# Evaluation of two vaginal, uterussparing surgical methods for pelvic organ prolapse reconstruction: modified Manchester operation (MM) and sacrospinal hysteropexy (SSH).

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Objective:The life-time risk for POP surgery is 20%, and 30% of these women will need surgery because of a recurrence. VaginalPOP surgery (VH, SSH and MM) is the first choice surgical treatment. The numbers of uterus sparing operations (SSH andMM)…

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| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Vulvovaginal disorders (excl infections and inflammations) |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON54613

**Source**
ToetsingOnline

**Brief title**
SAM-trial

### Condition

- Vulvovaginal disorders (excl infections and inflammations)
- Obstetric and gynaecological therapeutic procedures

**Synonym**
pelvic organ prolapse, vaginal descent

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Academisch Medisch Centrum
**Source(s) of monetary or material Support:** ZonMw Doelmatigheid

## Intervention

**Keyword:** composite outcome, pelvic organ prolapse, randomisation, surgical method, uterussparing

## Outcome measures

**Primary outcome**

OUTCOME PARAMETERS/TIME:

Primary outcome:

*Composite success*, defined as a combination of: 1) absence of POP beyond the

hymen in any compartment, 2) absence of

bulge symptoms and 3) absence of reoperation for POP. Absence of bulge symptoms

is defined as a negative response to the

question, *Do you see or feel a bulge in the vaginal area* (UDI domain genital

prolapse score: 0). This outcome is generally

referred to as Barber criteria.

The composite outcome was chosen as the most patient relevant outcome because

it accounts for anatomic changes in any

compartment, bulge symptoms, and the need for retreatment. Vaginal bulge

symptoms postoperatively had a significant

relationship with patient*s assessment of overall improvement, while anatomic

success alone did not. Success is defined as

achieving optimal anatomy and function in 1 operation and thus need for a

reoperation is defined as failure.

**Secondary outcome**

Secondary outcomes:

- Hospital parameters (surgery time, hospitalisation time)

- Surgery related morbidity/complications (including menstrual problems,

hematometra, any problems with uterine access such

as diagnostic cervical or endometrial sampling or IUD insertion)

- Further treatments for POP or UI

- POP-Q: anatomy in all compartments

- Generic quality of life: Euroqol 5D-5L (EQ-5D-5L) (6 questions)

- Disease specific quality of life:

Regarding symptoms: Pelvic Floor Distress Inventory (PDFI-20) (20 questions)

Regarding the impact of symptoms:

Patient Global Impression of Improvement (PGI-I) (1 question)

Pelvic Floor Impact Questionnaire (PFIQ-7) (7 questions)

- Sexual function: Pelvic Organ Prolapse/Urinary Incontinence Sexual

Questionnaire (PISQ-IR) (20 questions)

- Pain perception: VAS score pelvic pain: rest, activity (2 questions)

- Costs

# Study description

**Background summary**

INTRODUCTION/RATIONALE:
POP is highly prevalent (50% of vaginally parous women) and the symptoms have a high impact on quality of life. 20% of
Dutch women will undergo POP surgery during life time. According to guidelines, first choice surgical treatment of POP is a
vaginal POP operation. According to Kiwacharity, more than 17.000 of these operations are performed yearly in the
Netherlands. Vaginal POP operations consist of vaginal hysterectomy (VH), Modified Manchester operation (MM) or
sacrospinous hysteropexy (SSH), in combination with colporrhaphy when indicated. The most distinct difference between the
operations is that in VH the uterus is removed and in SSH and MM the uterus is attached to different pelvic ligaments.
These 3 types of surgery have lead to practice pattern variation (PPV) between hospitals and physicians. PPV is defined
as a difference in care that cannot be explained by the underlying medical condition. In general PPV is considered to be a
problem in controlling medical costs.
The comparison VH versus SSH has been made in the randomized SAVE-U study. That study showed non-inferior
effectiveness of SSH, but shorter operation times in SSH. In combination with a patient*s preference for uterus preservation,
the SAVE-U publications have provided arguments to choose for uterus sparing surgery. However, it is still unclear whether the
2 operations (SSH and MM) have equal outcome.
This study proposal is on a comparison of the two uterus sparing techniques (effectiveness and costs). We hypothesise that the
effectiveness of SSH is non-inferior to MM, but with shorter operation times.
The study will reveal whether the exsisting PPV is
unwanted or not significant in terms of effectiveness and cost.
HEALTH CARE EFFICIENCY PROBLEM:
Vaginal POP operations are subject to uncontrolled PPV due to lack of evidence. Only 13% of women prefered
hysterectomy, but in 2009 in 60% the uterus was removed (range 2 and 100% between hospitals). Between 1997 and
2009, the rise in MM and SSH was more than 5-fold. In the two hospitals in Nijmegen, 92% and 36% of POP procedures was
a MM, and in some Dutch centres no MM or SSH is performed at all. The variation and the fluctuation is not based on evidence
on a better outcome. The choice of operation thus depends mainly on the physican*s preference. This was confirmed in a
questionnaire study among 161 (uro)gynaecologists in 2011. The physician*s preference for VH, SSH or MM was equally
devided in women with stage 2 uterine descent (varying from 25-34%). Evidence

