

A Systematic Review Evaluating Health-Related Quality of Life, Work Impairment, and Health-Care Costs and Utilization in Abnormal Uterine Bleeding

Zhimei Liu, PhD,¹ Quan V. Doan, PharmD,¹ Paul Blumenthal, MD, MPH,² Robert W. Dubois, MD, PhD¹

¹Cerner LifeSciences, Beverly Hills, CA, USA; ²School of Medicine, Johns Hopkins University, Baltimore, MD, USA

ABSTRACT

Objectives: Abnormal uterine bleeding (AUB) impacts women's health-related quality of life (HRQoL) and puts a heavy economic burden on society. To date, this burden has not been systematically studied. We conducted a systematic review of the medical literature to evaluate the impact of AUB on HRQoL and to quantify the economic burden of AUB from a societal perspective.

Methods: We searched the PubMed and Cochrane databases, and article bibliographies for the period up to July 2005. Teams of two reviewers independently abstracted data from studies that reported outcomes of interest: prevalence, HRQoL, work impairment, and health-care utilization and costs associated with AUB.

Results: The search yielded 1009 English-language articles. Ninety-eight studies (including randomized controlled trials, observational studies, and reviews) that met the inclusion and exclusion criteria underwent a full-text review. The prevalence of AUB among women of reproductive age ranged

from 10% to 30%. The HRQoL scores from the 36-item Short-Form Health Survey Questionnaire (SF-36) suggested that women with AUB have HRQoL below the 25th percentile of that for the general female population within a similar age range. The conservatively estimated annual direct and indirect economic costs of AUB were approximately \$1 billion and \$12 billion, respectively. These figures do not account for intangible costs and productivity loss due to presenteeism.

Conclusions: The burden of AUB needs further and more thorough investigation. Additional research should prospectively evaluate the impact of AUB and the value of treatment provided to help guide future health resource allocation and clinical decision-making.

Keywords: abnormal uterine bleeding, health-care costs and utilization, health-related quality of life, systematic review, work impairment.

Introduction

Abnormal uterine bleeding (AUB) is a common gynecologic disorder affecting women of reproductive age. AUB is defined as change in frequency of menses, duration of flow, or amount of blood loss. AUB includes heavy menstrual bleeding (i.e., menorrhagia) and can be due to a functional abnormality (e.g., dysfunctional uterine bleeding [DUB]), organic abnormality (e.g., fibroids), or systemic disorder (e.g., von Willebrand disease) [1,2]. The commonly cited epidemiological information related to AUB is that up to 30% of reproductive age women suffer from menorrhagia [1].

The treatment for AUB includes both medical therapies and surgical procedures. Medical therapies are recommended as first-line treatments [3] and include

oral contraceptives (OCs), progestins, tranexamic acid, mefenamic acid, danazol, and gonadotropin-releasing hormone analogs. Women seeking treatment for AUB who also require contraception have a choice of OCs, long-acting progestogens, or the levonorgestrel-releasing intrauterine system (LNG-IUS) [1,4–9]. Hysterectomy is an invasive surgical option that usually is recommended only after other therapies for AUB have failed and for women who do not wish to retain their fertility. Endometrial ablation techniques, including first-generation (transcervical resection of the endometrium [TCRE], roller-ball, and laser ablation) and second-generation (thermal balloon, microwave, radiofrequency, cryoablation, and hydrothermal ablation), are less invasive surgical alternatives to hysterectomy [10,11].

Mortality and serious complications from AUB are extremely uncommon. The true burden of AUB is best characterized by its impact on health-related quality of life (HRQoL), as well as health-care utilization, direct costs, and indirect costs (e.g., work productivity loss).

Address correspondence to: Zhimei Liu, Cerner LifeSciences, 9100 Wilshire Boulevard, Suite 655E, Beverly Hills, CA 90212, USA. E-mail: zliu@cerner.com
10.1111/j.1524-4733.2007.00168.x

Nevertheless, no study has systematically described the burden of AUB in terms of these outcomes. The Global Burden of Disease Project, conducted as a collaboration of the World Health Organization, Harvard School of Public Health, and the World Bank, due to resource constraints did not include menstrual disorders (including AUB) among the 483 disabling diseases and injuries analyzed [12–14]. To fill this knowledge gap, we conducted a systematic review to characterize how AUB impacts HRQoL, work impairment, and health-care costs and utilization. Furthermore, we reviewed the literature that quantified the prevalence of AUB.

Methods

Literature Search and Review

We conducted a systematic review of the published literature to identify studies on AUB that reported any of our four outcomes of interest: 1) prevalence; 2) HRQoL; 3) health-care utilization and direct treatment cost; and 4) work impairment and indirect cost. We searched the PubMed and Cochrane databases for English-language articles published from 1980 to July 2005. MeSH terms and keywords were used in searches that combined disease conditions (AUB, DUB, menorrhagia, heavy menstrual bleeding) with outcomes of interest (prevalence, epidemiology, epidemiologic, quality of life, functioning, impairment, health services, utilization, care-seeking behavior, treatment-seeking behavior, burden, economics, economic, costs, cost, productivity, absenteeism, presenteeism, work impairment). We did not search for abstracts, posters, or conference proceedings.

Titles and abstracts were reviewed using explicit inclusion criteria to identify articles pertaining to our search objective. We excluded letters and case reports. After title and abstract review, we conducted a full-text review and included all studies that reported outcomes of interest. For studies on HRQoL, only those studies that used reportedly validated HRQoL instrument(s) were candidates for full-text review. During full-text review, we also searched article bibliographies to identify additional studies for full-text review.

At each stage of the review process, two reviewers conducted independent appraisals of the title/abstract or article and resolved disagreements by consensus. Inter-rater reliability was tested on a 10% sample, with Kappa values greater than 0.70 at each stage of the review.

Data from each accepted article were abstracted into an evidence table that detailed key information, including study design, sample size, study population characteristics, outcomes, and conclusions. Data were analyzed separately for each of the four outcomes of interest.

Data Synthesis

We assessed the prevalence qualitatively because the studies were few and the data were heterogeneous, thus precluding meta-analyses.

We assessed the impact of AUB on HRQoL either qualitatively or quantitatively based on the availability and heterogeneity of the data. We quantitatively evaluated studies that used the 36-item Short-Form Health Survey Questionnaire (SF-36), which is the most commonly used generic HRQoL instrument for various disease conditions including menorrhagia [15–18]. SF-36 includes 36 items that measure eight dimensions of HRQoL: physical functioning, physical role functioning, bodily pain, general health, energy/vitality, social functioning, emotional role functioning, and mental health. We used a conservative random-effects meta-analytic model to pool SF-36 scores for each of the eight domains. We then compared the pooled estimates with the US population normative values for women aged from 18 to 54 years, which was calculated as the weighted average across age groups [19]. We qualitatively assessed the rest of the studies on HRQoL.

We also estimated the total direct and indirect economic burden due to AUB from a societal perspective and at the population level. We based our estimate on the disease prevalence, health-care utilization, treatment costs, and indirect cost per person as identified from our literature review. Direct economic burden included treatment costs associated with AUB, while indirect economic burden included productivity loss due to work impairment, specifically absenteeism (i.e., productivity loss because of absence from work) and presenteeism (i.e., productivity loss while at work). We chose the lower and upper bound of each variable to provide the most conservative as well as a liberal economic estimate.

