Human Reproduction, Vol.32, No.2 pp. 315–324, 2017
Advanced Access publication on December 5, 2016 doi:10.1093/humrep/dew293

human reproduction

ORIGINAL ARTICLE ***Gynaecology***

World Endometriosis Society consensus on the classification of endometriosis

Neil P. Johnson[1,2,3,4,*], Lone Hummelshoj[1,5], G. David Adamson[5,6], Jörg Keckstein[7], Hugh S. Taylor[8], Mauricio S. Abrao[1,9], Deborah Bush[10], Ludwig Kiesel[1,11], Rulla Tamimi[12], Kathy L. Sharpe-Timms[1,13], Luk Rombauts[1,14], and Linda C. Giudice[1,5,15] for the World Endometriosis Society Sao Paulo Consortium

[1]World Endometriosis Society, Vancouver, Canada [2]Robinson Research Institute, University of Adelaide, Australia [3]University of Auckland, Auckland, New Zealand [4]Repromed Auckland and Auckland Gynaecology Group, Auckland, New Zealand [5]World Endometriosis Research Foundation, London, England [6]Palo Alto Medical Foundation, Fertility Physicians of Northern California, USA [7]KABEG Landeskrankenhaus, Villach, Austria [8]Yale School of Medicine, New Haven, USA [9]Sao Paulo University, Sao Paulo, Brazil [10]Endometriosis New Zealand, Christchurch, New Zealand [11]University of Münster School of Medicine, Münster, Germany [12]Harvard TH Chan School of Public Health, Boston, USA [13]University of Missouri, Columbia, USA [14]Monash University, Melbourne, Australia [15]University of California San Francisco, San Francisco, USA

*Correspondence address. World Endometriosis Society, 1201 West Pender Street, Suite 300, Vancouver, British Columbia V6E 2V2, Canada. Tel: +44 (0)77 1006 5164; E-mail: wes@endometriosis.ca

Submitted on October 24, 2016; resubmitted on October 24, 2016; accepted on October 30, 2016

STUDY QUESTION: What is the global consensus on the classification of endometriosis that considers the views of women with endometriosis?

SUMMARY ANSWER: We have produced an international consensus statement on the classification of endometriosis through systematic appraisal of evidence and a consensus process that included representatives of national and international, medical and non-medical societies, patient organizations, and companies with an interest in endometriosis.

WHAT IS KNOWN ALREADY: Classification systems of endometriosis, developed by several professional organizations, traditionally have been based on lesion appearance, pelvic adhesions, and anatomic location of disease. One system predicts fertility outcome and none predicts pelvic pain, response to medications, disease recurrence, risks for associated disorders, quality of life measures, and other endpoints important to women and health care providers for guiding appropriate therapeutic options and prognosis.

STUDY DESIGN, SIZE, DURATION: A consensus meeting, in conjunction with pre- and post-meeting processes, was undertaken.

PARTICIPANTS/MATERIALS, SETTING, METHODS: A consensus meeting was held on 30 April 2014 in conjunction with the World Endometriosis Society's 12th World Congress on Endometriosis. Rigorous pre- and post-meeting processes, involving 55 representatives of 29 national and international, medical and non-medical organizations from a range of disciplines, led to this consensus statement.

MAIN RESULTS AND THE ROLE OF CHANCE: A total of 28 consensus statements were made. Of all, 10 statements had unanimous consensus, however none of the statements was made without expression of a caveat about the strength of the statement or the statement itself. Two statements did not achieve majority consensus. The statements covered women's priorities, aspects of classification, impact of low resources, as well as all the major classification systems for endometriosis. Until better classification systems are developed, we propose a classification toolbox (that includes the revised American Society for Reproductive Medicine and, where appropriate, the Enzian and Endometriosis Fertility Index staging systems), that may be used by all surgeons in each case of surgery undertaken for women with endometriosis. We also propose wider use of the World Endometriosis Research Foundation Endometriosis Phenome and Biobanking Harmonisation Project surgical and clinical data collection tools for research to improve classification of endometriosis in the future, of particular relevance when surgery is not undertaken.

LIMITATIONS, REASONS FOR CAUTION: This consensus process differed from that of formal guideline development, although based on the same available evidence. A different group of international experts from those participating in this process may have yielded subtly different consensus statements.

WIDER IMPLICATIONS OF THE FINDINGS: This is the first time that a large, global, consortium–representing 29 major stake-holding organizations, from 19 countries – has convened to systematically evaluate the best available evidence on the classification of endometriosis and reach consensus. In addition to 21 international medical organizations and companies, representatives from eight national endometriosis organizations were involved, including lay support groups, thus generating and including input from women who suffer from endometriosis in an endeavour to keep uppermost the goal of optimizing quality of life for women with endometriosis.

STUDY FUNDING/COMPETING INTEREST(S): The World Endometriosis Society convened and hosted the consensus meeting. Financial support for participants to attend the meeting was provided by the organizations that they represented. There was no other specific funding for this consensus process. Mauricio Abrao is an advisor to Bayer Pharma, and a consultant to AbbVie and AstraZeneca; G David Adamson is the Owner of Advanced Reproductive Care Inc and Ziva and a consultant to Bayer Pharma, Ferring, and AbbVie; Deborah Bush has received travel grants from Fisher & Paykel Healthcare and Bayer Pharmaceuticals; Linda Giudice is a consultant to AbbVie, Juniper Pharmaceutical, and NextGen Jane, holds research grant from the NIH, is site PI on a clinical trial sponsored by Bayer, and is a shareholder in Merck and Pfizer; Lone Hummelshoj is an unpaid consultant to AbbVie; Neil Johnson has received conference expenses from Bayer Pharma, Merck-Serono, and MSD, research funding from AbbVie, and is a consultant to Vifor Pharma and Guerbet; Jörg Keckstein has received a travel grant from AbbVie; Ludwig Kiesel is a consultant to Bayer Pharma, AbbVie, AstraZeneca, Gedeon Richter, and Shionogi, and holds a research grant from Bayer Pharma; Luk Rombauts is an advisor to MSD, Merck Serono, and Ferring, and a shareholder in Monash IVF. The following have declared that they have nothing to disclose: Kathy Sharpe Timms; Rulla Tamimi; Hugh Taylor.

