‘The Endometriosis Enigma’

Miss Jessica Preshaw, Consultant Gynaecologist

NHS
North Bristol
NHS Trust

An enigmna……

‘a person, thing, or situation that is mysterious and difficult to understand’

Persistent (Chronic) Pelvic Pain

Pain in the lower abdomen, constant or intermittent, occurring for at least 6 months

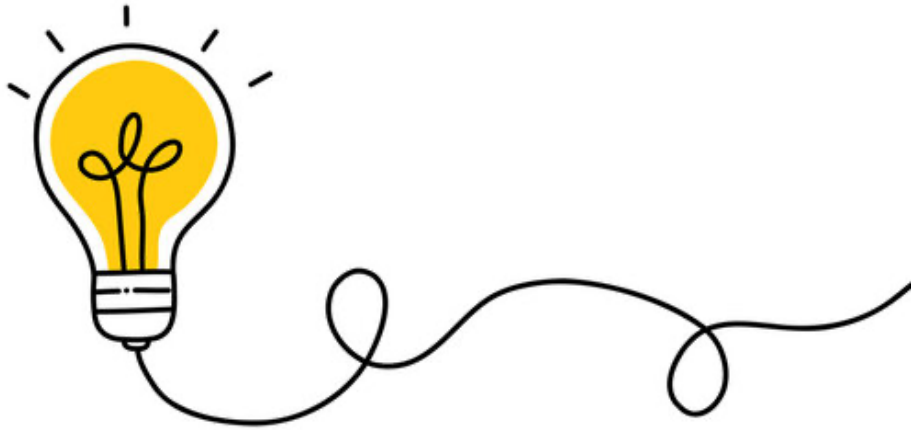
Endometriosis

Hormone mediated condition with ectopic endometrial like tissue forming lesions outside the uterus

Pain = information ≠ pathology

often mixed picture

Nociceptive	Neuropathic	Nociplastic
• Activation of peripheral nociceptors by actual tissue damage or potentially damaging stimuli	• Damage to the nervous system	• Pain from altered nociception, without evidence of actual or threatened tissue damage • Widespread or regional pain syndrome



Persistent Pelvic Pain

30% no cause found

Endometriosis/ Adenomyosis

Pelvic Inflammatory Disease

Interstitial Cystitis

Adhesions

Pelvic Organ Prolapse

Irritable Bowel Syndrome

Nerve entrapment incl. pudendal neuralgia

Musculoskeletal pain

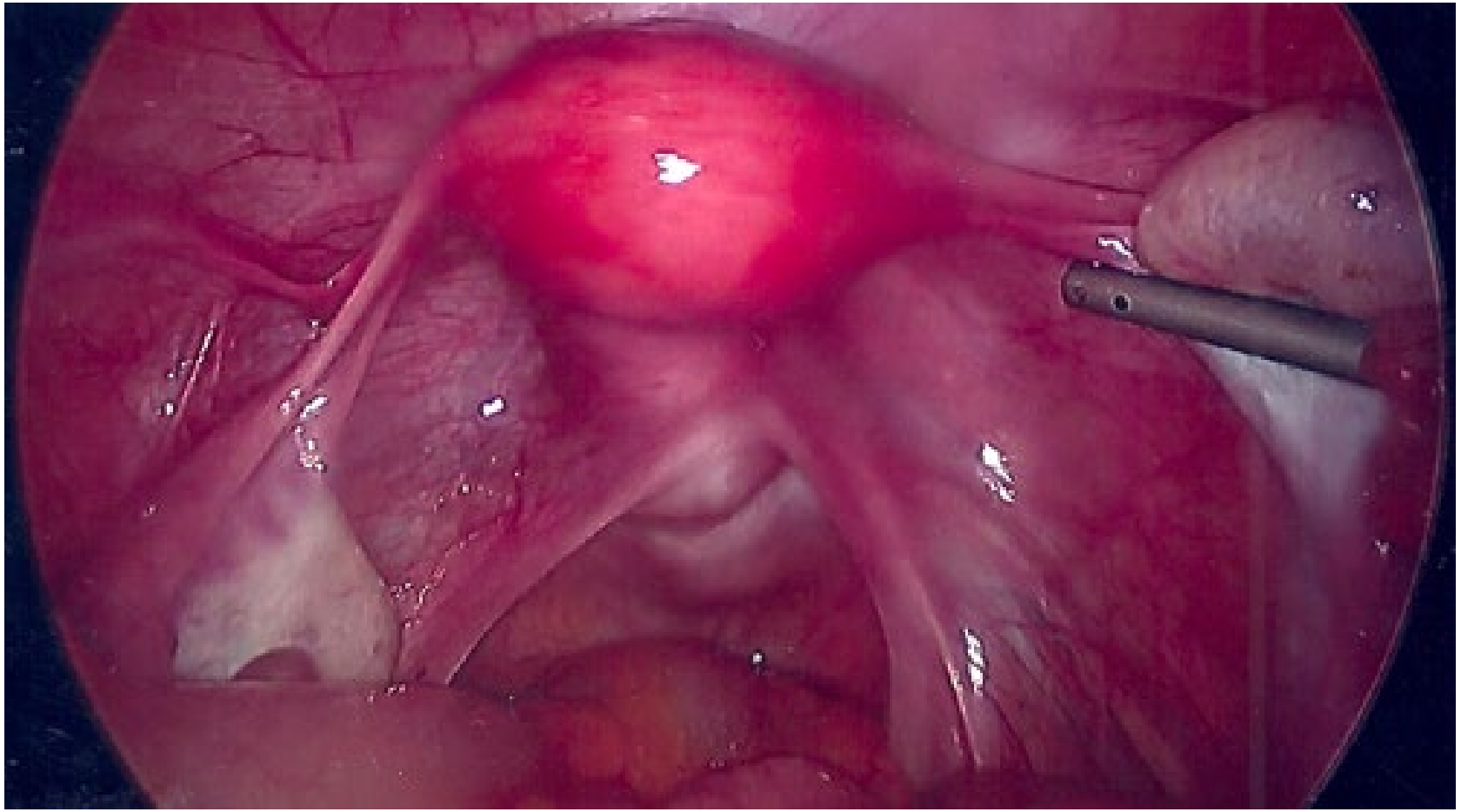
Depression

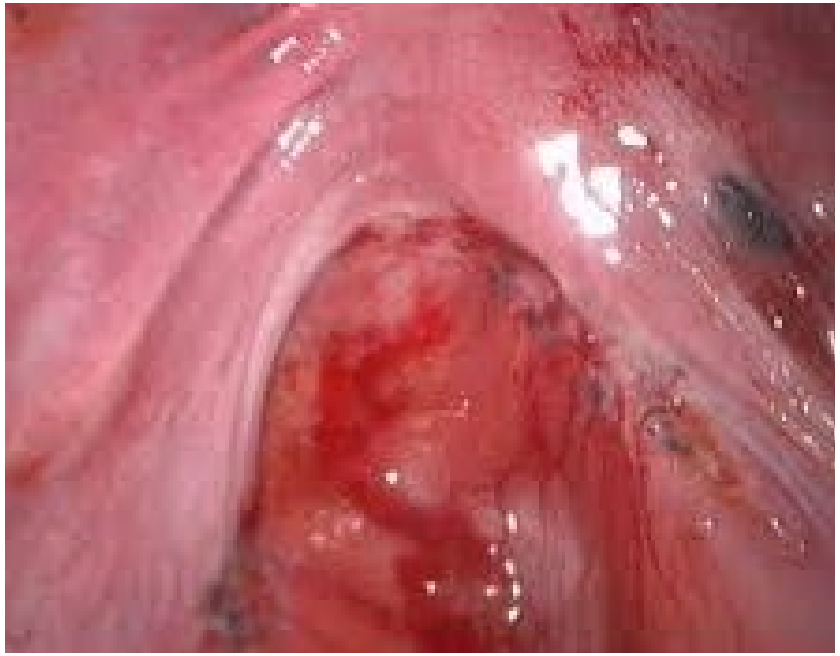
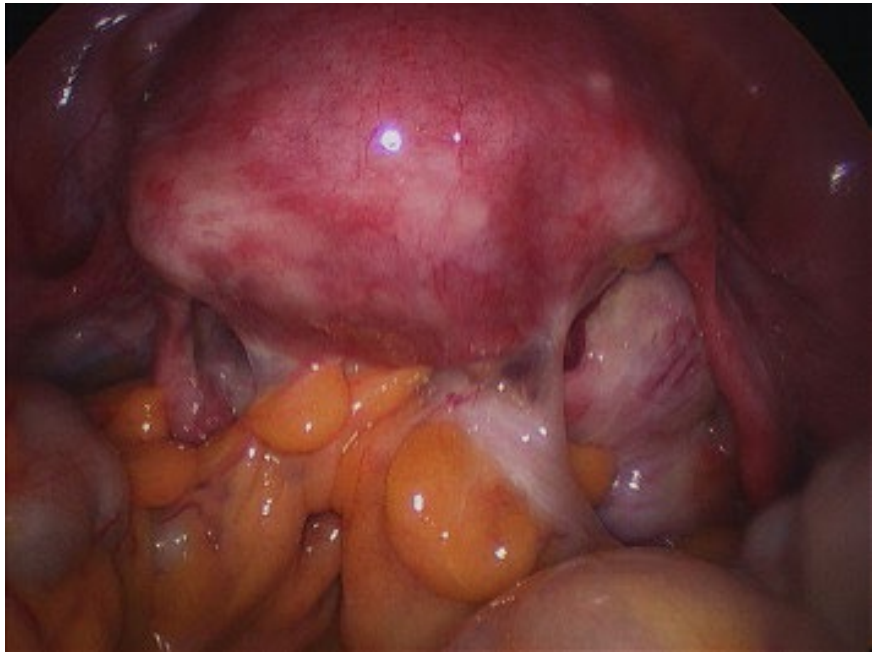
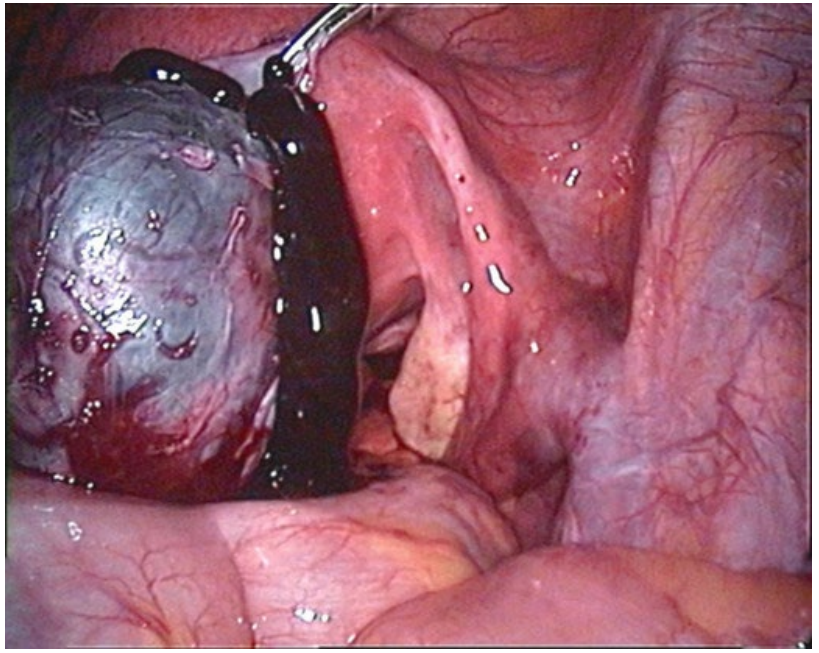
Traumatic experiences

