

Cost-effectiveness Analysis for Treatment of Symptomatic Uterine Fibroids Among Premenopausal Women Seeking to Retain Their Uterus

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BACKGROUND

- Uterine fibroids (leiomyoma) are a common condition in women, with an annual incidence rate of 9.2 per 1,000 women aged 25 to 44 years when confirmed by ultrasound or hysterectomy.¹
- Primary symptoms include excessive bleeding, dysmenorrhea (pain during menstruation), dyspareunia (pain during intercourse), infertility, pelvic pain, urinary urgency, and fatigue.^{2,3,4}
- Uterine fibroids are associated with circulating levels of estrogen and progesterone, and growth and incidence are generally reduced after menopause when the levels of these hormones decline.^{5,6}
- Therapies for uterine fibroids include:
 - Treatment of symptoms using hormonal agents (gonadotropin-releasing hormone [GnRH] agonists, oral contraceptives, or levonorgestrel-releasing intrauterine devices).
 - Removal or destruction of fibroid via surgical procedures (hysterectomy, myomectomy, and uterine artery embolization [UAE]).

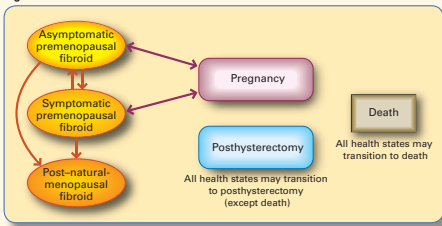
OBJECTIVE

To determine the cost-effectiveness of different treatment options and optimal number of treatments for symptomatic uterine fibroids in women who wish to retain their uterus.

METHODS

A database- and literature-based Markov model was developed to compare different treatment options, as well as to determine the optimal number of treatment options, for premenopausal women with symptomatic uterine fibroids who prefer to retain their uterus (Figure 1).

Figure 1. Structure of the Model



Model Structure

- The time horizon was defined as age of diagnosis to age of menopause or age 60 years, with a cycle time of 1 year for transitions between health states.
- The model limits the treatment options for premenopausal women desiring to retain their uterus to:
 - Watchful waiting (includes treatment, if needed, with oral contraceptives, intrauterine devices, or nonsteroidal anti-inflammatory drugs)
 - One-time use of GnRH for 6 months
 - Myomectomy (multiple procedures allowed)

- If treatment fails or symptoms recur, women undergo additional interventions; the model allows for treatment strategies to include up to four interventions.
- Nine treatment strategies were evaluated.
 - Watchful waiting only
 - GnRH only
 - GnRH followed by one myomectomy
 - GnRH followed by up to two myometomies
 - GnRH followed by up to three myometomies
 - A single myomectomy
 - Up to two myometomies
 - Up to three myometomies
 - Up to four myometomies

Model Assumptions and Parameters

- Probability of treatment success (symptomatic to asymptomatic) and probability of recurrence of symptoms (asymptomatic to symptomatic) were obtained from the literature and from an analysis of the PharMetrics database (Table 1).
- Probability of emergency hysterectomy during a myomectomy procedure was obtained from the PharMetrics database.
- Women naturally postmenopausal may undergo a hysterectomy but only for reasons other than uterine fibroids (e.g., cancer).
- Pregnancy rates, pregnancy outcome rates, and menopause rates were based on US population-based age-specific rates.^{7,8}
 - Relative risks were included to model the effect of fibroids on fertility and on pregnancy outcomes (reduction in ability to get pregnant and increased risk of unsuccessful pregnancy for women with symptomatic fibroids are 0.849 and 1.678, respectively).⁹

- Women who have had a hysterectomy or are menopausal no longer have symptoms from uterine fibroids.
- Mortality rates were based on age-specific, all-cause mortality data for a female US population.¹⁰
- The model included both uterine fibroid-related monitoring costs (based on the health-state a woman was in at any given time) and treatment costs (based on which treatments and how many treatments a woman underwent) (Table 2).
- Utility values were assigned to each health-state, and one-time utility decrements were included for complications and productivity losses associated with surgical interventions (Table 3).
- Costs (2007 US\$) and outcomes were discounted at 3% annually.¹¹

Model Outcomes and Sensitivity Analysis

- The base-case analysis was for women diagnosed at age 20 years and followed until menopause. Total discounted costs and quality-adjusted life years (QALYs) were calculated for each of the nine treatment strategies, and an efficiency frontier was plotted.
- Incremental cost per QALY gained was calculated for each strategy compared with the last nondominated strategy.
- One-way sensitivity analyses on key model parameters were conducted. The cost-effective strategy was identified using a willingness-to-pay threshold of \$100,000 per QALY gained.

