COMPARISON OF SHORT-TERM OUTCOMES BETWEEN TWO SACROSPINOUS SUTURE CAPTURE DEVICES:

A RANDOMISED CONTROLLED TRIAL

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DECLARATION OF ORIGINALITY

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ABSTRACT

BACKGROUND

Sacrospinous Fixation is a procedure for mid-compartment apical suspension in pelvic organ prolapse surgery with high success rates. The approach by traditional wide dissection has been well-documented. The literature is lacking however with regard to newer devices on the market that use less extensive dissection to perform this procedure.

METHODS

A randomised controlled trial was carried out comparing the Boston Scientific's Capio Slim® (control) and Bard's Fixt® (intervention) for bilateral sacrospinous fixation in women with mid-compartment prolapse requiring surgery and who met the study criteria. The primary outcome was time (in seconds) to successful bilateral suspension suture placements. Secondary outcomes examined were used to assess short-term safety and efficacy of the devices at the time of the procedure and at the six week follow-up.

RESULTS

Of the 51 women recruited to the trial, 27 were randomised to the Capio slim® control arm and 24 women to the Fixt ® intervention arm of the trial. Analysis was carried out by intention to treat. Most of the demographic characteristics and pre-operative prolapse questionnaire scores of participants in the two arms of the trial were similar. The mean pre-operative POP-Q point C was +1.185 (±3.990) in the Capio Slim® group and +1.458 (±4.452) in the Fixt® group (p value 0.8182). When comparing the Capio Slim® and Fixt® devices in this non-inferiority trial, no significant difference was found in the primary outcome, i.e. time (in seconds) to bilateral sacrospinous suture placements. The median time for the Capio Slim® was 170.5 (105 - 642) seconds and 222 (112 – 848) seconds with the Fixt® (p value of 0.3513). No significant difference was found in the secondary outcomes examined. This related to the number of throws required until a successful suture is placed (median of 1 throw on each side in both arms); adverse events intra-operatively and post-operatively; post-operative subjective pain assessments, post-operative symptoms and levels of satisfaction (both arms median score 5 out of 5). Improvement of POP-Q point C at 6 weeks was comparable with mean improvement of 7.96 cm with the Capio Slim® and 7.63 cm with the Fixt® (p value 0.7849). No statistical difference was found in the incidence of post-operative buttock pain related to pudendal nerve entrapment requiring release of the suspension suture (ROS incidence 7% Capio Slim®, 8% Fixt®).

CONCLUSIONS

Non-inferiority between the Capio Slim® and Fixt ® device was proven when comparing short-term outcomes in terms of their safety and efficacy. The anterior approach to the sacrospinous fixation was also shown to be an effective procedure for mid-compartment prolapse. Long-term trials are needed to assess the success of procedures performed with the above devices beyond 6 weeks. (Funding: Obstetrics & Gynaecology Departmental, GSH. South African National Clinical Trial Register www.sanctr.gov.za number: 5358)

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LIST OF ABBREVIATIONS

SSSCD	Sacrospinous Suture Capture Device trial
POP	Pelvic Organ Prolapse
WHI	Women's Health Initiative
BMI	Body Mass Index
PFIQ-7	Pelvic Floor Impact Questionnaire-7
PFDI-20	Pelvic Floor Distress Inventory-20
PISQ-IR	Pelvic Organ Prolapse/Incontinence Sexual Questionnaire, IUGA-Revised
POPDI-6	Pelvic Organ Prolapse Distress Inventory
UDI-6	Urinary Distress Inventory
CRADI-8	Colorectal-anal Distress Inventory
POP-Q	Prolapse Organ Prolapse-Quantification
PFMT	Pelvic floor muscle training
SSF	Sacrospinous Fixation
AVR	Anterior Vaginal Repair
PVR	Posterior Vaginal Repair
TVT	Tension-free Vaginal Tape insertion
EBL	Estimated Blood Loss
RTT	Return To Theatre
ROS	Removal Of Suture
TOVF	Trial Of Void Failure
PPA	Pre-operative Pain Assessment
IPPA D3	Immediate Post-operative Pain Assessment (day 3)
IPPA DC	Immediate Post-operative Pain Assessment on Discharge
STPPA	Short-term Post-operative Pain Assessment
WHO	World Health Organisation

BACKGROUND

Urogynaecology is a constantly evolving discipline, with cutting edge advances being made that impact greatly on the quality of life of women globally. Pelvic organ prolapse (POP) is a major contributor to the pathologies in this field.

With the rapidly ageing population, the demand for prolapse repair will increase by almost 50% over the next 30 years as the proportion of women older than 50 years old increases.[1] The mean age of women seeking medical care for pelvic organ prolapse was found to be 61 years[2].

Prolapse prevalence data was revealed in the Women's Health Initiative Hormone Replacement Therapy Clinical Trial, a large multi-centre trial in the United States. They found that in the 16 616 women with a uterus, the rate of objective prolapse was[3]:

- 34.3% with cystocele
- 18.6% with rectocele
- 14.2% with uterine prolapse

Of the 10,727 women who had had a hysterectomy, the prevalence was[3]:

- 32.9% with cystocele
- 18.3% with rectocele

(vault prolapse was not commented on)

Risk factors for pelvic organ prolapse were identified in the WHI trial for the (North American) population studied. The factors strongly associated with increased risk of pelvic organ prolapse was advanced age, parity and obesity[3]. They showed that the risk of prolapse increased as the body mass index (BMI) increased, i.e. with BMI 25-30 kg/m^2 prevalence increased by 31% for uterine prolapse, 38% for rectocele, and 39% for cystocele; BMI >30 kg/m^2 prevalence increased by 40% for uterine prolapse, 75% for rectocele, and 57% for cystocele. Risk of uterine prolapse increased with increasing parity up to 5 births, after which no additional risk was noted.[3]

Surgery for pelvic organ prolapse has been problematic due to the relatively high recurrence rates as well as a lack of evidence-based medical practice. Ohlsen et al found that by the age of 80 years, the risk of having a surgical repair for pelvic organ prolapse or urinary incontinence was 11.1%, with a reoperation rate of almost 30%.[4] With this as an indicator of burden of disease, it is essential that we

have evidence for best practice, i.e. which surgical technique has the lowest risk of complications and is least likely to result in failure requiring repeat surgery. A Cochrane review by Maher et al (2007) reviewing the different surgical approaches in the management of pelvic organ prolapse, uncovered a gap in the research around this condition. Too few well-powered randomised controlled trials were found to make adequate recommendations for best practice. A limited number of trials had been found addressing research around vaginal sacrospinous suspension. Three trials had found that abdominal sacrocolpopexy had lower rates of prolapse recurrence and dyspareunia than the vaginal sacrospinous colpopexy, but longer operating and recovery times as well as higher costs. When searching for trials addressing the vaginal surgical approach, no trials had been identified comparing McCall culdoplasty with sacrospinous colpopexy, or McCall culdoplasty and uterosacral ligament plication with vaginal sacrospinous colpopexy. The author concluded: "The data from randomised trials are currently insufficient …… Adequately powered randomised controlled clinical trials are urgently needed."[5] This trial, though not a long-term one, aims to contribute to partially filling this gap in research, with potential for long term follow up in the future.

Anatomy

Pelvic organ prolapse involves prolapse of the anterior, central or posterior compartments of the vagina. Anatomically this can be described as a cystocele, uterine or vault prolapse after hysterectomy, an enterocele or a rectocele respectively.

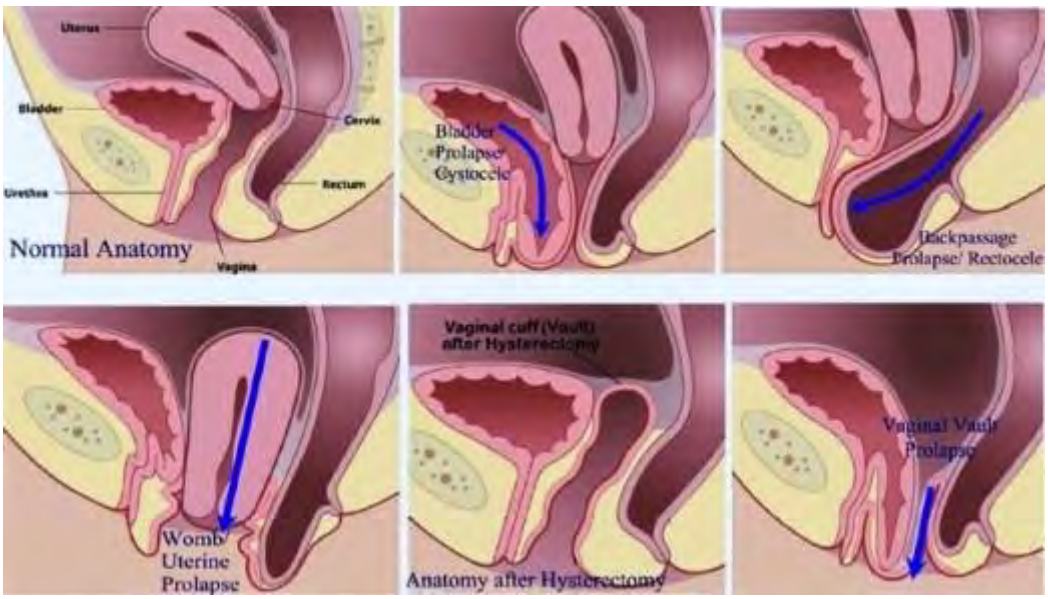


Figure 1. Anatomical changes in uterine and vault prolapse[6]

The pelvic organs are supported at a number of levels, with a suspension system made up of ligaments, pelvic floor muscles and fascia within the pelvis[7]:

- Level 1 support is the uterosacral and cardinal (transverse cervical) ligament complex that runs from the cervix to the sacrum posteriorly, and the cervix to lateral pelvic sidewall respectively. This level of support provides vaginal apical (mid-compartment) support, maintaining vaginal length.[1]
- Level 2 support involves the mid-portion of the vagina. It consists of the endopelvic fascia that attaches the lateral aspect of the vagina to arcus tendineus.[1]
- Level 3 support involves the pelvic floor muscles and fascia supporting the distal, most superficial aspect of the vagina and perineum. [1]

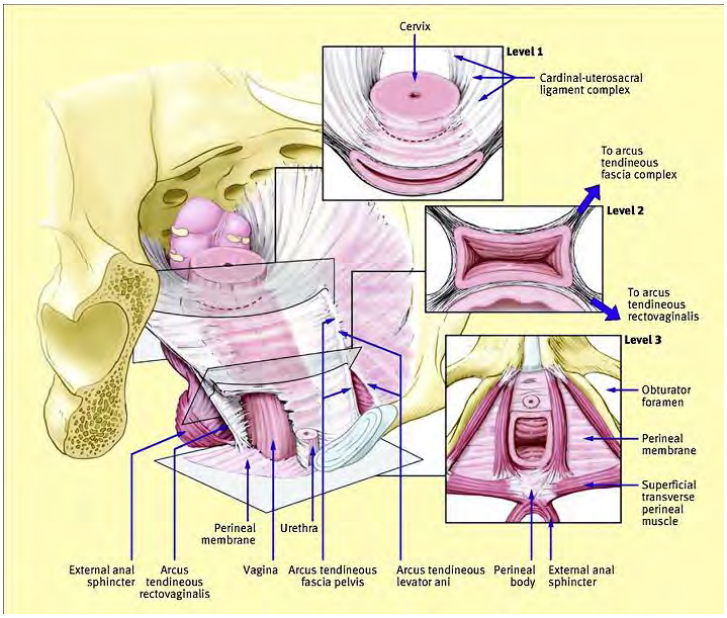


Figure 2. Complex 3D support of pelvic organs.[8]

The pelvic floor is made up of the pelvic diaphragm (levator ani and coccygeus muscles) and the urogenital diaphragm. (See Figure 3) The levator ani muscles in turn, consist of the pubococcygeus (puborectalis, pubovaginalis, pubourethralis) and iliococcygeus muscles.

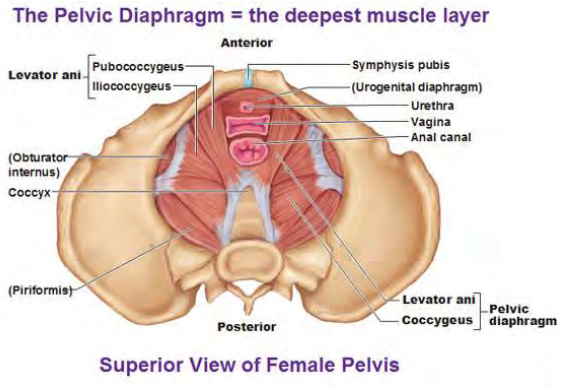


Figure 3. Superior View of the Female Pelvis[9]

Of note is the location of the sacrospinous ligament that runs from the ischial spine postero-medially to the lateral aspect of the sacrum. The pudendal nerve (from the S2, S3 and S4 spinal nerves) exits

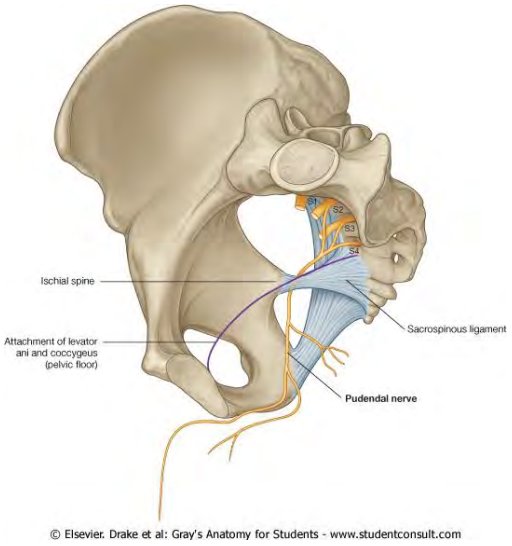


Figure 4. Course of Pudendal Nerve[10]

the pelvis through the greater sciatic foramen, runs superficial to the sacrospinous ligament at its lateral aspect and then enters the pelvis through the lesser sciatic foramen (S2, S3 and S4 spinal nerves) (see Figure 4). The pudendal nerve provides sensory innervation to the perineum, vulva perianal skin, clitoris, urethra and vaginal vestibule. Motor function is delivered to external anal sphincter, perineal muscles and urogenital diaphragm via this nerve.[1] The sacrospinous ligament's location provides an ideal position for surgical mid-compartment suspension. The pudendal nerve is however vulnerable to entrapment during the surgery, a well-recognised complication of the procedure. The Sciatic nerve, which runs deep to this ligament is also vulnerable to injury at this point, but to a much lesser degree.

