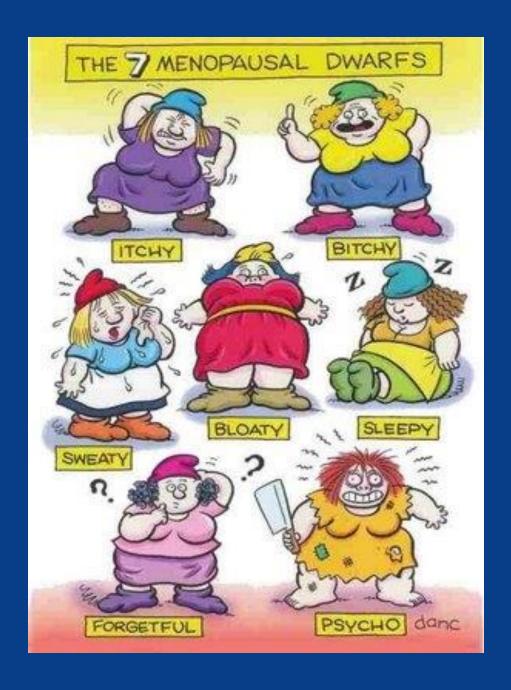
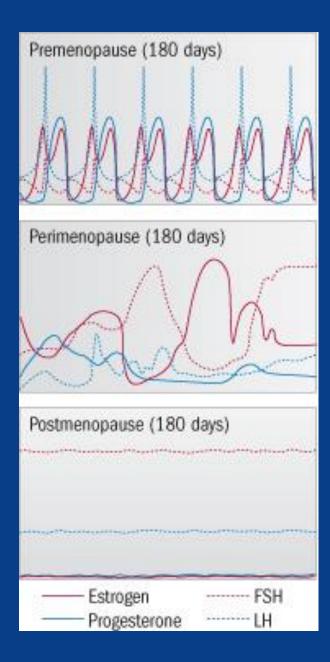
# Integrative Medicine for Menopausal Symptoms

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# Menopause transition

- Hot flushes
- Mood swings
- Fatigue
- Irritability
- Irregular menstrual cycles
- Sleep disruption



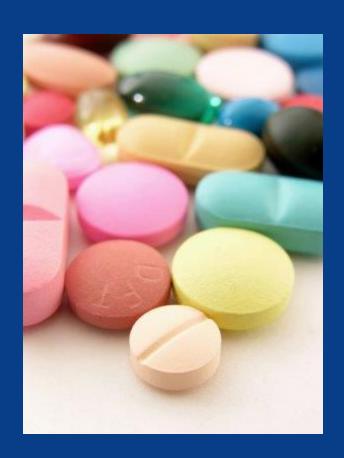


# Physiology of symptoms

- Narrowed thermoregulatory zone
- Late menopause transition:
  - HPA activation
  - ↑ cortisol and DHEAS
- Imbalance
  - Hyperestrogen and Hypoprogesterone
  - Sympathetic and Parasympathetic

#### Pharmaceuticals

- Hormone therapy (Estrogen/Progestogen)
- SSRIs
- SNRIs
- Clonidine
- Gabapentin



# IM approaches in menopause

- Mind-body medicine
- Yoga
- Acupuncture
- Botanical and Supplements

Disclaimer: not comprehensive review but representative

#### Does stress worsen hot flushes?

- RCT :lab stress versus non-stress
- 47-57% ↑ flushes with stress
- Both life stress and lab stress 

   flushes

Swartzman et al. Health Psychology 1990;9(5):529-45.

# Mind-body approaches

- If stress ↑ hot flushes...
- Can relaxation ↓ them?

# Mind-body approaches

- Multiple studies:
  - Relaxation response
  - Slow deep breathing
  - -MBSR
  - Hypnosis
  - -CBT
- Most show great improvement in HF

#### **MBSR**

- n=110
- MBSR vs WLC
- $\downarrow$  in bother from hot flashes
- No sig↓ in hot flash intensity
- Improvements maintained at 3 months
- Standard MBSR procedure

Carmody JF et al. Mindfulness training for coping with hot flashes: results of a randomized trial. Menopause 2011;18:611-620.

