

Treatment utilization for endometriosis symptoms: a cross-sectional survey study of lifetime experience

Ninet Sinaii, Ph.D.,^{a,b} Sean D. Cleary, Ph.D.,^b Naji Younes, Ph.D.,^c Mary Lou Ballweg, B.A.,^d and Pamela Stratton, M.D.^a

^aReproductive Biology and Medicine Branch, National Institute of Child and Human Development, National Institutes of Health, Bethesda, Maryland; ^bDepartment of Epidemiology and Biostatistics, School of Public Health and Health Services, The George Washington University, Washington, DC; ^cThe Biostatistics Center, The George Washington University, Rockville, Maryland; and ^dThe Endometriosis Association, International Headquarters, Milwaukee, Wisconsin

Objective: To examine the lifetime utilization and perceived benefit of medical treatments and surgical procedures for endometriosis-related symptoms.

Design: Cross-sectional study of self-reported survey data.

Setting: Academic research setting.

Patient(s): Self-reported surgically diagnosed endometriosis by 1,160 women responding to the 1998 Endometriosis Association survey.

Intervention(s): None.

Main Outcome Measure(s): Use, perceived helpfulness, and outcomes of medical treatments and surgical procedures.

Result(s): Ninety-five percent of respondents reported pelvic pain, had endured symptoms on average of 16 years, and were young (mean: 36 years), white, and educated. Many women (46%) had tried three or more medical treatments, and almost 20% took them for 10+ years. Many reported medical treatments as helpful for symptoms (range, 36.4%–61.9%), but some reported stopping because of ineffectiveness (range, 15.6%–26.1%) or side effects (range, 10.0%–43.5%). Danazol or medroxyprogesterone acetate (MPA) was most commonly stopped because of side effects (range, 40.7%–43.5%). Surgical procedures were performed at least three times on 42%. Nearly 20% had a hysterectomy or oophorectomy; these procedures were reported as most successful in improving symptoms (45.9% and 37.8%, respectively).

Conclusion(s): Despite reporting various treatments as helpful, women used many different types and endured symptoms for an average of almost two decades, indicating the profound effect of endometriosis on women's health. (Fertil Steril® 2007;87:1277–86. ©2007 by American Society for Reproductive Medicine.)

Key Words: Endometriosis, endometriosis treatment, hormones, laparoscopy, laparotomy

Although studies have looked at the short-term effectiveness of various treatments, the actual use and perceived benefit of different treatments for endometriosis-related symptoms is unknown. Currently, treatment of pain associated with endometriosis includes both medical treatment and surgical procedures. Unfortunately, either type of treatment has side effects and is often repeated when endometriosis symptoms return. Women may also seek alternative treatments such as acupuncture, hypnosis, dietary supplements, or massage.

Nonsteroidal anti-inflammatory drugs and oral contraceptives (OC) are often effective in treating endometriosis-related dysmenorrhea and pelvic pain. Second-line hormonal treatments lower estrogen (E) levels by inducing ovarian

suppression. These hormonal treatments have successfully demonstrated pain relief in women and are roughly equivalent: 84%–92% of women treated with danazol (1), 75%–89% with OCs (2), and 80% in those receiving GnRH agonists (3). Endometriotic implants have been shown to decrease in size in response to these medical therapies, although studies have been poorly controlled and do not include long-term follow-up.

With advancements in laparoscopic surgical techniques, women in the 1990s were more likely to have had surgery for the diagnosis of endometriosis. In randomized studies of surgical treatment versus diagnostic laparoscopy alone, 63%–80% of treated women versus 23%–32% of controls demonstrated significant improvement in symptoms at 6 months after surgery (4, 5). Approximately 90% of those having relief of pain at 6 months continued to have decreased pain at 1 year.

Women may use alternative treatments to relieve symptoms. Although acupuncture, hypnosis, and chiropractic manipulation have been investigated for pain relief or infertility (6–9), studies on the effectiveness in women who are known to have endometriosis are lacking.

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Reprint requests: Ninet Sinaii, Ph.D., 10 Center Drive, Building 10, CRC, Room 1-3140, Bethesda, MD 20892-1109 (FAX: 301-402-0884; E-mail: sinaii@mail.nih.gov).

The goal of this study is to report on the actual lifetime therapeutic practices and effectiveness of medical, surgical, and alternative treatments from the patient's perspective by analyzing data from more than 1,000 women with endometriosis. We hypothesized that women with endometriosis undergo multiple medical treatments and surgical procedures, which are not perceived as helpful, and are commonly stopped due to ineffectiveness or side effects.

MATERIALS AND METHODS

Data Source

Of the 4,745 (47.5%) respondents to the 1998 Endometriosis Association (headquarters, Milwaukee, WI) mailed questionnaire, data from a randomly selected subset of 1,276 women self-reporting endometriosis were entered into the Clinical Trials Database (CTDB) at the National Institute of Child Health and Human Development (NICHD, Bethesda, MD). Women completed detailed information about medical treatments, alternative treatments, and surgeries. Questionnaires were anonymized and deidentified to ensure confidentiality, and were approved as exempt from Investigational Review Board (IRB) reviews by the Office of Human Subjects Research at NICHD, and the Committee on Human Research, The George Washington University, Washington, DC.