TRIAL REGISTRATION NUMBER: N/A

Key words: endometriosis / evidence based / classification / staging / World Endometriosis Society Sao Paulo Consortium / consensus / r-ASRM / EFI / Enzian / WERF EPHect

Introduction

Endometriosis is an inflammatory disease associated with pelvic pain and infertility that is characterized by lesions of endometrial-like tissue outside of the uterus (Johnson and Hummelshoj, 2013). The prevalence of endometriosis has been estimated as 176 million women worldwide (Adamson *et al.*, 2010).

Classification of endometriosis has remained controversial and challenging, due to the many manifestations of the disease, wherein the focus has been on anatomy, histology and disease burden for 'surgical staging' and, more recently, on prognostic value. These efforts have largely struggled to yield a suitable solution to enhance the utility of disease classification in endometriosis-related symptom management, prognosis for response to therapies, recurrence, association with other disorders, quality of life and other elements of key concern to women with endometriosis.

The best-known classification system for endometriosis is the revised American Society for Reproductive Medicine (r-ASRM) classification (1997). In addition to the r-ASRM classification, emerging systems include the Enzian classification for deep endometriosis (Keckstein *et al.*, 2003; Haas *et al.*, 2013), the endometriosis fertility index (EFI) (Adamson and Pasta, 2010), and the American Association of Gynecological Laparoscopists (AAGL) classification (http://www.aagl.org/wp-content/uploads/2013/03/NewsScope_Oct-Dec_2012.pdf; accessed 1 February 2016; unpublished to date). However, the classification systems in current use continue to attract criticism from women with endometriosis and those providing care for them because of the poor correlation with disease symptoms as well as a lack of predictive prognosis and, to date, unclear pathways of treating pelvic pain and infertility based on its classification.

This lack of correlation has led to the pertinent question: why classify endometriosis? We propose that if classification of endometriosis ultimately has benefit for women suffering from the disease with informed counselling by health care providers, then it can form the bridge between diagnosing a woman with endometriosis and enabling her the most successful treatment possible based on her symptoms and the physical disease present.

Adamson (2011) highlighted the criteria for a good classification system, and one that should therefore benefit women with endometriosis. It should be simple (for doctors to explain and for women to understand) and easy to perform; allow a simple description of the disease; correlate well with problems experienced by women, especially pain and infertility; give prognostic information; predict response to treatment for (i) pain and (ii) infertility and (iii) recurrence of symptoms after treatment (Adamson, 2011). Additional good qualities of the ideal classification system are that it should be empirically and scientifically based; comprehensive for all cases; use unambiguously defined terms; have a simple translation from anatomic lesion to verbal description; reflect the progression of the disease (with scientifically derived, and not arbitrary, cut-off points that are clinically meaningful); finally, it should have general consensus (Adamson, 2011).

The World Endometriosis Society (WES) established a process to bring together representatives of national and international, medical and non-medical societies, patient organizations and pharmaceutical companies with an interest in endometriosis, aiming to derive a consensus on the classification of endometriosis from a global perspective in which the views of health care providers, researchers and women with endometriosis were represented. The aim was to attain a consensus around classification to enable a pathway that assists the healthcare team and women who present with symptoms of possible

endometriosis in securing effective treatment. This document contains a summary of the WES consensus on the classification of endometriosis: a full-length article can be found online at http://humrep.oxfordjournals.org/.

Materials and Methods

We developed a consensus process supported by a specific methodology, detailed in the full length article at http://humrep.oxfordjournals.org/), similar to that used for our previous consensus statement on the management of endometriosis (Johnson and Hummelshoj, 2013).

Results

The evidence tables (Table V in the full-length article at http://humrep.oxfordjournals.org/) provide the evidence that was considered to reach the consensus statements. The consensus statements, categorised as either 'strong' or 'weak', are summarised in Table I, along with the degree of consensus that applied to each statement. More detailed information, specifically relating to caveats to the evidence statements, is available in the full-length article at http://humrep.oxfordjournals.org/.

Discussion

We have developed the first international consensus statement on the classification of endometriosis through rigorous methodology. We recommend a classification toolbox that may be used by all surgeons in each case of surgery undertaken for women with endometriosis, from which surgeons may select the appropriate components and ensure this is documented in the patient medical/surgical record (Fig. 1).

No single classification system adequately classifies endometriosis. It has been demonstrated already that the available systems have little prognostic value, with the exception of the EFI, which probably works because it includes important clinical variables that have an effect on the likelihood of pregnancy independent of the presence of endometriosis. Although it has been raised that this may respect endometriotic lesions insufficiently, it is clear that classification systems relying solely on surgical findings have inadequate predictive value for outcomes important to women. Even for a description of the disease, in terms of correlation with severity of symptoms and infertility and their impact on women, the existing classification systems have shortcomings. However, a recent proposal for endometriosis classification from Koninckx *et al.* (2011) adding adenomyosis, peritoneal pocket lesions, and subtle endometriosis to the three more traditionally recognised lesion phenotypes (typical (peritoneal), cystic and deep endometriosis) and placing emphasis on the size of lesions is awaiting further appraisal and validation. While not all classification systems are well understood, those that have a level of acceptance are r-ASRM (whose main advantage is its longevity, universal familiarity and its embedding in many other classification systems), Enzian (for deep endometriosis) and the EFI (owing to its value in predicting fertility and the external validation of that) and thus these systems all have some merit. The inextricable interlinking of r-ASRM with newer classification systems (Enzian and EFI) means that a classification that has attracted no small measure of criticism appears to have been immortally enshrined. Although the AAGL classification has the investment of the opinions of a quorum of surgical opinion leaders involved in its development it is yet to be fully validated and published. The absence of consensus around the utility of the AAGL system reflects this.

