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: 12/16/2022
To: "Brett David Einerson" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-22-1956

RE: Manuscript Number ONG-22-1956

Clinical Expert Series: Placenta Accreta Spectrum

Dear Dr. Einerson:

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, and STATISTICAL EDITOR COMMENTS (if applicable) below.

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 01/06/2023, we will assume you wish to withdraw the manuscript from further consideration.

EDITOR COMMENTS:

Please note the following:

* Help us reduce the number of queries we add to your manuscript after it is revised by reading the Revision Checklist at https://journals.lww.com/greenjournal/Documents/RevisionChecklist_Authors.pdf and making the applicable edits to your manuscript.

* Figure 1: Is this figure original? Please upload as a figure file on Editorial Manager.

* Figures 2-3: Please upload as figure files on Editorial Manager.

REVIEWER COMMENTS:

Reviewer #1: This is a much needed and very clearly written review of contemporary practices and recommendations for care of patients with placenta accreta spectrum.

I applaud the authors for the very well-organized and comprehensive review of the topic. The images and tables are excellent.

I have the following minor recommendations:

1) I recommend balancing the discussion of use of MRI just a bit. There is some bias that clearly favors avoiding its use. The authors go on to state a few paragraphs after the initial recommendation to use MRI only if assessing differences with ultrasound, it is stated that MRI and ultrasound have similar diagnostic performance, which contradicts the original discussion about its utility. In the proper setting and "eyes," MRI has been shown in multiple smaller studies to be useful

with similar diagnostic accuracy. The same principles apply to the diagnostic capability of ultrasound, and this equipoise is not clearly represented in the discussion. I agree, like most, that ultrasound is first line due to its ubiquity, non-invasiveness and low cost, but MRI may be very helpful in select cases, in the right center(s).

2) There is a new publication that clarifies very nicely the steps and the caveats for single surgery focal resection and repair. Consider including and citing it in the section about focal resection. The biggest dilemma with this approach is that it can be difficult to know with certainty ahead of time, whether the extent of scarring and hypervascularity will permit this approach, even with antenatal imaging. This is where counseling patients about an attempt, with default to hysterectomy if needed is important. Knowing when to use this approach vs. proceeding directly to hysterectomy is perhaps a more nuanced skill than the surgical skills necessary for either approach. (Citation: Nieto-Calvache AJ, Palacios-Jaraquemada JM, Aryananda R, et al. How to perform one-step conservative surgery for placenta accreta spectrum move by move [published online ahead of print, 2022 Nov 10]. Am J Obstet Gynecol MFM. 2022;100802. doi:10.1016/j.ajogmf.2022.100802)

Reviewer #2:

Overall, I think the review is well presented by the authors and highlights many areas that lack quality research. I do think there are various areas of the manuscript that could be presented more clearly.

-throughout various places in the manuscript, recommend authors refer to Cesarean hysterectomy rather than hysterectomy alone if that is what they are trying to convey.
-several areas of data presented under Etiology and Risk Factors and Classification sections need corresponding references.

Incidence
-the paragraph has contradictory sentences. One states the incidence is increasing while another says it may be increasing as accurate data are hard to come by. Fix to be more clear.

Diagnosis

System Preparedness
-This section would be better under Antenatal Management after Diagnosis section
-Please make sure what is stated in this section is consistent with ACOG/SMFM guidelines

Diagnosis
-add consideration of cost of MRI as one of barriers.
-Recommend a table summarizing SMFM Task Force findings, or requesting permission to use Table 3 from their Special Report.

Assessment of Risk Section
-Review first trimester screening for low implantation cite or c-scar ectopic.
-Consider a table on a priori risk modification for more common risk factors.
-Consider including numbers (if available) on how rare PAS is if placenta is away from uterine scar.
-Move recommendation for transvaginal sweep to Ultrasound section.

Ultrasound
-Move discussion of risks from placenta previa to "Assessment of Risk" section

MRI
-use or the term "system-specific" is not clear here. This is a confusing term. Do you mean it is specific to the institution or healthcare system, or system (anatomic location) specific? I assumed the former.

Antenatal Staging and Morbidity Predictions
-Consider re-wording question…from "Where is the body of disease location" to "is there invasion into surrounding pelvic structures (i.e. bladder)?"

