

Targeted Update

Robot-assisted surgery in women undergoing hysterectomy

This is a **Targeted Update** of the Cochrane Review Liu H, Lawrie TA, Lu D, Song H, Wang L, Shi G. Robot-assisted surgery in gynaecology. Cochrane Database of Systematic Reviews 2014, Issue 12. Art. No.: CD011422. DOI: 10.1002/14651858.CD011422.

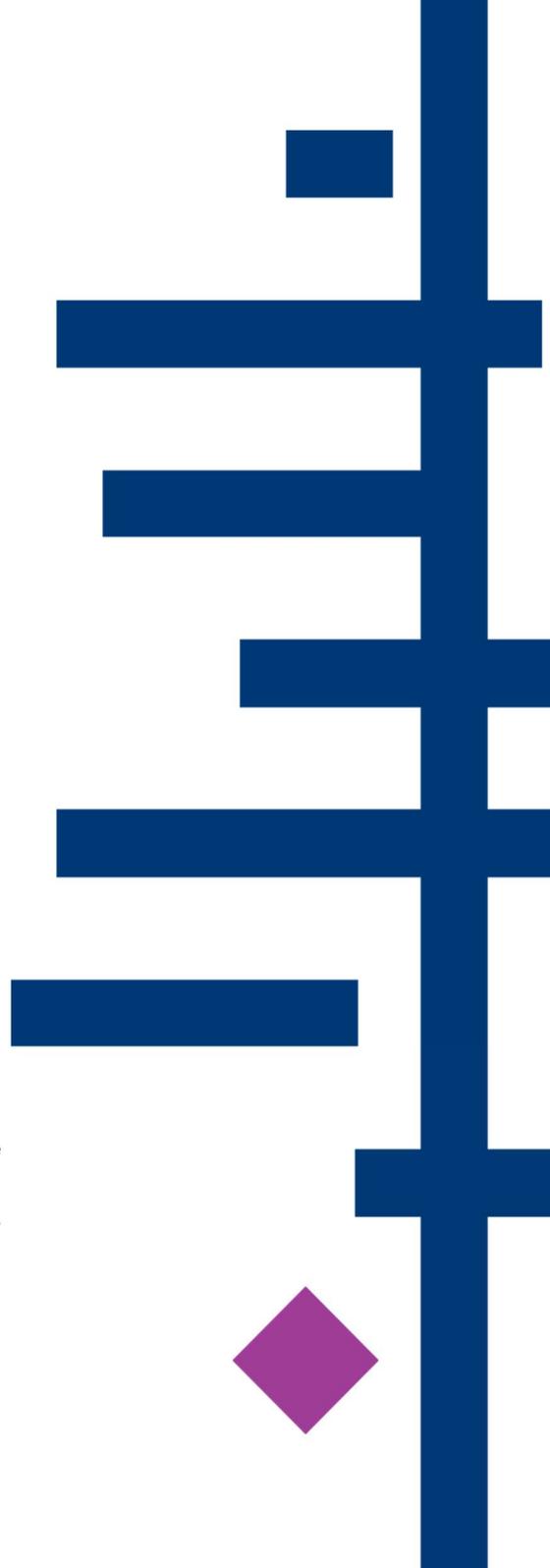
Latest search was performed: **8 January 2018**

Results of the search, details of updates to methods, study characteristics, risk of bias assessments, list of ongoing and excluded studies, and details of data analyses can be found in the **Supplementary material**.

This **Targeted Update** was prepared by Hanna Bergman¹. Data were taken from the published full review and results of the updating process, carried out by Hanna Bergman, and Nicola Maayan¹. The abstract was adapted from the published full review.

¹Cochrane Response, Cochrane, London, UK

Trusted evidence.
Informed decisions.
Better health.



What's a Targeted Update?

Targeted Updates are focussed documents that use the Cochrane Review as their foundation, but focus on updating only one or two important comparisons, and the most relevant outcomes. They include an updated Summary of Findings table, analyses, and abstract, and use Cochrane methodology. The full search results, risk of bias assessments, and references do not form part of the Targeted Update, but are available as supplementary information. Targeted Updates are intended for use by policy makers.

What's the context for this Targeted Update?

The Swiss Medical Board commissioned this Targeted Update to help develop a HTA report.

What's new

The comparison 'Robot-assisted surgery (RAS) versus conventional laparoscopic surgery (CLS) for hysterectomy' was in the focus of this Targeted update. Two new included studies with 245 participants and one new ongoing study were identified.

There may be little or no difference in intra- and post-operative complications, RAS may increase the risk of needing blood transfusion and may lead to higher total cost compared with CLS, however RAS may lead to slightly shorter hospital stay. We cannot say what effect RAS has on operating time, quality of life, and pain because the evidence was of very low certainty. There was no evidence on mortality and disease-free survival in cancer patients.

The Cochrane review that this Targeted Update is based on has a wider scope, includes two additional studies, and concluded that there is uncertainty as to whether RAS or CLS, when used for hysterectomy and sacrocolpopexy, has lower intraoperative and postoperative complication rates due to imprecision of the effect and inconsistency.

Key messages: Robot-assisted surgery for hysterectomy compared with conventional laparoscopic surgery

- may lead to little or no difference in intra- and post-operative complications (low certainty);
- may lead to slightly shorter overall duration of hospital stay (low certainty);
- may lead to a higher risk of needing a blood transfusion (low certainty);
- may lead to higher total cost (low certainty);
- we cannot say what effect RAS has on operating time, quality of life, and pain because the evidence was of very low certainty; and
- there was no evidence on mortality and disease-free survival in cancer patients

Background

Robot-assisted surgery (RAS) is a relatively new innovation in laparoscopic surgery that enables the surgeon to conduct the operation from a computer console, situated away from the surgical table. Hysterectomy, which is the most commonly performed major gynaecological operation, can be performed effectively via a laparoscopic approach.

Objectives

To assess the effectiveness and safety of RAS for hysterectomy in the treatment of women with benign and malignant gynaecological disease.

Search methods

The Cochrane Gynaecological Cancer Review Group Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, and EMBASE databases were searched on 8 January 2018.

www.ClinicalTrials.gov was searched on 16 January 2018.

Selection criteria

Randomised controlled trials of RAS compared with conventional laparoscopic surgery (CLS) in women undergoing hysterectomy.

Data collection and analysis

Relative risks (RRs) were calculated for binary outcome data. Mean differences (MDs) were calculated for continuous variable outcome data. A random effects model was applied. Medians and ranges or inter-quartile ranges (IQR) were tabulated for skewed data. Studies were grouped by condition: benign or cancer. Sensitivity analyses were carried out excluding one early study (Sarlos 2010) of RAS (see Appendix 2, supplementary materials).

Main Results

We included 6 RCTs; two of these were new to this Targeted Update. The studies were published 2010 to 2017 and included a total of 632 participants. Three ongoing RCTs were identified (see supplementary materials).

RAS was compared with CLS for hysterectomy in all six studies. Women in one study were diagnosed with endometrial cancer and underwent hysterectomy, bilateral salpingo-oophorectomy, and pelvic lymphadenectomy (Maenpaa 2016). The remaining studies included participants with benign conditions (pelvic pain, endometriosis, abnormal uterine bleeding, fibroids, previous failure of ablation treatment). Studies were carried

out in academic teaching hospitals in Finland, Sweden, Switzerland and the USA.

For most of the included studies the risk of bias was unclear, as allocation concealment and blinding of outcome assessment were not adequately described in the report. Further, blinding is difficult to achieve in this type of study, which could lead to risk of performance and detection bias. All studies were at unclear risk of other bias mainly due to unclear author conflict of interest.

There was low certainty evidence that RAS may result in little or no difference in the number of intra- and post-operative complications combined, both for benign conditions surgery (RR 0.76, 95% CI 0.38 to 1.53, 5 studies, n=486, I²=54%) and for endometrial cancer surgery (RR 1.47, 95% CI 0.79 to 1.72, 1 study, n=99, I²=0%). The early study of benign condition surgery had effect estimates favouring CLS (RR 1.53, 95% CI 0.83 to 2.82, n=95) whereas the 4 later studies of benign condition surgery had a pooled effect estimate favouring RAS (RR 0.52, 95% CI 0.27 to 0.97, n=391, I²=0% (see sensitivity analyses in Supplementary materials). There was moderate certainty evidence that RAS probably results in little or no difference in the number of intra-

operative complications in benign conditions surgery compared with CLS (RR 1.66, 95% CI 0.76 to 3.61, 4 studies, 388 participants, $I^2=0\%$). For endometrial cancer surgery there was low certainty evidence that RAS may result in little or no difference in the number of intra-operative complications compared with CLS (RR 0.11, 95% CI 0.01 to 1.97, $n=99$). There was low certainty evidence that RAS may result in fewer post-operative complications in benign condition surgery compared with CLS (RR 0.61, 95% CI 0.34 to 1.09, 4 studies, 434 participants, $I^2=0\%$); for endometrial cancer surgery there was low certainty evidence that RAS may result in more post-operative complications compared with CLS (RR 1.76, 95% CI 0.91 to 3.43, $n=99$).