There is no general consensus on the most appropriate methodology for consensus statements, particularly for disease classifications. Therefore we adopted a modified version (Table IV in the full length article at http://humrep.oxfordjournals.org/) of the GRADE system of grading the quality of evidence (Guyatt *et al.,* 2008), now recognised as the most relevant method of grading evidence and recommendations in guidelines. We adapted this to our consensus process, which we based on previous consensus documents, using a system promoted by the ACCEPT Group that is gaining wider acceptance (Kroon *et al,* 2011; Koch *et al.*, 2012; Johnson and Hummelshoj, 2013; Boothroyd *et al.*, 2015). It must also be acknowledged that a consensus statement from international experts would likely be different with a different group of experts, although it is hoped that our broad sample of participants in this consortium was representative of the spectrum of viewpoints of all the members of all the organizations and societies representing stakeholders in endometriosis research, clinical care and advocacy.

An obvious finding in the quest for a consensus statement is that absolute unanimity from a range of experts regarding any statement is difficult to attain. However, our methodology sequence, with an additional step to refine our consensus statements after our consensus meeting, then a second survey step to refine further selected statements in the case of statements for which it was judged to be required, was associated with higher degrees of consensus than with our previous consensus statement on the management of endometriosis (Johnson and Hummelshoj, 2013). From our survey that followed the consensus meeting, ten of the 28 statements were graded unanimous (α) consensus, even though none reached 100% agreement without expression of a caveat about either the statement or the strength of the statement; four of our 28 consensus statements were associated with a 0% disagreement rate from the survey respondents (consensus statements 2, 3, 6 and 13). In the case of only two statements were we unable to achieve a majority consensus (statements 4 and 23). It must also be stressed that, by its very definition, and the finding that there was 100% agreement without caveat for none of the consensus statements, these consensus statements will not be expected to completely reflect the views of all of the individual participants and their organizations.

The strengths of this consensus document are its established methodology, the broad international representation including individuals from 19 countries across medical, surgical, and fertility organizations—and included a viewpoint from the women themselves via participation of eight endometriosis organizations. There are potential weaknesses in a consensus process such as this. Few of our statements are based on strong research evidence and many statements are based on opinion and termed 'good practice points' (GPPs); however, such statements could still be associated with a strong consensus amongst the group of experts. It is possible that we have overlooked some statements that have relevance, in spite of the methodology and feedback from all participants. It is therefore intended that this consensus will be updated regularly in response to feedback and, hopefully, increasing research evidence in this field.

Table I World Endometriosis Society Sao Paulo Consensus Statements on classification of endometriosis.

Patient priorities	**Consensus grading**
1) The ideal classification system for endometriosis should be standardized, pragmatic, cost effective and user friendly (for affected women, health care professionals, and researchers) so that it results in achievable strategies that increase access to and attainment of outcomes important to women with endometriosis and promotes standardization of disease phenotypes to optimize research study design (strong GPP).	α
2) Classification of endometriosis should deliver tangible benefits to affected women, including an understanding of the severity of their disease; its likely impact on their fertility, pain symptoms, and consequently their quality of life; the prognosis without intervention; the likely response and quality of life following treatment for pain and/or infertility; the chance of recurrence of symptoms and disease after treatment (strong GPP).	β
Definition	**Consensus grading**
3) Endometriosis should be defined as an inflammatory disease process, characterized by lesions of endometrial-like tissue outside the uterus that is associated with pelvic pain and/or infertility (strong GPP).	β
4) A comprehensive, contemporary characterization of endometriosis should include other essential elements: incidence; pathogenesis; multifactorial aetiology including genetic factors with possible epigenetic influences; possible effects of environmental exposures; pain syndrome elements; proliferative nature; hormone responsiveness (oestrogen-dependence and progesterone resistance); overlap with other conditions characterized by pelvic–abdominal pain and infertility (weak).	δ
5) Deep endometriosis should be defined as lesions extending deeper than 5 mm under the peritoneal surface or those involving or distorting bowel, bladder, ureter or vagina (weak).	γ
Low resources	**Consensus grading**
6) In low resource settings, classification of endometriosis should be well enough understood by women and health care professionals to be helpful in directing utilization of scarce resources (strong GPP).	γ
7) In low resource settings, classification should focus on information about the impact on women through questions about pelvic–abdominal pain and infertility (strong GPP).	γ
8) In low resource settings, empirical classification may facilitate integration of endometriosis management into general healthcare strategies (including education, progestin-based contraceptives, family planning and lactation) (strong GPP).	γ
Historic and minor classification systems	**Consensus grading**
9) Numerous historic classification systems have been described, but lack external validation, have variable correlation with clinical symptoms, do not predict treatment outcomes or prognosis, have not gained wide acceptance, and thus should not be used in clinical practice (weak).	α
Revised American Society for Reproductive Medicine (r-ASRM) classification of endometriosis	**Consensus grading**
10) The r-ASRM classification system is the longest established method of describing operative findings in current use (strong GPP).	α
11) The r-ASRM classification system does not describe deep endometriosis adequately (strong GPP).	α
12) The r-ASRM classification system has poor correlation with fertility outcomes (weak).	β
13) The r-ASRM classification system has very poor correlation with pain symptoms and quality of life (weak).	α
14) The r-ASRM classification system gives poor prognostic information (weak).	β
15) The r-ASRM classification system has poor predictive accuracy with respect to treatment outcomes (weak).	α
16) The reasons not to abandon the r-ASRM classification system are its longevity, widespread clinical use, its prevalence in the literature describing the operative appearance of endometriosis, and its incorporation into other classification systems of potentially greater value (GPP).	γ
Enzian classification of endometriosis	**Consensus grading**
17) If the r-ASRM classification is to be used, the Enzian classification system should be employed when deep endometriosis is also present to give a complete description of the operative findings (GPP).	γ
18) Correlation of Enzian with symptoms and infertility is poor (weak).	β
19) Enzian has limited prognostic value for the course of symptoms, quality of life and infertility (weak).	β
20) The predictive capacity of Enzian to detect a women's likely response to treatment for pain and/or infertility is uncertain (weak).	α

