National Institute for Health and Care Excellence

Draft for consultation

Colorectal cancer (update)

[C3] Optimal surgical technique for rectal cancer

NICE guideline TBC

Evidence reviews

July 2019

Draft for Consultation

These evidence reviews were developed by the National Guideline Alliance hosted by the Royal College of Obstetricians and Gynaecologists

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ISBN:

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Optimal surgical technique for rectal cancer

This evidence review supports recommendations 1.3.6 to 1.3.9.

Review question

What is the optimal surgical technique for rectal cancer?

Introduction

Over the last couple of decades, laparoscopic surgery, a minimally invasive surgical technique, has become more and more common in rectal cancer surgery, offering an alternative to the conventional open surgical technique. In recent years manual laparoscopic surgery has been challenged by robotic surgery and transanal total mesorectal excision (TaTME) has been suggested as a surgical technique when performing anterior resection. The aim of this review is to compare the clinical and cost effectiveness of different surgical techniques in treating non-metastatic rectal cancer.

Summary of the protocol

Please see Table 1 for a summary of the population, intervention, comparison and outcomes (PICO) characteristics of this review.

Table 1: Summary of the protocol (PICO table)

Population	Adults with non-metastatic rectal cancer • T1-2 N1-2 • T3 N any • T4 N any • M0
Intervention	Surgical resection (for example abdominoperineal resection [APR] or low anterior resection [LAR]) • Open • Laparoscopic • Robotic • Transanal total mesorectal excision (TaTME; only anterior resection)
Comparison	Surgical techniques compared to each other

Outcomes	**Critical**
	• Overall survival
	• Quality of life
	  ○ Overall
	  ○ Sexual function
	  ○ Bladder function
	• Resection margins
	Important
	• Local recurrence
	• Length of hospital stay

	• 90-day mortality • Treatment-related complications: ○ Anastomotic leak (only relevant in anterior resection) ○ Surgical site infection ○ Blood loss

APR: abdominoperineal resection; LAR: lower anterior resection; TNM: cancer classification system, standing for tumour, nodal and metastasis stages.

For further details see the review protocol in appendix A.

Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual 2014. Methods specific to this review question are described in the review protocol in appendix A.

Declarations of interest were recorded according to NICE's 2014 conflicts of interest policy until 31 March 2018. From 1 April 2018, declarations of interest were recorded according to NICE's 2018 conflicts of interest policy. Those interests declared until April 2018 were reclassified according to NICE's 2018 conflicts of interest policy (see Register of Interests).

Clinical evidence

Included studies

Thirty-seven publications from 17 RCTs and 9 cohort studies were included in this review (ACOSOG Z6051 trial [Fleshman 2015; Fleshman 2018]; ALaCaRT trial [Stevenson 2015; Stevenson 2018]; Arteaga Gonzalez 2006; Bordeaux trial [Denost 2018; Pontallier 2016]; Braga 2007; Buonpane 2017; CLASICC trial [Green 2013; Guillou 2005; Jayne 2005; Jayne 2010; Quah 2002]; COLOR II trial [Andersson 2014; Andersson 2013; Bonjer 2015; van der Pas 2013]; Corbellini 2016; COREAN trial [Jeong 2014; Kang 2010]; Ielpo 2017; Ishibe 2017; Kim 2016; Kim 2017a; Kim 2017b; Law 2017; Liang 2011; Lujan 2011; Ng 2008; Ng 2009; Ng 2014; Park 2015; ROLARR trial [Jayne 2017]; Rouanet 2018; Yoo 2015; Zhou 2004).

The included studies are summarised in Table 2.

Fourteen RCTs (24 publications) compared laparoscopic surgery to open surgery in people with rectal cancer (comparison 1) (ACOSOG Z6051 trial [Fleshman 2015; Fleshman 2018]; ALaCaRT trial [Stevenson 2015; Stevenson 2018]; Arteaga Gonzalez 2006; Braga 2007; CLASICC trial [Green 2013; Guillou 2005; Jayne 2005; Jayne 2010; Quah 2002]; COLOR II trial [Andersson 2014; Andersson 2013; Bonjer 2015; van der Pas 2013]; COREAN trial [Jeong 2014; Kang 2010]; Ishibe 2017; Liang 2011; Lujan 2011; Ng 2008; Ng 2009; Ng 2014; Zhou 2004)).

Three cohort studies compared robotic surgery to open surgery in people with rectal cancer (comparison 2) (Buonpane 2017; Corbellini 2016; Kim 2016).

Two RCTs and 8 cohort studies compared robotic surgery to laparoscopic surgery in people with rectal cancer (comparison 3) (Corbellini 2016; Ielpo 2017; Kim 2016; Kim 2017a; Kim 2017b; Law 2017; Park 2015; ROLARR trial [Jayne 2017]; Rouanet 2018; Yoo 2015).

One RCT (3 publications) compared TaTME to laparoscopic anterior resection in people with rectal cancer (comparison 4) (Bordeaux' trial [Denost 2017; Denost 2018; Pontallier 2016]).

See the literature search strategy in appendix B and study selection flow chart in appendix C.

Excluded studies

Studies not included in this review with reasons for their exclusions are provided in appendix K.

Summary of clinical studies included in the evidence review

Summaries of the studies that were included in this review are presented in Table 2.

Table 2: Summary of included studies

Study	Population	Intervention/Comparison	Outcomes
Comparison 1: Laparoscopic versus open surgery			
ACOSOG Z6051 trial (Fleshman 2015; Fleshman 2018) RCT USA	N=486 Adenocarcinoma of the rectum within 12 cm of the anal verge; clinical stage II, IIA, or IIB; ≥18 years of age; BMI <34; ECOG performance score <3	Everyone received preoperative therapy. Laparoscopic surgery included 17% hand-assisted laparoscopic surgery and 14% robot-assisted laparoscopic surgery. ~75-80% LAR ~20-25% APR	• Positive resection margins • Local or locoregional recurrence • Length of hospital stay • Operative mortality • Anastomotic leak • Blood loss
ALaCaRT trial (Stevenson 2015; Stevenson 2018) RCT Australia	N=475 Adenocarcinoma of the rectum within 15 cm of the anal verge; ≥18 years of age; life expectancy of >12 weeks; adequate performance status; no comorbidity or condition that would preclude the use of either form of surgery	~50% received preoperative radiotherapy ~90% LAR ~10% APR	• Overall survival • Positive resection margins • Local or locoregional recurrence
Arteaga Gonzalez 2006 RCT Spain	N=40 Rectal carcinoma <15 cm from the anal verge ~25% TNM stage I	Preoperative radiotherapy: T3 or T4 middle and lower third tumours or mesorectal adenopathy without distant metastases ~50% LAR	• Positive resection margins • Length of hospital stay • Anastomotic leak • Blood loss

Study	Population	Intervention/Comparison	Outcomes
		~25% APR ~25% Hartmann	
Braga 2007 RCT Italy	N=168 Adenocarcinoma of the rectum; ≥18 years of age; suitable for elective surgery ~30% Duke's stage I	Preoperative chemoradiotherapy: preoperative T3 cancers ~90% LAR ~10% APR	• Positive resection margins • Local or locoregional recurrence • Length of hospital stay • Operative mortality • Anastomotic leak • Surgical site infection • Blood loss
CLASICC trial (Green 2013; Guillou 2005; Jayne 2005; Jayne 2010; Quah 2002) RCT UK	N=381 Rectal or colon cancer suitable for right melicolectomy, left hemicolectomy, sigmoid colectomy, anterior resection, or abdominoperineal resection (only data on people with rectal cancer were considered for this review) Proportion of the population with T1-2N0M0 cancer (exact proportion not clear)	Not clear how many received preoperative therapy. ~65% AR ~25% APR ~10% other 4% of laparoscopic surgery and 17% of open surgery was palliative surgery	• Overall survival • Quality of life • Positive resection margins • Operative mortality • Surgical site infection
COLOR II trial (Andersson 2013; Andersson 2014; Bonjer 2015; van der Pas 2013) RCT Belgium, Canada, Denmark, Germany, the Netherlands, Poland, South	N=1,103 A single rectal cancer within 15 cm of the anal verge; no evidence of distant metastases; candidate for elective surgery ~30% clinical stage I	Preoperative radiotherapy: ~60% Preoperative chemotherapy: ~30% ~60% resection with TME ~10% resection with partial mesorectal excision ~25% APR ~5% Hartmann	• Overall survival • Quality of life • Positive resection margins • Local or locoregional recurrence • Length of hospital stay • Operative mortality • Anastomotic leak • Surgical site infection

Study	Population	Intervention/Comparison	Outcomes
Korea, Spain, Sweden			
COREAN trial (Jeong 2014; Kang 2010) RCT South Korea	N=340 Mid- or low-rectal cancer; T3N0-2M0; previous preoperative chemoradiotherapy; 18-80 years of age	Everyone received preoperative chemoradiotherapy. ~85-90% LAR ~10-15% APR	• Overall survival • Positive resection margins • Local or locoregional recurrence • Operative mortality • Anastomotic leak
Ishibe 2017 RCT Japan	N=58 Colorectal adenocarcinoma; ≥75 years of age; clinical stage of up to T4a tumours; any N stage; no evidence of metastasis; elective surgery (only data on people with rectal cancer was considered for this review) Note that this study was among people 75 years or older.	No one received preoperative therapy. ~65% LAR ~20% high AR ~10% APR	• Overall survival • Local or locoregional recurrence
Liang 2011 RCT China	N=343 Rectal cancer; without lung or liver metastases; BMI ≤30; no preoperative therapy ~5% T1-2N0M0	No one received preoperative therapy. ~50% LAR ~50% APR	• Operative mortality • Anastomotic leak • Surgical site infection
Lujan 2009 RCT Spain	N=204 Mid and low rectal adenocarcinoma ~10-15% stage I	Preoperative therapy: ~75% ~75-80% AR ~20-25% APR	• Overall survival • Positive resection margins • Local or locoregional recurrence • Length of hospital stay • Operative mortality • Anastomotic leak

Study	Population	Intervention/Comparison	Outcomes
			• Surgical site infection • Blood loss
Ng 2008 RCT Hong Kong	N=99 Low rectal cancer within 5cm from the anal verge ~17-19% AJCC stage I	No one received preoperative therapy. 100% APR	• Overall survival • Positive resection margins • Local or locoregional recurrence • Length of hospital stay • Operative mortality • Surgical site infection • Blood loss
Ng 2009 RCT Hong Kong	N=153 Adenocarcinoma in the upper rectum (12-15cm from the anal verge) ~14-17% AJCC stage I	Preoperative therapy: not reported 100% AR	• Overall survival • Positive resection margins • Local or locoregional recurrence • Length of hospital stay • Operative mortality • Anastomotic leak • Surgical site infection • Blood loss
Ng 2014 RCT Hong Kong	N=80 Mid and low rectal cancer, lowest margin of tumour located between 5 and 12 cm from the anal verge ~13% AJCC stage I	No one received preoperative therapy. 100% sphincter-preserving surgery	• Overall survival • Positive resection margin • Local or locoregional recurrence • Length of hospital stay • Operative mortality • Surgical site infection • Anastomotic leak

Study	Population	Intervention/Comparison	Outcomes
			• Blood loss
Zhou 2004 RCT China	N=171 Rectal adenocarcinoma with the lowest margin of tumour located under the peritoneal reflection and 1.5 cm above the dentate line ~6% Duke's stage A	Preoperative therapy: not reported Laparoscopic surgery: anal sphincter-preserving resection Open surgery: type of surgery not clear	• Positive resection margins • Length of hospital stay • Operative mortality • Anastomotic leak • Surgical site infection
Comparison 2: Robotic versus open surgery			
Buonpane 2017 Retrospective cohort study This is a 3-arm study comparing robotic versus laparoscopic versus open surgery but only robotic versus open surgery is considered in this review. USA	N=16,672 Surgically resected rectal cancer Data obtained from a national oncology database. A proportion of the population with T1-2N0M0 (not clear how many) ~6-10% metastatic disease	Preoperative radiotherapy: ~60% Preoperative chemotherapy: ~60% Type of surgery not reported.	• Positive resection margins
Corbellini 2016 Prospective cohort study This is a 3-arm study comparing robotic versus laparoscopic versus open surgery. Italy	N=120 A single rectal cancer within 12 cm of the anal verge; without evidence of distant metastases; candidates for elective, good-chance surgeries ~20-25% pathologic stage I (clinical stage not reported)	Preoperative therapy recommended to locally advanced cancers. ~80-90% AR ~10-20% APR	• Overall survival • Positive resection margins
Kim 2016 Prospective cohort study This is a 3-arm study	N=1,628 Curatively resected adenocarcinoma of the rectum; stage ≤ III; ECOG performance status of 0-3; ≤75 years of age	Preoperative chemoradiotherapy: 32% robotic surgery, 51% open surgery ~85-95% LAR ~1-3% AR	• Overall survival • Quality of life • Positive resection margins

Study	Population	Intervention/Comparison	Outcomes
comparing robotic versus laparoscopic versus open surgery. South Korea	~25% AJCC clinical stage 0-I	~5-10% APR	
Comparison 3: Robotic versus laparoscopic surgery			
Corbellini 2016 Prospective cohort study This is a 3-arm study comparing robotic versus laparoscopic versus open surgery. Italy	N=105 A single rectal cancer within 12cm from the anal verge; without evidence of distant metastases; candidates for elective, good-chance surgeries ~25-35% pathologic stage I (clinical stage not reported) Italy	Preoperative therapy recommended to locally advanced cancers. ~90-95% AR ~3-10% APR	• Overall survival
Ielpo 2017 Retrospective cohort study Spain	N=198 Rectal cancer; underwent laparoscopic or robotic surgery; not T4 cancer Proportion of population with T1-2N0M0 not clear.	Preoperative therapy: ~77% ~65-70% LAR ~25-30% APR ~5% colo-anal anastomosis	• Overall survival
Kim 2016 Prospective cohort study This is a 3-arm study comparing robotic versus laparoscopic versus open surgery South Korea	N=1,628 Curatively resected adenocarcinoma of the rectum; stage ≤ III; ECOG performance status of 0-3; ≤75 years of age ~25% AJCC clinical stage 0-I	Preoperative chemoradiotherapy: 32% robotic surgery, 51% open surgery ~85-95% LAR ~1-3% AR ~5-10% APR	• Overall survival • Quality of life • Positive resection margins
Kim 2017a RCT South Korea	N=163 Rectal adenocarcinoma within 9 cm from the anal verge; without distant metastasis	Preoperative chemoradiotherapy: ~80% ~95-99% LAR ~1-3% APR	• Quality of life • Positive resection margins

Study	Population	Intervention/Comparison	Outcomes
	Proportion of population with T1-2N0M0 not clear.		
Kim 2017b Retrospective cohort study South Korea	N=448 Rectal adenocarcinoma within 15cm of the anal verge; underwent minimally invasive surgery for rectal cancer 28% pathologic TNM stage I (clinical stage was not reported)	Preoperative chemoradiotherapy: ~20% ~75% LAR ~2% AR ~15% intersphincteric resection ~5% APR	• Overall survival • Quality of life • Positive resection margins • Length of hospital stay • Anastomotic leak • Blood loss
Law 2017 Retrospective cohort study Hong Kong	N=391 Rectal cancer within 12cm from the anal verge; underwent elective radical resection ~30% stage 0-I	Preoperative radiotherapy: ~30-40% ~90-95% LAR ~5-8% APR ~1-3% Hartmann	• Overall survival
Park 2015 Prospective cohort study South Korea	N=217 Rectal adenocarcinoma; underwent low anterior resection by robotic or conventional laparoscopic approach ~30% postoperative pathologic stage I (preoperative/clinical stage not reported)	Preoperative chemoradiotherapy: ~11% 100% AR	• Overall survival
ROLARR trial (Jayne 2017) RCT Australia, Denmark, Finland, France, Germany, Italy, Singapore,	N=471 Adenocarcinoma of the rectum; fit for resectional surgery Proportion of population with T1-2N0M0 not clear.	Preoperative radiotherapy or chemoradiotherapy: ~46% ~65-70% LAR ~10% high AR ~20% APR	• Quality of life • Positive resection margins • Length of hospital stay • Operative mortality • Anastomotic leak • Surgical site infection

Study	Population	Intervention/Comparison	Outcomes
South Korea, UK, US			
Rouanet 2018 Retrospective cohort study France	N=400 Histologically proven adenocarcinoma located 12 cm from the anal verge who underwent minimally invasive surgery (laparoscopic or robotic TME), with no previous or concurrent malignancy and no evidence of distant metastasis at time of surgery.	Laparoscopic TME (n=200) vs robotic TME (n=200)	• Overall survival
Yoo 2015 Retrospective cohort study South Korea	N=70 Rectal cancer <5 cm from the anal verge; treated via laparoscopic or robotic intersphincteric resection Proportion of the population with T1-2N0M0 not clear. ~10% with metastatic disease South Korea	Preoperative chemoradiotherapy: 54% robotic, 27% laparoscopic 100% intersphincteric resection	• Overall survival
Comparison 4: TaTME versus laparoscopic surgery			
Bourdeaux' Trial (Denost 2018; Pontallier 2016) RCT France	N=100 Rectal cancer <6 cm from the anal verge; suitable for laparoscopic sphincter-saving resection Small proportion possibly with T1-2N0M0 but not clear (~80% T3-4 and ~60% N+)	Preoperative radiotherapy: ~80-90% Preoperative chemotherapy: ~80% Laparoscopic surgery: sphincter-preserving resection	• Overall survival • Quality of life • Positive resection margins • Local recurrence • Length of hospital stay • Operative mortality • Anastomotic leak (and/or abscess)

AJCC: American Joint Committee on Cancer; APR: abdominoperineal resection; AR: anterior resection; BMI: body mass index; ECOG: Eastern Cooperative Oncology Group; LAR: lower anterior resection; N: number; RCT: randomised controlled trial; T: tumour stage; TaTME: transanal total mesorectal excision: TME: total mesorectal excision; TNM: tumour, node, metastasis staging system

See the full evidence tables in appendix D and the forest plots in appendix E.

Quality assessment of clinical studies included in the evidence review

See the clinical evidence profiles in appendix F.

Economic evidence

Included studies

A systematic review of the economic literature was conducted but no economic studies were identified which were applicable to this review question.

Excluded studies

A global search of economic evidence was undertaken for all review questions in this guideline. See Supplement 2 for further information.

Economic model

An economic analysis was undertaken to estimate the cost-effectiveness of surgical techniques for rectal cancer (see appendix J for the full report of the economic analysis).

Methods

The analysis was developed in Microsoft Excel® and was conducted from the perspective of the NHS and Personal Social Services (PSS) as outlined in the NICE Reference Case (see Developing NICE guidelines: the manual). The model considered a lifetime horizon with future costs and benefits discounted at a rate of 3.5% (as recommended in the NICE reference case).

Clinical data and model approach

The economic analysis was based on clinical effectiveness data for each of the surgical techniques, which was sourced from the clinical evidence review. However, only the comparison between the open and laparoscopic approach provided sufficient data for all the key outcomes of interest for the economic analysis (overall survival, local recurrence and complications). As a result, a decision was made to separately consider two comparisons in the analysis. In the first, a comparison is made between the open and laparoscopic approach based on evidence from the clinical evidence review. In the second, all four surgical approaches are considered using available data from the clinical evidence review in combination with assumptions to fill in the missing data. The second analysis was therefore considered to be more speculative and the conclusions that can be drawn from the analysis were limited.

Costs

The costs considered in the model reflect the perspective of the analysis, thus only costs that are relevant to the UK NHS & PSS were included. Where possible, all costs were estimated in 2016/17 prices.

The majority of costs were sourced from NHS reference costs 2016/17 by applying tariffs associated with the appropriate Healthcare Resource Groups (HRG) code. However, note that the cost of the surgical procedure in NHS reference costs (FF31: complex large intestine procedures, 19 years and over) is the same regardless of the approach taken. Therefore, this cost was not estimated using the procedure code from NHS reference costs and an alternative approach was adopted in order to differentiate the various surgical techniques.

Surgical equipment costs were estimated using data from a cost-effectiveness analysis of surgical approaches in prostate cancer (Ramsay 2012), with costs inflated to 2016 prices. Equipment costs were estimated to be £1,502, £1,605, £4,628 and £1,815 for the open, laparoscopic, robotic and TaTME approaches, respectively. Operative time costs were estimated using average theatre time estimates reported in Ramsay 2012. A cost for an hour of operating theatre time was sourced from the cost-effectiveness analysis from Ramsay 2012 and inflated to 2016 prices (£1,266). Length of stay costs were estimated using data on the length of stay in hospital following each procedure from the studies included in the clinical evidence review combined with the cost of an excess bed day from NHS reference costs 2016/17.

Complication costs were estimated using the different costs associated with complication and co-morbidity (CC) scores for the surgical procedure from NHS reference costs. The difference between CC score 0-2 and an average of the other CC scores associated with complex large intestine procedures (FF31) was used as an estimate of complication costs.

Systemic chemotherapy costs were estimated assuming that patients would be treated with 6 cycles of FOLFIRI or FOLFOX. The chemotherapy delivery costs were sourced from NHS Reference Costs 2015/16 (assuming day case delivery) and drug costs were sourced from eMit.

The cost of palliative care was estimated using estimates from a costing report by the Nuffield Trust (Georghiou 2014). A cost of £7,287 was applied based on the average resource use of patients with cancer in the last three months of life.

Health-related quality of life

As recommended in the NICE reference case, the model estimates effectiveness in terms of quality adjusted life years (QALYs). These are estimated by combining life year estimates with quality of life (QoL) values associated with being in a particular health state.

QoL data for all comparisons were sourced from Rao 2017, a cost-effectiveness analysis that estimated QoL for recurrences (0.78) and for being recurrence free (0.86).

Base case results

The base case results of the analysis, based on the point estimates of the model inputs, are shown in Table 15 and Table 16 for the two-way and four-way comparison respectively. The results of the two-way comparison show the laparoscopic approach to be more effective (1.26 QALYs) and less costly than the open approach (£921) and it is therefore dominant. These results are driven by improvements in overall survival which are clinically significant.

In the four-way comparison, alternative approaches were compared using a net monetary benefit approach assuming a threshold of £20,000 per QALY. The results show the TaTME approach to be the least costly approach. All other strategies are found to be more costly and less effective than TaTME and are therefore dominated. Consequently, net monetary benefit was negative for all other interventions. However it should be noted for TaTME that the results are driven by improvements in overall survival and recurrence which were based on a hazard ratio for which the 95% confidence interval passed the line of no effect. It is therefore plausible that TaTME may result in lower QALYs and higher costs (through increased recurrence) compared to alternative approaches. These results should therefore be considered speculative.

Table 3: Base case results for two-way comparison

Strategy	Cost		QALYs		ICER (cost per QALY
	Total	Incremental	Total	Incremental	
Open	£11,963	-	9.08	-	-
Laparoscopic	£11,042	*-£921*	10.34	*1.26*	**Dominant**

ICER: incremental cost-effectiveness ratio; QALYs: quality adjusted life years

Table 4: Base case results for four-way comparison

Strategy	Cost		QALYs		ICER (cost per QALY	NMB
	Total	Incremental	Total	Incremental		
TaTME	£9,812	-	11.15	-	-	
Laparoscopic	£11,042	£1,230	10.34	-0.81	**Dominated**	*-£17,395*
Open	£11,963	£2,151	9.08	-2.07	**Dominated**	*-£43,575*
Robotic	£15,612	£5,800	9.92	-1.24	**Dominated**	*-£30,503*

ICER: incremental cost-effectiveness ratio; QALYs: quality adjusted life years NMB Net monetary benefit

Deterministic sensitivity results

A series of deterministic sensitivity analyses were conducted, whereby an input parameter is changed, the model is re-run and the new cost-effectiveness result is recorded. This is a useful way of estimating uncertainty and determining the key drivers of the model result. The results of the deterministic sensitivity analyses are presented in Table 5 and Table 6 for the two-way and four-way comparison, respectively.

In the two way comparison, it can again be seen that the conclusion of the analysis remains unchanged in the majority of modelled scenarios with the laparoscopic approach found to be cost-effective. Notably this includes a scenario in which only statistically significant effects are modelled. The conclusion of the analysis was found to change when the upper hazard ratio (HR) for overall survival was applied (meaning that overall survival is better with the open approach).

In the four way comparison, it can again be seen that the conclusion of the analysis remains unchanged in the majority of modelled scenarios with TaTME found to be cost-effective. However, notably, this does not includes a scenario in which only statistically significant effects are modelled (in which the laparoscopic approach is found to be cost-effective). The laparoscopic approach was also found to be cost-effective when the upper HR for overall survival for TaTME was applied or when overall survival was assumed to be equivalent with laparoscopic and TaTME. The open approach was found to be cost-effective when the upper HR for overall survival for TaTME and the laparoscopic approach was applied.

Table 5: Deterministic sensitivity results for two-way comparison

Modelled scenario	Optimal strategy
Base case	Laparoscopic
Overall survival – lower HR	Laparoscopic
Overall survival – upper HR	Laparoscopic
Local recurrence – lower RR	Laparoscopic
Local recurrence – upper RR	Laparoscopic
Complications – lower RR	Laparoscopic

Modelled scenario	Optimal strategy
Complications – upper RR	Laparoscopic
Statistically significant changes only	Laparoscopic
Number of robotic procedures per year = 50	Laparoscopic
Number of robotic procedures per year = 100	Laparoscopic
Number of robotic procedures per year = 200	Laparoscopic
Complication costs + 50%	Laparoscopic
Complication costs - 50%	Laparoscopic
No systemic chemotherapy costs	Laparoscopic
No palliative care costs	Laparoscopic
No recurrence disutility	Laparoscopic

1 *HR: hazard ratio: RR: relative risk*

2 **Table 6: Deterministic sensitivity results for four-way comparison**

Modelled scenario	Optimal strategy
Base case	TaTME
Overall survival – lower HR for laparoscopic	TaTME
Overall survival – upper HR for laparoscopic	TaTME
Overall survival – lower HR for TaTME	TaTME
Overall survival – upper HR for TaTME	***Laparoscopic***
Overall survival with TaTMEequivalent to laparoscopic	***Laparoscopic***
Overall survival – upper HR for TaTME and laparoscopic	***Open***
Absolute overall survival with robotic 10% higher	TaTME
Absolute overall survival with robotic 10% lower	TaTME
Local recurrence – lower RR for laparoscopic	TaTME
Local recurrence – upper RR for laparoscopic	TaTME
Absolute local recurrence with TaTME 10% higher	TaTME
Absolute local recurrence with TaTME 10% lower	TaTME
Local recurrence with TaTME equivalent to laparoscopic	TaTME
Complications – lower RR	TaTME
Complications – upper RR	TaTME
Statistically significant changes only	***Laparoscopic***
Number of robotic procedures per year = 50	TaTME
Number of robotic procedures per year = 100	TaTME
Number of robotic procedures per year = 200	TaTME
Complication costs + 50%	TaTME
Complication costs - 50%	TaTME
No systemic chemotherapy costs	TaTME
No palliative care costs	TaTME
No recurrence disutility	TaTME

3 *HR: hazard ratio; RR: relative risk; TaTME: transanal total mesorectal excision*

Evidence statements

Clinical evidence statements

Comparison 1: Laparoscopic versus open surgery

Critical outcomes

Overall survival

- Moderate quality evidence from 9 RCTs (N=2731; median follow-up 3.2 to 9.2 years) showed a clinically important improvement in the overall survival of people who underwent laparoscopic surgery for non-metastatic rectal cancer when compared to those who had open surgery.

Quality of life

- Very low quality evidence from 1 RCT (N=338) showed no clinically important difference in global quality of life at 4 weeks, 6 months or 12 months after surgery (self-assessed using QLQ-C30) between people who underwent laparoscopic or open surgery for non-metastatic rectal cancer.
- Very low quality evidence from 1 RCT (N=336) showed no clinically important difference in global health status at 4 weeks, 6 months or 12 months after surgery (self-assessed using EQ-VAS) between people who underwent laparoscopic or open surgery for non-metastatic rectal cancer.
- Very low quality evidence from 1 RCT (N=168) showed a clinically importantly higher general health score at 12 months after surgery (self-assessing using SF-36) in people who underwent laparoscopic surgery compared to those who underwent open surgery for non-metastatic rectal cancer. However, at 24 months after surgery there was no difference in the same general health score.
- Very low quality evidence from 1 RCT (N=1,103) showed no clinically important difference in sexual functioning at 4 weeks, 6, 12 or 24 months after surgery (self-assessed using QLQ-CR38) between people who underwent laparoscopic or open surgery for non-metastatic rectal cancer.
- Very low quality evidence from 1 RCT (N=1,103) showed no clinically important difference in sexual enjoyment at 6, 12 or 24 months after surgery (self-assessed using QLQ-CR38) between people who underwent laparoscopic or open surgery for non-metastatic rectal cancer.
- Very low quality evidence from 1 RCT (N=1,103) showed no clinically important difference in sexual problems at 6, 12 or 24 months after surgery (self-assessed using QLQ-CR38) between women who underwent laparoscopic or open surgery for non-metastatic rectal cancer.
- Very low quality evidence from 1 RCT (N=46) showed no clinically important difference in overall sexual dysfunction after surgery (self-assessed using FSFI) between women who underwent laparoscopic or open surgery for non-metastatic rectal cancer.
- Very low quality evidence from 1 RCT (N=1,103) showed no clinically important difference in sexual problems at 4 weeks, 6, 12 or 24 months after surgery (self-assessed using QLQ-CR38) between men who underwent laparoscopic or open surgery for non-metastatic rectal cancer.
- Very low quality evidence from 1 RCT (N=37) showed a clinically important increased risk of overall sexual dysfunction at median 3 years after surgery (self-assessed using IIEF) in previously sexually active men who underwent

laparoscopic surgery compared to those who underwent open surgery for non-metastatic rectal cancer.

- Very low quality evidence from 1 RCT (N=82) showed no clinically important difference in perceived severe change in overall level of sexual function after surgery (self-assessed using IIEF) in men who underwent laparoscopic or open surgery for non-metastatic rectal cancer.
- Very low quality evidence from 1 RCT (N=1,103) showed no clinically important difference in micturitional symptoms at 4 weeks, 6, 12, or 24 months after surgery (self-assessed using QLQ-CR38) between people who underwent laparoscopic or open surgery for non-metastatic rectal cancer.
- Very low quality evidence from 1 RCT (N=148) showed "no differences in bladder function, either in overall score or in individual symptom scores" at 2 weeks, 3, 6, and 18 months after surgery (self-assessed using IPSS and QLQ-CR38) between people who underwent laparoscopic or open surgery for non-metastatic rectal cancer (reported narratively only).

Resection margins

- Moderate quality evidence from 9 RCTs (N=2,246) showed no clinically important difference in positive CRM (defined as <1 mm, ≤1 mm or not defined) between people who underwent laparoscopic or open surgery for non-metastatic rectal cancer.
- Low quality evidence from 1 RCT (N=888) showed no clinically important difference in positive CRM (defined as <2 mm) between people who underwent laparoscopic or open surgery for non-metastatic rectal cancer.
- Low quality evidence from 5 RCTs (N=1,347) showed no clinically important difference in positive distal resection margin between people who underwent laparoscopic or open surgery for non-metastatic rectal cancer.
- Moderate quality evidence from 1 RCT (N=462) showed no clinically important difference in positive radial resection margin (defined as ≤1 mm) between people who underwent laparoscopic or open surgery for non-metastatic rectal cancer.
- Very low quality evidence from 1 RCT (N=40) showed no clinically important difference in positive radial resection margin (defined as ≤2 mm) between people who underwent laparoscopic or open surgery for non-metastatic rectal cancer.

Low quality evidence from 1 RCT (N=171) showed that 0 people who underwent either laparoscopic or open surgery for non-metastatic rectal cancer had positive resection margins (defined as "cancer cell found in the cut margins").

Important outcomes

Local recurrence

- Moderate quality evidence from 3 RCTs (N=701; median follow-up ranging from 3.2 to 4 years) showed no clinically important difference in local recurrence free survival between people who underwent laparoscopic or open surgery for non-metastatic rectal cancer.
- Low quality evidence from 9 RCTs (N=2,520; median follow-up ranging from 3 to 7.5 years) showed no clinically important difference in local or locoregional recurrence rates between people who underwent laparoscopic or open surgery for non-metastatic rectal cancer.

Length of hospital stay

- Meta-analysis of length of hospital stay showed considerable heterogeneity, therefore, subgroup analysis according to type of surgical resection was done.
- Very low quality evidence from 4 RCTs (N=1,750) showed no clinically important difference in mean length of hospital stay between people who underwent laparoscopic or open anterior resection or abdominoperineal resection for non-metastatic rectal cancer. Low quality evidence from one 1 RCT (N=381) showed no clinically important difference in median length of hospital stay between people who underwent laparoscopic or open anterior resection or abdominoperineal resection for non-metastatic rectal cancer.
- Low quality evidence from 4 RCTs (N=572) showed a clinically important lower mean length of hospital stay in people who underwent laparoscopic sphincter-preserving surgery compared to open sphincter-preserving surgery for non-metastatic rectal cancer. Moderate quality evidence from 2 RCTs (N=815) showed no clinically important difference in median length of hospital stay in people who underwent laparoscopic or open sphincter-preserving surgery for non-metastatic rectal cancer.
- Low quality evidence from 1 RCT (N=99) showed no clinically important difference in mean length of hospital stay in people who underwent laparoscopic or open abdominoperineal surgery for non-metastatic rectal cancer.

90-day mortality

- Low quality evidence from 4 RCTs (N=2,053) showed no clinically important difference in 30-day mortality between people who underwent laparoscopic or open surgery for non-metastatic rectal cancer.
- Moderate quality evidence from 1 RCT (N=340) showed no deaths within 90 days of surgery in people who underwent either laparoscopic or open surgery for non-metastatic rectal cancer.
- Low quality evidence from 6 RCTs (N=1,408) showed no clinically important difference in operative mortality (timeframe not defined) between people who underwent laparoscopic or open surgery for non-metastatic rectal cancer.

Treatment-related complications: anastomotic leak

- Low quality evidence from 10 RCTs (N=2,616) showed no clinically important difference in anastomotic leak between people who underwent laparoscopic or open surgery for non-metastatic rectal cancer.

Treatment-related complications: surgical site infection

- Low quality evidence from 10 RCTs (N=2,678) showed no clinically important difference in surgical site infection between people who underwent laparoscopic or open surgery for non-metastatic rectal cancer.

Treatment-related complications: blood loss

- Meta-analysis of blood loss showed considerable heterogeneity, therefore, subgroup analysis according to type of surgical resection was done.
- Moderate quality evidence from 3 RCTs (N=695) showed a clinically important lower mean blood loss in people who underwent laparoscopic anterior resection or abdominoperineal resection compared to those who underwent open anterior resection or abdominoperineal resection for non-metastatic rectal cancer. Moderate quality evidence from 1 RCT (N=1,044) showed that the median blood loss was significantly lower in people who underwent laparoscopic anterior

resection or abdominoperineal resection compared to those who underwent open anterior resection or abdominoperineal resection for non-metastatic rectal cancer.

- Moderate quality evidence from 4 RCTs (N=572) showed a clinically important lower mean blood loss in people who underwent laparoscopic sphincter-preserving surgery compared to those who underwent open sphincter-preserving surgery for non-metastatic rectal cancer. Moderate quality evidence from 2 RCTs (N=815) showed that the median blood loss was significantly lower in people who underwent laparoscopic sphincter-preserving surgery compared to those who underwent open sphincter-preserving surgery for non-metastatic rectal cancer.
- Low quality evidence from 1 RCT (N=99) showed no difference in mean blood loss between people who underwent laparoscopic or open abdominoperineal resection for non-metastatic rectal cancer.

Comparison 2: Robotic versus open surgery

Critical outcomes

Overall survival

- Very low quality evidence from 1 prospective and 1 retrospective cohort study (N=1,691) showed no clinically important difference in overall survival at 3 years between people who underwent robotic surgery compared to those who underwent open surgery for non-metastatic rectal cancer.

Quality of life

- Very low quality evidence from 1 prospective cohort study (N=473) showed a clinically important lower risk of moderate or severe sexual dysfunction in men 65 years or younger (self-assessed using VAS) who underwent robotic surgery compared to those who underwent open surgery for non-metastatic rectal cancer. When looking at severe and moderate sexual dysfunction separately, there was no difference in severe sexual dysfunction (VAS 4-5) between the groups but a clinically important lower risk of moderate sexual dysfunction (VAS 2-3) in men 65 years or younger who underwent robotic surgery compared to those who underwent open surgery.

Resection margins

- Very low quality evidence from 1 retrospective cohort study (N=16,672) showed a clinically important lower risk of positive resection margin (not defined) in people who underwent robotic surgery compared to those who underwent open surgery for non-metastatic rectal cancer.
- Very low quality evidence from 1 prospective cohort study (N=1,628) showed no clinically important difference in positive CRM (defined as ≤1 mm) between people who underwent robotic or open surgery for non-metastatic rectal cancer.
- Very low quality evidence from 1 prospective cohort study (N=120) showed no clinically important difference in R1 resection between people who underwent robotic or open surgery for non-metastatic rectal cancer.
- Very low quality evidence from 1 prospective cohort study (N=1,628) showed no clinically important difference in positive distal resection margin (defined as ≤5 mm) between people who underwent robotic or open surgery for non-metastatic rectal cancer.

Important outcomes

Local recurrence

No RCT evidence was identified to inform this outcome.

Length of hospital stay

No RCT evidence was identified to inform this outcome.

90-day mortality

No RCT evidence was identified to inform this outcome.

Treatment-related complications: anastomotic leak

No RCT evidence was identified to inform this outcome.

Treatment-related complications: surgical site infection

No RCT evidence was identified to inform this outcome.

Treatment-related complications: blood loss

No RCT evidence was identified to inform this outcome.

Comparison 3: Robotic versus laparoscopic surgery

Critical outcomes

Overall survival

- Very low quality evidence from 2 prospective and 6 retrospective cohort studies (N=2,771) with median follow-up 3 to 5 years showed no clinically important difference in overall survival between people who underwent robotic or laparoscopic surgery for non-metastatic rectal cancer.

Quality of life

- Very low quality evidence from 1 RCT (N=139) showed no clinically important difference in global health status at 3 weeks, 3 and 12 months after surgery (self-assessed using QLQ-C30) between people who underwent robotic or laparoscopic surgery for non-metastatic rectal cancer.
- Very low quality evidence from 1 RCT (N=139) showed a clinically important better sexual function score at 12 months (self-assessed using QLQ-CR38) in people who underwent robotic surgery compared to those who underwent laparoscopic surgery for non-metastatic rectal cancer.
- Very low quality evidence from 1 RCT (N=471) showed no clinically important difference in female sexual function at 6 months (self-assessed using FSFI) between women who underwent robotic or laparoscopic surgery for non-metastatic rectal cancer.
- Very low quality evidence from 1 RCT (N=471) showed no clinically important difference in male sexual function at 6 months (self-assessed using IIEF) between men who underwent robotic or laparoscopic surgery for non-metastatic rectal cancer.
- Very low quality evidence from 1 RCT (N=471) showed no clinically important difference in bladder function at 6 months (self-assessed using IPSS) between

people who underwent robotic or laparoscopic surgery for non-metastatic rectal cancer.

Resection margins

- Very low quality evidence from 2 RCTs (N=598) showed no clinically important difference in positive CRM (defined as ≤1 mm) between people who underwent robotic or laparoscopic surgery for non-metastatic rectal cancer.
- Very low quality evidence from 1 RCT (N=471) showed no clinically important difference in positive distal resection margin between people who underwent robotic or laparoscopic surgery for non-metastatic rectal cancer. In the same trial, no positive proximal resection margins were observed.

Important outcomes

Local recurrence

No RCT evidence was identified to inform this outcome.

Length of hospital stay

- Very low quality evidence from 2 RCTs (N=610) showed no clinically important difference in length of hospital stay between people who underwent robotic or laparoscopic surgery for non-metastatic rectal cancer.

90-day mortality

- Very low quality evidence from 1 RCT (N=471) showed no clinically important difference in 30-day mortality between people who underwent robotic or laparoscopic surgery for non-metastatic rectal cancer.

Treatment-related complications: anastomotic leak

- Very low quality evidence from 2 RCTs (N=500) showed no clinically important difference in anastomotic leak between people who underwent robotic or laparoscopic surgery for non-metastatic rectal surgery.

Treatment-related complications: surgical site infection

- Very low quality evidence from 1 RCT (N=471) showed no clinically important difference in surgical site infection within 30 days from the operation or between 30 days and 6 months from the operations between people wo underwent robotic or laparoscopic surgery for non-metastatic rectal cancer.

Treatment-related complications: blood loss

- Low quality evidence from 1 RCT (N=139) showed a clinically important higher blood loss in people who underwent robotic surgery compared to those who underwent laparoscopic surgery for non-metastatic rectal cancer.

Comparison 4: Transanal total mesorectal excision versus laparoscopic surgery

Critical outcomes

Overall survival

- Low quality evidence from 1 RCT (N=100) showed no clinically important difference in overall survival at 5 years between people who underwent TaTME or laparoscopic anterior resection for non-metastatic rectal cancer.

Quality of life

- Very low quality evidence from 1 RCT (N=51) showed a clinically important higher rate of maintained sexual activity at median 3.2 years after treatment in previously sexually active people who underwent TaTME compared to those who underwent laparoscopic anterior resection for non-metastatic rectal cancer.
- Very low quality evidence from 1 RCT (N=39) showed no clinically important difference in erectile function at median 3.2 years after treatment (self-assessed using IIEF) between men who underwent TaTME or laparoscopic anterior resection for non-metastatic rectal cancer.
- Very low quality evidence from 1 RCT (N=37) showed no clinically important difference in ejaculatory function at median 3.2 years after treatment (self-assessed using IIEF) between previously sexually active men who underwent TaTME or laparoscopic anterior resection for non-metastatic rectal cancer.
- Very low quality evidence from 1 RCT (N=8) showed no clinically important difference in female sexual function after treatment (self-assessed using FSFI) between previously sexually active female who underwent TaTME or laparoscopic anterior resection for non-metastatic rectal cancer.
- Very low quality evidence from 1 RCT (N=72) showed no sclinically important difference in median urinary function quality of life score or median urinary function total score after treatment (self-assessed using IPSS) in people who underwent TaTME or laparoscopic anterior resection for non-metastatic rectal cancer.

Resection margins

- Low quality evidence from 1 RCT (N=100) showed a clinically important lower risk of R1 resection (defined as positive CRM) in people who underwent TaTME compared to those who underwent laparoscopic anterior resection for non-metastatic rectal cancer.
- Low quality evidence from 1 RCT (N=100) showed no clinically important difference in positive distal margin between people who underwent TaTME or laparoscopic anterior resection for non-metastatic rectal cancer.

Important outcomes

Local recurrence

- Low quality evidence from 1 RCT (N=100) showed no clinically important difference in local recurrence at 5 years between people who underwent TaTME or laparoscopic anterior resection for non-metastatic rectal cancer.

Length of hospital stay

- Low quality evidence from 1 RCT (N=100) showed no clinically important difference in median length of hospital stay between people who underwent TaTME or laparoscopic anterior resection for non-metastatic rectal cancer.

90-day mortality

- Low quality evidence from 1 RCT (N=100) showed no clinically important difference in postoperative mortality between people who underwent TaTME or laparoscopic anterior resection for non-metastatic rectal cancer.

Treatment-related complications: anastomotic leak

- Low quality evidence from 1 RCT (N=100) showed no clinically important difference in anastomotic leak and/or abscess between people who underwent TaTME or laparoscopic anterior resection for non-metastatic rectal cancer.

Treatment-related complications: surgical site infection

No RCT evidence was identified to inform this outcome.

Treatment-related complications: blood loss

No RCT evidence was identified to inform this outcome.

Comparison 5: Transanal total mesorectal excision versus open surgery

No evidence was identified for this comparison.

Comparison 6: Transanal total mesorectal excision versus robotic surgery

No evidence was identified for this comparison.

Economic evidence statements

One bespoke economic model developed for this review question taking a UK NHS and PSS perspective and using clinical parameters from the accompanying clinical evidence review suggested that a laparoscopic approach was both cost saving and health improving compared to an open approach. Probabalistic sensitivity analysis concluded this result was robust with a 93% probability of laparoscopic approach being cost effective when QALYs are valued at £20,000 each. A speculative analysis gave very favourable results for TaTME compared to an open, laparoscopic and robotic approaches. However, there was great uncertainty around the inputs for this model and consequently the conclusions with results sensitive to assumptions around overall survival.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

Overall survival, quality of life and resection margins were considered critical outcomes for decision making. Overall survival was considered a critical outcome because ultimately the aim of cancer treatment is to improve survival. From the patient's perspective it is also critical to consider the effect on quality of life. Quality of life in terms of sexual function and bladder function were of particular interest to this review because of the potential effects that the different surgical techniques might

have on these. Impaired sexual function and bladder function can both have a significant impact on a person's quality of life. Resection margins were considered a critical outcome because a cancer-positive resection margin is a predictor for cancer recurrence.

Local recurrence, length of hospital stay, mortality within 90 days of surgery and treatment-related complications were considered important outcomes.

The quality of the evidence

Evidence was available for the comparison of laparoscopic versus open surgery (comparison 1), robotic versus open surgery (comparison 2), robotic versus laparoscopic surgery (comparison 3), and transanal total mesorectal excision (TaTME) versus laparoscopic surgery (comparison 4). No evidence was identified for the comparison of TaTME versus open surgery or of TaTME versus robotic surgery.

Evidence was available for all of the outcomes for comparison 1. The quality of the clinical evidence was assessed using GRADE and varied from low to moderate quality. For comparison 2, evidence was available for all critical outcomes but no evidence was available for important outcomes (local recurrence, length of hospital stay, 90-day mortality, and treatment–related complications). The quality of the evidence was assessed using GRADE and was of very low quality. For comparison 3 evidence was available for all outcomes except local recurrence and for comparison 4 evidence was available for all outcomes except surgical site infection and blood loss. The quality of the evidence for these comparisons was assessed using GRADE: for comparison 3 the evidence was mostly of very low quality and varied from very low to low and for comparison 4 it was mostly of low quality, varying from very low to low quality.

The main reasons for downgrading the quality of evidence were population indirectness, imprecision of the effect estimate, and risk of bias due to lack of blinding.

Some of the studies included a proportion of participants with early rectal cancer (T1-2, N0, M0) or metastatic rectal cancer which were out of the scope for this review and the quality of evidence was therefore downgraded for population indirectness.

For some outcomes, there was considerable uncertainty in the effect estimate due to the small number of participants or low number of events, in which case the evidence was downgraded for imprecision.

Blinding of personnel, patients and outcome assessors was generally not done or not possible to do. Lack of blinding might influence outcome measurement, particularly for outcomes that are subjective in nature. Therefore, for subjective outcomes such as quality of life, the quality of evidence was downgraded due to risk of detection bias.

Benefits and harms

Over time, minimally invasive surgical techniques, including laparoscopic surgery, have been developed in order to lower operative complications and adverse events and speeding up recovery without compromising the long-term effectiveness of surgery on survival and disease recurrence. Laparoscopic surgery for rectal cancer is commonly used in current practice alongside open surgery and the choice of technique is sometimes dependent on the skills and experience of the surgeon rather than the clinical effectiveness or appropriateness of either technique.

Clinical evidence on the long-term effectiveness of laparoscopic surgery compared to open surgery indicated an overall survival benefit with laparoscopic surgery with no clinically important difference in local recurrence rates.

The committee also considered the short-term effectiveness of laparoscopic surgery compared to open surgery. No overall difference was observed in positive resection margins. However, the committee discussed that there can be a long learning curve for laparoscopic surgery, which might be reflected in the results for resection margin and operative complications seen in some of the trials. The expectation is that the clinical effectiveness and safety of laparoscopic technique is now better than when most of the trials were conducted.

In general, there was no difference in length of hospital stay; however, a clinically important lower mean length of hospital stay was observed in people who underwent laparoscopic compared to open sphincter-preserving surgery for non-metastatic rectal cancer. No clinically important difference was observed in respect of quality of life, operative mortality, or anastomotic leak. As the committee expected, mean or median blood loss was lower in the laparoscopic group compared to the open group.

However, the committee agreed that in some cases open surgery is the most appropriate approach because of clinical or technical reasons. For example, scarring from previous abdominal or pelvic surgeries might make open surgery more feasible. Open surgery might also be more appropriate for technically demanding resection of adjacent organs or structures in locally advanced tumours.

In recent years robotic surgery has been introduced as another way of performing laparoscopic surgery. The robots are expensive but their technical advantages compared to the manual laparoscopic surgery include, for example, better visualisation, better freedom of movement, lack of tremor, and better ergonomics. Some clinical evidence was available comparing the robotic technique to either open or laparoscopic technique in rectal cancer surgery.

Low quality observational evidence was available comparing robotic surgery to open surgery. No difference was observed in overall survival. One study suggested a lower risk of positive resection margin with robotic approach, although two other studies found no difference between the groups. One study found less sexual dysfunction in men who underwent robotic surgery.

Robotic technique was compared to manual laparoscopic technique in one RCT and a few low quality observational studies. Overall, the evidence did not show the robotic approach to be better than manual laparoscopic approach. There was no difference in overall survival, overall quality of life, bladder function, resection margins, length of hospital stay, operative mortality, or anastomotic leak. One study showed better sexual function in the robotic group compared to manual laparoscopic group at 1 year after surgery.

TaTME is another relatively novel surgical approach to treat rectal cancers. TaTME has been suggested as a particularly useful approach in cancers in the low rectum in male patients because of the anatomical challenges of open or laparoscopic technique in this area, however, the evidence on this is lacking. The evidence base for this technique is small and the findings were statistically underpowered, therefore, the committee was not able to determine if TaTME is a clinically effective surgical technique to treat rectal cancer.

The committee was aware of the NICE interventional procedures guidance on transanal total mesorectal excision of the rectum (IPG514). The committee was also aware that TaTME has been suspended in Norway due to increased local recurrence

rates. Increased complication rates have also been attributed to TaTME, however, it is not impossible that these complications could happen in any operation in the pelvis. There is currently not enough evidence to show neither benefit nor harm from TaTME compared to more established techniques. COLOR III trial is currently recruiting patients to compare TaTME to laparoscopic technique.

After reviewing the clinical evidence on the different surgical techniques, the committee concluded that the clinical short- and long-term outcomes of laparoscopic technique were similar or better than of the open technique (although as discussed in certain cases the open approach is better) and that there seemed to be no difference between manual laparoscopic and robotic laparoscopic techniques. The committee agreed that in addition to the clinical effectiveness it is important to consider the costs of these difference techniques in order to assess which technique is the most cost effective approach in rectal cancer surgery.

The evidence showed no clinical benefit, clinically important higher blood loss but no other clinically important differences in complications no clinically important difference in complications (length of hospital stay, 90-day mortality, anastomotic leak, and surgical site infection) from the robotic technique. The committee recognised, however, that the robotic technique is already being used by certain centres in the UK. The committee would not want those centres with established programmes to stop performing robotic surgery but in the absence of clinical and cost effectiveness evidence in favour of robotic technique, the committee would only recommend robotic surgery to be considered within these established programmes. It was also considered important that audit data is collected within these programmes to assess the effectiveness and safety of robotic technique in clinical practice. The techniques and equipment of robotic surgery develop rapidly and more evidence on its usefulness will be available in the future.

Similarly, TaTME is used in some of centres in the UK. It was agreed that TaTME should be considered as a treatment option only within proctored programmes. These structured and supervised programmes should also collect outcome data for the national TaTME registry in order to enable assessment of the safety and effectiveness of TaTME in clinical practice.

Cost effectiveness and resource use

Bespoke economic modelling for this review question suggested that a laparoscopic approach to surgery would be both cost saving and health improving compared to an open approach. These increases in QALYs and cost savings were largely driven by survival parameters, which were clinically significant in the clinical evidence review favouring the laparoscopic approach. The deterministic and probabilistic sensitivity analysis results suggested that results were robust to alternative assumptions. The committee were therefore confident that recommending laparoscopic surgery was both cost effective and cost saving.

Whilst the bespoke economic analysis suggested that robotic surgery was not cost effective, the committee highlighted that this was a fast moving and expending area and as volumes increase (across all disease areas), costs of robotic surgery would decrease and, potentially, outcomes will also improve. For these reasons the committee thought that conclusions around cost effectiveness would become more favourable to robotic surgery potentially within a short period of time and recommending against it, based on current efficiency grounds, would be inappropriate. Given the above the committee recommended robotic surgery should only be considered in centres where there are already established programmes.

A speculative analysis as part of the bespoke economic analysis suggested that TaTME could be both cost saving and health improving compared to all other potential approaches. The committee however acknowledge that this was a new technique and that it was difficult to place a large amount of confidence in the results given the evidence to inform the model. The committee therefore only recommended its use in centres with structured and supervised programmes with appropriate auditing allowing for evaluation of the technique in future.

The committee were of the opinion that all recommendations were cost effective and all would potentially be cost saving within a short period of time compared to current practice. This would be largely driven by reducing the number of more intensive, expensive and potentially less effective procedures.

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Appendices

Appendix A – Review protocol

Review protocol for review question: What is the optimal surgical technique for rectal cancer?

Table 7: Review protocol for optimal surgical technique for rectal cancer

Field (based on PRISMA-P)	Content
Review question	What is the optimal surgical technique for rectal cancer?
Type of review question	Intervention
Objective of the review	To determine the optimal surgical technique for rectal cancer.
Eligibility criteria – population/disease/condition/issue/domain	Adults with non-metastatic rectal cancer based on TNM classification system: • T1-2 N1-2 • T3 N any • T4 N any • M0. Staging determined by ultrasound, MRI, computed tomography scan. Rectal cancer defined as any tumour within 15 cm from anal verge excluding anal canal. Exclusions: • bowel obstruction, metastatic cancer
Eligibility criteria – intervention(s)/exposure(s)/prognostic factor(s)	Surgical resection (for example abdominoperineal resection or low anterior resection) • Open • Laparoscopic • Robotic • Transanal total mesorectal excision (TaTME; only anterior resection)
Eligibility criteria – comparator(s)/control or reference (gold) standard	Surgical techniques compared to each other

Outcomes and prioritisation	**Critical outcomes:**
	• Overall survival (MID: statistical significance)
	• Quality of life measured using validated scales only (MID: from literature, see further down this document)
	  ○ Overall
	  ○ Sexual function
	  ○ Bladder function
	• Resection margins (positive/negative; MID: statistical significance)

Field (based on PRISMA-P)	Content

	Important outcomes:
	• Local recurrence (MID: statistical significance)
	• Length of hospital stay (MID: statistical significance)
	• 90-day mortality (MID: statistical significance)
	• Treatment-related complications (MID: statistical significance):
	  ○ Anastomotic leak (only relevant in anterior resection)
	  ○ Surgical site infection
	  ○ Blood loss
	
	Quality of life MIDs from the literature:
	• EORTC QLQ-C30: 5 points
	• EORTC QLQ-CR29: 5 points
	• EORTC QLQ-CR38: 5 points
	• EQ-5D: 0.09 to 0.10 using FACT-G quintiles
	• FACT-C: 5 points
	• FACT-G: 5 points
	• SF-12: >3.77 for the mental component summary and > 3.29 for the physical component summary of the Short Form SF-12 (SF-12)
	• SF-36: >7.1 for the physical functioning scale, >4.9 for the bodily pain scale, and >7.2 for the physical component summary

Eligibility criteria – study design	• Systematic reviews of (RCTs • RCTs • If eligible RCTs are not available for critical outcomes: comparative observational studies
Other inclusion exclusion criteria	Inclusion: • English-language • Published full texts • All settings will be considered that consider medications and treatments available in the UK • Studies published since 2000 Studies published 2000 onwards will be considered for this review question, as the GC felt that surgical techniques have evolved and evidence prior to 2000 would not be relevant any longer.
Proposed sensitivity/sub-group analysis, or meta-regression	In case of high heterogeneity in meta-analysis, the following subgroups will be considered: • People who underwent abdominoperineal resection • People who underwent (low) anterior resection • People who received preoperative radiotherapy or chemoradiotherapy • People who did not receive preoperative radiotherapy or chemoradiotherapy
Selection process – duplicate screening/selection/analysis	Sifting, data extraction, appraisal of methodological quality and GRADE assessment will be performed by the systematic reviewer. Resolution of any disputes will be with the senior systematic reviewer and the Topic Advisor. Quality control will be performed by the senior systematic reviewer.