Endometriosis

- 35-50% experience symptoms, variable clinical picture
- Affects every social group & ethnicity
- Prolonged time to diagnosis - 2017 APPG survey, why?
  1. Diagnostic complexities, low accuracy of examination, non-specific symptoms & overlapping with other conditions
  2. Failure to identify disease
  3. Failure to assess disease properly
  4. Failure to refer to the right people to manage & treat it
- Precise cause unclear
  - Retrograde menstruation; lymphatic or haematogenous spread; metaplastic transformation; genetics; immune dysfunction; embryologically patterned metaplasia

What is normal?



Types

- Ovarian
- Superficial
- Deep >5mm
- Not mutually exclusive
- Staging 1-4/ classification
- Extra pelvic

#Enzian

(Classification of Endometriosis)

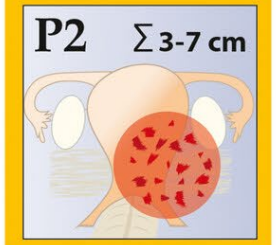
PERITONEUM

P Peritoneum

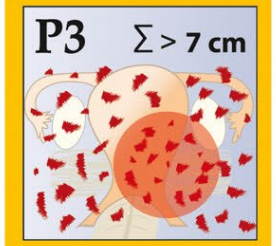
■ Sum of all diameters

P1 Σ < 3 cm

P2 Σ 3-7 cm



P3 Σ > 7 cm



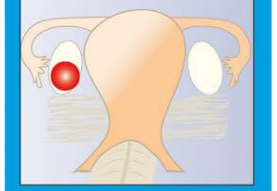
OVARY

O Ovary

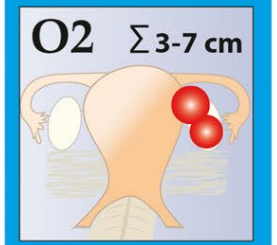
■ Sum of all diameters

left right

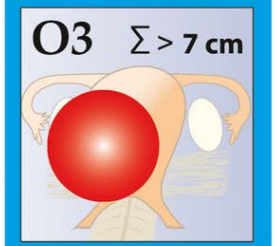
O1 Σ < 3 cm



O2 Σ 3-7 cm



O3 Σ > 7 cm



TUBE

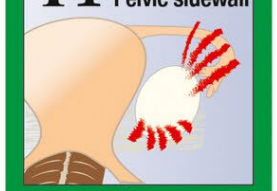
T Tubo-ovarian condition

■ Adhesions
■ Motility

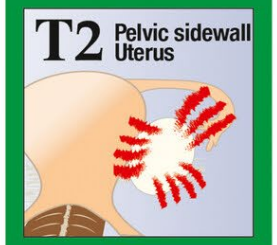
■ Patency test

left right

T1 Pelvic sidewall



T2 Pelvic sidewall Uterus



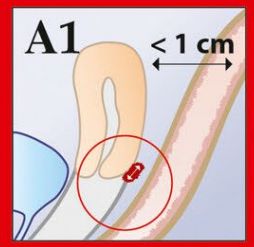
T3 Pelvic sidewall Uterus Bowel, USL

DEEP ENDOMETRIOSIS

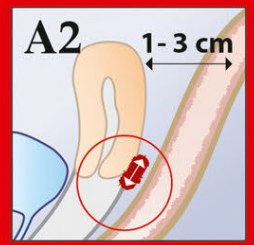
A Rectovaginal space Vagina Retrocervical area

■ Largest diameter

A1 < 1 cm



A2 1- 3 cm



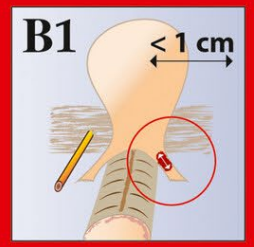
A3 > 3 cm

B Sacrouterine ligg. Cardinal ligaments Pelvic sidewall

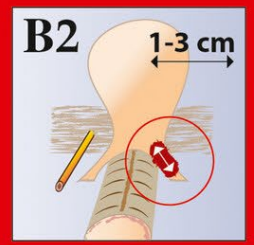
■ Largest diameter

left right

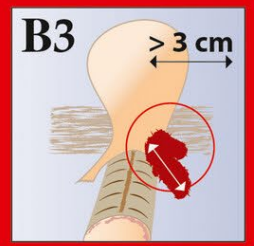
B1 < 1 cm



B2 1-3 cm



B3 > 3 cm



C Rectum

■ Largest diameter

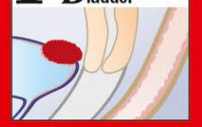
C1 < 1 cm

C2 1-3 cm

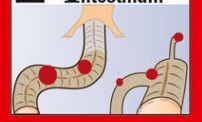
C3 > 3 cm

F Adenomyosis

F Bladder



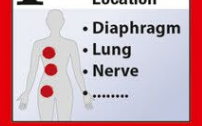
F Intestinum



F Ureter

F (.....) Location

- Diaphragm
- Lung
- Nerve
- .....



P _____

O ___ / ___
left right

m ovary is missing
x unknown / not visible

T ___ / ___
left right

m tube is missing
x unknown / not visible
+ or - Patency test

A _____

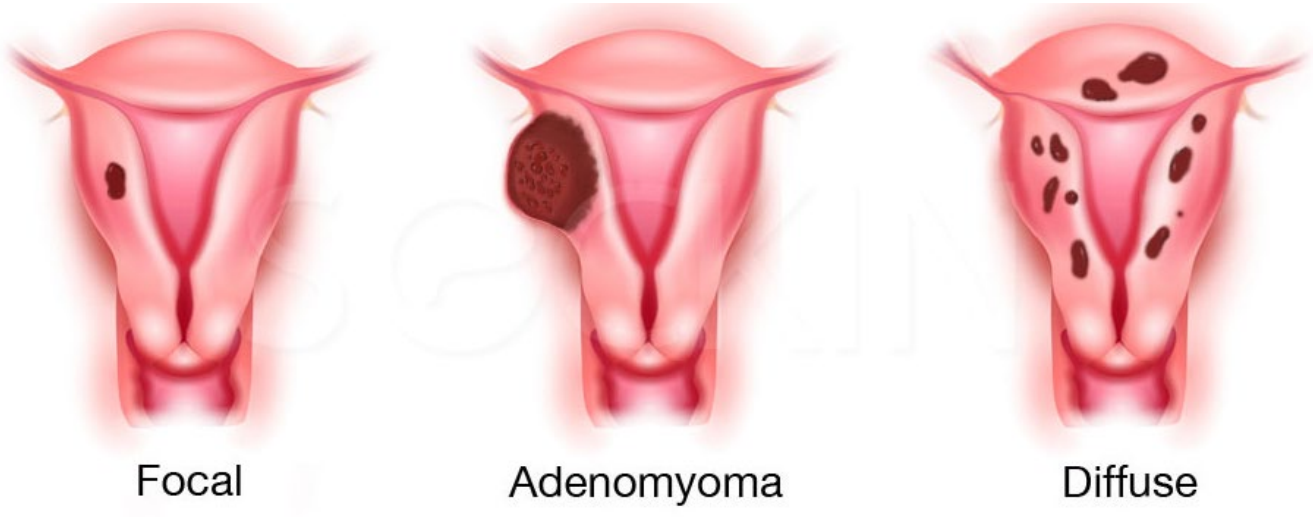
B ___ / ___
left right

C _____

F _____
(Location)

Adenomyosis

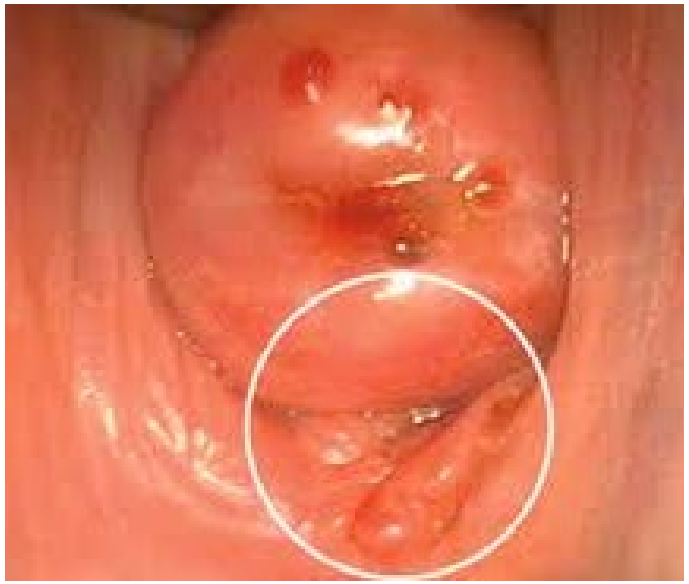
- Endometrial tissue deep in myometrium
- 1 in 10 women reproductive ages
- (40-50 years)
- (Parous)



Presentation: History

- Suspect endometriosis (including women ≤17 years) with:
  - Persistent pelvic pain
  - Dysmenorrhoea affecting daily activities & quality of life
  - Deep dyspareunia
  - Period-related or cyclical GI symptoms, particularly, painful bowel movements
  - Period-related or cyclical urinary symptoms, particularly, haematuria or bladder pain
  - Infertility in association with ≥1 of above
- Other symptoms:
  - Back pain
  - Chest symptoms
  - Nerve symptoms
  - Lumps
- Family history?

