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 and risk tolerance of women suffering from deep endometriosis (DE) with bowel involvement when they have to choose between conservative or surgical. Design Labelled Discrete Choice Experiment (DCE). Setting Dutch academic and non-academic hospitals and online recruitment. Population or Sample A total of 169 patients diagnosed with DE of the bowel. Methods Baseline characteristics and the fear for surgery were collected. Women were asked to rank attributes and choose between hypothetical conservative (medication) 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/or risk on pain, fatigue, pregnancy, endometriosis lesions, mood swings, osteoporosis, temporary stoma and permanent intestinal symptoms were used in this DCE. Results In the ranking osteoporosis is the least important attribute, while in the DCE, a lower chance of osteoporosis is one of the most important drivers when choosing a conservative treatment. Women with previous surgery show less fear for surgery compared to women without surgery. The low anterior resection syndrome is almost equally important for patients as the chance of pain reduction. Pain reduction has higher importance than improving fertility chances even in women with a future child wish. Conclusions The risk of suffering from LARS as a result of treatment is almost equally important as the reduction of pain symptoms. Women with previous surgery experience less fear for surgery compared to women without a surgical history.

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Running title: Discrete Choice Experiment in deep endometriosis

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Abstract

Objective

To study the preferences and risk tolerance of women suffering from deep endometriosis (DE) with bowel involvement when they have to choose between conservative or surgical.

Design

Labelled Discrete Choice Experiment (DCE).

Setting

Dutch academic and non-academic hospitals and online recruitment.

Population or Sample A total of 169 patients diagnosed with DE of the bowel.

Methods

Baseline characteristics and the fear for surgery were collected. Women were asked to rank attributes and choose between hypothetical conservative (medication) 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/or risk on pain, fatigue, pregnancy, endometriosis lesions, mood swings, osteoporosis, temporary stoma and permanent intestinal symptoms were used in this DCE.

Results

In the ranking osteoporosis is the least important attribute, while in the DCE, a lower chance of osteoporosis is one of the most important drivers when choosing a conservative treatment. Women with previous surgery show less fear for surgery compared to women without surgery. The low anterior resection syndrome is almost equally important for patients as the chance of pain reduction. Pain reduction has higher importance than improving fertility chances even in women with a future child wish.

Conclusions

The risk of suffering from LARS as a result of treatment is almost equally important as the reduction of pain symptoms. Women with previous surgery experience less fear for surgery compared to women without a surgical history.

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Key words:

Endometriosis, Discrete Choice Experiment, surgery, decision making, Deep Endometriosis

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Tweetable abstract: First discrete choice experiment in patients with deep endometriosis

Introduction

Patient centeredness, which is guided by patients' values, needs and preferences is an important quality dimension in modern healthcare (1). This approach is especially relevant in patients suffering from endometriosis, since endometriosis affects all facets of life (work, mood, quality of life, relationships, sexuality) (2). Even though endometriosis is a benign disease, it can cause significant decrease in the quality of life (QoL), social participation (e.g. loss of productivity) and sexual health (3) (4). Therefore, it is extremely important to realise that effective treatment goes beyond a purely somatic approach and should be patient centered.

Endometriosis is a disease in which endometrium-like tissue grows outside the uterus inducing chronic inflammation and adhesion formation (5). 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 curation, making endometriosis a chronic condition. Therefore, the main goal of these treatments is not to cure but to reduce pain, prevent further organ damage (e.g. ureteric obstruction), increase QoL and (potentially) increase the chance of pregnancy (6). Available data suggest that both conservative and surgical treatment are effective in reducing pain (7). The improvement of fertility chances with surgical treatment options remains uncertain, due to inconclusive study results on this topic (8). 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 side effects (e.g. depressive mood, weight gain, osteoporosis, menopause, decreased libido, headaches) which may cause treatment failure. Other reasons for treatment failure include therapy non-compliance or contraindications (deep venous thrombosis, other cardiovascular disease, hormone-sensitive tumours, active wish to conceive etc.) (7). On the other hand, surgical treatment options have the possible risks of severe complications and recurrence of disease. DE surgery is associated with significant complication rates up to 14% (9), which include bowel injury, anastomosis leakage, temporary or permanent stoma placement, urinary tract injury, formation of recto and or vesicovaginal fistulas (10). Making a careful and well-considered choice in endometriosis treatment options is especially relevant for deep endometriosis (DE), since these patients have to deal with complex treatment trade-offs.