#### **MBSR**

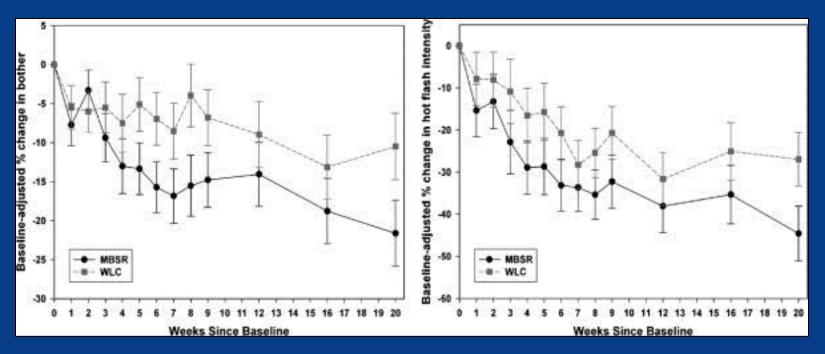


FIG. 2. Mean percent change since baseline (SE) in hot flash bother and hot flash intensity, weekly during the intervention (weeks 1-9) and at 12-, 16-, and 20-week follow-up.

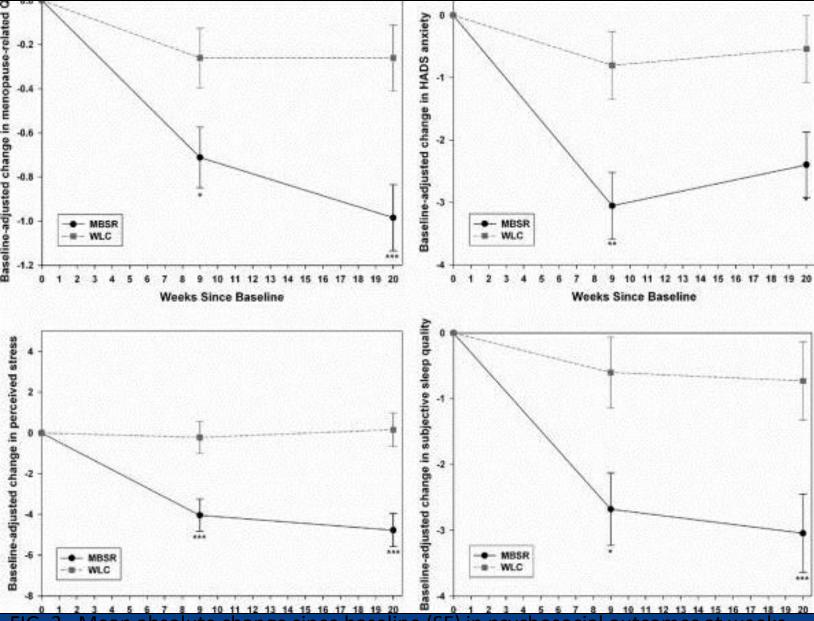


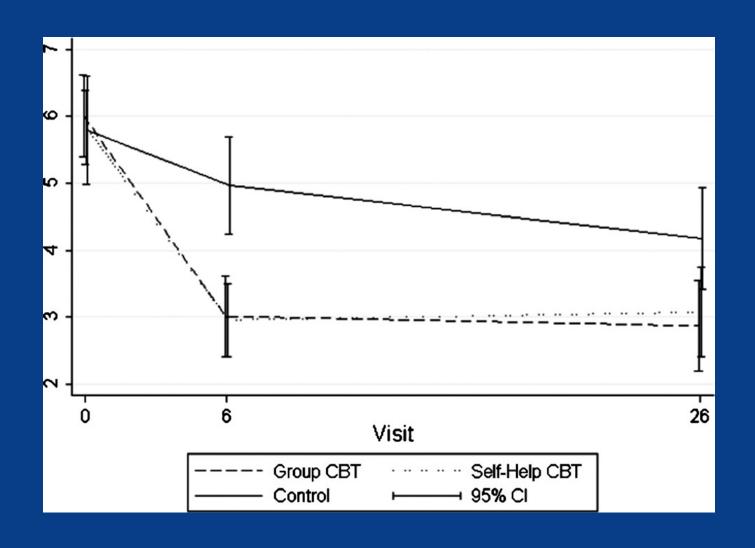
FIG. 3. Mean absolute change since baseline (SE) in psychosocial outcomes at weeks 9 and 20. For between-arm differences

# Cognitive Behavior Therapy

- N=140 3 arm RCT for 4 weeks
- Group CBT 2-hour /week for 4 weeks
- Self-help CBT
- Usual care