Results

Literature Review

Our initial search strategy yielded 1009 publications; 79 studies met our title/abstract inclusion criteria and underwent a full-text review. Bibliographic searches yielded 15 additional studies for full-text review. Of these 94 articles, 20 were reviews and their information served as background for this systematic review. The remaining 74 articles underwent data abstraction for the following outcomes: prevalence, 6; HRQoL, 34; health-care utilization, 30 (health-care utilization only, 25; the rest of the 30 studies also addressed HRQoL); and work impairment, 4.

Prevalence of AUB

Only six studies assessed prevalence of AUB; prevalence varied considerably depending on how blood loss

was measured. Data from population-based studies, conducted several decades ago and including samples of fewer than 1000 women, suggested that approximately 10% of reproductive-aged women had objective evidence of menorrhagia (i.e., menstrual blood loss more than 80 ml) [20,21]. In contrast, studies based on self-reported information suggested that approximately 30% of women of reproductive age were afflicted with heavy menstrual bleeding [22–24]. The discrepancy in subjective and objective measures of blood loss also was found in several other studies [25,26].

A completely objective measure, such as extracting hemoglobin from sanitary wear to assess blood loss (i.e., alkaline hematin technique), usually is impractical outside of controlled research settings. A mandate for objective assessment of blood loss may not be appropriate because the amount of blood loss does not fully predict women's care-seeking behavior [27,28]. Most gynecologists (96%) indicated that they diagnosed menorrhagia based on women's self-reported symptoms of excessive menstrual bleeding [25]. The pictorial blood loss assessment chart is a widely used alternative to measure blood loss. This semiobjective measure takes into account the number of items of sanitary wear used and the degree of staining of each item, and is easier to perform than the alkaline hematin technique, yet yields more objective results than self-reporting [29].

Discordance also existed depending on who assessed the condition. Gynecologists reported that only 8% of their patients complained of menorrhagia; this estimate is lower than the rate based on self-report [25], which suggests that not all women seek treatment for perceived menstrual disorders, among which AUB would be prominent. One study reported that 57.1% of patients who considered their symptoms as severe were rated by their physicians as having only moderate symptoms. Conversely, 28.7% of the patients reporting mild or moderate severity were diagnosed with severe symptoms [30].

Health-Related Quality of Life

Impact of AUB on HRQoL. AUB has a broad impact on HRQoL. Menorrhagia is the most common cause of iron-deficiency anemia in the developed world. Excessive menstrual bleeding (monthly blood loss in excess of 60 ml) can deplete iron stores, which leads to iron-deficiency anemia. Anemia may impact HRQoL by manifesting as weakness, fatigue, unexplained weight loss, mood swings, and impaired cognitive functioning [31].

Table 1 lists the eight studies that provided SF-36 scores in all eight domains attributable to AUB (i.e., before a specified treatment) and thus were included in the meta-analysis [32–39]. Two other studies also used

the SF-36, but provided only summary scores of the physical and mental components and were excluded from the meta-analysis [40,41]. All eight studies were randomized controlled trials (RCTs), and only one was conducted in the United States. For seven of the studies, the mean age of the study population was approximately 40 years; one study had a relatively young population (mean age: 29 years) [38]. Each study provided two sets of baseline SF-36 scores in all eight domains (because each study involved two treatments) and thus a total of 16 data points were available for the meta-analysis on each domain.

The results showed that women with AUB had lower SF-36 scores for all eight subscales compared with normative values for American women aged from 18 to 54 years. The most significantly affected domains were the physical role functioning and emotional role functioning subscales, which focus on work productivity and other daily activities. For six of the eight subscales, scores for women with AUB were below the 25th percentile of national norms. The biggest impact was observed for the physical role functioning domain, which was 23 points below the 25th percentile norms (60.3 vs. 83.2) (Table 2).

Sixteen studies used other validated HRQoL instruments, which measured the impact of AUB on various aspects of women's lives including sexual functioning, depression, anxiety, irritability, psychosocial adjustment, and personality [22,30,41–54]. Only four of these studies were conducted in the United States, and the mean age in most of the studies was approximately 40 years.

These studies showed that AUB affected sexual functioning [30,41], was associated with psychological morbidity [22,30,43–48,50,52–54], and affected social, professional, and family life [30,45,46,49,51]. For example, Kuppermann et al. reported that in women with AUB refractory to hormonal management (mean age: 41.8 years), the sexual functioning scores measured by the Medical Outcomes Study Sexual Problems Scales were only 55–69 as compared with 100 (optimal functioning) [41]. Greenberg and coworkers showed that mild-to-moderate neurotic depression was found in 62% of women with AUB referred to a gynecologic clinic [53]. Shaw et al. evaluated the impacts of menorrhagia using a multiattribute utility assessment tool. They found that the order of the impacts of menorrhagia (from most important to least important) was family life, physical health, work life, psychological health, practical difficulties, and social life [46].

Few studies expressed HRQoL as a preference or utility measure. A preference measure represents the value that one assigns to a health state (e.g., menorrhagia), typically on a scale from zero (representing death) to one (representing perfect health); a score of 0.5 therefore is equivalent to a half year of perfect

Table 1 Impact of AUB on HRQoL: studies reporting SF-36 scores

Reference	Author (Year)	Study setting	Treatment group (n)	Study population (Mean age)	Baseline domain scores: mean (SD)	
					Group 1	Group 2
[37]	Cooper et al. (2005)	UK	MEA (n = 116) vs. TCRE (n = 120)	41.4 vs. 42.4	PF: 84 (21) RP: 57 (43) BP: 57 (28) GH: 71 (21)	VT: 45 (23) SF: 60 (23) RE: 60 (42) MH: 63 (19)
[39]	Bongers et al. (2005)	The Netherlands	BEA (n = 40) vs. BRFEA (n = 75)	43.3 vs. 42.2	PF: 83 (16) RP: 73 (27) BP: 63 (22) GH: 76 (21)	VT: 54 (20) SF: 76 (21) RE: 80 (26) MH: 72 (18)
[36]	Bain et al. (2002)	Scotland	MEA (n = 120) vs. TCRE (n = 129)	41.1 vs. 42.2	PF: 84 (20) RP: 56 (43) BP: 56 (28) GH: 70 (22)	VT: 44 (23) SF: 60 (23) RE: 61 (42) MH: 63 (19)
[32]	Cooper et al. (2001)	UK	Medical (n = 71) vs. TCRE (n = 73)	41.8 vs. 41.6	PF: 78 (22) RP: 55 (39) BP: 56 (24) GH: 70 (21)	VT: 40 (17) SF: 70 (21) RE: 59 (43) MH: 58 (18)
[38]	Davis et al. (2000)	US	Placebo (n = 95) vs. OC (n = 97)	29.3 vs. 29.8	PF: 89 (30) RP: 75 (21) BP: 77 (11) GH: 77 (11)	VT: 60 (17) SF: 85 (22) RE: 83 (30) MH: 75 (17)
[33]	Cooper et al. (1999)	UK	Medical (n = 86) vs. TCRE (n = 87)	41.4 vs. 41.9	PF: 79 (21) RP: 53 (38) BP: 54 (24) GH: 68 (19)	VT: 40 (17) SF: 68 (21) RE: 57 (43) MH: 58 (18)
[35]	Cooper et al. (1999)	UK	MEA (n = 116) vs. TCRE (n = 124)	41.1 vs. 41.0	PF: 85 (19) RP: 57 (42) BP: 55 (28) GH: 70 (22)	VT: 44 (23) SF: 60 (23) RE: 62 (43) MH: 64 (19)
[34]	Cooper et al. (1997)	UK	Medical (n = 93) vs. TCRE (n = 93)	41.4 vs. 41.7	PF: 79 (21) RP: 54 (38) BP: 54 (25) GH: 68 (19)	VT: 41 (17) SF: 69 (21) RE: 58 (42) MH: 58 (18)
					PF: 82 (22) RP: 64 (41) BP: 63 (27) GH: 72 (20)	VT: 43 (24) SF: 60 (23) RE: 60 (43) MH: 63 (21)
					PF: 82 (19) RP: 79 (30) BP: 62 (20) GH: 73 (19)	VT: 56 (19) SF: 76 (19) RE: 85 (26) MH: 72 (18)
					PF: 83 (23) RP: 64 (41) BP: 63 (26) GH: 73 (19)	VT: 43 (24) SF: 60 (23) RE: 63 (43) MH: 63 (21)
					PF: 81 (20) RP: 53 (39) BP: 60 (25) GH: 65 (20)	VT: 40 (20) SF: 70 (24) RE: 52 (43) MH: 58 (19)
					PF: 89 (17) RP: 87 (25) BP: 71 (23) GH: 75 (15)	VT: 57 (18) SF: 84 (20) RE: 79 (31) MH: 73 (14)
					PF: 82 (19) RP: 57 (39) BP: 58 (25) GH: 66 (19)	VT: 41 (19) SF: 70 (24) RE: 55 (44) MH: 59 (19)
					PF: 82 (23) RP: 63 (42) BP: 64 (26) GH: 73 (19)	VT: 43 (24) SF: 60 (23) RE: 63 (43) MH: 64 (22)
					PF: 82 (19) RP: 57 (39) BP: 58 (26) GH: 65 (20)	VT: 42 (19) SF: 69 (24) RE: 53 (44) MH: 59 (19)