Pathology

Pelvic organ prolapse occurs due to weakening of the supportive structures of the vaginal canal i.e. muscles and connective tissue of the pelvic floor; fibromuscular tissue of the vaginal wall; and endopelvic connective tissue. For uterine or vault prolapse specifically, the defects of apical support involve weakening or loss of support of cardinal/uterosacral ligaments; and/or detachment, attenuation or tearing of the fibromuscular tissue of the vagina (which may occur at the time of vaginal birth).[1]

Clinical features

Pelvic organ prolapse can have significant impact on a woman's quality of life of women. Urinary symptoms include incontinence, difficulty voiding, urgency and frequency. Obstructive defecation symptoms may also be present as well as pelvic discomfort and dyspareunia.[1] In an article looking at symptoms in women with POP, severe bother was reported in 75% of women due to the sensation of a lump outside the introitus; 72% of women were bothered by the feeling of pelvic heaviness ; while 65% were bothered by urge incontinence. It was reported that of sexually active women, 57% had

mechanical or psychological problems because of their prolapse, and 35% complained of dyspareunia or vaginal dryness.[11]

Validated questionnaires are used to assess the level of distress and impact of these symptoms on women's lives. The Pelvic Floor Impact Questionnaire-7 (PFIQ-7) and Pelvic Floor Distress Inventory-20 (PFDI-20), two condition-specific quality-of-life questionnaires, were proven to be valid, reliable and a responsive measure of the impact of POP.[12] The Pelvic Organ Prolapse/Incontinence Sexual Questionnaire, IUGA-Revised (PISQ-IR), was shown to be valid, reliable and a responsive measure of sexual function in pelvic organ prolapse.[13]

In the clinical assessment of POP, two standardised methods are commonly used, i.e. the Baden-Walker halfway system and the Pelvic Organ Prolapse Quantification (POP-Q) system (see Table 1). The Baden-Walker classification describes the degree of prolapse in grades: 0 if no prolapse; 1 if descent halfway to the hymen; 2 if descent to the hymen; 3 if descent halfway past the hymen; and 4 if procidentia is present. The POP-Q system assesses the degree of prolapse using the hymen or remnants thereof as a point of reference in relation to six specific points within the vagina (Figure 5). Point C is the distal edge of the cervix or vaginal cuff in the assessment of mid-compartment prolapse.[15] A measurement of zero equates to a point C was at the hymen, above the hymen is a negative number in terms of the measurement, and beyond the hymen is a positive number.

anterior wall **Aa**	anterior wall **Ba**	cervix or cuff **C**
genital hiatus **gh**	perineal body **pb**	total vaginal length **tvl**
posterior wall **Ap**	posterior wall **Bp**	posterior fornix **D**

Table 1. Points of reference in assessment of POP [16]

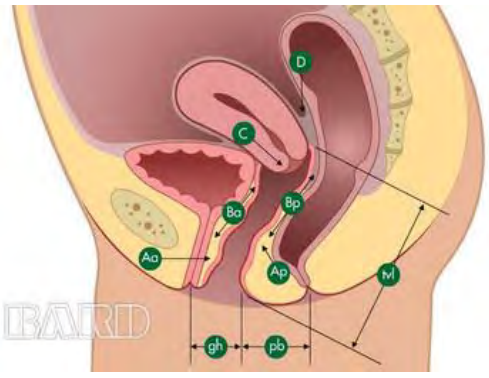


Figure 5. POP-Q 6 point measurements[14]

POINTS	DESCRIPTION	RANGE
Aa	Anterior wall 3cm from hymen	-3cm to +3cm
Ba	Most dependent portion of rest of anterior wall	-3cm to +tvl
C	**Cervix or vaginal cuff**	**+/-tvl**
D	Posterior fornix (if no previous hysterectomy)	+/- tvl or omitted
Ap	Posterior wall 3cm from hymen	-3cm to +3cm
Bp	Most dependent portion of rest of posterior wall	-3cm to +tvl

Table 2. Possible ranges of reference points in POP-Q assessment [16]

Management

Treatment options for uterine or vault prolapse are dependent on individualised holistic assessments. Expectant management may be instituted on a 'wait-and-see' basis in women who are not particularly bothered by the prolapse as long as complete bladder emptying can be demonstrated. Conservative non-surgical treatment is appropriate management for women not fit for surgery, or where the surgical option is declined. Conservative management includes lifestyle changes, pelvic floor muscle training and the use of vaginal pessaries.[1] Lifestyle changes suggested are reducing/avoiding increases in abdominal pressure; e.g. loss of weight, avoidance of constipation and lifting of heavy objects, treatment of chronic cough.[17] Pelvic floor muscle training (PFMT) is more beneficial in women with less severe prolapse i.e. Baden Walker grade 1 and 2.[17] The aim of pelvic floor exercises is to bulk up the pelvic floor muscles, increasing the tone and strength of the pelvic floor. A Cochrane review by Hagen showed that PFMT served to prevent worsening of the prolapse and improvement of prolapse-related symptoms.[18] The option of vaginal pessaries has been a successful alternative to surgery in the treatment of POP for the medically unfit patient and those who decline surgery. In a prospective study with 100 participants, Clemons et al reported a 90% improvement in bulge symptoms and 49% improvement in pressure symptoms, the most common mid-compartment prolapse symptoms, after 2 months with a vaginal pessary.[19] Though vaginal pessaries are usually well tolerated, logistical issues arise due to the need for regular (usually 6 monthly) checks of the pessary in an attempt to prevent the risks of sepsis, erosions and fistula formation associated with long-term unsupervised use.

Surgical options specifically for central compartment prolapse involve the apex which is the keystone of vaginal support. Apical suspension may either occur with the uterus in situ, or at the time of hysterectomy or as part of vault prolapse repair surgery. The approach may be abdominal (open or

laparoscopic) or vaginal. The abdominal mid-compartment prolapse repair procedures include mesh based procedures like sacrocolpopexy/sacrohysteropexy. For the purpose of this paper, the vaginal route will be focussed upon.

The decision for uterine preservation versus hysterectomy is made on an individual case-by-case basis. Maher et al showed that the subjective success rate for sacrospinous fixation with hysterectomy was 86% while that of sacrospinous hysteropexy (uterus in situ) was 78%. He showed no statistically significant difference between the two procedures with regards to the subjective or objective success rate.[20]

With vaginal hysterectomy, the options for apical suspension are: [21]

- McCall Culdoplasty
- High Uterosacral ligament suspension
- Sacrospinous fixation
- Illiococcygeus fixation

During vaginal vault prolapse repair surgery, various techniques may be employed to suspend the vault, which includes: [21]

- Sacrospinous Fixation (SSF)
- Illiococcygeus Fixation
- Mesh based procedures

Uterosacral ligament suspension involves suspension of the vaginal vault from the uterosacral ligament. McCall culdoplasty involves closure of Pouch of Douglas, apposing peritoneum and suspending the vault to uterosacral and cardinal ligaments. In Iliococcygeus fixation the suspension suture is placed through the iliococcygeal fascia medial and caudal to the Ischial spine.

Prolapse surgery though successful, was found to be not without adverse outcomes. Barber et al found that bilateral uterosacral ligament vault suspension had a 90% success rate in terms of prolapse symptom resolution, albeit in a small population size with relatively short-term follow-up (median post-operative follow-up of 15.5 months). There was however some reduction in vaginal length, as well as 11% incidence of intra-operative ureteric occlusion. Similar risks arose with McCall culdosplasty due to the use of uterosacral suspension.[22] High uterosacral ligament suspension refers to the vault

suspension suture being placed deeply enough postero-dorsally in the uterosacral ligament so as to avoid ureteric injury, as well as intra-operative cystoscopy to confirm urine flow from both ureters. By placing the suture high, this modified procedure was found to have a 5 fold decrease in ureteric injuries.[23] A recent randomised trial found no significant difference in terms of anatomic and functional outcomes, or adverse events when Sacrospinous fixation and high Uterosacral ligament suspension was compared.[24] In a prospective study by Krissi et al, iliococcygeal fixation was shown to be a relatively safe procedure, but was found to reduce total vaginal length that may be problematic in sexually active women undergoing the procedure.[25]

Numerous vaginal mesh kits are available for apical suspension in uterine or vault prolapse. A systematic review by Diwadkar et al comparing various apical suspension procedures, found that mesh-based procedures provided good apical support with lower prolapse recurrence rates requiring repeat surgery. However, reoperation rates for complications were higher than all other modalities. Significant complications noted were erosions and fistulae secondary to the mesh.[26]

Sacrospinous fixation (SSF) is an effective technique in vaginal reconstruction and has been shown to have high success and low recurrence rates for uterine and vault prolapse. In a study looking at the outcomes following SSF where either a Maiya needle passer or a Capio® device was used, 86% of participants reported total cure of prolapse, with a similar percentage reporting improved household and social activity, as well as some improvement in sexual activity. Long term success (2-4 year follow-up) in terms of sustained apical suspension was reported to be 94% in this study.[27]

Sacrospinous fixation can be performed with or without the uterus in-situ, and with concomitant anterior and/or posterior repair. A midline vaginal incision is made followed by sharp and blunt dissection of fascia to reach the ischial spine. This may be achieved with either an anterior or posterior vaginal approach. A suspension suture is then placed through the sacrospinous ligament approximately $1^1/_2$ to 2cm medial to the ischial spine and anchored in the vaginal apical tissue, either unilaterally or bilaterally. The suture is then either tied subepithelially or intravaginally. The placement of the suspension suture in this position avoids damage to the Pudendal nerve and vessels entering the pelvis at the ischial spine. Pudendal nerve entrapment at this vulnerable point is characterised by ipsilateral specific pin-point buttock pain worse on sitting, with possible perineal numbness. If this is present post-operatively, release of the suspension suture on the affected side is required.

Surgical devices have been developed to bypass the wide surgical dissection that was previously required for direct visualisation and suture placement through the sacrospinous ligament. The Boston Scientific Capio® used with the anterior approach, has been proven highly successful in suspension suture placement when compared with traditional wide dissection for direct visualisation of the sacrospinous ligament, as shown by Maggiore et al.[28, 29] The mean time to vaginal repair was 12.9 minutes (range 11–18 minutes) with median blood loss of 35 ml and a 2-year recurrence rate (Baden-Walker stage 2 or more) of 8.6%. No major intraoperative complications were noted.[28] The Boston Scientific Capio device has made the procedure simpler, decreased operative times by 32-46%, as well as significantly decreased estimated blood loss when compared with traditional methods.[29] No difference has been found, however, in the incidence of surgical complications or recurrence rates with follow-up of up to 3 years, when comparing the Capio® and traditional techniques. [28, 30, 31]This device allows for the suspension suture to be placed by palpation, avoiding the traditional extensive dissection for direct vision of the ligament.[29] It can also be used in mesh based procedures.[21] There is no published research comparing the Capio® with any other sacrospinous suture capture devices.

Newer devices are available, one being a modification of the original Boston Scientific Capio®, i.e. the Capio Slim® (Figure 6); another is Bard's Fixt® device (Figure 7). The differences between the specifications of the two devices have been tabulated below (see details Appendix 1 and 2):

	Shaft Diameter (mm)	Head Width (mm)	Device Weight (g)	Carrier Diameter (mm)
Fixt®	4.8	6.9	121.1	2.2
Capio Slim®	3.0	6.3	38.2	1.2

Table 3. Differences in specifications between Capio Slim® and Fixt®

Figure 6. Capio Slim ®

Figure 7. Fixt®

Below is a list of advantages and disadvantages based on local surgeons' experiences, when comparing the specifications and handling of the two devices:

ADVANTAGES

Fixt®	Capio Slim®
Narrower sweep of needle results in a smaller portion of the ligament captured in the suture	Smaller diameter needle allows for easier puncture of the ligament
Rigid metal shaft	Funnel-shaped catch
Ergonomic design	Thin shaft diameter
	Light weight design

Table 4. Advantages of Fixt ®and Capio Slim®

DISADVANTAGES

Fixt®	Capio Slim®
Wider diameter of shaft	Broader sweep of the needle results in bigger portion of the ligament captured in the suture
Wider diameter of needle	Less rigid shaft
Requires digital pressure when deploying the needle to achieve attachment of the suture	

Table 5. Disadvantages of Fixt® and Capio Slim®

For details of device specifications see Appendix 1 and 2.

Cost plays an important role in the clinician's decision as to which device to use. The cost of the individual devices are similar: Fixt® at R2 612,82 per device; Capio Slim® at R2612,95 per device. The suture per unit however differs, with the Fixt® suture costing R439,43 and the Capio Slim suture at R317,28 per unit.

The increasing incidence of pelvic organ prolapse in our ageing population demands effective, more definitive and low risk methods of repair. This demand has resulted in great strides being made in the very dynamic field of prolapse surgery. With evolving techniques and new devices being introduced into the market at a growing rate, it is of great importance to base our clinical decisions and actions on the best evidence available. The Capio Slim® and Bard Fixt® devices are both new entries into the market of Sacrospinous fixation devices. No evidence is currently available comparing the efficacy of the two devices. As mentioned above, there are some differences in their design. To guide clinicians' device choices in keeping with best evidence, this gap in knowledge had to be addressed. Therefore, motivating this randomised control trial was the need to establish whether any design differences that existed between the two devices were of clinical significance.

METHODS

This was a non-inferiority study, designed as a randomised controlled trial. Two devices used for sacrospinous fixation during vault or uterine suspension were compared; i.e. the Capio Slim® as the control and the Fixt® as the intervention.

OBJECTIVES

The objectives of this study were to compare the short term efficacy of the Fixt® with the Capio Slim®. This short term assessment was defined as the six week period after the surgical procedure.

Primary objectives:

- time until successful bilateral suspension suture placement (in seconds)

Secondary objectives:

- number of throws required until a successful suture is placed
- Intra-operative, immediate post-operative and short-term complications
- Patient satisfaction with regard to symptom relief 6 weeks after the procedure
- Change in POP-Q point C pre- and 6 weeks post-operatively

PARTICIPANTS

Participants were recruited from the Groote Schuur Hospital Urogynaecology Department, at the time of hospital admission for their surgical procedure. They included women with uterine or vaginal vault prolapse requiring and desiring surgical intervention. The original decision for surgery was made in the Urogynaecology outpatients' clinic by one of the two full time sub-specialist consultants in the Urogynaecology firm, several months prior to admission for surgery. These 2 sub-specialists were also the participating surgeons in the randomised control trial. One patient was recruited from Victoria Hospital, identified during an outreach clinic run by the same Urogynaecologists. Women attending these clinics were either self-referred or referred by their general practitioners or gynaecologists. All eligible women were recruited over a twelve month period (January 2014 to December 2014).

Participants were identified using the criteria listed below.

