

A large, stylized graphic of a leaf or petal, rendered in a light gray color, is positioned behind the text. It has a central vein and a curved, pointed shape.

***A CRITICAL EVALUATION OF THE  
CURRENT STAGING SYSTEMS OF  
ENDOMETRIOSIS***

***Kutay Biberoglu***  
***Ankara, Turkey***

**ACE 2014**  
3<sup>rd</sup> Asian Conference on Endometriosis

***3<sup>rd</sup> Asian Conference on Endometriosis (ACE 2014)***  
***October 24-26, 2014***  
***Seoul, Korea***

## ***Presentation outline***

- *Past & current classification systems*
  - *Why continue to develop classification systems for endometriosis?*
  - *Possible future systems*
  - *Implications for clinical practice*
- 
- The logo for ACE 2014 features a stylized, flowing grey graphic that resembles a ribbon or a leaf, curving around the text. The text "ACE 2014" is prominently displayed in a large, serif font, with "2nd Asian Conference on Endometriosis" written in a smaller, sans-serif font below it.

# Why should we classify endometriosis?

- *A good classification system can:*
  - *Create a common language*
  - *Enable specificity of diagnosis*
  - *Standardize comparisons*
  - *Facilitate research applications*
  - *Help guide and monitor treatment decisions*

Get Everyone on  
the Same Page



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# Past & current classification systems



- *First classification system proposed in 1979<sup>1</sup> by AFS (now ASRM) into 4 stages, on the premise that severity of disease would determine success of surgery*
- *Revised in 1995<sup>2</sup>*
- *Since then, revisions & new classification systems have been developed*

<sup>1</sup>AFS. Classification of endometriosis. Fertil Steril 1979;32:633–634

<sup>2</sup>Revised ASRM classification of endometriosis. Fertil Steril 1996; 67:817–821

**EXAMPLES & GUIDELINES**

**STAGE I (MINIMAL)**



**STAGE II (MILD)**



**STAGE III (MODERATE)**



PERITONEUM		
Superficial Endo	- 1-3cm	- 2
R. OVARY		
Superficial Endo	- < 1cm	- 1
Filmy Adhesions	- < 1/3	- 1
<b>TOTAL POINTS</b>		<b>4</b>

PERITONEUM		
Deep Endo	- >3cm	- 6
R. OVARY		
Superficial Endo	- <1cm	- 1
Filmy Adhesions	- <1/3	- 1
L. OVARY		
Superficial Endo	- <1cm	- 1
<b>TOTAL POINTS</b>		<b>9</b>

PERITONEUM		
Deep Endo	- >3cm	- 6
CULDESAC		
Partial Obliteration		- 4
L. OVARY		
Deep Endo	- 1-3cm	- 16
<b>TOTAL POINTS</b>		<b>26</b>

**STAGE III (MODERATE)**



**STAGE IV (SEVERE)**



**STAGE IV (SEVERE)**



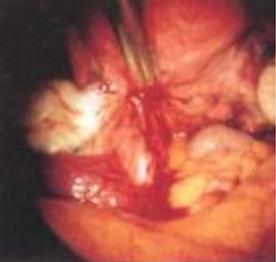
PERITONEUM		
Superficial Endo	- >3cm	- 4
R. TUBE		
Filmy Adhesions	- < 1/3	- 1
R. OVARY		
Filmy Adhesions	- < 1/3	- 1
L. TUBE		
Dense Adhesions	- < 1/3	- 16*
L. OVARY		
Deep Endo	- < 1 cm	- 4
Dense Adhesions	- < 1/3	- 4
<b>TOTAL POINTS</b>		<b>30</b>

PERITONEUM		
Superficial Endo	- >3cm	- 4
L. OVARY		
Deep Endo	- 1-3cm	- 32**
Dense Adhesions	- < 1/3	- 8**
L. TUBE		
Dense Adhesions	- < 1/3	- 8**
<b>TOTAL POINTS</b>		<b>52</b>

PERITONEUM		
Deep Endo	- >3cm	- 6
CULDESAC		
Complete Obliteration		- 40
R. OVARY		
Deep Endo	- 1-3cm	- 16
Dense Adhesions	- < 1/3	- 4
L. TUBE		
Dense Adhesions	- > 2/3	- 16
L. OVARY		
Deep Endo	- 1-3cm	- 16
Dense Adhesions	- > 2/3	- 16
<b>TOTAL POINTS</b>		<b>114</b>

\*Point assignment changed to 16

\*\*Point assignment doubled



**Red**



**Red-pink**



**White**



**Yellow-Brown**



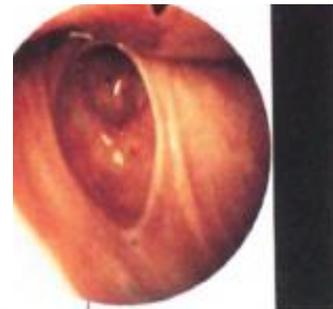
**Clear**



**Blue**



**Black**



**toneal defect**

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# Reliability of rASRM Staging