All studies are randomized controlled trials.

AUB, abnormal uterine bleeding; BEA, balloon endometrial ablation; BP, bodily pain/pain; BRFEA, bipolar radio frequency endometrial ablation; GH, general health perception; HRQoL, health-related quality of life; MEA, microwave endometrial ablation; MH, mental health; OC, oral contraceptive; PF, physical functioning; RE, role limitation/emotional; RP, role limitation/physical; SF, social functioning; TCRE, transcervical resection of the endometrium; VT, vitality/energy/fatigue.

Table 2 Impact of AUB on HRQoL: SF-36 subscale scores compared with the national norms (highest HRQoL = 100)

		Physical function	Role/physical	Pain	General health	Vitality	Social function	Role/emotional	Mental health
National norms*	25th percentile	83.3	83.2	60.9	64.2	46.2	72.1	70.4	63.6
	Mean	87.5	84.0	76.7	73.8	59.3	83.1	81.1	73.1
AUB	Meta-analysis (random-effects)	82.1	60.3	58.8	69.9	43.9	66.1	62.3	62.4

*Source: SF-36 Health Survey Manual & Interpretation Guide.

AUB, abnormal uterine bleeding; HRQoL, health-related quality of life.

health. In one study, preference for menorrhagia was solicited from the time trade-off technique, and it yielded a median of 0.55 (range: 0–0.95) and a mean of 0.5 (SE = 0.04) [55]. A generic instrument measuring health outcomes developed by the EuroQol group (i.e., the EQ-5D) is gaining favor as a measure of utility. Table 3 lists the four studies that provided baseline EQ-5D information regarding AUB; two studies were for the same population but with different lengths of follow-up [8,45,56,57]. The study conducted by Hurskainen et al. showed that the EQ-5D scores in women with AUB were significantly lower than the mean scores of Finnish or British women of the same age, suggesting that AUB may lead to significantly worse health [45].

Impact of AUB treatment on HRQoL. HRQoL was included as one of the outcomes in many studies evaluating treatment for AUB [11,58–64]. Among the 34 identified studies, 22 studies also provided baseline HRQoL information and thus were summarized in the previous section. The additional 12 studies had similar study characteristics as those for the 22 studies (i.e., most were conducted in European countries, and the mean age of the study population was approximately 40 years).

Studies showed that both first- and second-generation endometrial ablation techniques significantly improved HRQoL [35–37,39,42,44,56,57, 65,66]. For example, the two most recently published RCTs showed that various endometrial ablation techniques including TCRE, microwave endometrial

ablation, bipolar radio frequency endometrial ablation, and balloon endometrial ablation improved the majority of the eight SF-36 health domains, achieving SF-36 scores similar to those for the general population over both short term and long term [37,39]. Use of the LNG-IUS was associated with the improvements in HRQoL that were very similar to those seen with endometrial ablation techniques [67–69]. Hysterectomy also significantly improved HRQoL; its overall effect was similar to that of LNG-IUS or ablation, but may have been particularly effective at reducing bodily pain commonly experienced by women awaiting hysterectomy [8,41,45,47–51,54,70–74]. OCs, progestins, and other pharmacological therapies yielded the least improvement in HRQoL among the AUB treatments studied [30,32–34,38,40,75]. One review concluded that there was insufficient information on outcomes of medical management to guide clinical decision-making [76].

Health Services Utilization and Costs

Impact of AUB on health services utilization. In the United States, AUB is associated with significant utilization of resources in various health-care sectors. Women who reported heavier menstrual blood loss were more likely to visit a physician (OR = 1.48, $P \leq 0.01$), to receive emergency room care (OR = 1.79, $P \leq 0.01$), and to undergo a surgical procedure (OR = 1.56, $P \leq 0.01$) [77,78]. Data from the National Hospital Discharge Survey indicated that AUB contributed to more than 5 million hospitalizations, 2 million

Table 3 Effects of AUB on HRQoL: studies reporting baseline EQ-5D scores

Reference	Author (year)	Study setting	Study design	Study population (mean age)	Treatment group (n)	Baseline EQ-5D scores: mean (SD)	
						Group 1	Group 2
[56]	Hawe et al. (2003)	UK	RCT	Women with DUB (41.4 vs. 41.1)	Cavaterm (n = 34) vs. endometrial laser ablation (n = 33)	EQ-5D index: 0.78 (0.26) EQ-5D vas: 77.3 (14.2)	EQ-5D index: 0.65 (0.31) EQ-5D vas: 69.4 (18.0)
[57]	Abbott et al. (2003)	UK	RCT	Women with DUB (40.5 vs. 40.5)	Cavaterm (n = 17) vs. NovaSure (n = 37)	EQ-5D index: 0.66 (0.34) EQ-5D vas: 70.2 (25.8)	EQ-5D index: 0.71 (0.23) EQ-5D vas: 75.7 (18.1)
[45] [8]	Hurskainen et al. (2001)	Finland	RCT	Women with menorrhagia (43.1 vs. 43.0)	LNG-IUS (n = 119) vs. hysterectomy (n = 117)	EQ-5D index: 0.76 (0.70–0.80)	EQ-5D index: 0.78 (0.70–0.80)

AUB, abnormal uterine bleeding; DUB, dysfunctional uterine bleeding; HRQoL, health-related quality of life; LNG-IUS, levonorgestrel-releasing intrauterine system; RCT, randomized controlled trial.