Inclusion criteria:

- Women, 18 years and older who were deemed legally competent at the time of the trial
- Consented to participation in the study
- Symptoms of vaginal bulging or heaviness
- Uterine or vaginal vault prolapse with POP-Q Point C greater than or equal to -5
- Conservative management failed or declined
- Individualised assessment with senior clinician opinion that vaginal apical suspension with sacrospinous fixation would be the most appropriate technique
- Consented to a follow up visit six weeks after the operation

Exclusion criteria:

- Participant decision to opt out of trial
- Previous mesh or sacrospinous fixation surgery
- Any gynaecological condition requiring an abdominal or laparoscopic surgical approach

STUDY DESIGN

The trial was conducted in accordance with the protocol which was approved by the Human Research Ethics Committee of the University of Cape Town. Patients were initially seen and assessed for the need for sacrospinous suspension at the Groote Schuur Hospital outpatients department and Groote Schuur Hospital specialist-led outreach clinic at Victoria Hospital. This procedure requires highly specialised skill and therefore the assessment of patients who required this procedure was exclusively performed by the two Urogynaecologists based at Groote Schuur Hospital. Once the decision for surgery was made in the clinic, the patients were given a date for clerking and admission. Appropriate potential participants were identified pre-operatively at the time of clerking from this pool of patients. The POP-Q (Pelvic Organ Prolapse Quantification) point C, the measure of the distal edge of the cervix or vaginal cuff in relation to the hymen/hymenal remnant in the assessment of mid-compartment prolapse, was performed pre-operatively (as was routine practice for all pre-operative patients). Potential participants were counselled regarding the trial with the aid of the SSSCD trial Information Sheet (Appendix 5). Those willing to be part of the trial, were consented using the Consent Form (Appendix 6). The primary investigator was fluent in both English and Afrikaans (commonly spoken

local languages) and was available for any explanations required by participants. No Xhosa-speaking participants had been recruited, but this had been an incidental occurrence (possibly an indication of the local demographic profile of women with pelvic organ prolapse).

After participants were recruited to the trial and consent was obtained, demographic characteristics of participants and other medical information were obtained from the patient hospital folders. Validated symptom-directed questionnaires were administered by the primary investigator. These questionnaires are listed below (Appendices 3 and 4):

- PFIQ-7 (Pelvic Floor Impact Questionnaire)
- PFDI-20 (Pelvic Floor Distress Inventory)
    - POPDI-6 (Pelvic Organ Prolapse Distress Inventory)
    - UDI-6 (Urinary Distress Inventory)
    - CRADI-8 (Colorectal-anal Distress Inventory)
- PISQ-IR (Pelvic Organ Prolapse/Incontinence Sexual Questionnaire-IUGA Revised)

The PFIQ-7 questionnaire was used to assess the quality of life and measure of interference in activities of daily living with regard to bladder, bowel and prolapse symptoms. Each question has a range of possible answers translated to a score of 0 to 3, the higher number relating to a greater impact of symptoms on participants' lives. The subscales dealing with the level of bother of bladder-, bowel- and prolapse-related symptoms range from 0 to 100. With summation, the PFIQ-7 summary score is obtained with a maximum summary score of 300.

The PFDI-20 questionnaire consists of three subscales with a maximum summary score of 300, an addition of the subscales scores (out of 100). The subscales are the POPDI-6, UDI-6 and CRADI-8. These subscales are used to ascertain the severity of prolapse, urinary and bowel symptoms respectively. Individual questions within these subscales have a range of possible answers translated to a score of 1 to 4, the higher number equating to more severe symptomatology.

The sexual function (PSIQ-IR) questionnaire was administered to determine whether participants were sexually active or not. It also recorded the impact of vaginal prolapse and related symptoms on their sexual function; the degree of impact psychologically; and when participants were not sexually active, the reason for this inactivity.

The Wong Baker face scale subjective pain assessments were also carried out pre-operatively (Appendix 10). The Wong Baker face scale subjective pain assessments had score options of 0, 2, 4, 6,

8 or 10 as levels of bother/pain/discomfort relating to the condition , with 0=”No Hurt” and 10=”Hurts Worst”.

Recruited participants were assigned unique study identity numbers. These were used in all the trial documents, in lieu of their names. Groote Schuur Hospital has limited availability of Urogynaecologists and as a result the same two specialists who assessed patients for surgery also performed the surgical procedures. Confidential codes were assigned to both the surgeons and the devices. The surgeons were coded as Surgeon J and Surgeon T.

Computer generated 1:1 block randomisation was used to generate the sequence of allocation of devices to participants. Randomisation was stratified for the two surgeons performing the procedure. Equal amounts of cards for each of the devices were placed in sealed envelopes and placed in sequence in one of two secured boxes (one for each surgeon). Device assignment occurred in theatre just before the procedure was performed, where the surgeon involved blindly withdrew a card from the surgeon-specific box.

Women were randomised to either Device A (Capio Slim®) or Device B (Fixt®). These codes were added to the participants’ study identity numbers. In all but one case, both devices were readily available in theatre. In this one instance, the Capio Slim® device was found to be out of stock after randomisation of the participant to the control arm (Device A) had already occurred. In this event, Device B, the Fixt®, was used instead and analysed, as stated in the trial protocol, by intention to treat. One participant did not receive sacrospinous suspension after being randomised to Device A. Intra-operatively, after a vaginal hysterectomy was performed (where the cervix was found to be very long), the POP-Q point C then was less than -5 and she no longer required vault suspension. This data was also analysed on an intention to treat basis.

The anterior approach to the sacrospinous fixation was performed in all cases with the suture brought out intravaginally. The surgeons’ intra-operative experiences with the allocated devices, as well as any intra-operative complications were recorded on the Intra-operative Reporting Sheets (Appendix 7). The primary outcome measured was time to bilateral sacrospinous suture placement. The time was measured in minutes and seconds using the same stop watch in theatre for all cases. Start time was cued by the surgeon, measured from when the suture and device was picked up from the instrument table by the surgeon, to the time the second suture had been successfully placed, secured and clamped. The total time was converted into seconds and recorded on the Intra-operative Reporting

Sheet by the surgeon (Appendix 7). The remaining outcomes listed were secondary outcomes measured.

Being a procedural intervention, it was unavoidable that the surgeons were not blinded to the arm to which participants were enrolled. The primary investigator and participants, however, remained blinded to this until the trial had been completed.

On day 3 and day of discharge, participants' completed the Wong Baker pain assessment scale (Appendix 10). On the day of discharge, the Immediate Post-operative Reporting Sheets (Appendix 8) were completed. Six week post-operative follow-up visits were scheduled, where the Short-term Post-operative Reporting Sheets (Appendix 9) were completed. At this time, the Wong Baker pain assessment scale was repeated (Appendix 10), as well as the symptom-directed PFDI-20, PFIQ-7 Questionnaires and PISQ-IR sexual function questionnaire (Appendix 3). Vaginal speculum examinations were again performed at this 6 week follow-up visit, to assess the participants' post-operative POP-Q point C.

A scoring system was used to evaluate the level of participants' satisfaction with regard to their perception of success of the surgical procedure. The scoring system used a range of facial visual aids and numbers to discern the level of satisfaction, with 1 being very dissatisfied and 5 being very satisfied (see Appendix 9).

STATISTICAL METHODS

SAMPLE SIZE

The population size of this randomised trial was 51 participants. The statistical power calculation was based on presumed non-inferiority, using a one-sided Mann-Whitney test, assuming that the actual distribution was normal. Based on review of the literature, a 20% difference between the two devices in timing to bilateral suture placement, was regarded as non-inferior and achieved 99% power for this population size. The margin of non-inferiority was deemed 84 seconds or less.

ANALYSES

Trial data was captured using Excel and analysed statistically using the STATA programme. Datasets were compared using descriptive and comparative techniques. Shapiro Wilk tests were used to determine the normality of distribution of data. For continuous variables, normally distributed data was reported as means$\pm$SD, and medians with ranges used in skewed data. Categorical data was reported in frequencies. T-test, Chi-squared test, Mann-Whitney test and Fisher's exact test were used to determine the statistical significance of the results obtained, as appropriate. An intention to treat analysis was primarily performed, with per protocol analysis as an ancillary analysis. Analyses were performed by the primary investigator assisted by an independent statistician. The surgeon and device code assignments were only revealed to the primary investigator after the data analysis had been completed.

During trial data analysis, the following was reviewed:

- Demographics of participants in each arm
- Intra-operative Outcomes:
    - Time to application of bilateral sacrospinous sutures in seconds
    - Number of attempts required on each side for successful placement of the suture
    - Bladder injury
    - Rectal injury
    - Ureteric Injury

- Immediate Postoperative Outcomes:
    - Postoperative pain – appropriate post-operative pain versus severe localised unilateral / bilateral buttock pain
    - Return to theatre
    - Removal of sacrospinous suture

- Short term Outcomes (6 week follow-up):
    - Post-operative POP-Q point C
    - Pain/bother
    - Resolution or persistence of symptoms
    - Level of patient satisfaction

RESULTS

STUDY POPULATION

A total of 52 women were screened for inclusion in the trial within the time limit. One woman had surgery cancelled in theatre due to medical issues. This had occurred prior to randomisation and she had subsequently been lost to follow-up. All other women meeting the criteria (N=51) were recruited to the trial, randomly allocated to the control or intervention arm, and followed up 6 weeks post-surgery. One participant was recruited to the Capio Slim® arm of the trial, however the Fixt® device was used. This was due to the fact that the Capio Slim® was out of stock in theatre. The flow of participants through the trial can be seen in Figure 8. Analysis was carried out by intention to treat, where data from participants was analysed within the group they were randomised to, regardless of the actual device used.

Most of the baseline characteristics and pre-operative questionnaire scores of participants in the two arms of the trial were similar. There was a statistically significant difference in parity and severity of bother of prolapse-related symptoms. Median parity within the Capio Slim® arm was found to be 3 (range of 1 to 8), with that of the Fixt® arm being 3.5, ranging from 2 to 10 (P value 0.0267 in data with a skewed distribution). With a scoring system out of 100, an only slightly higher but statistically significant difference (P value 0.0289) in the POPDI-6 pre-operative score was discovered in the Capio Slim® group where the median score was 67 (range 46 to 100). The median score of the Fixt® was 63, ranging from 0 to 75.

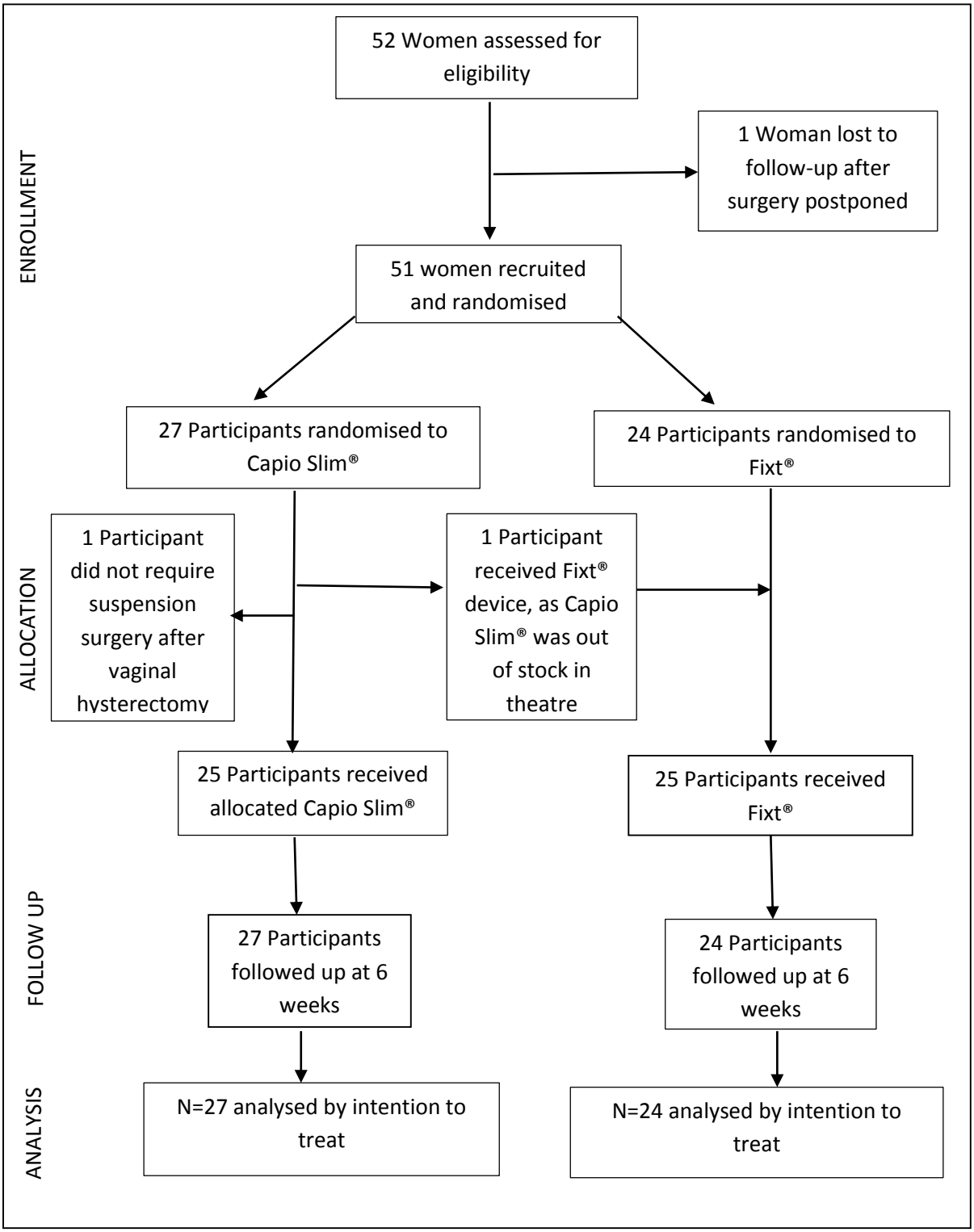


Figure 8. Participant Flow Diagram

The rest of the demographic characteristics of the two groups were comparable with regard to the parameters examined (see Table 6). The Capio Slim® group had a mean age of 62.1 years, while the

Fixt® group had a mean age of 60.6 years, in normally distributed data with a p value of 0.5530. Comparison of participants' Body Mass Index (BMI) was also similar, with Capio Slim® group's mean BMI of 30.3 and the Fixt® group of 30.7 (p value 0.8428). Of note, 17 of the 51 participants had no recorded measurements for BMI in their hospital folders. The prevalence of smokers within the 2 groups was found to be 22% in the Capio Slim® group and 41.667% in the Fixt® group, though this was not found to be statistically significant. At the time of recruitment 19 women reported being sexually active, 10 (52.6%) were in the Capio Slim® group and 9 (47%) in the Fixt® group. This created a prevalence within each group of 37% and 37.5% respectively (p value 0.973). Three of the 51 participants had documented use of hormone replacement therapy (HRT) prescribed by their General Practitioners or Gynaecologists for menopausal symptoms. Two occurred in the Capio Slim® group and 1 in the Fixt® group.

