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Preferences for Key Features of Gonadotropin-Releasing Hormone Analogues Among Women with Endometriosis in the United States

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INTRODUCTION

- Endometriosis is a chronic gynecological disease defined by the presence of abnormally or ectopically located endometrial tissue, which can cause pelvic pain and infertility.[1]
- The prevalence of endometriosis is difficult to accurately determine because surgery is required to verify diagnosis; previous studies suggest that approximately 10% of women aged 18–49 years in the United States have endometriosis.[2,3]
- Treatment options typically include analgesics to manage acute pain and regular use of hormone therapies, such as hormonal contraceptives and gonadotropin-releasing hormone (GnRH) analogues; surgery is recommended for more severe cases of endometriosis.[4]
- GnRH analogues currently available in the United States for endometriosis differ in efficacy, adverse effects, dosing schedule, mode of administration, and out-of-pocket (OOP) costs.[5]
- Given the availability of multiple options for GnRH analogue treatment, it is imperative to ascertain the patient perspective on key attributes of these medications and to assure patients' preferences are incorporated into physician treatment recommendations.

OBJECTIVE

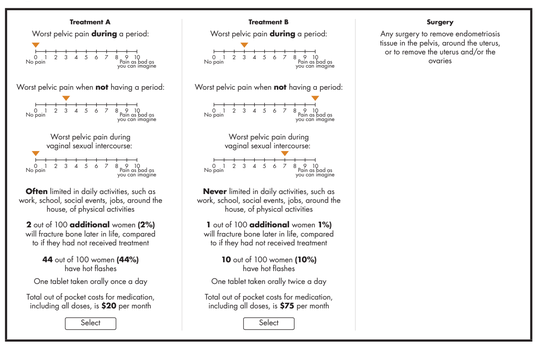
- This study aimed to quantify how US women with endometriosis value various features that differentiate GnRH analogues.

METHODS

Study design and sample

- A cross-sectional online survey, including a discrete choice experiment (DCE), was conducted; women were recruited via a healthcare research panel.
- The data for this interim analysis were collected from December 2021–April 2022.
- GnRH analogue attributes included in the DCE were identified through literature; cognitive interviews with women were conducted to qualitatively assess and refine the final survey instrument before its implementation.
- The DCE included a series of 14 choice tasks, each including 2 hypothetical GnRH analogue treatment profiles with varying levels of each attribute and a surgery opt-out option. An example choice task is shown in **Figure 1**.
- Attributes included in the DCE were reduction in dysmenorrhea, nonmenstrual pelvic pain, and dyspareunia; impact on daily activities; OOP cost (monthly); risks of bone fracture and hot flashes; and treatment administration (see **Figure 2** for attribute levels).
- The survey also collected data on patient sociodemographic and clinical characteristics, comorbidities, and past endometriosis treatments.

Figure 1. Example DCE Choice Task



Inclusion criteria

- English-speaking US resident
- Premenopausal women, aged 18–50 years
- Healthcare coverage for previous 3 years
- Self-reported laparoscopy-confirmed endometriosis diagnosis

Exclusion criteria

- Currently pregnant
- Currently enrolled in clinical trial
- Self-reported
  - Having had hysterectomy or oophorectomy
  - Receiving cancer diagnosis or cancer treatment in past 10 years
  - Having had surgical endometriosis treatment or other gynecological surgery in past 3 months
  - Having history of osteoporosis, bone disease, or uterine fibroids
- Unable or unwilling to provide informed consent
- Recruitment quotas were set to ensure an approximately even split of women with moderate-to-severe pain (rated ≥4 on a scale from 0 = no pain to 10 = pain as bad as you can imagine) during their most recent period who were treatment-naive and who were GnRH analogue-experienced.

Statistical analysis

- Descriptive statistics were reported for patient sociodemographic and clinical characteristics, comorbidities, and past endometriosis treatments.
- Hierarchical Bayesian modeling was used to analyze the DCE data; mean preference weights were computed for each attribute level.
  - The change in utility associated with a change in the levels of each attribute is represented by the difference between the preference weights for any 2 levels of an attribute.[†]
  - Larger differences indicate that the change between those 2 levels is more influential to overall utility.
- Attribute relative importance (RI) was computed by dividing the utility range of each attribute (preference weight of the most favorable level minus preference weight of the least favorable level) by the sum of the utility ranges of all attributes and multiplying by 100 to standardize.
  - RI estimates are ratio scaled; for example, an attribute with RI of 20 is twice as important to treatment choice as an attribute with RI of 10.
- Estimated preferences for hypothetical endometriosis treatment profiles were derived by summing the preference weights on an individual basis for each attribute level matching to a profile. Simulations were then performed to estimate the percentage of respondents who preferred each profile versus surgery.

