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- 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-20-2753


Dear Dr. Dahdouh:

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).

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 Dec 11, 2020, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:

The presented manuscript is a review of preimplantation genetic testing for aneuploidy during in vitro fertilization. The author presents a solid background and concise description of landmark randomized controlled trials on the topic. Additionally covered is a discussion of mosaicism and its impact on outcomes.

1. Line 125: briefly describe why the authors of this study in 2017 chose to use a day 3 biopsy as you have previously indicated that day 3 biopsy is not recommended.
2. Lines 148-149: recommend changing to "fewer embryo transfers, an increase in eSET, and a lower miscarriage rate..."
3. Lines 150-152: please briefly explain why polar biopsy is more expensive and causes greater workload.
4. Lines 153-155: this statement seems to contradict the only literature that you have presented on PGT-A of polar body biopsy, which was overall favorable.
5. Lines 168-169: please clarify which rate is stated here (I assume mosaic embryo rate).
6. Line 199: is this statement indicating that mosaicism decreasing with advancing maternal age?
7. Tables 1 and 2: I would recommend combining these into one table for ease of reference.

Reviewer #2:

The authors conduct a review of the evidence supporting the use of preimplantation genetic testing for aneuploidy (PGT-A) on trophectoderm biopsy samples as part of assisted reproductive technology (ART).

They summarize that "PGT-A does not improve ongoing pregnancy rates per cycle started, but seems to be a good embryo selection tool for patients with normal ovarian reserve"

In general this is an extremely relevant and important topic to the readership given the widespread use of PGT-A. The authors summarize the limited high quality data to support this practice and also discuss the evolution of the technology and special issues raised as a result of its use such as the controversy of mosaic embryo transfer. The authors include studies that are not completely relevant to today's practice of PGT-A such as RCTs of PGT-A performed on specimens from
polar body biopsy and cleavage stage biopsy. In parts of the manuscript the language used seems overly colloquial.

Abstract:
Would benefit from background information about frequency of use to highlight relevance. "X"% of cycles or X# of embryos transferred undergo PGT-A .

The objective of PGT'A is to select for transfer of a euploid embryo. Would exclude viable—this has connotations which authors may not intend.

Introduction:
Lines 76-77. Would expand upon the frequency of use—this is an important point where evidence may not support what has become general practice in some regions.

Lines 108-109. Cannot comment on miscarriage rate if non-significant.

Lines 122-24. A bit colloquial. Suggest "While favorable clinical outcomes were seen in this population and high volume laboratories, generalizability remains in question."

Line 125. As discussed in the introduction, cleavage stage biopsy was discarded years prior to this study, which raises the question of relevance of this RCT. It seems odd to be presenting this after the discussion of early RCTs of blastocyst biopsy for PGT-A

Line 143. Again, the question of relevance is raised here as polar body biopsy is infrequently pursued (for reasons stated). I think this trial should be removed from discussion as it is not clinically relevant.

Line 161. "nowadays." Used at other points in manuscript as well. This is perceived as overly colloquial for the journal.

Line 162. Would be helpful to know how "good ovarian reserve" was defined.

Line 169. 10.5% to 26.4% refers to range of euploid? Or mosaic embryos? Would include both data points.

Line 170. The consideration that mosaic embryo transfers may lead to normal babies is an important one but I don't think it has been discussed previously. Therefore, I would not say "raising again."

Line 199. Is this a consistent finding that mosaicism rates decrease with advancing age? I think rate of mosaicism has been reported to be relatively constant across the age spectrum but that a greater fraction of embryos are aneuploid with increasing age.

Line 217. Speculation about the possibility of human embryonic self-correction seems outside the scope of this review.

Would include new data confirming absent harm from trophectoderm biopsy and discussing outcomes associated with mosaic embryo transfer (RT Scott, A multicenter, prospective, blinded, non-selection study evaluating the predictive value of an aneuploid diagnosis using a targeted next-generation sequencing-based preimplantation genetic testing for aneuploidy assay and impact of biopsy, Fertil Steril, in press)

Any discussion of development of noninvasive PGT-A? Even if just a line or two as this is likely future of field?