VARIABLES	**CAPIO SLIM®** **N=27**	**FIXT®** **N=24**	**P VALUE**
AGE in years **mean (±SD)**	62.1 (9.21)	60.625 (8.46)	0.5530
BMI **mean (±SD)**	30.29333 (6.73832)	30.68947 (4.814434)	0.8428
PARITY **median (range)**	3 (1 - 8)	3.5 (2 - 10)	0.0267
SMOKING **YES (%) n=16**	6 (37.5)	10 (62.5)	0.135
SEXUALLY ACTIVE **YES (%) n=19**	10 (52.6)	9 (47)	0.973
HRT **YES (%) n=3**	2 (66.66667)	1 (33.333333)	0.588
PRE-OP PAIN ASSESSMENT **mean (±SD)**	5.407407 (3.543784)	5.083333 (2.500725)	0.7109
PRE-OP POP-Q POINT C **mean (±SD)**	1.185185 (3.99073)	1.458333 (4.452446)	0.8182

Table 6. Baseline Data

As mentioned above, the only statistically significant difference between the populations in the two arms in terms of their symptomatology pre-operatively, was revealed in the domain of the PFDI-20 questionnaire dealing with the severity of prolapse and related symptoms (POPDI-6). The remaining subscales of the PFDI-20 found no significant differences in the participants' reporting of the severity of their symptoms. The Urinary Distress Inventory (UDI-6) subscale (out of 100) had a median score of 54 (range 0 – 87) in the Capio Slim®; and 46 in the Fixt® group (range 0 – 96) with a p value of 0.5888. For the bowel related CRADI-8 subscale, the Capio Slim® had a median score of 31 out of a possible 100 (range 0 - 66); while the Fixt® had a median score of 28 with a range of 0 to 59 (P value 0.8087). The mean PFDI-20 summary score in the Capio Slim® group was 140.7 of a maximum possible score of 300; and 129.9 in the Fixt® group (P value 0.3355).

The median summary score for the level of bother questionnaire, the PFIQ-7, was 91 (range 0 - 262) in the Capio Slim® arm and 69 (range 0 - 176) in the Fixt® arm of the trial (P value 0.4845). No significant difference was found in the summary score, or within its subscales. With reference to the impact of bladder symptoms, the median subscale score was 33 (range 0 – 90) in the Capio Slim® group, and 33 (range 0 – 95) in the Fixt® group with a P value of 0.8941. Both arms of the trial had median subscale score of 0 for the level of bother of bowel related symptoms, ranges in the Capio Slim® arm of 0 to 86, and 0 to 62 in the Fixt® arm. Median scores for the impact of the "bulge"/prolapse symptoms was 43 of a maximum score of 100 for the Capio Slim® group (range 0 – 95); the Fixt not being statistically different (P value 0.2706), with a median score of 35.5 (range 0 – 86).

The mean pre-operative Wong Baker face scale pain assessment score in the Capio Slim® arm was 5.4 (± 3.5), and 5.083 (±2.5) in the Fixt® arm with a statistically non-significant p value of 0.7109.

VARIABLES	CAPIO SLIM® N=27	FIXT® N=24	P VALUE
PFDI-20:			
POPDI-6	67	63	0.0289
median (range)	(46 - 100)	(0 - 75)	
UDI 6	54	46	0.5888
median (range)	(0 – 87)	(0 – 96)	
CRADI 8	31	28	0.8087
median (range)	(0 – 66)	(0 - 59)	
PFDI-20*	140.7037	129.9167	0.3355
mean (±SD)	(38.86744)	(40.27289)	
PFIQ-7:			
BLADDER	33	33	0.8941
median (range)	(0 – 90)	(0 – 95)	
BOWEL	0	0	
median (range)	(0 – 86)	(0 – 62)	0.2285
BULGE	43	35.5	
median (range)	(0 – 95)	(0 – 86)	0.2706
PFIQ-7**	91	69	
median (range)	(0 – 262)	(0 – 176)	0.4845

Table 7. Pre-Operative Questionnaire Scores

** PFDI-20 score (maximum score of 300): summation of POPDI-6, UDI-6 AND CRADI-8 scores*

***PFIQ-7 score (maximum score of 300): summation of Bladder, Bowel and Bulge symptom subscale scores*

With regard to the pre-operative POP-Q point C, no significant statistical difference was found between the Capio Slim® group and the Fixt® group (P value 0.8182), where the mean POP-Q point C was +1.185 (±3.990) and +1.458 (±4.452) respectively.

Surgical characteristics were also compared and found to be similar with regard to estimated blood loss and total surgical time (see Table 8) and concomitant surgery (Table 9), these. No statistical difference was found in the numbers of participants in the two arms undergoing other procedures at the time of the Sacrospinous fixation, i.e. Anterior Vaginal (prolapse) Repair, Posterior Vaginal (prolapse) repair, Enterocele (prolapse) Repair, Perineorrhaphy (tightening of the perineal muscles) and Tension-free Vaginal Tape insertion (support of the urethra and bladder neck).

Surgical characteristics in terms of operative procedures and intra-operative events were similar between the two groups. Of the 45 patients without a uterus, either having had a hysterectomy previously or with the current surgery, 55% were in the Capio Slim® group, and 44% in the Fixt® group with the numbers not being statistically significantly different (Fisher's exact 0.402). Six participants underwent hysteropexy (mid-compartment suspension with the uterus in situ), 2 of whom were in the Capio Slim® arm and 4 in the Fixt® arm of the trial (P value 0.306).

VARIABLES	CAPIO SLIM ® N=27	FIXT® N=24	P VALUE
TIME TO BILATERAL SUTURE PLACEMENT (seconds) median (range)	170.5 (105 – 642)	222 (112 – 848)	0.3513
NUMBER THROWS RIGHT median (range)	1 (1 – 7)	1 (1 – 13)	0.5976
NUMBER THROWS LEFT median (range)	1 (1 – 6)	1 (1 – 8)	O.2897
NUMBER TOTAL ATTEMPTS median (range)	2.5 (2 – 8)	2 (2 – 17)	0.3629
DEVICE REPLACED YES (%) n=5	4 (80)	1 (20)	0.187
TOTAL SURGICAL TIME (min) mean (±SD)	112.3077 (28.81773)	122.5417 (34.10722)	0.2562
ESTIMATED BLOOD LOSS (ml) median (range)	150 (50 – 500)	150 (50 – 500)	0.8496
BLADDER INJURY YES (%) n=0	0	0	
RECTAL INJURY YES (%) n=0	0	0	
URETERIC INJURY YES (%) n=0	0	0	

Table 8. Intra-operative Outcomes and Events

VARIABLES	CAPIO SLIM ® N=27	FIXT® N=24	P VALUE
UTERUS - absent/removed			
NO (%) n=45	25 (55)	20 (44)	0.402 (Fisher's Exact)
YES (%) n=6	2 (33)	4 (66.6667)	0.306
AVR			
YES (%) n=43	23 (53)	20 (46.5)	1.000 (Fisher's Exact)
PVR			
YES (%) n=12	4 (33)	8 (66.7)	0.187 (Fisher's Exact)
ENTEROCELE			
YES (%) n=1	1 (100)	0 (0)	0.341
PERINEORRHAPHY			
YES (%) n=28	13 (46)	15 (53.57)	0.400 (Fisher's Exact)
TVT			
YES (%) n=11	4 (36)	7 (63.63)	0.310 (Fisher's Exact)

Table 9. Concomitant Surgery

OUTCOMES

The primary method of analysis was based on intention to treat. As expected in this non-inferiority trial, when comparing the Capio Slim® and Fixt® devices, no significant difference was found in the primary outcome, i.e. time (in seconds) to bilateral sacrospinous suture placements. The median time for the Capio Slim® was 170.5 seconds with a range of 105 to 642 seconds (see Table 8). For the Fixt®, the median time was 222 seconds with a range of 112 – 848 seconds and P value of 0.3513.

VARIABLES	CAPIO SLIM ® N=27	FIXT® N=24	P VALUE
BUTTOCK PAIN YES (%) n=8	3 (42)	5 (57)	0.341
UNILATERAL BUTTOCK PAIN YES (%) n=6	2 (33.333)	4 (66.667)	0.306
BILATERAL BUTTOCK PAIN YES (%) n=2	1 (50)	1 (50)	0.932
RETURN TO THEATRE YES (%) n=4	2 (50)	2 (50)	0.902
REMOVAL OF SUTURE YES (%) n=4	2 (50)	2 (50)	0.902
TRIAL OF VOID FAILURE YES (%) n=23	12 (52)	11 (47.8)	1.000 (Fisher's Exact)
IPPA D3 median (range)	2 (0 – 8)	4 (2 – 8)	0.3283
IPPA DC median (range)	2 (0 – 8)	2 (2 – 4)	0.4859
IMPROVED IPPA median (range)	0 (0 – 4)	0 (0 – 4)	0.5811
IN-HOSPITAL DAYS median (range)	4 (3 – 10)	4 (3 – 13)	0.3038
CATHETER DAYS median (range)	2 (1 – 12)	2 (1 -19)	0.8372
READMISSION YES (%) n=6	2 (33.333)	4 (66.667)	0.306

Table 10. Immediate Post-Operative Outcomes and Results

The secondary outcomes examined were all similar with regard to the number of throws required until a successful suture is placed; adverse events intra-operatively and post-operatively; post-operative subjective pain assessments, improvement of symptoms, levels of satisfaction and improvement of POP-Q point C (see Table 10). The number of throws required for successful bilateral placement of sacrospinous sutures was used as an indicator of ease of use of the two devices. The results were similar in this regard, with the Capio Slim® requiring a median of 2.5 and the Fixt® requiring a median of 2 throws to successfully place the sacrospinous suture on both sides The range of number of throws needed for successful placement of the suture on the right, was between 1 and 7 for the Capio Slim® and 1 to 13 for the Fixt®. On the left, the range of number of attempts was 1 to 6 for the Capio Slim® and 1 to 8 for the Fixt®. The p values for these parameters examined, showed no statistical difference between the Capio Slim® and the Fixt®, with all p values greater than 0.05. In 3 cases, bilateral suture placement was abandoned following difficulty and when the surgeon was satisfied that a unilateral suture provided adequate suspension of the vaginal mid-compartment. In one case where the Fixt® was used, the device had successfully deployed but the suture was damaged during diathermy and snapped after the vaginal vault was closed, it was subsequently not replaced. In the two cases involving the Capio Slim®, one was due to breakage of the suture material after tying; the second was due to a faulty device that failed to take an adequate bite of tissue after numerous attempts and change of device.

Device related or suture placement related issues arose in 10% of cases. A second device was needed in 5 cases for a number of reasons. A Fixt® device was replaced in one instance after numerous failed attempts at placement of the suture with the first device. In the second instance, the participant had been randomised to the Capio Slim® group, but the Fixt® was used due to the Capio being out of stock. A second Fixt device was needed due to difficulty with suture deployment with the initial device. With the second device, the stitch was eventually placed in the iliococcygeal fascia. There were 3 cases in which a second device was needed with the Capio Slim®. In 2 of these cases the second Capio device resulted in successful placement bilaterally, but on one occasion the surgeon was satisfied with suspension unilaterally and abandoned bilateral placement due to difficulty.

Total surgical time for the complete pelvic floor repair in each participant revealed no difference between the two groups (p value 0.2562), the Capio Slim® group had a mean operative time of 112 minutes, and the Fixt® group with a mean time of 122.5 minutes. The median estimated blood loss (EBL) per surgery performed was 150ml with ranges between 50ml and 500ml in both arms. No adverse events in terms of visceral injuries, i.e. ureteric, bladder or rectal injuries, were noted for the entire duration of the trial. No Dindo grade 4 complications were sustained (see Appendix 11).[34]

The immediate post-operative outcomes assessed participants for the presence of buttock pain indicative of possible pudendal nerve entrapment; need for sacrospinous suture removal due to complications (ROS); and need for the return to theatre for any number of reasons (RTT) (see Table 10), Dindo grade 3a and 3b (see Appendix 11).

A total of 8 participants complained of post-operative buttock pain. Three of these patients were in the Capio Slim® group, 1 of whom complained of bilateral buttock pain while the other 2 had unilateral buttock pain. The 2 participants with unilateral buttock pain had suspected pudendal nerve entrapment requiring removal of the suspension suture on the affected side (where suture was brought out intravaginally). One of these was removed in theatre while the other was removed in the ward. In both cases, the pain score halved from day 3 post-surgery when compared to the pain score on the day of discharge, from 4 to 2, and 8 to 4. The patient with bilateral buttock pain was found to be constipated. The pain resolved after stools were passed. Five participants in the Fixt® group had buttock pain, 4 of whom had unilateral pain and 1 with bilateral pain. The participant with bilateral pain had relief of pain after passing stools, with pain score improving from 6 to 2. Of the 4 patients within this arm of the trial with unilateral buttock pain, 2 required unilateral removal of the suspension suture due to persistent symptoms with subsequent improvement in pain scores from 8 to 4. The other 2 participants did not require removal of the suspension suture. One of these 2 participants' symptoms completely resolved after stools was passed, and the second participant's buttock pain and perianal paraesthesia improved slowly with time. Both participants' pain scores on day 3 after the surgical procedure was 4 with improvement on the day of discharge to 2.

Within the period of the elective admission for the surgical procedure, 4 participants returned to theatre after the original surgery due to complications, 2 from each arm of the trial. In the Capio Slim® arm, one participant had to return to theatre for the release of the TVT that had caused urinary retention. The other participant returned to theatre for the release of the suspension suture (as stated above). In the Fixt® arm of the trial, one participant who had resolved bilateral buttock pain on day 3 post-procedure when stools was passed, had to return to theatre on day 7 for release of the TVT due to urinary retention as well as for drainage of a vault haematoma. The second participant in this arm who needed to return to theatre, on day 7 underwent a washout of a vault abscess and removal of the right sacrospinous suspension suture due to pudendal nerve entrapment.

Additional information collected in the immediate post-operative period was failure of the trial of void (TOVF); number of days requiring transurethral catheterisation; visual aided pain scores; length of hospital stay; and need for readmission (see Table 10). The timing of the trial of void was based on the discretion of the surgeon, usually between day 1 and day 3 post-operatively. The trial of void was deemed failed when the residual urine measured after removal of the indwelling urinary catheter was more than 150ml. A total of 23 trial participants had trial of void failure requiring re-catheterisation, 12 within the Capio Slim® group and 11 in the Fixt® group (Fisher's exact 1.000). The median number of days requiring catheterisation was 2 days in each group. The range of catheterised days in the Capio Slim® arm was 1 to 12 days, and between 1 and 19 days in the Fixt® arm.

No statistical difference was found in the immediate post-operative Wong Baker pain assessment between the 2 groups. Both groups had a median pain assessment score of 2 on the day of discharge with a median of zero points improvement when compared to the pain assessment on day 3 post-procedure (expected day of discharge). The 2 trial arms both had a median of 4 days hospital stay. The ranges for this, was 3 to 10 days in the Capio Slim® arm, and 3 to 13 days in the Fixt® arm.

Six participants had unscheduled readmissions to hospital after discharge for post-operative complications. Two of these participants were in the Capio Slim® arm and 4 from the Fixt® arm (p value 0.306). The reasons for the readmission of the 2 participants in the Capio Slim® group was as a result of vault haematomas, 1 of which was septic requiring intravenous antibiotics (Dindo grade 1). In the Fixt® group, 3 of the 4 participants had vault haematomas, 1 of whom required drainage in

theatre (Dindo grade 3b). The fourth participant needed to return to theatre for release of the TVT that had caused urinary retention (Dindo grade 3b).

Examination of the short-term outcomes occurred 6 weeks after the surgical procedure at the scheduled outpatient follow-up visit. Assessed at this time was the post-operative POP-Q point C; short-term post-operative pain assessment (STPPA); distress and degree of bother related to prolapse, urinary and bowel symptoms (using the PDFI-20 and PFIQ-7 questionnaires); and the level of patient satisfaction after the procedure.

