Premenstrual Syndrome(s)

Understanding and management through case examples

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Conflicts of interest

- Educational sponsorship from Pharma
- Honorariums from Pharma

Premenstrual Syndrome - A timeline

Hippocrates' Aphorisms – (*370BC) '*shivering, lassitude and heaviness of the head denotes onset of menstruation….'

Henry Maudsley (1873) - First to make connection between PMS & cyclical ovarian activity

Frank (1931) - First use of term "Premenstrual tension"

Greene & Dalton (1953) – "Premenstrual syndrome"

*John Studd / Adam Magos (1986) – HT (Estro*gen Implants) for PMS

John Studd (1988) – "Ovarian Cycle Syndrome"

PMS O'Brien (2008) – International Society for Premenstrual Disorders

News Voices Culture Lifestyle Tech Sport Daily Edition

Lifestyle › Health & Families › Health News

Up to a million British women may suffer from psychosis due to PMS, gynaecologist warns

'I got psychosis and started seeing things which weren't there. It happened just like that', one woman told The Independent

Siobhan Fenton Health Correspondent | @siobhanfenton | Wednesday 19 October 2016 | 1 comment

4K shares

Dr Panay says women are being let down by a toxic mix of "poor education of the public regarding the condition; poor education of health professionals at university and postgraduate level; social stigma/taboo and prejudice that this is not a 'real' condition."

Oct 2016 The Independent

RCOG Guidelines for Premenstrual Syndrome
www.rcog.org.uk

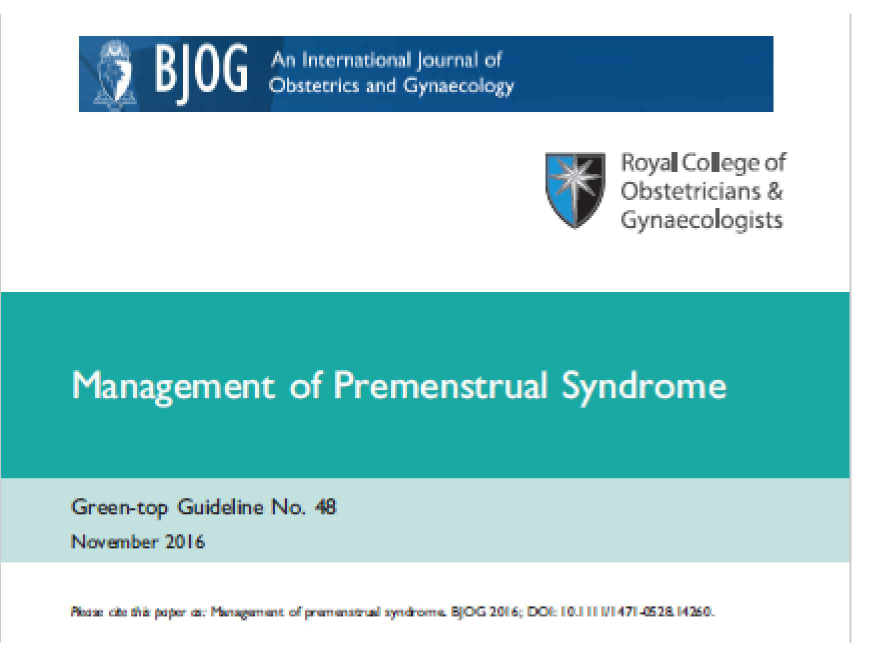
Development of consensus and guidelines on PMS essential to encourage acceptance of condition by patients/health professionals and regulatory authorities

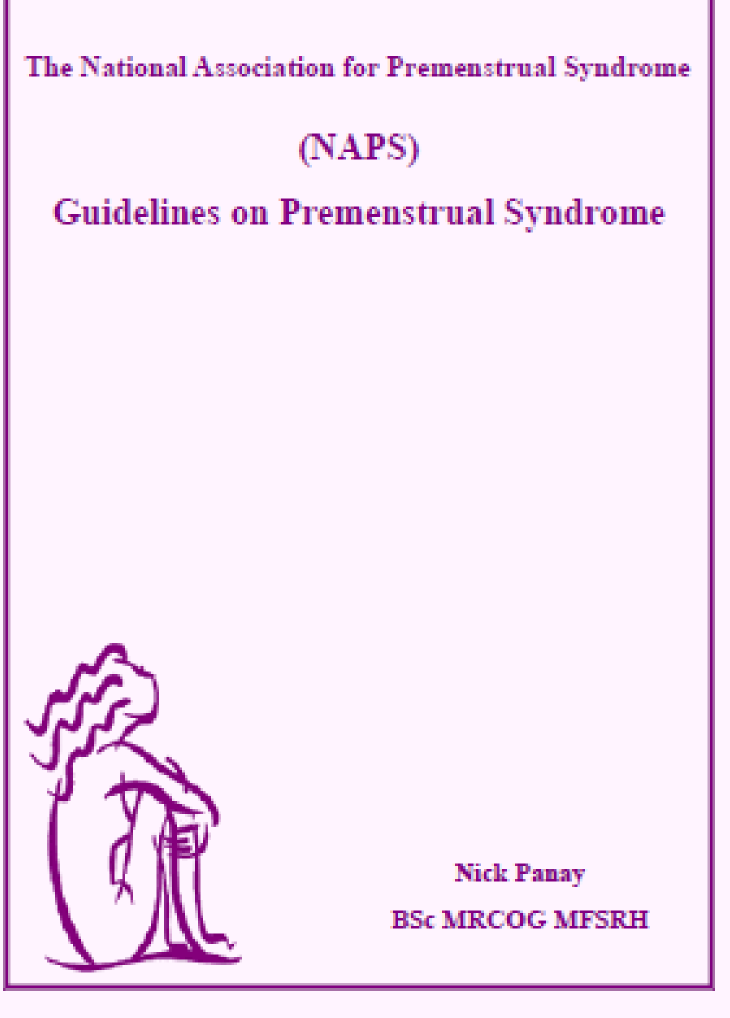
"Management of Premenstrual Syndrome"

