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ORIGINAL RESEARCH

# Quality of life 1 year after uterine artery embolization vs hysterectomy for symptomatic adenomyosis (QUESTA study)

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## Abstract

**Introduction:** Uterine artery embolization (UAE) is a less-invasive alternative for hysterectomy in therapy-resistant symptomatic adenomyosis. Comparative data are lacking. Our objective is to evaluate the non-inferiority of UAE compared with hysterectomy in improving health-related quality of life (HRQOL) for symptomatic adenomyosis, 1 year post-treatment.

**Material and Methods:** This multicenter randomized controlled trial was converted into a prospective cohort study. It was prospectively registered at 27-07-2015 (NL-OMON55436, https://onderzoekmetmensen.nl/en/trial/55436). From November 2015 to March 2022 participants with symptomatic adenomyosis eligible for hysterectomy were included and offered UAE as an alternative treatment. Primary endpoint was difference in 1-year HRQOL scores between UAE and hysterectomy, using WHO-QOL-Bref and SF-12. Non-inferiority margin was set at five points. Secondary

**Abbreviations:** HRQOL, health-related quality of life; ITT, intention-to-treat; MCS, mental component summary (of SF-12); MRI, magnetic resonance imaging; PCS, physical component summary (of the Short Form Health Survey (SF)-12); PP, per-protocol; RCT, randomized controlled trial; UAE, uterine artery embolization.

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endpoints: WHO-QOL-100 facets "Pain and Discomfort" and "Sexual Activity", adenomyosis-related symptoms, and satisfaction. Multivariable linear mixed models were used. All outcomes were analyzed in the per-protocol population, and repeated in the intention-to-treat population.

**Results:** Of 101 participants, 51 chose hysterectomy and 50 UAE. Both treatment groups were comparable at baseline, except for employment status, dysmenorrhea score, uterine volume, hemoglobin and CA125 (all adjusted for). Both treatments led to a significant increase in all HRQOL scores after 1 year. The effect differences between UAE and hysterectomy on all HRQOL domains in the per-protocol population were: SF-12 physical $\beta$ −4.20, (95% CI −9.53 to 1.12), SF-12 mental $\beta$ −4.95 (95% CI −10.83 to 0.94); WHO-QOL-Bref physical $\beta$ −7.42 (95% CI −18.51 to 3.68), psychological $\beta$ −4.28 (95% CI −13.30 to 4.74), social relations $\beta$ −2.23 (95% CI −13.09 to 8.63) and environment $\beta$ 0.35 (95% CI −8.39 to 9.09). Non-inferiority of UAE was not demonstrated within the predefined margin. Both hysterectomy and UAE improved "Pain and Discomfort" and "Sexual Activity", with greater effect on pain after hysterectomy ($\beta$ 17.17, 95% CI 4.94 to 29.41, $p = 0.007$). More participants were satisfied after hysterectomy (95%) than after UAE (73%).

**Conclusions:** Both UAE and hysterectomy significantly increased HRQOL for symptomatic adenomyosis. Neither non-inferiority nor inferiority of UAE could be established. One-year HRQOL scores were comparable; some secondary outcomes were in favor of hysterectomy. UAE is a valid less-invasive alternative to hysterectomy, with preservation of the uterus. Hysterectomy remains the treatment of choice for patients seeking a definite solution.

**KEYWORDS**
adenomyosis, hysterectomy, quality of life, uterine artery embolization

## 1 | INTRODUCTION

Adenomyosis, a benign uterine disease in women of reproductive age, is associated with symptoms, such as dysmenorrhea, heavy menstrual bleeding, chronic pelvic pain, dyspareunia, and subfertility.[1,2] These symptoms can have a great impact on women's quality of life; for example, one in three women quit daily activities because of menstrual symptoms,[3] and for 5% of women, these symptoms are a reason for sick leave.[4] The exact prevalence of adenomyosis is unknown, but the frequency of hysterectomies because of these symptoms may indicate its burden: among women with menorrhagia or abnormal uterine bleeding, the reported prevalence of histopathologically proven adenomyosis at hysterectomy ranges from 26% to 49%.[5]

Nowadays, hysterectomy is the only treatment option for women with symptomatic adenomyosis when conservative treatment (hormonal/non-hormonal) fails. Uterine artery embolization (UAE) has been suggested to be a less-invasive alternative to hysterectomy for symptomatic adenomyosis. UAE has already extensively been evaluated for symptomatic uterine fibroids and has been found to be safe and effective.[6] A randomized controlled trial (EMMY trial), evaluating UAE and hysterectomy for fibroids, found that UAE improved symptoms of menstrual bleeding, pain, and bulk symptoms[7] and health-related quality of life (HRQOL)[8] after a 2-year and even longer follow-up.[9,10] No differences were found regarding these outcomes when comparing UAE to hysterectomy. Ten years after randomization, 35% of UAE patients had a subsequent hysterectomy.[9]

A systematic review and meta-analysis reported symptom improvement in 89.6% (275/307) of patients with pure adenomyosis (adenomyosis without the presence of uterine fibroids) up to 12 months after UAE.[11] Both abnormal uterine bleeding and

**Key message**

Both uterine artery embolization and hysterectomy for symptomatic adenomyosis significantly improve health-related quality of life after 1 year, but neither non-inferiority nor inferiority for uterine artery embolization in comparison to hysterectomy could be demonstrated.

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dysmenorrhea seem to respond to UAE in patients with adenomyosis. 2.6% (8/307) underwent a subsequent hysterectomy within the first year after UAE, 7.2% (31/430) after a longer follow-up. Several small cohorts investigating the long-term outcomes of UAE reported improvement of HRQOL scores and symptom severity scores reductions.[12–14] However, studies comparing UAE with hysterectomy for symptomatic adenomyosis are lacking.

We hypothesized that UAE for symptomatic adenomyosis is non-inferior to hysterectomy in terms of quality of life. Therefore, we aim to prospectively evaluate HRQOL outcomes for UAE and hysterectomy up to 1 year post-intervention, focusing on mental and physical health, pain and sexual activity, and overall patient satisfaction.

## 2 | MATERIAL AND METHODS

The QUality of life after Embolization vs. hySTerectomy in Adenomyosis (QUESTA) study was approved by the ethics committee of the VU Medical Center Amsterdam and the boards of all participating hospitals. It was prospectively registered (NL-OMON55436, URL: https://onderzoekmetmensen.nl/en/trial/55436). The study was investigator-initiated and sponsored financially by Boston Scientific and Merit Medical consecutively, which provided embolization materials during their sponsoring period. They were not involved in data gathering, analysis, interpretation, or manuscript writing.

### 2.1 | Study design

The QUESTA study is a multicenter prospective cohort study in the Netherlands. The study protocol was published in 2018.[15] Initially launched as a randomized controlled trial (RCT) in November 2015, it transitioned to a prospective comparative cohort study, with consecutive inclusion, in March 2018 due to low inclusion rates. This adjustment allowed participants to choose their preferred treatment, resulting in an increased inclusion rate.

### 2.2 | Participants

The change to a prospective comparative cohort study and the required increase in sample size were the only modifications made to the original published protocol.[15] The study included premenopausal women with MRI-confirmed symptomatic adenomyosis (pure or predominant with fibroids), not wishing to conceive and requiring hysterectomy (i.e., conservative therapy was ineffective or undesired). MRI criteria were defined in the study protocol; a junctional zone thickness of >12 mm was seen as confirmative for the diagnosis.[15] Exclusion criteria were: age under 18, suspicion or presence of pelvic infection or malignancy, pregnancy, contraindications for angiography, deep endometriosis requiring surgery or risking intestinal stenosis (diagnosed using MRI), or removable submucous fibroids. Participants were consecutively enrolled between November 2015 and March 2022.