Measures

Ethnicity/race, education level, family's total annual income, and subject age were tabulated. Subjects reported symptoms of endometriosis, age at onset of symptoms, and year of endometriosis diagnosis. This information, along with age, were used to calculate duration of symptoms, average age and calendar year at onset of symptoms, time since diagnosis, and average age and calendar year at diagnosis. The sections on medical and alternative treatments included questions on [1] type, [2] duration, [3] helpfulness for symptoms of endometriosis, [4] stopping due to side effects, [5] stopping due to ineffectiveness, and [6] treatment order. The section on surgical treatments included [1] type/reason for surgery, [2] results/effectiveness, and [3] order of surgical procedure. Analyses were restricted to women with surgically diagnosed endometriosis ($n = 1,160$).

Medical treatments were categorized as first-line treatments of analgesics (nonsteroidal anti-inflammatory drugs and narcotics) and OCs. Second-line hormonal treatments were grouped by therapeutic class, including GnRH analogs (GnRH-a) (leuprolide [LA], nafarelin, goserelin, buserelin), danazol, and progestins (medroxyprogesterone acetate [MPA], norethindrone acetate, megestrol acetate, and progesterone).

Alternative treatments were classified using the National Center for Complementary and Alternative Medicine (NCCAM) (10) categories of: [1] whole medical systems and energy medicine (acupuncture, homeopathy, traditional Chinese medicine, immunotherapy and Candidiasis treat-

ment, ayurveda, naturopathy, bioenergetics, polarity, and reiki); [2] mind-body medicine (counseling, hypnosis, meditation, yoga, and biofeedback); [3] biologically based therapies (dietary supplements, herbs, diet-based practices, high colonics and detoxification, and aromatherapy); and [4] manipulative and body-based therapies (chiropractic and osteopathic manipulation, massage, and exercise).

For each type of medical and alternative treatment, a response of "yes" to the question "Did the treatment help you?" was considered helpful. Whether treatment was stopped because of bad side effects or because it did not work (ineffective) was indicated.

Surgeries included laparoscopies and laparotomies for diagnosis and excision of endometriosis, removal of reproductive organs (hysterectomy and oophorectomy), and surgery for adhesions. Women indicated the surgical outcomes of "successful," "resulted in additional problems," "surgery partly helped," and "surgery made no difference."

Data Analysis

Demographic characteristics of ethnicity/race, education level, total family annual income, and subject age were compared to 1998 female population rates from the 2001 US Census Bureau (11) data using Z-tests for proportions.

All medical and alternative treatments were described by specific type (e.g., LA, meditation) and category (e.g., GnRH-a, mind-body medicine), and included treatment use, average duration, helpfulness for symptoms, and stopping due to side effects and ineffectiveness. All quantifiable treatment duration responses were converted to months. For category summaries, the cumulative duration was calculated. If multiple treatments in the same category were listed with the same treatment order, they were assumed to be taken together. Weighted average percentages were calculated for summaries of treatment helpfulness, stopping due to side effects, and stopping for ineffectiveness.

The results and effectiveness of each surgical procedure were described, and were compared using χ^2 tests, with laparoscopy for diagnosis used as the reference group.

For those who designated a treatment order, the sequence of treatments or surgical procedures were described by Markov models, which were based on the probabilities of one treatment to be followed by another according to all treatment order information provided by subjects. For each model, categories of treatments or surgical procedures were used instead of specific therapies or procedures. The medical treatment model included the categories of analgesics, OCs, GnRH-a, and one category combining the different classes of danazol and progestins. The alternative treatment model used the NCCAM categories of whole medical system and energy medicine, mind-body medicine, biologically based therapies, and manipulative and body-based therapies.

Three different surgical treatment models were created. The first only included the sequence of procedures for endometriosis

that did not remove pelvic organs: [1] laparoscopy for diagnosis; [2] laparoscopy for removal of endometriosis; [3] laparotomy for diagnosis or removal of endometriosis; and [4] surgery for adhesions. The second combined procedure categories and included hysterectomy and oophorectomy. The combined categories were: [1] laparoscopy for diagnosis and removal of endometriosis; [2] laparotomy for diagnosis or removal of endometriosis, and surgery for adhesions; and [3] hysterectomy and oophorectomy. The third model excluded specific laparoscopic procedures for diagnosis or removal of endometriosis and was comprised of the following categories: [1] laparotomy for diagnosis or removal of endometriosis; [2] surgery for adhesions; [3] hysterectomy; and [4] oophorectomy.

For all tests, a *P* value of $\leq .05$ was considered statistically significant. The data were analyzed using SAS Release 8.02 (SAS Institute, Cary, NC).

RESULTS

Study Population

Respondents were primarily white, with fewer than 8% identifying themselves as black, Hispanic, Native American, Asian, and other (Table 1) (11). The mean age at the time of the survey was 36.0 years (range, 14–74 years), and 97.3% were of reproductive age (range, 15–50 years). The combined family income of more than half of the respondents (61.5%) was above \$50,000, and nearly all (91.1%) had at least some college education.

