Hormone Replacement and Menopausal Symptoms following Hysterectomy

Patricia Langenberg, Kristen H. Kjerulff, and Paul D. Stolley

Hormone replacement therapy (HRT) is recommended for most women who experience surgical menopause following hysterectomy/oophorectomy for noncancerous conditions; it is also commonly prescribed for postmenopausal women. Beginning in 1992, 1,299 women undergoing hysterectomy in 28 hospitals throughout Maryland were interviewed prior to hysterectomy and were subsequently followed over a 2-year period. Interviews included questions about HRT use and symptoms associated with menopause. The majority of the women (66 percent) were white, 55 percent had a high school education or better, 49 percent were obese (body mass index $\geq 27.3$), and 11 percent were postmenopausal. Over 40 percent of premenopausal women underwent bilateral oophorectomy. At 3 months posthysterectomy, 89 percent of these women were on HRT; this figure dropped to 85 percent at 24 months. Among postmenopausal women, 50 percent were on HRT both at 3 months and at 24 months posthysterectomy. Among premenopausal women who had unilateral oophorectomy, 21 percent were on HRT at 3 months, increasing to 35 percent at 24 months. Among premenopausal women who had no ovaries removed, 5 percent were on HRT at 3 months, increasing to 13 percent at 24 months. There were few within-group differences between HRT users and nonusers, except that among postmenopausal women, HRT users were younger and more likely to be white and had higher income and educational levels. Women who were postmenopausal or who underwent bilateral oophorectomy were less likely to have hot flashes if they were on HRT, but women with 0–1 ovary removed who were on HRT were more likely to have hot flashes than those not on HRT. Black women were significantly more likely to experience hot flashes than were white women, independent of HRT status and weight. Obese women were on HRT at approximately the same rates as nonobese women but were significantly more likely to have hot flashes, even when analyses controlled for HRT and race. Am J Epidemiol 1997;146:870–80.

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Abbreviations: CI, confidence interval; HRT, hormone replacement therapy; OR, odds ratio.

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Between 1988 and 1990, approximately 570,000 women per year in the United States made the decision to have a hysterectomy, and for about 50 percent of these women the surgery included bilateral oophorectomy, based on National Hospital Discharge data (1). The rate of concomitant bilateral oophorectomy has increased from 25 percent in 1965 and 41 percent in 1984 (2) to the current 50 percent level. For premenopausal women, the removal of both ovaries is considered surgical menopause, and it leads to a dramatic and rapid drop in endogenous estrogen levels, often accompanied by the onset of many menopausal symptoms. For those who have only one ovary removed (unilateral oophorectomy), there is a less dramatic loss of endogenous estrogen, although it is not entirely clear whether menopausal symptoms occur frequently (3). Among women who have had hysterectomies with no ovary removal, a diminution in estrogen levels and an increase in hot flashes has been reported (4, 5), but usually without severe menopausal symptoms. Several studies have reported a younger age of menopause among women who have had hysterectomies, even when both ovaries were retained (6, 7). For many women, hormone supplementation is prescribed following hysterectomy with or without oophorectomy (8), and since there is no longer a risk of endometrial cancer in these cases, hormone replacement therapy (HRT) usually involves estrogen without the addition of progestin.

There is increasing evidence of the benefits of HRT in prolonging life among postmenopausal women (9–13); one study (11) estimated a 46 percent reduction in all-cause mortality for estrogen users compared with age-matched controls. For a 50-year-old white woman with hysterectomy, who is no longer at risk for endometrial cancer, it has been estimated that long-term estrogen therapy will result in a net increase in life expectancy of 1.1 years (10). The principal benefit of
HRT in the prolongation of life appears to be reductions in coronary heart disease and other cardiovascular diseases (9–12). The Postmenopausal Estrogen/Progestin Interventions (PEPI) clinical trial (14) confirmed results of observational studies (15–19) that HRT had highly significant positive effects on metabolic risk factors for cardiovascular disease, with little difference being seen between estrogen only and estrogen plus progestin. Estrogen replacement therapy has also been shown to reduce progression of intimal-medial thickness in the carotid arteries (20).

