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Journal:	*BMJ*
Manuscript ID:	BMJ.2015.025142.R1
Article Type:	Research
BMJ Journal:	BMJ
Date Submitted by the Author:	29-Apr-2015
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Keywords:	uterine prolapse, hysterectomy, hysteropexy, randomised controlled trial

Sacrospinous hysteropexy versus vaginal hysterectomy with uterosacral ligament suspension in women with uterine prolapse stage two or higher: a multicentre randomised non-inferiority trial

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Word count

Abstract	271
Manuscript	4214

ABSTRACT

OBJECTIVE To investigate whether uterus preserving vaginal sacrospinous hysteropexy is non-inferior to vaginal hysterectomy with uterosacral ligament suspension in surgical treatment of uterine prolapse.

DESIGN A multicentre randomised controlled non-blinded non-inferiority trial (SAVE U) with 1:1 treatment allocation.

SETTING 4 Dutch non-university teaching hospitals

PARTICIPANTS 208 healthy women with uterine prolapse stage two or higher requiring surgery, without a history of prior pelvic floor surgery.

INTERVENTIONS Treatment with sacrospinous hysteropexy or vaginal hysterectomy with uterosacral ligament suspension. The predefined non-inferiority margin was an increase in surgical failure rate of 7%.

MAIN OUTCOME MEASURES Primary outcome was recurrent prolapse stage two or higher of the uterus or vaginal vault (apical compartment) evaluated by Pelvic Organ Prolapse Quantification examination in combination with bothersome bulge symptoms or repeat surgery for recurrent apical prolapse at 12 months follow-up. Secondary outcomes were overall anatomical recurrences, functional outcome, complications, hospital stay, post-operative recovery, and sexual functioning.

RESULTS Sacrospinous hysteropexy was non-inferior regarding anatomical recurrence of the apical compartment with bothersome bulge symptoms or repeat surgery (n=0, 0%) compared to vaginal hysterectomy with uterosacral ligament suspension (n=4, 4.0%, difference -3.9%; 95% CI for difference -8.6% to 0.7%). There were no differences in overall anatomical recurrences, functional outcome, quality of life, complications, hospital stay, measures on post-operative recovery and sexual functioning between the two groups. Five serious adverse events were reported during hospital stay. None of the events was assumed to be related to the type of surgery.

CONCLUSIONS Uterus preservation by sacrospinous hysteropexy was non-inferior to vaginal hysterectomy with uterosacral ligament suspension regarding surgical failure of the apical compartment at 12 months follow-up.

TRIAL REGISTRATION trialregister.nl Identifier: NTR1866.

Introduction

Pelvic organ prolapse is a very common health problem. With a prevalence rate up to 40% in women over 45 years of age, millions of women are affected and the incidence is still rising due to ageing and increased obesity rates.[1] Pelvic organ prolapse has a negative influence on women's quality of life and is associated with physical, psychological, and sexual distress.

The lifetime risk for prolapse surgery is 11-20% and worldwide vaginal hysterectomy is the most commonly performed surgical procedure for uterine prolapse. [2-6] Performing a hysterectomy for uterine prolapse is not an evidence based practice and whether or not the uterus should be removed is an important matter of debate. Uterus preserving procedures, such as vaginal sacrospinous hysteropexy, in which the uterus is attached to the sacrospinous ligament, are becoming more popular. In a recent study we found a trend towards more uterus preservation in The Netherlands, which is in line with the fact that also more women prefer to 'save' their uterus in case of equal outcome with hysterectomy. [6-9] Uterus preservation is thought to be less invasive and in prospective non-randomised and retrospective cohort studies sacrospinous hysteropexy was as effective as vaginal hysterectomy with a similar rate of recurrence and repeat surgery but with shorter operating time, less blood loss, faster recovery, and fewer complications. [10-12] A hysterectomy has known benefits as well: it prevents development of uterine cancer and stops menstrual bleeding in premenopausal women. On the other hand women after vaginal hysterectomy may be at increased risk of recurrent prolapse since hysterectomy disrupts supportive structures of the pelvic floor. [13] To prevent future vaginal vault prolapse after hysterectomy additional vault suspension is recommended. [14,15] Randomised controlled trials (RCT's) comparing uterus preserving techniques and hysterectomy with vault suspension are limited. One RCT found more recurrent uterine prolapse after sacrospinous hysteropexy after 12 months but recurrence rate was only a secondary endpoint. [16] Another RCT found no differences in sexual functioning after six months but did not report on anatomical outcome. [17]

Due to lack of well-executed RCT's and clear guidelines on the treatment of uterine prolapse the practice pattern variation in surgical management of uterine prolapse is enormous and a Cochrane meta-analysis on pelvic organ prolapse surgery concluded that more research on this subject is necessary. [18] The SAVE U trial was designed to test the hypothesis that sacrospinous hysteropexy was non-inferior to vaginal hysterectomy with uterosacral ligament suspension regarding surgical failure after 12 months follow-up.

Study Design

A detailed version of the SAVE U trial protocol has been published previously. [19] In short, all women with pelvic organ prolapse quantification (POP-Q) stage two or higher uterine prolapse (uterine prolapse 1 cm above the hymen or beyond) requiring surgery were asked for participation. Participants were randomly assigned to sacrospinous hysteropexy or vaginal hysterectomy with uterosacral ligament suspension in a non-blinded multicentre randomised controlled non-inferiority trial.

Patients with co-existing anterior and/or posterior vaginal wall prolapse were allowed to participate and cervical elongation together with uterine prolapse was no reason to exclude women for participation. Concomitant repair of anterior and/or posterior vaginal prolapse (colporrhaphy) was allowed including anti-incontinence surgery. Patients with previous pelvic floor or prolapse surgery, known malignancy or abnormal cervical smears, a wish to preserve fertility, language barriers, presence of immunological or haematological disorders interfering with recovery after surgery, abnormal ultrasound findings of the uterus or ovaries, or abnormal uterine bleeding, and those who were unwilling to return for follow-up were excluded.

All participating centres (n= 4) were Dutch large non-university teaching hospitals. Centres had to offer both treatment modalities and were asked for participation if they were known to perform the interventions in the same standardized manner. All gynaecologists were experienced and performed a minimum of 20 procedures of each intervention before the start of the trial. As the participating hospitals were teaching hospitals, residents were allowed to perform procedures under direct supervision of the gynaecologist. Gynaecologists and residents of the participating centres assessed eligibility of patients. The decision to treat uterine prolapse surgically was a shared decision by the woman and her gynaecologist. Written patient information was provided and informed consent prior to randomisation was obtained. The trial was approved by the medical ethical committee of the Isala hospital (MEC 09-625) and the local ethical committees of the participating centres, in accordance with the Declaration of Helsinki. Patients were randomly allocated in a 1:1 ratio using a web-based application with computer-generated randomization tables with a block size of four, stratified by hospital and POP-Q stage. The trial was non-blinded as it was impossible to blind the surgeon and patient for the surgical procedure to which the patient was allocated. An independent physician who was not in any way involved in the treatment carried out follow-up after 12 months.

