2021

Endometriosis classification, and staging and reporting systems: a systematic review on the road to a universally accepted endometriosis classification.

REVIEW REPORT

The draft of the paper “Endometriosis classification and staging systems: the road to a universally accepted and implemented system” (draft title) was open for stakeholder comments between 28 January and 28 February 2021.

The paper was published on the ESHRE website for open stakeholder review. ESGE submitted comments on behalf of their Executive board. ASRM submitted collated comments from multiple levels of simultaneous review: Practice Committee, members, executive Board, SRS, EndoSIG.

This report summarizes all reviewers, their comments and the reply of the writing group and is published on the societies’ website as supporting documentation to the paper.

A total of 81 comments were received.

The comments were focussed on the content of the paper (51 comments), language and style (19 comments), or were positive remarks that did not require a reply (11 comments). All suggested language corrections were adapted.

All comments to the content of the paper were checked by the working group and either addressed (in the paper) or a reply was formulated. Of the 51 comments, 19 resulted in an adaptation to the text, while 32 were replied to in this report.

Participants to the stakeholder review

Individual experts – contributing to the open review, organised by ESHRE

Reviewer	Country
Thomas D'Hooghe	Belgium
Philippe Koninckx	Belgium
Alison Maclean	UK
Gernot Hudelist	Austria
Carlos Calhaz-Jorge	Portugal
Chi Chiu Wang	Hong Kong
Marco Sbracia	Italy
Juan A Garcia-Velasco	Spain
Devin Namaky	USA
Mitranovici Melinda-Ildiko	Romania
Hunida ,M.Elmegrab	Libya
Svetlana Dubrovina	Russia
DEBBY PACQUING-SONGCO	PHILIPPINES
Puri Hernández-Vargas	Spain
Leila Adamyan	Russian Federation
Paul Yong	Canada
Theodoros D. Theodoridis	Greece
Justyna Sikora	Poland/Uk
Jennifer Mier Cabrera	Mexico
Horace Roman	France
Sun-Wei Guo	China
David Adamson	USA
Kaylon Bruner-Tran	USA

Experts contributing on behalf of ASRM

Collated comments from multiple levels of simultaneous review: Practice Committee, member, Board, SRS, EndoSIG 2-19-2021

Experts contributing on behalf of WES

Collated comments from the WES board members

Experts contributing on behalf of ESGE

Reviewer	Country
Ertan Saridogan	UK
Justin Clark	UK
Hélder Ferreira	Portugal
Michelle Nisolle	Belgium
Massimo Candiani	Italy
RABISCHONG	France

List of all comments and replies

	Name	Page	Line	Comment	Reply
1	Thomas D'Hooghe			I would suggest that the authors add another paragraph in the Discussion on the value of descriptive versus outcome-based classifications, and which criteria should be applied in their development and validation. Descriptive classification could be applied to both imaging and surgical classifications. Outcome Fertility has been well addressed with EFI, but outcome PAIN is much more difficult. This “next step” in classification development is a bit lacking, and I am sure that, with their collective expertise, the authors and societies they represent could add meaningful ideas here.	The reviewer suggests to add a paragraph in the discussion on the value of descriptive versus outcome-based classifications, and which criteria should be applied in their development and validation. The working group considers this a valid point, but there are insufficient data at this stage to make any valid conclusions or suggestions.
2	Thomas D'Hooghe			Excellent review, very well done, but vision for the future needs to be more articulated, see previous comment	Thank you.
3	Philippe Koninckx			I have read with interest the ‘ Endometriosis classification and staging systems: the road to a universally accepted and implemented system’. It is a nice description and overview of classifications. Please find below suggestions which might be biased by personal beliefs. Every bird has a different song. I am missing that before 1986 (1) subtle endometriosis was know known and therefore not reflected in the Acosta, Kistner, AFS classification. Also, deep endometriosis was only well recognised after 1990 (2). References 1. Jansen RPS, Russel P. Nonpigmented endometriosis: Clinical, laparoscopic, and pathologic definition. Am J Obstet Gynecol 1986;155:1154-9. 2. Cornillie FJ, Lauweryns JM, Seppala M, Riittinen L, Koninckx PR. Expression of endometrial protein PP14 in pelvic and ovarian endometriotic implants. Hum Reprod 1991;6:1411-5.	A sentence was added, reading “The different versions of the AFS/ASRM classification system reflect the progress made in the knowledge on endometriosis.”
4	Philippe Koninckx			An analysis of classification was made in 1991 demonstrating that if you omit adhesions from the AFS nothing changes since adhesions and cystic ovarian endo are so strongly associated (3) Also classes III and IV are cystic ovarian endometriosis (95%), deep endo is mainly represented in class II and the difference between I and II is the pelvic area with a cut-off around 3 cm2. A more extensive analysis was published in the report of the Quebec meeting of 1999 by late R. Maheux. References 3. Koninckx PR, Meuleman C, Demeyere S, Lesaffre E, Cornillie FJ. Suggestive evidence that pelvic endometriosis is a progressive disease, whereas deeply infiltrating endometriosis is associated with pelvic pain. Fertil Steril 1991;55:759-65.	The reviewer makes an interesting point, but providing such details on each of the different systems is not within the scope of the current paper.