based deimplementation of one the
procedures or shared decision making between patient and physician is not possible at this moment.

## Study objective

Objective:
The life-time risk for POP surgery is 20%, and 30% of these women will need surgery because of a recurrence. Vaginal
POP surgery (VH, SSH and MM) is the first choice surgical treatment. The numbers of uterus sparing operations (SSH and
MM) are rising more than 5-fold in recent years, at the expense of VH. Doctor*s preference was equally divided between the
three procedures in the patient group as defined in the present study proposal. There is maximal practice pattern variation
dictated by this doctor*s preference. Shared decision making is not possible due to this lack of evidence, mainly on
effectiveness of MM. MM is still performed approximately 3.000 times yearly in the Netherlands, which makes it undesirable to
neglect this knowledge gap.
This project will fill the knowledge gap on the effectiveness and costs of SSH versus MM. There are no other peer reviewed
publications, on going or planned studies on the topic. Guidelines do not advise one techniques over the other.
(Uro)gynaecologists do not expect relevant differences in the main outcomes (composite outcome). At this time point, we
do not know whether the substantial practice pattern variation in the Netherlands is detrimental or not. This study will provide
the answer to that question, and may lead to the need for deimplementation of one of the procedures.
Hypothesis: composite outcome of SSH after 2 years is non-inferior to MM but with shorter operation times in SSH.
Research questions:
1. Is SSH non-inferior to MM in women with signs and symptoms of POP in terms of composite outcome?
The composite outcome defines a successful operation in case of subjective and objective success achieved in the absence of
re-operation.
2. In case SSH is non-inferior, is deimplemenation of MM indicated based on a difference in costs in favour of SSH?

## Study design

DESIGN
The study is designed as a non-inferiority study, randomising each eligible patients giving informed consent for either the

Modified Manchester (MM) or Sacrospinous Hysteropexy (SSH) operating technique. The follow up period is 2 years.

The H0 for this trial is that SSH is non-inferior to MM regarding composite outcome for success. We consider SSH
inferior when the absolute difference in success rate exceeds 9% compared to the expected success rate of 89% - this is
comparable to a relative difference of 0.80/0.89 is 0.90. If the left border does not exceed the left border of the 9% CI with the
pre-defined threshold of 0.90 for inferiority we will consider SSH to be non-inferior to MM.
The analysis will be by intention-to-treat and per protocol. The primary outcome is defined as the composite of success (dichotomous) 1 year after surgery.
Results of secondary outcomes will be described as frequencies, absolute and relative risks, and hazard ratio*s for
dichotomous outcomes as appropriate, together with confidence intervals. Continuous outcomes will be described by mean/
median, mean difference, or standardized mean difference.
Subgroup analyses will be adjusted for relevant prognostic factors. No interim analyses for effectiveness, adverse effect, or
futility are planned. A Statistical Analysis Plan will be completed early during the trial, including ICT standards and a
data-monitoring plan.
Missing values are minimised though active trial monitoring within the Consortium. Data are routinely prospectively collected.
The software Castor (https://nl.castoredc.com) will be used to collect the questionnaire data. Therefore, the likelihood of
missing values for which data eventually cannot be obtained is very limited. If circumstance require however, a limited amount
of missing values (if missing not at random) may be imputated. In pertaining situations, sensitivity analyses will be carried out to
describe the effect of imputation.