Continued

Table I *Continued*

21) Enzian may be used preoperatively based on findings in clinical examination, transvaginal ultrasound and MRI, to assist planning of surgery by predicting the extent of deep endometriosis and the time required for surgery (weak).	γ
22) External validation of the value of Enzian in further studies is needed (strong GPP).	α
American Association of Gynecological Laparoscopists (AAGL) classification of endometriosis	**Consensus grading**
23) The AAGL classification system might, in the future, be used instead of the rASRM classification system, as a preliminary study suggests it may have better correlation with infertility, level of pain and surgical difficulty (weak).	δ
Endometriosis Fertility Index (EFI)	**Consensus grading**
24) The EFI is a simple, robust, and validated clinical tool that predicts fertility outcome for women following surgical staging of endometriosis and may have considerable utility in developing treatment plans for infertile women with endometriosis (strong).	γ
Overarching Consensus Statements on Classification of Endometriosis	**Consensus grading**
25) An endometriosis classification system for pain and/or quality of life should be developed using a similar methodology to the EFI in order to combine the factors most predictive of these outcomes (strong GPP)	α
26) We recommend standard methods of ascertaining symptoms, undertaking examination, and performing laparoscopic surgery to standardise the way in which classification of endometriosis is defined (strong GPP)	α
27) Classification systems should be developed for low resource settings and settings in which surgery is not undertaken (either through unavailability or through the choice of women) that have utility in predicting endometriosis and its extent; its likely impact on fertility, pain symptoms and thus quality of life; the prognosis without intervention; the likely response to treatment for pain and/or infertility; the chance of recurrence of problems after treatment (strong GPP).	γ
28) Until better classification systems are validated, all women with endometriosis undergoing surgery should have a r-ASRM (or possibly, when published, AAGL) score and stage completed, women with deep endometriosis should have an Enzian classification completed, and women for whom fertility is a future concern should have an EFI score completed, and documented in the medical/surgical records (strong GPP)	γ

GPP = good practice point; α = unanimous or near-unanimous (more than 80% agreed without caveat and fewer than 5% disagreed); β = unanimous with caveat (either more than 80% agreed without caveat but more than 5% disagreed, or, fewer than 5% disagreed but fewer than 80% agreed without caveat); γ = majority (50–80% agreed); δ = no consensus (fewer than 50% agreed with or without caveat).

Unsurprisingly, our consensus statements reflect the kind of differences that might be expected from the coalescence of an eclectic group of individuals with different perspectives. One of the real values to the participants in such an exercise is the opportunity to recognise a completely new perspective and interpretation of existing evidence—this can be applied in any multidisciplinary setting, where specialists in medical, surgical and fertility treatment join forces, in our case, with women affected by endometriosis. In some instances, the strength of our statements (and in some cases, even the GRADE score) or the content of statements themselves may be surprising. We endeavoured to make strong statements where (i) the classification system would be of value to women with endometriosis and where the evidence was moderate or strong, i.e. derived from a reliable and reproducible source that had been internally and externally validated with methodological rigour or (ii) where the risk or expense of application of a classification strongly justified its non-use in the context of marginal or insufficient evidence or (iii) where there was considerable potential for benefit from a simple, low invasive, low cost classification, to overcome a substantial burden of suffering, even in the face of only weak or absent research evidence (as in the case of our GPPs).

Given that surgery is the pivotal moment at which these classifications can be defined, until better systems become available, in order to derive the most information from the procedure, our recommendation is that all women undergoing surgery should have the r-ASRM classification completed, women with deep endometriosis should additionally have Enzian completed, and women for whom future fertility is a concern should additionally have the EFI completed. Hence the proposed classification toolbox (Fig. 1), that incorporates the r-ASRM, Enzian (if required) and EFI (if required), is the current recommended classification method, with possible replacement or addition of new classification systems as their utility is proven. So doing will increase the familiarity of surgeons, the multidisciplinary team involved in a woman's management, and, most importantly, the woman herself, with a greater common understanding about the disease, which we view as potentially beneficial for affected women. Perhaps the biggest barrier to the implementation of this approach is whether those undertaking surgery will have the time and willingness to complete these forms. However, we posit that this should not be used as a reason not to undertake this, as women who undergo laparoscopic surgery might be considered to be in a privileged minority compared to all women worldwide who suffer from endometriosis, and our view is that it is the duty of the caring surgeon to the woman with endometriosis to prioritize this. The ability to record—and later share and utilise—this information is one of the most important aspects of a resource that is not only the only universally accepted gold standard method of diagnosis and an effective treatment, but also an invasive intervention for the woman with endometriosis.