Table 4 Conservative estimation of the annual direct economic burden of AUB

Treatment	Utilization	Cost per person (2005 USD)	Total costs (2005 USD)
GP visit	3 million	35*	105 million
Drug therapy	1.8 million [†]	146 [‡]	263 million
Hysterectomy	125,000 [§]	4538	567 million
Endometrial ablation	35,714 [#]	1770 [#]	63 million
Total			998 million

*CPT = 99212 [114,115].

[†]Calculation is based on 72 million women aged 15–49 years, multiplied by 10% prevalence rate of AUB, and 1/4 seeking treatment [22,89,116].

[‡]3 months of supply of OCs (Ortho-Novum) [3,117].

[§]The total annual 500,000 hysterectomies multiplied by 25% attributable to AUB.

^{||}The sum of the physician fee of \$881 (CPT = 58150, 58260, 58550) and hospitalization costs of \$3657 (DRG = 359) [115,118].

[#]Based on rate ratio of 3.5:1 between hysterectomy and ablation.

[#]The sum of the physician fee of \$301 (CPT = 58353, 58563) and hospital outpatient service payment of \$1469 [115,119].

AUB, abnormal uterine bleeding; GP, general practitioner.

hysterectomies, and 20 million hospital days in the United States between 1980 and 1992 [79]. From 1988 to 1990, AUB was the fourth most common gynecologic cause for hospitalization, and 89% of those hospitalized underwent surgery [80]. AUB accounted for more than 3 million ambulatory care visits (mostly to physician offices) annually from 1999 to 2000 [81] and for more than 20% of all visits to obstetricians/gynecologists [82].

Treatment utilization. No study reported the rate of medical treatment in the United States. Clinical experts suggest that physicians normally would recommend at least 3 months of pharmaceutical therapy (e.g., OCs) as initial treatment. The rate of endometrial ablation also was rarely reported. In a study that analyzed data from Colorado, Maryland, New Jersey, Connecticut, New York, and Wisconsin, Farquhar et al. found that the ratios of total number of hysterectomy to endometrial ablation ranged from 1 to 3.5 in 1997. Because of the findings that over time the diffusion of endometrial ablation has had minimal impact on the rate of hysterectomy, they concluded that endometrial ablation was used as an adjunctive technology rather than a substitute for hysterectomy [83].

Hysterectomy remained second only to cesarean section as the most frequently performed major operation in the United States throughout the 1990s, with rates of 5.44, 5.23, 5.39, 5.60, and 4.40 per 1000 women aged 16 years or older in 1991, 1993, 1995, 1997, and 1999, respectively [84–87]. AUB is a frequently cited indication for hysterectomy and accounts for as many as 25% of all hysterectomies [49,88]. A study reported AUB as the main presenting problem in at least half of all the hysterectomies reported [89].

Treatment costs. Numerous studies compared the treatment costs of endometrial ablation with hysterectomy. Nevertheless, direct comparisons of these costs in absolute terms across studies were precluded by variations across study settings, study populations, year of reported cost, and cost components (e.g.,

whether or not direct or indirect costs were considered, or whether or not ablation failure rates were factored). Despite this heterogeneity, most studies suggested that hysterectomy cost twice as much as ablation [72,74,88,90–99].

In one randomized trial, the overall costs of LNG-IUS when used to treat AUB were approximately three times lower than for the hysterectomy group at 1 year of follow-up (averaging \$1529 vs. \$4222 per person, in 1996 US dollars) [45]. At 5 years of follow-up, the discounted direct and indirect costs in the LNG-IUS group remained substantially lower than in the hysterectomy group (\$2817 [95% CI: \$2222–3530] per participant vs. \$4660 [95% CI: \$4014–5180], in 2001 US dollars) [8]. The cost of LNG-IUS also compared favorably with the annual cost of available medical treatments including ibuprofen, OCs, mefenamic acid, progesterin, tranexamic acid, Provera, and danazol [100].

Estimated direct economic burden of AUB. Based on the reported prevalence, utilization rate, and unit costs, we estimated the total direct cost due to AUB as approximately \$1 billion annually (in 2005 US dollars). This included the costs of physician visits, drug therapy, and treatment with hysterectomy and ablation. Cost for hysterectomy alone may have accounted for approximately half of the total treatment cost (Table 4).

The total annual cost of \$1 billion is a very conservative estimate because we took the lower end value for each data element. For example, based on the results of Farquhar et al. we estimated that approximately 35,714 ablations are performed annually (Table 4). Nevertheless, in another study in our review, Gurtcheff and Sharp estimated that approximately 194,000 endometrial ablation procedures were performed through May 2003 using ThermaChoice, NovaSure, Her Option, and HydroThermAblator [101]. Based on their figures, after the number of years these devices had been on the market through 2003 was taken into account, the expected average number

of ablation procedures per year would be 52,606. Using this number, the total cost associated with endometrial ablation will increase to approximately \$93 million per year. Furthermore, assuming a 30% prevalence rate, the total cost for drug therapy will be \$789 million per year. Therefore, a less conservative estimate of the total costs associated with AUB is approximately \$1.55 billion, a 55% increase from the conservative estimate.

Work Impairment (Indirect Costs)

Impact of AUB on work impairment. Very few studies have assessed the impact of AUB on work productivity. Hurskainen et al. reported that among women with objective evidence of menorrhagia, 20% reported having missed work because of menorrhagia during the previous 6 months [102]. Pron et al. suggested that as many as 40% of women with fibroids (80% of whom reported heavy menstrual bleeding) reported taking time off work in the previous year for fibroid-related reasons—often several days a month, particularly around the time of menstruation [103]. Among women needing surgical treatment for menorrhagia, 39% to 55% reportedly took time off work in the previous 6 months [51].

Only one study reported indirect costs due to AUB. Cote et al. estimated that heavy bleeders worked 3.6 weeks fewer per year than nonheavy bleeders. They also estimated that the work loss from increased blood flow was \$1692 annually per woman [104]. Nevertheless, their estimation only took into account absenteeism, not presenteeism; therefore, productivity loss attributable to AUB in their study may have been substantially underestimated.

Estimated indirect economic burden of AUB. We estimated the annual indirect cost attributable to AUB as approximately \$12 billion based on the conservative estimate of the prevalence rate of AUB and the results of Cote et al.'s study (7.2 million sufferers multiplied by \$1692, in 2005 US dollars). When we assumed a prevalence rate of 30%, this number increased to \$36 billion. The indirect costs exceeded the direct costs attributable to AUB by 12-fold (conservative estimate) and 23-fold (liberal estimate). For the same reason mentioned earlier, the actual indirect cost estimate may be higher when presenteeism is taken into account.

Discussion

Epidemiological studies suggested that approximately 10% to 30% of reproductive-aged women were affected by menorrhagia. It is likely that the prevalence of AUB, which is a broader clinical condition than menorrhagia, could be higher than the estimated 10% to 30%. Accurately estimating the prevalence of AUB

is a challenge because some of the diagnostic methods are objective while others are subjective, and discordance exists between how patients and physicians rate severity of AUB symptoms. Studies suggested that subjective measures are better than objective measures in predicting women's treatment-seeking behavior [27,28]. Given that the studies employing subjective measures reported higher prevalence rates, this means that the direct and indirect economic burden of AUB may settle at the upper bound of our estimation instead of the conservative estimation. The true burden of AUB relies on an accurate estimate of AUB prevalence; therefore, it is very important to conduct epidemiologic studies using a standardized definition. Such research will help establish the burden of AUB and raise awareness for future policy and resource planning.

