Interventional procedure overview of vaginal transluminal endoscopic hysterectomy and adnexal surgery for benign gynaecological conditions

Contents

Table 1 Abbreviations

Abbreviation	Definition
CCT	Controlled clinical trials
CD	Clavien-Dindo (for example, CD-1 = Clavien-Dindo grade 1)
DVT	Deep venous thrombosis
EQ-5D-3L	EuroQol five-dimension three-level patient-reported outcome measure
NR	Not reported
PID	Pelvic inflammatory disease
QoL	Quality of life
RCT	Randomised controlled trials
RoB2	Risk of bias 2
ROBINS-I	Risk of bias in non-randomised studies
SE	Standard error
TLH	Total laparoscopic hysterectomy
TU-LESS	Transumbilical laparoendoscopic single-site surgery
VAS	Visual analogue scale
vNOTES	Transvaginal natural orifice transluminal endoscopic surgery

Indications and current treatment

Benign gynaecological conditions refer to non-cancerous conditions affecting the female reproductive systems. These include chronic pelvic pain, uterine prolapse, fibroids and abnormal vaginal bleeding. The causes of these types of conditions are not always known but can be linked to periods, hormones and genetics. Left untreated, these conditions can lead to severe and prolonged pain, infections, and reduced quality of life.

The typical treatments for these vaginal conditions are medications (such as antibiotics, painkillers and hormonal medicines), physiotherapy (such as pelvic floor exercises to relieve pain), and surgical intervention (such as hysterectomy).

The focus of this overview is on selected surgical interventions, namely hysterectomy, adnexectomy and myomectomy.

- Conventional hysterectomy is done through a cut in the abdomen or via the vagina. There are also laparoscopic approaches. A vaginal hysterectomy is usually preferred over an abdominal or laparoscopic hysterectomy because it's less invasive and involves a shorter stay in hospital. Limitations of vaginal hysterectomy includes poor visualisation and the limited space for manipulation.
- Adnexectomy is a surgical procedure which removes part of the adnexal tissue of the uterus and can be done with a hysterectomy or in isolation. Adnexectomies include the removal of one or both of the fallopian tubes (salpingectomy), the removal of one or both of the ovaries (oophorectomy) or the removal of ligaments that support the uterus and ovaries.
- A myomectomy is the surgical removal of fibroids that develop in or around the womb. These surgeries can be done as either keyhole or open surgeries depending on the size and position the fibroids.

What the procedure involves

The vaginal transluminal endoscopic hysterectomy procedure is done in a similar way to a conventional vaginal hysterectomy but uses an endoscopic view and laparoscopic instruments. The patient is placed in the lithotomy position. Under general anaesthesia, a circular incision is made in the vagina (around the cervix). Following anterior/posterior colpotomy and transecting the sacro-uterine ligaments, a keyhole instrument port is then inserted to improve access and

visibility. The abdominal cavity is accessed through the colpotomy and then insufflated. Laparoscopic instruments are inserted and the surgery is done in a Trendelenburg (head down) position. Then the uterus, fallopian tubes or ovaries are removed vaginally (depending on the procedure type). Then the instrument port is removed, the abdomen is deflated, and the vaginal incision is closed with absorbable sutures.

Outcome measures

The main outcomes included procedure success rates, operation time, intra- and postoperative complications, length of stay, readmission rates, postoperative pain and quality of life.

Evidence summary

Population and studies description

This interventional procedures overview is based on 3,980 people from 1 systematic review, 1 RCT, 2 prospective case series and 5 retrospective cohort studies. Of these 3,980 people, 2,178 had the procedure. This is a rapid review of the literature, and a flow chart of the complete selection process is shown in figure 1. This overview presents 9 studies as the key evidence in table 2 and table 3, and lists 24 other relevant studies in table 5.

The systematic review by Housmans et al. (2020) reported outcomes for 718 hysterectomy procedures in adult women, who were having removal of the uterus for benign gynaecological disease. There were 288 people in the vNOTES arms and 430 in the control arms. The studies included 1 RCT from Belgium, 1 retrospective cohort study from Taiwan, 2 retrospective cohort studies from South Korea, 1 retrospective cohort study from Turkey and 1 retrospective cohort study from China.

The RCT by Baekelandt et al. (2021) compared vNOTES with laparoscopy for adnexectomy in 67 adult women with an adnexal mass presumed to be benign. The study was done at a single centre in Belgium and randomly assigned 34 people to the vNOTES group and 33 to the laparoscopy group. The mean ages were 50 (plus or minus 10) and 52 (plus or minus 8.5), respectively. Follow up of 6 months captured pain and quality-of-life outcomes.

The study by Karkia et al. (2019) was a prospective case series in a UK setting. They investigated the safety and efficacy of hysterectomy and adnexectomy using vNOTES. The population included 33 women with benign uterine pathology or grade 1 stage 1 endometrial cancer suitable for hysterectomy at a local unit. The patients were aged between 35 and 70 with a mean age of 50. Indications for surgery included treatment resistant dysfunctional uterine bleeding (14), atypical endometrial hyperplasia (5), BRCA positive breast cancer (2), pelvic pain (7), post-menopausal bleeding (4) and endometrial cancer stage 1 (1). Follow-up data was captured at 3 months but is not publicly available.

The study by Baekelandt and Kapurubandara (2021) is a prospective case series study that captured perioperative outcome data for 1,000 people having vNOTES for benign gynaecological conditions. 73% of procedures were hysterectomies and the rest were adnexal surgeries (18%) or other. All the procedures were done at a single centre in Belgium. The mean age of this cohort of women was 46 years.

Huang et al. (2022) is a retrospective study of patient data at a single centre in China for people who had vNOTES surgery for gynaecological conditions. The procedures included 902 adnexal surgeries, 98 myomectomies, 82 hysterectomies, 51 pelvic floor reconstruction surgeries and 14 malignant tumour surgeries. The mean ages across surgery groups ranged from 30.89 (plus or minus 6.26) to 63.55 (plus or minus 9.12) years old.

Ovarian cystectomies were the subject of the retrospective cohort study by Huang et al. (2021). They analysed 296 people, with a mean age of 30.1 (plus or minus 7.65), in need of laparoscopic surgery for ovarian cysts. This was a study in China where 86 women had vNOTES procedures and 210 were in the TU-LESS group.

Yan et al. (2022) is a retrospective study of 361 women who had either a vNOTES (n=228) or TU-LESS (129) hysterectomy at a single-centre in China. The mean ages of each group were 53.03 (plus or minus 9.44) and 54.26 (plus or minus 10.33), respectively.

Temtanakitpaisan et al. (2018) retrospectively studied the outcomes of vNOTES hysterectomy across uterine sizes for benign pelvic organ lesions of the uterus, cervix or ovaries. The procedures were done for 275 women at a single centre in Taiwan. Group 1 included 191 people with uterine weights less than 500 g, group 2 included 67 people with uterine weights of 500 g to 999 g, and group 3 included 17 people with uterine weights of 1,000 g or higher. The mean ages of the groups were 48.68 (plus or minus 6.63), 47.22 (plus or minus 3.81) and 46.53 (plus or minus 2.96), respectively.

The study by Kaya et al. (2022) was a cross-sectional of surgical outcomes for vNOTES compared with laparoscopic hysterectomy for benign gynaecological conditions in women with obesity. The study was done in Turkey and the cohort (n=83) consisted of adult women with a BMI of 30 kg/m^2 or greater. The mean age in the laparoscopy arm was 49 years (range 40 to 71) and the mean age in the vNOTES group was 52 (range 40 to 74).

Table 2 presents study details.