Outcome measures

Surgical failure at 12 months follow-up was the initial primary outcome. As outcome definitions to evaluate prolapse surgery were improved after start of this trial, during enrolment and before data analysis the primary outcome was changed into the following composite outcome measure: recurrent prolapse POP-Q stage 2 or higher in the apical compartment (uterus or vaginal vault) with bothersome bulge symptoms or repeat surgery for recurrent apical prolapse at 12 months follow-up. The medical ethical committee approved this change and during enrolment the protocol was published in an open access online journal. [19]

The original primary outcome, overall anatomical failure (prolapse POP-Q stage two or higher in any compartment) was evaluated as secondary outcome together with two additional definitions of surgical failure/success: (I) composite outcome of success defined as no prolapse beyond the hymen, no bothersome bulge symptoms and no repeat surgery or pessary use for recurrent prolapse within 12 months follow-up and (II) overall surgical failure: prolapse POP-Q stage two or higher, pessary use or repeat surgery for recurrent prolapse in any compartment within 12 months. [20] Other secondary outcomes were functional outcome, quality of life, complications, hospital stay, post-operative recovery, and sexual functioning.

Interventions

A detailed description of the study interventions was used to warrant a uniform technique amongst surgeons. [19] All women received perioperative antibiotics, thrombosis prophylaxis and a bladder catheter according to local hospital protocol. Analgesics were given post-operatively in accordance with local hospital protocol. All patients were advised to abstain from heavy physical work for a period of 6 weeks.

Sacrospinous hysteropexy

Sacrospinous hysteropexy was performed unilaterally to the right sacrospinous ligament. Access to sacrospinous ligament was obtained through the pararectal space. Two permanent sutures (Prolene 1.0, Ethicon, Somerville, NJ, USA) were placed under direct vision at least 2 cm from the ischial spine. Hereafter, additional anterior and/or posterior vaginal wall repair or incontinence surgery was performed if indicated. The permanent sutures were placed through the posterior side of the cervix and the sutures were tightened and the cervix redressed. The posterior vaginal wall was closed with absorbable sutures (Vicryl 2, Ethicon,

Somerville, NJ, USA). https://www.youtube.com/watch?v=ySSfy2A1_RM and https://www.youtube.com/watch?v=wjct1r37sTw

Vaginal hysterectomy

The vaginal wall around the cervix was circumcised. After bladder dissection the anterior peritoneum was opened. Then the posterior peritoneum was opened and the Douglas cul-de-sac entered. The uterosacral ligaments were identified, transected and ligated. In several steps the uterus was removed using clamps and sutures. Following removal of the uterus, the adnexa were inspected and the surgical pedicles inspected for bleeding. The peritoneum was closed using a delayed-absorbable suture (Vicryl 1.0, Ethicon, Somerville, NJ, USA). Additional vault suspension in this study was performed by uterosacral ligament suspension. With uterosacral ligament suspension, the vaginal vault is reattached to the proximal uterosacral ligaments without plicating the uterosacral ligaments or obliterating the cul-de-sac. [21] Concomitant anterior and/or posterior vaginal wall repair and anti-incontinence surgery were performed afterwards if indicated.

Measurements and Procedures

Gynaecological examination prior to surgery included pelvic ultrasound to exclude uterine or ovarian disease, cervical PAP-smear and vaginal inspection in 45° semi-upright position for staging pelvic organ prolapse by using the The Pelvic Organ Prolapse Quantification (POP-Q) system. [22] The POP-Q system involves quantitative measurements of various points of the vaginal wall using the hymen as a reference point. The degree of prolapse of the anterior vaginal wall, the posterior vaginal wall, and the uterus or vaginal vault is measured in centimeters above or proximal to the hymen (negative number) or centimeters beyond or distal to the hymen (positive number) with the plane of the hymen being defined as zero. Also the genital hiatus, the perineal body, and the total vaginal length are measured. Based on POP-Q measurements, a POP-Q stage (0-4) is determined for each compartment. The overall POP-Q stage is equal to the POP-Q stage of the most severely prolapsed compartment. Patients came to the hospital for POP-Q examination at baseline and 6 weeks, 6 months, 12 months after surgery and annually thereafter till 60 months follow-up. At the time of the follow-up visits women completed validated health-related and disease-specific quality of life questionnaires: Short Form-36 (SF-36), Euroqol 5D (EQ5-D), Urogenital Distress Inventory (UDI), Defecatory Distress Inventory (DDI),

and Incontinence Impact Questionnaire (IIQ). [23-26] The presence of bothersome bulge symptoms after surgery was defined as a positive answer to any of the following two questions from the UDI: '' do you experience a sensation of bulging or protrusion from the vagina?'' and ''do you have a bulge or something falling out that you can see in the vagina?'' in combination with a response 'somewhat bothered' to 'very much bothered' to the question ''how much does this bother you?'' To assess sexual functioning the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12), translated from the validated questionnaire but not validated for Dutch language, was used. [27]

During hospitalisation and the first 6 weeks after surgery patients kept a diary to evaluate post-operative pain (range 0-10) measured by the validated Visual Analogue Scale, pain medication, and post-operative recovery measured with the validated Recovery Index-10 (RI-10). [28]

Data were entered and registered using a web-based application facilitated by the Dutch consortium for studies in women's health and reproductivity (www.studies-obsgyn.nl).

Statistical Analysis

The sample size for this trial is based on the current primary outcome. Recurrence rates after vaginal hysterectomy with respect to the apical compartment vary from 0-12%[29], so that a failure rate including bothersome symptoms and repeat surgery after sacrospinous hysteropexy of 10% or more might be regarded as high. As we expected a failure rate of 3% based on outcomes of vaginal hysterectomy in a previous randomised study [16,30] the non-inferiority margin was set at 7%. This means that when the upper limit of the 95% confidence interval (CI) for the estimated difference in recurrence rate after sacrospinous hysteropexy versus vaginal hysterectomy exceeds 7%, SH is inferior to vaginal hysterectomy. Assuming an absolute recurrence rate of 3% in both groups and a two-sided α risk of 0.05, with two groups of 94 patients the trial had 80% power with a pre-specified non-inferiority margin of 7% to assess non-inferiority of sacrospinous hysteropexy. Considering a 10 percent loss to follow-up, 104 women per arm were needed and in total 208 women.

Study outcomes were assessed by intention-to-treat (ITT) analysis. In case of missing data on anatomical outcome at 12 months we applied two strategies: first the last observation carried forward (LOCF) ITT approach using data of the six months follow-up visit if available. If 6-month data were not available,

patients were left out of the ITT-LOCF analysis. For the second ITT analysis we applied conservative imputation for all patients with missing data at 12 months (worst case scenario, i.e. failure). In case of a missing questionnaire, the presence or absence of bothersome bulge symptoms was obtained from the 12-month follow-up visit. Also per protocol (PP) analysis was carried out on the primary and secondary outcomes regarding anatomic and surgical failure. This analysis included patients who completed the entire treatment protocol as originally planned with availability of POP-Q score at 12 months and absence of major protocol deviations.

95% CIs for differences in proportions were calculated using the Agresti-Coull method.[31] For exploratory purposes, we compared proportions and continuous variables between the groups using Fisher's exact tests and Mann-Whitney U tests. To compare mean continuous data within groups, paired sample t-tests were used. After Bonferroni multiple testing adjustment a P value below 0.002 was considered statistically significant. [32] All statistical analyses were performed with SPSS for windows (version 22.0.0.1).

