MANAGING MENOPAUSAL SYMPTOMS WITHOUT MEDICATION

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THE UNIVERSITY OF MELBOURNE

the women's
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Cochrane

WHAT ARE MENOPAUSAL SYMPTOMS?

- Vasomotor symptoms (hot flushes and night sweats)
- Vaginal dryness
- Mood disturbance
- Sleep disturbance
- Sexual dysfunction

NIH State-of-the-Science Panel. *Ann Intern Med 2005*

GENITOURINARY SYNDROME OF MENOPAUSE

New terminology coined by North American Menopause Society in 2014 to replace "vulvovaginal atrophy"

Describes a "constellation of symptoms including vaginal dryness and pain with intercourse, itching, burning and irritation, dysuria, urinary frequency/urgency and recurrent urinary tract infections"

? affects 50% of postmenopausal women but varied interpretation

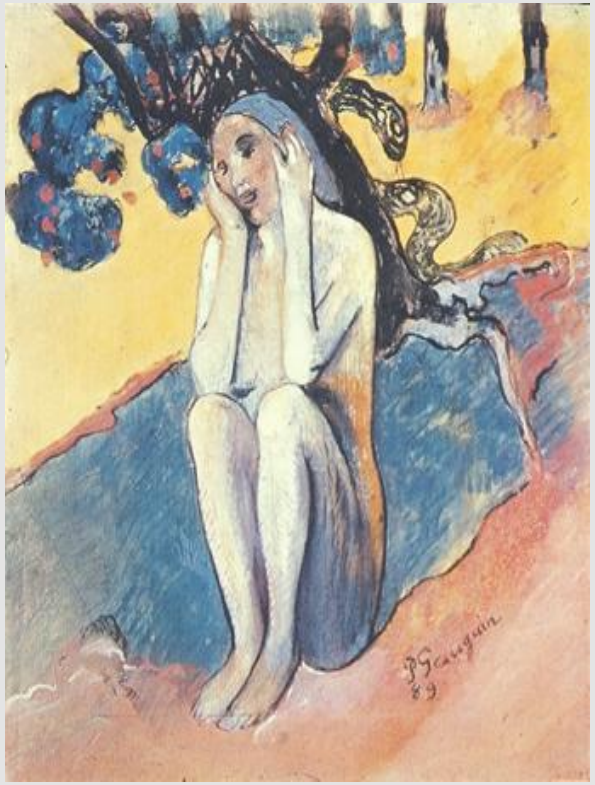
No diagnostic tools

No population-based data

Includes urinary symptoms (frequency, urgency, recurrent UTI) that are not associated with menopause

VASOMOTOR SYMPTOMS

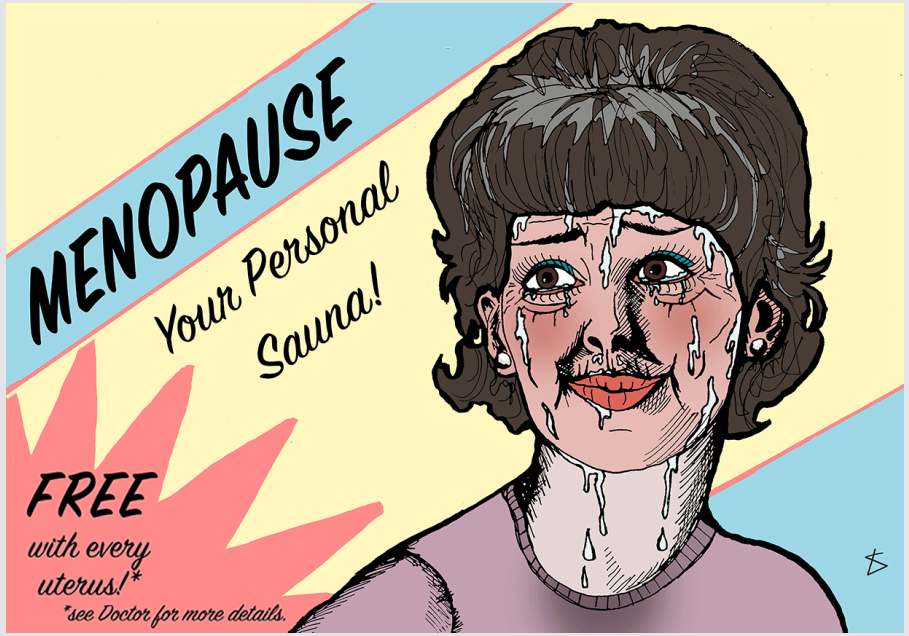
- Affect around 80% of women over the menopause transition
  - Up to 30% still symptomatic 10 years after menopause
- Described as "hot flushes" or "night sweats"
- Physiological characteristics similar but impact on women likely to be different
- Sleep disturbance due to night sweats may be more likely to lead to depression



Baker et al, 2018

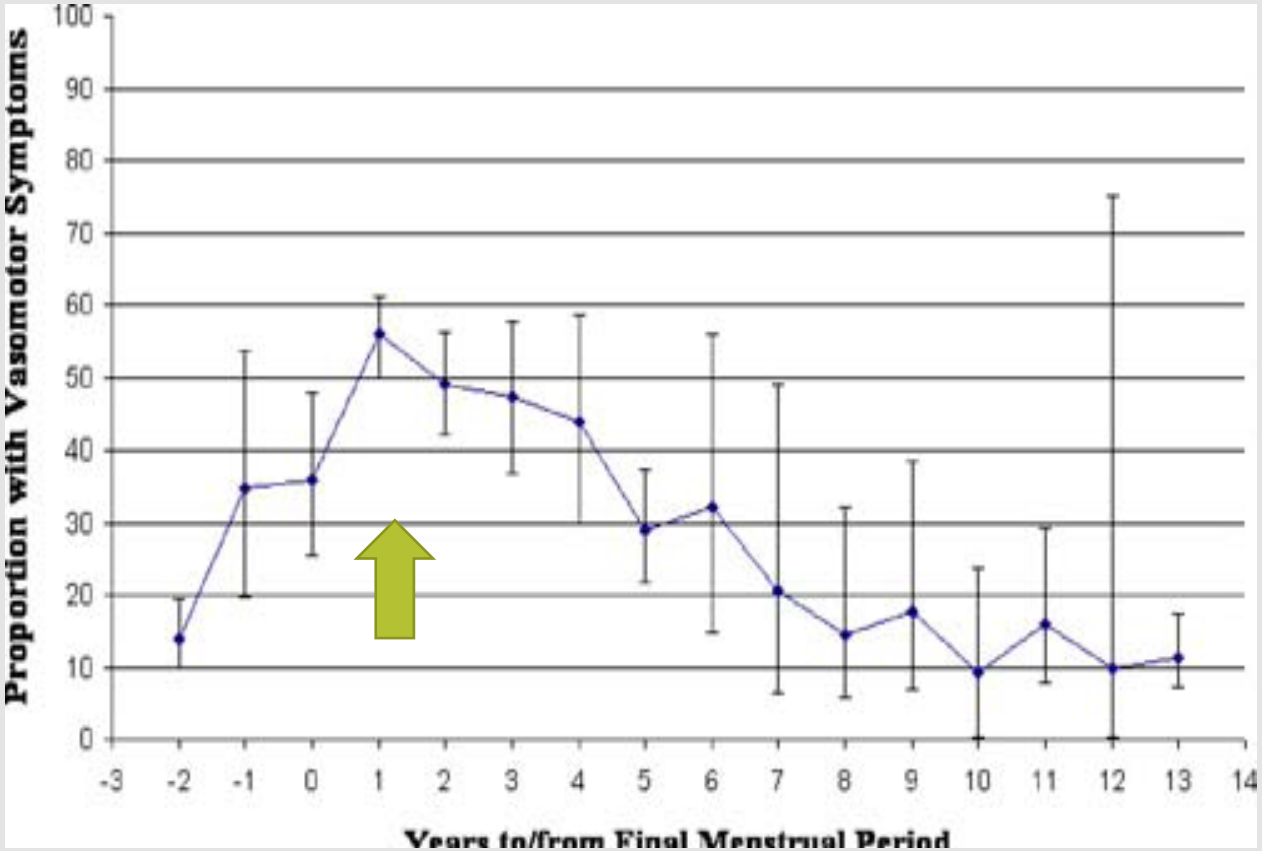
VASOMOTOR SYMPTOMS

- Main reason why women request treatment
- Leading patient priority for treatment
- Mean duration 7 years?
  - Includes women stopping and starting HT
- Duration after early/surgical/chemotherapy induced menopause is unknown