It is uncertain whether RAS reduces total operating time because the certainty of the evidence was assessed as very low (MD 41.18 minutes, 95% CI -6.17 to 88.53, 2 benign conditions studies, 148 participants, $I^2=80\%$; MD was not estimable for another 4 studies (438 participants) because medians and not means were reported due to skewed data, see *Forest plots and tabulated results* for medians and ranges).

There was low certainty evidence that RAS may lead to slightly shorter overall duration of hospital stay compared with CLS (MD -0.30 days, 95% CI -0.53 to -0.07 days, 2 benign conditions studies, 192 participants, $I^2=0\%$, but this slight difference was not considered clinically meaningful (95% CI 7/100th of a day to half a day); MD was not estimable for another 2 studies (243 participants) because medians and not means were reported

due to skewed data, see *Forest plots and tabulated results* for medians and ranges).

Based on the available evidence, graded as very low certainty, we cannot say what effect RAS has compared with CLS on mortality. One endometrial cancer study (Maenpaa 2016, $n=99$) reported that there were no deaths in either group (6 months follow-up). None of the other studies reported on mortality.

There was low certainty evidence that the risk of needing a blood transfusion during surgery may be higher with RAS compared with CLS both for benign conditions surgery (RR 1.94, 95% CI 0.30 to 12.76, 3 studies, $n=247$, $I^2=0\%$) and for endometrial cancer surgery (RR 2.94, 95% CI 0.62 to 13.87, 1 study, $n=99$).

Based on the available evidence, graded as very low certainty, we cannot say what effect RAS has compared with CLS on post-operative pain (MD -2.00 points, 95% CI -16.08 to 12.08 (scale range not reported), 1 benign conditions study, 36 participants; MD was not estimable for another 3 studies (269 participants) due to skewed data, see *Forest plots and tabulated results* for medians and ranges).

Based on the available evidence, graded as very low certainty, we cannot say what effect CLS has compared with RAS on quality of life (MD for SF-36 mean endpoint score at 6 months: -5.00 points, 95% CI -13.01 to 3.01, 1 benign conditions study, 38 participants; MD for EQ-5D mean change from baseline score at 6 weeks: -8.00 points, 95% CI -12.88 to -3.12, 1 benign conditions study, 95

participants; different scales and types of measures were not pooled, both quality of life scales ranged from 0-100 where a high score indicated a better outcome). Note that the direction of this comparison was inversed to be consistent with the other outcomes, as a higher quality of life score is a positive outcome.

There was low certainty evidence that the total cost of RAS may be higher than the total cost of CLS per patient undergoing hysterectomy (MD 1560 US dollars, 95% CI 1080 to 2050, 1 study, 97 participants).

No study reported on disease-free survival for women with cancer, the only study that included women with cancer (Maenpaa 2016) did not report on this outcome. This study reported on participant follow-up for 6 months.

Implications and conclusions

There was low certainty evidence that RAS may result in little or no difference in the number of intra- and post-operative complications compared to CLS, both for benign conditions and cancer surgery. The certainty of the evidence was generally low, mainly due to imprecision and inconsistency in the results, but also due to potential conflicts of interest among study authors. Further, it should be noted that technical training advances in both RAS and CLS systems will make any systematic review in this area subject to question of onward applicability. Therefore, further research is likely to have an important impact on the estimates, especially for endometrial cancer where only one study was identified.

Included studies (see Supplementary materials for more details)

	Setting	Participants	Risk of bias							
			Sequence	Allocation	Performance	Detection	Attrition	Reporting	Funding	Other
Deimling TA, Eldridge JL, Riley KA, Kunselman AR, Harkins GJ. Randomized controlled trial comparing operative times between standard and robot-assisted laparoscopic hysterectomy. <i>Int J Gynaecol Obstet</i> 2017;136(1):64-9.	USA, Pennsylvania	Benign conditions n=144	+	+	-	?	+	+	?	+
Green JL, Deimling T, Tam T, Davies MF, Harkins GJ. A randomized controlled trial comparing conventional laparoscopic hysterectomy with robot-assisted laparoscopic hysterectomy in a teaching institution. In: <i>Journal of Minimally Invasive Gynecology Conference: 42nd Global Congress of Minimally Invasive Gynecology, AAGL 2013 Washington, DC United States. 2013:S4.</i>	USA, Ohio	Benign conditions n=113	+	?	-	?	-	-	?	-
Lonnerfors C, Reynisson P, Persson J. A randomized trial comparing vaginal- and laparoscopic hysterectomy to robot-assisted hysterectomy. 2015 Jan; 22(1):78–86.	Sweden	Benign conditions n=122	+	?	-	?	+	?	?	?
Mäenpää MM, Nieminen K, Tomás EI, Laurila M, Luukkaala TH, Mäenpää JU. Robotic-assisted vs traditional laparoscopic surgery for endometrial cancer: a randomized controlled trial. <i>Am J Obstet Gynecol</i> 2016;215(5):588.e1-588.e7.	Finland	Endometrial cancer n=101	+	?	?	?	-	+	?	+
Paraiso MF, Ridgeway B, Park AJ, Jelovsek JE, Barber MD, Falcone T, et al. A randomized trial comparing conventional and robotically assisted total laparoscopic hysterectomy. <i>American Journal of Obstetrics and Gynecology</i> 2013;208(5):368.e361-368.e367.	USA, Ohio & Boston	Benign conditions n=62	+	?	+	+	?	+	?	+
Sarlos D, Kots L, Stevanovic N, von Felten S, Schar G. Robotic compared with conventional laparoscopic hysterectomy: a randomized controlled trial. <i>Obstetrics and Gynecology</i> 2012;3:604-11.	Switzerland	Benign conditions n=100	+	?	-	?	?	?	?	?

Summary of Findings: Robot-assisted surgery compared with conventional laparoscopic surgery for hysterectomy

Patients and setting: Women (18 to 80 years) with benign or malignant conditions scheduled to undergo hysterectomy at specialist settings (academic teaching hospitals) in Finland, Sweden, Switzerland, and the USA.

Comparison: Robot-assisted surgery (RAS) versus conventional laparoscopic surgery (CLS).

Outcome	Condition	Plain language summary	Anticipated absolute effects* (95% CI)		Relative effect (95% CI) N° participants & studies	Certainty of the evidence (GRADE)
			Risk with CLS	Risk with RAS		
Intra- and post-operative complications combined	Benign conditions	RAS may result in little or no difference to the proportion of women with benign conditions undergoing hysterectomy who experience intra-and post-operative complications compared with CLS.	146 per 1000	111 per 1000	RR 0.762 (0.38 to 1.53) Based on data from 486 participants in 5 studies	⊕⊕⊕⊕ LOW ^{1,2}
			Difference 35 fewer per 1000 (from 91 fewer to 77 more)			
	Endometrial cancer	RAS may result in little or no difference to the proportion of women with endometrial cancer undergoing hysterectomy who experience intra-and post-operative complications compared with CLS.	245 per 1000	360 per 1000	RR 1.47 (0.79 to 2.72) Based on data from 99 participants in 1 study	⊕⊕⊕⊕ LOW ³
			Difference 115 more per 1000 (from 51 fewer to 421 more)			
Intraoperative complications	Benign conditions	RAS probably results in little or no difference to the proportion of women with benign conditions undergoing hysterectomy who experience intra-operative complications compared with CLS.	44 per 1000	73 per 1000	RR 1.66 (0.76 to 3.61) Based on data from 388 participants in 4 studies	⊕⊕⊕⊕ MODERATE ^{2,4}
			Difference 29 more per 1000 (from 11 fewer to 115 more)			
	Endometrial cancer	RAS may result in little or no difference to the proportion of women with endometrial cancer undergoing hysterectomy who experience intra-operative complications compared with CLS.	82 per 1000	9 per 1000	RR 0.11 (0.01 to 1.97) Based on data from 99 participants in 1 study	⊕⊕⊕⊕ LOW ³
			Difference 73 fewer per 1000 (from 81 fewer to 79 more)			
Postoperative complications	Benign conditions	RAS may result in fewer women with benign conditions undergoing hysterectomy who experience post-operative complications compared with CLS.	124 per 1000	76 per 1000	RR 0.61 (0.34 to 1.09) Based on data from 434 participants in 4 studies	⊕⊕⊕⊕ LOW ^{5,6}
			Difference 48 fewer per 1000 (from 82 fewer to 11 more)			
	Endometrial cancer	RAS may result in more women with endometrial cancer undergoing hysterectomy who experience post-	204 per 1000	359 per 1000	RR 1.76 (0.91 to 3.43) Based on data from 99	⊕⊕⊕⊕ LOW ³
			Difference 155 more per 1000 (from 18 fewer to 496 more)			

