



A CRITICAL EVALUATION OF THE CURRENT STAGING SYSTEMS OF ENDOMETRIOSIS

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Presentation outline

- *Past & current classification systems*
 - *Why continue to develop classification systems for endometriosis?*
 - *Possible future systems*
 - *Implications for clinical practice*
- 
- The logo for the 2nd Asian Conference on Endometriosis (ACE 2014) is centered in the background. It features a large, stylized 'ACE 2014' in a serif font. Below the year, the text '2nd Asian Conference on Endometriosis' is written in a smaller, sans-serif font. The logo is flanked by two large, flowing, leaf-like shapes that curve upwards and outwards, creating a sense of movement and elegance.

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**



Past & current classification systems



- *First classification system proposed in 1979¹ by AFS (now ASRM) into 4 stages, on the premise that severity of disease would determine success of surgery*
- *Revised in 1995²*
- *Since then, revisions & new classification systems have been developed*

¹AFS. Classification of endometriosis. Fertil Steril 1979;32:633–634

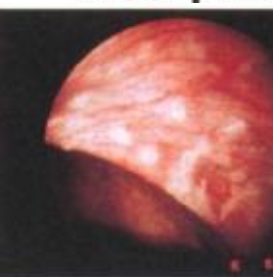
²Revised ASRM classification of endometriosis. Fertil Steril 1996; 67:817–821



Red



Red-pink



White



Yellow-Brown

EXAMPLES & GUIDELINES

STAGE I (MINIMAL)



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

STAGE II (MILD)



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

STAGE III (MODERATE)



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

STAGE III (MODERATE)



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
TOTAL POINTS		30

STAGE IV (SEVERE)



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

STAGE IV (SEVERE)



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
TOTAL POINTS		114

*Point assignment changed to 16

**Point assignment doubled



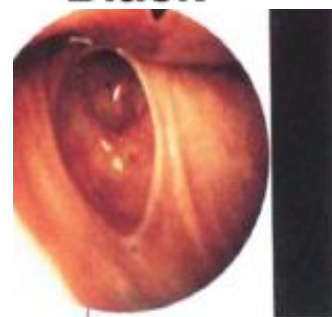
Clear



Blue



Black



toneal defect

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 2005³*
- *To supplement rASRM staging, particularly in DIE, retroperitoneal structures & intestine, ureter, bladder..*

