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The Cost-Effectiveness of the Levonorgestrel-Releasing Intrauterine System for the Treatment of Idiopathic Heavy Menstrual Bleeding in the United States

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ABSTRACT

Objectives: Heavy menstrual bleeding negatively impacts the health and quality of life of about 18 million women in the United States. Although some studies have established the clinical effectiveness of heavy menstrual bleeding treatments, few have evaluated their cost-effectiveness. Our objective was to evaluate the cost-effectiveness of the levonorgestrel-releasing intrauterine system (LNG-IUS) compared with other therapies for idiopathic heavy menstrual bleeding. **Methods:** We developed a model comparing the clinical and economic outcomes (from a US payer perspective) of three broad initial treatment strategies over 5 years: LNG-IUS, oral agents, or surgery. Up to three nonsurgical treatment lines, followed by up to two surgical lines, were allowed; unintended pregnancy was possible, and women could discontinue any time during nonsurgical treatments. Menstrual blood loss of 80 ml or more per cycle determined treatment failure. **Results:** Initiating treatment with LNG-IUS resulted in the fewest hysterectomies (6 per 1000 women), the most quality-adjusted life-years (3.78), and the lowest costs ($1137) among all the nonsurgical strategies. Initiating treatment with LNG-IUS was also less costly than surgery, resulted in fewer hysterectomies (vs. 9 per 1000 for ablation) but was associated with fewer quality-adjusted life-years gained per patient (vs. 3.80 and 3.88 for ablation and hysterectomy, respectively). Sensitivity analyses confirmed these results. **Conclusions:** LNG-IUS resulted in the lowest treatment costs and the fewest number of hysterectomies performed over 5 years compared with all other initial strategies and resulted in the most quality-adjusted life-years gained among nonsurgical options. Initial treatment with LNG-IUS is the least costly and most effective option for women desiring to preserve their fertility.

Keywords: cost-effectiveness, heavy menstrual bleeding, levonorgestrel-releasing intrauterine system, United States.

Introduction

Heavy menstrual bleeding (HMB), also referred to as menorrhagia, is a disorder characterized by heavy menstrual flow of 80 ml or more of blood loss per cycle that affects women of reproductive age [1]. HMB negatively impacts women's quality of life and work productivity by interfering with routine daily activities, work, and social engagements, and affects up to approximately 18 million women in the United States [2]. HMB can be caused by organic pathology (such as fibroids) or can occur without any pathology, in which case it is referred to as idiopathic or dysfunctional uterine bleeding [3,4]. This study focuses entirely on idiopathic HMB and therefore uses the term HMB.

Treatment options for women suffering from HMB include hormonal and nonhormonal medications, such as combined oral contraceptives (COCs), oral progestins, tranexamic acid (TXA [Lysteda]), nonsteroidal anti-inflammatory drugs, danazol, and the levonorgestrel-releasing intrauterine system (LNG-IUS [Mirena]), and surgical interventions such as endometrial ablation and hysterectomy. Nonsurgical treatment options are often used as first-line treatments and may be preferred by women who do not want to undergo a surgical treatment that will impair their fertility. For women who have not responded to these nonsurgical treatment options or who have completed childbearing, however, endometrial ablation and hysterectomy are used [5].

Although a number of trials have established the clinical evidence for the use of these treatment options [6–10], economic evidence is also needed to ensure efficient allocation of limited health care resources. A few studies, from perspectives other than the US health care payers, have investigated the cost-effectiveness and cost-utility of these treatments for women with HMB who also desire contraception [11–14]. Only one study, by Blumenthal et al. [15], has examined the cost-effectiveness of LNG-IUS, oral contraceptives, and surgical management of idiopathic HMB in the US population by considering three scenarios: women who have previously responded to a 3-month trial of COCs, women who did not respond to COCs, and women naive to medical therapy. After 5 years of treatment, costs associated with

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LNG-IUS were lower than those associated with other treatments in all scenarios; LNG-IUS was more effective among COC responders, but less effective among COC nonresponders and women who were treatment-naive.

The Blumenthal et al. [15] study, however, did not include surgery as a first-line treatment option, separately consider branded and generic COCs, or report outcomes in terms of quality-adjusted life-years (QALYs), making it difficult to evaluate incremental costs per outcome as reported in the broader literature. Our objective was, therefore, to evaluate (from a US payer perspective) the cost-effectiveness of LNG-IUS compared with surgical and nonsurgical treatments for women requiring treatment for HMB but who also desire contraception.