HRT has long been documented to reduce bone loss following menopause/oophorectomy. Recently, HRT has also been shown to be associated with gain in bone mineral density for postmenopausal women in the PEPI clinical trial (21) and with gain or reduced loss in a number of observational studies of surgically menopausal and other postmenopausal women (22–27). A report from a cross-sectional study indicates that HRT may reduce the return of endogenous lead from bone to the circulatory system (28).

Studies have reported beneficial effects of estrogen therapy on cognition (29, 30) in surgically menopausal women and a decreased risk of Alzheimer’s disease (31–33) in postmenopausal women. HRT use by women who have had a hysterectomy, with or without oophorectomy, has also been associated with lower levels of depression and greater well-being in comparison with women not using HRT (34).

The observational studies reporting beneficial effects of HRT suffer from the possibility of selection bias, since women taking replacement hormones tend to be healthier and better educated and to have higher incomes. In fact, Barrett-Connor (35) has shown that even within a homogeneous cohort with easy access to medical care, women on HRT tend to have better health behaviors, which may well be associated with earlier diagnosis and treatment of cancer and heart disease.

Breast cancer risk has been shown in some studies to be associated with HRT. All of these studies were observational in design, and results ranged from little or no evidence of risk (36–38) to a 32 percent increased risk (39) to an increased risk of 25–46 percent for long-term users (10, 39). Long-term HRT use has also been associated with fatal ovarian cancer; a 72 percent increased risk was found for current users with more than 6 years of use (40).

While there have been many studies of the risks and benefits of HRT, little is known about the extent of current use of HRT following hysterectomy/oophorectomy, the level of adherence to the regimen, or the perceived effectiveness of HRT in relieving symptoms thought to be sequelae of the surgery. This report concentrates on the experiences of 1,299 women who underwent hysterectomy in Maryland with respect to their utilization of HRT. Levels of postmenopausal symptoms experienced by users and nonusers over a 2-year period, factors associated with symptoms, and the women’s perceptions of adverse effects of exogenous hormone use are also discussed.

**MATERIALS AND METHODS**

**Study population**

Between 1992 and 1993, 1,299 women undergoing hysterectomy for noncancerous conditions in 28 hospitals throughout Maryland were recruited to participate in the Maryland Women’s Health Study. The hospitals chosen constituted a random sample of all hospitals in the state of Maryland, stratified by annual hysterectomy volume. The number of patients recruited from each stratum was proportional to the total number of hysterectomies from that stratum across the entire state. All attending gynecologists at each hospital were asked to participate (n = 663), and 406 (61 percent) agreed; many of those who declined indicated that they were obstetricians only, were in administrative or research positions, or for other reasons did not perform hysterectomies. Patients of participating physicians were identified via surgical posting schedules and were telephoned by study interviewers. Of the 1,600 patients contacted, 19 percent refused to join the study, in most cases because there was insufficient time for an interview before surgery. Otherwise, persons who refused did not differ significantly from participants by age, race, or indications for hysterectomy. To assess the representativeness of the sample, we compared study patients with all patients undergoing hysterectomy in Maryland in 1992–1993, using hospital discharge data. Participants did not differ significantly by race, marital status, principal diagnosis, complications, comorbidities, or type of procedure. Participants were younger, on average (43.3 years vs. 44.6 years), and had a shorter mean hospital stay (3.4 days vs. 3.8 days).

**Data collection**

Face-to-face interviews were conducted by trained interviewers in the homes of all participants prior to their surgery and at 6, 12, and 24 months following surgery. Telephone interviews were conducted at 3 and 18 months postsurgery. Of the original 1,299 participants, 1,244 (96 percent) were interviewed at 3 months, 1,225 (94 percent) at 6 months, 1,188 (91.5 percent) at 12 months, 1,173 (90 percent) at 18 months, and 1,162 (89.5 percent) at 24 months. Women who were lost to follow-up were significantly
more likely to be African-American and/or to have low incomes. No other significant differences were observed between those lost to follow-up and those remaining in the study.