³Tuttlies 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



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



E4bb = bilateral



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

F – EXTERNAL DISEASE



FA – Uterine adenomyosis



FB – deep infiltration of bladder



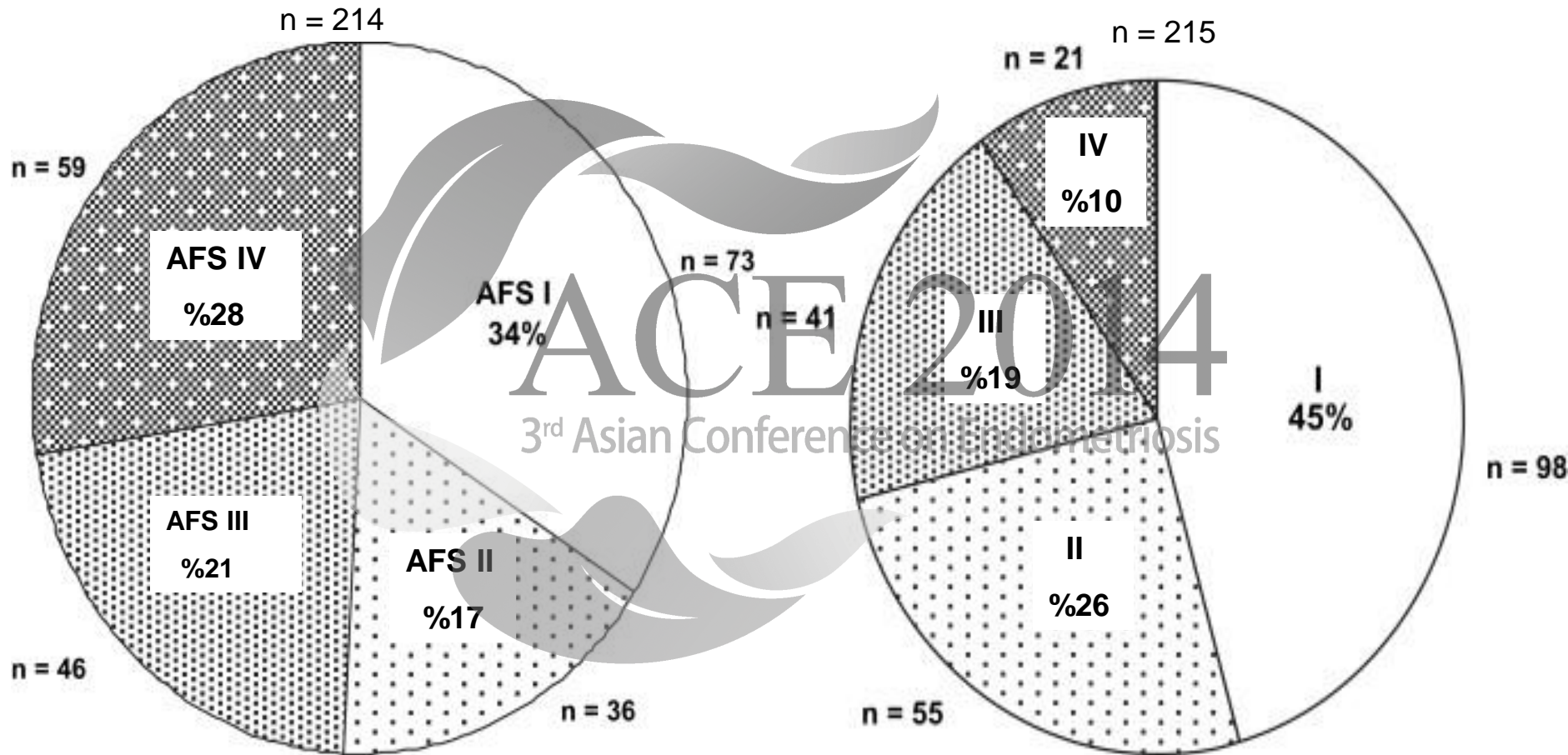
FU – intrinsic Ureteral infiltration



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

⁴Haas D et al. Fertil Steril 2011;95:1574–8

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

Pelvic compartment Level	A rectovaginal space vagina	B sacrouterine ligaments cardinal ligaments, pelvic sidewall external ureter compression	C lower bowel rectum / sigmoid
1 <1cm	A 1 	B 1 	C 1 
2 1-3 cm	A 2 	B 2 	C 2 
3 >3cm	A 3 	B 3 	C 3 

FA
uterine adenomyosis

FB
bladder

FU
intrinsic ureter

FI
intestine
sigma, coecum,
term. ileum

FO
other localisations
Diaphragma,....

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

Past & current classification systems



- *Developed by Adamson & Pasta in 2010⁶*
- *Predicts non-IVF fertility rates after surgery*
- *Uses rASRM as part of scoring system*
- *Validated in three studies up to 2013⁷⁻⁹*

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

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

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

⁹Tomassetti 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 =	Mild 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"/>

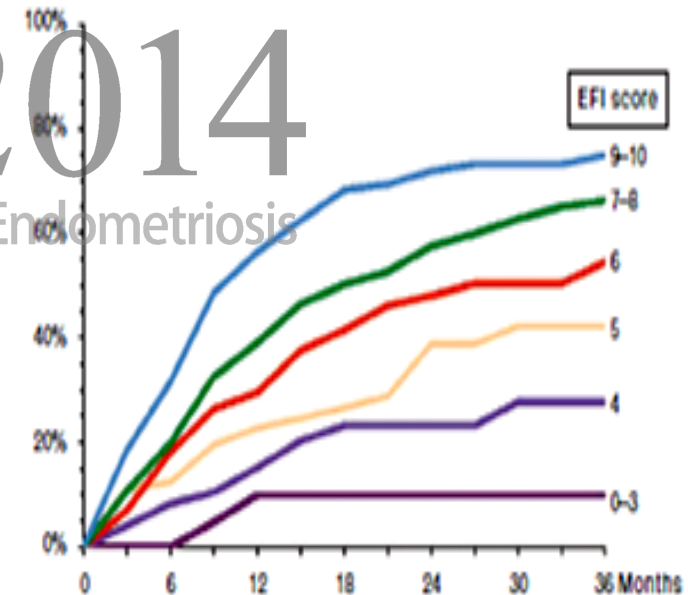
To calculate the LF score, add together the lowest score for the left side and the lowest score for the right side. If an ovary is absent on one side, the LF score is obtained by doubling the lowest score on the side with the ovary.