[†]Utility refers to the degree to which a specific product choice is valued or preferred by individuals; those options that are more valued or preferred have higher utility and vice versa.

RESULTS

Patient characteristics

- Overall, 244 women with endometriosis were included in the interim analysis. Patient characteristics are reported in **Table 1**.
- Most patients were White (84%); patients were a mean±SD of 32.2±7.3 years old and had been diagnosed with endometriosis for a mean±SD of 9.9±7.1 years.
- The endometriosis/menstrual symptoms reported most often were abdominal pain (98%) and pelvic pain (92%); the most frequently reported comorbidities were anxiety (71%) and depression (62%).
- Considering the past treatments used by respondents to manage their endometriosis symptoms and menstrual pain, over-the-counter (OTC) pain medications were most frequently mentioned (95%), followed by prescription (Rx) contraceptives (83%).

Table 1. Sample Characteristics

Variables	Total (N=244)
Age (Years): Mean ± SD (Median)	32.2±7.3 (31.0)
Race/Ethnicity: White, n (%)	205 (84.0)
Education: Less than college degree, n (%)	146 (59.8)
Employment: Employed full-time or part-time, n (%)	148 (60.7)
Comorbidities, n (%)*†	
Anxiety	173 (70.9)
Depression	150 (61.5)
Migraine	109 (44.7)
Lower back pain	89 (36.5)
Asthma	77 (31.6)
Polycystic ovary syndrome	61 (25.0)
Irritable bowel syndrome	60 (24.6)
Infertility	55 (22.5)
Time Since Diagnosis (Years): Mean ± SD (Median)**	9.9±7.1 (8.0)
Worst Dysmenorrhea Pain: Mean ± SD (Median)‡	7.6±1.7 (8.0)
Worst Nonmenstrual Pelvic Pain: Mean ± SD (Median)‡	5.4±2.6 (6.0)
Worst Dyspareunia Pain: Mean ± SD (Median)‡§	5.4±2.7 (6.0)
Endometriosis/Menstrual Symptoms Experienced, n (%)*††	
Abdominal pain	239 (98.0)
Pelvic pain	225 (92.2)
Back pain	216 (88.5)
Fatigue	216 (88.5)
Heavy bleeding during your period	211 (86.5)
Feeling unwell, faint, or nauseous during your period	204 (83.6)
Bloating	202 (82.8)
Headache/migraine	191 (78.3)
Gastrointestinal distress	188 (77.0)
Bleeding or spotting between periods	187 (76.6)
Endometriosis/Menstrual Pain Therapies Used, n (%)*	
OTC pain medications	232 (95.1)
Rx contraceptives	203 (83.2)
Rx medications	186 (76.2)
Surgery	154 (63.1)
Alternative therapies	108 (44.3)
OTC muscle relaxers	104 (42.6)
Prescribed physical therapy	46 (18.9)
GnRH Used, n (%)‡‡	
GnRH-experienced	96 (39.3)
GnRH-naive	148 (60.7)