Classification by hysterectomy/oophorectomy status

Women whose surgery includes bilateral oophorectomy (surgical menopause) or who are already postmenopausal have different indications for initiation of HRT than do premenopausal women who undergo hysterectomy only. For women who have unilateral oophorectomy, there is some evidence of a more rapid decline in levels of endogenous estrogen than for those whose ovaries remain intact (3). Thus, for purposes of analysis, the women were assigned to one of four mutually exclusive groups: postmenopausal (with or without oophorectomy); premenopausal with both ovaries removed (bilateral oophorectomy); premenopausal with one ovary removed (unilateral oophorectomy); and premenopausal with no ovaries removed.

Hormone replacement therapy and reported symptoms

Participants were asked at the prehysterectomy interview and at all posthysterectomy interviews whether they were currently taking replacement hormones, either estrogen only or estrogen and progesterin combined. They were asked for few details about specific regimens, formulations, or dosages. They were asked about the symptoms for which they were taking hormones and about problems/side effects that could be associated with these medications. The women were asked a set of general questions about the frequency of symptoms such as hot flashes, headaches, pain, incontinence, sleep disturbances, and breast sensitivity during the previous month. Answers to these symptom frequency questions were recorded on a six-point scale ranging from “all of the time” to “not at all.” Frequency of hot flashes was classified as “frequent” if women reported that hot flashes occurred “all of the time,” “most of the time,” or “a good bit of the time”; frequency was classified as “any” if women reported having any (including frequent) hot flashes. The symptom frequency questions were recorded on a six-point scale ranging from “all of the time” to “not at all.”

Characteristics by hysterectomy/oophorectomy status

RESULTS

Characteristics by hysterectomy/oophorectomy status

Of the 1,232 women who had nearly complete data at the 3-month interview, approximately 11 percent were postmenopausal, 37 percent were premenopausal and had had bilateral oophorectomy, 11 percent were premenopausal and had had unilateral oophorectomy, and 41 percent were premenopausal with no oophorectomy. Few differences were observed among the premenopausal subgroups in terms of demographic characteristics, except that women having bilateral oophorectomy were older (table 1). Postmenopausal women undergoing hysterectomy were less likely to be black (17 percent vs. 33 percent for premenopausal women), more likely to have low incomes (48 percent had incomes of $25,000 or less compared with about 25 percent of premenopausal women), more likely to have a lower educational level, and less likely to smoke. Nearly 50 percent of the women in this study were obese (body mass index \( \geq 27.3 \)), and the proportion differed little across status groups. Of the premenopausal women with bilateral oophorectomy, only 17 percent were under 40 years of age, while more than 50 percent of those with 0–1 ovary removed were under 40.

Table 2 shows that postmenopausal women were significantly more likely than premenopausal women to have bilateral oophorectomy (59 percent vs. 41 percent; \( p < 0.01 \)). Stratification by age revealed that there were no significant differences for women over 40 years of age: 57 percent of premenopausal women and 59 percent of postmenopausal women had both
ovaries removed. When women were asked what they believed to be the reasons for ovary removal, the principal reasons given were cysts or tumors (34 percent), fear of cancer (23 percent), and age (21 percent). Reasons were similar in the various status groups.

**Hormone replacement use**

Table 3 presents the characteristics of women who reported that they were on HRT 3 months posthysterectomy. Of premenopausal women with no oophorectomy, 5.4 percent were on HRT compared with 21.3 percent of those with unilateral oophorectomy and 89.3 percent of those with bilateral oophorectomy. Among postmenopausal women, 50.4 percent were on HRT—approximately the same percentage as before hysterectomy. Age was significantly and positively associated with hormone use in premenopausal women with no oophorectomy or unilateral oophorectomy. Age was not related to HRT in premenopausal women with bilateral oophorectomy, among whom almost 90 percent of all age groups were on HRT, and the postmenopausal group, in which HRT use dropped significantly in the women over 59 years of age. Differences by race were small, except among postmenopausal women, where a significantly higher percentage of white women (55.4 percent) than black women (29.2 percent) were taking hormones. HRT use was significantly associated with higher incomes for postmenopausal women and premenopausal women with bilateral oophorectomy, and with higher levels of