Figure 1 Flow chart of study selection

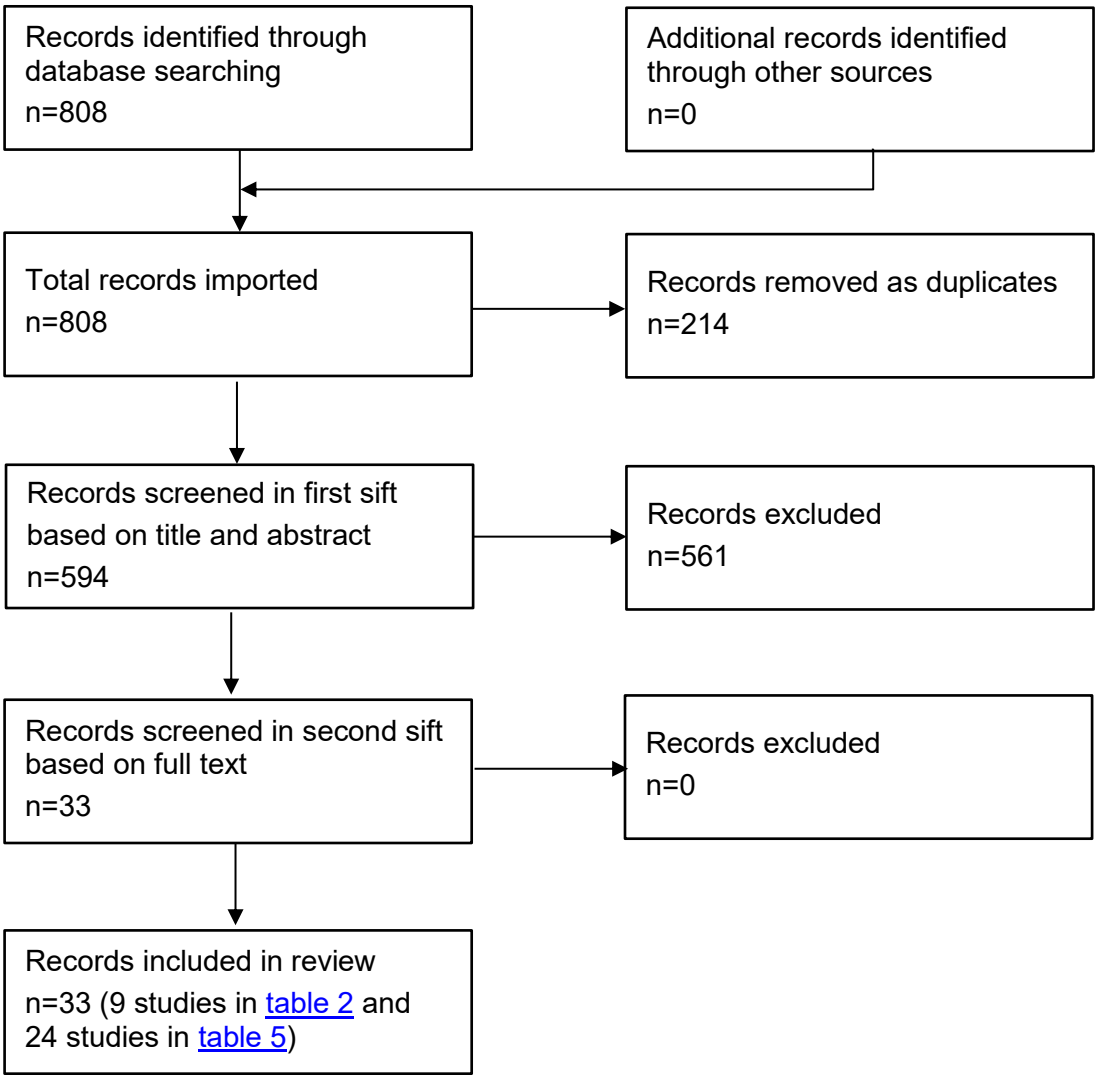

Table 2 Study details

Study no.	First author, date country	Patients (female)	Age (range)	Study design	Inclusion criteria	Intervention	Follow up
1	Housmans, 2020 Belgium	n=718 (n=288 in vNOTES arms)	Studies varied between 18 and 70 years	Systematic review	RCTs, CCTs, prospective or retrospective cohort studies that directly compares vNOTES to laparoscopy. Adult women having removal of the uterus for benign gynaecological disease. **Exclusions:** Genital prolapse Gynaecological malignancy	vNOTES hysterectomy compared with laparoscopic hysterectomy	NR
2	Baekelandt, 2021 Belgium	n=67 (n=34 in vNOTES arm)	Mean= 52 (plus or minus 11)	Randomised controlled trial	Women who were not pregnant, and were sexually active with an intact uterus and without obliteration of the pouch of Douglas scheduled to have removal of a benign adnexal mass. **Exclusions:** History of rectal surgery	vNOTES adnexectomy compared with laparoscopic adnexectomy	6 months pain/QoL

Study no.	First author, date country	Patients (female)	Age (range)	Study design	Inclusion criteria	Intervention	Follow up
					Suspected rectovaginal endometriosis Suspected malignancy Pelvic inflammatory disease Active lower genital tract infection		
3	Karkia, 2019 UK	n=33	Mean = 50 (35 to 75)	Prospective case series	Women with benign uterine pathology or grade 1 stage 1 endometrial cancer suitable for hysterectomy at a local unit. **Exclusions:** History of surgery to the rectovaginal pouch History of rectovaginal endometriosis Two or more caesarean sections Uterine prolapse	vNOTES hysterectomy and adnexectomy	NR
4	Baekelandt, 2020 Belgium	n=1,000	Mean= 46 (22 to 83)	Prospective case series	Women with benign gynaecological conditions. **Exclusions:** History of rectal surgery	vNOTES hysterectomy (n=730) vNOTES other (n=270)	NR

Study no.	First author, date country	Patients (female)	Age (range)	Study design	Inclusion criteria	Intervention	Follow up
					History of pelvic radiotherapy Suspected rectovaginal endometriosis Suspected malignancy Pelvic inflammatory disease Active lower genital tract infection		
5	Huang, 2022 China	n=1,147	Mean = 30.89 (plus or minus 6.26) to 63.55 (plus or minus 9.12)	Retrospective cohort	Women with gynaecological conditions. **Exclusions:** Unstable vital signs with intolerability of the procedure Acute infection Preoperative DVT or hypercoagulability Liver or kidney dysfunction Mental illness Other conditions that rendered the patient unable to tolerate laparoscopy (for example, severe	vNOTES hysterectomy, adnexal surgery, myomectomy, pelvic floor reconstruction or malignant tumour surgery	NR

Study no.	First author, date country	Patients (female)	Age (range)	Study design	Inclusion criteria	Intervention	Follow up
					cardiopulmonary disease) History of rectal surgery Suspected rectovaginal septum endometriosis or severe adhesions Virginity Pregnancy		
6	Huang, 2021 China	n=296	Mean = 30.1 (plus or minus 7.65)	Retrospective cohort	In need of laparoscopic surgery for unilateral ovarian cysts Stable vital signs and laparoscopic surgery can be tolerated Low probability of malignancy **Exclusions:** History of rectal surgery Suspected of rectovaginal septum endometriosis, tumors or severe adhesions Virginity Pregnancy	vNOTES ovarian cystectomy (n=86) compared with TU-LESS ovarian cystectomy (n=210)	NR

Study no.	First author, date country	Patients (female)	Age (range)	Study design	Inclusion criteria	Intervention	Follow up
7	Yan, 2022 China	n=361	Mean = 53.04 (plus or minus 9.44) to 54.26 (plus or minus 10.33)	Retrospective cohort	Woman with benign gynaecological conditions	vNOTES hysterectomy (n=232) compared with TU-LESS hysterectomy (n=129)	NR
8	Temtanakitpaisan, 2018 Taiwan	n=275	Mean= 46.53 (plus or minus 2.96) to 48.68 (plus or minus 6.63)	Retrospective cohort	Women with benign pelvic organ lesions of the uterus, cervix, or ovaries that need surgical intervention. **Exclusions:** Virginity History of tubo-ovarian abscess Severe endometriosis Suspected severe pelvic adhesion History of abandoned NOTES hysterectomy	vNOTES hysterectomy	NR
9	Kaya, 2022 Turkey	n=83	Mean= TLH, 49 (40 to 71) vNOTES, 52 (40 to 74)	Cross-sectional	Women who had hysterectomy for benign gynaecological conditions with a BMI of 30 kg/m^2 or greater. **Exclusions:**	vNOTES hysterectomy compared with total laparoscopic hysterectomy	NR

Study no.	First author, date country	Patients (female)	Age (range)	Study design	Inclusion criteria	Intervention	Follow up
					Active urinary tract or pelvic infections Pregnancy Endometriosis Gynaecological malignancy History of pelvic radiotherapy Trendelenburg position		

Table 3 Study outcomes (option 1)

First author, date	Efficacy outcomes	Safety outcomes
Housmans, 2020	**Procedure success:** Either none or one conversion procedures were reported across studies. **Operation time:** 5 out of 6 studies reported shorter operating times and 4 out of 5 were statistically significant. The mean difference was -16.73 minutes (95% CI -21.07 to -12.40) for vNOTES (p<0.00001). **Length of hospital stay:** 4 out of 6 studies reported statistically significant shorter stays than the control group.	**Readmissions:** 4 out of 6 studies reported on readmissions in vNOTES and control groups but there was no statistically significant difference. There was no statistically significant difference in the pooled analysis. Where studies had complication information in the vNOTES arms, 3 intraoperative, and 18 postoperative complications were reported. **Intraoperative:** 1 case of bleeding and 2 cases of bladder trauma.