Results

Between November 27, 2009, and March 12, 2012 208 women were randomly assigned to sacrospinous hysteropexy (n=103) or vaginal hysterectomy (n=105). Figure 1 shows the flow diagram. Baseline characteristics were similar between the groups (table 1) and no differences at baseline were found regarding pelvic measurements and characteristics (table 2).

In table 3 results on the primary outcome and the additional definitions of surgical failure are presented. Sacrospinous hysteropexy was non-inferior to vaginal hysterectomy regarding anatomical recurrence of the apical compartment with bothersome bulge symptoms or repeat surgery for recurrent apical prolapse: sacrospinous hysteropexy n=0, 0% versus vaginal hysterectomy n=4, 4.0%, difference -3.9% (95% CI -8.6% to 0.7%) for the ITT-LOCF approach. The ITT analysis with conservative imputation and the PP analysis also resulted in non-inferiority of sacrospinous hysteropexy. The original primary outcome parameter, overall anatomical failure, occurred 50.5% after sacrospinous hysteropexy, compared to 44.0% after vaginal hysterectomy (95% CI for difference -7.4% to 20.1%). No notable differences were found in anatomical recurrences in the different compartments, except for the posterior vaginal wall: sacrospinous hysteropexy 4.0% versus vaginal hysterectomy 14.1% (95% CI for difference -18.2% to -1.8%).

Intra- and postoperative details including the secondary outcomes complication rate and length of hospital stay are shown in table 4. Five serious adverse events (SAEs) during hospital stay were reported: two after hysterectomy and three after sacrospinous hysteropexy. One patient after vaginal hysterectomy developed a paralytic ileus. She experienced this problem also after previous orthopaedic surgery. Unfortunately she aspirated gastric content eight days after surgery, developed aspiration pneumonia and died because of multi-organ failure. The other SAEs were: 1. atrial fibrillation which required cardioversion (vaginal hysterectomy), 2. stroke two days after surgery; full recovery without any loss of function (sacrospinous hysteropexy), 3. postoperative pneumonia (sacrospinous hysteropexy) and 4. anaphylactic reaction on prophylactic antibiotics prior to the surgical procedure (sacrospinous hysteropexy); in this patient the surgical procedure was postponed until several months later, without any problems. None of the SAEs were judged to be related to the type of surgery.

Details on the other secondary outcomes can be found in table 5 and 6. There were no significant differences in functional outcome and quality of life between the groups (Table 5). Post-operative recovery was similar after both interventions with comparable RI-10 scores at 1, 2, 4 and 6 weeks after surgery (Table 6). Among the patients who completed the PISQ-12 before and after surgery, there was significant improvement in PISQ-12 scores in both the sacrospinous hysteropexy ($p<0.002$) and vaginal hysterectomy group ($p<0.002$) and there was no significant difference regarding total PISQ-scores between both interventions (Table 6).

VAS pain scores did not notably differ between both interventions except for day 14 in favour of hysterectomy. In eight out of nine patients who experienced buttock pain, a typical complaint after sacrospinous hysteropexy, the pain resolved (VAS<2) spontaneously within the first 6 weeks. One patient underwent suture cutting and vaginal hysterectomy after four months because of persistent pain localised at the place of the sacrospinous hysteropexy sutures. After this procedure she was free of symptoms.

Fourteen protocol deviations occurred: two patients received sacrospinous hysteropexy instead of vaginal hysterectomy due to technical difficulties during surgery (crossovers). In one patient allocated to vaginal hysterectomy, laparoscopic cystectomy prior to vaginal hysterectomy showed intra-abdominal adhesions and an abdominal hysterectomy was performed. In two women an exclusion criterion was ignored before randomisation: one patient had previous pelvic floor surgery (repair of posterior vaginal wall prolapse) and another patient suffered from primary sclerosing cholangitis with thrombocytopenia. Three patients who

were assigned to sacrospinous hysteropexy had abnormal PAP smears and were treated with electrosurgical excision (n=2) during prolapse surgery and/or follow-up. In six patients (6 of 102, 6%) apical suspension after vaginal hysterectomy was performed by a Mc Call culdoplasty instead of uterosacral ligament suspension. In the other patients uterosacral ligament suspension was performed (96 of 102, 94%). According to the ITT principle, we included these patients in the ITT analysis and all patients were analyzed as randomised. In the PP analysis these patients were excluded, except for the crossovers (n=2) as the primary outcome was related to efficacy and these women had no other protocol deviations, and the patients with abnormal PAP smears (n=3), as this was regarded as minor protocol deviation.

In the sacrospinous hysteropexy group three procedures (3%) and in the vaginal hysterectomy group 19 procedures (18%) were performed by residents. No statistically significant difference was found in overall surgical failure rate (recurrent prolapse, pessary use or repeat surgery) after surgery by either gynaecologist or resident (91 failures out of 180 procedures (50.6%) versus nine failures out of 19 procedures (47.4%), p=0.81). In one patient after sacrospinous hysteropexy (1.0%) endometrial cancer was diagnosed during follow-up and a laparoscopic hysterectomy was performed.

Urinary retention, which was defined as more than 150 ml urine retention after removal of the catheter, was similar between groups (table 4). These women received a transurethral catheter or were instructed to perform clean intermittent self-catheterisation. In all women spontaneous micturition was achieved after a maximum length of catheterisation of 40 days (median 5.0 days, range 1 - 40 days). After 12 months, 1 of 102 (1.0%) after sacrospinous hysteropexy versus 4 of 102 (3.9%, p=0.37) after vaginal hysterectomy had undergone subsequent surgical treatment for stress urinary incontinence.

Discussion

The SAVE U trial shows that treatment with sacrospinous hysteropexy is non-inferior to vaginal hysterectomy with uterosacral ligament suspension regarding surgical failure of the apical compartment both in the ITT and in the PP analysis. We found no notable differences in overall anatomical and surgical failure, functional outcome, quality of life, complications, post-operative recovery, hospital stay and sexual functioning between the interventions. Patients after sacrospinous hysteropexy reported more buttock pain after surgery but VAS pain scores were low and pain resolved within 6 weeks in the majority of cases.

Strengths and limitations of the study

Major strength of this study is the randomised multicentre design and sufficiently large study population. This is to our best knowledge the first randomised trial that compared uterus preservation with hysterectomy on a large scale using clinically relevant outcome measures. The study also has some limitations. First, our report is on a relatively short follow-up period of 12 months. However, results from registry studies suggest that the highest risk of prolapse surgery after hysterectomy is in the first year(s) after surgery. Furthermore not only long-term surgical outcome is important but also short-term secondary outcomes such as complication rate and postoperative recovery.[33, 34] Women gave consent for follow-up till 60 months after surgery and these data will be further analyzed.

After vaginal hysterectomy the ligatures of the uterosacral ligaments were to be sutured to the vaginal vault to aid in long-term vaginal support. However, in six patients the protocol was ignored and McCall culdoplasty was performed instead of uterosacral ligament suspension. During a McCall procedure, the uterosacral ligaments are plicated in the midline, incorporating the cul-de-sac peritoneum and posterior vaginal cuff. [35] Both procedures rely on the uterosacral ligaments for support of the vaginal apex but are considered different treatment modalities for vaginal vault suspension, which could have led to treatment differences. As far as we know, in literature there is no strong evidence on the best technique for vault suspension after vaginal hysterectomy and a recent published trial found similar outcomes after uterosacral ligament suspension and sacrospinous fixation for apical prolapse.[36] In the PP analysis these patients were excluded but this did not alter the conclusions.