- ↳ Intraoperative photographs reviewed by 4 academic & 4 local expert
- ↳ Images sent online, reviewed re: stage, size, type of lesions / adhesions
- ↳ Outcomes = \* lesion +/- \*\*clinical stage \*\*\*computer-assisted staging
- ✓ **\*Substantial reliability for endometriosis diagnosis** - interrater reliability among 8 surgeons : **0.69 (0.64 – 0.74)** (21% higher for academic vs local expert)
- ✓ **\*\*Moderate reliability for staging – agreement on rASRM staging 61% (52–75%) with moderate interrater reliability : 0.44 (0.41– 0.47)**
- ✓ **\*\*\*Almost perfect reliability with, computerized-assisted staging : 0.95 (0.89 – 0.99)**

# Past & current classification systems



- *First introduced in 2005<sup>3</sup>*
- *To supplement rASRM staging, particularly in DIE, retroperitoneal structures & intestine, ureter, bladder..*

<sup>3</sup>Tuttles F. et al. Zentralbi Gynakol 2005; 127:275–281

a : cul-de-sac  
& vagina

b : uterosacral lig.  
& cardinal lig.

c : rectum,  
rectosigmoid

**E – ENDOMETRIOSIS (severity 1-4)**



E1a = isolated nodule the pouch of Douglas



E1b = isolated nodule <1 cm from the uterine sacral ligament (USL)



E1bb = bilateral infiltration of the USL



E1c = isolated nodule in the rectovaginal space



E2a = infiltration of the upper third of the vagina



E2b = infiltration of the USL >1 cm



E2bb = bilateral



E2c = infiltration of rectum <1 cm



E3a = infiltration of the middle part of the vagina



E3b = infiltration of the cardinal ligament (without ureterohydronephrosis)



E3bb = bilateral



E3c = infiltration of the rectum 1-3 cm without stenosis



E4a = infiltration of uterus and/or lower third of the vagina and/or lower third of the vagina



E4b = infiltration of the cardinal ligament to pelvic side wall and/or ureterohydronephrosis cardinal ligament to pelvic side wall and/or ureterohydronephrosis



E4bb = bilateral



E4c = infiltration of the rectum >3 cm and/or rectal stenosis infiltration of the rectum >3 cm and/or rectal stenosis