Reviewer #3:
This is a thoughtful and well written review of an important topic. I have only four comments

1. The authors, in reviewing the first three RCT's, need to emphasize that the Forman trial cannot be used to contrast delivery rates- only implantation rates. While these are alluded to, the difference in transfer order allowed to study a different question, which is the ability of PGT-A to eliminate the need for multiple embryo transfer. The implantation rate remain relevant, but not the delivery rate per se in contrast to the other two studies with equivalent transfer orders where it is possible to compare live birth rates

2. In the review of the STAR trial, greater emphasis should be placed and the high rates of aneuploidy - especially in younger patients.
3. The authors really need to emphasize that data on one analytical platform should not really be compared to data from other platforms. The data to support that statement is enormous.

4. The authors need to emphasize how users of this technology should know the predictive values of an abnormal and a normal test for delivery rates. Predictive values are critical to using any diagnostic test. PGT-A is no exception. This requires great emphasis.

EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology are seeking to increase 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. Obstetrics & Gynecology uses an "electronic Copyright Transfer Agreement" (eCTA). When you are ready to revise your manuscript, you will be prompted in Editorial Manager (EM) to click on "Revise Submission." Doing so will launch the resubmission process, and you will be walked through the various questions that comprise the eCTA. Each of your coauthors will receive an email from the system requesting that they review and electronically sign the eCTA.

   Please check with your coauthors to confirm that the disclosures listed in their eCTA forms are correctly disclosed on the manuscript's title page.

3. 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.

4. 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 12 typed, double-spaced pages (3,000 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and print appendixes) but exclude references.

5. 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).

6. 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 Current Commentary articles is 250 words. Please provide a word count.

7. Only standard abbreviations and acronyms are allowed. A selected list is available online at [http://edmgr.ovid.com/ong/accounts/abbreviations.pdf](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.

8. The commercial name (with the generic name in parentheses) may be used once in the body of the manuscript. Use the generic name at each mention thereafter. Commercial names should not be used in the title, précis, or abstract.

9. 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.

10. 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.

If appropriate, please include number needed to treat for benefits (NNTb) or harm (NNTh). When comparing two procedures, please express the outcome of the comparison in U.S. dollar amounts.

Please standardize the presentation of your data throughout the manuscript submission. For P values, do not exceed three decimal places (for example, "P = .001"). For percentages, do not exceed one decimal place (for example, "11.1").

11. Please review the journal’s Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available online here: [http://edmgr.ovid.com/ong/accounts/table_checklist.pdf](http://edmgr.ovid.com/ong/accounts/table_checklist.pdf).

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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 reference you are citing is still current and available. If the reference you are citing has been updated (ie, 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 (exceptions could include manuscripts that address items of historical interest). All ACOG documents (e.g., Committee Opinions and Practice Bulletins) may be found at the Clinical Guidance page at https://www.acog.org/clinical (click on "Clinical Guidance" at the top).

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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 in a word processing format such as Microsoft Word. 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 Dec 11, 2020, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

John O. Schorge, MD
Associate Editor, Gynecology

2019 IMPACT FACTOR: 5.524
2019 IMPACT FACTOR RANKING: 6th out of 82 ob/gyn journals

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Montreal, November 27th 2020

John O. Schorge, MD
Associate Editor, Gynecology
Obstetrics & Gynecology

RE: Manuscript Number ONG-20-2753

Dear Editor,

Thank you for the opportunity to revise my manuscript for consideration and possible publication in Obstetrics & Gynecology. I have addressed each of the reviewers and editors’ comments, and I greatly appreciate their valuable suggestions and constructive recommendations.

Enclosed in this cover letter are my point-by-point responses to each of the referees’ comments. For an easy read, answers are written in Italic style and highlighted in blue. I also confirm that I have read and carefully reviewed the instructions for the Authors document.

I confirm that this manuscript has not been published before and is not considered for publication in any other journal. I appreciate the opportunity to publish it in your esteemed journal, and I thank you again for your consideration.

Sincerely,

Elias M. Dahdouh, MD, MSc
Founder & Medical Director
ART Centre, CHU Sainte-Justine
University of Montreal
Montreal, Canada
REVIEWER COMMENTS:

Reviewer #1:

The presented manuscript is a review of preimplantation genetic testing for aneuploidy during in vitro fertilization. The author presents a solid background and concise description of landmark randomized controlled trials on the topic. Additionally covered is a discussion of mosaicism and its impact on outcomes.

