

ZUYDERLAND MEDISCH CENTRUM



Vaginal hysterectomy versus vaginal **Assisted NOTES Hysterectomy (VANH)**: a randomised controlled trial

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PROTOCOL TITLE

'Vaginal hysterectomy versus vaginal Assisted NOTES Hysterectomy (VANH)': a randomised controlled trial

| | |
|--|---|
| Protocol ID | <include protocol ID given by sponsor or investigator> |
| Short title | VANH-trial |
| EudraCT number | Not applicable |
| Version | 2 |
| Date | 13-03-2021 |
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| Sponsor (in Dutch: verrichter/opdrachtgever) | Not applicable |
| Subsidising party | Not applicable |
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| Laboratory sites | Not applicable |
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LIST OF ABBREVIATIONS AND RELEVANT DEFINITIONS

| | |
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| ABR | General Assessment and Registration form (ABR form), the application form that is required for submission to the accredited Ethics Committee; in Dutch: Algemeen Beoordelings- en Registratieformulier (ABR-formulier) |
| AE | Adverse Event |
| AH | Abdominal hysterectomy |
| AR | Adverse Reaction |
| BMI | Body Mass Index |
| BWO | Bureau Wetenschappelijk Onderwijs |
| CA | Competent Authority |
| CCMO | Central Committee on Research Involving Human Subjects; in Dutch: Centrale Commissie Mensgebonden Onderzoek |
| CM | Centimeter |
| CTCM | Clinical Trial Centre Maastricht |
| CV | Curriculum Vitae |

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| DSMB | Data Safety Monitoring Board |
| eCRF | Case Report Form |
| EU | European Union |
| EudraCT | European drug regulatory affairs Clinical Trials |
| GCP | Good Clinical Practice |
| GDPR | General Data Protection Regulation; in Dutch: Algemene Verordening Gegevensbescherming (AVG) |
| HBO | Hoger Beroeps Onderwijs |
| IB | Investigator's Brochure |
| IC | Informed Consent |
| IMP | Investigational Medicinal Product |
| IMPD | Investigational Medicinal Product Dossier |
| KG | Kilogram |
| MBO | Middelbaar beroeps onderwijs |
| METC | Medical research ethics committee (MREC); in Dutch: medisch-ethische toetsingscommissie (METC) |
| Mg | Milligram |
| NFU | Nederlandse Federatie van Universitaire Medische Centra |
| (v)NOTES | (Vaginal) Natural Orifice Transluminal Endoscopic Surgery |
| NRS | Numeric Rating Scale |
| POPQ | Pelvic Organ Prolaps Quantification |
| QoL | Quality of Life |
| QoR-40 | Quality of Recovery – 40 |
| RCT | Randomized Controlled Trial |
| RH | Robot-assisted hysterectomy |
| RI-10 | Recovery Index 10 |
| (S)AE | (Serious) Adverse Event |
| SDD | Same day discharge |
| SPC | Summary of Product Characteristics; in Dutch: officiële productinformatie IB1-tekst |
| Sponsor | The sponsor is the party that commissions the organisation or performance of the research, for example a pharmaceutical company, academic hospital, scientific organisation or investigator. A party that provides funding for a study but does not commission it is not regarded as the sponsor, but referred to as a subsidising party. |
| SUSAR | Suspected Unexpected Serious Adverse Reaction |
| (T)LH | (Total) Laparoscopic Hysterectomy |
| UAVG | Dutch Act on Implementation of the General Data Protection Regulation; in Dutch: Uitvoeringswet AVG |
| VANH | Vaginal Assisted NOTES hysterectomy |
| VAS | Visual Analogue Scale |
| VH | Vaginal hysterectomy |
| WMO | Medical Research Involving Human Subjects Act; in Dutch: Wet Medisch-wetenschappelijk Onderzoek met Mensen |
| WO | Wetenschappelijk onderwijs |

SUMMARY

Rationale: Natural orifice transluminal endoscopic surgery (NOTES) is a minimal invasive technique using the natural body orifices like stomach, oesophagus, bladder, rectum and vagina to access the human body for surgery. In 2012, the first vaginal NOTES (vNOTES) hysterectomy was performed. Potential benefits of vNOTES hysterectomy, also called the vaginal assisted NOTES hysterectomy (VANH) are no visible scars, less pain and a shorter hospital stay compared with laparoscopic hysterectomy as shown in the HALON trial [1]. Up to now, no studies have compared the vNOTES hysterectomy with vaginal hysterectomy.

Objective: The aim of this study is to compare the vNOTES hysterectomy with the vaginal hysterectomy for same day-discharge (SDD), complications, treatment related outcomes, post-operative recovery, quality of life and cost-effectiveness.

Study design: The study concerns a single-blinded, multicentre, randomised controlled trial.

Study population: Eligible women who fulfil the inclusion criteria and will undergo a hysterectomy for benign indication.

Intervention: The study population will be randomly allocated to the VANH-group, who undergo a vaginal assisted NOTES hysterectomy (intervention group) or the vaginal hysterectomy group (control-group) and the participants will be single blinded. The pre- and postoperative care will be the same for both groups.

Main study parameters/endpoints: Primary outcome is the percentage of patients that underwent the hysterectomy as in SDD setting. A total of 41 patients should be included in the control group and a total of 83 patients in the intervention group, using an enrolment ratio of 1:2, with an alpha of 0.05 and a power of 0.8.

The secondary outcomes are complications, treatment related outcomes, post-operative recovery, quality of life and cost-effectiveness.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:

vNOTES is a new surgical technique, but a combination of two existing techniques namely the vaginal hysterectomy and the laparoscopic hysterectomy. Only one randomized controlled trial has been published, comparing the total laparoscopic hysterectomy (TLH) with the VANH, which shows no inferiority of the vNOTES technique compared to a laparoscopy [1]. A recent case series study has been published about the complication rate in VANH. There was a total complication rate in the hysterectomy group of 5.2%, in which 1.4% was intra-operative and 3.8% postoperative [2]. Theoretically it is possible that the VANH causes less intra-operative complications because of an improved view during the procedure. No further literature is known about VH versus VANH. Participants of the study should fill in multiple questionnaires before randomization and postoperative about their general health, pain experience and used analgesics.

1. INTRODUCTION AND RATIONALE

The hysterectomy is one of the most performed gynaecological surgeries worldwide [3, 4].

In the Netherlands about 14.500 hysterectomies are performed yearly [5]. The most common benign indications to perform a hysterectomy are abnormal uterine bleeding, uterine leiomyomas, endometriosis or adenomyosis, chronic pelvic pain, uterine prolapse, benign ovarian neoplasm, hyperplasia or atypia of the endometrium or cervical dysplasia [6-8].

The four approaches to perform a hysterectomy for benign disease are abdominal hysterectomy (AH), vaginal hysterectomy (VH), (total) laparoscopic hysterectomy ((T)LH) and robotic-assisted hysterectomy (RH) [4, 9].

VH appears to be superior to the AH, resulting in a quicker recovery [6]. The LH results in a quicker recovery than the AH and VH, but increases the risks of damage to the bladder or ureter [6]. That is why a recent Cochrane review advises to perform a VH when feasible for women undergoing a hysterectomy for a benign indication [6]. When VH is technically not feasible, a LH or AH is performed. LH resulted in more rapid recovery, fewer febrile episodes and less wound complications compared to AH [6]. The RH is not superior compared to the LH and is associated with higher costs [10].

Since the introduction of laparoscopy, the VH and AH decreased and the rate of LH significantly increased between 2002 and 2012 [11]. Performing a LH gives the opportunity to inspect the abdominal cavity and to easily perform an opportunistic salpingectomy compared to VH [10]. An opportunistic salpingectomy during a hysterectomy for benign indication might reduce the overall risk of ovarian cancer [12].

Additionally, patients experience less postoperative pain after a LH compared to a VH and therefore need less post-operative pain medication [10]. Advantages of the VH compared to the LH are a shorter operation duration, no visible scars and a lower chance of dehiscence of the vaginal cuff [10].

In 2004, a novel approach of endoscopic surgery was described, 'Natural Orifice Transluminal Endoscopic Surgery (NOTES)' by researchers at the John Hopkins University [13]. It is a surgical technique using natural orifices of the body (e.g. mouth, anus, urethra, vagina) to perform scarless surgery [14]. The vaginal approach is called the vNOTES technique. NOTES is an emerging field within minimal access surgery, evolves and presents multiple possibilities for innovation and development. The initial approach was trans gastric, but subsequently, NOTES has been evolved, resulting in trans rectal, trans gastric, transvaginal, and transurethral approaches nowadays [15-17].

In 2012, the first vNOTES hysterectomy, also called vaginal assisted NOTES hysterectomy (VANH) was performed [18]. vNOTES surgery can be used for different indications, for example hysterectomy, adnexectomy or salpingectomy in case of an ectopic pregnancy [19].

In 2018, the first randomised controlled trial (RCT) comparing TLH with VANH in 70 women was published [1]. This HALON trial showed VANH was non-inferior to TLH [1]. Compared to TLH, surgery time was significantly shorter, patients experience less post-operative pain and same day discharge (SDD) was possible in 77% of the women who underwent the VANH compared to 43% after TLH [1]. Besides, the VANH showed less post-operative complications [1].

Except for the HALON trial and two retrospective studies [20, 21] and case-control studies [22, 23] there is little literature about VANH.

No studies have been performed comparing the VH with the VANH. Because the VH is the preferred method to perform a hysterectomy for a benign indication [24], there is a need to compare VH with VANH and to explore the indications to perform a VANH.

The aim of this study is to compare the VANH with the VH for same day discharge (SDD), complications, treatment related outcomes, post-operative recovery, quality of life and cost-effectiveness.

We hypothesize that patients who underwent a VANH procedure are more often able to be treated in SDD setting.

2. OBJECTIVES

The aim of this study is to evaluate SDD, postoperative pain, safety, recovery and cost-effectiveness within 6 weeks after surgery, in woman undergoing two different surgical techniques; VANH or VH.

