National Institute for Health and Care Excellence

Final

Colorectal cancer (update)

[F1] Surgical volumes and outcomes for rectal cancer

NICE guideline NG151

Evidence reviews

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Developed by the National Guideline Alliance part of the Royal College of Obstetricians and Gynaecologists

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Contents

Surgical volumes and outcomes in the treatment of rectal cancer

This evidence review supports recommendations 1.3.11 to 1.3.12.

Review question

Is there a relationship between surgical volumes and outcomes in the treatment of rectal cancer (primary and recurrent disease)?

Introduction

Treatment for rectal cancer often involves the resection of the primary tumour in combination with adjuvant or neoadjuvant chemotherapy or chemoradiotherapy (Archampong 2012). There is conflicting evidence regarding the relationship between volume and outcomes in rectal surgery (Salz 2008). Typically, concentrating patient care for rare diseases with specialist surgeons enables the accumulation of experience and economic efficiency, but for more common diseases, the benefits of this concentration are less obvious (Archampong 2012). Recently, there has been a move to a more centralised provision of cancer services based on the assumption that high-volume providers are related to better patient outcomes. The effect of surgeon and hospital volumes on surgical outcomes has increasingly become a focus of national health policy due to the implications of the findings on the structure and delivery of services (Hogan 2009). Therefore, the aim of this review is to determine if there is a relationship between surgical volumes and outcomes in the treatment of primary and/or recurrent rectal cancer.

Summary of the protocol

Please see Table 1 for a summary of the population, predictors and outcomes (PPO) characteristics of this review.

Table 1: Summary of the protocol (PPO table)

Population	Adults with primary or recurrent rectal cancer undergoing surgery Sub-stratifications (analysed separately): • Primary rectal cancer • Recurrent rectal cancer
Predictors	Rectal cancer surgery volume: • By hospital • By surgeon Definition of volume as defined by the study. For example, the number of surgeries performed in a specific time period (1 year for example) by a surgeon or in a hospital. Surgery volume categorised into low, medium or high volume, as defined by the study.
Outcomes	**Critical** • Resection margins • Overall survival at 5 years • Perioperative complications: ○ Grade 3 or 4 complications

	○ Unplanned return to theatre **Important** • Local recurrence • Overall quality of life • Permanent stoma rates • Perioperative mortality

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

Nine publications included in 1 systematic review and 19 other population registry studies were included in this review.

The systematic review (Archampong 2012) included 9 population registry studies (Borowski 2010; Harling 2005; Hodgson 2003; Kressner 2009; Manchon-Walsh 2011; Meyerhardt 2004; Ptok 2007; Simunovic 2000; Wibe 2005). Data were available from 19 other population registry studies (Aquina 2016; Atkinson 2016; Baek 2013; Comber 2012; El Amrani 2018; Elferink 2010; Hohenberger 2013; Jonker 2017a; Jonker 2017b; Kladny 2007; Leonard 2014; Matthiessen 2006; NBOCA 2017 [Boyle 2017]; Ortiz 2016; Richardson 2014; Syk 2010; Yeo 2017; Yun 2012).

The included studies are summarised in Table 2.

Three studies reported on both hospital volumes and surgeon volumes (Archampong 2012 [Borowski 2010]; Aquina 2016; Comber 2012).

Twenty studies reported on hospital volumes (Archampong 2012 [Harling 2005; Hodgson 2003; Kressner 2009; Manchon-Walsh 2011; Meyerhardt 2004; Ptok 2007; Simunovic 2000; Wibe 2005]; Atkinson 2016; Baek 2013; El Amrani 2018; Elferink 2010; Jonker 2017a; Jonker 2017b; Leonard 2014; Matthiessen 2006; NBOCA 2017 [Boyle 2017]; Ortiz 2016; Syk 2010; Yun 2012).

Four studies reported on surgeon volumes (Hohenberger 2013; Kladny 2007; Richardson 2013; Yeo 2017).

The studies used their own definitions of low, medium and high volumes. To facilitate the generation of meaningful results and reduce statistical heterogeneity, this review stratified results by the case-per-year thresholds used to define each study's volume categories. Hospital volume results were analysed in increments of 10 and surgeon results in increments of 5. Adjacent volume categories were compared with each other: for example low versus medium volume and medium versus high volume, to explore the incremental effect of increasing the case volume threshold on outcomes.

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

2 **Excluded studies**

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

5 **Summary of clinical studies included in the evidence review**

6 A summary of the studies that were included in this review are presented in Table 2.
7 Variables included by studies in their multivariable models for each outcome are presented in
8 Table 3, Table 4, Table 5, Table 6, Table 7, and Table 8.

9 **Table 2: Summary of included studies**

Study	Population	Surgical volumes definition	Outcomes
Archampong 2012 Systematic review	Patients with a confirmed histological diagnosis of colorectal, colon and rectal cancer in prospective studies and patients with diagnostic codes for colorectal, colon and rectal cancer	Intervention: Surgery for colorectal, colon and rectal cancer performed by high volume and/or specialised units/hospitals or surgeons. In studies with more than two stratified groups, the highest volume category was used for comparative analysis. Control: Surgery for colorectal, colon and rectal cancer performed by low volume and/or non-specialised units/hospitals or surgeons.	• Five-year overall and/or cancer specific survival • Postoperative anastomotic leak rate • Five-year local recurrence rate • Permanent stoma rate for rectal cancer surgery • 30-day and inpatient mortality
Borowski 2010 Cancer registry study (included in Archampong 2012) UK	N= 7411 colorectal cancer patients undergoing resective surgery from 1998-2002. Prognostic factors adjusted for included sex, age, stage, comorbidity and presentation	Total number of hospitals/units=17 Total number of surgeons=140 Hospital volume LV= 14 to 33 MV=34 to 39 HV=40 to 71 Surgeon volume LV=0.2 to 13.5 MV=13.8 to 21.4 HV=22.3 to 29.2	• Five-year overall survival • Grade 3 or 4 complications • Permanent stoma rate • 30-day and inpatient mortality
Harling 2005 Cancer registry study (included in Archampong 2012) Denmark	N= 5021 rectal cancer patients undergoing resective surgery from 1994-1999 Prognostic factors adjusted for included sex, age and tumour height	Total number of hospitals=53 Caseload defined as average annual number of rectal cancer procedures Hospital volume LV=<15 (range NR) MV=15 to 30 HV=>30 (range NR)	• Five-year overall survival • Grade 3 or 4 complications • Permanent stoma rate • 30-day mortality

Study	Population	Surgical volumes definition	Outcomes
Hodgson 2003 Cancer registry study (included in Archampong 2012) US	N= 7257 rectal cancer patients undergoing surgical resection from 1994-1997 Prognostic factors adjusted for included sex, age, race, comorbidity, deprivation, tumour site, stage and number of examined lymph nodes	Total number of hospitals=367 Caseload defined as average annual number of rectal cancer operations performed in a year Hospital volume LV=1 to 7 MV= 7 to 13 HV= 14 to 20 VHV= 21 to 28	• Permanent stoma rate • 30-day mortality
Kressner 2009 Cancer registry study (included in Archampong 2012) Sweden	N= 10,425 rectal cancer patients undergoing resective surgery from 1995-2003 Prognostic factors adjusted for included sex, age, stage and radiotherapy	All hospitals in Sweden Caseload defined as average annual number of procedures in a year Hospital volume LV=<11 (range NR) MV=11 to 25 HV=>25 (range NR)	• Five-year overall survival • Grade 3 or 4 complications • Five year local recurrence rate • 30-day mortality
Manchon-Walsh 2011 Cancer registry study (included in Archampong 2012) Spain	N= 1831 rectal cancer patients that underwent curative intent surgery from 2005-2007 Prognostic factors adjusted for included sex, age, stage, comorbidity and presentation	Total number of hospitals=51 Caseload defined as number of procedures in a year Hospital volume LV=<12 (range NR) MV=12 to 30 HV=>30 (range NR)	• Resection margins • Grade 3 or 4 complications • Permanent stoma rate • 30-day mortality
Meyerhardt 2004 Cancer registry study (included in Archampong 2012) US	N= 1330 rectal cancer patients undergoing resective surgery for a primary tumour diagnosed from 1990-1992. Prognostic factors adjusted for included sex, age, stage, grade, comorbidity, presentation, ethnicity, hospital volume and clustering	Total number of hospitals/units=646 Caseload not derived from study but from Medicare data Hospital volume LV=0 to 8 MV= 9 to 16 HV=17 to 92	• Five-year overall survival • Five-year local recurrence rate
Ptok 2007 Cancer registry study (included in Archampong 2012) Germany	N= 1557 low rectal cancer patients undergoing resective surgery from 2000-2001. Prognostic factors adjusted for included stage, tumour perforation, procedure, and circumferential resection margin	Total number of hospitals/units= 75 Caseload defined as average number of potentially curative low rectal resections in a year Hospital volume LV=<10 (range NR) MV=10 to 19 HV=>19 (range NR)	• Resection margins • Five-year local recurrence rate
Simunovic 2000	N= 1072 primary invasive rectal cancer patients diagnosed in 1990 and undergoing	Total number of hospitals=124 Caseload defined as	• Five-year overall survival

Study	Population	Surgical volumes definition	Outcomes
Cancer registry study (included in Archampong 2012) Canada	resective surgery Prognostic factors adjusted for included sex, stage, comorbidity, procedure type, teaching hospital status for mortality. Referral to regional cancer centre added on for five year overall survival	average annual rectal cancer procedures in a year Hospital volume LV= <12 (range NR) MV=12 to 17 HV=>17 (range NR)	• Inpatient mortality
Wibe 2005 Cancer registry study (included in Archampong 2012) Norway	N= 3388 rectal cancer patients undergoing curative surgery from 1993-1999. Prognostic factors adjusted for included sex, age, stage, grade and site	Total number of hospitals=54 Caseload defined as annual hospital volume Hospital volume LV=1 to 9 MV=10 to 19 HV=20 to 29 VHV=30 to 34	• Resection margins • Five-year overall survival • Grade 3 or 4 complications • Five-year local recurrence rate • 30-day mortality
Aquina 2016 Cancer registry study US	N= 7798 patients 18 years of age or older with a primary or secondary diagnosis of rectal cancer who underwent LAR or APR from 2000 and 2011 Prognostic factors adjusted for included age, sex, race, insurance type, Elixhauser comorbidities previously validated for mortality prediction, type of operation (LAR vs APR), physician board certification in Surgery or Colorectal Surgery, years since completion of residency or fellowship training, hospital characteristics hospital designation and location (urban vs rural)	Individual surgeon and hospital volumes were calculated as the average number of rectal cancer resections performed during each of 3 time periods from 2000–2003, 2004– 2007, and 2008–2011 Non-HVS 1 to 9 resections HVS= ≥ 10 resections (range NR) Non-HVH= 1 to 24 resections HVH= ≥ 25 resections (range NR)	• Permanent stoma rate • 30-day mortality
Atkinson 2016 Cancer registry study US	N= 113,113 patients treated with LAR, LAR with coloanal anastomosis, APR, or pelvic exenterations for stage I-III rectal cancer Prognostic factors adjusted for included age, race, insurance status pathologic tumour (T) stage, nodal (N) stage, radiation sequence, tumour grade, tumour size and surgery performed	Volume quintiles were determined by taking 20th percentiles. VLV=≤6 (range NR) LV= 7 to 10 MV= 11 to 15 HV= 16 to 23 VHV= ≥ 24 (range NR)	• Resection margins
Baek 2013 Cancer registry study	N= 7187 patients diagnosed with rectal cancer who underwent surgery by LAR or APR	Hospital volume defined as the number of cases performed during the 6-year period. LV= 1 to 5 per annum MV= 6 to 10	• 30-day mortality