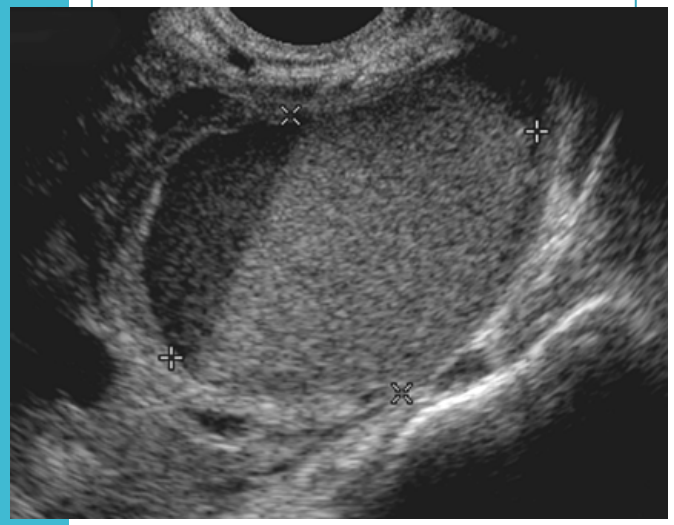
Presentation: Examination



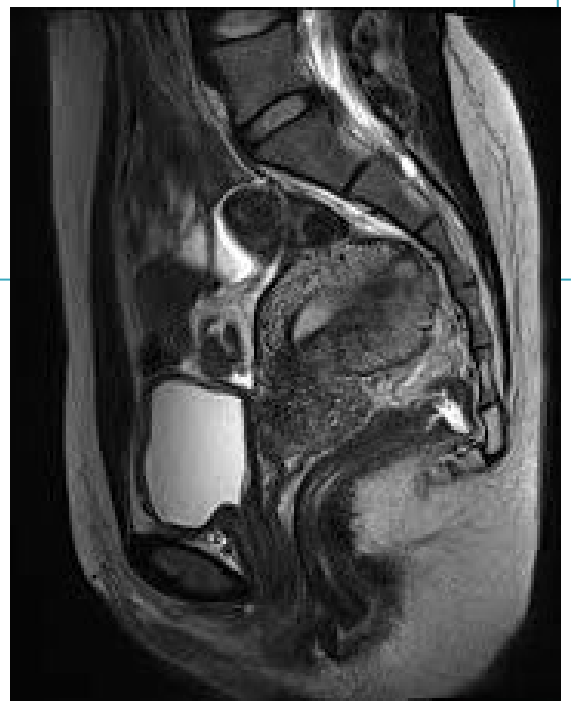
- Offer abdominal & pelvic exam to identify:
  - Masses
  - Reduced organ mobility
  - Tender nodularity in the posterior fornix
  - Endometriotic vaginal nodules

Diagnosis

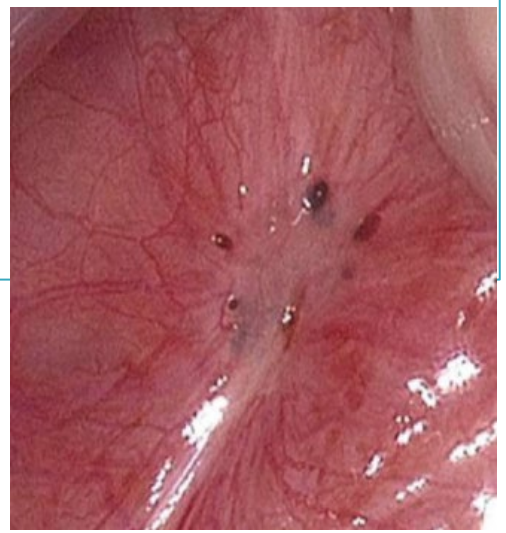
Ultrasound



MRI



Laparoscopy



Ziwig

What it is:

- CE-marked saliva test analysing >1000 microRNAs via NGS & AI
- Detects specific molecular signature of endometriosis
- Designed for women 18–43 with suggestive symptoms

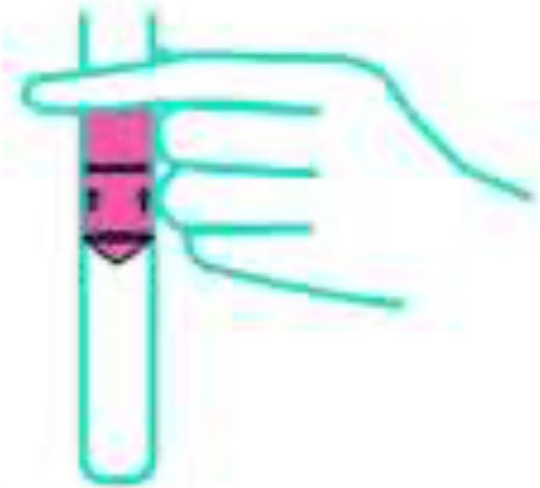
Clinical use:

- Non-invasive, painless, result in days
- Usable regardless of cycle phase or hormonal therapy

Performance:

- Sensitivity ~96-97%; specificity ~95-100%

Ziwig



Ziwig

Strengths:

- May reduce diagnostic delay
- Easy collection, suitable adjunct when imaging inconclusive

Limitations:

- Contraindications: pregnancy, saliva contamination, active infection, prior cancer/HIV
- Not yet in NICE or UK guidelines
- Access & cost may limit availability

Ziwig

Where Ziwig fits:

- High-performing non-invasive adjunct when suspicion is high but imaging non-diagnostic
- Positive result: supports expedited referral & targeted imaging
- Negative result: does not fully exclude disease; refer if symptoms persist.

Implications for GPs / Sexual Health Physicians:

- Could shorten diagnostic journey
- Need for local protocols: when to order, how to act on results
- Counsel patients: promising but not definitive

Endosure

What it is:

- Non-invasive diagnostic tool for endometriosis, using **electroviscerography (EVG)** to measure gastrointestinal myoelectrical activity (GIMA)
- Records electrical signals from smooth muscle in the abdomen, with electrode pads plus a respiratory belt
- Typically takes ~30 minutes of recording & prep time (~10 minutes baseline, water stimulus) to provoke GIMA response

Performance:

- ~99% accuracy (surgical verification) in detecting disease presence vs absence
- Detects disease at all stages, all subtypes / locations, broad age range (pre-teens to post-menopausal)

endo sure* TEST

Endosure

Strengths:

- Rapid, point-of-care-type test; results in same clinic visit in many cases
- Non-surgical, low risk, painless; could help reduce diagnostic delays

Limitations:

- Still emerging; availability currently limited
- Some prep required (fasting) to avoid interference
- Not yet FDA-approved for widespread use
- Need further peer reviewed, independent validation

endo sure* TEST

Endosure

Implications for GPs / Sexual Health Physicians:

- Could be offered when suspicion is high, imaging non-diagnostic, or patient reluctant for invasive diagnosis
- Positive: strong signal to refer, consider treatment planning
  Negative: symptom persistence still warrants investigation
- Need local protocols: who delivers test, cost, patient prep, interpretation of results.

endo sure* TEST

Treatment

Symptom based:
Pain
Fertility
Obstruction

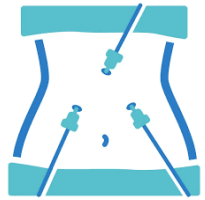
Personalised

Multimodal approach

Hormones

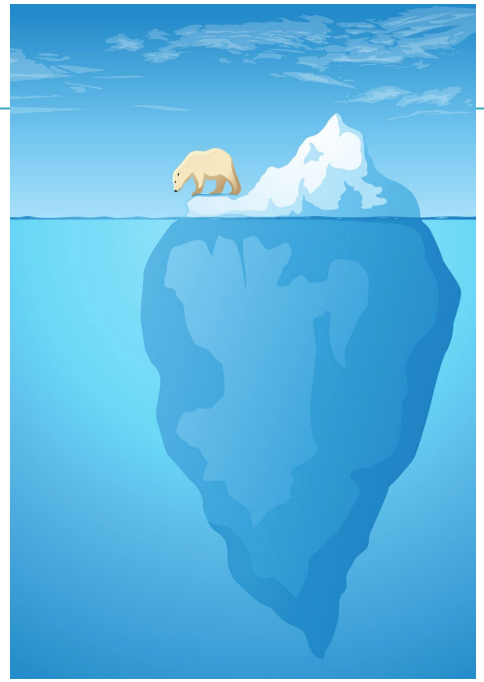
COCP; POP; Implanon; Depo-Provera; LNG-IUS; Dienogest; GnRHa