Coordinated Antenatal Care and Preparation
-Recommend restructuring this paragraph to start with determining a patient's a priori risk and obtaining imaging early in the pregnancy, in addition to reviewing the potential risk and health concerns.
-Are there any recommendations regarding hemoglobin/iron level targets, when to consider IV iron versus oral iron, when to start and how often to reassess, etc.?

Delivery Timing
-Please be very clear what is meant by "less sever disease" in the sentence "Delivery near term may be safe in cases of less severe disease or those without placenta previa." Does this include no previa but percreta suspected? If not, please clarify what is meant by this.

Delivery and Treatment
-Recommend this section be categorized into surgical and non-surgical management. Surgical management can be further categorized into immediate and delayed.

Immediate Hysterotomy
-Recommend addressing hysterectomy prior to viability, with fetus and placenta left in-situ, which is a rare but reasonable alternative for those who elect for pregnancy termination in the second trimester prior to viability.
-Please define or remove the "PAS" term preceding hysterectomy.
-"Some centers routinely make use of preoperative or intraoperative cystoscopy to delineate the position of the bladder and ureters, and prophylactic ureteral stent placement has been associated with reduced incidence of genitourinary injury in PAS cases." Recommend a separate section devoted to preoperative preparation and discussion of these techniques in more depth.

Partial Myometrial Dissection
-What types of studies are the authors citing in last sentence- case series, case reports?

Intrapartum Diagnosis
-Recommend authors summarize figure 1 more clearly in these 2-3 paragraphs. Give examples of when is it advisable to close the abdomen prior to creating a hysterectomy and transfer the patient to a PAS center. Mention the need for centers with fewer resources to have an action plan for this prior to encountering this type of situation, etc.

Postpartum care - Short term Postpartum care
-Recommend authors address anticipation and coordination of critical care, and specific OB needs during and after ICU care including post ICU syndrome.

Box 1
-Recommend creating a separate historical column rather than interspacing with current FIGO grade

Figure 1
-For second to right column, recommend stating BEFORE HYSTEROTOMY. For far right column, I am assuming the authors are advocating for closing uterus and abdomen prior to placental delivery. Maybe state AFTER DELIVERY WITH PLACENTA IN-SITU.

Editorial Office Note: This reviewer submitted additional edits for consideration directly to the Editor. These comments have been blinded and will be returned to you by in a separate email from Randi Zung.

Reviewer #3: Thank you for the opportunity to review this manuscript entitled, "Clinical Expert Series: Placenta Accreta Spectrum." This is a clinical expert series manuscript that reviews the etiology, diagnosis, and management of PAS disorders. The manuscript is well written, and I believe this will provide helpful guidance to our readership which includes clinicians who may encounter PAS disorders in their clinical practice. I have some comments outlined below:

-Page 4: Provide references for the sentence: "Accurate population-based statistics are hard to come by since PAS coding did not exist until recently in the ICD handbook and since disease definitions are evolving."

-Pages 5-6 (Classification): I suggest that the authors present the classification schemes in 1-2 sentences. Currently, the FIGO and PAS grades seem to come out of nowhere. Box 1 does not specify FIGO and PAS grades in the title or legend, just puts the references. This should be clarified.

-Page 6: For the sentence, "System preparedness is more important than an individual clinician's experience or skill in ensuring safe and effective PAS care," would suggest the word "may" instead of "is"

-Page 8-9: For the sentence, "Missed antenatal diagnosis leads to management in a less-prepared setting and results in worse outcomes," would suggest changing the wording of "missed antenatal diagnosis" as this implies that someone missed something. Also, perhaps avoid "a mistake made too commonly." While that could be the case in some cases, the limitations of our current diagnostic methods also contribute. This type of wording should be carefully used as this type of language could set up our medical community for medico-legal issues.

-Page 9: The sentence "its routine use is limited by lack of proven benefit and limited availability of expertise in MRI interpretation for PAS" should include references.

-Page 10: For sentence, "Transvaginal imaging with sweeps of the lower uterine segment can be invaluable to clarify this area in higher resolution," references should be provided as vaginal approach is the gold standard when evaluating previa and concern for PAS.