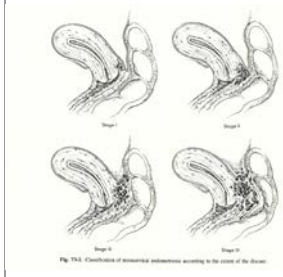
5	Philippe Koninckx			What I/we think about classification was published in Gyn Surgery which was not yet PUBMED listed (4). Essentially it says that The AFS is a nice classification but that subtle and deep should be classified separately and that volume/ severity should be taken into account. References 4. Koninckx PR, Ussia A, Adamyan LV, Wattiez A. An endometriosis classification, designed to be validated. Gynecol Surg 2011;8:1-6.	As described in the methodology section, the literature was limited to pubmed-indexed papers.
6	Philippe Koninckx			The ENZIAN classification is typically a classification by surgeons and reflects surgical expertise	It is clearly mentioned that the ENZIAN score is a surgical classification. This was not further explained
7	Philippe Koninckx			All classification today need validation. I hope that we can try together with J. Keckstein	The authors agree that any future or existing classification, staging or descriptive system needs evaluation and validation, and would certainly support such studies/collaborations
8	Philippe Koninckx			The Endometriosis Fertility Index is not a classification, but a self -fulfilling prophecy. When all parameters known to affect fertility are added we obviously predict fertility. What is missing, is a validation of the points given. More important this is still research, without a prediction and the variance of the MFR/CPR, which I expect to be irrealistic large	The working group considers EFI as a reporting system aiming to predict fertility after surgery. We have adapted the term "classification/staging" to "Classification, staging and reporting systems".
9	Alison Maclean			As stated in the introduction, adenomyosis is considered a separate entity by most definitions, but is included in some. This reader would be interested to know which of the classification systems discussed in this review include adenomyosis in their definitions. This could be included in the discussion, linking back to the comment in the introduction.	We have not looked specifically at classification systems for adenomyosis, but agree it has been included in existing endometriosis classification systems. Where relevant, this is mentioned in table II. We also added a sentence on adenomyosis in the methods section.
10	Alison Maclean	1	24	The sentence reads better as '*while for infertility* {insert comma} *surgery and/or assisted reproduction technologies (ART) have been used*'.	This was corrected
11	Alison Maclean	7	252	'*..for its intended purpose*, {insert: which is} *descriptive surgical staging'* to replace *'being'*.	This was corrected
12	Alison Maclean	7	255	In keeping with the paragraph, it would also be interesting to know if the UBESS and ECO classification systems have been evaluated for their intended goals, or not.	UBESS and ECO were evaluated for their intended purpose. This was added in the discussion.
13	Alison Maclean	7	269	'*…examined the classification systems for other purposes than the one for which* {insert: they were} *designed'* to replace *'it was'*.	This was corrected