Only those women (91.4%) reporting a surgical diagnosis of endometriosis were included in the analyses (Table 1). Six of these women were excluded because the treatment sections were missing.

Pelvic pain was the most common symptom and was experienced by 94.7%, either by itself (56.0%), or in combination with infertility (38.8%). Only 2.6% of women experienced infertility without pelvic pain and 2.7% denied having either.

Lifetime Treatment Utilization

All 1,111 (95.8%) subjects reporting use of any medical treatment selected at least one that was specifically listed. Alternative treatments were tried by 753 (64.9%) subjects. As seen in Figure 1, 63% of subjects reported using all three methods of treatments (medical, alternative, and surgical), and most of the remainder (32%) reported use of both medical treatments and surgical procedures. No one tried only alternative treatments for endometriosis.

At the time of completing the questionnaire, women had endured symptoms of endometriosis for an average duration of 16.3 ± 0.3 years, and had been diagnosed an average of 7.1 ± 0.2 years. The average age at onset of symptoms was 19.7 ± 0.2 years, in the calendar year 1982 (range, 1939–

TABLE 1
Characteristics of 1,160 respondents to the 1998 Endometriosis Association survey self-reporting surgically diagnosed endometriosis.

Characteristic	N (%)
Age (y)*	(n = 1,127)
<15	4 (0.4)
15–20	14 (1.2)
21–25	81 (7.2)
25–30	167 (14.8)
31–35	256 (22.7)
35–40	273 (24.2)
41–45	210 (18.6)
46–50	96 (8.5)
>50	26 (2.3)
Education level*	(n = 1,135)
Did not complete high school	5 (0.4)
High school graduate	70 (6.2)
Some college	226 (19.9)
College graduate	497 (43.8)
Postgraduate degree	311 (27.4)
Other	26 (2.3)
Combined family annual income*	(n = 1,076)
\$0–24,999	93 (8.6)
\$25,000–49,999	321 (29.8)
\$50,000–74,999	283 (26.3)
≥\$75,000	379 (35.2)
Race/ethnicity*	(n = 1,045)
White	967 (92.5)
Black	20 (1.9)
Hispanic	25 (2.4)
Native American	7 (0.7)
Asian	15 (1.4)
Other	11 (1.1)
Survey responses	(n = 1,276)
Indicated surgically diagnosed Endometriosis	1,166 (91.4)
Women included in study ^a	1,160 (90.9)
Endometriosis symptoms	(n = 1,160)
Pelvic pain	1,099 (94.7)
Infertility	480 (41.4)
Both pelvic pain and infertility	450 (39.9)
Duration of symptoms (y) ^b	16.3 ± 0.3
Time since diagnosis (y) ^b	7.1 ± 0.2
Treatment utilization	(n = 1,160)
Medical treatments	1,111 (95.8)
Alternative treatments	753 (64.9)
Surgical procedures	1,146 (98.8)

* $P < .0001$ compared to the general US female population data (1998) from the US Census Bureau (2001) (11) using Z-tests for proportions.

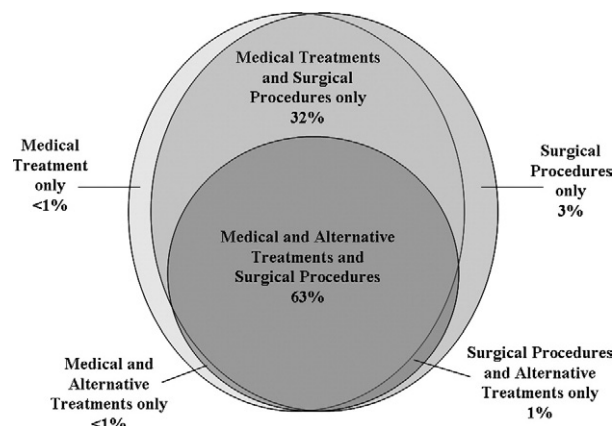
^a Six women were missing the treatment section of their surveys and therefore were excluded from analyses.

^b Mean \pm SE.

Sinaii. Experience with endometriosis treatments. *Fertil Steril* 2007.

FIGURE 1

Overall utilization of treatments for endometriosis.



Sinaii. Experience with endometriosis treatments. Fertil Steril 2007.

used them for 10 or more years. At least three surgical procedures were performed on 41.5% (range, 1–17 procedures). Alternative treatments had been taken by 16.7% for 5 or more years, with 41.5% having tried a minimum of three treatments (range, 1–13). Subject age, duration of symptoms, and time since diagnosis were not statistically different by method of treatment (data not shown).

Medical Treatments

Analgesics and OCs were the most common treatments (74.2% and 71.9%, respectively), followed by GnRH-a (51.3%), danazol (25.2%), and progestins (23.2%) (Table 2). Of those reporting GnRH-a treatment, LA was used most commonly (85.9%). Analgesics and OCs were used longest (77.5 ± 4.0 and 42.8 ± 2.1 months, respectively), translating into years of treatment for some women. Overall, GnRH-a were used on average for 6 months or less.

