This concept / comment is inherently wrong.

Thank you for this point. We have further clarified the statement that although the emphasis for NIPS is primarily and appropriately focused on helping individual patients obtain the necessary information pertaining to the health and wellbeing of their pregnancy, population wide screening does have an impact on the prevalence of disease and disability in the population at large (lines 66-67).

C. Lines # 73-74: cfDNA screening decreases invasive testing. All other prenatal screening tools entail a calculated 5% false positive rate. cfDNA screening bypasses this widely accepted clinical management paradigm, which knowingly entails unwarranted invasive testing (for a calculated 5% false positive rate).

Thank you for this point. We have strengthened our statement regarding how cfDNA screening currently decreases rates of invasive testing in accordance with this comment (lines 84-88).

D + E. The author(s) have not discussed cfDNA screening upon the notation of sonographically depicted structural fetal anomalies. In our inner-city teaching hospital, cfDNA screening has enabled prenatal diagnosis of two cases of Prader-Willi syndrome (third-trimester fetal growth restriction in the presence of polyhydraminos), one case of Angelman syndrome and others with microdeletions and microduplications of concern. cfDNA screening for Prader-Willi syndrome a life-long condition is noted to carry a PPV rate of approximately 15%. Our two cases demonstrate that the calculated PPV rate upon the diagnosis of structural concerns is likely considerably higher.

Thank you for this important point – we have added a statement distinguishing screening of low-risk patients and patients with identified structural abnormalities on ultrasound (lines 74-75).

F. Lines # 82-86: None of the microdeletions/microduplications conditions are of adult onset nature. All of these conditions are congenital, chronic, syndromic disorders without other reliable means of screening.

Thank you for this comment. The reviewer is correct – our statement regarding adult onset conditions was intended to project out into the future of NIPS, when adult onset conditions may also be included in screening. We have clarified this point (line 95).

G. Lines 84-86: Regarding the definition of the author(s) "reasonable level of accuracy". Expanded cfDNA screening (as described above, see points 5A, 5C-5E) is already changing prenatal care.

Thank you for this comment. We completely agree that cfDNA is changing prenatal care, and largely for the better. Our commentary is intended to offer a framework for evaluating
when new, expanded uses of cfDNA screening are ready for application in the general population. We have clarified this point in lines 98-100.

6. Newly developed technologies should be embraced and utilized appropriately, not withheld from the public. Developing technologies drive scientific development.

We fully agree with the reviewer and do not intend to suggest that new technologies should be withheld from the public, only that they be evaluated carefully before being widely offered.

7. In our view it is likely unethical to deny public insured patients access to cfDNA technology.

We agree that access to cfDNA should not depend on insurance status – public or private. We have broadened the statement in line 119 to clarify that patients should be able to access testing, if they desire (instead of just purchase out of pocket).

8+9. The time for appropriate utilization of expanded cfDNA screening has arrived, is being implemented and as mentioned above, is undoubtedly improving prenatal care. In general, I/we believe that cfDNA screening is a rapidly evolving technology, which will continue to enhance prenatal care.

Thank you for these comments. We take the Reviewer’s thoughts and opinions seriously and have made edits throughout the paper to clarify that we do not oppose expanded NIPS, but encourage the application of accepted standards for public health screening to NIPS, as is done for other types of health screening.

Reviewer #2:

The authors present a timely commentary on the use of non-invasive prenatal testing (NIPT) for rare chromosomal abnormalities. There are only a few comments/suggestions for the authors:

1. The majority of the readers of this journal are practicing ob/gyns without additional training in either genetics or ethics. The authors should consider explaining the technical terms that they freely use from these disciplines.

Thank you for this comment. We have added a short description of cfDNA testing in line 20-21.

2. The authors focus on "commercial companies", but expanded testing has been offered in some academic centers as well. It would be better to state that this commentary applies to "laboratories" offering expanded NIPT.

Thank you for this point – we have changed “companies” to “laboratories” in line 34 and deleted “commercial” in line 30.
3. Not all readers of this journal are also readers of the New York Times. A summary of the key points of the Times article would be useful to those who have not read that article and would help the reader understand the practical implications of a false positive test.

Since the original draft of this paper was written, the conversation has broadened far beyond the original New York Times article. Therefore, although we still cite the article, we do not describe it directly in the text.

4. A more in-depth discussion of the issues around false positive results with a specific example, such as the authors have done with Angelman syndrome, would strengthen their argument. For example, giving specific numbers on positive predictive values for a rare condition gives the reader a clear idea of how unlikely a positive test result is a true positive. That would give the practicing ob/gyn practical information in counseling his/her patient.

Thank you for this comment. We have added more specific data from a study of NIPS for microdeletions (see lines 76-78).