Study	Population	Surgical volumes definition	Outcomes
US	Prognostic studies controlled for included age, gender, race, ethnicity, and surgery type	HV= 11 to 24	
Comber 2012 Cancer registry study Ireland	N= 581 patients diagnosed with rectal cancer who underwent surgery Prognostic studies controlled for included gender, age, stage and functional status at diagnosis	Hospital volume and surgeon volume treated as a continuous outcome.	• Resection margins • Complications
El Amrani 2018 Cancer registry study France	N = 45,569 patients treated with proctectomy for rectal cancer from 2012 to 2016	Hospital volume was defined as the number of proctecomies per year: LV= <10 per annum MV= 10 to 40 HV= >40	• 90-day mortality
Elferink 2010 Cancer registry study The Netherlands	N= 16,039 patients with invasive rectal carcinoma, diagnosed from 2001 and 2006 Prognostic factors adjusted for included gender, age at diagnosis, grade, year of diagnosis, clinical stage, surgery, chemotherapy, radiotherapy and CCC-region	Hospital volume was defined as the number of resections per year LV= 9 to 24 MV= 25 to 49 HV= 50 to 92	• Five-year overall survival • 30-day mortality
Hagemans 2018 Cancer registry study The Netherlands	N=2104 patients with cT4 rectal cancer undergoing surgery from 2005 to 2013. Prognostic factors adjusted for included gender, age at diagnosis, grade, year of diagnosis, pathological stage, surgery, neoadjuvant therapy, type of surgery	Hospital volume was defined as the number of resections per year LV= 1 to 4 MV= 5 to 9 HV= >9	• Five-year overall survival
Hohenberger 2013 Cancer registry study Germany	N= 1028 patients with solitary invasive rectal carcinoma (invasion at least of the submucosa).	Surgeon caseload: LV= 1 to 3 MV= 4 to 6 HV= 7 to 23	• Resection margins • Five-year overall survival • Local recurrence • Grade 3 or 4 complications • Inpatient mortality
Jonker 2017a Cancer registry study The Netherlands	N= 2095 patients who underwent a registered rectal cancer resection.	Annual hospital volume was defined as the total number of rectal cancer resections performed in 2011. LV= < 20 (range NR) MV= 20 to 50 HV= > 50 (range NR)	• Resection margins • Grade 3 or 4 complications • 30-day or inpatient mortality

Study	Population	Surgical volumes definition	Outcomes
Jonker 2017b Cancer registry study The Netherlands	N= 14,651 patients operated for rectal cancer enrolled in the DSCA from January 2009 to December 2015.	Hospitals volumes were calculated as the number of cases per year. cT1-3 rectal cancer LV= < 20 (range NR) MV= 20 to 50 HV= > 50 (range NR) cT4 rectal cancer LV= 1 to 4 MV= 5 to 9 HV= ≥ 10 (range NR)	• Grade 3 or 4 complications • 30-day or inpatient mortality
Kladny 2007 Cancer registry study Poland	N= 286 patients with rectal cancer	Surgeon volume was defined as the average number of surgeries performed over the study period (5 years) LV= < 5 (range NR) HV= ≥ 5 (range NR)	• Five-year overall survival
Leonard 2014 Cancer registry study Belgium	N= 1469 patients with primary invasive adenocarcinoma of the rectum between 0 and 10 cm above the anal verge as determined by rigid or flexible endoscopy, who underwent elective TME Prognostic factors controlled for included node status, number of quadrants involved, pTNM stage and age.	Hospital volume was calculated as the average annual number of radical resections for rectal cancer at any level in the interval 2006 to mid-2008	• Five-year overall survival • Five-year local recurrence
Matthiessen 2006 Cancer registry study Sweden	N= 140 patients who underwent elective AR of the rectum.	Hospital caseload was divided arbitrarily into four categories, taking into consideration the existing differences in caseload in Sweden during the study period. VLV= 1 to 5 LV= 6 to <12 MV= 12 to <18 HV= 18 to 28	• Inpatient mortality
NBOCA 2017 [Boyle 2017] Cancer registry study UK	N= 4148 patients with new diagnoses of rectal cancer after 1 April 2013 Prognostics factors adjusted for included age (modelled as age plus age-squared), sex, ASA grade, Charlson comorbidity score, mode of admission, TNM stage, site of tumour.	Volume categories not used; results analysed per additional case	• Permanent stoma rate
Ortiz 2016 Cancer registry study Spain	N= 2910 patients who underwent one of three elective surgeries: AR, APR and Hartmann's procedure. Prognostic factors controlled for included age, categorized in 3 groups (<65, 65–80, >80 years); sex; severity of surgical risk	Stratifications were defined according to the mean number of patients treated annually LV= 12 to 23 MV= 24 to 35 HV= 36 to 56	• Five-year overall survival • Local recurrence

Study	Population	Surgical volumes definition	Outcomes
	(measured by the ASA anaesthesia risk classification); tumour location, categorized in 3 groups (0–6, 7–12, 13–15 cm); type of mesorectal excision (partial or total); type of resection (AR, APR, Hartmann procedure); pathological tumour stage and lymphadenopathies; state of circumferential resection margins; intraoperative perforation; use of neoadjuvant therapy; and the hospital case load		
Richardson 2013 Cancer registry study Canada	N= 521 patients with a new diagnosis of adenocarcinoma of the rectum between July 1, 2002 and June 30, 2006, who underwent resection with curative intent Prognostic factors controlled for included age, sex, body mass index, Charlson comorbidity score, tumour height, use of neoadjuvant therapy, and TNM stage.	Surgeon volume calculated as average number of cases per year LV= 1 to 5 HV= 6 to 14	• Five-year overall survival • Local recurrence • Permanent stoma rate
Syk 2010 Cancer registry study Sweden	N=2282 patients with rectal cancer who underwent abdominal resections Prognostic factors controlled for: gender, age, study period, tumour location, tumour size, T-stage, N-stage differentiation, radiotherapy, type of surgery, TME, intraoperative perforation of rectum, residual status, and case load	Hospital volume calculated as average number of cases per year LV= 5 to 29 HV= 30 to 62	• Local recurrence
Yeo 2017 Cancer registry study US	N= 14,833 patients undergoing major rectal resection, including rectosigmoid tumours, as their principal procedure during hospitalization between 2000 and 2013 Prognostic factors controlled for included patient demographics, surgery year, surgery approach and type, tumour characteristics (benign/malignant and location), comorbidities, emergency surgery and hospital volume	Surgeon volume was based on median surgeon volumes Cumulative volume: LC= 0-23 HC= ≥ 24 (range NR) Annual volume: LV= 0-4 HV= ≥ 5 (range NR)	• Grade 3 or 4 complications • Unplanned return to theatre
Yun 2012 Cancer registry study South Korea	N= 147,682 patients 20 years of age or older who had been diagnosed with cancer of the stomach, colon, rectum, pancreas, lung or breast	Hospital volume defined by number of operations per year LV= < 23 (range NR) HV= ≥ 23 (range NR)	• Five-year overall survival

Study	Population	Surgical volumes definition	Outcomes
	Prognostic factors controlled for included age, sex, Charlson scale, hospital type, insurance, radiotherapy, chemotherapy, type of medical care institution, year of diagnosis and hospital volume		

APR: abdominoperineal resection; AR: anterior resection; ASA: American Society of Anesthesiologists; CCC: Comprehensive Cancer Centre; DSCA: Dutch Surgical Colorectal Audit; HC: high cumulative; HV: high volume; HVH: high volume hospital; HVS: high volume surgeon; LAR: low anterior resection: LC: low cumulative; LV: low volume; MV: medium volume; NBOCA: National Bowel Cancer Audit; N: number; NR: not reported; TME: total mesorectal excision; TNM: cancer classification system, standing for tumour, nodal and metastases stages; VHV: very high volume; VLV: very low volume

Table 3: Variables included by studies in their multivariable models of positive resection margin

	Age	Year of diagnosis	Sex	Ethnicity	Deprivation	Insurance	Comorbidity	Fitness	Presentation	Surgical risk	Surgery type	Permanent stoma	Additional resection	Tumour stage	Tumour grade	Tumour site	Tumour size	Node stage	# nodes examined	Synchronous mets.	Chemotherapy	Radiotherapy	Doctor certification	Doctor years of work	Urban vs Rural hsp.	Hospital volume	Surgeon volume
Atkinson 2016	●	-	●	●	-	●	-	-	-	-	●	-	-	●	●	-	●	●	-	-	-	●	-	-	-	●	-
Comber 2012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	●	●
Harling 2005	●	-	●	-	-	-	-	-	-	-	-	-	-	●	-	-	-	●	-	●	-	-	-	-	-	●	-
Hohenberger 2013	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-	●

● *variable included; - variable not included*

Table 4: Variables included by studies in their multivariable models of overall survival

	Age	Year of diagnosis	Sex	Ethnicity	Deprivation	Insurance	BMI	Comorbidity	Fitness	Presentation	Surgical risk	Surgery type	Permanent stoma	Surgical margins	Surg. complications	Additional resection	Local recurrence	Tumour stage	Tumour grade	Tumour site	Tumour size	Node stage	# nodes examined	Synchronous mets.	Chemotherapy	Radiotherapy	Doctor certification	Doctor years of work	Hospital type	Hospital volume	Surgeon volume
Borowski 2010	●	-	●	-	-	-	-	-	●	●	-	-	-	-	-	-	-	●	-	●	-	-	-	-	-	-	-	-	●	●
Jonker 2017a	●	-	●	-	-	-	-	-	●	-	-	●	●	-	-	●	-	●	-	-	-	●	-	●	●	●	-	-	-	●	-
Hagemans 2018	●	●	●	-	-	-	-	-	-	-	-	●	-	-	-	-	-	●	-	-	-	●	-	-	●	●	-	-	-	●	-
Kladny 2007	●	-	-	-	-	-	-	-	-	-	-	-	-	-	●	●	-	-	●	●	-	●	-	-	-	-	-	-	●	-	●
Leonard 2014	●	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	●	-	●	-	●	-	●	●	-	-	-	-	●	-
Meyerhardt 2004	●	-	●	●	-	-	-	-	●	●	-	●	-	-	-	-	-	●	-	-	-	●	-	-	-	-	-	-	-	●	-
Ortiz 2016	●	-	●	-	-	-	-	-	●	-	-	●	-	●	-	-	-	●	-	●	-	●	-	-	●	●	-	-	-	●	-
Richardson 2013	●	-	-	-	-	-	●		●	-	-	-	-	-	-	-	-	●	-	●	-	●	-	-	●	●	-	-	-	-	●