SAMPLE SIZE CALCULATION
Sample sizes of 193 in group one and 193 in group two achieve 80% power to detect a
non-inferiority margin difference between the group proportions of -0.0900. The reference group proportion is 0.8900. The treatment group proportion is assumed to be 0.8000 under the null hypothesis of inferiority. The power was computed for the case when the actual treatment group proportion is 0.8900. The test statistic used is the one-sided Z test (unpooled). The significance level of the test was targeted at 0.0250.
The 9% non-inferiority margin was motivated by the margins used in two other large national studies SAVE-U (7%) and PEOPLE study (10%).
The anticipated number of patients is considered both feasible in terms of number of

patients available, willingness to participate and maximum available funding (see also Feasibility).

### Intervention

INTERVENTION(S)
Sacrospinous hysteropexy (SSH):
After opening the posterior vaginal wall, the pararectal space is explored at the right side and the sacrospinous ligament is
identified. The posterior side of the cervix is attached to the sacrospinous ligament with 2 non-absorbable Prolene sutures
approximately 2 cm medial of the ischial spine (to prevent damage to the pudendal nerve). Anterior and posterior colporrhaphy
as indicated.
Apeldoorn: https://www.youtube.com/watch?v=ySSfy2A1_RM
USUAL CARE/COMPARISON
Modified Manchester operation (MM):
The procedure consists of extraperitoneal plication of the uterosacral ligaments (and cardinal where possible) with use of three
or four Vicryl 1 sutures and amputation of the cervix. The most cranial suture is fixated through the posterior fornix of the
vagina. Anterior and posterior colporrhaphy as indicated.
Videoclip Enschede: https://www.youtube.com/watch?v=HYzWm7rRjho.

Anaesthesia, antibiotics and thrombosis prophylaxis, patient*s position on the OR table, postoperative catheterisation and
vaginal packing and standards for postoperative hospitalisation are similar for the procedures. Local protocols in the including
hospitals will be checked for differences between the treatments (e.g. duration of hospitalisation). In case of differences the
protocols will be made uniform (as far as possible) before the start of the study, but will otherwise be left to the discretion of the
surgeon.

### Study burden and risks

Burden: follow up with physical (gynaecological) examination at 1 and 2 years after surgery and questionnaires at 12 weeks, 1 and 2 years is not standard in all Dutch hospitals. This holds true for 5 and 10 years after surgery as well.
Risks: not applicable.

## Contacts

### Public

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

Women with symptomatic pelvic organ prolapse including uterine descent. The prolapse may be at any stage but POP-Q point D may not exceed minus 1cm.
Community dwelling
Capable of filling out questionnaires
Patients from the hospitals in Nijmegen, Zwolle, Almelo, Hengelo and Enschede) are asked to participate in a supine and upright MRI scan at the University of Twente.

## Exclusion criteria

- < 18 years
- Previous prolapse or other pelvic floor surgery Previous POP surgery
- Previous incontinence surgery
- POP-Q longer than 3 months ago at randomisation
- Need or wish for removal of the uterus

- Need for concomitant mid-urethral sling surgery
- Contraindication to uterus preservation (in case indicated, a pap-smear and/or pipelle endometrial biopsy should be normal before inclusion)
- Pregnancy or future wish for childbearing
- Insufficient understanding and reading of the Dutch language
- Not capable of filling out questionnaires

For the facultative MRI study additional exclusion criteria are in order, namely:
- Inability to stand for 15 minutes without assistance
- Hip width> 47cm (jeans size >44)
- Not allowed to do a maximum Valsalva manoeuvre because of cardiac or pulmonary disease
- Not eligible for MRI, in response to the MRI safety checklist

# Study design

## Design

**Study type:** Interventional

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| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Treatment |

## Recruitment

NL

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| Recruitment status: | Recruiting |
| Start date (anticipated): | 03-07-2018 |
| Enrollment: | 424 |
| Type: | Actual |

# Ethics review

Approved WMO

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| Date: | 29-11-2017 |
| Application type: | First submission |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |

Approved WMO

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| Date: | 26-02-2018 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 27-03-2018 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 10-04-2018 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 23-05-2018 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 30-07-2018 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 02-08-2018 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 05-11-2018 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 14-11-2018 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 24-04-2019 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO | |

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|---|---|
| Date: | 30-09-2020 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 26-09-2023 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
|---|---|
| CCMO | NL61904.091.17 |