Field (based on PRISMA-P)	Content
	Dual sifting will be undertaken for this question for a random 10% sample of the titles and abstracts identified by the search.
Data management (software)	Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5). 'GRADEpro' will be used to assess the quality of evidence for each outcome. NGA STAR software will be used for study sifting, data extraction, recording quality assessment using checklists and generating bibliographies/citations.
Information sources – databases and dates	Potential sources to be searched: Medline, Medline In-Process, CCTR, CDSR, DARE, HTA, Embase Limits (e.g. date, study design): • Apply standard animal/non-English language exclusion • Limit to RCTs and systematic reviews in first instance, but download all results • Dates: from 2000
Identify if an update	Not an update
Author contacts	https://www.nice.org.uk/guidance/indevelopment/gid-ng10060 Developer: NGA
Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual
Search strategy – for one database	For details please see appendix B.
Data collection process – forms/duplicate	A standardised evidence table format will be used, and published as appendix D (clinical evidence tables) or H (economic evidence tables).
Data items – define all variables to be collected	For details please see evidence tables in appendix D (clinical evidence tables) or H (economic evidence tables).
Methods for assessing bias at outcome/study level	Standard study checklists were used to critically appraise individual studies. For details please see section 6.2 of Developing NICE guidelines: the manual Appraisal of methodological quality: The methodological quality of each study will be assessed using an appropriate checklist: • ROBIS for systematic reviews • Cochrane risk of bias tool for RCTs • ROBINS-I tool for non-randomised studies (if applicable) The quality of the evidence for an outcome (i.e. across studies) will be assessed using GRADE. The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/
Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual

Field (based on PRISMA-P)	Content
Methods for quantitative analysis – combining studies and exploring (in)consistency	Synthesis of data: Pairwise meta-analysis of randomised trials will be conducted where appropriate. When meta-analysing continuous data, final and change scores will be pooled if baselines are comparable. If any studies reports both, the method used in the majority of studies will be analysed. MIDs: The guideline committee identified statistically significant differences as appropriate indicators for clinical significance for all outcomes except quality of life for which published MIDs from literature will be used (see outcomes section for more information).
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual. If sufficient relevant RCT evidence is available, publication bias will be explored using RevMan software to examine funnel plots.
Confidence in cumulative evidence	For details see sections 6.4 and 9.1 of Developing NICE guidelines: the manual.
Rationale/context – what is known	For details please see the introduction to the evidence review.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the guideline. The committee was convened by The National Guideline Alliance and chaired by Peter Hoskin in line with section 3 of Developing NICE guidelines: the manual. Staff from The National Guideline Alliance undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the guideline in collaboration with the committee. For details please see Supplement 1: methods.
Sources of funding/support	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists
Name of sponsor	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists
Roles of sponsor	NICE funds the National Guideline Alliance to develop guidelines for those working in the NHS, public health, and social care in England
PROSPERO registration number	Not registered

CCTR: Cochrane Central Register of Controlled Trials; CDSR: Cochrane Database of Systematic Reviews; DARE: Database of Abstracts of Reviews of Effects; EQ-5D: EuroQol five dimensions questionnaire; EORTC QLQ-C30: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 Items; EORTC QLQ-CR29: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire colorectal cancer module (29 items); EORTC QLQ-CR38: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire colorectal cancer module (38 items); FACT-C: Functional Assessment of Cancer Therapy questionnaire (colorectal cancer); FACT-G: Functional Assessment of Cancer Therapy questionnaire (general); GC: Guideline committee; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HTA: Health Technology Assessment; MID: minimal important difference; MRI: magnetic resonance imaging; NGA: National Guideline Alliance; NHS: National Health Service; NICE: National Institute for Health and Care Excellence; PRISMA-P: Preferred Reporting for Systematic review and Meta-Analysis Protocols; PROSPERO: international prospective register of systematic reviews; RCT: randomised controlled trial; ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions; ROBIS: a tool for assessing risk of bias in systematic reviews; SD: standard deviation; SF-

12: 12-Item Short Form Survey; SF-36: 36-Item Short Form Survey; TaTME: transanal total mesorectal excision; TNM: cancer classification, standing for tumour, nodal and metastasis stages

Appendix B – Literature search strategies

Literature search strategies for review question: What is the optimal surgery for rectal cancer?

A combined search was conducted for the following three review questions:

- What is the most effective treatment for early rectal cancer?
- What is the effectiveness of preoperative radiotherapy or chemoradiotherapy for rectal cancer?
- What is the optimal surgical technique for rectal cancer?

Database: Embase/Medline

Last searched on: 12/02/2019

#	Search
1	exp Rectal Neoplasms/ use prmz
2	*rectum cancer/ or *rectum tumor/
3	2 use oemezd
4	exp Adenocarcinoma/
5	(T1 or T2 or N0 or M0).ti,ab.
6	1 or 3
7	4 or 5
8	6 and 7
9	((rectal or rectum) adj3 (cancer* or neoplas* or malignan* or tumo?r* or carcinom* or adeno*)).ti,ab.
10	early rect* cancer.ti,ab.
11	6 or 8 or 9 or 10
12	exp radiotherapy/ or exp radiation oncology/ or exp external beam radiotherapy/ or exp Brachytherapy/ or exp preoperative care/ or exp neoadjuvant therapy/ or exp multimodality cancer therapy/ or exp chemotherapy/ or exp antineoplastic agent/ or exp drug therapy/ or exp chemoradiotherapy/ or exp fluorouracil/ or exp folinic acid/ or exp capecitabine/ or exp oxaliplatin/ or exp bevacizumab/ or exp methotrexate/ or exp radiation dose fractionation/ or exp tumor recurrence/
13	12 use oemezd
14	exp Radiotherapy/ or exp Radiation Oncology/ or exp Radiotherapy, Computer-Assisted/ or exp Brachytherapy/ or exp Preoperative Care/ or exp Neoadjuvant Therapy/ or exp Combined Modality Therapy/ or exp Chemoradiotherapy/ or exp Antineoplastic Combined Chemotherapy Protocols/ or exp Drug Therapy/ or exp Antineoplastic Agents/ or exp Fluorouracil/ or exp Leucovorin/ or exp Capecitabine/ or exp Bevacizumab/ or exp Methotrexate/ or exp Dose Fractionation/
15	14 use prmz
16	((radiotherap* or chemoradio* or radiation or brachytherapy* or chemotherapy*) adj (pre?op* or preop* or periop* or neoadjuvant)).ti,ab.
17	(5-fluorouracil or 5-FU or leucovorin or folinic acid or capecitabine or oxaliplatin or bevacizumab or methotrexate or dose* or fraction* or recurren*).ti,ab.
18	13 or 15 or 16 or 17
19	exp Laparoscopy/ or exp Transanal Endoscopic Microsurgery/ or exp Minimally Invasive Surgical Procedures/ or exp Endoscopy/ or exp Endoscopic Mucosal Resection/ or exp Surgical Procedures, Operative/ or exp Robotic Surgical Procedures/ or exp Surgery, Computer-Assisted/ or exp Dissection/
20	19 use prmz
21	exp laparoscopy/ or exp endoscopic surgery/ or exp transanal endoscopic microsurgery/ or exp endoscopy/ or exp minimally invasive surgery/ or exp endoscopic mucosal resection/ or exp surgery/ or exp robotic surgical procedure/ or exp computer assisted surgery/ or exp dissection/ or exp total mesorectal excision/ or exp excision/ or exp rectum resection/ or exp endoscopic polypectomy/ or exp polypectomy/ or exp endoscopic submucosal dissection/
22	21 use oemezd
23	(laparoscop* or endoscop* or transanal excision* or TAE or transanal endoscopic microsurger* or TEM or TEMS or transanal resection or TART or transanal minimally invasive surger* or TAMIS or total mesorectal excision* or TaTME or transanal total mesorectal excision* or TME or anterior resection* or abdominoperineal resection* or endoscopic resection* or polypectomy or endoscopic submucosal dissection* or ESD or endoscopic mucosal resection* or EMR or surger* or surgic* or operat*).ti,ab.
24	20 or 22 or 23
25	11 and 18
26	11 and 18 and 24
27	25 or 26
28	limit 27 to english language
29	limit 28 to yr="1997 -Current"
30	(conference abstract or letter).pt. or letter/ or editorial.pt. or note.pt. or case report/ or case study/ use oemezd
31	Letter/ or editorial/ or news/ or historical article/ or anecdotes as topic/ or comment/ or case report/ use prmz

#	Search
32	(letter or comment* or abstracts).ti.
33	or/30-32
34	randomized controlled trial/ use prmz
35	randomized controlled trial/ use oemezd
36	random*.ti,ab.
37	or/34-36
38	33 not 37
39	(animals/ not humans/) or exp animals, laboratory/ or exp animal experimentation/ or exp models, animal/ or exp rodentia/ use prmz
40	(animal/ not human/) or nonhuman/ or exp animal experiment/ or exp experimental animal/ or animal model/ or exp rodent/ use oemezd
41	(rat or rats or mouse or mice).ti.
42	38 or 39 or 40 or 41
43	29 not 42
44	clinical Trials as topic.sh. or (controlled clinical trial or pragmatic clinical trial or randomized controlled trial).pt. or (placebo or randomi#ed or randomly).ab. or trial.ti.
45	44 use prmz
46	crossover procedure/ or double blind procedure/ or randomized controlled trial/ or single blind procedure/ or (assign* or allocat* or crossover* or cross over* or ((doubl* or singl*) adj blind*) or factorial* or placebo* or random* or volunteer*).ti,ab.
47	46 use oemezd
48	or/45,47
49	43 and 48
50	epidemiologic studies/ or observational study/ or case control studies/ or retrospective studies/ or cohort studies/ or longitudinal studies/ or follow-up studies/ or prospective studies/ or cross-sectional studies/
51	50 use prmz
52	exp observational study/ or exp case control study/ or exp retrospective study/ or exp cohort analysis/ or exp longitudinal study/ or exp follow up/ or exp prospective study/ or exp cross-sectional study/
53	52 use oemezd
54	((retrospective* or cohort* or longitudinal or follow?up or prospective or cross section*) adj3 (stud* or research or analys*)).ti.
55	51 or 53 or 54
56	43 and 55
57	49 or 56
58	57 not 56
59	56 or 58

1 **Database: Cochrane Library**

2 Last searched on: 12/02/2019

#	Search
1	MeSH descriptor: [Rectal Neoplasms] explode all trees
2	MeSH descriptor: [Adenocarcinoma] explode all trees
3	T1 or T2 or N0 or M0
4	#2 or #3
5	#1 and #4
6	(rectal or rectum) near (cancer* or neoplas* or malignan* or tumo?r* or carcinom* or adeno*)
7	early rect* cancer
8	#1 or #5 or #6 or #7
9	MeSH descriptor: [Radiotherapy] explode all trees
10	MeSH descriptor: [Radiation Oncology] explode all trees
11	MeSH descriptor: [Radiotherapy, Computer-Assisted] explode all trees
12	MeSH descriptor: [Brachytherapy] explode all trees
13	MeSH descriptor: [Preoperative Care] explode all trees
14	MeSH descriptor: [Neoadjuvant Therapy] explode all trees
15	MeSH descriptor: [Combined Modality Therapy] explode all trees
16	MeSH descriptor: [Chemoradiotherapy] explode all trees
17	MeSH descriptor: [Antineoplastic Combined Chemotherapy Protocols] explode all trees
18	MeSH descriptor: [Drug Therapy] explode all trees
19	MeSH descriptor: [Antineoplastic Agents] explode all trees
20	MeSH descriptor: [Fluorouracil] explode all trees
21	MeSH descriptor: [Capecitabine] explode all trees
22	MeSH descriptor: [Bevacizumab] explode all trees
23	MeSH descriptor: [Methotrexate] explode all trees
24	MeSH descriptor: [Dose Fractionation] explode all trees
25	(radiotherap* or chemoradio* or radiation or brachytherapy* or chemotherapy*) near (pre?op* or preop* or periop* or neoadjuvant)
26	5-fluorouracil or 5-FU or leucovorin or folinic acid or capecitabine or oxaliplatin or bevacizumab or methotrexate or dose* or fraction* or recurren*

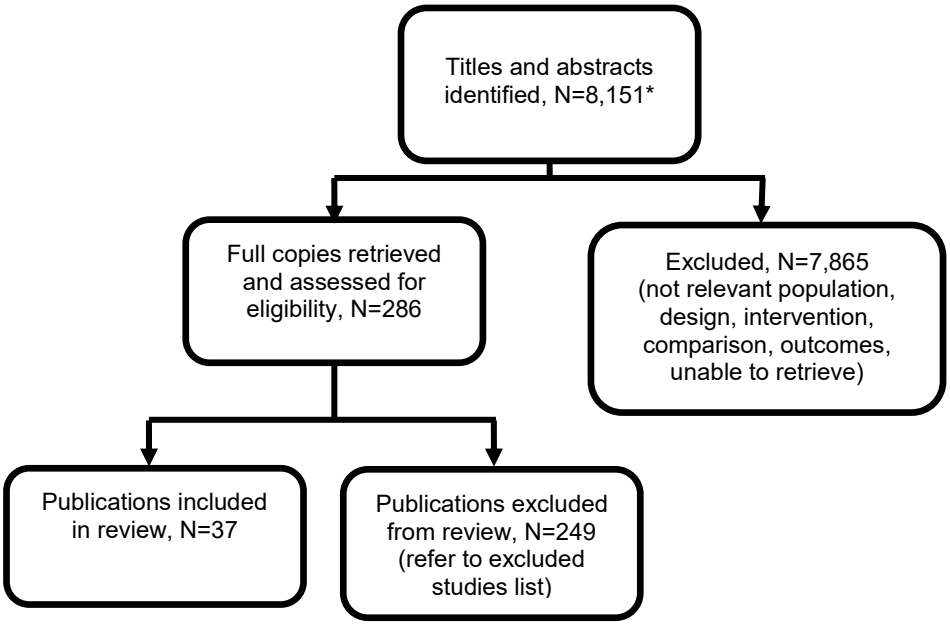
#	Search
27	#9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26
28	MeSH descriptor: [Laparoscopy] explode all trees
29	MeSH descriptor: [Transanal Endoscopic Microsurgery] explode all trees
30	MeSH descriptor: [Minimally Invasive Surgical Procedures] explode all trees
31	MeSH descriptor: [Endoscopy] explode all trees
32	MeSH descriptor: [Endoscopic Mucosal Resection] explode all trees
33	MeSH descriptor: [Surgical Procedures, Operative] explode all trees
34	MeSH descriptor: [Robotic Surgical Procedures] explode all trees
35	MeSH descriptor: [Surgery, Computer-Assisted] explode all trees
36	MeSH descriptor: [Dissection] explode all trees
37	laparoscop* or endoscop* or transanal excision* or TAE or transanal endoscopic microsurger* or TEM or TEMS or transanal resection or TART or transanal minimally invasive surger* or TAMIS or total mesorectal excision* or TME or anterior resection* or abdominoperineal resection* or endoscopic resection* or polypectomy or endoscopic submucosal dissection* or ESD or endoscopic mucosal resection* or EMR or surger* or surgic* or operat*
38	#28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37
39	#8 and #27
40	#8 and #27 and #38
41	#39 or #40 Publication Year from 1997 to 2017

1

Appendix C – Clinical evidence study selection

Clinical study selection for review question: What is the optimal surgery for rectal cancer?

Figure 1: Study selection flow chart



**The literature search was done for 3 review questions at once including the current review and review questions: 'What is the most effective treatment for early rectal cancer?' and 'What is the effectiveness of preoperative radiotherapy and chemoradiotherapy for rectal cancer?'. The number of titles and abstracts identified applies for all three reviews but all the other numbers are applicable to this specific review only. In addition, possibly relevant studies were added from systematic reviews.*

1 Appendix D – Clinical evidence tables

2 Clinical evidence tables for review question: What is the optimal surgery for rectal cancer?

3 Table 8: Clinical evidence tables

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Andersson, J., Abis, G., Gellerstedt, M., Angenete, E., Angeras, U., Cuesta, M. A., Jess, P., Rosenberg, J., Bonjer, H. J., Haglind, E., Patient-reported genitourinary dysfunction after laparoscopic and open rectal cancer surgery in a randomized trial (COLOR II), Br J Surg, 103, 1746, 2016 **Ref Id** 810630 **Country/ies where the study was carried out** **Study type**	**Sample size** See Bonjer 2015 (COLOR II trial). **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Aim of the study **Study dates** **Source of funding**					
Full citation Andersson, J., Angenete, E., Gellerstedt, M., Angeras, U., Jess, P., Rosenberg, J., Furst, A., Bonjer, J., Haglind, E., Health-related quality of life after laparoscopic and open surgery for rectal cancer in a randomized trial, Br J Surg, 100, 941-9, 2013 **Ref Id** 810631 **Country/ies where the study was carried out** **Study type**	**Sample size** See Bonjer 2015 (COLOR II trial). **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Aim of the study **Study dates** **Source of funding**					
Full citation Arteaga Gonzalez, I., Diaz Luis, H., Martin Malagon, A., Lopez-Tomassetti Fernandez, E. M., Arranz Duran, J., Carrillo Pallares, A., A comparative clinical study of short-term results of laparoscopic surgery for rectal cancer during the learning curve, International Journal of Colorectal Disease, 21, 590-595, 2006 **Ref Id** 745480 **Country/ies where the study was carried out**	**Sample size** N=40 randomised; n=20 laparoscopic surgery; n=20 open surgery **Characteristics** Age in years, mean±SD: Laparoscopic 66.6±12.6 Open 70.7±9.2 Male sex, n/n: Laparoscopic 11/20 Open 8/20 BMI, mean±SD Laparoscopic 26.0±2.9 Open 27.9±5.1 Tumour distance to anal verge, n/n: 0-5 cm Laparoscopic 9/20 Open 7/20 6-11 cm	**Interventions** Laparoscopic surgery versus open surgery Type of surgery, n/n: Haartmann Laparoscopic 5/20 Open 6/20 Lower anterior resection Laparoscopic 9/20 Open 10/20 Abdominoperineal resection Laparoscopic 6/20 Open 4/20 Total mesorectal excision (TME) was performed on all tumours located in the middle or lower thirds of the rectum. Laparoscopic surgery was performed with 4-6 ports.	**Details** Randomisation and allocation concealment No details provided. Blinding No blinding. Follow-up/outcomes Clinical and anatomopathological data were prospectively collected into a database. Statistical analysis Continuous variables compared using Student's t-test and categorical variables compared using Chi-squared or Fisher's exact test.	**Results** Outcome: Radial margin >2 mm Laparoscopic 20/20 Open 16/20 Outcome: Tumour-free distal margin Laparoscopic 20/20 Open 20/20 Outcome: Length of hospital stay in days, mean±SD Laparoscopic 9.1±5.7 (n=20) Open 15.6±6.1 (n=20) Outcome: Anastomotic leak Laparoscopic 0/20 Open 2/20 Outcome: Wound infection	**Limitations** Cochrane risk of bias tool Selection bias Random sequence generation: unclear risk (Details not reported.) Allocation concealment: unclear risk (Details not reported.) Performance bias Blinding of participants and personnel: high risk (No blinding.) Detection bias Blinding of outcome assessment: high risk (No blinding.) Attrition bias Incomplete outcome data: low risk (It is not clear if the **Sample size** reported is the original sample randomised. However, this paper only reports short-

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Spain **Study type** RCT **Aim of the study** To assess reliability and efficiency of laparoscopy in the curative treatment of rectal carcinoma. **Study dates** Enrolment between January 2003 to April 2004. **Source of funding** None reported.	Laparoscopic 6/20 Open 7/20 11-15 cm Laparoscopic 5/20 Open 6/20 TNM staging, n/n: I Laparoscopic 4/20 Open 7/20 II Laparoscopic 7/20 Open 5/20 III Laparoscopic 7/20 Open 3/20 IV Laparoscopic 2/20 Open 5/20 **Inclusion criteria** Carcinomas located less than 15 cm from the anal verge (determined with a flexible endoscope). **Exclusion criteria** Tumours with obstruction or perforation symptoms; preoperatively diagnosed T4 staging; tumours	Patients with preoperatively staged T3 or T4 middle and lower third tumours or mesorectal adenopathy without distant metastases received a regimen of preoperative radiotherapy (45 Gy in 4 weeks).		Laparoscopic 3/20 Open 6/20 Outcome: Blood loss in ml, mean±SD Laparoscopic 243.4±129.6 (n=20) Open 405.0±151.2 (n=20)	term outcomes and no one was lost to follow-up.) Reporting bias Selective reporting: low risk Other bias Other sources of bias: - **Other information** None

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	larger than 7 cm; candidates for local surgery.				
Full citation Bonjer, H. J., Deijen, C. L., Abis, G. A., Cuesta, M. A., Van Der Pas, M. H. G. M., De Lange-De Klerk, E. S. M., Lacy, A. M., Bemelman, W. A., Andersson, J., Angenete, E., Rosenberg, J., Fuerst, A., Haglind, E., A randomized trial of laparoscopic versus open surgery for rectal cancer, New England Journal of Medicine, 372, 1324-1332, 2015 **Ref Id** 745799 **Country/ies where the study was carried out**	**Sample size** N=1,103 randomised; n=739 allocated to laparoscopic surgery of which 40 were excluded, n=699 included in analysis ; n=364 allocated to open surgery of which 19 were excluded, n=345 included in analysis (main reasons for exclusion were that the participant had distant metastasis, did not have carcinoma, had T4 tumour, withdrew consent) **Characteristics** Age in years, mean±SD Laparoscopic 66.8±10.5 Open 65.8±10.9 Male sex, (%) Laparoscopic 448 (64) Open 211 (61) BMI, mean±SD Laparoscopic 26.1±4.5	**Interventions** Laparoscopic surgery versus open surgery All procedures had to comply with the principles of TME or partial mesorectal excision (PME). Resection with PME, n (%) Laparoscopic 72 (10) Open 35 (10) Resection with TME, n (%) Laparoscopic 418 (60) Open 230 (67) Abdominoperineal resection Laparoscopic 200 (29) Open 80 (23) Hartmann procedure Laparoscopic 36 (5) Open 25 (7) Preoperative radiotherapy, n (%) Laparoscopic 412 (59)	**Details** Randomisation and allocation concealment The participants were registered on the trial's website by the local investigator to ensure allocation concealment. Randomisation was done in a 2:1 ratio in accordance with a list of randomisation numbers and treatment allocation. This list was computer generated by the trial statistician. The randomisation was stratified by centre, tumour location, and preoperative radiotherapy. It was implemented by use of an internet application to allow central randomisation. Blinding No blinding. Follow-up/outcomes Minimal required follow-up included annual clinical examinations for 5 years after surgery. Three years	**Results** Outcome: Overall survival at 3 years Laparoscopic 86.7% Open 83.6% (No statistical difference between groups, narratively reported. No number of events, no HR, no p-values reported.) Outcome: Global quality of life (QLQ-C30; scale 0 to 100, higher score indicating better quality of life)* Baseline score Laparoscopic 72.8±20.18 (n=243) Open 68.6±20.81 (n=109) Mean difference at 4 weeks adjusted for baseline† Laparoscopic (n=230) - open (n=108)	**Limitations** Cochrane risk of bias tool Selection bias Random sequence generation: low risk Allocation concealment: low risk Performance bias Blinding of participants and personnel: high risk (No blinding.) Detection bias Blinding of outcome assessment: low/high risk (No blinding. High risk of bias for subjective outcomes.) Attrition bias Incomplete outcome data: low risk (Around 5% of the randomised were excluded from analysis because of distant metastasis, the patient had no carcinoma, withdrawal of consent etc.) Reporting bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Belgium, Canada, Denmark, Germany, the Netherlands, Poland, South Korea, Spain, Sweden **Study type** RCT (COLOR II trial) **Aim of the study** To compare 3-year rates of cancer recurrence in the pelvic or perineal area (locoregional recurrence) and survival after laparoscopic and open resection of rectal cancer. **Study dates** January 2004 to May 2010 **Source of funding** Ethicon Endo-Surgery Europe; Swedish	Open 26.5±4.7 Tumour distance from the anal verge, n (%) <5 cm Laparoscopic 203 (29) Open 93 (27) 5-<10 cm Laparoscopic 273 (39) Open 136 (39) 10-15 cm Laparoscopic 223 (32) Open 116 (34) Clinical stage, n (%) I Laparoscopic 201 (29) Open 96 (28) II Laparoscopic 209 (30) Open 107 (31) III Laparoscopic 257 (37) Open 126 (37) Missing Laparoscopic 32 (5) Open 16 (5) Pathological stage, n (%) I Laparoscopic 231 (33)	Open 199 (58) Preoperative chemotherapy, n (%) Laparoscopic 196/609 (32) Open 99/295 (34)	after the index surgery, CT or MRI of the pelvis combined with imaging of the liver and the chest were performed. The primary outcome was the proportion of patients with local recurrence at 3 years. For health-related quality of life, validated Swedish, Dutch, Danish, English and German translations of the following instruments were used: EQ-5D, EORTC QLQ-C30 and EORTC QLQ-CR38. (Information on quality of life scales is extracted from Andersson 2013.) The EQ-5D is a standardised non-disease-specific (generic) instrument for assessing self-reported health status. It comprises a description of the patient's health in five dimensions (mobility, self-care, daily activity, pain/discomfort and anxiety/depression). The EORTC QLQ-C30 is a 30-item questionnaire developed to assess the quality of life of patients with cancer. There are five	0.3 (95% CI -4.7 to 5.3) Mean difference at 6 months adjusted for baseline† Laparoscopic (n=221) - Open (n=106) -2.2 (95% CI -6.8 to 2.4) Mean difference at 12 months adjusted for baseline† Laparoscopic (n=208) - Open (n=97) -1.8 (95% CI -6.1 to 2.4) Outcome: Global health status (EQ-VAS; scale 0 to 100, higher score indicating better health status)* Baseline score Laparoscopic 77.3±16.6 (n=245) Open 74.9±16.6 (n=107) Mean difference at 4 weeks	Selective reporting: low risk Other bias Other sources of bias: - **Other information** None

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Cancer Society; the Health and Medical Care Committee of the Regional Executive Board, Region Västra Götaland, and an agreement concerning research and education of doctors, Sahlgrenska University Hospital, Gothenburg, Sweden; the Departments of Surgery and Biostatistics, Erasmus University Medical Center, Rotterdam, the Netherlands; the Department of Surgery, Dalhousie University, Halifax, NS, Canada; and the Department of Surgery, VU University	Open 107 (31) II Laparoscopic 180 (26) Open 91 (26) III Laparoscopic 180 (26) Open 125 (36) IV Laparoscopic 4 (1) Open 0 Missing Laparoscopic 18 (3) Open 3 (1) **Inclusion criteria** A single rectal cancer within 15 cm from the anal verge (confirmed at colonoscopy, rigid rectoscopy, or barium enema); no evidence of distant metastases; candidate for elective surgery **Exclusion criteria** T4 tumours or T3 tumours within 2 mm of		functional scales (physical, role, emotional, cognitive and social functioning), three symptom scales (fatigue, nausea/vomiting and pain), six single-item questions (about dyspnoea, insomnia, loss of appetite, constipation, diarrhoea and financial difficulties) and a global health/quality-of-life index. The latter assesses overall health and overall quality of life on a 7-point scale (1 indicating very poor and 7 indicating excellent). All other questions have four possible answers: 'not at all', 'a little', 'quite a bit' and 'very much'. The time frame was 'during the past week'. The EORTC QLQ-CR38 questionnaire is a 38-item questionnaire used to measure more specific information about quality of life in patients with colorectal cancer. The questions cover 4 functional scales/single items (body image, sexual functioning, sexual enjoyment, future perspective) and eight symptom scales/items	Laparoscopic (n=232) - Open (n=104) 1.6 (95% CI -3.3 to 6.5) Mean difference at 6 months Laparoscopic (n=219) - Open (n=102) 1.7 (95% CI -2.4 to 5.9) Mean difference at 12 months Laparoscopic (n=206) - Open (n=91) 0.6 (95% CI -3.4 to 4.7) Outcome: Sexual functioning (QLQ-CR38; scale 0 to 100, higher score indicating better functioning)** Baseline score Laparoscopic 19.9±22.4 (n=224) Open 24.3±24.7 (n=102) Mean difference at 4 weeks adjusted for baseline†	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Medical Center, Amsterdam	the endopelvic fascia (as determined on CT scan or MRI); T1 tumour treated with local transanal excision; rectal cancer other than adenocarcinoma; history of other malignancy except basocellular carcinoma of the skin or in-situ carcinoma of the cervix uteri; signs of acute intestinal obstruction; need for synchronous colorectal surgery; familial adenomatous polyposis coli; hereditary non-polyposis colorectal cancer; active Crohn's disease or active ulcerative colitis; absolute contraindications to general anaesthesia or prolonged pneumoperitoneum; ASA category >III; pregnancy.		(micturition problems, chemotherapy side-effects, gastrointestinal symptoms, male sexual problems, female sexual problems, defaecation problems, stoma-related problems and weight loss). For this review, sexual functioning, sexual enjoyment, micturition problems, male sexual problems and female sexual problems were considered. All questions have four possible responses: 'not at all', 'a little', 'quite a bit' and 'very much'. The time frame was previous 4 weeks. For both QLQ-30 and QLQ-CR38, the individual scores were converted to a score ranging from 0 to 100. A high score for the symptom/item scales represents a high level of symptoms/problems, whereas a high score for the functional scales and the global health/general quality-of-life index represents a high level of functioning, overall health and quality of life.	Laparoscopic (n=207) - Open (n=98) 2.5 (95% CI -0.3 to 6.3) Mean difference at 6 months adjusted for baseline† Laparoscopic (n=206) - Open (n=96) -0.8 (95% CI -5.5 to 3.9) Mean difference at 12 months adjusted for baseline† Laparoscopic (n=197) - Open (n=89) 3.1 (95% CI -1.7 to 7.9) Mean difference at 24 months adjusted for baseline† Laparoscopic (n=141) - Open (n=64) 4.6 (95% CI -1.7 to 10.9) Outcome: Sexual enjoyment (QLQ-CR38; scale 0 to 100, higher score	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
			Statistical analysis Kaplan–Meier method to estimate the difference in recurrence rates and survival between the study groups.	indicating better enjoyment)** Baseline score Laparoscopic 49.1±33.0 (n=97) Open 61.3±32.5 (n=50) Mean difference at 6 months adjusted for baseline Laparoscopic (n=72) - Open (n=37) 0.7 (95% CI -13.6 to 15.0) Mean difference at 12 months adjusted for baseline Laparoscopic (n=87) - Open (n=38) 8.0 (95% CI -5.0 to 21.0) Mean difference at 24 months adjusted for baseline Laparoscopic (n=41) - Open (n=21) -2.1 (95% CI -17.2 to 13.0) Outcome: Female sexual problems (QLQ-	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				CR38; scale 0 to 100, higher score indicating worse problems)** Baseline score Laparoscopic 10.9±15.6 (n=23) Open 12.2±19.4 (n=15) Mean difference at 6 months adjusted for baseline† Laparoscopic (n=19) - Open (n=10) 5.1 (95% CI -16.5 to 26.8) Mean difference at 12 months adjusted for baseline† Laparoscopic (n=19) - Open (n=14) 0.9 (95% CI -20.8 to 22.7) Mean difference at 24 months adjusted for baseline† Laparoscopic (n=7) - Open (n=5) 11.8 (95% CI -18.9 to 42.5) Outcome: Male sexual problems (QLQ-CR38; scale 0	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				to 100, higher score indicating worse problems)** Baseline score Laparoscopic 36.2±35.2 (n=124) Open 27.8±29.5 (n=54) Mean difference at 4 weeks adjusted for baseline† Laparoscopic (n=91) - Open (n=41) -6.5 (95% CI -19.9 to 6.8) Mean difference at 6 months adjusted for baseline† Laparoscopic (n=116) - Open (n=47) -6.9 (95% CI -20.5 to 6.7) Mean difference at 12 months adjusted for baseline† Laparoscopic (n=117) - Open (n=50) -9.8 (95% CI -22.3 to 2.6) Mean difference at 24	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				months adjusted for baseline† Laparoscopic (n=78) - Open (n=37) 1.1 (95% CI -12.2 to 14.4) Outcome: Micturitional symptoms (QLQ-CR38; scale 0 to 100, higher score indicating worse symptoms)** Baseline score Laparoscopic 24.0±18.1 (n=240) Open 23.3±17.7 (n=110) Mean difference at 4 weeks adjusted for baseline† Laparoscopic (n=219) - Open (n=103) 0.9 (95% CI -4.4 to 6.2) Mean difference at 6 months adjusted for baseline† Laparoscopic (n=219) - Open (n=101) -1.0 (95% CI -5.0 to 3.0)	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				Mean difference at 12 months adjusted for baseline† Laparoscopic (n=209) - Open (n=95) 2.2 (95% CI -2.0 to 6.4) Mean difference at 24 months adjusted for baseline† Laparoscopic (n=170) - Open (n=79) 2.4 (95% CI -2.4 to 7.2) Outcome: Positive CRM (<2 mm) Laparoscopic 56/588 Open 30/300 (denominator is the number without complete remission) Outcome: Locoregional recurrence at 3 years Laparoscopic 5.0% Open 5.0%	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				No statistical difference between groups, narratively reported. Outcome: Length of hospital stay, mean±SD; median (IQR)*** Laparoscopic 11.9±11.8; 8.0 (6.0-13.0) Open 12.1±10.6; 9.0 (7.0-14.0) Outcome: 28-day mortality*** Laparoscopic 8/699 Open 6/345 Outcome: Anastomotic leak*** Laparoscopic 58/461 Open 25/240 Outcome: Blood loss in ml, median (IQR)*** Laparoscopic 200 (100-400) Open 400 (200-700) p<0.0001	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				Outcome: Wound infection*** Laparoscopic 28/697 Open 17/345 *Data extracted from Andersson 2013. **Data extracted from Andersson 2014. ***Data extracted from van der Pas 2013. †The analysis of mean difference between groups at a specific time point was adjusted for differing baseline scores and/or **Characteristics**, however, it is not clear from the paper what was actually done and why the baseline scores were different even though the groups were randomly assigned.	
Full citation Braga, M., Frasson, M., Vignali, A., Zuliani, W., Capretti, G., Di	**Sample size** N=168 randomised; n=83 allocated to laparoscopic surgery; n=85 allocated to open surgery	**Interventions** Laparoscopic surgery versus open surgery Type of surgery, n/n Low anterior resection	**Details** Randomisation and allocation concealment Randomization list was generated by a computer program. Assignments were	**Results** Outcome: Quality of life - General health score at 12 months (modified SF-36;	**Limitations** Cochrane risk of bias tool Selection bias Random sequence generation: low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Carlo, V., Laparoscopic resection in rectal cancer patients: Outcome and cost-benefit analysis, Diseases of the Colon and Rectum, 50, 464-471, 2007 **Ref Id** 745870 **Country/ies where the study was carried out** Italy **Study type** RCT **Aim of the study** To evaluate the impact of laparoscopic rectal resection on short-term postoperative morbidity and costs.	**Characteristics** Age in years, mean±SD Laparoscopic 62.8±12.6 Open 65.3±10.3 Male sex, n/n Laparoscopic 55/83 Open 64/85 Obesity, n/n Laparoscopic 9/83 Open 5/85 Dukes stage, n/n I Laparoscopic 25/83 Open 24/85 II Laparoscopic 16/83 Open 19/85 III Laparoscopic 31/83 Open 29/85 IV Laparoscopic 11/83 Open 13/85 Tumour distance from the anal verge in cm, mean	Laparoscopic 76/83 Open 74/85 Abdominoperineal resection Laparoscopic 7/83 Open 11/85 In both laparoscopy and open groups TME was performed when cancer was located in the middle or low portion of the rectum. Patients with a preoperative diagnosis of T3 stage cancer received preoperative chemoradiotherapy: continuous infusion of 5-fluorouracil 20 mg/m² daily for 45 days plus 4,500 Gy distributed in 19 days (from day 14) plus oxaliplatin 100 mg/m² on days 1, 14, and 28.	made by means of sealed sequenced masked envelopes, which were opened before the induction of anaesthesia by a nurse unaware of the trial design. Blinding No blinding. Follow-up/outcomes Follow-up for infectious and noninfectious complications was performed for 30 days after hospital discharge by weekly office visits. Long-term follow-up was performed every six months by office visits. Quality of life was assessed by a modified version of the Medical Outcomes Study Short Form 36 (SF-36) questionnaire. **Statistical analysis** Intention-to-treat analysis was done. Survival curves were constructed with the Kaplan-Meier method and were compared with the log-rank test.	scale 0-100, higher indicating better) Laparoscopic 74 (n=83) Open 65 (n=85) p=0.0001 Outcome: Quality of life - General health score at 24 months (modified SF-36; scale 0-100, higher indicating better) Laparoscopic 72 (n=83) Open 68 (n=85) (p-value not reported but not significant difference between groups) Outcome: Positive distal margin Laparoscopic 0/83 Open 0/85 Outcome: Positive circumferential resection margin Laparoscopic 1/83 Open 2/85	Allocation concealment: low risk Performance bias Blinding of participants and personnel: high risk (No blinding.) Detection bias Blinding of outcome assessment: high risk (No blinding.) Attrition bias Incomplete outcome data: low risk (Intention-to-treat analysis was done. No losses to follow-up.) Reporting bias Selective reporting: low risk Other bias Other sources of bias: - **Other information** None

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study dates Not reported. **Source of funding** None reported.	Laparoscopic 9.1 Open 8.6 Tumour distance 10-15 cm from the anal verge, n/n Laparoscopic 30/83 Open 24/85 **Inclusion criteria** Adenocarcinoma of the rectum; age 18 years or older; suitability to elective surgery. **Exclusion criteria** Cancer infiltrating adjacent organs assessed by CT scan or MRI; cardiovascular dysfunction (New York Heart Association Class > 3); respiratory dysfunction (arterial pO2 < 70 mmHg); hepatic dysfunction (Child-Pugh Class C); ongoing infection; plasma neutrophil level < 2x10(9)/L.			Outcome: Local recurrence 3 years after surgery Laparoscopic 3/83 Open 4/85 Outcome: Length of hospital stay in days, mean±SD Laparoscopic 10±4.9 (n=83) Open 13.6±10 (n=85) Outcome: Operative mortality Laparoscopic 1/83 Open 1/85 Outcome: Anastomotic leak Laparoscopic 8/83 Open 9/85 Outcome: Wound infection Laparoscopic 6/83 Open 13/85 Outcome: Blood loss in ml, mean±SD Laparoscopic 213±236 (n=83)	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				Open 396±367 (n=85)	
Full citation Buonpane, C., Efiong, E., Hunsinger, M., Fluck, M., Shabahang, M., Wild, J., Halm, K., Long, K., Buzas, C., Blansfield, J., Predictors of utilization and quality assessment in robotic rectal cancer resection: A review of the national cancer database, American Surgeon, 83, 918-924, 2017 **Ref Id** 745976 **Country/ies where the study was carried out** US **Study type**	**Sample size** N=1,937 robotic surgery; N=7,185 laparoscopic surgery (not considered for this review because RCT data exists on critical outcomes); N=14,735 open surgery **Characteristics** Age, % 18-29 years Robotic Not reported (NR) Open 0.7 30-39 Robotic NR Open 3.5 40-49 Robotic 15.2 Open 13.1 50-59 Robotic 30.7 Open 27.1 60-69 Robotic 28.7 Open 27.8 70-79 Robotic 14.6 Open 18.6	**Interventions** Robotic surgery versus open surgery Neoadjuvant radiotherapy, n (%) Robotic 66.2 Open 58.0 Neoadjuvant chemotherapy, n (%) Robotic 64.5 Open 57.4	**Details** Randomisation and allocation concealment Not a randomised study. The data for this study was received from a national oncology database that captures more than 70% of all newly diagnosed malignancies in the US. Records of all surgically resected rectal cancers were obtained. Blinding Not applicable. Follow-up/outcomes Data from a database was used. **Statistical analysis** Analysis of outcomes of interest for this review were not adjusted for potential confounders or case-mix.	**Results** Outcome: Positive surgical margin Robotic 106/1,937 Open 1,256/14,735	**Limitations** ROBINS-I checklist for non-randomised studies of Interventions Pre-intervention Bias due to confounding: Serious risk of bias (This is a retrospective non-randomised observational study. No matching of groups was done. The study did not control for potential confounding in the analysis.) Bias in selection of participants into the study: Low risk of bias At intervention Bias in classification of Interventions: Low risk of bias Post-intervention Bias due to deviations from intended Interventions: Low risk of bias Bias due to missing data: Low risk of bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Retrospective cohort study **Aim of the study** To evaluate the use of robotic surgery in rectal cancer resection compared with open and laparoscopic techniques and to assess the quality of resection. **Study dates** 2010 to 2012 **Source of funding** None reported.	80+ Robotic 6.3 Open 9.2 Male sex, % Robotic 62.7 Open 60.2 T stage, % In situ Robotic NR Open 1.4 x Robotic 15.3 Open 21.3 T0 Robotic NR Open 0.3 T1 Robotic 9.3 Open 9.4 T2 Robotic 12.6 Open 12.2 T3 Robotic 57.8 Open 48.9 T4 Robotic 3.8 Open 6.5				Bias in measurement of outcomes: Low risk of bias Bias in selection of the reported result: Low risk of bias **Other information** None

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	N stage, n (%) x Robotic 7.7 Laparoscopic 7.7 Open 9.7 N0 Robotic 56.4 Open 57.7 N1 Robotic 29.6 Open 26.7 N2 Robotic 6.3 Open 5.9 Metastatic disease, % Robotic 5.8 Open 9.7 **Inclusion criteria** Surgically resected rectal cancers diagnosed from 2010 through 2012. **Exclusion criteria** If surgical approach for the resection of the primary tumour was not reported or if data required for analysis was missing.				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Corbellini, C, Biffi, R, Luca, F, Chiappa, A, Costa, S, Bertani, E, Bona, S, Lombardi, D, Tamayo, D, Botteri, E, Andreoni, B, Open, laparoscopic, and robotic surgery for rectal cancer: medium-term comparative outcomes from a multicenter study, Tumori, 102, 414-421, 2016 **Ref Id** 746335 **Country/ies where the study was carried out** Italy **Study type** A prospective, multi-centre cohort study.	**Sample size** N=65 patients received robotic surgery; N=40 patients received laparoscopic surgery (only considered for overall survival because for other critical outcomes there is RCT data); N=55 patients received open surgery **Characteristics** Age in years, median (range) Robotic 64 (39-78) Laparoscopic 64 (36-80) Open 62 (40-80) Male sex, n (%) Robotic 35 (54) Laparoscopic 23 (58) Open 36 (66) BMI, n (%) <25 Robotic 36 (55) Laparoscopic 17 (43) Open 33 (60) 25-30	**Interventions** Robotic versus laparoscopic versus open surgery Type of surgery, n (%) Anterior resection Robotic 58 (89) Laparoscopic 38 (95) Open 43 (78) Abdominoperinal resection Robotic 7 (11) Laparoscopic 1 (2.5) Open 11 (20) Hartmann Robotic 0 (0) Laparoscopic 1 (2.5) Open 1 (2) Choice of surgical technique was carried according to the surgeon's and the patient's preferences. TME with nerve preservation was performed in low and muddle rectal cancers and partial mesorectal excision was performed in upper rectal cancers.	**Details** Randomisation and allocation concealment This study was not a randomised study. Data was prospectively collected but the choice of surgical technique was done according to preference of the surgeon and the patient. Blinding No blinding. Follow-up/outcomes Follow-up visits were 3 months after surgery and every 6 months for the first 3 years, including a physical examination and tumour marker testing. Colonoscopy was done 1 and 3 years after surgery. Chest and abdominopelvic computer tomography was done once a year and abdominal ultrasound examination was done every 6 months. **Statistical analysis** Differences in survival were analysed using the log-rank	**Results** Outcome: Overall survival at 3 years Robotic 88.2% Laparoscopic 96.4% Open 93.9% p=0.522 Outcome: R1 Robotic 0/65 Open 2/55 Outcome: Distal surgical margin <2 cm (Abdominoperineal resection excluded) Robotic 22/58 Open 10/44	**Limitations** ROBINS-I checklist for non-randomised studies of Interventions Pre-intervention Bias due to confounding: Serious risk of bias (This is a non-randomised study, the groups were not matched by any characteristic. The study did not control for potential confounding or case-mix in the analysis.) Bias in selection of participants into the study: Low risk of bias At intervention Bias in classification of Interventions: Low risk of bias Post-intervention Bias due to deviations from intended Interventions: Low risk of bias Bias due to missing data: Low risk of bias Bias in measurement of outcomes: Low risk of bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Aim of the study To analyse and resolve advantages of robotic surgery with respect to open surgery and laparoscopic surgery in the management of rectal cancer. **Study dates** April 2009 to August 2011 **Source of funding** No financial support.	Robotic 23 (35) Laparoscopic 14 (35) Open 13 (24) >30 Robotic 6 (9) Laparoscopic 9 (23) Open 9 (16) Tumour distance from anal margin, n (%) <6 cm Robotic 21 (34) Laparoscopic 9 (23) Open 20 (37) 6-9.9 cm Robotic 18 (29) Laparoscopic 13 (33) Open 16 (30) >=10 cm Robotic 23 (37) Laparoscopic 18 (45) Open 18 (33) Pathologic staging, n (%) I Robotic 17 (26) Laparoscopic 15 (38)	All robotic-assisted laparoscopic anterior resection surgeries were performed by hybrid technique. Preoperative chemoradiotherapy and postoperative chemotherapy were recommended for patients with locally advanced rectal cancer.	test. No multivariate analysis was done.		Bias in selection of the reported result: Low risk of bias **Other information** None

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	Open 11 (20) II Robotic 17 (26) Laparoscopic 13 (33) Open 15 (27) III Robotic 31 (48) Laparoscopic 12 (30) Open 29 (53) **Inclusion criteria** A single rectal cancer within 12 cm from the anal verge; without evidence of distant metastases; candidates for elective, good-chance surgery. **Exclusion criteria** Tumours treated with local transanal excision; rectal cancers other than adenocarcinoma; recent history of other malignancies; familial adenomatous polyposis coli; hereditary nonpolyposis colorectal cancer; Chrohn disease or ulcerative colitis;				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	preoperative clinical stage IV.				
Full citation Denost, Q., Loughlin, P., Chevalier, R., Celerier, B., Didailler, R., Rullier, E., Transanal versus abdominal low rectal dissection for rectal cancer: long-term results of the Bordeaux' randomized trial, Surgical Endoscopy and Other Interventional Techniques, 1-9, 2017 **Ref Id** 746561 **Country/ies where the study was carried out** France **Study type** RCT (Bordeaux' trial)	**Sample size** N=100 randomised; n=50 allocated to transanal TME (TaTME); n=50 allocated to laparoscopic surgery **Characteristics** Age in years, median (range) TaTME 64 (39-82) Laparoscopic 63 (31-90) Male sex, n/n TaTME 37/50 Laparoscopic 32/50 BMI, median (range) TaTME 25.1 (17.3–33.2) Laparoscopic 25.6 (18.3–38.3) Tumour location from the anal verge in cm, median (range) TaTME 4 (2-6) Laparoscopic 4 (2-6) Tumour stage, n/n T1-2	**Interventions** TaTME versus laparoscopic TME Surgery was performed 6 weeks after the end of radiotherapy. Preoperative radiotherapy, n/n TaTME 40/50 Laparoscopic 44/50 Preoperative chemotherapy, n/n TaTME 39/50 Laparoscopic 42/50	**Details** Randomisation and allocation concealment The randomization of patients was performed by the assistant researcher the day before surgery, when the investigator has obtained the patient's written informed consent. Randomization was blind for the patient and was stratified by surgeon. No other details reported. Blinding No blinding. Follow-up/outcomes Follow-up visits were at 1 month, then every 4 months up to 2 years and 6 months subsequently. Postoperative surveillance included clinical examination, CEA level assessment and computer tomography scan. Colonoscopy was performed 1 year following surgery, then every 5 years.	**Results** Outcome: Overall survival, median 60.2 months of follow-up TaTME n=50, 7 events* Laparoscopic n=50, 13 events* p=0.135 Outcome: Urinary function median score (range) (IPSS, scale 0 to 35, higher indicating worse urinary function)** TaTME 5.5 (0-23) (n=38) Laparoscopic 3.5 (0-27) (n=34) p=0.821 Outcome: Urinary function quality of life median score (range) (IPSS, scale 0 to 6, lower indicating better quality of life)** TaTME 1 (0-6) (n=38)	**Limitations** Cochrane risk of bias tool Selection bias Random sequence generation: unclear risk (Limited details reported.) Allocation concealment: unclear risk (Details not reported.) Performance bias Blinding of participants and personnel: high risk (No blinding.) Detection bias Blinding of outcome assessment: low/high risk (No blinding. High risk of bias for subjective outcomes.) Attrition bias Incomplete outcome data: low/high risk (For recurrence, survival and perioperative outcomes intention-to-treat analysis was done. However, for sexual and urinary function only 72/100 participants

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Aim of the study To compare outcomes between transanal and laparoscopic rectal dissection in laparoscopic sphincter preservation for low rectal cancer. **Study dates** June 2008 to February 2012 **Source of funding** None reported.	TaTME 10/50 Laparoscopic 9/50 T3-4 TaTME 40/50 Laparoscopic 41/50 N1-2, n/n TaTME 30/50 Laparoscopic 33/50 **Inclusion criteria** Low rectal cancer (<6 cm from the anal verge); suitable for laparoscopic sphincter-saving resection. **Exclusion criteria** Exclusion criteria for functional outcome assessments were: death; local or recurrent disease; presence of a stoma.		Local recurrence was defined as any recurrence diagnosed or suspected in the pelvis. Recurrences were confirmed with radiological or histological examination. Overall survival was measured from the date of surgery to death. Assessment of urinary and sexual function was performed at least 12 months after stoma closure. (All data relating to urinary and sexual function extracted from Pontallier 2016.) Urinary function was assessed by the International Prostate Symptom score (IPSS). The IPSS questionnaire is based on 7 items (incomplete bladder emptying, frequency, intermittency, urgency, weak stream, straining and nocturia). Each item value is ranged from 0 to 5 (0=not at all; 1=less than one time; 2=less than half the time; 3=about half the time; 4=more than half the time; and 5=almost always). Total IPSS was calculated by	Laparoscopic 1 (0-5) (n=34) p=0.967 Outcome: Sexual activity maintained after treatment (in previously sexually active participants)** TaTME 20/28 Laparoscopic 9/23 p=0.02 Outcome: Sexual dysfunction at median 3.2 years after treatment (FSFI score ≤19) in previously sexually active female participants TaTME 2/5 Laparoscopic 2/3 p=1.00 Outcome: Erectile function median score (range) in sexually active men (IIEF, scale 5-25, higher indicating better erectile function)** TaTME 17.5 (5-25) (N not reported)	were included in the analysis.) Reporting bias Selective reporting: low risk Other bias Other sources of bias: - **Other information** The definition of local recurrence is unclear. The paper reports that local recurrence was defined as diagnosed or suspected recurrence in the pelvis, however, it also reports that all recurrences were confirmed by radiological or histological examination.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
			adding the score for each item and ranges from 0 (no urinary disorder) to 35 (major urinary disorder). The quality of urinary function was graded in three subgroups according to their IPSS: normal function (IPSS 0–7 points), moderate dysfunction (IPSS 8–19 points) and severe dysfunction (IPSS 20–35 points). The quality of life included in the IPSS questionnaire ranged from 0 (best) to 6 (worst). Male sexual function was assessed by the 5-item version of the International Index of Erectile Function questionnaire (IIEF-5; items included erection confidence, maintenance ability, maintenance frequency, erection firmness, and sexual satisfaction). Each item value is ranged from 0 to 5 (0=did not attempt intercourse; 1=almost never or never; 2=less than half the time; 3=about half the time; 4=more than half the time; and 5=almost always). The IIEF-5 score was	Laparoscopic 7 (5-21) (N not reported) p=0.119 Outcome: Erectile dysfunction (IIEF score <=21) after treatment** TaTME 67% (N not reported) Laparoscopic 93% (N not reported) p=0.108 Outcome: Normal ejaculatory function after treatment among sexually active men before surgery (IIEF)** TaTME 14/21 (67%) (denominator calculated from percentage reported) Laparossopic 7/16 (44%) (denominator calculated from percentage reported) p=0.224 Outcome: Positive distal margin (not defined)	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
			calculated by adding the score for each item and ranges from 5 to 25. A total score at or below 21 was considered ‘‘abnormal.’’ Erectile function in patients with sexual inactivity (score from 0 to 4) was not analysed. Female sexual function was assessed by the 6-item version of the Female Sexual Function Index (FSFI-6; items included sexual desire, sexual activity, lubrication, dyspareunia, sexual arousal and satisfaction). Each item value is ranged from 0 to 5 (0=did not attempt intercourse; 1=almost never or never; 2=less than half the time; 3=about half the time; 4=more than half the time; 5=almost always). The FSFI-6 score was calculated by adding the score for each item and ranges from 0 to 30. A total score at or below 19 was considered ‘‘abnormal.’’ Sexual activity in both male and female was assessed before and after treatment. In case of a loss of sexual activity after surgery,	TaTME 1/50 Laparoscopic 4/50 Outcome: "R1 resection (positive CRM)" (not defined) TaTME 2/50 Laparoscopic 9/50 Outcome: Local recurrence at 5 years TaTME 2.6% (95% CI 2.3% to 7.5%) Laparoscopic 4.8% (95% CI 1.7 to 11.3%) p = 0.300 Outcome: Length of hospital stay in days, median (range) TaTME 7 (3-54) (n=50) Laparoscopic 8 (2-29) (n=50) p=0.281 Outcome: Postoperative mortality TaTME 0/50 Laparoscopic 1/50	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
			patients should report whether this postoperative impairment was due or not to the surgical procedure. **Statistical analysis** Recurrence and survival were evaluated by the Kaplan–Meier method and compared with the log-rank test.	Outcome: Anastomotic leak and/or abscess TaTME 1/50 Laparoscopic 5/50 *Number of events calculated from the Kaplan-Meier curve. **Data extracted from Pontallier 2016.	
Full citation Denost Q, Loughlin P, Chevalier R et al. Transanal versus abdominal low rectal dissection for rectal cancer: long-term results of the Bordeaux' randomized trial. Surg Endosc. 2018 Mar;32(3):1486-1494. **Ref Id** 982355	**Sample size** (See Denost 2017 BORDEAUX trial)	**Interventions** (See Denost 2017 BORDEAUX trial)	Details (See Denost 2017 BORDEAUX trial)		**Limitations** (See Denost 2017 BORDEAUX trial) **Other information** None

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Country/ies where the study was carried out France **Study type** RCT (Bordeaux' trial) **Aim of the study** To compare outcomes between transanal and laparoscopic rectal dissection in laparoscopic sphincter preservation for low rectal cancer. **Study dates** June 2008 to February 2012 **Source of funding** None reported.					
Full citation Fleshman, J., Branda, M., Sargent, D. J., Boller, A. M.,	**Sample size** N=486 randomised; n=243 allocated to laparoscopic surgery but 3 did not receive	**Interventions** Laparoscopic surgery versus open surgery	**Details** Randomisation and allocation concealment Randomization was performed centrally.	**Results** Outcome: Negative distal margin (>=1 mm)	**Limitations** Cochrane risk of bias tool Selection bias Random sequence generation: low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
George, V., Abbas, M., Peters, W. R., Maun, D., Chang, G., Herline, A., Fichera, A., Mutch, M., Wexner, S., Whiteford, M., Marks, J., Birnbaum, E., Margolin, D., Larson, D., Marcello, P., Posner, M., Read, T., Monson, J., Wren, S. M., Pisters, P. W. T., Nelson, H., Effect of laparoscopic-assisted resection vs open resection of stage II or III rectal cancer on pathologic outcomes the ACOSOG Z6051 randomized clinical trial, JAMA - Journal of the American Medical Association, 314, 1346-1355, 2015 **Ref Id**	intervention as randomised, n=240 analysed; n=243 allocated to open surgery but 21 not included in analysis because did not undergo intervention as randomised or problem with consent, n=222 analysed. **Characteristics** Age in years, mean±SD Laparoscopic 57.7±11.5 Open 57.2±12.1 Male sex, n (%) Laparoscopic 156 (64.5) Open 158 (66.1) BMI, mean±SD Laparoscopic 26.4±4.0 Open 26.8±4.2 Location of tumour in the rectum, n (%) High Laparoscopic 33 (13.6) Open 28 (11.7) Middle Laparoscopic 85 (35.1)	Previous therapy received, n (%) Chemotherapy + radiotherapy Laparoscopic 227 (95.0) Open 217 (91.2) Radiotherapy alone Laparoscopic 8 (3.3) Open 13 (5.5) Chemotherapy alone Laparoscopic 4 (1.7) Open 8 (3.4) Unknown Laparoscopic 3 Open 1 Planned surgical approach, n (%) Abdominoperineal resection Laparoscopic 55 (22.7) Open 57 (23.8) Low anterior resection Laparoscopic 187 (77.3) Open 182 (76.2) Surgical approach used, n (%) Abdominoperineal resection Laparoscopic 58 (24.2)	Stratification by surgeon, site of primary tumor (high, middle, or low rectum according to the subclassification of the 12 cm of rectum into equal thirds), and planned operative procedure (lowanterior resectionwith anastomosis or abdominoperineal resection with colostomy). Blinding No blinding was done. Follow-up/outcomes Patients were assessed for complications at discharge from the hospital and at 4 to 6 weeks postoperatively. **Statistical analysis** Modified intention-to-treat. Patients who did not receive the randomised intervention were not included in the analysis but patients who had a conversion to open surgery were included in the analysis as originally allocated.	Laparoscopic 234/240 Open 218/222 Outcome: CRM > 1mm or distance = not applicable Laparoscopic 211/240 Open 205/222 Outcome: Distance to radial margin <=1 mm Laparoscopic 29/240 Open 17/222 >1 mm Laparoscopic 211/240 Open 205/222 Outcome: Local and regional recurrence* was 4.6% from laparoscopic resection and 4.5% for open resection. Outcome: Length of hospital stay in days, mean±SD Laparoscopic 7.3 (5.4)	Allocation concealment: unclear risk (Details not reported.) Performance bias Blinding of participants and personnel: high risk (No blinding.) Detection bias Blinding of outcome assessment: low/high risk (No blinding. High risk of bias on subjective outcomes.) Attrition bias Incomplete outcome data: unclear risk (Modified intention-to-treat analysis done. 3 in one group and 22 in one group of the originally randomised not analysed.) Reporting bias Selective reporting: low risk Other bias Other sources of bias: - **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
746895 **Country/ies where the study was carried out** US **Study type** RCT (ACOSOG Z6051 trial) **Aim of the study** To determine whether laparoscopic resection is noninferior to open resection. **Study dates** October 2008 to September 2013 **Source of funding** The National Cancer Institute; The American Society of Colon and Rectal Surgeons; The Society of	Open 95 (39.7) Low Laparoscopic 124 (51.2) Open 116 (48.5) Preoperative clinical stage, n (%) I Laparoscopic 2 (0.8) Open 3 (1.3) IIA Laparoscopic 99 (40.9) Open 92 (38.5) IIIA Laparoscopic 11 (4.5) Open 11 (4.6) IIIB Laparoscopic 114 (47.1) Open 114 (47.7) IIIC Laparoscopic 16 (6.6) Open 19 (7.9) **Inclusion criteria** Aged 18 years or older; BMI of 34 or less,; Eastern Cooperative Oncology Group	Open 47 (21.2) Low anterior resection Laparoscopic 69 (28.8) Open 73 (32.9) Low anterior resection + coloanal anastomosis Laparoscopic 110 (45.8) Open 96 (43.2) Low Hartmann Laparoscopic 1 (0.4) Open 0 Total proctocolectomy Laparoscopic 2 (0.8) Open 6 (2.7) Surgical technique in the laparoscopic arm, n (%) Laparoscopic 165 (68.8) Hand-assisted 41 (17.1) Robotic assisted 34 (14.2)		Open 7.0 (3.4) Outcome: 30-day mortality Laparoscopic 2/240 Open 2/222 Outcome: Anastomotic leak during postoperative period Laparoscopic 5/240 Open 5/222 Outcome: Blood loss in ml, mean±SD (median, IQR) Laparoscopic 256.1± 305.8 (150, 100-300) Open 318.4±331.7 (200±100-400) *Data extracted from Fleshman 2019.	Note that "laparoscopic surgery" includes robotic (14%), hand-assisted laparoscopic (17%) and conventional laparoscopic (69%) surgery.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
American Gastrointestinal and Endoscopic Surgeons	performance score less than 3; histologically proven adenocarcinoma of the rectum at or below 12 cm above the anal verge (by rigid proctoscopy); clinical stage II, IIIA, IIIB (T3N0M0, TanyN1 or 2, M0, and no T4) determined by rectal cancer protocol magnetic resonance imaging or transrectal ultrasonography **Exclusion criteria** History of invasive pelvic malignancy within 5 years; psychiatric or addictive disorders that affected compliance to the protocol; severe incapacitating disease (ASA classification IV or V); systemic disease that would preclude use of a laparoscopic approach (for example cardiovascular, renal, hepatic); conditions that would limit the success of laparoscopic resection (multiple previous				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	laparotomies or severe adhesions).				
Full citation Fleshman J, Branda ME, Sargent DJ, et al. Disease-free Survival and Local Recurrence for Laparoscopic Resection Compared With Open Resection of Stage II to III Rectal Cancer: Follow-up Results of the ACOSOG Z6051 Randomized Controlled Trial. Ann Surg. 2019 Apr;269(4):589-595. **Ref Id** 982405 **Country/ies where the study was carried out** US **Study type**	**Sample size** See Fleshman 2015	**Interventions**	**Details**	**Results**	**Limitations**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
RCT (ACOSOG Z6051 trial) **Aim of the study** To determine whether laparoscopic resection is noninferior to open resection. **Study dates** October 2008 to September 2013 **Source of funding** The National Cancer Institute; The American Society of Colon and Rectal Surgeons; The Society of American Gastrointestinal and Endoscopic Surgeons					
Full citation Green B, Marshall H, Collinson F et	**Sample size** See Jayne 2010 (CLASICC trial).	**Interventions**	**Details**	**Results**	**Limitations**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
al. (2013) Long-term follow-up of the Medical Research Council CLASICC trial of conventional versus laparoscopically assisted resection in colorectal cancer, British Journal of Surgery 100: 75-82 **Ref Id** 747298 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**	**Characteristics** **Inclusion criteria** **Exclusion criteria**				**Other information**
Full citation Guillou, P. J., Quirke, P., Thorpe, H.,	**Sample size** See Jayne 2010 (CLASICC trial).	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Walker, J., Jayne, D. G., Smith, A. M., Heath, R. M., Brown, J. M., Mrc Clasicc trial group, Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial, Lancet, 365, 1718-26, 2005 **Ref Id** 809742 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates**	**Characteristics** **Inclusion criteria** **Exclusion criteria**				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Source of funding					
Full citation Ielpo, B., Duran, H., Diaz, E., Fabra, I., Caruso, R., Malave, L., Ferri, V., Nunez, J., Ruiz-Ocana, A., Jorge, E., Lazzaro, S., Kalivaci, D., Quijano, Y., Vicente, E., Robotic versus laparoscopic surgery for rectal cancer: a comparative study of clinical outcomes and costs, International Journal of Colorectal Disease, 32, 1423-1429, 2017 **Ref Id** 747778 **Country/ies where the study was carried out**	**Sample size** N=86 robotic surgery; N=112 laparoscopic surgery **Characteristics** Age in years, mean±SD Robotic 63.9±9.5 Laparoscopic 61.6±11.9 Male sex, n/n Robotic 48/86 Laparoscopic 67/112 BMI, mean±SD Robotic 26.1±4.1 Laparoscopic 25.7±3.4 Tumour location from the anal verge, n (%) <5 cm Robotic 25/86 Laparoscopic 32/112 5-9 cm Robotic 30/86 Laparoscopic 39/112 10-15 cm Robotic 31/86 Laparoscopic 41/112	**Interventions** Robotic versus laparoscopic surgery Operative procedure, n (%) Lower anterior resection Robotic 62 (72) Laparoscopic 73 (65) Abdominoperineal resection Robotic 20 (23) Laparoscopic 32 (29) Colo-anal Robotic 4 (5) Laparoscopic 7 (6) Robotic surgery was performed with da Vinci Robotic Surgical System model Si and Xi. Patients with T3 or N+ cancer received neoadjuvant chemoradiation followed by surgery within 8 weeks. Neoadjuvant therapy, n (%) Robotic 65 (76)	**Details** Randomisation and allocation concealment This study was not a randomised study. The data was obtained from a prospectively collected database of rectal surgeries in the study institution. No matching of the groups was done. Blinding No blinding. Follow-up/outcomes Outcome data was obtained retrospectively from a prospectively-collected database. Follow-up assessments were performed at 15 postoperative days, at 1, 3 and 6 months, and every 6 months up to 5 years post-operation. A colonoscopy was performed at the year 1 and 3. A chestabdominal-pelvic CT-scan was used for the detection of locoregional or systemic recurrence at 2 and 6	**Results** Outcome: Overall survival at 3 years Robotic 91% Laparoscopic 94% p=0.7	**Limitations** ROBINS-I checklist for non-randomised studies of Interventions Pre-intervention Bias due to confounding: Serious risk of bias (This is a non-randomised study. No matching of groups was done. The study did not control for potential confounding in the analysis.) Bias in selection of participants into the study: Low risk of bias At intervention Bias in classification of **Interventions**: Low risk of bias Post-intervention Bias due to deviations from intended **Interventions**: Low risk of bias Bias due to missing data: Low risk of bias Bias in measurement of outcomes: Low risk of bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Spain **Study type** Retrospective cohort study **Aim of the study** To compare the clinical outcomes and cost differences of robotic versus laparoscopic surgery in the treatment of rectal cancer. **Study dates** October 2010 to March 2017 **Source of funding** This study has not been funded in whole or in part by any organisation.	**Inclusion criteria** Patients with diagnosed rectal cancer who underwent laparoscopic or robotic surgery. **Exclusion criteria** T4 rectal cancers	Laparoscopic 87 (78)	months after surgery, and every 6 months thereafter, or whenever suspected. **Statistical analysis** No adjustments for potential confounding or case-mix was done.		Bias in selection of the reported result: Low risk of bias **Other information** None
Full citation Ishibe, A., Ota, M., Fujii, S., Suwa, Y., Suzuki, S., Suwa, H., Momiyama, M.,	**Sample size** N=200 randomised in total of which 58 were rectal cancer patients; n=29 rectal cancer patients allocated to	**Interventions** Laparoscopic versus open surgery Medial-to-lateral approach in the	**Details** Randomisation and allocation concealment Details not reported. Blinding	**Results** Outcome: Overall survival at 3 years (rectal cancer) Laparoscopic 85.7% Open 83.1%	**Limitations** Cochrane risk of bias tool Selection bias Random sequence generation: unclear risk (Details not reported.)