### 2.3 | Study interventions

#### 2.3.1 | UAE

All embolization procedures were performed under patient-controlled epidural or intravenous analgesia (PCEA or PCIA) according to standard clinical practice or patient preference. The angiographic embolization endpoint was complete stasis of contrast in the horizontal part of both uterine arteries. Embolization particles used were either tightly calibrated Embozene™ (Boston Scientific) microspheres of 500 μm, possibly supplemented by >500 μm, or Embosphere® (Merit Medical) microspheres in sizes of 300–500 μm, possibly supplemented by 500–700 μm. Intervention radiologists were trained according to study protocol, with the first UAE procedures attended by the coordinating investigator (PL).[15]

#### 2.3.2 | Hysterectomy

Hysterectomy was preferably performed by total laparoscopic, robot-assisted laparoscopic, or vaginal hysterectomy, with optional (in-bag) morcellation. Abdominal and supracervical hysterectomy, concomitant adhesiolysis, or coagulation of mild endometriosis were permitted if necessary or desired.[15]

### 2.4 | Study measures/data collection

Sociodemographic data were assessed at baseline. Outcomes were measured at baseline, 6, 12, 26, and 52 weeks post-intervention using electronic case report forms (eCRF). The primary end-point quality of life was measured using the WHO-QOL-Bref and the SF-12. Secondary endpoints were adenomyosis-related symptom severity and satisfaction. All used questionnaires and endpoints are explained in Table 1.

### 2.5 | Statistical analyses

#### 2.5.1 | Sample size

The study aimed to demonstrate non-inferiority of UAE compared with hysterectomy if HRQOL (WHO-QOL-Bref and SF-12) scores did not differ more than five points, with a standard deviation of 9.[15] A sample size of 41 participants per group, excluding 10% drop-out, was calculated based on the EMMY trial assumptions, which used SF-36.[8] Due to a higher loss to follow-up and missing eCRFs identified at the time of the design change, we continued enrollment until 50 participants were reached in the UAE cohort.

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**TABLE 1** Primary and secondary endpoints.

| End-point | Questionnaire | Explanation |
|---|---|---|
| Quality of life | WHO-QOL-Bref[26] | 26-questions survey scoring quality of life in four domains (physical, psychological, social relationships and environment) on a 0–100 scale (100 being the optimal score) |
| Quality of life | SF-12[27] | 12-item survey providing the physical component summary (PCS) and mental component summary (MCS). Scores range from 0 to 100 (100 is optimal). A mean PCS or MCS score of 50 (SD 10) is a cut-off for below standard physical health or mental health, using normative data of the general Dutch population[22] |
| Pelvic pain | Numeric Rating Scale (NRS) | Monthly average pelvic pain and pelvic pain now (at time of the questionnaire) from 0 (no pain) to 10 (severest pain imaginable) |
| Pain | WHO-QOL-100 Facet Pain and discomfort[28] | Four questions out of the WHO-QOL-100 questionnaire, assessing the impact of pain on HRQOL. A higher score indicates lower HRQOL |
| Sexual activity | WHO-QOL-100 Facet Sexual activity[28] | Four questions out of the WHO-QOL-100 questionnaire, measuring sexual urge, desire, and satisfaction. A higher score indicates higher HRQOL |
| Pressure, micturition, defecation | 7-point Likert scale | Urinary leakage and frequency, uncomfortable feeling and pressure in pelvic area and difficulty passing stools were assessed at baseline. At follow-up change in comparison to before intervention is asked in a seven-point Likert scale (from no complaints to much more complaints) |
| Laboratory results | Mmol/L, kU/L | Hemoglobin mmol/L and Ca125 kU/L were measured at baseline and 6 months post-intervention |
| Satisfaction | 5-point Likert scale | Satisfaction about the received procedure was measured utilizing a five-point Likert scale (from very satisfied to not satisfied) |
| Recommend to friend | Yes/No | Participants were asked if they would recommend the received procedure to a friend |

*Note*: Used (validated) questionnaires at time of baseline and all follow-up points, if not stated otherwise.

### 2.5.2 | Statistical analysis

As usual for non-inferiority studies, all outcomes were analyzed in the per-protocol (PP) population, and were repeated in the intention-to-treat (ITT) population for sensitivity analysis.[16] Analyses were performed by SPSS version 28.

Baseline characteristics were compared using independent samples *T*-test or Mann–Whitney *U* test depending on data distribution. Chi-square or Fisher's exact test was used for categorical data. In case of multiple comparisons, Bonferroni correction was applied to test statistical significance. Linear mixed model analyses were used to analyze differences in the outcome variables between UAE and hysterectomy up to 1 year post-intervention. The model included treatment group, time, and the interaction between group and time. Time was treated as categorical and represented by dummy variables. All analyses were adjusted for BMI, age, comorbidity, smoking, baseline hemoglobin, baseline uterine volume, baseline CA125, partner, children, educational level, and employment.

Linear mixed model analyses were also used for analyzing the within-group development over time. In the analysis, all measurements, including the baseline measurement, were used as outcomes, and the model only included time (represented by dummy variables).

Change in pressure, micturition, and defecation symptoms were categorized and visualized in graphs. These symptom changes and laboratory changes from baseline to 6 months were tested using Mann–Whitney U tests.

Satisfaction was categorized in three options and analyzed using multinomial logistic mixed model analyses and the dichotomous "recommend to friend" question was analyzed using logistic generalized estimating equations.

A two-sided $p$-value of $<0.05$ was considered significant.

## 3 | RESULTS

Participants were enrolled consecutively between November 2015 and March 2022, resulting in 107 included participants. Figure 1 shows the flow of participants and data collection during follow-up. Eventually, after exclusion of six participants (five participants declined after having signed informed consent and

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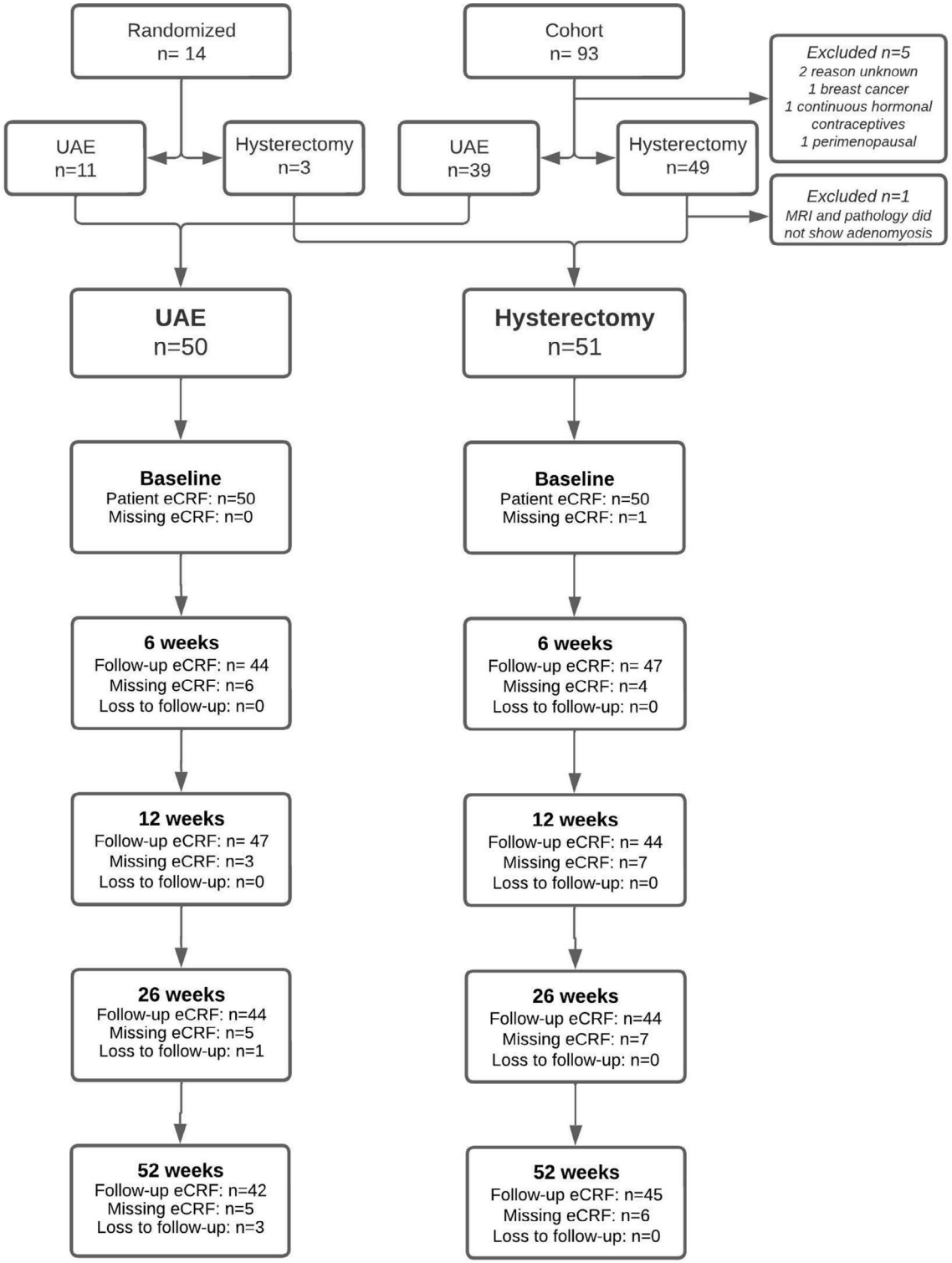


**FIGURE 1** Flow diagram.

one participant because MRI did not confirm adenomyosis) 50 underwent UAE and 51 hysterectomy. The following results are presented according to the PP analyses. ITT analyses are found in the Supporting Information. The outcomes are comparable, as only six UAE participants had a secondary hysterectomy in the first year after embolization.