Another limitation might be that residents were allowed to perform sacrospinous hysteropexy or vaginal hysterectomy under direct supervision of a gynaecologist because of their training position. Surgery by residents may have led to variation in procedures. In the hysterectomy group more procedures were performed by residents. No statistically significant difference was found in surgical failure rate in patients who underwent surgery by either gynaecologist or resident but the higher number of procedures performed by residents could have contributed to longer operation time in the vaginal hysterectomy group. Surgery performed by residents may improve the generalisability of the trial findings as their involvement in treatment of POP is common in the Dutch urogynaecological practice.

Comparison with other studies

The anatomical outcome after sacrospinous hysteropexy in our study is in line with previous studies [16,37] although the only previous randomised study showed opposite results: Dietz et al. have found a higher rate of anatomical recurrence of the apical compartment after sacrospinous hysteropexy (7 of 34 [21%] versus 1 in 31 [3%] after vaginal hysterectomy, p=0.03) after 12 months follow-up. Possible explanations for this difference might be differences in surgical protocol or skills, precise definition of the recurrence outcome, and sample size. The primary outcome in the study reported by Dietz et al. was recovery time instead of anatomical outcome. They considered a POP-Q stage two or higher of the uterus or vaginal vault as a recurrence. Recurrent prolapse was defined in our study as prolapse of the apical compartment POP-Q stage two or higher in combination with bothersome bulge symptoms or repeat surgery for recurrent apical prolapse. In our opinion, this composite outcome measure is more clinically relevant than outcome in terms of objective POP-Q scores alone. Barber et al. reported on different definitions of success after pelvic organ prolapse surgery in 2009.[20] Treatment success varied widely depending on the definition used, but definitions that included the absence of vaginal bulge symptoms had the strongest relationship with the patients assessment of overall improvement and treatment success. They furthermore concluded that the hymen is an important cut-off point for symptom development. As new trials probably will use these updated outcome definitions, we also analyzed our data using the hymen as anatomical threshold and also used their composite outcome measure, making this trial in the future comparable to others.

Although the presence of posterior vaginal wall prolapse in both groups was similar prior to surgery, more posterior vaginal wall repairs (colporrhaphies) were performed in the vaginal hysterectomy group. The surgeons were free to decide on concomitant surgery and in general this was decided intra-operative. One explanation might be that the surgeons felt that the more dorsal axis of the vagina after sacrospinous hysteropexy already protected against a recurrent posterior vaginal wall prolapse. Despite the higher number of posterior colporrhaphies more anatomical recurrences of the posterior compartment were found after hysterectomy with uterosacral ligament suspension, which supports this vision. The risk for recurrent anterior vaginal wall prolapse after sacrospinous hysteropexy is often discussed. We found no difference in occurrence of anatomical anterior vaginal wall prolapse. This is in line with previous studies: a retrospective study by Smilen et al. demonstrated that the occurrence of anterior vaginal wall prolapse was not altered by the

performance of a sacrospinous hysteropexy and the randomized study performed by Dietz and co-workers did not find more anterior vaginal wall prolapse after sacrospinous hysteropexy (51%) compared with a vaginal hysterectomy (64%) after one year.[12, 38]

Reoperation rates for (recurrent) pelvic organ prolapse did not differ. Two patients after uterine preservation ended up undergoing hysterectomy. In one patient this was because of persistent buttock pain. The overall rate of buttock pain after sacrospinous hysteropexy in our study (9%) is in line with other studies and the majority of patients had spontaneous resolution. [30] Preoperative counseling should include information about the potential risk of buttock pain postoperative. Endometrial carcinoma was found in 1 patient during follow-up (1%). A previous retrospective analysis of pathology findings after prolapse surgery with hysterectomy showed premalignant or malignant abnormalities in 17 of 644 patients (2.6%). [39] In that study, 2 patients (0.3%) had endometrial cancer diagnosed. Because of the low incidence and the early diagnosis of endometrial cancer due to blood loss we believe that future risk of malignancy should not be regarded as a valid reason to remove the uterus.

Clinical implications and future research

Uterus preservation has gained popularity during the last years among gynaecologists and patients. [6-9] A recent trial among 213 women from multiple study sites throughout the United States showed that 36% of the women preferred uterus preservation, 20% of the women preferred hysterectomy and 44% had no preference, assuming equal outcomes after both procedures.[7] Another preference study among 100 women showed that 60% would decline hysterectomy in case an equally efficacious alternative was available.[8] This trial provides evidence that sacrospinous hysteropexy is such an alternative and therefore this study has important implications for clinical practice. Women who want to avoid hysterectomy and preserve the uterus can be reassured that sacrospinous hysteropexy was found to be equally effective after short-term follow-up. However longer follow-up is necessary and also randomized controlled trials comparing other uterus preserving procedures are needed.

Conclusions

Based on the analysis after 12 months follow-up, we conclude that sacrospinous hysteropexy is non-inferior to vaginal hysterectomy with uterosacral ligament suspension regarding recurrent prolapse of the apical compartment with bothersome bulge symptoms or repeat surgery for recurrent apical prolapse. There were no differences in overall anatomical outcome, functional outcome, hospital stay, complications, post-operative recovery and sexual functioning.

WHAT IS ALREADY KNOWN ON THIS TOPIC

- Uterine prolapse is a very common health problem with increasing incidence due to ageing and increased obesity rates
- Vaginal hysterectomy is the standard treatment for uterine prolapse but uterus preservation is gaining popularity. No large randomised trials are available to compare both treatment options.

WHAT THIS STUDY ADDS

- Sacrospinous hysteropexy was non-inferior to vaginal hysterectomy with uterosacral ligament suspension regarding recurrent prolapse of the apical compartment with bothersome bulge symptoms or repeat surgery and no differences were found in overall anatomical outcome, quality of life, subjective outcome, hospital stay, recovery, complications and sexual functioning after 12 months
- Women can be offered the opportunity to choose for uterus preservation and avoid hysterectomy when uterine prolapse needs to be surgically corrected.

Author Contributions: All authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Detollenaere, den Boon, Vierhout, Van Eijnhoven

Acquisition of data: Detollenaere, den Boon, Stekelenburg, van Eijndhoven

Analysis and interpretation of data: Detollenaere, den Boon, Stekelenburg, IntHout, Vierhout, Kluivers, van Eijndhoven

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Statistical analysis: Detollenaere, IntHout, Kluivers.

Obtained funding: Detollenaere, van Eijndhoven

Administrative, technical, or material support: Detollenaere, den Boon, van Eijndhoven

Study supervision: Detollenaere, van Eijndhoven

Funding/Support: The SAVE U trial received an unrestricted grant from the Isala research foundation.

Role of the Sponsors: The funding source did not play any role in the design and conduct of the study; in the collection, management, analysis, or interpretation of the data; or in the preparation, review, or approval of the manuscript.