Treatment was stopped because of side effects in fewer than one-third of the subjects for each category, except for either danazol or progestins, for which nearly half indicated side effects as the reason for stopping. Relatively few reported stopping any medical treatment because it was ineffective (range, 15.6%–26.1%), and many reported them as

1998). The average age at diagnosis was 29.8 ± 0.2 years, in the calendar year 1991 (range, 1968–1998).

During a lifetime of symptoms, 45.5% of women used three or more medical treatments (range, 1–11), and 19.4%

TABLE 2

Medical treatment use, duration, helpfulness, and stopping due to side effects and ineffectiveness among 1,160 women self-reporting surgically diagnosed endometriosis.

Type of medical treatment	N (%)	Treatment duration months ± SE (available N)	Treatment helpful for endometriosis symptoms N (%) ^a	Reports of treatment cessation due to:	
				Side effects N (%) ^a	Ineffective N (%) ^a
First-line treatments					
Analgesics	861 (74.2)	77.5 ± 4.0 (n = 526)	533 (61.9)	86 (10.0)	210 (24.4)
Oral contraceptive pill	834 (71.9)	42.8 ± 2.1 (n = 709)	399 (47.8)	271 (32.5)	218 (26.1)
Second-line hormonal treatments					
GnRH analogs	595 (51.3)	7.0 ± 0.3 (n = 569)	360 (58.3)	186 (29.1)	106 (17.5)
Leuprolide	511 (44.1)	6.5 ± 0.2 (n = 483)	306 (59.9)	154 (30.1)	85 (16.6)
Nafarelin	118 (10.2)	6.0 ± 0.5 (n = 110)	67 (56.8)	30 (25.4)	23 (19.5)
Other GnRH analogs ^b	37 (3.2)	5.6 ± 0.8 (n = 33)	15 (40.5)	10 (27.0)	9 (24.3)
Danazol	292 (25.2)	8.5 ± 0.9 (n = 271)	144 (49.3)	127 (43.5)	60 (20.6)
Progestins	269 (23.2)	15.5 ± 2.1 (n = 228)	110 (38.6)	112 (39.0)	66 (22.7)
Medroxyprogesterone acetate	258 (22.2)	14.6 ± 2.2 (n = 207)	94 (36.4)	105 (40.7)	61 (23.6)
Other progestins ^c	32 (2.8)	18.1 ± 5.8 (n = 28)	18 (56.3)	8 (25.0)	5 (15.6)

^a Percentages are based on the number of women in the first column who used each medical treatment; category summary percentages are weighted to the number of women using each treatment within the category.

^b Goserelin, buserelin.

^c Norethindrone acetate, megestrol acetate, progesterone.

Sinaii. Experience with endometriosis treatments. Fertil Steril 2007.

helpful for their endometriosis symptoms (range, 36.4%–61.9%).

Alternative Treatments

The most commonly reported alternative treatments were biologically based therapies (51.6%) and manipulative and body-based therapies (40.9%). The helpfulness of different treatments varied (Table 3). Women used alternative treatments for years, with the longest duration of use for manipulative and body-based (46.7 ± 3.8 months) and biologically based practices (43.9 ± 3.3 months). Most continued therapy with few stopping for side effects or ineffectiveness.

Among those who used whole medical systems and energy medicine, acupuncture and Candidiasis treatment were the most popular (14.7% and 13.5%, respectively), and were generally helpful (61.8% and 61.4%, respectively). Homeopathy was frequently discontinued for ineffectiveness (33.0%), but not for side effects (1.1%). Mind–body medi-

cal practices (43.9 ± 3.3 months). Most continued therapy with few stopping for side effects or ineffectiveness.

TABLE 3

Alternative treatment use, duration, helpfulness, and stopping due to side effects and ineffectiveness among 1,160 women self-reporting surgically diagnosed endometriosis.