First author, date	Efficacy outcomes	Safety outcomes
	The mean difference was -0.58 days for vNOTES (p<0.00001). **Postoperative pain:** Only 1 paper reported a statistically significant difference, which was lower pain in the vNOTES group. There was no statistically significant difference in the pooled analysis. **Other:** The RCT reported no difference between arms for incidence and severity of dyspareunia, sexual wellbeing and quality of life.	There was no statistically significant difference in intraoperative complications in the pooled analysis. **Postoperative:** 10 transfusions, 5 fevers, 1 reintervention for bleeding, 1 infected hematoma and 1 case of suspected DVT. The odds of postoperative infection (fever or PID) were lower in the vNOTES groups (OR=0.41, 95% CI 0.17 to 0.99) compared with the control groups (p=0.05).
Baekelandt, 2021	**Procedure success:** Zero conversions were needed in either arm (vNOTES or laparoscopy). **Operation time:** The vNOTES procedure was on average 15 minutes quicker (95%CI 11 to 19) (p<0.001). **Length of hospital stay:** There was no statistically significant difference between day-0 discharge. **Postoperative pain:** The mean use of analgesics in the vNOTES arm was 6 units compared with 11 units in the laparoscopy arm. The mean difference is 5 units (95% CI 2 to 8) (p<0.001). **Longer term pain/QoL:** The risk difference of pelvic pain at 3 months was statistically significant with fewer people reporting pain in the vNOTES group (RD=24%, 95% CI 7% to 42%) (p<0.006). The difference in median VAS score for pelvic pain at 3 months was higher in the laparoscopy group	**Intraoperative complications:** 1 case of intraperitoneal spilling in the vNOTES group and none in the laparoscopy group **Postoperative complications:** 4 bleeding complications in the vNOTES group and 1 in the laparoscopy group. • **vNOTES:** 1 person needed revision and suturing and 3 had conservative treatment • **Laparoscopy:** 1 person had conservative treatment There were no cases of postoperative infection, readmission, lasting disability or death within 6 weeks after surgery.

First author, date	Efficacy outcomes	Safety outcomes
	(1.5, 95% CI 0.5 to 2.4) (p<0.002). All other pain and QoL differences were not statistically significant.	
Karkia, 2019	**Procedure success:** 33 people had vNOTES hysterectomy. 32/33 people had a planned and successful adnexectomy. Zero conversions were needed. **Operation time:** Mean operating time was 68.5 minutes (range 43 to 110). **Estimated blood loss:** Mean blood loss was 269ml (range 50 to 1,200). 15% of people had an estimated blood of 500 ml or more. **Length of hospital stay:** On average, people stayed in hospital for 1.4 nights after the procedure (range 1 to 2). **Postoperative pain:** The median VAS pain score at 6 hours after operation and at discharge was 0.	**Postoperative:** There were no major postoperative complications reported. 2 patients needed readmission and had conservative treatment.
Baekelandt, 2020	**Procedure success:** 1,000 procedures were completed, including hysterectomy (73%), adnexal surgery (18%), salpingectomy (4%), ovarian cystectomy (3%), myomectomy (1%) and other indications (1%). 4 out of 1,000 procedures needed conversion (3 to conventional laparoscopy and 1 to laparotomy). **Operation time:** The mean operating time for the hysterectomy group was 46 minutes (range 20 to	**vNOTES hysterectomy complications in 730 procedures (38)** • **Intraoperative (10):** 9 cystotomies and 1 case of bleeding requiring transfusion. • **Postoperative (28):** Complications included cystitis (6), haematoma (5), postoperative nausea and vomiting (2), wound infections (2), genital herpes (1), stress urinary incontinence (1), haematoma

First author, date	Efficacy outcomes	Safety outcomes
	250) and 33 minutes (range 14 to 150) in the vNOTES other group.	drainage (6), wound repair (4), and adhesiolysis (1). **vNOTES other complications in 270 procedures (1)** • **Postoperative (1):** cystitis (1).
Huang, 2022	**Adnexal surgery** Includes unilateral and bilateral forms of salpingectomies, ovarian cystectomies and adnexectomies. • **Procedure success:** 16 conversions were reported for 902 procedures. • **Operation time:** Mean operating times across adnexal surgeries range from 67.88 (plus or minus 25.99) to 115.74 (plus or minus 40.56) minutes. • **Length of hospital stay:** Mean hospital stays ranged from 3.26 (plus or minus 1.77) to 4.30 (plus or minus 2.68) days. • **Estimated blood loss:** Mean blood loss across adnexal surgeries ranged from 23.47 ml (plus or minus 17.34) to 48.87 ml (plus or minus 57.53). • **Postoperative pain:** Mean VAS pain scores ranged from 2.85 (plus or minus 0.41) to 2.97 (plus or minus 0.18) at 12 hours. At 24 hours, the range was 2.26	**Complications:** • **Adnexal surgery:** Complications occurred in 21 out of 902 procedures. • **Myomectomy:** Complications occurred in 4 out of 98 procedures. • **Hysterectomy:** Complications occurred in 2 out of 82 hysterectomy procedures. The nature of the complications for each type of surgery is unclear. Across all 5 vNOTES surgery types, 38 complications were reported in 1,147 procedures (**3.31% complication rate**). Complications were reported using the Clavien-Dindo classification. 27 were grade 1, 4 were grade 2 and 7 were grade 3 (including rectal injury, bladder injury and mesh exposure).

First author, date	Efficacy outcomes	Safety outcomes
	(plus or minus 0.75) to 2.39 (plus or minus 0.65). **Myomectomy** • **Procedure success:** 2 conversions were needed out of the 98 procedures. • **Operation time:** Mean operating time was 103.31 (plus or minus 45.09) minutes. • **Length of hospital stay:** Mean stay was 3.92 (plus or minus 1.95) days • **Estimated blood loss:** Mean blood loss was 81.53 ml (plus or minus 193.43). • **Postoperative pain:** Mean VAS pain scores were 2.91 (plus or minus 0.46) and 2.35 (plus or minus 0.56) at 12 and 24 hours, respectively. **Hysterectomy** • **Procedure success:** 0 conversions out of 82 procedures. • **Operation time:** Mean operating time was 107.40 (plus or minus 39.54) minutes. • **Length of hospital stay:** Mean stay was 4.72 (plus or minus 1.91) days. • **Estimated blood loss:** Mean blood loss was 113.29 ml (plus or minus 182.22).	

First author, date	Efficacy outcomes	Safety outcomes
	• **Postoperative pain:** Mean VAS pain scores were 2.98 (plus or minus 0.44) and 2.46 (plus or minus 0.67) at 12 and 24 hours, respectively.	
Huang, 2021	No significant difference in operation time or estimated blood loss between vNOTES and TU-LESS arms. **Procedure success:** No conversions to laparoscopy or laparotomy were needed. **Length of hospital stay:** Mean hospital stay was significantly shorter in the vNOTES group (3.39 days plus or minus 0.67) compared with the TU-LESS group (3.73 days plus or minus 0.97) (p<0.003). **Postoperative pain:** Mean VAS score at 24 hours after surgery was 0.99 (plus or minus 0.80) in the vNOTES group compared with 2.35 (plus or minus 1.05) in the TU-LESS group (p<0.001). **Other:** Time of flatus after surgery was significantly lower in the vNOTES group (15.8 hours plus or minus 5.27) compared with the TU-LESS group (19.5 plus or minus 4.60) (p<0.001). The mean cosmetic score in the vNOTES group was higher at 21.4 (plus or minus 1.39) compared with 19.1 (plus or minus 1.94) in the TU-LESS group (p<0.001).	**Complications** • **vNOTES:** 2 cases of fever (CD-1) were treated with antipyretic drugs. • **TU-LESS:** 4 cases of fever (CD-1) were treated with antipyretic drugs and 1 case of postoperative anaemia (CD-2) was treated with blood transfusion. No complications of CD-3, -4 or -5 were observed in either procedure group.