### 3.1 | Participant characteristics

In Tables 2 and 3 baseline characteristics of all included participants of the PP and ITT population are presented. The treatment indications were not statistically significantly different between the two groups. Chronic pelvic pain was similar in both groups, but

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**TABLE 2** Baseline characteristics of per-protocol and intention-to-treat population: Demographics, medical history.

| | Per-protocol population | | | Intention to treat population | | |
|---|---|---|---|---|---|---|
| | UAE $n=44$ *n* (%) | Hysterectomy $n=51$ *n* (%) | *p*-Value | UAE $n=50$ *n* (%) | Hysterectomy $n=51$ *n* (%) | *p*-Value |
| Age (years) | | | | | | |
| Mean (SD) | 44.4 (5.03) | 42.2 (5.33) | 0.061 | 44.1 (5.1) | 42.2 (5.3) | 0.061 |
| Body Mass Index (weight (kg)/length $(m)^2$) | $N=44$ | $N=48$ | | $N=50$ | $N=48$ | |
| Mean (SD) | 26.7 (5.41) | 28.6 (5.09) | 0.096 | 26.9 (5.2) | 28.6 (5.1) | 0.096 |
| Parity | | | | | | |
| 0 | 10 (23) | 6 (12) | 0.181 | 10 (20) | 6 (12) | 0.295 |
| ≥1 | 34 (77) | 43 (88) | | 40 (80) | 43 (88) | |
| Employed | 38/44 (86) | 33/49 (67) | 0.031 | 43/50 (86) | 33/49 (67) | 0.028 |
| Voluntary work | 5 (11) | 8 (16) | 0.491 | 7 (14) | 8 (16) | 0.747 |
| Comorbidity[1] | | | | | | |
| None | 31/43 (72) | 35/50 (70) | 0.825 | 37/49 (84) | 35/51 (80) | 0.538 |
| Diabetes Mellitus | 0 (0) | 2 (4) | | 0 (0) | 2 (4) | |
| Hypertension | 1 (2) | 2 (4) | | 1 (2) | 2 (4) | |
| Asthma | 4 (9) | 1 (2) | | 4 (9) | 1 (2) | |
| Systemic disease | 3 (7) | 2 (5) | | 3 (6) | 2 (5) | |
| Blood clotting disorder | 0 (0) | 3 (7) | | 0 (0) | 3 (7) | |
| Other | 6 (14) | 8 (16) | | 6 (12) | 8 (16) | |
| Marital status | | | | | | |
| Single | 6 (14) | 6 (12) | 0.520 | 7 (14) | 6 (12) | 0.571 |
| Married/cohabiting | 32 (73) | 39 (80) | | 37 (74) | 39 (80) | |
| Living Apart Together | 2 (5) | 2 (4) | | 2 (4) | 2 (4) | |
| Divorced | 4 (9) | 1 (2) | | 4 (8) | 1 (2) | |
| Widow | 0 (0) | 1 (2) | | 0 (0) | 1 (2) | |
| Smoking status | $N=44$ | $N=49$ | | | | |
| Current smoker | 4 (9) | 10 (20) | 0.143 | 5 (10) | 10 (20) | 0.133 |
| Former smoker | 12 (27) | 17 (35) | | 13 (26) | 17 (35) | |
| Non-smoker | 28 (64) | 22 (45) | | 32 (64) | 22 (45) | |
| Highest educational level | | | | | | |
| Primary | 0 (0) | 0 (0) | 0.138 | 0 (0) | 0 (0) | 0.247 |
| Vocational lower secondary education | 2 (5) | 2 (4) | | 2 (4) | 2 (4) | |
| General secondary education | 12 (27) | 25 (52) | | 16 (32) | 25 (52) | |
| Vocational upper secondary education | 5 (11) | 3 (6) | | 6 (12) | 3 (6) | |
| Higher professional education, University | 26 (59) | 18 (38) | | 26 (52) | 18 (38) | |

*Note*: Reported for all participants in the per-protocol or intention-to-treat population, unless stated otherwise. (1) The numbers do not add up because multiple options could have been selected.

the dysmenorrhea score was slightly lower in the UAE group than in the hysterectomy group (Numeric Rating Scale 7 vs. 8, $p=0.007$). Median uterine volume and CA125 were statistically significantly larger in the UAE group than in the hysterectomy group (252 vs. 149 $cm^3$ and 43.5 vs. 12.0 kU/L respectively). Median hemoglobin was slightly lower in the UAE group (7.9 vs. 8.3, $p=0.010$) and mean HRQOL (adjusted) domains were comparable at baseline. No differences existed in the presence of other symptoms. The majority of all participants had or were using hormonal treatment at inclusion and did not have comorbidities or previous abdominal surgery.

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**TABLE 3** Baseline characteristics of per-protocol and intention-to-treat population previous/current therapy, symptoms, sonographic assessment, laboratory results.

| | Per-protocol population | | | Intention to treat population | | |
|---|---|---|---|---|---|---|
| | UAE *n* = 44 *n* (%) | Hysterectomy *n* = 51 *n* (%) | *p*-Value | UAE *n* = 50 *n* (%) | Hysterectomy *n* = 51 *n* (%) | *p*-Value |
| Previous medical treatment | 36/43 (84) | 46/50 (92) | 0.218 | 41/49 (84) | 46/50 (92) | 0.204 |
| Current hormonal medication[1] | | | | | | |
| Total (%) | 22/43 (51) | 31/50 (62) | 0.202 | 25/49 (51) | 31/50 (62) | 0.270 |
| Oral contraceptives | 9 | 12 | | 9 | 12 | |
| Progestogens[2] | 7 | 6 | | 7 | 6 | |
| GnRH-analogue | 4 | 15 | | 8 | 15 | |
| Hormonal IUD | 3 | 7 | | 3 | 7 | |
| Current supportive treatment | | | | | | |
| NSAID | 10 | 16 | 0.852 | 12 | 16 | 0.863 |
| Tranexamic acid | 4 | 4 | | 4 | 4 | |
| Iron supplements | 7 | 6 | | 7 | 6 | |
| Blood transfusion in the last 3 months | 2 | 0 | | 2 | 0 | |
| Other | 2 | 6 | | 2 | 6 | |
| Previous surgical treatment[1] | *N* = 43 | *N* = 50 | | *N* = 49 | *N* = 50 | |
| None | 29 (67) | 30 (60) | 0.457 | 33 (67) | 30 (60) | 0.447 |
| Hysteroscopic resection fibroid | 4 (9) | 1 (2) | | 4 (8) | 1 (2) | |
| Hysteroscopic endometrial ablation + resection | 1 (2) | 3 (6) | | 1 (2) | 3 (6) | |
| Endometrial ablation | 3 (7) | 4 (8) | | 3 (6) | 4 (8) | |
| Myomectomy (laparotomic/laparoscopic) | 1 (2) | – | | 1 (2) | – | |
| Other[3] | 8 (19) | 15 (30) | | 10 (18) | 15 (30) | |
| Preassessment | | | | | | |
| HRQOL (adjusted mean, [95% CI]) | | | | | | |
| WHO-QOL-Bref Physical | 47.2 [39.0 to 55.5] | 44.4 [37.2 to 51.7] | 0.625 | 47.3 [39.9 to 54.7] | 44.8 [37.6 to 52.0] | 0.643 |
| WHO-QOL-Bref Psychological | 52.0 [45.6 to 58.3] | 60.8 [55.2 to 66.4] | 0.051 | 54.4 [48.4 to 60.4] | 60.7 [54.8 to 66.5] | 0.152 |
| WHO-QOL-Bref Social | 62.7 [55.1 to 70.3] | 65.7 [59.0 to 72.4] | 0.575 | 64.3 [57.4 to 71.1] | 65.6 [58.9 to 72.3] | 0.794 |
| WHO-QOL-Bref Environment | 69.9 [63.8 to 76.1] | 71.7 [66.3 to 77.2] | 0.682 | 71.0 [65.6 to 76.4] | 71.8 [66.5 to 77.0] | 0.846 |
| SF-12 Physical | 40.4 [36.0 to 44.8] | 38.0 [34.1 to 41.8] | 0.418 | 39.2 [35.3 to 43.1] | 38.2 [34.4 to 42.0] | 0.728 |
| SF-12 Mental | 37.2 [32.0 to 42.3] | 36.7 [32.2 to 41.3] | 0.898 | 36.7 [32.1 to 41.3] | 37.0 [32.5 to 41.5] | 0.935 |
| Indication for intervention[1,4] | *N* = 43 | *N* = 50 | | *N* = 49 | *N* = 50 | |
| AUB | 27 (63) | 22 (44) | 0.070 | 31 (63) | 22 (44) | 0.055 |
| Dysmenorrhea | 15 (35) | 31 (62) | .009[3] | 18 (37) | 31 (62) | 0.012 |
| Pelvic pain | 5 (12) | 7 (14) | 0.734 | 6 (12) | 7 (14) | 0.796 |
| Urinary symptoms | 1 (2) | 2 (4) | 1.000 | 1 (2) | 2 (4) | 1.000 |
| Defecation problems | 0 (0) | 0 (0) | - | 0 (0) | 0 (0) | - |
| Anemia | 2 (5) | 0 (0) | 0.211 | 2 (4) | 0 (0) | 0.240 |
| Mechanical symptoms | 1 (2) | 1 (2) | 1.000 | 1 (2) | 1 (2) | 1.000 |
| Other | 1 (2) | 3 (6) | 0.621 | 1 (2) | 3 (6) | 0.617 |