Pain Management/ Integrative therapies



Surgery

Laparoscopic excision



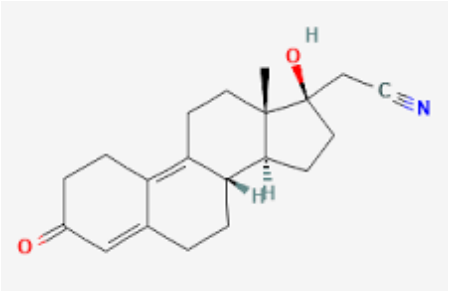
Dienogest

What it is:

- A **progestin** (19-nortestosterone derivative) with strong local progestogenic effect
- Selective action → suppresses oestradiol to mid-follicular range (30–50 pg/ml)
- Oral daily tablet (2 mg once daily)

Mechanism of action:

- Reduces endometrial proliferation & angiogenesis
- Induces decidualisation & atrophy of endometriotic lesions
- Anti-inflammatory & immunomodulatory effects



Indications:

- Licensed for treatment of **endometriosis-associated pain**
- Effective across all lesion types

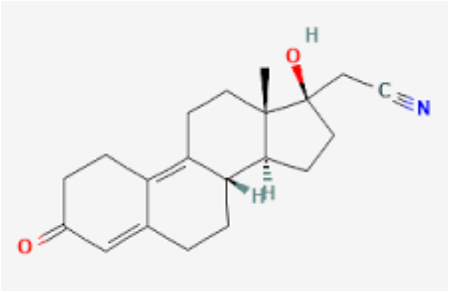
Clinical efficacy:

- Large RCTs show significant reduction in pelvic pain, dysmenorrhoea, dyspareunia, & improved quality of life
- Comparable efficacy to GnRH agonists but with better tolerability & bone safety

Dienogest

Advantages:

- Oral, once-daily dosing
- Long-term safety established (up to 5 years in studies)
- Favourable bone mineral density profile vs GnRH analogues
- Can be used continuously; return of menses/fertility after discontinuation
- Good tolerability: less hypoestrogenic symptom burden



Adverse effects:

- Irregular bleeding/spotting (common, usually improves over time)
- Headache, breast discomfort, mood changes, acne, weight change possible.
- Rare: thromboembolic risk lower than combined oral contraceptives, but consider other risk factors

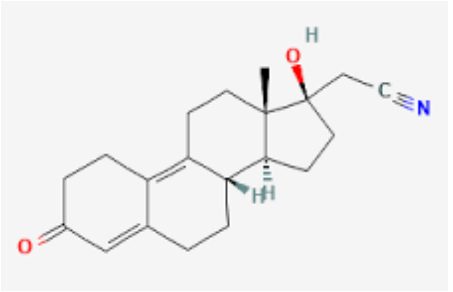
Dienogest

When to consider:

- Alternative if COCPs or alternative progestin not tolerated or contraindicated

Key counselling points:

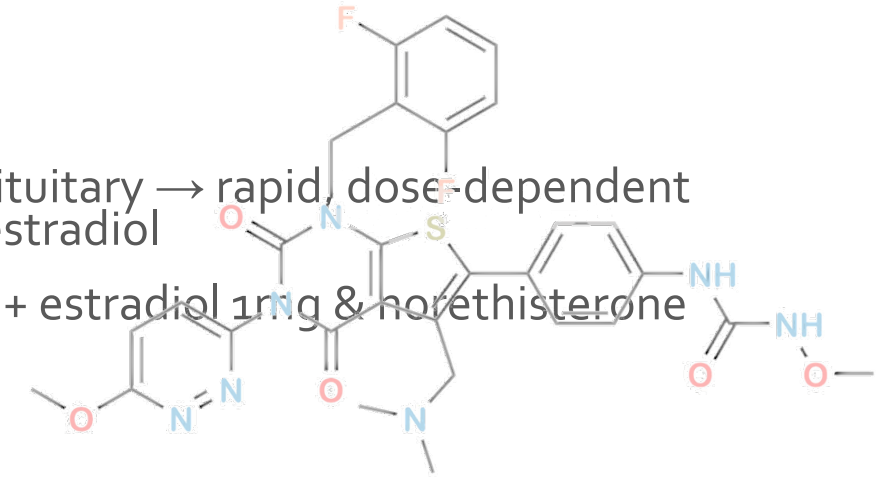
- Effectiveness relies on adherence
- Bleeding changes common - manage expectations
- Fertility returns after stopping; not contraceptive unless combined with barrier method
- Safe for longer-term use where effective & tolerated



Relugolix

What it is:

- Oral **GnRH receptor antagonist**
- Directly blocks GnRH receptors in pituitary → rapid, dose-dependent suppression of LH/FSH → lowers oestradiol
- **Fixed-dose combination** (relugolix + estradiol 1mg & norethisterone acetate 0.5mg)



Mechanism of action:

- Suppresses ovarian oestrogen production
- Reduces stimulation of ectopic endometrium
- Combination with low-dose add-back therapy preserves bone mineral density & mitigates hypo-oestrogenic symptoms

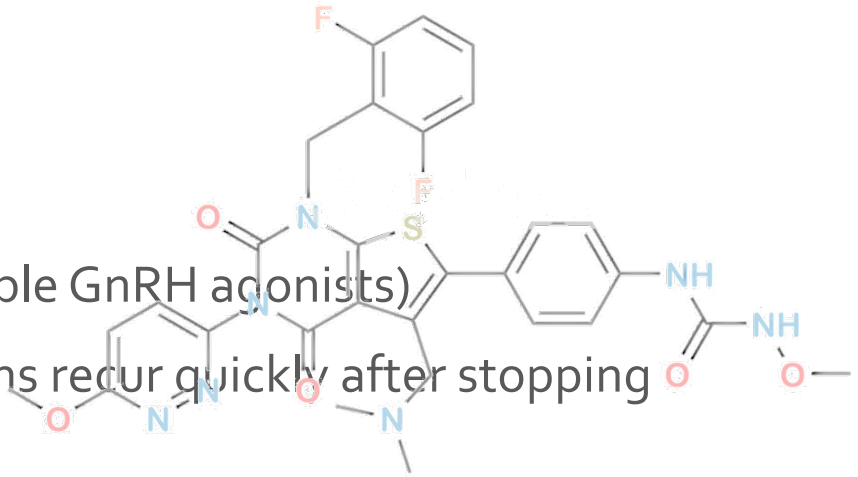
Indications:

- **Uterine fibroids** & for **moderate-to-severe pain associated with endometriosis**

Clinical efficacy:

- SPIRIT 1 & 2 trials (NEJM, 2022): significant reduction in dysmenorrhoea, non-menstrual pelvic pain, & dyspareunia vs placebo
- Sustained effect with combination therapy for up to 2 years with bone & metabolic safety maintained

Relugolix



Advantages:

- **Oral, once-daily** dosing (vs injectable GnRH agonists)
- Rapid onset and offset → symptoms recur quickly after stopping (useful if planning pregnancy
- With add-back, maintains bone density & reduces vasomotor side effects
- Flexible duration: licensed for long-term use (>24 months)

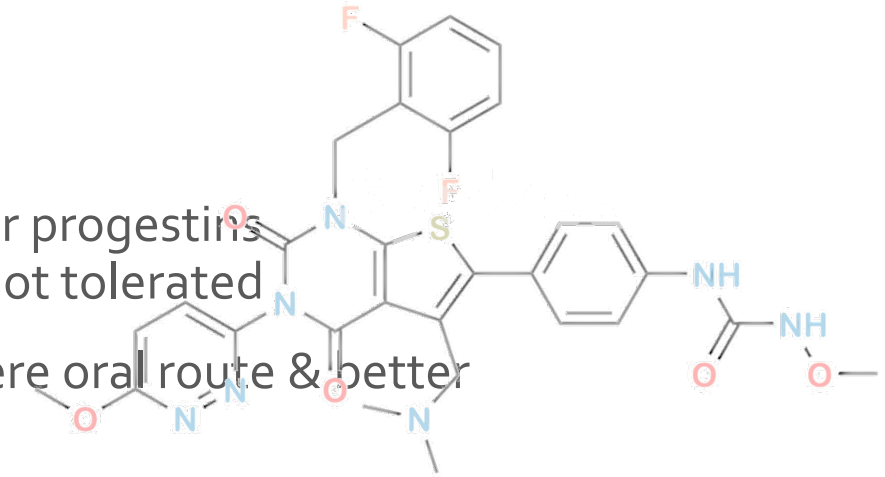
Adverse effects:

- Hypo-oestrogenic symptoms (hot flushes, headaches, mood changes) – less with combination therapy
- Irregular bleeding, nausea, fatigue
- No HRT flexibility

Relugolix

Considerations in primary care:

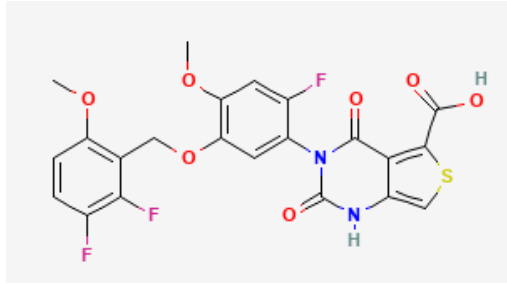
- Second-line if COCPs, LNG-IUS, or progestins (dienogest, NET) are ineffective/not tolerated
- Alternative to GnRH agonists where oral route & better side-effect profile preferred
- Initiated in specialist care



Key counselling points:

- Take daily at the same time
- Combination product improves tolerability
- Symptoms usually return rapidly if treatment stopped
- Additional contraception 1 month
- Oral ccHRT risks

Linzagolix



What it is:

- **GnRH receptor antagonist**
- Available in **100 mg & 200 mg** doses
- **Licensed in the UK** for moderate-to-severe endometriosis-associated pain in women who have not responded to prior medical or surgical treatments.