		operative complications compared with CLS.			participants in 1 study	
Total operating time [minutes]	Benign conditions	Due to risk of bias, inconsistency and imprecision, we cannot make any conclusions about total operating time for RAS compared with CLS.	Mean total operating time ranged across control groups from 75 to 103 minutes	Mean total operating time in the intervention groups ranged from 96 to 173 minutes	MD 41.18 (-6.17 to 88.53) Based on data from 148 participants in 2 studies	⊕○○○ VERY LOW ^{7,8}
		Due to skewed data, results from four studies (438 participants) could not be meta-analysed with the other studies. Their results (medians and ranges) are tabulated below.	Difference 41.18 minutes longer (from 6.17 minutes shorter to 88.53 minutes longer)			
Overall duration of hospital stay [days]	Benign conditions	RAS may result in slightly shorter overall duration of hospital stay compared with CLS after hysterectomy, but this difference was not considered to be clinically important	Mean hospital stay ranged across control groups from 1.4 to 3.6 days	Mean hospital stay in the intervention groups ranged from 1.1 to 3.3 days (0.3 days lower)	MD -0.30 (-0.53 to -0.07) Based on data from 192 participants in 2 studies	⊕⊕○○ LOW ⁹
		Due to skewed data, results from two studies (243 participants) could not be meta-analysed with the other studies. Their results (medians and ranges) are tabulated below.	Difference 0.3 days shorter (from 0.07 to 0.53 days shorter)			
Mortality	Endometrial cancer	We cannot make any conclusion based on the available evidence on mortality. One study (Maenpaa 2016, n=99) reported that there were no deaths in either group (6 months follow-up). None of the other studies reported on mortality.				⊕○○○ VERY LOW ^{10,11}
Blood transfusion	Benign conditions	The risk of needing a blood transfusion during surgery may be higher with RAS compared with CLS in women with benign conditions undergoing hysterectomy.	10 per 1000	20 per 1000	RR 1.94 (0.30 to 12.76) Based on data from 237 participants in 3 studies	⊕⊕○○ LOW ¹²
	Endometrial cancer		41 per 1000	120 per 1000		
Postoperative pain scale range not reported, low=good	Benign conditions	We cannot make any conclusion based on the available evidence on post-operative pain because the evidence was assessed as very low certainty.	Mean post-operative pain score in the control group was 17 points	Mean post-operative pain score in the intervention group was 19 points	MD -2.00 (-16.08 to 12.08) Based on data from 36	⊕○○○ VERY LOW ^{13,14}

follow-up: up to 2 weeks		Due to skewed data, results from three studies (269 participants) could not be meta-analysed with the other studies. Their results (medians and ranges) are tabulated below.	Difference 2 points less (from 16 points less to 12 points more)		participants in 1 study	
Quality of life, various scales, 0-100, high=good** follow-up: 6 weeks to 6 months	Benign conditions	We cannot make any conclusion based on the available evidence on Quality of life because the evidence was assessed as very low certainty. One study (Paraiso 2013) reported mean endpoint score for the SF-36 scale: MD -5.00 (-13.01 to 3.01, n=38) at 6 months. Another study (Sarlos 2010) reported mean change from baseline score for the EQ-5D scale: MD -8.00 (-12.88 to -3.12, n=95) at 6 weeks.			MD Not estimable Based on data from 133 participants in 2 studies	⊕⊕⊕⊕ VERY LOW ^{15,16}
Total cost [US dollars]	Benign conditions	The total cost of RAS may be higher than the total cost of CLS per patient undergoing hysterectomy.	Mean total cost per patient in the control group was 7059 US dollars	Mean total cost per patient in the intervention group was 8623 US dollars	MD 1560 (1080 to 2050) Based on data from 97 participants in 1 study	⊕⊕⊕⊕ LOW ^{17,18}
			Difference 1560 US dollars more (from 1080 to 2050 US dollars more)			
For cancer surgery: Disease-free survival	-	The only study that included cancer patients (Maenpaa 2016) did not report on disease free survival. This study reported on participant follow-up for 6 months.				-

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

**NB: the direction of the comparison for this outcome was inversed to enable graphical presentation consistent with the other outcomes

CI= confidence interval; CLS=conventional laparoscopic surgery; IQR= inter-quartile range; MD= mean difference; RAS= robot-assisted surgery; RR= risk ratio

¹ Downgraded one level for inconsistency: serious heterogeneity ($I^2=54\%$), the early study (RR 1.53, 95% CI 0.83 to 2.82, n=95) had an effect estimate favouring CLS whereas the 4 later studies had a pooled effect estimate favouring RAS (RR 0.52, 95% CI 0.27 to 0.97, n=391, $I^2=0\%$; see sensitivity analyses in Appendix 2, supplementary materials).

² Downgraded one level for imprecision: confidence intervals were wide including both appreciable benefit and appreciable harm for RAS, as well as no effect.

³ Downgraded two levels for imprecision: only one included study with a small sample size; confidence intervals were wide including both appreciable harm/benefit for RAS and no effect.

⁴ Although one early study (Sarlos 2010) contributed 12/14 adverse events in the RAS arm, sensitivity analysis does not suggest that effect estimate is likely to change significantly (see Appendix 2, supplementary materials). and we did not downgrade for inconsistency.

⁵ Downgraded one level for imprecision: confidence intervals were wide including both appreciable benefit for RAS, as well as no effect.

⁶ Downgraded one level for risk of bias: the early study had an effect estimate favouring CLS (RR 1.23, 95% CI 0.40 to 3.74, n=95), although CIs were wide, whereas the 3 later studies had a pooled, statistically significant effect estimate favouring RAS (RR 0.47, 95% CI 0.24 to 0.93, n=339, $I^2=0\%$).

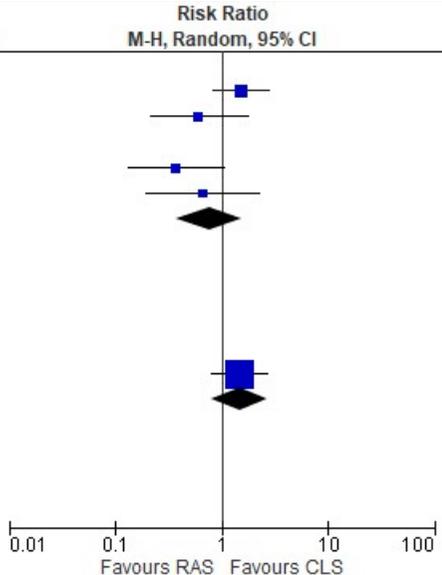
⁷ Downgraded one level for imprecision: confidence intervals were wide including both appreciable benefit for RAS and no effect.

- ⁸ Downgraded two levels for inconsistency: considerable heterogeneity ($I^2=80\%$), no plausible explanation was found for this inconsistency. In addition, four studies could not be included in the meta-analysis due to skewed data.
- ⁹ Downgraded two levels for risk of bias: From one of the two studies only data from a subgroup of the randomised control group was used: within the control group the surgeon decided who would receive CLS and who would receive vaginal hysterectomy, we included data from the CLS participants only. None of the studies were blinded which might have had an effect on this outcome, especially due to unclear funding bias. In addition, two studies could not be included in the meta-analysis due to skewed data.
- ¹⁰ Downgraded one level for risk of bias: Reporting bias, only one study reported on mortality.
- ¹¹ Downgraded two levels for imprecision: the studies included in this review did not have enough power to estimate a difference in mortality.
- ¹² Downgraded two levels for imprecision: sparse data leading to very wide CIs including both appreciable benefit and appreciable harm for RAS, as well as no effect.
- ¹³ Downgraded two levels for imprecision: small sample size, only 36 participants from one study were included. In addition, three studies could not be included in the meta-analysis due to skewed data.
- ¹⁴ Downgraded one level for risk of bias: there is limited information on the pain scale that was used, we do not know whether it is a validated scale or what the range was.
- ¹⁵ Downgraded one level for imprecision: small sample size, only 133 participants were included.
- ¹⁶ Downgraded two levels for risk of bias: one of the two studies was not blinded which might have had an effect on this subjective outcome. In addition, the follow-up for the non-blinded study (MD -8.00, 95% CI -12.88 to -3.12, n=95) was only 6 weeks whereas for the blinded study (MD -5.00, 95% CI -13.01 to 3.01, n=38) it was 6 months.
- ¹⁷ Downgraded one level for risk of bias: only data from a subgroup of the randomised control group was used: within the control group the surgeon decided who would receive CLS and who would receive vaginal hysterectomy, we included data from the CLS participants only.
- ¹⁸ Downgraded one level for imprecision: small sample size, only 97 participants were included.

Forest plots and tabulated results: Robot-assisted surgery compared with conventional laparoscopic surgery for hysterectomy

Patients and setting: Women (18 to 80 years) with benign or malignant conditions scheduled to undergo hysterectomy at specialist settings (academic teaching hospitals) in Finland, Sweden, Switzerland, and the USA.

Comparison: Robot-assisted surgery versus conventional laparoscopic surgery.