14	Gernot Hudelist			Please do update the reference regarding the Enzian – or now #Enzian classification – see The #Enzian classification: A comprehensive non-invasive and surgical description system for endometriosis. Keckstein J, Saridogan E, Ulrich UA, Sillem M, Oppelt P, Schweppe KW, Krentel H, Janschek E, Exacoustos C, Malzoni M, Mueller M, Roman H, Condous G, Forman A, Jansen FW, Bokor A, Simedrea V, Hudelist G.Acta Obstet Gynecol Scand. 2021 Jan 23. doi: 10.1111/aogs.14099. Furthermore, I do not see the necessitiy to create another additional classification system as the classification above - #ENZIAN provides a universal tool for classifying endometriosis.	We have incorporated the new #ENZIAN classification and noted that the reviewer does not agree with the need for a new system.
15	Carlos Calhaz-Jorge			Congratulations to the authors for the excellent overview	Thank you.
16	Carlos Calhaz-Jorge	1	14-15	"myometrium of the uterus" could be just "myometrium"	This was adapted
17	Carlos Calhaz-Jorge	Tables	Headings	I suggest "Prediction of difficulty of surgery" instead of "Difficulty of surgery"	This was adapted
18	Carlos Calhaz-Jorge	Table I	Valli system	Is it related with endometriosis? I have no access to the paper but hysteroscopy seems an odd option for evaluation of **endometriotic** lesions	We agree with the comment and have removed the valli system from the list of classification systems.
19	Carlos Calhaz-Jorge		Chapron classification	The final Reference list includes two papers of Chapron et al in 2003. Would it be possible to specify in this table which one is considered?	This was corrected
20	Carlos Calhaz-Jorge	6	221	Reference "Aletaha et al, 2010" is linked to a classification system on RA (line 217). A review was published two years later but the reference is again "Aletaha et al, 2010". Is it correct?	Thank you for spotting that the wrong reference was inserted. This is now corrected
21	Chi Chiu Wang		Results	Good idea to summary the previous studies, but it is better and more important to provide some recommendations. Currently it is rather provide a list of previous studies though.	The goal of this paper was to provide an overview of existing data, as one part of an international collaboration for endometriosis classification. Further project outcomes will focus on providing recommendations
22	Chi Chiu Wang		Evidence	Better to include level of evidence or frequency of the usage of each definition had been used, rather than just a single citation provided in the tables.	Ideally, the proposed classification systems would be evaluated in several reports focussing on the same outcomes, which would have allowed meta-analysis of the data. As this is not feasible with the current data, we refrained from any meta-analysis and applied a descriptive approach
23	Chi Chiu Wang	Introduction	17-19	To be consistent with the other Glossary review	The glossary describes the 3 major endometriosis phenotypes (peritoneal, deep and ovarian endometriosis), which is consistent with the sentence indicated in the review.
24	Chi Chiu Wang	Introduction	26-30	How to compare with the grading stage in the Glossary review, Table IV, GRADE I, II, III, IV, V	The glossary describes different levels of complications (Grade I to V). In the introduction there is no mentioning of complications, and hence no inconsistency to be corrected.
25	Chi Chiu Wang	Table 1		Each endometriosis classification staging system has differential and common items, it is worth to identify any items good for correlating classification with outcomes and prognosis.	The reviewer makes an interesting point, but assessing the similarities and differences of the different systems was not within the scope of the current paper.

