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Randomized trial of medical treatment versus hysterectomy for abnormal uterine bleeding: Resource use in the Medicine or Surgery (Ms) trial

Jonathan Showstack, PhD, MPH,[a,d] Feng Lin, MS,[b] Lee A. Learman, MD, PhD,[c] Eric Vittinghoff, PhD,[b] Miriam Kuppermann, PhD, MPH,[c] R. Edward Varner, MD,[e] Robert L. Summitt Jr, MD, PhD,[f] S. Gene McNeeley, MD,[g] Holly Richter, PhD, MD,[e] Stephen Hulley, MD, MPH,[b] A. Eugene Washington, MD, MSc,[c] for the Ms Research Group

Departments of Medicine,[a] Epidemiology and Biostatistics,[b] Obstetrics, Gynecology and Reproductive Sciences,[c] and Institute for Health Policy Studies,[d] University of California, San Francisco, CA; University of Alabama,[e] Birmingham, AL; University of Tennessee,[f] Memphis, TN; Wayne State University,[g] Detroit, MI

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Objective: This study was undertaken to compare resource use outcomes for participants in the Medicine or Surgery (Ms) randomized trial.

Study design: In a randomized controlled trial, we compared resources used during a 24-month follow-up period by women with abnormal uterine bleeding who were randomly assigned to either expanded medical treatment or hysterectomy.

Results: Women randomly assigned to hysterectomy used significantly more resources (medicine = $4479, hysterectomy = $6777; $P = .03$), with almost all the difference caused by the hysterectomy procedure. Fifty-three percent of women randomly assigned to medicine had a hysterectomy during the follow-up period; women who were able to continue on medical therapy had mean total resource use of $2595 compared with $6128 for medicine patients who eventually had surgery.

Conclusion: For women with abnormal uterine bleeding refractory to cyclic medroxyprogesterone acetate, compared with expanded medical treatment, hysterectomy increases resource use significantly and results in better clinical and 6-month quality-of-life outcomes.

Hysterectomy is 1 of the most common major surgical procedure performed in the United States, with approximately 600,000 performed in this country each year.[1,2] Most hysterectomies are elective and performed before menopause for abnormal uterine bleeding and other non–life-threatening reasons.[1]

The initial therapeutic approach to treating abnormal uterine bleeding is with medicines such as progestins, combinations of estrogen and progestin, prostaglandin synthetase inhibitors, and antifibrinolytics.[3-7] Because

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medical approaches do not always relieve symptoms and may have adverse side affects, hysterectomy is sometimes considered as an alternative to provide a definitive solution.

To compare treatment alternatives for women with abnormal uterine bleeding refractory to cyclic medroxyprogesterone acetate (MPA), we conducted a randomized clinical trial of expanded medical treatment versus hysterectomy (the "Ms" trial). We report here the results of an analysis that addresses the economic question, "How does total 24-month resource use compare among women assigned randomly to either expanded medical treatment or hysterectomy?"

Material and methods

The null hypothesis was that there would be no difference between randomly assigned groups in the amount or type of resources used during the 24 months after the date of randomization. The perspective of this analysis was relative resource use (not "costs" or "charges" to insurers, providers, or individual patients). The recruitment methods and study design,[8] and clinical[9] and quality-of-life[10] outcomes, of the Ms trial have been reported, including a diagram of the flow of participants through the trial.[8] Women who were randomly assigned to hysterectomy reported significantly more improvement in 9 of the 14 health-related quality-of-life and sexual functioning outcomes we measured at 6 months. Most of the differences were no longer significant at 2 years, because of the high rate of crossing-over to hysterectomy in the medicine group and the substantial improvements in the women who were able to continue on expanded medical treatment.[10]

Subjects were recruited from the gynecology clinics at the University of Alabama, Birmingham, University of Tennessee, Memphis, Wayne State University in Detroit, and clinics affiliated with the University of California, San Diego. The study was approved by the institutional review boards (IRBs) of the 4 clinical centers and the University of California, San Francisco, where the coordinating center was located.

Subjects included English-speaking premenopausal women, aged 30 to 50 years, with at least 2 months of abnormal uterine bleeding, defined as more than 7 days of flow each month or flow heavy enough to produce anemia (hematocrit $\leq$32%). Women older than 45 years were included if their follicle-stimulating hormone level did not exceed 30 mIU/mL and if their endometrial biopsy specimen did not show evidence of hyperplasia or carcinoma. Excluded were women with other causes of anemia, desire to preserve fertility, or evidence of pregnancy, endocrinopathy, or coagulopathy, as well as women who had received treatment with long-acting regimens (depot medroxyprogesterone acetate or gonadotrophin-releasing hormone agonist) within 6 months of screening or who had used oral contraceptive pills or intrauterine devices within 3 months of screening, and those who had contraindications to study medications, potential problems with subject compliance or follow-up, or were participating in another medication trial. In addition, we excluded women with evidence of pelvic pathology for which hysterectomy or other specific directed therapy was indicated (ie, ultrasound, hysterogram, hysteroscopy, and/or biopsy specimen showing endometrial polyp, submucous lieomyoma, endometrial hyperplasia or carcinoma, or cervical dysplasia or carcinoma).

Eligible women were informed that they would be assigned randomly to hysterectomy or medical treatment. Each participant signed a consent form approved by the local IRB. Methods and results of randomization have been reported.[8] The study's methods and consent procedures were approved by the IRBs at each of the study clinical sites and at the University of California, San Francisco (project number H657-15753-07 approved through July 27, 2005). Interim monitoring to assess safety was carried out by an independent Data and Safety Monitoring Board.

Sixty-three women were randomly assigned. Women were included in the analyses reported here only if they attended at least 5 of the 8 possible follow-up interviews during the 24 months postrandomization. This criterion ensured that the absence of any reported service use in a particular period was not due simply to the absence of a study follow-up visit; the criterion eliminated 2 women randomly assigned to expanded medical treatment and 2 women randomly assigned to hysterectomy. One additional hysterectomy subject was excluded because she was randomly assigned at a study site (San Diego) at which resource use data were not collected.

The resulting study cohort for the analyses reported here included 58 subjects: 30 medicine subjects and 28 hysterectomy subjects recruited at 3 of the study centers (Birmingham: Medicine n = 19, Hysterectomy n = 18; Memphis: Medicine n = 10, Hysterectomy n = 10; Detroit: Medicine n = 1, Hysterectomy n = 0). The primary intention-to-treat analyses included patients in their assigned groups irrespective of the treatment ultimately received. Secondary as-treated analyses included 14 medicine subjects, 16 medicine subjects who had a hysterectomy (medicine crossover patients); and 27 hysterectomy subjects (1 subject assigned to the hysterectomy group did not receive a hysterectomy; this patient was omitted from the as-treated analyses because she did not receive the standard treatment provided to patients assigned to the medicine group).

Subjects were monitored for 24 months after randomization. Data were collected from subjects in structured interviews at the time of randomization and during in-person visits at 12 and 24 months, and by telephone at 3, 6, 9, 15, 18, and 21 months after randomization. Baseline data collection included demographic characteristics and