Dear reviewer, thank you very much for your overall favorable evaluation of the manuscript.

1. Line 125: briefly describe why the authors of this study in 2017 chose to use a day 3 biopsy as you have previously indicated that day 3 biopsy is not recommended.

Thank you for this comment. The following explanation and statement were added to the manuscript: “Patients recruitment for this trial started in early 2012 when IVF centers in Europe had still limited experience in blastocyst biopsy.”

2. Lines 148-149: recommend changing to "fewer embryo transfers, an increase in eSET, and a lower miscarriage rate…”

Thank you. It was changed as requested.

3. Lines 150-152: please briefly explain why polar biopsy is more expensive and causes greater workload.

Thank you for your inquiry. It was already mentioned in the manuscript “... by increasing the number of biopsy procedures and genetic tests”. (more fertilized oocytes than blastocysts to be biopsied and tested are available in a given cycle).

4. Lines 153-155: this statement seems to contradict the only literature that you have presented on PGT-A of polar body biopsy, which was overall favorable.

Thank you. In fact, the cumulative LBR in one year (primary outcome) was similar in both groups. To avoid this confusion, the term “the literature indicates that…” was removed from this sentence.
The statement was therefore amended as follows: “For the aforementioned reasons, being only useful in countries where embryo biopsy is deemed illegal, PGT-A on the first and the second polar body has practically no indication in the current assisted reproduction practice”.

5. Lines 168-169: please clarify which rate is stated here (I assume mosaic embryo rate).

Thank you. It was indeed the mosaic rate. Both the euploid and the mosaic rates were included in the manuscript (as recommended by Reviewer#2) as follows:
“It is also worth mentioning that euploid and mosaic embryo rates were highly variable between clinics and genetic laboratories, varying from 26 to 60% and from 10.5% to 26.4%, respectively”.

6. Line 199: is this statement indicating that mosaicism decreasing with advancing maternal age?

Thank you for your valuable comment. In the paper by Munné et al. RBMOnline 2018, it was reported that mosaicism decreased with ARA. However, this finding was indeed inconsistent in the literature and therefore deleted from the present manuscript (as also suggested by Reviewer#2).

7. Tables 1 and 2: I would recommend combining these into one table for ease of reference.

Thank you for your recommendation. Tables 1 & 2 were combined in one Table (#1).

Reviewer #2:

The authors conduct a review of the evidence supporting the use of preimplantation genetic testing for aneuploidy (PGT-A) on trophectoderm biopsy samples as part of assisted reproductive technology (ART).

They summarize that "PGT-A does not improve ongoing pregnancy rates per cycle started, but seems to be a good embryo selection tool for patients with normal ovarian reserve"

In general this is an extremely relevant and important topic to the readership given the widespread use of PGT-A. The authors summarize the limited high quality data to support this practice and also discuss the evolution of the technology and special issues raised as a result of its use such as the controversy of mosaic embryo transfer. The authors include studies that are not completely relevant to today's practice of PGT-A such as RCTs of PGT-A performed on specimens from polar body biopsy and cleavage stage biopsy. In parts of the manuscript the language used seems overly colloquial.

Dear reviewer, thank you for your overall favorable assessment of the manuscript. I do recognize that Rubio et al. and ESTEEM trials are in fact not relevant to today’s practice. Yet, they were included in this review as being part of all the published RCTs on PGT-A applying CCS technology. I do also admit that in parts the language seems colloquial, some modifications have been integrated to make it more formal.

Abstract:
Would benefit from background information about frequency of use to highlight relevance. "X"% of cycles or X# of embryos transferred undergo PGT-A.
Thank you for your suggestion. Frequency and true number of PGT-A cycles are difficult to get as many cycles are not being reported to national ART registry. Nevertheless, some data can be extracted from the published SART data. I included in the Abstract: “Around 95,000 PGT cycles were carried out in the US between 2014 and 2016, the majority of which were performed for PGT-A”.

The objective of PGT-A is to select for transfer of a euploid embryo. Would exclude viable—this has connotations which authors may not intend.

Thank you. It was excluded as suggested (in the abstract and in the introduction sections).