-Page 14: For sentence, "Antenatal corticosteroid administration is indicated when delivery is planned as preterm," suggest making language less strong because antenatal corticosteroids may be intentionally deferred in the setting of late preterm in the setting of maternal diabetes or twin gestation and may not always be "indicated" in the preterm period.

-Page 16: When referring to FIGO or PAS grades, suggest again referencing Box 1.

-Page 23: Would provide more references for the section "Endovascular approaches to reduce blood loss."

-Box 1: see comments above

-Box 2: would suggest changing the title of this box to better clarify that this box gives suggestion of current knowledge gaps and are potential areas for future research

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Sincerely,
Jason D. Wright, MD
Editor-in-Chief

The Editors of Obstetrics & Gynecology

_____

RE: Manuscript Number ONG-22-1956

Clinical Expert Series: Placenta Accreta Spectrum

Jan 11, 2023

Thank you to the editors for considering this revised manuscript for the Clinical Expert Series on Placenta Accreta Spectrum. We are deeply appreciative of the reviewers for their expert suggestions and comments. We have addressed each prompt (below) and find that the revised submitted manuscript is improved significantly. Itt is also considerably longer as a result of responding to reviewer requests.

Please do let us know what else can be done. We hope you will find this submission suitable for publication in Obstetrics & Gynecology.

Very sincerely,
Brett D. Einerson, MD MPH

EDITOR COMMENTS:

* Figure 1: Is this figure original? Please upload as a figure file on Editorial Manager.
This is original. An simpler flow diagram was previously featured in OBG Management, but this one is sufficiently different to be considered original, in my opinion.

* Figures 2-3: Please upload as figure files on Editorial Manager.
This has been done.

REVIEWER COMMENTS:

Reviewer #1:

This is a much needed and very clearly written review of contemporary practices and recommendations for care of patients with placenta accreta spectrum.

I applaud the authors for the very well-organized and comprehensive review of the topic. The images and tables are excellent.
We appreciate these comments.

I have the following minor recommendations:

1) I recommend balancing the discussion of use of MRI just a bit. There is some bias that clearly favors avoiding its use. The authors go on to state a few paragraphs after the initial recommendation to use MRI only if assessing differences with ultrasound, it is stated that MRI and ultrasound have similar diagnostic performance, which contradicts the original discussion about its utility. In the proper setting and "eyes," MRI has been shown in multiple smaller studies to be useful with similar diagnostic accuracy. The same principles apply to the diagnostic capability of ultrasound, and this equipoise is not clearly represented in the discussion. I agree, like most, that ultrasound is first line due to its ubiquity, non-invasiveness and low cost, but MRI may be very helpful in select cases, in the right center(s).

We appreciate this perspective and we have edited this section to reflect the reviewer's comments (additions emphasized).

Lines 190-196

"Use of MRI for diagnosis may be preferred in some institutions and its use is under active investigation in PAS research centers, but clinicians should not presume that MRI will be a helpful adjunct to ultrasound in every setting. Expertise in the diagnosis of PAS varies by institution and, like with ultrasound, diagnostic accuracy of MRI is likely worse outside of experienced referral centers. Given its cost and uncertain utility, we believe that MRI should be used only when it is likely to offer important clinical information about the disease character or location *beyond what ultrasound can provide*."

2) There is a new publication that clarifies very nicely the steps and the caveats for single surgery focal resection and repair. Consider including and citing it in the section about focal resection. The biggest dilemma with this approach is that it can be difficult to know with certainty ahead of time, whether the extent of scarring and hypervascularity will permit this approach, even with antenatal imaging. This is where counseling patients about an attempt, with default to hysterectomy if needed is important. Knowing when to use this approach vs. proceeding directly to hysterectomy is perhaps a more nuanced skill than the surgical skills necessary for either approach. (Citation: Nieto-Calvache AJ, Palacios-Jaraquemada JM, Aryananda R, et al. How to perform one-step conservative surgery for placenta accreta spectrum move by move [published online ahead of print, 2022 Nov 10]. Am J Obstet Gynecol MFM. 2022;100802. doi:10.1016/j.ajogmf.2022.100802)

This is true and very helpful. Accordingly, we added these sentiments into the discussion of single surgery focal resection and repair (additions emphasized).

