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## RESEARCH ARTICLE

## Gynaecological Surgery

# Treatment preferences for medication or surgery in patients with deep endometriosis and bowel involvement – a discrete choice experiment

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**Abstract**

**Objective:** To study the preferences of women with deep endometriosis (DE) with bowel involvement when they have to choose between conservative (medication) or surgical treatment.

**Design:** Labelled discrete choice experiment (DCE).

**Setting:** Dutch academic and non-academic hospitals and online recruitment.

**Population or Sample:** A total of 169 women diagnosed with DE of the bowel.

**Methods:** Baseline characteristics and the fear of surgery were collected. Women were asked to rank attributes and choose between hypothetical conservative or surgical treatment in different choice sets (scenarios). Each choice set offered different levels of all treatment attributes. Data were analysed by using multinomial logistic regression.

**Main Outcome Measures:** The following attributes – effect on/risk of pain, fatigue, pregnancy, endometriosis lesions, mood swings, osteoporosis, temporary stoma and permanent intestinal symptoms – were used in this DCE.

**Results:** In the ranking, osteoporosis was ranked with low importance, whereas in the DCE, a lower chance of osteoporosis was one of the most important drivers when choosing a conservative treatment. Women with previous surgery showed less fear of surgery compared with women without surgery. Low anterior resection syndrome was almost equally important for patients as the chance of pain reduction. Pain reduction had higher importance than improving fertility chances, even in women with desire for a future child.

**Conclusions:** The risk of developing low anterior resection syndrome as a result of treatment is almost equally important as the reduction of pain symptoms. Women with previous surgery experience less fear of surgery compared with women without a surgical history.

Jeroen Metzemaekers and M. Elske van den Akker-van Marle share first authorship.

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**KEY WORDS**

decision-making, deep endometriosis, discrete choice experiment, endometriosis, surgery

**Tweetable Abstract:** First discrete choice experiment in patients with deep endometriosis.

## 1 | INTRODUCTION

Numerous treatment options are available for endometriosis, but there are two main strategies: conservative treatment (analgesics and/or hormones) and surgical treatment. However, none of these options offer a complete cure, making endometriosis a chronic condition. Available data suggest that conservative treatment and surgical treatment are effective in reducing pain.<sup>1</sup> The improvement of fertility chances with surgical treatment options remains uncertain because of inconclusive study results on this topic.<sup>2</sup> Although most of the treatment options are proven to be effective in reducing pain, they unfortunately do not come without consequences. On the one hand, conservative treatments may have potential harmful adverse effects (e.g. depressive mood, weight gain, osteoporosis), which may cause treatment failure. Other reasons for treatment failure include therapy non-compliance or contraindications (deep venous thrombosis, other cardiovascular disease).<sup>1</sup> On the other hand, surgical treatment options have the possible risks of severe complications and recurrence of disease. Surgery for deep endometriosis (DE) is associated with significant complication rates up to 14%,<sup>3</sup> which include bowel injury, anastomosis leakage and temporary or permanent stoma placement.<sup>4</sup> Making a careful and well-considered choice in endometriosis treatment options is especially relevant for DE because these patients have to deal with complex treatment trade-offs. Unfortunately, limited research has been performed to study the values and preferences in women with DE, which makes optimal counselling challenging. In addition, there is no conclusive evidence to advise patients of a particular treatment that is clearly superior.

This study aims to investigate patients' preferences in DE treatment options for conservative (focused on hormonal treatment) or surgical treatment options and which characteristics are relevant in their treatment choice. To achieve this, we performed a labelled discrete choice experiment (DCE).

## 2 | METHODS

### 2.1 | Study design

A DCE was used to gain insight into treatment preferences of women with DE and bowel involvement when they have to choose between conservative or surgical treatment. For the conservative treatment, we focused on hormonal treatment

and not on analgesics because otherwise the DCE would be too complex and too difficult to interpret. This DCE technique assumes that patients value different characteristics of a treatment, which will determine their preference. When presenting different choices, patients will usually choose the option that is most beneficial.<sup>5,6</sup>

### 2.2 | Participant recruitment

Enrollment took place between January 2019 and October 2020 in six Dutch academic hospitals (23.7% of the patients) and eight non-academic hospitals (46.7%) and also by the Dutch and Belgian endometriosis foundation (29.6%). Women who were interested could visit the website ([www.endokeuze.com](http://www.endokeuze.com)) for information about the study. Women willing to participate had to pass three inclusion questions, which are commonly used and accepted.<sup>7-9</sup> Women could not see which answer would include or exclude them. The following inclusion questions were used.

1. *Do you have deep endometriosis with bowel involvement, which is diagnosed by a doctor by ultrasound, MRI or surgery?* yes included.
2. *Are you prior to a treatment choice with medication or surgery?* yes included.
3. *Are you currently in a trajectory to become pregnant (e.g. hormonal treatment for ovulation induction, IVF)?* no included.