We attempted to quantify the burden of AUB by comparing scores from validated HRQoL instruments with population norms, using the meta-analysis technique. Despite the criticism of using a generic HRQoL instrument [15,16], the SF-36 assesses a breadth of HRQoL variables that are important to all patients and thus helps compare individuals with a given disease with the general population or with individuals with other diseases. We found that according to the SF-36 results, health with AUB was below the 25th percentile for the US general female population and AUB affected mostly the domains that were directly linked to the work productivity and daily activities.

We found only one study that quantified the costs stemming from absenteeism, but no studies for presenteeism. In estimating the indirect economic burden of AUB, these omitted costs (work loss due to presenteeism) could represent an important burden from the perspectives of society. Therefore, the current estimate of annual indirect costs could be a large underestimation. In future research, a more thorough evaluation of work impairment, with particular attention to presenteeism, is needed to assess the full impact of AUB.

There are certain issues regarding treatment utilization in AUB. There is evidence suggesting both undertreatment and overtreatment for AUB. Not all women suffering from AUB sought or received appropriate treatment. For example, studies suggested that only approximately 25% of women who complained of heavy menstrual bleeding actually sought health care [22,89]. The mean duration of AUB symptoms ranged from 3 to 9 years before treatment [38,67,69,98,105–107]. On the other hand, there was evidence suggesting that some of the hysterectomies performed to treat AUB may have been unnecessary [108–110]. In one study, one-third of women complaining of menorrhagia but without objective evidence of heavy menstrual bleeding still underwent hysterectomy [110]. This overutilization may be reflected in the estimated high proportion of costs associated with hysterectomy

among the estimated annual direct treatment costs for AUB. The high rate of hysterectomy for AUB may indicate either that women are not fully informed about the availability of the less invasive techniques or that there is a lack of communication between patients and their physicians, who greatly influence women's decision-making. Addressing these issues is likely to impact the health-care utilization and costs associated with AUB.

Studies have suggested that medical treatment with LNG-IUS and surgical treatment with endometrial ablation or hysterectomy can all significantly improve women's HRQoL. Choosing among these treatments may therefore depend on the relative cost-effectiveness or cost-utility of each treatment. In addition, women's preference strongly predicts the actual treatment [109]. Many women may prefer procedures that are less invasive than hysterectomy and would be willing to undergo these procedures even if the chance of success is relatively poor [34,111–113]. Studies are needed to evaluate the cost-effectiveness and cost-utility of various treatment options for AUB, and to reveal women's treatment preferences as less invasive options become available. If disseminated appropriately, this information is likely to help improve the quality of care and reduce the economic burden of AUB on payers and society.

We suggest that further research on AUB be directed to the areas of epidemiology, health economics, health services, and patient-reported outcomes. As awareness for the burden of AUB becomes greater, policymakers, clinicians, and patient advocacy groups are likely to demand better information. Although our systematic review reveals available literature in these various areas, the data are highly random and disconnected, thus contributing to low precision when quantifying burden of illness. In order for future research to be more useful, the definition of AUB needs to be standardized so that it can be easily applied to many types of research (such as clinical trials, epidemiological research, health services research, social science research, etc.). Payers will need to understand AUB-related resource utilization, predictors of utilization, and preferences for different services to treat AUB. Moreover, there is a need to understand the economic value of existing and emerging therapies for managing AUB to make better decisions regarding health-care spending. Policymakers will also need to understand the appropriateness of current utilization. Employers may also be interested in understanding the impact of AUB on work force productivity with particular attention to presenteeism.

Conclusion

Evaluation of the literature suggests that the prevalence of AUB is at least 10% to 30% among

reproductive-aged women. The impact of AUB encompasses all aspects of HRQoL, with six health domains measured by SF-36 below the 25th percentile of the US general female population. AUB may also cost the society \$1 billion to \$1.55 billion in annual direct treatment costs and \$12 billion to \$36 billion in annual indirect costs. The public as well as policymakers need to increase awareness of the impact of this common benign gynecologic disorder. Addressing issues such as better quantifying the burden of AUB as well as evaluating and disseminating information regarding the most cost-effective solutions will likely result in positive economic, health, and social impact.

We thank Berlex Laboratories, NJ for providing financial support for this project.

References

- 1 Vilos GA, Lefebvre G, Graves GR. SOGC clinical practice guidelines. Guidelines for the management of abnormal uterine bleeding. *J Obstet Gynaecol Can* 2001;106:1–6.
- 2 Albers JR, Hull SK, Wesley RM. Abnormal uterine bleeding. *Am Fam Physician* 2004;69:1915–26.
- 3 Royal College of Obstetricians and Gynaecologists. The Initial Management of Menorrhagia. National Evidence-Based Clinical Guidelines. Available from: <http://www.rcog.org.uk/index.asp?PageID=698> [Accessed May, 2005].
- 4 Roy SN, Bhattacharya S. Benefits and risks of pharmacological agents used for the treatment of menorrhagia. *Drug Saf* 2004;27:75–90.
- 5 Protheroe J. Modern management of menorrhagia. *J Fam Plann Reprod Health Care* 2004;30:118–22.
- 6 Royal College of Obstetricians and Gynaecologists. The Management of Menorrhagia in Secondary Care. National Evidence-Based Clinical Guidelines. Available from: <http://www.rcog.org.uk/index.asp?PageID=692> [Accessed May, 2005].
- 7 Faculty of Family Planning and Reproductive Health Care Guidance. The levonorgestrel-releasing intrauterine system (LNG-IUS) in contraception and reproductive health. *J Fam Plann Reprod Health Care* 2004;30:99–108.
- 8 Hurskainen R, Teperi J, Rissanen P, et al. Clinical outcomes and costs with the levonorgestrel-releasing intrauterine system or hysterectomy for treatment of menorrhagia: randomized trial 5-year follow-up. *JAMA* 2004;291:1456–63.
- 9 Hurskainen R, Paavonen J. Levonorgestrel-releasing intrauterine system in the treatment of heavy menstrual bleeding. *Curr Opin Obstet Gynecol* 2004;16:487–90.
- 10 Sowter MC. New surgical treatments for menorrhagia. *Lancet* 2003;361:1456–8.
- 11 Marjoribanks J, Lethaby A, Farquhar C. Surgery versus medical therapy for heavy menstrual bleeding. *Cochrane Database Syst Rev* 2003;CD003855.
- 12 Murray CJL, Lopez AD. The Global Burden of Disease: A Comprehensive Assessment of Mortality