(a) REVISED AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE CLASSIFICATION OF ENDOMETRIOSIS 1985

Patient's Name _____ Date: _____

Stage I (Minimal) 1-5 Laparoscopy_____Laparotomy_____Photography_____
Stage II (Mild) 6-15 Recommended Treatment _____
Stage III (Moderate) 16-40 _____
Stage IV (Severe) >40
Total _____ Prognosis _____

	ENDOMETRIOSIS	< 1 cm	1 – 3 cm	> 3 cm
Peritoneum	Superficial	1	2	4
	Deep	2	4	6
Ovary	R Superficial	1	2	4
	Deep	4	16	20
	L Superficial	1	2	4
	Deep	4	16	20
	POSTERIOR CULDESAC OBLITERATION	Partial		Complete
		4		40
	ADHESIONS	< 1/3 Enclosure	1/3-2/3 Enclosure	> 2/3 Enclosure
Ovary	R Filmy	1	2	4
	Dense	4	8	16
	L Filmy	1	2	4
	Dense	4	8	16
Tube	R Filmy	1	2	4
	Dense	4	8	16
	L Filmy	1	2	4
	Dense	4*	8*	16

*If the fimbriated end of the fallopian tube is completely enclosed, change the point assignment to 16.

Additional Endometriosis: _____ Associated Pathology: _____

To Be Used with Normal Tubes and Ovaries

L R

To Be Used with Abnormal Tubes and/or Ovaries

L R

Figure 1 Proposed Toolbox for Surgical Classification for Endometriosis.

a: Revised American Society for Reproductive Medicine scoring system for all women with endometriosis. Reprinted with permission from Elsevier from *Fertil Steril* 1997;**67**:817–821. American Society for Reproductive Medicine. Revised American Society for Reproductive Medicine classification of endometriosis: 1996. b: Enzian scoring system for women with deep endometriosis. Reprinted with permission from Professor Jörg Keckstein. Reference: www.endometriose-sef.de/dateien/ENZIAN_2013_web.pdf; accessed 1 February 2016. c: Endometriosis Fertility Index for women with endometriosis for whom future fertility is a consideration. Reprinted with permission from the American Society for Reproductive Medicine. Reference: Adamson GD, Pasta DJ. Endometriosis fertility index: the new, validated endometriosis staging system. *Fertil Steril* 2010;**94**:1609-1615.