Kronenburg 1990, Politi et al 2008, Col et al 2008, Freeman et al 2014

DURATION OF VASOMOTOR SYMPTOMS



- Mean duration is 4-10 years
- Most common in the year around the final menstrual period

Politi et al 2008, Col et al 2008, Freeman et al 2014, Avis et al 2015

DRUG-FREE TREATMENTS

- Many women prefer “natural” approaches to managing menopause
- Non-pharmacological approaches are effective
- Integrating these into clinical practice is challenging

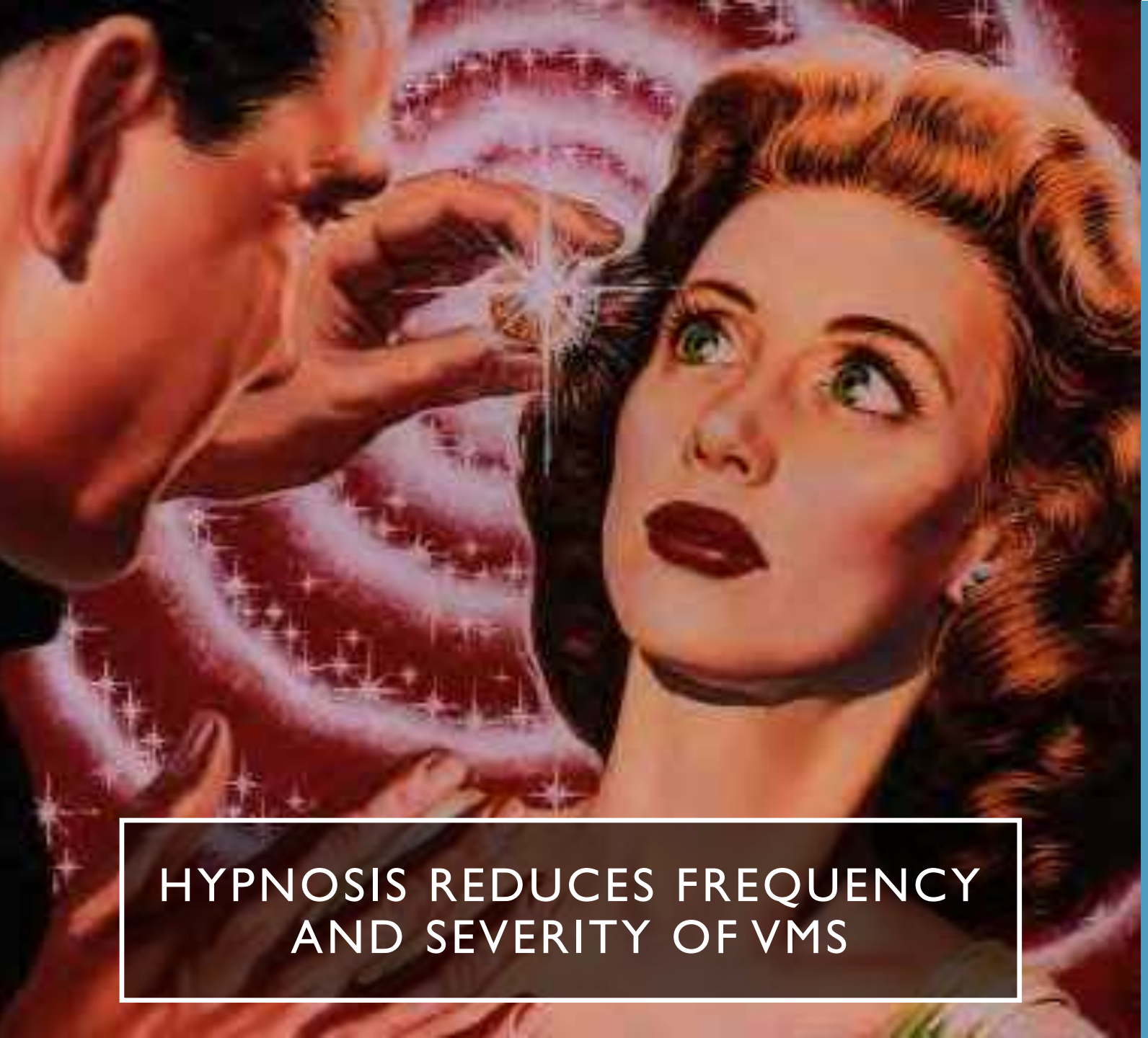
WHAT WORKS FOR VASOMOTOR SYMPTOMS?

DEPENDS ON WHAT YOU MEASURE

COGNITIVE BEHAVIOUR THERAPY: REDUCES PROBLEM RATING/INTERFERENCE

- Purpose designed CBT reduces the problem rating of vasomotor symptoms:
  - In healthy symptomatic women
  - After breast cancer
  - In working women
- "Side effects" improved mood, sleep and sexual function
- Recommended in international guidelines for managing menopause