- and Disability from Diseases, Injuries, and Risk Factors in 1990 and Projected to 2020. Cambridge, MA: World Health Organization and the World Bank, 1997.
- 13 Murray CJL, Lopez AD. Global Health Statistics: A Compendium of Incidence, Prevalence and Mortality Estimates for Over 200 Conditions. Cambridge, MA: World Health Organization and the World Bank, 1997.
 - 14 World Health Organization. Report on the informal consultation on DALYs and reproductive health, 27–28 April 1998. Division of Reproductive Health Technical Support (RHT). Available from: http://www.who.international/reproductive-health/publications/RHT_98_28/dalys_and_reproductive_health.pdf [Accessed November 1, 2005].
 - 15 Clark TJ, Khan KS, Foon R, et al. Quality of life instruments in studies of menorrhagia: a systematic review. *Eur J Obstet Gynecol Reprod Biol* 2002; 104:96–104.
 - 16 Jones GL, Kennedy SH, Jenkinson C. Health-related quality of life measurement in women with common benign gynecologic conditions: a systematic review. *Am J Obstet Gynecol* 2002;187:501–11.
 - 17 Barnard K, Frayne SM, Skinner KM, Sullivan LM. Health status among women with menstrual symptoms. *J Womens Health (Larchmt)* 2003;12: 911–19.
 - 18 Jenkinson C, Peto V, Coulter A. Making sense of ambiguity: evaluation in internal reliability and face validity of the SF 36 questionnaire in women presenting with menorrhagia. *Qual Health Care* 1996;5:9–12.
 - 19 Ware JE Jr, Kosinski M, Gandek B. SF-36 Health Survey: Manual & Interpretation Guide. Lincoln, RI: QualityMetric Incorporated, 2002.
 - 20 Cole SK, Billewicz WZ, Thomson AM. Sources of variation in menstrual blood loss. *J Obstet Gynaecol Br Commonw* 1971;78:933–9.
 - 21 Hallberg L, Hogdahl AM, Nilsson L, Rybo G. Menstrual blood loss—a population study. Variation at different ages and attempts to define normality. *Acta Obstet Gynecol Scand* 1966;45:320–51.
 - 22 Gath D, Osborn M, Bungay G, et al. Psychiatric disorder and gynaecological symptoms in middle aged women: a community survey. *Br Med J (Clin Res Ed)* 1987;294:213–18.
 - 23 Rees MC. Role of menstrual blood loss measurements in management of complaints of excessive menstrual bleeding. *Br J Obstet Gynaecol* 1991;98: 327–8.
 - 24 Shapley M, Jordan K, Croft PR. An epidemiological survey of symptoms of menstrual loss in the community. *Br J General Pract* 2004;54:359–63.
 - 25 Dilley A, Drews C, Lally C, et al. A survey of gynecologists concerning menorrhagia: perceptions of bleeding disorders as a possible cause. *J Womens Health Gend Based Med* 2002;11:39–44.
 - 26 Fraser IS, McCarron G, Markham R. A preliminary study of factors influencing perception of menstrual blood loss Volume. *Am J Obstet Gynecol* 1984; 149:788–93.
 - 27 Coulter A, Long A, Kelland J, et al. Managing menorrhagia. *Qual Health Care* 1995;4:218–26.
 - 28 Warner PE, Critchley HO, Lumsden MA, et al. Menorrhagia II: is the 80-mL blood loss criterion useful in management of complaint of menorrhagia? *Am J Obstet Gynecol* 2004;190:1224–9.
 - 29 Higham JM, O'Brien PM, Shaw RW. Assessment of menstrual blood loss using a pictorial chart. *Br J Obstet Gynaecol* 1990;97:734–9.
 - 30 Coulter A, Peto V, Jenkinson C. Quality of life and patient satisfaction following treatment for menorrhagia. *Fam Pract* 1994;11:394–401.
 - 31 Cohen BJ, Gibor Y. Anemia and menstrual blood loss. *Obstet Gynecol Surv* 1980;35:597–618.
 - 32 Cooper KG, Jack SA, Parkin DE, Grant AM. Five-year follow up of women randomised to medical management or transcervical resection of the endometrium for heavy menstrual loss: clinical and quality of life outcomes. *BJOG* 2001;108:1222–8.
 - 33 Cooper KG, Parkin DE, Garratt AM, Grant AM. Two-year follow up of women randomised to medical management or transcervical resection of the endometrium for heavy menstrual loss: clinical and quality of life outcomes. *Br J Obstet Gynaecol* 1999;106:258–65.
 - 34 Cooper KG, Parkin DE, Garratt AM, Grant AM. A randomised comparison of medical and hysteroscopic management in women consulting a gynaecologist for treatment of heavy menstrual loss. *Br J Obstet Gynaecol* 1997;104:1360–6.
 - 35 Cooper KG, Bain C, Parkin DE. Comparison of microwave endometrial ablation and transcervical resection of the endometrium for treatment of heavy menstrual loss: a randomised trial. *Lancet* 1999; 354:1859–63.
 - 36 Bain C, Cooper KG, Parkin DE. Microwave endometrial ablation versus endometrial resection: a randomized controlled trial. *Obstet Gynecol* 2002; 99:983–7.
 - 37 Cooper KG, Bain C, Lawrie L, Parkin DE. A randomised comparison of microwave endometrial ablation with transcervical resection of the endometrium; follow up at a minimum of five years. *BJOG* 2005;112:470–5.
 - 38 Davis A, Godwin A, Lippman J, et al. Triphasic norgestimate-ethinyl estradiol for treating dysfunctional uterine bleeding. *Obstet Gynecol* 2000;96: 913–20.
 - 39 Bongers MY, Bourdrez P, Heintz AP, et al. Bipolar radio frequency endometrial ablation compared with balloon endometrial ablation in dysfunctional uterine bleeding: impact on patients' health-related quality of life. *Fertil Steril* 2005;83:724–34.
 - 40 Kuppermann M, Varner RE, Summitt RL, et al. Effect of hysterectomy vs medical treatment on health-related quality of life and sexual functioning: the medicine or surgery (Ms) randomized trial. *JAMA* 2004;291:1447–55.
 - 41 Kuppermann M, Summitt RL Jr, Varner RE, et al. Sexual functioning after total compared with supracervical hysterectomy: a randomized trial. *Obstet Gynecol* 2005;105:1309–18.