In patient centered health care, decisions about treatment options are preferably made in consultation between the physician and the patient (11). Therefore, gynaecologists need to inform patients optimally by providing extensive information on the pros and cons of each treatment and by supporting the decision making process. This can only be achieved when gynaecologists are trained in guiding shared decision making (SDM) and understand which risks and benefits may be important to patients. Unfortunately, limited research has been performed to study the value and preferences in women with DE, which makes optimal counselling challenging. In addition, there is no conclusive evidence to advise patients for a particular treatment that is clearly superior. This makes preference sensitive care the most suitable form to use (12). In preference sensitive care, it remains important to make a well-considered choice that includes the patient's wishes, priorities, risks and benefits. Especially for women suffering from endometriosis, the decision making process can be difficult and complex, since it is not only a matter of choosing pills or surgery. Their choice is also highly dependent on the different phases of life (school going, career/work, wish to conceive or not), and some choices can have lifelong consequences (hysterectomy, low anterior resection etc.). Therefore, optimal counselling is mandatory to assist these women in their decision making.

A technique to gain insight in treatment preferences is a so-called discrete choice experiment (DCE). This DCE technique assumes that patients value different characteristics of a treatment, (e.g. pain reduction, pregnancy chance, risk of complications) which will determine their preference. When presenting different choices, patients will usually choose the option that is most beneficial (13, 14).

This study aims to investigate patients' preferences in DE treatment options for conservative or surgical treatment options and which characteristics are relevant in their treatment choice. To achieve this, we

performed a labeled discrete choice experiment.

Methods

Study design

A discrete choice experiment (DCE) was used to gain insight in treatment preferences of women with DE and bowel involvement when they have to choose between conservative or surgical treatment. This DCE technique assumes that patients value different characteristics of a treatment, (e.g. pain reduction, pregnancy chance, risk of complications) which will determine their preference. When presenting different choices, patients will usually choose the option that is most beneficial (13, 14).

Participant recruitment

Inclusion 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) for information about the study. It was especially noted that only women with DE and bowel involvement could participate in this study. Women willing to participate had to pass three inclusion questions, which are commonly used and accepted in endometriosis questionnaire studies (15) (16) (17). For this DCE only women with surgically or radiologically (ultrasound and/or MRI) diagnosed DE with bowel involvement, prior to a treatment decision and currently not in any fertility treatment trajectory could participate. Women could not see which answer would in- or exclude them. The first question was: *"Do you have deep endometriosis with bowel involvement, which is diagnosed by a doctor by ultrasound, MRI or surgery?"* Patients who answered this with 'yes' received a second question; *"Are you prior to a treatment choice with medication or surgery?"* Patients who answered this with 'yes' received a final question; *"Are you currently in a trajectory to become pregnant (e.g. hormonal treatment for ovulation induction, IVF)?"* Patients who answered these questions with 'no' were included in the study prior to a digital informed consent form. Patients who did not meet the inclusion criteria, were acknowledged for their interest in the study, but could not further participate. Further exclusion criteria were low health literacy, this was tested with three questions (18).

Further exclusion criteria were low health literacy, this was tested with three questions (18). We excluded patients who indicated to 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 with no informed consent, patients who did not complete the 10 DCE questions, patients who completed the whole survey in [?] 10 minutes time (this 'too fast' threshold was set after the pilot) and patients who gave the same answer on all questions in the first section of the survey and DCE, were excluded. A total of 641 patients started the survey (Supplementary table S1), 141 patients were excluded at inclusion question one (no DE with bowel involvement), 152 patients were excluded at inclusion question two (not prior to a treatment decision), 53 patients were excluded at inclusion question three (patients in fertility treatment). A total of 91 patients who met the inclusion criteria but stopped after reading the information were also excluded, five patients with no informed consent were excluded. One patient who filled in the same answer at all questions (survey fatigue), 24 patients who did not complete the DCE task, three patients with poor health literacy were excluded. One patient indicated to always have difficulties with understanding medical information about her disease and treatment, one patient always needed help with reading information about her disease and treatment and one patient who had no confidence at all in filling in medical forms. Furthermore, two patients were excluded who completed the DCE within 10 minutes. This resulted in 169 patients who met all inclusion criteria (26.4% of the initial amount of patients who started the survey).