Mann et al, 2012, Hunter et al, 2016, Green et al, 2019

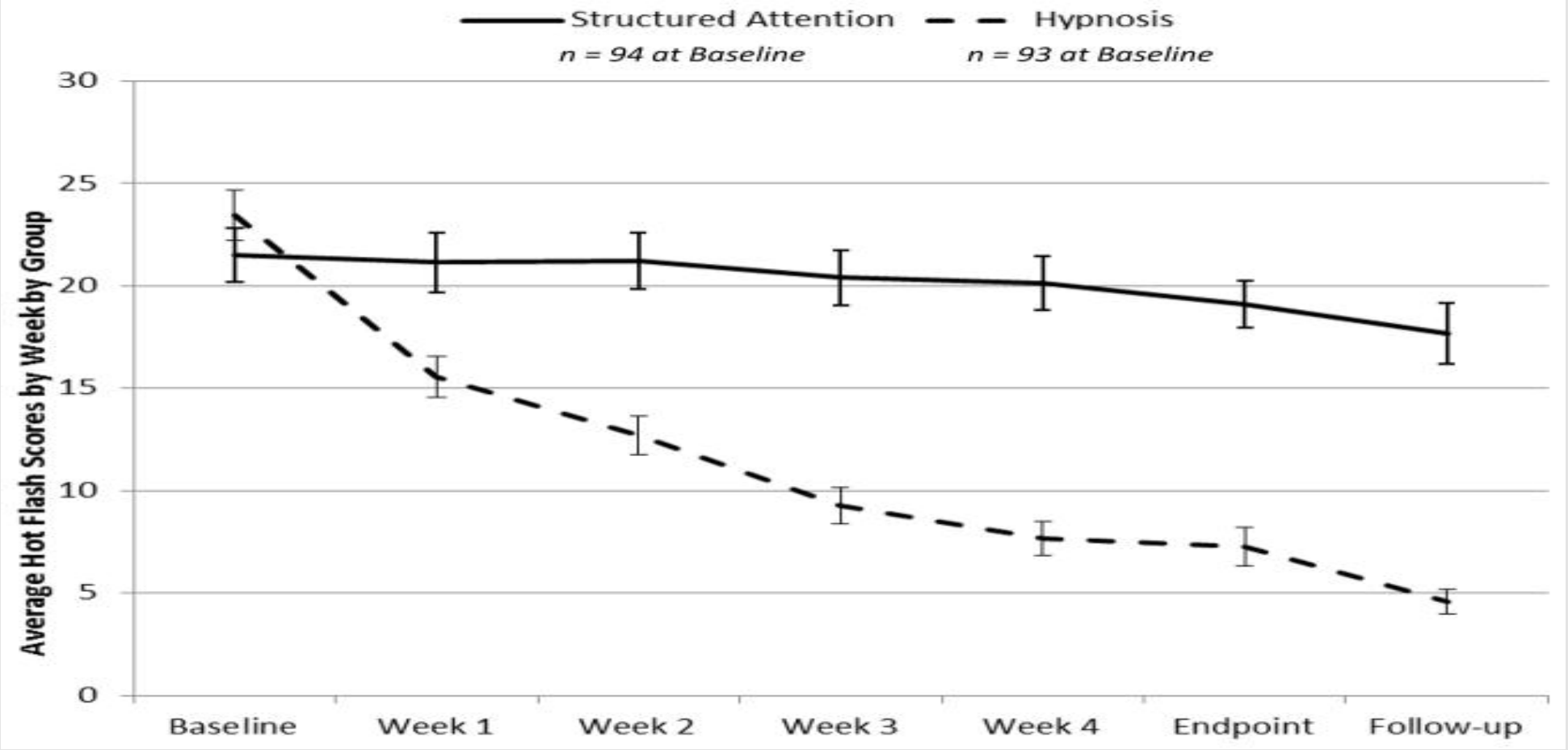


HYPNOSIS REDUCES FREQUENCY AND SEVERITY OF VMS

- Reduced frequency of vasomotor symptoms by 74% compared with 17% for controls
- Physiologically measured vasomotor symptoms reduced by 57% (vs 10% with controls)
- May also be effective after breast cancer

Elkins et al, 2008, 2013

REDUCTION IN HOT FLASH SCORE WITH HYPNOSIS COMPARED TO CONTROL



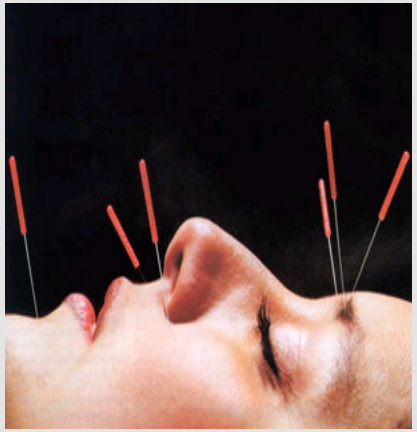
Elkins et al, 2013

WHAT DOES NOT WORK FOR VASOMOTOR SYMPTOMS

Yoga

Avoiding spicy food or hot drinks

Acupuncture



Vitamin E

Herbal supplements

Paced breathing

Exercise

Daley et al 2011, Cohen et al 2013, Woods et al 2013, Garcia et al 2013, Newton et al, 2014, Ee et al, 2016, Stefanopoulou and Grunfeld 2017