Improvements in mood, QOL, HF/NS

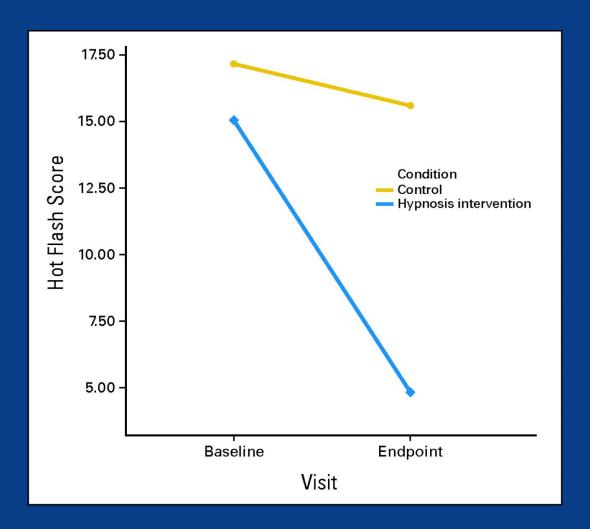
# Hot flush rating scale



# Hypnosis for Hot Flushes

- 65 breast cancer survivors
- 5 weekly sessions versus no treatment
- Standard transcript
- ↓ in:
  - hot flushes
  - Anxiety
  - Depression
  - sleep disruption

Elkins G et al. JCO 2008;26:5022-5026

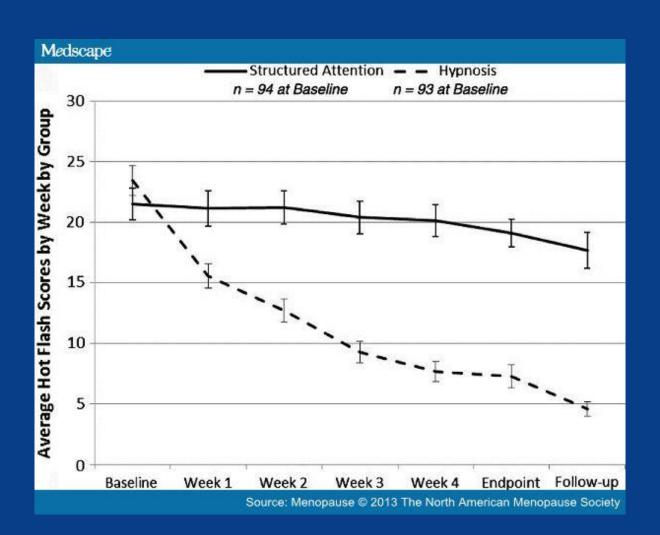


# **Hypnosis**

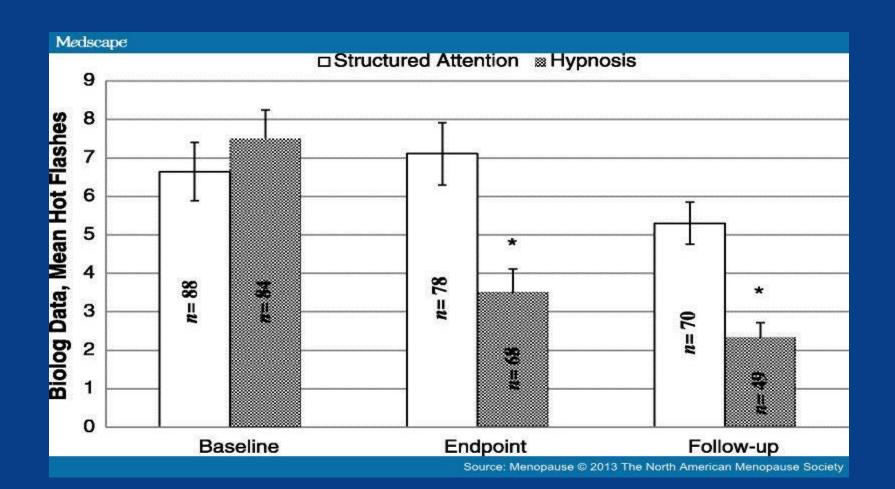
- Not confined to breast cancer patients
- >6 hot flushes per day
- RCT: hypnosis vs active structured-attention control
- Matched for therapist exposure, therapeutic environment, interpersonal exchange, and encouragement

Elkins et al. Clinical Hypnosis in the Treatment of Postmenopausal Hot Flashes: A Randomized Controlled Trial. Menopause 2013;20(3):291-298.

# Hypnosis: HF score



# Hypnosis: Objective HF



# Yoga

- N=200, ages 40-55 RCT
- Daily yoga vs no yoga for 3 months

Joshi S et al. Menopause Intl 2011;17:78-81.

Chattha R et al. Menopause 2008;15:862-870.