Lines 554-570

"Single-surgery partial myometrial resection and reconstruction of the uterus is a treatment approach in some areas of the world. This strategy involves *en bloc* resection of the placenta and attached myometrium in well-selected cases followed by repair and reconstruction of the remaining uterus and cervix. [the above citation added] This strategy is typically performed during the same surgery as cesarean delivery. Important to the success of this approach is experience in determining at the time of surgery whether to attempt resection or proceed directly to hysterectomy based on individual patient characteristics. These include sufficient viable myometrial tissue surrounding the affected area, degree of hypervascularity, and location and severity of pelvic adhesive disease. Knowing when to use this approach is a nuanced skill that comes only with experience. Some investigators couple resection and repair with pelvic devascularization procedures, compression suturing, incorporating the cervix into the closure, or tourniquet placement to reduce blood loss during uterine repair and reconstruction.

"This approach has not been commonly used (or at least has not been widely reported) in the U.S. SMFM and ACOG state that this approach should be "rare and considered individually." Patients considering this approach should understand that resection may not be possible or may result in significant bleeding that would require hysterectomy."

Reviewer #2:

Overall, I think the review is well presented by the authors and highlights many areas that lack quality research. I do think there are various areas of the manuscript that could be presented more clearly.
We appreciate the work of Reviewer 2 to provide a revised version of the manuscript that addresses many of the concerns below.

-throughout various places in the manuscript, recommend authors refer to Cesarean hysterectomy rather than hysterectomy alone if that is what they are trying to convey.
This has been updated, at the reviewer's request throughout the manuscript.

-several areas of data presented under Etiology and Risk Factors and Classification sections need corresponding references.
Agreed. Multiple references have been added in this section.

Incidence
-the paragraph has contradictory sentences. One states the incidence is increasing while another says it may be increasing as accurate data are hard to come by. Fix to be more clear.
This was edited by the reviewer, and those changes were accepted in the revised manuscript. This paragraph now states that PAS 'may be' increasing (line 52-58).

Diagnosis

System Preparedness
-This section would be better under Antenatal Management after Diagnosis section
System preparedness has been moved in accordance with the recommendation.

-Please make sure what is stated in this section is consistent with ACOG/SMFM guidelines
Changes made by the reviewer for consistency with ACOG/SMFM guidelines have been accepted in the revised version of the manuscript.

Diagnosis
-add consideration of cost of MRI as one of barriers.
We agree. See additions to 113 and 194.

"Magnetic resonance imaging (MRI) may be preferred for diagnosis in some institutions, but its routine use is limited by lack of proven benefit, <u>higher cost</u>, and limited availability of expertise in MRI interpretation for PAS.

-Recommend a table summarizing SMFM Task Force findings, or requesting permission to use Table 3 from their Special Report.
Thank you. We will request permission from AJOG for reproducing Table 3 from their Special Report, and if delayed or declined will adapt that content for this review.

Assessment of Risk Section
-Review first trimester screening for low implantation cite or c-scar ectopic.
This was a topic we decided in the original submission to exclude, given space and word-limit constraints. In this revision we offer a succinct description of the importance of first trimester sonographic evaluation of PAS and CSEP and added key citations to guide readers who are interested. If the editors want to see more detailed information in the text, we are happy to include this. New content is <u>emphasized</u> below.

Line 133-136.

“Patients with risk factors for PAS should undergo systematic evaluation of the placenta at multiple times starting early in pregnancy. Evidence of PAS or cesarean scar ectopic pregnancy (CSEP), particularly abnormal vascularity and low placental implantation, can be detected as early as the viability ultrasound at 6-10 weeks.”

-Consider a table on a priori risk modification for more common risk factors.

Thank you for this request. We have added additional data from available contemporary literature on risk modification based on more common risk factors for PAS within the text. While working to build a table for incidence and relative risk, we recognized that most of these estimates are likely non-comparable (coming from individual studies for individual risk factors) and are generally emanating from low-quality studies. In our opinion, the table is not particularly helpful and so we did not include it.

Line 76-79.