26	Chi Chiu Wang	Table 1		May consider to separate operative and non-operative classifications	The third column of the table specifies whether the system is based on surgical observation or other parameters. We consider it not necessary to further clarify this
27	Marco Sbracia		Endometriosis classification	The standardization of endometriosis classification systems is certainly necessary to give doctors a clear and easy-to-use supp01i to describe the stage of the disease. However the main problem is to define what we want to describe and what is the goal of the classification system. Endometriosis may present several different clinical features, especially associated with symptoms and anatomical presentation.	Thank you for this feedback. We largely agree with your comments.
28	Marco Sbracia		Metodology	The process for the standardization of endometriosis classification will take long time and needs an international cooperation to evaluate in a big data system the adherence of the classification system with the clinical reality of patients.	We agree with the reviewer on this comment and would like to stress that it is the aim of the working group to start such an international cooperation.
29	Marco Sbracia	1	31	Looking for a system of being able to include all the possible characteristics of the disease, including symptoms, prognosis and possible clinical outcome regarding pain and infertility seems a bit unrealistic and inconclusive. Perhaps it would be better to think for a classification well describing the spread of endometriosis in the pelvis and extra-pelvis, including deep endometriosis as well as the anatomic distortion produced in the pelvis.	We agree with this comment, but would like to point out the aim of the review was to provide an overview of existing classification systems and validation studies.
30	Marco Sbracia	7	233	The reference to the TNM classification for cancer is quite fitting, but to obtain the same for endometriosis it is necessary to establish a process of evaluation of the descriptive factors of the disease and then with a longitudinal study on patients which of these factors is more significant in predicting disease recurrence and the reappearance of symptoms.	We consider this a helpful comment and we will take this into consideration in further steps of the project to develop a classification for endometriosis.
31	Juan A Garcia-Velasco		General comment	My only comment is regarding the idea of a unified classification system. Endometriosis, as you clearly explain, is a very heterogeneous disease, with different aspects that are all group under the umbrella of “endometriosis”. However, it seems extraordinarily different to share a common classification. The fact that pain is not related to the ASRM classification, and the same for fertility prognosis (EFI is a good classification but prognostic value only after surgery and for natural pregnancy), should make us aware that we may need to have different classifications according to the problem that we are dealing with. This may sound counterintuitive when trying to unify concepts, but may be this is the time to separate the different entities “glued” together as endometriosis.	We consider this a helpful comment and will take this into consideration in further steps of the project to develop a classification for endometriosis.

32	Devin Namaky			Given that the goal is to map and assess the current publication systems, I think this review paper achieves this goal. Mostly importantly, I appreciate that this review highlights that any staging system should have objectives in mind. The lack of attention to this is exactly why I do not currently stage my patients. There is no simple system I can currently rely on to clinically represent the difficulty of treatment and excision, nor to predict pain. I recognize also that fertility prediction is also of concern for patients and clinicians. It would be nice if the system mimicked that of cancer staging: 1. Staged surgically, 2. Represents the level of difficulty in treatment (i.e. difficulty of excision), 3. Predicts pain and/or fertility response (outcomes).	Thank you for this feedback. We largely agree with your comments.
33	Mitranovici Melinda-Ildiko			I think a TNM-like staging system used for cancer is much better at aiming a clinical classification by anatomical extent. And it could also be used in treatment planning	Thank you for this feedback.
34	Mitranovici Melinda-Ildiko		166	EFI is a 10 point scoring system which I find useful	The aim of the review is to provide an overview of the different systems and the extent to which they are validated. We clearly state that we did not include an assessment of all positive and negative aspects of the classification systems as not to repeat other reviews.
35	Mitranovici Melinda-Ildiko		174	EFI has a good predictive value	The aim of the review is to provide an overview of the different systems and the extent to which they are validated. We clearly state that we did not include an assessment of all positive and negative aspects of the classification systems as not to repeat other reviews.
36	Mitranovici Melinda-Ildiko		184	The ENZIAN classification system is useful for surgical staging	The aim of the review is to provide an overview of the different systems and the extent to which they are validated. We clearly state that we did not include an assessment of all positive and negative aspects of the classification systems as not to repeat other reviews.
37	Hunida ,M.Elmegrab			Implementing a system that is feasible, reliable and reproducible is a hard task. Especially due to lack of validating researches Based on a personal experience and my observations in the clinical field of infertility I've found ENDORECT system easy, affordable and has high positive value in many aspects specially the medical treatment of endometriosis and I will include a file describing my experience using that system with my patients As your review shows EFI showed higher predictive value and included more aspects than the one it was designed for I'd like to suggest in regards of that is to integrate ENDORECT system and EFI to produce a more accurate, descriptive and easy to obtain system in terms of accessible, cost effective methods such as clinical examination, US and other imaging studies The chosen classification system should also cover more aspects than the one for which it was designed for. In my opinion further researches should be conducted to assess the validity of the suggested systems above.	Although we largely agree with these comments, the aim of the review is to provide an overview of the different systems and the extent to which they are validated. We clearly state that we did not include an assessment of all positive and negative aspects of the classification systems as not to repeat other reviews.

