# Adolescent endometriosis


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# Adolescence: Defintions

| | | | |
|---|---|---|---|
| **WHO** | **1980** | **Final report, Manila,<br>WHO Regional Office of Western Pacific** | **12 – 19 years** |
| | | | |
| **Sawyer SM *et al.*,** | **2018** | **Lancet Child Adolesc Health** | **10 – 24 years** |

# Adolescence and endometriosis: US signs

*Unselected consecutive population of adolescents (N = 270)*

| Unselected consucutive population of adolescents | US findings of endometriosis |
| --- | --- |
| N = 270 | 36 patients<br>13.3% |

Martire *et al .*, Fertil Steril (2020)

# Adolescence and endometriosis: US signs

*Unselected consecutive population of adolescents (N = 270)*

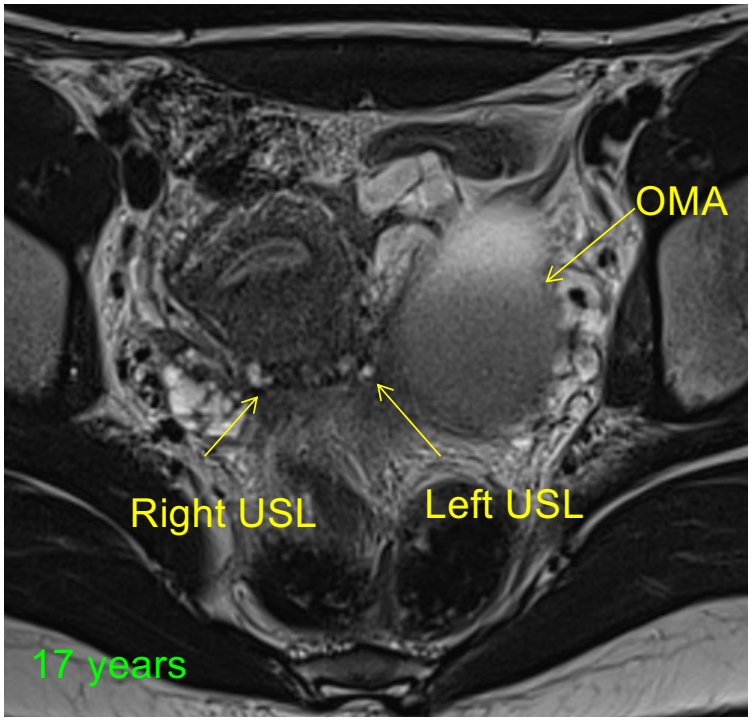
| Symptoms related to endometriosis | Total population (n = 270) | US findings of endometriosis | | |
|---|---|---|---|---|
| | | Present (n = 36) | Absent (n = 234) | *P* value |
| Dysmenorrhea | 147 (54.4) | 31 (86.1) | 116 (49.6) | <.001 |
| Dyspareunia | 24 (8.9) | 8 (22.2) | 16 (6.8) | .007 |
| Dysuria | 12 (4.4) | 3 (8.3) | 9 (3.8) | .205 |
| Dyschezia | 15 (5.5) | 5 (13.9) | 10 (4.3) | .391 |
| Heavy menstrual bleeding | 81 (30.0) | 20 (55.5) | 61 (26.1) | <.001 |
| Functional bowel symptoms | 9 (3.3) | 4 (11.1) | 5 (2.1) | .020 |
| Chronic pelvic pain | 21 (7.8) | 5 (13.9) | 16 (6.8) | .173 |

Martire *et al .*, Fertil Steril (2020)

# Adolescent dysmenorrhea: MRI endometrioisis appearence

*N = 308 patients*

| Adolescent dysmenoorrhea | MRI signs |
|---|---|
| | |
| **Endometriosis:** ***OMA and/or DIE*** | **121 (39.3%)** |

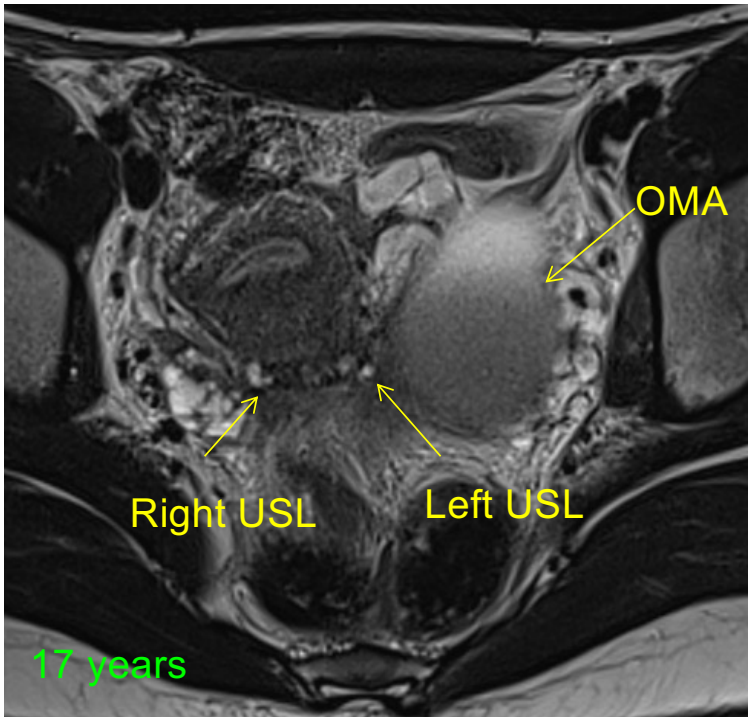



Millischer – Chapron *et al.*, 2021 (in progress)

# Adolescent dysmenorrhea: MRI endometrioisis appearence

*N = 308 patients*

| Adolescent dysmenoorrhea | MRI signs |
|---|---|
| | |
| **Endometriosis:** *OMA and/or DIE* | **121 (39.3%)** |
| | |
| **Adenomyosis** | **41 (13,3%)** |
| | |




Millischer – Chapron *et al.*, 2021 (in progress)

# Adolescent dysmenorrhea: MRI endometrioisis appearence

*N = 121 patients - 39.3%*

| Endometriotic lesions | MRI signs |
|---|---|
| | |
| **OMA** | **25 (20.7%)** |
| | |
| **DIE** | **110 (90.9%)** |
| - Retrocervical *(torus, US ligaments, vagina)** | 106 |
| - Rectosigmoid | 4 |
| - Ureter | 0 |
| - Bladder | 0 |
| | |
| **Associated adenomyosis** | **21 (17.4%)** |

*: 12 patients (11.3% with asociated OMA)

Millischer – Chapron *et al.*, 2021 (in progress)

# Adolescent dysmenorrhea: MRI endometrioisis appearence

*N = 121 patients - 39.3%*

| Endometriotic lesions | MRI signs Total 121 patients | MRI signs < 15 years | MRI signs 15 - 17 years | MRI signs 18- 20 years |
|---|---|---|---|---|
| | | | | |
| OMA | 25 (20.7%) | 1 (4.0%) | 7 (28.0%) | 17 (68.0%) |
| | | | | |
| DIE | 110 (90.9%) | | | |
| - Retrocervical * | 106 (87.6%) | 5 (4.7%) | 32 (30.2%) | 69 (65.1%) |
| - Rectosigmoid | 4 (3.4%) | 0 (0.0%) | 2 (50.0%) | 2 (50.0%) |
| - Ureter | 0 | 0 | 0 | 0 |
| - Bladder | 0 | 0 | 0 | 0 |

*: torus uterinum, US ligamet(s), vagina

Millischer – Chapron *et al.,* 2021 (in progress)