Lowest Score Left + Lowest Score Right = LF Score

Endometriosis Fertility Index (EFI)

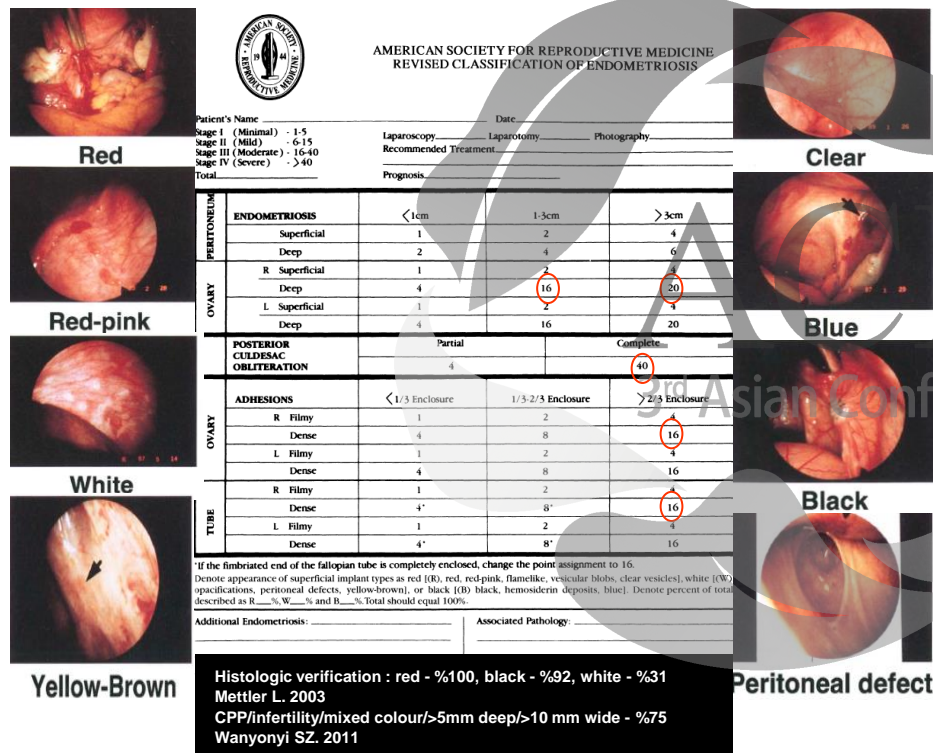
Historical Factors			Surgical Factors		
Factor	Description	Points	Factor	Description	Points
Age	If age is ≤ 35 years	2	LF Score	If LF Score = 7 to 8 (high score)	3
	If age is 36 to 39 years	1		If LF Score = 4 to 6 (moderate score)	2
	If age is ≥ 40 years	0		If LF Score = 1 to 3 (low score)	0
Years Infertile	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:			<div style="display: flex; align-items: center; justify-content: center;"> <div style="border: 1px solid black; width: 60px; height: 30px; margin-right: 5px;"></div> <div>+</div> <div style="border: 1px solid black; width: 60px; height: 30px; margin-right: 5px;"></div> <div>=</div> <div style="border: 1px solid black; width: 60px; height: 30px; margin-left: 5px;"></div> </div> <div style="display: flex; justify-content: space-around; margin-top: 5px;"> Historical Surgical EFI Score </div>		

Estimated percent pregnant by 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 Prognosis: _____
 Stage IV (Severe) - >40
 Total: _____

ENDOMETRIOSIS		<1cm	1-3cm	>3cm
PERITONEUM	Superficial	1	2	4
	Deep	2	4	6
	Total	3	6	10
OVARY	R Superficial	1	2	4
	R Deep	4	16	20
	L Superficial	1	2	4
L. Deep	4	16	20	
	Total	16	32	40
	POSTERIOR CULDESAC OBLITERATION	Partial	4	Complete
ADHESIONS	<1/3 Enclosure		1/3-2/3 Enclosure	>2/3 Enclosure
	R Filmy	1	2	4
	R Dense	4	8	16
	L Filmy	1	2	4
	L Dense	4	8	16
	Total	16	32	40
TUBE	R Filmy	1	2	4
	R Dense	4	8	16
	L Filmy	1	2	4
	L Dense	4	8	16

**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 diagnosis¹
 - Moderately reliable for staging¹
 - 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