Freedman and Woodward. Am J Obstet Gynecol 1992;167:436-9.

# Yoga versus Control

|           | Pre Yoga | Post yoga | Pre control | Post control |
|-----------|----------|-----------|-------------|--------------|
| MRS       | 9.37     | 4.36*     | 9.00        | 9.20         |
| Psych     | 4.57     | 1.85*     | 3.75        | 3.73         |
| Somatoveg | 3.34     | 1.61*     | 3.24        | 3.3          |

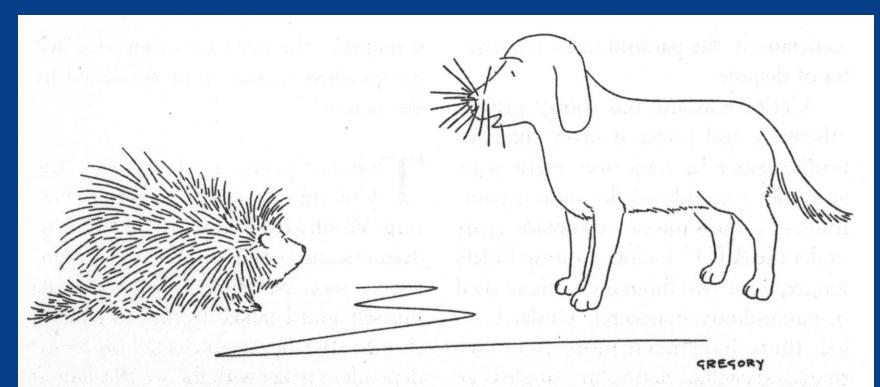
#### Similar Results

- Yoga compared to structured exercise
- Paced respiration compared to placebo

Yoga and diaphragmatic breathing are effective for hot flushes

Chattha R et al. Menopause 2008;15:862-870.

Freedman and Woodward. Am J Obstet Gynecol 1992;167:436-9.



"On the plus side, you've cured my back pain."

## Acupuncture

- Studied in menopausal women with and without breast cancer
- ↓ hot flushes, anxiety, depression
- Difficult to blind
- Control group:
  - usual care
  - superficial needling
  - telescoping needles

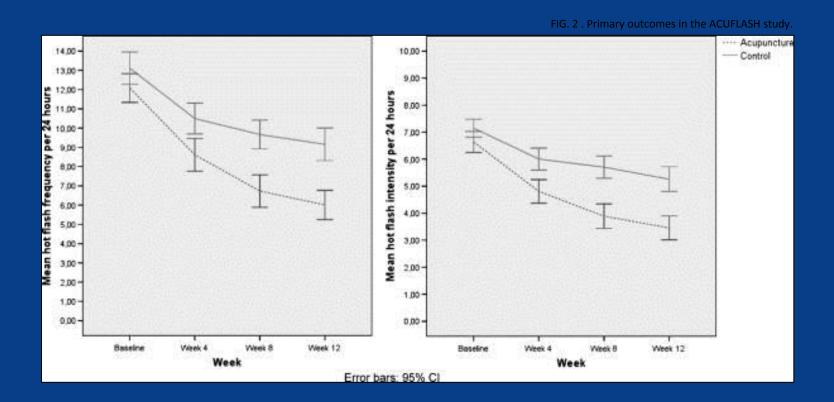


## Acupuncture

- N=267, Multicenter RCT
- Acupuncture and self-care vs self-care alone
- ACUFLASH study
- Primary outcome: HF freq and intensity
- Secondary outcomes: somatic, vasomotor, sleep improved

Borud et al. Menopause 2009;16:484-93

# Acupuncture versus self-care: ACUFLASH



# Acupuncture: true vs sham

- N=59 breast ca on tamoxifen
- True vs sham for 10 weeks
- Sham: superficial needling at non-a/p points
- ↓ HF and NS
- Improvement in Kupperman index