The median pain assessment Wong Baker score was zero in both trial groups, indicative of no pain or bother in the majority of participants at the 6 week post-operative follow-up. The range of scores was 0 to 4 in the Capio Slim arm and 0 to 6 in the Fixt® arm of the trial (P value 0.991).

VARIABLES	**CAPIO SLIM ®** N=27	**FIXT®** N=24	**P VALUE**
STPPA median (range)	0 (0 – 4)	0 (0 – 6)	0.9911
POST-OP POP-Q POINT C median (range)	-7 (-10 – +2)	-7 (-8 – 0)	0.2062
CHANGE POINT C mean (±SD)	7.962963 (4.228852)	7.625 (4.566537)	0.7849
PATIENT SATISFACTION median (range)	5 (2 – 5)	5 (1 – 5)	0.4594

Table 11. Short Term (Six Week) Post-Operative Outcomes and Results

The 6 week post-operative POP-Q point C had a median measurement of -7 in both groups. Interpretation of this is that the vaginal mid-compartment (vaginal vault or uterus) was successfully suspended 7cm above the hymenal remnant in both groups. The range for the measurement in the Capio Slim® group was -10 to +2. In the Fixt® group the range of the POP-Q point C measurement was from- 8 to 0 (P value 0.2062). The resultant change in the POP-Q point C measurement was ascertained by establishing the difference between the pre-operative and post-operative point C measurement. The mean change in the POP-Q point C measurement showed no statistical difference in the degree of improvement in both groups. There was 7.96cm (±4.23cm) mean improvement in mid-

compartment suspension in the Capio Slim® group and 7.63cm (±4.57cm) in the Fixt® group with a p value of 0.78.

The median level of satisfaction in both groups 6 weeks post-operatively was 5. The interpretation of this is that the majority of the trial participants were very satisfied with the outcome of their surgery. The range of satisfaction scores in the Capio Slim® arm of the trial was 2 to 5. One participant had a satisfaction score of 2, reporting initial right leg pain, decreased sensation of bladder filling and constipation that had resolved 1 month later. The rest of the participants in the Capio Slim® arm scored their satisfaction levels as 4 or 5 (satisfied or very satisfied). In the Fixt® arm, the satisfaction score range was 1 to 5. One participant rated her level of satisfaction as 1, i.e. very dissatisfied, as she had developed difficulty with urinary voiding and a grade 3 cystocele. In this case, the pre-op POP-Q measurement found no significant prolapse in the anterior vaginal compartment and hence an anterior vaginal repair had not been performed. One participant reported neutrality in her feeling of satisfaction with the outcomes of her surgery (score of 3). The reason stated was post-operative pudendal nerve entrapment requiring unilateral removal of the suspension suture followed by the need for readmission and TVT release, and slow recovery of perineal sensation. The remainder of the participants in the Fixt arm reported satisfaction scores of 4 and 5.

At the 6 week follow-up appointment, the questionnaires administered pre-operatively were repeated. No statistical difference was found between the 2 arms of the trial when comparing these questionnaire scores at the short-term post-operative assessment. The prolapse severity PFDI-20 questionnaire had low scores in both arms with a mean score of 82 out of a total of 300 in the Capio Slim® arm, and 86 in the Fixt® arm (P value 0.566). Within the subscales of the PFDI-20 related to prolapse, urinary and bowel symptoms, both arms had the same median scores with P values that showed no significant difference between the 2 groups. The PFIQ-7 level of bother questionnaire had median scores of zero in all subscales for both groups.

The only statistically significant difference in secondary outcomes was the magnitude of change between the pre-operative and post-operative prolapse-related symptoms of the POPDI-6, a subscale of the PFDI-20 questionnaire. The pre-operative score in the Capio Slim® group was statistically significantly greater than the Fixt® group (refer to section Study Population above), with comparable 6 week post-operative scores. The resultant difference in pre and post-operative scores was also found

to be statistically significantly greater (P value 0.0235) in the Capio Slim® group with a median of 38 point improvement versus 33 points in Fixt®, and a range of -25 to 75 (Fixt® range -25 to 50). No significant difference was found in the rest of the pre- and post-procedural scores.

VARIABLES	CAPIO SLIM ® N=27	FIXT® N=24	P VALUE
PFDI-20:			
POPDI-6	25	25	
median (range)	(25 - 100)	(25 – 42)	0.0927
UDI 6	29	29	
median (range)	(25 – 54)	(25 – 54)	0.5887
CRADI 8	25	25	
median (range)	(25 – 50)	(25 – 50)	0.7078
PFDI-20*	82	86	
mean (±SD)	(75 - 150)	(75 – 143)	0.5666
PFIQ-7:			
BLADDER	0	0	
median (range)	(0 – 62)	(0 – 29)	0.8647
BOWEL	0	0	
median (range)	(0 – 62)	(0 – 29)	0.9406
BULGE	0	0	
median (range)	(0 – 71)	(0 – 10)	0.5308
PFIQ-7	0	0	
median (range)	(0 – 195)	(0 – 39)	0.6396

Table 12. Short Term (6 Week) Post-operative Questionnaire Scores

The PISQ-IR questionnaires were also administered on follow-up. This data was not analysed as the majority of women, on advice from their attending doctor, were not sexually active at the time of their 6 week follow-up visit due to their recent surgery.

VARIABLES	CAPIO SLIM ® N=27	FIXT® N=24	P VALUE
CHANGE IN SCORES:			
CHANGE POPDI-6 median (range)	38 (-25 – 75)	33 (-25 – 50)	0.0235
CHANGE UDI 6 mean (±SD)	14.18519 (32.43341)	18.70833 (27.07876)	0.5939
CHANGE CRADI 8 median (range)	3 (-34 – 41)	0 (-38 – 31)	0.6955
CHANGE PFDI-20* mean (±SD)	52.55556 (46.07714)	40.04167 (35.00494)	0.2849
CHANGE PFIQ-7 mean (±SD)**	79 (88.04282)	71.58333 (54.67367)	0.7234
CHANGE BLADDER mean (±SD)	32.14815 (36.82568)	32.16667 (31.74308)	0.9985
CHANGE BOWEL median (range)	0 (-43 – 86)	0 (-29 – 62)	0.5353
CHANGE BULGE mean (±SD)	41.18519 (39.54942)	35.66667 (30.21613)	0.5818

Table 13. Change in Questionnaire Scores (pre- and post-operative)

Further analysis was performed on trial data to assess if any significant difference existed when comparing the two surgeons performing the procedures. When reviewing intra-operative performance using the Capio Slim® (see Table 14), both surgeons were similar with regard to the primary and secondary outcomes. Evaluation of the primary outcome i.e. time to successful bilateral suspension suture placements found Surgeon J to have a median time of 168 seconds versus 196 seconds for Surgeon T (P value 1.000). The median number of throws on the right and left was 1 on each side for both surgeons. Examining these procedure-related outcomes when the Fixt® was used had similar findings with no significant difference found between the 2 surgeons (see Table 15). The median time to successful suspension suture placement was 229 seconds by Surgeon J and 222 seconds with Surgeon T (P value 0.6441). The median number of throws for successful suture placement was 1 attempt on the left and right side for Surgeon J, and 1.5 times on either side for Surgeon T.

The post-operative course with both devices where comparable between the 2 surgeons. No suspension sutures placed with the Capio Slim® by Surgeon J required removal, whereas 2 unilateral sutures required removal in the suspension performed by Surgeon T using the same device. The numbers were small and hence no significant difference was found (P value 0.157). With the Fixt®, the need for the removal of the suspension suture and return to theatre was 0 in the group for Surgeon J, and 2 for Surgeon T with no statistical difference found (P value 0.140).

Failure of the trial of void when the Capio Slim® was used was 5 for Surgeon J and 7 for Surgeon T. Using the Fixt®, trial of void failure occurred in 3 of participants in the group where surgery was performed by Surgeon J and 8 in Surgeon T's group. In both devices, no statistical difference was found between the surgeons in this regard.

The 6 week post-operative POP-Q showed some difference in the point C measurement when the Capio Slim® was used (P value 0.467), with Surgeon J achieving mid-compartment suspension slightly higher than Surgeon T [mean point C -7.46cm versus -6.14cm above the hymenal remnant]. No significant difference was found in the amount of improvement of point C pre-operatively to post-operatively when comparing the 2 surgeon (mean change Surgeon J 7.38cm versus 8.5cm Surgeon T; P value 0.504). In the Fixt® group, no significant difference was found between surgeons with regard to the post-operative point C at 6 weeks or the improvement in the point C measurement when compared with the pre-operative measurement. Surgeon J had a median post-operative POP-Q point C measurement of -6cm above the hymenal remnant with a mean improvement of mid-compartment suspension by 7.58cm. Comparable measurements were found with Surgeon T who had median post-operative point C measurement of -7cm and mean improvement of 7.67cm.

VARIABLES	SURGEON J N=12	SURGEON T N=14	P VALUE
TIME TO BILATERAL SUTURE PLACEMENT (seconds) median (range)	168.5 (128 – 642)	196.5 (105 – 535)	1.0000
NUMBER THROWS RIGHT median (range)	1 (1 – 7)	1 (1 – 6)	0.9758
NUMBER THROWS LEFT median (range)	1 (1 – 3)	1 (1 -6)	0.1932
REMOVAL OF SUTURE YES (%) n= 2	0	2 (100)	0.157
RETURN TO THEATRE YES (%) n=2	0	2 (100)	0.157
TRIAL OF VOID FAILURE YES (%) n=12	5 (41.6667)	7 (58)	0.704 (Fisher's exact)
POST-OP POP-Q POINT C mean (±SD)	-7.461538 (1.450022)	-6.142857 (1.79131)	0.0467
CHANGE POP-Q POINT C mean (±SD)	7.384615 (4.05254)	8.5 (4.467834)	0.5042

Table 14. Surgeons' Performance with Capio Slim®

VARIABLES	SURGEON J N=12	SURGEON T N=12	P VALUE
TIME TO BILATERAL SUTURE PLACEMENT (seconds) median (range)	229 (148 – 768)	222 (112 – 848)	0.6441
NUMBER THROWS RIGHT median (range)	1 (1 – 7)	1.5 (1 – 13)	0.5675
NUMBER THROWS LEFT median (range)	1 (1 – 7)	1.5 (1 – 8)	0.3814
REMOVAL OF SUTURE YES (%) n=2	0	2 (100)	0.140
RETURN TO THEATRE YES (%) n=2	0	2 (100)	0.140
TRIAL OF VOID FAILURE YES (%) n=11	3 (27)	8 (72)	0.100 (Fisher's exact)
POST-OP POP-Q POINT C median (range)	-6 (-8 – 0)	-7 (-8 - -5)	0.0749
CHANGE POP-Q POINT C mean (±SD)	7.583333 (3.776924)	7.666667 (5.416026)	0.9655

Table 15. Surgeons' Performance with Fixt®

ANCILLARY ANALYSES

The principal form of analysis for this randomised controlled trial was by intention to treat (results as reported above). An additional method of analysis performed was per protocol analysis i.e. comparison of participants in two groups based on the actual device used in their suspension procedures (when this device differed for whatever reason to the arm of the trial to which they were randomised to).

VARIABLES	CAPIO SLIM ® N=25	FIXT® N=25	P VALUE
SURGEON J	12	12	1.000 (Fisher's exact)
SURGEON T	13	13	1.000 (Fisher's exact)
UTERUS NO (%) n=44 (absent/removed)	23 (52)	21 (47.7)	0.667 (Fisher's exact)
TIME TO BILATERAL SUTURE PLACEMENT (seconds) median (range)	169 (105 – 642)	223 (112 – 848)	0.2179
NUMBER THROWS RIGHT median (range)	1 (1 – 7)	1 (1 – 13)	0.7583
NUMBER THROWS LEFT median (range)	1 (1 – 3)	1 (1 – 8)	0.1219
DEVICE CHANGED YES (%) n=5	3 (60)	2 (40)	1.000 (Fisher's exact)

Table 16. Intra-operative Per Protocol Analysis

Within the Capio Slim® and the Fixt® groups, 25 devices each were used. Surgeon J had performed 12 procedures and Surgeon T performed 13 procedures using each device. No significant difference was found between the two groups with regard to the number of suspension procedures performed on the vaginal vault i.e. sacrospinous fixation versus sacrospinous hysteropexy with the uterus in-situ. The primary outcome of time to bilateral suture placement showed no statistical difference in this analysis, with the median time in the Capio Slim® arm of 169 seconds and 223 seconds in the Fixt® arm (P value 0.2179).

In terms of secondary outcomes, the number of throws required for successful suture placement was equal with a median of 1 attempt on each side in both groups. In the Capio Slim® arm there were 3 intra-operative changes of device and 2 in the Fixt® arm (Fisher's exact 1.000).

The immediate post-operative pain assessment on day 3 and on the day of discharge had a median score of 2 in both groups with no change between these 2 points in time. Of the 8 participants who reported post-operative buttock pain, 3 were within the Capio Slim® arm and 5 in the Fixt® arm (P value 0.440). Two participants in each group required the removal of a unilateral suspension suture and 2 within each group needed to return to theatre for either removal of the suspension suture or for other post-operative complications (drainage of vault abscesses, release of TVT causing urinary retention, etc.).

Twelve participants failed the post-operative trial of void in the Capio Slim® arm and 11 in the Fixt® arm. No difference was found with the Fisher's exact test (1.000).

Five participants required unscheduled urgent readmission for a number of reasons discussed previously, 1 within the Capio Slim® arm and 4 in the Fixt® arm of the trial.

VARIABLES	CAPIO SLIM ® N=25	FIXT® N=25	P VALUE
IPPA DC median (range)	2 (0 – 8)	2 (2 – 4)	0.6589
IPPA D3 median (range)	2 (0 – 8)	2 (2 – 8)	0.5201
IMPROVED IPPA median (range)	0 (0 – 4)	0 (0 – 4)	0.7375
POST-OP BUTTOCK PAIN YES (%) n=8	3 (37.5)	5 (62.5)	0.440
RETURN TO THEATRE YES (%) n=4	2 (50)	2 (50)	1.000
REMOVAL OF SUTURE YES (%) n=4	2 (50)	2 (50)	1.000
TRIAL OF VOID FAILURE YES (%) n=23	12 (52)	11 (47.8)	1.000 (Fisher's exact)

Table 17. Immediate Post-operative Per Protocol Analysis

At the 6 week follow-up visit, most participants reported no pain or bother, with a median pain assessment score of zero in both groups. At this time the POP-Q point C was measured again. Both groups had a median measurement of -7, with almost an 8cm improvement in the Capio Slim® arm and 7cm improvement in the Fixt® arm, when compared to the pre-operative measurement (P value of 0.8762). In both arms of the trial at this short-term follow-up visit, most participants reported a maximum (out of 5) satisfaction score of 5.