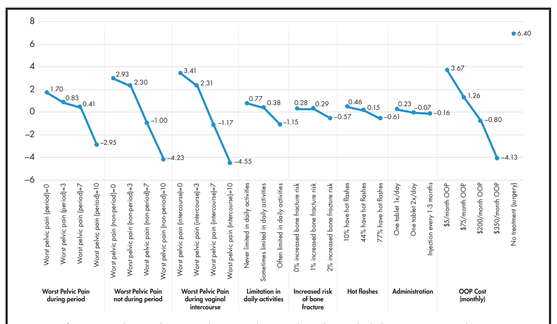
GnRH: gonadotropin-releasing hormone; OTC: over-the-counter; Rx: prescription; SD: standard deviation.
*Respondents could select >1 response option.
†Only those comorbidities reported by ≥20% of respondents are shown.
**2 patients were excluded from calculation of disease duration due to extreme outlier values on this variable.
‡Pain was rated on a scale from 0 (no pain) to 10 (pain as bad as you can imagine). Recall was based on the past month (nonmenstrual pain and dyspareunia) or the last period (menstrual pain).
§N=172 for worst dyspareunia pain.
††Only those symptoms reported by ≥75% of respondents are shown.
‡‡The GnRH-experienced group consisted of women who selected "yes" for use of Rx medications to manage menstrual pain/endometriosis symptoms and also selected "yes" on elagolix, leuprorelin, and/or another GnRH agonist in a follow-up item on Rx medications used. The GnRH-naive group consisted of women who selected "no" on use of Rx medications to manage menstrual pain/endometriosis symptoms and women who selected "yes" on use of Rx medications to manage menstrual pain/endometriosis symptoms and also selected "no" on elagolix, leuprorelin, and another GnRH agonist in a follow-up item on Rx medications used.

Treatment preferences

Trade-offs

- Across the DCE choice tasks, respondents chose a GnRH analogue profile 42% of the time versus the surgery opt-out option.
- Attribute level preference weights are depicted in **Figure 2**.
  - Respondents were willing to accept an increase in monthly OOP cost from $5 to $75 (mean change in preference weights: 3.7–1.3 = 2.4) for an improvement in
    - Dyspareunia pain rating from 7 to 3 (change in preference weight = 3.5)
    - Nonmenstrual pelvic pain rating from 7 to 3 (change in preference weight = 3.3)
  - Improvement in dysmenorrhea pain severity, improvement in daily activities, reduced administration burden, reduced risk of hot flashes, or reduced risk of bone fracture later in life had less impact on treatment choice.

Figure 2. Attribute Level Preference Weights

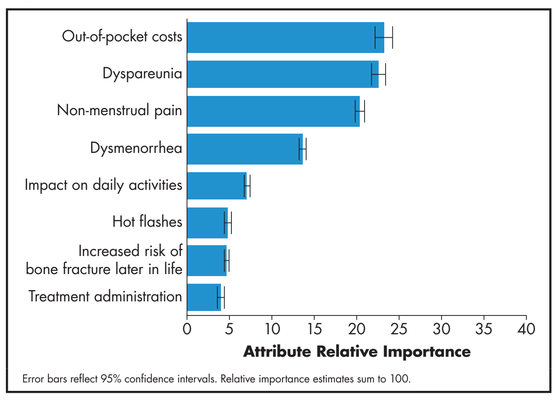


Mean preference weights are shown. Attributes are shown in the order in which they were presented to respondents in the DCE choice tasks; attributes are shown in purple text, with attribute levels shown in light blue text.

Attribute relative importance estimates

- Monthly OOP cost (RI=23.2) and reduction in dyspareunia (RI=22.5) were the most important attributes and were similarly valued by patients **(Figure 3)**.
  - These 2 attributes were significantly more influential ($p<0.05$, 2-tailed) to treatment choice than any of the other attributes included in the DCE.

Figure 3. Attribute Relative Importance Estimates



Error bars reflect 95% confidence intervals. Relative importance estimates sum to 100.