Further exclusion criteria were low health literacy, which was tested with three questions.<sup>10</sup> We excluded patients who always have difficulties with understanding medical information about their disease and treatment, always need help with reading information about their disease and treatment and have no confidence at all in filling in medical forms. Furthermore, patients who did not complete the ten DCE questions, patients who completed the survey in 10 minutes or less (this 'too fast' threshold was set after the pilot) and patients who gave the same answer on all questions, were excluded. A total of 641 patients started the survey; after exclusion, 169 patients were included (Table S1).

### 2.3 | Data collection

For hosting the internet survey and data collection, we used Sawtooth Software's SSI Web (Sawtooth Software. Orem,

UT, USA). As recommended, attributes and levels were based on literature review, qualitative research and an expert panel.<sup>11-13</sup> The four stages as described by Helter et al.<sup>14</sup> were applied, although we slightly customised these as seen in Figure 1. To find out which attributes were important for DE patients, we collected data by performing a literature search and qualitative study (Stage 1). We performed a survey among 28 patients, one focus group with eight patients before their decision-making<sup>15</sup> and a focus group with ten gynaecologists with expertise on DE. The results combined from Stage 1 resulted in 158 attributes. The second step in attribute development was data reduction (Stage 2). This was achieved by frequency and rank order by the researchers (JeM and JS) combined with thematic analysis, which resulted in 28 attributes. In the third and fourth stages, we removed inappropriate attributes.<sup>16</sup> This resulted in eight final attributes (Table 1).

The first part of the survey included questions about baseline characteristics, surgical fear measured with the validated Dutch surgical fear questionnaire<sup>17</sup> and three health literacy screening questions. We included the short surgical fear questionnaire, and hypothesised that the fear of surgery could influence the results of the DCE. Pain was recorded on a numerical rating scale, patients rated their pain intensity (from 0 = no pain to 10 = maximum pain, or inapplicable option).

Part two of this survey included information about the DCE (Table S2). Before the DCE, we asked the women to rank the eight attributes from most important<sup>1</sup> to least important<sup>8</sup> when making a treatment decision. To become familiar with the concept of a DCE, a simple DCE question for choosing a phone was included. Subsequently, the actual DCE was presented with ten choice sets. Each choice set consisted of two hypothetical treatment options labelled as conservative (pharmaceutical) treatment and surgical treatment. The women were asked to choose their preferred treatment of choice for each of the ten choice sets (Figure 2). The treatment options are shown in Table 1.

## 2.4 | Data analysis

NGENE software (version 1.2.1) was used to construct a fractional factorial efficient design. One constraint was taken into account to avoid implausible combinations. Thirty choice sets were created with each choice set consisting of a conservative and a surgical treatment option. In order to reduce the burden for the patient, the 30 choice sets were blocked into three versions of ten choice sets.

To assess if the DCE questionnaire was understood, we performed a pilot test with a group of pre-surgical patients. After the DCE was online and open for inclusion, an interim analysis was performed to test our expected direction of effect. The results were in line with our expectations; so no adjustments were made. For internal consistency, we included one fixed task, with the conservative treatment option more favourable compared with a surgical option with maximum adverse effects and little to no beneficial effects.

Optimal sample size calculation for estimating for non-linear discrete choice models is complicated because it depends on the true values of the unknown parameters estimated in the DCE.<sup>18</sup> Given the lack of a definite method for calculating a sample size, we based our sample size on a literature review.<sup>19</sup> Marshall et al. described that most studies published between 2005 and 2008 had a sample size of 100–300 respondents. We aimed for 300 respondents because we also wanted to study subgroups.

## 2.5 | Statistical analysis

IBM SPSS version 25.0 for Windows (IBM, Armonk, NY, USA) was used for our analysis and we used the Shapiro–Wilk test to evaluate the distribution of the data. Data are presented as mean ± standard deviation or median with interquartile range (IQR) for normally distributed or skewed data, respectively. We used Student's *t* test for normally distributed data. We considered a two-tailed *p* value less than 0.05 as statistically significant. For the DCE analysis we used NLOGIT software