Data collection

For hosting the internet survey and data collection, we used Sawtooth Software's (Orem, UT) SSI Web. As recommended by earlier studies, the identification and selection of the final attributes and levels was based on literature review, qualitative research and an expert panel (19) (20) (21). The four stages as described

by Heller et al were applied although we slightly customized these as seen in Figure 1, which means that we used several data sources in stage 1. To find out which attributes were important for DE patients, we firstly (Stage 1) collected data by performing a literature- and qualitative study. We performed a survey among 28 patients, one focus group with eight patients prior to their decision making (22) and a focus group with 10 gynaecologists with expertise on deep endometriosis. The results combined from stage 1 resulted in 158 attributes.

The second step (Stage 2) in attribute development is data reduction. This was achieved by frequency and rank order by the researchers (JeM and JS) combined with thematic analysis (grouping attributes with more or less the same theme), which resulted in 28 attributes. In the third and fourth stage, concerning respectively removing inappropriate attributes and wording of attributes, we selected attributes which comply with the research question, are relevant for the DE population, and are intelligible for all patients (23). The last process of attribute selection was performed in collaboration with all members of the research group, which resulted in eight final attributes (Table 1).

The first part of the survey included questions about baseline characteristics (i.e. age, educational level, medication use, medical history and pain symptoms), surgical fear measured with the validated Dutch surgical fear questionnaire (SFQ) (24) and three health literacy screening questions. We included the short surgical fear questionnaire, while we hypothesized that the fear for surgery could influence the results of the DCE. Women with surgical fear could have a tendency towards choosing the conservative treatment compared to women with less surgical fear. The surgical fear has a subscale sum score for short -and long term fear that ranges from 0 (no fear) to 40 (very afraid), the total sum score ranges from 0 (no fear) to 80 (very afraid). Pain was recorded on a numeric rating scale, patients rated their pain intensity (0 = no pain and 10 = maximum pain, or inapplicable option). The pain intensity score was obtained for menstrual cycle and non-cycle related pain, on the dimensions of dysmenorrhea, pelvic pain, dyspareunia, dysuria and dyschezia.

Part two of this survey included information about the DCE (Supplementary table S2 includes the attributes explanation). Prior to the DCE, we asked the women to rank the eight attributes from most important (1) to least important (8) when making a treatment decision. In the ranking we did not distinguish between conservative or surgical treatment. To get familiar with the concept of a DCE, a simple DCE question for choosing a phone. Subsequently, the actual DCE was presented with 10 choice sets. Each choice set consisted of two hypothetical treatment options labeled as pharmaceutical (conservative) and surgical treatment. The reason for choosing a labeled DCE is that both conservative and surgical treatment have a number of specific attributes and levels that are not generic for both treatments. The women were asked to choose their preferred treatment of choice for each of the 10 choice sets (Figure 2). The conservative treatment option included specific attributes like side effects of hormonal treatment: depressive feelings and the chance of developing osteoporosis. The surgical option included treatment specific risks like, the chance of getting a temporary stoma and the chance of permanent intestinal symptoms (LARS) (Table 1).

Data analysis

Ngene software (version 1.2.1) was used to construct a fractional factorial efficient design based on the selected attributes and their levels. In the design, one constraint was taken into account in order to avoid implausible combinations (if surgery removes the endometriosis as much as possible without major bowel surgery, then the chance of permanent intestinal symptoms can only be 10%). Thirty choice sets were created with each choice set consisting of two treatment options, that is conservative and surgical treatment. In order to reduce the burden for the patient, the thirty choice sets were blocked into three versions of 10 choice sets.

To assess if the DCE, levels, attributes, explanation text and baseline questions were understood, we performed a pilot test with a group of pre-surgical patients. Small adjustments were made, mainly in the information text of the attributes and levels. 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; therefore no adjustments were made. For the whole design of this DCE we followed the checklist of

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the ISPOR Conjoint Analysis Experimental Design Good Research Practices Task Force (25).

For internal consistency, we included one fixed task, with one dominant option (conservative treatment option) which is more favorable (higher chance of pain reduction and little side effects, compared to a surgical option with maximum side effects and little to no beneficial effects). However, it should be noted that this is not automatically and unambiguously always the 'best' treatment because some women can have a strong preference for a conservative treatment or surgery regardless of the specific levels of the attributes.

Optimal sample size calculation for estimating for non-linear discrete choice models is complicated as it depends on the true values of the unknown parameters estimated in the DCE (26). Given the lack of a definite method for calculating a sample size, we based our sample size on a literature review (27). Marshall et al. described that most studies published between 2005-2008 had a sample size of 100-300 respondents. We aimed for 300 respondents because we also wanted to study subgroups.