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**TABLE 3** (Continued)

| | Per-protocol population | | | Intention to treat population | | |
|---|---|---|---|---|---|---|
| | UAE $n=44$ $n$ (%) | Hysterectomy $n=51$ $n$ (%) | $p$-Value | UAE $n=50$ $n$ (%) | Hysterectomy $n=51$ $n$ (%) | $p$-Value |
| Duration of menstrual cycle (days) | $N=44$ | $N=50$ | | $N=50$ | $N=50$ | |
| Median [IQR] | 26.5 [11.0–29.8] | 21 [7.0–28.0] | 0.098 | 25 [13.0–30.0] | 21 [7.0–28.0] | 0.076 |
| Duration of symptoms (months) | $N=44$ | $N=50$ | | $N=50$ | $N=50$ | |
| Median [IQR] | 35 [15.3–97.8] | 60 [18.0–292.5] | | 36 [15.8–86.5] | 60 [18.0–292.5] | |
| Mean rank | 42.7 | 51.8 | 0.106 | 45.5 | 55.5 | 0.086 |
| Presence of other symptoms[1,3] | $N=44$ | | | $N=50$ | $N=50$ | |
| Urinary incontinence | 19 (43) | 17 (34) | 0.400 | 22 (44) | 17 (34) | 0.305 |
| Frequent micturition | 27 (61) | 24 (48) | 0.219 | 29 (58) | 24 (48) | 0.316 |
| Defecation symptoms | 14 (32) | 18 (37) | 0.666 | 15 (30) | 18 (37) | 0.477 |
| Pressure symptoms | 39 (89) | 46 (92) | 0.730 | 45 (90) | 46 (92) | 0.727 |
| Pain (NRS) (median [IQR]) | $N=44$ | $N=50$ | | $N=50$ | $N=50$ | |
| Current pain at time of inclusion | 4.00 [1.0–7.0] | 5.00 [2.0–7.0] | 0.404 | 4.50 [1.0–7.0] | 5.00 [2.0–7.0] | 0.501 |
| During menstruation | 7.00 [7.0–9.0] | 8.00 [8.0–9.0] | 0.007 | 7.00 [6.5–9.0] | 8.00 [8.0–9.0] | 0.012 |
| Average last month | 6.00 [4.0–8.0] | 7.00 [5.0–8.0] | 0.470 | 6.00 [4.0–8.0] | 7.00 [5.0–8.0] | 0.484 |
| Uterine volume ($cm^3$)[5] (on ultrasound) median [IQR] | $N=35$ 252 [157.1–399.2] | $N=39$ 149 [89.4–278.2] | 0.020 | $N=41$ 236 [156.8–387.4] | $N=39$ 149 [89.4–278.2] | 0.038 |
| Fibroids (on ultrasound) present ($n/N$) | 9/43 (19) | 6/48 (13) | 0.279 | 9/48 (19) | 6/48 (13) | 0.399 |
| Sonographic assessed adenomyosis form | $N=43$ | $N=48$ | | $N=48$ | $N=48$ | |
| Diffuse | 21 (49) | 32 (67) | 0.395 | 26 (54) | 32 (67) | 0.717 |
| Focal | 5 (12) | 5 (10) | | 5 (10) | 5 (10) | |
| Combined diffuse and focal | 9 (21) | 6 (13) | | 9 (19) | 6 (13) | |
| Not known | 8 (19) | 5 (10) | | 8 (17) | 5 (10) | |
| Sonographic features (present (%)) | | | | $N=48$ | $N=48$ | |
| Anechoic lacunae | 30 (70) | 27 (56) | 0.409 | 34 (71) | 27 (56) | 0.332 |
| Asymmetrical thickening of myometrium | 34 (79) | 30 (63) | 0.161 | 37 (77) | 30 (63) | 0.267 |
| Heterogeneous myometrial aspect | 35 (81) | 41 (85) | 0.656 | 40 (83) | 41 (85) | 0.721 |
| Linear striations | 32 (89) | 37 (82) | 0.401 | 35 (85) | 37 (82) | 0.693 |
| Diffuse vascular flow | 26 (60) | 28 (58) | 0.963 | 28 (58) | 28 (58) | 0.951 |
| Heterogenous endometrial-myometrial zone | 26 (74) | 28 (67) | 0.467 | 27 (68) | 28 (67) | 0.936 |
| Number of criteria per participant (median [IQR]) | 5 [3–6] | 4 [3–5] | 0.191 | 5 [3–5.3] | 4 [3–5] | 0.330 |
| Laboratory results (median [IQR]) | | | | | | |
| Hb (mmol/L) | 7.9 [6.9–8.4] | 8.3 [7.8–8.8] | 0.010 | 8.0 [7.0–8.4] | 8.3 [7.8–8.8] | 0.019 |
| Hb <7.0 ($n/N$) | 11/43 (26) | 1/49 (2.0) | | 11/48 (23) | 1/49 (2.0) | |
| CA 125 (kU/L) ($n=37/n=43$) | 43.5 [13.3–159.0] | 12.0 [9.0–30.0] | 0.003 | 36.0 [11.0–150.0] | 12.0 [9.0–30.0] | 0.013 |

*Note*: (1) The numbers do not add up because multiple options could have been selected; (2) Oral cyclic progesterone ulipristal, Implanon or depot medroxyprogesterone acetate; (3) Other: For example, diagnostic laparoscopy for endometriosis, adhesiolysis, curettage, cesarean section; (4) To address the issue of multiple comparisons, we applied the Bonferroni correction to the eight statistical tests performed in this study. The original significance threshold of $p<0.05$ was adjusted to $p<0.00625$ (0.05/8). (5) Uterine volume calculated as 0.5233 × longitudinal length, anterior–posterior height, and transverse width.

Abbreviations: AUB, abnormal uterine bleeding; Hb, hemoglobin; HRQOL, health-related quality of life; IQR, interquartile range; IUD, intrauterine device; NRS, numeric rate scale; NSAID non-steroid anti-inflammatory drugs.