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Watanabe, J., Watanabe, K., Taguri, M., Kunisaki, C., Endo, I., Midterm follow-up of a randomized trial of open surgery versus laparoscopic surgery in elderly patients with colorectal cancer, Surgical Endoscopy and Other Interventional Techniques, 31, 3890-3897, 2017 **Ref Id** 747811 **Country/ies where the study was carried out** Japan **Study type** RCT **Aim of the study** To compare open surgery with	laparoscopic surgery; n=29 rectal cancer patients allocated to open surgery **Characteristics** **Characteristics** in the total cohorts (both colon and rectal cancers): Age >=80 years, n (%) Laparoscopic 44 (45) Open 39 (42) Male sex, n (%) Laparoscopic 49 (50) Open 55 (60) BMI >=25, n (%) Laparoscopic 33 (34) Open 34 (37) Tumour site, n (%) Colon Laparoscopic 69 (70) Open 63 (69) Rectum Laparoscopic 29 (30) Open 29 (32) pStage, n (%)	laparoscopic surgery was performed in all patients in the laparoscopic group. High anterior resection of rectum, n/n Laparoscopic 5/29 Open 7/29 Low anterior resection of rectum Laparoscopic 19/29 Open 19/29 Abdominoperineal resection Laparoscopic 4/29 Open 2/29 Intersphincteric resection Laparoscopic 1/29 Open 0/29 Adjuvant chemotherapy, n (%) (for the total population, including colon and rectal cancers) Laparoscopic 16 (16) Open 10 (11)	No blinding. Follow-up/outcomes The follow-up schedule was specific to the disease stage. Stage 0 or I: outpatient examinations once a year for 5 years, including tumour marker measurements and computed tomography of the chest, abdomen, and pelvis. Stage II or IIIA: Computed tomography and tumour marker measurements every 6 months for the first 2 years, once a year from years 3 to 5. Stage IIIB or IIIC: Computed tomography and tumour marker measurements every 4 months for the first 2 years, and every 6 months from years 3 to 5. **Statistical analysis** Survival was analysed using the Kaplan–Meier method, difference between the groups was determined by log-rank test.	p = 0.557 Outcome: Local recurrence (median 42.5 months of follow-up) Laparoscopic 0/29 Open 4/29	Allocation concealment: unclear risk (Details not reported.) Performance bias Blinding of participants and personnel: high risk (No blinding.) Detection bias Blinding of outcome assessment: high risk (No blinding, high risk of bias for subjective outcomes.) Attrition bias Incomplete outcome data: low risk Reporting bias Selective reporting: low risk Other bias Other sources of bias: - **Other information** None

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
laparoscopic surgery in elderly patients with colorectal cancer. **Study dates** August 2008 to August 2012 **Source of funding** None.	0 Laparoscopic 5 (5) Open 2 (2) I Laparoscopic 27 (28) Open 24 (26) II Laparoscopic 36 (37) Open 33 (36) III Laparoscopic 30 (31) Open 33 (36) **Inclusion criteria** Age of 75 years or older; a histologically confirmed diagnosis of colorectal adenocarcinoma; a clinical stage of up to T4a tumours; any N stage; no evidence of metastasis (M0); elective surgery. **Exclusion criteria** Synchronous or metachronous (within 5 years) malignancy in another organ except carcinoma-in situ; multiple colorectal cancer needing				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	reconstruction two or more times; acute intestinal obstruction or perforation due to colorectal cancer; bulky tumour >8 cm in diameter; lower rectal cancer that required pelvic side wall lymphadenectomy; history of laparotomy for colorectal resection except appendectomy; pregnancy or breastfeeding; inability to tolerate pneumoperitoneum on the basis of general condition.				
Full citation Jayne, D. G., Brown, J. M., Thorpe, H., Walker, J., Quirke, P., Guillou, P. J., Bladder and sexual function following resection for rectal cancer in a randomized clinical trial of laparoscopic versus open	**Sample size** See Jayne 2010 (CLASICC trial). **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
technique, Br J Surg, 92, 1124-32, 2005 **Ref Id** 809743 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**					
Full citation Jayne, Dg, Thorpe, Hc, Copeland, J, Quirke, P, Brown, Jm, Guillou, Pj, Five-year follow-up of the Medical Research Council CLASICC trial of laparoscopically assisted versus open surgery for colorectal cancer,	**Sample size** N=794 randomised (both colon and rectal cancers) of which N=381 were rectal cancer patients; n=253 rectal cancer patients allocated to laparoscopic surgery; n=128 rectal cancer patients allocated to open surgery **Characteristics**	**Interventions** Laparoscopic versus open surgery Anterior resection (rectal cancer), n (%) Laparoscopic 167 (66) Open 79 (62) Abdominoperineal resection, n (%) Laparoscopic 63 (25) Open 34 (27)	**Details** Randomisation and allocation concealment Randomisation was done by telephone by the trial coordinator. Randomisation was stratified by surgeon, proposed site of operation, presence of liver metastases, and preoperative radiotherapy administration. Blinding	**Results** Outcome: Overall survival at 5 years (rectal cancer) Laparoscopic 62.8% Open 52.9% p=0.247 Outcome: Quality of life - Overall sexual dysfunction at median 3 years after surgery among	**Limitations** Cochrane risk of bias tool Selection bias Random sequence generation: unclear risk (Limited details reported.) Allocation concealment: unclear risk (Limited details reported.) Performance bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
British Journal of Surgery, 97, 1638-1645, 2010 **Ref Id** 747887 **Country/ies where the study was carried out** UK **Study type** RCT (CLASICC trial) **Aim of the study** To evaluate the technical and oncological safety and efficacy of laparoscopically assisted surgery in comparison with conventional open surgery for the treatment of colorectal cancer. **Study dates** July 1996 to July 2002	**Characteristics** of the total population (both colon and rectal cancers): Age in years, mean±SD Laparoscopic 69±11 Open 69±12 Female sex, n (%) Laparoscopic 230 (44) Open 123 (46) BMI, mean±SD Laparoscopic 25±4 Open 26±4 Tumour site, n (%) Colon Laparoscopic 273 (52) Open 140 (52) Rectum Laparoscopic 253 (48) Open 128 (48) pT stage, n (%) pT1 Laparoscopic 26 (6) Open 12 (5) pT2 Laparoscopic 68 (15)	Surgery with curative intent (rectal cancer), n (%) Laparoscopic 233 (92) Open 99 (77) Palliative surgery (rectal cancer), n (%) Laparoscopic 11 (4) Open 22 (17)	No blinding. Follow-up/outcomes Follow-up visits were at 1 and 3 months after surgery, then every 3 months for the first year, every 4 months for the second year, and every 6 months afterwards. Overall survival was calculated from the date of randomisation to the date of death from any cause. The International Prostate Symptom Score (I-PSS), International Index of Erectile Function (IIEF) and Female Sexual Function Index (FSFI) were used as symptom-specific tools to assess bladder and sexual function. A global question was added to each questionnaire to investigate the effect of surgery on sexual and bladder function from the patient's perspective. Quality of life was measured with the European Organization for Research and Treatment of Cancer (EORTC) colorectal module QLQ-CR38	previously sexually active men (IIEF; rectal cancer only)* Laparoscopic 7/15 Open 1/22 Outcome: Quality of life - A severe change in overall level of sexual function perceived in men (IIEF; rectal cancer only)** Laparoscopic 23/56 Open 6/26 Outcome: Quality of life - Overall level of sexual function decreased 'quite a lot' or 'severely' as a result of surgery in women (FSFI; rectal cancer only)** Laparoscopic 8/29 Open 3/17 Outcome: Quality of life - Bladder function (I-PSS; rectal cancer only)** "No differences in bladder function, either in overall score	Blinding of participants and personnel: high risk (No blinding.) Detection bias Blinding of outcome assessment: high risk (No blinding. High risk of bias for subjective outcomes such as quality of life.) Attrition bias Incomplete outcome data: low risk Reporting bias Selective reporting: unclear risk (Because this trial included patients with both colon and rectal cancers, not all outcomes were reported by the site of the tumour.) Other bias Other sources of bias: - **Other information** None

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Source of funding UK Medical Research Council	Open 35 (15) pT3 Laparoscopic 261 (56) Open 136 (56) pT4 Laparoscopic 70 (15) Open 33 (14) Missing Laparoscopic 33 (7) Open 24 (10) pN stage, n (%) pN0 Laparoscopic 244 (53) Open 129 (54) pN1 Laparoscopic 107 (23) Open 52 (22) pN2 Laparoscopic 72 (16) Open 38 (16) Not investigated Laparoscopic 4 (1) Open - Missing Laparoscopic 35 (8) Open 22 (9)		questionnaire, including 10 items relating to sexual and bladder function, with information being collected prospectively before operation, and 2 weeks (bladder function only), 3, 6 and 18 months after surgery. **Statistical analysis** Differences in survival and recurrences between groups were compared using Kaplan–Meier curves and tested with log-rank test.	or in individual symptom scores, were detected between the laparoscopic and open rectal resection groups." Outcome: Quality of life - Bladder function (QLQ-CR38; rectal cancer only)** "No differences in bladder function were detected at any time point between the laparoscopic and open rectal groups." Outcome: Local recurrence at 5 years (anterior resection for rectal cancer only) Laparoscopic 9.4% Open 7.6% p=0.740 Outcome: Length of hospital stay in days (rectal cancer), median (IQR)*** Laparoscopic 11 (9-15) Open 13 (9-18)	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	pM stage, n (%) pM0 Laparoscopic 167 (36) Open 91 (38) pM1 Laparoscopic 12 (3) Open 7 (3) Not investigated Laparoscopic 229 (50) Open 112 (46) Missing Laparoscopic 54 (12) Open 31 (13) **Inclusion criteria** Patients with cancer of the colon or rectum suitable for right hemicolectomy, left hemicolectomy, sigmoid colectomy, anterior resection, or abdominoperineal resection. **Exclusion criteria** Adenocarcinoma of the transverse colon;			Outcome: in-hospital mortality*** Laparoscopic 17/585 Open: 27/823 Outcome: Wound infection (rectal cancer)*** Laparoscopic 33/253 Open 15/125 *Data extracted from Quah 2002. ** Data extracted from Jayne 2005. ***Data extracted from Guillou 2005.	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	contraindications to pneumoperitoneum (chronic cardiac or pulmonary disease); acute intestinal obstruction; malignant disease in the past 5 years; synchronous adenocarcinomas; pregnancy; associated gastrointestinal disease needing surgical intervention.				
Full citation Jayne D, Pigazzi A, Marshall H, Croft J, Corrigan N, Copeland J, Quirke P, West N, Rautio T, Thomassen N, Tilney H, Gudgeon M, Bianchi PP, Edlin R, Hulme C, Brown J. Effect of Robotic-Assisted vs Conventional Laparoscopic Surgery on Risk of Conversion to Open Laparotomy Among Patients Undergoing Resection for	**Sample size** N=471 randomised; n=237 allocated to robotic surgery; n=234 allocated to laparoscopic surgery **Characteristics** Age in years, mean±SD Robotic 64.4±11 Laparoscopic 65.5±12 Male sex, n (%) Robotic 161 (68) Laparoscopic 159 (68) BMI ≥30, n (%) Robotic 54 (23) Laparoscopic 55 (24) Pathological T stage, n (%) pT0 Robotic 22 (9)	**Interventions** Robotic versus laparoscopic surgery Type of resection, n (%) High anterior resection Robotic 35 (15) Laparoscopic 34 (15) Low anterior resection Robotic 159 (67) Laparoscopic 158 (68) Abdominoperineal resection Robotic 43 (18) Laparoscopic 42 (18) Preoperative radiotherapy or chemoradiotherapy Robotic 111 (47) Laparoscopic 108 (46)	**Details** Randomisation and allocation concealment Randomisation was done with stratification for treating surgeon, sex, preoperative radiotherapy or chemoradiotherapy, intended procedure, and BMI. No other details reported. Blinding No blinding. Follow-up/outcomes Primary endpoint of the trial was conversion to open resection. Secondary endpoints included for example: CRM+ (defined as	**Results** Outcome: Female sexual function at 6 months (FSFI) Adjusted* difference in score Laparoscopic (n=29) minus robotic (n=25) 1.23 (95% CI -3.54 to 6.00), p=0.60 Outcome: Male sexual function at 6 months (IIEF) Adjusted* difference in score Laparoscopic (n=84) minus robotic (n=97) 0.80 (95% CI -4.10 to 5.70), p=0.75 Outcome: Bladder function at 6 months (IPSS)	**Limitations** Cochrane risk of bias tool Selection bias Random sequence generation: unclear risk (Details not reported.) Allocation concealment: unclear risk (Details not reported.) Performance bias Blinding of participants and personnel: high risk (No blinding.) Detection bias Blinding of outcome assessment: high risk (No blinding.)

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Rectal Cancer: The ROLARR Randomized Clinical Trial. JAMA 318(16), 1569-1580, 2017 **Ref Id** 839317 **Country/ies where the study was carried out** UK, Italy, Denmark, US, Finland, South Korea, Germany, France, Australia and Singapore **Study type** RCT (ROLARR trial) **Aim of the study** To compare robotic-assisted versus conventional laparoscopic surgery for risk of conversion to open laparotomy among patients undergoing	Laparoscopic 24 (10) pT1 Robotic 24 (10) Laparoscopic 20 (9) pT2 Robotic 64 (27) Laparoscopic 61 (27) pT3 Robotic 117 (50) Laparoscopic 114 (50) pT4 Robotic 5 (2) Laparoscopic 8 (4) Tx or missing Robotic 4 (2) Laparoscopic 3 (1) Pathological N stage, n (%) pN0 Robotic 146 (62) Laparoscopic 150 (65) pN1 Robotic 63 (27) Laparoscopic 58 (25) pN2 Robotic 25 (11) Laparoscopic 21 (9) Missing Robotic 2 (1) Laparoscopic 1 (0.4) **Inclusion criteria** Age ≥18 years; able to provide written informed consent; diagnosis of		tumour ≤1 mm), intraoperative and postoperative complications, postoperative 30-day mortality, and patient-reported sexual and bladder function at baseline and at 6 months. Female sexual function was self-assessed by the patients using Female Sexual Function Index (FSFI), with scores ranging from 2 to 36 and higher score indicating better functioning. Male sexual function was self-assessed by the patients using International Index of Erectile Function (IIEF), with scores ranging from 5 to 75 and higher scores meaning better functioning. Bladder function was self-assessed by the patients using International Prostate Symptom Score (IPSS), with scores ranging from 0 to 35, higher score indicating worse symptoms. **Statistical analysis** Intention-to-treat analysis was done.	Adjusted* difference in score Laparoscopic (n=176) minus robotic (n=175) 0.743 (95% CI -0.59 to 2.07), p=0.27 Outcome: Positive CRM Robotic 12/235 Laparoscopic 14/224 Outcome: Positive proximal resection margin Robotic 0/235 Laparoscopic 0/224 Outcome: Positive distal resection margin Robotic 0/235 Laparoscopic 1/224 Outcome: Length of hospital stay (mean±SD days) Robotic 8.0±5.85 (n=237) Laparoscopic 8.2±6.03 (n=234) Outcome: 30-day operative mortality Robotic 2/236 Laparoscopic 2/230 Outcome: Anastomotic leak (within 6 months)	Attrition bias Incomplete outcome data: low risk Reporting bias Selective reporting: low risk Other bias Other sources of bias: - **Other information** None

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
resection for rectal cancer. **Study dates** January 7th 2011 to September 30th 2014 **Source of funding** Efficacy and Mechanism Evaluation Programme, a partnership between Medical Research Council and National Institute for Health Research with contributions from the Chief Scientist Office in Scotland, the National Institute of Social Care and Health Research in Wales, and the Health and Social Care Research and Development Division, Public Health Agency in Northern Ireland; National Institute	rectal cancer amenable to curative surgery either by low anterior resection, high anterior resection, or abdominoperineal resection i.e. staged T1-3, N0-2, M0 by imaging as per local practice; rectal cancer suitable for resection by either standard or robotic-assisted laparoscopic procedure; fit for robotic-assisted or standard laparoscopic rectal resection; ASA physical status classification less than or equal to 3; capable of completing required questionnaires at time of consent. **Exclusion criteria** Benign lesions of the rectum; benign or malignant diseases of the anal canal; locally advanced cancers not amenable to curative surgery; locally advanced cancers requiring en bloc multi-visceral resection; synchronous colorectal tumours requiring multi-			Robotic 22/180 Laparoscopic 18/181 Outcome: Surgical site infection (within 30 days) Robotic 21/236 Laparoscopic 19/230 Outcome: Surgical site infection (between 30 days and 6 months) Robotic 4/236 Laparoscopic 8/230 *Adjusted for baseline scores and stratification factors (surgeon, sex, preoperative therapy, intended procedure and BMI)	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
for Health Research; Yorkshire Cancer Research; the Medical Research Council Bioinformation Initiative.	segment surgical resection; co-existent inflammatory bowel disease; clinical or radiological evidence of metastatic spread; concurrent or previous diagnosis of invasive cancer within 5 years that could confuse diagnosis; history of psychiatric or addictive disorder or other medical condition that, in the opinion of the investigator, would preclude the patient from meeting the trial requirements; pregnancy; participation in another rectal cancer clinical trial relating to surgical technique				
Full citation Jeong, S. Y., Park, J. W., Nam, B. H., Kim, S., Kang, S. B., Lim, S. B., Choi, H. S., Kim, D. W., Chang, H. J., Kim, D. Y., Jung, K. H., Kim, T. Y., Kang, G. H., Chie, E. K., Kim, S. Y., Sohn,	**Sample size** N=340 randomised; n=170 allocated to laparoscopic surgery; n=170 allocated to open surgery **Characteristics** Age in years, mean±SD Laparoscopic 57.8 (11.1) Open 59.1 (9.9)	**Interventions** Laparoscopic surgery versus open surgery Type of surgery, n (%) Abdominoperineal resection Laparoscopic 19 (11) Open 24 (14) Low anterior resection Laparoscopic 151 (89)	**Details** Randomisation and allocation concealment Computer-generated randomisation list was generated through Centre for Clinical Trials with a random permuted block design, 1:1 ratio, randomisation stratified by sex and preoperative chemotherapy regimen.	**Results** Outcome: Overall survival (median 4 years of follow-up; event is death from any cause) Laparoscopic N=170, 20 events Open N=170, 25 events HR 0.8 95% CI 0.44 to 1.45*	**Limitations** Cochrane risk of bias tool Selection bias Random sequence generation: low risk Allocation concealment: low risk Performance bias Blinding of participants and personnel: high risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
D. K., Kim, D. H., Kim, J. S., Lee, H. S., Kim, J. H., Oh, J. H., Open versus laparoscopic surgery for mid-rectal or low-rectal cancer after neoadjuvant chemoradiotherapy (COREAN trial): Survival outcomes of an open-label, non-inferiority, randomised controlled trial, The Lancet Oncology, 15, 767-774, 2014 **Ref Id** 747902 **Country/ies where the study was carried out** South Korea **Study type** RCT (COREAN trial) **Aim of the study**	Male sex, n (%) Laparoscopic 110 (65) Open 110 (65) BMI >25, n (%) Laparoscopic 63 (37) Open 64 (38) Tumour distance from anal verge, n (%) 0-3 cm Laparoscopic 35 (21) Open 46 (27) 3-6 cm Laparoscopic 66 (39) Open 59 (35) 6-9 cm Laparoscopic 69 (41) Open 65 (38) Clinical classification, n (%) cN0 Laparoscopic 59 (35) Open 52 (31) cN+ Laparoscopic 111 (65) Open 118 (69)	Open 146 (86) Laparoscopic surgery was done with 5 ports. Surgeries were done 6–8 weeks after completion of preoperative chemoradiotherapy. Radiotherapy was delivered to the whole pelvis at a dose of 45 Gy in 25 fractions, followed by a boost to the primary tumour of 5.4 Gy in three fractions during 5.5 weeks. Type of preoperative chemotherapy, n (%) Fluoropyrimidines alone Laparoscopic 156 (92) Open 156 (92) Capecitabine and irinotecan Laparoscopic 3 (2) Open 1 (1) Capecitabine, irinotecan, and cetuximab Laparoscopic 11 (6) Open 13 (8)	Randomisation was done at the coordinating centre via telephone. Blinding Patients and clinicians not blinded. During follow-up, radiologists and pathologists were blinded. Follow-up/outcomes Patients were followed-up every 3 months for the first 2 years, every 6 months for the next 3 years, and every 6 months or yearly thereafter. For the postoperative follow-up, a physical examination, complete blood-cell count, liver function tests, serum CEA tests, and chest radiography were done every 3 months or 6 months; abdominal and pelvic computer tomography were done every 6 months. Colonoscopic examinations were done 1 year postoperatively and once every 2 years thereafter. The primary outcome was disease-free survival (not of interest to this	Outcome: Positive CRM (<1 mm) Laparoscopic 5/170 Open 7/170 Outcome: Local recurrence (median 4 years of follow-up; event is local recurrence) Laparoscopic N=170, 2 events Open N=170, 4 events HR 0.40 95% CI 0.13 to 1.30* Outcome: Length of hospital stay in days, median (IQR)** Laparoscopic 8 (7-12) Open 9 (8-12) p=0.056 Outcome: 90-day mortality** Laparoscopic 0/170 Open 0/170 Outcome: Anastomotic leak**	(Patients and clinicians not blinded.) Detection bias Blinding of outcome assessment: low/high risk (Patients and clinicians not blinded but at follow-up radiologists and pathologists were blinded. High risk on subjective outcomes if no blinding done.) Attrition bias Incomplete outcome data: low risk (Intention-to-treat analysis done.) Reporting bias Selective reporting: low risk Other bias Other sources of bias: - **Other information** None

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
To compare survival outcomes of laparoscopic surgery with open surgery for patients with mid-rectal low-rectal cancer. **Study dates** April 4 2006 to August 26 2009 **Source of funding** National Cancer Center, (South Korea)	**Inclusion criteria** Mid-rectal or low-rectal cancer; cT3N0-2M0; previous preoperative chemoradiotherapy; 18–80 years of age **Exclusion criteria** Synchronous distant metastases, another primary malignancy, cardiopulmonary dysfunction, active uncontrolled infection, active uncontrolled psychosis, and intestinal perforation or obstruction.	Postoperative adjuvant chemotherapy was recommended for all patients, irrespective of the surgical pathology results.	review). Secondary outcomes were overall survival, local recurrence, and quality of life. Local recurrence was defined as any recurrence within the pelvic cavity or the perineum. Overall survival was defined as time from surgery to death from any cause. A validated Korean version of the European Organization for Research and Treatment of Cancer Quality-of-Life Questionnaire (EORTC QLQ)–C30 questionnaire (version 3.0) and the colorectal cancer module QLQ–CR38 to assess quality of life preoperatively and at months 3, 12, 24, and 36 after surgery. Statistical methods All analysis based on intention-to-treat population. Kaplan-Meier method with log-rank test to assess difference between groups.	Laparoscopic 2/170 Open 0/170 Outcome: Blood loss in ml, median (IQR)** Laparoscopic 200.0 (100.0-300.0) Open 217.5 (150.0-400.0) p=0.006 *The HR reported in the paper was inverted in order to have open surgery as the reference. **Data extracted from Kang 2010.	
Full citation Kang, S. B., Park, J. W., Jeong, S. Y., Nam, B. H.,	**Sample size** See Jeong 2014 (COREAN trial).	**Interventions**	Details	Results	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Choi, H. S., Kim, D. W., Lim, S. B., Lee, T. G., Kim, D. Y., Kim, J. S., Chang, H. J., Lee, H. S., Kim, S. Y., Jung, K. H., Hong, Y. S., Kim, J. H., Sohn, D. K., Kim, D. H., Oh, J. H., Open versus laparoscopic surgery for mid or low rectal cancer after neoadjuvant chemoradiotherapy (COREAN trial): Short-term outcomes of an open-label randomised controlled trial, The Lancet Oncology, 11, 637-645, 2010 **Ref Id** 748017 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates**	**Characteristics** **Inclusion criteria** **Exclusion criteria**				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Source of funding					
Full citation Kim, J., Baek, S. J., Kang, D. W., Roh, Y. E., Lee, J. W., Kwak, H. D., Kwak, J. M., Kim, S. H., Robotic Resection is a Good Prognostic Factor in Rectal Cancer Compared with Laparoscopic Resection: Long-term Survival Analysis Using Propensity Score Matching, Diseases of the Colon & Rectum, 60, 266-273, 2017 **Ref Id** 748152 **Country/ies where the study was carried out** South Korea **Study type**	**Sample size** N=224 robotic TME; N=224 laparoscopic TME (groups matched by sex, age, BMI, comorbidity, ASA score, tumour height from the anal verge, tumour location, preoperative chemoradiotherapy, and TNM stage) **Characteristics** Matched group **Characteristics**: Age in years, mean±SD Robotic 60.7±11.7 Laparoscopic 61.0±11.0 Male sex, n (%) Robotic 145 (65) Laparoscopic 141 (63) BMI, mean±SD Robotic 23.3±3.0 Laparoscopic 23.4 (3.3)	**Interventions** Robotic versus laparoscopic TME All robotic TME procedures were performed by a single docking totally robotic technique using the da Vinci Surgical System. Type of resection, n (%) Anterior resection Robotic 2 (1) Laparoscopic 7 (3) Lower anterior resection Robotic 169 (75) Laparoscopic 168 (75) Intersphincteric resection Robotic 41 (18) Laparoscopic 35 (16) Abdominoperineal resection Robotic 12 (5) Laparoscopic 14 (6) Preoperative concurrent chemoradiotherapy was	**Details** Randomisation and allocation concealment This was not a randomised study but a retrospective observational study. Matching of groups were done based on: Blinding Not applicable. Follow-up/outcomes For those who underwent chemotherapy, laboratory tests including CEA and abdominopelvic computer tomography scan were performed at 3- to 4-cycle intervals during chemotherapy. Other examinations such as chest CT, sigmoidoscopy or total colonoscopy, and positron emission tomography and CT were added when necessary. After chemotherapy, follow-up examinations were performed at 3-month intervals in the first 2 years,	**Results** Outcome: Overall survival at 5 years Stages I-III Robotic 90.5% Laparoscopic 78.0% p=0.323 Stage II Robotic 91.2% Laparoscopic 87.0% p=0.896 Stage III Robotic 83.1% Laparoscopic 64.2% p=0.526	**Limitations** ROBINS-I checklist for non-randomised studies of Interventions Pre-intervention Bias due to confounding: Moderate risk of bias (This is a retrospective observational study. Groups were matched.) Bias in selection of participants into the study: Low risk of bias At intervention Bias in classification of Interventions: Low risk of bias Post-intervention Bias due to deviations from intended Interventions: Low risk of bias Bias due to missing data: Low risk of bias Bias in measurement of outcomes: Low risk of bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Retrospective coh ort study **Aim of the study** To evaluate long term oncologic outcomes of robotic TME compared with laparoscopic TME. **Study dates** April 2007 to March 2014 **Source of funding** National Research Foundation of Korea; the Ministry of Science, ICT, and Future Planning (Republic of Korea)	Tumour location from the anal verge, n (%) Lower Robotic 128 (57) Laparoscopic 136 (61) Middle Robotic 88 (39) Laparoscopic 78 (35) Upper Robotic 8 (4) Laparoscopic 10 (5) Pathologic TNM stage, n (%) I Robotic 62 (28) Laparoscopic 63 (28) II Robotic 59 (26) Laparoscopic 54 (24) III Robotic 75 (34) Laparoscopic 75 (34) IV Robotic 28 (13) Laparoscopic 32 (14) **Inclusion criteria** Primary rectal cancer with pathologically proven adenocarcinoma	given selectively based on the following indications: T4; CRM positive or threatened; or suggestive metastasis of lateral pelvic lymph node, defined as a lymph node beyond the TME plane such as the iliac and obturator lymph nodes, on preoperative staging. Preoperative chemoradiotherapy, n (%) Robotic 50 (22) Laparoscopic 50 (22) The indications for postoperative radiotherapy were: T4; CRM or distal resection margin positive (CRM <2 mm, distal resection margin <5 mm); or lateral pelvic lymph nodes suspicious on preoperative diagnostic images but not receiving preoperative radiotherapy.	at 6-month intervals until 5 years, and annually thereafter, unless there was evidence of recurrence. **Statistical analysis** Propensity score matching was conducted to reduce the bias due to non-randomization of patients, based on: sex, age, BMI, comorbidity, ASA score, tumour height, tumour location, preoperative concurrent chemoradiotherapy, and TNM stage. Survival was analysed using the Kaplan-Meier method, and comparison of the survival between the groups was performed by the paired Prentice-Wilcoxon test.		Bias in selection of the reported result: Low risk of bias Other information None

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	within 15 cm of the anal verge; underwent minimally invasive surgery for rectal cancer. **Exclusion criteria** Patients with pathological stage IV cancer excluded from survival analysis.				
Full citation Kim, J. C., Yu, C. S., Lim, S. B., Park, I. J., Kim, C. W., Yoon, Y. S., Comparative analysis focusing on surgical and early oncological outcomes of open, laparoscopy-assisted, and robot-assisted approaches in rectal cancer patients, International Journal of Colorectal Disease, 31, 1179-1187, 2016 **Ref Id** 748163	**Sample size** N=2,114 consecutive rectal cancer patients; n=533 patients underwent robotic surgery; n=1,095 open surgery (n=486 laparoscopic surgery, not considered for this review because almost half of the population in this intervention group with stage 0 or I cancer) **Characteristics** Age in years, mean±SD Robotic 55±9 Open 59±9 Male sex, n (%) Robotic 333 (63) Open 700 (64)	**Interventions** Robotic versus open surgery All procedures included TME with at least unilateral pelvic autonomic nerve preservation. Type of surgery, n (%) Anterior resection Robotic 4 (1) Open 33 (3) Lower anterior resection Robotic 503 (94) Open 942 (86) Abdominoperineal resection Robotic 26 (5) Open 120 (11)	**Details** Randomisation and allocation concealment This was not a randomised study. Consecutive rectal cancer patients were provided with full information on the three procedures (open, laparoscopic, and robotic approaches) and chose one. Blinding No blinding. Follow-up/outcomes Follow-up examinations were done every 6 months for the first 3 years and annually thereafter until five postoperative years. Recurrence was confirmed either by imaging	**Results** Outcome: Overall survival at 3 years Robotic 94.6% Open 91.9% p=0.352 Outcome: Sexual dysfunction in men <=65 years of age (total; VAS; scale 0-5; 2-3 indicating moderate dysfunction; 4-5 indicating severe dysfunction) Robotic 27/141 Open 108/332 Outcome: Severe sexual dysfunction in men <=65 years of age (VAS 4-5)	**Limitations** ROBINS-I checklist for non-randomised studies of Interventions Pre-intervention Bias due to confounding: Serious risk of bias (This is a non-randomised study. The outcomes of interest were not controlled for potential confounding and case-mix in the analysis.) Bias in selection of participants into the study: Low risk of bias At intervention Bias in classification of Interventions: Low risk of bias Post-intervention

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Country/ies where the study was carried out South Korea **Study type** Prospective cohort study **Aim of the study** To compare open, laparoscopic, and robotic TME for rectal cancer in terms of sphincter-saving operation achievement, surgical complications, and early oncological outcomes. **Study dates** July 2010 to February 2015 **Source of funding** Korea Research Foundation; Ministry of Science, ICT, and Future Planning; the	BMI, mean±SD Robotic 24.1±3 Open 23.8±3 Tumour distance from the anal verge, n (%) Lower Robotic 258 (49) Open 429 (39) Middle Robotic 229 (43) Open 554 (51) Upper Robotic 45 (9) Open 112 (10) cStage (AJCC) 0 Robotic 10 (2) Open 112 (10) I Robotic 137 (26) Open 164 (15) II Robotic 101 (19) Open 197 (18) III Robotic 285 (54) Open 721 (66) **Inclusion criteria**	Preoperative chemoradiotherapy was principally indicated for patients with clinical stage III or T4 cancers but was ultimately determined by the surgeon. Postoperative chemoradiotherapy was administered in pathologic stage III patients without preoperative chemoradiotherapy. Patients with preoperative or postoperative chemoradiotherapy received a total of 45–50.4 Gy with fluorouracil + leucovorin or capecitabine. Preoperative chemoradiotherapy, n (%) Robotic 172 (32) Laparoscopic 61 (13) Open 553 (51)	studies or histologic examinations. Male sexual dysfunction was assessed at two postoperative years in ≤65 years old men by evaluating both erectile firmness and ejaculatory frequency using a visual analogue scale (VAS): 0-1 indicating none–mild dysfunction, 2-3 indicating moderate dysfunction, and 4-5 indicating severe dysfunction. **Statistical analysis** Survival outcomes and recurrences were compared using the Kaplan-Meier method with the log-rank test. Multivariate analysis was not done for the outcomes of interest.	Robotic 13/141 Open 37/332 Outcome: Moderate sexual dysfunction in men <=65 years of age (VAS 2-3) Robotic 14/141 Open 71/332 Outcome: Positive CRM (<=1 mm) Robotic 8/533 Open 26/1,095 Outcome: Positive distal resection margin (<=5 mm) Robotic 5/533 Open 13/1,095	Bias due to deviations from intended Interventions: Low risk of bias Bias due to missing data: Low risk of bias Bias in measurement of outcomes: Moderate risk of bias (The clinicians were not blinded to the intervention, therefore, subjective outcomes might be biased.) Bias in selection of the reported result: Low risk of bias **Other information** None

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Korea Health 21 R&D Project; Ministry of Health,Welfare, and Family Affairs (Republic of Korea).	Curatively resected adenocarcinoma of the rectum (≤stage III); an Eastern Cooperative Oncology Group performance status of 0–3; age ≤75 years. **Exclusion criteria** Previous history of any cancer; hereditary colorectal cancer; inflammatory bowel disease.				
Full citation Kim, M. J., Park, S. C., Park, J. W., Chang, H. J., Kim, D. Y., Nam, B. H., Sohn, D. K., Oh, J. H., Robot-assisted Versus Laparoscopic Surgery for Rectal Cancer: A Phase II Open Label Prospective Randomized Controlled Trial, Annals of Surgery., 25, 2017 **Ref Id**	**Sample size** N=163 randomised; n=82 allocated to robot-assisted surgery but n=16 dropped before allocated surgery, in the end n=66 included in analysis; n=81 allocated to laparoscopic surgery but 8 dropped before allocated surgery, in the end n=73 included in analysis **Characteristics** Age in years, mean±SD Robotic 60.4 (9.7) Laparoscopic 59.7 (11.7)	**Interventions** Robot-assisted surgery versus laparoscopic surgery Robotic surgery was performed with the da Vinci Surgical System. All study participants underwent TME and pelvic autonomic nerve preservation, and the operative extent was the same for both groups. Surgical approach, n (%) Low anterior resection with double stapling anastomosis	**Details** Randomisation and allocation concealment Randomisation was computer-generated, and allocation was communicated via telephone by the trial coordinator at the Clinical Trials Research office at the National Cancer Center. Randomisation was stratified according to sex and preoperative chemoradiotherapy adminis tration using a block permutation approach. Blinding	**Results** Outcome: Quality of life global health status score at baseline, at 3 weeks, 3 months and 12 months after surgery (QLQ-C30) No difference between the two groups. (Reported narratively and in a figure, no mean scores presented.) Outcome: Quality of life - sexual function subscale mean score at 12 months after surgery (QLQ-CR38)	**Limitations** Cochrane risk of bias tool Selection bias Random sequence generation: low risk Allocation concealment: low risk Performance bias Blinding of participants and personnel: high risk (No blinding.) Detection bias Blinding of outcome assessment: low/high risk (Pathologist was blinded but participants were not.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
748185 **Country/ies where the study was carried out** South Korea **Study type** RCT **Aim of the study** To compare the outcomes of robotic surgery with those of laparoscopic surgery in patients with rectal cancer. **Study dates** February 21 2012 to March 11 2015 **Source of funding** National Cancer Center (Republic of Korea)	Male sex, n (%) Robotic 51 (77) Laparoscopic 52 (71) BMI, mean±SD Robotic 24.1 (3.3) Laparoscopic 23.6 (3.0) Tumour location from the anal verge, n (%) <=5 cm Robotic 33 (50) Laparoscopic 35 (48) >5 cm Robotic 33 (50) Laparoscopic 38 (52) **Inclusion criteria** People with mid- or low-lying (within 9 cm from the anal verge) rectal adenocarcinoma w ithout distant metastasis. **Exclusion criteria** Cancer invading adjacent organs (T4), distant metastasis (M1),	Robotic 40 (61) Laparoscopic 48 (66) Low anterior resection with hand-sewn anastomosis Robotic 25 (38) Laparoscopic 22 (30) Abdominoperineal resection Robotic 1 (1.5) Laparoscopic 2 (2.7) Hartmann operation Robotic 0 (0) Laparoscopic 1 (1.4) Preoperative chemoradiotherapy received, n (%) Robotic 51 (77) Laparoscopic 58 (80)	No blinding of patients. Pathologists examining the macroscopic quality of the TME were blinded to allocation. Follow-up/outcomes The primary outcome of the trial was completeness of TME. Secondary outcomes included for example resection margins, morbidity and quality of life. Quality of life was evaluated before surgery and 3 weeks, 3 months, and 12 months after surgery using the validated Korean version of the EORTC QLQ-C30 questionnaire (version 3.0) and the colorectal cancer module QLQ-CR38. Scale was 0 to 100, higher score indication better quality of life for global health status and functioning scores. **Statistical analysis** Per protocol analysis was done.	(scale 0 to 100, higher indicating better) Robotic 35.2 (95% CI 26.9 to 43.5) SD 33.8 (n=66) Laparoscopic 23.0 (95% CI 15.7 to 30.2) SD 31.1 (n=73) Outcome: Positive CRM (<=1 mm) Robotic 4/66 Laparoscopic 4/73 Outcome: Length of hospital stay in days, mean±SD Robotic 10.3±3.4 (n=66) Laparoscopic 10.8±7.4 (n=73) Outcome: Anastomotic leak Robotic 8/66 Laparoscopic 5/73 Outcome: Blood loss in ml, median (range) Robotic 100 (0-1,000) (n=66)	High risk of bias for subjective outcomes.) Attrition bias Incomplete outcome data: unclear risk (Per protocol analysis done. 16/82 and 8/81 not included in analysis for robotic and laparoscopic groups, respectively. Reasons for these were reported (main reasons: participants refused the allocated surgery, or distant metastasis was detected). Reporting bias Selective reporting: low risk Other bias Other sources of bias: - **Other information** None

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	severe concomitant disease that might limit compliance or completion of the protocol, any other malignancy, pregnant or breastfeeding females, hereditary colorectal cancer, and emergency operation.			Laparoscopic 50 (0-300) (n=73)	
Full citation Law, W. L., Foo, D. C. C., Comparison of short-term and oncologic outcomes of robotic and laparoscopic resection for mid- and distal rectal cancer, Surgical Endoscopy and Other Interventional Techniques, 31, 2798-2807, 2017 **Ref Id** 748501 **Country/ies where the study was carried out**	**Sample size** N=220 robotic surgery; N=171 laparoscopic surgery **Characteristics** Age in years, median (range) Robotic 65 (34-90) Laparoscopic 67 (23-96) Male sex, n/n Robotic 148/220 Laparoscopic 97/171 BMI, mean Robotic 24.9 Laparoscopic 24.6 Tumour distance from the anal verge in cm, median (range) Robotic 7.0 (0-12)	**Interventions** Robotic versus laparoscopic surgery For robotic surgeries, the Da Vinci surgical robotic system was used. The majority of robotic surgeries were performed with the hybrid technique with left colon mobilisation and division of the inferior mesenteric vessels using the conventional laparoscopic technique. Type of surgery, n (%) Lower anterior resection Robotic 206 (94) Laparoscopic 152 (88) Abdominoperineal resection Robotic 11 (5) Laparoscopic 14 (8)	**Details** Randomisation and allocation concealment This was not a randomised study. The groups were not matched. Blinding No blinding. Follow-up/outcomes The patients were followed up at intervals of 2–3 months during the first 2 years and every 4–6 months from 3 to 5 years and annually thereafter. The visits included: history, physical examination, blood tests and serum CEA level. A digital rectal examination was performed at each visit to detect any anastomotic stricture or local recurrence.	**Results** Outcome: Overall survival at 5 years Robotic 71.8% Laparoscopic 74.3% p=0.423	**Limitations** ROBINS-I checklist for non-randomised studies of Interventions Pre-intervention Bias due to confounding: Serious risk of bias (This is a non-randomised, observational study, the groups were not matched by any characteristic. The study did not control for potential confounding or case-mix in the analysis.) Bias in selection of participants into the study: Low risk of bias At intervention Bias in classification of Interventions: Low risk of bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Hong Kong **Study type** Retrospective cohort study **Aim of the study** To compare the short-term operative as well as oncologic outcomes of laparoscopic and robotic rectal resection. **Study dates** January 2008 to June 2015 **Source of funding** None reported.	Laparoscopic 8.0 (0-12) **Inclusion criteria** People with rectal cancer within 12 cm from the anal verge and underwent elective radical resection. **Exclusion criteria** People who underwent open resection.	Hartmann Robotic 3 (1.4) Laparoscopic 5 (3) Neoadjuvant chemoradiation was offered to patients when the mesorectal margin was at risk (<1 mm by MRI) and to those with findings of poor prognosis with distal cancer destined for abdominoperineal resection or low anterior resection with hand-sewn coloanal anastomosis. Preoperative radiotherapy, n (%) Robotic 91 (41) Laparoscopic 50 (29) An enhanced recovery care program was adopted for patients following surgery for rectal cancer during the study period.	Colonoscopy was performed regularly for the detection of metachronous lesions. If recurrences were suspected, endoscopic examination, CT scan or other imaging studies were performed to determine whether salvage surgery could be performed. Data, including survival data, were prospectively collected in a database for rectal cancer. **Statistical analysis** Survival was analysed using the Kaplan–Meier method, and the groups were compared with the log-rank test. No matching or adjusting was done.		Post-intervention Bias due to deviations from intended Interventions: Low risk of bias Bias due to missing data: Low risk of bias Bias in measurement of outcomes: Low risk of bias Bias in selection of the reported result: Low risk of bias **Other information** None
Full citation Liang, X., Hou, S., Liu, H., Li, Y., Jiang, B., Bai, W.,	**Sample size** N=343 randomised;	**Interventions** Laparoscopic surgery versus open surgery	**Details** Randomisation and allocation concealment	**Results** Outcome: Overall survival at 3 years	**Limitations** Cochrane risk of bias tool Selection bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Li, G., Wang, W., Feng, Y., Guo, J., Effectiveness and safety of laparoscopic resection versus open surgery in patients with rectal cancer: a randomized, controlled trial from China, J Laparoendosc Adv Surg Tech A, 21, 381-5, 2011 **Ref Id** 809748 **Country/ies where the study was carried out** China **Study type** RCT **Aim of the study** To assess efficacy and safety of laparoscopic surgery for	n=169 allocated to laparoscopic surgery, 2 people lost to follow-up and n=167 included in analysis; n=174 allocated to open surgery, 2 people lost to follow-up and n=172 included in analysis. **Characteristics** Age in years, mean±SD Laparoscopic 57.3±14.1 Open 57.4±13.1 Male sex, n/n Laparoscopic 104/169 Open 92/174 BMI, mean (assumed to be mean, not reported) Laparoscopic 21.45 Open 22.31 TNM stage, n/n T1-2N0M0 Laparoscopic 9/169 Open 7/174 T3-4N0M0 Laparoscopic 72/169 Open 84/174 TxN1-2M0	Surgical approach, n/n Abdominoperineal resection Laparoscopic 83/169 Open 70/174 Lower anterior resection Laparoscopic 86/169 Open 104/174 No one received preoperative (chemo)radiotherapy (in fact that was an exclusion reason).	Randomisation was done on the day before surgery through sealed opaque envelopes. Blinding Short-term complications were reviewed by a single person blinded to treatment allocation. Otherwise no blinding. Follow-up/outcomes Patients were assessed for complications at the time of hospital discharge by a single reviewer blinded to the treatment assignments. Follow-up visits were at 1 and 3 months after surgery, every 3 months for the first 2 years and every 6 months thereafter. The visits included physical examination, abdominal and pelvic part ultrasonography, chest radiography, examination of alimentary tract tumour markers and colonofiberscope examination. Recurrence was confirmed by imaging or pathological examination.	Laparoscopic 76.0% Open 82.8% p=0.462 Outcome: 30-day mortality Laparoscopic 0/169 Open 0/174 Outcome: Anastomotic leak Laparoscopic 4/169 Open 6/174 Outcome: Wound infection Laparoscopic 9/169 Open 8/174 Outcome: Blood transfusion Laparoscopic 4/169 Open 8/174	Random sequence generation: unclear risk (No sufficient detail provided.) Allocation concealment: low risk Performance bias Blinding of participants and personnel: high risk (No blinding.) Detection bias Blinding of outcome assessment: high risk (No blinding.) Attrition bias Incomplete outcome data: low risk (2 patients in each group lost to follow-up and not included in survival analysis.) Reporting bias Selective reporting: low risk Other bias Other sources of bias: - **Other information** None

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
treatment of rectal cancer. **Study dates** May 2005 to April 2008 **Source of funding** None reported.	Laparoscopic 88/169 Open 83/174 **Inclusion criteria** Rectal cancer diagnosed by pathologic examination; written informed consent. **Exclusion criteria** Liver or lung metastases assessed by computer tomography, magnetic resonance imaging or ultrasonography; BMI of >30 kg/m²; acute intestinal obstruction; serious infection; previous abdominal surgery; patients who had received neoadjuvant therapy.		**Statistical analysis** For survival, Kaplan-Meier method was used and log-rank test was used to compare the interventions.		
Full citation Lujan, J., Valero, G., Hernandez, Q., Sanchez, A., Frutos, M. D., Parrilla, P., Randomized clinical trial comparing	**Sample size** N=204 randomised; n=101 allocated to laparoscopic surgery but n=97 included in analysis (2 excluded due to postoperative deaths and 2 excluded because	**Interventions** Laparoscopic versus open surgery All patients underwent TME with preservation of the hypogastric nerves.	Details Randomisation and allocation concealment Randomisation was computer-generated with the surgical approach concealed in a sealed	Results Outcome: Overall survival at 5 years Laparoscopic 72.1% (95% CI 54.1% to 90.1% Open 75.3% (95% CI 63.3% to 87.3%)	**Limitations** Cochrane risk of bias tool Selection bias Random sequence generation: low risk Allocation concealment: low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
laparoscopic and open surgery in patients with rectal cancer, British Journal of Surgery, 96, 982-989, 2009 **Ref Id** 748829 **Country/ies where the study was carried out** Spain **Study type** RCT **Aim of the study** To compare surgical outcomes after laparoscopic and open approaches for mid and low rectal cancers. **Study dates** January 2002 to February 2007	of tumour persistence); n=103 allocated to open surgery but n=96 included in analysis (3 excluded due to postoperative deaths and 4 excluded because of tumour persistence) **Characteristics** Age in years, mean±SD Laparoscopic 67.8 (12.9) Open 66.0 (9.9) Male sex, n/n Laparoscopic 64/103 Open 62/101 Tumour location from the anal verge in cm, mean±SD Laparoscopic 5.49 (3.04) Open 6.24 (2.91) Preoperative stage, n (%) I Laparoscopic 11 (11) Open 15 (15) II Laparoscopic 35 (35) Open 39 (38)	The laparoscopic surgery was performed with 4 or sometimes 5 ports. Surgical approach, n (%) Anterior resection Laparoscopic 77 (76) Open 81 (79) Abdominoperineal resection Laparoscopic 24 (24) Open 22 (21) Neoadjuvant therapy, n (%) Laparoscopic 73 (72) Open 77 (75)	envelope until the day of operation. Blinding No blinding. Follow-up/outcomes Postoperative complications were regarded as those occurring during admission or up to 30 days after surgery. All patients were followed up as outpatients every 3 months for the first 2 years and every 6 months thereafter. On each visit the participants had a physical examination, general blood tests and determination of the CEA level. Every 6 months they alternated between thoracic and abdominal computer tomography or abdominal ultrasonography and chest radiography. A complete colonoscopy was performed yearly. The primary endpoints were number of lymph nodes isolated, circumferential margin involvement, rate of complications and length of hospital stay. Secondary endpoints were local	p=0.980 Outcome: CRM involved (not defined) Laparoscopic 4/101 Open 3/103 Outcome: Distal margin involved (not defined) Laparoscopic 0/101 Open 0/103 Outcome: Local recurrence at 5 years Laparoscopic 4.8% (95% CI 0% to 11.5%) Open 5.3% (0% to 11.2%) p=0.781 Outcome: Length of hospital stay in days, mean±SD Laparoscopic 8.2±7.3 Open 9.9±6.8 Outcome: Postoperative mortality (up to 30 days after surgery)	Performance bias Blinding of participants and personnel: high risk (No blinding.) Detection bias Blinding of outcome assessment: low/high risk (No blinding. High risk of bias for subjective outcomes.) Attrition bias Incomplete outcome data: low risk (Intention-to-treat analysis done for most outcomes, for survival outcomes per-protocol analysis done.) Reporting bias Selective reporting: low risk Other bias Other sources of bias: - **Other information** None