Statistical analysis

IBM SPSS version 25.0 for Windows 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 (SD) or median (with interquartile range) for normally distributed or skewed data, respectively (baseline characteristics like age, time till diagnose etc.). We used Student's t-test for normally distributed data (surgical fear questionnaire). For the ranking exercise we calculated the mean and standard deviation, and ranked form low (ranked most important) to high (least important). We considered a 2-tailed p-value of < 0.05 as statistically significant.

For the DCE analysis we used Nlogit software version 6. Data were analyzed using a multinomial regression model. This model has the following regression equation

V(conservatie treatment/surgerij treatment) $=\beta 0+ \beta 1$*change of pain reduction_med $+ \beta 2$* change of fatigue $+ \beta 3$* change of pregnancy $+ \beta 4$*presence of endometriosis_med$+ \beta 5$ *change on depressed mood_med $+ \beta 6$ * change on osteoporosis_med$+ \beta 7$*change of pain reduction_surg $+ \beta 8$* presence of endometriosis_surg $+ \beta 9$* change on temporary stoma_surg $+ \beta 10$* permanent intestinal symptoms_surg $+ \beta 2$* change of fatigue $+ \beta 3$* change of pregnancy $+ \epsilon$

V represents the relative utility that a respondent derives from choosing conservative treatment or surgery. β_0 is the alternative specific constant, reflecting a preference for the label irrespective of the levels of the attributes

β1- β10 are the alternative specific coefficients of each attribute with the exception of β2 chance of fatigue and β3 chance of pregnancy. The levels of these attributes were generic across the treatments.

A priori, we expected that patients prefer a higher chance of pain reduction (positive coefficient), lower levels of fatigue (positive coefficient for decreasing fatigue, negative for increasing fatigue), higher pregnancy chance, reduction of endometriosis nodules/spots, low chance of getting a depressed mood, osteoporosis, temporary stoma and permanent intestinal symptoms.

ε is an unobserved component of the utility function or error term. Pain reduction, chance on depressed mood, chance on osteoporosis, chance on temporary stoma and permanent intestinal symptoms were included as continuous variables while for fatigue, chance on pregnancy and presence of endometriosis dummy coding was used. In addition, we performed subgroup analysis with women with or without a future child wish. 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 level of the same attribute (in 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 (28). A significance level of 5% was chosen to determine statistically significant coefficients.

Results

Table 2 shows the baseline characteristics of all participants. The mean age was 36.2 years. The median

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time to diagnosis was reported to be 9 years. The majority had a paid job (86.4%) and was currently in a relationship (82.8%). Looking at the obstetric history, 51.5% of the women had never been pregnant, and 34.9% of the participants had a future child wish. The total spontaneous conception percentage was 76.9% (133/173). The majority of participants rarely had difficulty with written medical information (39.6%), did not need help with reading medical information (55.0%) and had extreme trust in filling in medical forms (58.6%). 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). Regarding the surgical fear, the mean (SD) score for the short-term consequences was 15.5 ($\pm$8.9) and for the long-term consequences this was 18.1 ($\pm$10.0). The mean total score was 33.6 ($\pm$16.6).

Pain

Dysmenorrhea was reported with a mean (SD) numeric rating scale for pain of 7.9($\pm$1.5), and cycle related pelvic pain of 7.7($\pm$1.7), dyschezia 7.1($\pm$2.6), dyspareunia 6.1($\pm$2.8) and dysuria 4.4($\pm$3.2) (Table 3). Non-cycle related pain was reported for pelvic pain with a mean (SD) numeric rating scale for pain of 5.5($\pm$2.3), dyschezia 5.0($\pm$2.8), dyspareunia 5.0($\pm$2.7), and dysuria 3.1($\pm$2.8).

Subgroup analysis regarding surgical fear

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

Ranking of attributes prior the DCE

Reducing pain (1) was ranked most important followed by no permanent intestinal symptoms (LARS) (2), decrease of fatigue (3), reduction of endometriosis (4), no temporary stoma (5), stable mood (6), increase of pregnancy chances (7) and no osteoporosis (7) ranked equally important on the last place (Table 4). For the subgroup of women with a future child wish, the ranking was as followed: reducing pain (1), increase of pregnancy chances (2), no permanent intestinal symptoms (3), reduction of endometriosis (4), decrease of fatigue (4), no temporary stoma (5), stable mood (6) and no osteoporosis (7).

Attributes coefficients and relative importance

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

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 impact while the chance of a depressed mood did not show a significant effect. The three most important drivers for a 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%) are the most important drivers for the surgical treatment, accounting for 85% of the relative importance results.