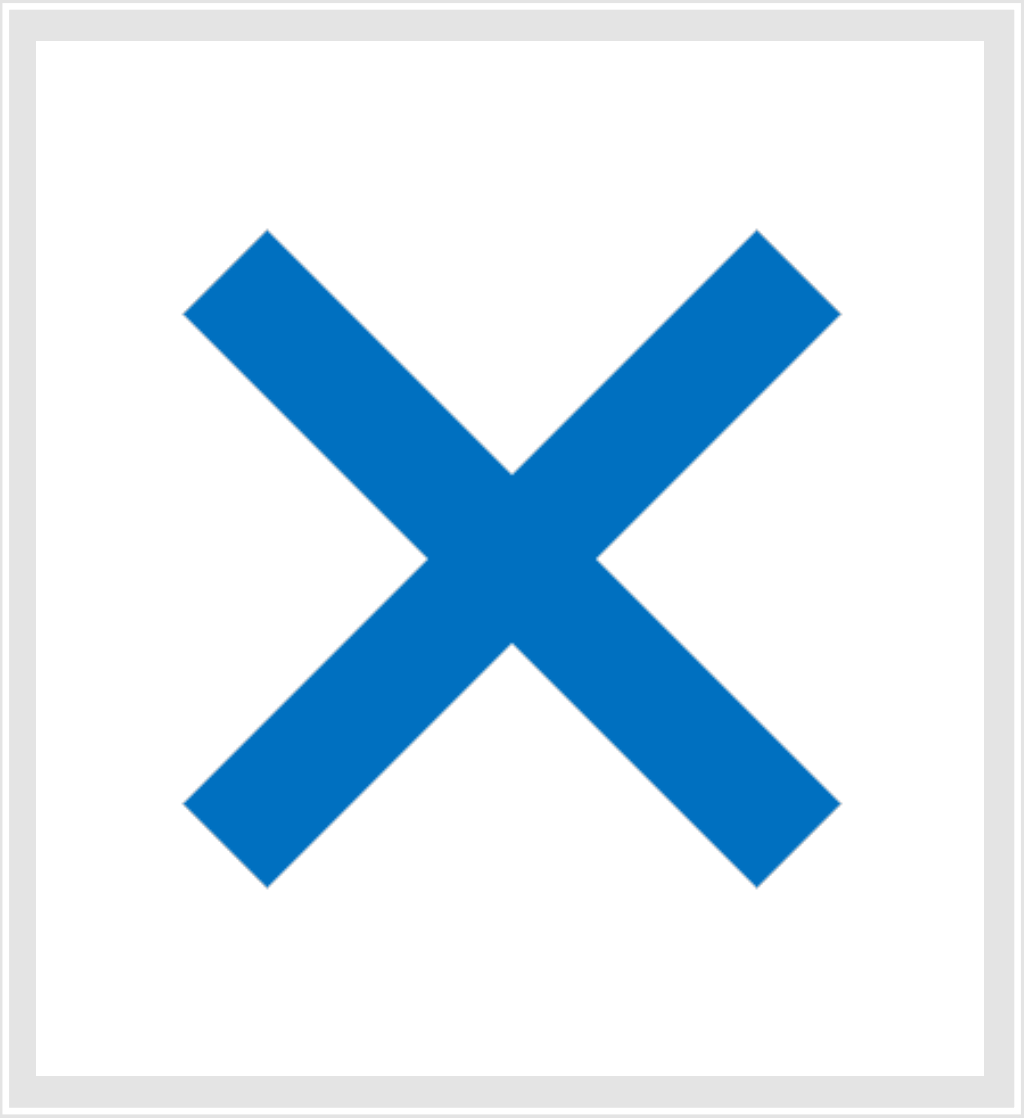
AVOID

Bio-identical compounds

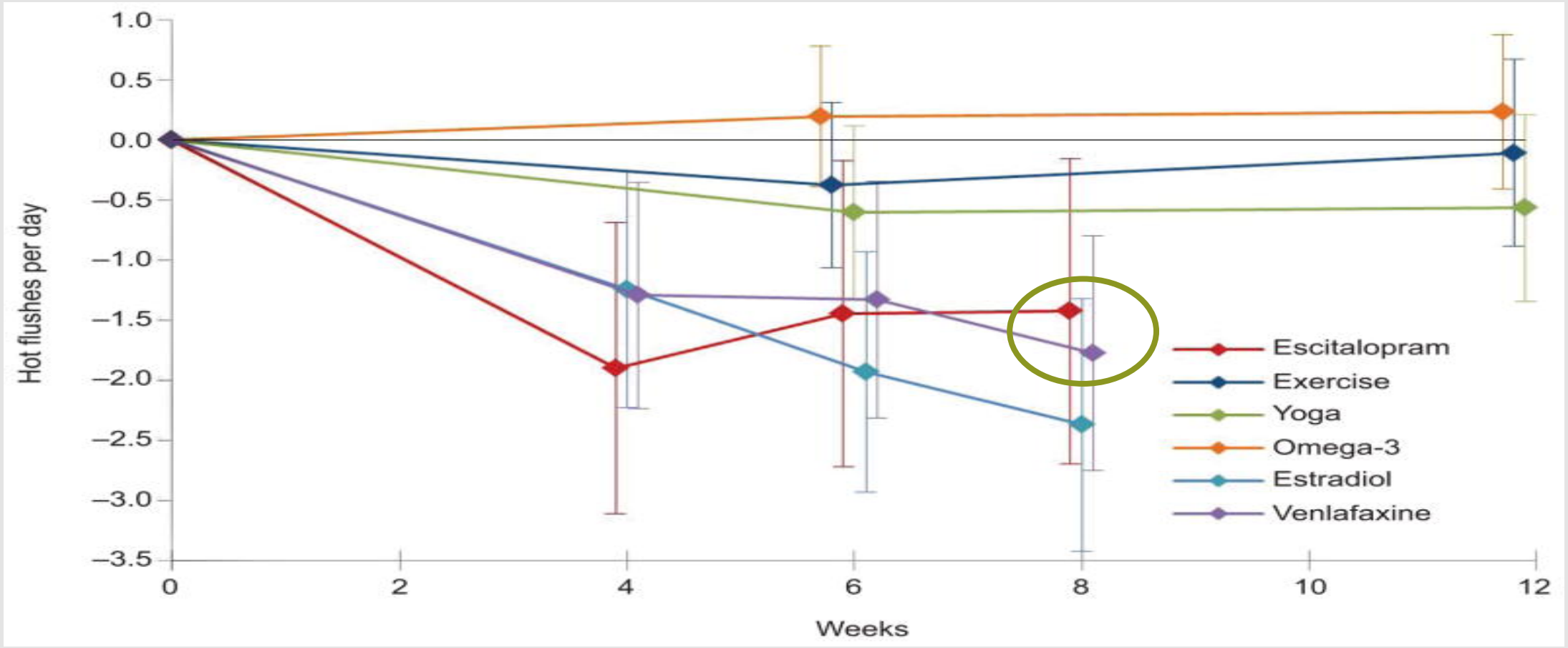
- May work but commonly contain high dose sex steroids including estrogen
- Progestogen creams do not provide endometrial protection

Other OTC products

- Limited evidence for benefit over placebo
- Concern about product content and safety

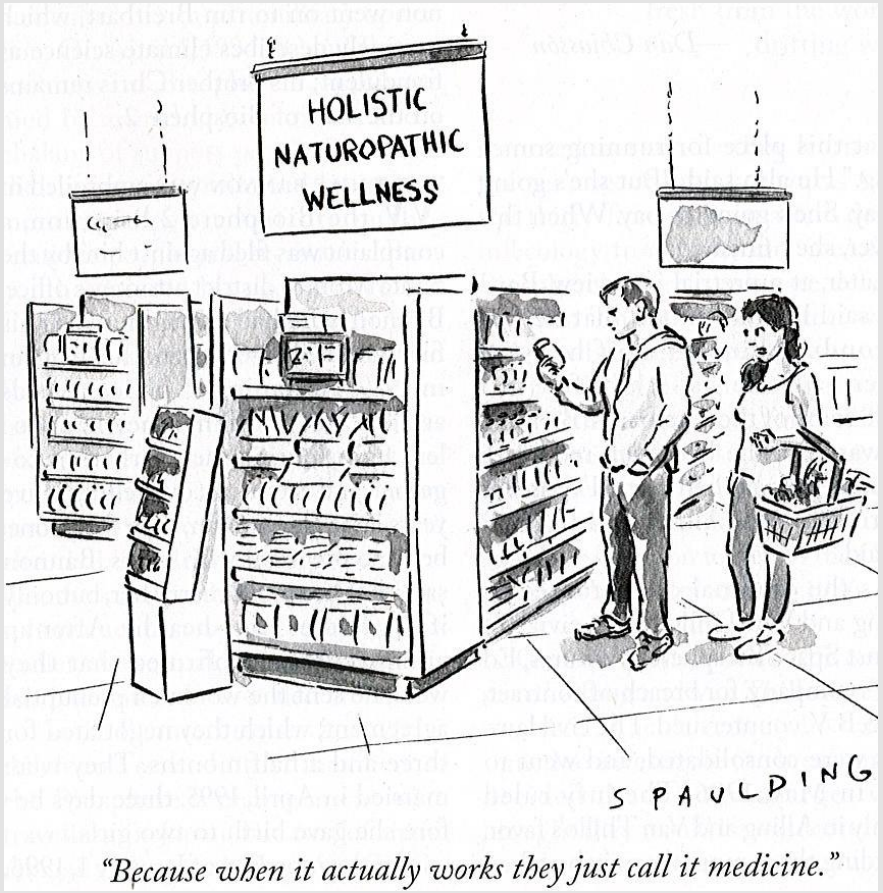


WHAT WORKS BEST FOR VASOMOTOR SYMPTOMS?



Effect of each intervention on changes from baseline in daily mean vasomotor symptom frequency, relative to control. *Guthrie et al, 2015*

WHEN IT WORKS, THEY CALL IT MEDICINE

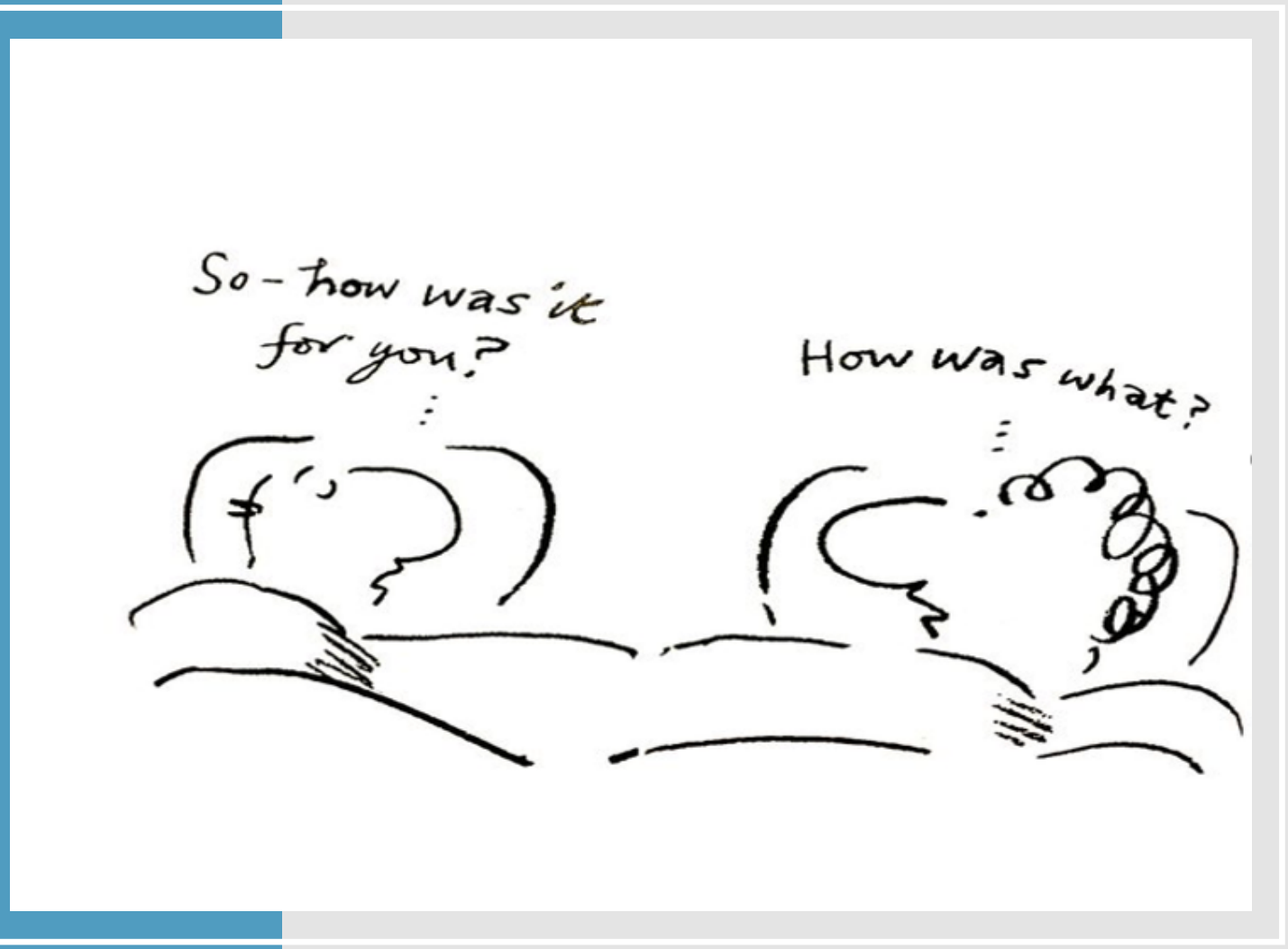


"Because when it actually works they just call it medicine."