Type of complementary and alternative treatment	N (%)	Treatment duration months ± SE (available N)	Treatment helpful for endometriosis symptoms N (%) ^a	Reports of treatment cessation due to:	
				Side effects N (%) ^a	Ineffective N (%) ^a
Whole medical systems and energy medicine	281 (24.2)	16.5 ± 1.6 (n = 241)	173 (56.9)	9 (2.6)	87 (21.6)
Acupuncture	170 (14.7)	12.7 ± 2.1 (n = 141)	105 (61.8)	4 (2.4)	39 (22.9)
Candidiasis treatment	156 (13.5)	17.9 ± 3.2 (n = 117)	96 (61.4)	6 (3.9)	24 (15.4)
Traditional Chinese medicine	131 (11.3)	12.3 ± 1.8 (n = 101)	70 (53.4)	3 (2.3)	31 (23.7)
Homeopathy	88 (7.6)	10.8 ± 1.4 (n = 71)	39 (44.3)	1 (1.1)	29 (33.0)
Immunotherapy	37 (3.2)	20.3 ± 4.4 (n = 25)	20 (54.1)	1 (2.7)	4 (10.8)
Other ^b	5 (0.4)	40.0 ± 14.4 (n = 3)	4 (80.0)	0 (0.0)	0 (0.0)
Mind–body medicine	131 (11.3)	29.3 ± 4.0 (n = 93)	36 (73.7)	1 (0.8)	19 (13.2)
Counseling	118 (10.2)	28.8 ± 4.2 (n = 86)	82 (69.5)	1 (0.9)	18 (15.3)
Meditation	8 (0.7)	38.0 ± 15.6 (n = 3)	8 (100.0)	0 (0.0)	0 (0.0)
Other ^c	11 (0.9)	19.9 ± 16.7 (n = 7)	11 (100.0)	0 (0.0)	0 (0.0)
Biologically based therapies	598 (51.6)	43.9 ± 3.3 (n = 408)	393 (58.5)	10 (1.0)	100 (12.3)
Dietary supplements	456 (39.3)	34.4 ± 2.9 (n = 289)	254 (55.7)	3 (0.7)	55 (12.1)
Diet-based	418 (36.0)	27.8 ± 2.3 (n = 268)	276 (66.0)	3 (0.7)	51 (12.2)
Herbs	137 (11.8)	18.6 ± 3.4 (n = 62)	62 (45.3)	3 (2.2)	14 (10.2)
Aromatherapy	46 (4.0)	13.3 ± 3.3 (n = 33)	25 (54.4)	1 (2.2)	11 (23.9)
High colonics/detoxification	6 (0.5)	10.6 ± 6.4 (n = 5)	5 (83.3)	0 (0.0)	0 (0.0)
Manipulative and body-based therapies	474 (40.9)	46.7 ± 3.8 (n = 278)	327 (35.1)	9 (0.9)	68 (8.7)
Exercise	418 (36.0)	43.7 ± 4.0 (n = 210)	273 (23.5)	5 (0.4)	31 (2.7)
Chiropractic manipulation	154 (13.3)	30.7 ± 4.1 (n = 115)	89 (57.8)	3 (2.0)	38 (24.7)
Massage	30 (2.6)	42.0 ± 9.8 (n = 13)	23 (76.7)	1 (3.3)	2 (6.7)
Other ^d	3 (0.3)	16.0 ± 7.0 (n = 3)	2 (66.7)	0 (0.0)	1 (33.3)
All others	7 (0.6)	6.4 ± 1.9 (n = 5)	6 (85.7)	0 (0.0)	1 (14.3)

^a Percentages are based on the number of women in the first column who used each alternative treatment; category summary percentages are weighted to the number of women using each treatment within the category.

^b Ayurveda, naturopathy, bioenergetics, polarity, and reiki.

^c Hypnosis, yoga, biofeedback, and other relaxation therapies.

^d Physical therapy, applied kinesiology, and osteopathic manipulation.

Sinaii. Experience with endometriosis treatments. Fertil Steril 2007.

TABLE 4

Utilization and results of surgical procedures for endometriosis among 1,160 women self-reporting surgically diagnosed disease.

Type of surgical procedure	N (%)	Results of surgery:			
		Surgery successful N (%) ^a	Partly helped N (%) ^a	Made no difference N (%) ^a	Additional problems N (%) ^a
Laparoscopy					
Diagnosis of endometriosis	875 (75.4)	281 (32.1)	205 (23.4)	230 (26.3)	70 (8.0)
Removal of endometriosis	802 (69.1)	244 (30.4)	402 (50.1) ^b	118 (14.7) ^b	83 (10.4)
Laparotomy					
Diagnosis or removal of endometriosis	326 (28.1)	97 (29.8)	148 (45.4) ^b	32 (9.8) ^b	60 (18.4) ^b
Removal of reproductive organs					
Oophorectomy	230 (19.8)	87 (37.8)	77 (33.5) ^c	12 (5.2) ^b	37 (16.1) ^b
Hysterectomy	209 (18.0)	96 (45.9) ^b	66 (31.6) ^c	6 (2.9) ^b	37 (17.7) ^b
Both	144 (12.4)	58 (40.3)	48 (33.3) ^c	8 (5.6) ^b	9 (6.3)
Surgery for adhesions	305 (26.3)	95 (31.2)	135 (44.3) ^b	27 (8.9) ^b	33 (10.8)

^a Percentages are based on the number of women in the first column who had each surgical procedure.

^b $P < .0001$ compared to laparoscopy for diagnosis using χ^2 test.

^c $P < .02$ compared to laparoscopy for diagnosis using χ^2 test.

Sinaii. Experience with endometriosis treatments. *Fertil Steril* 2007.

cine was uncommonly reported (11.3%), but was the most helpful (73.3%) of the alternative medicine categories and rarely was stopped for side effects (0.8%).

Surgical Procedures

Most women reported having had a laparoscopy for diagnosis of endometriosis (75.4%) (Table 4). Removal of endometriosis was performed more frequently by laparoscopy (69.1%) than by laparotomy (28.1%). Surgery for adhesions was indicated separately, independent of other surgeries by 305 women (26.3%). Despite the young age of women, hysterectomy (18.0%) and oophorectomy (19.8%) were commonly reported.