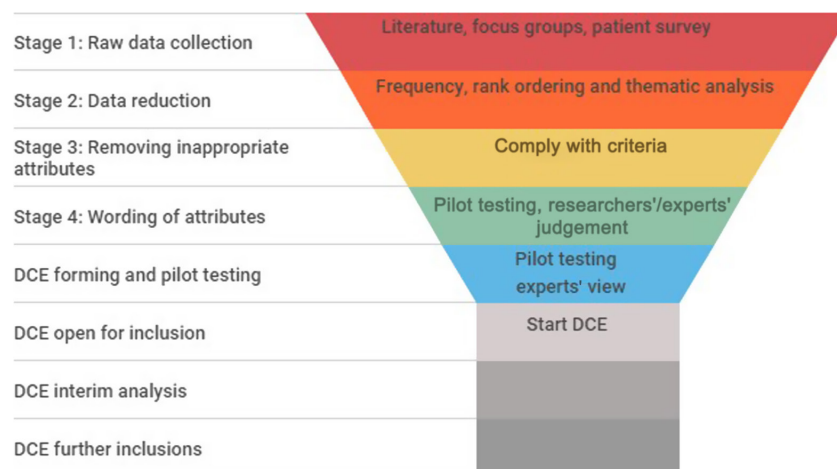


FIGURE 1 Customised stages to create attributes and forming of DCE

**TABLE 1** Treatment attributes and levels used in the discrete choice experiment

Attributes	Level pharmaceutical	Level surgical
Chance that pain disappears (%)	40%	50%
	60%	70%
	80%	90%
Chance of fatigue symptoms	Decreases	Decreases
	Does not change	Does not change
	Increases	Increases
Pregnancy chance after treatment	Increases	Increases
	No influence	No influence
Chance of the presence of endometriosis	Remains the same	Will be removed as much as possible, no chance of radical surgery
	Gets smaller	Will be completely removed, chance of radical surgery
Chance of depressed mood (%)	1%	–
	5%	–
	10%	–
Chance of osteoporosis (%)	1%	–
	5%	–
	10%	–
Chance of temporary stoma (%)	–	1%
	–	5%
	–	10%
Chance of permanent intestinal Symptoms (%)	–	10%
	–	50%
	–	80%
	–	–

version 6. Data were analysed using a multinomial regression model. This model has the following regression equation

$$\begin{aligned}
 V_{\text{conservative treatment}}(ct) = & \beta_0 \\
 & + \beta_1 * \text{chance of pain reduction}_{cv} \\
 & + \beta_2 * \text{chance of fatigue} + \beta_3 * \text{chance of pregnancy} \\
 & + \beta_4 * \text{presence of endometriosis}_{cv} \\
 & + \beta_5 * \text{chance of depressed mood}_{cv} \\
 & + \beta_6 * \text{chance of osteoporosis}_{cv} + \epsilon,
 \end{aligned}$$

$$\begin{aligned}
 V_{\text{surgical treatment}}(st) = & \beta_7 * \text{chance of pain reduction}_{st} \\
 & + \beta_8 * \text{presence of endometriosis}_{st} \\
 & + \beta_9 * \text{chance of temporary stoma}_{st} \\
 & + \beta_{10} * \text{permanent intestinal symptoms}_{st} \\
 & + \beta_2 * \text{chance of fatigue} + \beta_3 * \text{chance of pregnancy} + \epsilon.
 \end{aligned}$$

$V$  represents the relative utility that a respondent derives from choosing conservative treatment or surgery.  $\beta_0$  is the alternative specific constant, reflecting a preference for the label irrespective of the levels of the attributes.

$\beta_1$ – $\beta_{10}$  are the alternative specific coefficients of each attribute with the exception of  $\beta_2$  chance of fatigue and  $\beta_3$  chance of pregnancy. The levels of these attributes were generic across the treatments.

$\epsilon$  is an unobserved component of the utility function or error term. Pain reduction, chance of depressed mood,

chance of osteoporosis, chance of temporary stoma and permanent intestinal symptoms were included as continuous variables whereas for fatigue, chance of pregnancy and presence of endometriosis dummy coding were used. In addition, we performed subgroup analysis with women with or without desire for a child in the future. Relative importance was calculated by multiplying the coefficient of an attribute with the range used for the attribute levels or using the difference in coefficients between the best and worst levels of the same attribute (in the case of dummy coding). Subsequently, the resulting part-worth utility of each attribute was divided by the sum of all part-worth utilities, which gives the relative importance per attribute.<sup>20</sup> A significance level of 5% was chosen to determine statistically significant coefficients.

### 3 | RESULTS

Table 2 shows the baseline characteristics of all participants. The mean age was 36.2 years, 51.5% of the women had never been pregnant and 34.9% of the women wished for a child in the future. Hormonal medication for the endometriosis was used in 72.8% and 71.0% used painkillers. Looking at the surgical history, 69.2% had previous abdominal surgery with a total complication rate of 33% (ever experienced a surgical complication, ranging from cystitis to anastomosis leakage).