First author, date	Efficacy outcomes	Safety outcomes
Yan, 2022	**Procedure success:** 4 out of 232 vNOTES procedures needed conversion to TU-LESS because of multiple uterine myoma. 3 procedures failed because of the large size of myoma (up to 12 cm) and 1 because of adhesion between the uterus and pelvis. **Operation time:** Mean operation time was significantly shorter in the vNOTES group (p<0.001). vNOTES hysterectomy took, on average, 78.21 minutes (plus or minus 30.79) compared with 112.09 (plus or minus 44.05) in the TU-LESS group. **Estimated blood loss:** There was no statistically significant difference in median blood loss between both groups. **Length of hospital stay:** Median hospital stay was shorter in the vNOTES group (2.31 days plus or minus 0.69) compared with the TU-LESS group (3.77 days plus or minus 1.57) (p<0.001). **Postoperative pain:** 4.39% of vNOTES patients required postoperative analgesics compared with 15.50% in the TU-LESS group (p<0.001). **Other:** Duration of anal exhaust was statistically significant between groups. On average, this persisted for 18.80 hours (plus or minus 6.60) in the vNOTES group compared with 36.49 hours (plus or minus 13.71) in the TU-LESS group.	**Complications** • **vNOTES:** No complications were seen in this group. • **TU-LESS:** Exudation occurred in the umbilicus wound in 2 women in this group. No readmissions were needed in either group after 6 weeks.

First author, date	Efficacy outcomes	Safety outcomes
Temtanakitpaisan, 2018	**Procedure success:** 2 out of 275 procedures could not be done successfully and conversions to conventional laparoscopy were needed. **Operation time:** The differences of operation times between groups was statistically significant (p<0.0001). Group 1's mean operating time was 76.70 minutes (SE 0.68), group 2's was 99.99 minutes (SE 1.14) and group 3's was 152.88 minutes (SE 3.37). **Estimated blood loss:** Mean blood loss was statistically significant between groups (p<0.0001). Mean estimated blood loss in group 1 was 180.85 ml (SE 4.61), 342.57 ml (SE 6.98) for group 2 and 532.35 ml (SE 11.85) for group 3. **Length of hospital stay:** Mean hospital stays in each group ranged between 1.34 to 1.47 days but this was not statistically significant.	**Complications** • **Group 1 (n=191):** 4 cases of postoperative bleeding, 2 pelvic infection and 2 bladder injury. • **Group 2 (n=67):** 1 case of pelvic infection. • **Group 3 (n=17):** No complications reported.
Kaya, 2022	**Procedure success:** No conversions were needed in the vNOTES group. ***Operation time:** Mean operating time in the vNOTES arm was 80 minutes (35 to 170) compared with 135 minutes (105 to 220) in the TLH arm – a statistically significant difference (p<0.001). **Estimated blood loss:** 8 people in the TLH group and 7 in the vNOTES group had intraoperative blood loss of more than 300 ml.	**Peri/postoperative blood transfusion:** 6 transfusions needed in the TLH procedures and 7 in the vNOTES procedures. Not statistically significant. **Organ injury:** 1 case of primary bladder injury in the TLH group and no other complications reported in the vNOTES group.

First author, date	Efficacy outcomes	Safety outcomes
	***Length of hospital stay:** Mean stay was 48 hours (48 to 96) in the TLH arm and 48 hours (24 to 96) in the vNOTES arm. ***Postoperative pain:** Mean VAS pain score at 6 hours was 7 in TLH compared with 6 in vNOTES ($p<0.01$). Mean VAS pain score at 24 hours was 3 and 4, respectively ($p<0.01$). *Outcomes from the propensity score matched model (n=62)	

Procedure technique

Of the 9 studies, 5 studies compared a gynaecological vNOTES procedure with its laparoscopic equivalent (Housmans, 2020; Baekelandt, 2021; Huang, 2021; Yan, 2022; Kaya, 2022). Karkia (2019) alone investigated vNOTES hysterectomy with adnexal surgery. The remaining 3 studies investigated vNOTES hysterectomy alone (Temtanakitpaisan, 2018), or outcomes for vNOTES hysterectomies and other vNOTES procedures (Baekelandt, 2020; Huang, 2022).

The following multiple-instrument access ports were used across studies: GelPOINT mini advanced access platform (Baekelandt, 2020; Baekelandt, 2021), GelPOINT Alexis retractor or GelPOINT vPath (Karkia, 2019; Kaya 2022), HK-TH-60.4TY (Huang, 2022; Huang, 2021; Yan, 2022). Housmans (2020) and Temtanakitpaisan (2018) described limited details of the procedure.

In some people with uterine weights greater than 1,000 g the uterus could not be removed, which was associated with BMI and limited vaginal space. Uterus retrieval can also be difficult when the shape of large uteri is disproportionate to the pelvis. The suggested way to overcome this during procedure is to opt for manual morcellation of the uterus (Temtanakitpaisan, 2018).

Efficacy

Procedure success

All 9 studies reported procedure success. There was variability across the studies in the reporting of procedure success, where some studies only had inferred procedural success (by lack of conversion) while others stated procedure success (rates) explicitly as the proportion of women who successfully had treatment with the intended approach without conversion to any other procedure or technique.

The systematic review by Housmans (2020) reported on 288 vNOTES procedures across the 6 studies and up to 1 conversion procedure per study. The case series of 1,000 people reported 4 conversion procedures: 3 to conventional laparoscopy and 1 to laparotomy (Baekelandt, 2020). Huang (2022) reported 16 conversions in 902 adnexal surgery procedures, 2 conversions for the 98 myomectomies and 0 for the hysterectomies. Yan (2022) reported 4 conversions from vNOTES hysterectomy to TU-LESS hysterectomy because of myoma (3) and adhesion (1). The study on various uteri sizes reported 2 conversions to conventional laparoscopy out of 275 procedures (Temtanakitpaisan, 2018).

The Baekelandt (2021) RCT, the Karkia (2019) study, and the study on people with obesity (Kaya, 2022) reported that 0 conversion procedures were needed.

Operation time

All 9 studies reported operation time.

Three studies reported comparisons of operating time between vNOTES and laparoscopy. Of the 6 studies in the systematic review, 4 reported shorter operative times for vNOTES hysterectomy compared with laparoscopic hysterectomy that were statistically significant (Housmans, 2020). The pooled estimate for vNOTES operation time was a mean difference of -16.73 minutes (95% CI -21.07 to -12.40; $p<0.00001$). The RCT by Baekelandt (2021) estimated that vNOTES adnexectomy was, on average, 15 minutes (95% CI 11 to 19; $p<0.001$) quicker than laparoscopy. In the obesity study (Kaya, 2022), the operation time was 80 minutes (35 to 170) in the vNOTES hysterectomy arm, compared with 135 minutes (105 to 220) in the total laparoscopic hysterectomy arm ($p<0.0001$).

Karkia (2019) was the UK study of hysterectomy and adnexectomy, which had a mean operating time of 68.5 minutes (range 43 to 110). In the Baekelandt (2020)

case series, the mean operating time for vNOTES hysterectomy was 33 minutes (range 14 to 150) and 46 minutes (range 20 to 250) for other vNOTES procedures.

The Huang (2022) case series reported operation times for the various vNOTES procedures. Hysterectomy, adnexal and myomectomy were the 3 procedures of interest. The mean operation times for hysterectomies was 107.40 minutes (plus or minus 39.54) and 103.31 (plus or minus 45.09) for myomectomies. The mean operating times for adnexal surgeries ranged from 67.88 (plus or minus 25.99) to 115.74 (plus or minus 40.56) minutes.

Yan (2022) reported significantly shorter operation times in the vNOTES group of 78.21 minutes (plus or minus 30.79) compared with 112.09 minutes (plus or minus 44.05) in the TU-LESS group ($p<0.001$). Whereas Huang (2021) reported no significant difference in operation times.

Temtanakitpaisan (2018) reported statistically significant differences in operating times for vNOTES hysterectomies across the 3 uterine weight groups. The mean operating time (in minutes) for uteri size less than 500 g was 76.70, for 500 g to 999 g was 99.99 and for 1,000 g or more was 152.88.

Length of hospital stay

Eight of the studies reported length of hospital stay.