- 2007 RCOG Green-Top Guideline No 48
  - Panay et al.
- 2017 RCOG Green-Top Guideline No 48
  - Baker L, Panay N, Craig M, O'Brien PMS

*guidelines systematically developed using standardised evidence-based methodology

PMS Guidelines





https://doi.org/10.1111/1471-0528.14260

www.pms.org.uk

PMS: Aetiology & Prevalence

- Prevalence
  - Peak prevalence of severe PMS in 40-50y age group
  - Moderate PMS: 24% in SWS
  - Severe PMS (PMDD) 5-8%[2] in general population v 23% in perimenopausal women
- Aetiology
  - Likely to be multiple aetiologies (E2/serotonin, Progesterone-allopregnanolone/GABA)
  - (Cyclical) ovarian activity / hormonal fluctuations play an essential role in the genesis of symptoms, also in VMS
  - Probable genetic predisposition – unique ESR1 gene polymorphisms in PMDD sufferers v controls.

1.Sadler et al JWH 2010; 2.Reid NEJM 1991; 3.Chung at al JMM 2014 4. Miller et al 2010

International Society for PreMenstrual Disorders (ISPMD) Consensus on Definitions, Diagnosis and Management

- **Core Premenstrual Disorders (PMDs):** Classic PMS: Ovulatory cycles, functional impairment, post menstrual resolution

- **Variants**
  - **Premenstrual Exacerbation** e.g.epilepsy, migraine
  - **Non Ovulatory PMDs:** ovarian activity(perimenopause)
  - **Progestogen Induced:** side effects of OCP / HRT
  - **PMDs without Menstruation:** post TAH / ablation

PSYCHOLOGICAL & BEHAVIOURAL SYMPTOMS
Mood swings, depression
Tiredness, fatigue or lethargy, irritability
Anxiety, feeling out of control
Reduced cognitive ability, aggression, anger
Sleep disorders, , food cravings

PHYSICAL SYMPTOMS
Breast tenderness, skin rashes
Bloating, weight gain, clumsiness
Headaches, backache

O'Brien PMS, Backstrom T, Brown C, Dennerstein L, Endicott J, Epperson CN, Eriksson E, Freeman E, Halbreich, Ismail KMK, Panay N, Pearlstein T, Rapkin A, Reid R, Schmidt P, Steiner M, Studd J, Yonkers K. Arch Women's Ment Health 2011; 14: 13-21.
Women's Ment Health 2013; 16 (4) 279 – 291.

Premenstrual Dysphoric Disorder (PMDD) American Psychiatric Association DSM-5

A depressive disorder, with a 12-month prevalence ranging from 1.8% to 5.8% among women who menstruate

Factors that differentiate PMDD from other affective disorders include aetiology, duration, and temporal relationship with the menstrual cycle

- Demands 5 out of 11 stimulated symptoms, of which 1 must be mood
- Must occur in the luteal phase
- Is a distinct diagnosis but my occur with other psychopathology
- Clinically significant distress or interference with work, school, usual social activities, or relationships with others

- Criticism: the strict criteria may exclude women who may have a narrow range of severe symptoms
- Many women seek this diagnosis to legitimise their symptoms and desperate to be believed

www.psychiatry.org/psychiatrists/practice/dsm/educational-resources/dsm-5-fact-sheets

Definitions: PMS or PMDD?

- NAPS changed its name to the National Association for Premenstrual Syndromes from "…Syndrome" to reflect the variation in definitions and severities of this disorder.

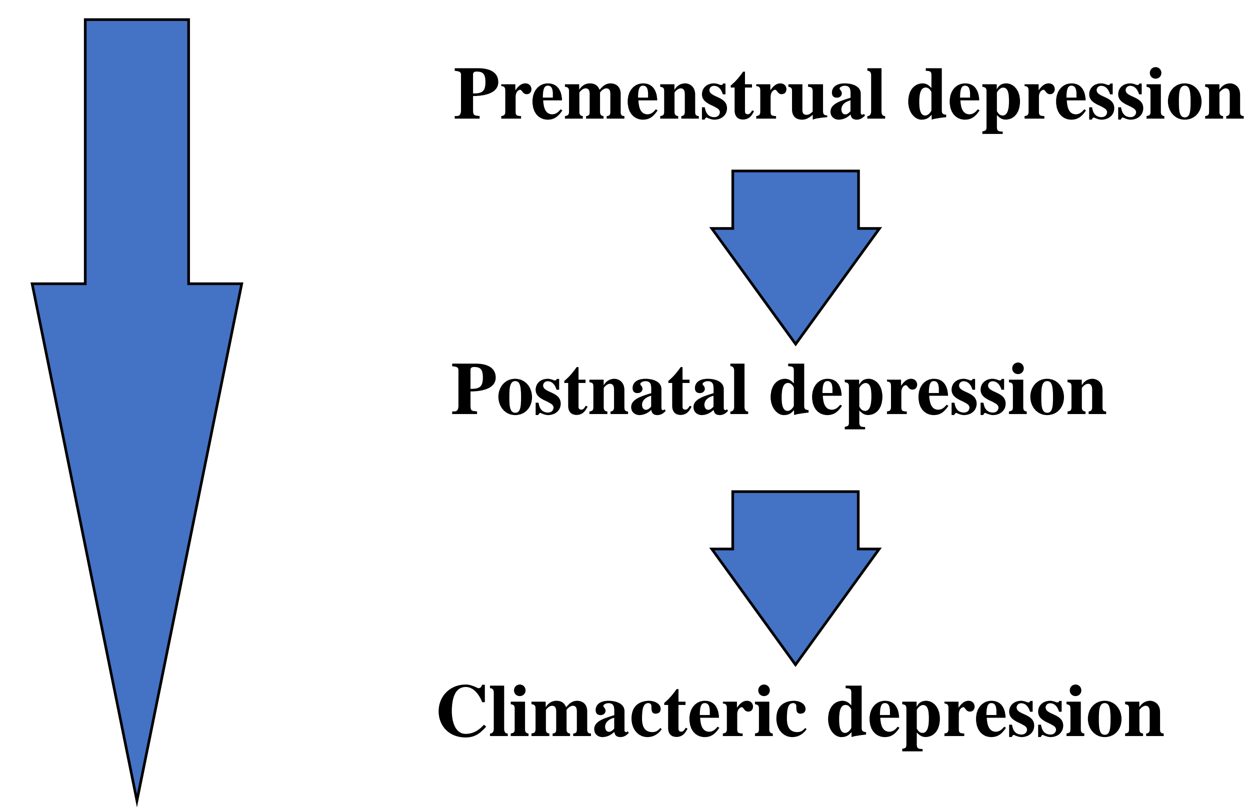
- Current PMS terminology should be maintained because PMDD refers to only one type of severe form of PMS.