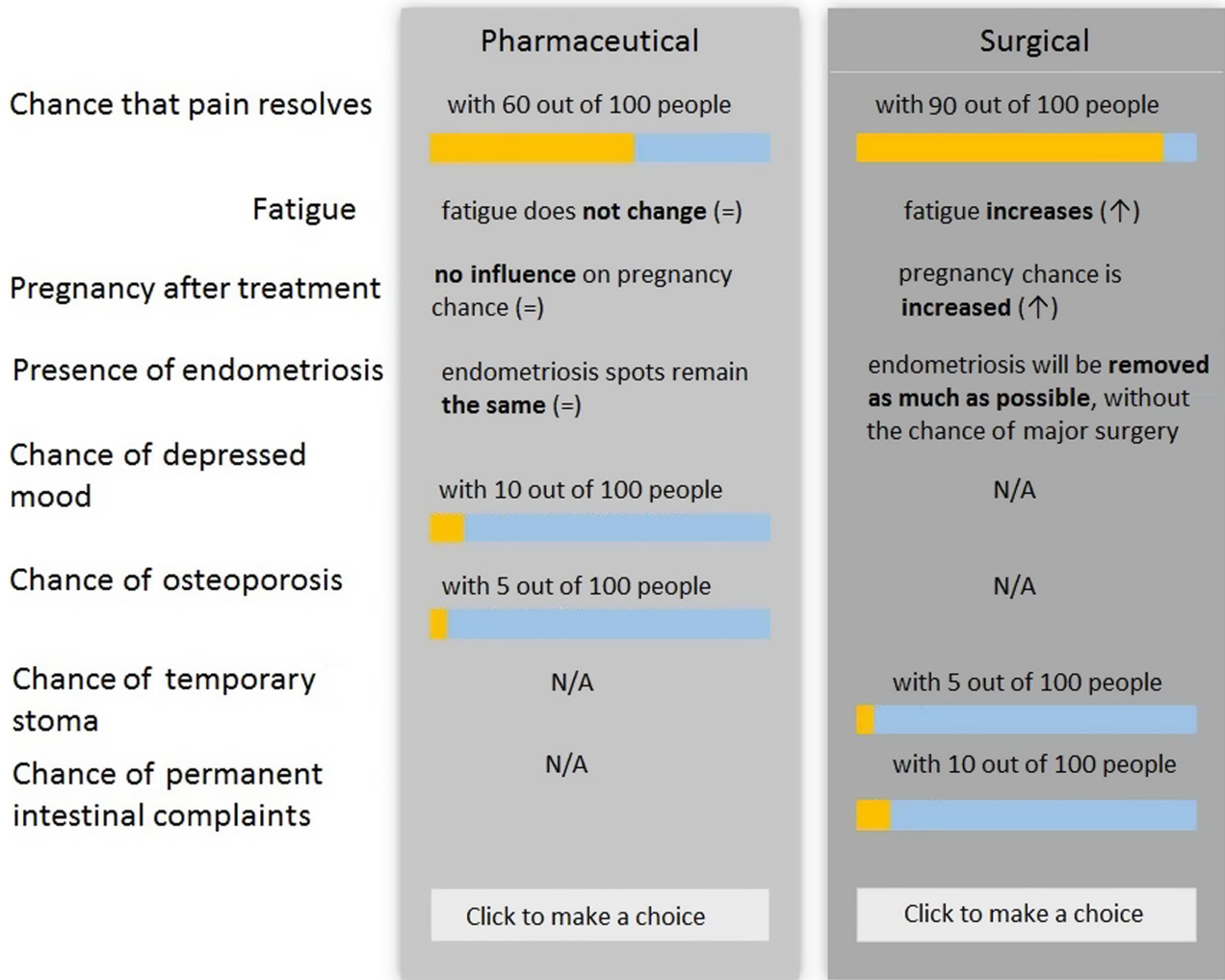


FIGURE 2 Choice task with two hypothetical treatment options

### 3.1 | Pain

Dysmenorrhoea was reported with median numeric rating scales of 8.0 (IQR 7–9) for pain, 8.0 (IQR 7–9) for cycle-related pelvic pain, 8.0 (IQR 6–9) for dyschezia, 7.0 (IQR 5–8) for dyspareunia and 5.0 (IQR 1–7) for dysuria (Table 3). Non-cycle-related pain was reported for pelvic pain with a median numeric rating scales of 6.0 (IQR 4–7) for pain, 6.0 (IQR 3–7) for dyschezia, 6.0 (IQR 3–7) for dyspareunia and 3.0 (IQR 0–6) for dysuria.

### 3.2 | Subgroup analysis regarding surgical fear

The total surgical fear was assessed for patients with or without the desire for a future child and patients with or without previous surgery. The surgical fear was significantly lower in the group of women with previous surgery (30.9 versus 39.8,  $p = 0.01$ ), no significant difference in surgical fear was seen between the groups of patients with and without a wish for a child (34.7 versus 30.9,  $p = 0.17$ ).

### 3.3 | Ranking of attributes before the DCE

Table 4 shows the ranking of attributes before the start of the DCE.

### 3.4 | Attributes coefficients and relative importance

Table 5 shows the main results of the DCE, which include the coefficients and relative importance in the main model and the subgroup of women with and without a wish for a future child.

### 3.5 | Main model

When making a choice for conservative treatment a lower chance of osteoporosis, an improvement in fatigue symptoms, a higher chance of reducing pain, a higher chance of pregnancy and a reduction of endometriosis lesions all had a significant