38	Hunida ,M.Elmegrab	7	250 251 252	Even though rASRM showed various negative values it should be further investigated and researches should be conducted to evaluate the system for it's intended goal which is the description of surgical staging	We agree with this comment, which is in line with the conclusion of the paper stating that "Any future evaluation of existing or newly developed classification, staging or descriptive system should primarily focus on assessing validity, feasibility and reproducibility, and on reliability related to the purpose for which the system was developed"
39	Svetlana Dubrovina	7	241-242	«The EFI system needs further evaluation with regards to the importance of the different parameters and whether to include the completeness of surgical treatment.» I totally agree with it in spite of the fact that it is one of best system. But new one should evaluate the adhesions not only between ovaries and tubes but also how intestine, for ex., is involved in abdominal adhesions.	The aim of the review is to provide an overview of the different systems and the extent to which they are validated. We clearly state that we did not include an assessment of all positive and negative aspects of the classification systems as not to repeat other reviews.
40	DEBBY PACQUING-SONGCO	Page 1	18	Endometrioma is already noted as a cyst. unless endometrial cyst will be used. Suggest cyst in conjunction with endometrioma	We have removed the word "cyst" as this is indeed redundant.
41	DEBBY PACQUING-SONGCO	Page 1	39	When is inception? Date? Better to put 1973 here then inception during discussion on page 6 line 203	Inception means the date of which papers are included in PUBMED/Medline. We clarified in the text that this is from 1966,
42	DEBBY PACQUING-SONGCO	Page 1	40	Papers gathered should only be focusing on endometriosis, no need to put not include papers not focusing on endometriosis	We agree with this comment, but consider it relevant to clarify the non-selection of 1152 references from all references collected through the literature search.
43	Puri Hernández-Vargas		Other references	Some recent proposed classification system has not been included in the report and they could introduce new perspectives for endometriosis classification (see doi:10.17219/acem/118849; doi:10.1093/hropen/hoaa053)	We have incorporated the new #ENZIAN classification in the overview.
44	Puri Hernández-Vargas		Title	The title seems to me a bit mis-leading as the report does not propose any universally accepted and implemented system. I therefore suggest revising that part of the title.	We have clarified the title, which now reads "Endometriosis classification and staging systems: a systematic review on the road to a universally accepted endometriosis classification."
45	Puri Hernández-Vargas	Figure 1	80-82	Only exclusion criteria for eligibility has been considered. Could you please show the exclusion criteria for screening (n=1152 records excluded)? Please clarify if they are the exclusion criteria cited in lines 39-41 (methods). If so, please, include them in figure footnotes.	The 1152 references were excluded based on the mentioned criteria "Non-English language studies, animal studies and papers not focusing on endometriosis". By following the reviewer's suggestion to include this in a footnote to figure 1, this is clarified to all readers
46	Puri Hernández-Vargas	Page 3 Page 7 and Figure 1	88-89 266	"Sixty-seven papers…classification or staging system in endometriosis (n=24) or evaluation one (n=43)". Only 23 papers have been included in Table I while 46 papers are in Table II. Could you please confirm the number of papers?	The inconsistency was due to the 2 references from Chapron, of which one was missing in table 1, Meanwhile the numbers were corrected and updated with the inclusion of #ENZIAN, The number of validation papers was adapted. Thank you for alerting us of this inconsistency
47	Puri Hernández-Vargas	Page 3 and Table I	104-106	"(1979, 1985…)" The reference is a bit confusing. Is it possible to include AFS?	This was corrected
48	Puri Hernández-Vargas	Table I and II		Tables titles should use a similar format.	This was corrected