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Source of funding None reported.	III Laparoscopic 45 (45) Open 44 (43) IV Laparoscopic 10 (10) Open 5 (5) **Inclusion criteria** Patients with mid and low rectal adenocarcinoma. **Exclusion criteria** Locally advanced disease (T4); familial adenomatous polyposis; those who underwent emergency surgery.		recurrence, disease-free and overall survival. (Only outcomes relevant for this review are reported here.) Local recurrence was defined as reappearance of tumour in the surgical field and it was confirmed by histological examination. **Statistical analysis** Kaplan–Meier estimation method and survival curves were compared with the log rank test.	Laparoscopic 2/101 Open 3/103 Outcome: Anastomotic leak (in anterior resection only) Laparoscopic 5/77 Open 10/81 Outcome: Surgical wound infection Laparoscopic 0/101 Open 2/103 Outcome: Blood loss in ml, mean±SD Total Laparoscopic 127.8±113.3 Open 234.2±174.3 t-test p=<0.001 Anterior resection Laparoscopic 109.6±117.3 Open 199.5±153.3 t-test p=0.001 Abdominoperineal resection Laparoscopic 187.5±74.9 Open 346.9±195.3	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				t-test p=0.006	
Full citation Ng, S. S. M., Leung, K. L., Lee, J. F. Y., Yiu, R. Y. C., Li, J. C. M., Teoh, A. Y. B., Leung, W. W., Laparoscopic-assisted versus open abdominoperineal resection for low rectal cancer: A prospective randomized trial, Annals of Surgical Oncology, 15, 2418-2425, 2008 **Ref Id** 749447 **Country/ies where the study was carried out** Hong Kong **Study type** RCT	**Sample size** N=99 randomised; n=51 allocated to laparoscopic surgery; n=48 allocated to open surgery **Characteristics** Age in years, mean±SD Laparoscopic 63.7±11.8 Open 63.5±12.6 Male sex, n/n Laparoscopic 31/51 Open 30/48 AJCC staging, n/n I Laparoscopic 10/51 Open 8/48 II Laparoscopic 13/51 Open 8/48 III Laparoscopic 17/51 Open 20/48 IV Laparoscopic 11/51	**Interventions** Laparoscopic-assisted abdominoperineal resection versus open abdominoperineal resection Laparoscopic surgery was performed with 3 ports. No one received preoperative (chemo)radiotherapy.	**Details** Randomisation and allocation concealment Randomisation was performed on the day before surgery according to a computer-generated random sequence kept concealed by an independent operating theatre coordinator. Blinding No blinding. Follow-up/outcomes All patients were followed up regularly at 3-month intervals in the first 2 years and then every 6 months thereafter for clinical examination and CEA testing. The survival status was cross-checked with the networked computer database of local hospital authority. **Statistical analysis**	**Results** Outcome: Overall survival after curative resection (stages I-III) (median 87 or 90 months of follow-up) Laparoscopic n=40, 12 events Open n=36, 17 events p=0.20 Outcome: CRM involvement (not defined) Laparoscopic 3/40 Open 2/36 Outcome: Local/peritoneal recurrence after curative resection (stages I-III) (median 87 or 90 months of follow-up) Laparoscopic 2/40 Open 4/36	**Limitations** Cochrane risk of bias tool Selection bias Random sequence generation: low risk Allocation concealment: unclear risk (No sufficient detail provided.) Performance bias Blinding of participants and personnel: high risk (No blinding.) Detection bias Blinding of outcome assessment: high risk (No blinding.) Attrition bias Incomplete outcome data: unclear risk (Not clear how many were lost to follow-up. Survival analysis not done on intention-to-treat population although the paper claims so.) Reporting bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Aim of the study To compare laparoscopic-assisted versus open abdominoperineal resection in patients with low rectal cancer. **Study dates** September 1994 to February 2005 **Source of funding** None reported.	Open 12/48 **Inclusion criteria** Patients diagnosed low rectal cancer within 5 cm from the anal verge. **Exclusion criteria** Tumour >6 cm; tumour infiltration to the adjacent organs on ultrasonography and/or computed tomography; recurrent disease; did not consent to randomisation; intestinal obstruction or perforation.		Survival and disease-free interval were calculated by the Kaplan-Meier method, and differences between groups were compared with the log-rank test. The paper claims to have done intention-to-treat analysis but survival analysis was not done on all randomised patients.	Outcome: Length of hospital stay in days, mean (range) Laparoscopic 10.8 (5-27) Open 11.5 (5-38) p=0.55 Outcome: Postoperative death (timeframe not provided) Laparoscopic 1/51 Open 1/48 Outcome: Perineal wound infection Laparoscopic 10/51 Open 6/48 Abdominal wound infection Laparoscopic - (not applicable) Open 4/48 Outcome: Blood loss in ml, mean (range)* Laparoscopic 321.7 (0–3000) Open 555.6 (0–4720) p=0.093	Selective reporting: low risk Other bias Other sources of bias: - **Other information** None

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Ng, S. S., Leung, K. L., Lee, J. F., Yiu, R. Y., Li, J. C., Hon, S. S., Long-term morbidity and oncologic outcomes of laparoscopic-assisted anterior resection for upper rectal cancer: ten-year results of a prospective, randomized trial, Dis Colon Rectum, 52, 558-66, 2009 **Ref Id** 809749 **Country/ies where the study was carried out** Hong Kong **Study type** RCT **Aim of the study**	**Sample size** N=153 randomised; n=76 allocated to laparoscopic anterior resection; n=77 allocated to open anterior resection **Characteristics** Age in years, mean±SD Laparoscopic 66.5±11.9 Open 65.7±12.0 Male sex, n/n Laparoscopic 37/76 Open 48/77 AJCC stage, n/n I Laparoscopic 11/76 Open 13/77 II Laparoscopic 29/76 Open 29/77 III Laparoscopic 20/76 Open 28/77 IV Laparoscopic 16/76 Open 7/77	**Interventions** Laparoscopic anterior resection versus open anterior resection	**Details** Randomisation and allocation concealment Blinding No blinding. Follow-up/outcomes After surgery, the patients were followed up regularly at 3-month intervals in the first 2 years and then every 6 months until year 5. Thereafter, patients were seen annually. Clinical examination, rigid sigmoidoscopy, and serum CEA testing were done at each visit. Colonoscopy was performed at one year after surgery, and thereafter every 3 years. If recurrence was suspected, computed tomography or positron emission tomography would be performed. Data regarding long-term morbidity, mortality, recurrence, and survival were prospectively recorded. The survival status was cross-checked with the networked computer database of the local hospital authority.	Results Outcome: Overall survival after curative resection (median 109 and 112.5 months of follow-up) Laparoscopic n=59, 22 events Open n=67, 26 events p=0.303 Outcome: CRM involvement Laparoscopic 2/76 Open 1/77 Outcome: Locoregional recurrence at 10 years Laparoscopic 7.1% Open 4.9% p=0.677 Outcome: Length of hospital stay in days, mean (range) Laparoscopic 8.4 (2-32) (n=76) Open 10.0 (3-39) (n=77)	**Limitations** Cochrane risk of bias tool Selection bias Random sequence generation: low risk Allocation concealment: unclear risk (No sufficient detail provided.) Performance bias Blinding of participants and personnel: high risk (No blinding.) Detection bias Blinding of outcome assessment: high risk (No blinding.) Attrition bias Incomplete outcome data: low risk (No losses to follow-up. Survival analysis not done on intention-to-treat population although the paper claims so.) Reporting bias Selective reporting: low risk Other bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
To compare laparoscopic and open resection in patients with upper rectal cancer. **Study dates** September 1993 to October 2002 **Source of funding** None reported.	**Inclusion criteria** Patients with upper rectal cancer (defined as adenocarcinoma in the rectum of which the lowest margin of the tumour was located between 12 and 15 cm from the anal verge as determined by rigid sigmoidoscopy). (The trial originally included rectosigmoid cancers and upper rectal cancers but this publication only reports outcomes for the subpopulation of people with upper rectal cancers.) **Exclusion criteria** Distal tumour needing anastomosis within 5 cm of the dentate line; tumour >6 cm; tumour infiltration to adjacent organs on sonography with or without computer tomography scan; previous abdominal operations near the region of the colorectal operation; individuals who did not consent to randomisation; those		Locoregional recurrence was defined as the presence of radiologically confirmed or histologically proven tumour restricted to the anastomosis or in the pelvis within the region of the primary surgery. **Statistical analysis** Data were analysed by the intention-to-treat principle. Survival and recurrence were calculated by the Kaplan-Meier method, and differences between the groups were compared by the log-rank test.	p=0.013 Outcome: Operative mortality Laparoscopic 2/76 Open 4/77 Outcome: Anastomotic leak Laparoscopic 1/76 Open 4/77 Outcome: Wound infection Laparoscopic 5/76 Open 9/77 Outcome: Blood loss in ml, mean (range) Laparoscopic 280.0 (0-3000) (n=76) Open 337.3 (0-2542) (n=77) p=0.338	Other sources of bias: - **Other information** None

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	with intestinal obstruction or perforation.				
Full citation Ng, Ss, Lee, Jf, Yiu, Ry, Li, Jc, Hon, Ss, Mak, Tw, Ngo, Dk, Leung, Ww, Leung, Kl, Laparoscopic-assisted versus open total mesorectal excision with anal sphincter preservation for mid and low rectal cancer: a prospective, randomized trial, Surgical Endoscopy, 28, 297-306, 2014 **Ref Id** 749442 **Country/ies where the study was carried out** Hong Kong **Study type** RCT	**Sample size** N=80 randomised; n=40 allocated to laparoscopic TME; n=40 allocated to open TME **Characteristics** Age in years, mean±SD Laparoscopic 60.2±11.3 Open 62.1±12.6 Male sex, n/n Laparoscopic 24/40 Open 22/40 BMI mean±SD Laparoscopic 23.1±3.4 Open 22.4±3.2 Tumour location from the anal verge in cm, mean±SD Laparoscopic 6.9±1.7 Open 7.1±2 AJCC staging, n/n I Laparoscopic 5/40 Open 6/40	**Interventions** Laparoscopic-assisted TME versus open TME All surgeries were done with anal sphincter preservation. Preoperative therapy was not given. (From September 2006 long-course preoperative chemoradiotherapy was offered to selected patients with radiologic T3 or T4 and/or N+ disease but those patients were excluded from this study.)	**Details** Randomisation and allocation concealment Randomisation was performed on the day before surgery according to a computer-generated random sequence kept concealed by an independent operating theatre coordinator. Blinding No blinding. Follow-up/outcomes The patients were followed up regularly at 3-month intervals in the first 2 years and then every 6 months until year 5. Thereafter, patients were seen annually. Clinical examination, rigid sigmoidoscopy, and serum CEA testing were done at each visit. Colonoscopy was performed at one year after surgery, and thereafter every three years. Data regarding perioperative outcome, long-term	**Results** Outcome: Overall survival after curative resection (stages I-III) (median 75.7 months of follow-up) Laparoscopic n=36, 6 events* Open n=36, 7 events* p=0.912 Outcome: CRM involvement (not defined) Laparoscopic 3/40 Open 2/40 Outcome: Locoregional recurrence after curative resection (stages I-III) (median 75.7 months of follow-up) Laparoscopic 1/36 Open 4/36 Outcome: Length of hospital stay in says, mean (range)	**Limitations** Cochrane risk of bias tool Selection bias Random sequence generation: low risk Allocation concealment: unclear risk (No sufficient detail provided.) Performance bias Blinding of participants and personnel: high risk (No blinding.) Detection bias Blinding of outcome assessment: high risk (No blinding.) Attrition bias Incomplete outcome data: low risk (No losses to follow-up. Survival analysis not done on intention-to-treat population although the paper claims so.) Reporting bias Selective reporting: low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Aim of the study To compare laparoscopic-assisted and open TME with anal sphincter preservation in patients with mid and low rectal cancer. **Study dates** August 2001 to August 2007 **Source of funding** This study was supported by any grant.	II Laparoscopic 15/40 Open 11/40 III Laparoscopic 16/40 Open 19/40 IV Laparoscopic 4/40 Open 4/40 **Inclusion criteria** Patients diagnosed with mid and low rectal cancer (lowest margin of the tumour was located between 5 and 12 cm from the anal verge as determined by rigid sigmoidoscopy). **Exclusion criteria** Tumour larger than 6 cm; tumour infiltration to the adjacent organs on computed tomography; recurrent disease; synchronous colorectal tumours; intestinal obstruction or perforation; patients who required neoadjuvant therapy; patients who did		morbidity, recurrence, and survival were prospectively recorded. The survival status was cross-checked with the networked computer database of the local hospital authority. If recurrence was suspected, computed tomography or positron emission tomography would be performed. Primary endpoints were short-term clinical outcome, including postoperative recovery and short-term morbidity. Secondary endpoints were long-term morbidity and survival. **Statistical analysis** Data were analysed by intention-to-treat principle. Recurrence and survival were calculated by the Kaplan-Meier method, and differences between the groups were compared with log-rank test.	Laparoscopic 10.5 (5-35) Open 15 (6-167) p=0.071 Outcome: Operative death Laparoscopic 0/40 Open 0/40 Outcome: Anastomotic leak Laparoscopic 1/40 Open 0/40 Outcome: Wound infection Laparoscopic 1/40 Open 7/40 Outcome: Blood loss in ml, mean (range) Laparoscopic 142 (0-2,000) Open 361 (5-2,500) p<0.001 *Number of events calculated from the Kaplan-Meier curve	Other bias Other sources of bias: - **Other information** None

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	not consent to randomisation.				
Full citation Park, E. J., Cho, M. S., Baek, S. J., Hur, H., Min, B. S., Baik, S. H., Lee, K. Y., Kim, N. K., Long-term oncologic outcomes of robotic low anterior resection for rectal cancer, Annals of Surgery, 261, 129-137, 2015 **Ref Id** 749686 **Country/ies where the study was carried out** South Korea **Study type** Prospective cohort study **Aim of the study** To evaluate the long-term	**Sample size** N=133 robotic lower anterior resection; N=84 laparoscopic lower anterior resection **Characteristics** Age in years, mean±SD Robotic 59.2±11.4 Laparoscopic 63.5±11.2 Male sex, n (%) Robotic 86 (65) Laparoscopic 60 (71) BMI, mean±SD Robotic 23.±2.9 Laparoscopic 22.9±2.8 Tumour location from the anal verge, n (%) 0-5 cm Robotic 33 (25) Laparoscopic 16 (19) 5.1-10 cm Robotic 60 (45) Laparoscopic 37 (44) 10.1-15 cm Robotic 40 (30)	**Interventions** Robotic versus laparoscopic lower anterior resection For robotic surgery, the da Vinci surgical system was used. All robotic-assisted lower anterior resections were performed by the hybrid technique. Chemoradiotherapy was given for stage T3-4N0 or N+ M0 low- and mid-rectal cancers. Majority of the patients underwent postoperative chemoradiotherapy due to the institute's treatment protocol at the time of the study. The regimen was based on 5-FU and leucovorin. Preoperative chemoradiotherapy, n (%) Robotic 15 (11) Laparoscopic 10 (12)	**Details** Randomisation and allocation concealment This was not a randomised study. The groups were not matched. Blinding No blinding. Follow-up/outcomes Data were collected from the Yonsei Colorectal Cancer Database. The follow-up visits were at 1 month, 3 months, and every 3 months for the first 3 years and then 6 months until 5 years after surgery. Regular laboratory tests with CEA and a physical examination were performed. Colonoscopy was done 1 year after surgery and at 5 years. Chest and abdominopelvic computed tomography scans were obtained every 6 months to detect local recurrence or systemic metastasis during the follow-up period.	**Results** Outcome: Overall survival at 5 years Stages I-III Robotic 92.8% Laparoscopic 93.5% p=0.829 Stage II Robotic 94.2% Laparoscopic 100% p=0.221 Stage III Robotic 86.8% Laparoscopic 87.8% p=0.916	**Limitations** ROBINS-I checklist for non-randomised studies of Interventions Pre-intervention Bias due to confounding: Moderate risk of bias (This is a non-randomised study, the groups were not matched by any characteristic but the study controlled for potential confounding or case-mix in the analysis.) Bias in selection of participants into the study: Low risk of bias At intervention Bias in classification of Interventions: Low risk of bias Post-intervention Bias due to deviations from intended Interventions: Low risk of bias Bias due to missing data: Low risk of bias Bias in measurement of outcomes: Low risk of bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
oncologic outcomes of robotic surgery for rectal cancer compared with conventional laparoscopic surgery. **Study dates** April 2006 to August 2011 **Source of funding** None reported.	Laparoscopic 31 (37) Postoperative pathologic TNM stage, n (%) I Robotic 49 (37) Laparoscopic 22 (26) II Robotic 36 (27) Laparoscopic 28 (33) III Robotic 48 (36) Laparoscopic 34 (41) **Inclusion criteria** People diagnosed with rectal adenocarcinoma; underwent low anterior resection by robotic or conventional laparoscopic approach. **Exclusion criteria** Open surgery; stage IV disease; patients lost to follow-up.		**Statistical analysis** Survival was analysed using the Kaplan-Meier method and the groups were compared with the log-rank test. Univariate analysis of clinicopathological factors upon overall survival was performed using the log-rank test to determine the prognostic value of the surgical methods, all statistically significant factors determined by univariate analysis were conducted for multivariate analysis by the Cox proportional hazards regression model with a forward selection of variables.		Bias in selection of the reported result: Low risk of bias **Other information** None
Full citation van der Pas, M. H., Haglind, E., Cuesta, M. A., Furst, A., Lacy, A.	**Sample size** See Bonjer 2015 (COLOR II trial). **Characteristics**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
M., Hop, W. C., Bonjer, H. J., C. Olorectal cancer Laparoscopic or Open Resection II Study Group, Laparoscopic versus open surgery for rectal cancer (COLOR II): short-term outcomes of a randomised, phase 3 trial, Lancet Oncology, 14, 210-8, 2013 **Ref Id** 751236 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**	**Inclusion criteria** **Exclusion criteria**				
Full citation Pontallier, A., Denost, Q., Van Geluwe, B., Adam, J. P.,	**Sample size** See Denost 2017 (Bordeaux' trial).	**Interventions**		Results	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Celerier, B., Rullier, E., Potential sexual function improvement by using transanal mesorectal approach for laparoscopic low rectal cancer excision, Surgical Endoscopy and Other Interventional Techniques, 30, 4924-4933, 2016 **Ref Id** 749925 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**	**Characteristics** **Inclusion criteria** **Exclusion criteria**				
Full citation	**Sample size**	**Interventions**	**Details**	**Results**	**Limitations**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Quah, H. M., Jayne, D. G., Eu, K. W., Seow-Choen, F., Bladder and sexual dysfunction following laparoscopically assisted and conventional open mesorectal resection for cancer, Br J Surg, 89, 1551-6, 2002 **Ref Id** 809751 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**	See Jayne 2010 (CLASICC trial). **Characteristics** **Inclusion criteria** **Exclusion criteria**				Other information
Full citation	**Sample size** N=400	**Interventions** N=400	**Details**	**Results**	**Limitations**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Rouanet P, Bertrand MM, Jarlier M et al. Robotic Versus Laparoscopic Total Mesorectal Excision for Sphincter-Saving Surgery: Results of a Single-Center Series of 400 Consecutive Patients and Perspectives. Ann Surg Oncol. 2018 Nov;25(12):3572-3579. **Ref Id** 982948 **Country/ies where the study was carried out** France **Study type** Retrospective cohort study **Aim of the study** To compare robotic total mesorectal	**Characteristics** Male, n (%) 131 65.5% (R-TME); 136 (68.0%) Median age years (range) 64 (25, 85 (R-TME); 63.5 (35, 86) (L-TME) Tumour location, n (%) Upper >/= 11 cm 27 (13.6); middle 6-10 cm 83 (41.9); low (</= 5 cm) 88 (44.4) (R-TME). Upper >/= 11 cm 39 (20.2); middle 6-10 cm 75 (38.9); low (</= 5 cm) 79 (40.9) (L-TME) **Inclusion criteria** Patients with histologically proven adenocarcinoma located \12 cm from the anal verge who underwent minimally invasive surgery (laparoscopic or robotic TME), with no previous or concurrent malignancy and no evidence of distant	R-TME (n=200) L-TME (n=200)	Prospectively collected records of 400 patients with mild or low rectal cancer who underwent curative conservative surgery Follow-up: NR **Statistical analysis:** Patient Characteristics, and surgical and pathology results were described using frequency and percentage for categorical variables and median and range for continuous variables. Data were compared using the Pearson Chi square test or the nonparametric Kruskal–Wallis test for categorical or continuous variables. Analysis of the QLQC30 questionnaires was performed according to EORTC guidelines.11 FSFI, IIEF, and IPSS scores are described as continuous variables, according to groups. Subgroup analyses were conducted to estimate the odds ratios (ORs) for conversion to laparotomy and CRM involvement between the groups. ORs	Overall survival: Follow-up 4.1 years (R-TME 3.1 years [95% CI 2.9, 3.4 years]; L-TME 5.7 years [95% CI 5.3, 6.0 years]) 3 year survival rate was 84.1% (95% CI 77.3, 88.9%) (R-TME) vs 88.4% (95% CI 82.9, 92.2%) (L-TME) Quality of life: Sexual results were similar in the two groups, in both female (FSFI assessment) and male (IIEF score) patients. Quality of life was similar in the two groups in the overall population and for a high-risk subgroup of patients (n=61) including men with BMI >/= 28 kg/m2 and low rectal tumour. A trend for better symptom scores was reported	ROBINS-I checklist for non-randomised studies of Interventions Pre-intervention Bias due to confounding: Moderate risk of bias (This is a non-randomised study, the groups were not matched by any characteristic.) Bias in selection of participants into the study: Low risk of bias At intervention Bias in classification of Interventions: Low risk of bias Post-intervention Bias due to deviations from intended Interventions: Low risk of bias Bias due to missing data: Low risk of bias Bias in measurement of outcomes: Low risk of bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
excision (R-TME) with laparoscopic TME (L-TME) in a series of consecutive rectal cancer patients **Study dates** 2008 to 2012 and 2012 to 2015 **Source of funding** Financial support was provided by Intuitive Surgical, Aubonne, Switzerland	metastasis at time of surgery. **Exclusion criteria** Not reported		and their 95% confidence intervals (95% CI) were estimated using a univariate logistic regression model. Overall survival was estimated using the Kaplan–Meier method, and survival curves were compared with the log-rank test. No imputation method was used in Laparoscopic Versus Robotic Proctectomy 3573 case of missing data. All tests were two-sided, and p value B 0.05 was considered statistically significant. Statistical analyses were performed using STATA 13.0 (StataCorp, College Station, TX, USA).	for the R-TME group in the high-risk patients although it was not significant	Bias in selection of the reported result: Low risk of bias **Other information** None
Full citation Stevenson, A. R. L., Solomon, M. J., Lumley, J. W., Hewett, P., Clouston, A. D., Gebski, V. J., Davies, L., Wilson, K., Hague, W., Simes, J., Effect of laparoscopic-assisted resection vs open resection	**Sample size** N=475 randomised; n=238 allocated to laparoscopic surgery; n=237 allocated to open surgery **Characteristics** Age in years, median (IQR) Laparoscopic 65 (56-74) Open 65 (56-73)	**Interventions** Laparoscopic surgery versus open surgery The open surgery was a hybrid operation in which the abdominal component (splenic flexure mobilization and vessel division) could be performed laparoscopically; however, the rectal mobilization had to be performed as an open	**Details** Randomisation and allocation concealment Randomisation was conducted at the National Health and Medical Research Council Clinical Trials Centre via the Internet using the method of minimization and stratified by the location of the tumour from the anal verge, the registering surgeon, the planned operative	**Results** Outcome: Negative C RM (>=1 mm) Laparoscopic 222/238 Open 228/235 Outcome: Negative distal resection margin (>=1 mm) Laparoscopic 236/238 Open 234/235	**Limitations** Cochrane risk of bias tool Selection bias Random sequence generation: unclear risk (Limited details reported.) Allocation concealment: unclear risk (Details not reported.) Performance bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
on pathological outcomes in rectal cancer: The ALaCaRT randomized clinical trial, JAMA - Journal of the American Medical Association, 314, 1356-1363, 2015 **Ref Id** 750805 **Country/ies where the study was carried out** Australia **Study type** RCT (ALaCaRT trial) **Aim of the study** To determine whether laparoscopic resection is noninferior to open rectal cancer resection for adequacy of cancer clearance. **Study dates**	Male sex, n (%) Laparoscopic 160 (67) Open 151 (64) Tumour location from the anal verge, n/n <5 cm Laparoscopic 82 (35) Open 83 (35) 5-10 cm Laparoscopic 103 (43) Open 102 (44) 10-15 cm Laparoscopic 53 (22) Open 50 (21) Tumour stage, n/n T1 Laparoscopic 18 (8) Open 11 (5) T2 Laparoscopic 68 (29) Open 68 (29) T3 Laparoscopic 151 (63) Open 155 (66) Nodal status, n/n N0 Laparoscopic 107 (45) Open 123 (53)	procedure under direct vision via a laparotomy. Laparoscopic-assisted procedures could include the use of a hand port, but robotic surgery was excluded. Planned surgical approach, n (%) Low anterior resection Laparoscopic 220 (92) Open 218 (93) Abdominoperineal resection Laparoscopic 18 (8) Open 17 (7) Surgical approach performed, n (%) Low anterior resection Laparoscopic 143 (60) Open 153 (65) Low anterior resection and coloanal anastomosis Laparoscopic 69 (29) Open 58 (25) Abdominoperineal resection Laparoscopic 25 (11) Open 23 (10)	procedure, body mass index, preoperative radiotherapy (yes or no), and distant metastasis (yes or no). No other details were provided. Blinding No blinding of participants. Pathologist blinded to allocation. Follow-up/outcomes A pathologist blinded to treatment allocation examined the surgical specimen. The specimens were photographed fresh and unopened to show the mesorectal dissection anteriorly and posteriorly before inking. The pathologist assessed the distal margin in the fresh and unstretched specimen. Other details not reported. **Statistical analysis** Wilcoxon rank sum test used to compare continuous data between groups.	Outcome: Length of hospital stay in days, median (IQR) Laparoscopic 8 (6-12) Open 8 (6-12) p=0.21 Outcome: Blood loss in ml, median (IQR) Laparoscopic 100 (50-200) Open 150 (55-300) p=0.02	Blinding of participants and personnel: high risk (No blinding.) Detection bias Blinding of outcome assessment: low/high risk (Pathologist was blinded. Surgical team or patient was not blinded.) Attrition bias Incomplete outcome data: low risk Reporting bias Selective reporting: low risk Other bias Other sources of bias: - **Other information** None

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
March 2010 to November 2014 **Source of funding** The Colorectal Surgical Society of Australia and New Zealand Foundation and the National Health and Medical Research Council.	N1 Laparoscopic 92 (39) Open 80 (34) N2 Laparoscopic 37 (16) Open 30 (13) Distant metastases Laparoscopic 10 (4) Open 10 (4) **Inclusion criteria** Aged 18 years or older; histological diagnosis of adenocarcinoma of the rectum within 15 cm of the anal verge; life expectancy of at least 12 weeks; adequate performance status (Eastern Cooperative Oncology Group Scale score of ≤2); no comorbidity or condition that would preclude the use of either form of surgery. **Exclusion criteria** T4 tumours or an involved CRM (determined by pretreatment pelvic MRI,	Preoperative radiotherapy, n (%) Laparoscopic 119 (50) Open 116 (49)			

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	or endorectal ultrasound if MRI was contraindicated); concurrent or previous invasive pelvic malignant tumours (cervical, uterine, or rectal; excluding the prostate) within 5 years before study enrolment. (Distant metastases was not an exclusion criterion.)				
Full citation Stevenson ARL, Solomon MJ, Brown CSB et al. Disease-free Survival and Local Recurrence After Laparoscopic-assisted Resection or Open Resection for Rectal Cancer: The Australasian Laparoscopic Cancer of the Rectum Randomized Clinical Trial. Ann Surg. 2019 Apr;269(4):596-602. **Ref Id**	**Sample size** (See Stevenson, 2015 (ALaCaRT study))	**Interventions**	**Details**	**Results** Median follow-up was 3.2 years (range: 0.1-5.4 yrs). Outcome OS 28 deaths within 2 years and a 2-year survival estimate 94% for LAP and 93% for OPEN (difference, 0.9%, 95% CI, -3.6% to -5.4%). HR 1.08 (95% CI 0.63, 1.86) Outcome: LRR cumulative incidence at 2 years: LAP 5.4%; OPEN 3.1% [difference, 2.3%; 95% confidence interval (CI), -1.5% to 6.1%; hazard ratio	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
983031 **Country/ies where the study was carried out** Australia **Study type** RCT (ALaCaRT trial) **Aim of the study** To determine whether laparoscopic resection is noninferior to open rectal cancer resection for adequacy of cancer clearance. **Study dates** March 2010 to November 2014 **Source of funding** The Colorectal Surgical Society of Australia and New Zealand Foundation and				(HR) 1.7; 95% CI, 0.74-3.9, p=0.21.	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
the National Health and Medical Research Council.					
Full citation Yoo, B. E., Cho, J. S., Shin, J. W., Lee, D. W., Kwak, J. M., Kim, J., Kim, S. H., Robotic Versus Laparoscopic Intersphincteric Resection for Low Rectal Cancer: Comparison of the Operative, Oncological, and Functional Outcomes, Annals of Surgical Oncology, 22, 1219-1225, 2015 **Ref Id** 751717 **Country/ies where the study was carried out** South Korea **Study type** Retrospective cohort study	**Sample size** N=44 robotic intersphincteric resection; N=26 laparoscopic intersphincteric resection **Characteristics** Age in years, mean±SD Robotic 59.8±12,3 Laparoscopic 60.5±10.8 Male sex, n (%) Robotic 35 (80) Laparoscopic 19 (73) BMI, mean±SD Robotic 24.13.3 Laparoscopic 21.4±3.1 Tumour distance from the anal verge in cm, mean Robotic 3.2±0.8 Laparoscopic 3.7±0.9 Clinical T stage, n (%)	**Interventions** Robotic versus laparoscopic intersphincteric resection Robotic surgery was performed with the da Vinci Surgical System by a single surgeon. Preoperative chemoradiotherapy (5,080 cGy in 28 fractions and 5-fluorouracil) was given s electively to locally advanced cancers if the CRM was suspicious/threatened/positive or if lymph nodes that escaped the TME plane were detected using MRI or CT scan. Surgeries were performed 8 weeks after preoperative chemoradiotherapy.	**Details** Randomisation and allocation concealment This was not a randomised study. The groups were not matched. Blinding No blinding. Follow-up/outcomes Data was retrospectively obtained from a prospectively-collected database. No details about follow-up visits reported. **Statistical analysis** Survival was analysed using the Kaplan-Meier method, the differences between the groups were compared by log-rank test. The groups were not matched and the analysis did not control for potential confounding or case-mix.	**Results** Outcome: Overall survival at 3 years Robotic 95.2% Laparoscopic 88.5% p=0.174	**Limitations** ROBINS-I checklist for non-randomised studies of **Interventions** Pre-intervention Bias due to confounding: Serious risk of bias (This is a non-randomised study, the groups were not matched by any characteristic. The study did not control for potential confounding or case-mix in the analysis.) Bias in selection of participants into the study: Low risk of bias At intervention Bias in classification of **Interventions**: Low risk of bias Post-intervention Bias due to deviations from intended **Interventions**: Low risk of bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Aim of the study To compare the operative, oncological, and functional outcomes of low rectal cancer patients who underwent robotic or laparoscopic intersphincteric resection. **Study dates** September 2006 to August 2011 **Source of funding** None reported.	T1 Robotic 2 (5) Laparoscopic 3 (12) T2 Robotic 15 (34) Laparoscopic 4 (15) T3 Robotic 22 (50) Laparoscopic 18 (69) T4 Robotic 5 (11) Laparoscopic 1 (4) Clinical N stage, n (%) N0 Robotic 17 (39) Laparoscopic 14 (54) N1 Robotic 16 (36) Laparoscopic 2 (8) N2 Robotic 11 (25) Laparoscopic 10 (39) Clinical M stage, n (%) M0 Robotic 39 (89) Laparoscopic 24 (92) M1 Robotic 5 (11) Laparoscopic 2 (8)	Preoperative chemoradiotherapy, n (%) Robotic 24 (54) Laparoscopic 7 (27)			Bias due to missing data: Low risk of bias Bias in measurement of outcomes: Low risk of bias Bias in selection of the reported result: Low risk of bias **Other information** None

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	Inclusion criteria Patients with low rectal cancer (<5 cm from the anal verge) treated via laparoscopic or robotic intersphincteric resection. **Exclusion criteria** Patients with synchronous tumours or clinical T4 stage tumours that did not respond to neoadjuvant treatment.				
Full citation Zhou, Z. G., Hu, M., Li, Y., Lei, W. Z., Yu, Y. Y., Cheng, Z., Li, L., Shu, Y., Wang, T. C., Laparoscopic versus open total mesorectal excision with anal sphincter preservation for low rectal cancer, Surg Endosc, 18, 1211-5, 2004 **Ref Id**	**Sample size** n=82 underwent laparoscopic surgery; n=89 underwent open surgery. How many were originally randomised and allocated to each group is not reported. **Characteristics** Age in years, mean (range) Laparoscopic 44 (26-85) Open 45 (30-81) Male sex, n/n	**Interventions** Laparoscopic surgery versus open surgery Open resection with TME. Laparoscopic resection with TME and anal sphincter preservation.	**Details** Randomisation and allocation concealment No details reported. Blinding No blinding. Follow-up/outcomes Clinical data collected. **Statistical analysis** Chi-square test and Student's t-test was performed to determine	**Results** Outcome: Positive resection margin ("cancer cell found in the cut margins") Laparoscopic 0/82 Open 0/89 Outcome: Length of hospital stay in days, mean±SD Laparoscopic 8.1±3.1 (n=82) Open 13.3±3.4 (n=89) p=0.001	**Limitations** Cochrane risk of bias tool Selection bias Random sequence generation: unclear risk (Details not reported.) Allocation concealment: unclear risk (Details not reported.) Performance bias Blinding of participants and personnel: high risk (No blinding.) Detection bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
809754 **Country/ies where the study was carried out** China **Study type** RCT **Aim of the study** To compare open versus laparoscopic low and ultralow anterior resections, to assess the feasibility and efficacy of the laparoscopic approach of TME with anal sphincter preservation and to analyse the short-term results of patients with low rectal cancer. **Study dates** June 2001 to September 2002	Laparoscopic 46/82 Open 43/89 Dukes stage, n/n A Laparoscopic 5/82 Open 6/89 B Laparoscopic 10/82 Open 8/89 C1 Laparoscopic 33/82 Open 35/89 C2 Laparoscopic 30/82 Open 33/89 D Laparoscopic 4/82 Open 7/89 **Inclusion criteria** Patients diagnosed with rectal adenocarcinoma, with the lowest margin of tumour located under the peritoneal reflection and 1.5 cm above the dentate line.		difference between the laparoscopic and open groups.	Outcome: Operative mortality (timeframe not reported) Laparoscopic 0/82 Open 0/89 Outcome: Anastomotic leak Laparoscopic 1/82 Open 3/89 Outcome: Postoperative infection Laparoscopic 2/82 Open 3/89 Outcome: Blood loss in ml, mean (range) Laparoscopic 20 (5-120) (n=82) Open 92 (50-200) (n=89) p=0.025	Blinding of outcome assessment: high risk (No blinding.) Attrition bias Incomplete outcome data: unclear risk (The original number randomised not reported. Only outcomes immediate to surgery reported, therefore, no losses to follow-up.) Reporting bias Selective reporting: unclear risk (Not clear which outcomes should be reported.) Other bias Other sources of bias: - **Other information** None

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Source of funding National Outstanding Youth Foundation of China	**Exclusion criteria** Low rectal cancer of other pathological type (for example lymphoma); lowest margin of tumour within 1.5 cm above the dentate line; those in emergency situations (for example acute obstruction during enema, haemorrhage, and perforation); Dukes stage D with local infiltration affecting adjacent organs; those unwilling to take part in the study.				

5-FU: 5-fluorouracil; AJCC: American Joint Committee on Cancer; ASA: American Society of Anestheologists; BMI: body mass index; c: clinical; CEA: carcinoembryonic antigen; cGy: centigray unit; CI: confidence interval; CRM: circumferential resection margin; CT: computed tomography; EORTC: European Organisation for Research and Treatment of Cancer; EQ-5D: EuroQol five dimensions questionnaire; EQ-VAS: EuroQol visual analogue scale; FSFI: Female Sexual Function Index; Gy: Gray unit; HR: hazard ratio; IIEF: International Index of Erectile Function; IQR: interquartile range; IPSS: International Prostate Symptom score; LAP: laparoscopic resection; L-TME: laparoscopic total mesorectal excision; ml: millilitre; M0-1: distant metastasis stage; MRI: magnetic resonance imaging; N0-2: nodal stage; N: number; NR: not reported; p: pathological; OPEN: open resection; OR: odds ratio; PME: partial mesorectal excision; QLQ-C30: Quality of Life Questionnaire Core 30 Items; QLQ-CR38: Quality of Life Questionnaire colorectal cancer module (38 items); RCT: randomised controlled trial; ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions; R-TME: robotic total mesorectal excision; SD: standard deviation; SF-36: 36-Item Short Form Survey; T0-4: tumour stage; TME: total mesorectal excision; TNM: cancer classification system, standing for tumour, nodal and metastasis stages; VAS: visual analogue scale

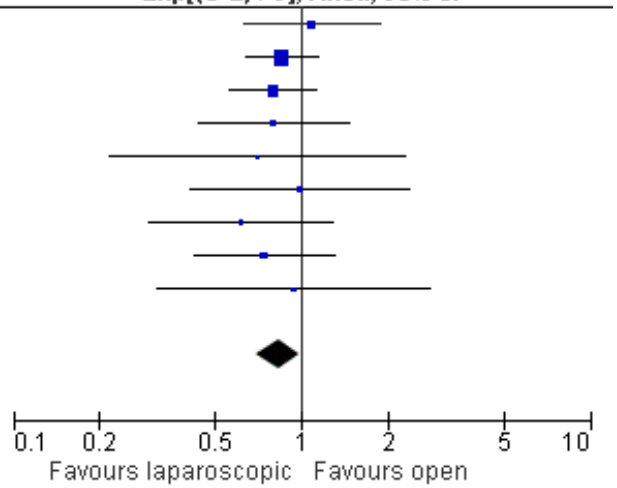
Appendix E – Forest plots

Forest plots for review question: What is the optimal surgery for rectal cancer?

Figure 2: Comparison 1: Laparoscopic versus open surgery for rectal cancer – Overall survival (median 3.2 to 9.2 years of follow-up, event is death from any cause)

	Laparoscopic		Open					Hazard Ratio	Hazard Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**O-E**	**Variance**	**Weight**	**Exp[(O-E) / V], Fixed, 95% CI**	**Exp[(O-E) / V], Fixed, 95% CI**
ALaCaRT (Stevenson 2019)	27	225	26	225	1	13	9.9%	1.08 [0.63, 1.86]	
CLASICC (Green 2013) (1)	0	253	0	128	-7.35	45.39	34.7%	0.85 [0.64, 1.14]	
COLOR II (Bonjer 2015) (2)	0	692	0	344	-7.16	31.67	24.2%	0.80 [0.56, 1.13]	
COREAN (Jeong 2014)	20	170	25	170	-2.41	10.8	8.3%	0.80 [0.44, 1.45]	
Ishibe 2017	4	29	7	28	-0.97	2.75	2.1%	0.70 [0.22, 2.29]	
Lujan 2009	9	97	11	96	-0.06	5	3.8%	0.99 [0.41, 2.37]	
Ng 2008	12	40	17	36	-3.4	7.03	5.4%	0.62 [0.29, 1.29]	
Ng 2009	22	59	26	67	-3.56	11.92	9.1%	0.74 [0.42, 1.31]	
Ng 2014	6	36	7	36	-0.2	3.23	2.5%	0.94 [0.32, 2.80]	
Total (95% CI)		**1601**		**1130**			**100.0%**	**0.83 [0.70, 0.99]**	
Total events	100		119						

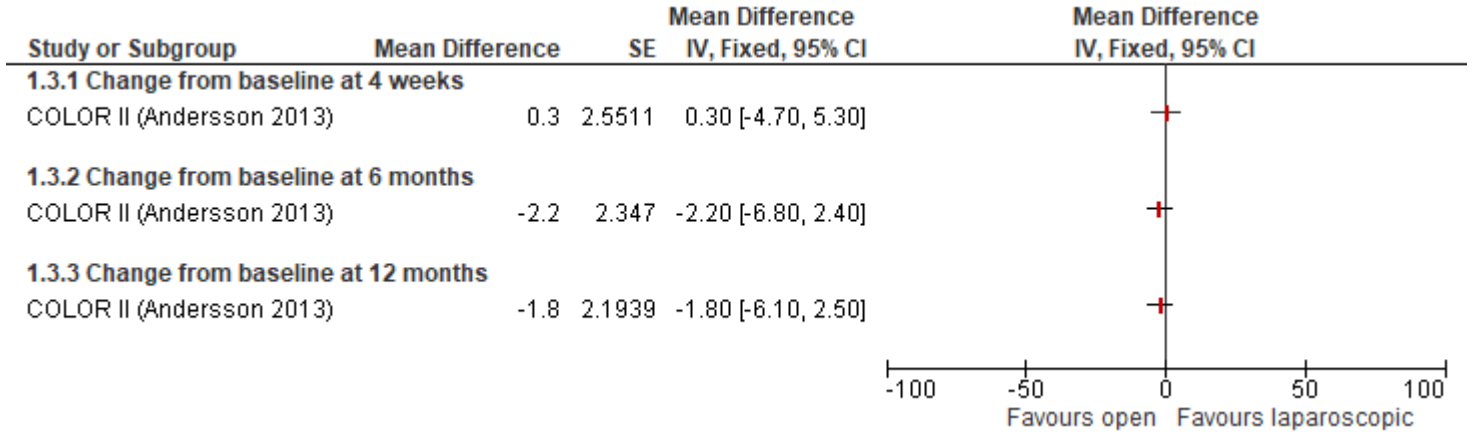
Heterogeneity: Chi² = 2.04, df = 8 (P = 0.98); I² = 0%
Test for overall effect: Z = 2.11 (P = 0.04)



Footnotes
(1) Number of events not reported
(2) Number of events not reported

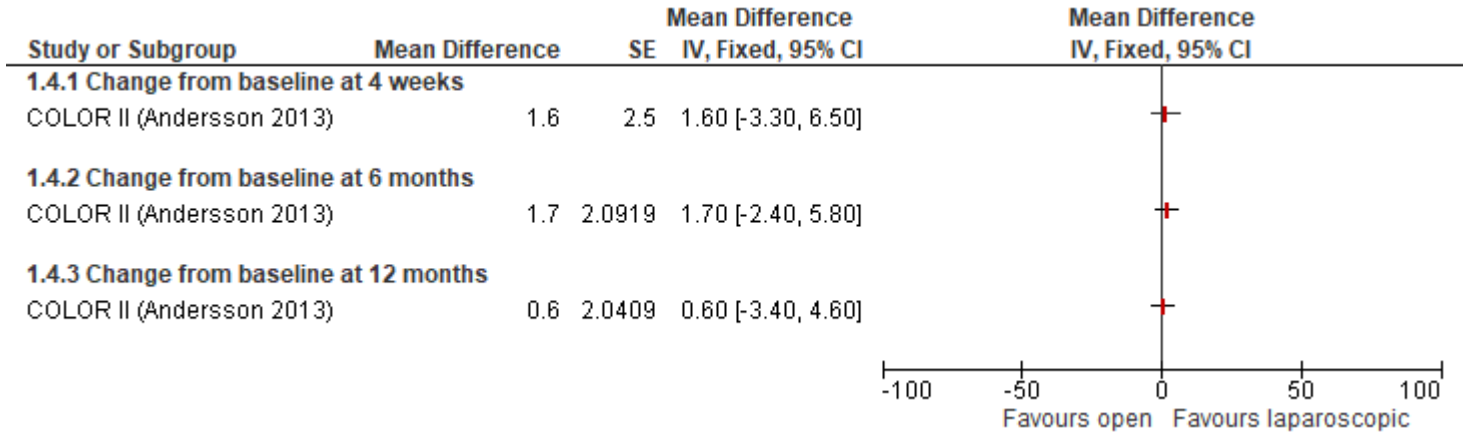
CI: confidence interval; O-E: observed minus expected; V: variance

Figure 3: Comparison 1: Laparoscopic versus open surgery for rectal cancer – Quality of life - Global quality of life score (QLQ-C30; scale 0-100; better indicated by higher values)



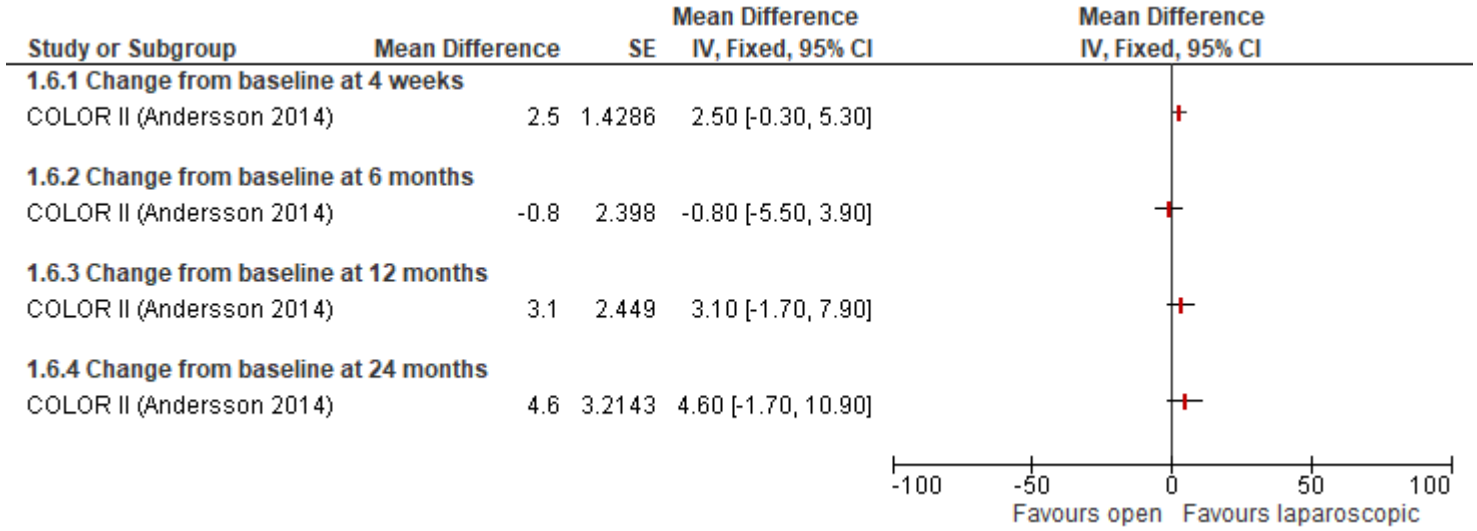
CI: confidence interval; IV: inverse variance; QLQ-C30: Quality of Life Questionnaire Core 30 Items; SE: standard error

Figure 4: Comparison 1: Laparoscopic versus open surgery for rectal cancer – Quality of life - Global health status (EQ-VAS; scale 0-100; better indicated by higher values)



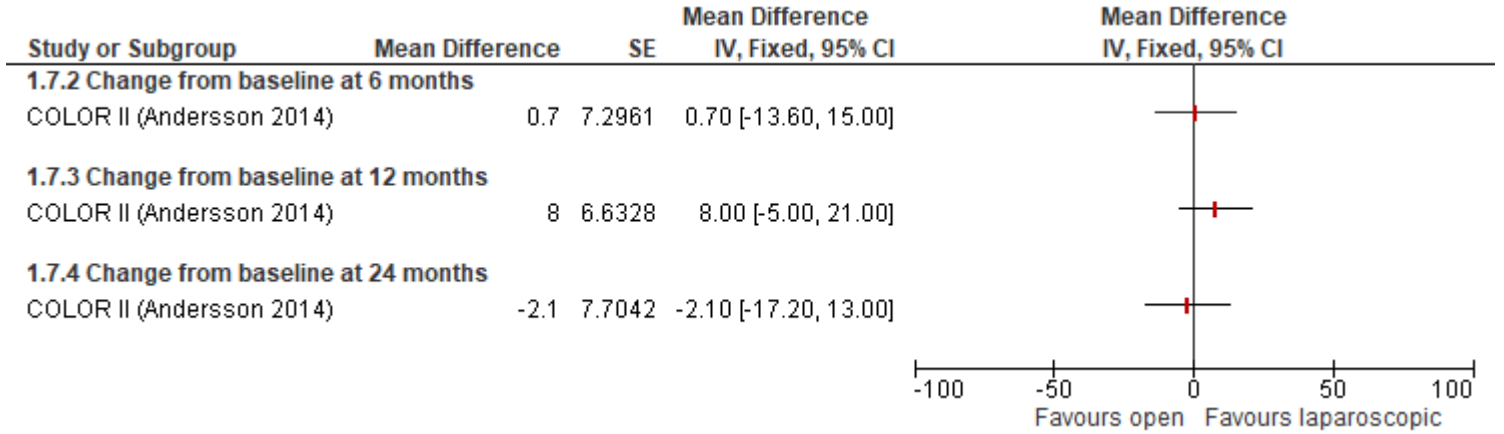
CI: confidence interval; EQ-VAS: EuroQol visual analogue scale; IV: inverse variance; SE: standard error

Figure 5: Comparison 1: Laparoscopic versus open surgery for rectal cancer – Quality of life - Sexual functioning (QLQ-CR38; scale 0-100; better indicated by higher values)



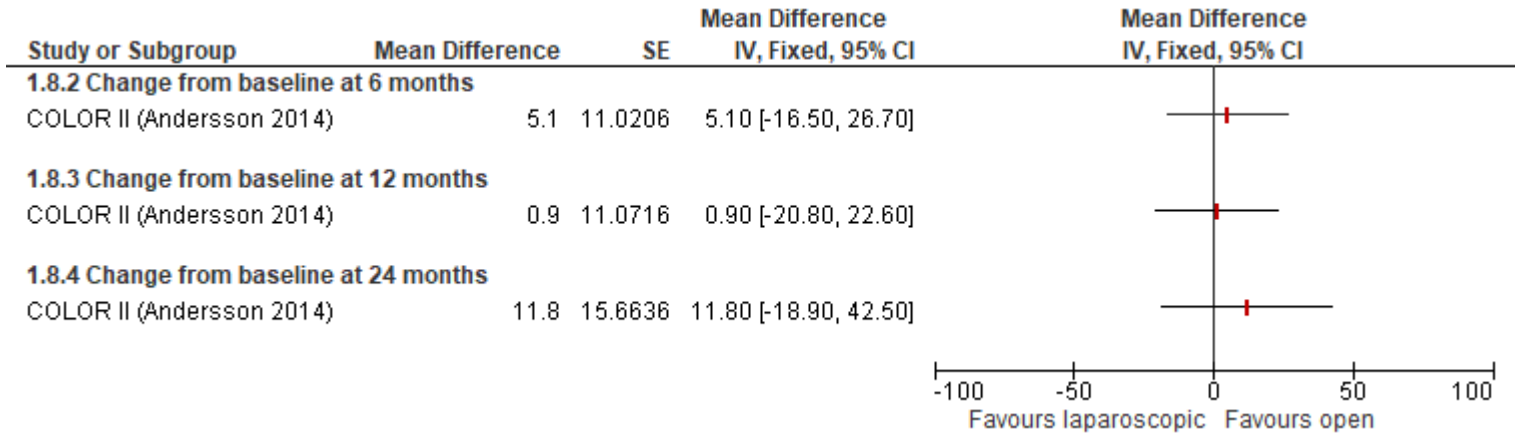
CI: confidence interval; IV: inverse variance; QLQ-CR38: Quality of Life Questionnaire colorectal cancer module (38 items); SE: standard error

Figure 6: Comparison 1: Laparoscopic versus open surgery for rectal cancer – Quality of life - Sexual enjoyment (QLQ-CR38; scale 0-100; better indicated by higher values)



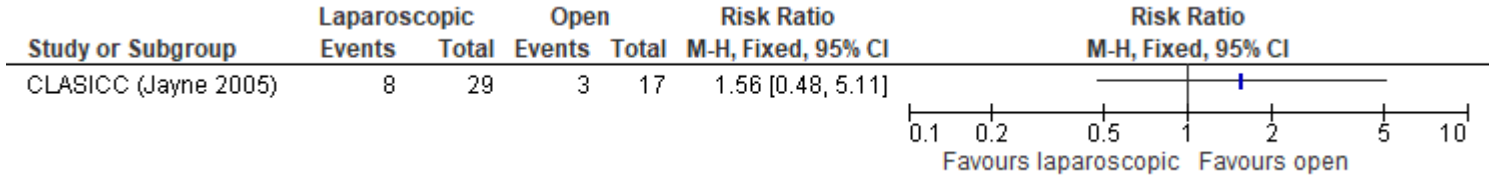
CI: confidence interval; IV: inverse variance; QLQ-CR38: Quality of Life Questionnaire colorectal cancer module (38 items); SE: standard error

Figure 7: Comparison 1: Laparoscopic versus open surgery for rectal cancer – Quality of life - Female sexual problems (QLQ-CR38; scale 0-100; better indicated by lower values)



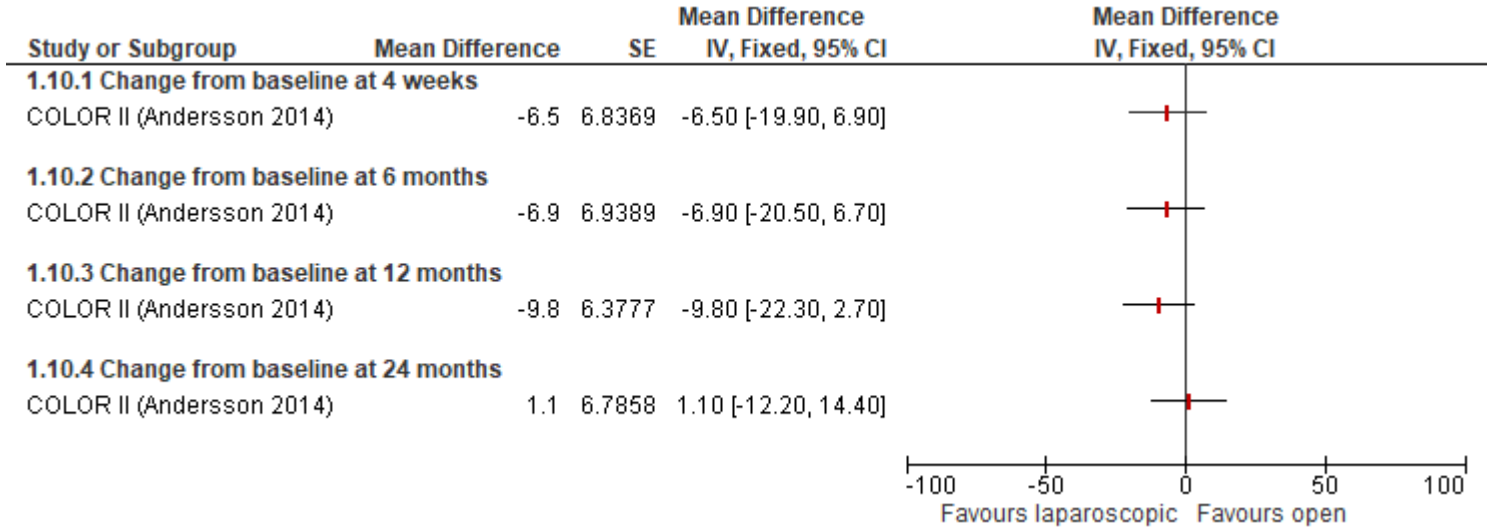
CI: confidence interval; IV: inverse variance; QLQ-CR38: Quality of Life Questionnaire colorectal cancer module (38 items); SE: standard error

Figure 8: Comparison 1: Laparoscopic versus open surgery for rectal cancer – Quality of life - Overall level of sexual function decreased 'quite a lot' or 'severely' as a result of surgery in women (FSFI)



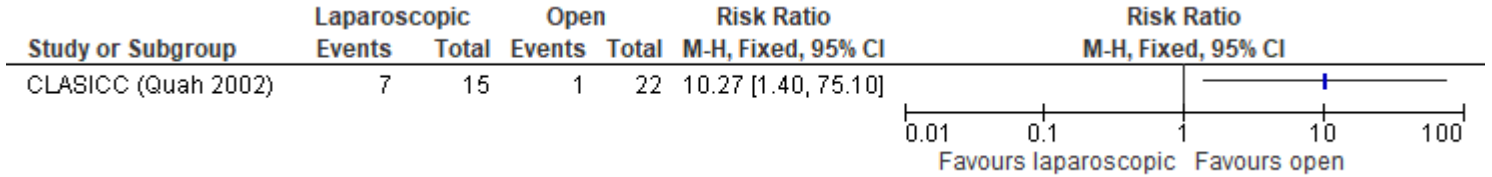
CI: confidence interval; FSFI: Female Sexual Function Index; M-H: Mantel Haenszel method

Figure 9: Comparison 1: Laparoscopic versus open surgery for rectal cancer – Quality of life - Male sexual problems (QLQ-CR38; scale 0-100; better indicated by lower values)



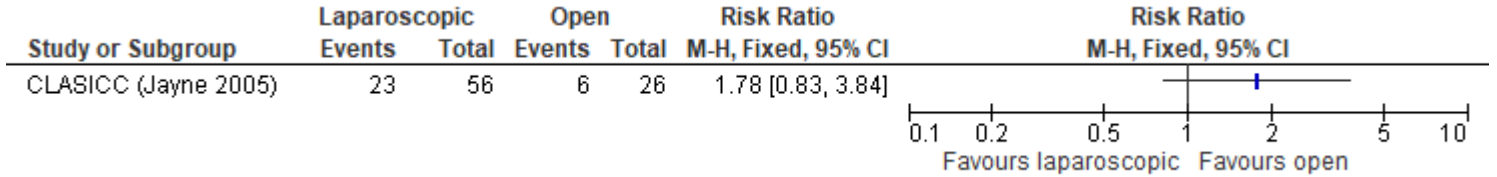
CI: confidence interval; IV: inverse variance; QLQ-CR38: Quality of Life Questionnaire colorectal cancer module (38 items); SE: standard error