TABLE 2 Patient characteristics

		<i>n</i> = 169
Age (years), mean ± SD		36.2 ± 7.0
Time till diagnosis (years), median (IQR)		9.0 (3.0–15.0)
		<i>n</i> (%)
Currently in a relationship		140 (82.8%)
Country of birth	The Netherlands	146 (86.4%)
	Surinam	3 (1.8%)
	Antilles	4 (2.4%)
	Other	16 (9.5%)
Highest completed education	Secondary education	15 (8.9%)
	Secondary vocational education	56 (33.1%)
	Higher professional education	68 (40.2%)
	University education	29 (17.2%)
	Other	1 (0.6%)
Currently having a paid job		146 (86.4%)
Obstetric history		
Gravida	0	87 (51.5%)
	≥1	82 (48.5%)
Total conception	Natural	133/173 (76.9%)
	IVF/ICSI	28/173 (16.2%)
	Other	12/173 (6.9%)
Future child wish	Yes	59 (34.9%)
	No	87 (51.5%)
	Unknown at the moment	23 (13.6%)
Medication for endometriosis		
Hormonal medication use		123 (72.8%)
Painkiller use for endometriosis		120 (71.0%)
Surgical history and fear of surgery		
Previous abdominal surgery		117 (69.2%)
Ever experienced a surgical complication		34 (33%) <sup>a</sup>
Surgical Fear Questionnaire, mean ± SD <sup>b</sup>		
	Fear of short-term consequences <sup>c</sup>	15.5 ± 8.9
	Fear of long-term consequences <sup>c</sup>	18.1 ± 10.0
	Total score <sup>d</sup>	33.6 ± 16.6

Abbreviations: ICSI, intracytoplasmic sperm injection; IVF, in vitro fertilisation.

<sup>a</sup>Fourteen missing values, 34/103 = 33%.

<sup>b</sup>Five missing values.

<sup>c</sup>Sum score subscale range from 0 (no fear) to 40 (very afraid).

<sup>d</sup>Sum score total range from 0 (no fear) to 80 (very afraid).

TABLE 3 Numeric rating scale for pain (0–10)

Pain symptoms numeric rating scale	During menstruation		Not related to menstruation	
	Median (IQR)	<i>n</i>	Median (IQR)	<i>n</i>
Dysmenorrhoea	8.0 (7–9)	122	–	–
Pelvic pain	8.0 (7–9)	121	6.0 (4–7)	148
Dyschezia	8.0 (6–9)	125	6.0 (3–7)	149
Dyspareunia	7.0 (5–8)	91	6.0 (3–7)	127
Dysuria	5.0 (1–7)	122	3.0 (0–6)	139

impact, but the chance of a depressed mood did not show a significant effect. The three most important drivers for conservative treatment were lower chance of osteoporosis (33%), improvement of fatigue (25%) and a higher chance of reducing pain (24%), accounting for 82% of the relative importance results. The improvement of fertility (9.4%) and the reduction of endometriosis lesions (8.5%) showed low relative importance.

When making a choice for surgery, a lower chance of permanent intestinal symptoms, reducing pain, improving fatigue symptoms, improving fertility, a lower chance of getting a temporary stoma all have a significant effect with the exception of the attribute reducing endometriosis nodules/spots. A lower chance of permanent intestinal symptoms (38%), reducing pain (25%) and improvement of fatigue (22%) were the most important drivers for the surgical treatment, accounting for 85% of the relative importance results.

### 3.6 | Subgroup analysis in women with a future child wish

In the subgroup model, it is shown that improving fatigue symptoms (34%) together with reducing pain (28%) and improving fertility (24%) are the three most important attributes when making a choice for conservative treatment (86% of the relative importance).

The subgroup model also showed that the chance of permanent intestinal symptoms (35%), reducing pain (21%) and improving fatigue symptoms (19%) were the most important attributes when making a choice for surgery (75% of the relative importance).

## 4 | DISCUSSION

### 4.1 | Main findings

Translating the main findings of this DCE with women with DE and bowel involvement towards the clinical setting we can conclude the following. 1. In the ranking, osteoporosis was ranked with low importance. 2. The three most important drivers for the choice of conservative treatment were lower chance of developing osteoporosis (gonadotrophin-releasing hormone [GnRH] analogues), higher chance of improving fatigue symptoms and higher chance of reducing

**TABLE 4** Ranking of attributes

Attributes (1 = most important, 6 = least important)	Total patients		Attributes	Patients with future child wish	
	<i>n</i> = 155 <sup>a</sup>			<i>n</i> = 58 <sup>b</sup>	
	Median	IQR		Median	IQR
1. Reducing pain	1	1–2	1. Reducing pain	1	1–2
2. No permanent intestinal symptoms	3	2–5	2. Pregnancy change increase	3	2–4
3. Fatigue decrease	4	2–5	3. No permanent intestinal symptoms	4	2–5
3. Endometriosis reduction	4	3–6	3. Endometriosis reduction	4	2–7
4. No temporary stoma	5	3–7	3. Fatigue decrease	4	3–6
4. Stable mood	5	4–7	4. No temporary stoma	5	3–7
5. No osteoporosis	6	5–7	5. Stable mood	6	5–7
6. Pregnancy change increase	8	4–8	6. No osteoporosis	7	6–8

<sup>a</sup>Fourteen missing data.<sup>b</sup>One missing data.**TABLE 5** Attributes coefficients and relative importance