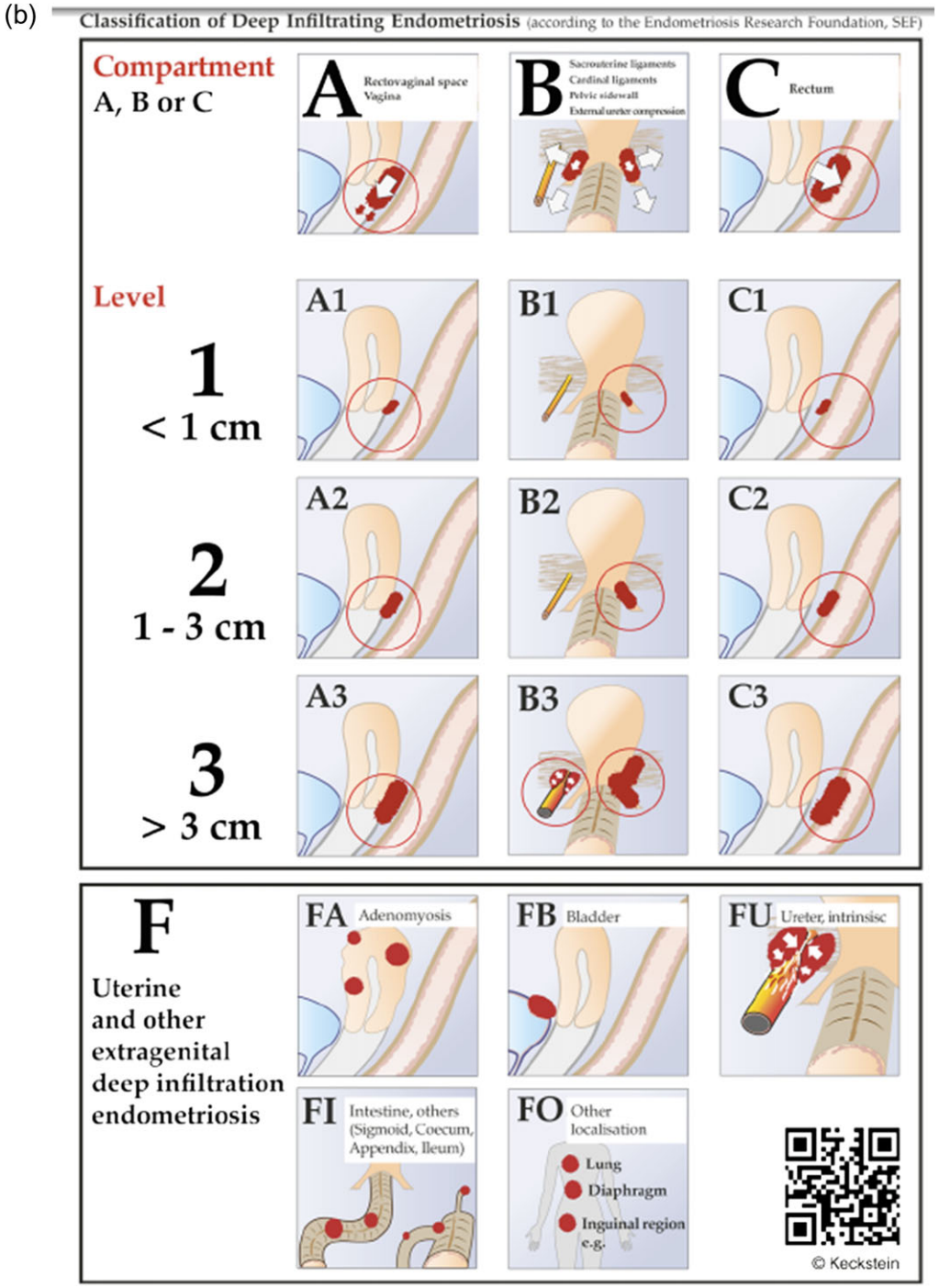

Figure 1 *Continued*

Several important issues have been raised by this consensus process that we have not addressed, or for which we have not attained consensus. These themes may form topics merit-worthy of further research. First, regarding definitions, we did not address 'subtle' endometriosis (Koninckx *et al.*, 2011), which some consider should be classified separately. Many authorities argue that the concept of microscopic endometriosis as a cause of pain, infertility, or more severe endometriosis has never been proven. Some have called for recognition of 'stage 0' disease, which could mean strongly suspected endometriosis based on combinations of symptoms and examination findings strongly predictive of endometriosis in women who have not undergone surgical diagnosis; visualized but not histologically confirmed endometriosis in the context of pain symptoms; occult or invisible (microscopic) lesions that are confirmed histologically in biopsy

(c)

ENDOMETRIOSIS FERTILITY INDEX (EFI) SURGERY FORM

LEAST FUNCTION (LF) SCORE AT CONCLUSION OF SURGERY

Score	Description
4	= Normal
3	= Mild Dysfunction
2	= Moderate Dysfunction
1	= Severe Dysfunction
0	= Absent or Nonfunctional

	Left	Right	
Fallopian Tube			
Fimbria			
Ovary			
Lowest Score		+	=
	Left	Right	LF Score

To calculate the LF score, add together the lowest score for the left side and the lowest score for the right side. If an ovary is absent on one side, the LF score is obtained by doubling the lowest score on the side with the ovary.

ENDOMETRIOSIS FERTILITY INDEX (EFI)

Historical Factors			Surgical Factors		
Factor	Description	Points	Factor	Description	Points
Age			LF Score		
	If age is ≤ 35 years	2		If LF Score = 7 to 8 (high score)	3
	If age is 36 to 39 years	1		If LF Score = 4 to 6 (moderate score)	2
	If age is ≥ 40 years	0		If LF Score = 1 to 3 (low score)	0
Years Infertile			AFS Endometriosis Score		
	If years infertile is ≤ 3	2		If AFS Endometriosis Lesion Score is < 16	1
	If years infertile is > 3	0		If AFS Endometriosis Lesion Score is ≥ 16	0
Prior Pregnancy			AFS Total Score		
	If there is a history of a prior pregnancy	1		If AFS total score is < 71	1
	If there is no history of prior pregnancy	0		If AFS total score is ≥ 71	0
Total Historical Factors			Total Surgical Factors		

EFI = TOTAL HISTORICAL FACTORS + TOTAL SURGICAL FACTORS: [ ] Historical + [ ] Surgical = [ ] EFI Score

ESTIMATED PERCENT PREGNANT BY EFI SCORE

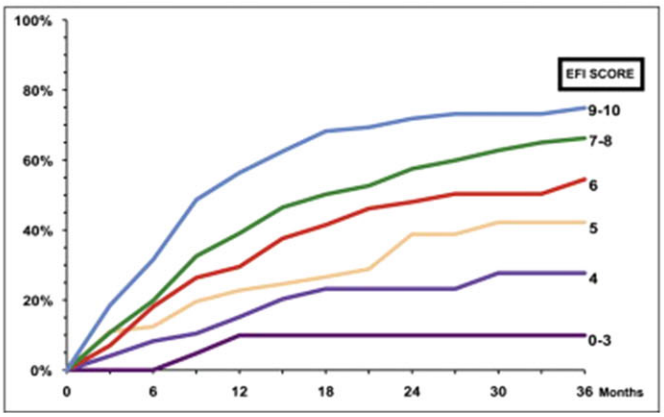

Figure 1 *Continued*

samples as endometriosis. 'Subtle' endometriosis (whether defined as this stage 0—or even stage 0 and r-ASRM stage 1) might simply be a natural condition rather than a pathological disease. There is a groundswell of opinion that subtle endometriosis (as well as deep endometriosis) should be classified separately. We did not address in detail what role adenomyosis should have on the classification of endometriosis. We also did not address how recurrence of endometriosis should be defined. Second, we have called for an endometriosis

classification system for pain and/or quality of life to be developed using a similar methodology to the EFI in order to combine the factors most predictive of these outcomes. Such a comprehensive classification system should incorporate all types of endometriosis including those features of deep endometriosis found to have prognostic value. Standardization is crucial to the development of such new classification systems. Formerly, there were no guidelines to standardize even the way in which information is obtained when diagnostic laparoscopy is performed. We now have such standardization available and the World Endometriosis Research Foundation Endometriosis Phenome and Biobanking Harmonisation Project (WERF EPHect) tools (Becker *et al.*, 2014; Vitonis *et al.*, 2014) are expected to transform uniquely the surgical and clinical data collection for women with endometriosis. Third, there is an imperative for the development of an 'empirical' classification system for circumstances in which laparoscopic surgery is not undertaken. Some argue that without laparoscopy there can be no diagnosis, thus no classification. However there may be particular utility for a predictive empirical classification system for women with pelvic/abdominal pain and/or infertility, when other causes have been ruled out. Finally, the possibility that molecular and genetic diagnostics may assist in staging endometriosis, as we have seen in many other diseases including breast cancer, will be an important theme of research over the coming decade. Molecular markers that allow directed treatments based on prognosis and response to treatment have the potential to be directed to women who will benefit most through classifications based on prognosis and response to treatment. Collaborative data collection in a manner described in the WERF EPHect papers highlighting the need for harmonisation of the endometriosis phenome (i.e. the set of all phenotypes expressed), data collection, and specimen handling (Becker *et al.*, 2014; Vitonis *et al.*, 2014; Rahmioglu *et al.*, 2014; Fassbender *et al.*, 2014) is the key to unlock this considerable potential.