Primary Objective:

The primary objective is the difference in percentage of SDD in both groups.

Secondary Objective(s):

- Complications, severity scored by Clavien-Dindo classification (see attachment 6)
 - Injuries to bowel, bladder, ureter, vessels, nerves
 - Thrombo-embolic events
 - Haematoma requiring surgical intervention
 - Haemorrhage requiring transfusion or surgical intervention

- Wound dehiscence requiring surgical intervention
- Wound infections including vaginal vault abscesses
- Treatment related outcomes
 - Conversion rate
 - Time in operation room (measured from entering the operating theatre until leaving the theatre to the recovery)
 - Surgery time (start of incision and end of surgical procedure)
 - Blood loss (measured in mL)
 - Pain measured in numeric rating scale (NRS) at: 1 hours postoperative, 8 hours postoperative and 24 hours postoperative
 - Recovery of pain (measured in NRS) within the first week after surgery
 - Use of analgesics (daily use of paracetamol, NSAIDs, opioids)
 - Resumption of daily activity
 - Hospital readmission within 6 weeks after surgery
 - Post-operative pain the first 7 days after surgery (measured on a numeric rating scale (NRS))
- Intended number of salpingectomies in each group
- Number of salpingectomies performed in each group
- Recovery index-10 (RI-10) measured on different moments pre- and post-operative
- Health-related quality of life (EQ-5D-5L questionnaire)
- Costs (including intervention costs, hospital costs, healthcare costs outside the hospital and costs due to loss of productivity; using an adapted version of iMCQ questionnaire) (see attachment 5 and 8).
- Cost-effectiveness (of VANH versus VH)

3. STUDY DESIGN

The design of this study is a single-blind, multicentre, randomised controlled trial (RCT). Eligible patients will be randomised in either the VH group and receive a vaginal hysterectomy or in the VANH-group and the hysterectomy is performed by vaginal assisted NOTES surgery.

4. STUDY POPULATION

4.1 Population (base)

Women who fulfil the inclusion criteria and have an indication for a hysterectomy.

4.2 Inclusion criteria

To be eligible to participate in this study, a subject must meet all the following criteria:

- Written and orally given informed consent
- 18 years and older
- Native Dutch speaker or in control of the Dutch language in speaking and writing
- Indication for hysterectomy for benign indication
- Possible to perform a VH judged by experienced (resident) gynaecologist during gynaecological examination

4.3 Exclusion criteria

The following exclusion criteria are defined:

- Any contra-indication for VH (for example, large uterus myomatosis, not enough descensus, etc) as judged by experienced gynaecologist
- History of more than 1 caesarean section
- History of endometriosis
- History of rectal surgery
- History of pelvic radiation
- Suspected rectovaginal endometriosis
- History of pelvic inflammatory disease, especially prior tubo-ovarian or pouch of Douglas abscess or suspected adhesions due to (ruptured) inflammatory disease (for example ruptured appendicitis)
- Virginity
- Pregnancy
- Indication for anterior or posterior colporrhaphy during the same surgery
- Indication of mid urethral slings
- Uterus myomatosis will not be an exclusion criteria but the surgeon will indicate if it is possible to remove the uterus vaginally.

4.4 Sample size calculation

We are planning a study of independent cases with an enrolment ratio of 1:2 in favour of the VANH-group (2 cases VANH for 1 VH).

According to literature, the mean postoperative hospital stay differs from 1.13 days to 2.2 days [25-29]. There is also literature that says that a VH can be performed as a day-care treatment, wherein 63.9% of the patients is able to go home within 12 hours after surgery [30]. As mentioned earlier, 77% of the patients undergoing a VANH procedure is able to go home within 12 hours after surgery [1].

We hypothesize 50% SDD is feasible in the control group and 77% SDD in the intervention group. With an alpha of 0.05 and a power of 0.8 and enrolment ratio of 1:2, this will result in a total of 36 patients in the control group and 72 patients in the intervention group, which makes a total of 108 in the whole trial. Taking 15% lost to follow up in account, we strive to a total of 124 patients, 41 patients randomized in the control group and 83 patients in the intervention group. The sample size was calculated using the website <https://clincalc.com/stats/samplesize.aspx>.

The Zuyderland Medical Centre performs between 95-120 VH each year. Since the introduction of the VANH in 2019 an increase of the VANH procedure has been seen and a decrease of VH. In 2019 a total of 75 VH was performed compared to 21 VANH procedures. The VANH-team of Zuyderland Medical Centre (dr. Martine Wassen and dr. Nicol Smeets) have performed over 75 VANH in total, which results in more than 35 procedures per surgeon.

We planned to start with this study in May 2021. We strive to include 75% of the patients with an indication for vaginal hysterectomy. This concludes in 75 patients a year, which results in 115 patients after 18 months.

5. TREATMENT OF SUBJECTS

5.1 Investigational product/treatment

The study population will be randomly divided into the intervention group (VANH-group) or the control group (VH-group).

VANH hysterectomy:

All planned VANH hysterectomies are scheduled in the morning before 12.00u pm. All VANH procedures will be performed by surgeons who have the skills to perform a VANH. This means that the surgeons will be experienced in performing a

VANH and must have performed at least 25 VANH independently, as it is demonstrated that the learning curve consists of 25 cases [31].

Elective salpingectomy will be performed after counselling on the outpatient clinic, subsequently on patients request. Pre-operative cefazolin 2 gram and 500 mg metronidazole is administered intravenously.

The patient is placed in lithotomy position. After disinfection and sterile draping, a urinary bladder catheter is inserted into the bladder. At start of the procedure descensus uteri will be classified according to the Pelvic Organ Prolaps Quantification classification (POPQ-classification), using the point 'C'[32]. This anatomical point 'C' will be classified when there is traction on the cervix.

Access to the peritoneal cavity will be performed similar to vaginal surgery by a circular incision around the cervix, anterior and posterior colpotomy and transecting the sacro-uterine ligaments.

The vNOTES port (GelPOINT V-Path, Applied Medical) will be placed to get access to the abdominal cavity and a pneumoperitoneum will be created. After positioning in 20° degree Trendelenburg laparoscopic instruments will be introduced (30° laparoscope, a grasping forceps and sealing device through three trocars). The peritoneal cavity and ureters are inspected. The hysterectomy is performed by dissecting from caudally to cranially. The fallopian tubes will be removed elective after counselling in the outpatient clinic and the ovaries will be removed on indication only.

Finally, haemostasis is checked and the vNOTES port and the uterus are removed trans-vaginally and the pneumoperitoneum is deflated. The vaginal cuff will be closed using a running Vicryl-1 suture. The urinary bladder catheter will be removed directly postoperative.

VH:

All planned vaginal hysterectomies are scheduled in the morning before 12.00u pm. In women allocated to the VH, surgery will be performed by competent surgeons. Elective salpingectomy will be performed after counselling on the outpatient clinic, subsequently on patients request. Pre-operative cefazolin 2 gram and 500 mg metronidazole is administered intravenously. The patient is placed in lithotomy position. After disinfection and sterile draping, a urinary bladder catheter is inserted into the bladder. At start of the procedure descensus uteri will be classified according to the Pelvic Organ Prolaps Quantification classification (POPQ-classification), using the point 'C'[32]. This anatomical point 'C' will be classified when there is traction on the cervix. A circumferential incision is made around the cervix. Access to the peritoneal cavity will be performed through anterior and posterior colpotomy. The sacro-uterine ligaments, ligamenta cardinalia uterine arteries will be clamped and dissected. Finally, the ovarian ligament, round ligament and fallopian tubes will be dissected and tied. The uterus will be removed and the vagina will be closed. The urinary bladder catheter will be removed directly postoperative.

5.2 Use of co-intervention (if applicable)

Not applicable

5.3 Escape medication (if applicable)

Not applicable

6. INVESTIGATIONAL PRODUCT

6.1 Name and description of investigational product(s)

The Alexis wound retractor provides 360 degrees of circumferential, atraumatic and hand free retraction of the operating area.

The GelPOINT V-Path is a GelSeal Cap, which provides flexible fulcrum for unmatched triangulation of standard laparoscopic instrumentation. It maintains insufflation for continuous access. It has two valves to facilitate smoke evacuation and accommodate standard laparoscopic insufflation tubing and it facilitates large specimen extraction with simple detachment from the Alexis Retractor.

The CE-number of the products are known. The products have a combined CE number, namely CE0843.

6.2 Summary of findings from non-clinical studies

An animal study in pigs was performed in 2004, performing a endoscopic per oral, trans gastric approach to enter the peritoneal cavity [13]. This study showed that the NOTES technique was feasible and has the potential to be an alternative to laparoscopy and laparotomy [13].

6.3 Summary of findings from clinical studies

There are some comparative studies and case series-studies which show that the vNOTES method is a safe method to perform a hysterectomy [20, 22, 23].

Only one RCT has been performed yet. This is the HALON-trial, which compares the hysterectomy by vNOTES versus the TLH in a day-care procedure. This study concluded that vNOTES is non-inferior to a laparoscopy for successfully performing a hysterectomy without conversion. Next to this, patients who underwent a vNOTES hysterectomy are more often treated in a day-care setting and the duration of the vNOTES surgery was significantly shorter [1]. And there were less postoperative complications compared to the laparoscopy and patients experienced less post-operative pain and used less pain medication postoperative [1].

Recently a case series study has been published about the complication rate of 1000 vNOTES cases. In 730 cases a hysterectomy was performed. A total complication rate of 5.2% was found of which 1.4% was intra-operative and 3.8% postoperative. 2.3% of the postoperative complications were classified a Clavien Dindo classification I or II. 1.5% was classified as Clavien Dindo classification III. No grade IV or V classifications were reported [2].

6.4 Summary of known and potential risks and benefits

For the VH potential risks are, according to literature, injury to the bladder, ureter or intestines, per-operative haemorrhage, arterial or venous injury postoperative cuff hematoma or abscess, urinary tract infection and thrombosis, according to literature [6]. Urinary tract injury can occur in 1.6%, vascular injury is seen in 1.2% bleeding occurs in 2.9% and an unintended laparotomy occurs every 2.4% [6].