**F – EXTERNAL DISEASE**



FA – Uterine adenomyosis



FB – deep infiltration of bladder



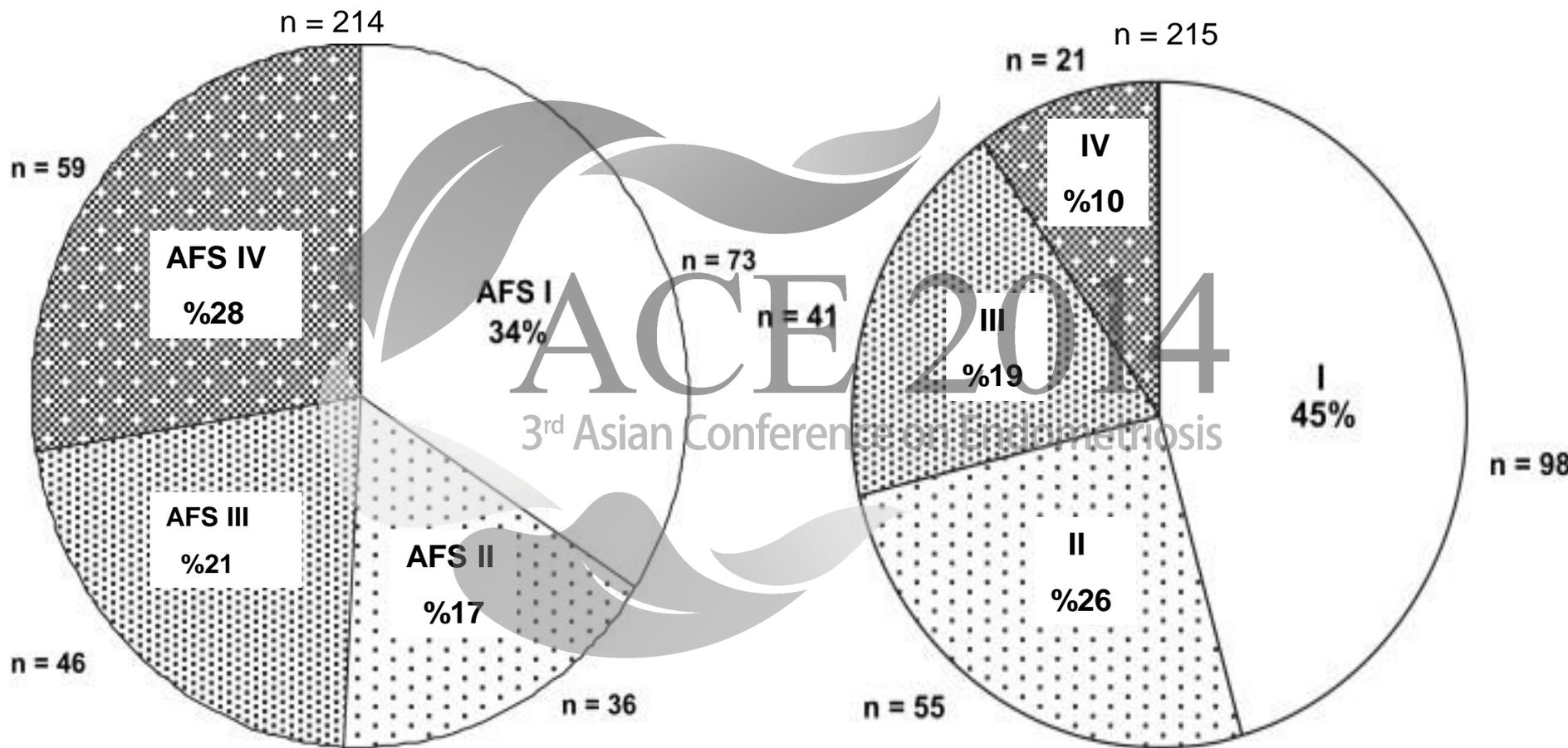
FU – intrinsic Ureteral infiltration



FI – intestinal infiltration other than rectum/sigmoid

FO – other locations

## Does the ENZIAN score complement the rAFS, or do both signify a duplicate registration of the same phenomena?



58/160 had superficial peritoneal foci in cul-de-sac & uterosacral lig (E1a/1b/1bb), already classified by rAFS. When excluded from the ENZIAN, Dx of DIE were reduced by 58 (36%).

\*3 compartments intersect each other in three-dimensional space – overlap / duplication