Mechanism of Action:

- Blocks GnRH receptors → suppresses LH/FSH → reduces oestradiol levels
- At **200 mg,** induces full oestradiol suppression (<20 pg/ml)
- At **100 mg,** maintains oestradiol in the 20–60 pg/ml range, reducing hypo-oestrogenic side effects

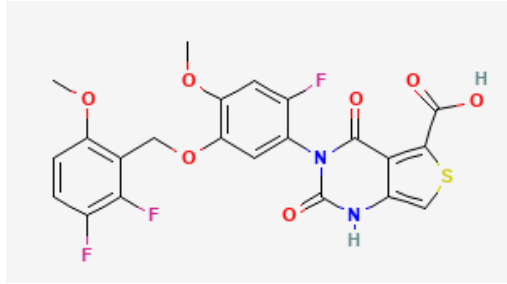
Clinical Efficacy:

- **EDELWEISS 3 trial** (2024): 200 mg & add-back therapy (ABT) significantly reduced:
  - Dysmenorrhoea: 72.9% response vs 23.5% placebo.
  - Non-menstrual pelvic pain: 47.3% vs 30.9% placebo.
- 75 mg monotherapy showed significant improvement in dysmenorrhoea but not non-menstrual pain.

Safety Profile:

- Add-back therapy (1 mg oestradiol & 0.5 mg norethisterone acetate) mitigates:
  - Bone mineral density loss (<1%)
  - Hot flushes & other hypo-oestrogenic symptoms
- Low rates of adverse events; well-tolerated in clinical trials

Linzagolix



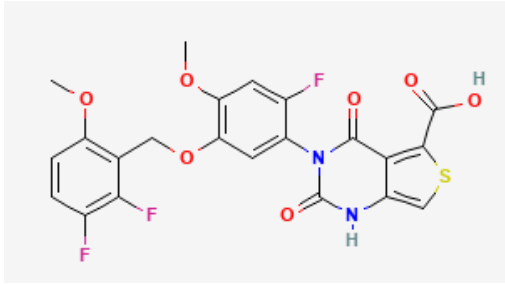
Advantages:

- **Oral, once-daily** dosing
- Flexible dosing:
  - 100 mg for partial suppression (preferred for bone safety)
  - 200 mg for full suppression
- Suitable for long-term use; licensed for up to 2 years
- Can be used when no response to other treatments
- HRT flexibility

Limitations:

- Requires concurrent add-back therapy to prevent hypo-oestrogenic side effects

Linzagolix



Considering in Primary Care:

- Second-line treatment after failure of COCPs, LNG-IUS, or progestins
- Alternative to GnRH agonists for patients preferring oral medication
- Consider in patients with contraindications to other hormonal therapies

Key Counselling Points:

- Take once daily at the same time each day
- Use with add-back therapy to mitigate side effects
- Monitor for any signs of hypo-oestrogenic symptoms or bone density loss
- Not a contraceptive; use additional contraception if pregnancy is not desired

Management to consider

Medical

Analgesics

Hormonal treatment

Neuropathic agents

Antidepressants

Antispasmodics, antidiarrheal medication, laxatives

Melatonin, zopiclone

Non-Medical

Exercise on Referral, yoga

Mindfulness & relaxation, sleep

Social prescribing

Diet, supplements (NAC, Vit E)

Talking therapies/ counselling

Acupuncture, TENS

Pelvic physiotherapy

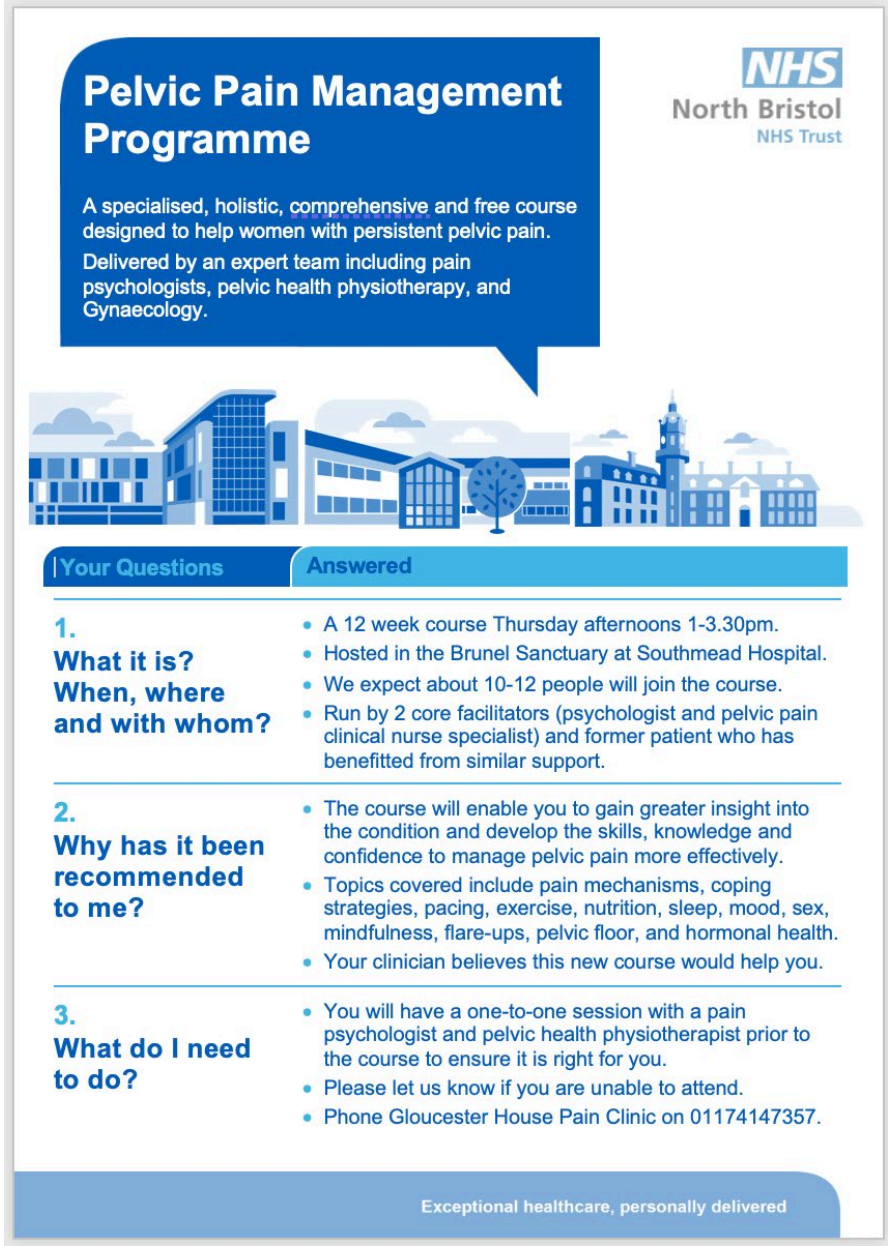
Pain management Tool kit Complementary

pelvic pain SUPPORT NETWORK

ENDOMETRIOSIS UK

Pelvic Pain Management Programme

- PMPs: an evidence-based, multidisciplinary approach to addressing chronic pain
- Often generic, not addressing the challenges of PPP
- Hence the importance of a dedicated PPMP



Pelvic Pain Management Programme

NHS North Bristol NHS Trust

A specialised, holistic, comprehensive and free course designed to help women with persistent pelvic pain.

Delivered by an expert team including pain psychologists, pelvic health physiotherapy, and Gynaecology.

Your Questions	Answered
1. What it is? When, where and with whom?	• A 12 week course Thursday afternoons 1-3.30pm. • Hosted in the Brunel Sanctuary at Southmead Hospital. • We expect about 10-12 people will join the course. • Run by 2 core facilitators (psychologist and pelvic pain clinical nurse specialist) and former patient who has benefitted from similar support.
2. Why has it been recommended to me?	• The course will enable you to gain greater insight into the condition and develop the skills, knowledge and confidence to manage pelvic pain more effectively. • Topics covered include pain mechanisms, coping strategies, pacing, exercise, nutrition, sleep, mood, sex, mindfulness, flare-ups, pelvic floor, and hormonal health. • Your clinician believes this new course would help you.
3. What do I need to do?	• You will have a one-to-one session with a pain psychologist and pelvic health physiotherapist prior to the course to ensure it is right for you. • Please let us know if you are unable to attend. • Phone Gloucester House Pain Clinic on 01174147357.

Exceptional healthcare, personally delivered

Content

Session	Intro	Topic 1	Topic 2	End
1		Psychometrics & ground rules	Programme aims Consequences of PPP	Group hopes
2		Pain Mechanisms & nervous system	Impact of pain on the self, exploring values SMART goal setting	
3		Activity management, pacing, reintroducing movement	CBT model	
4		Mindfulness intro	Stress (drive/threat/soothe model) Soothing rhythm breathing	
5		Mindfulness of posture & avoidance of positions/movement Body scan & recognising threat	Self-criticism vs self-compassion Development of compassionate self	
6		Restorative/mindful movement Stretch	Relationships & communication	
7		Hormones & cycles	Flare-up management	
8		Pelvic floor anatomy, pelvic exercise Bladder & bowel function	Nutrition	
9		Building confidence in exercise Strengthening movements	Problem solving	
10		Mood & emotions Mindfulness of feelings associated with pain & how to live with them	Intimacy & sex	
11		Translating exercise into meaningful activity Trouble shooting activities	Sleep	
12		Pulling together & reflections	Setting long term intentions Psychometrics	

Welcome & weekly feedback

Small group goal setting

Outcomes

All participants made clinically meaningful change on at least two indices measured

Construct	Tool
Mood	HADS
Pain Catastrophising	Coping strategy questionnaire
Health related QOL/occupation/disability	EQ-5D-5L
Pain self-efficacy	PSEQ
Pain intensity & distress	Brief pain inventory
Fear of movement	Tampa Scale of Kinesiophobia (TSK)
Fatigue	Chalder Fatigue Questionnaire (CFQ)
Patient activation	Patient activation measure PAM

Feedback


Alternative therapies
Validation
Understanding
New information
Stuck
Relatable group
Connection

Surgery:

Laparoscopic including robotic
Excisional
Symptom focused

Anterior compartment: bladder

Middle compartment: uterus, tubes, ovaries, ligaments

Posterior compartment: bowel including appendix

Shave vs Disc vs Resection

Extra pelvic: thoracic, scar, nerve

A multi-centre randomised controlled trial to determine the effectiveness of laparoscopic removal of isolated superficial peritoneal endometriosis for the management of chronic pelvic pain in women

Obstetrics and gynaecology
Research

Laparoscopic excision of deep rectovaginal endometriosis in BSGE endometriosis centres: a multicentre prospective cohort study

Dominic Byrne [1], Tamara Curnow [2], Paul Smith [3], Alfred Cutner [4], Ertan Saridogan [4], T Justin Clark [5] on behalf of BSGE Endometriosis Centres

Correspondence to Professor T Justin Clark; t.j.clark@doctors.org.uk

Abstract

Objective To estimate the effectiveness and safety of laparoscopic surgical excision of rectovaginal endometriosis.