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TABLE 3. Percentage of women on hormone replacement therapy 3 months after hysterectomy, by oophorectomy/postmenopausal status and demographic variables, Maryland, 1992–1995

<table>
<thead>
<tr>
<th>Race</th>
<th>No oophorectomy</th>
<th>Unilateral oophorectomy</th>
<th>Bilateral oophorectomy</th>
<th>Postmenopausal women</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>6.8 (21/309)</td>
<td>22.2 (20/90)</td>
<td>91.5 (280/306)</td>
<td>55.4 (62/112)</td>
</tr>
<tr>
<td>Black</td>
<td>3.3 (6/183)</td>
<td>20.8 (10/48)</td>
<td>85.1 (114/134)</td>
<td>29.2 (7/24)</td>
</tr>
<tr>
<td>Other</td>
<td>0.0 (0/11)</td>
<td>0.0 (0/3)</td>
<td>80.0 (8/10)</td>
<td>0.0 (0/2)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Annual income</th>
<th>No oophorectomy</th>
<th>Unilateral oophorectomy</th>
<th>Bilateral oophorectomy</th>
<th>Postmenopausal women</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤$25,999</td>
<td>2.2 (3/132)</td>
<td>22.9 (8/35)</td>
<td>83.3 (75/90)</td>
<td>36.7 (22/60)</td>
</tr>
<tr>
<td>$26,000–$50,000</td>
<td>6.7 (13/195)</td>
<td>17.9 (10/56)</td>
<td>88.0 (162/184)</td>
<td>56.5 (26/48)</td>
</tr>
<tr>
<td>&gt;$50,000</td>
<td>6.9 (11/160)</td>
<td>21.3 (10/47)</td>
<td>93.3 (154/165)</td>
<td>84.2 (16/19)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Education (years)</th>
<th>No oophorectomy</th>
<th>Unilateral oophorectomy</th>
<th>Bilateral oophorectomy</th>
<th>Postmenopausal women</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–12</td>
<td>5.1 (11/214)</td>
<td>16.4 (10/61)</td>
<td>88.6 (171/193)</td>
<td>40.7 (33/81)</td>
</tr>
<tr>
<td>13–16</td>
<td>4.9 (13/286)</td>
<td>27.3 (18/66)</td>
<td>89.9 (195/217)</td>
<td>68.3 (28/41)</td>
</tr>
<tr>
<td>≥17</td>
<td>13.0 (3/23)</td>
<td>14.3 (2/14)</td>
<td>90.0 (36/40)</td>
<td>50.0 (8/16)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Obese*</th>
<th>No oophorectomy</th>
<th>Unilateral oophorectomy</th>
<th>Bilateral oophorectomy</th>
<th>Postmenopausal women</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>5.1 (13/254)</td>
<td>20.9 (14/67)</td>
<td>90.8 (198/218)</td>
<td>54.4 (37/68)</td>
</tr>
<tr>
<td>Yes</td>
<td>5.2 (12/231)</td>
<td>19.1 (12/63)</td>
<td>88.3 (189/214)</td>
<td>44.4 (28/65)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Current smoker</th>
<th>No oophorectomy</th>
<th>Unilateral oophorectomy</th>
<th>Bilateral oophorectomy</th>
<th>Postmenopausal women</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>7.5 (27/359)</td>
<td>20.8 (22/106)</td>
<td>91.0 (304/334)</td>
<td>49.2 (61/124)</td>
</tr>
<tr>
<td>Yes</td>
<td>4.9 (7/144)</td>
<td>25.7 (9/35)</td>
<td>91.4 (106/116)</td>
<td>50.0 (7/14)</td>
</tr>
</tbody>
</table>

* Data in parentheses, number of women/total number.
† Body mass index (weight (kg)/height (m)^2) ≥ 27.3.

education for postmenopausal women. No significant differences were observed for any of the status groups by obesity level or smoking status.