Three studies compared length of hospital stay between vNOTES and laparoscopy. In the systematic review, 4 out of 6 studies reported statistically significantly shorter stays in the vNOTES group than in the control group (Housmans 2020). The mean difference was -0.58 days for vNOTES hysterectomy compared with laparoscopic hysterectomy ($p<0.00001$). The RCT reported the number of people who were discharged from hospital on day 0 (Baekelandt 2021). In both procedure arms, most of the people were discharged

on day 0. There were 88% of laparoscopic adnexectomy people discharged on day 0 compared with 94% in the vNOTES arm, but there was no statistically significant difference. Kaya (2022) reported no difference between length of hospital stay between vNOTES hysterectomy and TLH.

The mean hospital stay was 1.4 nights (range 1 to 2) in the Karkia (2019) paper. Hospital stays of 1.34 to 1.47 days were reported in the Temtanakitpaisan (2018) paper. There was no statistically significant difference between groups of different uterine weights.

For vNOTES hysterectomy procedures in the Huang (2022) study, the mean length of hospital stay was 4.72 days (plus or minus 1.91). Mean stay for myomectomies was 3.92 days (plus or minus 1.95) and between 3.26 (plus or minus 1.77) and 4.30 (plus or minus 2.68) across the 6 variations of adnexal procedures.

Huang (2021) reported mean hospital stays of 3.39 days (plus or minus 0.67) in the vNOTES ovarian cystectomy group compared with 3.73 days (plus or minus 0.97) in the TU-LESS group ($p<0.003$).

Yan (2022) reported median length of hospital stays for both hysterectomy groups. The median stay in the vNOTES group was significantly shorter at 2.31 days (plus or minus 0.69) compared with 3.77 days (plus or minus 1.57) in the TU-LESS group.

Postoperative pain

Seven studies reported postoperative pain.

Only one of the studies in the systematic review, a retrospective chart analysis, reported a statistically significant difference in postoperative pain (Housmans,

2020). The mean difference in VAS score on day 1 was 1.25 lower in the vNOTES group.

The RCT by Baekelandt (2021) captured postoperative pain by the average use of analgesics in each group. The mean analgesics use in the vNOTES group was 6 units compared with 11 in the laparoscopy group, which is a statistically significant mean difference of 5 units (95% CI 2 to 8; p<0.001). People were asked whether they experienced pelvic or vaginal pain at 3 and 6 months after operation, and were asked to provide VAS pain scores. The only statistically significant difference was at 3 months, when fewer people reported pain in the vNOTES group, representing a risk difference of 24% (95% CI 7% to 42%; p=0.006) compared with the laparoscopy group. The difference in median VAS score for pelvic pain at 3 months was higher in the laparoscopy group (median difference 1.5, 95% CI 0.5 to 2.4; p=0.002).

Statistically significant differences in mean VAS pain scores were captured at 6 and 24 hours after operation in the study on people with obesity (Kaya, 2022). At 6 hours, the mean score in the TLH group was 7 compared with 6 in vNOTES (p<0.01). At 24 hours, the respective mean VAS pain scores were 3 and 4 (p<0.01).

In the UK study for vNOTES hysterectomy and adnexectomy, the median VAS pain score at 6 hours after operation and at discharge was 0 (Karkia, 2019).

The Huang (2022) study captured VAS pain scores at 12 and 24 hours after surgery. In the hysterectomy group, the mean VAS pain scores were 2.98 (plus or minus 0.44) at 12 hours and 2.46 (plus or minus 0.67) at 24 hours. In the adnexal surgeries group, the mean pain score ranged from 2.85 (plus or minus 0.41) to 2.97 (plus or minus 0.18) at 12 hours and then ranged from 2.26 (plus or minus 0.75) to 2.39 (plus or minus 0.65) at 24 hours. In the myomectomy group,

the postoperative mean VAS pain score was 2.91 (plus or minus 0.46) at 12 hours and 2.35 (plus or minus 0.56) at 24 hours.

In the Huang (2021) study, postoperative pain was captured at 24 hours after surgery using the VAS score. The mean score was reported as 0.99 (plus or minus 0.80) in the vNOTES ovarian cystectomy group and 2.35 (plus or minus 1.05) in the TU-LESS group.

In Yan (2022), postoperative pain was indicated by the number of people who needed analgesics after the hysterectomy. A statistically significant difference was seen between groups, where 4.39% of people needed analgesics in the vNOTES group compared with 15.50% in the TU-LESS group.

Quality of life

One study reported quality-of-life measures.

Quality-of-life data was captured at 3 and 6 months after operation in the Baekelandt (2021) RCT using the EQ-5D-3L. There was no statistically significant difference between the two groups at each time interval.

Safety

Readmissions

Three studies reported readmissions.

The Housmans (2020) systematic review included 4 studies that captured readmissions. One readmission occurred across the vNOTES groups (n=288) for suspicion of DVT, which needed CT angiography. There were 10 readmissions noted across the laparoscopy control groups (n=430) because vault hematoma (2), pain (2), cuff infection (1), repair of a vesicovaginal fistula (1), pulmonary

embolism with ICU admission (1) and pelvic inflammatory disease (3). None of the readmission findings were significant in the individual studies.

In the Karkia (2019) paper, 2 out of 33 people had been readmitted and had conservative treatment.

No readmissions were needed in either vNOTES or TU-LESS hysterectomy groups at 6 weeks in the Yan (2022) study.

Intraoperative complications

Four studies reported intraoperative complications.

In the vNOTES arm of the systematic review, there were 3 intraoperative complications from 288 procedures, compared with 7 in the 430 laparoscopic procedures (Housmans, 2020). The vNOTES complications were because of bleeding (1) and bladder trauma (2). Baekelandt (2020) also reported 1 case of intraoperative bleeding that needed transfusion in the 730 vNOTES hysterectomies. Also, 9 cystotomies had to be done during these procedures.

One case of intraperitoneal spilling was reported in the vNOTES group of the Baekelandt (2021) RCT. No intraoperative complications were reported for the laparoscopy group.

Postoperative complications

In the vNOTES arm of the systematic review, there were 18 intraoperative complications from 288 procedures, compared with 105 in the 430 laparoscopic procedures (Housmans, 2020). The vNOTES complications were because of blood transfusions (10), fever (5), reintervention for bleeding (1), suspected DVT (1), and infected hematoma (1).

In addition to the systematic review, 4 other studies reported postoperative bleeding complications. During the Baekelandt (2021) trial, bleeding

complications occurred in 4 out of 34 vNOTES adnexal procedures and in 1 out of 33 laparoscopy procedures. The person who had laparoscopy and 3 of the - people who had vNOTES had conservative treatment, while 1 person who had vNOTES needed revision and suturing. There were 4 people in the less than 500 g uterine weight group (n=191) who experienced bleeding after surgery (Temtanakitpaisan, 2018). Blood transfusion was needed in 7 out of 31 vNOTES hysterectomies in the cohort of people with obesity compared with 6 out of 31 in the laparoscopy control group (Kaya, 2022). No bleeding complications were seen in the vNOTES arm, but 1 person in the TU-LESS ovarian cystectomy needing a blood transfusion (Huang, 2021).

The Baekelandt (2020) case series reported 28 postoperative complications in the vNOTES hysterectomy procedures (n=730) and 1 case of cystitis in the vNOTES other procedures (n=270). The complications in the hysterectomy group included cystitis (6), hematoma drainage (6), hematoma (5), wound repair (4), nausea and vomiting (2), wound infections (2), genital herpes (1), stress urinary incontinence (1) and adhesiolysis (1).

Huang (2022) reported 38 complications collectively for the 5 types of vNOTES procedures (n=1,147) for an overall complication rate of 3.31%. Complications occurred in 2 out of 82 hysterectomies, 21 out of 902 adnexal surgeries and 4 out of 98 myomectomies. The 38 complications (which includes unrelated surgeries) are reported using Clavien-Dindo classifications; 27 were grade 1, 4 were grade 2 and 7 were grade 3 (including rectal injury, bladder injury and mesh exposure).

Fever was seen in 2 people in the vNOTES hysterectomy group and 4 people in the TU-LESS hysterectomy group of the Yan (2022) study. All had treatment with antipyretic drugs.

There were 3 cases of pelvic infection recorded by Temtanakitpaisan (2018). Two were in the less than 500 g uterine weight group (n=191) and 1 was in the 500 g to 999 g group (n=67).