49	Puri Hernández-Vargas	Figure I	Line 55-line 69	Two editing errors (spaces before brackets) should be corrected.	This was corrected
50	Leila Adamyan		Deep infiltrating endometriosis	Since deep endometriosis is not scored in the rAFS classification, and specific classification is of great need. Leila Adamyan classified retrocervical endometriosis into four stages according to the extent of disease in the retrocervical area: in stage I, endometriotic lesions are confined to rectovaginal cellular tissue in the area of the vaginal vault; stage II exists when endometriotic tissue invades the cervix and penetrates the vaginal wall, causing fibrosis and small cyst formation; in stage III, lesions spread into the uterosacral ligaments and the rectal serosa. The last and most severe stage, IV, exists when the rectal wall, rectosigmoid zone, and retro-uterine peritoneum are completely involved, and the recto-uterine pouch is totally obliterated.  Leila Adamyan created this classification to describe the extent of the disease and proposed treatment approaches for each of the classes. This classification has been referenced at various international scientific meetings and serves as a foundation for monographs, chapters, and national standards of care. Reference: Adamyan LV. Additional international perspectives. In: Nichols DH (ed) Gynecologic and obstetric surgery. Mosby, St Louis, 1993, pp 1167–1182	We explain in the paper that we have restricted our overview to classification systems published in peer reviewed papers and available through PUBMED/MEDLINE. Although locally used and/or unpublished systems are available and can be valuable, the relevance of including them in the current review was considered low, as they would not be widely applied, nor evaluated by (independent) researchers. For universal use of a classification system, it is pivotal that the system is accessible, validated, reliable and reproducible. As such, the Adamyan system could not be added
51	Paul Yong		TNM	One thing that makes endometriosis different – which goes beyond anatomic and molecular subtype classification in TNM – is the importance of comorbidities for outcomes such as pain level and pain recurrence. I'm not sure a purely anatomic/molecular classification will be prognostic for pain, without consideration of myofascial, bladder, bowel, central nervous system variables. Similar idea to the EFI, where anatomic findings had to supplemented with fertility "comorbidities" (e.g. age, years infertility, previous pregnancy).	We consider this a helpful comment and will take this into consideration in further steps of the project to develop a classification for endometriosis.
52	Paul Yong	1	24	"…suppress the production of estrogen from the ovaries" – I think there is evidence that hormonal therapies can also directly suppress lesions?	As this paper is focussed on classification system, we have removed this sentence and made it more general.
53	Theodoros D. Theodoridis			Execellent work, I have no comments to add	Thank you.

54	Justyna Sikora		rASRM	The rASRM classification is the most widely used all over the world . In theory, it is easy to use, and it is helpful for clinicians to simply explain the severity of endometriosis in simple terms to the patients I am aware that it is not without flaws disadvantages. First, it can be a difference between histologically diagnosed endometriosis and the visual stage. Second, the reproducibility of the rASRM result is poor. Third, the severity of pain and infertility is not correlated with the severity of rASRM. Fourth, the rASRM classification does not take into account the presence of endometriosis at various sites such as the uterosacral ligaments, bladder, vagina and intestines. Due to its commonness, it is also often used by researchers trying to explain the causes and development of endometriosis. They test comparing the various degrees of disease with each other in order to establish the relationship between them. They very often combine 1st and 2nd degree, and 3rd and 4th endometriosis. Especially in this case, it may be worth standardizing the nomenclature. Researchers use early and late endometriosis, either moderate and advanced or severe disease. Standardization could prove very useful not only in basic research but also in epidemiological research.	The aim of the review is to provide an overview of the different systems and the extent to which they are validated. We clearly state that we did not include an assessment of all positive and negative aspects of the classification systems as not to repeat other reviews. Standardisation of nomenclature is the aim of the glossary paper.
55	Jennifer Mier Cabrera		OK	I consider this paper a great opportunity to implement a universally accepted system. I apologize in advance, I'm a dietitian and I do not have credentials or expertise to review this paper.	Thank you for this comment
56	Horace Roman	6	184	ENZIAN classification has recently been modified, and it definitively classifies all endometriosis localizations: ovary, superficial, tubal patency, rare localizations. Although it is too late to modify the whole review, I think the last article should simply be mentioned in a sentence: Keckstein J, Saridogan E, Ulrich UA, Sillem M, Oppelt P, Schweppe KW, Krentel H, Janschek E, Exacoustos C, Malzoni M, Mueller M, Roman H, Condous G, Forman A, Jansen FW, Bokor A, Simedrea V, Hudelist G. The #Enzian classification: A comprehensive non-invasive and surgical description system for endometriosis. Acta Obstet Gynecol Scand. 2021 Jan 23. doi: 10.1111/aogs.14099.	We have incorporated the new #ENZIAN classification in the overview.
57	Sun-Wei Guo	6	201--	Ideally, a good classification system should correlate with either the severity of symptoms or prognosis (recurrence risk), or help to choose the best treatment modality or to plan for surgery. EFI has a very good prognostic power for fertility (but not for pain) but for all the other classification systems, there are still lots of unknowns. Much more research is needed in this regard.	The aim of the review is to provide an overview of the different systems and the extent to which they are validated. We clearly state that we did not include an assessment of all positive and negative aspects of the classification systems as not to repeat other reviews. We agree the need for more research.
58	Sun-Wei Guo			Nicely written, very informative.	Thank you.
59	ASRM		1	Line 16, not consistent with endometrioma and adenomyosis	We have revised the sentence in line 16, but could not identify any inconsistency, and decided not to adapt the sentence based on the comment.