Prehysterectomy, 10 percent of premenopausal women and 49 percent of postmenopausal women were on HRT. Between 3 months and 24 months posthysterectomy, the proportion of women on HRT in each of the status groups changed little (figure 1), although there were gradual increases over time for premenopausal women who retained one or both ovaries and a small decline in those with bilateral oophorectomy. Table 4 presents data on changes in HRT use between 3 months and 24 months. At 24 months, for premenopausal women, an additional 8 percent of those with no oophorectomy and 15 percent of those with unilateral oophorectomy had started HRT, while 3 percent or fewer had stopped. For women with surgical menopause, 4 percent started HRT and 7 percent stopped, while for those with natural menopause, 7 percent started and 10 percent stopped. When questioned about adherence to the HRT regimen, 85 percent of women reported skipping their hormones none of the time or only a little of the time. At 3 months posthysterectomy, most of the women reported taking HRT orally. However, 8.4 percent of postmenopausal women and 16.4 percent of premenopausal women on HRT reported transdermal administration.

Symptoms

Participants in the study were questioned about a number of symptoms that they may have perceived to be associated with hysterectomy, oophorectomy, or menopause. Those on HRT were also specifically questioned about symptoms that they believed to be associated with hormone use. There were no significant differences among status groups in these symptoms, which included breast enlargement (21 percent), headaches (19 percent), sleep disturbances (18 percent),
HRT and Menopausal Symptoms after Hysterectomy

The symptom most commonly reported among all women in the study was hot flashes within the previous month: 39 percent reported experiencing them at 24 months postsurgery. Figure 2 presents the prevalence of hot flashes within status and HRT subgroups both prehysterectomy and 24 months posthysterectomy. Among premenopausal women whose ovaries were not removed, those on HRT were significantly more likely to experience hot flashes than those not on HRT. For women who had bilateral oophorectomy or were postmenopausal, those on HRT were significantly less likely to experience hot flashes than those not on HRT. Further investigation revealed that 94 percent of premenopausal women who reported taking hormones because of hot flashes were having some or frequent hot flashes, while only 35 percent of those taking hormones for other reasons reported having hot flashes. Those percentages were similar across oophorectomy groups; however, a much larger percentage of women with bilateral oophorectomy were on HRT than those who had had one or no ovaries removed.

When the prevalence of hot flashes 24 months postsurgery was examined by race, black women were more likely than non-black women to experience hot flashes in nearly all subgroups (table 5). For women on HRT, blacks were more than twice as likely as non-blacks to have hot flashes (odds ratio (OR) = 2.4, 95 percent confidence interval (CI) 1.6–3.5); for women not taking hormones, the odds ratio was 1.2 (95 percent CI 0.9–1.8). We also compared obese women with nonobese women regarding the prevalence of hot flashes and observed similar differences: For women on HRT, the odds ratio was 1.7 (95 percent CI 1.2–2.4), and for women not on HRT, it was 1.5 (95 percent CI 1.1–2.1) (table 5). However, we also observed that in every status group, black women were significantly more likely to be obese; for all women combined, 70 percent of black women and 39 percent of non-black women were obese. We carried out similar analyses for frequent hot flashes (as opposed to any), and the results in both race and body mass index groups were very similar (data not shown).