Bladder injury was reported in 2 studies. There were 2 instances of bladder injury during the 191 vNOTES hysterectomies for the less than 500 g uterine weight group (Temtanakitpaisan, 2018). There was 1 case in the laparoscopy control group of the cohort with obesity and no other organ injury complications were reported in the vNOTES group (Kaya, 2022).

Karkia (2019) reported no major postoperative complications in their study. No complications were seen in the vNOTES arm of the Yan (2022) study, while 2 women experienced exudation in the umbilicus wound in the TU-LESS arm.

Anecdotal and theoretical adverse events

Expert advice was sought from consultants who have been nominated or ratified by their professional Society or Royal College. They were asked if they knew of any other adverse events for this procedure that they had heard about (anecdotal), which were not reported in the literature. They were also asked if they thought there were other adverse events that might possibly occur, even if they have never happened (theoretical).

They listed the following anecdotal adverse events:

- Operative risks include infection, bleeding, conversion (to laparoscopy or laparotomy), cystotomy and organ injuries. Rates of injuries to the bladder, ureter and bowel are estimated at 1 to 2 per 100, 1 per 100 and 1 per 100, respectively.
- Hip, pelvic or vaginal pain, and vaginal wound complications or dehiscence.
- Dyspareunia and impaired sexual function (both estimated to be uncommon), or problems with urinary retention.

- Deep venous thrombosis or pulmonary embolus.

They listed the following theoretical adverse events:

- Reduced ability to control unexpected haemorrhage.
- Difficulties from unexpected adhesions.
- Rectal injury from inadvertent placement of laparoscope in women with obliteration of pouch of Douglas.
- Risk of endometrial cancer cells spilled from the cervix.
- Risk of vesicovaginal fistula (very rare).

Thirteen professional expert questionnaires for this procedure were submitted. Find full details of what the professional experts said about the procedure in the specialist advice questionnaires for this procedure.

Validity and generalisability

- Nine studies were included in the key evidence summary, including 1 systematic review, 1 RCT, 2 prospective case series and 5 retrospective cohort studies. Research was done in various countries worldwide (Belgium, UK, China, Taiwan, Turkey and South Korea), but only 1 was from a UK setting.
- The systematic review contained mostly retrospective comparative studies and only 1 single-blinded, non-inferiority RCT. The smallest study had a sample of 48 people. The RCT was assessed with the Cochrane RoB2 tool and deemed to have low risk of bias across the board. The remaining papers' risk was assessed with the ROBINS-I tool and were all deemed to have moderate overall risk of bias. Mean ages in studies were quite representative with all but the Kaya paper under 50.
- The main direction of the efficacy and safety data across the 34 studies was either positive or comparable to conventional laparoscopic hysterectomy.

- The mean age across the key evidence (excluding the systematic review) tended to be around 50 or lower.
- Sample sizes varied considerably – from 29 people to 1,147 across studies. The only prospective UK analysis had only 33 people.
- There was variability across the studies in the outcomes they reported. For example, some studies only had inferred procedural success (by lack of conversion) while others stated procedure success (rates) explicitly.
- The studies were lacking long-term follow up. The only longer-term outcomes that were captured were self-reported pain or quality of life (up to 6 months) (Baekelandt, 2021).
- Mostly consistent, but some variability, in patient inclusion and exclusion criteria.
- Some variability in the procedure technique (where described) and access ports were often devices by 1 company (Applied Medical) or tended to be single-use, constructed-for-purpose ports or made by other companies (Beijing Aerospace Kadi Technology Development Institute).
- Some study authors are prominent (featured often) in the literature for this procedure and were involved in multiple studies that make up this overview.
- Disclosures included Jan Baekelandt (a prominent study author), Supuni Kapurubandara who have provided services for/been associated with Applied Medical.
- Ongoing trials include NCT04886791, NCT05150275, NCT04324034, NCT05031182, KCT0004605.

Related NICE guidance

Interventional procedures

NICE international procedures guidance on laparoscopic techniques for hysterectomy (Recommendation: normal arrangements).

Professional societies

- Royal College of Obstetricians and Gynaecologists (RCOG)
- British Society of Urogynaecology (BSUG)
- British Society for Gynaecological Endoscopy
- Royal College of Anaesthetists.

Company engagement

NICE asked companies who manufacture a device potentially relevant to this procedure for information on it. NICE received 1 completed submission. This was considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

References

1. Housmans, S., Noori, N., Kapurubandara, S., Bosteels, J. J., Cattani, L., Alkatout, I., ... & Baekelandt, J. (2020). Systematic review and meta-analysis on hysterectomy by vaginal natural orifice transluminal endoscopic surgery (vNOTES) compared to laparoscopic hysterectomy for benign indications. *Journal of clinical medicine*, *9*(12), 3959.
2. Baekelandt, J., De Mulder, P. A., Le Roy, I., Mathieu, C., Laenen, A., Enzlin, P., ... & Bosteels, J. J. (2021). Adnexectomy by vaginal Natural Orifice Transluminal Endoscopic Surgery versus laparoscopy: results of a first randomised controlled trial (NOTABLE trial). *BJOG: An International Journal of Obstetrics & Gynaecology*, *128*(11), 1782-1791.
3. Karkia, R., Giacchino, T., Taylor, J., Ghaffar, A., Gupta, A., & Kovoor, E. (2019). Hysterectomy and Adenextomy via transvaginal natural orifice transluminal endoscopic surgery (vNOTES): a UK perspective with a case series of 33 patients. *European journal of obstetrics & gynecology and reproductive biology*, *242*, 29-32.
4. Baekelandt, J., & Kapurubandara, S. (2021). Benign Gynaecological procedures by vaginal Natural Orifice Transluminal Endoscopic Surgery (vNOTES): Complication data from a series of 1000 patients. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, *256*, 221-224.

5. Huang, L., Feng, D., Gu, D. X., Lin, Y. H., Gong, Z. L., Liu, D. D., Zhang, Q., Li, Y., Huang, L. Q., & He, L. (2022). Transvaginal natural orifice transluminal endoscopic surgery in gynecological procedure: Experience of a Women's and Children's Medical Center from China. *The journal of obstetrics and gynaecology research*, *48*(11), 2926–2934.
6. Huang, L., Lin, Y. H., Yang, Y., Gong, Z. L., & He, L. (2021). Comparative analysis of vaginal natural orifice transluminal endoscopic surgery versus transumbilical laparoendoscopic single-site surgery in ovarian cystectomy. *Journal of Obstetrics and Gynaecology Research*, *47*(2), 757-764.
7. Yan, B., Miao, H. X., Wang, Y., Xu, J. M., Lu, X. Q., He, W. H., ... & Lou, W. H. (2022). Hysterectomy by Transvaginal Natural Orifice Transluminal Endoscopic Surgery versus Transumbilical Laparoscopic Single-Site Surgery: A Single-Center Experience from East China. *BioMed Research International*, *2022*.
8. Temtanakitpaisan, T., Wu, K. Y., Huang, C. Y., Jaiswal, A., Yen, C. F., & Lee, C. L. (2018). The outcomes of transvaginal NOTES hysterectomy in various uterine sizes. *Taiwanese Journal of Obstetrics and Gynecology*, *57*(6), 842-845.
9. Kaya, C., Yıldız, Ş., Alay, İ., Aslan, Ö., Aydıner, İ. E., & Yaşar, L. (2022). The comparison of surgical outcomes following laparoscopic hysterectomy and vNOTES hysterectomy in obese patients. *Journal of Investigative surgery*, *35*(4), 862-867.

Methods

NICE identified studies and reviews relevant to vaginal transluminal endoscopic hysterectomy and adnexal surgery for benign gynaecological conditions from the medical literature. The following databases were searched between the date they started to 22 November 2022: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the internet were also searched (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following inclusion criteria were applied to the abstracts identified by the literature search.

- Publication type: clinical studies were included with emphasis on identifying good quality studies. Abstracts were excluded if they did not report clinical outcomes. Reviews, editorials, and laboratory or animal studies, were also excluded and so were conference abstracts, because of the difficulty of appraising study methodology, unless they reported specific adverse events that not available in the published literature.
- Patients with benign gynaecological conditions.
- Intervention or test: vaginal natural orifice transluminal endoscopic surgery (vNOTES).
- Outcome: articles were retrieved if the abstract contained information relevant to the safety, efficacy, or both.

If selection criteria could not be determined from the abstracts the full paper was retrieved.

Potentially relevant studies not included in the main evidence summary are listed in the section on other relevant studies.