- 42 Rosenbaum SP, Fried M, Munro MG. Endometrial hydrothermablation: a comparison of short-term clinical effectiveness in patients with normal endometrial cavities and those with intracavitary pathology. *J Minim Invasive Gynecol* 2005;12:144–9.
- 43 Shapley M, Jordan K, Croft PR. Increased vaginal bleeding and psychological distress: a longitudinal study of their relationship in the community. *BJOG* 2003;110:548–54.
- 44 Wright B, Gannon MJ, Greenberg M, et al. Psychiatric morbidity following endometrial ablation and its association with genuine menorrhagia. *BJOG* 2003;110:358–63.
- 45 Hurskainen R, Teperi J, Rissanen P, et al. Quality of life and cost-effectiveness of levonorgestrel-releasing intrauterine system versus hysterectomy for treatment of menorrhagia: a randomised trial. *Lancet* 2001;357:273–7.
- 46 Shaw RW, Brickley MR, Evans L, Edwards MJ. Perceptions of women on the impact of menorrhagia on their health using multi-attribute utility assessment. *Br J Obstet Gynaecol* 1998;105:1155–9.
- 47 Alexander DA, Naji AA, Pinion SB, et al. Randomised trial comparing hysterectomy with endometrial ablation for dysfunctional uterine bleeding: psychiatric and psychosocial aspects. *BMJ* 1996;312:280–4.
- 48 Gath D, Rose N, Bond A, et al. Hysterectomy and psychiatric disorder: are the levels of psychiatric morbidity falling? *Psychol Med* 1995;25:277–83.
- 49 Clarke A, Black N, Rowe P, et al. Indications for and outcome of total abdominal hysterectomy for benign disease: a prospective cohort study. *Br J Obstet Gynaecol* 1995;102:611–20.
- 50 Carlson KJ, Miller BA, Fowler FJ Jr. The Maine Women's Health Study: I. Outcomes of hysterectomy. *Obstet Gynecol* 1994;83:556–65.
- 51 Dwyer N, Hutton J, Stirrat GM. Randomised controlled trial comparing endometrial resection with abdominal hysterectomy for the surgical treatment of menorrhagia. *Br J Obstet Gynaecol* 1993;100:237–43.
- 52 Salter JR. Gynaecological symptoms and psychological distress in potential hysterectomy patients. *J Psychosom Res* 1985;29:155–9.
- 53 Greenberg M. The meaning of menorrhagia: an investigation into the association between the complaint of menorrhagia and depression. *J Psychosom Res* 1983;27:209–14.
- 54 Gath D, Cooper P, Day A. Hysterectomy and psychiatric disorder: I. Levels of psychiatric morbidity before and after hysterectomy. *Br J Psychiatry* 1982;140:335–42.
- 55 Sculpher M. A cost-utility analysis of abdominal hysterectomy versus transcervical endometrial resection for the surgical treatment of menorrhagia. *Int J Technol Assess Health Care* 1998;14:302–19.
- 56 Hawe J, Abbott J, Hunter D, et al. A randomised controlled trial comparing the Cavaterm endometrial ablation system with the Nd:YAG laser for the treatment of dysfunctional uterine bleeding. *BJOG* 2003;110:350–7.
- 57 Abbott J, Hawe J, Hunter D, Garry R. A double-blind randomized trial comparing the Cavaterm and the NovaSure endometrial ablation systems for the treatment of dysfunctional uterine bleeding. *Fertil Steril* 2003;80:203–8.
- 58 Beaumont H, Augood C, Duckitt K, et al. Danazol for heavy menstrual bleeding. *Cochrane Database Syst Rev* 2002;CD001017.
- 59 Lethaby A, Hickey M. Endometrial destruction techniques for heavy menstrual bleeding. *Cochrane Database Syst Rev* 2002;CD001501.
- 60 Iyer V, Farquhar C, Jepson R. Oral contraceptive pills for heavy menstrual bleeding. *Cochrane Database Syst Rev* 2000;CD000154.
- 61 Lethaby AE, Cooke I, Rees M. Progesterone/progestogen releasing intrauterine systems versus either placebo or any other medication for heavy menstrual bleeding. *Cochrane Database Syst Rev* 2000;CD002126.
- 62 Hickey M, Higham J, Fraser IS. Progestogens versus oestrogens and progestogens for irregular uterine bleeding associated with anovulation. *Cochrane Database Syst Rev* 2000;CD001895.
- 63 Lethaby A, Irvine G, Cameron I. Cyclical progestogens for heavy menstrual bleeding. *Cochrane Database Syst Rev* 2000;CD001016.
- 64 Lethaby A, Farquhar C, Cooke I. Antifibrinolytics for heavy menstrual bleeding. *Cochrane Database Syst Rev* 2000;CD000249.
- 65 Ulmsten U, Carstensen H, Falconer C, et al. The safety and efficacy of MenoTreat, a new balloon device for thermal endometrial ablation. *Acta Obstet Gynecol Scand* 2001;80:52–7.
- 66 Clark TJ, Gupta JK. Outpatient thermal balloon ablation of the endometrium. *Fertil Steril* 2004;82:1395–401.
- 67 Crosignani PG, Vercellini P, Mosconi P, et al. Levonorgestrel-releasing intrauterine device versus hysteroscopic endometrial resection in the treatment of dysfunctional uterine bleeding. *Obstet Gynecol* 1997;90:257–63.
- 68 Soysal M, Soysal S, Ozer S. A randomized controlled trial of levonorgestrel releasing IUD and thermal balloon ablation in the treatment of menorrhagia. *Zentralbl Gynakol* 2002;124:213–19.
- 69 Henshaw R, Coyle C, Low S, Barry C. A retrospective cohort study comparing microwave endometrial ablation with levonorgestrel-releasing intrauterine device in the management of heavy menstrual bleeding. *Aust NZJ Obstet Gynaecol* 2002;42:205–9.
- 70 Lahteenmaki P, Haukkamaa M, Puolakka J, et al. Open randomised study of use of levonorgestrel releasing intrauterine system as alternative to hysterectomy. *BMJ* 1998;316:1122–6.
- 71 Hurskainen R, Teperi J, Aalto AM, et al. Levonorgestrel-releasing intrauterine system or hysterectomy in the treatment of essential menorrhagia: predictors of outcome. *Acta Obstet Gynecol Scand* 2004;83:401–3.