Table 6 presents the results of repeated-measures logistic regression analysis for the prevalence of either frequent or any hot flashes at 6, 12, 18, and 24 months posthysterectomy among women who were premenopausal at hysterectomy. The results were adjusted for age as a continuous variable. No significant time effect was observed, nor were there significant interactions with time, which indicates that there were not great changes in the prevalence of hot flashes between 6 months and 24 months, either for all women or within subgroups. Black women were significantly more likely than non-black women to have either frequent (OR = 1.78, 95 percent CI 1.30–2.43) or any (OR = 1.68, 95 percent CI 1.34–2.09) hot flashes, adjusted for obesity, status group, and HRT variables. Obese women were more likely to have frequent hot flashes and significantly more likely to have any hot flashes, after data were adjusted for race. Smokers were significantly more likely to have frequent or any hot flashes than were nonsmokers. The association be-

![Figure 1. Percentage of Maryland women reporting use of hormone replacement therapy (HRT) prior to hysterectomy and in post-hysterectomy interviews conducted up to 24 months after surgery, by oophorectomy/menopausal status, 1992-1995.](image-url)
FIGURE 2. Percentage of Maryland women reporting any hot flashes prior to hysterectomy and during the 24-month period following hysterectomy, by use of hormone replacement therapy (HRT) and oophorectomy/menopausal status, 1992–1995.

tween HRT and hot flashes differed across status groups, such that for premenopausal women with bilateral oophorectomy, HRT had a protective effect against hot flashes, with an odds ratio of 0.65 (95 percent CI 0.40–1.06) for frequent hot flashes and an odds ratio of 0.74 (95 percent CI 0.51–1.07) for any hot flashes. For premenopausal women who retained one or both ovaries, those on HRT were more likely to experience hot flashes. Similar analyses were not carried out for postmenopausal women because of sample size limitations; furthermore, some of these women were well past menopause and the period of frequent hot flashes, but the date of cessation of menses was not known.

Another symptom reported by many of the women was vaginal dryness. Because the pattern of results was very similar to that for hot flashes, although somewhat less significant, it is not presented here.

DISCUSSION

To our knowledge, this is the most detailed study of hysterectomy outcomes that has been conducted to date, and one of the few studies that has followed women from a point before surgery to 24 months postsurgery. Overall, 42 percent of these women had bilateral oophorectomies (41 percent of premenopausal women and 59 percent of postmenopausal women). These proportions are similar to those reported by Wilcox (1), who estimated on the basis of 1988–1990 National Hospital Discharge data that 50 percent of all US women undergoing hysterectomy also had bilateral oophorectomy: 37.4 percent of those aged 25–44 years, 73.5 percent of those aged 45–54 years, and 59 percent of those aged ≥55 years. Our lower overall percentage resulted from the fact that 40 percent of hysterectomies among premenopausal women in our study were in women under 40, only 17 percent of whom had both ovaries removed. Most of the women in our study (94 percent) reported having discussed ovary removal with their physicians, and gave as principal reasons cysts or tumors, age, and fear of cancer. These study results lead to the conclusion that a large percentage of the gynecologic surgeons in Maryland and across the United States believe that it is often necessary and/or appropriate to remove the ovaries of older women concomitantly with hysterectomy.
### TABLE 5. Percentage of women with hot flashes 24 months after hysterectomy, by oophorectomy/menopausal status and other variables, Maryland, 1992-1995

<table>
<thead>
<tr>
<th>HRT* and oophorectomy status</th>
<th>Black women</th>
<th>Non-black women</th>
<th>Body mass index &lt;27.3</th>
<th>Body mass index ≥27.3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Users of HRT</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No oophorectomy</td>
<td>41 (7/17)‡</td>
<td>42 (19/45)</td>
<td>60 (9/15)</td>
<td>44 (8/18)</td>
</tr>
<tr>
<td>Unilateral oophorectomy</td>
<td>69 (11/16)</td>
<td>37 (11/30)</td>
<td>58 (7/12)</td>
<td>41 (7/17)</td>
</tr>
<tr>
<td>Bilateral oophorectomy</td>
<td>68 (64/54)</td>
<td>44 (125/292)</td>
<td>51 (95/187)</td>
<td>42 (81/195)</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>40 (2/5)</td>
<td>29 (18/55)</td>
<td>45 (3/29)</td>
<td>17 (6/36)</td>
</tr>
<tr>
<td>All users combined</td>
<td>64 (64/32)</td>
<td>42 (171/412)</td>
<td>51 (124/243)</td>
<td>38 (102/266)</td>
</tr>
<tr>
<td>Adjusted odds ratio§</td>
<td>2.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(95% CI†)</td>
<td>(1.6–3.5)</td>
<td></td>
<td></td>
<td>(1.2–2.4)</td>
</tr>
</tbody>
</table>