Outcome	Forest plot	Certainty of the evidence (GRADE)																																																																																																																																																																																																			
Intra- and post-operative complications combined	<table border="1"> <thead> <tr> <th rowspan="2">Study or Subgroup</th> <th colspan="2">RAS</th> <th colspan="2">CLS</th> <th rowspan="2">Weight</th> <th colspan="2">Risk Ratio</th> <th rowspan="2">Year</th> </tr> <tr> <th>Events</th> <th>Total</th> <th>Events</th> <th>Total</th> <th>M-H, Random, 95% CI</th> <th>M-H, Random, 95% CI</th> </tr> </thead> <tbody> <tr> <td colspan="9">1.1.1 Benign conditions</td> </tr> <tr> <td>Sarlos 2010</td> <td>18</td> <td>47</td> <td>12</td> <td>48</td> <td>34.6%</td> <td>1.53</td> <td>[0.83, 2.82]</td> <td>2010</td> </tr> <tr> <td>Green 2013 (1)</td> <td>6</td> <td>61</td> <td>6</td> <td>37</td> <td>22.8%</td> <td>0.61</td> <td>[0.21, 1.74]</td> <td>2013</td> </tr> <tr> <td>Paraiso 2013</td> <td>0</td> <td>26</td> <td>0</td> <td>26</td> <td></td> <td>Not estimable</td> <td></td> <td>2013</td> </tr> <tr> <td>Lonnerfors 2014 (2)</td> <td>5</td> <td>61</td> <td>8</td> <td>36</td> <td>23.2%</td> <td>0.37</td> <td>[0.13, 1.04]</td> <td>2015</td> </tr> <tr> <td>Deimling 2017</td> <td>4</td> <td>72</td> <td>6</td> <td>72</td> <td>19.4%</td> <td>0.67</td> <td>[0.20, 2.26]</td> <td>2017</td> </tr> <tr> <td>Subtotal (95% CI)</td> <td></td> <td>267</td> <td></td> <td>219</td> <td>100.0%</td> <td>0.76</td> <td>[0.38, 1.53]</td> <td></td> </tr> <tr> <td>Total events</td> <td colspan="2">33</td> <td colspan="2">32</td> <td colspan="4"></td> </tr> <tr> <td colspan="9">Heterogeneity: Tau² = 0.28; Chi² = 6.58, df = 3 (P = 0.09); I² = 54%</td> </tr> <tr> <td colspan="9">Test for overall effect: Z = 0.77 (P = 0.44)</td> </tr> <tr> <td colspan="9">1.1.2 Endometrial cancer</td> </tr> <tr> <td>Maenpaa 2016</td> <td>18</td> <td>50</td> <td>12</td> <td>49</td> <td>100.0%</td> <td>1.47</td> <td>[0.79, 2.72]</td> <td>2016</td> </tr> <tr> <td>Subtotal (95% CI)</td> <td></td> <td>50</td> <td></td> <td>49</td> <td>100.0%</td> <td>1.47</td> <td>[0.79, 2.72]</td> <td></td> </tr> <tr> <td>Total events</td> <td colspan="2">18</td> <td colspan="2">12</td> <td colspan="4"></td> </tr> <tr> <td colspan="9">Heterogeneity: Not applicable</td> </tr> <tr> <td colspan="9">Test for overall effect: Z = 1.23 (P = 0.22)</td> </tr> <tr> <td colspan="9">Test for subgroup differences: Chi² = 1.92, df = 1 (P = 0.17), I² = 48.0%</td> </tr> <tr> <td colspan="9"><u>Footnotes</u></td> </tr> <tr> <td colspan="9">(1) Per protocol data</td> </tr> <tr> <td colspan="9">(2) Excluding 25 women who underwent a vaginal hysterectomy in the control arm</td> </tr> </tbody> </table> 	Study or Subgroup	RAS		CLS		Weight	Risk Ratio		Year	Events	Total	Events	Total	M-H, Random, 95% CI	M-H, Random, 95% CI	1.1.1 Benign conditions									Sarlos 2010	18	47	12	48	34.6%	1.53	[0.83, 2.82]	2010	Green 2013 (1)	6	61	6	37	22.8%	0.61	[0.21, 1.74]	2013	Paraiso 2013	0	26	0	26		Not estimable		2013	Lonnerfors 2014 (2)	5	61	8	36	23.2%	0.37	[0.13, 1.04]	2015	Deimling 2017	4	72	6	72	19.4%	0.67	[0.20, 2.26]	2017	Subtotal (95% CI)		267		219	100.0%	0.76	[0.38, 1.53]		Total events	33		32						Heterogeneity: Tau ² = 0.28; Chi ² = 6.58, df = 3 (P = 0.09); I ² = 54%									Test for overall effect: Z = 0.77 (P = 0.44)									1.1.2 Endometrial cancer									Maenpaa 2016	18	50	12	49	100.0%	1.47	[0.79, 2.72]	2016	Subtotal (95% CI)		50		49	100.0%	1.47	[0.79, 2.72]		Total events	18		12						Heterogeneity: Not applicable									Test for overall effect: Z = 1.23 (P = 0.22)									Test for subgroup differences: Chi ² = 1.92, df = 1 (P = 0.17), I ² = 48.0%									<u>Footnotes</u>									(1) Per protocol data									(2) Excluding 25 women who underwent a vaginal hysterectomy in the control arm									<p>⊕⊕⊕⊕ LOW</p> <p>⊕⊕⊕⊕ LOW</p>
	Study or Subgroup		RAS		CLS			Weight	Risk Ratio		Year																																																																																																																																																																																										
Events		Total	Events	Total	M-H, Random, 95% CI	M-H, Random, 95% CI																																																																																																																																																																																															
1.1.1 Benign conditions																																																																																																																																																																																																					
Sarlos 2010	18	47	12	48	34.6%	1.53	[0.83, 2.82]	2010																																																																																																																																																																																													
Green 2013 (1)	6	61	6	37	22.8%	0.61	[0.21, 1.74]	2013																																																																																																																																																																																													
Paraiso 2013	0	26	0	26		Not estimable		2013																																																																																																																																																																																													
Lonnerfors 2014 (2)	5	61	8	36	23.2%	0.37	[0.13, 1.04]	2015																																																																																																																																																																																													
Deimling 2017	4	72	6	72	19.4%	0.67	[0.20, 2.26]	2017																																																																																																																																																																																													
Subtotal (95% CI)		267		219	100.0%	0.76	[0.38, 1.53]																																																																																																																																																																																														
Total events	33		32																																																																																																																																																																																																		
Heterogeneity: Tau ² = 0.28; Chi ² = 6.58, df = 3 (P = 0.09); I ² = 54%																																																																																																																																																																																																					
Test for overall effect: Z = 0.77 (P = 0.44)																																																																																																																																																																																																					
1.1.2 Endometrial cancer																																																																																																																																																																																																					
Maenpaa 2016	18	50	12	49	100.0%	1.47	[0.79, 2.72]	2016																																																																																																																																																																																													
Subtotal (95% CI)		50		49	100.0%	1.47	[0.79, 2.72]																																																																																																																																																																																														
Total events	18		12																																																																																																																																																																																																		
Heterogeneity: Not applicable																																																																																																																																																																																																					
Test for overall effect: Z = 1.23 (P = 0.22)																																																																																																																																																																																																					
Test for subgroup differences: Chi ² = 1.92, df = 1 (P = 0.17), I ² = 48.0%																																																																																																																																																																																																					
<u>Footnotes</u>																																																																																																																																																																																																					
(1) Per protocol data																																																																																																																																																																																																					
(2) Excluding 25 women who underwent a vaginal hysterectomy in the control arm																																																																																																																																																																																																					

	RAS		CLS		Risk Ratio		Risk Ratio		
	Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% CI
Intraoperative complications	1.2.1 Benign conditions								
	Sarlos 2010	12	47	7	48	85.9%	1.75 [0.76, 4.06]	2010	
	Paraiso 2013	0	26	0	26		Not estimable	2013	
	Lonnerfors 2014 (1)	1	61	1	36	8.1%	0.59 [0.04, 9.15]	2015	
	Deimling 2017	1	72	0	72	6.0%	3.00 [0.12, 72.44]	2017	
	Subtotal (95% CI)		206		182	100.0%	1.66 [0.76, 3.61]		
	Total events	14		8					
	Heterogeneity: Tau ² = 0.00; Chi ² = 0.69, df = 2 (P = 0.71); I ² = 0%								
	Test for overall effect: Z = 1.27 (P = 0.20)								
	Postoperative complications	1.3.1 Benign conditions							
Sarlos 2010		6	47	5	48	26.8%	1.23 [0.40, 3.74]	2010	
Green 2013 (1)		6	61	6	37	30.0%	0.61 [0.21, 1.74]	2013	
Lonnerfors 2014 (2)		4	61	7	36	24.9%	0.34 [0.11, 1.07]	2015	
Deimling 2017		3	72	6	72	18.4%	0.50 [0.13, 1.92]	2017	
Subtotal (95% CI)			241		193	100.0%	0.61 [0.34, 1.09]		
Total events		19		24					
Heterogeneity: Tau ² = 0.00; Chi ² = 2.59, df = 3 (P = 0.46); I ² = 0%									
Test for overall effect: Z = 1.67 (P = 0.09)									
Postoperative complications		1.3.2 Endometrial cancer							
	Maenpaa 2016	18	50	10	49	100.0%	1.76 [0.91, 3.43]	2016	
	Subtotal (95% CI)		50		49	100.0%	1.76 [0.91, 3.43]		
	Total events	18		10					
	Heterogeneity: Not applicable								
	Test for overall effect: Z = 1.67 (P = 0.09)								
	Test for subgroup differences: Chi ² = 5.57, df = 1 (P = 0.02), I ² = 82.1%								
	<u>Footnotes</u>								
	(1) High risk of bias (per protocol data). [Infection (1 vs 3), bleeding (1 vs 0), vaginal cuff dehiscence (3 vs 3), other (1 vs 1)]								
	(2) Excluding 25 women who underwent a vaginal hysterectomy in the control arm								