Until now, no studies have compared these results for the VH and the VANH. A case series study of 730 vNOTES hysterectomy procedures shows an incidence of urinary tract injury 1.4%, per-operative haemorrhage in need of blood transfusion 0.1%, postoperative cystitis 0.8%, hematoma 1.5% and wound infection 2 patients 0.3% [2].

With the scarce literature, there is no evidence to suggest performing VANH increases the operation risk and complication rate. Theoretically it is maybe even possible that the VANH causes less intra-operative complications compared to the VH because of an improved view during surgery.

6.5 Description and justification of route of administration and dosage

Not applicable

6.6 Dosages, dosage modifications and method of administration

Not applicable

6.7 Preparation and labelling of Investigational Medicinal Product

Not applicable

6.8 Drug accountability

Not applicable

7. NON-INVESTIGATIONAL PRODUCT**7.1 Name and description of non-investigational product(s)**

Not applicable

7.2 Summary of findings from non-clinical studies

Not applicable

7.3 Summary of findings from clinical studies

Not applicable

7.4 Summary of known and potential risks and benefits

Not applicable

7.5 Description and justification of route of administration and dosage

Not applicable

7.6 Dosages, dosage modifications and method of administration

Not applicable

7.7 Preparation and labelling of Non Investigational Medicinal Product

Not applicable

7.8 Drug accountability

Not applicable

8. METHODS**8.1 Study parameters/endpoints****8.1.1 Main study parameter/endpoint**

The primary objective is the percentage of SDD in both groups.

8.1.2 Secondary study parameters/endpoints (if applicable)

- Complications, severity scored by Clavien-Dindo classification (see attachment 6)
 - Injuries to bowel, bladder, ureter, vessels, nerves
 - Thrombo-embolic events

- Haematoma requiring surgical intervention
- Haemorrhage requiring transfusion or surgical intervention
- Wound dehiscence requiring surgical intervention
- Wound infections including vaginal vault abscesses
- Treatment related outcomes
 - Conversion rate
 - Time in operation room (measured from entering the operating theatre until leaving the theatre to the recovery)
 - Surgery time (start of incision and end of surgical procedure)
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 - Recovery of pain (measured in NRS) within the first week after surgery
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 - Resumption of daily activity
 - Hospital readmission within 6 weeks after surgery
 - Post-operative pain the first 7 days after surgery (measured on a numeric rating scale (NRS))
- Intended number of salpingectomies in each group
- Number of salpingectomies performed in each group
- Recovery index-10 (RI-10) measured on different moments pre- and post-operative
- Health-related quality of life (EQ-5D-5L questionnaire)
- Costs (including intervention costs, hospital costs, healthcare costs outside the hospital and costs due to lost of productivity; using an adapted version of iMCQ questionnaire) (see attachment 5 and 8).
- Cost-effectiveness (of VANH versus VH)

8.1.3 Other study parameters (if applicable)

The following baseline characteristics will be collected pre-operatively; age, BMI, ethnicity, education level, vaginal parity, medication use, intoxications, co-morbidities, surgical history, indication of surgery, chronic pain during > 6 months not related to surgery indication (see attachment 1) and the EQ-5D-5L questionnaire (see attachment 3).

Other characteristics are collected per-operatively: ASA-classification, indication of the surgery, duration of complete surgery, intra-abdominal pressure (mmHg), total CO₂ used, amount of blood loss, weight of the uterus, POP-Q classification point C (see attachment 2).

8.2 Randomisation, blinding and treatment allocation

After giving written informed consent, the patient will be randomized to VANH or VH by the Datamanagement randomisation programme of Research Manager. Randomisation will be 1:2 for control group and the intervention-group. The study will be a single blinded (participant) study. Treatment allocation concealment will be used. Both Zuyderland Medical Centre as Catharina Medical Centre will be able to randomise patients using the Datamanagement module of Research Manager. We will use block randomisation using a different block per centre, thus stratified randomisation with permuted blocks. Given the 1:2 ratio this means we will use blocks of 6, for example AABBA, or ABAABA.

8.3 Study procedures

Women who have a benign indication for a hysterectomy will be informed about the study during their visit at the outpatient clinic. Eligible patients who fulfil the inclusion criteria will be identified and counselled by the research coordinator or staff

of the participating centres. Those patients will receive a patient information folder and every patient who received a folder will be noted in the database (both electronic patient record and study database), even if they eventually will not participate in the study.

When eligible patients do not want to be randomized in this trial, informed consent will be asked to use their data in a cohort study. When the reason of not participating is known, this will be noted. Patients are not obligated to give a reason for not participating in the study.

During the consultation at the outpatient clinic patients will be counselled for an elective salpingectomy during the surgery. Before entry into the study, the research coordinator and/or the staff will explain to potential participants the aims, methods, reasonably anticipated benefits, and potential hazards of the study. They will be informed that their participation is voluntary and that they may withdraw consent to participate at any time during the study. They will be informed that choosing not to participate will not affect their care. After giving sufficient information, written informed consent must be obtained. Patients will receive oral and written information and have a minimum of 7 days to consider their participation in the study. Eligible patients receive the patient information folder and when they decide to participate in the study, this folder will be handed to their doctor during the next visit.

After receiving written informed consent, the randomization procedure will be performed by submitting the patient in Research Manager. Pre-operatively a multiple base-line questionnaires will be filled in.

All participants will be counselled for SDD. The surgery will be planned before 12 pm. The length of hospital stay is dependent from clinical recovery. Clinical recovery depends, among other things, on pain experience, nausea or vomiting, patients wish to stay in the hospital or to go home.

Intervention (VANH-group):

The participants randomized into the VANH-group will undergo the VANH procedure. When arrived in the hospital, they will be admitted at the day-care ward. Pre-operative cefazolin 2 gram and 500 mg metronidazole is administered intravenously. Elective salpingectomy will be performed after counselling on the outpatient clinic and subsequently patients request. During surgery, the surgeon will estimate surgical feasibility and safety. This is a subjective estimation based on clinical experience of the surgeon.

The participants receive the standard pain medication according to the local pain protocol (see below). Based on their NRS-score (4 or higher), additional pain medication will be proposed. When a patient reports a NRS-score of 4 or higher, extra pain medication will be proposed. The patient can choose whether to take the pain medication.

Control (VH group):

The participants randomized in the control group will receive a vaginal hysterectomy. When arrived in the hospital, they will be admitted at the day-care ward. Pre-operative cefazolin 2 gram and 500 mg metronidazole is administered intravenously. Elective salpingectomy will be performed after counselling on the outpatient clinic and subsequently patients request. During surgery, the surgeon will estimate surgical feasibility and safety. This is a subjective estimation based on clinical experience of the surgeon.

The participants receive the standard pain medication according to the local pain protocol (see below). Based on their NRS-score (4 or higher), additional pain medication will be proposed. When a patient reports a NRS-score of 4 or higher, extra pain medication will be proposed. The patient can choose whether to take the pain medication.

For the Zuyderland Medical Centre this is:

Step 1: paracetamol

Step 2: paracetamol and NSAID

For the Catharina Medical Centre this is:

Step 1: paracetamol

Step 2: NSAID

Step 3: oxynorm

Study schedule

Outpatient clinic

- Study information is provided
- Informed consent after 7 days reflection period
- Counselling salpingectomy
- Randomization after receiving informed consent and planning surgery

Baseline = Pre-operative ward on day of surgery (when arriving on ward)

1. VANH-group = Baseline questionnaire, pre-operative NRS and EQ-5D-5L questionnaire
2. Control group (VH group) = Baseline questionnaire, pre-operative NRS and EQ-5D-5L questionnaire

T0 = Postoperative on the recovery ward (1 hour after surgery)

1. VANH-group = pain score (NRS) and given pain medication
2. Control-group (VH group) = pain score (NRS) and given pain medication

T1= Postoperative on the ward (4 hours after surgery)

1. VANH-group = pain score (NRS) and given pain medication
2. Control-group (VH group) = pain score (NRS) and given pain medication

T2 = Postoperative on the ward or at home (24 hours after surgery)

1. VANH-group = pain score (NRS) in morning and evening, pain medication used, using a logbook (see attachment 7)
2. Control-group (VH group) = pain score (NRS) in morning and evening, pain medication used, using a logbook (see attachment 7)

T3 = 2 days after surgery

1. VANH-group = pain score (NRS) in morning and evening, pain medication used, using a logbook (see attachment 7), RI-10 questionnaire.
2. Control-group (VH group) = pain score (NRS) in morning and evening, pain medication used, using a logbook (see attachment 7)

T4 – 8 = 3- 6 days after surgery

1. VANH-group = pain score (NRS) in morning and evening, pain medication used, using a logbook (see attachment 7), RI-10 questionnaire.
2. Control-group (VH group) = pain score (NRS) in morning and evening, pain medication used, using a logbook (see attachment 7)

T9= 7 days after surgery

1. VANH-group = pain score (NRS) in morning and evening, pain medication used, RI-10 questionnaire. Patients will receive the questionnaires by email*.
2. Control-group (VH group) = pain score (NRS) in morning and evening, pain medication used, RI-10 questionnaire. Patients will receive the questionnaires by email*.

T10 = 4 weeks after surgery

1. VANH-group = RI-10 questionnaire. Patients will receive the questionnaires by email*.
2. Control-group (VH group) = RI-10 questionnaire. Patients will receive the questionnaires by email*.

T11 = 6 weeks after surgery

1. VANH-group = EQ-5D-5L questionnaire + RI-10 questionnaire + evaluation of complications postoperative at outpatient clinic. Patients will receive the questionnaires by email* and adapted iMCQ questionnaire.
2. Control-group (VH group) = EQ-5D-5L questionnaire + RI-10 questionnaire + evaluation of complications postoperative at outpatient clinic. Patients will receive the questionnaires by email* and adapted iMCQ questionnaire.