| Nonusers of HRT             |             |                 |                      |                      |
| No oophorectomy             | 31 (43/140) | 25 (66/266)     | 32 (67/209)          | 24 (58/240)          |
| Unilateral oophorectomy     | 28 (9/32)   | 44 (25/57)      | 38 (19/50)           | 22 (11/51)           |
| Bilateral oophorectomy      | 59 (19/32) | 50 (11/22)      | 70 (16/23)           | 67 (10/15)           |
| Postmenopausal              | 64 (7/11)  | 33 (18/48)      | 41 (12/29)           | 42 (13/31)           |
| All nonusers combined       | 36 (78/215) | 30 (118/395) | 37 (114/311)         | 27 (92/337)          |
| Adjusted odds ratio§        | 1.2         |                 |                      | 1.5                  |
| (95% CI†)                   | (0.9–1.8)   |                 |                      | (1.1–2.1)            |

* HRT, hormone replacement therapy; CI, confidence interval.
† Weight (kg/height (m)^2.
‡ Data in parentheses, number of women/total number.
§ Comparison between groups for frequency of hot flashes, adjusted for hysterectomy/oophorectomy status.

### TABLE 6. Estimated odds ratios for hot flashes after hysterectomy among women who were premenopausal at the time of surgery, Maryland, 1992-1995*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Very frequent</th>
<th>Any</th>
</tr>
</thead>
<tbody>
<tr>
<td>HRT‡ versus no HRT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilateral oophorectomy</td>
<td>0.65</td>
<td>0.74</td>
</tr>
<tr>
<td>Unilateral oophorectomy</td>
<td>2.45</td>
<td>1.44</td>
</tr>
<tr>
<td>No oophorectomy</td>
<td>3.19</td>
<td>1.56</td>
</tr>
<tr>
<td>Black race</td>
<td>1.78</td>
<td>1.68</td>
</tr>
<tr>
<td>Obesity§</td>
<td>1.24</td>
<td>1.31</td>
</tr>
<tr>
<td>Current smoking</td>
<td>1.67</td>
<td>1.66</td>
</tr>
<tr>
<td>Time (6-month change)</td>
<td>1.00</td>
<td>1.00</td>
</tr>
</tbody>
</table>

* Results of repeated-measures logistic regression analysis (generalized estimating equations method) of data obtained 6, 12, 18, and 24 months posthysterectomy.
† OR, odds ratio; CI, confidence interval; HRT, hormone replacement therapy.
‡ Adjusted for age (continuous variable).
§ Adjusted for body mass index (weight (kg)/height (m)^2 ≥ 27.3.

Reports on the use of HRT after hysterectomy by US women in the 40- to 60-year age range have varied over the past 25 years, but data seem to indicate a gradual increase in use over time. Perhaps the results reported in the form most comparable with ours are those on current usage of HRT by women with bilateral oophorectomies. Our study found that 89 percent of women in this group were users 3 months after surgery, with the percentage dropping to 87 at 24 months. In comparison, other studies reported 44 percent in 1976–1977 (43); 11 percent and 29 percent in 1981 (44, 45); 35, 40, and 47 percent in 1983–1986 (44, 46, 47); and 34, 60, 60, and 71 percent in the 1987–1993 period (36, 48–50). All of these percentages are considerably lower than that found in this study. Reports of HRT usage among women without oophorectomy are more consistent with our finding of 7–12 percent; previous studies conducted between 1975 and 1991 reported HRT use ranging from 10 percent to 25 percent (36, 43, 44, 47). Our findings that women with higher income and educational levels and white women versus black women are more likely to be on HRT are consistent with the literature (36, 44, 45, 47, 48, 51). However, some investigators have...
reported that smokers and women with high body mass indices are less likely to be on HRT (36, 45, 47), while we found no differences.