Subgroup analysis in women with a future child wish

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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). Reducing endometriosis (14%) shows a low relative importance. Lower chance on osteoporosis and impact on mood did not show a significant effect.

The subgroup model also shows that the chance of permanent intestinal symptoms (35%), reducing pain (21%) and improving fatigue symptoms (19%) are the most important attributes when making a choice for surgery (75% of the relative importance). Improving fertility (14%) and the chance of getting a temporary stoma (10%) have low relative importance. Reducing endometriosis nodules/spots do not show a significant effect.

Discussion

Main findings

Translating the main findings of this DCE with women suffering from DE and bowel involvement towards the clinical setting we can conclude that 1) In the general ranking, osteoporosis is ranked as least important attribute, while in the DCE, a lower chance of osteoporosis is one of the most important drivers for making a choice in the conservative treatment. 2) Osteoporosis, fatigue symptoms, pain symptoms, pregnancy rates and the presence of endometriosis nodules all have a significant impact on the preference for conservative treatment. The three most important drivers for conservative treatment are lower chance of developing osteoporosis (gonadotropin-releasing hormone (GnRH) analogues), higher chance of improving fatigue symptoms and higher chance of reducing pain symptoms. For surgery, the attributes with a significant impact are getting intestinal symptoms (LARS), pain symptoms, fatigue symptoms, pregnancy rates and getting a temporary stoma. The three most important drivers for surgery are lower chance of getting bowel symptoms (LARS), higher chance of reducing pain symptoms and higher chance of improving fatigue symptoms. 3) The chance of getting a temporary stoma plays a less important role in the context of this study compared to pain reduction and the risk of LARS. 4) Women with a future child wish put pain reduction above possible improvement of fertility chances. 5) Women with previous surgery have significant lower fear for surgery compared to women without a surgical history (DE surgery).

Comparing the results of the direct ranking method and those of the relative importance of the DCE shows discrepancy between both methods. In particular the attribute chance of osteoporosis is considered least important in the ranking exercise while one of the most important attributes when choosing conservative treatment in the DCE. However, as described by Louviere and Islam (29), 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 and thus, 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 therefore more challenging to make. Solely ranking attributes is easy, but it should be kept in mind that no considerations about the levels are taken into account.

The risk of permanent intestinal symptoms being almost equally important as pain reduction is an important finding, since the debate about radical DE bowel surgery (resection) versus conservative surgery (shaving/discoid) is ongoing and still undecided. Believers of radical surgery have an approach (radical as possible) almost similar to oncological surgical approaches (30) (31) 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 permanent intestinal symptoms (LARS) (32). Surgeons who believe in a more reluctant 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) (33) (34) (35). However, regarding the good results from the more reluctant surgical approach from Donnez it has to be noted that these patients were treated with progesterone afterwards and only followed up for one year. Long term effects and patients without progesterone should

be studied as well to support the more reluctant surgical DE approach.

Strengths and limitations

The main strength of this study is the extensive preparation (qualitative study) in order to correctly identify the attributes of importance. Identifying the attributes is seen as the key aspect of the design of a DCE. Attributes should be relevant to the target population, should be relevant to the decision making context and the research question and the attributes should be defined in a way that is intelligible for patients. Without extensive work in defining the attributes, a DCE will not provide valid preferences, while important attributes could be missed that would have been paramount in making a treatment choice. With our qualitative, quantitative 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%) who were suitable for our DCE and would comply to our research question. Completing a DCE is a complex task and requires concentration and a certain level of intellect. With the three inclusion questions we aimed to select only patients with DE and bowel endometriosis, were not in actual fertility treatment and prior to a treatment decision. Furthermore, we excluded patients with poor health literacy, patients who filled in the DCE unreasonable quickly, patients who showed signs of being survey fatigue by filling in the same answer on almost all questions and finally we excluded patients who did not complete the DCE part of the survey. This way we aimed to select patients without linguistic bias, were focused, and took the time to fill in this DCE.

This study has two main limitations. The first limitation is the method of recruitment. The vast majority of patients (70.4%) were recruited by their gynaecologist and 29.6% through advertisement via the Dutch and Belgian endometriosis foundation. Ideally we only included patients via their gynaecologist who also confirmed the deep endometriosis with bowel involvement, but because deep endometriosis is less prevalent ([?] 1/10 of the general endometriosis population), we anticipated on the fact that recruitment would not be sufficient if we only included patients through their treating gynaecologists. We specifically choose advertising via official endometriosis organisations to reduce the potential bias recruiting patients without endometriosis, although there was no actual benefit in completing this DCE (no financial fee). To reduce the potential bias of patients without deep endometriosis we included three inclusion questions, whereby it was not clear for the participant which question would in or exclude the participant. This method of inclusion had been used more often, also in endometriosis research (15) (16) (17).