MANAGING SEXUAL DYSFUNCTION WITHOUT MEDICATION

DIAGNOSING SEXUAL DYSFUNCTION

- Hypoactive sexual desire disorder affects 10% of women
- Lack of motivation
- Lack of desire or response
- Causes distress



Clayton et al, 2018

MULTIPLE CAUSES FOR SEXUAL DYSFUNCTION

- Vaginal dryness – worse with aromatase inhibitors
- Changes in body image
- Changes in relationships
- Anxiety and depression
- Grief and anger

WHAT WORKS FOR VAGINAL DRYNESS: VAGINAL LUBRICANTS AND MOISTURISERS

- Vaginal dryness can lead to painful and discomfort during sexual activity

- Lubricants
  - Wide range of products available
  - Limited evidence to support clinical recommendations

Mitchell et al, 2018

WHAT WORKS FOR VAGINAL DRYNESS: LUBRICANTS

- **Olive Oil, Vaginal Exercise, and MoisturizeR (OVERcome) for breast cancer patients**
  - Significant improvements in dyspareunia, sexual function, and quality of life
- **Sexuality after Breast Cancer (SAB)**
  - Double blind RCT of water vs silicone based lubricant in breast cancer patients with sexual discomfort (n=38):
  - Primary outcome: Discomfort during sexual activity
  - Secondary outcomes: acceptability, distress, pleasure, habit
- **Results**
  - >90% reported distress at baseline
  - 88% continued to report distress despite lubricant use
  - Greater pain relief with silicone lubricant (OR 5.4, 95% CI 1.3-22.1, p=0.02).
  - Women preferred silicone-based to water-based (65% vs 35%)

Juraskova et al 2013, Marino et al, 2016, Hickey et al, 2017

WHAT WORKS FOR SEXUAL PROBLEMS: SEX THERAPY?

- Education
- Manage contributory factors
  - Depression, pain, incontinence
  - Sex therapy
    - CBT
    - Mindfulness
  - Evidence base for efficacy is uncertain
  - Preferred approach is unclear

(New Yorker)

WHAT DOES NOT WORK FOR SEXUAL PROBLEMS?

- Moisturisers: no good evidence for efficacy despite US market of >$200m
- Pelvic floor exercises
- Vaginal laser
  - Insufficient evidence for safety or efficacy
  - Potential for harm: increased pain after laser vs vaginal estrogen

Lara et al, 2012, Mitchell et al, 2018, Cruz et al, 2018, Hickey and Richards, 2019

- Used in cosmetic surgery to cause local inflammation and tissue remodelling
- Data from small observational studies and randomised trials show equivocal results
  - Less effective than vaginal estrogen
  - Varied outcome measures used
  - No sham control arm
  - Increased pain with laser vs vaginal estrogen

Hickey and Richards 2019

VAGINAL LASERS

- TGA: Not listed for this indication in Australia
- Ongoing sham randomised trials vs estrogen and in breast cancer patients will report in 2020
  - **Until then – don't do it!**

"These products have serious risks and don't have adequate evidence to support their use for these purposes. We are deeply concerned women are being harmed."

FDA, 2018

MANAGING SLEEP DISTURBANCE WITHOUT MEDICATION

SLEEP DISTURBANCE AND MENOPAUSE

- Sleep disturbance is one of the most common reasons women seek treatment at menopause
- Around one third report new onset sleep disturbance during the menopause transition
  - Difficulty falling asleep
  - Multiple awakenings, difficulty getting back to sleep
  - Reduced sleep quality
  - Daytime tiredness and poor concentration
- Vasomotor symptoms only account for one third of time spent awake

Kravitz et al 2008, Soares et al 2007, Polo-Kantola 2011, Ameratunga et al 2012, Xu et al 2014, Baker et al, 2018

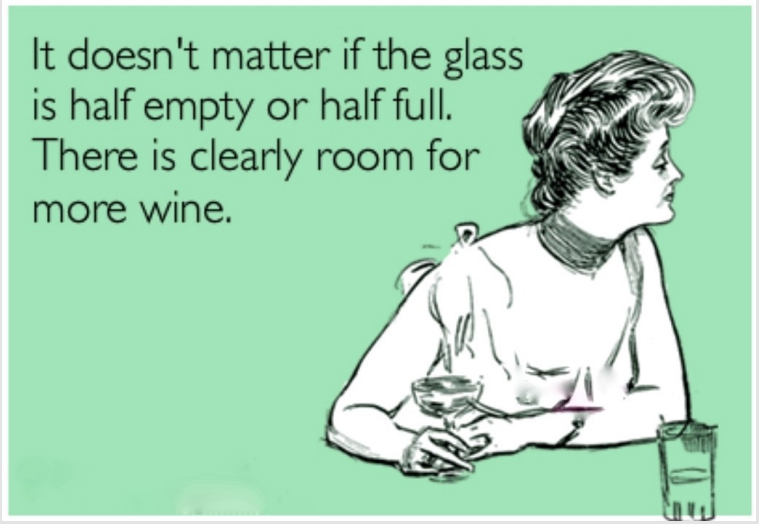
EVALUATING SLEEP DISTURBANCE AT MENOPAUSE

What is the problem?

- Difficulty falling asleep?
- Early morning wakening? Think depression
- Multiple awakenings? Think menopause

Other sources of sleep disturbance?

- Snoring partner
- Nocturia
- Evening alcohol consumption
- Clinically significant anxiety or depression

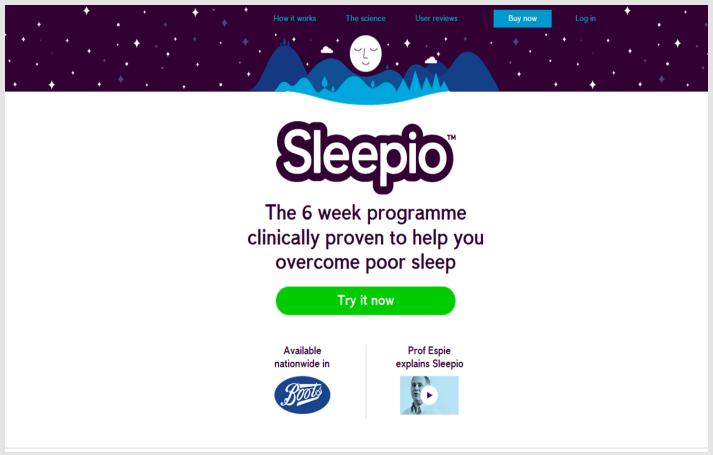


WHAT WORKS? COGNITIVE BEHAVIOUR THERAPY

- 8 week telephone-based CBT for insomnia in perimenopausal women
- Improved sleep (Insomnia severity index)
- Reduced sleep latency, wake time, and improved sleep efficiency
- Reduced interference due to vasomotor symptom