Design A multicentre, prospective cohort study.

Setting 51 hospitals accredited as specialist endometriosis centres.

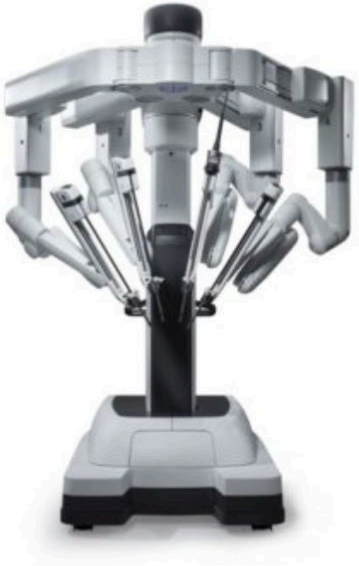
Outcomes

- N=5000, prospective data
- Colorectal surgeon needed 27.6%
- Bowel surgery in 63%
- Urologist needed 6.8%
- Overall improvement in QoL: 6 months – 24 months
- Analgesia reduction
- All symptoms improve excluding voiding difficulties

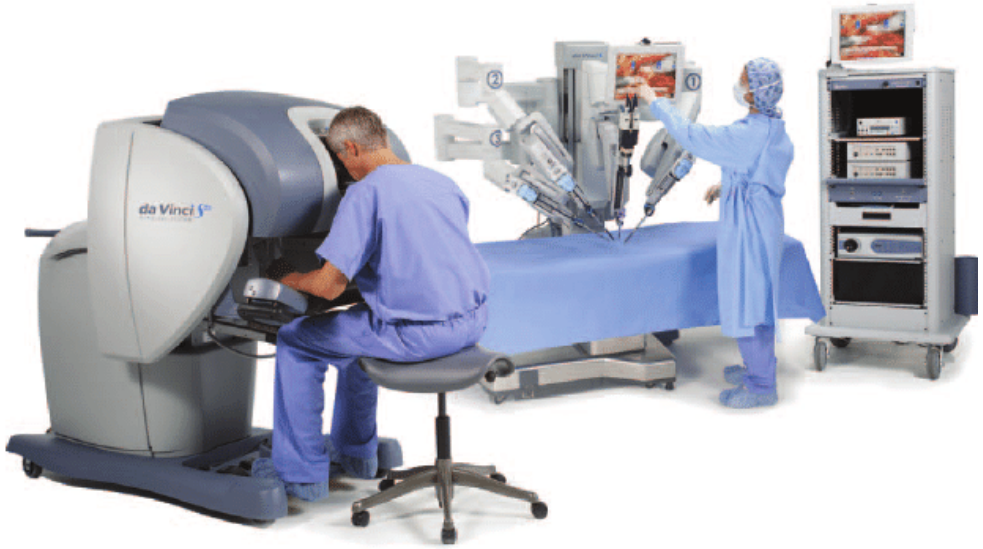
Outcomes

Overall surgical complications 6.8% (bleeding, ureteric)

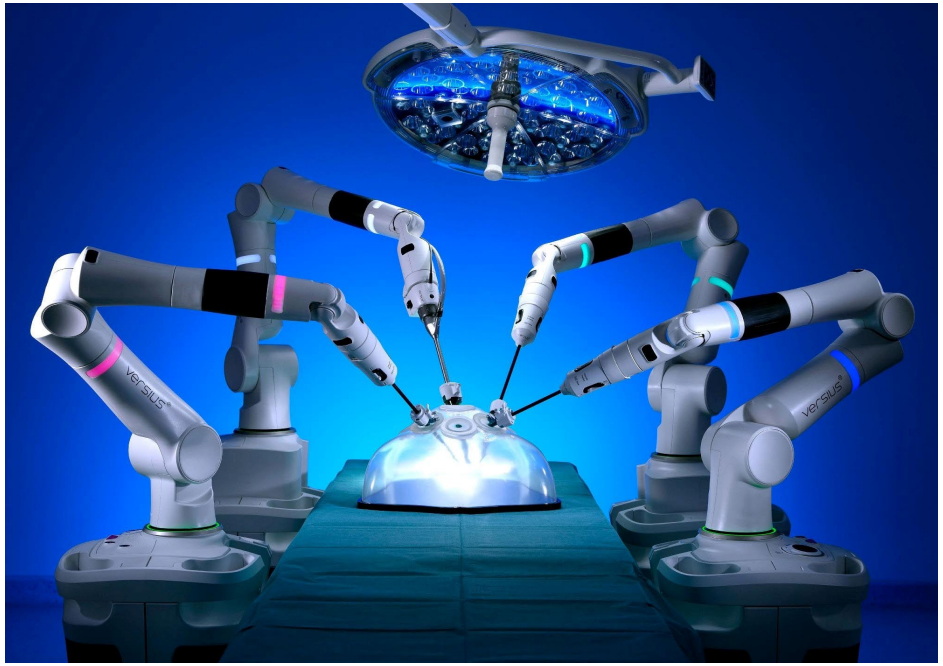
Bowel related 1.1%



INTUITIVE



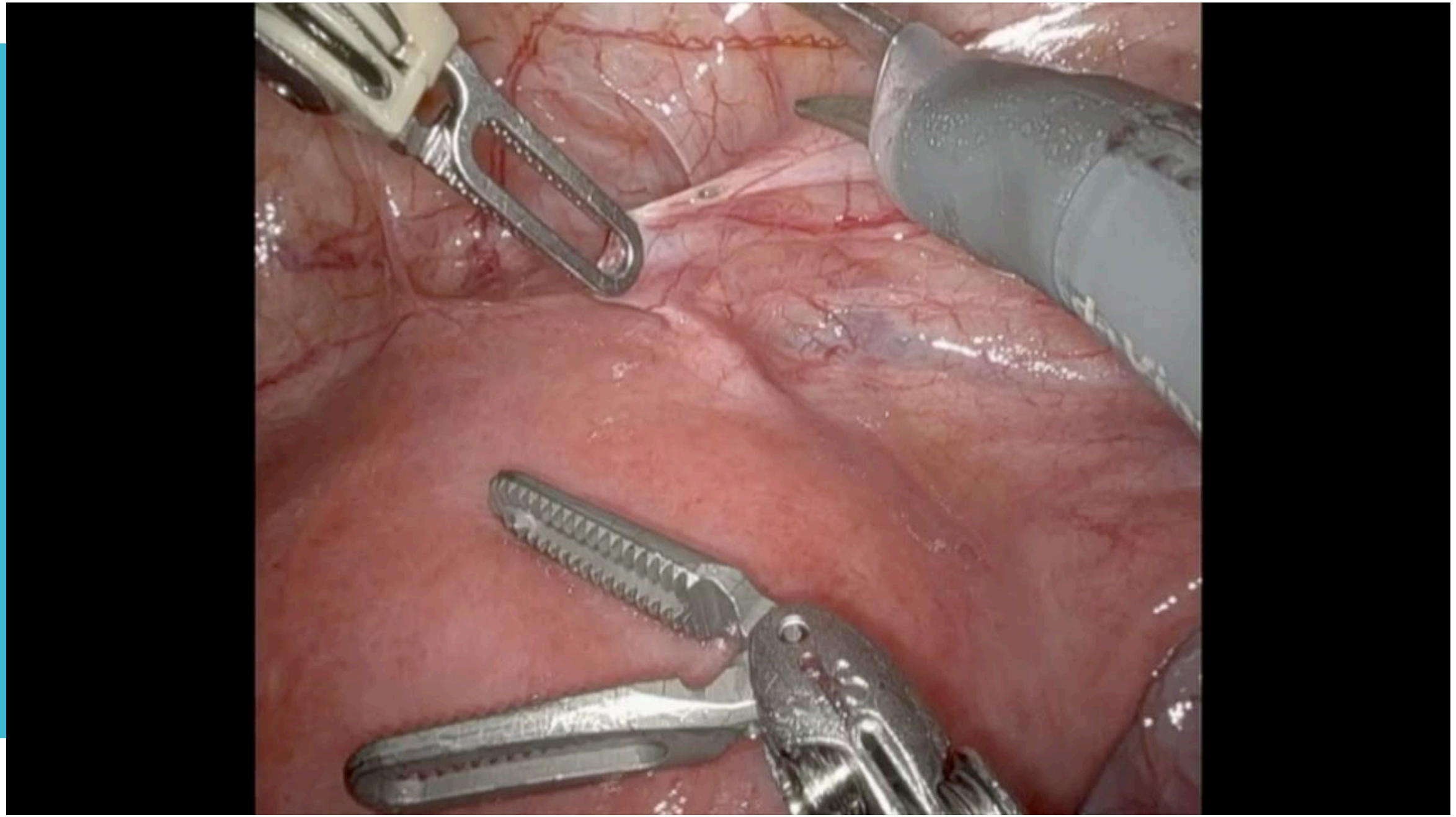
Robotic Assisted Surgical Systems



CMR SURGICAL

Medtronic

Robotic Assisted Surgical Systems



ITV NEWS

Inside the Bristol hospital using robotic-assisted surgery to help reduce NHS waiting times