T12 = 12 weeks after surgery

1. VANH-group = EQ-5D-5L questionnaire + RI-10 questionnaire and adapted iMCQ questionnaire. Patients will receive the questionnaires by email*.
2. Control-group (VH group) = EQ-5D-5L questionnaire + RI-10 questionnaire and adapted iMCQ questionnaire. Patients will receive the questionnaires by email*.

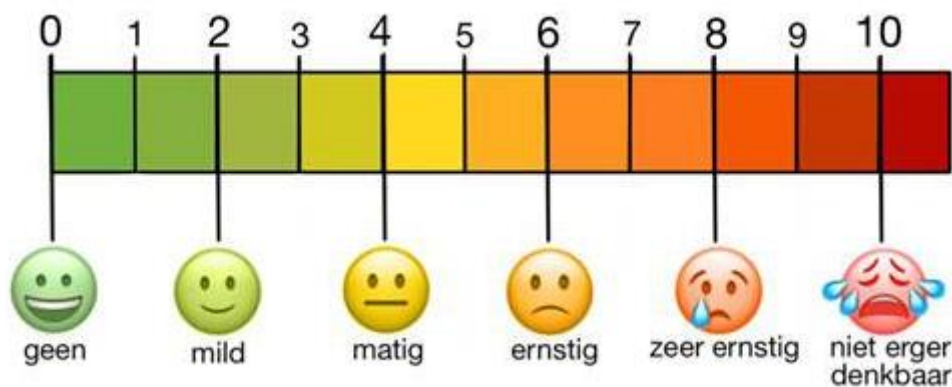
* = When patients do not respond or do not fulfil the questionnaires, they will receive a reminder 1 day after the first email. When they still not respond, the second day after the email they will receive a phone-call by one of the researchers.

Questionnaires:Baseline questionnaire (see attachment 1):

The baseline questionnaire will collect the following variables: age, BMI, ethnicity, education level, vaginal parity, medication use, intoxications, comorbidities, surgical history, indication of surgery, chronic pain defined as pain > 6 months not related to indication of surgery, NRS before surgery.

NRS before surgery:

Do you experience abdominal pain before surgery? If yes, how do you experience the pain before surgery?

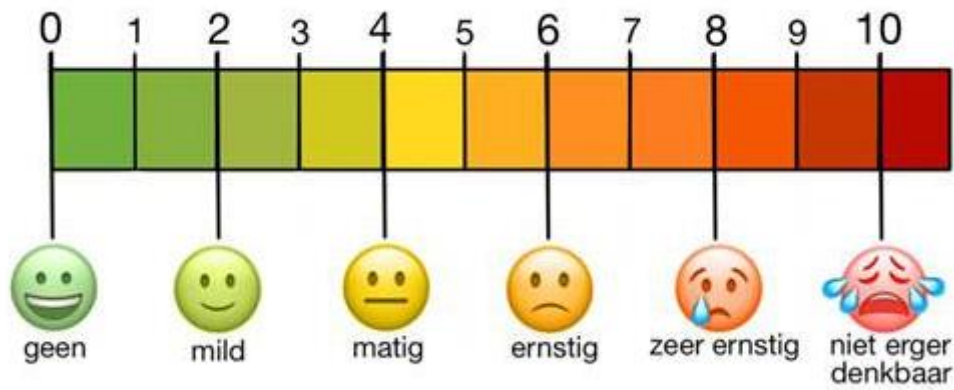


No pain

Worst imaginable pain

NRS after surgery:

How did you experience the pelvic and/or vaginal pain after surgery?



No pain

Worst imaginable pain

EQ-5D-5L questionnaire (see attachment 3):

EQ-5D-5L is a generic Health Related Quality of Life (HRQoL) measure, which is broadly used in economic evaluation [33, 34]. The instrument examines a patient's HRQoL on the day of the interview. It consists of the EQ-5D-5L descriptive system and the EQ-Visual Analogue Scale. The descriptive system comprises five dimensions: mobility, self-care, usual activities, pain/ discomfort and anxiety/depression. Each dimension has five levels: no problems, slight problems, moderate problems, severe problems, and extreme problems. Responses to the 5 items result in a patient's health state that can be transformed into an index score representing health-related quality of life, ranging between 0 (death) and 1 (full health) [35]. These index scores are combined with length of life to calculate the QALY. The EQ-VAS records the patient's self-rated health with endpoints labelled 'the best health you can imagine' at the top and 'the worst health you can imagine' at the bottom.

RI-10 questionnaire: (see attachment 4)

This is a standardized questionnaire to measure 5 levels of recovery. This includes for example feelings, pain, mobility, and self-care.

Resource use survey (iMCQ questionnaire) (see attachment 5)

Costs outside the hospital are calculated by estimating resource use by means of a questionnaire based on the iMTA Medical Consumption Questionnaire [36], completed by patients. The questionnaire has a recall period of 6 weeks. Questions focus on resource use outside the hospital (e.g. general practitioner visits, medication, etcetera), and also the use of informal care and productivity losses.

Study schedule

| | Informed consent | Baseline questionnaire | EQ-5D-5L | RI-10 | iMCQ | Pain score (NRS) |
|---|------------------|------------------------|----------|-------|------|------------------|
| Outpatient clinic | | | | | | |
| Baseline (T0) 1. VANH-group 2. control group | | | | | | |
| 1 hour postoperative (T1) 1. VANH-group 2. Control-group | | | | | | |
| 8hours postoperative (T1) 1. VANH-group 2. Control-group | | | | | | |
| 24 hours postoperative (T2) 1. VANH-group 2. Control-group | | | | | | |
| 2 days after surgery (T3) 1. VANH-group 2. Control-group | | | | | | |

| | | | | | | |
|---|--|--|--|--|--|--|
| 3-6 days after surgery (T4-8) 1. VANH-group 2. Control-group | | | | | | |
| 7 days after surgery (T9) 1. VANH-group 2. Control-group | | | | | | |
| 4 weeks after surgery (T10) 1. VANH-group 2. Control-group | | | | | | |
| 6 weeks after surgery (T11) 1. VANH-group 2. Control-group | | | | | | |
| 12 weeks after surgery (T12) 1. VANH-group 2. Control-group | | | | | | |

8.4 Withdrawal of individual subjects

Subjects can leave the study at any time for any reason if they wish to do so without any consequences. The investigator can decide to withdraw a subject from the study for urgent medical reasons.

8.4.1 Specific criteria for withdrawal (if applicable)

We do not expect specific complaints or side effects of the VANH-surgery, other than the known complications of a vaginal hysterectomy, which are reason to withdraw from the study.

8.5 Replacement of individual subjects after withdrawal

After withdrawal of a participant before surgery, we will try to include a new patient to reach the sample size. If a patient decides to stop participating in the study, the data will be registered in the cohort study.

8.6 Follow-up of subjects withdrawn from treatment

After withdrawal from a participant, the patient is asked to agree with obtaining the measurements (NRS score, anxiety score etcetera) and using this data. When she wants to withdraw completely, she cannot be replaced by a new participant.

8.7 Premature termination of the study

We do not expect the study will be terminated premature before enrolling the required participants. No interim analysis will be performed because of the small number of subjects that will be included.

9. SAFETY REPORTING

9.1 Temporary halt for reasons of subject safety

In accordance with section 10, subsection 4, of the WMO, the sponsor will suspend the study if there is sufficient ground that continuation of the study will jeopardize subject health or safety. If there will be more than 3 intraoperative complications (3% of total cohort) in one of both groups the sponsor will notify the accredited METC without undue delay of a temporary halt including the reason for such an action. This action will also be performed if there are more than 8 postoperative complications. These numbers are based on the largest series concerning VANH demonstrating an intraoperative complication rate of 1,4% and a postoperative complication rate of 3,8% (total complication rate 5,2%) [2]. The sponsor will notify the accredited METC without undue delay of a temporary halt including the reason for such an action. The study will be suspended pending a further positive decision by the accredited METC. The investigator will take care that all subjects are kept informed.

9.2 AEs, SAEs and SUSARs

9.2.1 Adverse events (AEs)

Adverse events are defined as any undesirable experience occurring to a subject during the study, whether or not considered related to the experimental intervention. All adverse events reported spontaneously by the subject or observed by the investigator or his staff will be recorded.

9.2.2 Serious adverse events (SAEs)

A serious adverse event is any untoward medical occurrence or effect that

- results in death;
- is life threatening (at the time of the event);
- requires hospitalisation or prolongation of existing inpatients' hospitalisation (re-admission will also be considered as a SAE);
- results in persistent or significant disability or incapacity;
- is a congenital anomaly or birth defect; or
- any other important medical event that did not result in any of the outcomes listed above due to medical or surgical intervention but could have been based upon appropriate judgement by the investigator.

An elective hospital admission will not be considered as a serious adverse event.

May a serious adverse event occur, this will be reported by the head-investigator within one week after the event at the website <http://www.toetsingonline.nl>. The sponsor will report the SAEs through the web portal *ToetsingOnline* to the accredited METC that approved the protocol, within 7 days of first knowledge for SAEs that result in death or are life threatening followed by a period of maximum of 8 days to complete the initial preliminary report. All other SAEs will be reported within a period of maximum 15 days after the sponsor has first knowledge of the serious adverse events.

9.2.3 Suspected unexpected serious adverse reactions (SUSARs)

Not applicable

9.3 Annual safety report

Not applicable

9.4 Follow-up of adverse events

All AEs will be followed until they have abated, or until a stable situation has been reached. Depending on the event, follow up may require additional tests or medical procedures as indicated, and/or referral to the general physician or a medical specialist.

SAEs need to be reported till end of study within the Netherlands, as defined in the protocol.

9.5 [Data Safety Monitoring Board (DSMB) / Safety Committee]

Not applicable

10. STATISTICAL ANALYSIS

The data will be analysed using the program SPSS (version 26). A Chi-square test will be used to assess categorical variables, and the independent sample T-test will be used for continuous variables in case of normal distribution based on the skewness, kurtosis, and graphical representation (histogram) of the continuous variables, to compare both groups. The mean NRS-score with standard deviation will be calculated for pain in both groups, when the data is normally divided. When the data is not normally divided, then a median with interquartile range will be calculated. For categorical variables, frequency and percentage will be calculated. Depending on the amount of missing values, the missing values will be excluded or imputed. This depends on the amount of missing values. There will be performed an intention to treat analysis and per protocol analysis.