Figure 10: Comparison 1: Laparoscopic versus open surgery for rectal cancer – Quality of life - Overall sexual dysfunction median 3 years after surgery among previously sexually active men (IIEF)



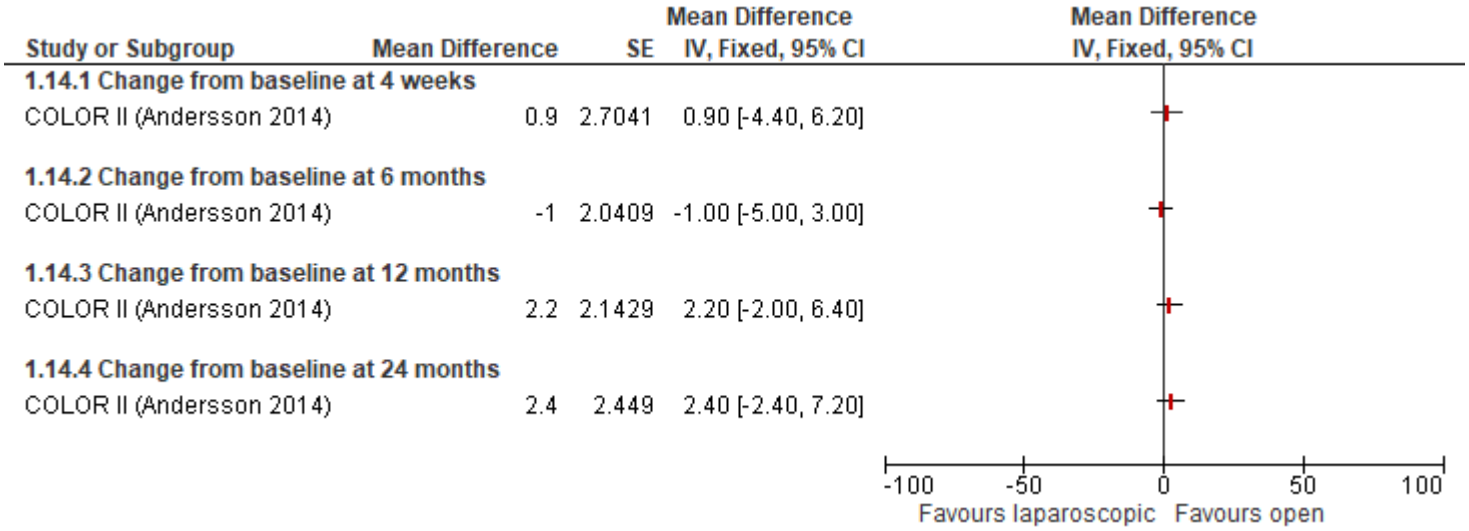
CI: confidence interval; IIEF: International Index of Erectile Function; M-H: Mantel Haenszel method

Figure 11: Comparison 1: Laparoscopic versus open surgery for rectal cancer – Quality of life - A severe change in overall level of sexual function perceived in men (IIEF)



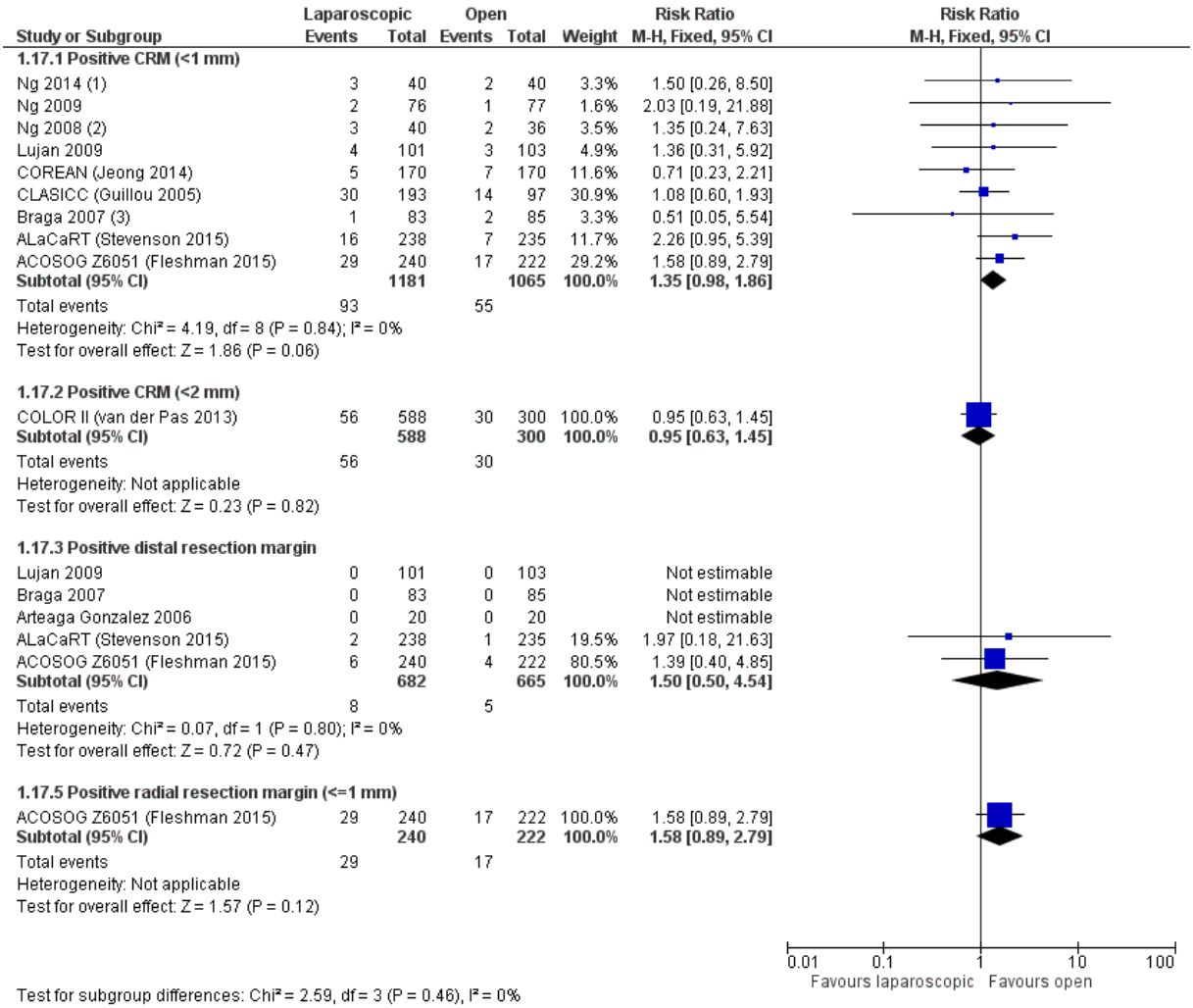
CI: confidence interval; IIEF: International Index of Erectile Function; M-H: Mantel Haenszel method

Figure 12: Comparison 1: Laparoscopic versus open surgery for rectal cancer – Quality of life - Micturitional symptoms (QLQ-CR38; scale 0-100; better indicated by lower values)



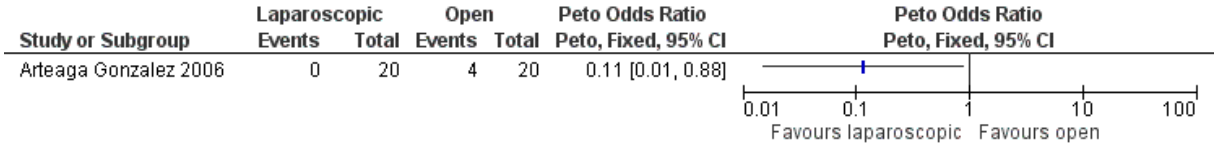
CI: confidence interval; IV: inverse variance; QLQ-CR38: Quality of Life Questionnaire colorectal cancer module (38 items); SE: standard error

Figure 13: Comparison 1: Laparoscopic versus open surgery for rectal cancer – Positive resection margins



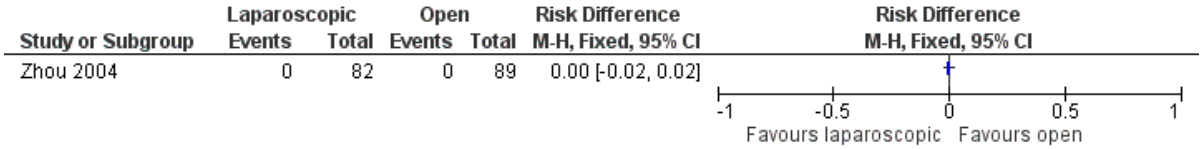
CI: confidence interval; CRM: circumferential resection margin; M-H: Mantel Haenszel method

Figure 14: Comparison 1: Laparoscopic versus open surgery for rectal cancer – Positive radial resection margin ≤ 2 mm



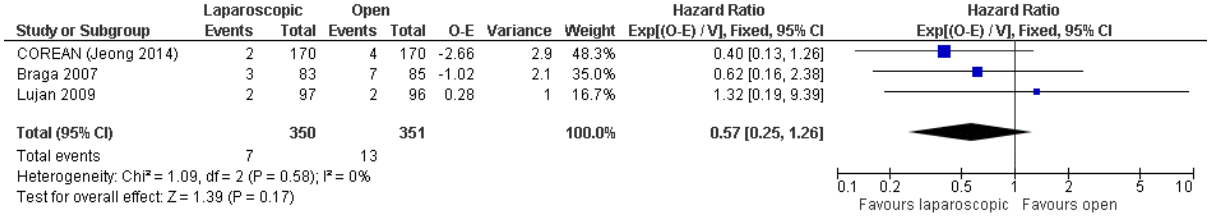
CI: confidence interval

Figure 15: Comparison 1: Laparoscopic versus open surgery for rectal cancer – Positive resection margin ("cancer cell found in the cut margin")



CI: confidence interval; M-H: Mantel Haenszel method

Figure 16: Comparison 1: Laparoscopic versus open surgery for rectal cancer – Local recurrence (time to event outcome; median 3.2 to 4 years of follow-up)

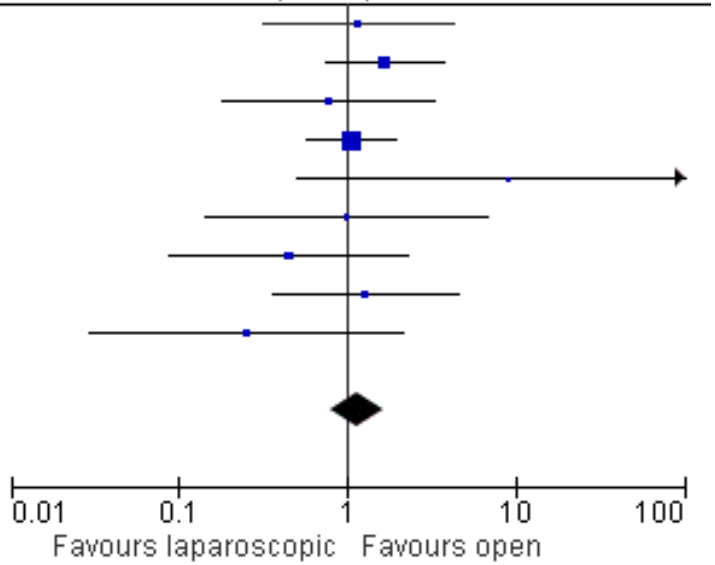


CI: confidence interval; O-E: observed minus expected; V: variance

Figure 17: Comparison 1: Laparoscopic versus open surgery for rectal cancer – Local or locoregional recurrence (median 3 to 7.5 years of follow-up)

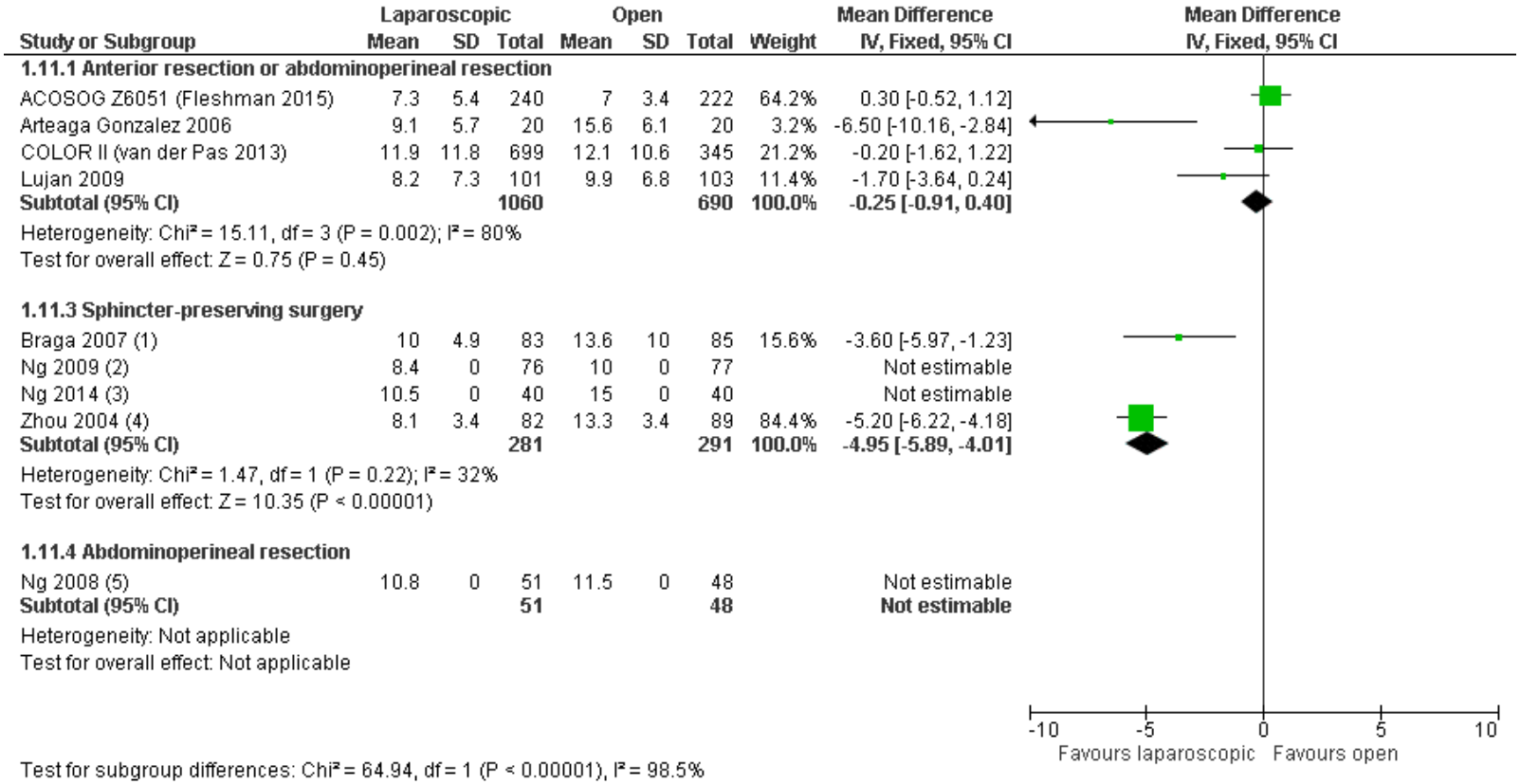
Study or Subgroup	Laparoscopic Events	Laparoscopic Total	Open Events	Open Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ACOSOG Z6051 (Fleshman 2019)	5	240	4	222	8.0%	1.16 [0.31, 4.25]
ALaCaRT (Stevenson 2019)	15	225	9	225	17.4%	1.67 [0.74, 3.73]
Braga 2007	3	83	4	85	7.6%	0.77 [0.18, 3.33]
COLOR II (Bonjer 2015)	31	588	15	300	38.4%	1.05 [0.58, 1.92]
Ishibe 2017	4	29	0	29	1.0%	9.00 [0.51, 159.94]
Lujan 2009	2	97	2	96	3.9%	0.99 [0.14, 6.88]
Ng 2008	2	40	4	36	8.1%	0.45 [0.09, 2.31]
Ng 2009	5	76	4	77	7.7%	1.27 [0.35, 4.54]
Ng 2014	1	36	4	36	7.7%	0.25 [0.03, 2.13]
Total (95% CI)		**1414**		**1106**	**100.0%**	**1.13 [0.78, 1.62]**
Total events	68		46			

Heterogeneity: Chi² = 6.38, df = 8 (P = 0.61); I² = 0%
Test for overall effect: Z = 0.64 (P = 0.52)



CI: confidence interval; M-H: Mantel Haenszel method

Figure 18: Comparison 1: Laparoscopic versus open surgery for rectal cancer – Length of hospital stay (days)



Study or Subgroup	Laparoscopic Mean	SD	Total	Open Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.11.1 Anterior resection or abdominoperineal resection								
ACOSOG Z6051 (Fleshman 2015)	7.3	5.4	240	7	3.4	222	64.2%	0.30 [-0.52, 1.12]
Arteaga Gonzalez 2006	9.1	5.7	20	15.6	6.1	20	3.2%	-6.50 [-10.16, -2.84]
COLOR II (van der Pas 2013)	11.9	11.8	699	12.1	10.6	345	21.2%	-0.20 [-1.62, 1.22]
Lujan 2009	8.2	7.3	101	9.9	6.8	103	11.4%	-1.70 [-3.64, 0.24]
Subtotal (95% CI)			**1060**			**690**	**100.0%**	**-0.25 [-0.91, 0.40]**
Heterogeneity: Chi² = 15.11, df = 3 (P = 0.002); I² = 80%								
Test for overall effect: Z = 0.75 (P = 0.45)								
1.11.3 Sphincter-preserving surgery								
Braga 2007 (1)	10	4.9	83	13.6	10	85	15.6%	-3.60 [-5.97, -1.23]
Ng 2009 (2)	8.4	0	76	10	0	77		Not estimable
Ng 2014 (3)	10.5	0	40	15	0	40		Not estimable
Zhou 2004 (4)	8.1	3.4	82	13.3	3.4	89	84.4%	-5.20 [-6.22, -4.18]
Subtotal (95% CI)			**281**			**291**	**100.0%**	**-4.95 [-5.89, -4.01]**
Heterogeneity: Chi² = 1.47, df = 1 (P = 0.22); I² = 32%								
Test for overall effect: Z = 10.35 (P < 0.00001)								
1.11.4 Abdominoperineal resection								
Ng 2008 (5)	10.8	0	51	11.5	0	48		Not estimable
Subtotal (95% CI)			**51**			**48**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								

Test for subgroup differences: Chi² = 64.94, df = 1 (P < 0.00001), I² = 98.5%

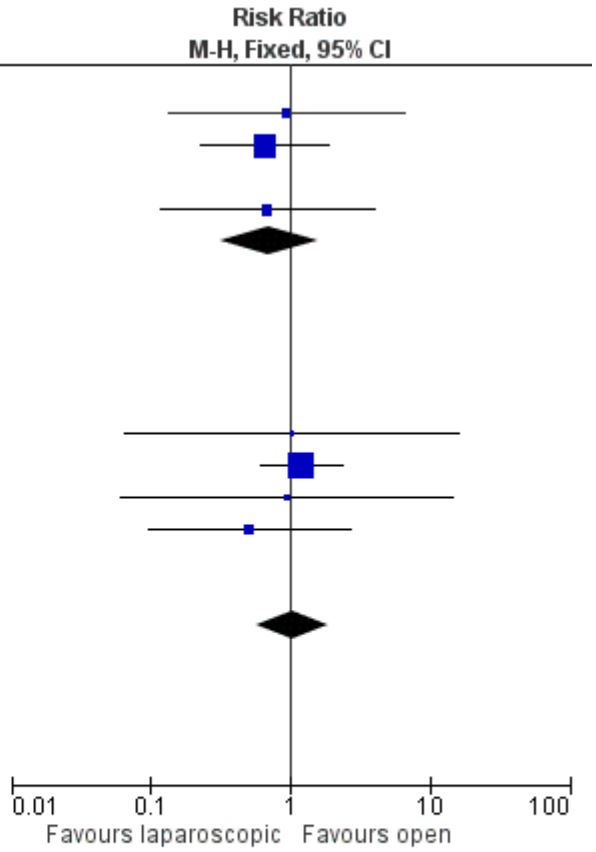
Footnotes

(1) Around 90% lower anterior resection.
(2) SD not reported, range 2-32 versus 3-39, p=0.013. 100% anterior resection.
(3) SD not reported, range 5-35 versus 6-167, p=0.071. 100% sphincter-preserving surgery.
(4) 100% sphincter-preserving surgery.
(5) SD not reported, range 5-27 versus 5-38, p=0.55. 100% abdominoperineal resection.

CI: confidence interval; IV: inverse variance; SD: standard deviation

Figure 19: Comparison 1: Laparoscopic versus open surgery for rectal cancer – Operative mortality

Study or Subgroup	Laparoscopic Events	Laparoscopic Total	Open Events	Open Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.24.1 30-day mortality						
ACOSOG Z6051 (Fleshman 2015)	2	240	2	222	15.9%	0.93 [0.13, 6.51]
COLOR II (van der Pas 2013) (1)	8	699	6	345	61.4%	0.66 [0.23, 1.88]
Liang 2011 (2)	0	169	0	174		Not estimable
Lujan 2009	2	101	3	103	22.7%	0.68 [0.12, 3.98]
Subtotal (95% CI)		**1209**		**844**	**100.0%**	**0.71 [0.31, 1.60]**
Total events	12		11			
Heterogeneity: Chi² = 0.09, df = 2 (P = 0.95); I² = 0%						
Test for overall effect: Z = 0.84 (P = 0.40)						
1.24.3 Operative mortality (timeframe not defined)						
Braga 2007	1	83	1	85	4.8%	1.02 [0.07, 16.10]
CLASICC (Guillou 2005)	13	253	21	484	70.6%	1.18 [0.60, 2.33]
Ng 2008	1	51	1	48	5.0%	0.94 [0.06, 14.63]
Ng 2009	2	76	4	77	19.5%	0.51 [0.10, 2.68]
Ng 2014 (3)	0	40	0	40		Not estimable
Zhou 2004 (4)	0	82	0	89		Not estimable
Subtotal (95% CI)		**585**		**823**	**100.0%**	**1.03 [0.57, 1.86]**
Total events	17		27			
Heterogeneity: Chi² = 0.86, df = 3 (P = 0.83); I² = 0%						
Test for overall effect: Z = 0.11 (P = 0.92)						



Test for subgroup differences: Chi² = 0.55, df = 1 (P = 0.46), I² = 0%

Footnotes

(1) 28-day mortality

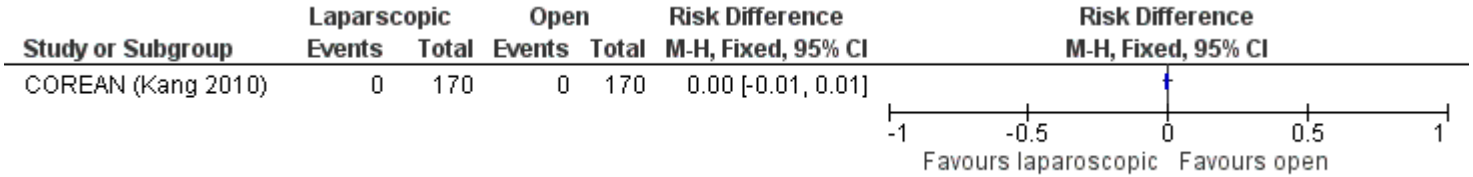
(2) RR not estimable because no events.

(3) RR not estimable because no events.

(4) RR not estimable because no events.

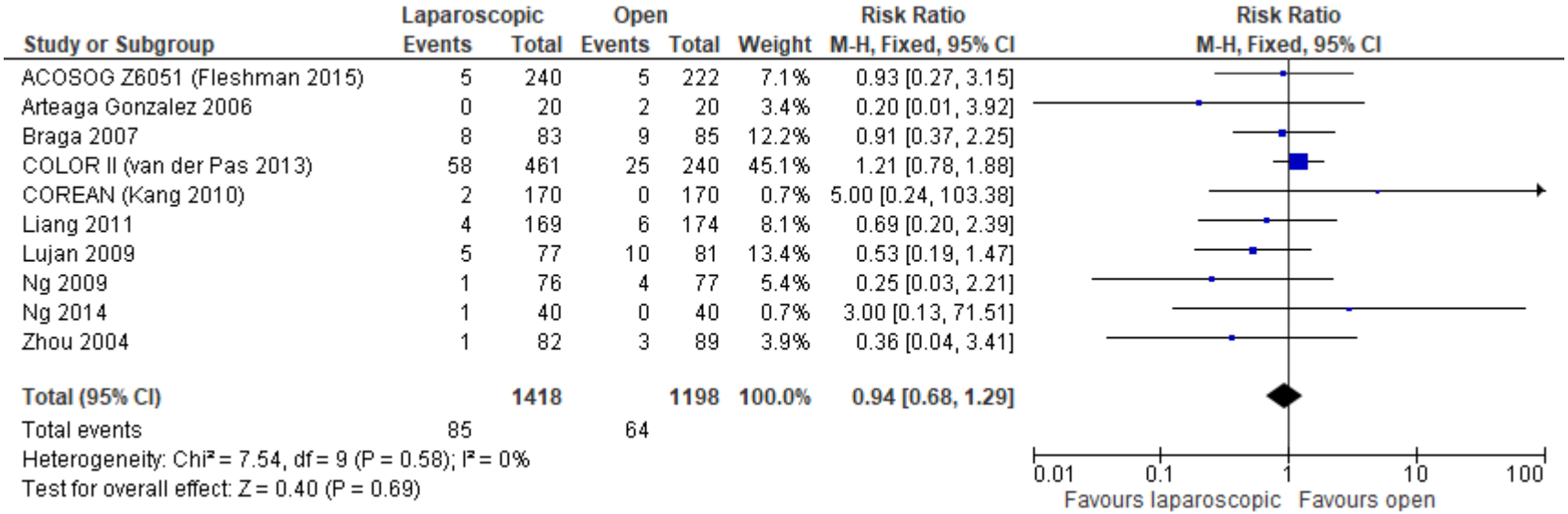
CI: confidence interval; M-H: Mantel Haenszel method

Figure 20: Comparison 1: Laparoscopic versus open surgery for rectal cancer – 90-day operative mortality



CI: confidence interval; M-H: Mantel Haenszel method

Figure 21: Comparison 1: Laparoscopic versus open surgery for rectal cancer – Anastomotic leak

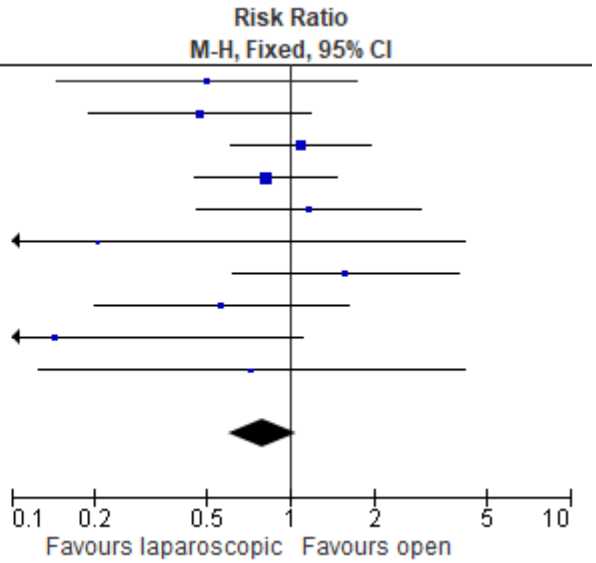


CI: confidence interval; M-H: Mantel Haenszel method

Figure 22: Comparison 1: Laparoscopic versus open surgery for rectal cancer – Surgical site infection

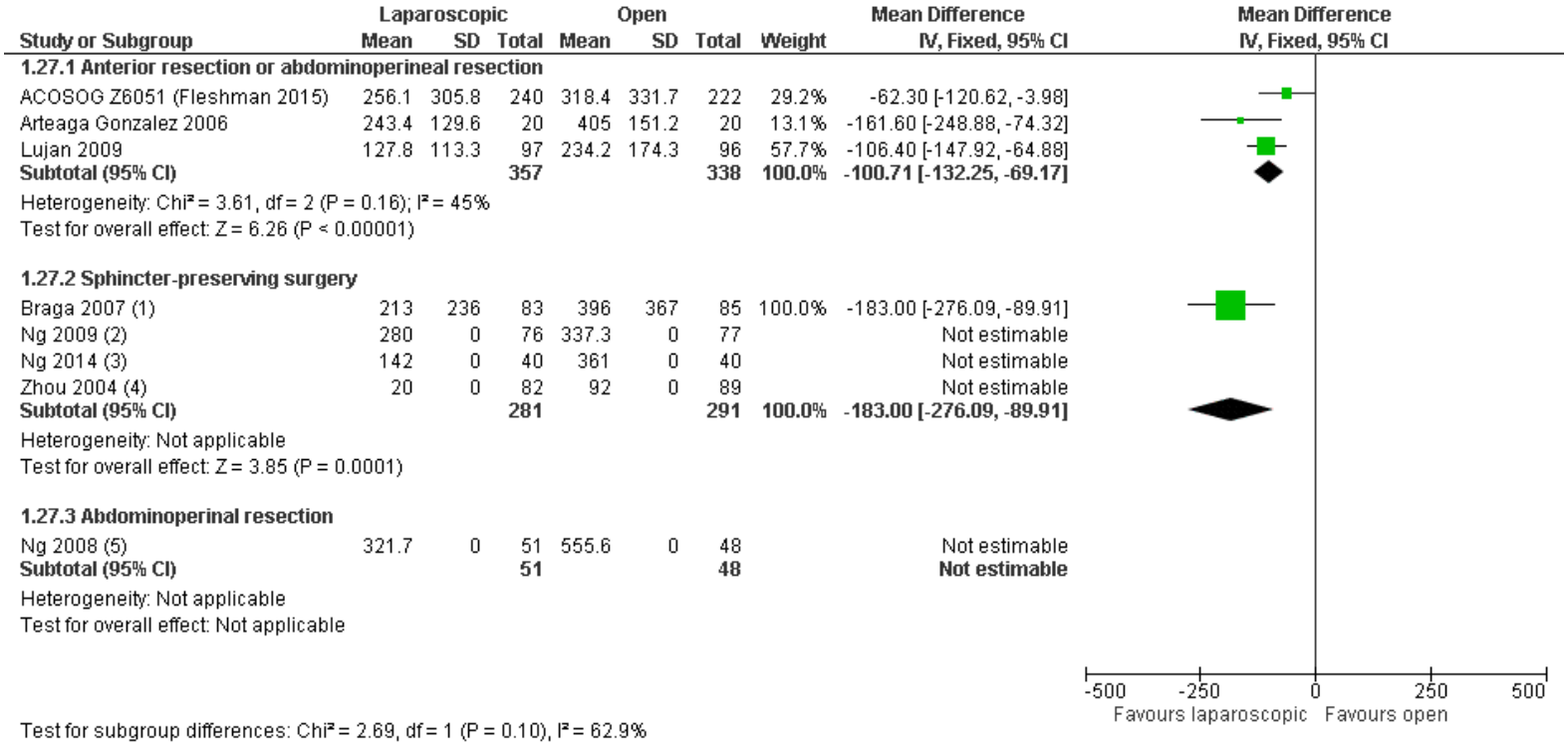
Study or Subgroup	Laparoscopic Events	Laparoscopic Total	Open Events	Open Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Arteaga Gonzalez 2006	3	20	6	20	6.2%	0.50 [0.14, 1.73]
Braga 2007	6	83	13	85	13.2%	0.47 [0.19, 1.18]
CLASICC (Guillou 2005)	33	253	15	125	20.7%	1.09 [0.61, 1.92]
COLOR II (van der Pas 2013)	28	697	17	345	23.4%	0.82 [0.45, 1.47]
Liang 2011	9	169	8	174	8.1%	1.16 [0.46, 2.93]
Lujan 2009	0	101	2	103	2.6%	0.20 [0.01, 4.20]
Ng 2008	10	51	6	48	6.4%	1.57 [0.62, 3.98]
Ng 2009	5	76	9	77	9.2%	0.56 [0.20, 1.60]
Ng 2014	1	40	7	40	7.2%	0.14 [0.02, 1.11]
Zhou 2004	2	82	3	89	3.0%	0.72 [0.12, 4.22]
Total (95% CI)		**1572**		**1106**	**100.0%**	**0.79 [0.60, 1.05]**
Total events	97		86			

Heterogeneity: Chi² = 9.51, df = 9 (P = 0.39); I² = 5%
Test for overall effect: Z = 1.60 (P = 0.11)



CI: confidence interval; M-H: Mantel Haenszel method

Figure 23: Comparison 1: Laparoscopic versus open surgery for rectal cancer – Blood loss (ml)



Test for subgroup differences: Chi² = 2.69, df = 1 (P = 0.10), I² = 62.9%

Footnotes

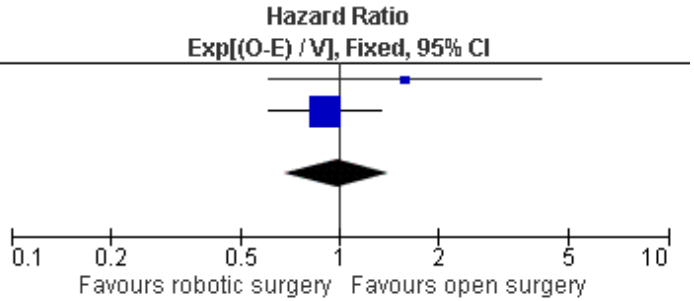
(1) Around 90% lower anterior resection.
(2) SD not reported, range 0-3,000 versus 0-2,542, p=0.338. 100% anterior resection.
(3) SD not reported, range 0-2,000 versus 5-2,5000, p<0.001. 100% sphincter-preserving surgery.
(4) SD not reported, p=0.025. 100% sphincter-preserving surgery.
(5) SD not reported, range 0-3,000 versus 0-4,720, p=0.093. 100% abdominoperineal resection.

CI: confidence interval; IV: inverse variance; SD: standard deviation

Figure 24: Comparison 2: Robotic versus open surgery for rectal cancer – overall survival (median follow-up 3 years)

Study or Subgroup	Robotic Events	Robotic Total	Open Events	Open Total	O-E	Variance	Weight	Hazard Ratio Exp[(O-E) / V], Fixed, 95% CI
Corbellini 2016	7	63	3	61	1.95	4.25	14.7%	1.58 [0.61, 4.09]
Kim 2016 (1)	0	533	0	1095	-2.45	24.59	85.3%	0.91 [0.61, 1.34]
Total (95% CI)		**596**		**1156**			**100.0%**	**0.98 [0.68, 1.42]**
Total events	7		3					

Heterogeneity: Chi² = 1.13, df = 1 (P = 0.29); I² = 12%
Test for overall effect: Z = 0.09 (P = 0.93)

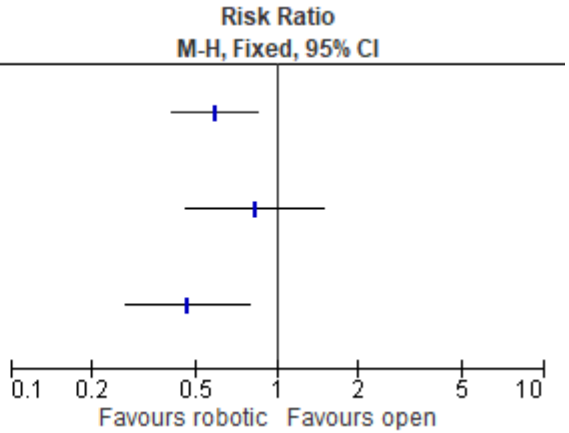


Footnotes
(1) Event rate not reported

CI: confidence interval; O-E: observed minus expected; V: variance

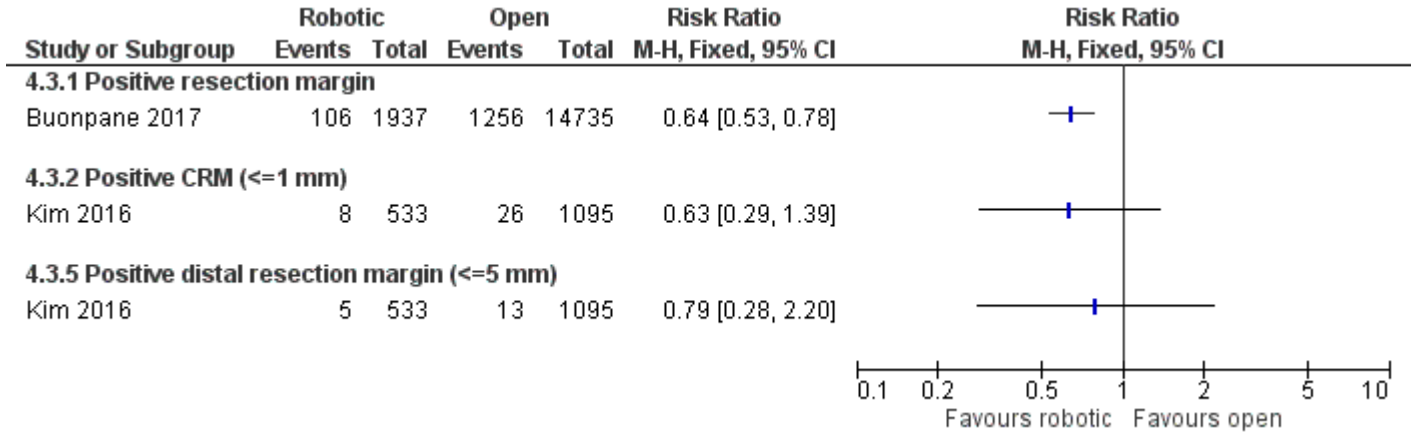
Figure 25: Comparison 2: Robotic versus open surgery for rectal cancer – Quality of life - Sexual dysfunction in men ≤65 years

Study or Subgroup	Robotic Events	Robotic Total	Open Events	Open Total	Risk Ratio M-H, Fixed, 95% CI
4.2.1 Moderate or severe sexual dysfunction in men <=65 years (VAS 2-5)					
Kim 2016	27	141	108	332	0.59 [0.41, 0.85]
4.2.2 Severe sexual dysfunction in men <=65 years (VAS 4-5)					
Kim 2016	13	141	37	332	0.83 [0.45, 1.51]
4.2.3 Moderate sexual dysfunction in men <=65 years (VAS 2-3)					
Kim 2016	14	141	71	332	0.46 [0.27, 0.80]



CI: confidence interval; M-H: Mantel Haenszel method; VAS: visual analogue scale

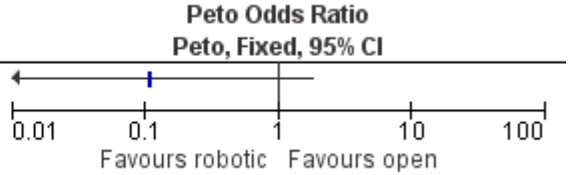
Figure 26: Comparison 2: Robotic versus open surgery for rectal cancer – Positive resection margins



CI: confidence interval; CRM: circumferential resection margin; M-H: Mantel Haenszel method

Figure 27: Comparison 2: Robotic versus open surgery for rectal cancer – positive resection margin (R1)

Study or Subgroup	Robotic Events	Robotic Total	Open Events	Open Total	Peto Odds Ratio Peto, Fixed, 95% CI
Corbellini 2016	0	65	2	55	0.11 [0.01, 1.81]

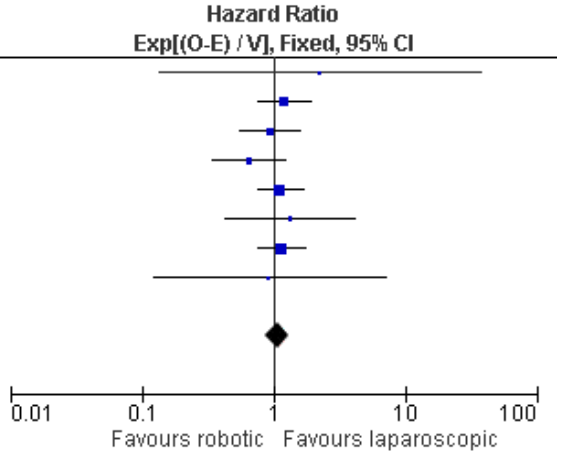


CI: confidence interval

Figure 28: Comparison 3: Robotic versus laparoscopic surgery for rectal cancer – overall survival (median follow-up 3 to 5 years)

Study or Subgroup	Robotic Events	Robotic Total	Laparoscopic Events	Laparoscopic Total	O-E	Variance	Weight	Hazard Ratio Exp[(O-E) / V], Fixed, 95% CI
Corbellini 2016	7	63	1	29	0.4	0.49	0.5%	2.26 [0.14, 37.20]
Ielpo 2017 (1)	0	86	0	112	3.27	18.01	19.4%	1.20 [0.76, 1.90]
Kim 2016 (2)	0	533	0	486	-0.78	14.13	15.2%	0.95 [0.56, 1.59]
Kim 2017b (3)	0	192	0	192	-3.93	9.39	10.1%	0.66 [0.35, 1.25]
Law 2017 (4)	0	220	0	171	2.84	24.43	26.3%	1.12 [0.76, 1.67]
Park 2015	8	133	4	84	0.86	2.98	3.2%	1.33 [0.43, 4.15]
Rouanet 2018 (5)	0	200	0	200	3.39	22.66	24.4%	1.16 [0.77, 1.75]
Yoo 2015	1	44	3	26	-0.07	0.93	1.0%	0.93 [0.12, 7.08]
Total (95% CI)		**1471**		**1300**			**100.0%**	**1.07 [0.87, 1.31]**
Total events	16		8					

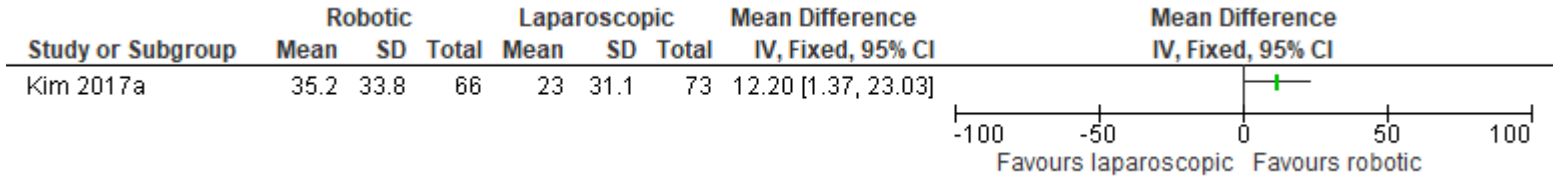
Heterogeneity: Chi² = 3.31, df = 7 (P = 0.85); I² = 0%
Test for overall effect: Z = 0.62 (P = 0.54)



Footnotes
(1) Number of events not reported
(2) Number of events not reported
(3) Number of events not reported
(4) Number of events not reported
(5) Number of events not reported

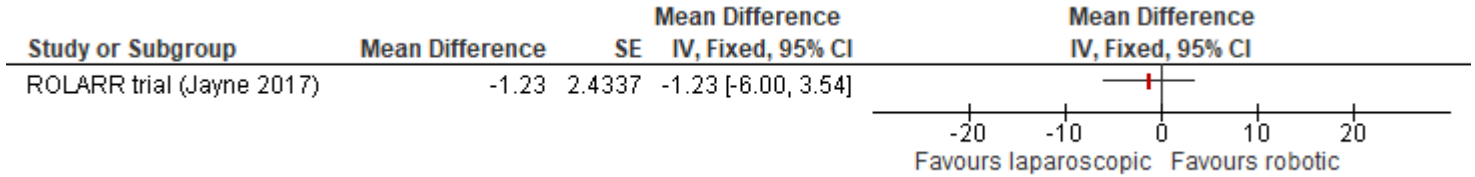
CI: confidence interval; O-E: observed minus expected; V: variance

Figure 29: Comparison 3: Robotic versus laparoscopic surgery for rectal cancer – Quality of life - Sexual function mean score at 12 months (QLQ-CR38; scale 0-100; better indicated by higher values)



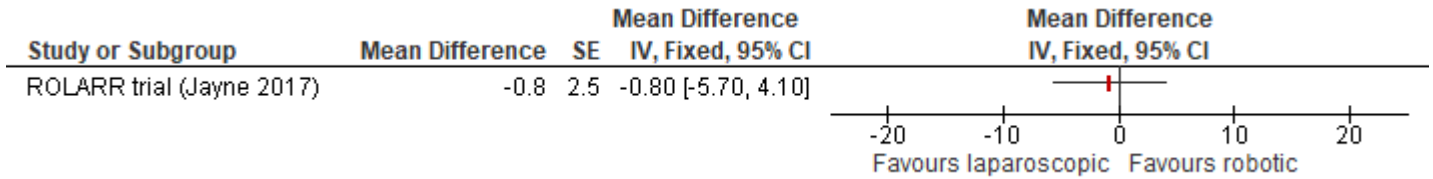
CI: confidence interval; IV: inverse variance; QLQ-CR38: Quality of Life Questionnaire colorectal cancer module (38 items); SD: standard deviation

Figure 30: Comparison 3: Robotic versus laparoscopic surgery for rectal cancer – Quality of life – Female sexual function adjusted mean score difference at 6 months (FSFI; scale 2-36; better indicated by higher values)



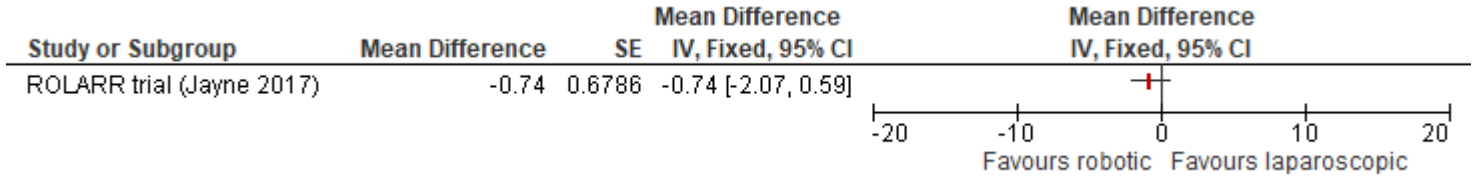
CI: confidence interval; FSFI: Female Sexual Function Index; IV: inverse variance; SE: standard error

Figure 31: Comparison 3: Robotic versus laparoscopic surgery for rectal cancer – Quality of life – Male sexual function adjusted mean score difference at 6 months (IIEF; scale 5-75; better indicated by higher values)



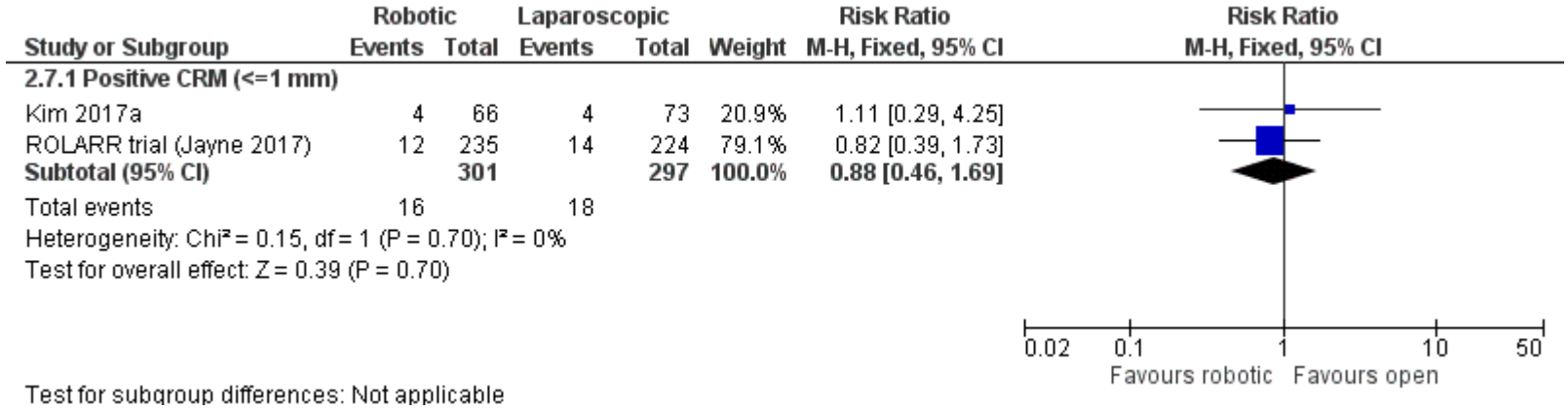
CI: confidence interval; IIEF: International Index of Erectile Function; IV: inverse variance; SE: standard error

Figure 32: Comparison 3: Robotic versus laparoscopic surgery for rectal cancer – Quality of life – Bladder function adjusted mean score difference at 6 months (IPSS; scale 0-35; better indicated by lower values)



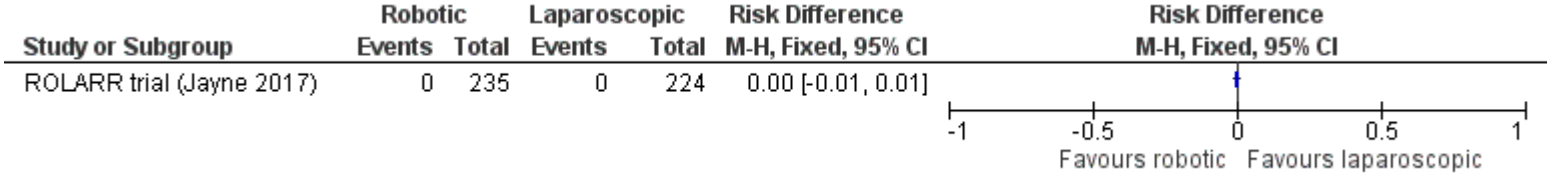
CI: confidence interval; IPSS: International Prostate Symptom Score; IV: inverse variance; SE: standard error

Figure 33: Comparison 3: Robotic versus laparoscopic surgery for rectal cancer – Positive resection margins



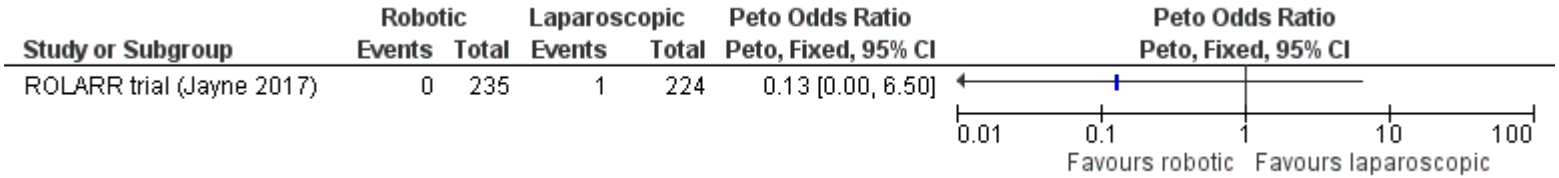
CI: confidence interval; CRM: circumferential resection margin; M-H: Mantel Haenszel method

Figure 34: Comparison 3: Robotic versus laparoscopic surgery for rectal cancer – Positive proximal resection margin



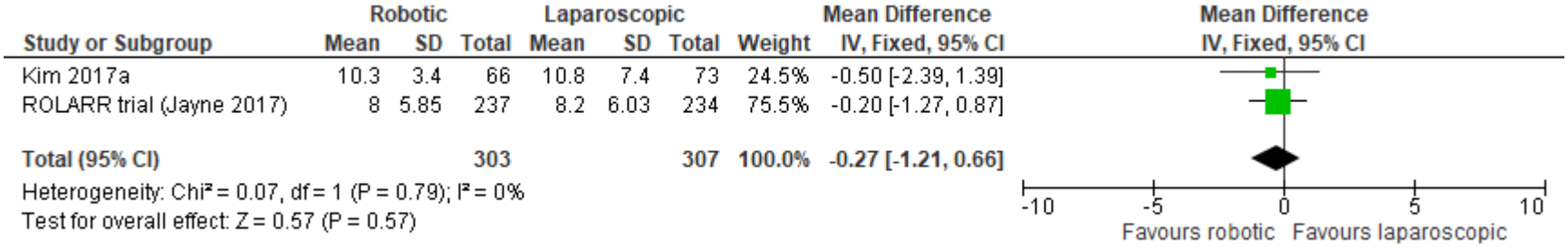
CI: confidence interval; M-H: Mantel Haenszel method

Figure 35: Comparison 3: Robotic versus laparoscopic surgery for rectal cancer – Positive distal resection margin



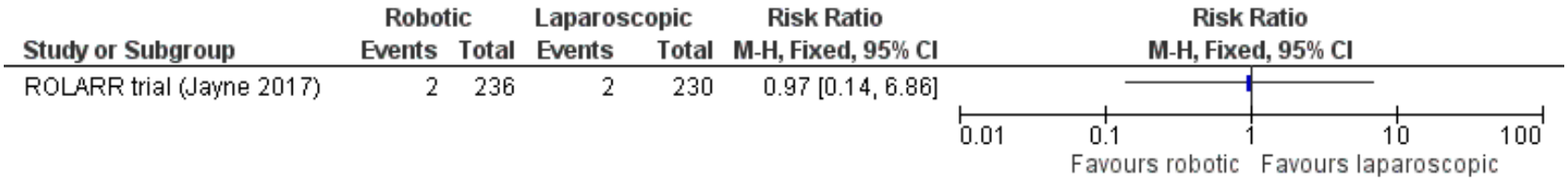
CI: confidence interval

Figure 36: Comparison 3: Robotic versus laparoscopic surgery for rectal cancer – Length of hospital stay (days)



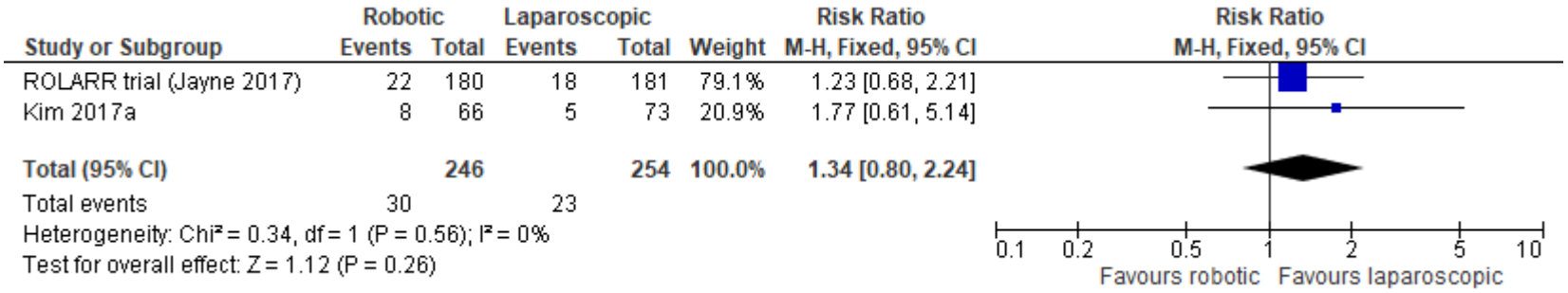
CI: confidence interval; IV: inverse variance; SD: standard deviation

Figure 37: Comparison 3: Robotic versus laparoscopic surgery for rectal cancer – 30-day operative mortality



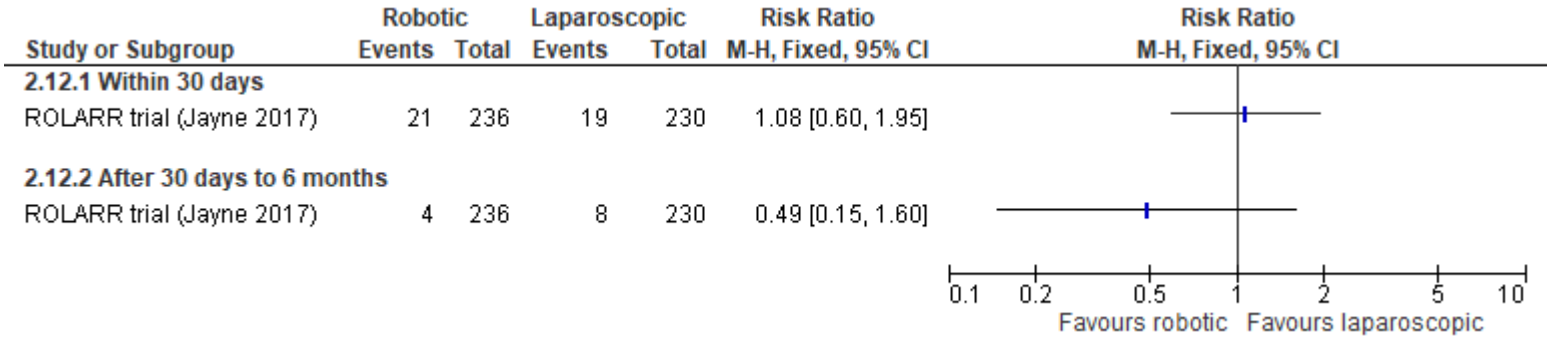
CI: confidence interval; M-H: Mantel Haenszel method

Figure 38: Comparison 3: Robotic versus laparoscopic surgery for rectal cancer – Anastomotic leak