One hundred forty-four (12.4%) women had both hysterectomy and oophorectomy (Table 4). Having had either hysterectomy or oophorectomy successfully improved symptoms in the highest proportion of women (45.9% and 37.8%, respectively), whereas only one-third of women with other surgical procedures reported successful treatment. In considering the success of a procedure, only hysterectomy was more successful in relieving symptoms ($P < .0001$; Table 4), but all other procedures were perceived as somewhat helpful compared to laparoscopy for diagnosis ($P < .02$; Table 4). However, any therapeutic procedure, particularly laparotomy for diagnosis or removal of endometriosis (18.4%), more commonly led to additional problems than laparoscopy for diagnosis ($P < .0001$; Table 4).

Markov Models

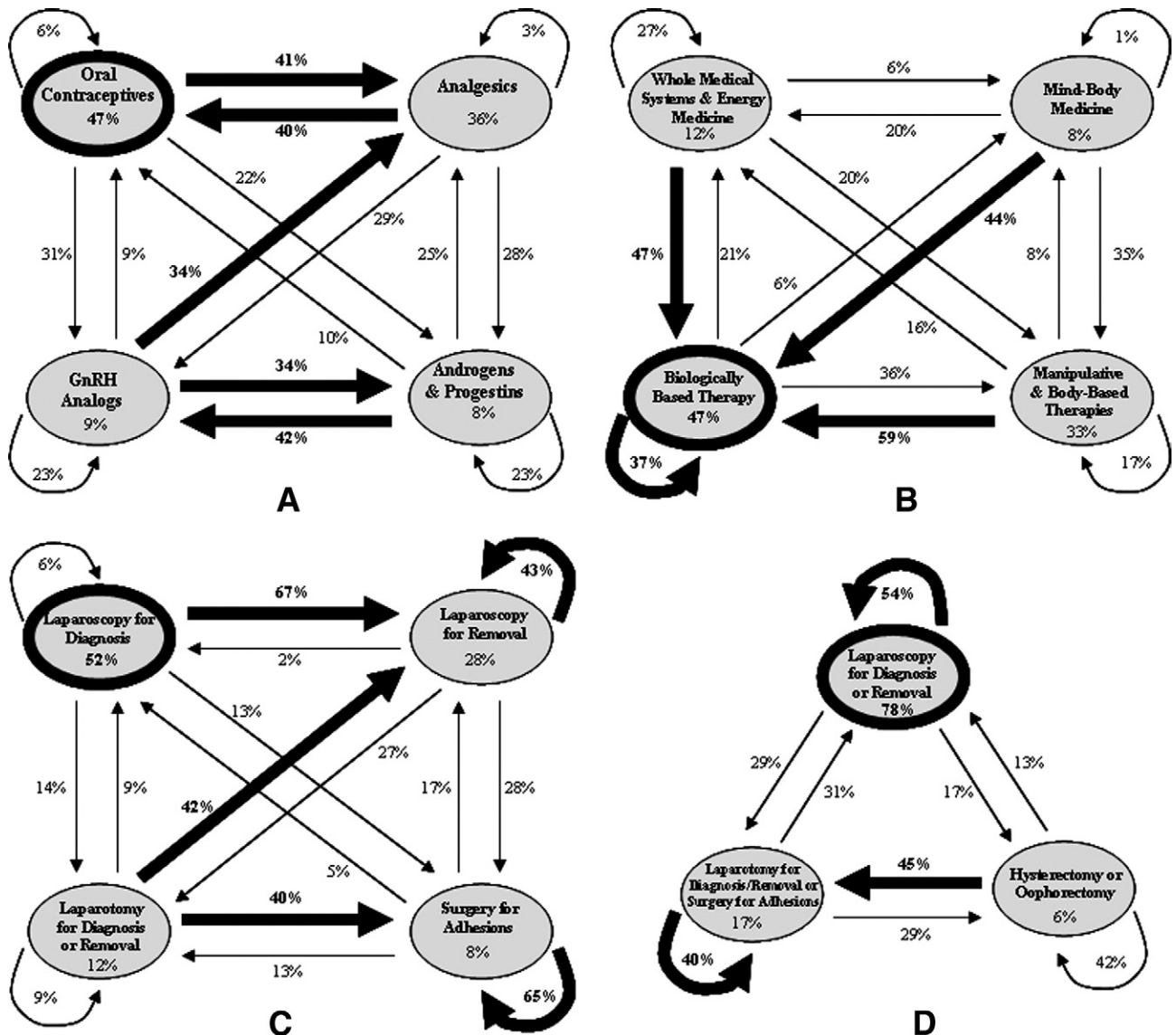
Figure 2 depicts the Markov models to describe the sequence of treatments used that were based on the calculated probabilities of one treatment to be followed by another from all quantifiable treatment orders provided by subjects. Figure 2A confirms the usual pattern of medical treatments for pain from endometriosis, in that OCs or analgesics were taken first 83% of the time (47% and 36%, respectively). Women taking OCs most often took analgesics next (41%). Similarly, those taking analgesics went on to take OCs (40%). Very few (6%) took OCs again. Results were similar for analgesics. Surprisingly, 17% started with a second-line hormone as their initial treatment. Of those taking GnRH-a, most then took analgesics (34%), or either danazol or progestins (34%). For women who took either danazol or progestins, most took a GnRH-a next (42%).