Introduction:
Lines 76-77. Would expand upon the frequency of use—this is an important point where evidence may not support what has become general practice in some regions.

Thank you. The following sentence was added in the introduction: “Between 2014 and 2016, the proportion of IVF cycles that underwent PGT increased from 13% to 27% in the US. During this time, a total number of 94,935 PGT cycles were undertaken, the majority of which were performed for PGT-A”.

Lines 108-109. Cannot comment on miscarriage rate if non-significant.

Thank you. This sentence was deleted as suggested.

122-24. A bit colloquial. Suggest "While favorable clinical outcomes were seen in this population and high-volume laboratories, generalizability remains in question."

Thank you for your valuable comment. It was changed accordingly as suggested.

Line 125. As discussed in the introduction, cleavage stage biopsy was discarded years prior to this study, which raises the question of relevance of this RCT. It seems odd to be presenting this after the discussion of early RCTs of blastocyst biopsy for PGT-A.

Thank you. Though I agree that Rubio’s RCT is in fact not relevant to today’s practice, this trial was presented in order to include in this review all the published RCTs on PGT-A using CCS technology in a chronological manner (date of publication).

Line 143. Again, the question of relevance is raised here as polar body biopsy is infrequently pursued (for reasons stated). I think this trial should be removed from discussion as it is not clinically relevant.

Thank you. Though I agree that the ESTEEM trial is in fact not relevant to today’s practice, this trial was presented in order to include in this review all the published RCTs on PGT-A using CCS technology in a chronological manner (date of publication).
Line 161. "nowadays." Used at other points in manuscript as well. This is perceived as overly colloquial for the journal.

*Thank you. “Nowadays” was deleted from the sentence.*

Line 162. Would be helpful to know how "good ovarian reserve" was defined.

*Thank you for this comment. In fact, this trial excluded diminished ovarian reserve patients. The term “with good ovarian reserve” was replaced by “with no diminished ovarian reserve”.*

Line 169. 10.5% to 26.4% refers to range of euploid? Or mosaic embryos? Would include both data points.

*Thank you. It refers to the mosaic rate. Both the euploid and the mosaic rates were included.*

Line 170. The consideration that mosaic embryo transfers may lead to normal babies is an important one but I don't think it has been discussed previously. Therefore, I would not say "raising again."

*Thank you. The term “…again…” was deleted.*

Line 199. Is this a consistent finding that mosaicism rates decrease with advancing age? I think rate of mosaicism has been reported to be relatively constant across the age spectrum but that a greater fraction of embryos are aneuploid with increasing age.

*Thank you for your valuable comment. In the paper by Munné et al. in RBMOnline 2018, it was reported that mosaicism decreased with ARA. However, this finding was indeed inconsistent in the literature and therefore deleted from the present manuscript.*

Line 217. Speculation about the possibility of human embryonic self-correction seems outside the scope of this review.

*Thank you. However, I believe that it could be of great interest to the journal readers to present this speculation in only two sentences. This might explain how mosaic embryo transfers can eventually lead to healthy babies.*

Would include new data confirming absent harm from trophectoderm biopsy and discussing outcomes associated with mosaic embryo transfer (RT Scott, A multicenter, prospective, blinded, non-selection study evaluating the predictive value of an aneuploid diagnosis using a targeted next-generation sequencing-based preimplantation genetic testing for aneuploidy assay and impact of biopsy, Fertil Steril, in press)
Thank you. Findings and data from this key paper (Tiegs et al. 2020) were included in the manuscript at the end of the STAR trial section. It was also referenced in the introduction where it was commented on the harmless effect of TE biopsy.

Any discussion of development of noninvasive PGT-A? Even if just a line or two as this is likely future of field?

Thank you. A brief description of this new technique was included in two sentences with key references at the end of the discussion section:
“Recently, a noninvasive form of PGT-A has been introduced into clinical practice; it consists of testing embryonic cell-free DNA in the blastocyst culture media. This technique has shown high concordance with TE results, and can avoid the invasive biopsy procedure while decreasing cost”.

Reviewer #3:

This is a thoughtful and well written review of an important topic. I have only four comments.

Dear reviewer, thank you for your overall favorable evaluation of the manuscript.