Conflict of Interest Disclosures: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Detollenaere - Nothing to disclose; den Boon - Astellas: Scientific Medical Advisor, writing an e-learning on incontinence for general practioners receiving consulting fee; Stekelenburg - Nothing to disclose; IntHout - Nothing to disclose; Kluivers KB - Nothing to disclose; Vierhout ME- Astellas: Advisory Committee Member receiving consulting fee; Van Eijndhoven - Johnson & Johnson / AMS / BARD: trainer receiving honoraria

Transparency: The corresponding author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; No important aspects of the study have been omitted and any discrepancies from the study as planned have been explained.

Data sharing: No additional data available.

Additional Contributions: We are thankful to the staff at participating centres for their assistance with study enrolment; We greatly appreciate the involvement of N. van Rijn for assistance with data collection and administrative support;

References

1 Slieker-ten Hove MC, Pool-Goudzwaard AL, Eijkemans MJ, Steegers-Theunissen RP, Burger CW, Vierhout ME. The prevalence of pelvic organ prolapse symptoms and signs and their relation with bladder and bowel disorders in a general female population. *Int Urogynecol J Pelvic Floor Dysfunct* 2009;20:1037–45.

2 Olsen AL, Smith VJ, Bergstrom JO, Colling JC, Clark AL. Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. *Obstet Gynecol* 1997;89:501–6.

3 De Boer TA, Slieker-ten Hove MC, Burger CW, Kluivers KB, Vierhout ME. The prevalence and factors associated with previous surgery for pelvic organ prolapse and or urinary incontinence in a cross sectional study in the Netherlands. *Eur J Obstet Gynecol Reprod Biol* 2011;158:343–9.

4 Jha S, Moran P. The UK national prolapse survey: 5 years on. *Int Urogynecol J* 2011;22:517–28.

5 Vanspauwen R, Seman E, Dwyer P. Survey of current management of prolapse in Australia and New Zealand. *Aust N Z J Obstet Gynaecol* 2010;50:262–7.

6 Detollenaere RJ, den Boon J, Kluivers KB, Vierhout ME, van Eijndhoven HW. Surgical management of pelvic organ prolapse and uterine descent in the Netherlands. *Int Urogynecol J* 2013;24:781–8.

7 Korbly NB, Kassis NC, Good MM, et al. Patient preferences for uterine preservation and hysterectomy in women with pelvic organ prolapse. *Am J Obstet Gynecol* 2013;209:470.e1–6.

8 Frick AC, Barber MD, Paraiso MF, Ridgeway B, Jelovsek JE, Walters MD. Attitudes toward hysterectomy in women undergoing evaluation for uterovaginal prolapse. *Female Pelvic Med Reconstr Surg* 2013;19:103–9.

9 Wu MP, Long CY, Huang KH, Chu CC, Liang CC, Tang CH. Changing trends of surgical approaches for uterine prolapse: an 11-year population-based nationwide descriptive study. *Int Urogynecol J* 2012;23:865–72.

10 Maher CF, Cary MP, Slack MC, Murray CJ, Milligan M, Schluter P. Uterine preservation or hysterectomy at sacrospinous colpopexy for uterovaginal prolapse? *Int Urogynecol J Pelvic Floor Dysfunct* 2001;12:381–4.

11 Brummen HJ, van de Pol G, Aalders CIM, Heintz APM, van der Vaart. Sacrospinous hysteropexy compared to vaginal hysterectomy as primary surgical treatment for a descensus uteri: effect on urinary symptoms. *Int Urogynecol J Pelvic Floor Dysfunct* 2003;14:350–5.

12 Hefni MA, El-Toukhy TA, Bhaumik J, Katsimanis E. Sacrospinous cervicocolpopexy with uterine conservation for uterovaginal prolapse in elderly women: an evolving concept. *Am J Obstet Gynecol* 2003;188:645–50.

13 Dällenbach P, Kaelin-Gambirasio I, Jacob S, Dubuisson JB, Boulvain M. Incidence rate and risk factors for vaginal vault prolapse repair after hysterectomy. *Int Urogynecol J Pelvic Floor Dysfunct* 2008;19:1623–9.

14 Kantartzis KL, Turner LC, Shepherd JP, Wang L, Winger DG, Lowder JL. Apical support at the time of hysterectomy for uterovaginal prolapse. *Int Urogynecol J* 2014; doi 10.1007/s00192-014-2474-y.

15 Bulletins-Gynecology ACoP (2007) ACOG practice bulletin No.85: pelvic organ prolapse. *Obstet Gynecol* 110:717-729. doi:10.1097/01. AOG.0000263925.97887.72.

16 Dietz V, van der Vaart CH, van der Graaf Y, Heintz P, Schraffordt Koops SE. One-year follow-up after sacrospinous hysteropexy and vaginal hysterectomy for uterine descent: a randomized study. *Int Urogynecol J Pelvic Floor Dysfunct* 2010;2:209–16.

17 Jeng CJ, Yang YC, Tzeng CR, Shen J, Wang LR. Sexual functioning after vaginal hysterectomy or transvaginal sacrospinous hysteropexy for uterine prolapse: a comparison. *J Reprod Med* 2005;50:669–74.

18 Maher C, Feiner B, Baessler K, Schmid C. Surgical management of pelvic organ prolapse in women. *Cochrane Database Syst Rev* 2013; 30;4:CD004014.

19 Detollenaere RJ, den Boon J, Stekelenburg J et al. Treatment of uterine prolapse stage 2 or higher: a randomized multicenter trial comparing sacrospinous fixation with vaginal hysterectomy (SAVE U trial). *BMC Womens Health* 2011;15;11:4.

20 Barber MD, Brubaker L, Nygaard I et al. Defining success after surgery for pelvic organ prolapse. *Obstet Gynecol* 2009;114:600–9.

21 Cruikshank SH. Preventing posthysterectomy vaginal vault prolapse and enterocele during vaginal hysterectomy. *Am J Obstet Gynecol* 1987:156:1433-40.

21 Bump RC, Mattiasson A, Bo K et al. The standardization of terminology of female pelvic organ prolapse and pelvic floor dysfunction. *Am J Obstet Gynecol* 1996;175:10–7.

23 Ware JE, Kosinski M, and Keller SD. SF-36 physical and mental component summary measures-a users' manual. 1994. Boston: New England Medical Center, The Health Institute.

24 van der Vaart CH, de Leeuw JR, Roovers JP, Heintz AP. Measuring health-related quality of life in women with urogenital dysfunction: the urogenital distress inventory and incontinence impact questionnaire revisited. *Neurourol Urodyn* 2003;22:97–104.

25 Roovers JP, van der Bom JG, van der Vaart CH, Heintz AP. Prediction of findings at defecography in patients with genital prolapse. *BJOG* 2005; 112:1547–53.

26 Lamers LM, Stalmeier PF, McDonnell J, Krabbe PF, van Busschbach JJ. Measuring the quality of life in economic evaluations: the Dutch EQ-5D tariff. *Ned Tijdschr Geneeskd* 2005;149:1574–8.

27 Schweitzer KJ, de Jong M, Milani AL: Prolaps en seks: hoe meten we de relatie? *Ned Tijdschr Obst Gyn* 2008;121:79-82.

28 Kluivers KB, Hendriks JC, Mol BW et al. Clinimetric properties of 3 instruments measuring postoperative recovery in a gynecologic surgical population. *Surgery* 2008;144:12–21.