“Other risk factors include other uterine surgeries, Asherman syndrome, prior endometrial ablation, multifetal pregnancy, and in vitro fertilization, with relative risks in the literature ranging on the order of 2-7 compared to baseline and persisting when adjusted for factors such as maternal age and prior cesarean delivery.”

-Consider including numbers (if available) on how rare PAS is if placenta is away from uterine scar.
Getting at this exact number is hard and we were unable to find a reference to support the statement as written. We have therefore re-written it to clarify that this is an experience-based opinion (emphasis added).

Line 141-142

“If the placenta is located well-above and away from the level of the prior scar(s), the risk of PAS involving the lower uterine segment is likely exceedingly low.”

-Move recommendation for transvaginal sweep to Ultrasound section.
Thank you. Done.

Ultrasound
-Move discussion of risks from placenta previa to "Assessment of Risk" section
We appreciate that previa is commonly described as a risk factor for placenta accreta spectrum. Our intention in including it here is to remind obstetricians than previa is also an ultrasound sign of PAS. As such, we believe it is important to emphasize that here in the ultrasound section.

MRI
-use or the term "system-specific" is not clear here. This is a confusing term. Do you mean it is specific to the institution or healthcare system, or system (anatomic location) specific? I assumed the former.
This has been clarified using the language suggested by the reviewer, deleting “system specific,” which was, admittedly, vague.

Line 176-178.

“The role of magnetic resonance imaging (MRI) in PAS diagnosis is less well defined. MRI may provide helpful information in select cases and in institutions with special expertise in interpreting placental MRI.”

Antenatal Staging and Morbidity Predictions
-Consider re-wording question…from "Where is the body of disease location" to "is there invasion into surrounding pelvic structures (i.e. bladder)?"
We appreciate this comment, although we find the concept of invasion into pelvic structures is misunderstood. We revised this to read instead "Where exactly is the placenta located in the uterus and pelvis?" (line 210).

Coordinated Antenatal Care and Preparation
-Recommend restructuring this paragraph to start with determining a patient's a priori risk and obtaining imaging early in the pregnancy, in addition to reviewing the potential risk and health concerns.
We appreciate this recommendation and have revised the paragraph as suggested by the reviewer. Line 288-302.
-Are there any recommendations regarding hemoglobin/iron level targets, when to consider IV iron versus oral iron, when to start and how often to reassess, etc.?
We have expanded this paragraph to include ACOG recommended screening and treatment thresholds for anemia as well as specific considerations for patients with PAS, inclusive of 2 added references. Line 309-316.
"Laboratory screening for anemia at 24-28 weeks and treatment for hemoglobin levels under 10.5 g/dL and/or serum ferritin levels under 30 ng/dL, which is recommended in all pregnancies, is critical in this population. Optimizing hemoglobin prior to delivery may require high concentration iron replacement using IV iron formulations. Treatment thresholds in PAS for hemoglobin or serum ferritin have not been established, but given safety and efficacy data, strong consideration for late second or early third trimester adminstration of IV iron rather than oral iron is advisable."

Delivery Timing
-Please be very clear what is meant by "less sever disease" in the sentence "Delivery near term may be safe in cases of less severe disease or those without placenta previa." Does this include no previa but percreta suspected? If not, please clarify what is meant by this.
This was revised based on this question.

Line 342-345.

"Later delivery near term may be safe in selected cases, including those without placenta previa, but it is unclear what combination of other reassuring factors (e.g. history of term birth, long cervical length, or less severe disease) might contribute to robust risk stratification for later delivery."

Delivery and Treatment
-Recommend this section be categorized into surgical and non-surgical management. Surgical management can be further categorized into immediate and delayed.
We are happy to do this if the editors prefer it. But for this revision we have left it in the order originally written for two reasons. First, non-surgical may be misunderstood since many conservatively managed cases require surgery (cesarean for many, hysteroscopy or other procedures after initial management for some). Second, the third and fourth strategies mentioned (delayed hyst and resection) are approaches that may be best understood as alternative treatments to address the limitations or risks of cesarean hysterectomy (CH) and conservative in situ management (CM). As such, their ordering after both CH and CM makes the most sense within the context of the manuscript, in our opinion. A preferrable alternative would be to split treatment options into uterine-sparing and not

uterine-sparing.