BBC NEWS UK

Hospital equals national record for robotic surgeries

What to do

- Organise pelvic ultrasound
- Vaginal swabs if indicated
- (Do not use CA125 to diagnose endometriosis)

- Offer initial management with a trial (e.g. 3 months) of:
  - Analgesics
  - Hormonal treatment
  - Consider neuromodulator

- Suggest keeping a pain & symptom diary

Flo period tracker Clue Period calender

- Signpost:

ENDOMETRIOSIS UK pelvic pain SUPPORT NETWORK

Refer when:

* Trial of analgesia provides inadequate pain relief

* Hormonal treatment not effective, not tolerated or contraindicated

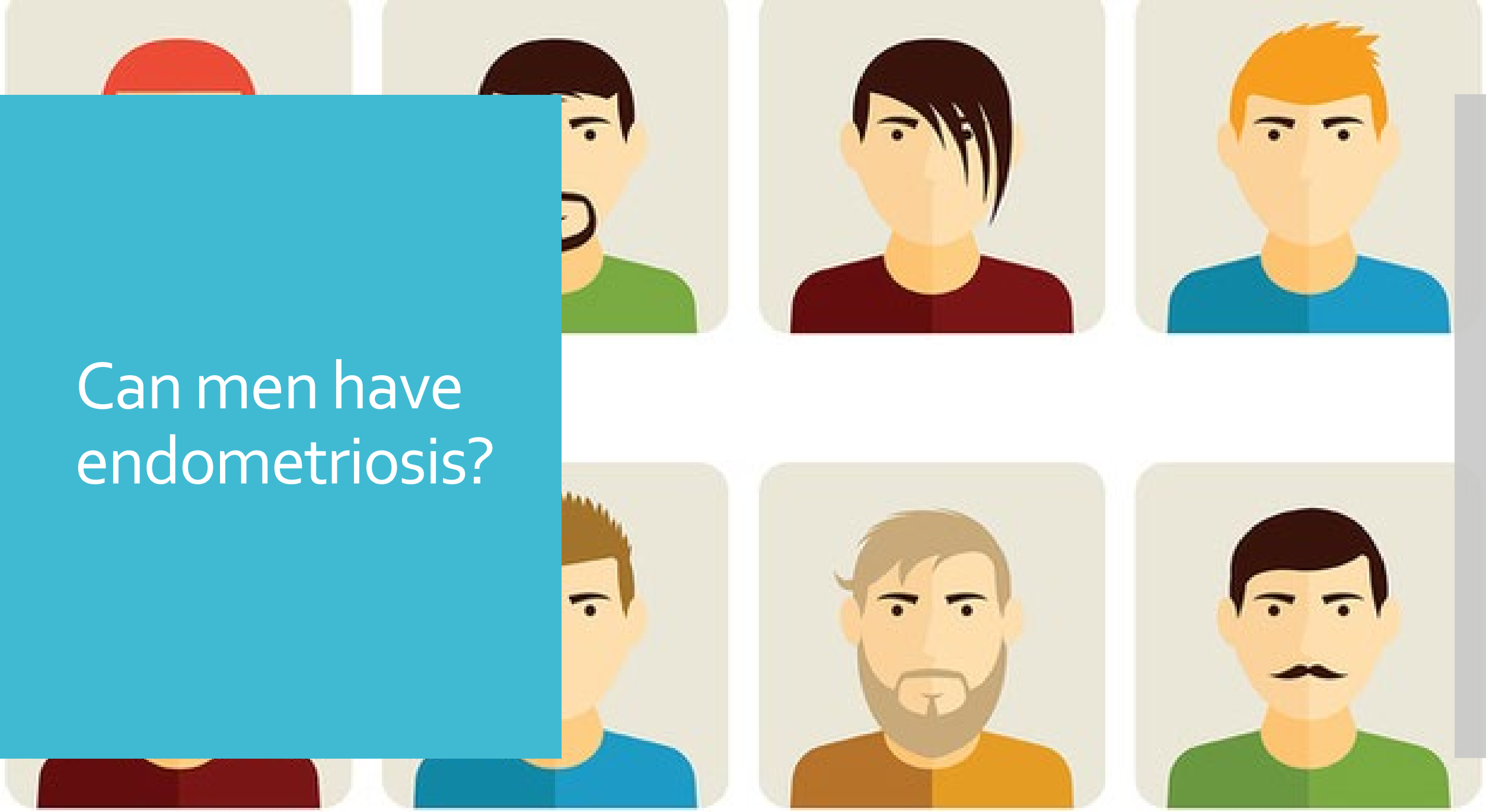
- Refer to a gynaecology service:
  - If initial management is not effective, not tolerated or is contraindicated
  - for persistent or recurrent symptoms of endometriosis
  - for symptoms which impact daily life
  - for pelvic signs of endometriosis, unless deep endometriosis suspected
- Endometriosis Centre:
  - Deep endometriosis including involving bowel, bladder, ureter
  - Endometrioma
  - Extra pelvic endometriosis e.g., thoracic endometriosis
- Refer young people (17 & under) to PAG or Endometriosis Centre

BSGE

The MDT

- Primary care
- Gynaecology, including fertility
- PAG
- CNS
- Colorectal
- Urology
- Radiology
- Upper GI/HPB
- Thoracics
- Anaesthetist
- Pain team
- Psychology
- Occupational therap
- Psychiatry
- Nutritionist
- Physiotherapist
- Psychosexual
- Residents

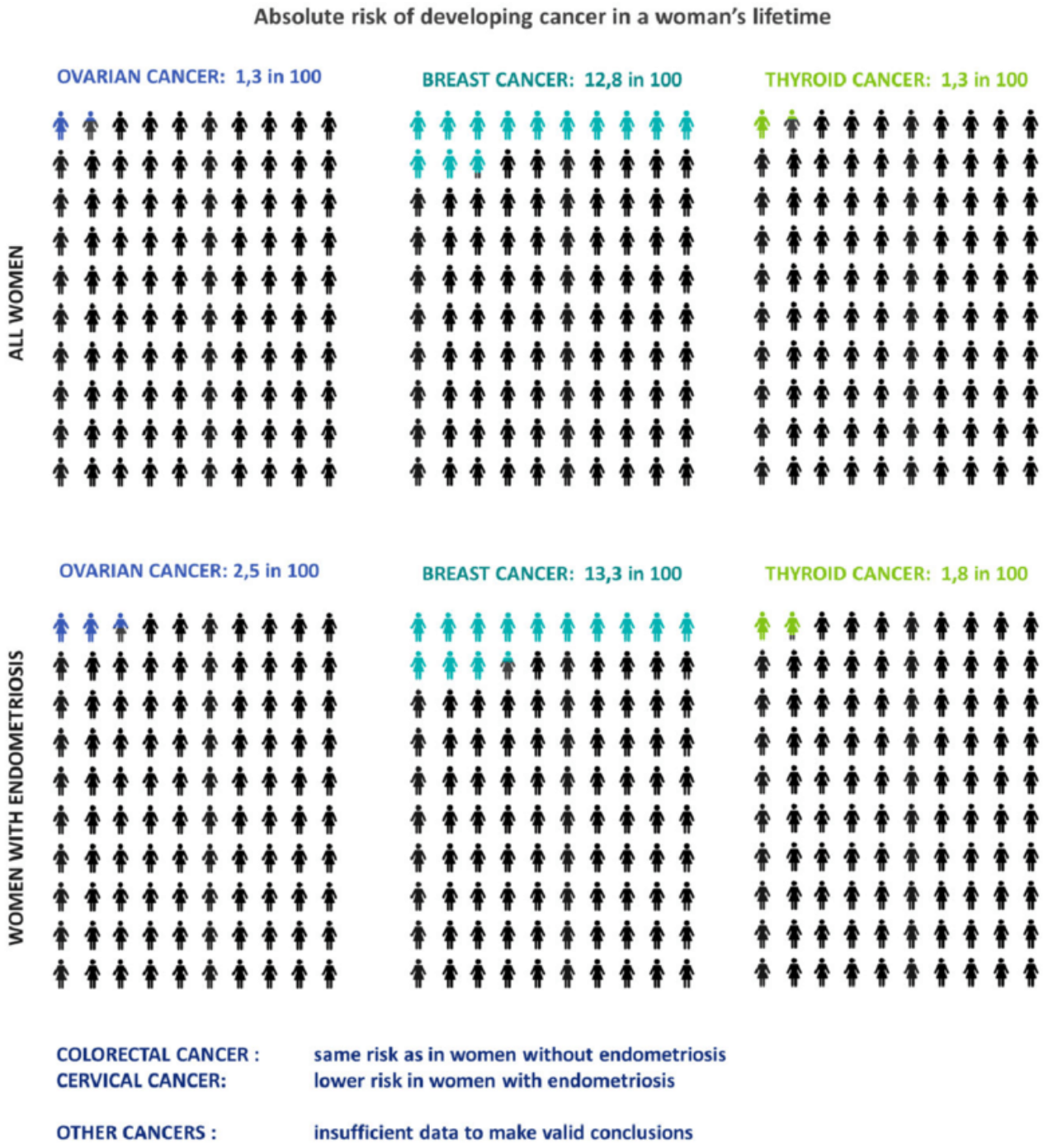
Can men have endometriosis?