	Age	Year of diagnosis	Sex	Ethnicity	Deprivation	Insurance	BMI	Comorbidity	Fitness	Presentation	Surgical risk	Surgery type	Permanent stoma	Surgical margins	Surg. complications	Additional resection	Local recurrence	Tumour stage	Tumour grade	Tumour site	Tumour size	Node stage	# nodes examined	Synchronous mets.	Chemotherapy	Radiotherapy	Doctor certification	Doctor years of work	Hospital type	Hospital volume	Surgeon volume
Simunovic 2000	●	-	●	-	-	-	-	●	-	●	-	●	-	-	-	-	-	●	-	-	-	●	-	-	-	-	-	-	●	●	-
Wibe 2005	●	-	●	-	-	-	-	-	-	-	-	●	-	●	-	-	-	●	●	●	-	●	-	-	●	●	-	-	●	●	-
Yun 2012	●	●	●	-	-	●	-	-	●	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	●	●	-	-	●	●	-

● *variable included; - variable not included; BMI: body mass index*

Table 5: Variables included by studies in their multivariable models of positive perioperative complications

	Age	Year of diagnosis	Sex	Ethnicity	Deprivation	Insurance	Comorbidity	Fitness	Presentation	Surgical risk	Surgery type	Permanent stoma	Surgical margins	Additional resection	Tumour stage	Tumour grade	Tumour site	Tumour size	Node stage	# nodes examined	Synchronous mets.	Chemotherapy	Radiotherapy	Doctor certification	Doctor years of work	Urban vs Rural hsp.	Hospital volume	Surgeon volume
Borowski 2010	●	-	●	-	-	-	-	●	●	-	-	-	-	-	●	-	●	-	-	-	-	-	-	-	-	-	●	●
Comber 2012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	●	●
Harling 2005	●	-	●	-	-	-	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-	●	-
Hohenberger 2013	-	-	-	-	-	-	-	-	●	-	●	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	●
Jonker 2017b (T4)	-	-	●	-	-	-	●	●	-	-	●	-	-	●	●	-	-	●	-	-	-	-	-	-	-	-	●	-
Manchon-Walsh 2011	●	●	●	-	-	-	-	●	-	-	-	-	-	-	●	-	-	-	●	-	●	-	-	-	-	-	●	-
Yeo 2017	-	-	-	-	-	-	●	-	●	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	●	●

● *variable included; - variable not included*

Table 6: Variables included by studies in their multivariable models of local recurrence

	Age	Year of diagnosis	Sex	Ethnicity	Deprivation	Insurance	BMI	Comorbidity	Fitness	Presentation	Surgical risk	Surgery type	Perforation	Permanent stoma	Surgical margins	Additional resection	Tumour stage	Tumour grade	Tumour site	Tumour size	Node stage	# nodes examined	Synchronous mets.	Chemotherapy	Radiotherapy	Doctor certification	Doctor years of work	Hospital type	Hospital volume	Surgeon volume
Leonard 2014	●	-	-	-	-	-	-	-	-	-	-	-		-	-	-	●	-	●	-	●	-	●	-	-	-	-	-	●	-
Meyerhardt 2004	●	-	●	●	-	-		-	●	●	-	●		-	-	-	●	-	-	-	●	-	-	-	-	-	-	-	●	-
Ortiz 2016	●	-	●	-	-	-		-	●	-	-	●		-	●	-	●	-	●	-	●	-	-	●	●	-	-	-	●	-
Ptok 2007	-	-	-	-	-	-	-	-	-	-	-	●	●	-	●	-	●	-	-	-	●	-	-	-	-	-	-	-	●	-
Richardson 2013	●	-	-	-	-	-	●	-	●	-	-	-	-	-	-	-	●	-	●	-	●	-	-	●	●	-	-	-	-	●
Wibe 2005	●	-	●	-	-	-	-	-	-	-	-	●	-	-	●	-	●	●	●	-	●	-	-	●	●	-	-	●	●	-
Syk 2010	●	●	●	-	-	-	-	-	-	-	-	●	●	-	●	-	●	●	●	●	●	-	-	-	●	-	-	-	●	-

● *variable included; - variable not included; BMI: body mass index*

Table 7: Variables included by studies in their multivariable models of permanent stoma rate

	Age	Year of diagnosis	Sex	Ethnicity	Deprivation	Insurance	BMI	Comorbidity	Fitness	Presentation	Surgical risk	Surgery type	Surgical margins	Additional resection	Tumour stage	Tumour grade	Tumour site	Tumour size	Node stage	# nodes examined	Synchronous mets.	Chemotherapy	Radiotherapy	Doctor certification	Doctor years of work	Hospital type	Hospital volume	Surgeon volume
Aquina 2016	●	●	●	-	-	●	-	●	-	-	-	●	-	-	-	-	-	-	-	-	●	-	-	●	●	●	●	●
Baek 2013	●	-	●	●	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	●	-
Harling 2005	●	-	●	-	-	-	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-	●	-
Hodgson 2003	●	-	●	●	●	-	-	●	-	-	-	-	-	-	●	-	●	-	●	●	-	-	-	-	-	-	●	-
Meyerhardt 2004	●	-	●	●	-	-	-	-	●	●	-	●	-	-	●	-	-	-	●	-	-	-	-	-	-	-	●	-
NBOCA 2017	●	-	●	-	-	-	-	-	●	●	●	-	-	-	●	-	●	●	●	-	-	-	-	-	-	-	●	-
Richardson 2013	●	-	-	-	-	-	●	-	●	-	-	-	-	-	●	-	●	-	●	-	-	●	●	-	-	-	-	●

● *variable included; - variable not included; BMI: body mass index*

Table 8: Variables included by studies in their multivariable models of perioperative mortality

	Age	Year of diagnosis	Sex	Ethnicity	Deprivation	Insurance	Comorbidity	Fitness	Presentation	Surgical risk	Surgery type	Symptom. leakage	Intra op AEs	Permanent stoma	Surgical margins	Additional resection	Tumour stage	Tumour grade	Tumour site	Tumour size	Node stage	# nodes examined	Synchronous mets.	Chemotherapy	Radiotherapy	Doctor certification	Doctor years of work	Hospital region	Hospital type	Hospital volume	Surgeon volume
Aquina 2016	●	●	●	-	-	-	●	-	-	-	●	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	●	●	●
Baek 2013	●	-	●	●	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	●	-
Borowski 2010	●	-	●	-	-	-	-	●	●	-	-	-	-	-	-	-	●	-	●	-	-	-	-	-	-	-	-	-	-	-	●
Elferink 2010	●	-	●	-	-	-	-	-	-	-	●	-	-	-	-	-	●	-	-	-	●	-	-	-	-	-	-	●	●	●	-
El-Amrani 2018	●	-	●	-	-	-	●	-	-	-	●	-	-	-	-	-	-	-	●	-	-	-	-	●	-	-	-	-	-	●	-
Harling 2005	●	-	●	-	-	-	-	-	-	-	-	-	-	-	-	-	●	-	-	-	●	-	●	-	-	-	-	-	-	●	-
Hohenberger 2013	●	-	●	-	-	-	-	-	●	-	-	-	-	●	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	●
Kladny 2007	●	-	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	●	-	●	-	-	●	-	-	-	-	●	-	●
Kressner 2009	●	-	●	-	-	-	-	-	-	-	-	-	-	-	-	-	●	-	-	-	●	-	●	-	●	-	-	-		●	-
Manchon-Walsh 2011	●	●	●	-	-	-	-	●	-	-	●	-	-	-	-	-	●	-	-	-	●	-	●	-	-	-	-	-	-	●	-
Matthiessen 2006	●	-	●	-	-	-	-	-	-	-	-	●	●	-	-	-	●	-	-	-	●	-	●	-	-	-	-	-	-	●	-
Simunovic 2000	●	-	●	-	-	-	●	-	-	-	●	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	●	●	-

● *variable included; - variable not included; AEs: adverse events*

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

Quality assessment of clinical outcomes 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

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation.

Evidence statements

Clinical evidence statements

Outcomes by hospital volume of rectal cancer surgery

Critical outcomes

Positive resection margins

Hospital volume cut-off 1 to 9 cases/year

- Moderate quality evidence came from 2 population registry studies (N=113,694) none of which showed a clinically important difference in positive resection margins between high and low case volume hospitals when thresholds were set between 1 and 9 cases per year.

Hospital volume cut-off 10 to 19 cases/year

- Moderate quality evidence came from 1 population registry study (N=113,113) which showed no clinically important difference in positive resection margins between high and low case volume hospitals when the threshold was set between 10 and 19 cases per year.

Hospital volume cut-off 20 to 29 cases/year

- Moderate quality evidence came from 1 population registry study (N=113,113) which showed no clinically important difference between in positive resection margins high and low case volume hospitals when the threshold was set between 20 and 29 cases per year..

Per additional case

- Very low quality evidence from 1 population registry study (N=581) showed no clinically important difference in positive resection margins per additional case.

Overall survival

Hospital volume cut-off 1 to 9 cases/year

- Moderate quality evidence came from 3 population registry studies (N=4,903) none of which showed a clinically important difference in overall survival between high and low case volume hospitals when thresholds were set between 1 and 9 cases per year.

Hospital volume cut-off 10 to 19 cases/year

- Moderate quality evidence came from 4 population registry studies (N=7,894) 1 of which showed a clinically important difference in overall survival in favour of high case volume hospitals when thresholds were set between 10 and 19 cases per year.

Hospital volume cut-off 20 to 29 cases/year

- Moderate quality evidence from 4 population registry studies (N=10,405) none of which showed a clinically important difference in overall survival between high and low case volume hospitals when thresholds were set between 20 and 28 cases per year.

Hospital volume cut-off 30 to 39 cases/year

- Moderate quality evidence came from 4 population registry studies (N=16,021) 2 of which showed a clinically important difference in overall survival in favour of high case volume hospitals when thresholds were set between 30 and 39 cases per year.

Hospital volume cut-off 40 to 49 cases/year

- Moderate quality evidence came from a population registry study (N=7,441) which showed no clinically important difference in overall survival between high and low case volume hospitals when the threshold was set between 40 and 49 cases per year.