Our findings indicate high adherence to the HRT regimen over time. For premenopausal women with bilateral oophorectomy who were using HRT, only 7 percent reported stopping the therapy during the 21-month study period, and approximately 4 percent started using HRT during that time. Usage by postmenopausal women remained close to 50 percent from prehysterectomy to 24 months postsurgery, with 10 percent stopping and 7 percent starting. Usage by premenopausal women with unilateral oophorectomy and no oophorectomy increased by approximately 12 percent and 6 percent, respectively, with less than 3 percent stopping. These rates of adherence are considerably higher than those reported in the literature, although few studies have reported rates by hysterectomy/oophorectomy status. A study carried out in seven British group medical practices between 1991 and 1994 reported that, of 158 hysterectomized women who had been randomly assigned to estrogen therapy, 67 percent were still using it after 2 years (52). A 1990 study of 220 postmenopausal private patients at New York University Medical Center found that only 7 percent had discontinued therapy by 1 year (53), and a 1990 multicenter study reported that 5 percent of 1,330 menopausal women had stopped therapy at 1 year (53); rates for hysterectomized women were not reported for either of these studies. A 1996 study based on prescription records from a health maintenance organization found 24 percent to 62 percent compliance at 1 year for postmenopausal women, the range being based on how compliance with HRT therapy was defined (54).

Studies have reported that the two major reasons for discontinuation of treatment have been withdrawal bleeding (not applicable to hysterectomized women) and fear of cancer (53, 55–59). Reasons given for cessation of HRT in our study showed no consistent patterns, and the numbers for each reason were small.

Our findings indicate that among premenopausal women, black women are significantly more likely to experience hot flashes than non-black women after adjustment for differences in obesity, smoking, and other factors. Obese women were also more likely to experience hot flashes in this study, contrary to common belief. These results are consistent with those of den Tonkelaar et al. (60), who found, in a large population-based study, a strong positive association between hot flashes and both body mass index and waist:hip ratio in women aged 40–44 years. Anderson et al. (61), in a study of participants who visited a menopause clinic primarily because of phys-

ical symptoms, found that 53 percent were obese. However, Schwingl et al. (62), in her 1994 North Carolina study of risk factors for hot flashes in naturally menopausal women, found no relation for race and a negative association for high body mass index among women who smoked.

HRT was protective against hot flashes in women with surgical menopause but was associated with hot flashes in the other two premenopausal groups. This result can be partially explained by the fact that 94 percent of the premenopausal women across all groups who reported taking HRT because of hot flashes were still having hot flashes, and about 45 percent were experiencing them frequently. When this information is combined with the fact that a smaller proportion of the women who did not have bilateral oophorectomy were on HRT for hot flashes, and only a small proportion of these women were on HRT at all, we see why HRT use appears to be associated with hot flashes in those groups: Women having hot flashes were requesting hormone therapy. However, it is not clear why such a large percentage of women who were taking HRT for hot flashes would be continuing to experience them, unless for many of them the dosage was insufficient to alleviate symptoms.

Another interesting finding is that premenopausal women with unilateral oophorectomy were, in most cases, very similar to women in the no oophorectomy group in terms of symptoms experienced across time. With loss of half of the primary source of estrogen production, one might expect these women to experience menopausal symptoms sooner and at levels between those with surgical menopause and those with no oophorectomy. It has been the prevailing view that menopause results from an exhaustion of ovarian follicles, although an alternate theory proposes that age-related changes in the nervous system initiate the menopausal transition and that the exhaustion of ovarian follicles is a consequence (3). Clearly, our understanding of the factors associated with the menopausal transition and the role of hysterectomy, especially oophorectomy, in progression toward this transition is limited at present. Strategies for relieving some of the adverse symptoms of menopause, beyond prescription of estrogen supplementation, will only be developed with a better understanding of the physiologic processes underlying the transition.

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