Total operating time [minutes]	<table border="1"> <thead> <tr> <th rowspan="2">Study or Subgroup</th> <th colspan="3">RAS</th> <th colspan="3">CLS</th> <th colspan="3">Mean Difference</th> <th rowspan="2">Year</th> <th rowspan="2">Mean Difference IV, Random, 95% CI [min]</th> </tr> <tr> <th>Mean [min]</th> <th>SD [min]</th> <th>Total</th> <th>Mean [min]</th> <th>SD [min]</th> <th>Total</th> <th>Weight</th> <th>IV, Random, 95% CI [min]</th> </tr> </thead> <tbody> <tr> <td colspan="12">1.4.1 Benign conditions</td> </tr> <tr> <td>Sarlos 2010</td> <td>96</td> <td>28</td> <td>47</td> <td>75</td> <td>21</td> <td>48</td> <td>58.9%</td> <td>21.00</td> <td>[11.03, 30.97]</td> <td>2010</td> <td rowspan="3"> </td> </tr> <tr> <td>Paraiso 2013</td> <td>172.8</td> <td>89</td> <td>26</td> <td>102.7</td> <td>63.7</td> <td>27</td> <td>41.1%</td> <td>70.10</td> <td>[28.30, 111.90]</td> <td>2013</td> </tr> <tr> <td>Subtotal (95% CI)</td> <td></td> <td></td> <td>73</td> <td></td> <td></td> <td>75</td> <td>100.0%</td> <td>41.18</td> <td>[-6.17, 88.53]</td> <td></td> </tr> <tr> <td colspan="12">Heterogeneity: Tau² = 965.00; Chi² = 5.01, df = 1 (P = 0.03); I² = 80% Test for overall effect: Z = 1.70 (P = 0.09)</td> </tr> <tr> <td colspan="12">Total (95% CI)</td> </tr> <tr> <td colspan="12">Heterogeneity: Tau² = 965.00; Chi² = 5.01, df = 1 (P = 0.03); I² = 80% Test for overall effect: Z = 1.70 (P = 0.09) Test for subgroup differences: Not applicable</td> </tr> </tbody> </table>											Study or Subgroup	RAS			CLS			Mean Difference			Year	Mean Difference IV, Random, 95% CI [min]	Mean [min]	SD [min]	Total	Mean [min]	SD [min]	Total	Weight	IV, Random, 95% CI [min]	1.4.1 Benign conditions												Sarlos 2010	96	28	47	75	21	48	58.9%	21.00	[11.03, 30.97]	2010		Paraiso 2013	172.8	89	26	102.7	63.7	27	41.1%	70.10	[28.30, 111.90]	2013	Subtotal (95% CI)			73			75	100.0%	41.18	[-6.17, 88.53]		Heterogeneity: Tau ² = 965.00; Chi ² = 5.01, df = 1 (P = 0.03); I ² = 80% Test for overall effect: Z = 1.70 (P = 0.09)												Total (95% CI)												Heterogeneity: Tau ² = 965.00; Chi ² = 5.01, df = 1 (P = 0.03); I ² = 80% Test for overall effect: Z = 1.70 (P = 0.09) Test for subgroup differences: Not applicable												<p>⊕⊕⊕⊕ VERY LOW</p>																								
	Study or Subgroup	RAS			CLS			Mean Difference			Year		Mean Difference IV, Random, 95% CI [min]																																																																																																																													
		Mean [min]	SD [min]	Total	Mean [min]	SD [min]	Total	Weight	IV, Random, 95% CI [min]																																																																																																																																	
1.4.1 Benign conditions																																																																																																																																										
Sarlos 2010	96	28	47	75	21	48	58.9%	21.00	[11.03, 30.97]	2010																																																																																																																																
Paraiso 2013	172.8	89	26	102.7	63.7	27	41.1%	70.10	[28.30, 111.90]	2013																																																																																																																																
Subtotal (95% CI)			73			75	100.0%	41.18	[-6.17, 88.53]																																																																																																																																	
Heterogeneity: Tau ² = 965.00; Chi ² = 5.01, df = 1 (P = 0.03); I ² = 80% Test for overall effect: Z = 1.70 (P = 0.09)																																																																																																																																										
Total (95% CI)																																																																																																																																										
Heterogeneity: Tau ² = 965.00; Chi ² = 5.01, df = 1 (P = 0.03); I ² = 80% Test for overall effect: Z = 1.70 (P = 0.09) Test for subgroup differences: Not applicable																																																																																																																																										
<p>Total operating time [min]: in addition, four studies reported medians and ranges or IQRs* due to skewed distribution of data</p> <table border="1"> <thead> <tr> <th rowspan="2">Condition</th> <th rowspan="2">Study</th> <th colspan="3">RAS</th> <th colspan="3">CLS</th> </tr> <tr> <th>Median</th> <th>Range</th> <th>N</th> <th>Median</th> <th>Range</th> <th>N</th> </tr> </thead> <tbody> <tr> <td rowspan="3">Benign</td> <td>Deimling 2017</td> <td>67</td> <td>59-83*</td> <td>72</td> <td>65.5</td> <td>57-90.5*</td> <td>72</td> </tr> <tr> <td>Green 2013</td> <td>90</td> <td>74-104</td> <td>61</td> <td>88</td> <td>75-105</td> <td>37</td> </tr> <tr> <td>Lonnerfors 2014</td> <td>76</td> <td>43-210</td> <td>61</td> <td>104</td> <td>53-223</td> <td>36</td> </tr> <tr> <td>Cancer</td> <td>Maenpaa 2016</td> <td>139</td> <td>86-197</td> <td>50</td> <td>170</td> <td>126-259</td> <td>49</td> </tr> </tbody> </table>											Condition	Study	RAS			CLS			Median	Range	N	Median	Range	N	Benign	Deimling 2017	67	59-83*	72	65.5	57-90.5*	72	Green 2013	90	74-104	61	88	75-105	37	Lonnerfors 2014	76	43-210	61	104	53-223	36	Cancer	Maenpaa 2016	139	86-197	50	170	126-259	49																																																																																				
Condition	Study	RAS			CLS																																																																																																																																					
		Median	Range	N	Median	Range	N																																																																																																																																			
Benign	Deimling 2017	67	59-83*	72	65.5	57-90.5*	72																																																																																																																																			
	Green 2013	90	74-104	61	88	75-105	37																																																																																																																																			
	Lonnerfors 2014	76	43-210	61	104	53-223	36																																																																																																																																			
Cancer	Maenpaa 2016	139	86-197	50	170	126-259	49																																																																																																																																			
Overall duration of hospital stay [days]	<table border="1"> <thead> <tr> <th rowspan="2">Study or Subgroup</th> <th colspan="3">RAS</th> <th colspan="3">CLS</th> <th colspan="3">Mean Difference</th> <th rowspan="2">Year</th> <th rowspan="2">Mean Difference IV, Random, 95% CI [days]</th> </tr> <tr> <th>Mean [days]</th> <th>SD [days]</th> <th>Total</th> <th>Mean [days]</th> <th>SD [days]</th> <th>Total</th> <th>Weight</th> <th>IV, Random, 95% CI [days]</th> </tr> </thead> <tbody> <tr> <td colspan="12">1.5.1 Benign conditions</td> </tr> <tr> <td>Sarlos 2010</td> <td>3.3</td> <td>0.9</td> <td>47</td> <td>3.6</td> <td>3.9</td> <td>48</td> <td>4.1%</td> <td>-0.30</td> <td>[-1.43, 0.83]</td> <td>2010</td> <td rowspan="3"> </td> </tr> <tr> <td>Lonnerfors 2014 (1)</td> <td>1.1</td> <td>0.52</td> <td>61</td> <td>1.4</td> <td>0.6</td> <td>36</td> <td>95.9%</td> <td>-0.30</td> <td>[-0.54, -0.06]</td> <td>2015</td> </tr> <tr> <td>Subtotal (95% CI)</td> <td></td> <td></td> <td>108</td> <td></td> <td></td> <td>84</td> <td>100.0%</td> <td>-0.30</td> <td>[-0.53, -0.07]</td> <td></td> </tr> <tr> <td colspan="12">Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 1.00); I² = 0% Test for overall effect: Z = 2.55 (P = 0.01)</td> </tr> <tr> <td colspan="12">Total (95% CI)</td> </tr> <tr> <td colspan="12">Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 1.00); I² = 0% Test for overall effect: Z = 2.55 (P = 0.01) Test for subgroup differences: Not applicable</td> </tr> <tr> <td colspan="12"><u>Footnotes</u></td> </tr> <tr> <td colspan="12">(1) Excluding 25 women who underwent a vaginal hysterectomy in the control arm</td> </tr> </tbody> </table>											Study or Subgroup	RAS			CLS			Mean Difference			Year	Mean Difference IV, Random, 95% CI [days]	Mean [days]	SD [days]	Total	Mean [days]	SD [days]	Total	Weight	IV, Random, 95% CI [days]	1.5.1 Benign conditions												Sarlos 2010	3.3	0.9	47	3.6	3.9	48	4.1%	-0.30	[-1.43, 0.83]	2010		Lonnerfors 2014 (1)	1.1	0.52	61	1.4	0.6	36	95.9%	-0.30	[-0.54, -0.06]	2015	Subtotal (95% CI)			108			84	100.0%	-0.30	[-0.53, -0.07]		Heterogeneity: Tau ² = 0.00; Chi ² = 0.00, df = 1 (P = 1.00); I ² = 0% Test for overall effect: Z = 2.55 (P = 0.01)												Total (95% CI)												Heterogeneity: Tau ² = 0.00; Chi ² = 0.00, df = 1 (P = 1.00); I ² = 0% Test for overall effect: Z = 2.55 (P = 0.01) Test for subgroup differences: Not applicable												<u>Footnotes</u>												(1) Excluding 25 women who underwent a vaginal hysterectomy in the control arm												<p>⊕⊕⊕⊕ LOW</p>
	Study or Subgroup	RAS			CLS			Mean Difference			Year		Mean Difference IV, Random, 95% CI [days]																																																																																																																													
		Mean [days]	SD [days]	Total	Mean [days]	SD [days]	Total	Weight	IV, Random, 95% CI [days]																																																																																																																																	
1.5.1 Benign conditions																																																																																																																																										
Sarlos 2010	3.3	0.9	47	3.6	3.9	48	4.1%	-0.30	[-1.43, 0.83]	2010																																																																																																																																
Lonnerfors 2014 (1)	1.1	0.52	61	1.4	0.6	36	95.9%	-0.30	[-0.54, -0.06]	2015																																																																																																																																
Subtotal (95% CI)			108			84	100.0%	-0.30	[-0.53, -0.07]																																																																																																																																	
Heterogeneity: Tau ² = 0.00; Chi ² = 0.00, df = 1 (P = 1.00); I ² = 0% Test for overall effect: Z = 2.55 (P = 0.01)																																																																																																																																										
Total (95% CI)																																																																																																																																										
Heterogeneity: Tau ² = 0.00; Chi ² = 0.00, df = 1 (P = 1.00); I ² = 0% Test for overall effect: Z = 2.55 (P = 0.01) Test for subgroup differences: Not applicable																																																																																																																																										
<u>Footnotes</u>																																																																																																																																										
(1) Excluding 25 women who underwent a vaginal hysterectomy in the control arm																																																																																																																																										
<p>Overall hospital stay [days]: in addition, two studies reported medians and IQRs due to skewed distribution of data</p> <table border="1"> <thead> <tr> <th rowspan="2">Condition</th> <th rowspan="2">Study</th> <th colspan="3">RAS</th> <th colspan="3">CLS</th> </tr> <tr> <th>Median</th> <th>IQR</th> <th>N</th> <th>Median</th> <th>IQR</th> <th>N</th> </tr> </thead> <tbody> <tr> <td>Benign</td> <td>Deimling 2017</td> <td>0.92</td> <td>0.40-1.00</td> <td>72</td> <td>0.92</td> <td>0.79-1.04</td> <td>72</td> </tr> <tr> <td>Cancer</td> <td>Maenpaa 2016</td> <td>1</td> <td>1-2</td> <td>50</td> <td>2</td> <td>1-2</td> <td>49</td> </tr> </tbody> </table>											Condition	Study	RAS			CLS			Median	IQR	N	Median	IQR	N	Benign	Deimling 2017	0.92	0.40-1.00	72	0.92	0.79-1.04	72	Cancer	Maenpaa 2016	1	1-2	50	2	1-2	49																																																																																																		
Condition	Study	RAS			CLS																																																																																																																																					
		Median	IQR	N	Median	IQR	N																																																																																																																																			
Benign	Deimling 2017	0.92	0.40-1.00	72	0.92	0.79-1.04	72																																																																																																																																			
Cancer	Maenpaa 2016	1	1-2	50	2	1-2	49																																																																																																																																			