McCurry et al, 2016

WHAT WORKS: ONLINE CBT



CBT-I improves sleep at menopause

Espie et al 2012: http://www.sleepio.com/, (Morin & Benca 2012; Howell et al., 2014, McCurry et al 2016)

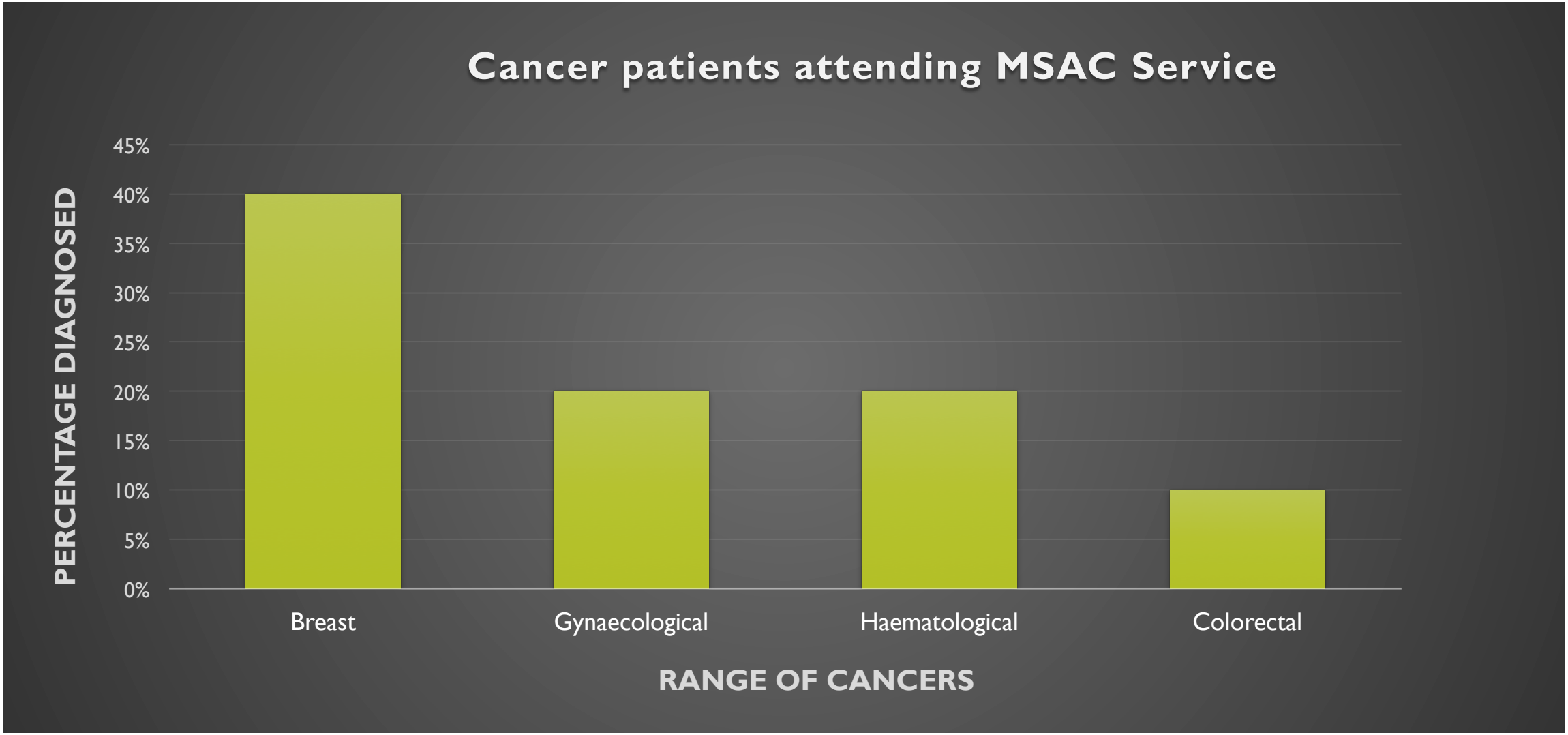
WHAT WORKS: STEPPED CARE

Component 1	• Development of self-management sleep resource
Component 2	• Implementation stepped-care sleep management program
Component 3	• Workforce development training and education

MULTIDISCIPLINARY MANAGEMENT OF MENOPAUSAL SYMPTOMS AFTER CANCER

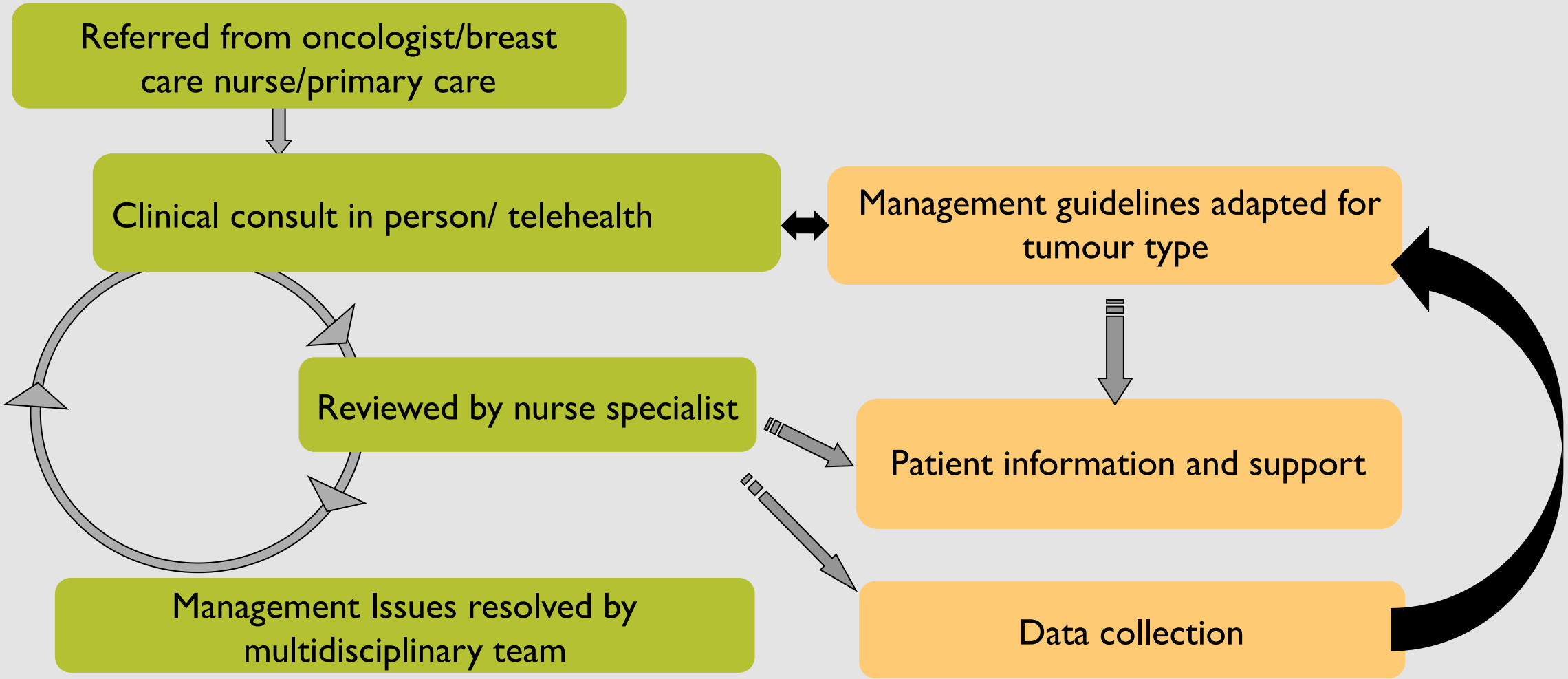
MULTIDISCIPLINARY MANAGEMENT OF MENOPAUSE AFTER CANCER (MSAC)