The baseline characteristics in both groups will be compared to check if both groups are comparable after randomization, or if statistical differences exist between both groups.

Imputation of the results will be executed according the guidelines of Jakobsen et al [37].

10.1 Primary study parameter(s)

The percentage of patients that had the surgery in SDD will be calculated. The differences will be calculated using the Fisher's exact test.

10.2 Secondary study parameter(s)

The NRS-scores at the different moments will be calculated into means with standard deviation. The differences in postoperative mean NRS-scores between both groups (VANH-group and VH-group) will be analysed using the linear mixed models analysis. The mean NRS-score of the VANH-group and VH-group will be compared to see whether the pain experience post-operative differs. Different variables, like age, BMI, ethnicity, education level, marital status, vaginal parity, ASA-classification, medication use, intoxications, chronic pain, surgical history, indication of surgery, type of planned surgery, will be considered in the statistical analysis. These are taken into account because these variables can be possible confounders in the results of the study.

The NRS-score pre-operative will also be included in the linear mixed models analysis of the NRS-score post-operative, because differences in pre-operative pain score can have effect on the post-operative pain score. The surgery duration, length of hospital stay and consumption of analgesics will be calculated into means with standard deviation (only when the results are normally distributed) in the VANH group and VH group. If the results are not normally distributed a median and (interquartile) range will be calculated. The total costs, divided in surgery costs, hospital costs etcetera will also be divided into means with standard deviation.

All the differences in the means between both groups will be analysed using the multivariable linear regression analysis. If the variable 'length of hospital stay' is not normally distributed, a different test (for example Poisson regression analysis) will be used.

We want to compare the baseline characteristics to see whether the groups are equally divided. The QoR-40 and RI-10 questionnaires are continuous variables, so we will use the independent sample t-test. When the baseline characteristics or questionnaire results are not normally distributed, we will use the Mann-Whitney U test.

Categorical variables like intra-operative complications, postoperative complications and hospital re-admission will be compared using the chi-square test or the Fisher exact test. A multivariable logistic regression analysis will be performed to adjust the association between the VANH and VH groups and these secondary outcomes for possible confounders (for example age, BMI etcetera).

Cost-effectiveness analysis

An economic evaluation will be performed alongside the clinical trial to determine the cost-effectiveness of VANH compared to VH. The evaluation adopts a societal perspective and has a time horizon of 3 months. The design of the economic evaluation follows the principles of a cost-utility analysis and adheres to the Dutch guideline for economic evaluations in health care and the Dutch manual for costing research [38, 39]. Outcome measures for the economic evaluation will be costs, health-related quality of life, and quality adjusted life years (QALYs). The EQ-5D-5L survey is used to estimate health-related quality of life and to calculate Quality Adjusted Life Years (QALYs) using area under the curve calculations. The EQ-5D is completed at baseline, 6 and 12 weeks. Costs will be measured using medical records, provider information systems and a self-developed questionnaire to be completed by patients (at baseline, 6 and 12 weeks). The latter is based on the validated iMTA Medical Consumption Questionnaire [36]. The Dutch manual for costing research will be used to determine prices for each volume of resource use [38].

The cost-effectiveness analysis will be conducted with an intention-to-treat approach and cost-effectiveness is expressed in (incremental) cost per QALY. Non-parametric bootstrapping with 5000 replicates of the joint distribution of costs and QALYs will estimate the probability of VANH being cost-effective compared to VH, for a range of maximum monetary values that a decision-maker might be willing to pay for a QALY gained, presented in a cost-effectiveness acceptability curve (CEAC). Several one-way sensitivity analyses and scenario analyses will be performed to assess the robustness of results.

10.3 Other study parameters

Not applicable

10.4 Interim analysis (if applicable)

Not applicable

11. ETHICAL CONSIDERATIONS

11.1 Regulation statement

The study will be conducted according to the principles of the Declaration of Helsinki (version 64, WMA General Assembly, Fortaleza, Brazil, October 2013)) and in accordance with the Medical Research Involving Human Subjects Act (WMO).

11.2 Recruitment and consent

Women who have an indication for vaginal hysterectomy will be informed about the study during their visit at the outpatient clinic. Eligible patients who fulfil the inclusion criteria will be identified and counselled by the research coordinator or staff of the participating centres. Before entry into the study, the research coordinator and/or the staff will explain to potential participants the aims, methods, reasonably anticipated benefits, and potential hazards of the study. They will be informed that their participation is voluntary and that they may withdraw consent to participate at any time during the study. They will be informed that choosing not to participate will not affect their care. After giving sufficient information, written informed consent must be obtained. Patients will receive oral and written information and have a minimum of 7 days to consider their participation in the study.

11.3 Objection by minors or incapacitated subjects (if applicable)

Not applicable

11.4 Benefits and risks assessment, group relatedness

The risks of this research will be small, according to the Clinical Trial Centre Maastricht (CTCM). Women undergoing VANH can experience the same complications as vaginal hysterectomy. VANH is a hybrid technique based on TLH (instruments, camera) and VH (access to peritoneal cavity). Possible benefits of the study will be: reduced pain after the VANH-hysterectomy in the postoperative period compared to the vaginal hysterectomy and consequently less consumption of pain medication and a shorter hospital admittance.

11.5 Compensation for injury

The sponsor/investigator has a liability insurance which is in accordance with article 7 of the WMO.

The sponsor (also) has an insurance which is in accordance with the legal requirements in the Netherlands (Article 7 WMO). This insurance provides cover for damage to research subjects through injury or death caused by the study.

The insurance applies to the damage that becomes apparent during the study or within 4 years after the end of the study.

11.6 Incentives (if applicable)

Not applicable.

12. ADMINISTRATIVE ASPECTS, MONITORING AND PUBLICATION

12.1 Handling and storage of data and documents

The pre- and postoperative data will be collected on a paper eCRF which travels with the patient during the day of surgery. An encrypted Excel key file will be made. In this file, the patient numbers will be linked to the concerning study number. Only the principal investigators will have access to this file. The obtained (paper) data will be saved as eCRF in the program 'Research Manager'. Also, here only the (head) investigators have access. The data will be saved for 15 years, according to the regular agreements. As well as for the Excel key file as for the Research Manager a password is necessary. All paper documents (informed consent, eCRF and questionnaires) will be stored in one folder. This folder will be saved in a locked closet in the room of the head investigator. On the informed consent form no study number will be mentioned, so that a study number cannot be traced back on paper to a patient. The data will be collected in a digital data management system (research manager).

When data of a patient must be derived from the electronic patient files, then this will be done by investigator I. Bekkers. In principle, all the information can be given by the patient, and the patient file does not have to be seen.

When the patient participates in the study, this will be noted in the patients document of the hospital.

The study number will be determined at the time of randomization. The inclusion will be done by one of the doctors of the Gynaecology department of the participating centres. They will be instructed how to include the patients and which patients are suitable to be included in the study. Data of the study will not be shared with persons and/or organizations other than the participating centres.

12.2 Monitoring and Quality Assurance

According to the local guidelines of 'Bureau Wetenschappelijk Onderzoek (BWO)' the study will be monitored by CTCM. The CTCM classified the study as 'negligible/low risk'. They are producing the monitoring plan. When the monitoring plan is finished, it will be uploaded on Research Manager.

In our opinion, this study adds a negligible risk according to the risk classification of the "Nederlandse Federatie van Universitaire Medische Centra" (NFU). Monitoring will be conducted in accordance with negligible risk monitoring guidelines of the NFU, which will be reported in a monitoring plan.

12.3 Amendments

Amendments are changes made to the research after a favourable opinion by the accredited METC has been given.

All substantial amendments will be notified to the METC and to the competent authority.

Non-substantial amendments will not be notified to the accredited METC and the competent authority, but will be recorded and filed by the sponsor.

12.4 Annual progress report

The investigator will submit a summary of the progress of the trial to the accredited METC once a year. Information will be provided on the date of inclusion of the first subject, numbers of subjects included and numbers of subjects that have completed the trial, serious adverse events/ serious adverse reactions, other problems, and amendments.

12.5 Temporary halt and (prematurely) end of study report

The investigator/sponsor will notify the accredited METC of the end of the study within a period of 8 weeks. The end of the study is defined as the last patient's last visit.

The sponsor will notify the METC immediately of a temporary halt of the study, including the reason of such an action.

In case the study is ended prematurely, the sponsor will notify the accredited METC within 15 days, including the reasons for the premature termination.

Within one year after the end of the study, the investigator/sponsor will submit a final study report with the results of the study, including any publications/abstracts of the study, to the accredited METC.

12.6 Public disclosure and publication policy

The trial will be registered at www.clinicaltrials.gov, under the study name 'VANH-trial', before including the first patient.

The principle investigator will publish the results of the study as soon as appropriate.

13. STRUCTURED RISK ANALYSIS

Not applicable

13.1 Potential issues of concern

Not applicable

13.2 Synthesis

Not applicable

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15. ATTACHMENTSAttachment 1: Baseline questionnaire:

Age, BMI, ethnicity, education level, marital status, vaginal parity, medication use, intoxications, chronic pain, surgical history, indication of surgery

Beste deelnemer,

Onderstaande vragenlijst omvat persoonlijke vragen. De vragen zijn zowel open als meerkeuze.