	Coefficient significance		Relative importance	%
Medication main model				
Lower chance of developing osteoporosis	-0.16058	0.05	1.45	33.4
Higher chance of improving fatigue symptoms	0.38772	0.01	1.09	25.1
Higher chance of reducing pain symptoms	0.02538	0.01	1.02	23.5
Higher chance of improving pregnancy rates	0.40875	0.01	0.41	9.4
Higher chance of reducing endometriosis nodules	0.37096	0.01	0.37	8.5
Lower chance of developing a depressed mood	-0.10284	NS	-	-
Surgery main model				
Lower chance of developing intestinal symptoms (LARS)	-0.02734	0.01	1.91	38.0
Higher chance of reducing pain symptoms	0.03092	0.01	1.24	24.7
Higher chance of improving fatigue symptoms	0.38772	0.01	1.09	21.7
Higher chance of improving pregnancy rates	0.40875	0.01	0.41	8.2
Lower chance of getting a temporary stoma	-0.04165	0.05	0.37	7.4
Higher chance of reducing endometriosis nodules	0.02234	NS	-	-
Medication subgroup: desire for a child in the future				
Higher chance of improving fatigue symptoms	0.42426	0.01	1.05	34.2
Higher chance of reducing pain symptoms	0.02158	0.01	0.86	28.0
Higher chance of improving pregnancy rates	0.73626	0.01	0.74	24.1
Higher chance of reducing endometriosis nodules	0.41927	0.05	0.42	13.7
Lower chance of developing osteoporosis	0.05322	NS	-	-
Lower chance of developing a depressed mood	-0.16129	NS	-	-
Surgery subgroup: desire for a child in the future				
Lower chance of developing intestinal symptoms (LARS)	-0.02725	0.01	1.91	35.2
Higher chance of reducing pain symptoms	0.02893	0.01	1.16	21.4
Higher chance of improving fatigue symptoms	0.42426	0.01	1.05	19.4
Higher chance of improving pregnancy rates	0.73626	0.01	0.74	13.7
Lower chance of getting a temporary stoma	-0.06208	0.01	0.56	10.3
Higher chance of reducing endometriosis nodules	0.03034	NS	-	-



pain symptoms. For surgery, the three most important drivers were lower chance of low anterior resection syndrome (LARS), higher chance of reducing pain symptoms and higher chance of improving fatigue symptoms. 3. The chance of getting a temporary stoma played a less important role in the context of this study compared with pain reduction and the risk of LARS. 4. Women with a desire for a child in the future put pain reduction above possible improvement of fertility chances. 5. Women with previous surgery had significantly lower fear of surgery compared with women without a history of surgery (DE surgery).

Comparing the results of the direct ranking method and those of the relative importance of the DCE shows discrepancies between both methods. In particular, the attribute chance of osteoporosis was considered of low importance in the ranking exercise but was one of the most important attributes when choosing conservative treatment in the DCE. However, as described by Louviere and Islam,<sup>21</sup> explicit context, like in this case information about the type of treatment, the description of the attributes and the associated levels, might explain the difference between the methods. For the ranking exercise, no levels were provided, so in contrast with the discrete choice experiment, a trade-off between levels of different attributes when making a choice for conservative treatment or surgery was not required. We believe that the DCE in this study provides more detailed and reliable outcomes, but also requires more intellectual effort from the participants and is therefore more challenging.

The risk of permanent intestinal symptoms being almost equally important as pain reduction is an important finding, because the debate about radical DE bowel surgery (resection) versus conservative surgery (shaving/discoid) is ongoing. Supporters of radical surgery have an approach almost similar to oncological surgical approaches<sup>22,23</sup> and aim to reduce pain, prevent recurrence and perhaps even cure women with DE. The potential price they have to pay for this approach is theoretically more severe complications and the risk of LARS.<sup>24</sup> Surgeons who believe in a more cautious approach aim to reduce pain symptoms and accept possible recurrence/incomplete removal of endometriosis, but try to reduce severe complications and prevent possible permanent bowel symptoms (LARS).<sup>25-27</sup>

## 4.2 | Strengths and limitations

The main strength of this study is the extensive preparation made to identify the treatment attributes. With our qualitative study and literature search we believe that we used all possible information sources for an optimal selection of relevant attributes, and therefore increased the chance of valid preferences.

The second strength of this study is the strict selection of appropriate patients (26.3%). With the three inclusion questions we aimed to select only patients with DE and bowel endometriosis, who were not receiving fertility treatment and before a treatment decision.

The first limitation is the method of recruitment. The vast majority of patients (70.4%) were recruited by their gynaecologist and 29.6% through an advertisement via the Dutch and Belgian endometriosis foundation. To reduce the potential bias of patients without DE, strict inclusion limits were set, as described in the Methods section.

The second limitation could be the sample size. We did not reach the aimed 300 inclusions, because recruitment took more time than expected. We took several steps to increase the number of participants, including advertising through the Dutch and Belgian endometriosis population. Lancsar and Louviere<sup>18</sup> state that based on empirical experience per questionnaire version, more than 20 respondents are rarely needed – although that number has to increase when performing extensive subgroup analyses. Given that we used three blocks (questionnaire versions) and performed one subgroup analysis, we calculated that our sample size of 169 was sufficient for reliable analysis.