- Established in 2001
- Victorian service manages around 1000 women pa
  - Clinical team: gynaecologist, endocrinologist, GP specialising in sexual counselling
- Range of tumour types:
  - Breast (40%)
  - Gynaecological (20%)
  - Haematological (20%)
  - Colorectal cancers (10%)
- High-risk women pre and post risk-reducing bilateral salpingo-oophorectomy



Hickey et al, 2019

MANAGEMENT MODEL



- Establish
- Nature and timing of troublesome symptoms
- What the patient wants from treatment
- Provide information: Menopausal symptom, lifestyle modification

Troublesome vasomotor symptoms

Non-pharmacological treatments

- Purpose-designed CBT
- Hypnosis
- Consider acupuncture

Pharmacological treatments*

- Escitalopram or citalopram (10-20 mg)
- Venlafaxine 75mg CR
- Paroxetine (10-20 mg)**
- Gabapentin 100-900 mg/day or nocte
- Clonidine 0.1mg

Review efficacy after 1-2 months

Troublesome vaginal symptoms

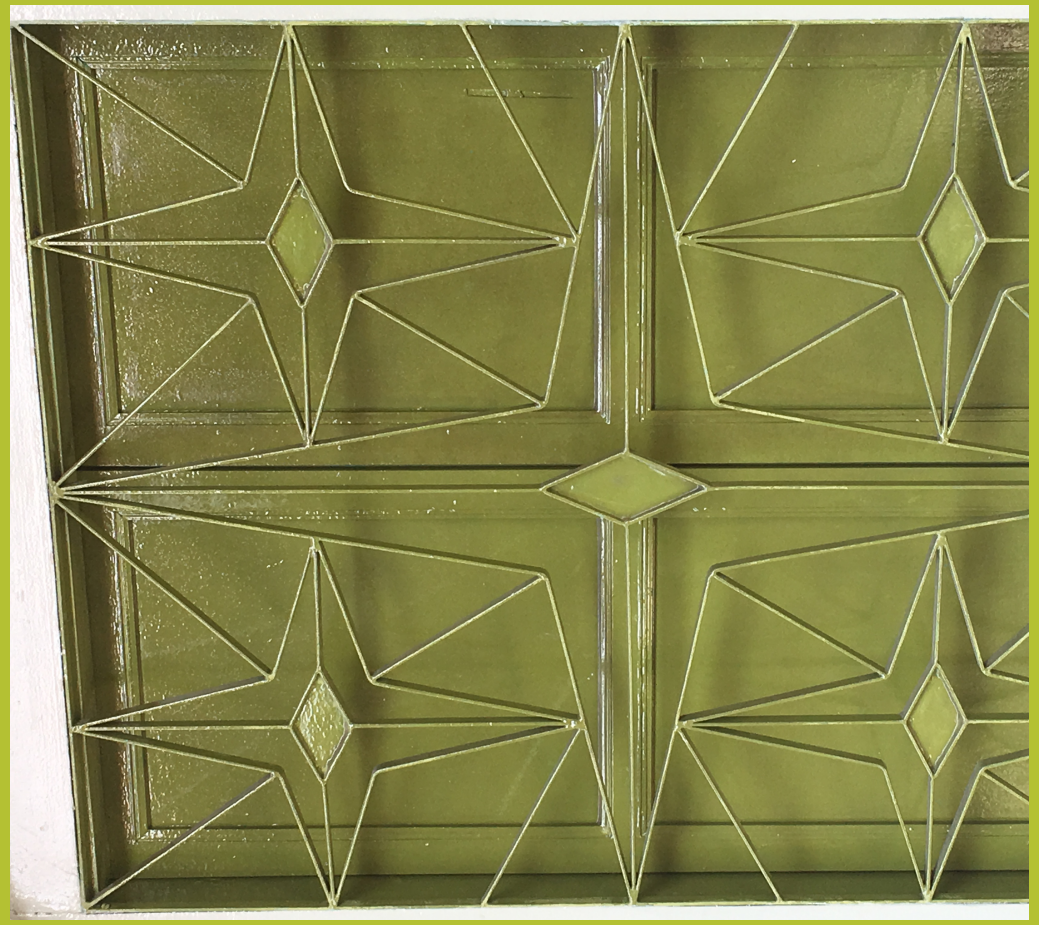
Exclude GVHD (autologous SCT)
Discuss vaginal estrogen with patient and treating oncologist (breast cancer)

For discomfort during sexual activity:
- Silicone based lubricants
- Water based lubricants
- Consider 4% lignocaine to the vulva

*no one pharmacological treatment has been shown to be superior to others

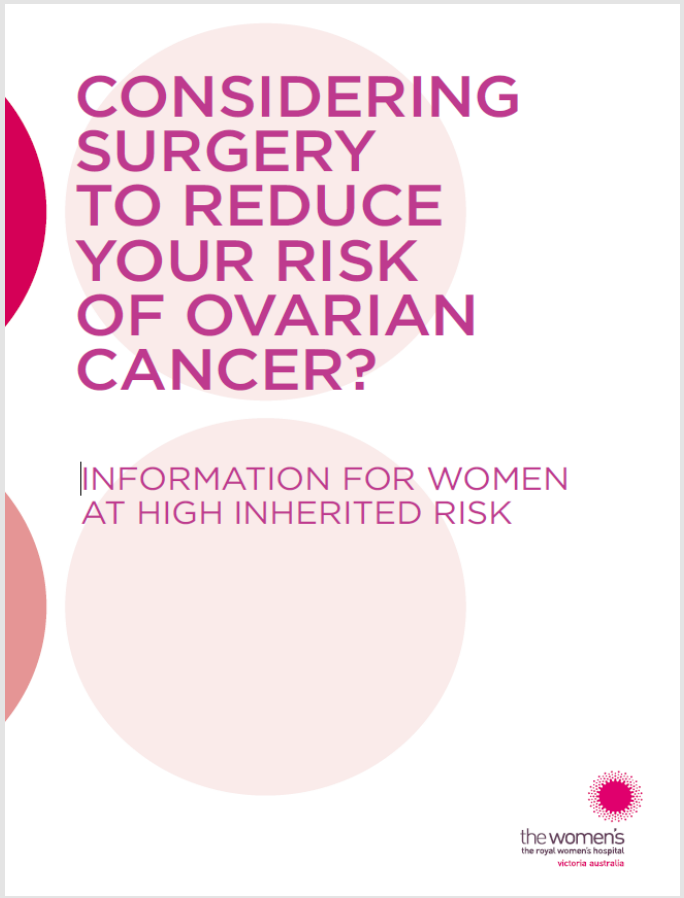
** avoid with tamoxifen

Hickey et al, BMJ 2017



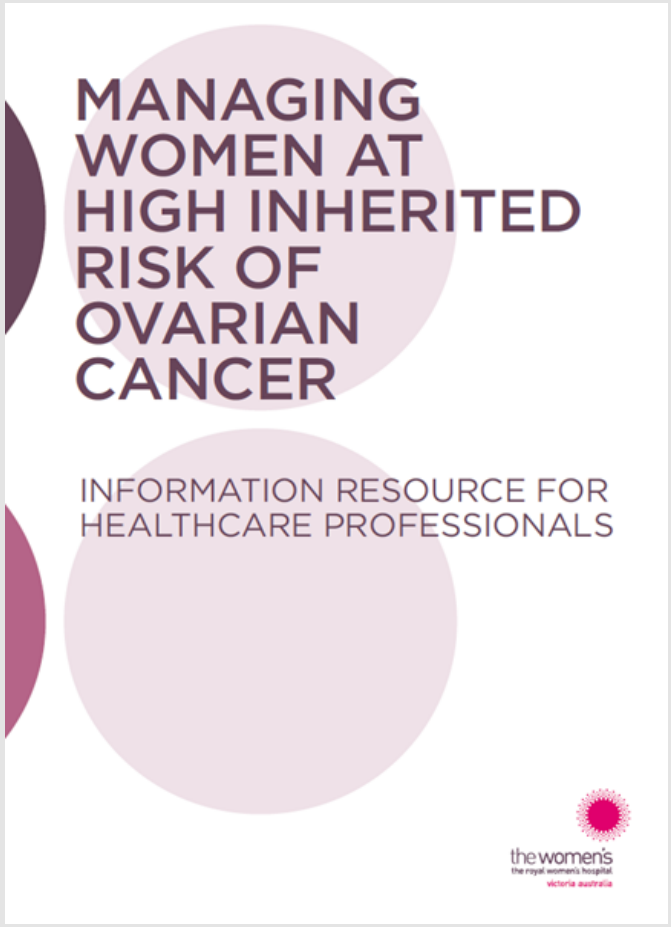
AROUND ONE IN 300 WOMEN ARE AT HIGH RISK OF OVARIAN CANCER