VARIABLES	CAPIO SLIM ® N=25	FIXT® N=25	P VALUE
READMISSION YES (%) n=5	1 (20)	4 (80)	0.157
STTPA median (range)	0 (0 – 4)	0 (0 – 6)	0.7569
POST-OP POP-Q POINT C median (range)	-7 (-10 - -2)	-7 (-8 – 0)	0.1382
CHANGE POP-Q POINT C median (range)	8 (2 – 17)	7 (1 – 18)	0.8762
PATIENT SATISFACTION median (range)	5 (2 – 1)	5 (1 – 5)	0.6500

Table 18. Short-term Post-operative Per Protocol Analysis

When assessing improvement of symptomatology, changes in pre- and post-operative symptom severity and level of impact questionnaire scores were reviewed. A significant difference was found in the prolapse distress inventory POPDI-6 score with a 42 point improvement in the Capio Slim group and 29 point improvement in the Fixt® group (P value 0.0134). The remainder of the PFDI-20 questionnaire related to the urinary and bowel distress inventory showed no difference in score improvement between the 2 groups. No difference was also found between the Capio Slim® and Fixt® groups with regard to the amount of improvement in the level of impact PFIQ-7 score and its subscales.

VARIABLES	CAPIO SLIM ® N=25	FIXT® N=25	P VALUE
CHANGE POPDI-6 median (range)	42 (-25 – 75)	29 (-25 – 50)	0.0134
CHANGE UDI 6 mean (±SD)	12.96 (33.24841)	18.64 (26.51082)	0.5074
CHANGE CRADI 8 median (range)	3 (-34 – 41)	-3 (-38 – 31)	0.4387
CHANGE PFDI-20* mean (±SD)	53.88 (47.38435)	39.12 (34.57639)	0.2144
CHANGE PFIQ-7 mean (±SD)**	78.68 (89.43886)	69.28 (54.74754)	0.6560
CHANGE BLADDER mean (±SD)	31.12 (35.85424)	30.88 (31.73368)	0.9801
CHANGE BOWEL median (range)	0 (-43 – 86)	0 (-29 – 62)	0.4430
CHANGE BULGE mean (±SD)	41.44 (40.56587)	34.8 (29.89565)	0.5131

Table 19. Per Protocol Analysis of Change in Questionnaire Scores

DISCUSSION

The hypothesis for conducting this randomised controlled trial was that of non-inferiority of the devices inspected, i.e. the Boston Scientific Capio Slim® and Bard Fixt®. This was based on the premise that they were equal in terms of their safety and performance with regard to the short-term outcomes examined. This randomised controlled trial went on to prove this hypothesis to be true.

INTERPRETATION

The outcomes studied inferred ease of use of the device, resultant post-operative sequelae and participants' level of satisfaction after the procedure. The primary outcome of time to successful bilateral sacrospinous suture placement, the main contributor to this inference of ease of use, showed no difference between the two devices. The median time, when converted to minutes, was 2.8 minutes with the Boston Scientific Capio Slim® and 3.7 minutes with the Bard Fixt®, a 54 second difference in the medians. This was less than the non-inferiority estimate of 84 seconds (20% difference) calculated for this highly powered study (power 99%). Non-inferiority was thus proven for the primary outcome. There is no literature available to compare these results with, apart from Maggiore's trial comparing the Capio® (median time 12.9 minutes) with traditional wide dissection for sacrospinous fixation.[28] The points of reference for timing of the procedures in this study when compared to the current trial were, however, different.

All secondary outcomes examined found no difference between the two devices. The number of throws needed to successfully place the suspension suture, examined as an intra-operative outcome, was used as another indicator of ease of use of the devices. Both devices required a median of 1 throw on each side for the successful suture placement. Hence, when examining the two outcomes mentioned above, it can be interpreted that the Boston Scientific Capio Slim® and the Bard Fixt® were comparable with regard to ease of use and **efficiency**.

By per protocol analysis, the device needed to be replaced 3 times in the Capio Slim® group, and twice in the Fixt® group (no statistically significant difference). Reasons for the device change can only be assumed based on the surgeons' report of intra-operative events and cannot be proven to be secondary to device fault or failure as subsequent testing of the devices had not been performed.

Reported reasons for device change with the Capio Slim® was “faulty device” in 2 cases and a suspected calcified sacrospinous ligament in the third case; and with the Fixt® reasons were “faulty device” and difficult surgical access.

Other intra-operative outcomes examined referring to **safety** of the devices**,** were comparable between the two devices. When examining the surgically associated complications, the Clavien-Dindo classification was used (See Appendix 11). There were no grade 4 complications i.e. no life-threatening complications causing organ dysfunction. No rectal, bladder or ureteric injuries were sustained during the entire duration of the trial and no other major intra-operative or post-operative adverse events were reported. There was however a moderate amount of grade 3a and 3b complications, requiring intervention without (3a) or with (3b) general anaesthesia. Great overlap exists regarding the possible causes for these adverse outcomes. This is because these complications cannot distinctly be related to the device, the users or the environment in which the devices were used. It therefore cannot be concluded that these devices are completely safe to use, but in well-trained hands and in the appropriate circumstances, these devices are comparable in their adequate display of safety. The anterior approach for sacrospinous fixation was also proven to be a safe procedure to perform for mid-compartment suspension. This observation of safety of the procedure itself is highlighted by its comparison with an 11% incidence of ureteric occlusion in Barber’s study of bilateral uterosacral ligament suspension for mid-compartment prolapse.[22]

Secondary post-operative outcomes went on to reiterate the non-inferiority of the Fixt® when compared to the Capio Slim®. No statistical difference was found in the incidence of post-operative buttock pain related to pudendal nerve entrapment requiring release of the suspension suture (ROS incidence 7% Capio Slim®, 8% Fixt®). Return to theatre rates were the same as the ROS rates (though not all sutures were removed in theatre). Two sutures were removed in the ward, additional reasons for return to theatre were drainage of vault haematoma/abscess and release of TVTs for urinary retention. The post-operative complication rates of buttock pain related to pudendal nerve entrapment requiring release of the suspension suture were not only comparable between the two devices, but these rates were also shown to be lower than Karram et al who quoted a prevalence of nerve-related buttock pain of 10-15%.[32]

As stated previously, no visceral injury occurred intra-operatively. The only major complication related to SSF was pudendal nerve entrapment discussed above. Participants were counselled pre-operatively about the risk of its occurrence. Measures were also undertaken to prevent it by ensuring that the sacrospinous suture placement was at least 2cm from the ischial spine. Despite these measures, 4 participants required unilateral suture removal for pudendal nerve entrapment. This can be explained by individual variations in the location of the pudendal nerve as well as Barkesdale et al's histological findings that nerve fibres were present and widely distributed within the sacrospinous ligament.[33] With timeous recognition and subsequent removal of the ipsilateral suspension suture, there was immediate resolution of the related buttock pain and return of perineal sensation in all affected participants. At the 6 week follow-up, all the cases that had had a sacrospinous suture removed still had an adequately suspended mid-compartment with the remaining unilateral sacrospinous suture.

With regard to the short-term **efficacy** of the devices, no difference was found between the two devices in the 6 week post-procedural assessment. The procedure was proven successful in the short-term, with a well suspended mid-compartment at this 6 week assessment, a nearly 8cm improvement from the pre-operative measurement (median post-operative point C measurement -7 in both arms). The median short-term post-operative pain assessment was zero with most participants reporting no pain or bother, low symptom severity and level of impact questionnaire scores, and high overall satisfaction levels in both arms. Questionnaire reported symptom improvement in the Capio Slim® group was 70.85% and 66.85% in the Fixt® group. Overall rates of participant satisfaction related to the subjective success of the suspension procedure was 92%, where 96% of participants in the Capio Slim® reported being satisfied or very satisfied and 87,5% in the Fixt® arm.

This marked improvement in symptom severity and impact as well as participants post-procedural assessment. The procedure was proven successful in the short-t similar data by Ghoniem et al looking at the outcomes following SSF (86% total subjective cure of prolapse; improved household and social activity; some improvement in sexual activity).[27]

Some statistical differences were found between the two groups in the study population, the significance of which is however uncertain. A difference was found in median parity (3 births in Capio Slim® group and 3.5 in Fixt® group), but the clinical significance of this is questionable. This was bearing in mind the Women's Health Initiative pelvic organ prolapse article (2002) stating that women's risk

of uterine prolapse increased with every birth up to 5 births after which no further increase in risk was found.[4] The pre-operative POP-Q point C was found to be similar with no statistical difference found between the two groups. Hence, the difference in parity was not thought to be clinically significant.

No clear explanation can be found for the difference that arose between the two arms in the pre-operative POPDI-6 prolapse related questionnaire score. Participants in the Capio Slim® arm scored higher in this subscale (median score of 67) when compared to the Fixt® arm (subscale score 63). The median post-operative POPDI-6 scores were similar, hence a statistical difference existed in the calculated change between the pre-operative and post-operative scores. With randomisation to the different arms performed in theatre by the surgeons independent of the questionnaires administered by the primary investigator (who was blinded to the randomisation), no clear forms of bias or corrupted data could be found. The questionnaires were only validated in English. The primary investigator, fluent in English and Afrikaans, therefore verbally translated the questionnaires into Afrikaans in a non-directive manner. This was a possible source for corrupted data but it would have been implicated all of the questionnaires. This difference was thus thought to be a coincidental finding.

The World Health Organisation recommends that medical devices "*should be designed and manufactured in such a way that, when used under the conditions and for the purposes intended and, where applicable, by virtue of the technical knowledge, experience, education or training of intended users, they will not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety.*"[34]

In light of the above statement, based on the short-term outcomes examined in this trial both devices comply equally with the World Health Organisation's medical device regulations of safety with regard to risk management and hazards (adverse events); as well as clinical effectiveness as an indicator of device performance.[35] Not only were the devices comparable, but the anterior approach sacrospinous fixation was found to be a valuable procedure in mid-compartment prolapse surgery. The devices and procedure were shown to be highly effective with relatively low risks in the short-term assessment.

GENERALISABILITY

The generalizability of this trial is twofold relating firstly to the population observed and secondly to the surgeons performing the procedures. Firstly, the results of the outcomes examined cannot be extrapolated to the general female population because of the specific inclusion and exclusion criteria stipulated for this trial. External validity however exists for the population requiring or desiring surgical repair of their mid-compartment prolapse. Scrutiny of the study population in the two different arms showed homogeneity in all but two characteristics (parity and pre-operative prolapse severity score, POPDI-6). The significance of the differences between the two arms in the above regard was uncertain and was not thought to affect the internal validity of this trial. The demographics of the study population concurred with what the literature has revealed as risk factors for pelvic organ prolapse. The mean age of participants within this study population was 61.4 years (Capio Slim® 62.1 years; Fixt® 60.6 years) corresponding with Luber et al who found that the mean age of women seeking medical care for pelvic organ prolapse was 61 years.[2] The WHI trial showed that the risk of prolapse increased as BMI increased with significant increases of prolapse in all compartments when the BMI was more than 30 kg/m^2. [3] The trial participants' mean BMI was 30.5 kg/m^2 (Capio Slim® 30.3 kg/m^2; Fixt® 30.7 kg/m^2) reiterating the WHI findings.

By assessing the differences in the performance of the two surgeons involved in the trial, an attempt was made to infer generalizability in terms of operators of the devices with regard to the outcomes examined. Analysis comparing surgeons' performances with the Capio Slim® found that there was a statistical difference in the post-operative POP-Q point C (the objective measure of mid-compartment suspension). Change in pre-and post-operative measurements, however, found no difference. The rest of the outcomes measured comparing the surgeons' performances with the Capio Slim® and the Fixt® found no further significant differences. As no statistical differences were found in the outcomes of the two surgeons who performed the procedures in this trial the results could most likely be inferred to the population of adequately trained operators who perform this procedure on a regular basis, with minimal inter-operator variability (20 procedures or more per year as was performed in the trial).

STRENGTHS AND LIMITATIONS

A number of limitations were recognised in this trial. This randomised controlled trial was powered to the primary outcome of time to successful placement of bilateral suspension sutures. The strength of this trial is that it achieved a high power of 99% power for this outcome. However, the reliability and validity of the secondary outcomes may be questioned for the small population size observed. With this in mind, the non-inferiority between the two devices in terms of these secondary outcomes cannot be stated as an absolute as the population size would need to be powered for each outcome examined.

Further strengths of this trial was that of the design as a randomised trial, with good methodology and maintenance of blinding of the primary investigator throughout the trial until results had been established. This prevented the occurrence of selection bias affecting the results. Intention to treat analysis performed prevented alteration of results from crossover of participants for varying reasons between arms as well as dropout of participants from the trial. There was a zero percent dropout rate in this trial, with all participants being followed up for the specified trial period. As a result, the effects of attrition bias was negated.

Two relatively new devices (Capio Slim® and Fixt®) and approach (anterior approach to sacrospinous suture placement) were used in the trial. While both surgeons had extensive experience with the older Boston Scientific Capio® device; the Capio Slim® and Fixt® were newer on the market. Both surgeons had little experience with either the Capio Slim or the Fixt before the initiation of the trial. The impact of the learning curve therefore needs to be considered when reviewing this trial.

Analysis stratification was not performed for comparisons of outcomes of procedures performed with or without the uterus in-situ. The impact on subjective and objective improvement of prolapse when concomitant procedures were performed at the time of sacrospinous fixation was also not analysed. These aspects were beyond the scope of this trial. Using the source data from this trial, however, these points have potential for further scrutiny.

Possible reporting bias may have been introduced with regard to the objective post-operative assessment where clinicians performing the POP-Q measurements were aware of the devices used. However, with no differences existing between the two arms of the trial concerning the subjective symptom improvement and level of participant satisfaction, this is less likely to be a significant form of bias.

Comment with regard to post-procedural subjective and objective observations is also limited due to the short follow-up period. The six week trial follow-up period was too short to comment on prolapse recurrence, or to review whether any differences existed between the two arms of the trial in this regard. Post-operative results from this trial can thus not be compared to most other trials which tend to have longer follow-up periods.

Improvement or alterations in subjective sexual function could also not be commented upon as the majority of participants, on advice from their attending doctors, where not yet sexually active at the time of their six week follow-up visits.

These limitations related to the short duration of the trial, has potential for further investigation. One year and five year (or longer) follow-up of this trial population may provide valuable information related to long term surveillance of symptomatology, recurrence of prolapse and effect on sexual function.

IMPLICATIONS

At present, no other trials have been published comparing sacrospinous suspension suture capture devices. This trial has highlighted the advantages of the anterior approach to Sacrospinous Fixation using either of the two suture capture devices, with its short procedural time and relatively low complication rates (reversibility and resolution with regard to pudendal nerve entrapment). With these suspension suture capture devices being disposable, cost plays a big role in the decision to use them to perform sacrospinous fixation for mid-compartment prolapse.

In the South African context, for several years only the Capio® had been available for use in sacrospinous fixation without wide dissection. Now its modification, Boston Scientific's Capio Slim® as well as Bard's Fixt® are on the market. Knowing that the safety and efficacy of these devices are equal (with regard to the outcomes examined in this trial), surgeons are provided with more options to perform sacrospinous fixation. This could introduce competition into the market that may have implications on costing in the future.