## 4.3 | Interpretation

From the findings in our study, we can conclude that pain reduction should not be the only motivation for surgery at all costs. Pain can negatively impact the quality of life, but the chance of LARS in more radical surgery as the result of bowel resection is also debilitating and has major impact on the quality of life.<sup>28</sup> For this reason, women with DE who have an indication for bowel resection should be counselled for the possible benefits and potential risk of developing LARS. Consequently, a multidisciplinary approach with shared decision-making should enable a patient to make a well-informed choice that is based on the patient's preferences and the clinical judgement of her physician.

The risk of bone loss with GnRH treatment is a major concern, as reduction of bone density in young to middle-aged women increases the risk of osteoporotic fractures later in life.<sup>29</sup> To reduce the effect of osteoporosis, add-back therapy is mandatory and the duration of GnRH administration should be minimised as much as possible.<sup>29</sup> With add-back therapy, estrogen is given back in low dose to prevent osteoporosis, but does not activate endometriosis implants.<sup>30</sup> In this way, the use of GnRH is safe and the risk of osteoporosis is reduced to a minimum, which should be counselled when prescribed.

### 4.3.1 | Increased chance of getting pregnant with conservative treatment?

In this DCE it has to be noted that the levels are hypothetical, but based on the current literature. In literature there is still no consensus as to whether conservative treatment (with GnRH) increases the chances of fertility.<sup>31</sup> Further high-quality trials are needed to determine the effect of GnRH treatment on fertility outcomes, and women should be counselled about this uncertainty.

In our DCE, it was interesting to find that women put pain reduction above the possible improvement of fertility chances. One explanation might be that in the short-term pain reduction is more important, whereas fertility could be a future treatment goal. A different explanation could be that the pain is so unbearable that the fertility wish is less important even in women with a fertility wish. One quote from our qualitative study<sup>32</sup> highlights this issue: one woman said 'I was in so much pain, I couldn't function anymore. I thought "if I have that pain any longer, then I'm done with it, I don't want to live like that".' If pain is so intolerable and life defining, then other important life goals could become insignificant.

## 5 | CONCLUSION

The aim of the present study was to gain insight into preferences for a conservative or surgical treatment approach of patients with DE. The three most important drivers for choosing conservative treatment are lower chance of developing osteoporosis, higher chance of improving fatigue symptoms and higher chance of reducing pain symptoms. For choosing surgery, a lower chance of LARS, higher chance of reducing pain symptoms and higher chance of improving fatigue symptoms are important. Women with previous surgery have significantly lower fear for surgery compared with women without a surgical history. The current results can be used to assist shared decision-making, e.g. by developing decision aids aimed at providing relevant information and assisting patients in treatment choices in DE care.

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## CONFLICT OF INTERESTS

None declared.

## AUTHOR CONTRIBUTION

JeM and JS conducted the qualitative research, the DCE was designed by all researchers, JeM and ET were responsible for collecting data, BE and JeM performed the analyses. JeM, JM, FJ, EA and BE took the lead in writing the manuscript. All authors were responsible for interpreting the data and for final review of the manuscript. All authors approved the final manuscript.

## ETHICS APPROVAL

The Medical Ethical Committee of the two executive centres Leiden University Medical Centre (P18.142) and Máxima Medisch Centrum (N18.088) approved the study protocol and procedure (online recruitment).

## DATA AVAILABILITY STATEMENT

Due to privacy and ethical concerns, neither the data nor the source of the data can be made available.

## REFERENCES

- Berlanda N, Somigliana E, Frattaruolo MP, Buggio L, Drudi D, Vercellini P. Surgery versus hormonal therapy for deep endometriosis: is it a choice of the physician? *Eur J Obstet Gynecol Reprod Biol.* 2017;209:67–71.
- Iversen ML, Seyer-Hansen M, Forman A. Does surgery for deep infiltrating bowel endometriosis improve fertility? A systematic review. *Acta Obstet Gynecol Scand.* 2017;96(6):688–93.
- Kondo W, Bourdel N, Tamburro S, Cavoli D, Jardon K, Rabischong B, et al. Complications after surgery for deeply infiltrating pelvic endometriosis. *BJOG.* 2011;118(3):292–8.
- Brouwer R, Woods R. Rectal endometriosis: results of radical excision and review of published work. *ANZ J Surg.* 2007;77:562–71.
- Ryan M, Netten A, Skátun D, Smith P. Using discrete choice experiments to estimate a preference-based measure of outcome—an application to social care for older people. *J Health Econ.* 2006;25(5):927–44.
- Burton C, Entwistle V, Elliott A, Krucien N, Porteous T, Ryan M. The value of different aspects of person-centred care: a series of discrete choice experiments in people with long-term conditions. *BMJ Open.* 2017;7:e015689.
- Saha R, Mariens L, Tornvall P. Validity of self-reported endometriosis and endometriosis-related questions in a Swedish female twin cohort. *Fertil Steril.* 2017;107(1):174–8.e2.
- Moradi M, Parker M, Sneddon A, Lopez V, Ellwood D. The Endometriosis Impact Questionnaire (EIQ): a tool to measure the long-term impact of endometriosis on different aspects of women's lives. *BMC Womens Health.* 2019;19(1):64.
- Greene R, Stratton P, Cleary SD, Ballweg ML, Sinai N. Diagnostic experience among 4,334 women reporting surgically diagnosed endometriosis. *Fertil Steril.* 2009;91(1):32–9.
- Chew L, Bradley K, Boyko E. Brief questions to identify patients with inadequate health literacy. *Fam Med.* 2004;36:588–94.
- Brownstone D, Train K. Forecasting new product penetration with flexible substitution patterns. *Journal of Econometrics.* 1998;89(1–2):109–29.
- Ubach C, Scott A, French F, Awramenko M, Needham G. What do hospital consultants value about their jobs? A discrete choice experiment. *BMJ.* 2003;326(7404):1432.
- Phillips K, Maddala T, Johnson F. Measuring preferences for health care interventions using conjoint analysis: an application to HIV testing. *Health Serv Res.* 2003;37:1681–705.
- Helter, TM, Boehler, CE. Developing attributes for discrete choice experiments in health: a systematic literature review and case study of alcohol misuse interventions. *J Subst Use.* 2016;21(6):662–8.
- Metzemaekers J, Slotboom S, Sampat J, Vermolen P, Smeets Elske van den Akker-van Marle M, et al. Crossroad decisions in deep endometriosis treatment options: a qualitative study among patients. *Fertil Steril.* 2021;115(3):702–14.
- Coast J, Al-Janabi H, Sutton EJ, Horrocks SA, Vosper AJ, Swancutt DR, et al. Using qualitative methods for attribute development for discrete choice experiments: issues and recommendations. *Health Econ.* 2012;21(6):730–41.
- Theunissen M, Peters ML, Schouten EG, Fiddelaers AA, Willemsen MG, Pinto PR, et al. Validation of the surgical fear questionnaire in adult patients waiting for elective surgery. *PLoS One.* 2014;9(6):e100225.