1. Leeftijd (in jaren)

..... jaar

2. Lengte (in centimeters)

..... cm

3. Gewicht (in kilogram)

.....kg

4. Ras (indien u deze vraag liever niet invult, mag u hier 'onbekend' invullen)

- ☐ Kaukasisch
- ☐ Latijns-Amerikaans
- ☐ Aziatisch
- ☐ Afrikaans
- ☐ Turks
- ☐ Andere afkomst namelijk,
- ☐ Onbekend

5. Welke opleiding van onderstaande opleidingen heeft u voltooid? (Indien u deze vraag liever niet invult, mag u hier 'onbekend' invullen)

- ☐ Basisschool
- ☐ Middelbare school
- ☐ Lager beroeps onderwijs
- ☐ MBO
- ☐ HBO
- ☐ WO
- ☐ Onbekend

6. Burgerlijke staat (indien u deze vraag liever niet invult, mag u hier 'onbekend' invullen)

- ☐ Alleenstaand
- ☐ Samenwonend
- ☐ Gehuwd
- ☐ Onbekend

7. Roken

- ☐ Ja,..... sigaren/sigaretten per dag/week/maand
- ☐ Nee

8. Alcohol

- ☐ Ja, glazen per dag/week/maand
- ☐ Nee

9. Drugs

- ☐ Ja
Welke? per dag/week/maand
- ☐ Nee

10.Aantal bevallingen (vaginaal)

- ☐ 0
- ☐ 1
- ☐ 2
- ☐ 3
- ☐ 4
- ☐ >5

11. Aantal keizersnedes

- ☐ 0
- ☐ 1
- ☐ 2
- ☐ 3
- ☐ 4
- ☐ >5

12. Medicijn gebruik (onder medicatie verstaan wij alle medicatie die een arts aan u voorgeschreven heeft)

.....

.....

.....

.....

.....

.....

13. Indien u medicijnen gebruikt, gebruikt u morfine-achtige medicatie? (oxycodon, oxycontin, morfine, fentanyl, et cetera)

.....

.....

14. Heeft u klachten van langdurige pijn (langer dan 6 maanden bestaand) niet gerelateerd aan de reden van operatie?

- ☐ Ja
- ☐ Nee

15. Heeft u eerder operaties ondergaan?

- ☐ Ja
- ☐ Nee

16. Indien u bij vraag 15 'Ja' heeft ingevuld, waaraan bent u eerder geopereerd?

.....

.....

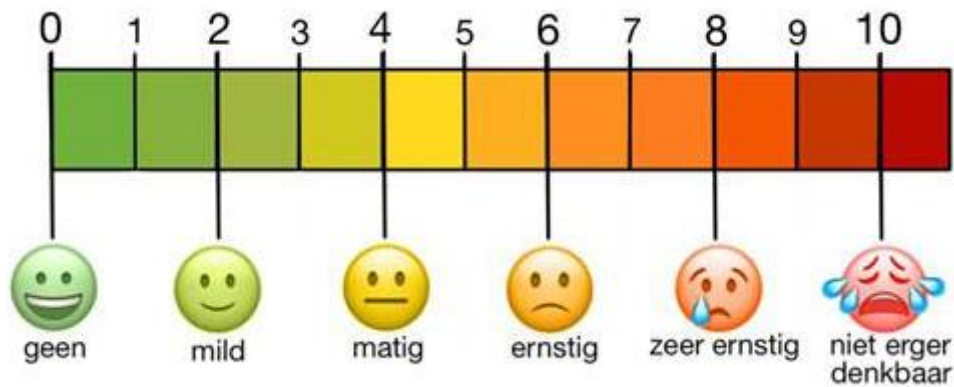
.....

.....

17. Heeft u momenteel pijn in de onderbuik?

- ☐ Ja
- ☐ Nee

18. Indien u bij vraag 17 'ja' heeft ingevuld, welk cijfer zou u dan aan deze buikpijn geven als 0 geen pijn is, en 10 de meest erg denkbare pijn?



Attachment 2: (Pre-)operative characteristics

1. ASA classification
 - a) ASA I
 - b) ASA II
 - c) ASA III
 - d) ASA III
2. Indication of surgery
3. Descensus uteri according to POPQ (point C on traction)
4. Length of complete surgery (in minutes)
5. When VANH: intra-abdominal pressure (in mmHg)
6. When VANH: total amount of CO₂ (in L)
7. Amount of blood loss (in mL)
8. Weight of the uterus (in grams)
9. Complexity of the surgery as judged by the surgeon (low, moderate, high)
 - a) Low
 - b) Moderate
 - c) High

Attachment 3 EQ-5D-5L vragenlijst

Zet bij iedere groep in de lijst hieronder een kruisje in het hokje dat het best past bij uw gezondheid VANDAAG

MOBILITEIT

- Ik heb geen problemen met lopen ☐
- Ik heb een beetje problemen met lopen ☐
- Ik heb matige problemen met lopen ☐
- Ik heb ernstige problemen met lopen ☐
- Ik ben niet in staat om te lopen ☐

ZELFZORG

- Ik heb geen problemen met mijzelf wassen of aankleden ☐
- Ik heb een beetje problemen met mijzelf wassen of aankleden ☐

| | | |
|--|--------------------------|---|
| Ik heb matige problemen met mijzelf wassen of aankleden | <input type="checkbox"/> | De beste gezondheid die u zich kunt voorstellen 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 De slechtste gezondheid die u zich kunt voorstellen |
| Ik heb ernstige problemen met mijzelf wassen of aankleden | <input type="checkbox"/> | |
| Ik ben niet in staat mijzelf te wassen of aan te kleden | <input type="checkbox"/> | |
| DAGELIJKSE ACTIVITEITEN (bijv. Werk, studie, huishouden, gezins- en vrijetijdsactiviteiten) | | |
| Ik heb geen problemen met mijn dagelijks activiteiten | <input type="checkbox"/> | |
| Ik heb een beetje problemen met mijn dagelijks activiteiten | <input type="checkbox"/> | |
| Ik heb matige problemen met mijn dagelijks activiteiten | <input type="checkbox"/> | |
| Ik heb ernstige problemen met mijn dagelijks activiteiten | <input type="checkbox"/> | |
| Ik ben niet in staat mijzelf mijn dagelijks activiteiten uit te voeren | <input type="checkbox"/> | |
| PIJN/ONGEMAK | | |
| Ik heb geen pijn of ongemak | <input type="checkbox"/> | |
| Ik heb een beetje pijn of ongemak | <input type="checkbox"/> | |
| Ik heb matige pijn of ongemak | <input type="checkbox"/> | |
| Ik heb ernstige pijn of ongemak | <input type="checkbox"/> | |
| Ik heb extreme pijn of ongemak | <input type="checkbox"/> | |
| ANGST/SOMBERHEID | | |
| Ik ben niet angstig of somber | <input type="checkbox"/> | |
| Ik ben een beetje angstig of somber | <input type="checkbox"/> | |
| Ik ben matig angstig of somber | <input type="checkbox"/> | |
| Ik ben erg angstig of somber | <input type="checkbox"/> | |
| Ik ben extreem angstig of somber | <input type="checkbox"/> | |

Wij willen weten hoe goed of slecht uw gezondheid VANDAAG is.

Deze meetschaal loopt van 0-100.

- 100 staat voor de beste gezondheid die u zich kunt voorstellen
- 0 staat voor de slechtste gezondheid die u zich kunt voorstellen

Markeer een X op de meetschaal om aan te geven hoe uw gezondheid VANDAAG is

Noteer het getal waarbij u de X geplaatst heeft =

Attachment 4 – Recovery Index 10

Om een inzicht te krijgen in het herstel na de operatie die u heeft ondergaan, vragen wij u deze vragenlijst in te vullen. Geef u daarvoor alstublieft bij elke vraag het antwoord dat het beste weergeeft hoe u zich de afgelopen week voelde. Dit gebeurt op een schaal van 1-5. Boven de gevallen staat de betekenis van de getallen.

Volledige mee oneens

Volledig mee eens

| | | | | | |
|--|---|---|---|---|---|
| 1. Ik ben snel moe | 1 | 2 | 3 | 4 | 5 |
| 2. Overdag moet ik regelmatig rusten | 1 | 2 | 3 | 4 | 5 |
| 3. Ook als ik niets doe, heb ik regelmatig last van buikpijn | 1 | 2 | 3 | 4 | 5 |
| 4. Zelfs lichte inspanning (bijv koffie zetten) kan ik nauwelijks doen | 1 | 2 | 3 | 4 | 5 |
| 5. Ik voel me volledig hersteld na de operatie. | 1 | 2 | 3 | 4 | 5 |
| 6. Ik kan mijn normale dagelijkse bezigheden in huis helemaal doen. | 1 | 2 | 3 | 4 | 5 |
| 7. Sinds de operatie heb ik moeite met slapen. | 1 | 2 | 3 | 4 | 5 |
| 8. De operatie en het herstel daarna zijn minder goed verlopen dan ik mij had voorgesteld. | 1 | 2 | 3 | 4 | 5 |
| 9. Ik heb in het algemeen veel pijn gehad na de operatie. | 1 | 2 | 3 | 4 | 5 |
| 10. De klachten waarvoor ik ben geopereerd zijn volledig verdwenen. | 1 | 2 | 3 | 4 | 5 |

Attachment 5: iMCQ

Toelichting

Wij willen graag weten met welke dokters u in de afgelopen 6 weken een afspraak had gerelateerd aan uw vaginale baarmoederverwijdering.

Het gaat om afspraken voor uzelf. Ook andere zorgverleners tellen mee. Bijvoorbeeld de fysiotherapeut.

Welke afspraken tellen mee?

- Controles
- Afspraken omdat u een lichamelijke of psychische klacht had
- Afspraken waarbij de dokter bij u thuis kwam
- Telefonische afspraken
- Telefoontjes met de receptenlijn

Wat telt niet mee?

- Afspraken voor een ander, bijvoorbeeld voor uw kind
- Telefoontjes om een afspraak te maken

Weet u niet precies hoeveel afspraken het waren? Schrijf dan op hoeveel het er ongeveer waren.

Vraag 1a. Heeft u in de afgelopen 6 weken afspraken gehad met huisarts of praktijkondersteuner gerelateerd aan uw operatie? Praktijkondersteuner wordt ook wel POH genoemd.

- ☐ Nee
☐ Ja

Heeft u "Ja" aangekruist? Beantwoord dan vraag 1b.
 Ga anders verder met vraag 2.