Hospital volume cut-off 50 to 59 cases/year

- Moderate quality evidence came from a population registry study (N=2,095) which showed no clinically important difference in overall survival between high and low case volume hospitals when the threshold was set between 50 and 59 cases per year.

Per additional case

- High quality evidence from 1 population registry study (N=1,469) showed no clinically important difference in overall survival years per additional case.

Perioperative complications – Grade 3 or 4 complications

Hospital volume cut-off 1 to 9 cases/year

- Very low quality evidence came from 1 population registry study (N=581) which showed no clinically important difference in Grade 3 or 4 complications between high and low case volume hospitals when the threshold was set between 1 and 9 cases per year.

Hospital volume cut-off 10 to 19 cases/year

- Moderate quality evidence came from 2 population registry studies (N=6,852) 1 of which showed a clinically important difference in Grade 3 or 4 complications in favour of high case volume hospitals when thresholds were set between 10 and 19 cases per year.

Hospital volume cut-off 20 to 29 cases/year

- Low quality evidence came from a population registry study (N=1,511) which showed no clinically important difference in Grade 3 or 4 complications between high and low case volume hospitals when the threshold was set between 20 and 29 cases per year.

Hospital volume cut-off 30 to 39 cases/year

- Moderate quality evidence came from 3 population registry studies (N=14,293) none of which showed a clinically important difference in Grade 3 or 4 complications between high and low case volume hospitals when thresholds were set between 30 and 39 cases per year.

Hospital volume cut-off 40 to 49 cases/year

- Moderate quality evidence came from a population registry study (N=7,441) which showed no clinically important difference in Grade 3 or 4 complications between high and low case volume hospitals when the threshold was set between 40 and 49 cases per year.

Hospital volume cut-off 50 to 59 cases/year

- Low quality evidence came from a population registry study (N=1,511) which showed no clinically important difference in Grade 3 or 4 complications between high and low case volume hospitals when the threshold was set between 50 and 59 cases per year.

Per additional case

- Very low quality evidence from 1 population registry study (N=581) showed no clinically important difference in Grade 3 or 4 complications per additional case.

Perioperative complications – Unplanned return to theatre

No evidence was identified to inform this outcome.

Important outcomes

Local recurrence

Hospital volume cut-off 1 to 9 cases/year

- Moderate quality evidence came from 2 population registry studies (N=2,799) none of which showed a clinically important difference in local recurrence between high and low case volume hospitals when thresholds were set between 1 and 9 cases per year.

Hospital volume cut-off 10 to 19 cases/year

- Moderate quality evidence came from 2 population registry studies (N=4,718) 1 of which showed a clinically important difference in local recurrence in favour of high case volume hospitals when thresholds were set between 10 and 19 cases per year.

Hospital volume cut-off 20 to 29 cases/year

- Moderate quality evidence came from 3 population registry studies (N=7,855) 1 of which showed a clinically important difference in local recurrence in favour of high case volume hospitals when thresholds were set between 20 and 29 cases per year.

Hospital volume cut-off 30 to 39 cases/year

- Moderate quality evidence came from 2 population registry studies (N=6,298) 1 of which showed a clinically important difference in local recurrence in favour of high case volume hospitals when thresholds were set between 30 and 39 cases per year.

Per case (hospital volumes not specified) – High versus low volume

- Moderate quality evidence from 1 population registry study (N=1,469) showed no clinically important difference in local recurrence per additional case.

Overall quality of life

No evidence was identified to inform this outcome.

Permanent stoma rates

Hospital volume cut-off 1 to 9 cases/year

- Moderate quality evidence came from 4 population registry studies (N=19,922) none of which showed a clinically important difference in permanent stoma rates between high and low case volume hospitals when thresholds were set between 1 and 9 cases per year.

Hospital volume cut-off 10 to 19 cases/year

- Moderate quality evidence came from 4 population registry studies (N=20,795) 3 of which showed a clinically important difference in permanent stoma rates in favour of high case volume hospitals when thresholds were set between 10 and 19 cases per year.

Hospital volume cut-off 20 to 29 cases/year

- Moderate quality evidence came from 2 population registry studies (N=15,055) none of which showed a clinically important difference in permanent stoma rates between high and low case volume hospitals when thresholds were set between 20 and 29 cases per year.

Hospital volume cut-off 30 to 39 cases/year

- Moderate quality evidence came from a population registry study (N=5,021) which showed no clinically important difference in permanent stoma rates between high and low case volume hospitals when the threshold was set between 30 and 39 cases per year.

Per additional case

- High quality evidence from 1 population registry study (N=4,622) showed no clinically important difference in permanent stoma rates per additional case.

Perioperative mortality

Hospital volume cut-off 1 to 9 cases/year

- Moderate quality evidence came from 3 population registry studies (N=14,584) 1 of which showed a clinically important difference in perioperative mortality in favour of high case volume hospitals when thresholds were set between 1 and 9 cases per year.

Hospital volume cut-off 10 to 19 cases/year

- Moderate quality evidence came from 10 population registry studies (N=79,714) 2 of which showed a clinically important difference in perioperative mortality in favour of high case volume hospitals when thresholds were set between 10 and 19 cases per year.

Hospital volume cut-off 20 to 29 cases/year

- Moderate quality evidence came from 4 population registry studies (N=41,519) none of which showed a clinically important difference in perioperative mortality between high and low case volume hospitals when thresholds were set between 20 and 29 cases per year.

Hospital volume cut-off 30 to 39 cases/year

- Moderate quality evidence came from 3 population registry studies (N=14,293) none of which showed a clinically important difference in perioperative mortality between high and low case volume hospitals when thresholds were set between 30 and 39 cases per year.

Hospital volume cut-off 40 to 49 cases/year

- Moderate quality evidence came from 2 population registry studies (N=53,010) 1 of which showed a clinically important difference in perioperative mortality in favour of high case volume hospitals when thresholds were set between 40 and 49 cases per year.

Hospital volume cut-off 50 to 59 cases/year

- Moderate quality evidence came from a population registry study (N=16,039) which showed no clinically important difference between high and low case volume hospitals when the threshold was set between 50 and 59 cases per year.

Outcomes by surgeon volume

Critical outcomes

Positive resection margins

Surgeon volume cut-off 1 to 4 cases/year

- Low quality evidence came from 2 population registry studies (N=1,609) none of which showed a clinically important difference in positive resection margins between high and low case volume surgeons when thresholds were set between 1 and 4 cases per year.

Surgeon volume cut-off 5 to 9 cases/year

- Low quality evidence came from a population registry study (N=1,028) which showed a clinically important difference in positive resection margins in favour of high case volume surgeons when the threshold was between 5 and 9 cases per year.

Overall survival

Surgeon volume cut-off 5 to 9 cases/year

- Low quality evidence came from 2 population registry studies (N=807) none of which showed a clinically important difference in overall survival in positive resection margins between high and low case volume surgeons when thresholds were set between 5 and 9 cases per year.

Surgeon volume cut-off 10 to 14 cases/year

- Moderate quality evidence came from a population registry study (N=7,441) which showed a clinically important difference in overall survival in favour of high case volume surgeons when the threshold was between 10 and 14 cases per year.

Surgeon volume cut-off 20 to 24 cases/year

- Moderate quality evidence came from a population registry study (N=7,441) which showed no clinically important difference in overall survival between high and low case volume surgeons when the threshold was set between 20 and 24 cases per year.

Perioperative complications – Grade 3 or 4 complications

Surgeon volume cut-off 1 to 4 cases/year

- Moderate quality evidence came from 2 population registry studies (N=1,609) none of which showed a clinically important difference in Grade 3 or 4 complications between high and low case volume surgeons when thresholds were set between 1 and 4 cases per year.

Surgeon volume cut-off 5 to 9 cases/year

- Moderate quality evidence came from 2 population registry studies (N=15,861) 1 of which showed a clinically important difference in Grade 3 or 4 complications in favour of high case volume surgeons when thresholds were set between 5 and 9 cases per year.

Surgeon volume cut-off 10 to 14 cases/year

- Moderate quality evidence came from a population registry study (N=7,441) which showed no clinically important difference in Grade 3 or 4 complications between high and low case volume surgeons when the threshold was set between 10 and 14 cases per year.

Surgeon volume cut-off 20 to 24 cases/year

- Moderate quality evidence came from a population registry study (N=7,441) which showed a clinically important difference in Grade 3 or 4 complications in favour of high case volume surgeons when the threshold was between 20 and 24 cases per year.

Per additional case

- Very low quality evidence from 1 population registry study (N=581) showed no clinically important difference in Grade 3 or 4 complications per additional case.

Perioperative complications – Unplanned return to theatre

Surgeon volume cut-off 5 to 9 cases/year

- Moderate quality evidence from 1 population registry study (N=14,833) showed no clinically important difference in unplanned return to theatre between high and low case volume surgeons when the threshold was set between 10 and 14 cases per year.

Important outcomes

Local recurrence

Surgeon volume cut-off 5 to 9 cases/year

- Moderate quality evidence came from a population registry study (N=521) which showed a clinically important difference in local recurrence in favour of high case volume surgeons when the threshold was between 5 and 9 cases per year.

Overall quality of life

No evidence was identified to inform this outcome.

Permanent stoma rates

Surgeon volume cut-off 5 to 9 cases/year

- Low quality evidence came from a population registry study (N=521) which showed a clinically important difference permanent stoma rate in favour of high case volume surgeons when the threshold was between 5 and 9 cases per year.

Surgeon volume cut-off 10 to 14 cases/year

- Moderate quality evidence came from a population registry study (N=7,798) which showed no clinically important difference in permanent stoma rate between high and low case volume surgeons when the threshold was set between 10 and 14 cases per year.

Perioperative mortality

Surgeon volume cut-off 1 to 4 cases/year

- Low quality evidence came from a population registry study (N=1,028) which showed no clinically important difference in perioperative mortality between high and low case volume surgeons when the threshold was set between 1 and 4 cases per year.

Surgeon volume cut-off 5 to 9 cases/year

- Low quality evidence came from a population registry study (N=1,028) which showed no clinically important difference in perioperative mortality between high and low case volume surgeons when the threshold was set between 5 and 9 cases per year.

Surgeon volume cut-off 10 to 14 cases/year

- Moderate quality evidence came from 2 population registry studies (N=15,239) 1 of which showed a clinically important difference in perioperative mortality in favour of high case volume surgeons when thresholds were set between 10 and 14 cases per year.

Surgeon volume cut-off 20 to 24 cases/year

- Moderate quality evidence came from a population registry study (N=7,441) which showed no clinically important difference in perioperative mortality between high and low case volume surgeons when the threshold was set between 20 and 24 cases per year.

Economic evidence statements

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

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

Resection margins were a critical outcome because they indicate the achievement of a curative resection, which is associated with lower morbidity, mortality and improved postoperative quality of life. Overall survival at 5 years was also a critical outcome for decision making because it indicates how likely a patient is to survive after surgery for primary or recurrent rectal cancer. Perioperative complications, including grade 3 or 4 complications and unplanned return to theatre, were considered critical outcomes because they can impact a patient's postoperative quality of life.