29 Dietz V, Schraffordt Koops SE, van der Vaart CH (2009) Vaginal surgery for uterine descent; which options do we have? A review of the literature. *Int Urogynecol J Pelvic Floor Dysfunct* 20:349–56

30 Dietz V, Schraffordt Koops S, van der Graaf Y, Heintz P, van der Vaart C. Sacrospinous hysteropexy and vaginal hysterectomy for uterine descent: a randomized study. *Int Urogynecol J* 2008;19:S1-166.

31 Agresti A, Coull B. Approximate is better than 'exact' for interval estimation of binomial proportions. *The American Statistician* 1998;52:119–26.

32 Bland JM, Altman DG. Multiple significance tests: the Bonferroni method. *BMJ*. 1995;310:170.

33 Lykke R, Blaakær J, Ottesen B, Gimbel H. Pelvic organ prolapse (POP) surgery among Danish women hysterectomized for benign conditions: age at hysterectomy, age at subsequent POP operation, and risk of POP after hysterectomy. *Int Urogynecol J.* 2015;26:527-32.

34 Altman D, Falconer C, Cnattinguis S, Granath F. Pelvic organ prolapse surgery following hysterectomy on benign indications. *Am J Obstet Gynecol* 2008;198:572.e1-6

35 McCall ML. Posterior culdoplasty; surgical correction. *Obstet Gynecol* 1957:10:595.

36 Barber MD, Brubaker L, Burgio KL et al. Comparison of 2 transvaginal surgical approaches and

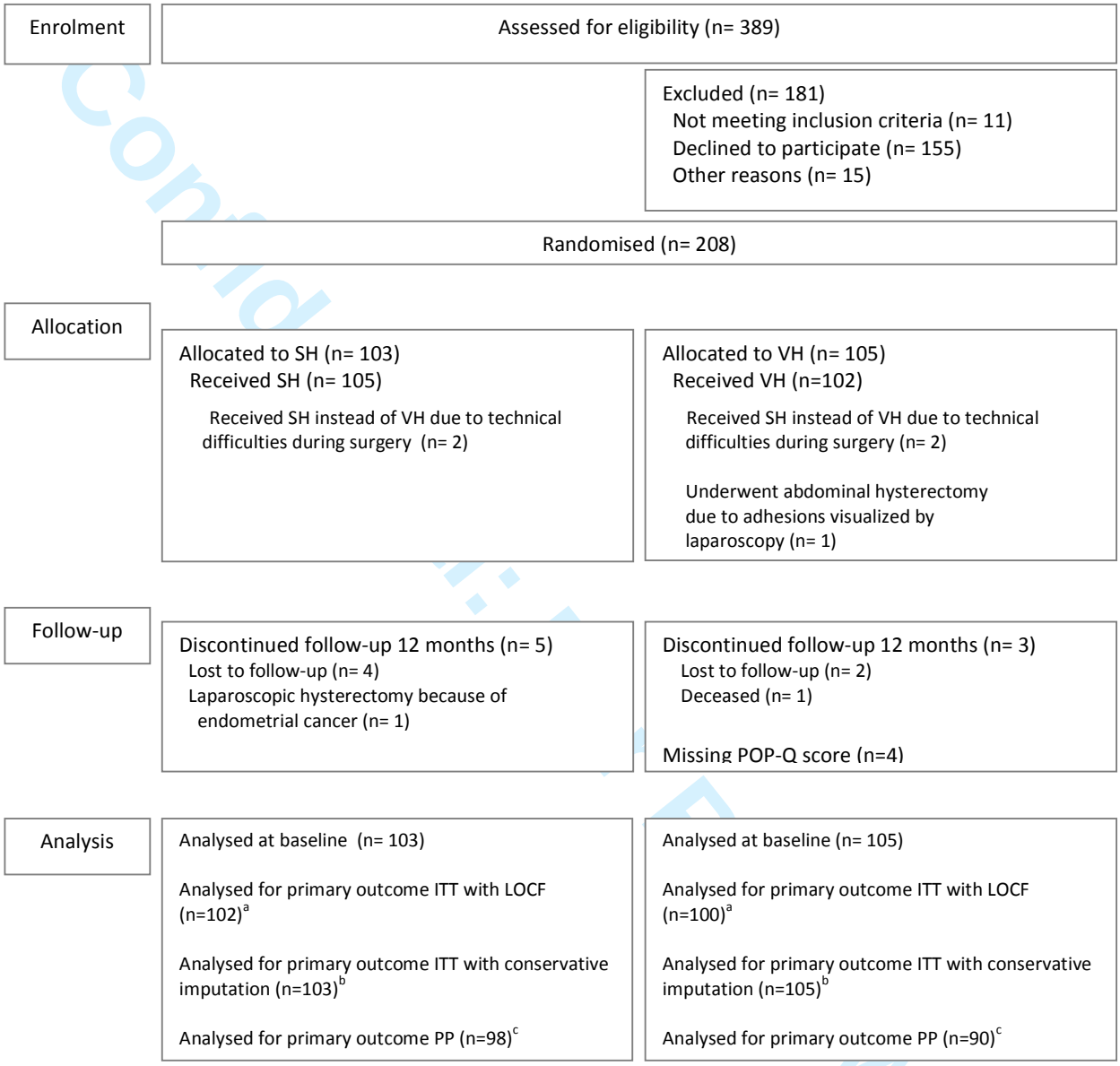
perioperative behavioral therapy for apical vaginal prolapse: the OPTIMAL randomized trial. *JAMA* 2014;311:1023-34.

37 Gutman R, Maher C. Uterine-preserving POP surgery. *Int Urogynecol J* 2013;24:1803–1813.

38 Smilen SW, Saine J, Wallach SJ, Porges RF. The risk of cystocele after sacrospinous ligament fixation. *Am J Obstet Gynecol* 1998;179:1465-1471.

39 Renganathan A, Edwards R, Duckett JR. Uterus conserving prolapse surgery—what is the chance of missing a malignancy? *Int Urogynecol J* 2010;21:819–821.

***Figure 1*. Study flowdiagram SAVE U trial**



ITT= intention to treat; LOCF= last observation carried forward; PP= per protocol; SH=sacrospinous hysteropexy; VH=vaginal hysterectomy;

[a] ITT: 2 patients allocated to VH received SH and were analysed in the VH group. In the SH group 6 month follow-up data were not available for LOCF in 1 patient; in the VH group LOCF data were not available in 6 patients; 1 patient after VH had a recurrent apical prolapse confirmed by the surgeon but POP-Q was missing, this patient was included in the ITT-LOCF analysis.

[b] missed data imputed as failure

[c] PP analysis: 2 patients allocated to VH received SH and were analysed in the SH group; Excluded PP-analysis: lost for follow-up at 12 months (n=8), POP-Q score was missing or incomplete (n=5) and major protocol deviations (n=9); Two patients met two criteria to be excluded from PP analysis.