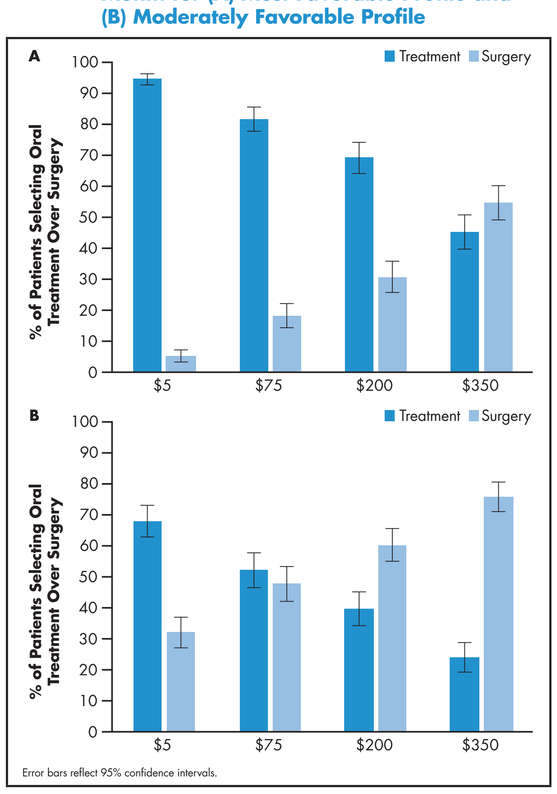
Estimated preference share

- Hypothetical GnRH analogue treatment profiles used for estimating preference share are shown in **Table 2**.
- For the most favorable treatment profile (highest efficacy and lowest risk), most patients would prefer oral treatment (vs surgery) at each monthly OOP cost level up to $200 **(Figure 4A)**.
- For the moderately favorable treatment profile (moderately high efficacy and risk), a majority would prefer oral treatment (vs surgery) at monthly OOP cost level up to $75 **(Figure 4B)**.

Table 2. Hypothetical Treatment Profiles

Attributes	Attribute Levels of Hypothetical Most Favorable Treatment Profile	Attribute Levels of Hypothetical Moderately Favorable Treatment Profile
Dysmenorrhea	Worst pelvic pain during a period = **0** (0, no pain, to 10, pain as bad as you can imagine)	Worst pelvic pain during a period = **3** (0, no pain, to 10, pain as bad as you can imagine)
Nonmenstrual Pain	Worst pelvic pain when not having a period = **0** (0, no pain, to 10, pain as bad as you can imagine)	Worst pelvic pain when not having a period = **3** (0, no pain, to 10, pain as bad as you can imagine)
Dyspareunia	Worst pelvic pain during vaginal sexual intercourse = **0** (0, no pain, to 10, pain as bad as you can imagine)	Worst pelvic pain during vaginal sexual intercourse = **3** (0, no pain, to 10, pain as bad as you can imagine)
Impact on Daily Activities	**Never** limited in daily activities, such as work, school, social events, jobs around the house, or physical activities	**Sometimes** limited in daily activities, such as work, school, social events, jobs around the house, or physical activities
Increased Risk of Bone Fracture Later in Life	**0** out of 100 additional women (**0%**) will fracture a bone later in life, compared to if they had not received treatment	**2** out of 100 additional women (**2%**) will fracture a bone later in life, compared to if they had not received treatment
Treatment Administration	How the medication is taken: **1 tablet taken orally once a day**	How the medication is taken: **1 tablet taken orally once a day**
Hot Flashes	**10** out of 100 women (**10%**) have hot flashes	**44** out of 100 women (**44%**) have hot flashes

Figure 4. Estimated Percentage of Patients Preferring Oral Treatment vs Surgery by OOP Cost Per Month for (A) Most Favorable Profile and (B) Moderately Favorable Profile



Error bars reflect 95% confidence intervals.

LIMITATIONS

- The DCE cannot accommodate all factors that could potentially influence treatment preferences or real-world treatment decisions. Accordingly, stated preferences may not have perfect fidelity to the actual treatment choices of women with endometriosis.
- Data on clinical characteristics, treatment, and diagnosed endometriosis and comorbid health conditions were self-reported and could not be medically confirmed for accuracy.
- The study sample may not be fully representative of the overall population of women with endometriosis in the United States, which may limit generalizability.
- The final analysis results (N=300) may slightly diverge from those found in this interim analysis.

CONCLUSIONS

- **Nearly all women used pain medications and prescription contraceptives to treat endometriosis symptoms.**
- **A majority selected surgery over a GnRH analogue. Given endometriosis recurs in up to 67% of cases after surgery,[6] it is possible that some women may erroneously believe that surgery is curative, presenting an opportunity for physicians to better inform their patients about the benefits and risks of available treatment options.**
- **When monthly OOP costs are minimal-to-moderate, the treatment preferences of women with endometriosis are most influenced by reducing the severities of dyspareunia and nonmenstrual pelvic pain.**
- **Overall, findings suggest that for women with endometriosis, 2 factors are most important when selecting a treatment: dyspareunia pain relief and OOP cost. These factors should be discussed in endometriosis treatment shared decision-making.**
- **Additional research is needed to quantify and qualify patients' perceptions of risk, including the importance of risk duration, in order to further elucidate the factors underlying the treatment preferences of women with endometriosis.**

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