# Adolescent dysmenorrhea: MRI endometrioisis appearence

*N = 121 patients - 39.3%*

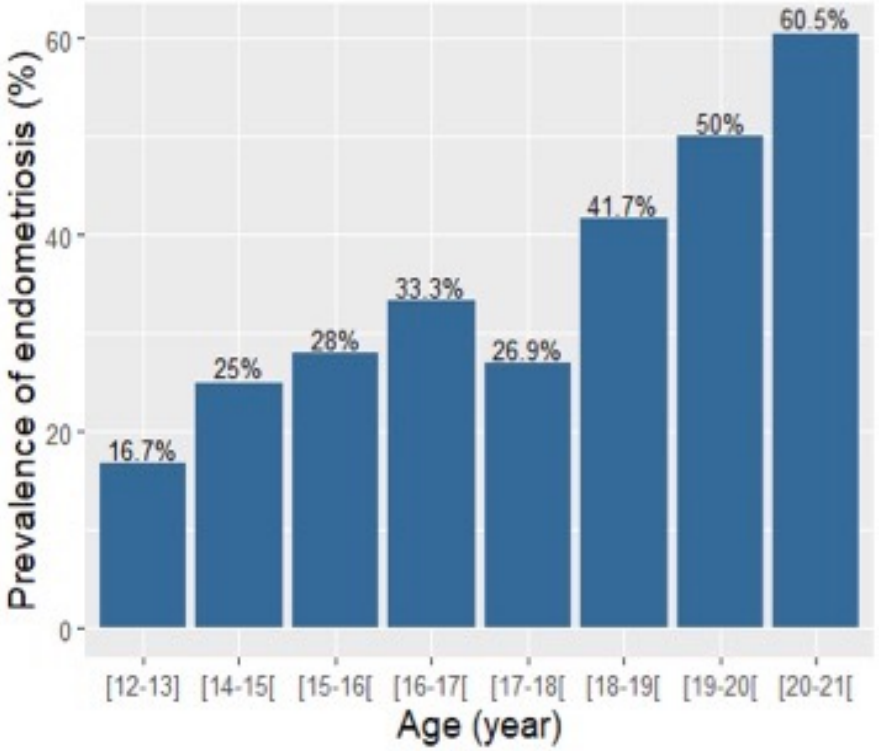
| Endometriotic lesions | MRI signs Total 121 patients | MRI signs < 15 years 6 patients: 5.0% | MRI signs 15 - 17 years 36 patients: 29.7% | MRI signs 18- 20 years 79 patients: 65.3% |
|---|---|---|---|---|
| | | | | |
| OMA | 25 (20.7%) | 1 (16.7%) | 7 (19.4%) | 17 (21.5%) |
| | | | | |
| DIE | 110 (90.9%) | 5 (83.3%) | 34 (94.4%) | 71 (89.9%) |
| - Retrocervical * | 106 (87.6%) | 5 (83.3%) | 32 (88.9%) | 69 (87.3%) |
| - Rectosigmoid | 4 (3.4%) | 0 (0.0%) | 2 (5.5%) | 2 (2.5%) |
| - Ureter | 0 | 0 | 0 | 0 |
| - Bladder | 0 | 0 | 0 | 0 |

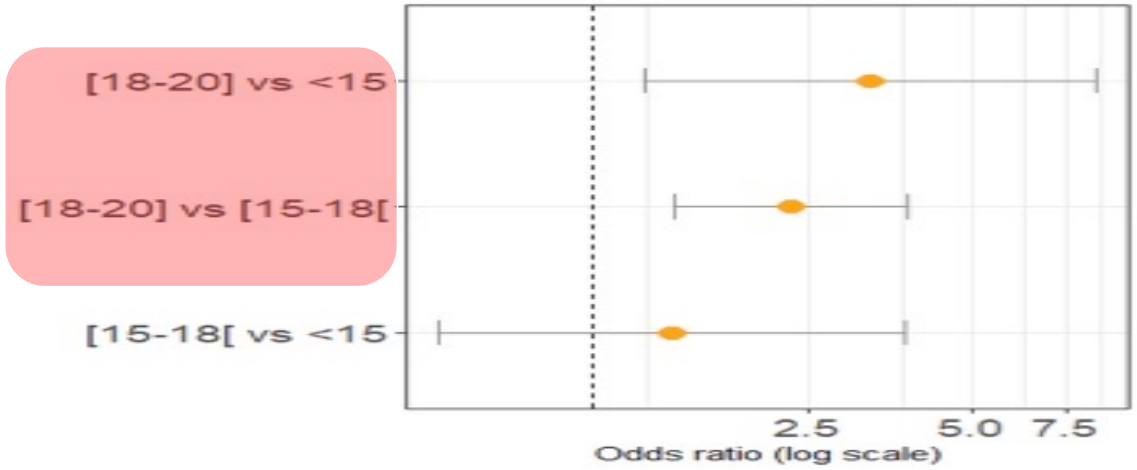
*: torus uterinum, US ligamet(s), vagina

Millischer – Chapron *et al.*, 2021 (in progress)

# Adolescent dysmenorrhea: MRI endometrioisis appearence

*N = 308 patients*



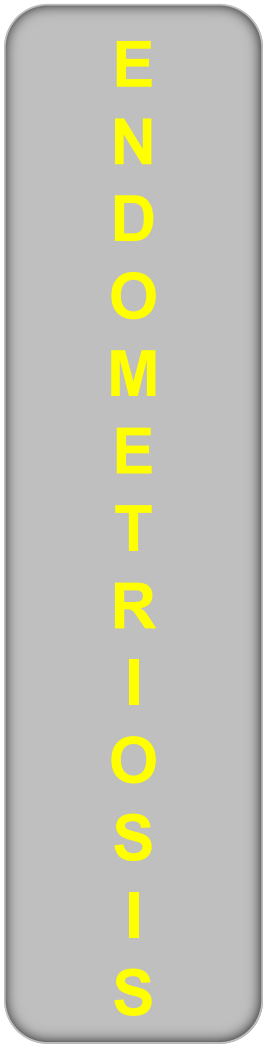




Odds ratio and confidence intervals for each pairwise comparison between age groups - Population without superficial endometriosis (alone or combined with± adenomyosis). N= 308.

| Age (year) | N1 | N2 | Odds ratio [95% CI] | p-value |
|---|---|---|---|---|
| [15-18[ vs <15 | 122 | 26 | 1.4 [0.5-3.8] | 0.51 |
| [18-20] vs [15-18[ | 160 | 122 | 2.3 [1.4-3.8] | < 0.01 |
| [18-20] vs <15 | 160 | 26 | 3.3 [1.2-8.5] | 0.02 |

Millischer – Chapron *et al.,* 2021 (in progress)

# Rethinking endometriosis diagnosis




→ **Diagnosis**

What is the difficulty ? Pain is THE cardinal symptom

What is the challenge for the gynecologist ?

To determine when the pain is caused by endometriosis
and not due to other gynecologic conditions
or chronic pain syndromes

# Endometriosis diagnosis: Questionning

## Family history *(1st degree relatives)*

| Authors (year) | Country | n | Sisters (%) | Mothers (%) | Mothers or sisters (%) | Controls (%) |
|---|---|---|---|---|---|---|
| Simpson *et al.* (1980) | USA | 123 | 5.8 | 8.1 | 6.9 | 1.0 |
| Lamb *et al.* (1986) | USA | 43 | 3.8[a] | 6.2[a] | 4.9[a] | 1.9[a] |
| Moen and Magnus (1993) | Norway | 515 | 4.8 | 3.9 | 4.3 (OR: 7.2) | 0.7 |
| Coxhead and Thomas (1993) | UK | 64 | — | — | 9.4 | 1.6 |
| Kennedy *et al.* (1998) | UK | 29 | — | — | 14.3 | — |
| dos Reis *et al.* (1999) | Brazil | 81 | — | — | 8.6 | 0 |
| Stefansson *et al.* (2002) | Iceland | 750 | (RR: 5.2) | — | — | — |
| Kashima *et al.* (2004) | Japan | 339 | 8.8 (RR: 5.7) | — | — | 1.5 |
| Matalliotakis *et al.* (2008) | USA | 485 | 5.6[b] | 3.9[b] | 9.5[b] (OR: 10.2)[b] | 1.0[b] |