***Table 1*. Baseline characteristics**

	SH (n=103)	VH (n=105)
Age in years, median (range)	62.7 (45 to 85)	61.9 (33 to 82)
Highest educational level		
Primary / secondary school	14 (14%)	7 (7%)
High school	78 (77%)	82 (80%)
Bachelor, master or academic degree	9 (9%)	13 (13%)
Comorbidity		
Cardiovascular disease	39 (38%)	32 (31%)
Diabetes mellitus	5 (5%)	5 (5%)
Respiratory disease	3 (3%)	7 (7%)
Current smoker	13 (14%)	9 (10%)
Vaginal deliveries, median (range)	2 (0 to 7)	3 (0 to 7)
Caesarean deliveries, median (range)	0 (0 to 1)	0 (0 to 2)
Body Mass Index (kg/m^2), mean (SD)	26.0 (3.3)	25.9 (3.5)

SH=sacrospinous hysteropexy; VH=vaginal hysterectomy; Data are number of patients (percentage) unless otherwise specified. Percentages were calculated using non-missing data. All patients were analyzed as allocated.

***Table 2*. Pelvic measurements and characteristics at baseline**

	SH (n=103)	VH (n=105)
POPQ stage uterine prolapse (POP-Q point C) [a]		
2	67 (65.0%)	66 (62.9%)
3	28 (28.2%)	29 (27.6%)
4	8 (7.8%)	10 (9.5%)
Anterior prolapse POP-Q stage 2 to 4 (Ba ≥ -1)	94 (94.0%)	95 (92.2%)
Posterior prolapse POP-Q stage 2 to 4 (Bp ≥ -1)	29 (29.0%)	33 (32.0%)
Prolapse beyond the hymen		
Apical (POP-Q C > 0)	48 (48.0%)	43 (41.7%)
Anterior (POP-Q Aa or Ba > 0)	71 (71.0%)	72 (70.0%)
Posterior (POP-Q Ap or Bp > 0)	11 (11.0%)	11 (10.7%)
Overall POP-Q stage prolapse [a]		
2	25/100 (25.0%)	36/103 (35.0%)
3	70/100 (70.0%)	62/103 (60.2%)
4	5/100 (5.0%)	5/103 (4.9%)
Vaginal bulge symptoms		
Any	94/101 (93.1%)	98/103 (95.1%)
Bothersome	93/100 (93.0%)[b]	96/101 (95.0%)

POP-Q=Pelvic Organ Prolapse Quantification; SH=sacrospinous hysteropexy; VH=vaginal hysterectomy; Data are number of patients (percentage) or mean (standard deviation) unless otherwise specified. Percentages were calculated using non-missing data. All patients were analyzed as allocated. 5 POP-Q scores were missing at baseline.

[a] The POP-Q system involves quantitative measurements of various points of the vaginal wall using the hymen as a reference point. The degree of prolapse of the anterior vaginal wall (Aa and Ba), the posterior vaginal wall (Ap and Bp), and the uterus or vaginal vault (C) is measured in centimeters above or proximal to the hymen (negative number) or centimeters beyond or distal to the hymen (positive number) with the plane of the hymen being defined as zero.POP-Q stage 2: the most distal prolapse is between 1 cm above and 1 cm beyond the hymen; stage 3: the most distal prolapse is prolapsed > 1 cm beyond the hymen but no further than 2 cm less than the total vaginal length; stage 4: represents total prolapse.

[b] not all patients were 'bothered' at baseline. The questionnaire was provided after patients consented for participation and the amount of bother could differ as reported at the outpatient clinic.

Table 3. **Pelvic organ prolapse outcomes and pelvic measurements at 12 months follow-up**

	SH	VH	Difference (95%CI)
Recurrent apical prolapse stage ≥2 with bothersome symptoms or repeat surgery for apical prolapse[a]			
ITT analysis with LOCF	0/102 (0.0%)	4/100 (4.0%)	-3.9% (-8.6 to 0.7)
ITT analysis with conservative imputation	6/103 (5.8%)	10/105 (9.5%)	-3.6% (-11.2 to 3.9)
PP analysis	0/98 (0.0%)	3/90 (3.3%)	-3.3% (-8.0 to 1.3)
Overall surgical failure: prolapse POP-Q stage ≥ 2 (any compartment) or repeat surgery or pessary use			
ITT analysis with LOCF	52/102 (51.0%)	49/100 (49.0%)	1.9% (-11.8 to 15.7)
ITT analysis with conservative imputation	55/103 (53.4%)	54/105 (51.4%)	1.9% (-11.6 to 15.5)
PP analysis	51/98 (52.0%)	44/90 (48.9%)	3.1% (-11.2 to 17.4)
Composite outcome success: no prolapse beyond the hymen and absence of bothersome bulge symptoms and no repeat surgery or pessary use			
ITT analysis with LOCF	91/102 (89.2%)	83/100 (83.0%)	6.1% (-3.6 to 15.8)
ITT analysis with conservative imputation	87/103 (84.5%)	82/105 (78.1%)	6.2% (-4.5 to 16.9)
PP analysis	87/98 (88.8%)	75/90 (83.3%)	5.3% (-4.7 to 15.5)
Overall anatomical failure: prolapse POP-Q stage ≥2 (any compartment)[b]	51/101 (50.5%)	44/100 (44.0%)	6.4% (-7.4 to 20.1)
Anatomical failure apical compartment	2/102 (2.0%)	7/100 (7.0%)	-5.0% (-11.1 to 1.2)
Anatomical failure anterior compartment	47/101 (46.5%)	33/99 (33.3%)	12.9% (-0.5 to 26.4)
Anatomical failure posterior compartment	4/101 (4.0%)	14/99 (14.1%)	-10.0% (-18.2 to -1.8)
Prolapse beyond the hymen[b]			
Apical (POP-Q C > 0)	0/102 (0.0%)	4/100 (4.0%)	-3.9% (-8.6 to 0.7)
Anterior (POP-Q Ba > 0)	8/101 (7.9%)	6/99 (6.1%)	1.8% (-5.6 to 9.2)
Posterior (POP-Q Bp > 0)	0/101 (0.0%)	2/99 (2.0%)	-2,0 (-5.9 to 1.9)
Surgery[b]			
Repeat surgery for recurrent prolapse	1/102 (1.0%)	4/102 (3.9%)	-2.9% (-7.8 to 2.0)
Repeat surgery apical compartment	0/102 (0.0%)	2/102 (2.0%)	-1.9% (-5.7 to 1.8)
Repeat surgery anterior compartment	1/102 (1.0%)	4/102 (3.9%)	-2.9% (-7.8 to 2.0)
Repeat surgery posterior compartment	0/102 (0.0%)	1/102 (1.0%)	-1.0% (-4.2 to 2.3)
Primary surgery different site[c]	0/102 (0.0%)	3/102 (2.9%)	-2.9% (-7.1 to 1.3)
Surgery for non-prolapse conditions			
Anti-incontinence	1/102 (1.0%)	4/102 (3.9%)	-2.9% (-7.8 to 2.0)
Hysterectomy	2/100 (2.0%)	-	

ITT=intention to treat; LOCF= last observation carried forward; POP-Q=Pelvic Organ Prolapse Quantification; PP=per protocol; SH=sacrospinous hysteropexy; VH= vaginal hysterectomy; Data are number of patients (percentage) or mean (standard deviation) unless otherwise specified. Percentages were calculated using non-missing data. P values were calculated using Fisher's exact test; 95% confidence intervals (CI) were calculated using the method of Agresti and Coull.

[a] Primary outcome of this study.