60	ASRM		2	Line 19, convention is Deep Infiltrating Endometriosis (DIE)	The terminology “Deep Endometriosis (DE)” has been previously agreed on and has been used in 2 collaborative paper from ESGE, ESHRE and WES. DE is also used in the glossary for endometriosis.
61	ASRM		3	Lines 22-25 don't make much sense	The text was adapted
62	ASRM		4	Line 178, can you provide confidence intervals?	We have added the confidence interval as suggested
63	ASRM		5	Line 142- should this be rAFS not rASF ?	Thank you, this error was corrected
64	ASRM		6	Line 164-165 I’m not certain that I understand this sentence. How does one evaluate the classification system for being a descriptive system?	We have adapted the sentence in the paper to clarify.
65	ASRM		7	First paragraph in the discussion goes back and forth between verb tenses, which I found confusing, Line 208-9. It does not appear that the classification systems have ever been studied as to their association with pain or quality of life----At least looking at Table 1. So I don’t think you can say that they don’t correlate—this outcome just hasn’t been studied, correct?	The text was adapted as suggested
66	ASRM		8	I think a sentence should be added to this paragraph stating that the classification systems have been studied to look at fertility outcomes and one has been shown to be associated with fertility outcomes.	The text was adapted as suggested
67	ASRM		9	While it is an extensive review of the literature, it doesn’t seem to offer new insights nor describe a concrete path forward	We have clarified that this review, mapping the current landscape, is to be considered a first step. We have adapted the conclusion of the review.
68	ASRM		11	We should be very cautious about replacing a well established and familiar staging system that is documented in almost all prior studies with another system without clear improvements in clinical utility	The aim of the review is to provide an overview of the different systems and the extent to which they are validated. We clearly state that we did not include an assessment of all positive and negative aspects of the classification systems as not to repeat other reviews. We have slightly modified the conclusion to fit with the intended purpose of the review
69	ASRM		12	Nice review why our present classifications systems for endometriosis do not address their intended purpose. Their conclusion “there seems to be a need for an internationally accepted descriptive system for endometriosis” The main problem with this document is that there is no proposal on how they intend to proceed. It would seem logical that they should at least propose some solution to this well-known observation.	The aim of the review is to provide an overview of the different systems and the extent to which they are validated. We clearly state that we did not include an assessment of all positive and negative aspects of the classification systems as not to repeat other reviews. We have slightly modified the conclusion to fit with the intended purpose of the review
70	ESGE - Ertan Saridogan			This is a useful and comprehensive review of most of the classification systems and would be useful to the reader.	Thank you for this comment.
71	ESGE - Ertan Saridogan		Table 1	An updated version of the Enzian classification system, #Enzian has just been published and would be worth including in this table.	We have incorporated the new #ENZIAN classification in the overview.
72	ESGE - Justin Clark			I would stratify the table into the different classification systems (subheadings to break it up and make easier to read) – at the moment it lists e.g. UBESS on a number of rows as each row refers to a different paper. That’s fine but provide the subheadings e.g. Enzian; UBESS; RAFS etc	We have adapted the table according to this suggestion