Adaptated from Dalsgaard *et al.*, Hum Reprod (2013)

| Endometriosis mother exposure | Daughters N (%) | Osis N (%) | Rate ratio (95% CI) |
|---|---|---|---|
| | | | |
| YES *(n = 24 691)* | 12 389 | 455 (3.7) | |
| | | | 2.12 (1.89-2.37) |
| NO *(n = 98 764)* | 52 371 | 908 (1.7) | |

Dalsgaard *et al.*, Hum Reprod (2013)

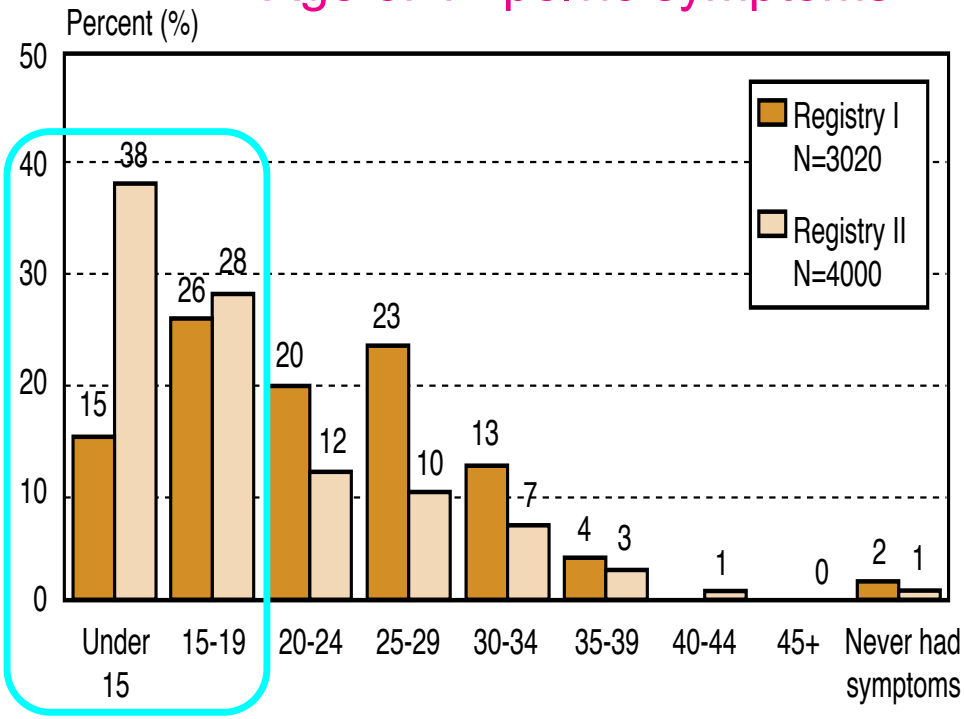
# Endometriosis: Questioning

| Onset of symptoms | |
|---|---|
| | |
| Adolescents | 67.1% |
| | |
| Adults | 39.2% |

| Onset of symptoms | Time from seeking medical attention to diagnosis |
|---|---|
| | |
| Adolescents | 6.0 ± 0.2 years |
| | |
| Adults | 2.0 ± 0.3 years |

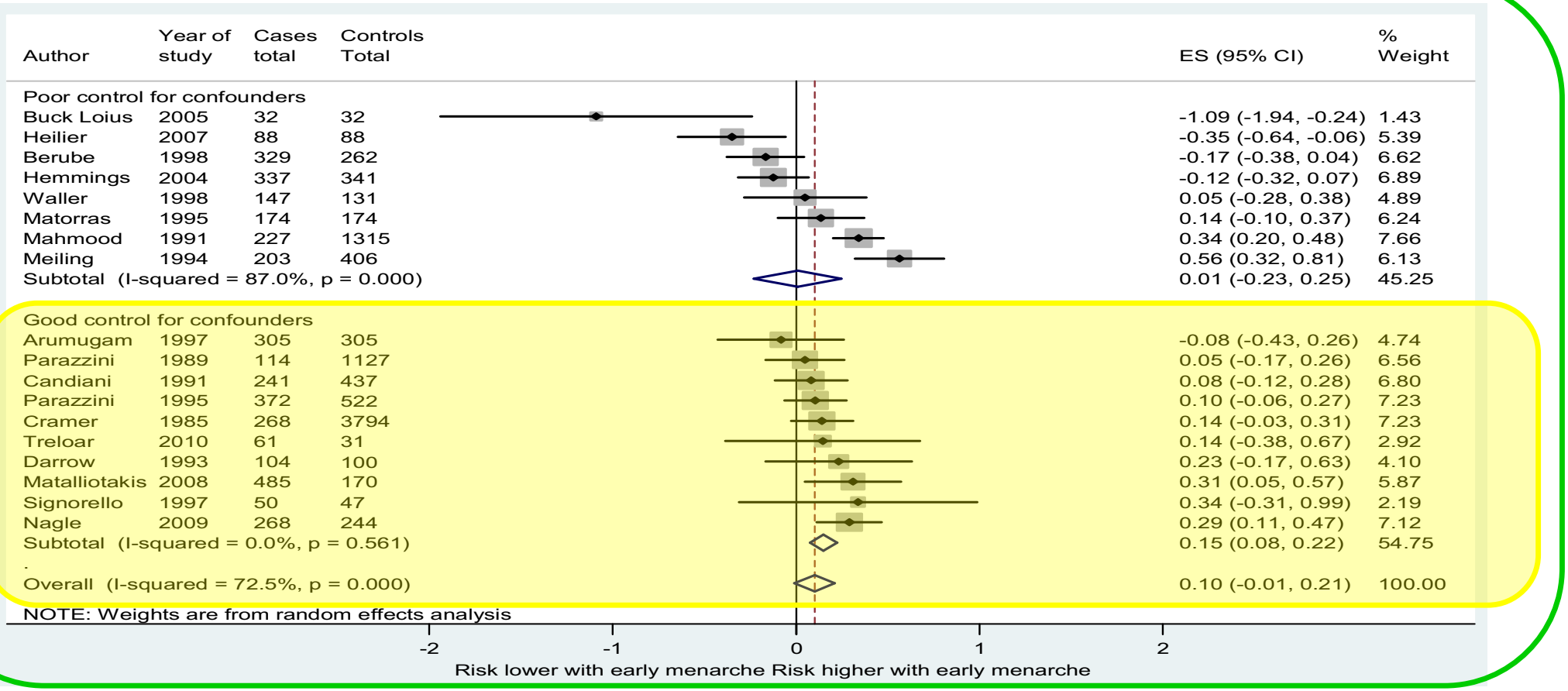
Greene *et al.*, Fertil Steril (2009)

Age of 1st pelvic symptoms




Ballweg ML (2004)

# Endometriosis: Age at menarche




Nnoaham *et al.*, Hum Reprod (2012)

# Early menstrual characteristics and subsequent endometriosis diagnosis

| Dysmenorrhea | Cases *N (%)* | Controls *N (%)* | | |
|---|---|---|---|---|
| Never/seldom | 35 (30) | 54 (48) | 1.0 | |
| Sometimes | 20 (16) | 19 (17) | 1.7 (0.6–5.1) | |
| Often | 65 (54) | 39 (35) | 2.6 (1.1–6.2) | .03 |

Treolar *et al.,* AJOG (2010)