<p>Blood transfusion</p>	<table border="1"> <thead> <tr> <th rowspan="2">Study or Subgroup</th> <th colspan="2">RAS</th> <th colspan="2">CLS</th> <th rowspan="2">Weight</th> <th colspan="2">Risk Ratio</th> <th rowspan="2">Year</th> <th rowspan="2">Risk Ratio M-H, Random, 95% CI</th> </tr> <tr> <th>Events</th> <th>Total</th> <th>Events</th> <th>Total</th> <th>M-H, Random, 95% CI</th> <th>Year</th> </tr> </thead> <tbody> <tr> <td colspan="10">1.6.1 Benign conditions</td> </tr> <tr> <td>Green 2013 (1)</td> <td>1</td> <td>61</td> <td>0</td> <td>37</td> <td>35.2%</td> <td>1.84</td> <td>[0.08, 44.00]</td> <td>2013</td> <td rowspan="4"> </td> </tr> <tr> <td>Paraiso 2013</td> <td>2</td> <td>26</td> <td>1</td> <td>26</td> <td>64.8%</td> <td>2.00</td> <td>[0.19, 20.72]</td> <td>2013</td> </tr> <tr> <td>Lonnerfors 2014 (2)</td> <td>0</td> <td>61</td> <td>0</td> <td>36</td> <td></td> <td>Not estimable</td> <td></td> <td>2015</td> </tr> <tr> <td>Subtotal (95% CI)</td> <td></td> <td>148</td> <td></td> <td>99</td> <td>100.0%</td> <td>1.94</td> <td>[0.30, 12.76]</td> <td></td> </tr> <tr> <td>Total events</td> <td>3</td> <td></td> <td>1</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td colspan="10">Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.97); I² = 0%</td> </tr> <tr> <td colspan="10">Test for overall effect: Z = 0.69 (P = 0.49)</td> </tr> <tr> <td colspan="10">1.6.2 Endometrial cancer</td> </tr> <tr> <td>Maenpaa 2016</td> <td>6</td> <td>50</td> <td>2</td> <td>49</td> <td>100.0%</td> <td>2.94</td> <td>[0.62, 13.87]</td> <td>2016</td> <td rowspan="2"> </td> </tr> <tr> <td>Subtotal (95% CI)</td> <td></td> <td>50</td> <td></td> <td>49</td> <td>100.0%</td> <td>2.94</td> <td>[0.62, 13.87]</td> <td></td> </tr> <tr> <td>Total events</td> <td>6</td> <td></td> <td>2</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td colspan="10">Heterogeneity: Not applicable</td> </tr> <tr> <td colspan="10">Test for overall effect: Z = 1.36 (P = 0.17)</td> </tr> <tr> <td colspan="10">Test for subgroup differences: Chi² = 0.11, df = 1 (P = 0.74), I² = 0%</td> </tr> <tr> <td colspan="10"><u>Footnotes</u></td> </tr> <tr> <td colspan="10">(1) per protocol data</td> </tr> <tr> <td colspan="10">(2) Excluding 25 women who underwent a vaginal hysterectomy in the control arm</td> </tr> </tbody> </table>	Study or Subgroup	RAS		CLS		Weight	Risk Ratio		Year	Risk Ratio M-H, Random, 95% CI	Events	Total	Events	Total	M-H, Random, 95% CI	Year	1.6.1 Benign conditions										Green 2013 (1)	1	61	0	37	35.2%	1.84	[0.08, 44.00]	2013		Paraiso 2013	2	26	1	26	64.8%	2.00	[0.19, 20.72]	2013	Lonnerfors 2014 (2)	0	61	0	36		Not estimable		2015	Subtotal (95% CI)		148		99	100.0%	1.94	[0.30, 12.76]		Total events	3		1							Heterogeneity: Tau ² = 0.00; Chi ² = 0.00, df = 1 (P = 0.97); I ² = 0%										Test for overall effect: Z = 0.69 (P = 0.49)										1.6.2 Endometrial cancer										Maenpaa 2016	6	50	2	49	100.0%	2.94	[0.62, 13.87]	2016		Subtotal (95% CI)		50		49	100.0%	2.94	[0.62, 13.87]		Total events	6		2							Heterogeneity: Not applicable										Test for overall effect: Z = 1.36 (P = 0.17)										Test for subgroup differences: Chi ² = 0.11, df = 1 (P = 0.74), I ² = 0%										<u>Footnotes</u>										(1) per protocol data										(2) Excluding 25 women who underwent a vaginal hysterectomy in the control arm										<p>⊕⊕⊕⊕ LOW</p> <p>⊕⊕⊕⊕ LOW</p>
Study or Subgroup	RAS		CLS		Weight	Risk Ratio		Year	Risk Ratio M-H, Random, 95% CI																																																																																																																																																																																									
	Events	Total	Events	Total		M-H, Random, 95% CI	Year																																																																																																																																																																																											
1.6.1 Benign conditions																																																																																																																																																																																																		
Green 2013 (1)	1	61	0	37	35.2%	1.84	[0.08, 44.00]	2013																																																																																																																																																																																										
Paraiso 2013	2	26	1	26	64.8%	2.00	[0.19, 20.72]	2013																																																																																																																																																																																										
Lonnerfors 2014 (2)	0	61	0	36		Not estimable		2015																																																																																																																																																																																										
Subtotal (95% CI)		148		99	100.0%	1.94	[0.30, 12.76]																																																																																																																																																																																											
Total events	3		1																																																																																																																																																																																															
Heterogeneity: Tau ² = 0.00; Chi ² = 0.00, df = 1 (P = 0.97); I ² = 0%																																																																																																																																																																																																		
Test for overall effect: Z = 0.69 (P = 0.49)																																																																																																																																																																																																		
1.6.2 Endometrial cancer																																																																																																																																																																																																		
Maenpaa 2016	6	50	2	49	100.0%	2.94	[0.62, 13.87]	2016																																																																																																																																																																																										
Subtotal (95% CI)		50		49	100.0%	2.94	[0.62, 13.87]																																																																																																																																																																																											
Total events	6		2																																																																																																																																																																																															
Heterogeneity: Not applicable																																																																																																																																																																																																		
Test for overall effect: Z = 1.36 (P = 0.17)																																																																																																																																																																																																		
Test for subgroup differences: Chi ² = 0.11, df = 1 (P = 0.74), I ² = 0%																																																																																																																																																																																																		
<u>Footnotes</u>																																																																																																																																																																																																		
(1) per protocol data																																																																																																																																																																																																		