73	ESGE - Justin Clark			Nice review but no clinical use although I know this was not the purpose of the paper. Hopefully this summary can be used as a basis for researchers developing new ones. I am aware of at least 2 new classifications in development. Some sort of collaborative development project seems in order as opposed to consenus statements / reviews	Thank you for this comment. We fully agree. The review was performed in a first step of a international working group to develop an internationally accepted classification.
74	ESGE - Hélder Ferreira			The literature review is robust. The information organized in tables seems clear and well organized. I think that the recent paper, published by several experts, entitled "The #Enzian classification: A comprehensive non-invasive and surgical description system for endometriosis" may be included.	We have incorporated the new #ENZIAN classification in the overview.
75	WES			Recently another paper was published describing the #ENZIAN classification. #ENZIAN means to further develop ENZIAN classification. The publication is in Acta Obstetricia et Gynecologica Scandinavica. I realize this publication was not available for consideration in this publication for obvious reasons. I just wanted to suggest at least mentioning it in the review.	We have incorporated the new #ENZIAN classification in the overview.
76	WES	Final comment in main text	Line 274 - 276	Any future evaluation of existing or newly developed classification, staging or descriptive system should primarily focus on assessing validity, feasibility and reproducibility, **should be patient-centered rather than reflecting only the anatomical and/or severity of disease** and on reliability related to the purpose for which the system was developed.	We consider that an evaluation of a classification system should focus on assessing validity, feasibility, reproducibility, and reliability. Patient centredness can be an appropriate outcome for some classification systems, but may not always be the focus.
77	David Adamson			Congratulations to the organizations and authors on this initiative, especially its collaborative nature, and the excellent articles.	Thank you.
78	David Adamson	Literature search	43	With respect to the history of endometriosis classification and staging systems, I believe several earlier efforts have not been included. Almost certainly they came up in your literature search and I assume were excluded. However, since the first paper by Sampson was 100 years ago now, and since the variable approaches and limitations emphasize the difficulties of this journey for over a century and still today, I believe a paragraph at least summarizing these earlier efforts is justified. I have attached a presentation on this from 2002 that lists some major studies with some brief characteristics of each approach. I believe it is essential to include these earlier efforts that laid the foundation for later efforts. I am certain the committee can source these original documents, review them, and make an appropriate summary to recognize their importance.	As described in the methodology section, the literature was limited to pubmed-indexed papers, which date back to 1966. We considered it would not add much value to include older resources.

79	David Adamson	EFI	242	The statement, “The EFI system needs further evaluation with regards to the importance of the different parameters and whether to include the completeness of surgical treatment (Maheux-Lacroix, et al., 2017) may benefit from further clarification. The Least Function Score (LFS) of the EFI takes into account the completeness of surgery in that if surgery is incomplete the ability of the structure to function, which is the basis of the LFS, should be reduced and so the Least Function Score would be lower and so take into account the completeness of surgery. It is true this applies only to the tube, fimbria, and ovary but it has not been demonstrated that removal of deep endometriosis affects the probability of pregnancy. The authors will decide if this additional information is worth including.	The reviewer makes an interesting point, but providing such details on each of the different systems is not within the scope of the current paper.
80	Kaylon Bruner-Tran	Fig 1	Top, right	Seems odd to list a block “additional records, N=0”. This is explained on p7 so perhaps here a footnote could be added here with examples of other sources that were considered, but rejected.	A footnote was added to the figure, but the flowchart, which is the official PRISMA 2009 Flow Diagram was not adapted.
81	Kaylon Bruner-Tran	Table 1	Adhesion line (first system)	It is not clear why the checkmark under “prediction of conception” is in parentheses.	We removed the parentheses as to avoid any confusion.