- Education of public and HCPs is the key issue going forward.

- It is vital that there is universal recognition of the severe impact that PMS can have, whatever terminology is used.

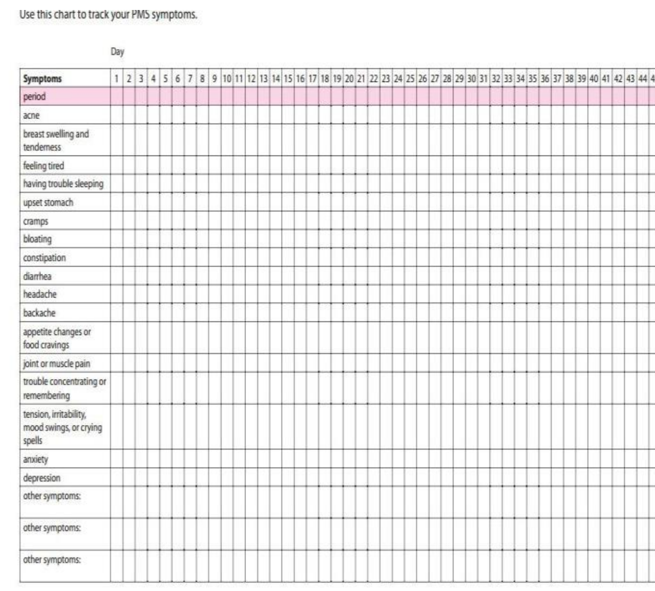
NAPS trustees' consensus statement (Sept 2017)

The triad of estrogen responsive depressive disorders



Studd J, Panay N. Hormones and depression in women. Climacteric. 2004 Dec;7(4):338-46.

Symptom diaries – key to diagnosis


Use this chart to track your PMS symptoms.

Day

Symptoms	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45
period																																													
acne																																													
breast swelling and tenderness																																													
feeling tired																																													
having trouble sleeping																																													
upset stomach																																													
cramps																																													
bloating																																													
constipation																																													
diarrhea																																													
headache																																													
backache																																													
appetite changes or food cravings																																													
joint or muscle pain																																													
trouble concentrating or remembering																																													
tension, irritability, mood swings, or crying spells																																													
anxiety																																													
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- Symptoms should be recorded prospectively, over two cycles using a symptom diary
- Retrospective recall of symptoms is unreliable

- Many symptom diaries available on line
- Cycle tracking apps becoming increasingly popular
- Daily Record of Severity of Problems (RSP) is well established and simple to use (www.rcog.org.uk)
- Screening question: How many good days do you have a month?

http://www.pms.org.uk/app/uploads/2019/10/NAPS-MENSTRUAL-DIARY.docx

Screening and Differentiation: PMS and other common psychiatric disorders

- Screening question: How many good days do you have a month?

- DDx: Bipolar disorder, borderline personality disorder
  - Psychiatric disorders do not follow the regularity of the ovarian cycle[¥]
  - Other psychiatric disorders may be co-morbid or exacerbated

- Differentiation: Symptoms cause significant impairment during the luteal phase of the menstrual cycle, resolving with menstruation.

[¥] Exception: PMDD

PMS – that's too complicated for me?

- Hormones are not completed
- They follow a logic
- They go in a cyclical predictable pattern
- The menstrual cycle is a seesaw
- Push one side, the other reacts

- PMS treatment principles aim to maintain status quo
- Balance and equilibrium
- Daily balance with no variability = No PMS