Hervik J et al. Breast Cancer Res Treat 2009;116:311-316

# Acupuncture vs sham: HF/day

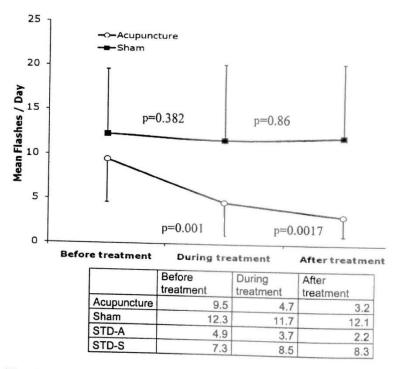


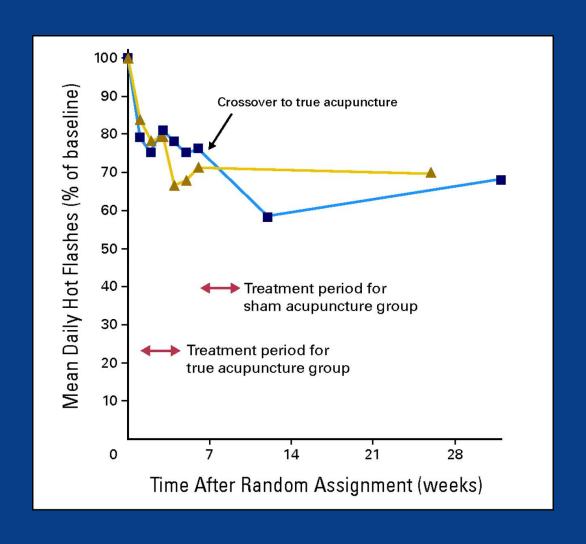
Fig. 1 Hot flashes, daytime

#### In contrast with

- 72 breast ca survivors
- Sham telescoping needles vs true ap
- Sham group crossed over to true at 7 weeks
- Similar acupuncture points
- Not statistically significant differences between groups, but...

Deng G et al. JCO;25:5584-90.

# True vs sham acupuncture



# Similar findings

- Comparing acupuncture to venlafaxine
  - Equally effective but results last longer with ap

- Comparing acupuncture to relaxation
  - Equally effective

Nedstrand et al. Climacteric 2005;8:243-50

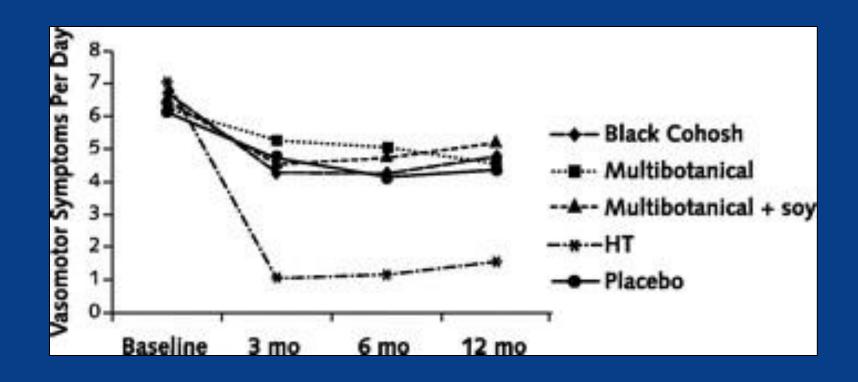
Walker EM et al. JCO 2010:28;634-640.

#### Botanical medicine

- Systematic review from 1948-2009
- Black cohosh vs placebo: no sig effect
- Bl cohosh/St Johns Wort: ↓ sxs vs placebo
- SJW/Vitex: no effect



# HT vs botanicals vs placebo



#### St Johns Wort

- RCT of SJW vs placebo
- N=100, av age 50.4
- SNRIs and SSRIs are effective for HF
- $\downarrow$  in duration, frequency, and severity

Abdali K et al. Menopause 2010;17:326-331.



#### TABLE 2

| Frequency                 | Baseline |      | 4th week of intervention |       | 8th week of intervention |      |
|---------------------------|----------|------|--------------------------|-------|--------------------------|------|
|                           | Mean     | SD   | Mean                     | SD    | Mean                     | SD   |
| St John's wort            | 3.88     | 0.85 | 2.84                     | 0.99  | 1.8                      | 1.03 |
| Placebo                   | 3.88     | 0.76 | 3.37                     | 0.69  | 2.65                     | 0.81 |
| Significance <sup>a</sup> | P = 0    | .526 | P = 0                    | 0.005 | P < 0                    | .001 |

<sup>&</sup>lt;sup>a</sup>Tukey post hoc comparison showed that the differences between the St John's wort and placebo groups were statistically significant in frequency on the 4th and 8th weeks of intervention.

#### TABLE 2. Mean number of hot flashes during 24 hours

# Phytoestrogens

- Clinically modest improvement in vasomotor symptoms and mood vs placebo
- Unclear role on breast stimulation
- Unlikely to stimulate endometrium

# Menopause transition

- Hormonal
- Autonomic
- IM approaches in menopause:
  - Mind-body
  - Acupuncture
  - Yoga
  - ?Herbs/supplements
  - Others under investigation