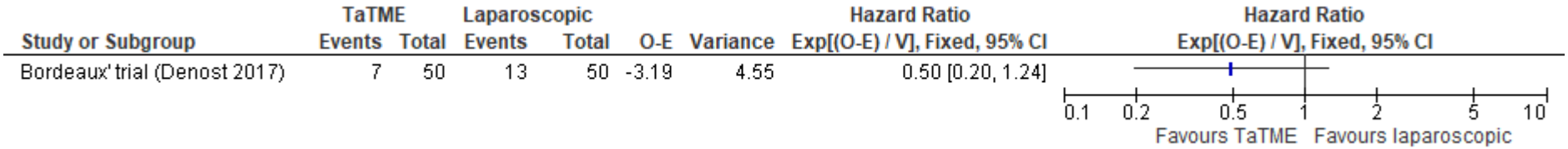
CI: confidence interval; M-H: Mantel Haenszel method

Figure 39: Comparison 3: Robotic versus laparoscopic surgery for rectal cancer – Surgical site infection



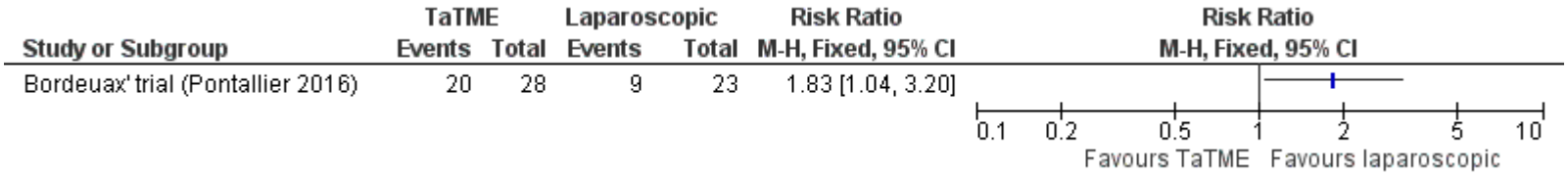
CI: confidence interval; M-H: Mantel Haenszel method

Figure 40: Comparison 4: Transanal total mesorectal excision versus laparoscopic surgery for rectal cancer – Overall survival (median 5 years of follow-up)



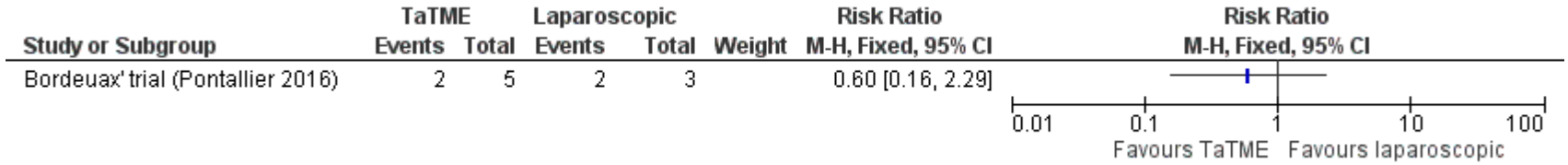
CI: confidence interval; O-E: observed minus expected; TaTME: transanal total mesorectal excision; V: variance

Figure 41: Comparison 4: Transanal total mesorectal excision versus laparoscopic surgery for rectal cancer – Quality of life - Sexual activity maintained at median 3.2 years after treatment (in previously sexually active participants)



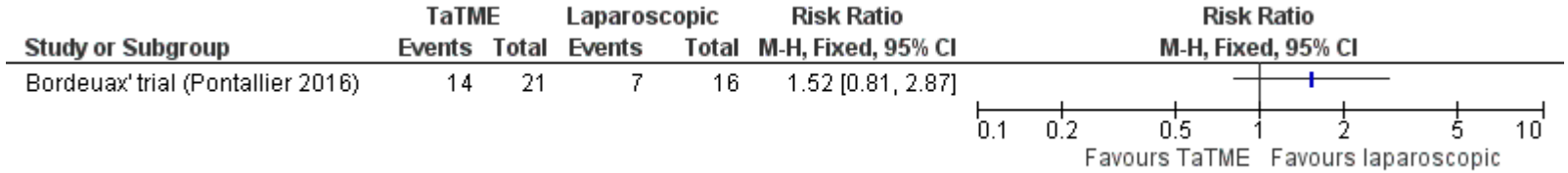
CI: confidence interval; M-H: Mantel Haenszel method; TaTME: transanal total mesorectal excision

Figure 42: Comparison 4: Transanal total mesorectal excision versus laparoscopic surgery for rectal cancer – Quality of life - Sexual dysfunction at median 3.2 years after treatment (FSFI score ≤19) in previously sexually active women



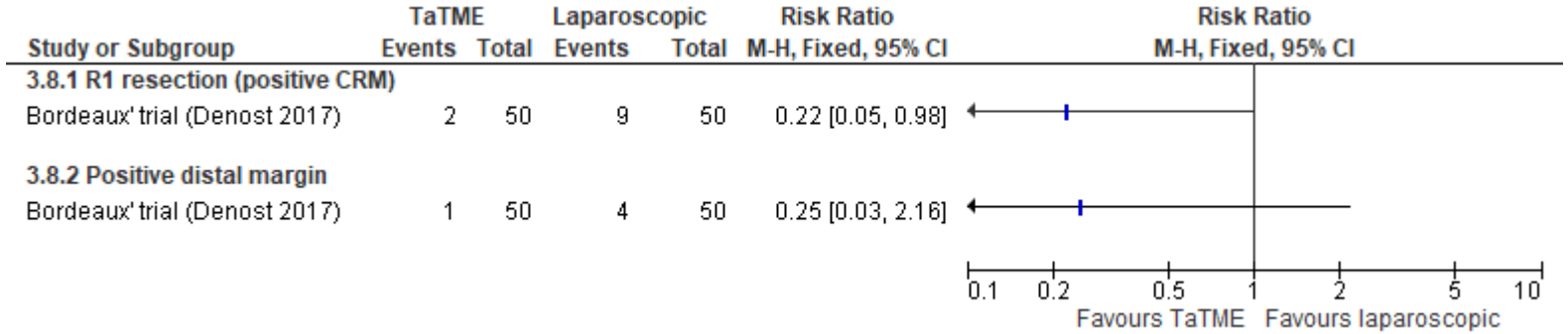
CI: confidence interval; FSFI: Female Sexual Function Index; M-H: Mantel Haenszel method; TaTME: transanal total mesorectal excision

Figure 43: Comparison 4: Comparison 4: Transanal total mesorectal excision versus laparoscopic surgery for rectal cancer – Quality of life - Normal ejaculatory function at median 3.2 years after treatment in previously sexually active men (IIEF)



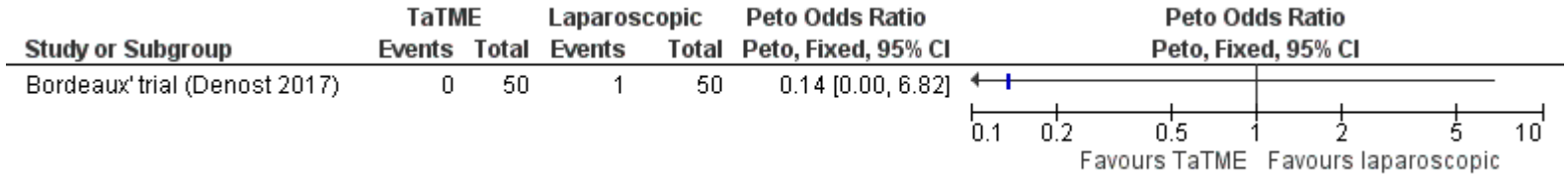
CI: confidence interval; IIEF: International Index of Erectile Function; M-H: Mantel Haenszel method; TaTME: transanal total mesorectal excision

Figure 44: Comparison 4: Transanal total mesorectal excision versus laparoscopic surgery for rectal cancer – Positive resection margins



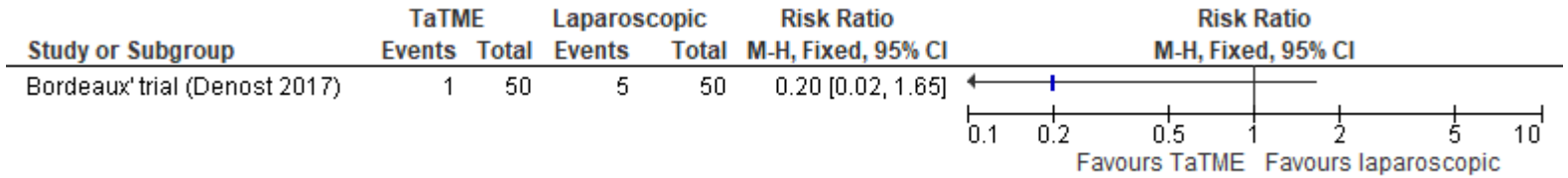
CI: confidence interval; CRM: circumferential resection margin; M-H: Mantel Haenszel method; TaTME: transnal total mesorectal excision

Figure 45: Comparison 4: Transanal total mesorectal excision versus laparoscopic surgery for rectal cancer – Postoperative mortality



CI: confidence interval; TaTME: transanal total mesorectal excision

Figure 46: Comparison 4: Transanal total mesorectal excision versus laparoscopic surgery for rectal cancer – Anastomotic leak and/or abscess



CI: confidence interval; M-H: Mantel Haenszel method; TaTME: transanal total mesorectal excision

1 Appendix F – GRADE tables

2 GRADE tables for review question: What is the optimal surgery for rectal cancer?

3 Table 9: Clinical evidence profile for comparison 1: Laparoscopic versus open surgery for rectal cancer

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Laparoscopic surgery**	**Open surgery**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Overall survival (median 3.2 to 9.2 years of follow-up; event is death from any cause)												
9	randomised trials	no serious risk of bias	no serious inconsistency	serious[3]	no serious imprecision	none	1,601	1,130	HR 0.83 (0.70 to 0.99)	At 5 years open 85%[2], laparoscopic 87.4% (85.1% to 89.2%)	MODERATE	CRITICAL
Quality of life - Global quality of life (QLQ-C30) - Change from baseline at 4 weeks (range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	serious[6]	none	230	108	-	MD 0.3 higher (4.7 lower to 5.3 higher)	VERY LOW	CRITICAL
Quality of life - Global quality of life (QLQ-C30) - Change from baseline at 6 months (range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	serious[6]	none	221	106	-	MD 2.2 lower (6.8 lower to 2.4 higher)	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Laparoscopic surgery**	**Open surgery**	**Relative (95% CI)**	**Absolute**		
Quality of life - Global quality of life (QLQ-C30) - Change from baseline at 12 months (range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	serious[6]	none	208	97	-	MD 1.8 lower (6.1 lower to 2.5 higher)	VERY LOW	CRITICAL
Quality of life - Global health status (EQ-VAS) - Change from baseline at 4 weeks (range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	serious[1]	none	232	104	-	MD 1.6 higher (3.3 lower to 6.5 higher)	VERY LOW	CRITICAL
Quality of life - Global health status (EQ-VAS) - Change from baseline at 6 months (range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	serious[1]	none	219	102	-	MD 1.7 higher (2.4 lower to 5.8 higher)	VERY LOW	CRITICAL
Quality of life - Global health status (EQ-VAS) - Change from baseline at 12 months (range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	serious[1]	none	206	91	-	MD 0.6 higher (3.4 lower to 4.6 higher)	VERY LOW	CRITICAL
Quality of life - General health score (SF-36) - At 12 months (range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	serious[1]	none	83	85	-	Laparoscopic: 74 Open 65 p=0.0001	VERY LOW	CRITICAL
Quality of life - General health score (SF-36) - At 24 months after surgery (range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	serious[1]	none	83	85	-	Laparoscopic: 72 Open: 65 Not significant (p-value not reported)	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Laparoscopic surgery	Open surgery	Relative (95% CI)	Absolute	Quality	Importance
Quality of life - Sexual functioning (QLQ-CR38) - Change from baseline at 4 weeks (range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	serious[6]	none	207	98	-	MD 2.5 higher (0.3 lower to 5.3 higher)	VERY LOW	CRITICAL
Quality of life - Sexual functioning (QLQ-CR38) - Change from baseline at 6 months (range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	serious[6]	none	206	96	-	MD 0.8 lower (5.5 lower to 3.9 higher)	VERY LOW	CRITICAL
Quality of life - Sexual functioning (QLQ-CR38) - Change from baseline at 12 months (range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	serious[6]	none	197	89	-	MD 3.1 higher (1.7 lower to 7.9 higher)	VERY LOW	CRITICAL
Quality of life - Sexual functioning (QLQ-CR38) - Change from baseline at 24 months (range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	serious[6]	none	141	64	-	MD 4.6 higher (1.7 lower to 10.9 higher)	VERY LOW	CRITICAL
Quality of life - Sexual enjoyment (QLQ-CR38) - Change from baseline at 6 months (range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	very serious[7]	none	72	37	-	MD 0.7 higher (13.6 lower to 15 higher)	VERY LOW	CRITICAL
Quality of life - Sexual enjoyment (QLQ-CR38) - Change from baseline at 12 months (range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	very serious[7]	none	87	38	-	MD 8 higher (5 lower to 21 higher)	VERY LOW	CRITICAL
Quality of life - Sexual enjoyment (QLQ-CR38) - Change from baseline at 24 months (range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	very serious[7]	none	41	21	-	MD 2.1 lower (17.2 lower to 13 higher)	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Laparoscopic surgery**	**Open surgery**	**Relative (95% CI)**	**Absolute**		
Quality of life - Female sexual problems (QLQ-CR38) - Change from baseline at 6 months (range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	very serious[5]	none	19	10	-	MD 5.1 higher (16.5 lower to 26.7 higher)	VERY LOW	CRITICAL
Quality of life - Female sexual problems (QLQ-CR38) - Change from baseline at 12 months (range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	very serious[7]	none	19	14	-	MD 0.9 higher (20.8 lower to 22.6 higher)	VERY LOW	CRITICAL
Quality of life - Female sexual problems (QLQ-CR38) - Change from baseline at 24 months (range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	very serious[7]	none	7	5	-	MD 11.8 higher (18.9 lower to 42.5 higher)	VERY LOW	CRITICAL
Quality of life - Overall level of sexual function decreased 'quite a lot' or 'severely' as a result of surgery in women (FSFI)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	serious[1]	none	8/29 (27.6%)	3/17 (17.6%)	RR 1.56 (0.48 to 5.11)	99 more per 1000 (from 92 fewer to 725 more)	VERY LOW	CRITICAL
Quality of life - Male sexual problems (QLQ-CR38) - Change from baseline at 4 weeks (range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	very serious[7]	none	91	41	-	MD 6.5 lower (19.9 lower to 6.9 higher)	VERY LOW	CRITICAL
Quality of life - Male sexual problems (QLQ-CR38) - Change from baseline at 6 months (range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	very serious[7]	none	116	47	-	MD 6.9 lower (20.5 lower to 6.7 higher)	VERY LOW	CRITICAL
Quality of life - Male sexual problems (QLQ-CR38) - Change from baseline at 12 months (range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	serious[6]	none	117	50	-	MD 9.8 lower (22.3 lower to 2.7 higher)	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Laparoscopic surgery	Open surgery	Relative (95% CI)	Absolute		
Quality of life - Male sexual problems (QLQ-CR38) - Change from baseline at 24 months (range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	very serious[7]	none	78	37	-	MD 1.1 higher (12.2 lower to 14.4 higher)	VERY LOW	CRITICAL
Quality of life - Overall sexual dysfunction median 3 years after surgery among previously sexually active men (IIEF)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	serious[1]	none	7/15 (46.7%)	1/22 (4.5%)	RR 10.27 (1.4 to 75.1)	421 more per 1000 (from 18 more to 1000 more)	VERY LOW	CRITICAL
Quality of life - A severe change in overall level of sexual function perceived in men (IIEF)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	serious[1]	none	23/56 (41.1%)	6/26 (23.1%)	RR 1.78 (0.83 to 3.84)	180 more per 1000 (from 39 fewer to 655 more)	VERY LOW	CRITICAL
Quality of life - Micturitional symptoms (QLQ-CR38) - Change from baseline at 4 weeks (range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	serious[6]	none	219	103	-	MD 0.9 higher (4.4 lower to 6.2 higher)	VERY LOW	CRITICAL
Quality of life - Micturitional symptoms (QLQ-CR38) - Change from baseline at 6 months (range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	serious[6]	none	219	101	-	MD 1 lower (5 lower to 3 higher)	VERY LOW	CRITICAL
Quality of life - Micturitional symptoms (QLQ-CR38) - Change from baseline at 12 months (range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	serious[6]	none	209	95	-	MD 2.2 higher (2 lower to 6.4 higher)	VERY LOW	CRITICAL
Quality of life - Micturitional symptoms (QLQ-CR38) - Change from baseline at 24 months (range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	serious[6]	none	170	79	-	MD 2.4 higher (2.4	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Laparoscopic surgery	Open surgery	Relative (95% CI)	Absolute	Quality	Importance
										lower to 7.2 higher)		
Quality of life - Bladder function at 2 weeks, 3, 6, and 18 months after surgery (IPSS and QLQ-CR38)												
1	randomised trials	serious[5]	no serious inconsistency	serious[3]	serious[1]	none	98	50	-	"No differences in bladder function were detected at any time point between the laparoscopic and open rectal groups."	VERY LOW	CRITICAL
Positive CRM												
9	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	93/1,181 (7.9%)	55/1,065 (5.2%)	RR 1.35 (0.98 to 1.86)	18 more per 1000 (from 1 fewer to 44 more)	MODERATE	CRITICAL
Positive CRM (<2 mm)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious[3]	serious[1]	none	56/588 (9.5%)	30/300 (10%)	RR 0.95 (0.63 to 1.45)	5 fewer per 1000 (from 37 fewer to 45 more)	LOW	CRITICAL
Positive distal resection margin												
5	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	8/682 (1.2%)	5/665 (0.75%)	RR 1.50 (0.50 to 4.54)	4 more per 1000 (from 4 fewer to 27 more)	MODERATE	CRITICAL
Positive radial resection margin (≤1 mm)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	29/240 (12.1%)	17/222 (7.7%)	RR 1.58 (0.89 to 2.79)	44 more per 1000 (from 8 fewer to 137 more)	MODERATE	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Laparoscopic surgery**	**Open surgery**	**Relative (95% CI)**	**Absolute**		
Positive radial resection margin (≤2 mm)												
1	randomised trials	serious[4]	no serious inconsistency	serious[3]	serious[1]	none	0/20 (0%)	4/20 (20%)	Peto odds ratio 0.11 (0.01, 0.88)	173 fewer per 1000 (from 198 fewer to 20 fewer)	VERY LOW	CRITICAL
Positive resection margin ("cancer cell found in the cut margins")												
1	randomised trials	serious[4]	no serious inconsistency	no serious indirectness	serious[1]	none	0/82 (0%)	0/89 (0%)	RD 0.00 (-0.02, 0.02)	0 fewer per 1000 (from 20 fewer to 20 more)	LOW	CRITICAL
Local recurrence (time to event outcome; median 3.2 to 4 years of follow-up)												
3	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	7/350 (3.9%)	13/351 (3.1%)	HR 0.57 (0.25 to 1.26)	At 3 years open 4.9%[8], laparoscopic 2.8% (1.2% to 6.6 %)	MODERATE	IMPORTANT
Local or locoregional recurrence (median 3 to 7.5 years of follow-up)												
9	randomised trials	no serious risk of bias	no serious inconsistency	serious[3]	serious[1]	none	68/1,414 (4.8%)	46/1,106 (4.2%)	RR 1.13 (0.78 to 1.62)	5 more per 1000 (from 9 fewer to 26 more)	LOW	IMPORTANT
Length of hospital stay (days) - Anterior resection or abdominoperineal resection												
4	randomised trials	no serious risk of bias	very serious[9]	serious[3]	no serious imprecision	none	1,060	690	-	MD 0.25 lower (0.91 lower to 0.4 higher)	VERY LOW	IMPORTANT
1	randomised trials	no serious risk of bias	no serious inconsistency	serious	serious[1]	none	253	128	-	Laparoscopic: median 11 (IQR 9-15) Open: median 13 (IQR 9-18) No difference	LOW	IMPORTANT

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Laparoscopic surgery**	**Open surgery**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
										between groups, narratively reported.		
Length of hospital stay (days) - Sphincter-preserving surgery												
4	randomised trials	serious[5]	no serious inconsistency	serious[3]	no serious imprecision	none	281	291	-	MD 4.95 lower (5.89 to 4.01 lower)	LOW	IMPORTANT
1	randomised trials	no serious risk of bias	no serious inconsistency	serious[3]	no serious imprecision	none	238	237	-	Laparoscopic: median 8 (IQR 6-12) Open: median 8 (IQR 6-12) p=0.21	MODERATE	IMPORTANT
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	170	170	-	Laparoscopic: median 8 (IQR 7-12) Open: median 9 (IQR 8-12) p=0.056	MODERATE	IMPORTANT
Length of hospital stay (days) - Abdominoperineal resection												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious[3]	serious[1]	none	51	48	-	Laparoscopic: mean 10.8 (range 5-27) Open: mean 11.5 (range 5-38) p=0.55	LOW	IMPORTANT
30-day mortality												
4	randomised trials	no serious	no serious inconsistency	serious[3]	serious[1]	none	12/1,209 (0.99%)	11/844 (1.3%)	RR 0.71 (0.31 to 1.6)	4 fewer per 1000 (from 9	LOW	IMPORTANT

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Laparoscopic surgery	Open surgery	Relative (95% CI)	Absolute	Quality	Importance
		risk of bias								fewer to 8 more)		
90-day mortality												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	0/170 (0%)	0/170 (0%)	RD 0.00 (-0.01, 0.01)	0 fewer per 1000 (from 10 fewer to 10 more)	MODERATE	IMPORTANT
Operative mortality (timeframe not defined)												
6	randomised trials	no serious risk of bias	no serious inconsistency	serious[3]	serious[1]	none	17/585 (2.9%)	27/823 (3.3%)	RR 1.03 (0.57 to 1.86)	1 fewer per 1000 (from 14 fewer to 28 more)	LOW	IMPORTANT
Anastomotic leak												
10	randomised trials	no serious risk of bias	no serious inconsistency	serious[3]	serious[1]	none	85/1,418 (6%)	64/1,198 (5.3%)	RR 0.94 (0.68 to 1.29)	3 fewer per 1000 (from 17 fewer to 15 more)	LOW	IMPORTANT
Surgical site infection												
10	randomised trials	no serious risk of bias	no serious inconsistency	serious[3]	serious[1]	none	97/1,572 (6.2%)	86/1,106 (7.8%)	RR 0.79 (0.6 to 1.05)	16 fewer per 1000 (from 31 fewer to 4 more)	LOW	IMPORTANT
Blood loss (ml) - Anterior resection or abdominoperineal resection												
3	randomised trials	no serious risk of bias	serious[10]	no serious indirectness	no serious imprecision	none	357	338	-	MD 100.71 lower (132.25 to 69.17 lower)	MODERATE	IMPORTANT
1	randomised trials	no serious risk of bias	no serious inconsistency	serious[3]	no serious imprecision	none	699	345	-	Laparoscopic: median 200 (IQR 100-400) Open: median 400 (IQR 200-700)	MODERATE	IMPORTANT

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Laparoscopic surgery	Open surgery	Relative (95% CI)	Absolute	Quality	Importance
										p<0.0001		
Blood loss (ml) - Sphincter-preserving surgery												
4	randomised trials	no serious risk of bias	no serious inconsistency	serious[3]	no serious imprecision	none	281	291	-	MD 183 lower (276.09 to 89.91 lower)	MODERATE	IMPORTANT
1	randomised trials	no serious risk of bias	no serious inconsistency	serious[3]	no serious imprecision	none	238	237	-	Laparoscopic: median 100 (IQR 50-200) Open: median 150 (55-300) p=0.02	MODERATE	IMPORTANT
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	170	170	-	Laparoscopic: median 200 (IQR 100-300) Open: median 217.5 (IQR 150-400) p=0.006	MODERATE	IMPORTANT
Blood loss (ml) - Abdominoperinal resection												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious[3]	serious[1]	none	51	48	-	Laparoscopic: mean 321.7 (range 0-3000) Open: mean 555.6 (range 0-4720) p=0.093	LOW	IMPORTANT

1 *CI: confidence interval; CRM: circumferential resection margin; EQ-VAS: EuroQol visual analogue scale; FSFI: Female Sexual Function Index; HR: hazard ratio; IIEF: International*
2 *Index of Erectile Function questionnaire; IPSS: International Prostate Symptom score; IQR: interquartile range; MD: mean difference; QLQ-C30: Quality of Life Questionnaire Core*
3 *30 Items; QLQ-CR38: Quality of Life Questionnaire colorectal cancer module (38 items); RD: risk difference; RR: relative risk; SF-36: 36-item Short Form health survey*
4 *1 Quality of evidence downgraded by 1 because of imprecision of the effect estimate (<300 events for dichotomous outcomes or sample size <400 for continuous outcomes).*

2 Survival percentage at 5 years in the control group estimated using 5-year survival data from Ng 2014 and Ng 2008, and 3-year survival data from COREAN trial (Jeong 2014) and 10-year survival data from Ng 2009.
3 Quality of evidence downgraded by 1 because a considerable proportion of the population had or likely had (not clearly reported) early (T1-2N0M0 or stage 0/I) rectal cancer.
4 Quality of evidence downgraded by 1 because of risk of selection bias (method of randomisation or allocation concealment were not reported).
5 Quality of evidence downgraded by 1 because of risk of detection bias (there was no blinding of intervention which might affect assessment of outcome).
6 Quality of evidence downgraded by 1 because the imprecision of the effect estimate (95% CI crosses 1 MID).
7 Quality of evidence downgraded by 2 because of the imprecision of the effect estimate (95% CI crosses 2 MIDs).
8 Local recurrence percentage at 3 years in the control group taken from COREAN trial (Jeong 2014).
9 Quality of evidence downgraded by 2 because of serious heterogeneity.
10 Quality of evidence downgraded by 1 because of heterogeneity.

Table 10: Clinical evidence profile for comparison 2: Robotic versus open surgery for rectal cancer

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Robotic surgery**	**Open surgery**	**Relative (95% CI)**	**Absolute**		
Overall survival (median follow-up 3 years; event is death from any cause)												
2	observational studies	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	596	1,156	HR 0.98 (0.68 to 1.42)	At 3 years open 92%, robotic 92% (89% to 95%)[5]	VERY LOW	CRITICAL
Quality of life - Moderate or severe sexual dysfunction in men ≤65 years (VAS 2-5)												
1	observational studies	very serious[1,4]	no serious inconsistency	serious[2]	serious[3]	none	27/141 (19.1%)	108/332 (32.5%)	RR 0.59 (0.41 to 0.85)	133 fewer per 1000 (from 49 fewer to 192 fewer)	VERY LOW	CRITICAL
Quality of life - Severe sexual dysfunction in men ≤65 years (VAS 4-5)												
1	observational studies	very serious[1,4]	no serious inconsistency	serious[2]	serious[3]	none	13/141 (9.2%)	37/332 (11.1%)	RR 0.83 (0.45 to 1.51)	19 fewer per 1000 (from 61 fewer to 57 more)	VERY LOW	CRITICAL
Quality of life - Moderate sexual dysfunction in men ≤65 years (VAS 2-3)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Robotic surgery**	**Open surgery**	**Relative (95% CI)**	**Absolute**		
1	observational studies	very serious[1,4]	no serious inconsistency	serious[2]	serious[3]	none	14/141 (9.9%)	71/332 (21.4%)	RR 0.46 (0.27 to 0.8)	115 fewer per 1000 (from 43 fewer to 156 fewer)	VERY LOW	CRITICAL
Positive resection margin												
1	observational studies	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	106/1,937 (5.5%)	1,256/14,735 (8.5%)	RR 0.64 (0.53 to 0.78)	31 fewer per 1000 (from 19 fewer to 40 fewer)	VERY LOW	CRITICAL
Positive CRM (≤1 mm)												
1	observational studies	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	8/533 (1.5%)	26/1,095 (2.4%)	RR 0.63 (0.29 to 1.39)	9 fewer per 1000 (from 17 fewer to 9 more)	VERY LOW	CRITICAL
Postive resection margin (R1)												
1	observational studies	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	0/65 (0%)	2/55 (3.6%)	Peto odds ratio 0.11 (0.01, 1.81)	32 fewer per 1000 (from 36 fewer to 28 more)	VERY LOW	CRITICAL
Positive distal resection margin (≤5 mm)												
1	observational studies	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	5/533 (0.94%)	13/1,095 (1.2%)	RR 0.79 (0.28 to 2.2)	2 fewer per 1000 (from 9 fewer to 14 more)	VERY LOW	CRITICAL
Local recurrence												
0	No RCT evidence available	-	-	-	-	-	-	-	-	-	-	IMPORTANT

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Robotic surgery	Open surgery	Relative (95% CI)	Absolute		
Length of hospital stay (days)												
0	No RCT evidence available	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Operative mortality												
0	No RCT evidence available	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Treatment-related complications												
0	No RCT evidence available	-	-	-	-	-	-	-	-	-	-	IMPORTANT

CI: confidence interval; CRM: circumferential resection margin; R1: positive resection margin; RCT: randomised controlled trial; RR relative risk; VAS: visual analogue scale
1 Quality of evidence downgraded by 1 because of risk of bias due to lack of adjustment for confounding or case mix.
2 Quality of evidence downgraded by 1 because a considerable proportion of the population had or likely had (not clearly reported) early (T1-2N0M0 or stage 0/I) rectal cancer.
3 Quality of evidence downgraded by 1 because of imprecision of the effect estimate (less than 300 events for dichotomous outcomes or sample size less than 400 for continuous outcomes).
4 Quality of evidence downgraded by 1 because of no blinding.
5 Estimated using the 3 year overall survival in the open surgery group from Kim 2016

Table 11: Clinical evidence profile for comparison 3: Robotic versus laparoscopic surgery for rectal cancer

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Robotic surgery	Laparoscopic surgery	Relative (95% CI)	Absolute		
Overall survival (median follow-up 3 to 5 years; event is death from any cause)												
8	observational studies	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	1,471	1,300	HR 1.07 (0.87 to 1.31)	At 3 years laparoscopic 94%,	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Robotic surgery	Laparoscopic surgery	Relative (95% CI)	Absolute	Quality	Importance
										robotic 94% (92% to 95%)[7]		
Quality of life - Global health status (QLQ-C30)												
1	randomised trials	serious[4]	no serious inconsistency	serious[2]	serious[3]	none	66	73	No difference between the two groups at 3 weeks, 3 months, and 12 months after surgery.	-	VERY LOW	CRITICAL
Quality of life - Sexual function mean score at 12 months (QLQ-CR38) (range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[4]	no serious inconsistency	serious[2]	serious[3]	none	66	73	-	MD 12.2 higher (1.37 to 23.03 higher)	VERY LOW	CRITICAL
Quality of life – Female sexual function at 6 months (FSFI) (range of scores: 2-36; Better indicated by higher values)												
1	randomised trials	serious[4,5]	no serious inconsistency	serious[2]	serious[3]	none	25	29	-	Adjusted[6] MD -1.23 (-6.00 to 3.54)	VERY LOW	CRITICAL
Quality of life – Male sexual function at 6 months (IIEF) (range of scores: 5-75; Better indicated by lower values)												
1	randomised trials	serious[4,5]	no serious inconsistency	serious[2]	serious[3]	none	97	84	-	Adjusted[6] MD -0.80 (-5.70 to 4.10)	VERY LOW	CRITICAL
Quality of life – Bladder function at 6 months (IPSS) (range of scores 0-35; Better indicated by lower values)												

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Robotic surgery**	**Laparoscopic surgery**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
1	randomised trials	serious[4,5]	no serious inconsistency	serious[2]	serious[3]	none	175	176	-	Adjusted[6] MD -0.74 (-2.07 to 0.59)	VERY LOW	CRITICAL
Positive CRM (≤1 mm)												
2	randomised trials	serious[5]	no serious inconsistency	serious[2]	serious[3]	none	16/301 (5.3%)	18/297 (6.1%)	RR 0.88 (0.46 to 1.69)	7 fewer per 1000 (from 33 fewer to 42 more)	VERY LOW	CRITICAL
Positive proximal resection margin												
1	randomised trials	serious[5]	no serious inconsistency	serious[2]	serious[3]	none	0/235 (0%)	0/224 (0%)	RD 0 .00 (-0.01., 0.01)	0 fewer per 1000 (from 10 fewer to 10 more	VERY LOW	CRITICAL
Positive distal resection margin												
1	randomised trials	serious[5]	no serious inconsistency	serious[2]	serious[3]	none	0/235 (0%)	1/224 (0.45%)	Peto odds ratio 0.13 (0.00, 6.50)	4 fewer per 1000 (from 0 fewer to 24more)	VERY LOW	CRITICAL
Local recurrence												
0	No RCT evidence available	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Length of hospital stay (days)												
2	randomised trials	serious[5]	no serious inconsistency	serious[2]	serious[3]	none	303	307	-	MD 0.27 lower (1.21 lower to 0.66 higher)	VERY LOW	IMPORTANT
30-day operative mortality												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Robotic surgery**	**Laparoscopic surgery**	**Relative (95% CI)**	**Absolute**		
1	randomised trials	serious[5]	no serious inconsistency	serious[2]	serious[3]	none	2/236 (0.85%)	2/230 (0.87%)	RR 0.97 (0.14 to 6.86)	0 fewer per 1000 (from 7 fewer to 51 more)	VERY LOW	IMPORTANT
Anastomotic leak												
2	randomised trials	serious[5]	no serious inconsistency	serious[2]	serious[3]	none	30/246 (12.2%)	23/254 (9.1%)	RR 1.34 (0.8 to 2.24)	31 more per 1000 (from 18 fewer to 112 more)	VERY LOW	IMPORTANT
Surgical site infection within 30 days												
1	randomised trials	serious[5]	no serious inconsistency	serious[2]	serious[3]	none	21/236 (8.9%)	19/230 (8.3%)	RR 1.08 (0.6 to 1.95)	7 more per 1000 (from 33 fewer to 78 more)	VERY LOW	IMPORTANT
Surgical site infection between 30 days and 6 months after surgery												
1	randomised trials	serious[5]	no serious inconsistency	serious[2]	serious[3]	none	4/236 (1.7%)	8/230 (3.5%)	RR 0.49 (0.15 to 1.6)	18 fewer per 1000 (from 30 fewer to 21 more)	VERY LOW	IMPORTANT
Blood loss (ml)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	serious[3]	none	66	73	-	Robotic: median 100 (range 0-1,000) Laparoscopic: median 50 (range 0-300) p<0.0001	LOW	IMPORTANT

1 *CI: confidence interval; CRM: circumferential resection margin; FSFI: Female Sexual Function Index; IIEF: International Index of Erectile Function; IPSS: International Prostate*
2 *Symptom Score; MD: mean difference; QLQ-C30: Quality of Life Questionnaire Core 30 Items; QLQ-CR38: Quality of Life Questionnaire colorectal cancer module (38 items); RCT:*

randomised controlled trial; RD: risk difference; RR: relative risk
1 Quality of evidence downgraded by 1 because of risk of bias due to lack of adjustment for confounding or case mix.
2 Quality of evidence downgraded by 1 because considerable proportion of the population had or likely had (not clear from the paper) early (T1-2N0M0 or stage 0-I) rectal cancer.
3 Quality of evidence downgraded by 1 because of imprecision of the effect estimate (less than 300 events for dichotomous outcomes or sample size less than 400 for continuous outcomes).
4 Quality of evidence downgraded by 1 because of no blinding.
5 Quality of evidence downgraded by 1 because details about randomisation and allocation concealment were not reported.
6 Adjusted for baseline scores and stratification factors (surgeon, sex, preoperative therapy, intended procedure and BMI).
7 Estimated using the 3 year overall survival in the laparascopic surgery group from Kim 2016

Table 12: Clinical evidence profile for comparison 4: Transanal total mesorectal excision versus laparoscopic surgery for rectal cancer

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**TaTME**	**Laparoscopic surgery**	**Relative (95% CI)**	**Absolute**		
Overall survival (median 5 years of follow-up; event is death from any cause)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious[1]	serious[2]	none	7/50 (14%)	13/50 (26%)	HR 0.50 (0.20 to 1.24)	At 5 years laparoscopic 74.4%[3], TaTME 86.3% (69.3% to 94.3%)	LOW	CRITICAL
Quality of life - Sexual activity maintained at median 3.2 years after treatment (in previously sexually active participants)												
1	randomised trials	serious[4]	no serious inconsistency	serious[1]	serious[2]	none	20/28 (71.4%)	9/23 (39.1%)	RR 1.83 (1.04 to 3.2)	325 more per 1000 (from 16 more to 861 more)	VERY LOW	CRITICAL
Quality of life - Sexual dysfunction at median 3.2 years after treatment (FSFI score ≤19) in previously sexually active women												
1	randomised trials	serious[4]	no serious inconsistency	serious[1]	serious[2]	none	2/5 (40%)	2/3 (66.7%)	RR 0.6 (0.16 to 2.29)	267 fewer per 1000 (from 560 fewer to 860 more)	VERY LOW	CRITICAL
Quality of life - Erectile function score at median 3.2 years after treatment (IIEF) (range of scores: 5-25; Better indicated by higher values)												
1	randomised trials	serious[4]	no serious inconsistency	serious[1]	serious[2]	none	23	16	-	TaTME: median	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	TaTME	Laparoscopic surgery	Relative (95% CI)	Absolute		
										17.5 (range 5-25) Laparoscopic: median 7 (range 5-21) p=0.119		
Quality of life - Normal ejaculatory function at median 3.2 years after treatment in previously sexually active men (IIEF)												
1	randomised trials	serious[4]	no serious inconsistency	serious[1]	serious[2]	none	14/21 (66.7%)	7/16 (43.8%)	RR 1.52 (0.81 to 2.87)	227 more per 1000 (from 83 fewer to 818 more)	VERY LOW	CRITICAL
Quality of life - Urinary function quality of life score at median 3.2 years after treatment (IPSS) (range of scores: 0-6; Better indicated by lower values)												
1	randomised trials	serious[4]	no serious inconsistency	serious[1]	serious[2]	none	38	34	-	TaTME: median 1 (range 0-6) Laparoscopic: median 1 (range 0-5) p=0.967	VERY LOW	CRITICAL
Quality of life - Urinary function total score at median 3.2 years after treatment (IPSS) (range of scores: 0-35; Better indicated by lower values)												
1	randomised trials	serious[4]	no serious inconsistency	serious[1]	serious[2]	none	38	34	-	TaTME: median 5.5 (range 0-23) Laparoscopic: median 3.5 (range 0-27) p=0.821	VERY LOW	CRITICAL
R1 resection (positive CRM)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**TaTME**	**Laparoscopic surgery**	**Relative (95% CI)**	**Absolute**		
1	randomised trials	no serious risk of bias	no serious inconsistency	serious[1]	serious[2]	none	2/50 (4%)	9/50 (18%)	RR 0.22 (0.05 to 0.98)	140 fewer per 1000 (from 4 fewer to 171 fewer)	LOW	CRITICAL
Positive distal margin												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious[1]	serious[2]	none	1/50 (2%)	4/50 (8%)	RR 0.25 (0.03 to 2.16)	60 fewer per 1000 (from 78 fewer to 93 more)	LOW	CRITICAL
Local recurrence												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious[1]	serious[2]	none	50	50	Insufficient data to calculate	At 5 years laparoscopic 4.8%, TaTME 2.6 (2.3% to 7.5%)	LOW	IMPORTANT
Length of hospital stay (days)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious[1]	serious[2]	none	50	50	-	TaTME: median 7 (range 3-54) Laparoscopic: median 8 (range 2-29) p=0.281	LOW	IMPORTANT
Postoperative mortality												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious[1]	serious[2]	none	0/50 (0%)	1/50 (2%)	Peto odds ratio 0.14 (0.00, 6.82)	17 fewer per 1000 (from 0 fewer to 102 more)	LOW	IMPORTANT

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**TaTME**	**Laparoscopic surgery**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Anastomotic leak and/or abscess												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious[1]	serious[2]	none	1/50 (2%)	5/50 (10%)	RR 0.2 (0.02 to 1.65)	80 fewer per 1000 (from 98 fewer to 65 more)	LOW	IMPORTANT
Surgical site infection												
0	No evidence available	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Blood loss (ml)												
0	No evidence available	-	-	-	-	-	-	-	-	-	-	IMPORTANT

CI: confidence interval; CRM: circumferential resection margin; FSFI: Female Sexual Function Index; HR: hazard ratio; IIEF: International Index of Erectile Function questionnaire; IPSS: International Prostate Symptom score; MD: mean difference; R1: positive margin; RR: relative risk; TaTME: transanal total mesorectal excision

1 Quality of evidence downgraded by 1 because considerable proportion of the population likely had (not clear from the paper) early (T1-2N0M0 or stage 0-I) rectal cancer.

2 Quality of evidence downgraded by 1 because of imprecision of the effect estimate (less than 300 events for dichotomous outcomes or sample size less than 400 for continuous outcomes).

3 Survival percentage at 5 years in the control group taken from the Bordeaux' trial (Denost 2018).

4 Quality of evidence downgraded by 1 because of no blinding.

Appendix G – Economic evidence study selection

Economic evidence study selection for review question: What is the optimal surgical technique for rectal cancer?

A global search of economic evidence was undertaken for all review questions in this guideline. See Supplement 2 for further information.

Appendix H – Economic evidence tables

Economic evidence study selection for review question: What is the optimal surgical technique for rectal cancer?

No economic evidence was identified which was applicable to this review question.

Appendix I – Economic evidence profiles

Economic evidence profiles for review question: What is the optimal surgical technique for rectal cancer?

No economic evidence was identified which was applicable to this review question.

Appendix J – Economic analysis

Economic evidence analysis for review question: What is the optimal surgical technique for rectal cancer?

An economic analysis was undertaken to estimate the cost-effectiveness of surgical techniques for rectal cancer.

Methods

The analysis was developed in Microsoft Excel® and was conducted from the perspective of the NHS and Personal Social Services (PSS) as outlined in the NICE Reference Case (see Developing NICE guidelines: the manual). The model considered a lifetime horizon with future costs and benefits discounted at a rate of 3.5% (as recommended in the NICE reference case).

Clinical data and model approach

The economic analysis was based on clinical effectiveness data for each of the surgical techniques, which was sourced from the clinical evidence review. However, only the comparison between the open and laparoscopic approach provided sufficient data for all the key outcomes of interest for the economic analysis (overall survival, local recurrence and complications). As a result, a decision was made to separately consider two comparisons in the analysis. In the first, a comparison is made between the open and laparoscopic approach based on evidence from the clinical evidence review. In the second, all four surgical approaches are considered using available data from the clinical evidence review in combination with assumptions to fill in the missing data. The second analysis was therefore considered to be more speculative and the conclusions that can be drawn from the analysis were limited.

The clinical values applied in the analysis are detailed in the relevant sections below. In all cases it should be noted that there is considerable uncertainty around the estimates (as shown by the reported Cis). Furthermore, it should be noted that the four way comparison relies on making some assumptions were values were missing and also necessitates making indirect treatment comparisons which further increases uncertainty.

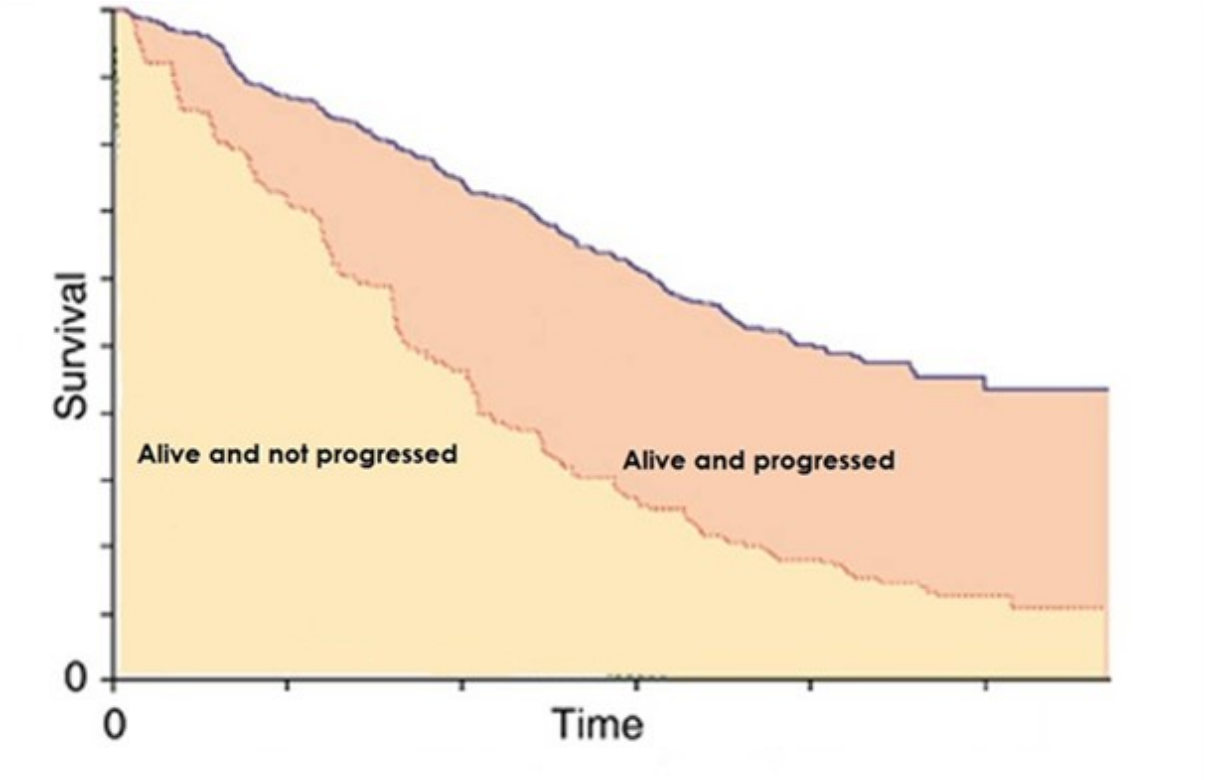
Model Structure

A partitioned survival analysis was developed to estimate the expected life expectancy, quality adjusted life years (QALYs) and costs associated with the approaches considered in this economic analysis. A partitioned survival analysis divides the model cohort between different health states based on survival curves derived for overall survival (OS) and recurrence free survival (RFS) derived from the accompanying clinical evidence review. The expected OS and RFS are then calculated from the area under the respective curves. For our model, 3 mutually exclusive health states were derived for the cohort to be partitioned into:

- alive without progressed disease (equal to the area under the RFS curve)
- alive with progressed disease (equal to the area between the RFS curve and the OS curve)
- death (area above the OS curve).

An illustrative example of the structure of the partitioned survival analysis is shown in Figure 47.

Figure 47: Illustrative example of partitioned survival analysis



A partitioned survival analysis approach was chosen over other modelling approaches, for example, a state transition model as only absolute survival estimates at limited set time points were reported by the identified studies and these were the only survival estimates synthesised and reported by the meta-analyses in the accompanying clinical evidence review. Consequently all OS and RFS estimates in the model were derived from these outcomes. Given the scarcity of the time points at which these were reported it was difficult to estimate plausible transition probabilities for use in a state transition model. It was also possible to extrapolate survival beyond that reported by the studies in the accompanying clinical evidence review. This approach is widely used in models of the cost effectiveness of oncology interventions. A review of recent NICE technology appraisals in oncology found that this approach was used in 73% of submissions (Woods 2017).

While not a consideration in choosing the most appropriate modelling approach, a partitioned survival analysis is a more intuitive modelling approach for metastases in cancer than state transition models. Evidence from trials and observational studies where survival is a key outcome are almost exclusively reported as median overall and progression-free survival with accompanying hazard ratio and Kaplan Meier survival curves. As these are the primary inputs for partitioned survival analysis the inputs can be easily compared with those observed in the included trials and other external sources. The model can also be more easily compared, for validity, with any potential future study which consider the relevant interventions.

A partitioned survival analysis was performed for both interventions considered in the economic evaluation and for the two further interventions considered in the further speculative analysis and the total time spent in each health state for the model cohort was calculated. Each health state was assigned a quality of life weighting so that survival could be adjusted to QALYs.

The economic component of the model was built and run in Microsoft Excel 2013. The model had a cycle length of 1 year. The model had a time horizon of 36 years for which, based on Office of National Statistics (ONS) life tables, over 99.9% of a general population sample would have died. This percentage would be even higher for a population with rectal cancer. The model would therefore comfortably cover a sufficient time horizon to capture all outcomes, QALYs and costs. The model took a NHS and Personal Social Services perspective (PSS) and only outcomes relevant to either organisation were considered.

For the reporting of outcomes in the model the open approach was considered the comparator and laparoscopic approach the intervention. Costs and outcomes are reported on a per person basis.

Overall survival

Overall survival estimates for the comparison between the open and laparoscopic surgical approach were based upon values from the clinical evidence review. Absolute survival estimates showed that 85.0% of patients were alive at five years following treatment with the open surgical approach. The laparoscopic approach was found to reduce overall mortality in comparison to the open approach with an estimated HR of 0.83 (95% CI 0.70-0.99).

Overall survival estimates for the comparison between all four surgical approaches were also based upon values from the clinical evidence review. Overall survival values for the open and laparoscopic approach were based on the same methodology used in the two-way comparison between these approaches. Overall survival with the robotic approach was based on an estimated RR of 1.02. This value was estimated from absolute 3 year survival estimates obtained from 1 study (Rouanet 2018) the clinical evidence review which gave survival rates of 88.4% and 84.1% for the laparoscopic and robotic approach, respectively. Overall survival for the TaTME approach was based on the HR of 0.5 (95% CI 0.20-1.24) reported in the clinical evidence review for the comparison between TaTME and the laparoscopic approach. All calculations follow the usual proportional hazard assumptions.

Local recurrence

Local recurrence estimates for the comparison between the open and laparoscopic surgical approach were based upon values from the clinical evidence review. Absolute estimates from 1 study (Jeong 2014) identified in the accompanying clinical evidence review showed that 4.9% of patients had local recurrence at 3 years following treatment with the open surgical approach. From this study, the laparoscopic approach had lower local recurrence in comparison to the open approach and estimated a HR of 0.40 (95% CI 0.13-1.26). This estimate was chosen for use in the economic model over the pooled estimate from the clinical evidence review as this was the largest and most recent study identified and was considered most applicable to technologies used today. The pooled estimate of 0.57 (95% CI 0.25-1.26) would be less favourable to a laparoscopic approach however both estimates have 95% confidence intervals that pass the line of no effect.

Local recurrence estimates for the comparison between all four surgical approaches were also based upon values from the clinical evidence review. Local recurrence values for the open and laparoscopic approach were based on the same methodology used in the two-way comparison between these approaches. Local recurrence estimates were not available for the robotic approach. It was therefore assumed that it would be equivalent to local recurrence with the laparoscopic approach. A RR estimate of 1.00 was therefore applied. Local recurrence with the TaTME approach was based on an estimated RR of 0.54. This

value was estimated from absolute local recurrence estimates obtained from the clinical evidence review which gave local recurrence rates of 4.8% and 2.6% at 5 years for the laparoscopic and robotic approach, respectively. As with overall survival the usual proportional hazard assumptions apply.

Complications

The accompanying clinical evidence review found evidence for 3 types of surgical complications in this comparison: anastomical leak, surgical site infection and excess blood loss. Excess blood loss is not an uncommon occurrence in surgery and it was likely that in all but rare severe cases there will be limited impact on quality of life and costs. This complication was therefore not included in the economic model. Other complications which were highlighted as important such as reduction in sexual function and bladder problems, even though they would have a significant impact upon quality of life were not included in the model. This is because the accompanying evidence review did not find any evidence around these outcomes and it is uncertain, from clinical opinion, whether these would be more favourable in either open or laparoscopic groups.

All complications were assumed to have only a short impact upon quality of life and morbidity. No longer-term morbidity was modelled. Whilst anastomical leaks can lead to operative mortality this would beincluded in the perioperative mortality model inputs.

The proportion of treatment related complications were estimated for the comparison between the open and laparoscopic surgical approach using values from the clinical evidence review. Absolute estimates for patients treated with the open approach showed that 5.3% had an anastomotic leak and 7.8% had a surgical site infection. Complications after the laparoscopic approach were estimated using RRs from the clinical evidence review which suggest that the laparoscopic approach reduces complications with RRs of 0.94 (95% CI 0.68-1.29) and 0.79 (95% CI 0.60-1.05) for anastomotic leak and surgical site infection, respectively.

Complication estimates for the comparison between all four surgical approaches were also based upon values from the clinical evidence review. Complication estimates for the open and laparoscopic approach were based on the same methodology used in the two-way comparison between these approaches. The proportion of patients with an anastomotic leak after treatment with the robotic approach was based on a reported RR of 1.34 (95% CI 0.80-2.24) in comparison to the laparoscopic approach. There was no data on the proportion of patients with a surgical site infection after treatment with the robotic approach. Therefore this was assumed to be equivalent to laparoscopic approach (i.e. assuming RR of 1.00). The proportion of patients with an anastomotic leak after treatment with the TaTME approach was based on a reported RR of 0.20 (95% CI 0.02-1.65) in comparison to the laparoscopic approach. There was no data on the proportion of patients with a surgical site infection after treatment with the TaTME approach. Therefore this was assumed to be equivalent to laparoscopic approach (i.e. assuming RR of 1.00).

Costs

The costs considered in the model reflect the perspective of the analysis, thus only costs that are relevant to the UK NHS & PSS were included. Where possible, all costs were estimated in 2016/17 prices. All costs used in the model are presented in Table 13 with the exception of palliative care costs which are presented in Table 14.

The majority of costs were sourced from NHS reference costs 2016/17 by applying tariffs associated with the appropriate Healthcare Resource Groups (HRG) code. However, note that the cost of the surgical procedure in NHS reference costs (FF31: complex large intestine procedures, 19 years and over) is the same regardless of the approach taken. Therefore this cost was not estimated using the procedure code from NHS reference costs and an alternative approach was adopted in order to differentiate the various surgical techniques.

Surgical equipment costs

Surgical equipment costs were estimated using data from a cost-effectiveness analysis of surgical approaches in prostate cancer (Ramsay 2012), with costs inflated to 2016 prices. Equipment costs were estimated to be £1,502, £1,605, £4,628 and £1,815 for the open, laparoscopic, robotic, and TaTME approaches, respectively. Operative time costs were estimated using average theatre time estimates from the studies included in the clinical evidence review. A cost for an hour of operating theatre time was sourced the cost-effectiveness analysis from Ramsay 2012 and inflated to 2016 prices (£1,266). Length of stay costs were estimated using data on the number of days for each procedure from the studies included in the clinical evidence review combined with the cost of an excess bed day from NHS reference costs 2016/17. The length of hospital stay was meta-analysed by type of resection in the clinical evidence review given heterogeneity. This economic analysis does not investigate the cost effectiveness of the interventions by these subgroup so a pooled estimate of all length of stays was used in the economic model. This distribution was given a wide uniform distribution in the probabilistic sensitivity analysis given the considerations around heterogeneity.

Complication costs

Complication costs were estimated using the different costs associated with complication and co-morbidity (CC) scores for the surgical procedure from NHS reference costs. The difference between CC score 0-2 (used as a best estimate for no complications) and a weighted average of the other CC scores associated with complex large intestine procedures (FF31) was used as an estimate of complication costs.

Systemic chemotherapy costs

Systemic chemotherapy costs were estimated assuming that patients would be treated with 6 cycles of FOLFIRI or FOLFOX. The chemotherapy delivery costs were sourced from NHS Reference Costs 2015/16 (assuming day case delivery) and drug costs were sourced from eMit.

Inpatient and outpatient management costs

The cost of palliative care was estimated using estimates from a costing report by the Nuffield Trust (Georghiou 2014). A cost of £7,287 was applied based on the average resource use of patients with cancer in the last three months of life.