Vraag 1b. Hoeveel afspraken had u in de afgelopen 6 weken met uw huisarts en/of praktijkondersteuner (POH) gerelateerd aan uw operatie?

- ☐ afspraken huisarts
☐ afspraken praktijkondersteuner (POH)

Vraag 2. Hoeveel afspraken had u in de afgelopen 6 weken met een maatschappelijk werker gerelateerd aan uw operatie?

- ☐ Geen enkele afspraak
☐ afspraken

Vraag 3. Hoeveel afspraken had u in de afgelopen 6 weken met een fysiotherapeut gerelateerd aan uw operatie? Of met een caesartherapeut, therapeut mensendieck of een manueel therapeut? Tel alle afspraken met deze therapeuten bij elkaar op.

- ☐ Geen enkele afspraak
☐ afspraken

Vraag 4. Hoeveel afspraken had u in de afgelopen 6 weken met een ergotherapeut gerelateerd aan uw operatie?

- ☐ Geen enkele afspraak
☐ afspraken

Vraag 5. Hoeveel afspraken had u in de afgelopen 6 weken met een logopedist gerelateerd aan uw operatie?

- ☐ Geen enkele afspraak
☐ afspraken

Vraag 6. Hoeveel afspraken had u in de afgelopen 6 weken met een diëtist gerelateerd aan uw operatie?

- ☐ Geen enkele afspraak
☐ afspraken

Vraag 7. Hoeveel afspraken had u in de afgelopen 6 weken met een homeopaat gerelateerd aan uw operatie? Of met een acupuncturist? Tel alle afspraken met deze zorgverleners bij elkaar op.

- ☐ Geen enkele afspraak
☐ afspraken

Vraag 8. Hoeveel afspraken had u in de afgelopen 6 weken met een psycholoog gerelateerd aan uw operatie? Of met een psychotherapeut of psychiater? Tel alle afspraken met deze zorgverleners bij elkaar op.

- ☐ Geen enkele afspraak
☐ afspraken

Vraag 9. Hoeveel afspraken had u in de afgelopen 6 weken met de bedrijfsarts gerelateerd aan uw operatie?

- ☐ Geen enkele afspraak
☐ afspraken

Vraag 10a. Heeft u in de afgelopen 6 weken hulp van de thuiszorg gehad gerelateerd aan uw operatie?

- ☐ Nee
☐ Ja

Heeft u "Ja" aangekruist? Beantwoord dan vraag 10b tot en met 10d.
Ga anders verder met vraag 11.

Vraag 10b. Wat voor hulp van de thuiszorg heeft u gehad in de afgelopen 6 weken gerelateerd aan uw operatie? U kunt meer dan 1 hokje aankruisen.

- ☐ Huishoudelijke hulp
voorbeeld: stofzuigen, bed opmaken, boodschappen doen
- ☐ Verzorging van uzelf
voorbeeld: hulp bij douchen of aankleden
- ☐ Verpleging
voorbeeld: verband omdoen, medicijnen geven, bloeddruk meten

Vraag 10c. Hoeveel weken heeft u deze thuiszorg gehad gerelateerd aan uw operatie? Tel alle weken in de afgelopen 6 weken bij elkaar op.

Huishoudelijke hulp: ... weken in de afgelopen 6 weken
Verzorging van uzelf: ... weken in de afgelopen 6 weken
Verpleging: ... weken in de afgelopen 6 weken

Vraag 10d. Hoeveel uur thuiszorg kreeg u in deze weken gemiddeld?

Huishoudelijke hulp: gemiddeld ... uur in de week
Verzorging van uzelf: gemiddeld ... uur in de week
Verpleging: gemiddeld ... uur in de week

Vraag 11a. Heeft u in de afgelopen 6 weken medicijnen gebruikt?

- ☐ Nee
☐ Ja

Heeft u "Ja" aangekruist? Vul dan bij vraag 11b in welke medicijnen en hoeveel.
 Ga anders verder met vraag 12.

Vraag 11b. Welke medicijnen heeft u in de afgelopen 6 weken gebruikt? Met medicijnen bedoelen we alle medicijnen die u hebt gekregen op recept en geneesmiddelen die u hebt gekocht bij de apotheek of de drogist. U ziet eerst drie voorbeelden.

Let op: pak de verpakking erbij! Daarop staat hoeveel u per keer moest nemen. En hoe vaak u dat moest doen. Heeft u meer of minder gebruikt? Vul dan in hoeveel u ook echt gebruikt heeft.

| Hoe heet het medicijn? | Hoeveel heeft u per keer genomen? Kijk op de verpakking | Hoe vaak op een dag heeft u dit gedaan? Kijk op de verpakking | Op hoeveel dagen in de afgelopen 6 weken heeft u het medicijn gebruikt? |
|--|--|--|---|
| voorbeeld 1 Metoprolol (tegen hoge bloeddruk) | voorbeeld 100mg | voorbeeld 1 keer | voorbeeld 90 dagen |
| voorbeeld 2 Furosemide (plastabletten) | voorbeeld 40 mg | voorbeeld 1 keer | voorbeeld 26 dagen (2 x per week; 13 weken) |
| voorbeeld 3 Hydrocortison crème | voorbeeld - | voorbeeld 1 | voorbeeld 14 dagen |
| | | | |
| | | | |
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| | | | |
| | | | |

Vraag 12. Hoe vaak bent u in de afgelopen 6 weken op de spoedeisende eerste hulp van een ziekenhuis geweest gerelateerd aan uw operatie? Een andere naam voor spoedeisende eerste hulp is EHBO.

- ☐ Geen enkele keer
☐ ... keer

Vraag 13. Hoe vaak bent u in de afgelopen 6 weken met een ambulance naar het ziekenhuis gebracht gerelateerd aan uw operatie? Een andere naam voor ambulance is ziekenauto.

- ☐ Geen enkele keer
☐ ... keer

Vraag 14a. Had u in de afgelopen 6 weken een afspraak bij de polikliniek van het ziekenhuis gerelateerd aan uw operatie? Het gaat om afspraken voor uzelf met een dokter. Bijvoorbeeld met de cardioloog, reumatoloog of neuroloog.

- ☐ Nee
☐ Ja

Heeft u "Ja" aangekruist? Vul dan bij vraag 14b in bij welke soorten dokters u geweest bent. En hoe vaak. Op de eerste rij staat een voorbeeld.
 Ga anders verder met vraag 15.

Vraag 14b. Bij welke soorten dokters bent u in de afgelopen 6 weken in het ziekenhuis geweest gerelateerd aan uw operatie? En hoe vaak?

| Bij welke soort dokter bent u in het ziekenhuis geweest? | Hoe vaak bent u in de afgelopen 6 weken bij deze dokter geweest? |
|--|--|
| voorbeeld cardioloog | voorbeeld 2 keer |
| | ... keer |
| | ... keer |
| | ... keer |
| | ... keer |
| | ... keer |
| | ... keer |
| | ... keer |

Vraag 15a. Bent u in de afgelopen 6 weken overdag in het ziekenhuis geweest voor een behandeling gerelateerd aan uw operatie? U bleef dus niet slapen. U kwam bijvoorbeeld voor een bloedtransfusie, nierdialyse of chemokuur.

- ☐ Nee
☐ Ja

Heeft u "Ja" aangekruist? Beantwoord dan vraag 15b en 15c.
 Ga anders verder met vraag 16.

Vraag 15b. Voor welke soort behandeling was dit? Was dit voor meer dan 1 soort behandeling? Vul dan alle soorten behandelingen in.

Behandeling 1:

Behandeling 2:

Behandeling 3:

Vraag 15c. Hoeveel keer moest u in de afgelopen 6 weken voor deze behandelingen naar het ziekenhuis gerelateerd aan uw operatie?

..... keer voor behandeling 1

..... keer voor behandeling 2

..... keer voor behandeling 3

Vraag 16a. Bent u in de afgelopen 6 weken ergens anders geweest voor een behandeling overdag gerelateerd aan uw operatie? U bleef dus niet slapen. U ging bijvoorbeeld naar de dagopvang van een woon-/zorgcentrum of een psychiatrische instelling. Of naar de dagbehandeling van een revalidatiecentrum.

- ☐ Nee
☐ Ja

Heeft u "Ja" aangekruist? Beantwoord dan vraag 16b en 16c.
 Ga anders verder met vraag 17.

Vraag 16b. Wat voor instelling was dit? Kruis het goede antwoord aan. U kunt meer dan 1 hokje aankruisen.

- ☐ Woon-/zorgcentrum
☐ Revalidatiecentrum
☐ Psychiatrische instelling
☐ Een andere instelling, namelijk

Vraag 16c. Hoe vaak moest u hier in de afgelopen 6 weken naartoe gerelateerd aan uw operatie? Heeft u bij vraag 16b meer dan 1 hokje aangekruist? Vul dan hieronder voor iedere instelling in hoe vaak u er bent geweest.

Naar het woon-/zorgcentrum: keer in de afgelopen 6 weken

Naar het revalidatiecentrum: keer in de afgelopen 6 weken

Naar de psychiatrische instelling: keer in de afgelopen 6 weken

Naar de andere instelling: keer in de afgelopen 6 weken

Vraag 17a. Heeft u in de afgelopen 6 weken weleens in het ziekenhuis gelegen gerelateerd aan uw operatie? U moest dus blijven slapen. Bijvoorbeeld omdat u geopereerd was en niet meteen naar huis kon.

- ☐ Nee
☐ Ja

Heeft u "Ja" aangekruist? Beantwoord dan vraag 17b en 17c.
 Ga anders verder met vraag 18.

Vraag 17b. Hoe vaak heeft u in de afgelopen 6 weken in het ziekenhuis gelegen gerelateerd aan uw operatie?
 keer in de afgelopen 6 weken

Vraag 17c. Hoe lang heeft u in het ziekenhuis gelegen gerelateerd aan uw operatie? Heeft u meer dan 1 keer in het ziekenhuis gelegen in de afgelopen 6 weken Tel dan alle dagen bij elkaar op.
 dagen in totaal in de afgelopen 6 weken

Vraag 18a. Moest u in de afgelopen 6 weken ergens anders blijven slapen voor uw gezondheid gerelateerd aan uw operatie? Bijvoorbeeld in een woon-/zorgcentrum, psychiatrische instelling of revalidatiecentrum.