RESEARCH OUTCOMES: NEW RESOURCES FOR HIGH-RISK WOMEN



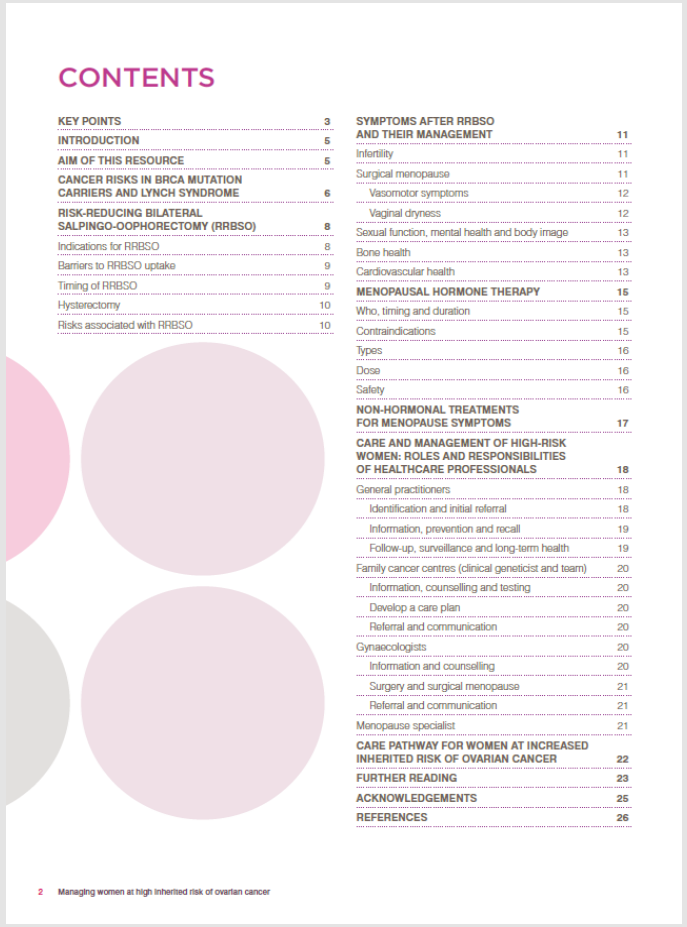
Hickey et al, 2019

RESEARCH OUTCOMES: NEW RESOURCES FOR HEALTHCARE PROFESSIONALS


MANAGING WOMEN AT HIGH INHERITED RISK OF OVARIAN CANCER

INFORMATION RESOURCE FOR HEALTHCARE PROFESSIONALS

the women's
the royal women's hospital
victoria australia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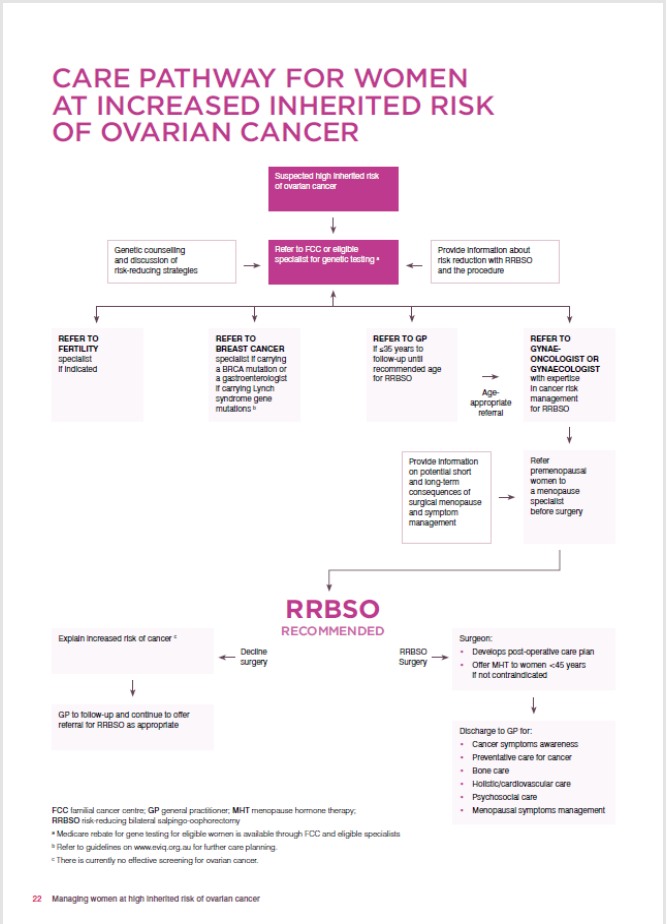
CARE PATHWAY FOR WOMEN AT INCREASED INHERITED RISK OF OVARIAN CANCER

Suspected high inherited risk of ovarian cancer

Genetic counselling and discussion of risk-reducing strategies

Refer to FCC or eligible specialist for genetic testing *

Provide information about risk reduction with RRBSO and the procedure

REFER TO FERTILITY specialist if indicated

REFER TO BREAST CANCER specialist if carrying a BRCA mutation or a gastroenterologist if carrying Lynch syndrome gene mutations [b]

REFER TO GP if ≤35 years to follow-up until recommended age for RRBSO

Age-appropriate referral

REFER TO GYNAE-ONCOLOGIST OR GYNAECOLOGIST with expertise in cancer risk management for RRBSO

Provide information on potential short and long-term consequences of surgical menopause and symptom management

Refer premenopausal women to a menopause specialist before surgery

RRBSO RECOMMENDED

Explain increased risk of cancer [c]

Decline surgery

RRBSO Surgery

Surgeon:
- Develops post-operative care plan
- Offer MHT to women <45 years if not contraindicated

GP to follow-up and continue to offer referral for RRBSO as appropriate

Discharge to GP for:
- Cancer symptoms awareness
- Preventative care for cancer
- Bone care
- Holistic/cardiovascular care
- Psychosocial care
- Menopausal symptoms management

FCC familial cancer centre; GP general practitioner; MHT menopause hormone therapy; RRBSO risk-reducing bilateral salpingo-oophorectomy

* Medicare rebate for gene testing for eligible women is available through FCC and eligible specialists

[b] Refer to guidelines on www.eviq.org.au for further care planning.

[c] There is currently no effective screening for ovarian cancer.

Hickey et al, 2019

COMMA: CORE OUTCOMES IN MENOPAUSE

COMMA: Core Outcomes in Menopause

- Menopausal symptoms are inconsistently measured in clinical trials
- Prevents data pooling and comparisons between treatments
- Clinical relevance of some outcome measures uncertain
- Vaginal pH and Percentage of parabasal cells

Core Outcome Sets

- Set of well-defined, discriminatory and feasible outcome
- Reflect the priorities of clinicians, researchers and patients
- To be included as a minimum dataset in all intervention studies

CORE OUTCOMES IN MENOPAUSE

Illiodromiti et al, accepted BJOG 2019, Christmas et al, in prep

THANKS!

Flesh after Fifty

Changing images of older women in Art

28 March – 3 May 2020