18. Lancsar E, Louviere J. Conducting discrete choice experiments to inform healthcare decision making: a user's guide. *Pharmacoeconomics*. 2008;26(8):661–77.
19. Marshall D, Bridges JF, Hauber B, Cameron R, Donnalley L, Fyie K, et al. Conjoint analysis applications in health - how are studies being designed and reported?: An update on current practice in the published literature between 2005 and 2008. *Patient*. 2010;3(4):249–56.
20. Malhotra NK, Nunan D, Birks DF. *Marketing research: an applied approach*. London: Pearson Education Limited; 2017.
21. Louviere J, Islam T. A comparison of importance weights and willingness-to-pay measures derived from choice-based conjoint, constant sum scales and best-worst scaling. *J Business Res*. 2008;61:903–11.
22. Régenet N, Métairie S, Cousin GM, Lehur PA. Endométriose colorectale. Diagnostic et prise en charge. *Ann Chir*. 2001;126(8):734–42.
23. Jerby B, Kessler H, Falcone T, Milsom J. Laparoscopic management of colorectal endometriosis. *Surg Endosc*. 1999;13(11):1125–8.
24. Heinz-Partington S, Costa W, Martins WP, Condous G. Conservative vs radical bowel surgery for endometriosis: a systematic analysis of complications. *Aust N Z J Obstet Gynaecol*. 2021;61(2):169–76.
25. Donnez J, Squifflet J. Complications, pregnancy and recurrence in a prospective series of 500 patients operated on by the shaving technique for deep rectovaginal endometriotic nodules. *Hum Reprod*. 2010;25(8):1949–58.
26. Roman H, Vassilief M, Gourcerol G, Savoye G, Leroi AM, Marpeau L, et al. Surgical management of deep infiltrating endometriosis of the rectum: pleading for a symptom-guided approach. *Hum Reprod*. 2011;26(2):274–81.
27. Donnez O, Donnez J. Deep endometriosis: the place of laparoscopic shaving. *Best Pract Res Clin Obstet Gynaecol*. 2021;71:100–13.
28. Pape E, Pattyn P, Van Hecke A, Somers N, Van de Putte D, Ceelen W, et al. Impact of low anterior resection syndrome (LARS) on the quality of life and treatment options of LARS – A cross sectional study. *Eur J Oncol Nurs*. 2021;50: 101878.
29. Sauerbrun-Cutler M-T, Alvero R. Short- and long-term impact of gonadotropin-releasing hormone analogue treatment on bone loss and fracture. *Fertil Steril*. 2019;112(5):799–803.
30. Barbieri RL. Hormone treatment of endometriosis: the estrogen threshold hypothesis. *Am J Obstet Gynecol*. 1992;166:740–5.
31. Georgiou EX, Melo P, Baker PE, Sallam HN, Arici A, Garcia-Velasco JA, et al. Long-term GnRH agonist therapy before in vitro fertilisation (IVF) for improving fertility outcomes in women with endometriosis. *Cochrane Database Syst Rev*. 2019;11.
32. Metzemaekers J, Slotboom S, Sampat J, Vermolen P, Smeets MJGH, Elske van den Akker-van Marle M, et al. Crossroad decisions in deep endometriosis treatment options: a qualitative study among patients. *Fertil Steril*. 2021;115(3):702–14.

## SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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