1. The authors, in reviewing the first three RCT’s, need to emphasize that the Forman trial cannot be used to contrast delivery rates- only implantation rates. While these are alluded to, the difference in transfer order allowed to study a different question, which is the ability of PGT-A to eliminate the need for multiple embryo transfer. The implantation rate remains relevant, but not the delivery rate per se in contrast to the other two studies with equivalent transfer orders where it is possible to compare live birth rates.

Thank you for pointing out this interesting comment. I agree that in Forman trial the implantation rates are main relevant outcomes because of the difference in transfer order (eSET in PGT-A vs. eDET in controls). The purpose of the research was to show that despite only one embryo transferred from PGT-A vs. two in control groups, the OPR were equal, yet implantation rates were higher with PGT-A owing to dramatic decrease in multiples. These findings will eliminate the indication for DET favoring eSET practice with PGT-A. I believe that these comments were already included in the original manuscript. The OPR (being the primary outcome of the Forman trial) were kept, and implantations rates were added to the manuscript.

2. In the review of the STAR trial, greater emphasis should be placed and the high rates of aneuploidy - especially in younger patients.

Thank you for this comment. I included in the STAR trial section the high rates of aneuploidy:
“In this trial, only 43.1% of the blastocysts analyzed by PGT-A were reported as euploid and 54.2% as aneuploid. Furthermore, the percentage of aneuploid embryos was particularly high, ranging from 49.3% in the patients under 35 years to 61.9% in patients over 35.”

3. The authors really need to emphasize that data on one analytical platform should not really be compared to data from other platforms. The data to support that statement is enormous.

4. The authors need to emphasize how users of this technology should know the predictive values of an abnormal and a normal test for delivery rates. Predictive values are critical to using any diagnostic test. PGT-A is no exception. This requires great emphasis

Answers to comments 3. and 4.: 

Thank for your valuable comments. These two points are indeed very helpful to users of this technology and should be addressed in this manuscript. Data indicating clinical error rates and discrepancies between different platforms used in PGT-A were included. Recent published work from a nonselection study on NGS for PGT-A by Tiegs et al. Fertil Steril 2020 evaluating the predictive value of an aneuploid diagnosis was also incorporated as follows:

At the end of the introduction section, the following sentences were included:
“Despite the potential benefits of the newer version of PGT-A, a misdiagnosis can still occur with each CCS platform. For example, the technical error rate of aCGH and qPCR were estimated around 2% and 0.2-0.3% respectively.(15, 16) Additionally, a study by Scott et al. calculated a 41% positive predictive value for the ability of the SNP microarray technology to predict a euploid live birth, and a negative predictive value of 96%. (17) On the other hand, recent published data from Friedenthal et al. estimated the clinical error rates of NGS at 0.7% per embryo, at 1% per pregnancy with gestational sac, and at 0.1% per live birth.(18) While the overall error rate is low, these results make comparison of the clinical outcomes from different platforms inappropriate and thus require a complete genetic counselling for patients undergoing PGT-A”.

In the STAR trial section, the following two sentences were included:
“However, a recent nonselection study by Tiegs et al. showed that the predictive value for a live birth of a euploid embryo diagnosed by a targeted NGS assay was 64.7%. Conversely, the likelihood of an embryo tested as aneuploid by the same platform and progressing to live birth was 0%”.
EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology are seeking to increase 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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   A. OPT-IN: Yes, please publish my point-by-point response letter.

2. Obstetrics & Gynecology uses an "electronic Copyright Transfer Agreement" (eCTA). When you are ready to revise your manuscript, you will be prompted in Editorial Manager (EM) to click on "Revise Submission." Doing so will launch the resubmission process, and you will be walked through the various questions that comprise the eCTA. Each of your coauthors will receive an email from the system requesting that they review and electronically sign the eCTA.

   I reviewed and signed the eCTA

   Please check with your coauthors to confirm that the disclosures listed in their eCTA forms are correctly disclosed on the manuscript's title page.

3. 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.

   No problem encountered.

4. 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 12 typed, double-spaced pages (3,000 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and print appendixes) but exclude references.

Word Count (body of the manuscript): 2829.

5. 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).

Nothing to disclose.

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Will do. Thank you.