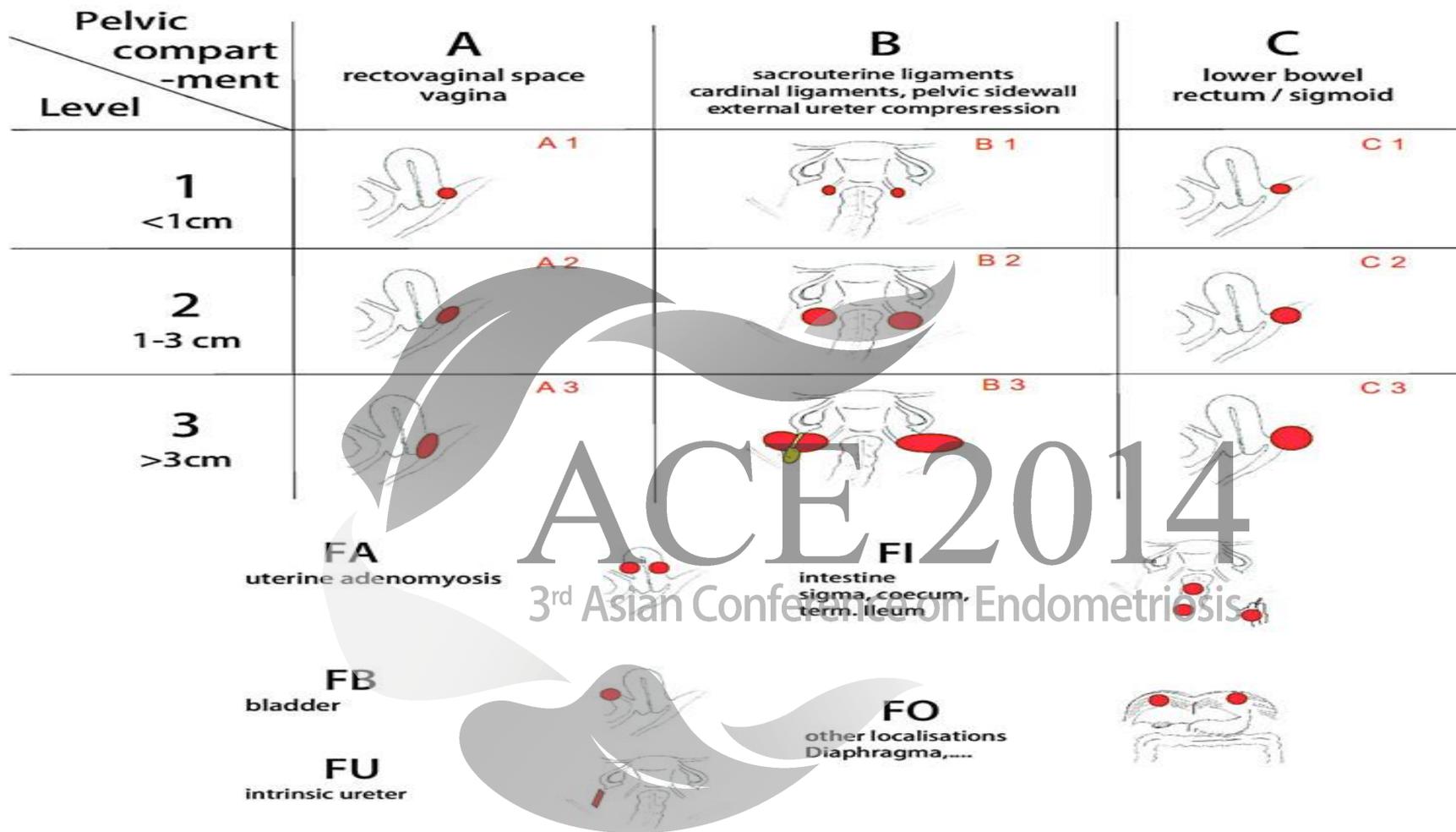
# Past & current classification systems



- Revised in 2011 (*rENZIAN*)<sup>4</sup>
- Re-revised in 2013 (*rENZIAN*)<sup>5</sup>
- Superficial peritoneal foci (E1a/1b/1bb) excluded ; DIE reduced by %36
- There were no cases classified twice on *rASRM* & *Enzian* systems

<sup>4</sup>Haas D et al. Fertil Steril 2011;95:1574–8

<sup>5</sup>Haas D. et al. Arch Gynecol Obstet 2013; 287:941–945



Axes, minor peritoneal lesions in the cul-de-sac, Grade 4 excluded

# Past & current classification systems



- *Developed by Adamson & Pasta in 2010* <sup>6</sup>
- *Predicts non-IVF fertility rates after surgery*
- *Uses rASRM as part of scoring system*
- *Validated in three studies up to 2013* <sup>7-9</sup>

<sup>6</sup>Adamson GD, Pasta DJ. Fertil Steril 2010; 94: 1609–1615

<sup>7</sup>Wei DM et al. Zhonghua Fu Chan Ke Za Zhi 2011; 46:806–808

<sup>8</sup>Yacoub A et al. World Congress Endometriosis. Montpellier, France. S#10-4. 7 September 2011

<sup>9</sup>Tomassetti C et al. Hum Reprod. 2013;28(5):1280-8

# Endometriosis Fertility Index (EFI) Surgery form

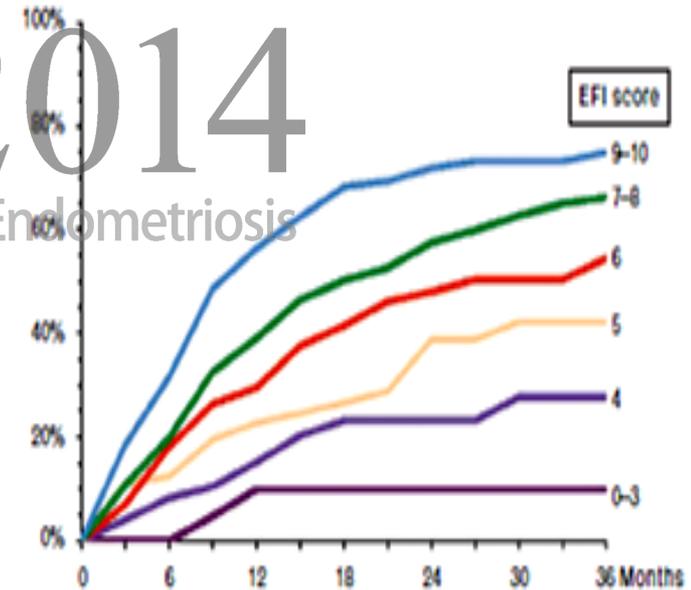
## Least function (LF) score at conclusion of surgery

Score	Description	Left	Right
4	= Normal	<input type="checkbox"/>	<input type="checkbox"/>
3	= Mid Dysfunction	<input type="checkbox"/>	<input type="checkbox"/>
2	= Moderate Dysfunction	<input type="checkbox"/>	<input type="checkbox"/>
1	= Severe Dysfunction	<input type="checkbox"/>	<input type="checkbox"/>
0	= Absent or Nonfunctional	<input type="checkbox"/>	<input type="checkbox"/>

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.