(2) Excluding 25 women who underwent a vaginal hysterectomy in the control arm																																																																																																																																																																																																		
<p>Postoperative pain scale range not reported, low=good follow-up: up to 2 weeks</p>	<table border="1"> <thead> <tr> <th rowspan="2">Study or Subgroup</th> <th colspan="2">RAS</th> <th colspan="2">CLS</th> <th rowspan="2">Weight</th> <th colspan="2">Mean Difference</th> <th rowspan="2">Year</th> <th rowspan="2">Mean Difference IV, Random, 95% CI</th> </tr> <tr> <th>Mean</th> <th>SD</th> <th>Mean</th> <th>SD</th> <th>IV, Random, 95% CI</th> <th>Year</th> </tr> </thead> <tbody> <tr> <td colspan="10">1.7.1 Benign conditions</td> </tr> <tr> <td>Paraiso 2013 (1)</td> <td>17</td> <td>20</td> <td>18</td> <td>19</td> <td>23</td> <td>18</td> <td>100.0%</td> <td>-2.00</td> <td>[-16.08, 12.08]</td> <td>2013</td> <td rowspan="2"> </td> </tr> <tr> <td>Subtotal (95% CI)</td> <td></td> <td></td> <td>18</td> <td></td> <td></td> <td>18</td> <td>100.0%</td> <td>-2.00</td> <td>[-16.08, 12.08]</td> <td></td> </tr> <tr> <td colspan="10">Heterogeneity: Not applicable</td> </tr> <tr> <td colspan="10">Test for overall effect: Z = 0.28 (P = 0.78)</td> </tr> <tr> <td colspan="10">Total (95% CI)</td> </tr> <tr> <td></td> <td></td> <td></td> <td>18</td> <td></td> <td></td> <td>18</td> <td>100.0%</td> <td>-2.00</td> <td>[-16.08, 12.08]</td> <td></td> </tr> <tr> <td colspan="10">Heterogeneity: Not applicable</td> </tr> <tr> <td colspan="10">Test for overall effect: Z = 0.28 (P = 0.78)</td> </tr> <tr> <td colspan="10">Test for subgroup differences: Not applicable</td> </tr> <tr> <td colspan="10"><u>Footnotes</u></td> </tr> <tr> <td colspan="10">(1) Pain at rest</td> </tr> </tbody> </table> <p>Pain (10-point analogue scale) at post-operation to 2 days follow-up: in addition, two studies reported medians and ranges or IQRs (*IQR, **25th-75th percentile) due to skewed distribution of data</p> <table border="1"> <thead> <tr> <th rowspan="2">Condition</th> <th rowspan="2">Study</th> <th colspan="3">RAS</th> <th colspan="3">CLS</th> </tr> <tr> <th>Median</th> <th>Range</th> <th>N</th> <th>Median</th> <th>Range</th> <th>N</th> </tr> </thead> <tbody> <tr> <td rowspan="2">Benign</td> <td>Deimling 2017 (2 hours)</td> <td>3</td> <td>2-5.5*</td> <td>72</td> <td>4</td> <td>2-5.5*</td> <td>72</td> </tr> <tr> <td>Green 2013 (post-operation)</td> <td>5</td> <td>3-7**</td> <td>61</td> <td>4</td> <td>3-6**</td> <td>37</td> </tr> <tr> <td>Cancer</td> <td>Maenpaa 2016 (2 days)</td> <td>2</td> <td>0-6</td> <td>13</td> <td>2</td> <td>0-6</td> <td>14</td> </tr> </tbody> </table>	Study or Subgroup	RAS		CLS		Weight	Mean Difference		Year	Mean Difference IV, Random, 95% CI	Mean	SD	Mean	SD	IV, Random, 95% CI	Year	1.7.1 Benign conditions										Paraiso 2013 (1)	17	20	18	19	23	18	100.0%	-2.00	[-16.08, 12.08]	2013		Subtotal (95% CI)			18			18	100.0%	-2.00	[-16.08, 12.08]		Heterogeneity: Not applicable										Test for overall effect: Z = 0.28 (P = 0.78)										Total (95% CI)													18			18	100.0%	-2.00	[-16.08, 12.08]		Heterogeneity: Not applicable										Test for overall effect: Z = 0.28 (P = 0.78)										Test for subgroup differences: Not applicable										<u>Footnotes</u>										(1) Pain at rest										Condition	Study	RAS			CLS			Median	Range	N	Median	Range	N	Benign	Deimling 2017 (2 hours)	3	2-5.5*	72	4	2-5.5*	72	Green 2013 (post-operation)	5	3-7**	61	4	3-6**	37	Cancer	Maenpaa 2016 (2 days)	2	0-6	13	2	0-6	14	<p>⊕⊕⊕⊕ VERY LOW</p>															
Study or Subgroup	RAS		CLS		Weight	Mean Difference		Year	Mean Difference IV, Random, 95% CI																																																																																																																																																																																									
	Mean	SD	Mean	SD		IV, Random, 95% CI	Year																																																																																																																																																																																											
1.7.1 Benign conditions																																																																																																																																																																																																		
Paraiso 2013 (1)	17	20	18	19	23	18	100.0%	-2.00	[-16.08, 12.08]	2013																																																																																																																																																																																								
Subtotal (95% CI)			18			18	100.0%	-2.00	[-16.08, 12.08]																																																																																																																																																																																									
Heterogeneity: Not applicable																																																																																																																																																																																																		
Test for overall effect: Z = 0.28 (P = 0.78)																																																																																																																																																																																																		
Total (95% CI)																																																																																																																																																																																																		
			18			18	100.0%	-2.00	[-16.08, 12.08]																																																																																																																																																																																									
Heterogeneity: Not applicable																																																																																																																																																																																																		
Test for overall effect: Z = 0.28 (P = 0.78)																																																																																																																																																																																																		
Test for subgroup differences: Not applicable																																																																																																																																																																																																		
<u>Footnotes</u>																																																																																																																																																																																																		
(1) Pain at rest																																																																																																																																																																																																		
Condition	Study	RAS			CLS																																																																																																																																																																																													
		Median	Range	N	Median	Range	N																																																																																																																																																																																											
Benign	Deimling 2017 (2 hours)	3	2-5.5*	72	4	2-5.5*	72																																																																																																																																																																																											
	Green 2013 (post-operation)	5	3-7**	61	4	3-6**	37																																																																																																																																																																																											
Cancer	Maenpaa 2016 (2 days)	2	0-6	13	2	0-6	14																																																																																																																																																																																											