Table 13: Costs and cost weightings used in the economic model

	Weight	Cost	Source
Complex Large Intestine Procedures, 19 years and over			
with CC Score 9+ (FF31A)	3%	£13,567.94	NHS Reference costs 2016/17
with CC Score 6-8 (FF31B)	6%	£10,626.33	NHS Reference costs 2016/17
with CC Score 3-5 (FF31C)	22%	£8,810.93	NHS Reference costs 2016/17
with CC Score 0-2 (FF31D)	70%	£7,370.66	NHS Reference costs 2016/17
Weighted average	100%	***£8,026.32***	
Complex Large Intestine Procedures, 19 years and over-Excess bed days			
with CC Score 9+ (FF31A)	6%	£247.57	NHS Reference costs 2016/17
with CC Score 6-8 (FF31B)	18%	£298.73	NHS Reference costs 2016/17

	Weight	Cost	Source
with CC Score 3-5 (FF31C)	23%	£354.04	NHS Reference costs 2016/17
with CC Score 0-2 (FF31D)	53%	£326.78	NHS Reference costs 2016/17
Weighted average	100%	***£323.36***	
Operative and length of stay costs			
Operative time cost per hour of surgery		£1,265.90	Ramsay 2012
LOS - cost per day		£323.36	Ramsay 2012
Open approach			
Equipment cost		£1,501.93	Ramsay 2012
Operative time		181 minutes	Ramsay 2012
Operative time cost		£3,813.41	
LOS - number of days		9.68 days	Ramsay 2012
LOS cost		£3,130.12	
Total cost of open approach		**£8,445.46**	
Laparoscopic approach			
Equipment cost		£1,605.41	Ramsay 2012
Operative time		225 minutes	Ramsay 2012
Operative time cost		£4,744.40	
LOS - number of days		8.27 days	Ramsay 2012
LOS cost		£2,674.18	
Total cost of laparoscopic approach		**£9,024.00**	
Robotic approach			
Equipment cost		£4,627.63	Ramsay 2012
Operative time		282 minutes	Ramsay 2012
Operative time cost		£5,950.57	
LOS - number of days		7.77 days	Ramsay 2012
LOS cost		£2,512.50	
Total cost of robotic approach		**£13,090.70**	
TaTME approach			
Equipment cost		£1,814.81	Ramsay 2012
Operative time		205 minutes	Ramsay 2012
Operative time cost		£4,329.50	
Surgeon cost per working hour		£107.00	Ramsay 2012
Cost for second surgeon		£365.95	Ramsay 2012
LOS - number of days		7.24 days	Ramsay 2012
LOS cost		£2,339.91	

	Weight	Cost	Source
Total cost of TaTME approach		**£8,850.16**	
Systemic chemotherapy costs			
FOLFOX			
Deliver complex chemotherapy at first attendance		£385.99	NHS Reference costs 2016/17
Dexamethasone 8mg		£1.52	eMit
Ondansetron 16mg		£0.17	eMit
Chlorphenamine 10mg		£3.01	eMit
Oxaliplatin 85mg/m2		£16.04	eMit
Folinic Acid 350mg		£10.42	eMit
Fluorouracil 400mg/m2		£3.94	eMit
Fluorouracil 2400mg/m2		£8.36	eMit
Cost per cycle		£429.45	
Total cost for 6 cycles		**£2,576.72**	
FOLFIRI			
Deliver complex chemotherapy at first attendance		£385.99	NHS Reference costs 2016/17
Atropine 250mcg		£0.12	eMit
Irinotecan 180mg/m2		£17.35	eMit
Folinic Acid 350mg		£10.42	eMit
Fluorouracil 400mg/m2		£3.94	eMit
Fluorouracil 2400mg/m2		£8.36	eMit
Cost per cycle		£426.18	
Total cost for 6 cycles		**£2,557.09**	
Average cost of systemic chemotherapy regimens		**£2,566.91**	

FOLFIRI: folinic acid, fluorouracil and irinotecan; FOLFOX: folnic acif, fluorouracil and oxaliplatin; LOS: length of stay; CC: clinical complications; eMit: Drugs and pharmaceutical electronic market information tool

Cost of palliative care

Given the life expectancy of the model cohort and that the majority of patients would die as a result of their disease a one off cost of palliative care was applied to the entirety of the cohort during their final year of life. This is to represent the increase in resource use experienced during the final months of a patient's life. This one off cost was taken from Georghiou 2014. The study used medical records of over 1,836 patients with cancer at multiple UK hospitals and hospices to estimate resource use and publically available UK costs to estimate a total cost for the final 90 days of life. An average cost for patients with cancer was used from the report. These costs are presented in Table 14.

Table 14: Costs of palliative care for patients with cancer from Georghiou 2014

Type of care	Cost
Cost of all hospital contacts	£5,890
Local authority-funded care	£444
District nursing care	£588
GP contacts	£365
Total palliative care cost per patient	**£7,287**

The above costs includes 'local authority-funded care'. The methods of calculation from the original report may include costs, such as personal contributions to care, which are not strictly covered by the NHS & PSS perspective used for this economic model. A deterministic sensitivity analysis was therefore undertaken which removed this cost from the total palliative care cost estimate.

Health-related quality of life

As recommended in the NICE reference case, the model estimates effectiveness in terms of quality adjusted life years (QALYs). These are estimated by combining life year estimates with quality of life (QoL) values associated with being in a particular health state.

QoL data for all comparisons were sourced from Rao 2017, a cost-effectiveness analysis that estimated QoL for recurrences (0.78) and for being recurrence free (0.86).

Sensitivity analysis

Uncertainty was assessed in the economic model through deterministic and probabilistic sensitivity analysis. A series of deterministic sensitivity analyses were conducted, whereby an input parameter was changed, the model was re-run and the new cost-effectiveness result was recorded. This form of analysis is a useful way of estimating uncertainty and determining the key drivers of the model results.

Probabilistic sensitivity analysis (PSA) was conducted to assess the combined parameter uncertainty in the model. In this analysis, the mean values that were utilised in the base-case were replaced with values drawn from distributions around the mean values.

Results

Overall and recurrence free survival

Overall (Figure 48) and recurrence free survival (Figure 49), based on the deterministic point estimates, were unsurprisingly in line with the HRs and RRs used as inputs. There is over a 20 percentage point difference between TaTME and the open approach for both overall and recurrence free survival at the greatest point of difference although the uncertainty around the TaTME estimates of both types of survival should be noted.

Figure 48: Overall survival estimated in the economic model

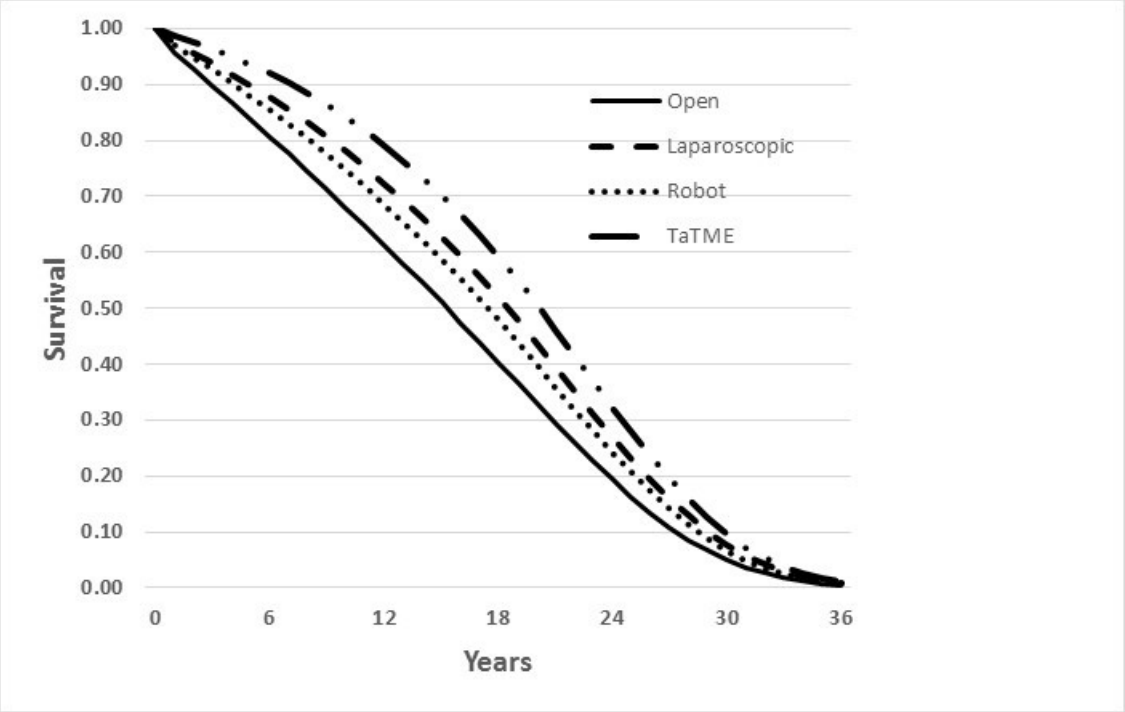
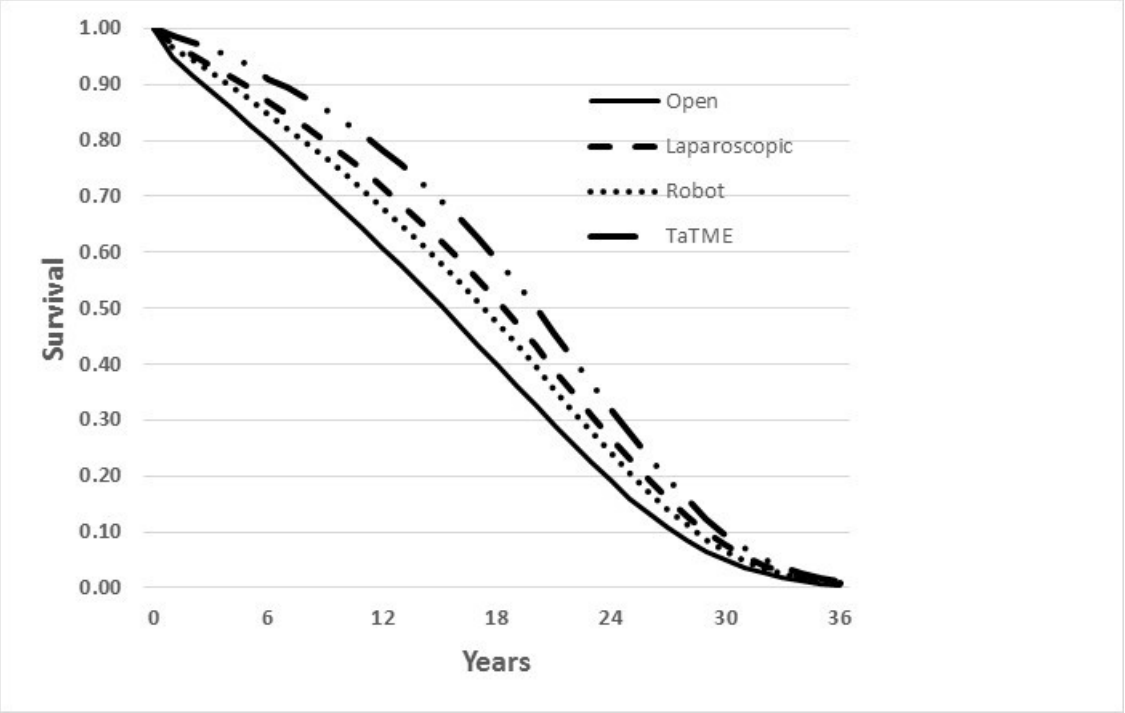


Figure 49: Recurrence free survival estimated in the economic model



Base-case results

The base case resultsof the analysis, based on the point estimates of the model inputs, are shown in Table 15 and Table 16 for the two-way and four-way comparison respectively. The results of the two way comparison show the laparoscopic approach to be more effective (1.26 QALYs) and less costly than the open approach (£921) and it is therefore dominant. These results are driven by improvements in overall survival which are clinically significant.

In the four-way comparison, alternative approaches were compared using a net monetary benefit approach assuming a threshold of £20,000 per QALY. The results show the TaTME approach to be the least costly approach. All other strategies are found to be more costly and less effective than TaTME and are therefore dominated. Consequently, net monetary benefit was negative for all other interventions. However it should be noted for TaTME that the results are driven by improvements in overall survival and recurrence which were based on a hazard ratio for which the 95% confidence interval passed the line of no effect. It is therefore plausible that TaTME may result in lower QALYs and higher costs (through increased recurrence) compared to alternative approaches. These results should therefore be considered speculative.

Table 15: Base case results for two-way comparison

Strategy	Cost		QALYs		ICER (cost per QALY
	Total	Incremental	Total	Incremental	
Open	£11,963	-	9.08	-	-
Laparoscopic	£11,042	*-£921*	10.34	*1.26*	**Dominant**

ICER: incremental cost-effectiveness ratio; QALYs: quality adjusted life years

Table 16: Base case results for four-way comparison

Strategy	Cost		QALYs		ICER (cost per QALY	NMB
	Total	Incremental	Total	Incremental		
TaTME	£9,812	-	11.15	-	-	
Laparoscopic	£11,042	£1,230	10.34	-0.81	**Dominated**	*-£17,395*
Open	£11,963	£2,151	9.08	-2.07	**Dominated**	*-£43,575*
Robotic	£15,612	£5,800	9.92	-1.24	**Dominated**	*-£30,503*

ICER: incremental cost-effectiveness ratio; QALYs: quality adjusted life years NMB Net monetary benefit

Disaggregated costs are presented in Table 17. The majority of total costs (>60% of total costs) for all interventions is the upfront treatment cost of the surgical procedure.Systemic chemotherapy and palliative care costs are zero for both robotic and TaTME given the assumptions around disease specific mortality.

Table 17: Disaggregated costs for four-way analysis

	Upfront treatment costs	Complication costs	Recurrence costs	Systemic chemotherapy	Palliative care costs
TaTME	£8,850	£259	£1,154	£0	£0
Laparoscopic	£9,024	£404	£1,182	£319	£907
Open	£8,445	£475	£1,209	£805	£2,284
Robotic	£8,850	£259	£1,154	£0	£0

Deterministic sensitivity results

A series of deterministic sensitivity analyses were conducted whereby an input parameter is changed, the model is re-run and the new cost-effectiveness result is recorded. This is a useful way of estimating uncertainty and determining the key drivers of the model result. The results of the deterministic sensitivity analyses are presented in Table 18 and Table 19 for the two-way and four-way comparison, respectively.

In the two-way comparison, it can again be seen that the conclusion of the analysis remains unchanged in the majority of modelled scenarios with the laparoscopic approach found to be cost effective. Notably this includes a scenario in which only statistically significant effects

are modelled. The conclusion of the analysis was found to change when the upper HR for overall survival was applied (meaning that overall survival is better with the open approach).

In the four-way comparison, it can again be seen that the conclusion of the analysis remains unchanged in the majority of modelled scenarios with TaTME found to be cost effective. However, notably, this does not include a scenario in which only statistically significant effects are modelled (in which the laparoscopic approach is found to be cost effective). The laparoscopic approach was also found to be cost effective when the upper HR for overall survival for TaTME was applied or when overall survival was assumed to be equivalent with laparoscopic and TaTME. The open approach was found to be cost effective when the upper HR for overall survival for TaTME and the laparoscopic approach was applied.

Table 18: Deterministic sensitivity results for two-way comparison

Modelled scenario	Optimal strategy
Base case	Laparoscopic
Overall survival – lower HR	Laparoscopic
Overall survival – upper HR	Laparoscopic
Local recurrence – lower RR	Laparoscopic
Local recurrence – upper RR	Laparoscopic
Complications – lower RR	Laparoscopic
Complications – upper RR	Laparoscopic
Statistically significant changes only	Laparoscopic
Number of robotic procedures per year = 50	Laparoscopic
Number of robotic procedures per year = 100	Laparoscopic
Number of robotic procedures per year = 200	Laparoscopic
Complication costs + 50%	Laparoscopic
Complication costs - 50%	Laparoscopic
No systemic chemotherapy costs	Laparoscopic
No palliative care costs	Laparoscopic
No recurrence disutility	Laparoscopic

HR: hazard ratio; RR: relative risk

Table 19: Deterministic sensitivity results for four-way comparison

Modelled scenario	Optimal strategy
Base case	TaTME
Overall survival – lower HR for laparoscopic	TaTME
Overall survival – upper HR for laparoscopic	TaTME
Overall survival – lower HR for TaTME	TaTME
Overall survival – upper HR for TaTME	***Laparoscopic***
Overall survival with TaTME equivalent to laparoscopic	***Laparoscopic***
Overall survival – upper HR for TaTME and laparoscopic	***Open***
Absolute overall survival with robotic 10% higher	TaTME
Absolute overall survival with robotic 10% lower	TaTME
Local recurrence – lower RR for laparoscopic	TaTME
Local recurrence – upper RR for laparoscopic	TaTME
Absolute local recurrence with TaTME 10% higher	TaTME
Absolute local recurrence with TaTME 10% lower	TaTME
Local recurrence with TaTME equivalent to laparoscopic	TaTME
Complications – lower RR	TaTME

Modelled scenario	Optimal strategy
Complications – upper RR	TaTME
Statistically significant changes only	***Laparoscopic***
Number of robotic procedures per year = 50	TaTME
Number of robotic procedures per year = 100	TaTME
Number of robotic procedures per year = 200	TaTME
Complication costs + 50%	TaTME
Complication costs - 50%	TaTME
No systemic chemotherapy costs	TaTME
No palliative care costs	TaTME
No recurrence disutility	TaTME

HR: hazard ratio; RR: relative risk; TaTME: transanal total mesorectal excision; TME: total mesorectal excision

Probabilistic sensitivity results

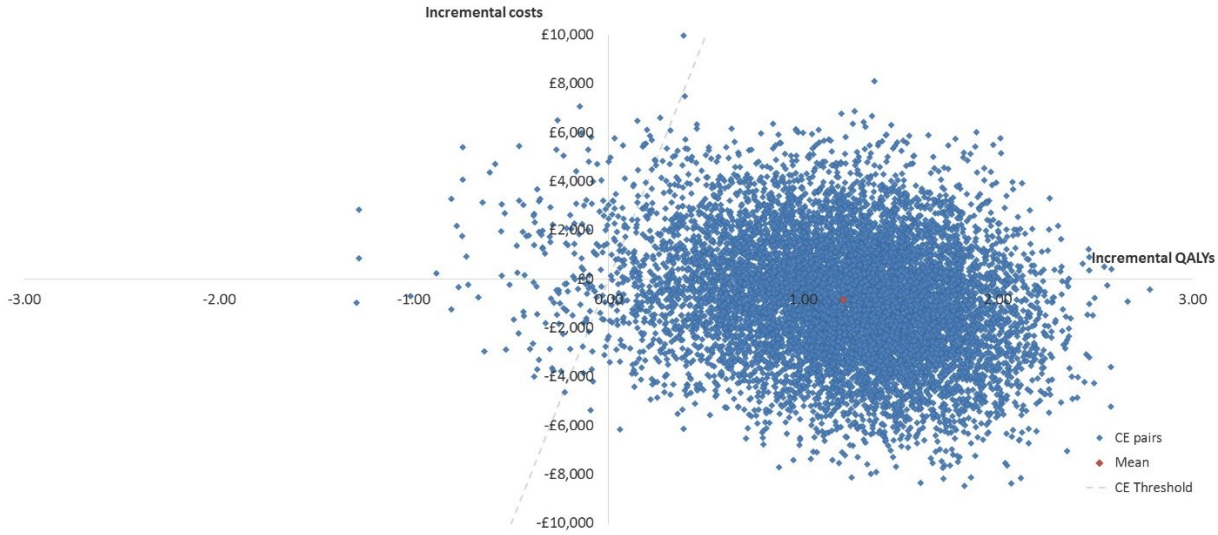
The results of 10,000 runs of the PSA are shown using ICER scatterplots and cost-effectiveness acceptability curves (CEAC). The ICER scatter plots show the incremental costs and QALYs associated with each of the 10,000 runs of the PSA along with the mean result. The CEAC graphs show the probability of each strategy being considered cost-effective at the various cost-effectiveness thresholds on the x axis.

Figure 50 shows the ICER scatterplot for the comparison between the open and laparoscopic surgical approach. It can be seen that, while the results are spread across all four domains of the scatterplot, the majority of the results reside on the East side of the graph. This indicates that in the majority of cases, the laparoscopic approach was found to be more effective. Furthermore, it can be seen that the majority of the cost effectiveness pairs reside below the cost-effectiveness threshold line (£20,000 per QALY) meaning that in the majority of cases, the laparoscopic strategy was found to be cost effective.

Figure 51 shows the CEAC for the comparison between the open and laparoscopic surgical approach. It can be seen that the likelihood of the laparoscopic approach being deemed cost-effective increases as the cost-effectiveness threshold increases. At the NICE threshold of £20,000 per QALY, the laparoscopic approach was found to have a 9% probability of being cost effective, while the open approach has a 2% probability of being cost effective.

Figure 52 shows the CEAC for the comparison between all four surgical approaches. It can be seen that the likelihood of the TaTME strategy being cost-effective increases as the cost-effectiveness threshold increases while the likelihood of all other strategies being cost-effective decrease. At the NICE threshold of £20,000 per QALY, the TaTME strategy was found to have an 86% probability of being cost effective, while the laparoscopic, open and robotic approach were found to have a 13%, 2% and 0% probability of being cost effective, respectively.

Figure 50: ICER scatterplot for the comparison between the open and laparoscopic surgical approach



CE: cost-effectiveness; QALYs: quality-adjusted live years

Figure 51: Cost-effectiveness acceptability curve (CEAC) for the comparison between the open and laparoscopic surgical approach

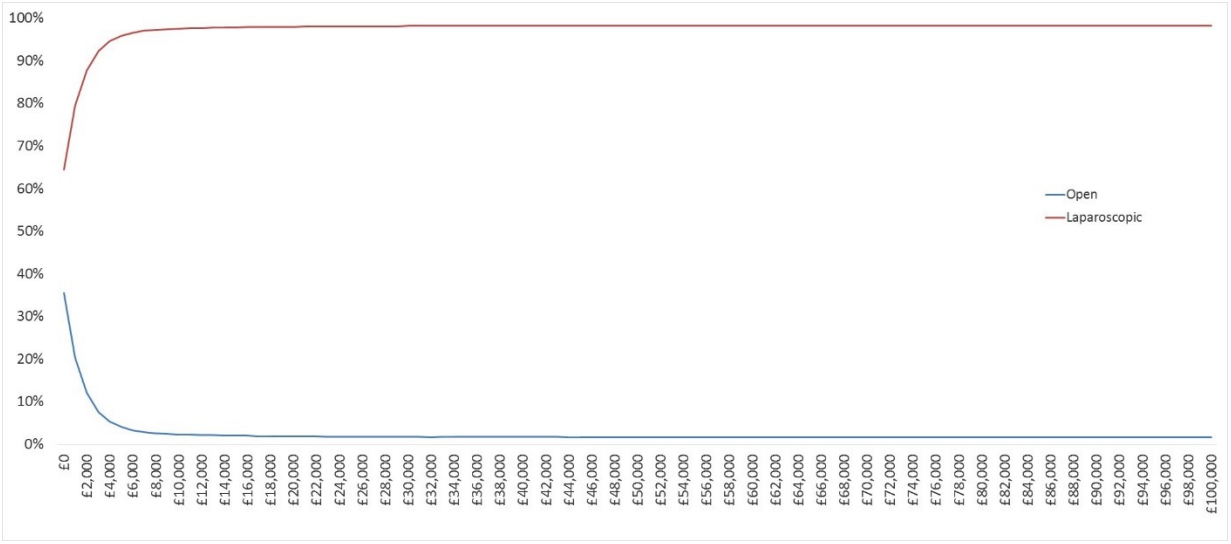
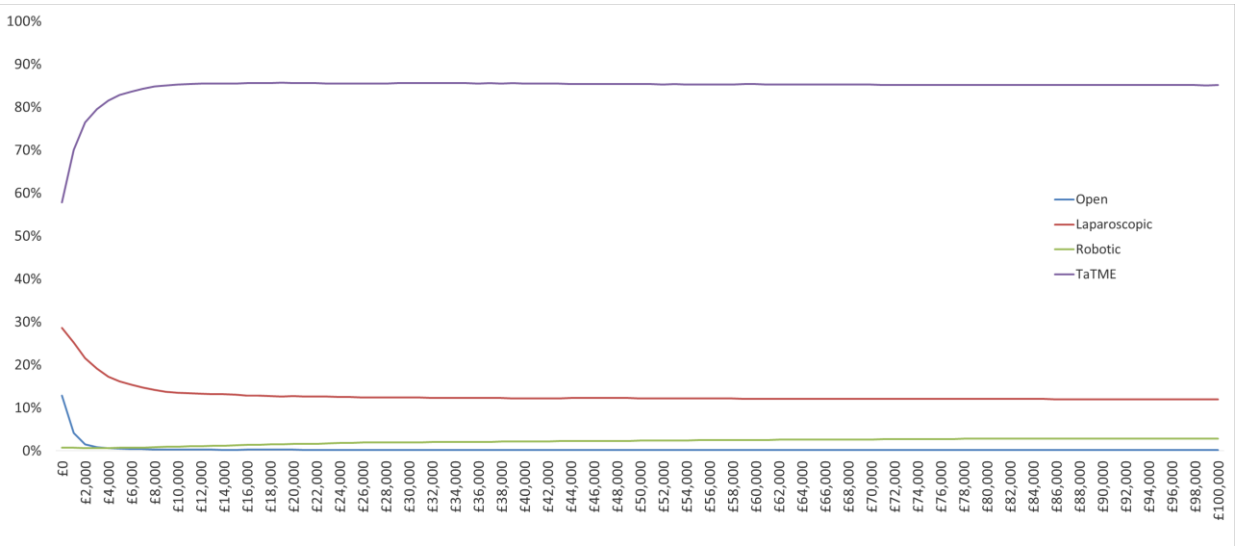


Figure 52: Cost-effectiveness acceptability curve (CEAC) for the comparison between all four surgical approaches



TaTME: transanal total mesorectal excision

Conclusions

The results of the analysis suggest that the laparoscopic approach may be cost effective for rectal cancer surgery. However, there is some uncertainty around the approach, largely driven by the uncertainty around some of the clinical effectiveness estimates especially around recurrence. A speculative analysis comparing the open, laparoscopic, robotic and TaTME approaches suggests that the TaTME may be cost-effective. However, the lack of clear data as well as the assumptions required to run this four-way comparison severely limit the conclusions that can be drawn from the analysis.

1 Appendix K – Excluded studies

2 Excluded clinical studies for review question: What is the optimal surgical 3 technique for rectal cancer?

4 **Table 20: Excluded studies and reasons for their exclusion**

Study	Reason for exclusion
Anon. Short-term surgical outcomes and patient quality of life between robotic and laparoscopic extralevator abdominoperineal excision for adenocarcinoma of the rectum	A conference abstract
Abdujapparov A, Ten Y, Korakhadjaev B. The results of neoadjuvant chemoradiation therapy in combined treatment of rectal cancer. European Journal of Cancer. 2017;72:S50.	A conference abstract
Abraha I, Aristei C, Palumbo I, Lupattelli M, Trastulli S, Cirocchi R, et al. Preoperative radiotherapy and curative surgery for the management of localised rectal carcinoma. Cochrane Database Syst Rev. 2018;10:CD002102.	Wrong comparison: (comparison potentially relevant for review C1). A systematic review and meta-analysis of RCTs comparing preoperative radiotherapy and surgery versus surgery alone.
Agha, A., Benseler, V., Hornung, M., Gerken, M., Iesalnieks, I., Furst, A., Anthuber, M., Jauch, K. W., Schlitt, H. J., Long-term oncologic outcome after laparoscopic surgery for rectal cancer, Surgical Endoscopy and Other Interventional Techniques, 28, 1119-1125, 2014	A non-randomised study comparing laparoscopic and open surgery.
Agha, A., Furst, A., Iesalnieks, I., Fichtner-Feigl, S., Ghali, N., Krenz, D., Anthuber, M., Jauch, K. W., Piso, P., Schlitt, H. J., Conversion rate in 300 laparoscopic rectal resections and its influence on morbidity and oncological outcome, International Journal of Colorectal Disease, 23, 409-417, 2008	A non-randomised study comparing laparoscopic and open surgery.
Ahmad, N. Z., Racheva, G., Elmusharaf, H., A systematic review and meta-analysis of randomized and non-randomized studies comparing laparoscopic and open abdominoperineal resection for rectal cancer, Colorectal Disease, 15, 269-277, 2013	Systematic review of laparoscopic versus open rectal surgery including both RCTs and non-RCTs and studies published pre-2000. Included RCTs checked for relevance.
Alecu, L., Stanciulea, O., Poesina, D., Tomulescu, V., Vasilescu, C., Popescu, I., Robotically performed total mesorectal excision for rectal cancer, Chirurgia (Bucuresti), 110, 137-43, 2015	No comparison group.
Ali, S., Taylor, B. M., Schlachta, C. M., Evaluation of pilot experience with robotic-assisted proctectomy and coloanal anastomosis for rectal cancer, Canadian journal of surgery, Journal canadien de chirurgie. 58, 188-192, 2015	Insufficient number of participants to get meaningful data. (Robot group included a total of 3 participants.)
Allaix, M. E., Giraudo, G., Ferrarese, A., Arezzo, A., Rebecchi, F., Morino, M., 10-Year Oncologic Outcomes After Laparoscopic or Open Total Mesorectal Excision for Rectal Cancer, World Journal of Surgery, 40, 3052-3062, 2016	A non-randomised study comparing laparoscopic and open surgery.

Alvim, Rg, Queiroz, Fld, Lacerda-Filho, A, Silva, Rg, Male sexual function after total mesorectal excision: a comparison between laparoscopic and open surgery during the learning curve period, Surgical Laparoscopy, Endoscopy & Percutaneous Techniques, 25, e51-e56, 2015	A non-randomised study comparing laparoscopic and open surgery.
Aly, E. H., Laparoscopic colorectal surgery: Summary of the current evidence, Annals of the Royal College of Surgeons of England, 91, 541-544, 2009	A non-randomised study comparing laparoscopic and open surgery.
Anderson, C, Uman, G, Pigazzi, A, Oncologic outcomes of laparoscopic surgery for rectal cancer: a systematic review and meta-analysis of the literature (Structured abstract), European Journal of Surgical Oncology, 34, 1135-1142, 2008	Systematic review of laparoscopic versus open rectal surgery including both RCTs and non-RCTs and studies published pre-2000. Included RCTs checked for relevance.
Anthuber, M., Fuerst, A., Elser, F., Berger, R., Jauch, K. W., Outcome of laparoscopic surgery for rectal cancer in 101 patients, Diseases of the Colon and Rectum, 46, 1047-1053, 2003	A non-randomised study comparing laparoscopic and open surgery.
Araujo, S. E. A., Seid, V. E., Bertoncini, A., Campos, F. G., Sousa Jr, A., Nahas, S. C., Cecconello, I., Laparoscopic total mesorectal excision for rectal cancer after neoadjuvant treatment: Targeting sphincter-preserving surgery, Hepato-Gastroenterology, 58, 1545-1554, 2011	A non-randomised study comparing laparoscopic and open surgery.
Araujo, S. E., da Silva eSousa, A. H., Jr., de Campos, F. G., Habr-Gama, A., Dumarco, R. B., Caravatto, P. P., Nahas, S. C., da Silva, J., Kiss, D. R., Gama-Rodrigues, J. J., Conventional approach x laparoscopic abdominoperineal resection for rectal cancer treatment after neoadjuvant chemoradiation: results of a prospective randomized trial, Revista do Hospital das Clinicas; Faculdade de Medicina Da Universidade de Sao Paulo, 58, 133-40, 2003	Population not relevant (more than half of the population with early rectal cancer).
Arezzo, A., Passera, R., Salvai, A., Arolfo, S., Allaix, M. E., Schwarzer, G., Morino, M., Laparoscopy for rectal cancer is oncologically adequate: A systematic review and meta-analysis of the literature, Surgical Endoscopy and Other Interventional Techniques, 29, 334-348, 2015	Systematic review of laparoscopic versus open rectal surgery, includes non-RCTs. Included RCTs checked for relevance.
Aziz, O., Constantinides, V., Tekkis, P. P., Athanasiou, T., Purkayastha, S., Paraskeva, P., Darzi, A. W., Heriot, A. G., Laparoscopic versus open surgery for rectal cancer: A meta-analysis, Annals of Surgical Oncology, 13, 413-424, 2006	Systematic review of laparoscopic versus open rectal surgery including both RCTs and non-RCTs and studies published pre-2000. Included RCTs checked for relevance.
Baek, J. H., Pastor, C., Pigazzi, A., Robotic and laparoscopic total mesorectal excision for rectal cancer: A case-matched study, Surgical Endoscopy and Other Interventional Techniques, 25, 521-525, 2011	Population not according to protocol :almost half of the participants with TNM stage 0 or I cancer.
Baek, S. J., Al-Asari, S., Jeong, D. H., Hur, H., Min, B. S., Baik, S. H., Kim, N. K., Robotic versus laparoscopic coloanal anastomosis with	Non-randomised study comparing robotic versus laparoscopic surgery. RCT evidence is available for critical outcomes, apart from overall survival, therefore, data from non-randomised studies will

or without intersphincteric resection for rectal cancer, Surgical Endoscopy, 27, 4157-63, 2013	only be considered for overall survival. This study does not report overall survival.
Baek, S. J., Kim, S. H., Cho, J. S., Shin, J. W., Kim, J., Robotic versus conventional laparoscopic surgery for rectal cancer: a cost analysis from a single institute in Korea, World Journal of Surgery, 36, 2722-9, 2012	A non-randomised study comparing robotic versus laparoscopic surgery but no critical outcomes of interest reported.
Baik, S. H., Kwon, H. Y., Kim, J. S., Hur, H., Sohn, S. K., Cho, C. H., Kim, H., Robotic versus laparoscopic low anterior resection of rectal cancer: Short-term outcome of a prospective comparative study, Annals of Surgical Oncology, 16, 1480-1487, 2009	Non-randomised study comparing robotic versus laparoscopic surgery. RCT evidence is available for critical outcomes, apart from overall survival, therefore, data from non-randomised studies will only be considered for overall survival. This study does not report overall survival.
Baik, Sh, Gincherman, M, Mutch, Mg, Birnbaum, Eh, Fleshman, Jw, Laparoscopic vs open resection for patients with rectal cancer: comparison of perioperative outcomes and long-term survival, Diseases of the Colon and Rectum, 54, 6-14, 2011	A non-randomised study comparing laparoscopic and open surgery.
Baker, R. P., White, E. E., Titu, L., Duthie, G. S., Lee, P. W. R., Monson, J. R. T., Does laparoscopic abdominoperineal resection of the rectum compromise long-term survival?, Diseases of the Colon and Rectum, 45, 1481-1485, 2002	A non-randomised study comparing laparoscopic and open surgery.
Barendse RM, Musters GD, de Graaf EJR, van den Broek FJC, Consten ECJ, Doornebosch PG, et al. Randomised controlled trial of transanal endoscopic microsurgery versus endoscopic mucosal resection for large rectal adenomas (TREND Study). Gut. 2018;67(5):837-46.	A systematic review of RCTs and non-RCTs; included RCTs checked
Bianchi, P. P., Ceriani, C., Locatelli, A., Spinoglio, G., Zampino, M. G., Sonzogni, A., Crosta, C., Andreoni, B., Robotic versus laparoscopic total mesorectal excision for rectal cancer: a comparative analysis of oncological safety and short-term outcomes, Surg Endosc, 24, 2888-94, 2010	Non-randomised study comparing robotic versus laparoscopic surgery. RCT evidence is available for critical outcomes, apart from overall survival, therefore, data from non-randomised studies will only be considered for overall survival. This study does not report overall survival.
Boller, A. M., Nelson, H., Colon and rectal cancer: Laparoscopic or open?, Clinical Cancer Research, 13, 6894S-6896S, 2007	A non-randomised study comparing laparoscopic and open surgery.
Boutros, M., Hippalgaonkar, N., Silva, E., Allende, D., Wexner, S. D., Berho, M., Laparoscopic resection of rectal cancer results in higher lymph node yield and better short-term outcomes than open surgery: A large single-center comparative study, Diseases of the Colon and Rectum, 56, 679-688, 2013	A non-randomised study comparing laparoscopic and open surgery.
Breukink, S., Pierie, J., Wiggers, T., Laparoscopic versus open total mesorectal excision for rectal cancer, Cochrane Database of Systematic Reviews, (4) (no pagination), 2006	A non-randomised study comparing laparoscopic and open surgery.
Capussotti, L., Massucco, P., Muratore, A., Amisano, M., Bima, C., Zorzi, D., Laparoscopy as a prognostic factor in curative resection for node positive colorectal cancer: results for a	A non-randomised study comparing laparoscopic and open surgery.

single-institution nonrandomized prospective trial, Surgical Endoscopy, 18, 1130-5, 2004	
Chen K, Xie G, Zhang Q, Shen Y, Zhou T. Comparison of short-course with long-course preoperative neoadjuvant therapy for rectal cancer: A meta-analysis. J Cancer Res Ther. 2018;14(Supplement):S224-S31.	Wrong comparison: (comparison relevant for review question): Systematic review and meta-analysis of studies comparing preoperative CRT with or without additional CT.
Chen, C. C., Lai, Y. L., Jiang, J. K., Chu, C. H., Huang, I. P., Chen, W. S., Cheng, A. Y. M., Yang, S. H., Transanal Total Mesorectal Excision Versus Laparoscopic Surgery for Rectal Cancer Receiving Neoadjuvant Chemoradiation: A Matched Case-Control Study, Annals of Surgical Oncology, 23, 1169-1176, 2016	Non-randomised study comparing TaTME to laparoscopic surgery. Evidence on critical outcomes already available from a RCT.
Chen, H., Zhao, L., An, S., Wu, J., Zou, Z., Liu, H., Li, G., Laparoscopic Versus Open Surgery Following Neoadjuvant Chemoradiotherapy for Rectal Cancer: A Systematic Review and Meta-analysis, Journal of Gastrointestinal Surgery, 18, 617-626, 2014	Systematic review of laparoscopic versus open rectal surgery including both RCTs and non-RCTs. Included RCTs checked for relevance.
Chen, K., Cao, G., Chen, B., Wang, M., Xu, X., Cai, W., Xu, Y., Xiong, M., Laparoscopic versus open surgery for rectal cancer: A meta-analysis of classic randomized controlled trials and high-quality Nonrandomized Studies in the last 5 years, International Journal of Surgery, 39, 1-10, 2017	Systematic review of laparoscopic versus open rectal surgery including both RCTs and non-RCTs. Included RCTs checked for relevance.
Chen, W., Li, Q., Qiu, P., Jiang, L., Fu, Z., Fan, Y., Li, D., Liu, P., Tang, L., Comparison of perioperative outcomes between laparoscopic and open surgery for mid-low rectal cancer with total mesorectal excision following neoadjuvant chemoradiotherapy, Journal of Cancer Research and Therapeutics, 12, C199-C204, 2016	A non-randomised study comparing laparoscopic and open surgery.
Chen, Y., Guo, R., Xie, J., Liu, Z., Shi, P., Ming, Q., Laparoscopy combined with transanal endoscopic microsurgery for rectal cancer: A prospective, single-blinded, randomized clinical trial, Surgical Laparoscopy, Endoscopy and Percutaneous Techniques, 25, 399-402, 2015	Population not relevant. More than hald of the participants with early rectal cancer (Duke's A).
Chi, P., Huang, S. H., Lin, H. M., Lu, X. R., Huang, Y., Jiang, W. Z., Xu, Z. B., Chen, Z. F., Sun, Y. W., Ye, D. X., Laparoscopic Transabdominal Approach Partial Intersphincteric Resection for Low Rectal Cancer: Surgical Feasibility and Intermediate-Term Outcome, Annals of Surgical Oncology, 22, 944-951, 2015	A non-randomised study comparing laparoscopic and open surgery.
Chiu, H. H., Chen, J. B., Wang, H. M., Tsai, C. Y., Laparoscopic abdominoperineal resection for low rectal cancer, Formosan Journal of Surgery, 35, 23-27, 2002	A non-randomised study comparing laparoscopic and open surgery.
Cho, M. S., Baek, S. J., Hur, H., Min, B. S., Baik, S. H., Lee, K. Y., Kim, N. K., Short and long-term outcomes of robotic versus laparoscopic total mesorectal excision for rectal cancer: a case-matched retrospective study, Medicine, 94, e522, 2015	Population not according to the protocol: >40% of the population with TNM stage 0 or I cancer.

Cleary RK, Morris AM, Chang GJ, Halverson AL. Controversies in Surgical Oncology: Does the Minimally Invasive Approach for Rectal Cancer Provide Equivalent Oncologic Outcomes Compared with the Open Approach? Ann Surg Oncol. 2018;25(12):3587-95.	Systematic review of RCTs. All included studies are either included in our review or are too old for inclusion in our review.
Collinson, F. J., Jayne, D. G., Pigazzi, A., Tsang, C., Barrie, J. M., Edlin, R., Garbett, C., Guillou, P., Holloway, I., Howard, H., Marshall, H., McCabe, C., Pavitt, S., Quirke, P., Rivers, C. S., Brown, J. M., An international, multicentre, prospective, randomised, controlled, unblinded, parallel-group trial of robotic-assisted versus standard laparoscopic surgery for the curative treatment of rectal cancer, International Journal of Colorectal Disease, 27, 233-41, 2012	The summary of the ROLARR trial protocol. No results presented.
Cui, Z. L., Sun, X., Song, X. L., Zhang, Y. D. Feasibility study of neoadjuvant XELOX for local advanced lower rectal cancer. Chinese journal of cancer prevention and treatment. 2017; 1091-1093.	Wrong comparison; study does not compare surgical techniques
Da Luz Moreira, A., Mor, I., Geisler, D. P., Remzi, F. H., Kiran, R. P., Laparoscopic resection for rectal cancer: A case-matched study, Surgical Endoscopy and Other Interventional Techniques, 25, 278-283, 2011	A non-randomised study comparing laparoscopic and open surgery.
D'Ambrosio G, Picchetto A, Campo S, Palma R, Panetta C, De Laurentis F, et al. Quality of life in patients with loco-regional rectal cancer after ELRR by TEM versus VLS TME after nChRT: long-term results. Surg Endosc. 2019;33(3):941-8.	Wrong comparison: (comparison relevant for review question what is the most effective treatment for early rectal cancer?)
D'Annibale, A., Morpurgo, E., Fiscon, V., Trevisan, P., Sovernigo, G., Orsini, C., Guidolin, D., Robotic and laparoscopic surgery for treatment of colorectal diseases, Dis Colon Rectum, 47, 2162-8, 2004	Population includes people with both colonic and rectal tumours as well as benign and malignant tumours and results are not stratified.
D'Annibale, A., Pernazza, G., Monsellato, I., Pende, V., Lucandri, G., Mazzocchi, P., Alfano, G., Total mesorectal excision: A comparison of oncological and functional outcomes between robotic and laparoscopic surgery for rectal cancer, Surgical Endoscopy and Other Interventional Techniques, 27, 1887-1895, 2013	Not clear if population is according to the protocol: >50% T0-2 and 70% N0 most assumed to be outside the population of interest.
Dat, Anthony D, Poon, Flora, Robotic surgery for rectal cancer, Cochrane Database of Systematic Reviews, 2011	A protocol for a Cochrane systematic review. No full text has been published.
Day, W., Lau, P. Y. Y., Li, K. M., Kwok, S. Y., Yip, A. W. C., Clinical outcome of open and laparoscopic surgery in Dukes'B and C rectal cancer: Experience from a regional hospital in Hong Kong, Hong Kong Medical Journal, 17, 26-32, 2011	A non-randomised study comparing laparoscopic and open surgery.
de'Angelis, N., Portigliotti, L., Azoulay, D., Brunetti, F., Transanal total mesorectal excision for rectal cancer: a single center experience and systematic review of the literature, Langenbeck's Archives of Surgery, 400, 945-959, 2015	Non-randomised study comparing TaTME to laparoscopic surgery. Evidence on critical outcomes already available from a RCT.

Deijen, C. L., Velthuis, S., Tsai, A., Mavroveli, S., de Lange-de Klerk, E. S., Sietses, C., Tuynman, J. B., Lacy, A. M., Hanna, G. B., Bonjer, H. J., COLOR III: a multicentre randomised clinical trial comparing transanal TME versus laparoscopic TME for mid and low rectal cancer, Surgical Endoscopy, 30, 3210-5, 2016	A protocol of the COLOR III trial. This trial is still recruiting and no results have been published yet.
Delaney,C.P., Lynch,A.C., Senagore,A.J., Fazio,V.W., Comparison of robotically performed and traditional laparoscopic colorectal surgery, Diseases of the Colon and Rectum, 46, 1633-1639, 2003	A case-series of 6 robotic surgeries and 6 laparoscopic surgeries of both colon and rectum tumours.
Denost, Q., Adam, J. P., Rullier, A., Buscail, E., Laurent, C., Rullier, E., Perineal transanal approach: A new standard for laparoscopic sphincter-saving resection in low rectal cancer, a randomized trial, Annals of Surgery, 260, 993-999, 2014	The Bordeaux' trial is included in the review, however, this publication does not report any additional outcomes.
Denost Q, Loughlin P, Chevalier R et al. (2017) Transanal versus abdominal low rectal dissection for rectal cancer: long-term results of the Bordeaux' randomized trial. Surgical Endoscopy and Other Interventional Techniques 1-9	This publication is a duplicate of the included trial: Denost et al., 2018. This publication record the EPub record..
Denoya, P., Wang, H., Sands, D., Nogueras, J., Weiss, E., Wexner, S. D., Short-term outcomes of laparoscopic total mesorectal excision following neoadjuvant chemoradiotherapy, Surgical Endoscopy and Other Interventional Techniques, 24, 933-938, 2010	A non-randomised study comparing laparoscopic and open surgery.
DeSouza, A. L., Prasad, L. M., Ricci, J., Park, J. J., Marecik, S. J., Zimmern, A., Blumetti, J., Abcarian, H., A comparison of open and robotic total mesorectal excision for rectal adenocarcinoma, Diseases of the Colon and Rectum, 54, 275-282, 2011	Non-randomised study comparing robotic versus laparoscopic surgery. RCT evidence is available for critical outcomes, apart from overall survival, therefore, data from non-randomised studies will only be considered for overall survival. This study does not report overall survival.
Ding, K. F., Chen, R., Zhang, J. L., Li, J., Xu, Y. Q., Lv, L., Wang, X. C., Sun, L. F., Wang, J. W., Zheng, S., Zhang, S. Z., Laparoscopic surgery for the curative treatment of rectal cancer: Results of a Chinese three-center case-control study, Surgical Endoscopy and Other Interventional Techniques, 23, 854-861, 2009	A non-randomised study comparing laparoscopic and open surgery.
Draeger T, Volkel V, Gerken M, Klinkhammer-Schalke M, Furst A. Long-term oncologic outcomes after laparoscopic versus open rectal cancer resection: a high-quality population-based analysis in a Southern German district. Surg Endosc. 2018;32(10):4096-104.	A non-randomised study comparing laparoscopic and open surgery.
Dural, A. C., Keskin, M., Balik, E., Akici, M., Kunduz, E., Yamaner, S., Asoglu, O., Gulluoglu, M., Bugra, D., The role of the laparoscopy on circumferential resection margin positivity in patients with rectal cancer: Long-term outcomes at a single high-volume institution, Surgical Laparoscopy, Endoscopy and Percutaneous Techniques, 25, 129-137, 2015	A non-randomised study comparing laparoscopic and open surgery.

Ellis-Clark, J. M., Lumley, J. W., Stevenson, A. R. L., Stitz, R. W., Laparoscopic restorative proctectomy - hybrid approach or totally laparoscopic?, ANZ journal of surgery, 80, 807-812, 2010	A non-randomised study comparing laparoscopic and open surgery.
Feliciotti, F., Guerrieri, M., Paganini, A. M., De Sanctis, A., Campagnacci, R., Perretta, S., D'Ambrosio, G., Lezoche, G., Lezoche, E., Long-term results of laparoscopic vs open resections for rectal cancer for 124 unselected patients, Surgical Endoscopy and Other Interventional Techniques, 17, 1530-1535, 2003	A non-randomised study comparing laparoscopic and open surgery.
Feng B, Lu J, Zhang S, Yan X, Li J, Xue P, et al. Laparoscopic abdominoperineal excision with trans-abdominal individualized levator transection: interim analysis of a randomized controlled trial. Colorectal Dis. 2017;19(7):O246-O52.	Wrong comparison (compares laparoscopic APE vs trans-abdominal individualised levator transection)
Feroci, F., Vannucchi, A., Bianchi, P. P., Cantafio, S., Garzi, A., Formisano, G., Scatizzi, M., Total mesorectal excision for mid and low rectal cancer: Laparoscopic vs robotic surgery, World Journal of Gastroenterology, 22, 3602-3610, 2016	Population not according to protocol: >40% with stage I cancer.
Formisano, G., Marano, A., Bianchi, P. P., Spinoglio, G., Challenges with robotic low anterior resection, Minerva chirurgica, 70, 341-354, 2015	A review of literature on robotic rectal surgery. No additional data/references.
Franks, P. J., Bosanquet, N., Thorpe, H., Brown, J. M., Copeland, J., Smith, A. M., Quirke, P., Guillou, P. J., Clasicc trial participants, Short-term costs of conventional vs laparoscopic assisted surgery in patients with colorectal cancer (MRC CLASICC trial), Br J Cancer, 95, 6-12, 2006	Population is people with colorectal cancer, results are not stratified by colon/rectum.
Fujii, S, Inomata, M, Akagi, T, Katayama, H, Mizusawa, J, Saito, S, Saida, Y, Munakata, Y, Sato, T, Bandou, H, Sekimoto, M, Yamamoto, H, Shimada, Y, Kitano, S, Transitional impact of short and long-term outcomes of a randomized controlled trial to evaluate laparoscopic versus open surgery for colorectal cancer from Japan clinical oncology group study JCOG0404, European journal of cancer., 51, S139, 2015	A conference abstract. This trial is on colon cancer.
Fujimoto, Y., Akiyoshi, T., Kuroyanagi, H., Konishi, T., Ueno, M., Oya, M., Yamaguchi, T., Safety and feasibility of laparoscopic intersphincteric resection for very low rectal cancer, Journal of Gastrointestinal Surgery, 14, 645-650, 2010	A non-randomised study comparing laparoscopic and open surgery.
Ge, L, Wang, Hj, Zhao, Zl, Yang, Xh, Zhao, Wm, Hati, P, Liu, L, Evaluation of short-term efficacy and safety after laparoscopic resection for mid-low rectal cancer, Zhonghua yi xue za zhi, 92, 98-101, 2012	A non-randomised study comparing laparoscopic and open surgery.
Gezen, C., Altuntas, Y. E., Kement, M., Aksakal, N., Okkabaz, N., Vural, S., Oncel, M., Laparoscopic and conventional resections for low rectal cancers: A retrospective analysis on	A non-randomised study comparing laparoscopic and open surgery.

perioperative outcomes, sphincter preservation, and oncological results, Journal of Laparoendoscopic and Advanced Surgical Techniques, 22, 625-630, 2012	
Gezen, C., Altuntas, Y. E., Kement, M., Vural, S., Civil, O., Okkabaz, N., Aksakal, N., Oncel, M., Complete versus partial mobilization of splenic flexure during laparoscopic low anterior resection for rectal tumors: a comparative study, Journal of Laparoendoscopic & Advanced Surgical Techniques. Part A, 22, 392-6, 2012	A non-randomised study comparing laparoscopic and open surgery.
Ghezzi, T. L., Luca, F., Valvo, M., Corleta, O. C., Zuccaro, M., Cenciarelli, S., Biffi, R., Robotic versus open total mesorectal excision for rectal cancer: Comparative study of short and long-term outcomes, European Journal of Surgical Oncology, 40, 1072-1079, 2014	Population not according to protocol: >40% with stage 0 or I cancer.
Gijn, W, Marijnen, Ca, Nagtegaal, Id, Kranenbarg, Em, Putter, H, Wiggers, T, Rutten, Hj, Påhlman, L, Glimelius, B, Velde, Cj, Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer: 12-year follow-up of the multicentre, randomised controlled TME trial, The lancet. Oncology, 12, 575-582, 2011	A non-randomised study comparing laparoscopic and open surgery.
Gleeson, F. C., Clain, J. E., Rajan, E., Topazian, M., Wang, K. K., Levy, M. J., Surveillance EUS FNA following transanal excision of primary rectal cancer facilitates early detection of local recurrence, Gastrointestinal Endoscopy, 1), AB170, 2011	A non-randomised study comparing laparoscopic and open surgery.
Gong, J., Shi, D. B., Li, X. X., Cai, S. J., Guan, Z. Q., Xu, Y., Short-term outcomes of laparoscopic total mesorectal excision compared to open surgery, World Journal of Gastroenterology, 18, 7308-7313, 2012	Population not according to protocol: people with cT3-4 and cTxN tumours were excluded.
Gonzalez, Q. H., Rodriguez-Zentner, H. A., Moreno-Berber, J. M., Vergara-Fernandez, O., de Leon, H. T. C., Lopez, R. F., Jonguitud, L. A., Ramos, R., Castaneda-Argaiz, R., Laparoscopic vs. open total mesorectal excision for treatment of rectal cancer, Revista de Investigacion Clinica, 60, 205-211, 2008	A non-randomised study comparing laparoscopic and open surgery.
Gonzalez, Q. H., Rodriguez-Zentner, H. A., Moreno-Berber, J. M., Vergara-Fernandez, O., Tapia-Cid de Leon, H., Jonguitud, L. A., Ramos, R., Moreno-Lopez, J. A., Laparoscopic versus open total mesorectal excision: a nonrandomized comparative prospective trial in a tertiary center in Mexico City, American Surgeon, 75, 33-8, 2009	A non-randomised study comparing laparoscopic and open surgery.
Gouvas, N., Tsiaoussis, J., Pechlivanides, G., Zervakis, N., Tzortzinis, A., Avgerinos, C., Dervenis, C., Xynos, E., Laparoscopic or open surgery for the cancer of the middle and lower rectum short-term outcomes of a comparative non-randomised study, International Journal of Colorectal Disease, 24, 761-769, 2009	A non-randomised study comparing laparoscopic and open surgery.

Gresham, G., Cheung, W. Y., Speers, C., Woods, R., Kennecke, H., Time to adjuvant chemotherapy and survival outcomes among patients with stage 2 to 3 rectal cancer treated with preoperative chemoradiation, Clinical Colorectal Cancer, 14, 41-5, 2015	A non-randomised study comparing laparoscopic and open surgery.
Guillerme, F., Kurtz, J. E., Clavier, J. B., Schumacher, C., Brigand, C., Noel, G., A retrospective outcome study in the elder patient with locally advanced rectal cancer treated with hypofractionated or conventional preoperative radiotherapy, Journal of Solid Tumors, 3, 25-34, 2013	A non-randomised study comparing laparoscopic and open surgery.
Gunka, I., Dostalik, J., Martinek, L., Gunkova, P., Mazur, M., Vavra, P., Long-term results of laparoscopic versus open surgery for nonmetastatic colorectal cancer, Acta chirurgica Belgica, 112, 139-147, 2012	A non-randomised study comparing laparoscopic and open surgery.
Haddock, M. G., Gunderson, L. L., Nelson, H., Cha, S. S., Devine, R. M., Dozois, R. R., Wolff, B. G., Intraoperative irradiation for locally recurrent colorectal cancer in previously irradiated patients, International journal of radiation oncology, biology, physics, 49, 1267-74, 2001	A non-randomised study comparing laparoscopic and open surgery.
Hall, N. R., Finan, P. J., al-Jaberi, T., Tsang, C. S., Brown, S. R., Dixon, M. F., Quirke, P., Circumferential margin involvement after mesorectal excision of rectal cancer with curative intent. Predictor of survival but not local recurrence?, Diseases of the Colon & Rectum, 41, 979-83, 1998	A non-randomised study comparing laparoscopic and open surgery.
Hamel, C. T., Metzger, J., Curti, G., Degen, L., Harder, F., von Flue, M. O., Ileocecal reservoir reconstruction after total mesorectal excision: functional results of the long-term follow-up, International Journal of Colorectal Disease, 19, 574-9, 2004	A non-randomised study comparing laparoscopic and open surgery.
Han, K. S., Sohn, D. K., Kim, D. Y., Kim, B. C., Hong, C. W., Chang, H. J., Kim, S. Y., Baek, J. Y., Park, S. C., Kim, M. J., Oh, J. H., Endoscopic criteria for evaluating tumor stage after preoperative chemoradiation therapy in locally advanced rectal cancer, Cancer Research and Treatment, 48, 567-573, 2016	A non-randomised study comparing laparoscopic and open surgery.
Han, S. L., Zeng, Q. Q., Shen, X., Zheng, X. F., Guo, S. C., Yan, J. Y., The indication and surgical results of local excision following radiotherapy for low rectal cancer, Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland, 12, 1094-1098, 2010	A non-randomised study comparing laparoscopic and open surgery.
Hartley, J. E., Mehigan, B. J., Qureshi, A. E., Duthie, G. S., Lee, P. W., Monson, J. R., Total mesorectal excision: assessment of the laparoscopic approach, Diseases of the Colon & Rectum, 44, 315-21, 2001	A non-randomised study comparing laparoscopic and open surgery.
Hida K, Okamura R, Sakai Y, Konishi T, Akagi T, Yamaguchi T, et al. Open versus	A non-randomised study comparing laparoscopic and open surgery.