Lowest Score Left + Lowest Score Right = LF Score

## Estimated percent pregnant by EFI score



## Endometriosis Fertility Index (EFI)

Historical Factors			Surgical Factors				
Factor	Description	Points	Factor	Description	Points		
Age	If age is ≤ 35 years	2	LF Score	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	If years infertile is ≤ 3	2	AFS Endometriosis Score	If AFS Endometriosis Lesion Score is < 16	1		
	If years infertile is > 3	0		If AFS Endometriosis Lesion Score is ≥ 16	0		
Prior Pregnancy	If there is a history of a prior pregnancy	1	AFS Total Score	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:			<input type="text"/>	+	<input type="text"/>	=	<input type="text"/>
			Historical		Surgical		EFI Score

# What do we have, so far?

## Reflecting more on rASRM

**AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE  
REVISED CLASSIFICATION OF ENDOMETRIOSIS**

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: \_\_\_\_\_

PERITONEUM	ENDOMETRIOSIS		
	<1cm	1-3cm	>3cm
Superficial	1	2	4
Deep	2	4	6
<b>R</b> Superficial	1	2	4
<b>R</b> Deep	4	16	20
<b>L</b> Superficial	1	2	4
<b>L</b> Deep	4	16	20

OVARY	POSTERIOR CULDESAC OBLITERATION	
	Partial	Complete
	4	40

OVARY	ADHESIONS		
	<1/3 Enclosure	1/3-2/3 Enclosure	>2/3 Enclosure
<b>R</b> Filmy	1	2	4
<b>R</b> Dense	4	8	16
<b>L</b> Filmy	1	2	4
<b>L</b> Dense	4	8	16
<b>R</b> Filmy	1	2	4
<b>R</b> Dense	4*	8*	16
<b>L</b> Filmy	1	2	4
<b>L</b> Dense	4*	8*	16

TUBE	ADHESIONS		
	<1/3 Enclosure	1/3-2/3 Enclosure	>2/3 Enclosure
<b>R</b> Filmy	1	2	4
<b>R</b> Dense	4*	8*	16
<b>L</b> Filmy	1	2	4
<b>L</b> Dense	4*	8*	16

\*If the fimbriated end of the fallopian tube is completely enclosed, change the point assignment to 16.  
 Denote appearance of superficial implant types as red (R), red-pink, flame-like, vesicular blots, clear vesicles, white (W), opacifications, peritoneal defects, yellow-brown, or black (B) black, hemosiderin deposits, blue. Denote percent of total described as R, W, Y, B, and L. Total should equal 100%.

Additional Endometriosis: \_\_\_\_\_ Associated Pathology: \_\_\_\_\_

**Histologic verification : red - %100, black - %92, white - %31  
 Mettler L. 2003  
 CPP/infertility/mixed colour/>5mm deep/>10 mm wide - %75  
 Wanyonyi SZ. 2011**

- The most widely known & commonly used classification system
  - Reliable for diagnosis<sup>1</sup>
  - Moderately reliable for staging<sup>1</sup>
  - Commonly used in RCTs & studies
- But, its usefulness in clinical setting is questioned:
  - Wide-ranging and arbitrary scoring
  - No correlation between pain & staging of disease
  - Doesn't account for DIE or organ involvement
  - Does not guide treatment or predict outcome

<sup>1</sup>Schliep KC et al. Obstet Gynecol 2012;120:104–12

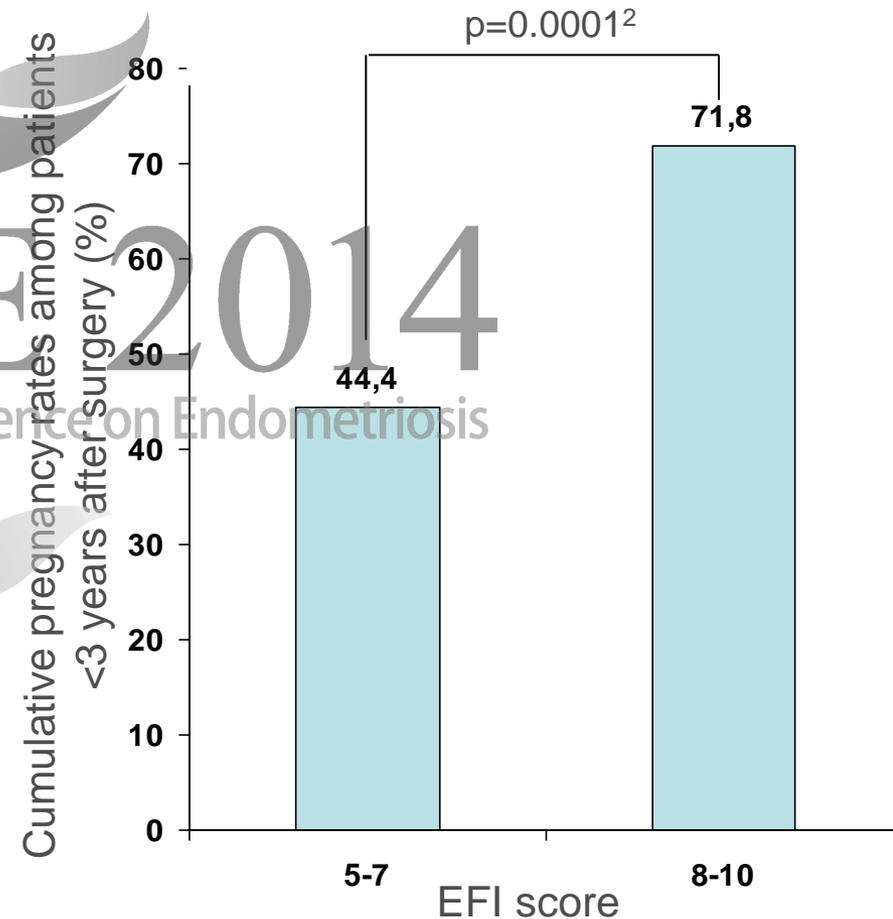
# What else do we have?