Table 1. Annual Probabilities

Parameter Description	Probability
Treatment success and fibroid recurrence	
Watchful waiting ^a	
Success (symptomatic to asymptomatic)	0.0%
Recurrence (asymptomatic to symptomatic)	NA
GnRH	
Success (symptomatic to asymptomatic) ¹²	92.1%
Recurrence (asymptomatic to symptomatic) ^{b, 13}	3.7%
Myomectomy	
Success (symptomatic to asymptomatic) ¹⁴	96.8%
Recurrence (asymptomatic to symptomatic) ¹⁵	3.6%
Hysterectomy	
Success (symptomatic to asymptomatic) ^c	100.0%
Recurrence (asymptomatic to symptomatic)	0.0%
Procedural complications	
Myomectomy ^{d,16}	21.3%
Hysterectomy ¹⁶	35.9%
Emergency hysterectomy during myomectomy procedure ¹²	3.14%
Non-fibroid-related hysterectomy	
Premenopausal ¹⁷	0.51%
Postmenopausal ¹⁷	0.29%

NA = not applicable.

^a Assumption that watchful waiting has no efficacy in treating symptomatic fibroids.

^b The annualized percentage of asymptomatic women who underwent surgery each year following diagnosis of uterine fibroids using the PharMetrics Database. Asymptomatic was defined as not having a procedure within the first year of diagnosis.

^c Assumption that women who have had a hysterectomy no longer have symptoms from uterine fibroids.

^d The probability of complications from myomectomy is assumed equal to that of UAE because no significant difference in complication rates was found in a head-to-head trial between myomectomy and UAE.¹⁴

Table 2. Costs (2007 US\$)

Parameter Description	Costs
Annual uterine fibroid-related monitoring costs	
Asymptomatic premenopausal fibroid ^{a,18}	\$199.00
Symptomatic premenopausal fibroid ^{a,18}	\$199.00
Posthysterectomy ^a	\$0.00
Pregnancy ^{a, 18}	\$137.00
Natural menopause ^{d,18}	\$63.00
1-year treatment costs	
Watchful waiting ^{a,19,20}	\$134.63
GnRH ²⁰	\$3,094.98
Myomectomy ^{1,21}	\$14,465.00
Non-fibroid-related hysterectomy ^{1,21}	\$15,702.78
Cost of pregnancy	
Successful ²²	\$9,318.00
Unsuccessful ²²	\$536.87

^a Assumes 1 physician visit (CPT code 99213) and 1 ultrasound (CPT code 76801).

^b Assumes no uterine fibroid-related monitoring costs.

^c Assumes 1 ultrasound (CPT code 76801).

^d Assumes 1 physician visit (CPT code 99213).

^e Weighted average based on the percentage of women on watchful waiting taking symptom drug treatments.

^f Costs include the mean procedure cost plus the 1-year follow-up cost (includes complication and emergency hysterectomy costs).

Table 3. Utilities

Parameter Description	Utility Value/Utility Decrement
Health state utilities	
Asymptomatic premenopausal fibroid ¹⁶	0.8250
Symptomatic premenopausal fibroid ¹⁶	0.7050
Posthysterectomy ^{a,16,23}	0.8050
Natural menopause ¹⁶	0.8250
Utility decrements (QALY adjustment in first year)	
Procedural complications ¹⁶	0.0079
Loss of productivity after myomectomy ¹⁶	0.0022
Loss of productivity after hysterectomy ¹⁶	0.0070

^a Posthysterectomy includes a 0.02 utility decrement for a woman's presumed unwanted loss of her uterus.²³

RESULTS

- Base-case results show treatment of symptomatic fibroids with GnRH followed by up to three myomectomy procedures for women whose symptoms recurred resulted in the most discounted QALYs (18.79) (Table 4).
- Base-case results indicate that for women diagnosed with symptomatic fibroids at age 20 years, watchful waiting and treatment strategies including one-time use of GnRH were on the efficiency frontier; treatment strategies including myomectomy only were dominated (Table 4, Figure 2).
- Additional procedures for women whose symptoms recurred led to increased medical costs and increased QALYs, resulting in an incremental cost per QALY gain of \$13,307, \$15,433, and \$17,555 for the first, second, and third myomectomy, respectively (Table 4, Figure 2).
- One-time use of GnRH followed by myomectomy for women whose symptoms recurred was more costly and more effective than watchful waiting in treating uterine fibroids over a woman's lifetime (incremental cost per QALY gained range: \$3,789-\$7,456).