Local recurrence, overall quality of life, permanent stoma rates, and perioperative mortality were considered important outcomes. Local recurrence was considered an important outcome because local recurrence suggests ineffective treatment of the disease, potentially requiring further treatment. Overall quality of life was an important outcome because of the impact and potential long-term adverse effects of surgical interventions on patients. Permanent stoma rates were also considered important outcomes because of the effect a permanent stoma can have on a person's quality of life. Perioperative mortality was considered an important outcome for decision making because it can indicate the success and safety of the operation.

The quality of the evidence

Evidence was available that compared the effect of hospital volume and surgeon volume, respectively, on outcomes for rectal cancer surgery. Evidence was available for all of the outcomes except quality of life.

The quality of the evidence was assessed using modified GRADE and varied from very low to high quality. The key methodological limitation was that in most studies case volume (a continuous outcome) was dichotomised for analysis using various arbitrary thresholds, reducing the statistical power to detect a relation between case volume and patient outcome. In some studies patient characteristics were not well reported, attrition not accounted for or outcome measurement not described. There was also imprecision for some of the rarer outcomes, such as perioperative mortality or surgical complications, especially for the studies of surgeon case volume. There were additional complexities with surgeon-level data (i.e. consultants may do more complex surgeries, but fewer of them, and a consultant might be involved with other surgeries but not be the named surgeon) as well as with hospital-level data (i.e. old, international data with inconsistent staging across studies). As a result the committee were cautious in their interpretation of the evidence.

Benefits and harms

Due to differences between studies in the variables used for case-mix adjustment, effect estimates could not be pooled, however wherever clinically significant effects were seen in studies they favoured higher case volume hospitals or surgeons. There was some evidence

that when the threshold is set between 10 and 20 rectal cancer surgery cases per year higher volume hospitals have better outcomes than lower volume hospitals in terms of overall survival, local recurrence, permanent stoma rates and perioperative mortality. Similarly there was some evidence of benefit with a surgeon case volume threshold of between 5 and 10 cases per year in terms of resection margins, local recurrence and permanent stoma rates. Setting these minimum threshold levels could lead to patients living longer and experiencing fewer complications.

An audit of rectal cancer surgeries in the UK has indicated that the majority of hospitals in the UK perform at least 20 cases of rectal cancer surgery per year. However, given the uncertainties in the data, the committee agreed that the evidence was not strong enough to recommend a minimum cut-off of 20 cases a year, as doing so would have a large effect on those hospitals that are currently performing less than 20 cases a year.

The committee recognised that the reorganisation of services could result in some people having to travel further to attend treatment.

Cost effectiveness and resource use

Given that the majority of hospitals in the UK currently perform at least 20 rectal cancer surgeries per year, the recommendation for a minimum threshold of 10 cases per year at a hospital-level will not have a large impact on current practice. Based on their clinical knowledge, the committee were aware that some surgeons in the UK currently undertake fewer than 5 cases per year so the recommendation that surgeons perform at least 5 cases a year could have an impact on these surgeons. The centralisation of surgeons with fewer surgeons performing more cases will have related staffing and resource costs.

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1 Appendices

2 Appendix A – Review protocol

3 Review protocol for review question: Is there a relationship between 4 surgical volumes and outcomes in the treatment of rectal cancer 5 (primary and recurrent disease)?

6 **Table 9: Review protocol for relationship between surgical volumes and** 7 **outcomes in the treatment of rectal cancer (primary and recurrent** 8 **disease).**

Field (based on PRISMA-P)	Content
Review question in guideline	Is there a relationship between surgical volumes and outcomes in the treatment of rectal cancer (primary and recurrent disease)?
Type of review question	Prognostic
Objective of the review	To determine if is there a relationship between surgical volumes and outcomes in the treatment of rectal cancer (primary and recurrent disease).
Eligibility criteria – population/disease/condition/issue/domain	Adults with primary or recurrent rectal cancer undergoing surgery Sub-stratifications (analysed separately): • Primary rectal cancer • Recurrent rectal cancer Exclusion: people undergoing surgery for colorectal cancer unless data for people with rectal cancer can be extracted separately. Rectal cancer defined as any tumour within 15 cm from the anal verge, excluding the anal canal.
Eligibility criteria – intervention(s)/exposure(s)/prognostic factor(s)	**Predictors** Rectal cancer surgery volume: • By hospital • By surgeon Definition of volume as defined by the study. For example, the number of surgeries performed in a specific time period (1 year for example) by a surgeon or in a hospital. Surgery volume categorised into low, medium or high volume, as defined by the study.
Eligibility criteria – comparator(s)/control or reference (gold) standard	Not applicable
Outcomes and prioritisation	**Critical:**

Field (based on PRISMA-P)	Content

	• Resection margins (MID: statistical significance)
	• Overall survival at 5 years (MID: statistical significance)
	• Perioperative complications
	  ○ Grade 3 or 4 complications (MID: statistical significance)
	  ○ Unplanned return to theatre (MID: statistical significance)
	
	Important:
	• Local recurrence (MID: statistical significance)
	• Overall quality of life measured using validated scales (MID: from literature, see further down this document)
	• Permanent stoma rates (MID: statistical significance)
	• Perioperative mortality (MID: statistical significance)
	
	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 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 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 cohort studies • Population-based registry studies • Prospective or retrospective comparative cohort studies
Other inclusion exclusion criteria	Inclusion: • English-language • All settings will be considered that consider medications and treatments available in the UK • Studies published post-2000 Studies conducted post-2000 will be considered for this review question because the guideline committee considered that treatment techniques have evolved and evidence prior to 2000 would no longer be relevant.

Field (based on PRISMA-P)	Content
Proposed sensitivity/sub-stratification analysis, or meta-regression	All studies should include multivariate analysis controlling for the following confounding factors: • Age of patient or performance status • Primary or recurrent cancer • Tumour characteristics (TNM stage, location) • Preoperative radiotherapy and/or Chemotherapy • Surgical procedure (sphincter preservative or not) • Emergency or elective surgery • Sex • Deprivation • Ethnicity
Selection process – duplicate screening/selection/analysis	The quality of the evidence will be assessed on a per study basis using the tools specified in the Methods for assessing bias at outcome/study level section of the protocol. 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. 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)	Analyses will be performed using Cochrane Review Manager (RevMan5) where possible (for example, if studies have adjusted for the same confounding factors). 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 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

Field (based on PRISMA-P)	Content
	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: • CHARMS checklist for systematic reviews of risk prediction modelling studies • QUIPS tool for prognostic factor studies • PROBAST tool for risk prediction modelling studies • CASP checklist for clinical prediction rule The quality of the evidence for an outcome (i.e. across studies) will be assessed using GRADE. The certainty in the evidence was evaluated for each outcome using an adaptation of 'Grading of Recommendations Assessment, Development and Evaluation (GRADE)' methodology (see methods supplement).
Criteria for quantitative synthesis (where suitable)	For details please see section 6.4 of Developing NICE guidelines: the manual
Methods for analysis – combining studies and exploring (in)consistency	Synthesis of data: Odds ratios and hazard ratios will be calculated where appropriate. Minimally important differences: 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.
Assessment of confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual
Rationale/context – Current management	For details please see the introduction to the evidence review.

Field (based on PRISMA-P)	Content
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.
Sources of funding/support	The NGA is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists
Name of sponsor	The NGA is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists
Roles of sponsor	NICE funds the NGA to develop guidelines for those working in the NHS, public health, and social care in England
PROSPERO registration number	Not registered

CASP: Critical Appraisal Skills Programme; CCTR: Cochrane controlled trials register; CDSR: Cochrane database of systematic reviews; CHARMS: Checklist for critical appraisal and data extraction for systematic Reviews of prediction Modelling Studies; DARE: Database of Abstracts of Reviews of Effects; EQ-5D: EuroQol five dimensions questionnaire; EORTC QLQ-C30: European Organisation for Re-search 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);GRADE: Grading of Recommendations Assessment, Development and Evaluation; HTA: Health Technology Assessment; NGA: National Guideline Alliance; NHS: National Health Service; NICE: National Institute for Health and Clinical Excellence; PRISMA-P: Preferred Reporting Items for Systematic reviews and Meta-Analysis Protocols; PROBAST: Prediction model Risk Of Bias Assessment Tool; PROSPERO: International prospective register of systematic reviews; QUIPS: Quality in Prognosis Studies; SF-12: 12-Item Short Form Survey; SF-36: 36-Item Short Form Survey; TNM: tumour, node, metastasis

1 Appendix B – Literature search strategies

2 Literature search strategies for review question: Is there a relationship between 3 surgical volumes and outcomes in the treatment of rectal cancer (primary and 4 recurrent disease)?

5 Databases: Embase/Medline

6 Last searched on: 12/02/2019

#	Search
1	exp rectum tumor/ use emez
2	exp rectal neoplasms/ use ppez
3	((rectal or rectum) adj3 (adenocarcinoma* or cancer* or carcinoma* or malignan* or neoplas* or oncolog* or tumo?r*)).tw.
4	or/1-3
5	exp surgical procedures, operative/ use ppez or surgery/ use emez
6	(excis* or resect* or surg*).tw.
7	or/5-6
8	4 and 7
9	hospital volume/ use emez
10	surgeon volume/ use emez
11	hospitals/
12	workload/
13	caseload/ use emez
14	high volume hospital/ use emez
15	low volume hospital/ use emez
16	Hospitals, high-volume/ use ppez
17	hospitals, Low-volume/ use ppez
18	((low* or high* or medium or mid) adj3 volume?).tw.
19	(caseload? or case load? or service load? or workload? or work load?).tw.
20	((case or center or center level or centre level or doctor? or hospital? or individual? or medical practitioner or operator? or personal or physician? or private or provider? or procedural or service? or surgeon? or surger* or surgical) adj2 volume?).tw.
21	(volume? adj2 (standard? or outcome?)).tw.
22	or/9-21
23	8 and 22
24	Letter/ use ppez
25	letter.pt. or letter/ use emez
26	note.pt.
27	editorial.pt.
28	Editorial/ use ppez
29	News/ use ppez
30	exp Historical Article/ use ppez
31	Anecdotes as Topic/ use ppez
32	Comment/ use ppez
33	Case Report/ use ppez
34	case report/ or case study/ use emez
35	(letter or comment*).ti.
36	or/24-35
37	randomized controlled trial/ use ppez
38	randomized controlled trial/ use emez
39	random*.ti,ab.
40	or/37-39