- **ENZIAN**

- Supplements rASRM staging
- Pain & fertility still absent
- Poorly accepted (attributed to its complexity)<sup>1</sup>

- **EFI**

- Uses rASRM as part of scoring system
- Fallopian tube and ovarian dysfunction - subjective
- Significant correlation between EFI score & the time to non-ART pregnancy<sup>2</sup>
- Informs treatment decisions



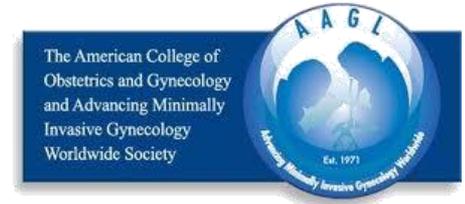
<sup>1</sup>Adamson GD. Curr Opin Obstet Gynecol 2011; 23: 213–220

<sup>2</sup>Tomassetti C et al. Hum Reprod. 2013;28(5):1280-8

# Summary of current systems

	rASRM	rENZIAN	EFI
Peritoneal	✓		
Ovarian/OMA	?		
DIE		✓	
Fertility			✓
<b>Pain</b>	<b>✗</b>	<b>✗</b>	<b>✗</b>
Guides treatment?			✓
Simple			?

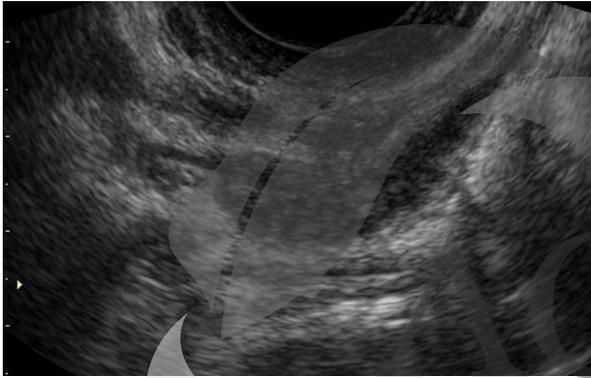
# Possible future classification systems



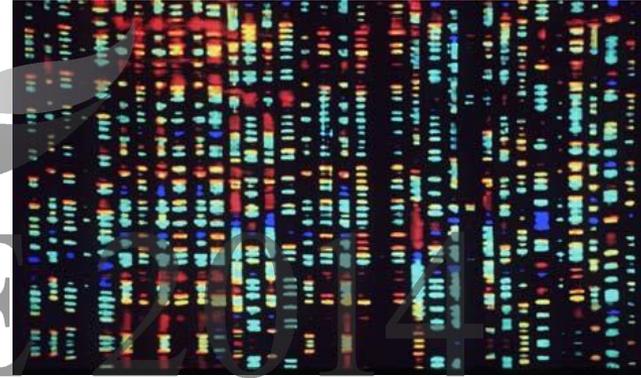
- **AAGL**

- *Project initiated by AAGL special interest group on reproductive surgery and endometriosis in 2007*
- *Experts give weighted score to anatomical factors felt to be important with respect to pain & infertility*
- *Hypothesis: if disease can be described accurately, a practical classification system may eventually be developed from analysis of the descriptions*
- *Data from 30 experts analyzed and scores assigned*
- *AAGL is now about to propose a new classification system*
- *Preliminary results correlate with pain, infertility and surgical difficulty*