Find out more about how NICE selects the evidence for the committee.

Table 4 literature search strategy

Databases	Date searched	Version/files
MEDLINE (Ovid)	22/11/2022	1946 to November 07, 2022
MEDLINE In-Process (Ovid)	22/11/2022	1946 to November 07, 2022
MEDLINE Epubs ahead of print (Ovid)	22/11/2022	1946 to November 07, 2022
EMBASE (Ovid)	22/11/2022	1974 to 2022 November 07
EMBASE Conference (Ovid)	22/11/2022	1974 to 2022 November 07
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	22/11/2022	Issue 11 of 12, November 2022

Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	22/11/2022	Issue 10 of 12, October 2022
International HTA database (INAHTA)	22/11/2022	-

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

MEDLINE search strategy

1 exp hysterectomy/ or exp vaginal hysterectomy/ 82,798
2 ovariectomy/ 39,874
3 salpingectomy/ 5,840
4 salpingooophorectomy/ 17,545
5 (Hysterectom* or ovariect* or salping*).tw. 108,064
6 (Adnex* adj4 disease*).tw. 595
7 adnexectom*.tw. 1,803
8 exp adnexa disease/ 263,667
9 ((uter* or womb* or ovar* or (fallop* adj tube*)) adj4 (remov* or excis* or cut* or prolapse*)).tw. 13,193
10 or/1-9 398,588
11 natural orifice transluminal endoscopic surgery/ 2,985
12 (NOTES or vNOTES or VAHN or TVHN or VAMIS).tw. 67,232
13 ((vagin* or transvagin* or translumin*) adj4 (NOTES or endosc* surg*)).tw. 2,052
14 (Natur* adj4 Orific* adj4 Endoscop* adj4 Surg*).tw. 2,414
15 or/11-14 68,569
16 10 and 15 1,431
17 GelPOINT-V-PATH.tw,dv,dm. 8
18 16 or 17 1,433
19 Nonhuman/ not Human/ 5,072,852
20 18 not 19 1,408
21 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. 5,346,653
22 20 not 21 700
23 20 and 21 708

Other relevant studies

Other potentially relevant studies to the IP overview that were not included in the main evidence summary (tables 2 and 3) are listed in table 5.

Table 5 additional studies identified

Article	Number of patients and follow up	Direction of conclusions	Reason study was not included in main evidence summary
Aharoni, S., Matanes, E., Lauterbach, R., Mor, O., Weiner, Z., & Lowenstein, L. (2021). Transvaginal natural orifice transluminal endoscopic versus conventional vaginal hysterectomy with uterosacral ligament suspension for apical compartment prolapse. European Journal of Obstetrics & Gynecology and Reproductive Biology, 260, 203-207.	Retrospective cohort n=135	Lower mean operative time ($p<0.005$), fewer intraoperative complications ($p<0.05$), less blood loss ($p<0.05$) and longer median hospital stay ($p<0.05$) in the vNOTES uterosacral ligament suspension group compared with the conventional group.	Prolapse not focal to this overview.
Badiglian-Filho, L., Chaves Faloppa, C., Narciso de Oliveira Menezes, A., Mantoan, H., Kumagai, L. Y., & Baiocchi, G. (2021). Vaginally assisted NOTES hysterectomy with adnexectomy (vNOTES) compared with conventional laparoscopy. A retrospective observational cohort study. International	Retrospective cohort n=86	No statistically significant differences in complications, conversions, reoperations or hospital stays between vNOTES hysterectomy (and adnexectomy) and conventional laparoscopy. 0 complications reported in both groups.	Studies with larger samples were included.

Journal of Gynecology & Obstetrics, 153(2), 351-356.			
Baekelandt, J. F., De Mulder, P. A., Le Roy, I., Mathieu, C., Laenen, A., Enzlin, P., ... & Bosteels, J. J. (2018). Transvaginal natural orifice transluminal endoscopic surgery (vNOTES) adnexectomy for benign pathology compared with laparoscopic excision (NOTABLE): a protocol for a randomised controlled trial. BMJ open, 8(1), e018059.	Study protocol		Study which was produced from this trial is included as the Baekelandt (2021) RCT
Baekelandt, J., & Cavens, D. (2016). GelPOINT (Applied Medical) is a suitable port for transvaginal NOTES procedures. Journal of Gynecologic Surgery, 32(5), 257-262.	Retrospective cohort n=110	110 successful vNOTES hysterectomy (n=77) and adnexal (n=33) procedures. Evidence of vNOTES being efficacious and safe with the GelPOINT port.	Device-focused study
Baekelandt, J., De Mulder, P. A., Le Roy, I., Mathieu, C., Laenen, A., Enzlin, P., ... & Bosteels, J. J. (2016). HALON—hysterectomy by transabdominal laparoscopy or natural orifice transluminal endoscopic surgery: a randomised controlled trial (study protocol). BMJ open, 6(8), e011546.	Study protocol		Study which was produced from this trial is included in the Housmans (2020) systematic review

Basol, G., Cora, A. O., Gundogdu, E. C., Mat, E., Yildiz, G., Kuru, B., ... & Kale, A. (2021). Hysterectomy via transvaginal natural orifice transluminal endoscopic surgery versus single-port laparoscopy: Comparison of early outcomes. Journal of Obstetrics and Gynaecology Research, 47(9), 3288-3296.	Retrospective cohort n=60	vNOTES was significantly superior to single-port laparoscopy for length of hospital stay and pain at 1 and 18 hours postop. 0 complications in the vNOTES arm which was statistically significant (p=0.023).	Studies with larger samples were included.
Corcoran, C., Taylor, L., Thomas, L., Mason, A., Bush, S., & Bush, S. (2021). Vaginal Natural Orifice Transluminal Endoscopic Surgery: A Pilot Study in a Residency Training Program. Journal of Gynecologic Surgery, 37(3), 232-235.	Retrospective pilot study n=29	2 out of 29 vNOTES adnexal surgeries alongside hysterectomy were converted to traditional surgery. 1 readmission required for a vaginal cuff hematoma. 0 intraoperative complications occurred.	Studies with larger samples were included.
Kaya, C., Alay, I., Cengiz, H., Yıldız, G. O., Baghaki, H. S., & Yasar, L. (2021). Comparison of hysterectomy cases performed via conventional laparoscopy or vaginally assisted natural orifice transluminal endoscopic surgery: a paired sample cross-sectional study. Journal of Obstetrics and Gynaecology, 41(3), 434-438.	Cross-sectional study n=99	After matching, n=30 in vNOTES hysterectomy and 30 in total laparoscopic hysterectomy. Mean vNOTES operative time is 44 minutes shorter than laparoscopy (p<0.001). Mean vNOTES hospital stay is 15 hours shorter than laparoscopy (p=0.004).	Included in the Housmans (2020) systematic review

Kaya, C., Yıldız, Ş., Alay, İ., Karakaş, S., Durmuş, U., Güraslan, H., & Ekin, M. (2022). Comparison of surgical outcomes of total laparoscopic hysterectomy and vNOTES hysterectomy for undescended-enlarged uteri. Journal of Investigative surgery, 35(4), 918-923.	Cross-sectional study n=78	115-minute shorter operative time (p<0.001) and 24-hour shorter hospitalisation (p<0.001) and lower median 24-hour VAS pain score (p=0.003) with vNOTES hysterectomy than total laparoscopic hysterectomy.	Studies with larger samples focussing on uterine size were included.
Kim, M. S., Noh, J. J., & Kim, T. J. (2021). Hysterectomy and adnexal procedures by vaginal natural orifice transluminal endoscopic surgery (VNH): initial findings from a Korean surgeon. Frontiers in Medicine, 7, 583147.	Prospective cohort n=34	Complications occurred in 3 out of 34 people. 2 cases of bladder injury and 1 person needed transumbilical single-port surgery because of late-onset postoperative bleeding on the thirteenth postoperative day. Statistically significant correlation between longer port-installation time and greater pain (4+ VAS pain score) (p=0.013).	Surgeon experience/learning curve focus.
Koythong, T., Thigpen, B., Sunkara, S., Erfani, H., Delgado, S., & Guan, X. (2021). Surgical outcomes of hysterectomy via robot-assisted versus traditional transvaginal natural orifice transluminal endoscopic surgery. Journal of minimally invasive gynecology, 28(12), 2028-2035.	Retrospective cohort n=114	Robotically assisted vNOTES seems like a safe and feasible option. None of the R-vNOTES procedures needed conversion (but not a statistically significant difference). No difference between traditional or robotic vNOTES for operative time, blood loss, length of hospital stay	Robotic assistance not focal to this overview.