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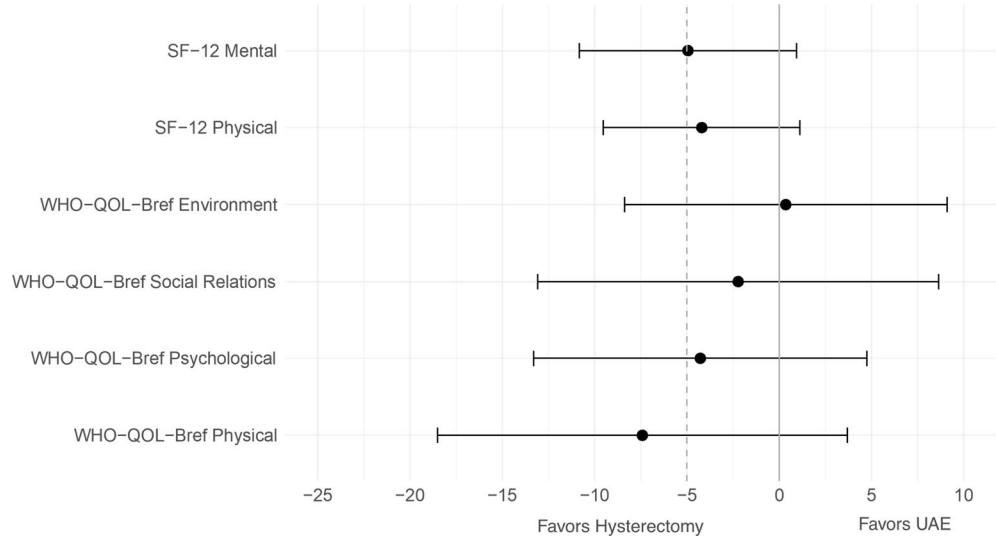


**FIGURE 2** Forest plots of effect difference between UAE, with 95% CI, for all HRQOL outcomes at 52 weeks in per protocol population. Dotted vertical line is the non-inferiority margin (delta 5). <0 favors hysterectomy, >0 favors UAE. Non-inferiority of UAE can be claimed when the lower bound of the 95% CI does not exceed −5. UAE is inferior when the upper bound of the 95% CI is lower than −5.

The majority of hysterectomies were performed laparoscopically (94.3%); the remaining was done vaginally. In four patients, a concomitant bilateral salpingo-oophorectomy was performed, and in three patients, coagulation of endometriosis was also done.

## 3.2 | HRQOL

Non-inferiority of UAE compared with hysterectomy could not be demonstrated for any of the six HRQOL domains at 1-year follow-up, as visualized in Figure 2. Also, inferiority could not be demonstrated. This is similar in the ITT population (Table S2). Additionally, the PP groups were comparable at all follow-up points for the WHO-QOL-Bref domains and SF-12 scores (Table 4) as analyzed using linear mixed model for repeated measurements. The ITT population revealed significant differences between the two treatment groups for both the Physical Component Summary (PCS-12) and the Mental Component Summary (MCS-12) scores of the SF-12 favoring hysterectomy at 1-year follow-up (PCS $\beta$ −6.17, 95% CI −11.26 to −1.09; MCS $\beta$ −6.93, 95% CI −12.53 to -1.34). Tables S1 and S2 detail the results of both the PP and ITT populations. Figure 3 depicts the results of the linear mixed model analyses on the per protocol population.

Within group analyses showed significant improvement of all HRQOL scores compared with baseline in both UAE and hysterectomy groups at almost all follow-up points. WHO-QOL-Bref Physical, Psychological, Environment, and SF-12 Physical and Mental improved significantly at all time points after both UAE and hysterectomy (Table 4). WHO-QOL-Bref Social relations improved statistically significantly at all time points after hysterectomy, and only at 52 weeks after UAE. The effects of both treatments in the ITT population on HRQOL scores (within group effect) are shown in Table S3.

## 3.3 | Symptom severity

### 3.3.1 | Pain

Within group analyses of WHO-QOL-100 Pain and Discomfort showed improvement in both groups at all follow-up points (Table 5), the biggest improvement is found in the first 6 weeks. Between group analysis revealed a greater decrease after hysterectomy at 12, 26, and 52 weeks in the PP population (Table 5) and at all follow-up points in the ITT population (Table S6). Figure 4A shows the change in time after UAE and hysterectomy for WHO-QOL-100: facet pain and discomfort.

One year after intervention, pain now (at time of questionnaire) expressed in the Numeric Rating Scale was higher after UAE in comparison to hysterectomy ($\beta$ 1.35, 95% CI 0.22 to 2.48), plotted in Figure 5A (Table 5). 82.5% of participants after UAE reported their pain now as less or no pain at all, in comparison to 97.7% of the participants after hysterectomy (Figure 6A). Average pain (last 6 weeks) at 52 weeks after intervention in comparison to average pain 6 weeks before intervention was less or not present for 32 participants after UAE (80.0%) vs. 41 participants after hysterectomy (93.2%) (Figure 6B). This is also reflected in the difference of adjusted mean Numeric Rating Scale scores ($\beta$ 2.45, 95% CI 1.18 to 3.72) (Table 5), plotted in Figure 5B.

### 3.3.2 | Sexual activity

Figure 3B demonstrates the change in time after UAE and hysterectomy for WHO-QOL-100 Sexual activity. After hysterectomy WHO-QOL-100 facet sexual activity improves significantly at each time point, for UAE is statistically significant improvement is found at 26 and 52 weeks (Table 5). The adjusted effects of hysterectomy

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**TABLE 4** Within group effect ($\beta$) and between group effect difference ($\Delta$), results from linear mixed model analyses.

| | Week 6 | | | | Week 12 | | | | Week 26 | | | | Week 52 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | UAE $\beta$ | Hyst $\beta$ | Effect Δ (95% CI) | p-Value | UAE $\beta$ | Hyst $\beta$ | Effect Δ (95% CI) | p-Value | UAE $\beta$ | Hyst $\beta$ | Effect Δ (95% CI) | p-Value | UAE $\beta$ | Hyst $\beta$ | Effect Δ (95% CI) | p-Value |
| Bref Physical | **18.47** | **22.85** | 1.61 (−9.69 to 12.91) | 0.777 | **24.03** | **28.47** | −3.34 (−14.00 to 7.32) | 0.533 | **23.41** | **30.34** | −4.19 (−14.69 to 6.31) | 0.428 | **21.58** | **33.51** | −7.42 (−18.51 to 3.68) | 0.186 |
| Bref psycho-logical | **9.98** | **10.67** | −5.71 (−14.43 to 3.01) | 0.195 | **11.35** | **8.79** | −3.03 (−12.11 to 6.06) | 0.508 | **12.46** | **13.10** | −5.15 (−14.24 to 3.94) | 0.262 | **13.36** | **13.96** | −4.28 (−13.30 to 4.74) | 0.346 |
| Bref social relations | 3.72 | **8.91** | −5.18 (−15.86 to 5.51) | 0.336 | 4.96 | **8.98** | −4.29 (−14.74 to 6.15) | 0.415 | 3.26 | **8.72** | −6.13 (−4.81 to 17.06) | 0.268 | **6.42** | **9.91** | −2.23 (−13.09 to 8.63) | 0.683 |
| Bref environ-ment | **4.38** | **5.64** | −2.30 (−11.76 to 5.77) | 0.497 | **6.91** | **6.54** | −1.21 (−9.73 to 7.32) | 0.778 | **7.11** | **7.65** | 0.70 (−8.01 to 9.41) | 0.873 | **6.45** | **6.86** | 0.35 (−8.39 to 9.09) | 0.936 |
| SF-12 physical | **5.61** | **4.68** | 4.50 (−1.71 to 10.72) | 0.153 | **7.83** | **11.74** | −0.90 (−6.45 to 4.64) | 0.746 | **9.36** | **12.72** | −1.92 (−3.20 to 7.04) | 0.456 | **8.10** | **13.74** | −4.20 (−9.53 to 1.12) | 0.120 |
| SF-12 mental | **3.96** | **7.53** | −0.81 (−7.25 to 5.63) | 0.803 | **5.25** | **10.31** | −3.18 (−9.32 to 2.97) | 0.306 | **7.75** | **12.15** | −3.99 (−10.20 to 2.22) | 0.205 | **7.05** | **12.43** | −4.95 (−10.83 to 0.94) | 0.098 |

*Note*: Adjusted for covariates, in per protocol population. Effect in bold is significant within group effect in comparison to baseline. Effect in bold is significant within group effect in comparison to baseline.

and UAE are comparable (non-significant effect differences) at all time points in the PP population (Table 5 and Figure 4B). In the ITT population, a statistically significant greater adjusted effect of hysterectomy for sexual activity was found at 26 weeks ($\beta$ −15.80, 95% CI −28.92 to −2.68) (Table S6).