Conclusion

This paper is the outcome of the first attempt to bring a global collaborative consensus to the classification of endometriosis, reflecting the best scientific evidence available and keeping uppermost the goal of improving quality of life for women with endometriosis. Our recommendation is that, until better classification systems have been developed, surgeons should use a toolbox for surgical classification of endometriosis (that includes the r-ASRM system and, where appropriate, the Enzian and EFI staging systems) to maximise the information available to women following their surgery.

Acknowledgements

This workshop was organised by the World Endometriosis Society. The views expressed in this consensus document represent the consensus of the individuals in the World Endometriosis Society Sao Paulo Consortium and not necessarily those of the organisations they represented.

Authors' roles

N.P.J. and L.H. conceptualised the idea and invited the societies. N.P.J., L.H., G.D.A., J.K., H.S.T., M.S.A., D.B., L.K., R.N.T., K.L.S-T., L.R. and L.C.G. all undertook literature reviews and made presentations at the consensus meeting. N.P.J., L.H. and G.D.A. drafted and, ultimately, finalised the article. The contributions of all members of the World Endometriosis Society Sao Paulo Consortium are outlined in Table II in the full-length article at http://humrep.oxfordjournals.org/. All named authors reviewed and approved the manuscript.

Funding

No funding was received for the consensus meeting. Members of the World Endometriosis Society Sao Paulo Consortium did not receive any payment.

Conflict of interest

The following disclosures were provided by the participants: Mauricio Abrao is an advisor to Bayer Pharma, and a consultant to AbbVie and AstraZeneca; G. David Adamson is the Owner of Advanced Reproductive Care Inc. and Ziva and a consultant to Bayer Pharma, Ferring and AbbVie; Arnold Advicula is a consultant to Blue Endo, Cooper Surgical, Intuitive Surgical, SurgiQuest, and Titan Medical; Catherine Allaire is a consultant to AbbVie, Actavis and Bayer Pharma; Joan-Carles Arche is an employee of Ferring; Christian Becker holds a research grant from Bayer Healthcare; Deborah Bush has received travel grants from Fisher & Paykel Healthcare and Bayer Pharmaceuticals; Kristof Chwalisz is an employee of AbbVie Inc and owns stock and stock options in AbbVie; Hilary Critchley has received travel support from AbbVie, Bayer Pharma, Gedeon Richter, Preglem and Vifor Pharma UK, and research grants from Bayer Pharma, Preglem and the Medical Research Council (UK); Thomas D'Hooghe is a consultant to Bayer Pharma, Proteomika, Pharmaplex, Astellas, Roche Diagnostics and Actavis, and holds research grants from Ferring, Merck Serono, Merck, Besins and Pharmaplex; Johannes L.H. Evers is the Editor-in-Chief of Human Reproduction; Thomas Faustmann is an employee of Bayer Pharma; Idhalez Flores holds a research grant from the Puerto Rico Science, Technology and Research Trust; Axel Forman is a principal investigator for a trial launched by Bayer AG; Ian Fraser lectures for and is an advisor to Bayer Healthcare, Merck/MSD, Daiichi Sankyo, and Vifor Pharma, and holds research funding from Bayer Healthcare, Merck/MSD, Daiichi Sankyo and Vifor Pharma; Linda Giudice is a consultant to AbbVie, Juniper Pharmaceutical and NextGen Jen, holds research grant from the NIH, is site PI on a clinical trial sponsored by Bayer, and is a shareholder in Merck and Pfizer; Lone Hummelshoj is an unpaid consultant to AbbVie; Neil Johnson has received conference expenses from Bayer Pharma, Merck-Serono, and MSD, research funding from AbbVie, and is a consultant to Vifor Pharma and Guerbet; Jörg Keckstein has received a travel grant from AbbVie; Ludwig Kiesel is a consultant to Bayer Pharma, AbbVie, AstraZeneca, Gedeon Richter and Shionogi, and holds a research grant from Bayer Pharma; Philippe Koninckx is a shareholder in Endosat Ltd and eSaturnus Ltd; Bruce Lessey is a scientific advisor to Abbvie; Ben Mol is a consultant to ObsEva; Carlos Petta is a consultant to and speaker for Bayer Pharma and Merck-Serono; Fernando Reis is participating in multicentre trials sponsored by AbbVie (M12-671) and Libbs Farmacêutica Ltda (LB1203); Edgardo Rolla is the principal investigator in clinical trials for AbbVie and Bayer Pharma; Luk Rombauts is an advisor to MSD, Merck Serono and Ferring, and a shareholder in Monash IVF; Pamela Stratton is working on a project that has a clinical

trials agreement with Allergan; Wilma Verhagen-Kamerbeek is an employee of Roche Diagnostics International; Krina Zondervan is part of a scientific collaboration between Oxford University and Bayer Healthcare Ltd for the purpose of drug target identification in endometriosis, and has in recent years been a consultant for Abbvie Inc, Bayer HealthCare, and Roche Diagnostics. The following have declared that they have nothing to disclose: Elisabet Andersson; George Condous; Bianca de Bie; Gerard Dunselman; Cindy Farquhar; Rui Ferriani; Jessica Fourquet; Heather Guidone; Sun-Wei Guo; M. Louise Hull; Louis Marcellin; Joy Marriott; Stacey Missmer; Alan Lam; Peter Maher; Uche Menakaya; Vicki Nisenblat; Dana Paredes; Tamer Seckin; Kathy Sharpe Timms; David Soriano; Rulla Tamimi; Hugh Taylor; Robert Taylor; Jim Tsaltas.