# Menstrual disorder of teenagers

| Symptom<br>Top ten symptoms reported | Frequency | Number of respondents | % (95% CI) |
|---|---|---|---|
| Feeling really tired | 791 | 1019 | 78 (75–80) |
| Pelvic pain – cramping | 701 | 986 | 71 (68–74) |
| Feeling down or depressed | 654 | 1011 | 65 (62–68) |
| Headaches | 641 | 1004 | 64 (61–67) |
| Bloating | 618 | 1003 | 62 (59–65) |
| Pelvic pain – aching | 604 | 976 | 62 (59–65) |
| Changes in appetite | 607 | 1005 | 60 (57–63) |
| Lower back pain | 580 | 1002 | 58 (55–61) |
| Pelvic pain – stabbing | 370 | 917 | 40 (37–44) |
| Nausea | 372 | 1002 | 37 (34–40) |

93% of adolescents reported pain with menstruation

Parker *et al.*, BJOG (2010)

Interferences of menstruation with life activities

| Activity | Number of respondents | N/A | High interference* | Low interference** |
|---|---|---|---|---|
| Sexual activity | 1020 | 358 | 255 (38.5) | 407 (61.5) |
| Sport and exercise | 1030 | 37 | 336 (33.8) | 657 (66.2) |
| Social activities | 1027 | 23 | 262 (26.1) | 742 (73.9) |
| Relationship with family | 1031 | 31 | 237 (23.7) | 763 (76.3) |
| Relationship with partner | 1020 | 153 | 151 (19.7) | 616 (80.3) |
| Completing school work | 1031 | 32 | 158 (15.8) | 841 (84.2) |
| Relationship with friends | 1032 | 32 | 153 (15.3) | 847 (84.7) |
| Casual paid work | 1025 | 167 | 117 (13.6) | 741 (86.4) |
| Attending school | 1035 | 27 | 120 (11.9) | 888 (88.1) |

# DIE: Importance of questioning

| Parameters | No DIE *(n = 131)* | DIE *(n = 98)* | p | OR 95% CI |
|---|---|---|---|---|
| | | | | |
| Absenteism from school during menstruation | 33 (25.2%) | 37 (37.7%) | 0.04 | 1.7 (1 - 3) |

Chapron *et al.*, Fertil Steril (2011)

# Adolescents with pain not responding to conventional therapy:

## Endometriosis prevalence

| Author | Year | N Adolescents | N patients with endometriosis | Rate (%) |
|---|---|---|---|---|
| | | | | |
| Reese | 1996 | 67 | 49 | 73.1 |
| Laufer | 1997 | 46 | 32 | 69.6 |
| Opoku-Anane | 2012 | 117 | 115 | 98.3 |
| | | | | |
| Total | | 230 | 196 | 82.2 |

# DIE: Importance of questioning

| Parameters | No DIE *(n = 131)* | DIE *(n = 98)* | p | OR 95% CI |
|---|---|---|---|---|
| | | | | |
| Prescription of OCPs because of severe 1st DM | 15 (25.9%) | 29 (58.0%) | 0.001 | 4.5 (1.9 - 10.4) |
| Age *(years)* | 18.1 ± 3.2 | 16.5 ± 2.4 | | 0.07 |
| Duration of use *(years)* | 5.1 ± 3.8 | 8.4 ± 4.2 | | 0.02 |

Chapron *et al.*, Fertil Steril (2011)

# Adolescents with pain not responding to conventional therapy:

## Nature of pain in cases of endometriosis

| Nature of pain | N | Rate (%) |
|---|---|---|
| | | |
| Cyclic only | 58/115 | 50.4 |
| Acyclic only | 12/115 | 10.4 |
| Both cyclic and acyclic | 45/115 | 39.1 |
| Gastrointestinal | 18/115 | 15.7 |
| Urinary | 3/115 | 2.6 |

Opoku-Anane and Laufer, J Pediatr Adolesc Gynecol (2012)

# Menstrual disorder of teenagers:

## Possible underlying endometriosis: Atypical symptoms

| Symptom | Frequency | Number of respondents | % (95% CI) |
|---|---|---|---|
| Pain when emptying bowels | 116 | 996 | 12 (10–14) |
| Pain before or when passing wind | 93 | 999 | 9 (8–11) |
| Pain with full bladder | 190 | 992 | 19 (17–22) |
| Pain during or after passing urine | 95 | 993 | 10 (8–11) |
| Pain during or after sexual intercourse | 133 | 1007 | 13 (11–15) |

Parker *et al.*, BJOG (2010)

# Endometriosis symptoms in women diagnosed during adolescence vs adulthood

| Did you experience nausea with your pain? n (%) | Adolescents at diagnosis (*n* = 295) | Adults at diagnosis (*n* = 107) | |
|---|---|---|---|
| No | 57 (30.5) | 40 (48.8) | .004 |
| Yes | 130 (69.5) | 42 (51.2) | |

DiVasta *et al.*, AJOG (2018)

# *Adolescent endometriosis: Associated comorbidities*

| | |
|---|---|
| **Autoimmune inflammatory diseases** | **Systemic lupus erythematosus** |
| | **Multiple sclerosis, Rheumatoid arthritis** |
| | **Sjogren's syndrome** |
| **Chronic pain conditions** | **Migraines, Fibromyalgia** |
| | **Interstitial cystitis** |
| | **Chronique fatigue syndrome** |
| | **Irritable bowel syndrome** |
| **Endocrine diseases** | **Hypothyroidism** |
| **Respiratory conditions** | **Allergies, Asthma** |
| **Psychosocial disorders** | **Depression, Anxiety, Sexual abuse** |

Adaptated from Youngster *et al.,* Curr Opin Pediatr (2013)

# Migraines in adolescents with endometriosis

| Endometriosis | With migraines | Without migraines | Ad OR (95% CI) |
|---|---|---|---|
| | | | |
| No | 30 (12.8%) | 65 (41.7%) | 1.00 (Ref) |
| Yes | 205 (87.2%) | 91 (58.3%) | 4.77 (2.53 – 9.02 |

| Migraine pain severity score | With endometriosis | Without endometriosis | Ad OR (95% CI) |
|---|---|---|---|
| | | | |
| 0 - 3 | 34 (16.8%) | 10 (33.3%) | 1.00 (Ref) |
| 4 - 6 | 67 (33.0%) | 9 (30.0%) | 3.03 (0.88 - 10.4) |
| 7 - 10 | 102 (50.3%) | 11 (36.7%) | 3.35 (1.04 - 10.8) |
| | | | |
| Mean score | 6.2 ± 2.6 | 4.9 ± 3.0 | 1.22 (1.03 - 1.44) |

Miller *et al.*, *Fertil Steril* (2018)

# Endometriosis diagnosis: Questionning

## In utero or early childhood exposure

Prematurity
Neonatal uterine bleeding
Low birth weight
Formula-fed infant
Early life body size
Maltreatment

| Visible NUB | Newborns N | Bleeding N | Incidence (%) |
|---|---|---|---|
| | | | |
| Rosa *(1955)* | 976 | 29 | 3.0 |
| Lévy *(1964)* | 1207 | 57 | 4.7 |
| Kaiser *(1974)* | 153 | 8 | 5.2 |
| Huber *(1976)* | 350 | 12 | 3.4 |
| Berić (1985) | 2477 | 96 | 3.9 |

**Neonatal uterine bleeding as antecedent of pelvic endometriosis**

Hum Reprod (2013)

Ivo Brosens[1,*], Jan Brosens[2], and Giuseppe Benagiano[3]

| | | Endometriosis (N = 98) | p - value |
|---|---|---|---|
| Birth weight (mean) | 3251 | 3119 | 0.002 |

Multivariate analysis :

- < 2500 g : Increased risk of Osis — OR = 1.8 (1.1 - 2.9) p = 0.02
- < 1500 g: Increased risk of DIE

Borghese - Chapron *et al.*, PlusOne (2015)

| Variable | Multivariate analysis |
|---|---|
| | |
| Prematurity | 4.55 (2.05 - 10.1) |
| | |
| Formula – fed infant | 1.98 (1.12 - 3.52) |