The second limitation could be the sample size. Prior to the start of the DCE we aimed to include 300 inclusions. We did not reach that amount of inclusions because recruitment took more time as previously anticipated. We took several steps to increase the number of participants like advertisement through the Dutch and Belgian endometriosis population. Finally, we were able to include 169 patients. Lancsar (26) states that based on empirical experience per questionnaire version rarely more than 20 respondents are 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.

Interpretation

From the findings in our study we can conclude that pain reduction should not be the only motivation for surgery at all costs. This new insight in patients' considerations could help in the shared decision making process and should be considered as an important factor in the final treatment decision. Pain can negatively impact the quality of life, but the chance on LARS in more radical surgery due to bowel resection (faecal incontinence or urgency, frequent or fragmented bowel movements, emptying difficulties) is also debilitating and has major impact on the quality of life (36). Therefore DE patients with an indication for bowel resection should be counselled for the possible benefits and potential risk of developing permanent intestinal symptoms (LARS). Consequently, a multidisciplinary approach with SDM should enable a patient to make a well informed choice that is based on patients' preferences and clinical judgement of their treating physician (gynaecologist/surgeon) to ensure treatment satisfaction and improved quality of life after the treatment and

recovery process.

Regarding surgical fear, women with previous surgery have significant lower surgical fear compared to women without a surgical history. This is also an important finding which could be useful in the shared decision making process. The physician should be aware that women without surgery might have more fear towards surgery, which could influence their decision. This is in line with the findings of patients undergoing cataract surgery, they found lower surgical fear in the group who underwent the second surgery (37).

However, this information could also mean that women with previous surgery and less fear have a tendency to choose surgery more easily and pay less attention to the possible complications or long term side effects (LARS). The clinician should be aware of both possibility's when counseling women (with and without a surgical history) in the SDM process.

Conclusion

The aim of the present study was to gain insight in preferences for a conservative or surgical treatment approach of patients suffering from DE. This is the first DCE on treatment preferences from a nationally representative cohort of patients with deep endometriosis. These findings make several contributions to the current literature in DE. The risk of permanent intestinal symptoms (from the treatment) is almost equally important for patients as the chance of reduction in pain symptoms. The results of this study can be used in the decision-making process between doctor and patient, where it is important that symptoms arising from the endometriosis are treated such as pain reduction and improvement of fatigue. However, it is also important to pay attention, when choosing a treatment to consider the short and long term risks. In which the risk of getting LARS during surgery needs attention, as well as a long term risk such as osteoporosis when choosing certain conservative treatment (GnRH analogues). Women with previous surgery showed less surgical anxiety, this information could help to inform anxious women without a surgical history, but who need surgery in their decision process. The current results can be used to assist SDM, e.g. by developing a decision aid aimed at providing relevant information and assisting patients in difficult treatment choices in DE care. Further studies regarding the role of decision making in non-DE would be worthwhile.

Disclosure of interest

None declared.

Contribution to authorship

Je.M. and J.S. conducted the qualitative research, the DCE was designed by all researchers, Je.M. and E.T. were responsible for collecting data, B.E. and JeM performed the analyses. Je.M., J.M., F.J., E.A., and B.E. took the lead in writing the manuscript. All authors were responsible for interpreting the data and final review of the manuscript. All authors approved the final manuscript.

Details of ethics approval

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

Acknowledgements

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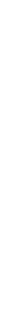
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	Pharmaceutical	Surgical
Chance that pain resolves	with 60 out of 100 people	with 90 out of 100 people
Fatigue	fatigue does **not change** (=)	fatigue **increases** (↑)
Pregnancy after treatment	**no influence** on pregnancy chance (=)	pregnancy chance is **increased** (↑)
Presence of endometriosis	endometriosis spots remain **the same** (=)	endometriosis will be **removed as much as possible**, whitout the chance on major surgery
Chance on depressed mood	with 10 out of 100 people	N/A
Chance on osteoporosis	with 5 out of 100 people	N/A
Chance on temporarely stoma	N/A	with 5 out of 100 people
Chance on permanent intestinal complains	N/A	with 10 out of 100 people
	Click to make a choice	Click to make a choice