¹Schliep KC et al. Obstet Gynecol 2012;120:104–12

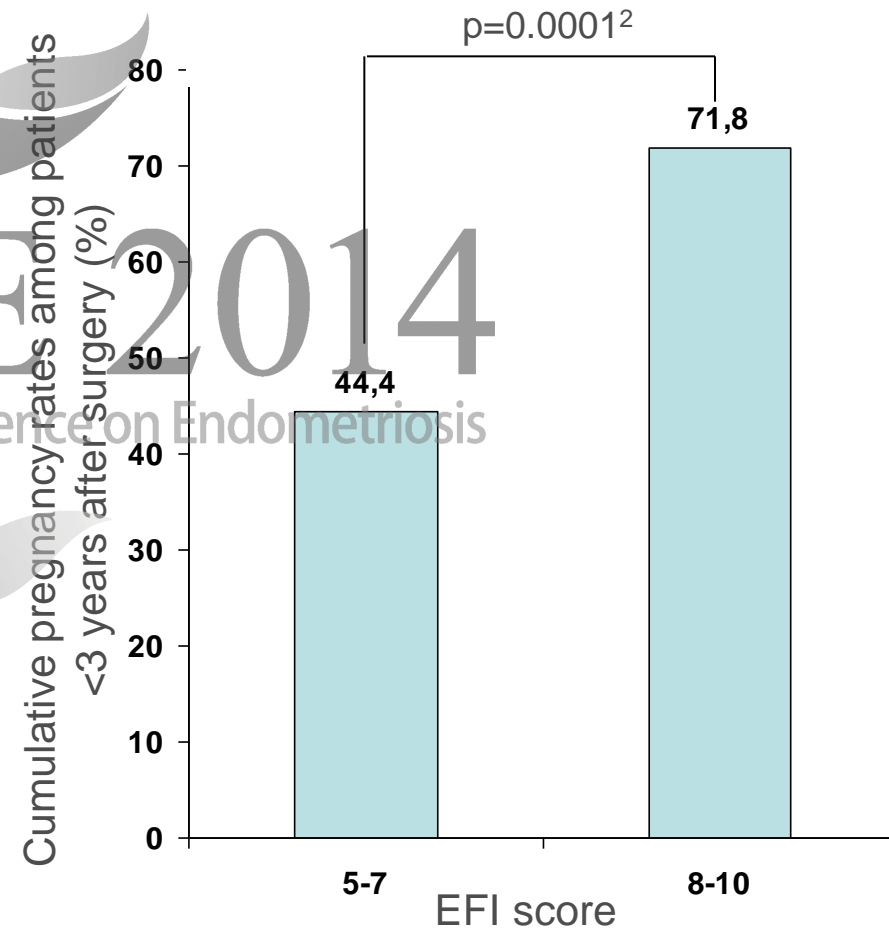
What else do we have?

- **ENZIAN**

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

- **EFI**

- Uses rASRM as part of scoring system
- Fallopian tube and ovarian dysfunction - subjective
- Significant correlation between EFI score & the time to non-ART pregnancy²
- Informs treatment decisions



¹Adamson GD. Curr Opin Obstet Gynecol 2011; 23: 213–220

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

Summary of current systems

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

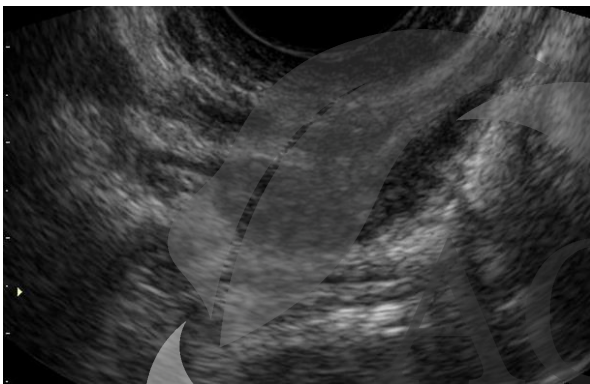
Possible future classification systems



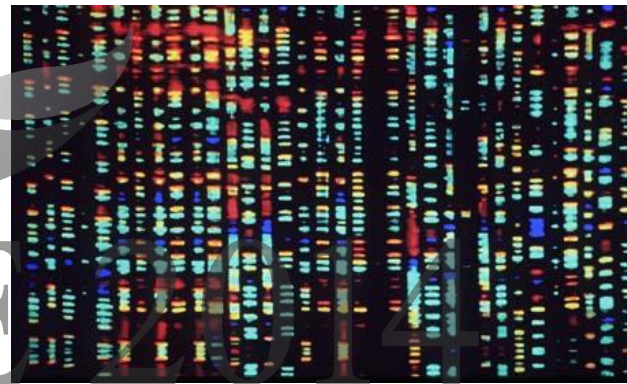
- **AAGL**

- *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 ¹



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 ²
- **AMH serum levels** and an association with severity²
- **Annexin V, VEGF, CA-125 & sICAM-1/or glycodelin** diagnosis in endometriosis undetectable by US with a sensitivity of 81–90% & a specificity of 63–81%^{2 3}

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

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

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

² Shebl O et al. Gynecol Endocrinol 2009; 25:713–716

² Vodolazkaia A et al. Hum Reprod 2012; 27:2698–2711

³ 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.