Vannuccini *et al.*, Fertil Steril (2016)

# Endometriosis diagnosis: Questionning

## In utero or early childhood exposure

Prematurity
Neonatal uterine bleeding
Low birth weight
Formula-fed infant
Early life body size
Maltreatment

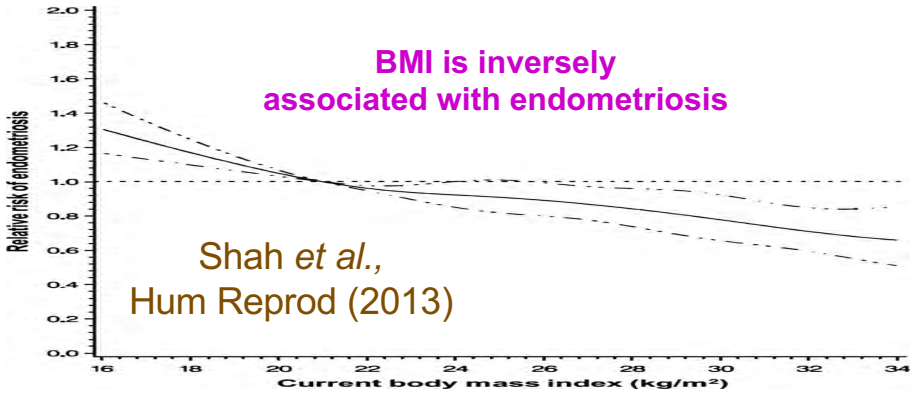
| Adverse childhood experiences | Women with endometriosis *(421 patients; N, %)* | Control women *(421 patients; N, %)* | P-value |
|---|---|---|---|
| Sexual abuse | 82 (19%) | 59 (14%) | 0.0338 |
| Emotional abuse | 185 (44%) | 116 (28%) | 0.0000 |
| Emotional neglect | 211 (50%) | 174 (41%) | 0.0104 |
| Inconsistency | 223 (53%) | 174 (41%) | 0.0007 |
| Mean number | 1.97 ± 0.08 | 1.51 ± 0.07 | 0.0000 |

| Adverse childhood experiences | Odds ratio | 95% CI | P-value |
|---|---|---|---|
| | | | |
| Sexual abuse | 1.1 | 1.00 - 2.71 | 0.0498 |
| Emotional abuse | 1.2 | 1.10 - 1.27 | 0.0000 |
| Emotional neglect | 1.1 | 1.01 - 1.17 | 0.0175 |
| Emotional abuse/neglect | 1.1 | 1.04 - 119 | 0.0030 |
| Sexual + emotional abuse | 1.2 | 1.07 - 1.12 | 0.0001 |
| No of abuse/neglect experiences | 1.1 | 1.02 - 1.06 | 0.0001 |
| Inconsistency in family origin | 1.1 | 1.04 - 119 | 0.0016 |

Liebermann *et al.*, Hum Reprod (2018)

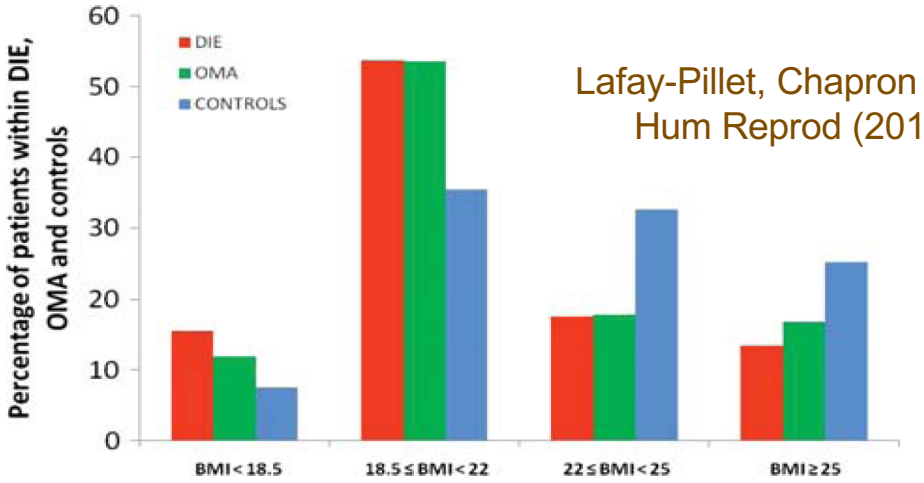
# Endometriosis diagnosis: Questionning

## Phenotype

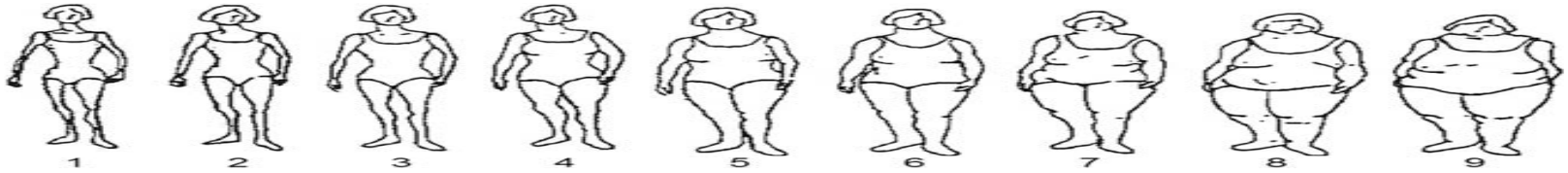



**BMI is inversely associated with endometriosis**

Shah *et al.*,
Hum Reprod (2013)




Lafay-Pillet, Chapron *et al.*,
Hum Reprod (2012)



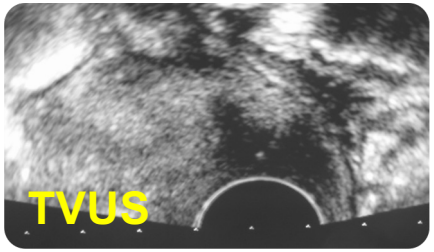

Vitonis *et al.*,
Hum Reprod (2010)

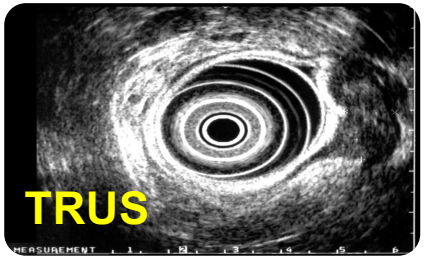
| | | | | | |
|---|---|---|---|---|---|
| Change from ages 10–20 years | | | | | |
| Decreased | 312 | 146 908 | 1.07 | 1.05 (0.91, 1.20) | 1.17 (1.00, 1.37) |
| No change | 556 | 280 438 | 1.00 | 1.00 | 1.00 |
| Increased 1 level | 697 | 310 055 | 1.10 | 1.12 (1.00, 1.25) | 1.05 (0.94, 1.18) |
| Increased 2 or more levels | 252 | 94 508 | 1.29 | 1.22 (1.05, 1.42) | 1.13 (0.96, 1.32) |
| Change from ages 5–20 years | | | | | |
| Decreased | 228 | 107 618 | 1.09 | 1.07 (0.91, 1.25) | 1.21 (1.02, 1.43) |
| No change | 492 | 255 098 | 1.00 | 1.00 | 1.00 |
| Increased 1 level | 690 | 306 368 | 1.14 | 1.14 (1.02, 1.28) | 1.07 (0.94, 1.21) |
| Increased 2 or more levels | 407 | 162 826 | 1.25 | 1.19 (1.04, 1.36) | 1.06 (0.92, 1.23) |

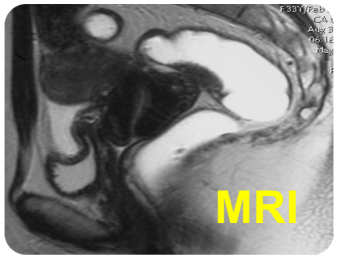
# Endometriosis: How optimize the diagnosis?