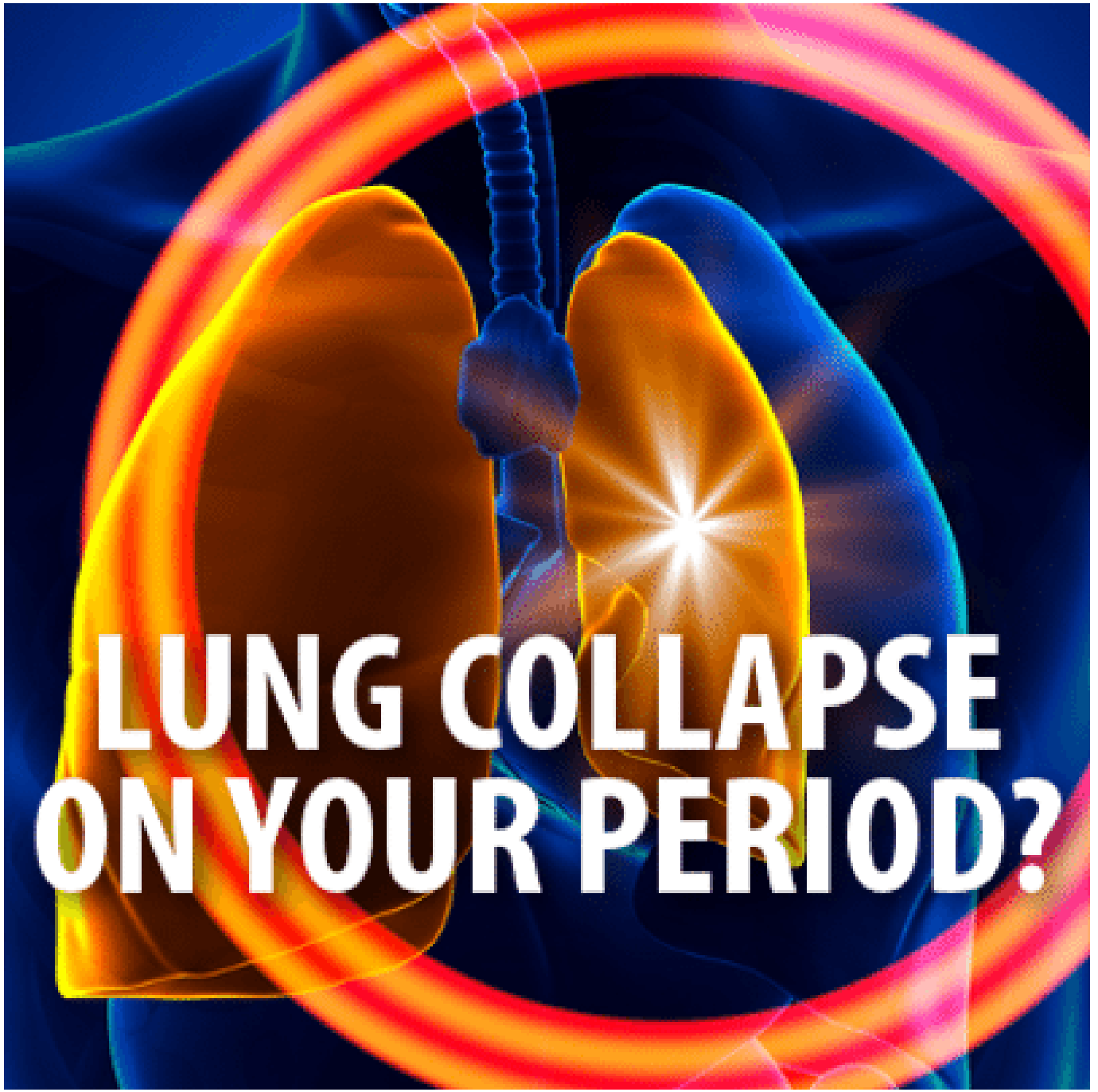
Should I worry about ovarian cancer?

- Risk of malignant transformation low (<2%)
  - Life risk ovarian cancer 1.3% in general pop
  - With endometriosis 1.8-2.5%
  - Very low compared with other cancers e.g., breast, bowel
- Endometrioma in higher risk groups (post menopause/ =>9cm), consider surveillance or surgery
- Routine prophylactic surgery in lower risks groups (asymptomatic) not advised
- Surgery higher risk due to adhesions
- CA125 unhelpful

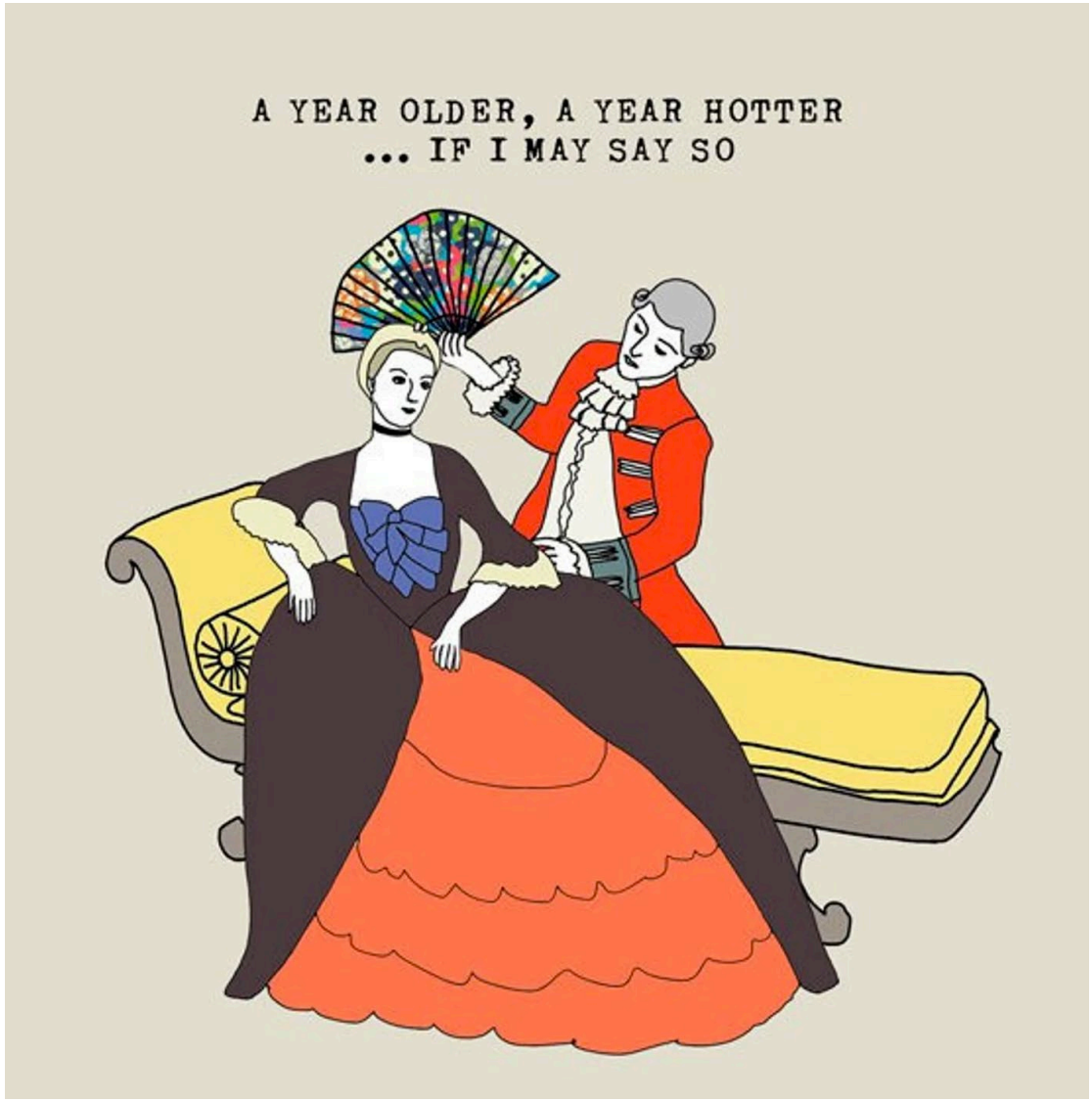
Endometriosis and cancer



Can this happen?



Can I prescribe HRT?



Key points

- Complex multifactorial condition
- Significant burden & morbidity
- Multimodal, personalised approach
- Multidisciplinary input vital

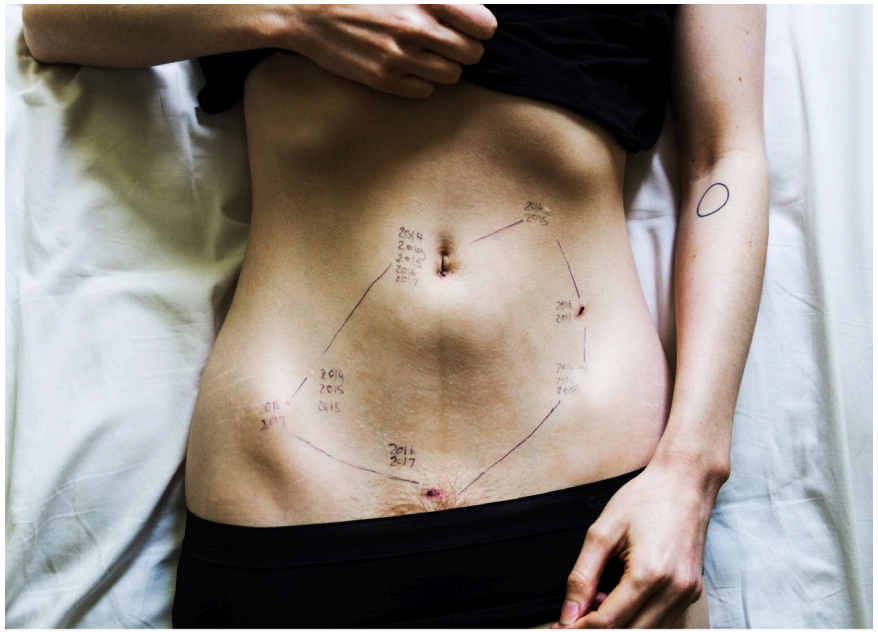


PHOTO BY GEORGIE WILEMAN

Thank you
Any questions?

jessica.preshaw@nbt.nhs.uk