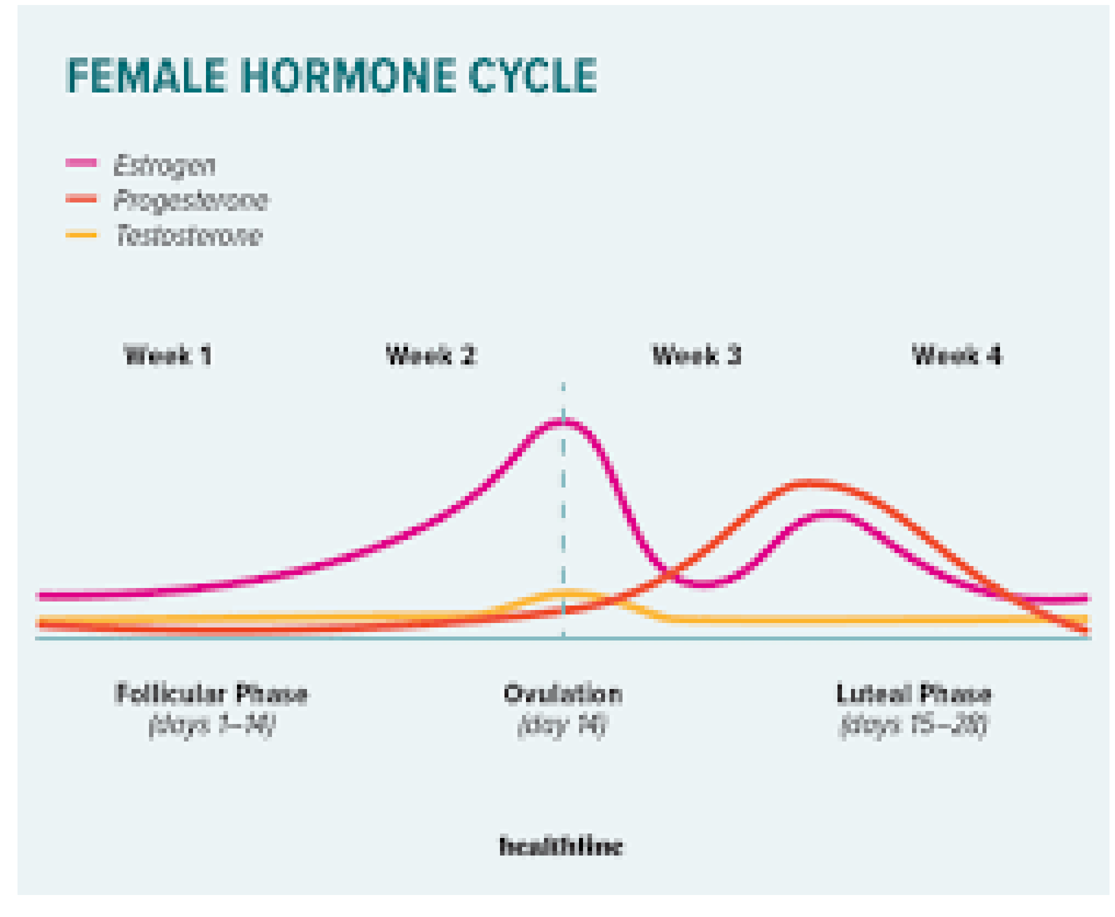
- Finding the individual treatment combination is the challenge

Explaining PMS – Dx from clinical presentation

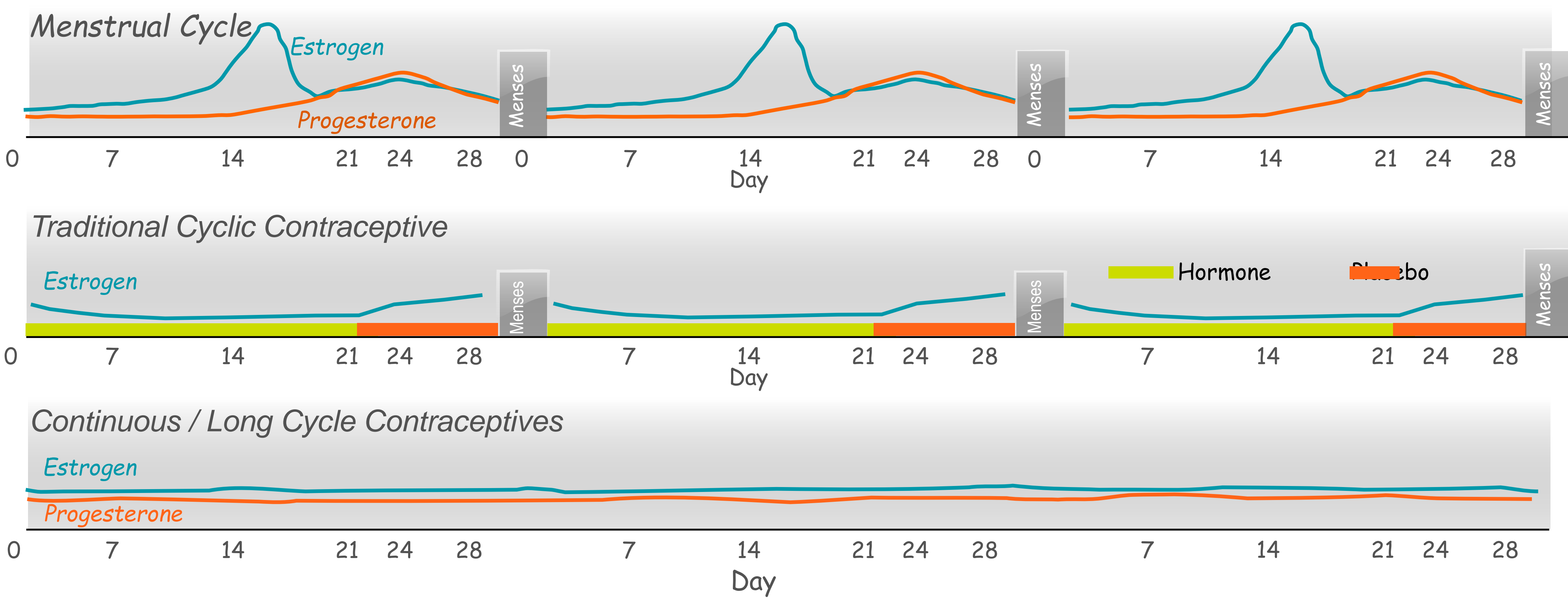
There are no diagnostic tests for PMS

- Light switch

- Seesaw



Moderation of Hormonal Fluctuations



PMS, Pregnancy, Progesterone

- ‘I felt the most well when pregnant’
- ‘The best time of my life’

WHY?