5. Do the authors believe that obstetrician gynecologists are well-position to counsel their patients? I would argue that they have limited resources to adequately counsel their patients that isn't provided by the testing laboratories.

Thank you for this important point. It is true that unfortunately, OB/GYNs often have limited time to have in-depth discussions about the different genetic testing options with patients. However, until genetic counselors are much more broadly available to have these conversations, we believe OB/GYNs are the best positioned (if not perfectly well-positioned).

6. The final line of the discussion should be changed to "has met accepted scientific and ethical criteria".

Thank you – we have made this change.

Reviewer #3:

This is a beautifully written and well-argued piece. I have two comments for the author to consider.

1. The final conclusion - that patients should be able to purchase commercially available tests out of respect for their autonomy - seems inconsistent with the arguments made about regulation and also reflects a rather thin conception of autonomy, in that commercial offers of (associated with marketing of) a product that may have profoundly problematic and hidden harms may not in fact respect autonomy in what ethicists call the "thick" sense of the word, and instead undermine it. Perhaps the authors could offer some nuance to this sentence in the conclusion, or delete it. I think in the context of the paper it is confusing and potentially misleading.
Thank you for this excellent point. We agree that respect for autonomy does not require allowing patients to access whatever kind of testing, no matter how problematic. At the same time, we believe that if tests are vetted by agencies such as the FDA and FTC and meet at least basic thresholds for accuracy and truthfulness in advertising AND patients are thoroughly counseled on the low PPV and possible need for invasive follow-up testing, they should be permitted to access the test. The alternative would be to ban certain kinds of testing outright, which could have far-reaching, unintended consequences. We have expanded on this point in the conclusion.

2. The authors do a great job of pointing to some of the moral problems associated with NIPT as a public health screening tool, but miss one that seems important which is that treatment where NIPT is concerned is not necessarily amelioration or elimination of the condition, but, where termination is concerned, elimination of the individual (the fetus) who is affected by it. This distinction is often lost in conversations about genetic testing but it seems to me that it should not be glossed over in this piece, where a framework for public health screening is being considered.

Thank you for this point. We have strengthened our paragraph on pregnancy termination (lines 60-71) by using the reviewer’s language regarding elimination of the affected fetus.

EDITORIAL OFFICE COMMENTS:

We do not respond point-by-point to the editorial comments below, but have ensured that our draft abides by Green Journal standards.

1. The Editors of Obstetrics & Gynecology have increased transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:

A. **OPT-IN: Yes, please publish my point-by-point response letter.**
B. **OPT-OUT: No, please do not publish my point-by-point response letter.**

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:
   * Include your title page information in the main manuscript file. The title page should appear as the first page of the document. Add any previously omitted Acknowledgements (ie, meeting presentations, preprint DOIs, assistance from non-byline authors).
   * Funding information (ie, grant numbers or industry support statements) should be disclosed on the title page and in the body text. For industry-sponsored studies, the Role of the Funding Source section should be included in the body text of the manuscript.
   * 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 uses an "electronic Copyright Transfer Agreement" (eCTA), which must be completed by all authors. When you uploaded your manuscript, each co-author received an email with the subject, "Please verify your authorship for a submission to Obstetrics & Gynecology." Please check with your coauthors to confirm that they received and completed this form, and that the disclosures listed in their eCTA are included on the manuscript's title page.

4. Our journal requires that all evidence-based research submissions be accompanied by a transparency declaration statement from the manuscript's lead author. The statement is as follows: "The lead author* affirms 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 (and, if relevant, registered) have been explained." *The manuscript's guarantor.

If you are the lead author, please include this statement in your cover letter. If the lead author is a different person, please ask him/her to submit the signed transparency declaration to you. This document may be uploaded with your submission in Editorial Manager.

5. 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://urldefense.com/v3/__https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-obstetrics-data-definitions__;!!MXfaZl3l!IEY8Z_wGB0EYEVI8lS6c82MoXmeXFG6ELZfpvYZ--51F1HhqYABcf5DRWutjTE4gCFvZ_gSCC5yIA$ and the gynecology data definitions at https://urldefense.com/v3/__https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-gynecology-data-definitions__;!!MXfaZl3l!IEY8Z_wGB0EYEVI8lS6c82MoXmeXFG6ELZfpvYZ--51F1HhqYABcf5DRWutjTE4gCFvZ_ghiehdZQS$. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

6. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Current Commentary articles should not exceed 3,000 words. Stated word limits include the title page, précis, abstract, text, tables, boxes, and figure legends, but exclude references.

7. Specific rules govern the use of acknowledgments in the journal. Please note the following guidelines:

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