### 3.3.3 | Pressure, micturition, and defecation symptoms

The self-reported change of pressure, micturition, and defecation symptoms at all follow-up moments in comparison to before intervention is shown in Figure 6. One year after UAE, more participants reported less or no problems regarding urinary incontinence (85.0%) and frequency (72.0%) compared with participants 1 year after hysterectomy (61.4% and 52.3% respectively, $p=0.025$ and $p=0.024$). Change in problems with defecation was comparable between both groups after 1 year ($p=0.479$). Pressure symptoms improved for 95.5% of participants 1 year after hysterectomy in comparison to 80.0% after UAE ($p=0.058$).

### 3.3.4 | Laboratory results

Baseline hemoglobin was comparable to hemoglobin 6 months after UAE (7.9–8.1; $p=0.272$) and hysterectomy (8.3–8.4, $p=0.145$). Ca125 significantly decreased after both UAE (43.5 to 35.0 kU/L, $p=0.022$) and hysterectomy (12.0 to 7.6 kU/L, $p=0.001$). No differences in the change of hemoglobin and Ca125 were found between groups ($p=0.812$ and $p=0.922$ respectively).

### 3.3.5 | Satisfaction

Table 6 presents an overview of satisfaction scored at all follow-up moments after UAE and hysterectomy. Due to low numbers in the neutral and unsatisfied categories, multinomial logistic mixed model analyses could not be performed. At 52 weeks, most participants in both intervention groups were satisfied (73% in the UAE group and 95% in the hysterectomy group) about the received procedure. Differences are found between the PP analyses and ITT analyses; the ITT population revealed more participants being unsatisfied after UAE than in the PP population (Table S7).

At 52 weeks post-intervention, UAE participants were less inclined to recommend the received intervention to a friend compared with the hysterectomy participants ($\beta$ −3.31, 95% CI −5.46 to −1.15) (Table 5).

## 4 | DISCUSSION

UAE is thought to be a promising and less-invasive alternative for hysterectomy in therapy-resistant symptomatic adenomyosis;

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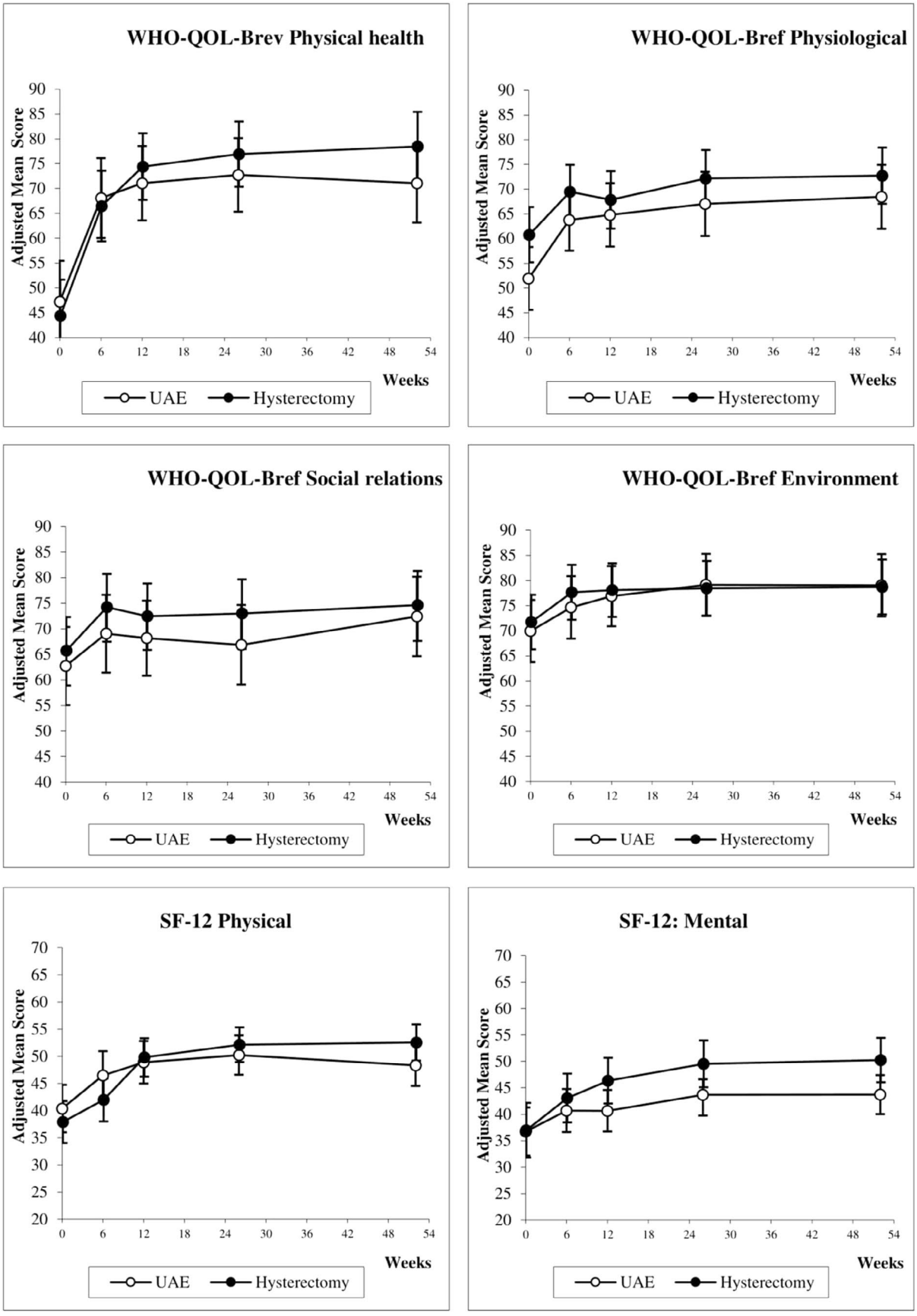


FIGURE 3 Graphs show the estimated adjusted means (95% CI) at the different timepoints of the different health-related quality of life (HRQOL) scores as a result of the linear mixed model analyses in the per protocol population. All HRQOL scores range from 0 to 100. Asterisk (*): Significant ($p \leq 0.05$) effect difference.

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**TABLE 5** Within group effect ($\beta$) and between group effect difference ($\Delta$) of secondary outcomes from linear mixed model analyses.

| | Week 6 | | | | Week 12 | | | | Week 26 | | | | Week 52 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | UAE $\beta$ | Hyst $\beta$ | Effect Δ (95% CI) | *p*-Value | UAE $\beta$ | Hyst $\beta$ | Effect Δ (95% CI) | *p*-Value | UAE $\beta$ | Hyst $\beta$ | Effect Δ (95% CI) | *p*-Value | UAE $\beta$ | Hyst $\beta$ | Effect Δ (95% CI) | *p*-Value |
| Pain and discomfort | **−24.97** | **−32.99** | 10.68 (−1.80 to 23.16) | 0.092 | **−29.17** | **−38.90** | 21.34 (9.27 to 33.41) | <0.001 | **−29.91** | **−38.26** | 18.65 (6.83 to 30.46) | 0.002 | **−27.64** | **−41.13** | 17.17 (4.94 to 29.41) | 0.007 |
| Sexual activity | 1.99 | **12.24** | −5.89 (−20.13 to 8.36) | 0.412 | 4.06 | **15.15** | −6.53 (−20.76 to 7.69) | 0.362 | **7.10** | **19.70** | −9.87 (−23.76 to 4.02) | 0.160 | **11.47** | **20.86** | −4.73 (−18.83 to 9.36) | 0.504 |
| Average pain (NRS) | **−2.33** | **−2.60** | 0.50 (−0.80 to 1.80) | 0.447 | **−3.18** | **−4.60** | 1.85 (0.76 to 2.93) | 0.001 | **−3.46** | **−4.84** | 1.77 (0.67 to 2.87) | 0.002 | **−2.81** | **−5.00** | 2.45 (1.18 to 3.72) | <0.001 |
| Pain now (NRS) | **−2.64** | **−3.28** | 0.45 (−0.66 to 1.57) | 0.420 | **−1.83** | **−3.49** | 2.67 (1.44 to 3.91) | <0.001 | **−2.37** | **−3.88** | 1.32 (0.05 to 2.59) | 0.042 | **−2.65** | **−4.07** | 1.35 (0.22 to 2.48) | 0.021 |
| Recommend to friend | | | −5.22 (−8.82 to −1.62) | 0.004 | | | −3.32 (−5.59 to −1.06) | 0.005 | | | −5.30 (−8.26 to −2.34) | <0.001 | | | −3.31 (−5.46 to −1.15) | 0.003 |