- ☐ Nee
☐ Ja

Heeft u "Ja" aangekruist? Beantwoord dan vraag 18b en 18c.
 Ga anders naar het einde van de vragenlijst.

Vraag 18b. Wat voor instelling was dit? U kunt meer dan 1 hokje aankruisen.

- ☐ Woon-/zorgcentrum
☐ Revalidatiecentrum
☐ Psychiatrische instelling
☐ Een andere instelling, namelijk

Vraag 18c. Hoe lang bent u in deze instelling geweest? Heeft u bij vraag 18b meer dan 1 hokje aangekruist? Vul dan hieronder voor iedere instelling in hoe lang u er bent geweest.

Bent u ergens meer dan 1 keer geweest in de afgelopen 6 weken? Tel dan alle dagen bij elkaar op.

In het woon-/zorgcentrum: dagen in de afgelopen 6 weken

In het revalidatiecentrum: dagen in de afgelopen 6 weken

In de psychiatrische instelling: dagen in de afgelopen 6 weken

In de andere instelling: dagen in de afgelopen 6 weken

Vraag 19a. Heeft u in de afgelopen 6 weken hulp gekregen van een familielid of een bekende vanwege uw lichamelijke of psychische problemen gerelateerd aan uw operatie?

- ☐ Nee
☐ Ja

Heeft u "Ja" aangekruist? Beantwoord dan vraag 19b tot en met 19d.

Ga anders verder met vraag 20.

Vraag 19b. Wat voor hulp van familieleden of bekenden heeft u gehad in de afgelopen 6 weken? U kunt meer dan 1 hokje aankruisen.

- ☐ Huishoudelijke hulp
 voorbeeld: stofzuigen, bed opmaken, boodschappen doen, klaarmaken van eten en drinken, verzorgen van kinderen

☐ Verzorging van uzelf
 voorbeeld: hulp bij douchen of aankleden, hulp bij het eten en drinken of het geven van medicijnen

☐ Praktische hulp
 voorbeeld: ondersteuning bij wandelen, het maken van uitstapjes of bezoeken aan bekenden, bezoeken aan de huisarts of het ziekenhuis, het regelen van hulp of het regelen van financiële zaken

Vraag 19c. Hoeveel weken heeft u deze hulp gehad? Tel alle weken in de afgelopen 6 weken bij elkaar op.

Huishoudelijke hulp: ... weken in de afgelopen 6 weken

Verzorging van uzelf: ... weken in de afgelopen 6 weken

Praktische hulp: ... weken in de afgelopen 6 weken

Vraag 19d. Hoeveel uur hulp kreeg u in deze weken gemiddeld?

Huishoudelijke hulp: gemiddeld ... uur in de week

Verzorging van uzelf: gemiddeld ... uur in de week

Praktische hulp: gemiddeld ... uur in de week

Vraag 20a. Welke wijze van vervoer heeft u gebruikt om van huis naar het ziekenhuis te gaan gerelateerd aan uw operatie?

- ☐ Niet van toepassing
☐ Te voet
☐ Fiets
☐ Auto

☐ Openbaar vervoer
☐ Taxi
☐ Anders, namelijk

Vraag 20b. Wat was de enkele reisafstand tussen uw huis en het ziekenhuis?

Deze afstand bedroeg: kilometer

Dit was de laatste vraag.

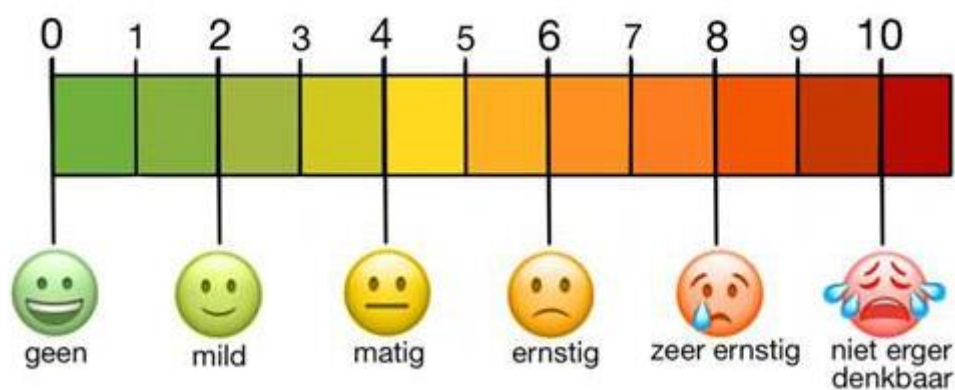
Attachment 6 Clavien Dindo classification:

TABLE 1. Classification of Surgical Complications

| Grade | Definition |
|------------|--|
| Grade I | Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside |
| Grade II | Requiring pharmacological treatment with drugs other than such allowed for grade I complications Blood transfusions and total parenteral nutrition are also included |
| Grade III | Requiring surgical, endoscopic or radiological intervention |
| Grade IIIa | Intervention not under general anesthesia |
| Grade IIIb | Intervention under general anesthesia |
| Grade IV | Life-threatening complication (including CNS complications)* requiring IC/ICU management |
| Grade IVa | Single organ dysfunction (including dialysis) |
| Grade IVb | Multiorgan dysfunction |
| Grade V | Death of a patient |
| Suffix "d" | If the patient suffers from a complication at the time of discharge (see examples in Table 2), the suffix "d" (for "disability") is added to the respective grade of complication. This label indicates the need for a follow-up to fully evaluate the complication. |

*Brain hemorrhage, ischemic stroke, subarachnoidal bleeding, but excluding transient ischemic attacks.
CNS, central nervous system; IC, intermediate care; ICU, intensive care unit.

Attachment 7 Participant's pain logbook and used medication:



Wij vragen uw pijn te scoren aan de hand van bovenstaande meter waarin 0 helemaal geen pijn betekent en 10 de meest denkbare pijn.

Dag 1 na operatie:

Pijnscore ochtend:

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|----|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| | | | | | | | | | | |

Pijnscore avond:

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|----|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| | | | | | | | | | | |

| | Aantal MG | Aantal tabletten | Tijdstip inname |
|----------------------------|-----------|------------------|-----------------|
| Paracetamol | | | |
| Ibuprofen | | | |
| Anderen, namelijk:..... | | | |

Dag 2 na operatie

Pijnscore ochtend:

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|----|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| | | | | | | | | | | |

Pijnscore avond:

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|----|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| | | | | | | | | | | |

| | Aantal MG | Aantal tabletten | Tijdstip inname |
|----------------------------|-----------|------------------|-----------------|
| Paracetamol | | | |
| Ibuprofen | | | |
| Anderen, namelijk:..... | | | |

Dag 3 na operatie:

Pijnscore ochtend:

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|----|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| | | | | | | | | | | |

Pijnscore avond:

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|----|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| | | | | | | | | | | |

| | Aantal MG | Aantal tabletten | Tijdstip inname |
|----------------------------|-----------|------------------|-----------------|
| Paracetamol | | | |
| Ibuprofen | | | |
| Anderen, namelijk:..... | | | |

Dag 4 na operatie:

Pijnscore ochtend:

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|----|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| | | | | | | | | | | |

Pijnscore avond:

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|----|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| | | | | | | | | | | |

| | Aantal MG | Aantal tabletten | Tijdstip inname |
|----------------------------|-----------|------------------|-----------------|
| Paracetamol | | | |
| Ibuprofen | | | |
| Anderen, namelijk:..... | | | |

Dag 5 na operatie:

Pijnscore ochtend:

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|----|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| | | | | | | | | | | |

Pijnscore avond:

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|----|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| | | | | | | | | | | |

| | Aantal MG | Aantal tabletten | Tijdstip inname |
|----------------------------|-----------|------------------|-----------------|
| Paracetamol | | | |
| Ibuprofen | | | |
| Anderen, namelijk:..... | | | |

Dag 6 na operatie:

Pijnscore ochtend:

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|----|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| | | | | | | | | | | |

Pijnscore avond:

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|----|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| | | | | | | | | | | |

| | Aantal MG | Aantal tabletten | Tijdstip inname |
|----------------------------|-----------|------------------|-----------------|
| Paracetamol | | | |
| Ibuprofen | | | |
| Anderen, namelijk:..... | | | |

Dag 7 na operatie:

Pijnscore ochtend:

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|----|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| | | | | | | | | | | |

Pijnscore avond:

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|----|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| | | | | | | | | | | |

| | Aantal MG | Aantal tabletten | Tijdstip inname |
|----------------------------|-----------|------------------|-----------------|
| Paracetamol | | | |
| Ibuprofen | | | |
| Anderen, namelijk:..... | | | |

Attachment 8 Financial costs**Medical costs:**Admission patient

- Ward (day)

Surgery:

- Surgery team costs (hour)
- Costs products
 - o Surgical devices

Health care providers:

- Gynaecologist (hour)
- Anaesthetist (hour)
- Resident gynaecology (hour)

Anaesthesia:

- Opiates (gift)
- Sedatives

Medications postoperative:

- Paracetamol (prescription)
- Diclofenac (prescription)
- Anti-emetic (prescription)
- Opiates (prescription)

Complications:

- Clavien Dindo classification

Post-operative hospital care:

- Medication (prescription)
- Urine bladder retention (procedure)
- Laboratory tests (procedure)
- Clinical care (procedure)

Post-operative other health care:

- Alternative health care (procedure)
- General practiser (GP) (consult)
- Other specific costs form GP (consult)
- Medications (prescription)
- dentist (procedure)
- Physiotherapist (procedure)

Non-medical costs

- Home care (hour)
- Domestic care (hour)
- Informal care (hour)
- Travel costs –car (total)

Indirect costs:

- Productivity loss (hour)