Symptom science: Clinical trials for alleviating menopausal hot flashes

Janet S. Carpenter, PhD, RN, FAAN
IU School of Nursing
Historical Context of Menopause Research

- Growth in research this century
- Greater emphasis on inclusion of women in research and on women’s health
- Worldwide more women living post-menopause

1907, E. Pratt, “A case of sudden death at the climacteric”
- **Postmenopausal women**
  - 477 million in 1998 worldwide
  - 1.1 billion in 2025 worldwide
  - 6,000 women reach menopause *daily* in USA

- **85%** have symptoms

- **80%** consult a health care provider
  - Health care expenditures 55% higher for midlife women than midlife men
Etiology?

Serotonin
Norepinephrine
Estrogen
GABA
Orexin
Kisspeptin
Neurokinin B
Dynorphin
Electrolytes
Glucose

Central? Peripheral? Both?

White matter hyperintensities
Menopausal Hot Flash Measurement

Repetitive, multidimensional, centrally-mediated, physiological events

NIH measurement workshop, NIH SBIR funding, MsFLASH measurement recommendations

Total costs per system: $1200 to $4000
Vasomotor symptoms = hot flashes/flushes + night sweats

<table>
<thead>
<tr>
<th>Hot Flash Phrases</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>les bouffées de chaleur</td>
<td>France</td>
</tr>
<tr>
<td>hitzewallengun</td>
<td>Germany</td>
</tr>
<tr>
<td>vampate di calore</td>
<td>Italy</td>
</tr>
<tr>
<td>los sofocos</td>
<td>Spain, Mexico</td>
</tr>
<tr>
<td>návaly horka</td>
<td>Czech Republic</td>
</tr>
<tr>
<td>goroom vap laga</td>
<td>Bangladesh</td>
</tr>
<tr>
<td>sicak basmasi</td>
<td>Turkey</td>
</tr>
</tbody>
</table>

Menopausal Hot Flash Measurement

Cited in 171 scientific papers

Translated in 12 languages: Afrikaans, Danish, Farsi, Flemish, French, Italian, Mandarin, Norwegian, Portugese, Spanish, Swedish, Taiwanese
MsFLASH and Other PI/CoI Treatment Trials
Preventing BrCA Through Non-hormonal Menopause Management

- Breathing
- Exercise
- Yoga
- Hypnosis

Supplements
- Omega-3 fatty acids

Medications
- Venlafaxine
- Escitalopram
- Estrogen

Integrative/Alternative

100 BEST SUPPLEMENTS FOR WOMEN
# MsFLASH 01: Escitalopram vs. Placebo

<table>
<thead>
<tr>
<th>SCREENING</th>
<th>TREATMENT</th>
<th>POST-TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escitalopram 10 mg po qd</td>
<td>Continue 10 mg po qd</td>
<td>Stop → Follow-up</td>
</tr>
<tr>
<td></td>
<td>Increase to 20 mg po qd</td>
<td>Taper off Follow-up</td>
</tr>
</tbody>
</table>

2 week screening → Baseline →

<table>
<thead>
<tr>
<th>Placebo 1 po qd</th>
<th>Continue 1 po qd</th>
<th>Stop → Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Increase to 2 po qd</td>
<td>Taper off Follow-up</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Week</th>
<th>V</th>
<th>V</th>
<th>Ph</th>
<th>V</th>
<th>V</th>
<th>V</th>
<th>V</th>
<th>Ph</th>
</tr>
</thead>
<tbody>
<tr>
<td>-1</td>
<td>V</td>
<td>V</td>
<td>Ph</td>
<td>V</td>
<td>V</td>
<td>V</td>
<td>V</td>
<td>Ph</td>
</tr>
<tr>
<td>0*</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>1</td>
<td>9</td>
<td>10</td>
<td>11</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Stratified randomization by race & clinical Site

V = visit, Ph = phone
MsFLASH02: 3x2 Factorial Trial of Omega-3, Yoga, Exercise vs. Placebo

<table>
<thead>
<tr>
<th>SCREENING</th>
<th>TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 week screening → Baseline →</td>
<td>Omega-3 fatty acids (EPA [1275mg] + DHA [300mg])</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
</tr>
<tr>
<td></td>
<td>Omega -3 Plus Exercise (3 times/week)</td>
</tr>
<tr>
<td></td>
<td>Placebo + Exercise</td>
</tr>
<tr>
<td></td>
<td>O3 Plus Yoga</td>
</tr>
<tr>
<td></td>
<td>Placebo + Yoga</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>V</th>
<th>V</th>
<th>Ph</th>
<th>M</th>
<th>V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week</td>
<td>-1</td>
<td>0*</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

V = visit, Ph = phone

*Stratified randomization by race & clinical Site
Effect of escitalopram on hot flash interference: a randomized, controlled trial

Janet S. Carpenter, PhD, RN,1 Katherine A. Guthrie, PhD,2 Joseph C. Larson, MS,3 Ellen W. Freeman, PhD,4 Hadine Joffe, MD,5 Saara Reid, MD,6 Kristine E. Ensrud, MD, MPH,7 Sheryl Sherman, PhD,8 Mary D. Sammel, ScD,9 Kurt Kroenke, PhD,10 Joseph C. Larson, MS,5 and Andrea Z. LaCroix, PhD2

Clinical hypnosis in the treatment of postmenopausal hot flashes: a randomized controlled trial

Gary R. Elkins, PhD,1 William I. Fisher, MA,1 Aimee K. Johnson, MA,1 Janet S. Carpenter, PhD, RN, FAAN,2 and Timothy Z. Keith, PhD3
North American Menopause Society

Non-hormonal management of menopausal symptoms

Expert panel reviewed 340 original research articles and 105 systematic reviews

Treatments classified according to level of evidence and implications for practice
# NAMS Recommendations

<table>
<thead>
<tr>
<th>Recommended</th>
<th>Recommend with Caution</th>
<th>Do Not Recommend at this Time</th>
</tr>
</thead>
</table>
| • Cognitive behavioral therapy  
• Clinical hypnosis  
• Paroxetine (FDA approved) and other SSRI / SSNRI  
• Gabapentin  
• Clonidine | • Weight loss  
• Mindfulness-based stress reduction  
• Soy extracts  
• Stellate ganglion block | • Paced respiration, relaxation training  
• Exercise, yoga  
• Acupuncture  
• Avoiding triggers  
• Cooling techniques |
Novel Treatment Trials

Integrative/Alternative

Supplements

Medications
Questions?