Immediate Hysterotomy
-Recommend addressing hysterectomy prior to viability, with fetus and placenta left in-situ, which is a rare but reasonable alternative for those who elect for pregnancy termination in the second trimester prior to viability.
-Please define or remove the "PAS" term preceding hysterectomy.
This has been clarified using the language suggested by the reviewer in line 417-419.

“If diagnosis is made before viability, gravid hysterectomy with placenta and fetus left in-situ is a rare but reasonable options for patients with PAS.

-"Some centers routinely make use of preoperative or intraoperative cystoscopy to delineate the position of the bladder and ureters, and prophylactic ureteral stent placement has been associated with reduced incidence of genitourinary injury in PAS cases." Recommend a separate section devoted to preoperative preparation and discussion of these techniques in more depth.
We are happy to expand this discussion, although we initially left it out due to word count constraints. Other than cystoscopy and ureteral stents, it is unclear to us what else the reviewer may have had in mind. This new, much more detailed discussion of Preoperative Preparation was moved to Antenatal section (line 351-391), as recommended by the reviewer.

Partial Myometrial Dissection
-What types of studies are the authors citing in last sentence- case series, case reports?
This has been clarified in 581-582.

“The few case series addressing these questions are not definitive to rule out significant harm.”

Intrapartum Diagnosis
-Recommend authors summarize figure 1 more clearly in these 2-3 paragraphs. Give examples of when is it advisable to close the abdomen prior to creating a hysterectomy and transfer the patient to a PAS center. Mention the need for centers with fewer resources to have an action plan for this prior to encountering this type of situation, etc.
Per the reviewers’ request, we have added further detail to our discussion of management of intrapartum diagnosis of PAS. We appreciate the suggestion to include the importance of an action plan for transfers to higher level of care and have added this to the section.

Line 598-613.

“In cases of fetal or maternal instability, rapid delivery may be necessary; however, definitive management of PAS with hysterectomy or alternative strategy is not absolutely or immediately required once stabilization has occurred. In fact, a finding of PAS at laparotomy in an otherwise stable patient is an opportunity to pause and assess whether proceeding with delivery is in the patient’s best interest. Often, when a center lacks resources or expertise, transport prior to delivery is the best course of action. Another timepoint for assessment is after delivery. If PAS is encountered following delivery of the fetus, closing the uterus and abdomen with the placenta in situ may be safer than attempting hysterectomy in low-resource settings. The same is true for PAS suspected after vaginal delivery, where failure of placental separation necessitates surgical planning.

Depending on a facility's resources and expertise, this is a time point to decide whether transport to a higher level of care is preferable and feasible to proceeding with delivery and or hysterectomy. This decision is ideally based on prior and ongoing assessment of system resources, expertise, and an established relationship and action plan for transitioning care to a designated referral center. Throughout, continued assessment of a patient's hemodynamic stability and provision of life-saving and resuscitative care such as volume repletion, blood product transfusion, antifibrinolytic agent is paramount."

Postpartum care - Short term Postpartum care
-Recommend authors address anticipation and coordination of critical care, and specific OB needs during and after ICU care including post ICU syndrome.
We appreciate the advice to incorporate consideration of post-intensive care syndrome. We have expanded this section to specify the coordination of care between OB and critical care, as well as detection and mitigation of post-intensive care syndrome.

Line 670-678.

"After initial treatment for PAS, patients require attention to specialized needs, often including critical care, in addition to routine postpartum care. Anticipation of critical care needs depends on clear communication between the obstetric team and critical care team(s). This process can start early with antenatal consults at PAS diagnosis and should allow for coordinated multidisciplinary daily care including the obstetrician even in critical care units that traditionally place care under the full responsibility of the intensivist. The PAS patient needs the intensivists' expertise in standard measures to reduce the impact of post-intensive care syndrome (PICS), as well as the obstetricians' expertise in achieving attainable elements of the normal postpartum experience."

Box 1
-Recommend creating a separate historical column rather than interspacing with current FIGO grade
This has been done. Thank you.

Figure 1
-For second to right column, recommend stating BEFORE HYSTEROTOMY. For far right column, I am assuming the authors are advocating for closing uterus and abdomen prior to placental delivery. Maybe state AFTER DELIVERY WITH PLACENTA IN-SITU.
We agree with these changes, which were made in Figure 1.