Ethics

This study abided by the important principles set out in the Declaration of Helsinki (Appendix 12). The intent of this trial was to be of **benefit** to the general population. Firstly, with the use of a well-designed study, it aimed to ascertain the best device to use for sacrospinous fixation (if any differences existed). Secondarily it aimed to assess the success and satisfaction with the procedure performed. The concept of **non-maleficence** was adhered to as the surgeons performing the procedure are deemed experts in their field with participants included only if appropriate. With the same principle in mind, no significant difference was found between the two devices used and no major irreversible adverse events had occurred within the duration of the trial and hence no harm was identified within the trial.

Participants had complete **autonomy** in terms of recruitment and continued participation in the trial, with no negative implications on services rendered with refusal of inclusion, or reprisal for withdrawal from the trial. **Justice** and fairness was maintained in terms of treatment for both non-participants and participants in either arm of the trial. After a comprehensive explanation of the proposed research, the participants signed a **consent** form (Appendix 6). Only participants older than 18 and deemed legally competent were included in the trial.

All data collected was handled confidentially with respect to participants' **privacy**. Participants' names and other identifying information were kept separately from research data in a password protected programme, with anonymity being maintained through the use of computer generated study identity numbers. Participants will have access to the results of the trial should they desire so. There is no conflict of interest as the primary investigator and supervisors have no vested interest in the outcomes of the trial.

FUNDING

The funding requirements for this trial was minimal. Participants were recruited from the pool of patients already scheduled for surgery. These patients would have undergone sacrospinous fixation whether part of the clinical trial or not. At Groote Schuur Hospital both the Capio Slim® and Fixt® devices have been received on state tender and were available. As a result, the cost of the hospital stay, theatre time, devices and procedure was borne by the hospital. There was no necessity to reimburse the women recruited to the trial since no additional out of the pocket expenses was created. The assessments of patients for surgery, as well as the actual procedures, were performed by hospital specialists. The enrolment of participants into the trial had no influence on the care they received as patients. For these reasons it was not deemed necessary for study insurance. The health professionals and patients were covered by the standard hospital insurance. All other expenses of the trial was covered by the Obstetrics and Gynaecology Department Research Fund.

CONCLUSION

Before this study had been performed there was very little evidence in the literature comparing safety and efficacy of devices used for sacrospinous fixation. This randomised controlled trial has now proven the non-inferiority of the Capio Slim® and Fixt® for the short-term outcomes compared. The devices as well as the anterior approach for sacrospinous fixation were shown to be relatively safe (though a fair number of Dindo 3b complications arose) and effective with short operative times. This study looking at short term outcomes should be followed up by trials examining the long-term safety and efficacy of these devices.

REGISTRATION OF TRIAL

South African National Clinical Trial Register number: 5358

www.sanctr.gov.za

APPENDICES

Appendix 1

Appendix 2a

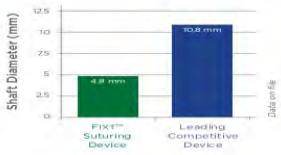
Hard-to-reach, meet easy-to-handle.

For deep suturing in tight operating spaces, intuitive, easy-to-wield tools are key to maximizing accuracy and minimizing patient trauma. You need an introducer that works as simply and solidly as your own hand—in a fraction of the space, with a fraction of the effort.

ELEGANT

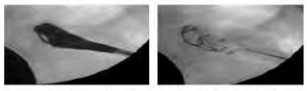
REDUCED SHAFT DIAMETER

The FIXT™ Suturing Device shaft is half the diameter of that of the leading suture delivery device.



ROBUST

Light but solid metal construction means one FIXT™ Suturing Device can finish the job.



FIXT™ Suturing Device *Leading Competitive Device*

ERGONOMIC

Easy-grip handle makes the FIXT™ Suturing Device an extension of the hand in tight spaces.

EFFICIENT

Solidly constructed. Easy to hold. Easy to use. Elegantly simple. Just aim and "click" for simple, one-pass success.

EFFECTIVE

Straight-line insertion means decreased manipulation—no unnecessary pushing or prodding.

Appendix 2b

PELVIC FLOOR RECONSTRUCTION

For more information about the **FIXT™ Suturing Device** and other BARD® products, please contact your BARD sales representative, or call 800.526.4455.

Order #	Product Name	Quantity
SD100	FIXT™ Suturing Device	1
SD105	FIXT™ Suturing Device Multi-Pack	Box of 5

Catalog #	Suture Material	Needle Configuration	Size	Length	Closest Equivalent
DEK100	Polypropylene Nonabsorbable Surgical Suture	Double armed with FX45 dilating tip and C-2 tapercut needle	0	48"	Prolene®
DEK200	Polypropylene Nonabsorbable Surgical Suture	Double armed with FX45 dilating tips	0	48"	Prolene®
TEV100	Polyester Nonabsorbable Surgical Suture	Double armed with FX45 dilating tip and C-2 tapercut needle	0	48"	Ethibond®
TEV200	Polyester Nonabsorbable Surgical Suture	Double armed with FX45 dilating tips	0	48"	Ethibond®
BON100	Polyglycolic Acid (PGA) Synthetic Absorbable Surgical Suture	Double armed with FX45 dilating tip and C-2 tapercut needle	0	48"	Dexon™/Vicryl™
BON200	Polyglycolic Acid (PGA) Synthetic Absorbable Surgical Suture	Double armed with FX45 dilating tips	0	48"	Dexon™/Vicryl™
MON100	Synthetic Polydioxanone (PDO) Absorbable Surgical Suture	Double armed with FX45 dilating tip and C-2 tapercut needle	0	48"	PDS™ II
MON200	Synthetic Polydioxanone (PDO) Absorbable Surgical Suture	Double armed with FX45 dilating tips	0	48"	PDS™ II

PELVIC HEALTH

BARD | MEDICAL

C. R. Bard, Inc.
8195 Industrial Boulevard
Covington, GA 30014
1.800.526.4455
www.bardmedical.com

PELVIC FLOOR RECONSTRUCTION

For more information about the **FIXT™ Suturing Device** and other BARD® products, please contact your BARD sales representative, or call 800.526.4455.

Order #	Product Name	Quantity
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MON100	Synthetic Polydioxanone (PDO) Absorbable Surgical Suture	Double armed with FX45 dilating tip and C-2 tapercut needle	0	48"	PDS™ II
MON200	Synthetic Polydioxanone (PDO) Absorbable Surgical Suture	Double armed with FX45 dilating tips	0	48"	PDS™ II

PELVIC HEALTH

BARD | MEDICAL

C. R. Bard, Inc.
8195 Industrial Boulevard
Covington, GA 30014
1.800.526.4455
www.bardmedical.com

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1006-48 R01/11 THP P01/11 SM

Appendix 3a

SYMPTOM DIRECTED QUESTIONNAIRES

PELVIC FLOOR DISTRESS INVENTORY QUESTIONNAIRE – 1

Study ID No: _____ Date: _____

Pelvic Organ Prolapse Distress Inventory 6 (POPDI-6)

Do you experience, and, if so, how much are You bothered by	Not at all	Somewhat	Moderately	Quite a bit
Usually experience pressure in the lower abdomen?				
Usually experience heaviness or dullness in the pelvic area?				
Usually have a bulge or something falling out that you can see or feel in your vaginal area?				
Ever have to push on the vagina or around the rectum to have or complete a bowel movement?				
Usually experience a feeling of incomplete bladder emptying?				
Ever have to push up on the bulge in the vaginal area with your fingers to start or complete urination?				

Pelvic Floor Impact Questionnaire

Instructions: Some women find that bladder, bowel, or vaginal symptoms affect their activities, relationships, and feeling. For each question place an **X** in the response that best describes how much you're activities, relationships, or feelings have been affected by your bladder, bowel, or vaginal symptoms or conditions **over the last 3 months**. Please make sure you mark an answer in **all 3 columns** for each question.

How do symptoms or conditions relate to the following →→→ Usually affect your ↓	*Bladder or Urine*	*Bowel or Rectum*	*Vagina or Pelvis*
1. Ability to do household chores (cooking, housecleaning, laundry)?	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit
2. Ability to do physical activities such as walking, swimming, or other exercise?	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit
3. Entertainment activities such as going to a movie or concert?	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit
4. Ability to travel by car or bus for a distance greater that 30 minutes away from home?	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit
5. Participating in social activities outside your home>	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit
6. Emotional health (nervousness, depression, etc)?	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit
7. Feeling frustrated?	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit

Appendix 3b

PELVIC FLOOR DISTRESS INVENTORY – 2

Study ID No: _____ Date: _____

Urinary Distress Inventory 6 (UDI-6)

Do you experience, and, if so, how much are You bothered by	Not at all	Somewhat	Moderately	Quite a bit
Usually experience frequent urination?				
Usually experience urine leakage associated with a feeling of urgency, this is, a strong sensation of needing to go to the bathroom?				
Usually experience urine leakage related to coughing, sneezing, or laughing?				
Usually experience small amounts of urine leakage (that is, drops)?				
Usually experience difficulty emptying your bladder?				
Usually experience pain or discomfort in the lower abdomen or genital region?				

Colorectal-Anal Distress Inventory 8 (CRADI-8)

Do you experience, and, if so, how much are You bothered by	Not at all	Somewhat	Moderately	Quite a bit
Feel you need to strain too hard to have a bowel movement?				
Feel you have not completely emptied your bowel at the end of a bowel movement?				
Usually lose stool beyond your control if your stool is well formed?				
Usually lose stool beyond your control if your stool is loose?				
Usually lose gas from the rectum beyond your control?				
Do you usually have pain when you pass your stool?				
Experience a strong sense of urgency and have to rush to the bathroom to have a bowel movement?				
Does part of your bowel ever pass through the rectum and bulge outside during or after a bowel movement?				

Appendix 4a

SYMPTOM DIRECTED QUESTIONNAIRES

SEXUAL FUNCTION QUESTIONNAIRE (PISQ) – 1

Study ID No: _____ Date: _____

Q1 Which of the following best describes you:

Not sexually active at all 1 ☐ → Go to item Q2 (Section 1)

Sexually active with or without a partner 2 ☐ → Skip to item Q7 (Section 2)

Section 1: For those who are not Sexually Active

☞ If you engage in sexual activity please check this box ☐ and skip to Page 3

Q2 The following are a list of reasons why you might not be sexually active, for each one please indicate how strongly you agree or disagree with it as a reason that you are not sexually active.

	STRONGLY AGREE	SOMEWHAT AGREE	SOMEWHAT DISAGREE	STRONGLY DISAGREE
a No partner	☐1	☐2	☐3	☐4
b No Interest	☐1	☐2	☐3	☐4
c Due to bladder or bowel problems (urinary or fecal incontinence) or due to prolapse (a feeling of or a bulge in the vaginal area)	☐1	☐2	☐3	☐4
d Because of my other health problems	☐1	☐2	☐3	☐4
e Pain	☐1	☐2	☐3	☐4

Q3 How much does the fear of leaking urine and/or stool and/or a bulging in the vagina (either the bladder, rectum or uterus falling out) cause you to avoid or restrict your sexual activity?

1 ☐ Not at All
2 ☐ A Little
3 ☐ Some
4 ☐ A Lot

Q4 For each of the following, please circle the number between 1 and 5 that best represents how you feel about your sex life.

		RATING					
a.	Satisfied	1	2	3	4	5	Dissatisfied
b.	Adequate	1	2	3	4	5	Inadequate

Appendix 4b

SEXUAL FUNCTION QUESTIONNAIRE - 2

Study ID No: _____ Date: _____

Q5 How strongly do you agree or disagree with each of the following statements:

	STRONGLY AGREE	SOMEWHAT AGREE	SOMEWHAT DISAGREE	STRONGLY DISAGREE
a. I feel frustrated by my sex life	☐1	☐2	☐3	☐4
b. I feel sexually inferior because of my incontinence and/or prolapse	☐1	☐2	☐3	☐4
c. I feel angry because of the impact that incontinence and/or prolapse has on my sex life	☐1	☐2	☐3	☐4

Q6 Overall, how bothersome is it to you that you are not sexually active?

1 ☐ Not at All
2 ☐ A Little
3 ☐ Some
4 ☐ A Lot

End of Items for Not Sexually Active

Appendix 4c

SEXUAL FUNCTION QUESTIONNAIRE – 3

Study ID No: _____ Date: _____

Section 2: For Those Who are Sexually Active

The remaining items in the survey are about a topic that one is not often asked to report on in a survey please answer as honestly and clearly as you possibly can.

Q7 How often do you feel sexually aroused (physically excited or turned on) during sexual activity?

1 ☐ Never
2 ☐ Rarely
3 ☐ Sometimes
4 ☐ Usually
5 ☐ Always

Q8 When you are involved in sexual activity, how often do you feel each of the following:

	NEVER	RARELY	SOMETIMES	USUALLY	ALMOST ALWAYS
a. Fulfilled	☐[1]	☐[2]	☐[3]	☐[4]	☐[5]
b. Shame	☐[1]	☐[2]	☐[3]	☐[4]	☐[5]
c. Fear	☐[1]	☐[2]	☐[3]	☐[4]	☐[5]

Q9 How often do you leak urine and/or stool with <u>any type</u> of sexual activity?

1 ☐ Never
2 ☐ Rarely
3 ☐ Sometimes
4 ☐ Usually
5 ☐ Always

Q10 Compared to orgasms you have had in the past, how intense are your orgasms now?

1 ☐ Much less intense
2 ☐ Less intense
3 ☐ Same intensity
4 ☐ More intense
5 ☐ Much more intense

Appendix 4d

SEXUAL FUNCTION QUESTIONNAIRE - 4

Study ID No: _____ Date: _____

Q11 How often do you feel pain during sexual intercourse? (If you don't have intercourse check this box ☐ and skip to the next item.)

1 ☐ Never
2 ☐ Rarely
3 ☐ Sometimes
4 ☐ Usually
5 ☐ Always

Q12 Do you have a sexual partner?

1 ☐ Yes ➜ Go to Q13
2 ☐ No ➜ Skip to Q15

Q13 How often does your partner have a problem (lack of arousal, desire, erection ,etc.) that limits your sexual activity?

1 ☐ All of the time
2 ☐ Most of the time
3 ☐ Some of the time
4 ☐ Hardly ever/Rarely

Q14 In general, would you say that your partner has a positive or negative impact on each of the following:

	VERY POSITIVE	SOMEWHAT POSITIVE	SOMEWHAT NEGATIVE	VERY NEGATIVE
a. Your sexual desire	☐[1]	☐[2]	☐[3]	☐[4]
b. The frequency of your sexual activity	☐[1]	☐[2]	☐[3]	☐[4]

Q15 When you are involved in sexual activity, how often do you feel that you want more?

1 ☐ Never
2 ☐ Rarely
3 ☐ Sometimes
4 ☐ Usually
5 ☐ Always

Q16 How frequently do you have sexual desire, this may include wanting to have sex, having sexual thoughts or fantasies, etc.?

1 ☐ Daily
2 ☐ Weekly
3 ☐ Monthly
4 ☐ Less often than once a Month
5 ☐ Never

Appendix 4e

SEXUAL FUNCTION QUESTIONNAIRE - 5

Study ID No: _____ Date: _____

Q17 How would you rate your level (degree) of sexual desire or interest?