Methods

Model Description

We developed a probabilistic state-transition model that simulated the costs and outcomes, from a US payer perspective, of hypothetical women with HMB who also desired contraception. To capture the complex nature of disease progression, variations in treatment patterns, and the importance of treatment history, we implemented a patient-level (microsimulation) approach using Visual Basic for Applications in Microsoft Excel. Patients started treatment in one of three broad initial treatment strategies: LNG-IUS, oral treatments, or surgery. Oral treatments included generic COCs, branded COCs, TXA, and oral progestins; surgery included endometrial ablation and hysterectomy. Because TXA does not have contraceptive properties, we assumed that women using TXA were also using condoms for contraception. Consistent with the approved maximum duration of LNG-IUS use in the United States, we tracked patients, in the base case, for 5 years during which time they could have initiated, switched, or discontinued treatments. We tracked patients for 10 years in a sensitivity analysis; a longer time horizon is unlikely to be applicable because many potential influences on HMB can change over this duration such as contraceptive needs and preferences, pregnancy and breast-feeding (which will stop menstruation for some time, after which HMB may or may not return), and transition to menopause.

In this model, women could have received up to three nonsurgical lines of therapy and up to two surgical lines of therapy (Fig. 1). Treatment response probabilities are discussed below and presented in Table 1, and the probabilities of treatment switching and of other subsequent events are presented in Appendix Tables 1 to 3 in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2012.11.011.

Women continued using their initial nonsurgical (i.e., LNG-IUS or oral) therapy until their menstrual blood loss was 80 ml or more per cycle (i.e., they no longer responded to their treatment), they became pregnant (i.e., experienced contraceptive failure), they discontinued for other reasons, or they died. Women who were not responding to the therapy could have switched to another nonsurgical line of therapy, had surgery, or discontinued treatment.

Initial surgical options for HMB included endometrial ablation and hysterectomy. Women who had an ablation, either as their initial therapy or as a non–first-line therapy (i.e., they switched from a previous nonsurgical line), could have stopped responding but, by assumption, could not become pregnant or discontinue for other reasons. Women who no longer responded could have elected to either undergo a hysterectomy or not to receive further

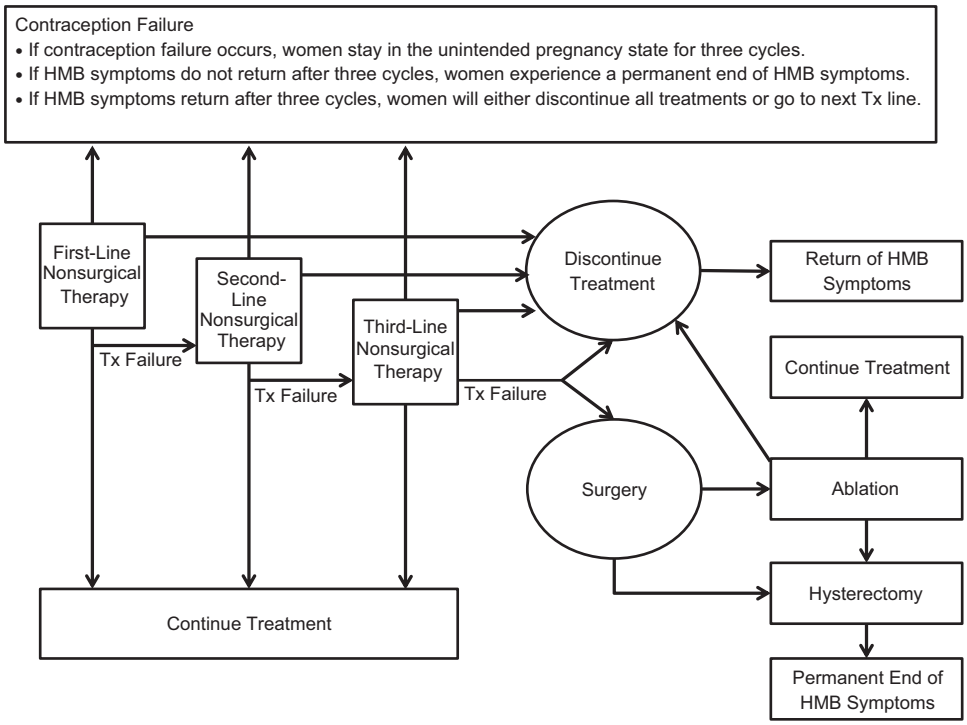

Fig. 1 – Model structure. Each model cycle represents 3 months. Women can initiate treatment with nonsurgical or surgical therapies. Women who continue treatment remain on the same therapy until treatment failure, unintended pregnancy, or they discontinue for other reasons. Women who fail their first- or second-line nonsurgical therapies can switch directly to the surgical therapy option. Women who discontinue their current nonsurgical treatment can either discontinue all treatments or switch to the next line of therapy. The model pathways for first-line surgery begin with the surgery node. Women can die at any point in the model. HMB, heavy menstrual bleeding; Tx, treatment.