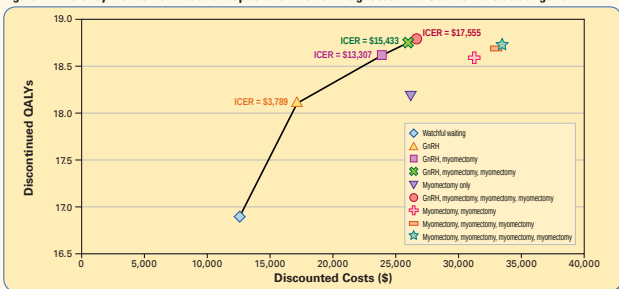
Table 4. Discounted Results for Women Diagnosed With Symptomatic Fibroids at Age 20 Followed Until Menopause

Treatment Strategy	Costs	QALYs	Incremental Cost per QALY Gained
Watchful waiting only	\$12,613	16.90	-
GnRH only	\$17,205	18.11	\$3,789 ^a
GnRH, myomectomy	\$23,963	18.62	\$13,307 ^a
GnRH, up to 2 myometomies	\$26,127	18.76	\$15,433 ^a
Myomectomy only	\$26,213	18.19	Dominated ^b
GnRH, up to 3 myometomies	\$26,742	18.79	\$17,555 ^a
Up to 2 myometomies	\$31,337	18.59	Dominated ^b
Up to 3 myometomies	\$33,035	18.70	Dominated ^b
Up to 4 myometomies	\$33,526	18.73	Dominated ^b

^a Compared with the last nondominated treatment.

^b Other strategies cost less and result in more QALYs.

Figure 2. Efficiency Frontier for Treatment Options for Women Diagnosed With Uterine Fibroids at Age 20



ICER = incremental cost-effectiveness ratio.

Sensitivity Analysis

- Cost-effectiveness results were sensitive to age at diagnosis, number of interventions, and the long-term disutility associated with a woman losing her uterus via emergency hysterectomy (Table 5).
- Similar to the base-case analysis, treatment strategies that included pharmacotherapy with GnRH for 6 months were dominant compared with no GnRH.
- The incremental cost per QALY gained of any treatment (i.e., pharmacotherapy, surgical procedure, or both) compared with watchful waiting increased as the age of diagnosis increased.
- For women whose symptoms recurred, each additional myomectomy procedure became increasingly less cost-effective as women approached menopausal age.
- For older women, GnRH for 6 months was dominant compared with myomectomy and cost an additional \$55,794 per QALY gained compared with watchful waiting.

Table 5. Sensitivity Analysis Results

Parameter	Value	Cost-effective Strategy	Incremental Cost per QALY Gained
Base case	20 years	GnRH, up to 3 myometomies	\$17,555 ^a
Age at diagnosis	30 years	GnRH, up to 3 myometomies	\$27,198 ^a
Age at diagnosis	40 years	GnRH, up to 3 myometomies	\$61,851 ^a
Age at diagnosis	50 years	GnRH, up to 1 myomectomy	\$88,754 ^a
Age at diagnosis	55 years	GnRH only	\$55,794 ^a
Utility posthysterectomy (base-case value = 0.8050)			
Low	0.7750	GnRH, up to 3 myometomies	\$19,563 ^a
High	0.8250	GnRH, up to 3 myometomies	\$16,430 ^a

^a Compared with the last nondominated treatment (GnRH followed by up to 2 myometomies).

^b Compared with the last nondominated treatment (GnRH only).

^c Compared with the last nondominated treatment (watchful waiting).

CONCLUSIONS

- Treatment strategies including one-time use of GnRH led to better health outcomes and lower costs (i.e., dominant) compared with strategies containing myomectomy only, because of the lack of risk of emergency hysterectomy associated with pharmacotherapy.
- For women of all ages, initial treatment with one-time use of GnRH leads to better long-term health outcomes compared with initial treatment with myomectomy.
- Pharmacotherapy with GnRH for 6 months should be considered for treating symptomatic fibroids in women desiring to retain their uterus before surgical procedures, such as myomectomy, with a risk of emergency hysterectomy are considered.
- Treatment options are limited for a woman seeking to retain her uterus. This model is the first to assess the cost-effectiveness of the treatment options for a woman who would like to retain her uterus.

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