# Possible future classification systems



**Transvaginal sonography**  
& contrast-enhanced magnetic  
resonance-colonography for DIE <sup>1</sup>



**Genome-wide profiling -**  
subtelomeric location of  
hypermethylation in endometriosis

- **Serological markers** in correlation with symptoms & rAFS
  - CA-125, TNF, IL-1, IL-6, IL-8 <sup>2</sup>
- **AMH serum levels** and an association with severity<sup>2</sup>
- **Annexin V, VEGF, CA-125 & sICAM-1/or glycodeclin** diagnosis in endometriosis undetectable by US with a sensitivity of 81–90% & a specificity of 63–81%<sup>2 3</sup>

<sup>1</sup> Vimercati A et al. Ultrasound Obstet Gynecol 2012; 40: 592–603

<sup>1</sup> Coccia ME, Rizzello F. Ann N Y Acad Sci 2011; 1221:61–69

<sup>2</sup> Socolov R et al. Eur J Obstet Gynecol Reprod Biol 2011; 154:215–217

<sup>2</sup> Shebl O et al. Gynecol Endocrinol 2009; 25:713–716

<sup>2</sup> Vodolazkaia A et al. Hum Reprod 2012; 27:2698–2711

<sup>3</sup> Borghese B et al. Mol Endocrinol 2010; 24:1872–1885

# So, how should we manage our patients today?

- Current systems in endometriosis do not meet needs & require visualisation via laparoscopy
- ..whilst no marker was conclusively shown to diagnose endometriosis, **endometrial nerve fibres and molecules involved in cell-cycle control, cell adhesion and angiogenesis are promising** candidates for future biomarker research
- Recommend **a pragmatic, patient-centric approach**:
  - Keep classification for clinical trials
  - Perform classification only if therapeutic surgery is to be performed at the same time
  - Use **EFI** if goal of surgical treatment is **to assist fertility**
  - No staging necessary for patients with pain
    - Monitoring with **B&B** or **VAS** scores and **ultrasound**

***Since the staging systems are not clinically accurate enough..***

- to guide the treatment plan, to predict clinical response to treatment and to foresee the risk of recurrence

***..and since endometriosis is present in 70-75% of women with chronic pelvic pain***

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- it is important that treatment decisions in endometriosis should be made not only on the basis of disease staging
- but should also take into account the needs and circumstances of the individual patient

## *Is surgical diagnosis always necessary?*

“The common belief that a preliminary laparoscopy must always be performed in order to definitely diagnose endometriosis should be challenged, as the nonsurgical diagnosis has been demonstrated to be highly reliable”

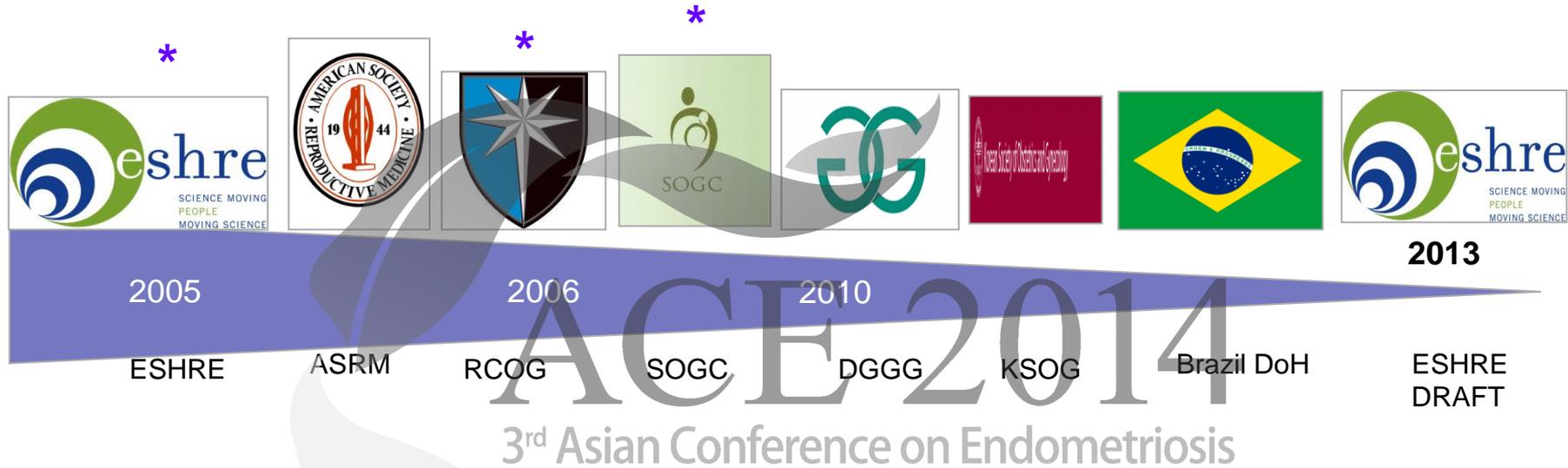
“..often reveals no obvious cause for pain”

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If signs of DIE or ovarian endometriosis are not present, it can be argued that laparoscopy should not be performed just to find peritoneal disease and treat it, especially in adolescents and young adults. It has not been shown that treatment of peritoneal disease influences the natural course of the disease.