#	Search
41	36 not 40
42	animals/ not humans/ use ppez
43	animal/ not human/ use emez
44	nonhuman/ use emez
45	exp Animals, Laboratory/ use ppez
46	exp Animal Experimentation/ use ppez
47	exp Animal Experiment/ use emez
48	exp Experimental Animal/ use emez
49	exp Models, Animal/ use ppez
50	animal model/ use emez
51	exp Rodentia/ use ppez
52	exp Rodent/ use emez
53	(rat or rats or mouse or mice).ti.
54	or/41-53
55	23 not 54
56	limit 55 to (yr="2000 - current" and english language)
57	remove duplicates from 56

1 **Database: Cochrane Library**

2 Last searched on: 12/02/2019

#	Search
1	MeSH descriptor: [Rectal Neoplasms] explode all trees
2	((rectal or rectum) near/3 (adenocarcinoma* or cancer* or carcinoma* or malignan* or neoplas* or oncolog* or tumo?r*)):ti,ab,kw
3	#1 or #2
4	MeSH descriptor: [Surgical Procedures, Operative] explode all trees
5	(excis* or resect* or surg*):ti,ab,kw
6	#4 or #5
7	#3 and #6
8	MeSH descriptor: [Hospitals] this term only
9	MeSH descriptor: [Workload] explode all trees
10	MeSH descriptor: [Hospitals, High-Volume] this term only
11	MeSH descriptor: [Hospitals, Low-Volume] this term only
12	((low* or high* or medium or mid) near/3 volume?):ti,ab,kw
13	(caseload? or case load? or service load? or workload? or work load?):ti,ab,kw
14	((case or center or center level or centre level or doctor? or hospital? or individual? or medical practitioner or operator? or personal or physician? or private or provider? or procedural or service? or surgeon? or surger* or surgical) near/2 volume?):ti,ab,kw
15	(volume? near/2 (standard? or outcome?)):ti,ab,kw
16	{or #8-#15}
17	#7 and #16 Publication Year from 2000 to 2018

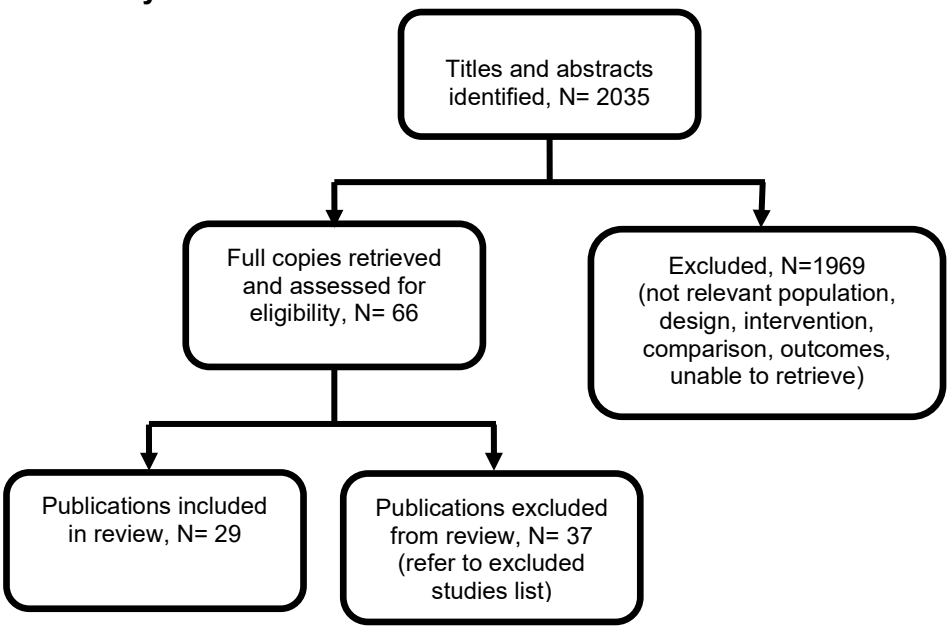
3

4

1 Appendix C – Clinical evidence study selection

2 Clinical study selection for review question: Is there a relationship between 3 surgical volumes and outcomes in the treatment of rectal cancer (primary and 4 recurrent disease)?

Figure 1: Study selection flow chart



5

Appendix D – Clinical evidence tables

Clinical evidence tables for review question: Is there a relationship between surgical volumes and outcomes in the treatment of rectal cancer (primary and recurrent disease)?

Table 10: Clinical evidence tables

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Aquina, C. T., Probst, C. P., Becerra, A. Z., Iannuzzi, J. C., Kelly, K. N., Hensley, B. J., Rickles, A. S., Noyes, K., Fleming, F. J., Monson, J. R. T., High volume improves outcomes: The argument for centralization of rectal cancer surgery, Surgery (United States), 159, 736-748, 2016 **Ref Id** 865104 **Country/ies where the study was carried out** USA **Study type** Retrospective population based registry study **Aim of the study**	**Sample size** n=7798 **Characteristics** Non-HVS and/or non-HVH, n=6496 Age, years, n < 65= 3079 65-79= 2583 ≥ 80=879 Male, n=3722 Distant metastasis, n=710 Operative characteristics, n Low anterior resection=4042 Abdominoperineal resection=2454 Ileostomy=1107 Colostomy=3227 Surgeon board-certification status, n General surgery=4220 Colorectal surgery=2276 Hospital characteristics Academic=2920 Urban= 6012 HVS and/or HVH, n=1302 Age, years, n < 65=798	**Interventions** Total number of hospitals /units= Total number of surgeons= Individual surgeon and hospital volumes were calculated as the average number of rectal cancer resections performed during each of 3 time periods from 2000–2003, 2004– 2007, and 2008–2011. Procedure volume was categorized as non-high-volume surgeons (non-HVSs) at non high- volume hospitals (non-HVHs), high-volume surgeon (HVS) only, high-volume hospital (HVH) only, and HVSs at HVHs. non-HVS < 10 resections/year non-HVH= < 25 resections/year HVS= ≥ 10 resections/year HVH= ≥ 25 resections/year	**Details** Data collection: The study collected data from the Statewide Planning and Research Cooperative System (SPARCS) which abstracted data from medical records. Prognostic factors controlled for: age, sex, race, insurance type, Elixhauser comorbidities previously validated for mortality prediction, and type of operation (LAR vs APR).26 In addition to surgeon volume, the American Medical Association/American Board of Medical Specialties database was used to obtain information regarding physician board certification in Surgery or Colorectal Surgery as well as years since completion of residency or fellowship training. Hospital characteristics included major academic status based on the Council of Teaching Hospitals designation and location (urban vs rural). Outcomes: nonrestorative proctectomy and 30-day postoperative mortality	**Results** Perioperative mortality: surgeon vol. NR-10 vs 10-NR cases p.a. OR 0.72 (0.32 to 1.62) Perioperative mortality: hospital vol. NR-25 vs 25-NR cases p.a. OR 1.06 (0.52 to 2.15) Stoma rate: surgeon vol. NR-10 vs 10-NR cases p.a. OR 0.84 (0.6 to 1.17) Stoma rate: hospital vol. NR-25 vs 25-NR cases p.a. OR 0.86 (0.7 to 1.05)	**Limitations** Quality of the study assessed with the QUIPS checklist for prognostic factor studies 1. Study participation: Low risk 2. Study attrition: Low risk 3. Prognostic factor measurement: Low risk 4. Outcome measurement: Low risk 5. Study confounding: Low risk 6. Statistical analysis reporting: Low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
To assess the relationship between case volume and the postoperative outcomes of restorative proctectomy and 30-day mortality **Study dates** 2000-2011 **Source of funding** Not reported	65-79=407 ≥ 80=97 Male, n=766 Distant metastasis, n=346 Operative characteristics, n Low anterior resection=984 Abdominoperineal resection=318 Ileostomy=592 Colostomy=391 Surgeon board-certification status, n General surgery=615 Colorectal surgery=687 Hospital characteristics Academic=1300 Urban=1302 **Inclusion criteria** Elective admissions associated with a primary or secondary diagnosis of rectal cancer. Patients older than 18 years of age who underwent low anterior resection (LAR; ICD-9 = 48.62–48.63) or abdominoperineal resection (APR; ICD-9 = 48.5) between 2000 and 2011 were selected. **Exclusion criteria** Patients with a diagnosis of rectosigmoid cancer (ICD-9 = 154.0, 154.8). patients who underwent pull-through resection (ICD-9 = 48.4),		Follow up: 1 year follow up to determine permanent colostomy status Data analysis: Clinically appropriate variables with P < .1 were entered in multivariable analysis. To account for clustering by surgeon and hospital, a 3-level, generalized estimating equation model with a logistic link function was used to assess factors associated with nonrestorative proctectomy and 30-day mortality		**Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	transsacral resection (ICD- 9 = 48.61), or posterior resection (ICD-9 = 48.64) were excluded. Further exclusion criteria included urgent/emergent admission, patients with a permanent address outside of NY State, a concurrent diagnosis of rectosigmoid cancer (ICD-9 = 154.0), anal cancer (ICD-9 = 154.2, 154.3), or a carcinoid tumor (ICD-9 = 209.17), a missing unique surgeon identifier, and no surgeon board-certification match within the database of the American Medical Association Physician Masterfile and American Board of Medical Specialties.				
Full citation Archampong, David, Borowski, David, Wille-Jørgensen, Peer, Iversen, Lene H, Workload and surgeon´s specialty for outcome after colorectal cancer surgery, Cochrane Database of Systematic Reviews, 2012 **Ref Id** 624820 **Country/ies where the study was carried out** N/A	**Sample size** **Of relevant studies:** **Borowski 2010** n= 7411 **Harling 2005** n= 5021 **Hodgson 2003** n=7257 **Kressner 2009** n= 10425 **Manchon-Walsh 2011** n=1831 **Meyerhardt 2004** n=1330 **Ptok 2007** n= 1557 **Simunovic 2000** n= 1072 **Wibe 2005**	**Interventions** **Of relevant studies:** **Borowski 2010** Total number of hospitals /units=17 Total number of surgeons=140 Hospital volume LV=<87 MV=87-109 HV=>109 Surgeon volume LV=<27 MV=27-40 HV=>40 **Harling 2005** Total no of hospitals=53 Caseload defined as average annual number of rectal	**Details** **Of relevant studies:** **Borowski 2010** Methods: prospective population based registry study (UK) Prognostic factors adjusted for: sex, age, stage, comorbidity and presentation Outcomes: Overall five year survival, 30 day and inpatient mortality, anastomotic leak rate, permanent stoma rate **Harling 2005** Methods: Retrospective population based registry study (Denmark) Prognostic factors adjusted for: sex, age and tumour height Outcomes: Overall five year survival (Not included in case mix	**Results** See evidence table rows for: • Borowski 2010 • Harling 2005 • Hodgson 2003 • Kressner 2009 • Manchon-Walsh 2011 • Meyerhardt 2004 • Ptok 2007 • Simunovic 2000 • Wibe 2005	**Limitations** See individual study for quality assessment **Other information** Quality appraisal performed with the CHARMS checklist for systematic reviews of prediction models 1) Participants: Low risk 2) Outcome(s) to be predicted: Low risk 3) Candidate predictors: Low risk 4) Sample size: Low risk 5) Missing data: Low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study type Cochrane systematic review **Aim of the study** The aim of the review was to assess the effects of hospital volume, surgeon caseload and specialisation on the outcomes of colorectal, colon and rectal cancer surgery. **Study dates** Electronic search from January 1990 to September 2011 **Source of funding** Not reported	n= 3388 **Characteristics Of relevant studies:** **Borowski 2010** Patient characteristics according to volume groups LV, MV, HV Surgeon volume Sex M=57.1%, 57.7%, 57.5% F=42.9%, 42.3%, 42.5% Age (years) <65= 26.4%, 29.6%, 30.5% 65-74= 35.8%, 35.1%, 36.2% 75-84= 31.2%, 28.2%, 28.2% 85+= 6.6%, 7.2%, 5.1% Tumour stage (Dukes') A= 11.4%, 15.2%, 16.4% B= 30.8%, 32.0%, 31.3% C= 27.5%, 26.2%, 26.7% D=21.7%, 18.3%, 17.3% No resection=6.6%, 6.2%, 5.9% Unknown=2.1%, 2.1%, 2.4% **Harling 2005** Patient characteristics according to volume/caseload groups LV, MV, HV Tumour stage (Dukes') A=15%, 15.1%, 12.9% B= 28.1%, 28.6%, 30.7% C= 29.6%, 26.5%, 27% D=15.8%, 19.3%, 17.7% **Hodgson 2003** Patient characteristics according to volume/caseload groups LV, MV, HV, VHV	cancer procedures Hospital volume LV=<15 MV=15-30 HV=>30 **Hodgson 2003** Total number of hospitals=367 Caseload defined as average annual number of rectal cancer operations performed in a year Hospital volume LV=<7 MV= 7-13 HV= 14-20 VHV= >20 **Kressner 2009** All hospitals in Sweden Caseload defined as average annual number of procedures in a year Hospital volume LV=<11 MV=11-25 HV=>25 **Manchon-Walsh 2011** Total no of hospitals=51 Caseload defined as number of procedures in a year Hospital volume LV=<11 MV=12-30 HV=>30 **Meyerhardt 2004** Total number of hospitals /units=646 Caseload not derived from study but from medicare data Hospital volume	adjustments), 30 day mortality, anastomotic leak rate, permanent stoma rate **Hodgson 2003** Methods: Retrospective population based registry study (USA) Prognostic factors adjusted for: sex, age, race, comorbidity, deprivation, tumour site, stage and number of examined lymph nodes Outcomes: 30 day mortality, permanent stoma rate **Kressner 2009** Methods: Prospective population based registry study (Sweden) Prognostic factors adjusted for: sex, age, stage and radiotherapy Outcomes: Overall five year survival, 30 day mortality (Not included in case mix adjustments), Five year local recurrence rate (Not included in case mix adjustments), anastomotic leak rate **Manchon-Walsh 2011** Methods: Retrospective population based registry study (Spain) Prognostic factors adjusted for: sex, age, stage, comorbidity and presentation Outcomes: 30 day mortality, anastomotic leak rate (Not included in case mix adjustments), permanent stoma rate (Not included in case mix adjustments) **Meyerhardt 2004** Methods: Selected cohort for chemotherapy trial 0114 (USA) Prognostic factors adjusted for: sex, age, stage, harvested lymph nodes, comorbidity, presentation,		6) Model development: Low risk 7) Model performance: Unclear risk (did not discuss calibration measures (calibration plot, Hosmer-Lemeshow test) or discrimination (e.g. log-rank) measures with confidence intervals 8) Model evaluation: Unclear risk (did not discuss methods for testing model performance such as using a developmental dataset or separate external validation) 9) Results: Low risk 10) Interpretation and discussion: Low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	Hospital volume Sex M=54.7%, 57.4%, 55.3%, 54.8% F=45.3%, 42.6%, 44.7%, 45.2% Median age (years) (range) 68.7 (61-78), 68.8 (61-78), 67.5 (60-77), 67.6 (60-76) Tumour stage (AJCC) I= 31.6%, 33.6%, 36.0%, 34.4% II= 36.7%, 34.0%, 31.7%, 31.3% III= 31.7%, 32.4%, 32.3%, 34.4% **Kressner 2009** Patient characteristics according to volume/caseload groups LV, MV, HV Hospital volume Sex M=60%, 57%, 57% F=40%, 43%, 43% Mean age (years) 70.4, 69.6, 69.4 Tumour stage (UICC) Stage 1=22%, 23%, 23% Stage 2=35%, 32%, 31% Stage 3= 30%, 33%, 31% Stage 4=12%, 11%, 13% Missing= 1%, 1%, 2% **Manchon-Walsh 2011** Patient characteristics for entire cohort Hospital volume Sex M=65.2%, F=34.8% Median age (years)	LV=0-8 MV= 9-16 HV=17-92 **Ptok 2007** Total number of hospitals /units= 75 Caseload defined as average number of potentially curative low rectal resections in a year Hospital volume LV=<10 MV=10-19 HV=>19 **Simunovic 2000** Total no of hospitals=124 Caseload defined as average annual rectal cancer procedures in a year Hospital volume LV= <12 MV=12-17 HV=>17 **Wibe 2005** Total number of hospitals=54 Caseload defined as annual hospital volume Hospital volume LV=<10 MV=10-19 HV=20-29 VHV=>30	ethnicity, hospital volume and clustering Outcomes: Overall five year survival, five year local recurrence rate, APER rate **Ptok 2007** Methods: Prospective multicentre study (Germany) Prognostic factors adjusted for: stage, tumour perforation, procedure, and CRM (circumferential resection margin) Outcomes: Five year local recurrence rate, APER rate (Not included in case mix adjustments) **Simunovic 2000** Methods: Retrospective population based registry study (Canada) Prognostic factors adjusted for: sex, stage, comorbidity, procedure type, teaching hospital status for mortality. Referral to regional cancer centre added on for five year overall survival Outcomes: Overall five year survival, inpatient mortality **Wibe 2005** Methods: Prospective population based registry study (Norway) Prognostic factors adjusted: included sex, age, stage, grade and site Outcomes: Overall five year survival, 30 day mortality (Not included in case mix adjustments), five year local recurrence rate, anastomotic leak rate (Not included in case mix adjustments), APER rate (Not included in case mix adjustments)		