		or pain at 1, 2 and 3 weeks postop.	
Li, C. B., & Hua, K. Q. (2020). Transvaginal natural orifice transluminal endoscopic surgery (vNOTES) in gynecologic surgeries: a systematic review. Asian journal of surgery, 43(1), 44-51.	Literature review	vNOTES is a promising procedure across many indications. Many small studies with disparate cohorts and procedures. Many studies reported no, or low, complications.	Review of literature. Many studies with small samples and no (pooled) analysis.
Liu, J., Tan, L., Thigpen, B., Koythong, T., Zhou, X., Liu, Q., ... & Guan, X. (2022). Evaluation of the learning curve and safety outcomes in robotic assisted vaginal natural orifice transluminal endoscopic hysterectomy: a case series of 84 patients. The International Journal of Medical Robotics and Computer Assisted Surgery, 18(3), e2385.	Retrospective cohort n=84	2 out of 84 R-vNOTES hysterectomy procedures needed conversion to robotic assisted laparoscopy. 15.48% (13/84) complication rate including 2 CD-I, 9 CD-II and 2 CD-III grade complications. Mean hospital stay is 0 days. Mean postoperative pain VAS score was reduced by 2.36 (p=0.001) at 2 weeks and by 4.36 (p=0.001) at 3 weeks, when compared with preoperative pain.	Learning curve and robotic-assistance focus.
Merlier, M., Collinet, P., Pierache, A., Vandendriessche, D., Delporte, V., Rubod, C., ... & Giraudet, G. (2022). Is V-NOTES hysterectomy as safe and feasible as outpatient surgery compared with vaginal hysterectomy?. Journal of Minimally	Retrospective cohort n=100	No statistical difference in intra- or postoperative complications, length of hospital stay and conversions between groups. 0 readmissions in the vNOTES group and 2 in the vaginal group but not a statistically significant difference.	Studies with larger samples were included.

Invasive Gynecology, 29(5), 665-672.			
Noh, J. J., Kim, M. S., Kang, J. H., Jung, J. H., Chang, C. S., Jeon, J., & Kim, T. J. (2022). Comparison of surgical outcomes of hysterectomy by vaginal natural orifice transluminal endoscopic surgery (vNOTES) versus single-port access (SPA) surgery. Journal of Personalized Medicine, 12(6), 875.	Prospective cohort n=73	VAS pain score was significantly lower in the vNOTES group than the laparoscopy group. Average port installation was 13 minutes longer in the vNOTES group ($p<0.001$) but time for vaginal closure and total operative time were shorter ($p<0.001$). 1 complication reported which was injury to the distal ureter in the vNOTES group. No conversion procedures needed.	Studies with larger samples were included.
Nulens, K., Bosteels, J., De Rop, C., & Baekelandt, J. (2021). vNOTES hysterectomy for large uteri: a retrospective cohort study of 114 patients. Journal of Minimally Invasive Gynecology, 28(7), 1351-1356.	Retrospective cohort n=114	4 complications in 114 procedures; 3 postoperative bleeding complications and 1 minor late complication. 1 conversion to laparotomy needed. Operative time positively associated with uterine size.	Studies with larger samples were included.
Ozceltik, G., Hortu, I., Itil, I. M., & Yeniel, A. O. (2022). Vaginal approach versus laparoscopy for hysterectomy in transgender men. Journal of Gynecology Obstetrics and Human Reproduction, 51(2), 102286.	Retrospective cohort n=90	No intraoperative complications or conversions in the vNOTES hysterectomy group. 1 reoperation in the vNOTES group because of late-onset intraabdominal bleeding.	Studies with larger samples were included.

		Median operative time was 25 minutes shorter and mean hospital stay was shorter in the vNOTES arm (p<0.001). Lower VAS pain scores at 12 and 24 hours postop (p<0.001), but no difference at 2, 6 or 48 hours. 1 complication in the laparoscopy group.	
Puisungnoen, N., Yantapant, A., & Yanaranop, M. (2020). Natural orifice transluminal endoscopic surgery-assisted vaginal hysterectomy versus total laparoscopic hysterectomy: a single-center retrospective study using propensity score analysis. Gynecology and Minimally Invasive Therapy, 9(4), 227.	Retrospective cohort n=100	No difference between vNOTES hysterectomy and total laparoscopic hysterectomy for operative time, complications or requirement of blood transfusion. Statistically significant difference for less pain and shorter length of stay for vNOTES.	More pertinent studies were included.
Wang, C. J., Go, J., Huang, H. Y., Wu, K. Y., Huang, Y. T., Liu, Y. C., & Weng, C. H. (2019). Learning curve analysis of transvaginal natural orifice transluminal endoscopic hysterectomy. BMC surgery, 19, 1-7.	Retrospective cohort n=240	239 out of 240 procedures completed successfully. 1 procedure was converted to laparoscopy. Blood transfusion in 5.4% of procedures. Complications in 5 procedures. Transfusion, complications and uteri size had statistically significant impacts on operation time.	Learning curve focus

Wang, C. J., Huang, H. Y., Huang, C. Y., & Su, H. (2015). Hysterectomy via transvaginal natural orifice transluminal endoscopic surgery for nonprolapsed uteri. Surgical endoscopy, 29, 100-107.	Retrospective cohort n=512	vNOTES hysterectomy leads to less blood loss ($p<0.001$) and fewer blood transfusions ($p=0.004$) compared with laparoscopically assisted vaginal hysterectomy. Efficiency: vNOTES hysterectomy is on average a 21-minute quicker procedure ($p<0.001$) and leads to shorter in-hospital stays ($p<0.001$).	Included in the Housmans (2020) systematic review
Wang, X., Li, J., Hua, K., & Chen, Y. (2020). Transvaginal natural orifice transluminal endoscopic surgery (vNOTES) hysterectomy for uterus weighing≥ 1 kg. BMC surgery, 20, 1-7.	Retrospective cohort n=39	Blood transfusion in 5.1% of procedures. 3 out of 39 (7.7%) procedures needed a conversion to laparoscopy because of being unable to posterior colpotomy. Statistically significant improvements in operation time, blood loss and hospital stay following first 20 procedures (learning curve).	Studies with larger samples were included.
Weerakiet, S., Uckara, W., Soimongkol, K., Daungroedeeswas, R., Pongphonkit, J., Chanasabaeng, S., & Sutjaritphong, P. (2021). Comparison of surgical outcomes between natural orifice transluminal endoscopic surgery for hysterectomy and conventional total laparoscopic hysterectomy.	Retrospective cohort n=65	Lower operative time ($p<0.0001$) and lower median VAS pain scores at 6, 24 and 48 hours ($p<0.001$) in the vNOTES hysterectomy group compared with total laparoscopic hysterectomy. Statistically significant lower need for added analgesics in the	Studies with larger samples were included.

JOURNAL OF THE MEDICAL ASSOCIATION OF THAILAND, 104(8), 1255-62.		vNOTES group (p=0.001).	
Yang, C. Y., Shen, T. C., Lin, C. L., Chang, Y. Y., Huang, C. C., & Lin, W. C. (2020). Surgical outcomes of hysterectomy by transvaginal natural orifice transluminal endoscopic surgery (vNOTES) compared with laparoscopic total hysterectomy (LTH) in women with non-prolapsed and benign uterine diseases. Taiwanese Journal of Obstetrics and Gynecology, 59(4), 565-569.	Retrospective chart analysis n=183	No difference between vNOTES hysterectomy and total laparoscopic hysterectomy for operative time, blood loss, uterine weight, decrease in haemoglobin level on postoperative day 1, complications, hospital stay and readmission rate. Statistically significantly less pain in vNOTES group for postoperative pain.	Included in the Housmans (2020) systematic review
Yang, E., Nie, D., & Li, Z. (2019). Comparison of major clinical outcomes between transvaginal notes and traditional laparoscopic surgery: a systematic review and meta-analysis. Journal of Surgical Research, 244, 278-290.	Systematic review and meta-analysis n=1,340	No difference between vNOTES and laparoscopy for risk of complications. Positive findings regarding pain and recovery for people having vNOTES.	Most studies did, or patients had, cholecystectomy – 2 out of 13 studies pertinent.