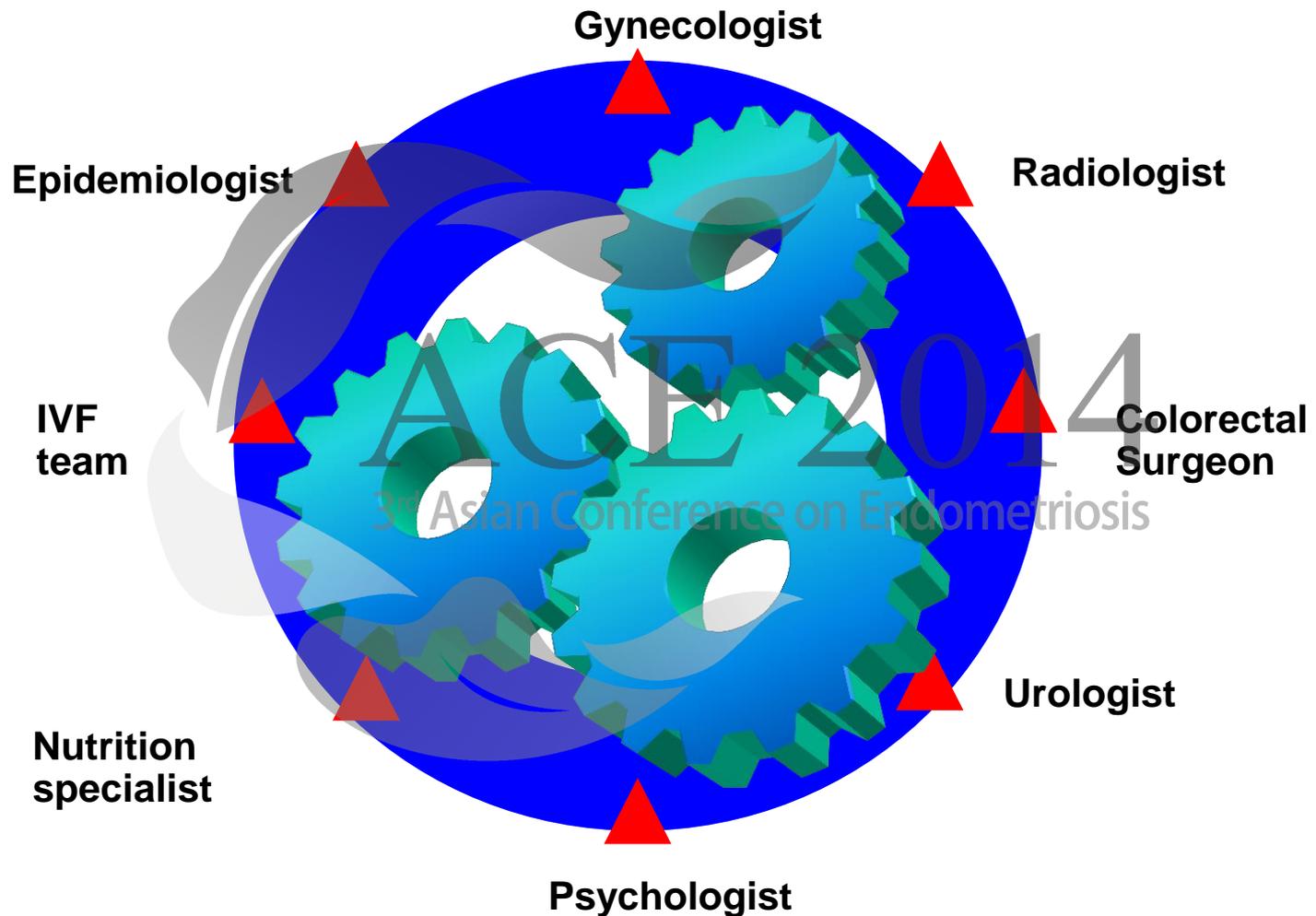
# Guidelines for endometriosis management



## Empirical treatment for pain symptoms without a definitive diagnosis \*

ESHRE=European Society of Human Reproduction and Embryology;  
ASRM=The American Society for Reproductive Medicine;  
RCOG=Royal College of Obstetricians and Gynaecologists;  
SOGC=Society of Obstetricians and Gynaecologists of Canada.  
DGGG=German society for gynecology and obstetrics,  
KSOG – Korean Society of Obstetrics and Gynecology  
DoH = Brazilian Department of Health

## *The complexities of endometriosis require a multidisciplinary team*



**From a patient perspective, conservative measures should be offered before surgery to women with painful symptoms with the purpose of reducing pain before, not after, surgery**