Figure 2B represents the pattern of alternative treatments. Biologically based therapies were used first by most women (47%). Regardless of which treatment women took, the next treatment was almost always a biologically based therapy.

The sequence of surgical procedures that did not remove pelvic organs, depicted in Figure 2C, shows what one might expect: laparoscopy for diagnosis was the most common first procedure (52%). For these women, the next most commonly used procedure was laparoscopy for removal of endometriosis (67%), but very few had a second laparoscopy for diagnosis. Laparoscopy for removal of endometriosis was also repeated for 43% of women who had a previous laparoscopic removal of endometriosis, as well as for those

FIGURE 2

(A–D) Markov models describing the sequence of treatments used. Each oval represents the category of treatment or surgical procedure, and the percentages in the ovals indicate the proportion of women using a treatment in that category first. The most common type of treatment initially used is represented by the bold oval. The arrows represent the proportion of women who move on to the next treatment. Those arrows that are arced specify use of the same treatment or another treatment in the same category next. The bold arrows indicate the most popular next treatment. (A) Medical treatments Markov model (n = 1,077); (B) alternative treatments Markov model (n = 655); (C) surgical procedures Markov model A (n = 1,043); and (D) surgical procedures Markov model B (n = 1,063).



Smaii. Experience with endometriosis treatments. *Fertil Steril* 2007.

who had endometriosis removed by laparotomy. Interestingly, laparotomy for diagnosis or removal of endometriosis was most commonly followed by surgery for adhesions (40%) or laparoscopy for removal of endometriosis (42%) as the next procedure. Surgery for adhesions led to another surgery for adhesions for 65% of women.

When categories were combined in the model as shown in Figure 2D, laparoscopic diagnosis or removal of endometriosis was often the first procedure (78%), which was followed most commonly (54%) by another laparoscopic diagnosis or removal. Laparotomy for diagnosis or removal of endometriosis, or surgery for adhesions, was most commonly fol-

lowed by another laparotomy for diagnosis or removal, or surgery for adhesions (40%). Surprisingly, those having hysterectomy and oophorectomy often had another surgical procedure, which was usually laparotomy for diagnosis or removal of endometriosis, or surgery for adhesions (45%).

In the third surgical model (data not shown), surgery for adhesions usually followed laparotomy for diagnosis or removal of endometriosis (43%), oophorectomy (61%), and a prior surgery for adhesions (62%). However, oophorectomy was the most common next procedure (49%), after hysterectomy.

DISCUSSION

The use and perceived benefit of treatments for endometriosis-related symptoms were reported by 1,160 women self-reporting surgically diagnosed endometriosis who completed the 1998 Endometriosis Association survey. Nearly all women were treated with medical and surgical treatments and two-thirds also used alternative therapies. Surgical procedures were performed at least three times on 42%. Nearly 20% of these young women had a hysterectomy or oophorectomy. Forty-six percent tried three or more medical treatments, and almost 20% took them for 10 years or longer. Three different types of alternative treatments were used by 42%. Danazol and progestins were used less commonly and, overall, were stopped because of side effects about 50% of the time.

The Markov models confirmed that OCs or analgesics were most commonly used first. Nearly one-quarter to one-third stopped OCs because they were ineffective for symptoms or resulted in side effects. Almost half believed they were helpful for endometriosis symptoms. Although other studies suggest OCs decrease pain in 75%–89% (2), during the long-term, this effectiveness may decrease.

Second-line hormonal treatments were also quite common, taken by about half of the cohort. The 17% who used a second-line hormone as their initial treatment may have begun it after a surgery. In addition, women may not have considered any treatment (OCs and analgesics, for example) before surgical diagnosis as a therapy for symptoms. Compared to previous studies reporting pain relief in women with endometriosis, GnRH agonists in this cohort were not as helpful (80% vs. 58%, respectively) (3). Fifty percent of those taking danazol or progestins stopped taking them because of side effects. The helpfulness of danazol for symptoms was much less in this study than previously reported (49% vs. 84%–92%, respectively) (1).

Of the alternative treatments, biologically based therapies were the most common alternative treatments for more than half the women and, regardless of which alternative treatment was used first, women always moved toward biologically based therapies. Women also found them helpful. The reasons for this preference of biologically based therapy is not well understood but may be explained by the Associa-

tion's publicity on dietary recommendations for coping with the disease. In addition to biological effects, they are taken orally and are most like conventional medical therapy. Perhaps the belief that they could work, similar to the placebo effect (12), contributed to the effectiveness. In addition, bowel symptoms, commonly experienced by women with endometriosis (13, 14), may decrease with use of natural products or diet-based therapies.

