SEATTLE MIDLIFE WOMEN'S HEALTH STUDY

OVERVIEW

The Seattle Midlife Women’s Health Study (SMWHS) studied the natural menopausal transition in a population-based sample from 1990 to 2006. The primary focus of SMWHS throughout the 17 years was on symptoms, hormones, stress and stages of the menopausal transition.

To find eligible women to participate in the study, 11,222 households were contacted by phone. 508 women between the ages of 35 and 55 were recruited between 1990 and 1992. After the initial interview 390 (77%) agreed to provide data annually by questionnaire, daily menstrual calendar, or health diary. At the end of 5 years, 242 of 300 women who were still eligible to participate (81%), agreed to continue in the study with 176 of these (73%) providing 3-day diaries or first morning urine specimens. Between 2000 and 2002, 174 women provided a buccal cell smear for genotyping.

Participation in SMWHS 1990-2006

<table>
<thead>
<tr>
<th>Reason</th>
<th>Number</th>
<th>Percent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Still in study as of Dec. 31, 2006</td>
<td>64</td>
<td>12.6</td>
</tr>
<tr>
<td>Lost to follow-up</td>
<td>153</td>
<td>30.1</td>
</tr>
<tr>
<td>Ineligible</td>
<td>121</td>
<td>23.8</td>
</tr>
<tr>
<td>Too busy</td>
<td>73</td>
<td>14.4</td>
</tr>
<tr>
<td>Personal/family reason making it difficult to participate</td>
<td>26</td>
<td>5.1</td>
</tr>
<tr>
<td>Moved, unwilling to continue</td>
<td>14</td>
<td>2.8</td>
</tr>
<tr>
<td>Lost interest</td>
<td>57</td>
<td>11.2</td>
</tr>
<tr>
<td>Total</td>
<td>508</td>
<td>100.0</td>
</tr>
</tbody>
</table>
Menopausal Transition (MT)

- The MT can be divided into specific stages (Mitchell, Woods & Mariella, 2000):
  - Early stage - cycles are still regular but length of periods, amount of flow or cycle length has changed
  - Middle stage - cycles become irregular. Consecutive cycles are 7 or more days different from each other.
  - Late stage - periods are skipped; there are 60 or more days between the start of consecutive periods.

- The length of a period, time between periods and amount of bleeding increase as women age. The length of a period and amount of bleeding increases steadily across the MT stages (In progress).

- On average women enter Middle stage at age 46.1 and stay in the stage for an average of 2.8 years. On average, women enter Late stage at age 49.1 and stay in this stage for an average of 2.6 years. The average age for the final menstrual period (start of postmenopause) is 51.6 years (In progress).

- Women themselves define MT as the cessation of periods, the end of reproductive ability, a time of hormonal changes, change of life, changing body and emotions and an aging process. Very few women define the MT as a time of symptom or disease risk (Woods & Mitchell, 1999).

Midlife

- Women describe midlife as a time of many transitions, of getting older, of changing bodies, outlooks and relationships. Personal achievements and employment are central to the lives of midlife women in this study (Woods & Mitchell, 1997).

- After publication of Women’s Health Initiative findings (2002) linking hormone therapy (HT) with increased risk of breast cancer, stroke, heart attacks and other health problems the percent of women taking hormones during the MT decreased from 49% in 1999 to 35% in 2003. Reasons to not take HT increased between 1999 and 2003 as follows: concerns raised by news reports, from 20% to 66%; imbalance between benefits and risks, from 39% to 86%; worry about cancer from 37% to 73%, concerns about side effects from 35% to 68%, and viewing menopause as natural from 29% to 59%. Advice against taking estrogen increased from 13% to 36% (Smith-DiJulio, Mitchell, Woods, 2005).
**Hormonal Changes**

- FSH (follicle-stimulating hormone, the driver of hormone secretion from the ovary) rises as women go from Middle to Late MT stage and to early postmenopause (PM) (Mitchell, Woods & Mariella, 2003).

- Estrone levels do not drop until at least one year after the beginning of Late stage (Estrone is one of the 3 estrogens secreted by the ovary and the one we measured.) (In progress).

- Cortisol (a stress hormone) increases during Late stage. Women with increased cortisol levels have more severe hot flashes than those without a cortisol increase. Other factors such as age, body mass index, FSH, estrone, exercise level, depressed mood, sleep disruption or stress level do not differentiate between women with high or low cortisol levels (Woods, Carr, Tao, et al., 2006).

**Symptoms**

- At the beginning of the study 58% of the women said they had PMS (premenstrual syndrome) at some point in their lives; half of those with a moderate or extreme level. Women with PMS have more life stress than women without PMS. PMS is more likely among women with 12 years or less education; younger women, women who can tell when they ovulate, and those whose mothers had similar symptoms. There is no difference between women with and without PMS on number of cigarettes smoked, alcoholic drinks consumed or amount of exercise (In progress).