## Questionning

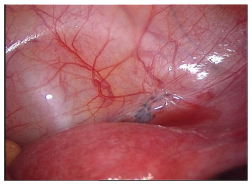
## Imaging



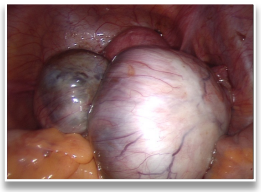




Endometriosis diagnosis

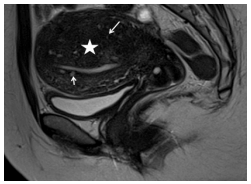


SUP



OMA

DIE



AdOsis

Endometriosis phenotypes

Chapron *et al.*, Nat Rev Endocrinol (2019)

# Take home messages

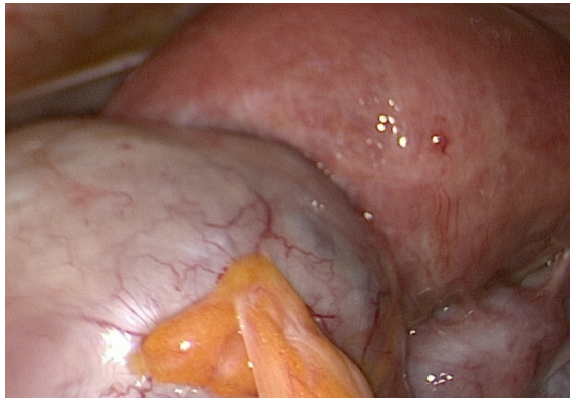


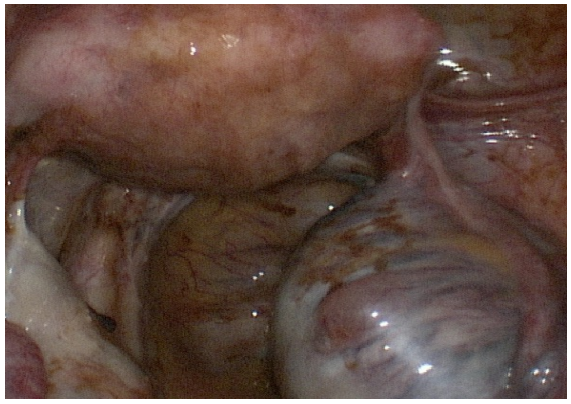
# Adolescent endometriosis

- Not so rare

# Adolescent endometriosis
# Prevalence of endometriomas

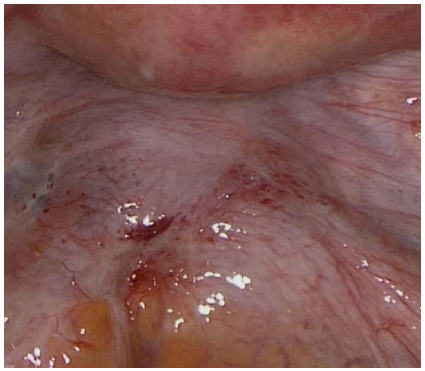
| Author | Year | N | Age | N of OMAs | Rate (%) |
|---|---|---|---|---|---|
| | | | | | |
| Audebert | 2000 | 40 | 13 - 19 | 8 | 20 |
| | | | | | |
| Tandoi | 2011 | 57 | ≤ 21 | 43 | 75 |
| | | | | | |
| Audebert | 2015 | 55 | 12 - 19 | 19 | 34 |

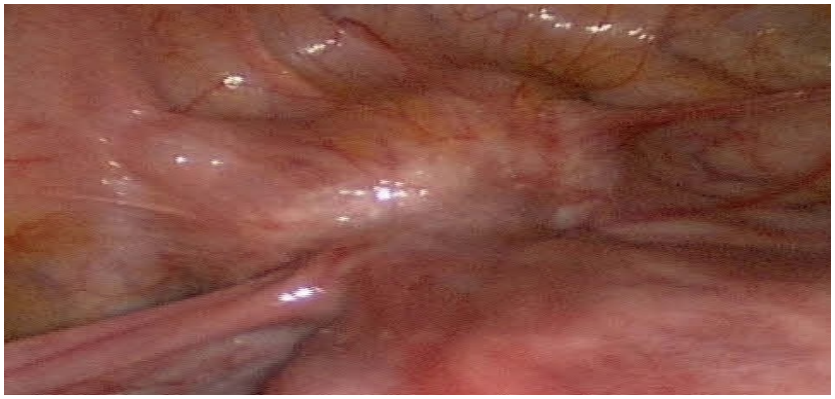




# Adolescent endometriosis
# Prevalence of deep endometriosis

| Author | Year | N | N of DIE | Rate (%) |
|---|---|---|---|---|
| | | | | |
| Tandoi | 2011 | 57 | 11 | 19 |
| | | | | |
| Audebert | 2015 | 55 | 6 | 11 |





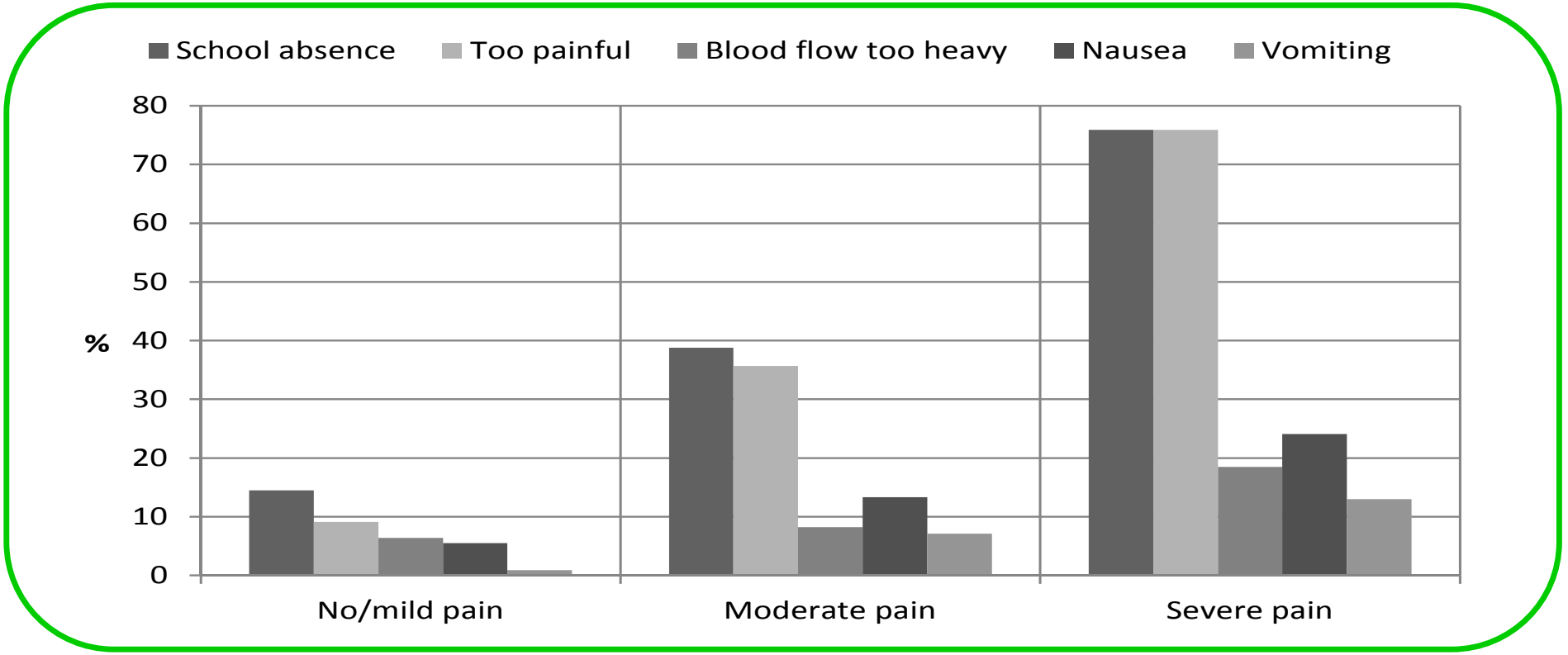
# Adolescent endometriosis

- Not so rare

- Early detection:

  + Shorten the time to diagnosis
  + Prevent enormous impact on adolescent's QOL

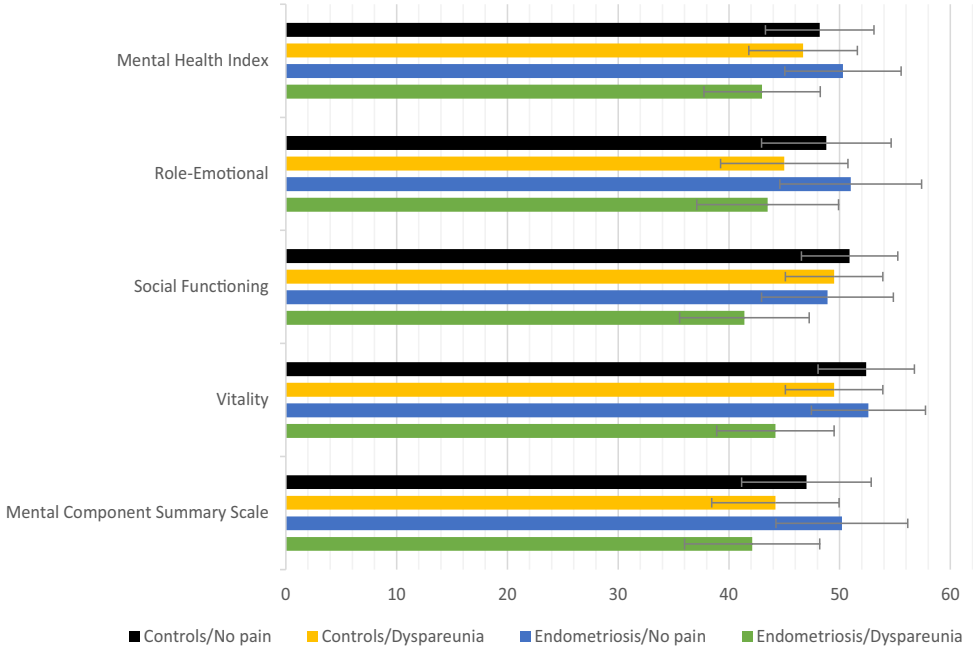
# DM: Impact on QOL among adolescents



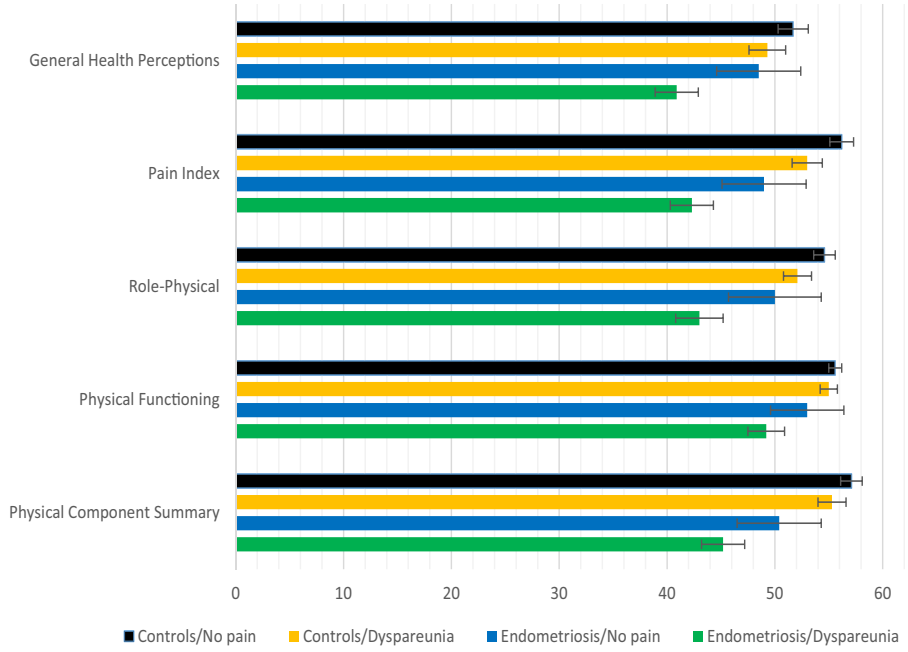

Al-Jefout *et al.,* J Pediatr Adolesc Gynecol (2015)

# QOL in adolescents and YAW with DP and endometriosis

## Short Form-36 (SF-36) QOL survey




SF-36 MENTAL component scores




SF-36 PHYSICAL component scores

Schneider *et al.*, J Pediatr Adolesc Health (2020)

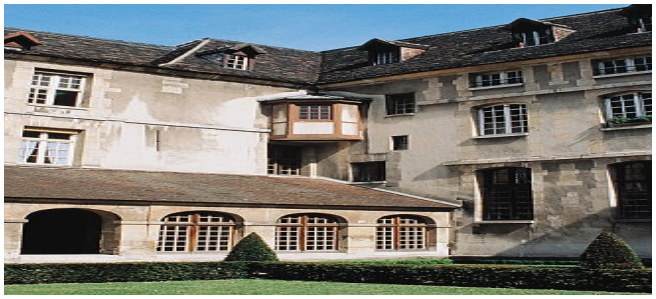
# Adolescent endometriosis

- Not so rare

- Early detection:

  + Shorten the time to diagnosis
  + Prevent enormous impact on adolescent's QOL

+ Referral center for endometriosis: Specific consultations for adolescents
  + Communicating endometriosis with young women: *school, internet, magazines*
  + Development of new specific questionnaire for adolescents
  + Teaching programs: gynecologists, GP, pediatricians, school nurses, pharmacists



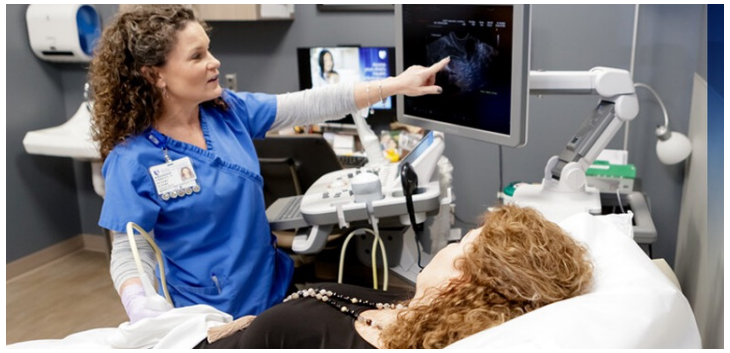
# Take home messages

## Endometriosis / Adenomyosis diagnosis

### Strong collaboration


Gynecologists

***and***



Radiologists

Chapron *et al.,* Nat Rev Endocrinol (2019)

# Repeat laparoscopy in treated adolescent endometriosis

| Author *(year)* | N | Age | Design | Follow-up | % |
|---|---|---|---|---|---|
| | | | | | |
| Roman *(2010)* | 20 | ≤ 20 | Prospect | 2.6 years | 10 |
| | | | | | |
| Yeung *(2011)* | 17 | < 20 | Prospect | 23.1 months | 47.1 |
| | | | | | |
| Tandoi *(2011)* | 57 | ≤ 21 | Retro | 5 years | 19.3 |
| | | | | | |
| Audebert *(2015)* | 55 | < 20 | Retro | 97.5 months | 32.1 |