[b] ITT with LOCF

[c] reoperation for POP in non-operated compartment

***Table 4*. Intra- and postoperative details**

	SH (n=103)	VH (n=105)	Difference (95%)
Intraoperative			
Operating time (min)	59 (13)	72 (21)	-13.5 (-18.5 to -8.6)
Estimated blood loss (mL)	202 (74)	209 (112)	-6.5 (-32.8 to 20.0)
Complications			
Related to use antibiotics	1 (1%)	0 (0%)	1.0 (-2.2 to 4.2)
Related to surgery	0 (0%)	1 (1%)[a]	-1.0 (-4.2 to 2.2)
Concomitant surgery			
Anti-incontinence	4 (4%)	4 (4%)	0.1 (-5.7 to 5.8)
Anterior colporrhaphy	100 (97%)	104 (99%)	-1.9 (-6.5 to 2.6)
Posterior colporrhaphy	30 (29%)	52 (50%)	-20 (-33.0 to -7.0)
Anterior and posterior colporrhaphy	30 (29%)	52 (50%)	-20 (-33.0 to -7.0)
Surgeon			
Gynaecologist	98 (97%)	85 (82%)	13.9 (5.1 to 22.7)
Resident	3 (3%)	19 (18%)	-14.9 (-23.2 to -6.6)
Postoperative			
Length of hospitalisation (days)	3 (1)	3 (1)	-0.1 (-0.4 to 0.2)
Complications during hospital stay			
Death	0 (0%)	1 (1%)	-1.0 (-4.2 to 2.2)
Re-operation because of bleeding	0 (0%)	1 (1%)	-1.0 (-4.2 to 2.2)
Cerebrovasculair accident	1 (1%)	0 (0%)	1.0 (-2.2 to 4.2)
Buttock pain	9 (9%)	0 (0%)	8.6 (2.6 to 14.5)
Urinary retention	15 (15%)	12 (11%)	3.1 (-6.2 to 12.4)
Infection needing antibiotics	3 (3%)	0 (0%)	2.9 (-1.3 to 7.0)
Other			
Endometrial carcinoma	1 (1%)	0 (0%)	1.0 (-2.2 to 4.2)

SH=sacrospinous hysteropexy; VH=vaginal hysterectomy. Data are number of patients (percentage) or mean (standard deviation) unless otherwise specified. Percentages were calculated using non-missing data. All patients were analyzed as allocated (ITT).

[a] bowel injury during abdominal hysterectomy

Table 5. **Functional outcome and quality of life (median and interquartile ranges of domain scores) after SH and VH at 12 months follow-up**

	Before surgery		12 months after surgery		
	SH (n=101)	VH (n=104)	SH (n=97)	VH (n=99)	P value*
UDI domain scores [a]					
Overactive bladder	0 (0, 44)	22 (0, 33)	0 (0, 11)	0 (0, 11)	0.34
Urinary incontinence	17 (0, 33)	17 (0, 33)	0 (0, 17)	0 (0, 17)	0.11
Obstructive micturition	8 (0, 33)	17 (0, 33)	0 (0, 0)	0 (0, 0)	0.71
Genital prolapse	50 (33, 67)	67 (33, 67)	0 (0, 0)	0 (0, 0)	0.86
Pain	17 (0, 33)	17 (0, 33)	0 (0, 0)	0 (0, 0)	0.86
DDI domain scores [a]					
Obstipation	0 (0, 17)	0 (0, 17)	0 (0, 0)	0 (0, 0)	0.65
Obstructive defecation	0 (0, 17)	0 (0, 10)	0 (0, 8)	0 (0, 8)	0.85
Pain	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0.42
Incontinence	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0.38
Flatus	33 (0, 33)	33 (0, 33)	0 (0, 33)	33 (0, 33)	0.20
IIQ domain scores [b]					
Mobility	11 (0, 33)	11 (0, 22)	0 (0, 11)	0 (0, 11)	0.50
Physical	0 (0, 33)	0 (0, 33)	0 (0, 0)	0 (0, 0)	0.81
Social	11 (0, 22)	0 (0, 11)	0 (0, 0)	0 (0, 0)	0.99
Embarrasment	0 (0, 17)	0 (0, 17)	0 (0, 0)	0 (0, 0)	0.12
Emotion	0 (0, 33)	0 (0, 22)	0 (0, 0)	0 (0, 0)	0.56
SF-36 domain scores [c]					
Physical functioning	80 (55, 90)	80 (65, 90)	90 (75, 100)	85 (70, 95)	0.27
Social functioning	94 (75, 100)	88 (75, 100)	100 (88, 100)	100 (75, 100)	0.20
Role limitations physical	75 (6, 100)	100 (50, 100)	100 (100, 100)	100 (75, 100)	0.89
Role limitations emotional	100 (75, 100)	100 (100, 100)	100 (100, 100)	100 (100, 100)	0.78
Mental health	84 (72, 92)	84 (72, 88)	84 (76, 92)	84 (72, 92)	0.57
Vitality	70 (50, 80)	70 (55, 80)	75 (55, 80)	75 (65, 80)	0.39
Bodily pain	78 (59, 100)	80 (67, 100)	100 (67, 100)	100 (78, 100)	0.92
General health perception	75 (55, 85)	75 (61, 85)	75 (60, 90)	75 (60, 90)	0.72
Health change	50 (25, 50)	50 (50, 50)	75 (50, 100)	75 (50, 100)	0.52

DDI: defecatory distress inventory; IIQ: incontinence impact questionnaire; SF-36: short-form 36; SH: sacrospinous hysteropexy; UDI: urogenital distress inventory; VH: vaginal hysterectomy; Data are presented as median (interquartile range). All patients were analyzed as allocated.

[a] UDI and DDI: 0=no symptoms or not bothersome and 100=most bothersome symptoms.

[b] IIQ: 0=best quality of life and 100=worst quality of life.

[c] SF-36: 0= worst quality of life and 100= best quality of life.

* P value for exploratory purposes: Mann-Whitney U test of SH vs VH.

Table 6. **Post-operative recovery and sexual functioning after SH and VH after 12 months follow-up**

	SH		VH		P value*
	n=	Score	n=	Score	
Recovery index-10[a]					
Week 1	99	32 (7)	99	33 (6)	0.66
Week 2	100	34 (7)	99	34 (7)	0.58
Week 4	98	36 (7)	98	36 (6)	0.82
Week 6	98	38 (8)	99	38 (9)	0.87
PISQ-12 [b]					
Total PISQ-12 score baseline	56	33 (6)	64	35 (5)	0.05
Total PISQ-12 score follow-up 12 months	49	37 (5)[‡]	56	37 (4)[‡]	0.62

SH=sacrospinous hysteropexy; VH=vaginal hysterectomy; PISQ-12: pelvic organ prolapse/urinary incontinence sexual questionnaire; Data are presented as mean (standard deviation).
[a:] RI-10 is a 10-item questionnaire measuring postoperative recovery on 5-point Likert scales. The summary scale score ranges from 10 to 50, where 50 indicates a perfect recovery.
[b:] Total PISQ-12 scores ranges from 0, which represents poorest sexual function, to 48 best sexual function.
P* value for exploratory purposes: independent samples t-test of SH vs VH.
[‡] not showed: paired sample test baseline score and follow-up score (SH <0.002 and VH <0.002)