*Note*: Adjusted for covariates, in per protocol population. Effect in bold is significant within group effect in comparison to baseline. "Pain and Discomfort" and "Sexual activity" are facets parts of the WHO-QOL-100.

however, comparative data are lacking. HRQOL (measured with WHO-QOL-Bref and SF-12) and adenomyosis-related symptoms were assessed at 6, 12, 26, and 52 weeks in 50 participants after UAE and 51 after hysterectomy.

Both interventions showed significant improvements in all 1-year HRQOL outcomes. Neither non-inferiority nor inferiority of UAE compared with hysterectomy could be demonstrated for any HRQOL domain. After 1 year, all HRQOL domains were comparable between the two groups in the PP population. Statistically significant differences favoring hysterectomy were observed in the ITT population in the adjusted PCS-12 and MCS-12 scores (PCS Δ −6.17, $p=0.018$, MCS Δ −6.93, $p=0.016$). Significant pain reduction and improvement in sexual activity were found after both UAE and hysterectomy, but the effect of hysterectomy concerning pain was greater (at 52 weeks $\beta$ 17.17, $p=0.007$). At 1 year, more participants were satisfied after hysterectomy than after UAE (95% vs. 73% respectively) and were more likely to recommend the received treatment ($\beta$ −3.31, $p=0.003$).

HRQOL is known to be affected in women with menstrual symptoms and adenomyosis, and is one of the core outcome measures in clinical research on uterine-sparing treatments of adenomyosis as defined by doctors, researchers, and patients.[17] No other studies investigated general HRQOL outcomes after UAE in patients with adenomyosis; we can only compare our results to studies that compared UAE vs. hysterectomy for the treatment of fibroids.[18] The EMMY (EMbolisation vs. hysterectoMY) trial[8] used SF-36 (comparable to the SF-12 in our study) and found comparable improvement of HRQOL after both UAE and hysterectomy.

Symptom severity has been more extensively reported in research on UAE for adenomyosis. Consistent with QUESTA's findings, a decrease in pain after UAE has previously been shown,[13,19,20] as well as improvements in pelvic heaviness and urinary frequency.[19] Sexual activity improved significantly after both procedures. Improvement in sexuality after hysterectomy was in line with the results found in a meta-analysis that also found a significant improvement in sexual function after hysterectomy without the removal of ovaries.[21]

Non-inferiority of HRQOL scores was predefined as a margin of five points, considered as the minimal clinically important difference,[15] however, both SF-12 and WHO-QOL-Bref have not been validated in a population with adenomyosis or menstrual symptoms. In the Questa study, a mean difference of 5.7 in PCS and 9.9 in MCS was found when comparing neutral and satisfied participants with those who were not satisfied. This suggests that larger margins might be more appropriate to capture the minimal clinically significant differences in HRQOL for adenomyosis patients. Normative Dutch data[22] were used to obtain SF-12 values. Women in the QUESTA study had lower mean MCS and PCS scores compared with the normative Dutch sample of women aged 40–49 (QUESTA-MCS 36.7 (SD 11.5) vs. Dutch-MCS 49.8 (SD 9.5); QUESTA-PCS 38.7 (SD 8.9) vs. Dutch-PCS 51.97 (SD 7.5)). This highlights the impact of adenomyosis on mental and physical health. Both hysterectomy and UAE reduced this gap, though MCS score remained lower, indicating

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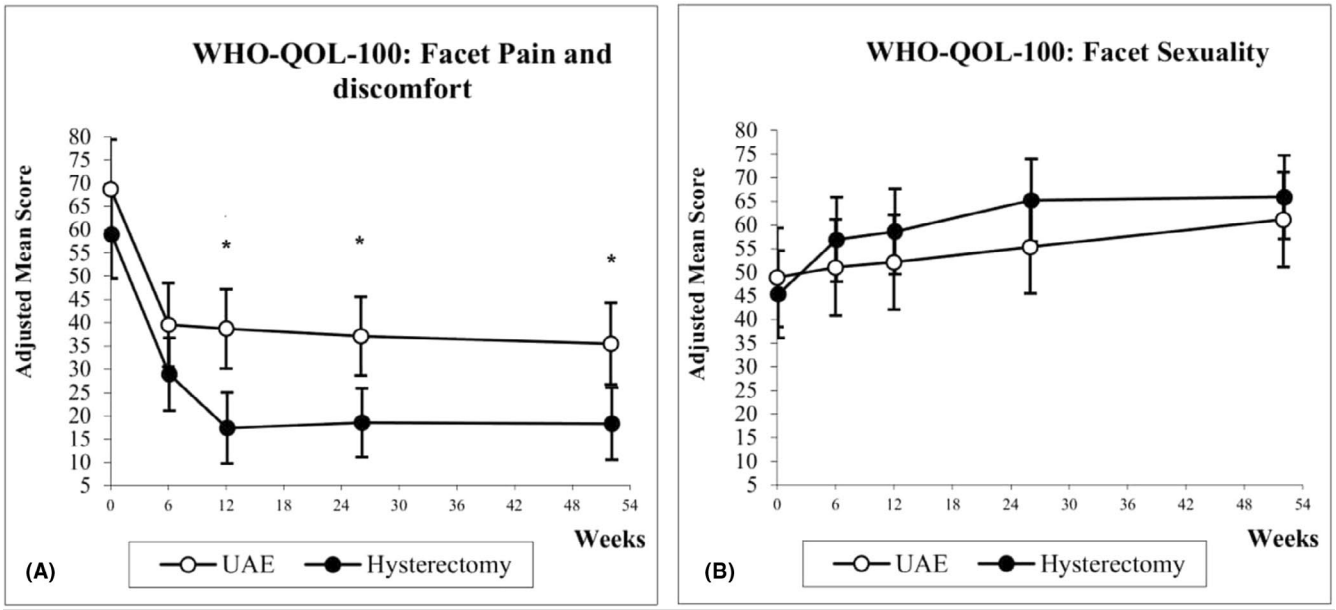


FIGURE 4 Graphs show the plotted adjusted means with 95% CI of WHO-QOL-100 facet Pain and Discomfort (A) and facet Sexual Activity (B) in per protocol population. A lower score in facet Pain and Discomfort means higher quality of life; a higher score in facet Sexual Activity scores higher in quality of life. Significant differences between groups per time point are marked with an asterisk (*). All HRQOL scores range from 0 to 100.