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	70 Tumour stage (UICC) 0=1.0% I=12.3% II=28.0% III=43.3% IV=7.4% Missing=8.1% **Meyerhardt 2004** Patient characteristics according to volume/caseload for entire rectal cancer cohort LV, MV, HV Hospital volume Sex M=62.4%, 64.7%, 65.6% F=37.6%, 35.3%, 34.4% Mean age (years), 60.1%, 60.7%, 62.1% T stage T0, T1, T2=15.4%, 15.8%, 14.8% T3=73.2%, 76.8%, 77.2% T4= 11.4%, 7.4%, 8.0% N stage N0= 32.9%, 32.1%, 30.8% N1=44.5%, 41.7%, 46.0% N2=22.6%,26.2%, 24.0% **Ptok 2007** Patient characteristics according to volume/caseload groups LV, MV, HV Hospital volume Sex M=60.5%, 60.8% 62.7%, F=39.5%, 39.2%, 37.3% Median age (years) 67.0, 66.0, 65.0 Tumour stage (UICC) I= 33.0%, 35.2%, 33.0%				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	II= 25.9%, 26.0%, 32.2% III= 41.1%, 38.7%, 34.8% Comorbidity (ASA) 1=11.0%, 15.0%, 15.6% 2=51.1%, 54.3%, 57.9% 3=36.3%, 30.0%, 25.2% 4=1.6%, 0.7%, 1.3% **Simunovic 2000** Patient characteristics according to volume/caseload groups LV, MV, HV Hospital volume Sex M=64.5%, 63.0%, 61.8% F=35.5%, 37.0%, 38.2% Age (years) 20-59= 23.4%, 25.1%, 31.5% 60-69= 34.5%, 35.2%, 30.6% >70=42.1%, 39.7%, 37.9% **Wibe 2005** Patient characteristics according to volume/caseload groups LV, MV, HV, VHV Hospital volume Sex M=58.6%, 60.0%, 55.9%, 55.9% F=41.45, 40.0%, 44.1%, 44.1% Age(years) <60= 17.6%, 18%, 20.6%, 19.6% 60-69= 27.2%, 25.9%, 28.2%, 27% 70-79= 35.8%, 39.1%, 34.3%, 36.4% >80= 19.4%, 16.9%, 16.9%, 16.9% Tumour stage (Dukes') A= 26.2%, 28.2%, 30.6%,				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	32.3% B= 38%, 37.9%, 37.2%, 35.8% C= 35.8%, 33.9%, 32.2%, 31.9% Tumour grade/differentiation High= 6.6%, 10.1%, 5.4%, 7.4% Moderate= 79.2%, 72.6%, 78.3% 76.6% Low= 8.8%, 10.2%, 8.8%, 10.1% **Inclusion criteria** Non-randomised cohort and observational studies of patients with "a confirmed histological diagnosis of colorectal, colon and rectal cancer in prospective studies and patients with diagnostic codes for colorectal, colon and rectal cancer, derived from International classification of diseases, 9th Revision (ICD-9-CM) for retrospective studies." **Exclusion criteria** Not reported				
Full citation Atkinson, S. J., Daly, M. C., Midura, E. F., Etzioni, D. A., Abbott, D. E., Shah, S. A., Davis, B. R., Paquette, I. M., The effect of hospital volume on resection	**Sample size** n=113,113 **Characteristics** Negative margin, n=106,559 Male, %= 58.4	**Interventions** Volume quintiles were determined by taking 20th percentiles of cases per year. VLV= <6 cases per year LV= 7-10 cases per year MV= 8-15 cases per year HV=16-23 cases per year	**Details** Data collection: Data was collected from the National Cancer Data Base, which contains oncologic outcomes from 1500+ hospitals in the USA. Prognostic factors controlled for: age, race, and insurance	**Results** Positive surgical margins: hospital vol. NR-7 vs 7-11 cases p.a. OR 1.04 (0.93 to 1.15)	**Limitations** Quality of the study assessed with the QUIPS checklist for prognostic factor studies 1. Study participation: Low risk 2. Study attrition: Low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
margins in rectal cancer surgery, Journal of Surgical Research, 204, 22-28, 2016 **Ref Id** 865114 **Country/ies where the study was carried out** USA **Study type** Retrospective population registry study **Aim of the study** The aim of the study was to assess the variation in the rates of positive resection margins after surgery for rectal cancer **Study dates** 1998-2010 **Source of funding** No funding	Age, year, mean= 64.5 Charlson-Deyo score, % 0=77 1=18.1 2=4.9 Surgical procedure, %= Low anterior resection=66.1 LAR with coloanal anastomosis=7.0 APR=25.0 Pelvic exenteration=2.0 Facility type, %= Community cancer program=15.8 Comprehensive community cancer program=52.8 Academic or research program= 30.0 Other specified type of cancer program=1.4 Positive margin, n=6554 Male, n=59.5 Age, year, mean=64.9 Charlson-Deyo score, % 0=76.5 1=18.1 2=5.4 Surgical procedure, n= Low anterior resection=53.6 LAR with coloanal anastomosis=6.0 APR=35.8 Pelvic exenteration=4.5 Facility type, %= Community cancer program=16.9 Comprehensive community cancer program=53.6 Academic or research program= 28.5	VHV= > 24 cases per year.	status) were included in the patient risk score. Tumour variables included were pathologic tumour (T) stage, nodal (N) stage, radiation sequence, tumour grade, tumour size, and surgery performed. Outcomes: Surgical resection margin, defined as macroscopic residual tumour (R2), microscopic residual tumour (R1), or no residual tumour (R0) Follow up: Not reported Data analysis: Univariate analysis was conducted using logistic regression to identify patient, tumour, and hospital factors associated with positive resection margin. After determining patient and tumour factors associated with margin positivity, we combined these patient and tumour factors into a patient risk score.	Positive surgical margins: hospital vol. 11-16 vs 16-24 cases p.a. OR 0.88 (0.76 to 1.03) Positive surgical margins: hospital vol. 16-24 vs 24-NR cases p.a. OR 1.01 (0.86 to 1.18)	3. Prognostic factor measurement: Low risk 4. Outcome measurement: Low risk 5. Study confounding: Low risk 6. Statistical analysis reporting: Low risk **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	Other specified type of cancer program=1.1 **Inclusion criteria** Patients treated with low anterior resection, low anterior resection with coloanal anastomosis, abdominoperineal resection, or pelvic exenterations for stage I-III rectal cancer **Exclusion criteria** Patients who underwent a local excision or patients with a pathologic complete response to neoadjuvant chemoradiation (yPT0) were excluded from analysis. Hospitals with less than one surgical case per year				
Full citation Baek, J. H., Alrubaie, A., Guzman, E. A., Choi, S. K., Anderson, C., Mills, S., Carmichael, J., Dagis, A., Qian, D., Kim, J., Garcia-Aguilar, J., Stamos, M. J., Bening, L., Pigazzi, A., The association of hospital volume with rectal cancer surgery outcomes, International Journal of Colorectal Disease, 28, 191-196, 2013	**Sample size** n=7187 **Characteristics** By hospital volume Low, n=2364 Age, n < 65=828 ≥ 65=1279 Unknown=257 Male, n=1118 Medium, n=2686 Age, n	**Interventions** Hospital volume was categorized as low, medium, or high depending on the total number of rectal cancer operations performed during the 6-year period. Low-, middle-, and high-volume hospitals were defined as the completion of ≤30, 31–60, and >60 cancer operations, respectively, during the 6-year period.	**Details** Data collection: Data was collected from the California Office of Statewide Health Planning and Development database. Data for patients diagnosed with rectal cancer was assessed. Prognostic factors controlled for: age, gender, race, ethnicity, and surgery type Outcomes: Surgical morbidity, mortality (in hospital rate of death) and rates of sphincter-preserving surgery Follow up: Not reported	**Results** Perioperative mortality: hospital vol. 1-6 vs 6-11 cases p.a. OR 0.46 (0.27 to 0.78) Perioperative mortality: hospital vol. 6-11 vs 11-24 cases p.a. OR 0.98 (0.48 to 2.01)	**Limitations** Quality of the study assessed with the QUIPS checklist for prognostic factor studies 1. Study participation: Low risk 2. Study attrition: Low risk 3. Prognostic factor measurement: Low risk 4. Outcome measurement: Low risk 5. Study confounding: Low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Ref Id 865127 **Country/ies where the study was carried out** USA **Study type** Retrospective population registry study **Aim of the study** The aim of the study was to assess differences in surgical outcomes for patients with rectal cancer according to hospital volume **Study dates** 2000-2005 **Source of funding** Not reported	< 65=1036 ≥ 65=1393 Unknown=257 Male, n=1351 High, n=2137 Age, n < 65=870 ≥ 65=854 Unknown=413 Male, n=940 **Inclusion criteria** All patients diagnosed with rectal cancer who underwent surgery by low anterior resection or abdominoperineal resection **Exclusion criteria** Patients with colon or rectosigmoid cancer were excluded.		Data analysis: For univariate analysis, a Mantel–Haenszel chi-square test with ordered categories was performed. A multivariate logistic regression analysis was used to identify differences in mortality and sphincter preservation in relation to hospital volume controlling for confounders. Tests were two-sided and statistical significance was set at p <0.05.	Stoma rate: hospital vol. 1-6 vs 6-11 cases p.a. OR 0.88 (0.78 to 1.01) Stoma rate: hospital vol. 6-11 vs 11-24 cases p.a. OR 0.7 (0.59 to 0.83)	6. Statistical analysis reporting: Low risk **Other information**
Full citation Borowski, D. W., Bradburn, D. M., Mills, S. J., Bharathan, B., Wilson, R. G., Ratcliffe, A. A., Kelly, S. B., Northern Region Colorectal Cancer Audit,	**Sample size** See Cochrane review Archampong 2012 for study details **Characteristics**	**Interventions**	**Details**	**Results** Perioperative mortality: hospital vol. 14-34 vs 34-40 cases p.a. OR	**Limitations** Quality of the study assessed with the QUIPS checklist for prognostic factor studies