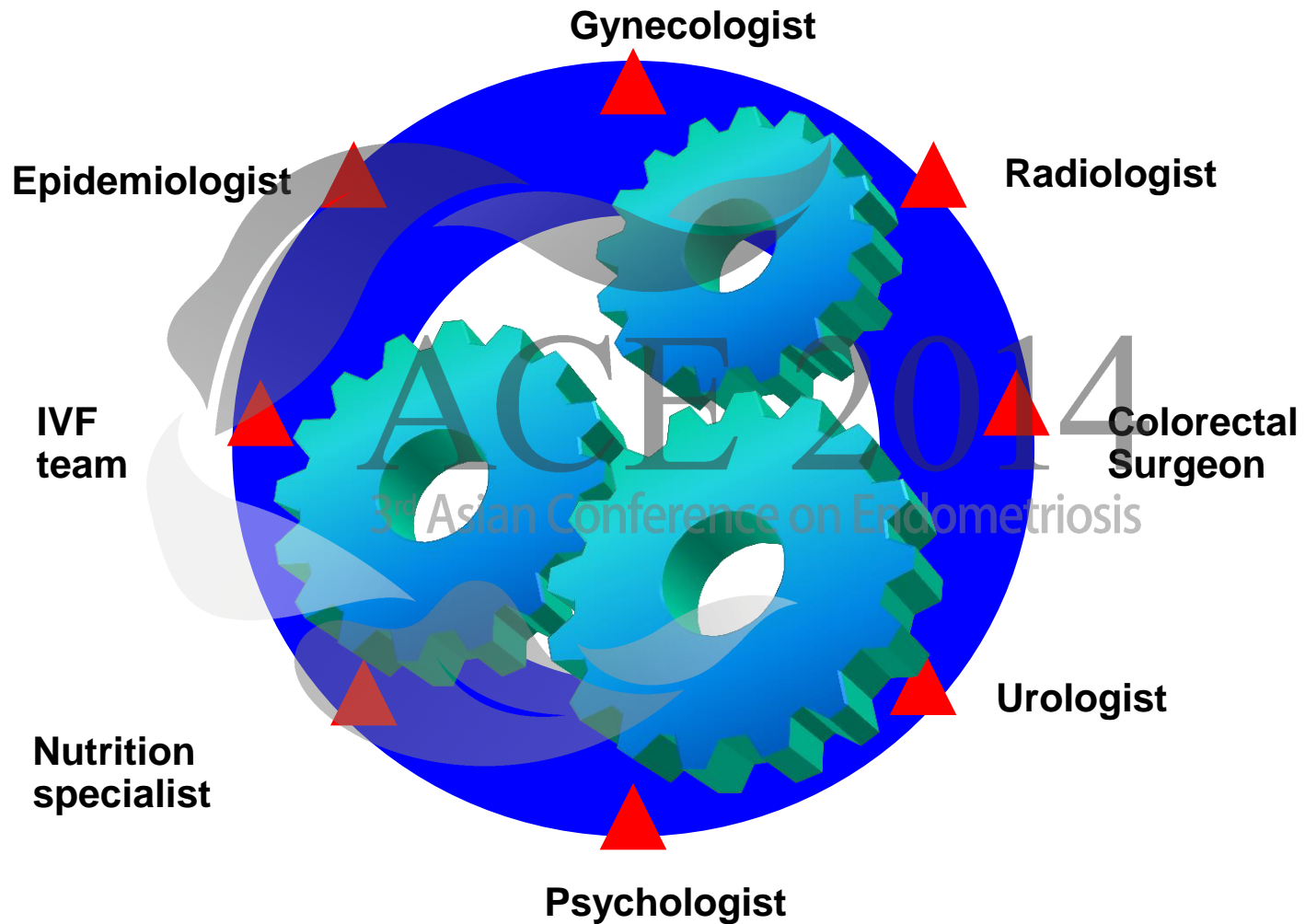
Guidelines for endometriosis management



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