1 ☐ Very high
2 ☐ High
3 ☐ Moderate
4 ☐ Low
5 ☐ Very low or none at all

Q18 How much does the fear of leaking urine, stool and/or a bulging in the vagina(prolapse) cause you to avoid sexual activity?

1 ☐ Not at All
2 ☐ A Little
3 ☐ Some
4 ☐ A Lot

Q19 For each of the following, please circle the number between 1 and 5 that best represents how you feel about your sex life.

		RATING					
a	Satisfied	1	2	3	4	5	Dissatisfied
b	Adequate	1	2	3	4	5	Inadequate
c	Confident	1	2	3	4	5	Not Confident

Q20 How strongly do you agree or disagree with each of the following statements:

	STRONGLY AGREE	SOMEWHAT AGREE	SOMEWHAT DISAGREE	STRONGLY DISAGREE
a. I feel frustrated by my sex life	☐[1]	☐[2]	☐[3]	☐[4]
b. I feel sexually inferior because of my incontinence and/or prolapse	☐[1]	☐[2]	☐[3]	☐[4]
c. I feel embarrassed about my sex life	☐[1]	☐[2]	☐[3]	☐[4]
d. I feel angry because of the impact that incontinence and/or prolapse has on my sex life	☐[1]	☐[2]	☐[3]	☐[4]

Appendix 5

Sacrospinous Suture Capture Device Trial

Information Sheet

This Informed Consent Form is for women attending the Urogynaecology clinic with uterine or vault prolapse ("womb or vagina dropping down"). You have been invited to be part of this research run by Groote Schuur Hospital doctors, with Dr. Lamees Ras as the main researcher. This Informed Consent Form has two parts:

- Information Sheet (to tell you about the research)
- Certificate of Consent (for you to sign if you agree to take part)

You will be given a copy of the full Informed Consent Form. The process will be explained to you by the doctor seeing you. If there is anything that you do not understand please feel free to ask questions at any point.

Information Sheet

The research we are doing is looking at two new tools used to do vaginal vault or uterine suspension (operation to lift the vagina or womb when it has prolapsed –"hanging out"). We are doing this to try to improve our care for patients by making sure that the tools we use in the operation work well, are comfortable for the surgeons to handle and have the best outcome. We are comparing the two tools to see if there is any difference in the time it takes to do the operation; things that go wrong during the operation (complications); your symptoms after the operation; how satisfied you are with the result and if the prolapse returns (vaginal vault or womb drops again).

Your doctor has examined you and decided that the best treatment for your womb/vault drop is to have an operation to lift the womb/vaginal vault. The procedure will be explained to you by your doctor. It will be done through the vagina and involves pulling up the vaginal vault or womb using a stitch high in the pelvis. The stitch is placed using one of two tools and we will compare their performance. The names of the two devices are the Capio Slim® and the Fixt®. Pamphlets on these two tools can be shown to you if you would like to know more about them. Both these tools have been used before by the doctors who will be performing your operation. The tool that is used for your operation will be randomly chosen. In order to be sure that our results are reliable you will not know what tool was used until after the research is done.

Sacrospinous Suture Capture Device Trial

Information Sheet

Continued…

You will need to fill out some forms before and after the operation that tell us about your symptoms and pain before the operation and the difference after the operation. We will be recording information about the operation and its success during and after the operation.

We will schedule the routine 6 week follow-up visit after you have been discharged, to see how you have recovered and if your symptoms have improved. This will help us to see if the operation was successful.

All the risks related to the operation itself will be explained to you by your doctor. We expect very little risk to you taking part in the research as these tools have been specially designed for the operation you are having. What we are aiming to show is that there is no difference between the Capio Slim® and the Fixt®.

You have a choice to take part in this research or not. If you decide not to take part in the research, you will still get all the treatment you need for your condition. You can decide at any point to leave the research project if you want to. This will not have a negative effect on the treatment you receive. If you decide to take part in the research, the results will help us by advising us as to the best tool to use in the future and this will improve patient care. If you are part of the research, your information will be handled with the utmost care and confidentiality. A research code will be used instead of your name so that you remain anonymous.

Once the trial has been completed in January 2015, the results will be available for you to see. The results of the trial may also be published publically but your personal information will not be made known. This proposal has been reviewed and approved by the Ethics committee, which is a committee that makes sure that research participants are protected from harm. No study insurance will be available for this trial. If any issues arise, you will be directed to the Groote Schuur Hospital medico-legal department.

For any queries, contact: Dr Lamees Ras 0722182220 or Dr Kendall Brouard (021) 4046020

If you have any further questions or unsatisfied by our response; or if you have concerns about your rights or welfare as a research participant, contact the Human Research Ethics Committee (HREC) on: Tel (021) 406 6338 or Fax (021) 406 6411

Appendix 6

Sacrospinous Suture Capture Device Trial

Informed Consent

I have read the information above, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked has been answered to my satisfaction. I consent voluntarily to participate as a participant in this research.

Print Name of Participant _____

Signature of Participant _____ or thumbprint

Date _____

Day/Month/Year

(Official Use)

Statement by person taking consent

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands the procedure.

I confirm that the participant was given the opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

Print Name of person taking the consent_____

Signature of person taking the consent _____

Date _____

Day/Month/Year

Appendix 7


Sacrospinous Suture Capture Device Trial

Intra-operative Reporting Sheet

Study ID No: _____ (include device code and surgeon's code)

Date: _____

Time to application of bilateral sacrospinous sutures (seconds): ☐

Number of attempts required: Right ☐

Left ☐

Rectal injury: yes ☐ no ☐

Bladder injury: yes ☐ no ☐

Comments:_____
_____
_____
_____
_____
_____

Appendix 8


Sacrospinous Suture Capture Device Trial

Immediate Post-operative Reporting Sheet

(To be completed on day of discharge)

Study ID No: _____ (include device code and surgeon's code)

Date: _____

Length of hospital stay (days): ☐

Post-operative buttock pain: yes ☐ no ☐

(Tick appropriate box)

Unilateral ☐ Bilateral ☐

Return to theatre: yes ☐ no ☐

Removal of suture: yes ☐ no ☐

Comments:_____
_____
_____
_____
_____

Appendix 9

Sacrospinous Suture Capture Device Trial

Short Term Post-operative Reporting Sheet

(To be completed at six week follow-up visit)

Study ID No: _____ (include device code and surgeon's code)

Date: _____

Recurrence of prolapse: yes ☐ no ☐

POP-Q score - pre-operative: ☐

post-operative: ☐

Patient level of satisfaction: (tick appropriate box)

1 = Very dissatisfied ☐ 

2 = Dissatisfied ☐ 

3 = Neutral ☐ 

4 = Satisfied ☐ 

5 = Very satisfied ☐ 

Comments:_____
_____
_____
_____

Appendix 10 a

Sacrospinous Suture Capture Device Trial

Pre-operative Pain Assessment

(To be completed pre-op; immediate post-op; six week follow up visit)

Study ID No: _____ (include device code and surgeon's code)

Date: _____

Rate your level of pain 0-10:

(tick appropriate box)

☐ ☐ ☐ ☐ ☐ ☐

Appendix 10 b

Sacrospinous Suture Capture Device Trial

Immediate Post-operative Pain Assessment

(To be completed pre-op; immediate post-op; six week follow up visit)

Study ID No: _____ (include device code and surgeon's code)

Date: _____

Rate your level of pain 0-10:

(tick appropriate box)

☐ ☐ ☐ ☐ ☐ ☐

Appendix 10 c

Sacrospinous Suture Capture Device Trial

Short term Post-operative Pain Assessment

(To be completed pre-op; immediate post-op; six week follow up visit)

Study ID No: _____ (include device code and surgeon's code)

Date: _____

Rate your level of pain 0-10:

(tick appropriate box)

☐ ☐ ☐ ☐ ☐ ☐

Appendix 11

The Clavien-Dindo Classification of Surgical Complications

Grades	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, analgesics, diuretics and 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 III-a:	intervention not under general anesthesia
Grade III-b:	intervention under general anesthesia
Grade IV:	Life-threatening complication (including CNS complications)requiring IC/ICU-management:
Grade IV-a:	single organ dysfunction (including dialysis)
Grade IV-b:	multi organ dysfunction
Grade V:	Death of a patient
Suffix 'd':	If the patients suffers from a complication at the time of discharge, 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.

Appendix 12

World Medical Association Declaration of Helsinki

Ethical Principles for Medical Research Involving Human Subjects

Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964; amended by the 29th WMA General Assembly, Tokyo, Japan, October 1975; 35th WMA General Assembly, Venice, Italy, October 1983; 41st WMA General Assembly, Hong Kong, September 1989; 48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996, and the 52nd WMA General Assembly, Edinburgh, Scotland, October 2000

Introduction

1. The World Medical Association has developed the Declaration of Helsinki as a statement of ethical principles to provide guidance to physicians and other participants in medical research involving human subjects. Medical research involving human subjects includes research on identifiable human material or identifiable data.
2. It is the duty of the physician to promote and safeguard the health of the people. The physician's knowledge and conscience are dedicated to the fulfillment of this duty.
3. The Declaration of Geneva of the World Medical Association binds the physician with the words, ''The health of my patient will be my first consideration,'' and the International Code of Medical Ethics declares that, ''A physician shall act only in the patient's interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient.''
4. Medical progress is based on research which ultimately must rest in part on experimentation involving human subjects.
5. In medical research on human subjects, considerations related to the well-being of the human subject should take precedence over the interests of science and society.
6. The primary purpose of medical research involving human subjects is to improve prophylactic, diagnostic and therapeutic procedures and the understanding of the aetiology and pathogenesis of disease. Even the best proven prophylactic, diagnostic, and therapeutic methods must continuously be challenged through research for their effectiveness, efficiency, accessibility and quality.
7. In current medical practice and in medical research, most prophylactic, diagnostic and therapeutic procedures involve risks and burdens.
8. Medical research is subject to ethical standards that promote respect for all human beings and protect their health and rights. Some research populations are vulnerable and need special protection. The particular needs of the economically and medically disadvantaged must be recognized. Special attention is also required for those who cannot give or refuse consent for themselves, for those who may be subject to giving consent under duress, for those who will not benefit personally from the research and for those for whom the research is combined with care.
9. Research Investigators should be aware of the ethical, legal and regulatory requirements for research on human subjects in their own countries as well as applicable international requirements. No national ethical, legal or regulatory requirement should be allowed to reduce or eliminate any of the protections for human subjects set forth in this Declaration.

Basic principles for all medical research

1. It is the duty of the physician in medical research to protect the life, health, privacy, and dignity of the human subject.
2. Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and on adequate laboratory and, where appropriate, animal experimentation.
3. Appropriate caution must be exercised in the conduct of research which may affect the environment, and the welfare of animals used for research must be respected.
4. The design and performance of each experimental procedure involving human subjects shou ld be clearly formulated in an experimental protocol. This protocol should be submitted for c onsideration, comment, guidance, and where appropriate, approval to a specially appointed ethical review committee, which must be independent of the investigator, the sponsor or an y other kind of undue influence. This independent committee should be in conformity with t he laws and regulations of the country in which the research experiment is performed. The c ommittee has the right to monitor ongoing trials. The researcher has the obligation to provid e monitoring information to the committee, especially any serious adverse events. The resea rcher should also submit to the committee, for review, information regarding funding, spons ors, institutional affiliations, other potential conflicts of interest and incentives for subjects.
5. The research protocol should always contain a statement of the ethical considerations involved and should indicate that there is compliance with the principles enunciated in this Declaration.
6. Medical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given consent.
7. Every medical research project involving human subjects should be preceded by careful assessment of predictable risks and burdens in comparison with foreseeable benefits to the subject or to others. This does not preclude the participation of healthy volunteers in medical research. The design of all studies should be publicly available.
8. Physicians should abstain from engaging in research projects involving human subjects unless they are confident that the risks involved have been adequately assessed and can be satisfactorily managed. Physicians should cease any investigation if the risks are found to outweigh the potential benefits or if there is conclusive proof of positive and beneficial results.
9. Medical research involving human subjects should only be conducted if the importance of the objective outweighs the inherent risks and burdens to the subject. This is especially important when the human subjects are healthy volunteers.
10. Medical research is only justified if there is a reasonable likelihood that the populations in which the research is carried out stand to benefit from the results of the research.
10. The subjects must be volunteers and informed participants in the research project.
11. The right of research subjects to safeguard their integrity must always be respected. Every precaution should be taken to respect the privacy of the subject, the confidentiality of the patient’s information and to minimize the impact of the study on the subject’s physical and mental integrity and on the personality of the subject.
12. In any research on human beings, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations

of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail. The subject should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal. After ensuring that the subject has understood the information, the physician should then obtain the subject's freely-given informed consent, preferably in writing. If the consent cannot be obtained in writing, the non-written consent must be formally documented and witnessed.

13. When obtaining informed consent for the research project the physician should be particularly cautious if the subject is in a dependent relationship with the physician or may consent under duress. In that case the informed consent should be obtained by a well-informed physician who is not engaged in the investigation and who is completely independent of this relationship.
14. For a research subject who is legally incompetent, physically or mentally incapable of giving consent or is a legally incompetent minor, the investigator must obtain informed consent from the legally authorized representative in accordance with applicable law. These groups should not be included in research unless the research is necessary to promote the health of the population represented and this research cannot instead be performed on legally competent persons.
15. When a subject deemed legally incompetent, such as a minor child, is able to give assent to decisions about participation in research, the investigator must obtain that assent in addition to the consent of the legally authorized representative.
16. Research on individuals from whom it is not possible to obtain consent, including proxy or advance consent, should be done only if the physical/mental condition that prevents obtaining informed consent is a necessary characteristic of the research population. The specific reasons for involving research subjects with a condition that renders them unable to give informed consent should be stated in the experimental protocol for consideration and approval of the review committee. The protocol should state that consent to remain in the research should be obtained as soon as possible from the individual or a legally authorized surrogate.
17. Both authors and publishers have ethical obligations. In publication of the results of research, the investigators are obliged to preserve the accuracy of the results. Negative as well as positive results should be published or otherwise publicly available. Sources of funding, institutional affiliations and any possible conflicts of interest should be declared in the publication. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.

Additional principles for medical research combined with medical care

18. The physician may combine medical research with medical care, only to the extent that the research is justified by its potential prophylactic, diagnostic or therapeutic value. When medical research is combined with medical care, additional standards apply to protect the patients who are research subjects.
19. The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not exclude the use of placebo, or no treatment, in studies where no proven prophylactic, diagnostic or therapeutic method exists.

20. At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study.
21. The physician should fully inform the patient which aspects of the care are related to the research. The refusal of a patient to participate in a study must never interfere with the patient–physician relationship.
22. In the treatment of a patient, where proven prophylactic, diagnostic and therapeutic methods do not exist or have been ineffective, the physician, with informed consent from the patient, must be free to use unproven or new prophylactic, diagnostic and therapeutic measures, if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering. Where possible, these measures should be made the object of research, designed to evaluate their safety and efficacy. In all cases, new information should be recorded and, where appropriate, published. The other relevant guidelines of this Declaration should be followed.

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