During pregnancy there are no cyclical hormones

Hormone leaves increase serotonin and improves mood

Consequence

- Led to licenced progestogens for PMS
- Encouraged use of COCP
- Synthetic progestogens generally not tolerated and exacerbate symptomology

PMS Guidelines RCOG & NAPS

First line	Exercise, cognitive behavioural therapy, vitamin B6 Combined new generation pill (cyclically or continuously) Continuous or luteal phase (day 15–28) low dose SSRIs, e.g. citalopram/escitalopram 10 mg

↓

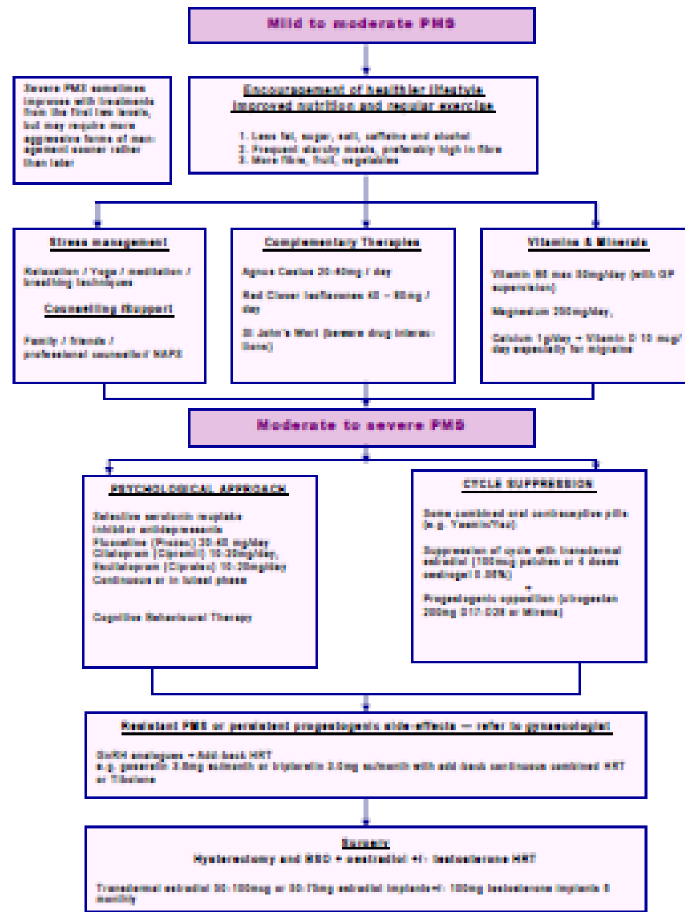
Second line	Estradiol patches (100 micrograms) + micronised progesterone (100 mg or 200 mg [day 17–28], orally *or* vaginally) or LNG-IUS 52 mg Higher dose SSRIs continuously or luteal phase, e.g. citalopram/escitalopram 20–40 mg

↓

Third line	GnRH analogues + add-back HRT (continuous combined estrogen + progesterone [e.g. 50–100 micrograms estradiol patches *or* 2–4 doses of estradiol gel combined with micronised progesterone 100 mg/day] or tibolone 2.5 mg)

↓

Fourth line	Surgical treatment ± HRT



https://doi.org/10.1111/1471-0528.14260

www.pms.org.uk

1. Case Study – Sally – Classical PMS

- Indra was 16 years old, troubled teenager at school
- Regular menses
- Regularly excluded for aggressive outburst
- Self harmed
- High achiever - failing in her studies
- High parental expectations
- Socially isolated
- Labelled borderline personality disorder
- Not sexually active
- Grandmother noticed a cyclical pattern of behaviour related symptoms