Appendix

The complete list of people representing the World Endometriosis Society Sao Paulo Consortium is:

Mauricio Abrao; G. David Adamson; Arnold Advincula; Catherine Allaire; Elisabet Andersson; Joan-Carles Arche; Christian Becker; Deborah Bush; Kristof Chwalisz; George Condous; Hilary Critchley; Bianca de Bie; Thomas D'Hooghe; Gerard Dunselman; Johannes (Hans) Evers; Cindy Farquhar; Thomas Faustmann; Rui Ferriani; Idhalez Flores; Axel Forman; Jessica Fourquet; Ian Fraser; Linda Giudice; Heather Guidone; Sun-Wei Guo; Louise Hull; Lone Hummelshoj; Neil Johnson; Jorg Keckstein; Ludwig Kiesel; Philippe Koninckx; Alan Lam; Bruce Lessey; Peter Maher; Louis Marcellin; Joy Marriott; Uche Menakaya; Stacey Missmer; Ben Mol; Vicki Nisenblat; Dana Paredes; Carlos Petta; Fernando Reis; Edgardo Rolla; Luk Rombauts; Tamer Seckin; Kathy Sharpe Timms; David Soriano; Pamela Stratton; Rulla Tamimi; Hugh Taylor; Robert Taylor; Jim Tsaltas; Wilma Verhagen-Kamberbeek; Krina Zondervan.

References

Adamson GD, Kennedy SH, Hummelshoj L. Creating solutions in endometriosis: global collaboration through the World Endometriosis Research Foundation. *J Endometr* 2010;**2**:3–6.

Adamson GD, Pasta DJ. Endometriosis fertility index: the new, validated endometriosis staging system. *Fertil Steril* 2010;**94**:1609–1615.

Adamson GD. Endometriosis classification: an update. *Curr Opin Obstet Gynecol* 2011;**23**:213–220.

American Society for Reproductive Medicine. Revised American Society for Reproductive Medicine classification of endometriosis: 1996. *Fertil Steril* 1997;**67**:817–821.

Becker CM, Laufer MR, Stratton P, Hummelshoj L, Missmer SA, Zondervan KT, Adamson GD, WERF EPHect Working Group. World Endometriosis Research Foundation Endometriosis Phenome and Biobanking Harmonisation Project: I. Surgical phenotype data collection in endometriosis research. *Fertil Steril* 2014;**102**:1213–1222.

Boothroyd C, Karia S, Andreadis N, Rombauts L, Johnson N, Chapman M, Australasian CREI Consensus Expert Panel on Trial evidence (ACCEPT) group. Consensus statement on prevention and detection of ovarian hyperstimulation syndrome. *Aust N Z J Obstet Gynaecol* 2015; **55**:523–534.

Fassbender A, Rahmioglu N, Vitonis AF, Viganò P, Giudice LC, D'Hooghe TM, Hummelshoj L, Adamson GD, Becker CM, Missmer SA *et al*. World Endometriosis Research Foundation Endometriosis Phenome and Biobanking Harmonisation Project: IV. Tissue collection, processing, and storage in endometriosis research. *Fertil Steril* 2014;**102**:1244–1253.

Haas D, Oppelt P, Shebl O, Shamiyeh A, Schimetta W, Mayer R. Enzian classification: does it correlate with clinical symptoms and the rASRM score? *Acta Obstet Gynecol Scand* 2013;**92**:562–566.

Johnson NP, Hummelshoj L, for The World Endometriosis Society Montpellier Consortium. Consensus on current management of endometriosis. *Hum Reprod* 2013;**28**:1552–1568.

Keckstein J, Ulrich U., Possover M, Schweppe KW. ENZIAN-Klassifikation der tief infiltrierenden Endometriose. *Zentralbl Gynäkol* 2003;**125**:291.

Koch J, Rowan K, Rombauts L, Yazdani A, Chapman M, Johnson N. Endometriosis and infertility—a consensus statement from ACCEPT (Australasian CREI Consensus Expert Panel on Trial evidence). *Aust N Z J Obstet Gynaecol* 2012;**52**:513–522.

Koninckx PR, Ussia A, Adamyan L, Wattiez A. An endometriosis classification, designed to be validated. *Gynecol Surg* 2011;**8**:1–6.

Kroon B, Johnson N, Chapman M, Yazdani A, Hart R, Australasian CREI Consensus Expert Panel on Trial evidence (ACCEPT) group. Fibroids in infertility—consensus statement from ACCEPT (Australasian CREI Consensus Expert Panel on Trial evidence). *Aust N Z J Obstet Gynaecol* 2011;**51**:289–295.

Rahmioglu N, Fassbender A, Vitonis AF, Tworoger SS, Hummelshoj L, D'Hooghe TM, Adamson GD, Giudice LC, Becker CM, Zondervan KT, Missmer SA; WERF EPHect Working Group. World Endometriosis Research Foundation Endometriosis Phenome and Biobanking Harmonization Project: III. Fluid biospecimen collection, processing, and storage in endometriosis research. *Fertil Steril* 2014;**102**:1233–1243.

Vitonis AF, Vincent K, Rahmioglu N, Fassbender A, Buck Louis GM, Hummelshoj L, Giudice LC, Stratton P, Adamson GD, Becker CM *et al*. World Endometriosis Research Foundation Endometriosis Phenome and biobanking harmonization project: II. Clinical and covariate phenotype data collection in endometriosis research. *Fertil Steril* 2014;**102**: 1223–1232.