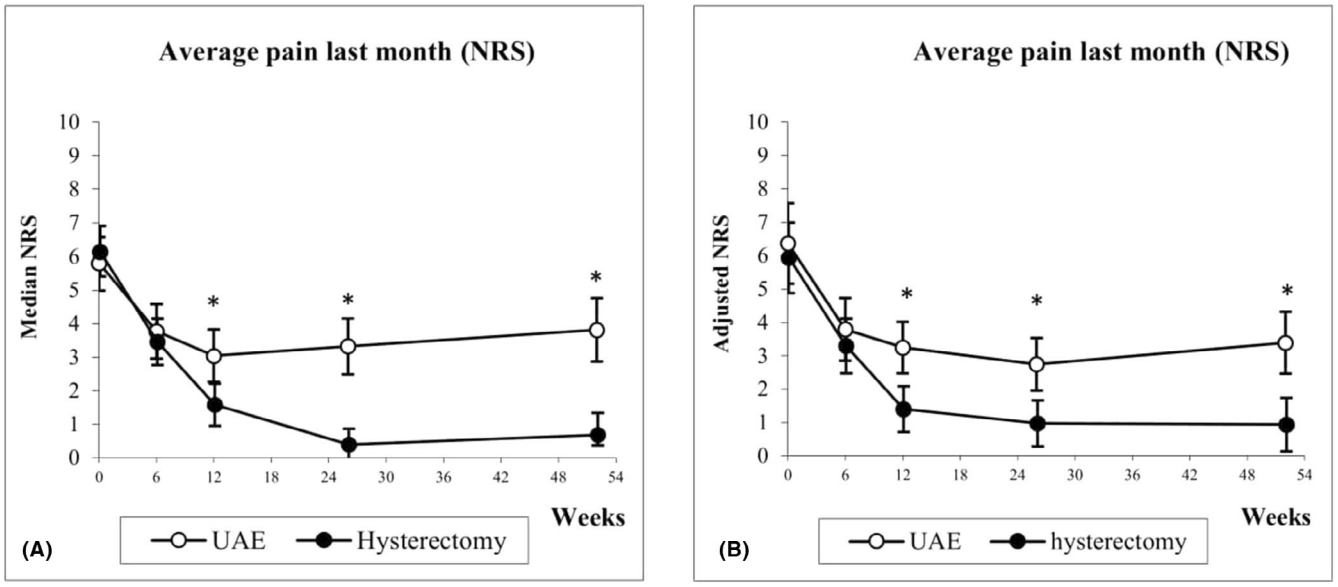


FIGURE 5 Plotted adjusted pain scores (NRS) at different time points for UAE and Hysterectomy in per protocol population. Average NRS score (A) and NRS score at time of questionnaire (B) improved significantly at every time point for both groups. Significant differences between groups per time point are marked with an asterisk (*).

worse mental health than the average Dutch female population even after intervention.

Similar to the EMMY trial, QUESTA participants were less satisfied with UAE 1 year after the procedure compared with hysterectomy,[8] despite the positive effect of UAE on HRQOL. This suggests that validated HRQOL questionnaires may not fully capture what adenomyosis patients consider important for their quality of life. This stresses the need for a disease-specific QOL questionnaire for adenomyosis. Future studies should compare UAE with other uterus-preserving therapies using an adenomyosis-specific QOL tool.

This study had several limitations. Firstly, due to low inclusion rates, the study design was changed from an RCT to a prospective comparative cohort. This is seen quite often in gynecological and obstetrical RCTs; a recent review reported a 55% failure of targeted recruitment in the preplanned study period in the Netherlands.[23] On the one hand, this might cause selection bias and confounding, as

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FIGURE 6 Severity of symptoms (no, less, same or more symptoms) at different follow-up moments in comparison to before the intervention (Per-protocol population). (A) Pain now (at time of filling out questionnaire). (B) Pain average in the last 6 weeks. (C) Pelvic pressure in the last 6 weeks. (D) Problems with defecation. (E) Urinary incontinence. (F) Micturition frequency.

reflected in some differences in baseline characteristics. To overcome this problem, we adjusted for these differences in our statistical analyses. On the other hand, changing the design from an RCT to a comparative study in which patients could choose their preferred treatment better reflects daily practice that improves the generalizability of our findings and increases external validity.[24] This is in line with the conclusions of a recent meta-analysis comparing RCTs with partially randomized patient preference trials.[25] Furthermore, the relatively small sample size may bias the reliability of clinical and baseline characteristics with low prevalence and result in relatively wide confidence intervals of HRQOLs, complicating conclusions on non-inferiority. Finally, we reduced the potential risk of bias caused by differences in multiple participating centers by implementing predefined MRI diagnostic criteria, an embolization protocol, and visitation by the coordinating investigator (PL).

## 5 | CONCLUSION

After 1 year, both UAE and hysterectomy significantly improved HRQOL for patients with symptomatic adenomyosis. Neither non-inferiority nor inferiority could be established within the predefined

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**TABLE 6** Satisfaction regarding the intervention (per protocol population).

| | 6 weeks | | 12 weeks | | 26 weeks | | 52 weeks | |
|---|---|---|---|---|---|---|---|---|
| | UAE $n=37$ $n$ (%) | Hyst $n=44$ $n$ (%) | UAE $n=39$ $n$ (%) | Hyst $n=38$ $n$ (%) | UAE $n=38$ $n$ (%) | Hyst $n=42$ $n$ (%) | UAE $n=40$ $n$ (%) | Hyst $n=43$ $n$ (%) |
| Satisfied | 23 (62) | 42 (96) | 30 (77) | 38 (100) | 30 (79) | 40 (95) | 29 (73) | 41 (95) |
| Neutral | 8 (22) | 2 (4) | 5 (13) | – | 5 (13) | 1 (2) | 6 (15) | 1 (2) |
| Unsatisfied | 6 (16) | – | 4 (10) | – | 3 (8) | 1 (2) | 5 (13) | 1 (2) |

*Note*: Moderately satisfied, satisfied, and very satisfied are combined in the group satisfied; not satisfied and not unsatisfied are named neutral; and moderately unsatisfied, unsatisfied, and very unsatisfied are combined in the group unsatisfied.

Abbreviations: Hyst, hysterectomy; UAE, uterine artery embolization.

margins. HRQOL after 1 year was comparable in all HRQOL domains after UAE vs. hysterectomy. Both UAE and hysterectomy improved sexual activity and pain, although hysterectomy had a significantly greater effect on pain. More participants were satisfied after hysterectomy. Even though hysterectomy performs better on several domains, UAE is a good alternative in adenomyosis patients and can be offered to patients who do not want to undergo surgery or want to preserve their uterus. For patients seeking a definitive solution, hysterectomy remains the treatment of choice. Further ongoing research on cost-effectiveness and long-term outcomes will provide additional insights into the potential benefits of UAE.

## AUTHOR CONTRIBUTIONS

Lisa M. Trommelen: validation, formal analysis, investigation, resources, data curation, writing – original draft, writing – review and editing, visualization, project administration. Annika Semmler: writing – review and editing, investigation. Annefleur M. De Bruijn: conceptualization, methodology, software, resources, writing – Review and Editing, project administration, investigation. Marissa Harmsen: methodology, software, resources, project administration, investigation. Marieke Smink, Petra F. Janssen, Ilse Van Rooij, Jeroen Van Bavel, Peggy Geomini, Jacques W.M. Maas, Celine M. Radder, Paul Van Kesteren, Janet Kwee, Erica Bakkum, Marleen De Lange, Freek Groenman, Velja Mijatovic, Anne Timmermans, Rutger Lely, Armand Lamers, Douwe Vos, Gretel Van Hoecke, Otto Elgersma, Huib A.A.M. Van Vliet, Lonneke Sf Yo, Dries A.R.H. Twijnstra, Frank W. Jansen, Catharina S.P. Van Rijswijk, Han Kruimer, Carroll Tseng, Sjors Coppus, Mark Arntz, Aloys F.J. Wust, Joost G.A.M. Blomjous, Laurens Van Boven, Alexander Venmans: resources, data curation, writing – review and editing, investigation. Robert A. De Leeuw: software, resources, data curation, writing – review and editing, investigation. Jos W.R. Twisk: methodology, formal analysis, writing – review and editing. Judith A.F. Huirne: conceptualization, methodology, writing – review and editing, investigation. Paul N.M. Lohle: conceptualization, methodology, writing – review and editing, supervision, project administration, funding acquisition, investigation. Wouter J.K. Hehenkamp: conceptualization, methodology, writing – review and editing, supervision, project administration, funding acquisition, investigation.


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## CONFLICT OF INTEREST STATEMENT

Wouter J.K. Hehenkamp and Paul N.M. Lohle received research funding from Boston Scientific and Merit Medical consecutively. It was investigator-initiated; the sponsors were not involved in data

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gathering, analysis, interpretation, or writing. They approved the study protocol beforehand and agreed on the publication of the results, irrespective of the outcome. Both sponsors were manufacturers of embolization material; their product was used during their sponsoring period. The remaining authors report no conflict of interest.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## ETHICS STATEMENT

The QUality of life after Embolization vs. hySTerectomy in Adenomyosis (QUESTA) study was approved by the ethics committee of the VU Medical Center Amsterdam (Reference number 2015/211) on July 27, 2015 and the boards of all participating hospitals.

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