Legal & practical considerations

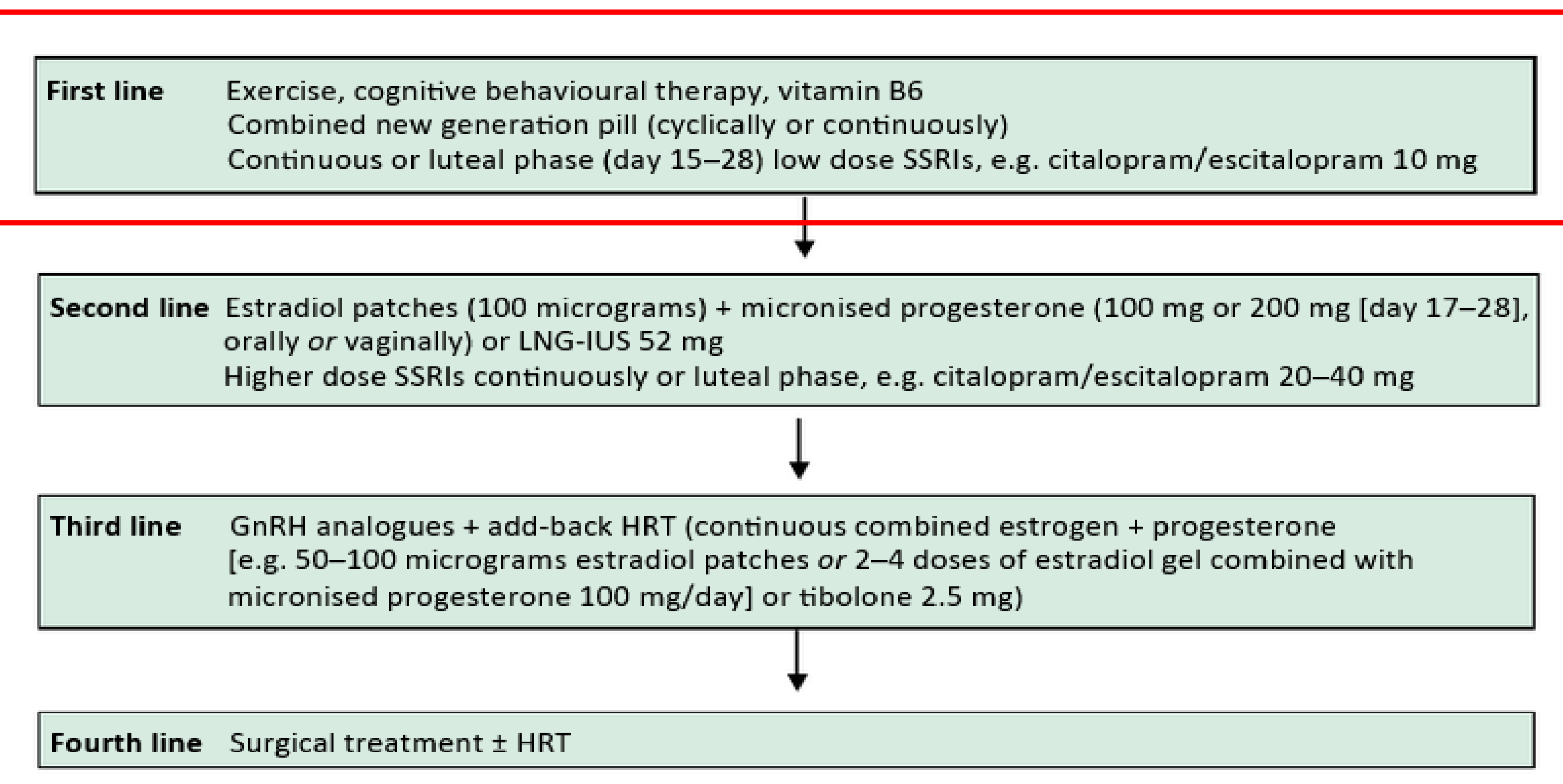
Legal

- Gillick competence
- Mental capacity
- Safeguarding vulnerable children
- Prescribing off-label drugs and regimens in children

Practical

- Engaging a teenager is not easy – compliance, peer pressure
- Parents with own agendas and ideas
- Parental support
- GP support

RCOG decision making algorithm



- CBT
- Parental education
- After school club-social skills / confidence
- School support
- Yasmin COCP, B2B (Drospirenone)
- @ 4/12 changed to Zoely COCP with estradiol, B2B (nomegestrol acetate)
- @ age 24, graduated with 1st class hons degree in engineering

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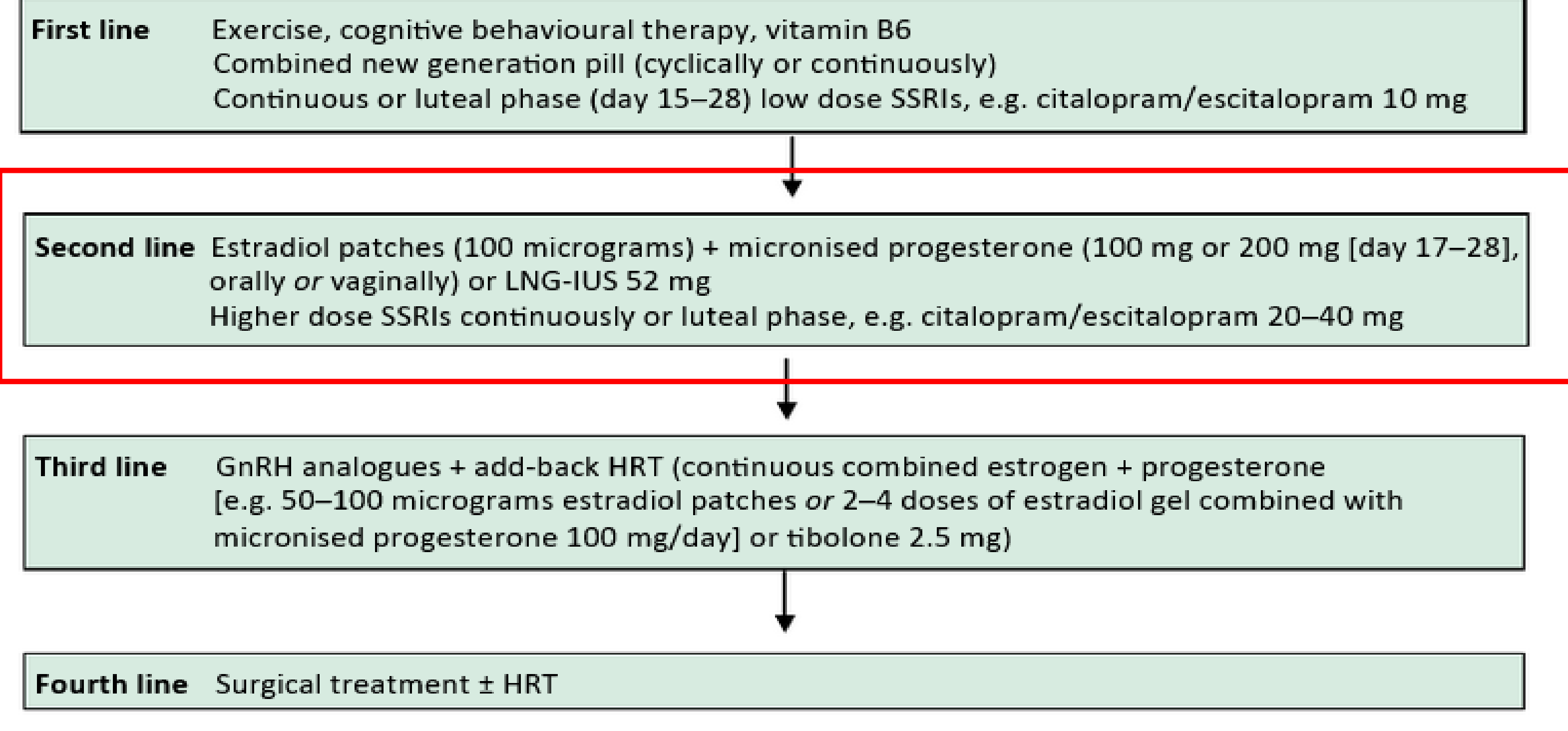
2. Case Study – Miriam - PMDD

- Miriam was 26 years old, para 1 age 18 months
- Menstrual cycles returned regularly
- New onset cyclical depression, anxiety, suicidal ideation
- ‘Jekale and Hyde’ each month
- No background psychopathology
- Never tolerated the COCP-very depressed
- Marital relationship breaking down
- Tried self help strategies and CBT
- Self diagnosis PMDD
- Rx: Citalopram – helped a little
- Contraception: Condoms
- Symptom diary consistent with prestation