Editorial Office Note: This reviewer submitted additional edits for consideration directly to the Editor. These comments have been blinded and will be returned to you by in a separate email from Randi Zung.
This approach was helpful. Thank you.

Reviewer #3: Thank you for the opportunity to review this manuscript entitled, "Clinical Expert Series: Placenta Accreta Spectrum." This is a clinical expert series manuscript that reviews the etiology, diagnosis, and management of PAS disorders. The manuscript is well written, and I believe this will provide helpful guidance to our readership which includes clinicians who may encounter PAS disorders in their clinical practice. I have some comments outlined below:

-Page 4: Provide references for the sentence: "Accurate population-based statistics are hard to come by since PAS coding did not exist until recently in the ICD handbook and since disease definitions are evolving."
This has been done in line 56.

-Pages 5-6 (Classification): I suggest that the authors present the classification schemes in 1-2 sentences. Currently, the FIGO and PAS grades seem to come out of nowhere. Box 1 does not specify FIGO and PAS grades in the title or legend, just puts the references. This should be clarified.
Thank you for pointing out this opportunity for clarification. We have added additional description of the classification schemes within the text and have also edited the Box 1 title and headers to reflect that the information is from the expert consensus guidelines for both pathologic and clinical (FIGO) classification.

-Page 6: For the sentence, "System preparedness is more important than an individual clinician's experience or skill in ensuring safe and effective PAS care," would suggest the word "may" instead of "is"
We agree and have modified this sentence in line 224.

-Page 8-9: For the sentence, "Missed antenatal diagnosis leads to management in a less-prepared setting and results in worse outcomes," would suggest changing the wording of "missed antenatal diagnosis" as this implies that someone missed something. Also, perhaps avoid "a mistake made too commonly." While that could be the case in some cases, the limitations of our current diagnostic methods also contribute. This type of wording should be carefully used as this type of language could set up our medical community for medico-legal issues.
This is very reasonable request. Language implying culpability has been removed in line 109-110.

“The tools for diagnosis of PAS are imperfect, and many patients are not diagnosed until the time of delivery. When diagnosis is not made until delivery, this may lead to management in a hospital setting lacking necessary resources which can result in worse outcomes. Investigation of promising biomarkers for PAS is underway, but broadly available and clinically useful blood or urine tests to predict PAS are not currently available. Importantly, a patients’ *a priori* risk should not be dismissed based on a reassuring ultrasound study.”

-Page 9: The sentence "its routine use is limited by lack of proven benefit and limited availability of expertise in MRI interpretation for PAS" should include references.
This is a an introductory comment that is further justified later in the section. No changes were made in response to this comment.

-Page 10: For sentence, "Transvaginal imaging with sweeps of the lower uterine segment can be invaluable to clarify this area in higher resolution," references should be provided as vaginal approach is the gold standard when evaluating previa and concern for PAS.
A reference has been added to this statement (which was moved to line 162-163 as part of another recommended edit)

-Page 14: For sentence, "Antenatal corticosteroid administration is indicated when delivery is planned as preterm," suggest making language less strong because antenatal corticosteroids may be intentionally deferred in the setting of late preterm in the setting of maternal diabetes or twin gestation and may not always be "indicated" in the preterm period.
This has been changed to add the nuance described by the reviewer, in line 326.

“Antenatal corticosteroid administration may be indicated when a preterm delivery is planned.”

-Page 16: When referring to FIGO or PAS grades, suggest again referencing Box 1.
Thank you. This has been done.

“In the absence of very severe disease (FIGO 3B or 3C or PAS Grade 3E, see Box 1), and in the hands of an experienced surgical team, some experts believe this approach reduces the risk of the worst outcomes compared to alternative approaches.”

-Page 23: Would provide more references for the section "Endovascular approaches to reduce blood loss."
Several additional references are now included.

-Box 1: see comments above
Confirmed.

-Box 2: would suggest changing the title of this box to better clarify that this box gives suggestion of current knowledge gaps and are potential areas for future research
Thank you. The title of Box 2 is now “Suggested innovations, knowledge gaps, and research priorities for the future of PAS care”