- 72 Sculpher MJ, Dwyer N, Byford S, Stirrat GM. Randomised trial comparing hysterectomy and transcervical endometrial resection: effect on health related quality of life and costs two years after surgery. *Br J Obstet Gynaecol* 1996;103:142-9.
- 73 Crosignani PG, Vercellini P, Apolone G, et al. Endometrial resection versus vaginal hysterectomy for menorrhagia: long-term clinical and quality-of-life outcomes. *Am J Obstet Gynecol* 1997;177:95-101.
- 74 Sculpher MJ, Bryan S, Dwyer N, et al. An economic evaluation of transcervical endometrial resection versus abdominal hysterectomy for the treatment of menorrhagia. *Br J Obstet Gynaecol* 1993;100:244-52.
- 75 Carlson KJ, Miller BA, Fowler FJ Jr. The Maine Women's Health Study: II. Outcomes of nonsurgical management of leiomyomas, abnormal bleeding, and chronic pelvic pain. *Obstet Gynecol* 1994;83:566-72.
- 76 Hidlebaugh DA. Cost and quality-of-life issues associated with different surgical therapies for the treatment of abnormal uterine bleeding. *Obstet Gynecol Clin North Am* 2000;27:451-65.
- 77 Cote I, Jacobs P, Cumming DC. Use of health services associated with increased menstrual loss in the United States. *Am J Obstet Gynecol* 2003;188:343-8.
- 78 Shapley M, Jordan K, Croft PR. An investigation in primary care of the relationship between consultation behaviour, increased vaginal bleeding and mental disorder. *J Obstet Gynaecol* 2004;24:684-6.
- 79 Thompson BL, Ponce DL, Kieke B, et al. Trends in hospitalizations for abnormal uterine bleeding in the United States: 1980-1992. *J Womens Health* 1997;6:73-81.
- 80 Velebil P, Wingo PA, Xia Z, et al. Rate of hospitalization for gynecologic disorders among reproductive-age women in the United States. *Obstet Gynecol* 1995;86:764-9.
- 81 Burt CW, Schappert SM. Ambulatory care visits to physician offices, hospital outpatient departments, and emergency departments: United States, 1999-2000. *Vital Health Stat* 2004;13:1-70.
- 82 Long CA. Evaluation of patients with abnormal uterine bleeding. *Am J Obstet Gynecol* 1996;175:784-6.
- 83 Farquhar CM, Naom S, Steiner CA. The impact of endometrial ablation on hysterectomy rates in women with benign uterine conditions in the United States. *Int J Technol Assess Health Care* 2002;18:625-34.
- 84 Popovic JR, Hall MJ. 1999 National Hospital Discharge Survey. Advance Data from Vital and Health Statistics; no 319. Hyattsville, MD: National Center for Health Statistics, 2001.
- 85 Farquhar CM, Steiner CA. Hysterectomy rates in the United States 1990-1997. *Obstet Gynecol* 2002;99:229-34.
- 86 Graves EJ. National hospital discharge survey. *Vital Health Stat* 1992;13:1-62.
- 87 Keshavarz H, Hillis S, Kieke B, Marchbanks P. Hysterectomy surveillance—United States, 1994-1999. *MMWR CDC Surveill Summ* 2002;51:1-8. Available from: <http://www.cdc.gov/mmwr/preview/mmwrhtml/ss5105a1.htm> [Accessed November 1, 2005].
- 88 London R, Holzman M, Rubin D, Moffitt B. Payer cost savings with endometrial ablation therapy. *Am J Manag Care* 1999;5:889-97.
- 89 Vessey MP, Villard-Mackintosh L, McPherson K, et al. The epidemiology of hysterectomy: findings in a large cohort study. *Br J Obstet Gynaecol* 1992;99:402-7.
- 90 Gannon MJ, Holt EM, Fairbank J, et al. A randomised trial comparing endometrial resection and abdominal hysterectomy for the treatment of menorrhagia. *BMJ* 1991;303:1362-4.
- 91 Brooks PG, Clouse J, Morris LS. Hysterectomy vs. resectoscopic endometrial ablation for the control of abnormal uterine bleeding. A cost-comparative study. *J Reprod Med* 1994;39:755-60.
- 92 Hidlebaugh DA. A health maintenance organization's initial experience with laparoscopic-assisted vaginal hysterectomy and endometrial ablation. *J Am Assoc Gynecol Laparosc* 1995;2:311-18.
- 93 Vilos GA, Pispidikis JT, Botz CK. Economic evaluation of hysteroscopic endometrial ablation versus vaginal hysterectomy for menorrhagia. *J Am Assoc Gynecol Laparosc* 1996;(Suppl. 3):S54.
- 94 Ransom SB, McNeeley SG, White C, Diamond MP. A cost analysis of endometrial ablation, abdominal hysterectomy, vaginal hysterectomy, and laparoscopic-assisted vaginal hysterectomy in the treatment of primary menorrhagia. *J Am Assoc Gynecol Laparosc* 1996;4:29-32.
- 95 Cameron IM, Mollison J, Pinion SB, et al. A cost comparison of hysterectomy and hysteroscopic surgery for the treatment of menorrhagia. *Eur J Obstet Gynecol Reprod Biol* 1996;70:87-92.
- 96 Brumsted JR, Blackman JA, Badger GJ, Riddick DH. Hysteroscopy versus hysterectomy for the treatment of abnormal uterine bleeding: a comparison of cost. *Fertil Steril* 1996;65:310-16.
- 97 Hidlebaugh DA, Orr RK. Long-term economic evaluation of resectoscopic endometrial ablation versus hysterectomy for the treatment of menorrhagia. *J Am Assoc Gynecol Laparosc* 1998;5:351-6.
- 98 Grant AM, Bhattacharya S, Mollison J, McIntosh E. A randomised trial of endometrial ablation versus hysterectomy for the treatment of dysfunctional uterine bleeding: outcome at four years. Aberdeen Endometrial Ablation Trials Group. *Br J Obstetgynaecol* 1999;106:360-6.
- 99 Fernandez H, Kobelt G, Gervaise A. Economic evaluation of three surgical interventions for menorrhagia. *Hum Reprod* 2003;18:583-7.
- 100 Radesic B, Sharma A. Levonorgestrel-releasing intrauterine system for treating menstrual disorders: a patient satisfaction questionnaire. *Aust NZJ Obstet Gynaecol* 2004;44:247-51.

- 101 Gurtcheff SE, Sharp HT. Complications associated with global endometrial ablation: the utility of the MAUDE database. *Obstet Gynecol* 2003;102:1278–82.
- 102 Hurskainen R, Aalto AM, Teperi J, et al. Psychosocial and other characteristics of women complaining of menorrhagia, with and without actual increased menstrual blood loss. *BJOG* 2001;108:281–5.
- 103 Pron G, Cohen M, Soucie J, et al. The Ontario Uterine Fibroid Embolization Trial. Part 1. Baseline patient characteristics, fibroid burden, and impact on life. *Fertil Steril* 2003;79:112–19.
- 104 Cote I, Jacobs P, Cumming D. Work loss associated with increased menstrual loss in the United States. *Obstet Gynecol* 2002;100:683–7.
- 105 Bonduelle M, Walker JJ, Calder AA. A comparative study of danazol and norethisterone in dysfunctional uterine bleeding presenting as menorrhagia. *Postgrad Med J* 1991;67:833–6.
- 106 Kennedy AD, Sculpher MJ, Coulter A, et al. Effects of decision aids for menorrhagia on treatment choices, health outcomes, and costs: a randomized controlled trial. *JAMA* 2002;288:2701–8.
- 107 Grant C, Gallier L, Fahey T, et al. Management of menorrhagia in primary care: impact on referral and hysterectomy: data from the Somerset Morbidity Project. *J Epidemiol Community Health* 2000;54:709–13.
- 108 Roberts RN, Norman BP, Harrison CG, et al. A medical audit and patient survey of hysterectomies performed for menstrual disorders. *Scott Med J* 1996;41:44–6.
- 109 Vuorma S, Rissanen P, Aalto AM, et al. Factors predicting choice of treatment for menorrhagia in gynaecology outpatient clinics. *Soc Sci Med* 2003;56:1653–60.
- 110 Higham J, Reid P. A preliminary investigation of what happens to women complaining of menorrhagia but whose complaint is not substantiated. *J Psychosom Obstet Gynaecol* 1995;16:211–14.
- 111 Nagele F, Rubinger T, Magos A. Why do women choose endometrial ablation rather than hysterectomy? *Fertil Steril* 1998;69:1063–6.
- 112 Geller SE, Bernstein SJ, Harlow SD. The decision-making process for the treatment of abnormal uterine bleeding. *J Womens Health* 1997;6:559–67.
- 113 Bourdrez P, Bongers MY, Mol BW. Treatment of dysfunctional uterine bleeding: patient preferences for endometrial ablation, a levonorgestrel-releasing intrauterine device, or hysterectomy. *Fertil Steril* 2004;82:160–6. quiz.
- 114 Current Procedural Terminology (CPT) 2005. Chicago, IL: American Medical Association, 2003.
- 115 Centers for Medicare & Medicaid Services. 2005 Medicare Physician Fee Schedule. Available from <http://www.cms.hhs.gov/apps/pfslookup/step0.asp>. [Accessed November 1, 2005].
- 116 2000 US Census. Available from: <http://www.census.gov> [Accessed November 1, 2005].
- 117 2005 Drug Topics. Red Book. Montvale, NJ: Medical Economics Company, Inc, 2005.
- 118 2005 DRG Expert: A Comprehensive Reference to the DRG Classification System (21st ed.). Salt Lake City, UT: Ingenix, Inc, 2005.
- 119 Centers for Medicare & Medicaid Services. 42 CFR Parts 410 and 419 Medicare Program; Changes to the Hospital Outpatient Prospective Payment System and Calendar Year 2004 Payment Rates; Final Rule. *Federal Register*. Vol. 68. No. 216. November 7, 2005. Available from: <http://www.cms.hhs.gov/providerupdate/regs/cms1471fc.pdf> [Accessed November 1, 2005].