RCOG decision making algorithm



First line	Exercise, cognitive behavioural therapy, vitamin B6 Combined new generation pill (cyclically or continuously) Continuous or luteal phase (day 15–28) low dose SSRIs, e.g. citalopram/escitalopram 10 mg
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Third line	GnRH analogues + add-back HRT (continuous combined estrogen + progesterone [e.g. 50–100 micrograms estradiol patches *or* 2–4 doses of estradiol gel combined with micronised progesterone 100 mg/day] or tibolone 2.5 mg)
Fourth line	Surgical treatment ± HRT

- SSRI changed to sertraline via GP
- Psychotherapy and ongoing GP reviews to assess suicide risk
- Cycle suppression with Estradiol 100mcg patches
- Cyclical utrogestan 200mg PO, then PV off label to reduce side-effects
- @4/12 changed to Kyleena off label with twice yearly USS
- @12 months relationship now back on track

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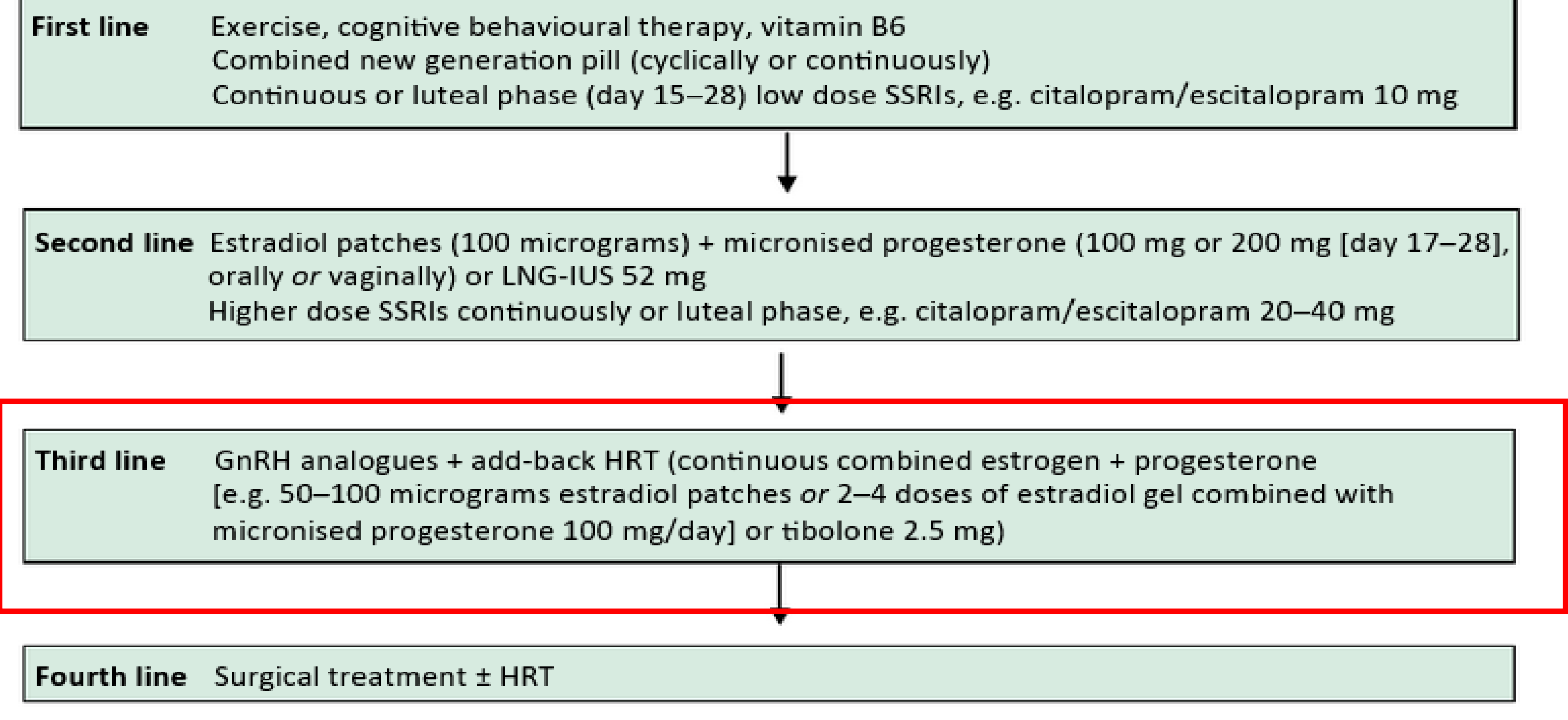
3. Case Study – Iona – PMDD
Our typical patient in clinic

- Iona age 36, para 0
- PMS since age 21, getting worse each year
- ‘I’m two people each month, I don’t recognise myself’
- ‘I’m desperate, I can’t go on. I’m very happy expect these 7 days’
- Self medicates with alcohol
- Does not want children at any time
- Contraception: condoms
- Wants a hysterectomy
- Tried depo provera, cocp, mirena - ‘I went mad, I was very suicidal’