Generally, more women in this cohort used alternative treatments than the average use of about 50% in the general US population (15), perhaps due to the chronic nature of endometriosis that may motivate women to try other methods of therapy. The type and indication for alternative treatments used also differed. Alternative therapies are used by the general population for back, neck, or joint pain, head or chest colds, and anxiety or depression, a different indication than that of women with pelvic pain (16). For instance, use of natural products (39%) and diet-based therapies (36%) were much more common in the study population than the 9% and 4%, respectively, use in the general population, whereas prayer (10%), meditation (8%), deep-breathing exercises (12%), yoga (5%), and massage (5%) were used much more frequently in the general population than the study cohort. A likely explanation for the difference may be that only 13 different therapies were listed in the Endometriosis Association survey. As a result, women may not have listed all alternative therapies used, especially if they were unsure whether certain treatments would be considered "alternative."

Randomized studies have found up to 80%–90% success in symptom improvement by surgical treatment of endometriosis versus 32% by diagnostic laparoscopy alone (4, 5). In this cohort, when combining partially helpful and successful categories, all surgical procedures for treatment had similar effectiveness (70%–80%), similar to the 80% observed in randomized studies. Diagnostic laparoscopy was significantly less effective but more effective than in randomized studies, perhaps because diagnosis itself was considered a successful result by the women. Although hysterectomy was significantly more successful than the other therapies, when considering the combined category of successful and partly helped, laparoscopy for removal of endometriosis was the most effective.

The Markov models confirmed the need for surgery for adhesions, as adhesions are a known sequelae of both endometriosis and any surgical procedure (17, 18). Additional surgery for adhesions was also done after removal of reproductive organs.

The OCs and analgesics were used for an average duration of 3.5 and 7 years, respectively. Despite an initially long period of treatment with these agents, women often did not use them again, even after second-line hormonal treatments. Other medical treatments were used for a much shorter time. The GNRH-a were used for the usual prescribed duration of about 6 months, as would be expected given treatment rec-

ommendations at the time of survey completion. Surprisingly, danazol and progestins were used for longer, 8.5 and 15.5 months, respectively, although they were ultimately stopped when they became ineffective or side effects became intolerable. Interestingly, progestins were used for up to 2 years despite the high occurrence of treatment cessation due to side effects and less effectiveness. Provera, the progestin listed in the questionnaire, which has either an oral or depot form, was used for longer. It is known to cause side effects of depression, weight gain, and moodiness (19, 20) at a higher frequency than other progestins, like norethindrone acetate, which was not specifically listed in the questionnaire.

This study has several strengths. First, the large sample size offers ample statistical power for testing the hypothesis and provides valuable information from more than 1,000 women. Second, the survey collected detailed information regarding the long-term use, helpfulness, side effects, and effectiveness of a wide range of treatments for endometriosis that has previously not been available. Third, by restricting the sample to those self-reporting surgical diagnosis of endometriosis, it is likely that the treatments listed were used for endometriosis, and extrapolations can be made to women with endometriosis and pain who belong to the Endometriosis Association. Another important study strength was the use of Markov models as a novel pictorial representation of women's sequence of treatments. However, because the probabilities of transitioning from one treatment to the next might be affected by treatment helpfulness, side effects, or concurrent treatments, the models are only useful for providing an overall impression of the order of treatments or surgical procedures.

Despite the study strengths, women completing the survey were self-selected members of the Endometriosis Association, and then chose to respond to this questionnaire, thus introducing selection bias and limiting generalizability. In addition, anonymized self-reported data cannot be confirmed by reviewing medical records and are subject to reporting errors. Whether or not a woman was experiencing pain or other symptoms at the time of survey completion may have influenced responses to questions on effectiveness of treatments. Her understanding of each treatment or procedure may be limited, especially if she was not adequately informed or did not inquire for detailed information. Furthermore, the reported "reason" for surgery may be in error, if the patient mistakenly attributed her symptoms to endometriosis.

The order and duration of each treatment received may not have been reported reliably among women who took many treatments for a lifelong condition. More women were also likely to report the duration of treatments if they were used for a shorter period of time. Furthermore, it is not possible to determine the age of the patient while she was on treatment, or to determine and control for multiple types of treatments being simultaneously or sequentially used. The effectiveness

of different treatments cannot be compared to each other, primarily because of the different types of questions that were asked for each method of treatment.

In conclusion, this study is the first to describe the type, order, and duration of treatments in 1,160 women with pelvic pain from endometriosis responding to the Endometriosis Association survey. Helpfulness for treating symptoms, and rate of stopping them due to ineffectiveness or side effects, were also described. Although it is not possible to recommend therapy for endometriosis based on these data, our study showed that women sought numerous different treatments for endometriosis, but they were overall helpful, at least initially, and few stopped treatment because of side effects. Despite reporting various treatments as helpful, women used many different types and endured symptoms for an average of almost two decades. Endometriosis has a profound effect on the health of women and it appears effective therapies are urgently needed.

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