- Women experience the following: depressed mood, hot flashes, decreased sexual desire, vaginal dryness, forgetfulness, difficulty concentrating, awakening during the night or early morning awakening, not all of which can be attributed to the MT (Mitchell & Woods, 1996).

- Hot flashes are related to a rise in FSH and a drop in estrone during the MT and early PM (Woods, Smith-DiJulio, Percival, et al., under review).

- Hot flash experiences across the MT are highly variable. Hormone therapy relieves hot flashes with 75% of women reporting fewer and less severe hot flashes (Smith-DiJulio, Mitchell, Woods, 2005), but this effect is not predictable, ie, not all women can count on relief of hot flashes with hormones use (In progress).

- Decreased sexual desire is associated with a decline in estrone levels. Vaginal dryness is related to a rise in FSH and a decline in testosterone during the MT and early PM (Woods, Smith-DiJulio, Percival, et al., under review).

- Forgetfulness increases along with FSH levels. Difficulty concentrating is associated with lower levels of testosterone (Woods, Smith-DiJulio, Percival, et al., under review).
• Depressed mood is not directly associated with hot flashes, but is associated with early morning awakening and awakening during the night. Early morning awakening and awakening during the night are directly associated with hot flashes (Woods, Smith-DiJulio, Percival, et al., under review).

• Women with a consistently depressed mood are more likely to have hot flashes, stress, history of premenstrual syndrome and postpartum blues than other women (Woods & Mitchell, 1996). Depressed mood increases slightly with age, hot flashes, and number of life events; more substantially with use of antidepressants (In progress).

• Most women experience the MT without a high level of depressed mood. A small group of women have their mood worsen. Another small group has their mood improve (Woods, Mariella & Mitchell, 2006).

• The occurrence of depressed mood is highly variable. It increases with aging, hot flash activity, use of antidepressants, stress and Late transition stage (In progress).

• About 72% of women report problems remembering names at least some of the time. About 50% have a problem remembering where they put things, recent phone numbers, things others told them (or they told others), keeping up correspondence and forgetting what they were doing. However, none of these events are considered a serious problem (Woods, Mitchell, & Adams, 2000).

• Many types of problems with memory are related to lower ratings of health and depressed mood. Problems with current memory and remembering past events are associated with higher levels of reported stress, which women attribute to the burden of meeting multiple role demands (Woods, Mitchell, & Adams, 2000).

• Women in the Early and Middle stages of the MT and those who use hormones have more problems with memory than women in Late stage (Woods, Mitchell, & Adams, 2000).

Genetic Influences

• Women with a specific genetic variations have more severe and frequent hot flashes during the Middle and Late MT stages and PM and have higher estrone levels during Middle and Late stages (Woods, Mitchell, Tao, et. al., 2006).

• Genetic differences influence the age of first menstruation, the age of entry into Middle and Late stage and age at final menstrual period. How long a woman is in Middle or Late stage is not influenced by genetic variation (Under review).
The data you gave us has been used as part of an international collaboration to assess ways to identify MT stages and to determine whether to support adoption of specific hormonal criteria to define the MT. This collaboration recommends the adoption of ≥7 day difference in repeated consecutive cycle lengths as the method to define onset of irregularity and the start of the MT. Also recommended is the use of at least 60 days of no bleeding as the approach for defining onset of late menopausal transition (Harlow, et al, 2006; Randolph, et al, 2006; Harlow, et al., Under review).

After 16 years, SMWHS is coming to a close. As of January 1, only Ellen Mitchell, Nancy Woods and Kathy Smith-DiJulio will remain to write the final report, finish writing papers and close the offices. You can imagine all the data that has to be stored! After June 1, Ellen Mitchell will be the only person maintaining the study and contacting you. Her goal is to support your participation in the study until you have reached 5 years after your final menstrual period. As seen in the Table on the first page, 64 women are continuing in the study. During this time Ellens focus will be on what happens in terms of symptoms during the early postmenopausal period. Not much is known about this particular phase in the reproductive lives of women so thank you to all of you for continuing to participate and provide data that will help fill existing gaps in knowledge.

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**Manuscripts Under Review**


**Manuscripts In Progress**


Woods, N.F., Smith-DiJulio, Percival, D.P., and Mitchell, E.S. “Stress and stress arousal across the menopausal transition and early postmenopause”.

Mitchell, E.S., Woods, N.F., Smith-DiJulio, K., Tao, E.Y., Percival, D.P. “Patterns of change in menstrual bleeding across the menopausal transition”.
Smith-DiJulio, K., Mitchell, E.S., Percial, D.P., Tao, E.Y., and Woods, N.F. “Hot flash severity in hormone therapy users and nonusers across the menopausal transition and early postmenopause”.


Woods, N.F., Smith-DiJulio, K., Mitchell, E.S. and Percival, D.P. “Sexuality and the menopausal transition”.