Laparoscopic Surgery for Advanced Low Rectal Cancer: A Large, Multicenter, Propensity Score Matched Cohort Study in Japan. Annals of surgery. 2018;268(2):318-24.	
Hida, K., Okamura, R., Sakai, Y., Konishi, T., Akagi, T., Yamaguchi, T., Akiyoshi, T., Fukuda, M., Yamamoto, S., Yamamoto, M., Nishigori, T., Kawada, K., Hasegawa, S., Morita, S., Watanabe, M., Open versus Laparoscopic Surgery for Advanced Low Rectal Cancer: A Large, Multicenter, Propensity Score Matched Cohort Study in Japan, Annals of Surgery., 16, 2017	A non-randomised study comparing laparoscopic and open surgery.
Holmer C, Kreis ME. Systematic review of robotic low anterior resection for rectal cancer. Surg Endosc. 2018;32(2):569-81.	A systematic review of studies evaluating robotic surgery (included studies checked and accounted for)
Hong, D, Tabet, J, Anvari, M, Laparoscopic vs. open resection for colorectal adenocarcinoma, Diseases of the Colon and Rectum, 44, 10-8; discussion 18-9, 2001	A non-randomised study comparing laparoscopic and open surgery.
Hu, J. J., Liang, J. W., Wang, Z., Zhang, X. M., Zhou, H. T., Hou, H. R., Zhou, Z. X., Short-term outcomes of laparoscopically assisted surgery for rectal cancer following neoadjuvant chemoradiotherapy: A single-center experience, Journal of Surgical Research, 187, 438-444, 2014	A non-randomised study comparing laparoscopic and open surgery.
Huang, Mj, Liang, Jl, Wang, H, Kang, L, Deng, Yh, Wang, Jp, Laparoscopic-assisted versus open surgery for rectal cancer: a meta-analysis of randomized controlled trials on oncologic adequacy of resection and long-term oncologic outcomes (Structured abstract), International Journal of Colorectal DiseaseInt J Colorectal Dis, 26, 415-421, 2011	Systematic review of laparoscopic versus open rectal surgery, not all studies are relevant to our review according to PICO in protocol.
Huang, Y. M., Huang, Y. J., Wei, P. L., Outcomes of robotic versus laparoscopic surgery for mid and low rectal cancer after neoadjuvant chemoradiation therapy and the effect of learning curve, Medicine (United States), 96 (40) (no pagination), 2017	Non-randomised study comparing robotic versus laparoscopic surgery. RCT evidence is available for critical outcomes, apart from overall survival, therefore, data from non-randomised studies will only be considered for overall survival. This study does not report overall survival.
Ishihara, S., Watanabe, T., Fukushima, Y., Akahane, T., Horiuchi, A., Shimada, R., Nakamura, K., Hayama, T., Yamada, H., Nozawa, K., Matsuda, K., Hashiguchi, Y., Safety and factors contributing to the difficulty of laparoscopic surgery for rectal cancer treated with preoperative chemoradiotherapy, Techniques in Coloproctology, 18, 247-55, 2014	A non-randomised study comparing laparoscopic and open surgery.
Jackson, T D, Kaplan, G G, Arena, G, Page, J H, Rogers, S O, Laparoscopic versus open resection for colorectal cancer: a metaanalysis of oncologic outcomes (Structured abstract), Journal of the American College of Surgeons, 204, 439-446, 2007	Systematic review of laparoscopic versus open colorectal surgery, includes both colon and rectal cancers, included RCTs checked for relevance.
Jayne, D. G., Guillou, P. J., Thorpe, H., Quirke, P., Copeland, J., Smith, A. M. H., Heath, R. M., Brown, J. M., Randomized trial of laparoscopic-assisted resection of colorectal carcinoma: 3-	This trial (CLASICC) is included in this review, however, this paper does not report any additional outcomes.

Year results of the UK MRC CLASICC trial group, Journal of Clinical Oncology, 25, 3061-3068, 2007	
Jefferies, M. T., Evans, M. D., Hilton, J., Chandrasekaran, T. V., Beynon, J., Khot, U., Oncological outcome after laparoscopic abdominoperineal excision of the rectum, Colorectal Disease, 14, 967-971, 2012	A non-randomised study comparing laparoscopic and open surgery.
Jeong, W. K., Park, J. W., Choi, H. S., Jeong, S. Y., Oh, J. H., Comparison of peristomal adhesion formation between laparoscopic and open low anterior resection of rectal cancer, World Journal of Surgery, 37, 2683-2687, 2013	A non-randomised study comparing laparoscopic and open surgery.
Jiang, J. B., Jiang, K., Wang, J. J., Dai, Y., Xie, F. B., Li, X. M., Short-term and Long-term Outcomes Regarding Laparoscopic Versus Open Surgery for Low Rectal Cancer: A Systematic Review and Meta-Analysis, Surgical Laparoscopy, Endoscopy & Percutaneous Techniques, 25, 286-96, 2015	Systematic review of laparoscopic versus open rectal surgery including both RCTs and non-RCTs. Included RCTs checked for relevance.
Jimenez Rodriguez, R. M., Diaz Pavon, J. M., de La Portilla de Juan, F., Prendes Sillero, E., Hisnard Cadet Dussort, J. M., Padillo, J., [Prospective randomised study: robotic-assisted versus conventional laparoscopic surgery in colorectal cancer resection], Cir Esp, 89, 432-8, 2011	Full text in Spanish.
Jimenez-Rodriguez, R., Quezada, F., Lynn, P., Strombon, P., Paty, P. S., Martin, W. R., Garcia Aguilar, J. Similar short-term oncolgical outcomes for robotic and open total mesorectal excision in patients with rectal cancer. 2018 American Society of Colon and Rectal Surgeons Annual Meeting, ASCRS 2018. United States	A conference abstract
Jones K, Qassem MG, Sains P, Baig MK, Sajid MS. Robotic total meso-rectal excision for rectal cancer: A systematic review following the publication of the ROLARR trial. World J Gastrointest Oncol. 2018;10(11):449-64.	Systematic review evaluating the effectiveness of robotic TME. Included studies checked for relevance.
Kang, J., Yoon, K. J., Min, B. S., Hur, H., Baik, S. H., Kim, N. K., Lee, K. Y., The impact of robotic surgery for mid and low rectal cancer: a case-matched analysis of a 3-arm comparison--open, laparoscopic, and robotic surgery, Annals of Surgery, 257, 95-101, 2013	Population not according to protocol, the exact proportion are unclear but T3-4 or TxN appear to be less than half of the population.
Katsuno, H., Shiomi, A., Ito, M., Koide, Y., Maeda, K., Yatsuoka, T., Hase, K., Komori, K., Minami, K., Sakamoto, K., Saida, Y., Saito, N., Comparison of symptomatic anastomotic leakage following laparoscopic and open low anterior resection for rectal cancer: a propensity score matching analysis of 1014 consecutive patients, Surgical Endoscopy and Other Interventional Techniques, 30, 2848-2856, 2016	A non-randomised study comparing laparoscopic and open surgery.
Keller, D. S., Champagne, B. J., Reynolds, H. L., Stein, S. L., Delaney, C. P., Cost-effectiveness of laparoscopy in rectal cancer, Diseases of the Colon and Rectum, 57, 564-569, 2014	A non-randomised study comparing laparoscopic and open surgery.

Keller, D. S., Khorgami, Z., Swendseid, B., Champagne, B. J., Reynolds, H. L., Jr., Stein, S. L., Delaney, C. P., Laparoscopic and converted approaches to rectal cancer resection have superior long-term outcomes: a comparative study by operative approach, Surgical Endoscopy, 28, 1940-8, 2014	A non-randomised study comparing laparoscopic and open surgery.
Keller, D. S., Park, K. J., Augestad, K. M., Delaney, C. P., Integration of open and laparoscopic approaches for rectal cancer resection: Oncologic and short-term outcomes, Surgical Endoscopy and Other Interventional Techniques, 28, 2129-2136, 2014	A non-randomised study comparing laparoscopic and open surgery.
Kellokumpu, I. H., Kairaluoma, M. I., Nuorva, K. P., Kautiainen, H. J., Jantunen, I. T., Short - and long-term outcome following laparoscopic versus open resection for carcinoma of the rectum in the multimodal setting, Diseases of the Colon and Rectum, 55, 854-863, 2012	A non-randomised study comparing laparoscopic and open surgery.
Keskin, M., Akici, M., Agcaoglu, O., Yegen, G., Saglam, E., Bugra, D., Bulut, M. T., Balik, E., Open Versus Laparoscopic Surgery for Rectal Cancer: Single-Center Results of 587 Cases, Surgical Laparoscopy, Endoscopy and Percutaneous Techniques, 26, e62-e68, 2016	A non-randomised study comparing laparoscopic and open surgery.
Khaikin, M., Bashankaev, B., Person, B., Cera, S., Sands, D., Weiss, E., Nogueras, J., Vernava, Iii A., Wexner, S. D., Laparoscopic versus open proctectomy for rectal cancer: Patients' outcome and oncologic adequacy, Surgical Laparoscopy, Endoscopy and Percutaneous Techniques, 19, 118-122, 2009	A non-randomised study comparing laparoscopic and open surgery.
Kim HJ, Choi GS, Park JS, Park SY, Yang CS, Lee HJ. The impact of robotic surgery on quality of life, urinary and sexual function following total mesorectal excision for rectal cancer: a propensity score-matched analysis with laparoscopic surgery. Colorectal Dis. 2018;20(5):O103-O13.	A non-randomised study comparing laparoscopic and robotic surgery.
Kim MJ, Park SC, Park JW, Chang HJ, Kim DY, Nam BH, et al. Robot-assisted Versus Laparoscopic Surgery for Rectal Cancer: A Phase II Open Label Prospective Randomized Controlled Trial. Annals of surgery. 2018;267(2):243-51.	Outcomes
Kim, J. C., Lim, S. B., Yoon, Y. S., Park, I. J., Kim, C. W., Kim, C. N., Completely abdominal intersphincteric resection for lower rectal cancer: Feasibility and comparison of robot-assisted and open surgery, Surgical Endoscopy and Other Interventional Techniques, 28, 2734-2744, 2014	The cohort in this study is included in another bigger cohort study from the same hospital (see Kim 2016).
Kim, J. G., Heo, Y. J., Son, G. M., Lee, Y. S., Lee, I. K., Suh, Y. J., Cho, H. M., Chun, C. S., Impact of laparoscopic surgery on the long-term outcomes for patients with rectal cancer, ANZ journal of surgery, 79, 817-823, 2009	A non-randomised study comparing laparoscopic and open surgery.
Kim, J. H., Ahn, B. K., Park, S. J., Park, M. I., Kim, S. E., Baek, S. U., Lee, S. H., Park, S. S., Long-term Outcomes of Laparoscopic versus	A non-randomised study comparing laparoscopic and open surgery.

Open Surgery for Rectal Cancer: A Single-center Retrospective Analysis, The Korean journal of gastroenterology = Taehan Sohwagi Hakhoe chi, 65, 273-282, 2015	
Kim, K. Y., Hwang, D. W., Park, Y. K., Lee, H. S., A single surgeon's experience with 54 consecutive cases of multivisceral resection for locally advanced primary colorectal cancer: can the laparoscopic approach be performed safely?, Surgical Endoscopy, 26, 493-500, 2012	A non-randomised study comparing laparoscopic and open surgery.
King, P. M., Blazeby, J. M., Ewings, P., Franks, P. J., Longman, R. J., Kendrick, A. H., Kipling, R. M., Kennedy, R. H., Randomized clinical trial comparing laparoscopic and open surgery for colorectal cancer within an enhanced recovery programme, Br J Surg, 93, 300-8, 2006	Population is people with colorectal cancer, only a few rectal cancers and results are not stratified by colon/rectum.
King, P. M., Blazeby, J. M., Ewings, P., Kennedy, R. H., Detailed evaluation of functional recovery following laparoscopic or open surgery for colorectal cancer within an enhanced recovery programme, International Journal of Colorectal Disease, 23, 795-800, 2008	Population is people with colorectal cancer, no stratification of results by colon/rectum.
Kitano, S., Inomata, M., Sato, A., Yoshimura, K., Moriya, Y., Japan Clinical Oncology Group, Study, Randomized controlled trial to evaluate laparoscopic surgery for colorectal cancer: Japan Clinical Oncology Group Study JCOG 0404, Japanese Journal of Clinical Oncology, 35, 475-7, 2005	A protocol for the JCOG 0404 trial (population with colon cancer).
Koedam TWA, Veltcamp Helbach M, Penna M, Wijsmuller A, Doornebosch P, van Westreenen HL, et al. Short-term outcomes of transanal completion total mesorectal excision (cTaTME) for rectal cancer: a case-matched analysis. Surg Endosc. 2019;33(1):103-9.	Wrong comparison (a non-randomised study comparing TaTME vs cTATME)
Koedam, T. W. A., Deijen, C. L., Velthuis, S., Tsai, A., Mavroveli, S., De Lange-De Klerk, E. S. M., Sietses, C., Tuynman, J. B., Lacy, A. M., Hanna, G. B., Bonjer, H. J., COLOR III trial, Surgical Endoscopy and Other Interventional Techniques, 31 (2 Supplement 1), S376, 2017	A conference abstract. This trial is still recruiting and no results have been published.
Koh, F., Tan, K. K., Lieske, B., Tsang, M., Tsang, C., Koh, D., Endowrist versus wrist: A case-controlled study comparing robotic versus hand-assisted laparoscopic surgery for rectal cancer, Surgical Laparoscopy, Endoscopy and Percutaneous Techniques, 24, 452-456, 2014	A non-randomised study comparing robotic versus laparoscopic surgery but no critical outcomes of interest reported.
Koulas, S. G., Pappas-Gogos, G., Spirou, S., Roustanis, E., Tsimogiannis, K. E., Tsirves, G., Tsimoyiannis, E. C., Evaluations of laparoscopic proctocolectomy versus traditional technique in patients with rectal cancer, Journal of the Society of Laparoendoscopic Surgeons, 13, 564-573, 2009	A non-randomised study comparing laparoscopic and open surgery.
Kusano, T., Inomata, M., Hiratsuka, T., Akagi, T., Ueda, Y., Tojigamori, M., Shiroshita, H., Etoh, T., Shiraishi, N., Kitano, S., A comparison of laparoscopic and open surgery following pre-operative chemoradiation therapy for locally	A non-randomised study comparing laparoscopic and open surgery.

advanced lower rectal cancer, Japanese Journal of Clinical Oncology, 44, 305-310, 2014	
Kwak, J. M., Kim, S. H., Kim, J., Son, D. N., Baek, S. J., Cho, J. S., Robotic vs laparoscopic resection of rectal cancer: Short-term outcomes of a case-control study, Diseases of the Colon and Rectum, 54, 151-156, 2011	Non-randomised study comparing robotic versus laparoscopic surgery. RCT evidence is available for critical outcomes, apart from overall survival, therefore, data from non-randomised studies will only be considered for overall survival. This study does not report overall survival.
Lacy, Fb, Fernandez-Hevia, M, Delgado, S, Bravo, R, Tasende, M, Jimenez, M, Diaz, Del Gobbo G, Castells, A, Lacy, Am, Transanal versus laparoscopic total mesorectal excision for rectal cancer: comparison of the 2-year follow-up, Surgical endoscopy and other interventional techniques., 30, S26, 2016	A conference abstract.
Lai, Yl, Chu, Cc, Huang, Ip, Chen, Cc, Cheng, Ts, Chen, Cm, Comparison of laparoscopic versus conventional surgery for rectal cancer after neoadjuvant chemoradiation-a matched case-controlled study, Surgical endoscopy and other interventional techniques., 29, S155, 2015	A non-randomised study comparing laparoscopic and open surgery.
Lam, H. D., Stefano, M., Tran-Ba, T., Tinton, N., Cambier, E., Navez, B., Laparoscopic versus open techniques in rectal cancer surgery: A retrospective analysis of 121 sphincter-saving procedures in a single institution, Surgical Endoscopy and Other Interventional Techniques, 25, 454-462, 2011	A non-randomised study comparing laparoscopic and open surgery.
Larson, D. W., Boostrom, S. Y., Cima, R. R., Pemberton, J. H., Larson, D. R., Dozois, E. J., Laparoscopic surgery for rectal cancer: Short-term benefits and oncologic outcomes using more than one technique, Techniques in Coloproctology, 14, 125-131, 2010	A non-randomised study comparing laparoscopic and open surgery.
Laurent, C., Leblanc, F., Wutrich, P., Scheffler, M., Rullier, E., Laparoscopic versus open surgery for rectal cancer: long-term oncologic results, Annals of Surgery, 250, 54-61, 2009	A non-randomised study comparing laparoscopic and open surgery.
Laurent, C., Paumet, T., Leblanc, F., Denost, Q., Rullier, E., Intersphincteric resection for low rectal cancer: laparoscopic vs open surgery approach, Colorectal Disease, 14, 35-41; discussion 42-3, 2012	A non-randomised study comparing laparoscopic and open surgery.
Law WL, Foo DCC. Comparison of early experience of robotic and transanal total mesorectal excision using propensity score matching. Surg Endosc. 2019;33(3):757-63.	A non-randomised study comparing robotic and TaTME surgery.
Law, W. L., Poon, J. T. C., Fan, J. K. M., Lo, S. H., Comparison of outcome of open and laparoscopic resection for stage II and stage III rectal cancer, Annals of Surgical Oncology, 16, 1488-1493, 2009	A non-randomised study comparing laparoscopic and open surgery.
Lee SH, Kim DH, Lim SW. Robotic versus laparoscopic intersphincteric resection for low rectal cancer: a systematic review and meta-analysis. Int J Colorectal Dis. 2018;33(12):1741-53.	A systematic review evaluating studies comparing robotic with laparoscopic. Included studies checked

Lelong, B., Bege, T., Esterni, B., Guiramand, J., Turrini, O., Moutardier, V., Magnin, V., Monges, G., Pernoud, N., Blache, J. L., Giovannini, M., Delpero, J. R., Short-term outcome after laparoscopic or open restorative mesorectal excision for rectal cancer: A comparative cohort study, Diseases of the Colon and Rectum, 50, 176-183, 2007	A non-randomised study comparing laparoscopic and open surgery.
Leung, K. L., Kwok, S. P., Lam, S. C., Lee, J. F., Yiu, R. Y., Ng, S. S., Lai, P. B., Lau, W. Y., Laparoscopic resection of rectosigmoid carcinoma: prospective randomised trial, Lancet, 363, 1187-92, 2004	This study is among people with rectosigmoid cancer, therefore, not the right population.
Leung, K. L., Lai, P. B., Ho, R. L., Meng, W. C., Yiu, R. Y., Lee, J. F., Lau, W. Y., Systemic cytokine response after laparoscopic-assisted resection of rectosigmoid carcinoma: A prospective randomized trial, Ann Surg, 231, 506-11, 2000	This study is among people with rectosigmoid cancer, therefore, not the right population.
Leung, Kl, Yiu, Ry, Lai, Pb, Lee, Jf, Thung, Kh, Lau, Wy, Laparoscopic-assisted resection of colorectal carcinoma: five-year audit, Diseases of the Colon and Rectum, 42, 327-32; discussion 332-3, 1999	A non-randomised study comparing laparoscopic and open surgery.
Levic, K., Donatsky, A. M., Bulut, O., Rosenberg, J., A Comparative Study of Single-Port Laparoscopic Surgery Versus Robotic-Assisted Laparoscopic Surgery for Rectal Cancer, Surgical Innovation, 22, 368-375, 2015	Non-randomised study comparing robotic versus laparoscopic surgery. RCT evidence is available for critical outcomes, apart from overall survival, therefore, data from non-randomised studies will only be considered for overall survival. This study does not report overall survival.
Lezoche, E., Guerrieri, M., De Sanctis, A., Campagnacci, R., Baldarelli, M., Lezoche, G., Paganini, A. M., Long-term results of laparoscopic versus open colorectal resections for cancer in 235 patients with a minimum follow-up of 5 years, Surgical Endoscopy and Other Interventional Techniques, 20, 546-553, 2006	A non-randomised study comparing laparoscopic and open surgery.
Li, S., Chi, P., Lin, H., Lu, X., Huang, Y., Long-term outcomes of laparoscopic surgery versus open resection for middle and lower rectal cancer: An NTCLES study, Surgical Endoscopy and Other Interventional Techniques, 25, 3175-3182, 2011	A non-randomised study comparing laparoscopic and open surgery.
Li, S., Jiang, F., Tu, J., Zheng, X., Long-term oncologic outcomes of laparoscopic versus open surgery for middle and lower rectal cancer, PLoS ONE, 10 (9) (no pagination), 2015	A non-randomised study comparing laparoscopic and open surgery.
Lim, D. R., Bae, S. U., Hur, H., Min, B. S., Baik, S. H., Lee, K. Y., Kim, N. K., Long-term oncological outcomes of robotic versus laparoscopic total mesorectal excision of mid-low rectal cancer following neoadjuvant chemoradiation therapy, Surgical Endoscopy and Other Interventional Techniques, 31, 1728-1737, 2017	Population not according to protocol: 45% of participants in one arm with stage 0-I rectal cancer.
Lin Y, Lin H, Xu Z, Zhou S, Chi P. Comparative Outcomes of Preoperative Chemoradiotherapy and Selective Postoperative Chemoradiotherapy	Wrong comparison (compares preoperative chemoradiotherapy with/without postoperative chemotherapy)

in Clinical Stage T3N0 Low and Mid Rectal Cancer. J Invest Surg. 2018:1-9.	
Liu, F. L., Lin, J. J., Ye, F., Teng, L. S., Hand-assisted laparoscopic surgery versus the open approach in curative resection of rectal cancer, Journal of International Medical Research, 38, 916-922, 2010	Hand-assisted laparoscopic colorectal surgery is rarely performed in England and therefore not relevant for this review.
Liu, L., Cao, Y., Zhang, G., Zhang, L., Wang, P., Gong, J., Long-term outcomes after laparoscopic total mesorectal excision for advanced rectal cancer, South African Journal of Surgery, 49, 186-189, 2011	A non-randomised study comparing laparoscopic and open surgery.
Liu, Y., Lu, X. M., Niu, Y. F., Tao, K. X., Wang, G. B., Application of laparoscopic total mesorectal excision combined with sphincter-preserving surgery in low or ultralow rectal cancer, Journal of Innovative Optical Health Sciences, 9 (5) (no pagination), 2016	A non-randomised study comparing laparoscopic and open surgery.
Liu, Z., Kang, L., Huang, M., Luo, Y., Wang, L., Lan, P., Cui, J., Wang, J., Open surgery against laparoscopic surgery for mid-rectal or low-rectal cancer of male patients: Better postoperative genital function of laparoscopic surgery, Surgical Laparoscopy, Endoscopy and Percutaneous Techniques, 25, 444-448, 2015	A non-randomised study comparing laparoscopic and open surgery.
Lujan, J., Parrila, P., Authors' reply: Randomized clinical trial comparing laparoscopic and open surgery in patients with rectal cancer (Br J Surg 2009; 96: 982-989), British Journal of Surgery, 96, 1496, 2009	Author's reply. The trial this comment refers to is included in the review.
Lujan, J., Valero, G., Biondo, S., Espin, E., Parrilla, P., Ortiz, H., Laparoscopic versus open surgery for rectal cancer: Results of a prospective multicentre analysis of 4,970 patients, Surgical Endoscopy and Other Interventional Techniques, 27, 295-302, 2013	A non-randomised study comparing laparoscopic and open surgery.
Marks, J. H., Montenegro, G. A., Salem, J. F., Shields, M. V., Marks, G. J., Transanal TATA/TME: a case-matched study of taTME versus laparoscopic TME surgery for rectal cancer, Techniques in Coloproctology, 20, 467-473, 2016	Non-randomised study comparing TaTME to laparoscopic surgery. Evidence on critical outcomes already available from a RCT.
Matsuhashi, N., Takahashi, T., Tanahashi, T., Matsui, S., Imai, H., Tanaka, Y., Yamaguchi, K., Osada, S., Yoshida, K., Safety and feasibility of laparoscopic intersphincteric resection for a lower rectal tumor, Oncology Letters, 14, 4142-4150, 2017	A non-randomised study comparing laparoscopic and open surgery.
Matsumoto, A, Arita, K, Tashiro, M, Haruki, S, Usui, S, Laparoscopic versus open resection for rectal cancer (RA and RB) based on 10 year data: results of our hospital study in 217 rectal cancer patients, Surgical endoscopy and other interventional techniques., 29, S102, 2015	A non-randomised study comparing laparoscopic and open surgery.
Milsom, Jw, Böhm, B, Hammerhofer, Ka, Fazio, V, Steiger, E, Elson, P, A prospective, randomized trial comparing laparoscopic versus conventional techniques in colorectal cancer	Published 1998. Includes both colon and rectal tumours and results are not stratified according to tumour location.

surgery: a preliminary report, Journal of the American College of Surgeons, 187, 46-54; discussion 54-5, 1998	
Mirza, M. S., Longman, R. J., Farrokhyar, F., Sheffield, J. P., Kennedy, R. H., Long-term outcomes for laparoscopic versus open resection of nonmetastatic colorectal cancer, Journal of Laparoendoscopic and Advanced Surgical Techniques, 18, 679-685, 2008	A non-randomised study comparing laparoscopic and open surgery.
Mohamed, Z. K., Law, W. L., Outcome of tumor-specific mesorectal excision for rectal cancer: the impact of laparoscopic resection, World Journal of Surgery, 38, 2168-2174, 2014	A non-randomised study comparing laparoscopic and open surgery.
Morelli, L., Guadagni, S., Lorenzoni, V., Di Franco, G., Cobuccio, L., Palmeri, M., Caprili, G., D'Isidoro, C., Moglia, A., Ferrari, V., Di Candio, G., Mosca, F., Turchetti, G., Robot-assisted versus laparoscopic rectal resection for cancer in a single surgeon's experience: a cost analysis covering the initial 50 robotic cases with the da Vinci Si, International Journal of Colorectal Disease, 31, 1639-48, 2016	Population not according to protocol: only around 40% of population with T3 or N cancer, T4 were excluded.
Morino, M, Allaix, Me, Giraudo, G, Corno, F, Garrone, C, Laparoscopic versus open surgery for extraperitoneal rectal cancer: a prospective comparative study, Surgical Endoscopy and Other Interventional Techniques, 19, 1460-1467, 2005	A non-randomised study comparing laparoscopic and open surgery.
Morino, M., Allaix, M. E., Giraudo, G., Corno, F., Garrone, C., Laparoscopic versus open surgery for extraperitoneal rectal cancer: A prospective comparative study, Surgical Endoscopy and Other Interventional Techniques, 19, 1460-1467, 2005	A non-randomised study comparing laparoscopic and open surgery.
Nagasaki, T., Akiyoshi, T., Ueno, M., Fukunaga, Y., Nagayama, S., Fujimoto, Y., Konishi, T., Yamaguchi, T., Laparoscopic salvage surgery for locally recurrent rectal cancer, Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract, 18, 1319-1326, 2014	A non-randomised study comparing laparoscopic and open surgery.
Nakamura, H., Uehara, K., Arimoto, A., Kato, T., Ebata, T., Nagino, M., The feasibility of laparoscopic extended pelvic surgery for rectal cancer, Surgery Today, 46, 950-956, 2016	A non-randomised study comparing laparoscopic and open surgery.
Nakamura, T., Kokuba, Y., Mitomi, H., Onozato, W., Hatate, K., Satoh, T., Ozawa, H., Ihara, A., Watanabe, M., Comparison between the oncologic outcome of laparoscopic surgery and open surgery for T1 and T2 rectosigmoidal and rectal carcinoma: Matched case-control study, Hepato-Gastroenterology, 54, 1094-1097, 2007	A non-randomised study comparing laparoscopic and open surgery.
NCT. Laparoscopic Surgery or Robotic-Assisted Laparoscopic Surgery in Treating Patients With Rectal Cancer That Can Be Removed By Surgery. 2010	A clinical trial record; no results (no data)
NCT. Optimisation of Response for Organ Preservation in Rectal Cancer : neoadjuvant	A clinical trial record; no results (no data)

Chemotherapy and Radiochemotherapy vs. Radiochemotherapy. 2015	
NCT. Phase III Study Comparing Preoperative Chemoradiotherapy Alone Versus Neoadjuvant Chemotherapy With Folfirinox Regimen Followed by Preoperative Chemoradiotherapy for Patients With Resectable Locally Advanced Rectal Cancer. 2013	A clinical trial record; no results (no data)
NCT. Preoperative Chemoradiotheray for Rectal Cancer. 2009	Wrong comparison for this research question. A clinical trial record; no results (no data) (linked to Park et al., 2012 [evidence review C1])
Neijenhuis, Pa, Buurma, M, Reimers, M, Kroon, Hm, Laparoscopic colorectal surgery leads to increased overall survival when compared to a conventional open approach, Surgical endoscopy and other interventional techniques., 29, S104, 2015	A non-randomised study comparing laparoscopic and open surgery.
Ng, S. S. M., Lee, J. F. Y., Yiu, R. Y. C., Li, J. C. M., Hon, S. S. F., Mak, T. W. C., Leung, W. W., Leung, K. L., Long-term oncologic outcomes of laparoscopic versus open surgery for rectal cancer: A pooled analysis of 3 randomized controlled trials, Annals of Surgery, 259, 139-147, 2014	This is a pooled analysis of 3 randomised trials from the same hospital in Hong Kong. The three trials focused on different rectal tumour locations (lower, middle, upper), and the type of surgery was therefore different (APR or AR). All of these trials have been included in this review.
Nienhuser H, Heger P, Schmitz R, Kulu Y, Diener MK, Klose J, et al. Short- and Long-Term Oncological Outcome After Rectal Cancer Surgery: a Systematic Review and Meta-Analysis Comparing Open Versus Laparoscopic Rectal Cancer Surgery. J Gastrointest Surg. 2018;22(8):1418-33.	A systematic review and meta-analysis comparing laparoscopic and open surgery. Included studies checked.
Nonaka, T., Fukuda, A., Maekawa, K., Nagayoshi, S., Tokunaga, T., Takatsuki, M., Kitajima, T., Taniguchi, K., Fujioka, H., Clinical and oncological outcomes of laparoscopic versus open surgery for advanced rectal cancer, Anticancer Research, 36, 5419-5424, 2016	A non-randomised study comparing laparoscopic and open surgery.
Odermatt, M., Flashman, K., Khan, J., Parvaiz, A., Laparoscopic-assisted abdominoperineal resection for low rectal cancer provides a shorter length of hospital stay while not affecting the recurrence or survival: a propensity score-matched analysis, Surgery Today, 46, 798-806, 2016	A non-randomised study comparing laparoscopic and open surgery.
Ohtani H, Maeda K, Nomura S, Shinto O, Mizuyama Y, Nakagawa H, et al. Meta-analysis of Robot-assisted Versus Laparoscopic Surgery for Rectal Cancer. In Vivo. 2018;32(3):611-23.	A systematic review and meta-analysis comparing robotic and laparoscopic surgery. Included studies checked.
Ohtani, H., Tamamori, Y., Azuma, T., Mori, Y., Nishiguchi, Y., Maeda, K., Hirakawa, K., A Meta-analysis of the Short- and Long-Term Results of Randomized Controlled Trials That Compared Laparoscopy-Assisted and Conventional Open Surgery for Rectal Cancer, Journal of Gastrointestinal Surgery, 15, 1375-1385, 2011	Systematic review of laparoscopic versus open rectal surgery, all included studies checked for relevance but not all studies are relevant to our review according to protocol.
Pai, A., Marecik, S. J., Park, J. J., Melich, G., Sulo, S., Prasad, L. M., Oncologic and Clinicopathologic Outcomes of Robot-Assisted	No comparison group.

Total Mesorectal Excision for Rectal Cancer, Diseases of the Colon & RectumDis Colon Rectum, 58, 659-67, 2015	
Pan, R., Zheng, S., Cai, W., Wang, Z., Zheng, M., Retrospective study on the effect of laparoscopic and open total mesorectal excision for middle/low T3 rectal cancer, International Journal of Clinical and Experimental Medicine, 9, 21708-21715, 2016	A non-randomised study comparing laparoscopic and open surgery.
Pan, Yf, Zhang, Xh, Jia, Xj, Qu, Jm, Xiang, Yq, Yang, K, Lin, Br, Zheng, Xf, Zheng, J, Laparoscopic abdominoperineal resection for low rectal cancer, Zhonghua wei chang wai ke za zhi [Chinese journal of gastrointestinal surgery], 10, 253-256, 2007	Full text in Chinese.
Park, I. J., Choi, G. S., Lim, K. H., Kang, B. M., Jun, S. H., Laparoscopic resection of extraperitoneal rectal cancer: a comparative analysis with open resection, Surgical Endoscopy, 23, 1818-24, 2009	A non-randomised study comparing laparoscopic and open surgery.
Park, J. S., Choi, G. S., Jun, S. H., Hasegawa, S., Sakai, Y., Laparoscopic versus open intersphincteric resection and coloanal anastomosis for low rectal cancer: Intermediate-term oncologic outcomes, Annals of Surgery, 254, 941-946, 2011	A non-randomised study comparing laparoscopic and open surgery.
Park, J. S., Choi, G. S., Jun, S. H., Park, S. Y., Kim, H. J., Long-term outcomes after laparoscopic surgery versus open surgery for rectal cancer: A propensity score analysis, Annals of Surgical Oncology, 20, 2633-2640, 2013	A non-randomised study comparing laparoscopic and open surgery.
Park, J. S., Choi, G. S., Lim, K. H., Jang, Y. S., Jun, S. H., S052: a comparison of robot-assisted, laparoscopic, and open surgery in the treatment of rectal cancer, Surgical Endoscopy, 25, 240-8, 2011	Population not according to protocol: people with T3-4 or TxN cancer are a minority in this study.
Park, J. S., Kang, S. B., Kim, D. W., Lee, K. H., Kim, Y. H., Laparoscopic versus open resection without splenic flexure mobilization for the treatment of rectum and sigmoid cancer: a study from a single institution that selectively used splenic flexure mobilization, Surgical Laparoscopy, Endoscopy & Percutaneous Techniques, 19, 62-8, 2009	A non-randomised study comparing laparoscopic and open surgery.
Park, J. S., Kim, N. K., Kim, S. H., Lee, K. Y., Lee, K. Y., Shin, J. Y., Kim, C. N., Choi, G. S., Korean Laparoscopic Colorectal Surgery Study, Group, Multicentre study of robotic intersphincteric resection for low rectal cancer, British Journal of Surgery, 102, 1567-73, 2015	Population not according to the protocol: >40% of people in one arm outside the population defined in the protocol (T3-4 or N , M0).
Park, Js, Kim, Nk, Kim, Sh, Lee, Ky, Sin, Jy, Kim, Cn, Choi, Gs, Kim, Hj, Long-term results: of robotic intersphincteric resection with coloanal anastomosis for low rectal cancer-the Korean laparoscopic colorectal surgery study group, Surgical endoscopy and other interventional techniques., 30, S33, 2016	A conference abstract.

Pasupathy, S., Eu, K. W., Ho, Y. H., Seow-Choen, F., A comparison between open versus laparoscopic assisted colonic pouches for rectal cancer, Techniques in Coloproctology, 5, 19-22, 2001	A non-randomised study comparing laparoscopic and open surgery.
Patankar, S. K., Larach, S. W., Ferrara, A., Williamson, P. R., Gallagher, J. T., DeJesus, S., Narayanan, S., Prospective comparison of laparoscopic vs. open resections for colorectal adenocarcinoma over a ten-year period, Diseases of the Colon and Rectum, 46, 601-611, 2003	A non-randomised study comparing laparoscopic and open surgery.
Patel, C. B., Ragupathi, M., Ramos-Valadez, D. I., Haas, E. M., A three-arm (laparoscopic, hand-assisted, and robotic) matched-case analysis of intraoperative and postoperative outcomes in minimally invasive colorectal surgery, Dis Colon Rectum, 54, 144-50, 2011	Population not relevant: mostly people with benign rectosigmoid tumours.
Patriti, A., Ceccarelli, G., Bartoli, A., Spaziani, A., Biancafarina, A., Casciola, L., Short- and medium-term outcome of robot-assisted and traditional laparoscopic rectal resection, Journal of the Society of Laparoendoscopic Surgeons, 13, 176-83, 2009	Non-randomised study comparing robotic versus laparoscopic surgery. RCT evidence is available for critical outcomes, apart from overall survival, therefore, data from non-randomised studies will only be considered for overall survival. This study does not report overall survival. Population not according to protocol: 46% in one arm with stage I rectal cancer.
Pechlivanides, G., Gouvas, N., Tsiaoussis, J., Tzortzinis, A., Tzardi, M., Moutafidis, M., Dervenis, C., Xynos, E., Lymph node clearance after total mesorectal excision for rectal cancer: laparoscopic versus open approach, Digestive Diseases, 25, 94-9, 2007	No relevant outcomes.
Pedziwiatr, M., Malczak, P., Mizera, M., Witowski, J., Torbicz, G., Major, P., Pisarska, M., Wysocki, M., Budzynski, A., There is no difference in outcome between laparoscopic and open surgery for rectal cancer: a systematic review and meta-analysis on short- and long-term oncologic outcomes, Techniques in Coloproctology, 21, 595-604, 2017	Systematic review and meta-analysis comparing laparoscopic and open rectal surgery. More studies are included in our review.
Perdawood, S. K., Al Khefagie, G. A. A., Transanal vs laparoscopic total mesorectal excision for rectal cancer: Initial experience from Denmark, Colorectal Disease, 18, 51-58, 2016	Non-randomised study comparing TaTME to laparoscopic surgery. Evidence on critical outcomes already available from a RCT.
Popescu, I., Vasilescu, C., Tomulescu, V., Vasile, S., Sgarbura, O., The minimally invasive approach, laparoscopic and robotic, in rectal resection for cancer. A single center experience, Acta chirurgica Iugoslavica, 57, 29-35, 2010	Population not according to protocol: around 40% of participants with stage 0-I rectal cancer.
Prytz M, Ledebo A, Angenete E, Bock D, Haglind E. Association between operative technique and intrusive thoughts on health-related Quality of Life 3 years after APE/ELAPE for rectal cancer: results from a national Swedish cohort with comparison with normative Swedish data. Cancer Med. 2018;7(6):2727-35.	Wrong comparison
Rasulov, Ao, Mamedli, Zz, Dzhumabaev, Ke, Kulushev, Vm, Kozlov, Na, Total mesorectal excision in rectal cancer management:	Full text not in English.

laparoscopic or transanal?, Khirurgiia, 37-44, 2016	
Rickert, A., Herrle, F., Doyon, F., Post, S., Kienle, P., Influence of conversion on the perioperative and oncologic outcomes of laparoscopic resection for rectal cancer compared with primarily open resection, Surgical Endoscopy and Other Interventional Techniques, 27, 4675-4683, 2013	A non-randomised study comparing laparoscopic and open surgery.
Sajid, M. S., Ahamd, A., Miles, W. F., Baig, M. K., Systematic review of oncological outcomes following laparoscopic vs open total mesorectal excision, World Journal of Gastrointestinal Endoscopy, 6, 209-19, 2014	Systematic review of laparoscopic versus open rectal surgery, all included studies checked for relevance but not all studies are relevant to our review according to protocol.
Saklani, A. P., Lim, D. R., Hur, H., Min, B. S., Baik, S. H., Lee, K. Y., Kim, N. K., Robotic versus laparoscopic surgery for mid-low rectal cancer after neoadjuvant chemoradiation therapy: Comparison of oncologic outcomes, International Journal of Colorectal Disease, 28, 1689-1698, 2013	Population not according to protocol: 46% in one arm with stage 0-I rectal cancer.
Sambasivan, C. N., Deveney, K. E., Morris, K. T., Oncologic outcomes after resection of rectal cancer: Laparoscopic versus open approach, American Journal of Surgery, 199, 599-603, 2010	A non-randomised study comparing laparoscopic and open surgery.
Schmidt, C. E., Bestmann, B., Kuchler, T., Longo, W. E., Kremer, B., Ten-year historic cohort of quality of life and sexuality in patients with rectal cancer, Diseases of the Colon and Rectum, 48, 483-492, 2005	A non-randomised study comparing laparoscopic and open surgery.
Schwandner, O., Schiedeck, T. H. K., Killaitis, C., Bruch, H. P., A case-control-study comparing laparoscopic versus open surgery for rectosigmoidal and rectal cancer, International Journal of Colorectal Disease, 14, 158-163, 1999	A non-randomised study comparing laparoscopic and open surgery.
Serin, K. R., Gultekin, F. A., Batman, B., Ay, S., Kapran, Y., Saglam, S., Asoglu, O., Robotic versus laparoscopic surgery for mid or low rectal cancer in male patients after neoadjuvant chemoradiation therapy: comparison of short-term outcomes, Journal of robotic surgery, 9, 187-194, 2015	Non-randomised study comparing robotic versus laparoscopic surgery. RCT evidence is available for critical outcomes, apart from overall survival, therefore, data from non-randomised studies will only be considered for overall survival. This study does not report overall survival.
Serra-Aracil X, Pericay C, Golda T, Mora L, Targarona E, Delgado S, et al. Non-inferiority multicenter prospective randomized controlled study of rectal cancer T2-T3s (superficial) N0, M0 undergoing neoadjuvant treatment and local excision (TEM) vs total mesorectal excision (TME). Int J Colorectal Dis. 2018;33(2):241-9.	Wrong comparison (compares local excision with total mesorectal excision)
Seshadri RA, Swaminathan R, Srinivasan A. Laparoscopic versus open surgery for rectal cancer after neoadjuvant chemoradiation: Long-term outcomes of a propensity score matched study. J Surg Oncol. 2018;117(3):506-13.	A non-randomised study comparing laparoscopic and open surgery.
Seshadri, R. A., Srinivasan, A., Tapkire, R., Swaminathan, R., Laparoscopic versus open	A non-randomised study comparing laparoscopic and open surgery.

surgery for rectal cancer after neoadjuvant chemoradiation: a matched case-control study of short-term outcomes, Surgical Endoscopy, 26, 154-61, 2012	
Shiomi, A., Kinugasa, Y., Yamaguchi, T., Kagawa, H., Yamakawa, Y., Robot-assisted versus laparoscopic surgery for lower rectal cancer: the impact of visceral obesity on surgical outcomes, International Journal of Colorectal Disease, 31, 1701-1710, 2016	Population not according to protocol: only 25-30% with T3-4 tumour and <20% with N .
Sikorszki, L., Temesi, R., Liptay-Wagner, P., Bezsilla, J., Botos, A., Vereczkei, A., Horvath, O. P., Case-matched comparison of short and middle term survival after laparoscopic versus open rectal and rectosigmoid cancer surgery, European Surgery - Acta Chirurgica Austriaca, 47, 303-311, 2015	A non-randomised study comparing laparoscopic and open surgery.
Simillis C, Lal N, Thoukididou SN, Kontovounisios C, Smith JJ, Hompes R, et al. Open Versus Laparoscopic Versus Robotic Versus Transanal Mesorectal Excision for Rectal Cancer: A Systematic Review and Network Meta-analysis. Annals of surgery. 2019.	A systematic review comparing laparoscopic and open surgery. Included studies checked
Sindhu, R. S. N., Natesh, B., Rajan, R., Shanavas, K., Sukumaran, G., Gayathri, L. K., Low-tie IMA and selective D3 lymph node sampling in laparoscopic rectal resection for carcinoma rectum: Comparison of surgical and oncological outcomes with the open technique, Journal of Gastrointestinal Oncology, 8, 850-857, 2017	A non-randomised study comparing laparoscopic and open surgery.
Sinukumar, S., Mehta, S., Ostwal, V., Jatal, S., Saklani, A., Impact of type of surgery (laparoscopic versus open) on the time to initiation of adjuvant chemotherapy in operable rectal cancers, Indian Journal of Gastroenterology, 34, 310-3, 2015	A non-randomised study comparing laparoscopic and open surgery.
Spiegel DY, Boyer MJ, Hong JC, Williams CD, Kelley MJ, Moore H, et al. Long-term Clinical Outcomes of Nonoperative Management With Chemoradiotherapy for Locally Advanced Rectal Cancer in the Veterans Health Administration. Int J Radiat Oncol Biol Phys. 2019;103(3):565-73.	Wrong comparison (non-operative management)
Spinoglio, G., Summa, M., Priora, F., Quarati, R., Testa, S., Robotic colorectal surgery: First 50 cases experience, Diseases of the Colon and Rectum, 51, 1627-1632, 2008	Population includes both colonic and rectal tumours and results are not stratified. Large proportion of participants with stage I cancer.
Stamopoulos, P., Theodoropoulos, G. E., Papailiou, J., Savidis, D., Golemati, C., Bramis, K., Panoussopoulos, S. G., Leandros, E., Prospective evaluation of sexual function after open and laparoscopic surgery for rectal cancer, Surgical Endoscopy, 23, 2665-74, 2009	A non-randomised study comparing laparoscopic and open surgery.
Steele, S. R., Randomized clinical trial comparing laparoscopic and open surgery in patients with rectal cancer, Diseases of the Colon and Rectum, 53, 369, 2010	A conference abstract.

Stewart, D. B., Hollenbeak, C., Boltz, M., Laparoscopic and Open Abdominoperineal Resection for Cancer: How Patient Selection and Complications Differ by Approach, Journal of Gastrointestinal Surgery, 15, 1928-1938, 2011	A non-randomised study comparing laparoscopic and open surgery.
Strohlein, M. A., Grutzner, K. U., Jauch, K. W., Heiss, M. M., Comparison of laparoscopic vs. open access surgery in patients with rectal cancer: A prospective analysis, Diseases of the Colon and Rectum, 51, 385-391, 2008	A non-randomised study comparing laparoscopic and open surgery.
Tajima, T., Mukai, M., Noguchi, W., Higami, S., Uda, S., Yamamoto, S., Hasegawa, S., Nomura, E., Sadahiro, S., Yasuda, S., Makuuchi, H., Comparison of hand-assisted laparoscopic surgery and conventional laparotomy for rectal cancer: Interim results from a single center, Molecular and Clinical Oncology, 3, 533-538, 2015	A non-randomised study comparing laparoscopic and open surgery.
Takiyama H, Kawai K, Ishihara S, Yasuda K, Otani K, Nishikawa T, et al. Different Impacts of Preoperative Radiotherapy and Chemoradiotherapy on Oncological Outcomes in Patients with Stages II and III Lower Rectal Cancer: A Propensity Score Analysis. Dig Surg. 2018;35(3):212-9.	Wrong comparison (compares preoperative radiotherapy and chemoradiotherapy)
Tan, K. K., Chong, C. S., Tsang, C. B., Koh, D. C., Outcomes following surgery for distal rectal cancers: A comparison between laparoscopic and open abdomino-perineal resection, Medical Journal of Malaysia, 68, 348-352, 2013	A non-randomised study comparing laparoscopic and open surgery.
Tang, C. L., Eu, K. W., Tai, B. C., Soh, J. G., MacHin, D., Seow-Choen, F., Randomized clinical trial of the effect of open versus laparoscopically assisted colectomy on systemic immunity in patients with colorectal cancer, Br J Surg, 88, 801-7, 2001	This trial includes both colon and rectal cancers. No relevant outcomes reported stratified by colon/rectum.
Taylor, G. W., Jayne, D. G., Brown, S. R., Thorpe, H., Brown, J. M., Dewberry, S. C., Parker, M. C., Guillou, P. J., Adhesions and incisional hernias following laparoscopic versus open surgery for colorectal cancer in the CLASICC trial, Br J Surg, 97, 70-8, 2010	No relevant outcomes presented.
Tjandra, J. J., Chan, M. K. Y., Yeh, C. H., Laparoscopic- vs. hand-assisted ultralow anterior resection: A prospective study, Diseases of the Colon and Rectum, 51, 26-31, 2008	A non-randomised study comparing laparoscopic and open surgery.
Vaughan-Shaw, P. G., Cheung, T., Knight, J. S., Nichols, P. H., Pilkington, S. A., Mirnezami, A. H., A prospective case-control study of extralevator abdominoperineal excision (ELAPE) of the rectum versus conventional laparoscopic and open abdominoperineal excision: Comparative analysis of short-term outcomes and quality of life, Techniques in Coloproctology, 16, 355-362, 2012	A non-randomised study comparing laparoscopic and open surgery.
Veenhof, A. A. F. A., Engel, A. F., Craanen, M. E., Meijer, S., De Lange-De Klerk, E. S. M., Van	A non-randomised study comparing laparoscopic and open surgery.

Der Peet, D. L., Meijerink, W. J. H. J., Cuesta, M. A., Laparoscopic versus open total mesorectal excision: A comparative study on short-term outcomes: A single-institution experience regarding anterior resections and abdominoperineal resections, Digestive Surgery, 24, 367-374, 2007	
Veenhof, A. A. F. A., Sietses, C., Von Blomberg, B. M. E., Van Hoogstraten, I. M. W., Vd Pas, M. H. G. M., Meijerink, W. J. H. J., Vd Peet, D. L., Vd Tol, M. P., Bonjer, H. J., Cuesta, M. A., The surgical stress response and postoperative immune function after laparoscopic or conventional total mesorectal excision in rectal cancer: A randomized trial, International Journal of Colorectal Disease, 26, 53-59, 2011	A sub-study of the COLOR II trial. No relevant outcomes reported.
Veltcamp Helbach M, Koedam TWA, Knol JJ, Velthuis S, Bonjer HJ, Tuynman JB, et al. Quality of life after rectal cancer surgery: differences between laparoscopic and transanal total mesorectal excision. Surg Endosc. 2019;33(1):79-87.	A non-randomised study comparing laparoscopic and transanal total mesorectal excision.
Velthuis, S., Nieuwenhuis, D. H., Ruijter, T. E., Cuesta, M. A., Bonjer, H. J., Sietses, C., Transanal versus traditional laparoscopic total mesorectal excision for rectal carcinoma, Surgical Endoscopy, 28, 3494-9, 2014	Non-randomised study comparing TaTME to laparoscopic surgery. Evidence on critical outcomes already available from a RCT. Population not according to protocol: Around half of participants with T1-2 and more than half with N0, T4 were excluded.
Vennix, S., Pelzers, L., Bouvy, N., Beets, G. L., Pierie, J. P., Wiggers, T., Breukink, S., Laparoscopic versus open total mesorectal excision for rectal cancer, The Cochrane database of systematic reviews, 4, CD005200, 2014	Systematic review of laparoscopic versus open rectal surgery, all included studies checked for relevance but not all studies are relevant to our review according to protocol.
Wang F, Fan W, Peng J, Lu Z, Pan Z, Li L, et al. Total mesorectal excision with or without preoperative chemoradiotherapy for resectable mid/low rectal cancer: a long-term analysis of a prospective, single-center, randomized trial. Cancer Commun (Lond). 2018;38(1):73.	Wrong comparison (compares any preoperative therapy with surgery alone)
Wang X, Zheng B, Lu X, Bai R, Feng L, Wang Q, et al. Preoperative short-course radiotherapy and long-course radiochemotherapy for locally advanced rectal cancer: Meta-analysis with trial sequential analysis of long-term survival data. PLoS One. 2018;13(7):e0200142.	Wrong comparison (a systematic review of short course radiotherapy with long course radiotherapy)
Wang, Y. W., Huang, L. Y., Song, C. L., Zhuo, C. H., Shi, D. B., Cai, G. X., Xu, Y., Cai, S. J., Li, X. X., Laparoscopic vs open abdominoperineal resection in the multimodality management of low rectal cancers, World Journal of Gastroenterology, 21, 10174-10183, 2015	A non-randomised study comparing laparoscopic and open surgery.
Wang, Z., Zhang, X. M., Liang, J. W., Hu, J. J., Zeng, W. G., Zhou, Z. X., Evaluation of short-term outcomes after laparoscopically assisted abdominoperineal resection for low rectal cancer, ANZ journal of surgery, 84, 842-846, 2014	A non-randomised study comparing laparoscopic and open surgery.

Westerholm, J., Garcia-Osogobio, S., Farrokhyar, F., Cadeddu, M., Anvari, M., Midterm outcomes of laparoscopic surgery for rectal cancer, Surgical Innovation, 19, 81-88, 2012	A non-randomised study comparing laparoscopic and open surgery.
Wu QB, Deng XB, Zhang XB, Kong LH, Zhou ZG. & Wang ZQ.Short-Term and Long-Term Outcomes of Laparoscopic Versus Open Surgery for Low Rectal Cancer. J Laparoendosc Adv Surg Tech A, 2018, 28, 637-644.	A non-randomised study comparing laparoscopic and open surgery.
Wu, Y., Sun, X., Qi, J., Wei, G., Cui, F., Gao, Q., Yu, J., Wang, K., Zheng, J., Comparative study of short-and long-term outcomes of laparoscopic-assisted versus open rectal cancer resection during and after the learning curve period, Medicine (United States), 96 (19) (no pagination), 2017	A non-randomised study comparing laparoscopic and open surgery.
Xanthis A, Greenberg D, Jha B, Olafimihan O, Miller R, Fearnhead N, et al. Local recurrence after 'standard' abdominoperineal resection: do we really need ELAPE? Ann R Coll Surg Engl. 2018;100(2):111-5.	Wrong intervention
Xiao, J., Teng, W. H., Liu, S., Wei, C., Liu, W. J., Chen, S., Zang, W. D. Short-course radiotherapy with delayed surgery versus conventional chemoradiotherapy: Comparison of short-term outcomes in patients with rectal cancer. 2018	Wrong comparison
Xiong, B., Ma, L., Huang, W., Zhao, Q., Cheng, Y., Liu, J., Robotic versus laparoscopic total mesorectal excision for rectal cancer: a meta-analysis of eight studies, Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract, 19, 516-526, 2015	Systematic review of robotic versus laparoscopic rectal surgery, not all studies are relevant to our review according protocol.
Xiong, B., Ma, L., Zhang, C., Cheng, Y., Robotic versus laparoscopic total mesorectal excision for rectal cancer: A meta-analysis, Journal of Surgical Research, 188, 404-414, 2014	Systematic review of robotic versus laparoscopic rectal surgery, not all studies are relevant to our review according protocol.
Xu J, Wei Y, Ren L, Feng Q, Chen J, Zhu D, et al. 482PD Robot-assisted vs laparoscopic vs open abdominoperineal resections for low rectal cancer: Short-term outcomes of a single-center prospective randomized controlled trial. Annals of Oncology. 2017;28(suppl_5).	A conference abstract
Yang, Y., Wang, F., Zhang, P., Shi, C., Zou, Y., Qin, H., Ma, Y., Robot-assisted versus conventional laparoscopic surgery for colorectal disease, focusing on rectal cancer: A meta-analysis, Annals of Surgical Oncology, 19, 3727-3736, 2012	Systematic review of TaTME versus laparoscopic rectal surgery, not all studies are relevant to our review according protocol.
Yu, J, Zhang, C, Wang, Yn, Hu, Yf, Cheng, X, Li, Gx, Laparoscopic versus open total mesorectal excision for the middle-lower rectal cancer: a clinical comparative study, Zhonghua wei chang wai ke za zhi [Chinese journal of gastrointestinal surgery], 12, 573-576, 2009	A non-randomised study comparing laparoscopic and open surgery.

Zhang X, Gao Y, Dai X, Zhang H, Shang Z, Cai X, et al. Short- and long-term outcomes of transanal versus laparoscopic total mesorectal excision for mid-to-low rectal cancer: a meta-analysis. Surg Endosc. 2019;33(3):972-85.	Meta-analysis of transanal versus laparoscopic rectal surgery, not all studies are relevant to our review according protocol.
Zhang X, Wu Q, Hu T, Gu C, Bi L, Wang Z. Laparoscopic Versus Conventional Open Abdominoperineal Resection for Rectal Cancer: An Updated Systematic Review and Meta-Analysis. J Laparoendosc Adv Surg Tech A. 2018;28(5):526-39.	Systematic review of laparoscopic versus open rectal surgery, not all studies are relevant to our review according protocol.
Zhang, F. W., Zhou, Z. Y., Wang, H. L., Zhang, J. X., Di, B. S., Huang, W. H., Yang, K. H., Laparoscopic versus open surgery for rectal cancer: a systematic review and meta-analysis of randomized controlled trials, Asian Pacific journal of cancer prevention : APJCP, 15, 9985-9996, 2014	Systematic review of laparoscopic versus open rectal surgery, all included studies checked for relevance but not all studies are relevant to our review according to protocol.
Zhang, X. M., Wang, Z., Ma, S. H., Zhou, Z. X., Advantages of laparoscopic abdominoperineal resection for anastomotic recurrence of rectal cancer, Asian Pacific journal of cancer prevention : APJCP, 15, 4295-4299, 2014	A non-randomised study comparing laparoscopic and open surgery.
Zhao, J. K., Chen, N. Z., Zheng, J. B., He, S., Sun, X. J., Laparoscopic versus open surgery for rectal cancer: Results of a systematic review and meta-analysis on clinical efficacy, Molecular and Clinical Oncology, 2, 1097-1102, 2014	Systematic review of laparoscopic versus open rectal surgery, all included studies checked for relevance but not all studies are relevant to our review according to protocol.
Zheng, J., Feng, X., Yang, Z., Hu, W., Luo, Y., Li, Y., The comprehensive therapeutic effects of rectal surgery are better in laparoscopy: A systematic review and meta-analysis, Oncotarget, 8, 12717-12729, 2017	Systematic review of laparoscopic versus open rectal surgery including both RCTs and non-RCTs. Included RCTs checked for relevance.
Zheng, M. H., Feng, B., Hu, C. Y., Lu, A. G., Wang, M. L., Li, J. W., Hu, W. G., Zang, L., Mao, Z. H., Dong, T. T., Dong, F., Cai, W., Ma, J. J., Zong, Y. P., Li, M. K. W., Long-term outcome of laparoscopic total mesorectal excision for middle and low rectal cancer, Minimally Invasive Therapy and Allied Technologies, 19, 329-339, 2010	A non-randomised study comparing laparoscopic and open surgery.
Zhou, T., Zhang, G., Tian, H., Liu, Z., Xia, S., Laparoscopic rectal resection versus open rectal resection with minilaparotomy for invasive rectal cancer, Journal of Gastrointestinal Oncology, 5, 36-45, 2014	A non-randomised study comparing laparoscopic and open surgery.
Zhou, X., Liu, F., Lin, C., You, Q., Yang, J., Chen, W., Xu, J., Lin, J., Xu, X., Hand-assisted laparoscopic surgery compared with open resection for mid and low rectal cancer: A case-matched study with long-term follow-up, World Journal of Surgical Oncology, 13 (1) (no pagination), 2015	A non-randomised study comparing laparoscopic and open surgery.
Zhou, Z. X., Zhao, L. Y., Lin, T., Liu, H., Deng, H. J., Zhu, H. L., Yan, J., Li, G. X., Long-term oncologic outcomes of laparoscopic vs open surgery for stages II and III rectal cancer: A retrospective cohort study, World Journal of Gastroenterology, 21, 5505-5512, 2015	A non-randomised study comparing laparoscopic and open surgery.

Zhou, Z; Li, L; Shu, Y; Yu, Y; Cheng, Z; Lei, W;, [Laparoscopic total mesorectal excision for low or ultralow anterior resection of rectal cancer with anal sphincter preservation], Zhonghua wai ke za zhi [Chinese journal of surgery], 40, 899-901, 2007	Full text in Chinese.

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Appendix L – Research recommendations

Research recommendations for review question: What is the optimal surgical technique for rectal cancer?

No research recommendations were made for this review question.