<p>Quality of life *** Follow-up: 6 weeks to 6 months</p>	<table border="1"> <thead> <tr> <th rowspan="2">Study or Subgroup</th> <th colspan="3">CLS</th> <th colspan="3">RAS</th> <th rowspan="2">Weight</th> <th rowspan="2">Mean Difference IV, Random, 95% CI</th> <th rowspan="2">Year</th> <th rowspan="2">Mean Difference IV, Random, 95% CI</th> </tr> <tr> <th>Mean</th> <th>SD</th> <th>Total</th> <th>Mean</th> <th>SD</th> <th>Total</th> </tr> </thead> <tbody> <tr> <td colspan="11">1.8.1 EQ-5D mean change from baseline</td> </tr> <tr> <td>Sarlos 2010</td> <td>5</td> <td>14</td> <td>48</td> <td>13</td> <td>10</td> <td>47</td> <td>100.0%</td> <td>-8.00 [-12.88, -3.12]</td> <td>2010</td> <td></td> </tr> <tr> <td>Subtotal (95% CI)</td> <td></td> <td></td> <td>48</td> <td></td> <td></td> <td>47</td> <td>100.0%</td> <td>-8.00 [-12.88, -3.12]</td> <td></td> <td></td> </tr> <tr> <td colspan="11">Heterogeneity: Not applicable Test for overall effect: Z = 3.21 (P = 0.001)</td> </tr> <tr> <td colspan="11">1.8.2 SF-36 mean endpoint score</td> </tr> <tr> <td>Paraiso 2013 (1)</td> <td>45</td> <td>14</td> <td>19</td> <td>50</td> <td>11</td> <td>19</td> <td>100.0%</td> <td>-5.00 [-13.01, 3.01]</td> <td>2013</td> <td></td> </tr> <tr> <td>Subtotal (95% CI)</td> <td></td> <td></td> <td>19</td> <td></td> <td></td> <td>19</td> <td>100.0%</td> <td>-5.00 [-13.01, 3.01]</td> <td></td> <td></td> </tr> <tr> <td colspan="11">Heterogeneity: Not applicable Test for overall effect: Z = 1.22 (P = 0.22)</td> </tr> <tr> <td colspan="11">Test for subgroup differences: Chi² = 0.39, df = 1 (P = 0.53), I² = 0%</td> </tr> <tr> <td colspan="11"><u>Footnotes</u> (1) 36 item short form health survey (mental component summary score). Physical summary scores were similar.</td> </tr> </tbody> </table>	Study or Subgroup	CLS			RAS			Weight	Mean Difference IV, Random, 95% CI	Year	Mean Difference IV, Random, 95% CI	Mean	SD	Total	Mean	SD	Total	1.8.1 EQ-5D mean change from baseline											Sarlos 2010	5	14	48	13	10	47	100.0%	-8.00 [-12.88, -3.12]	2010		Subtotal (95% CI)			48			47	100.0%	-8.00 [-12.88, -3.12]			Heterogeneity: Not applicable Test for overall effect: Z = 3.21 (P = 0.001)											1.8.2 SF-36 mean endpoint score											Paraiso 2013 (1)	45	14	19	50	11	19	100.0%	-5.00 [-13.01, 3.01]	2013		Subtotal (95% CI)			19			19	100.0%	-5.00 [-13.01, 3.01]			Heterogeneity: Not applicable Test for overall effect: Z = 1.22 (P = 0.22)											Test for subgroup differences: Chi ² = 0.39, df = 1 (P = 0.53), I ² = 0%											<u>Footnotes</u> (1) 36 item short form health survey (mental component summary score). Physical summary scores were similar.											<p>⊕⊕⊕⊕ VERY LOW</p>
Study or Subgroup	CLS			RAS			Weight	Mean Difference IV, Random, 95% CI					Year	Mean Difference IV, Random, 95% CI																																																																																																																			
	Mean	SD	Total	Mean	SD	Total																																																																																																																											
1.8.1 EQ-5D mean change from baseline																																																																																																																																	
Sarlos 2010	5	14	48	13	10	47	100.0%	-8.00 [-12.88, -3.12]	2010																																																																																																																								
Subtotal (95% CI)			48			47	100.0%	-8.00 [-12.88, -3.12]																																																																																																																									
Heterogeneity: Not applicable Test for overall effect: Z = 3.21 (P = 0.001)																																																																																																																																	
1.8.2 SF-36 mean endpoint score																																																																																																																																	
Paraiso 2013 (1)	45	14	19	50	11	19	100.0%	-5.00 [-13.01, 3.01]	2013																																																																																																																								
Subtotal (95% CI)			19			19	100.0%	-5.00 [-13.01, 3.01]																																																																																																																									
Heterogeneity: Not applicable Test for overall effect: Z = 1.22 (P = 0.22)																																																																																																																																	
Test for subgroup differences: Chi ² = 0.39, df = 1 (P = 0.53), I ² = 0%																																																																																																																																	
<u>Footnotes</u> (1) 36 item short form health survey (mental component summary score). Physical summary scores were similar.																																																																																																																																	
<p>Total cost [1,000 US dollars]</p>	<table border="1"> <thead> <tr> <th rowspan="2">Study or Subgroup</th> <th colspan="3">RAS</th> <th colspan="3">CLS</th> <th rowspan="2">Weight</th> <th rowspan="2">Mean Difference IV, Random, 95% CI</th> <th rowspan="2">Year</th> <th rowspan="2">Mean Difference IV, Random, 95% CI</th> </tr> <tr> <th>Mean</th> <th>SD</th> <th>Total</th> <th>Mean</th> <th>SD</th> <th>Total</th> </tr> </thead> <tbody> <tr> <td colspan="11">1.9.1 Benign conditions</td> </tr> <tr> <td>Lonnerfors 2014 (1)</td> <td>8.623</td> <td>1.018</td> <td>61</td> <td>7.059</td> <td>1.26</td> <td>36</td> <td>100.0%</td> <td>1.56 [1.08, 2.05]</td> <td>2015</td> <td></td> </tr> <tr> <td>Subtotal (95% CI)</td> <td></td> <td></td> <td>61</td> <td></td> <td></td> <td>36</td> <td>100.0%</td> <td>1.56 [1.08, 2.05]</td> <td></td> <td></td> </tr> <tr> <td colspan="11">Heterogeneity: Not applicable Test for overall effect: Z = 6.33 (P < 0.00001)</td> </tr> <tr> <td>Total (95% CI)</td> <td></td> <td></td> <td>61</td> <td></td> <td></td> <td>36</td> <td>100.0%</td> <td>1.56 [1.08, 2.05]</td> <td></td> <td></td> </tr> <tr> <td colspan="11">Heterogeneity: Not applicable Test for overall effect: Z = 6.33 (P < 0.00001) Test for subgroup differences: Not applicable</td> </tr> <tr> <td colspan="11"><u>Footnotes</u> (1) 1,000 US dollars; Excluding 25 women who underwent a vaginal hysterectomy in the control arm</td> </tr> </tbody> </table>	Study or Subgroup	RAS			CLS			Weight	Mean Difference IV, Random, 95% CI	Year	Mean Difference IV, Random, 95% CI	Mean	SD	Total	Mean	SD	Total	1.9.1 Benign conditions											Lonnerfors 2014 (1)	8.623	1.018	61	7.059	1.26	36	100.0%	1.56 [1.08, 2.05]	2015		Subtotal (95% CI)			61			36	100.0%	1.56 [1.08, 2.05]			Heterogeneity: Not applicable Test for overall effect: Z = 6.33 (P < 0.00001)											Total (95% CI)			61			36	100.0%	1.56 [1.08, 2.05]			Heterogeneity: Not applicable Test for overall effect: Z = 6.33 (P < 0.00001) Test for subgroup differences: Not applicable											<u>Footnotes</u> (1) 1,000 US dollars; Excluding 25 women who underwent a vaginal hysterectomy in the control arm											<p>⊕⊕⊕⊕ LOW</p>																																	
Study or Subgroup	RAS			CLS			Weight	Mean Difference IV, Random, 95% CI					Year	Mean Difference IV, Random, 95% CI																																																																																																																			
	Mean	SD	Total	Mean	SD	Total																																																																																																																											
1.9.1 Benign conditions																																																																																																																																	
Lonnerfors 2014 (1)	8.623	1.018	61	7.059	1.26	36	100.0%	1.56 [1.08, 2.05]	2015																																																																																																																								
Subtotal (95% CI)			61			36	100.0%	1.56 [1.08, 2.05]																																																																																																																									
Heterogeneity: Not applicable Test for overall effect: Z = 6.33 (P < 0.00001)																																																																																																																																	
Total (95% CI)			61			36	100.0%	1.56 [1.08, 2.05]																																																																																																																									
Heterogeneity: Not applicable Test for overall effect: Z = 6.33 (P < 0.00001) Test for subgroup differences: Not applicable																																																																																																																																	
<u>Footnotes</u> (1) 1,000 US dollars; Excluding 25 women who underwent a vaginal hysterectomy in the control arm																																																																																																																																	

*Inter quartile range (IQR) **25th-75th percentile ***The direction of the comparison for this outcome was inverted to enable graphical presentation consistent with the other outcomes

CI= confidence interval; CLS=conventional laparoscopic surgery; IQR= inter-quartile range; MD= mean difference; RAS= robot-assisted surgery; RR= risk ratio; SD= standard deviation