RCOG decision making algorithm



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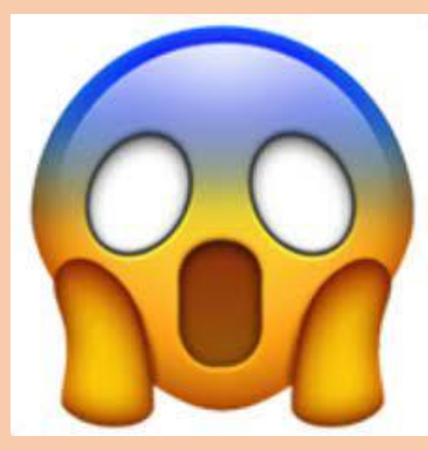
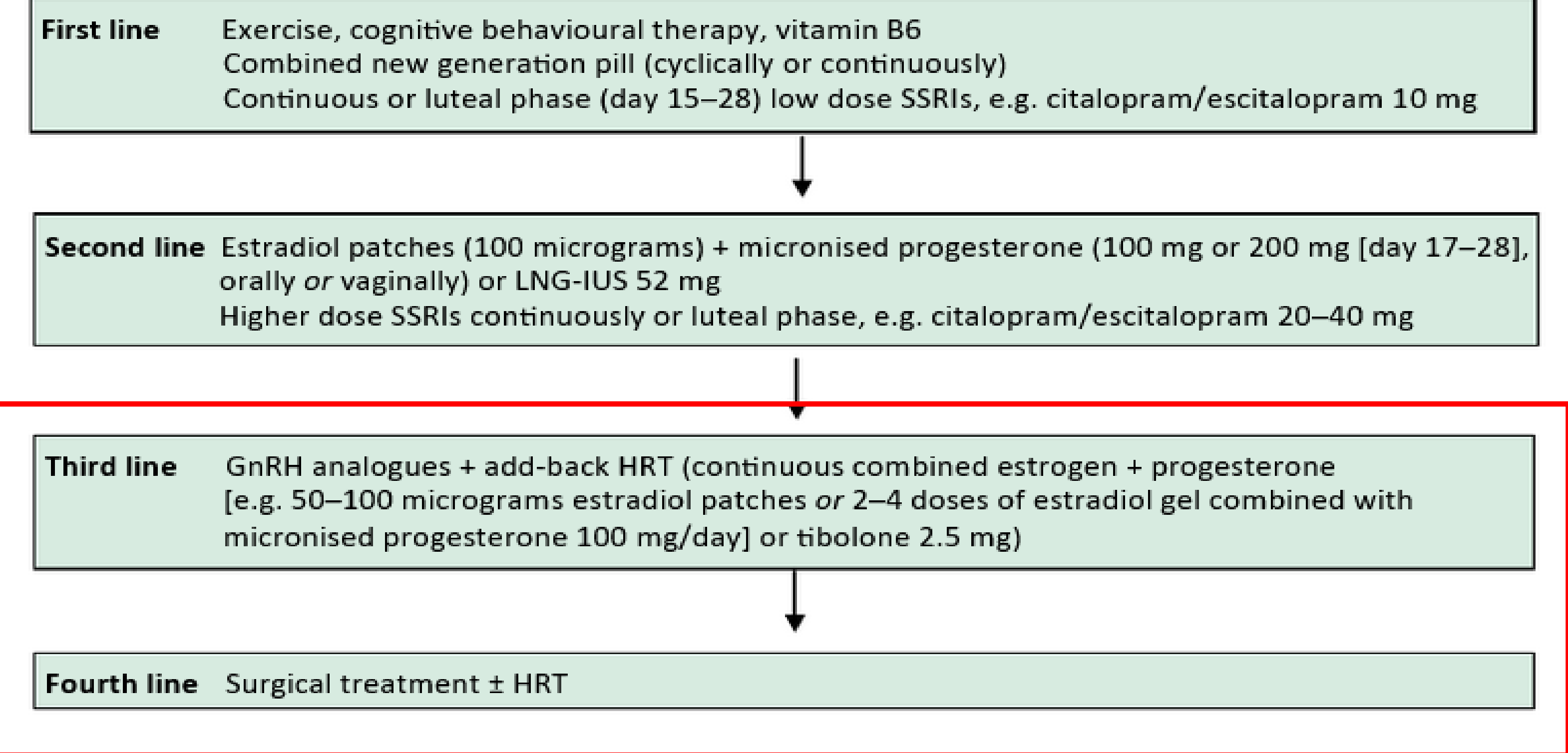
- Second line options attempted but cycle suppression not achieved
- Utrogestan poorly tolerated PV off-label and 'messy'
- Cyclical depression and suicidal ideation escalating
- Decapeptyl 11.25mg 10-12 weekly + estradiol 75mcg add back
- Contraception condoms
- Changed to dydrogesterone (DGN) 5mg daily
- @6/12, all symptoms resolved
- @18/12, agreed to continue regimen indefinitely without hysterectomy
- @age 48, still on Rx with BMD every 18 months
- No longer abuses alcohol - 9 years sober
- GnRHa to be discontinued between ages 51-55

4. Case Study – Nadia – Variant PMS

- Nadia was 38 years old, para 3
- Primary school teacher
- Brittle unstable asthma since menarche
- Regularly admitted to A&E and ICU (monthly)
- Asthma diary consistent with cyclical attacks and admissions
- On maximum asthma intervention
- Very positive can do attitude to life



RCOG decision making algorithm



- Third line intervention as with previous patient
- Intolerant to all progestogens – IUC admission
- Acute allergic reaction to GnRHa – IUC admission
- Elective TAHBSO – post op crash call x2
- Estrogen only replacement
- All cyclical exacerbations now stopped.
- @ age 49, still brittle asthma with regular A&E attendances but QOL significantly improved
- Crash trolley always at hand in clinic!

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Heads Together

'Too often, people feel afraid to admit that they are struggling with their mental health. This fear of prejudice and judgement stops people from getting help and can destroy families and end lives.'

(www.headstogether.org.uk/)

…. Or is it that sometimes we are too afraid to listen and act because be don't understand or don't believe?

What do we really mean when we say – first do no harm?

So here is the challenge of PMS…. to hear what's being said, to see its impact, and take time to understand

NHS
THANK YOU

Resources

NAPS - National Association for Premenstrual Syndrome

- https://www.pms.org.uk

Management of Premenstrual Syndrome - RCOG

- https://www.rcog.org.uk/globalassets/documents/guidelines/gt48... · PDF fil

Self-care for PMDD | Mind, the mental health charity ...

- https://www.mind.org.uk/information-support/types-of-mental-health...

PMS (premenstrual syndrome) - NHS

- https://www.nhs.uk/conditions/pre-menstrual-syndrome

Premenstrual syndrome (PMS) | Office on Women's Health

- https://www.womenshealth.gov/menstrual-cycle/premenstrual-syndrome

Premenstrual syndrome | Health topics A to Z | CKS | NICE

- https://cks.nice.org.uk/topics/premenstrual-syndrome