Recurrence rate: 38/149 = 25.5% - Mean Follow-up: 52,95 months; 4.41 years

# Endometriosis: Causes for recurrence

## Incomplete removal of endometriotic lesions

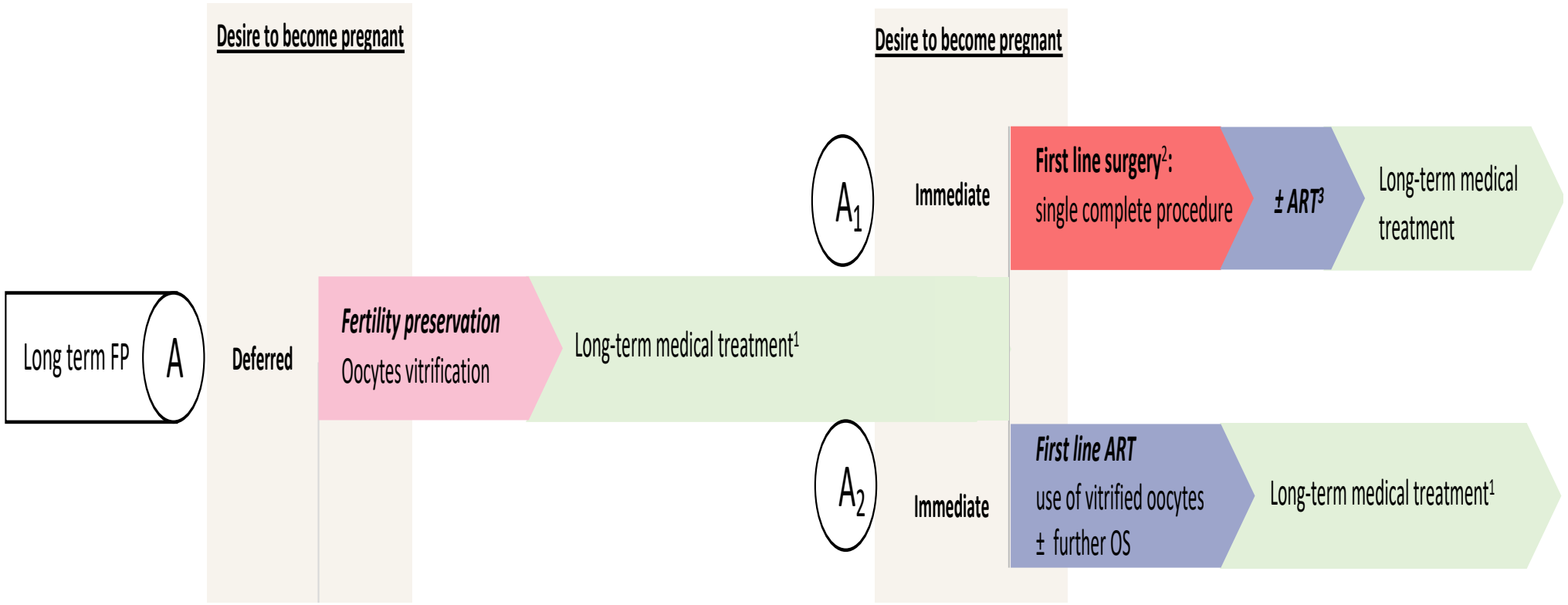
| Age *(year)* | 36-months rate of recurrence (%) *(reoperation or medical treatment)* | p-value |
|---|---|---|
| | | |
| < 25 | 54 | 0.007 |
| 26 - 30 | 23 | |
| 31 - 35 | 13 | |
| > 35 | 0 | |

Importance of patients's age
as the major risk factor for recurrence

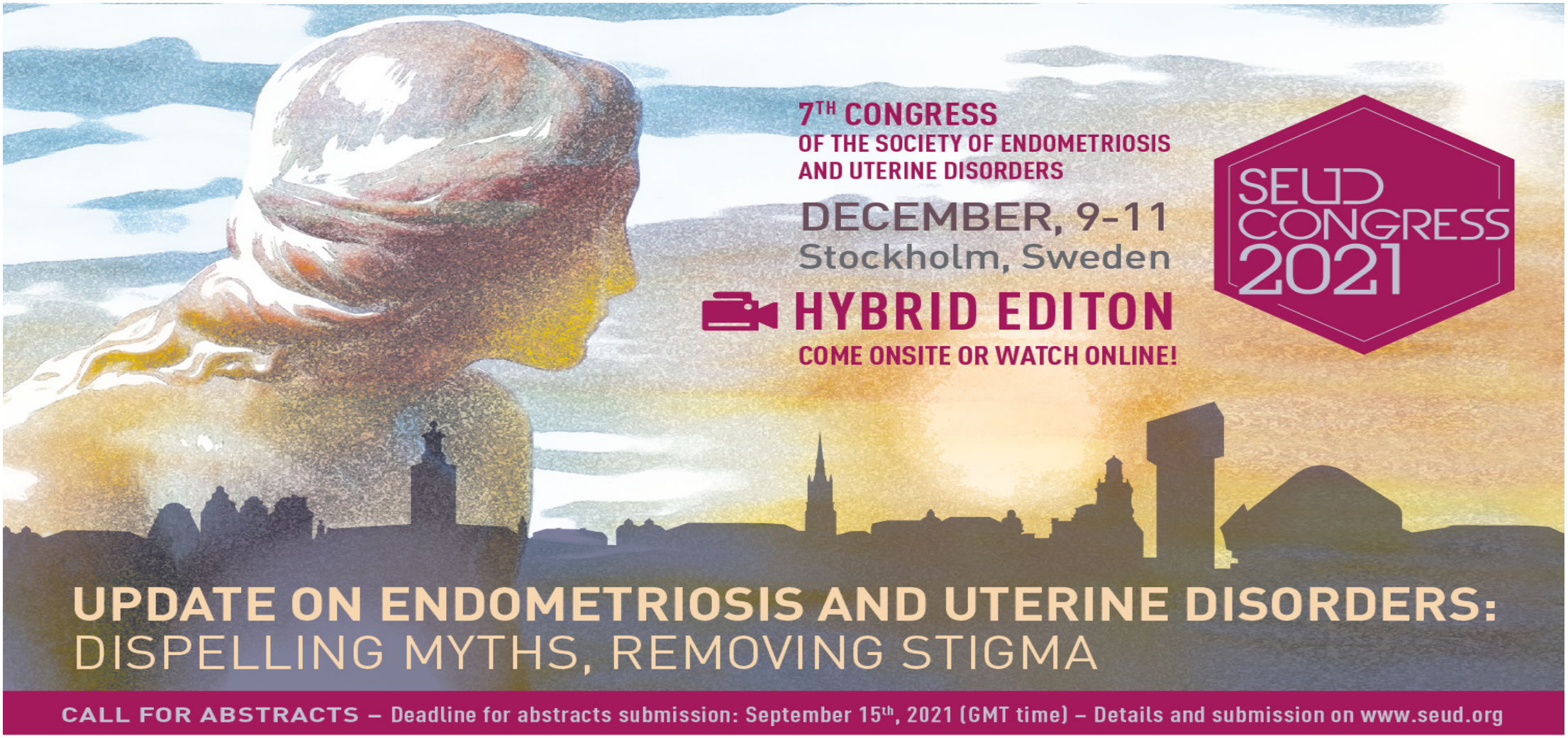
Fedele *et al.*, Am J Obstet Gynecol (2004)

# Rethinking endometriosis management

## Place of fertility preservation




Santulli, Bourdon, Chapron *et al.,* RBM Online (in press)




**CALL FOR ABSTRACTS – Deadline for abstracts submission: September 15th, 2021 (GMT time) – Details and submission on www.seud.org**

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