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Group, Volume-outcome analysis of colorectal cancer-related outcomes, The British journal of surgery, 97, 1416-1430, 2010 **Ref Id** 865186 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**	**Inclusion criteria** **Exclusion criteria**			0.86 (0.68 to 1.09) Perioperative mortality: hospital vol. 34-40 vs 40-71 cases p.a. OR 1.29 (0.97 to 1.71) Perioperative mortality: surgeon vol. 0.2-13.8 vs 13.8-22.3 cases p.a. OR 0.74 (0.58 to 0.93) Perioperative mortality: surgeon vol. 13.8-22.3 vs 22.3-29.2 cases p.a. OR 0.89 (0.67 to 1.18) Complications: hospital vol. 14-34 vs 34-40 cases p.a. OR 1.38 (0.93 to 2.04) Complications: hospital vol. 34-40 vs 40-71 cases p.a. OR 1.01 (0.64 to 1.61)	1. Study participation: Low risk 2. Study attrition: Low risk 3. Prognostic factor measurement: Low risk 4. Outcome measurement: Low risk 5. Study confounding: Low risk 6. Statistical analysis reporting: Low risk **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				Complications: surgeon vol. 0.2-13.8 vs 13.8-22.3 cases p.a. OR 0.97 (0.66 to 1.44) Complications: surgeon vol. 13.8-22.3 vs 22.3-29.2 cases p.a. OR 0.61 (0.37 to 0.99) Overall survival: surgeon vol. 0.2-13.8 vs 13.8-22.3 cases p.a. HR 0.88 (0.81 to 0.97) Overall survival: surgeon vol. 13.8-22.3 vs 22.3-29.2 cases p.a. HR 1.06 (0.95 to 1.17) Overall survival: hospital vol. 14-34 vs 34-40 cases p.a. HR 0.89 (0.82 to 0.96) Overall survival: hospital vol. 34-40 vs 40-71 cases p.a. HR 1.03 (0.94 to 1.14)	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Boyle. Jemma, Braun, Michael, Eaves, Elizabeth, Hill, Jim, Kuryba, Angela, Roe, Alison, Vallance, Abigail, Van der Meulen, Jan, Walker, Kate, National Bowel Cancer Audit Annual Report 2017 Version 2, 2017 **Ref Id** 893425 **Country/ies where the study was carried out** UK **Study type** Prospective registry study **Aim of the study** The aim of the audit is to measure the quality of care and outcomes of patients with bowel cancer in England and Wales. **Study dates** April 1, 2015- March 31 2016	**Sample size** N= 4622 **Characteristics** Patient characteristics reported by treatment type: No preop treatment recorded; long-course RT pre-surgery; short-course RT pre-surgery; other treatment pre-surgery N= 2817; 1232; 386; 188 Male sex, n= 1811; 788; 253; 122 Pre-treatment T-stage, n T1= 167; 4; 6; 1 T2= 1056; 127; 86; 30 T3= 1240; 860; 257; 110 T4= 149; 201; 22; 37 TX= 88; 5; 4; 2 T9= 117; 34; 11; 8 Pre-treatment N-stage, n N0= 1631; 254; 141; 58 N1= 774; 492; 146; 67 N2= 219; 433; 78; 52 Nx= 60; 14; 9; 2 N9= 133; 38; 12; 9 Pre-treatment M-stage, n M0= 2314; 1042; 312; 108 M1= 121; 67; 23; 60 Mx= 222; 78; 41; 9 M9= 160; 44; 10; 11 **Inclusion criteria**	**Interventions** Hospital volume assessed on a per additional case basis	**Details** Data collection: "All data for patients diagnosed with colorectal cancer from 1 April 2013 was submitted via NHS Digital's Clinical Audit Platform (CAP). Data is collected at the trust level in England and centrally from the Cancer Network Information System Cymru (CaNISC) system in Wales. Only patients with a new primary diagnosis of bowel cancer are included." Prognostic factors controlled for: age (modelled as age plus age-squared), sex, ASA grade, Charlson comorbidity score, mode of admission, TNM stage, site of tumour Outcomes: Permanent stoma rate Follow up: 1 year Data analysis: Multivariable logistic regression	**Results** Adjusted analysis for permanent stoma rate – OR 1.00 [1.00 to 1.01] per additional hospital case per annum	**Limitations** Quality of the study assessed with the QUIPS checklist for prognostic factor studies 1. Study participation: Low risk 2. Study attrition: Low risk 3. Prognostic factor measurement: Low risk 4. Outcome measurement: Low risk 5. Study confounding: Low risk 6. Statistical analysis reporting: Low risk **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Source of funding NHS England and Welsh Government	Patients with a new diagnosis of colorectal cancer during the study period **Exclusion criteria** Not reported				
Full citation Comber, H., Sharp, L., Timmons, A., Keane, F. B. V., Quality of rectal cancer surgery and its relationship to surgeon and hospital caseload: A population-based study, Colorectal DiseaseColorectal Dis, 14, e692-e700, 2012 **Ref Id** 625051 **Country/ies where the study was carried out** Ireland **Study type** Retrospective population registry study **Aim of the study** The aim of the study was to assess how surgeon and hospital caseload affect measures of quality in rectal cancer surgery	**Sample size** n=581 **Characteristics** Not reported **Inclusion criteria** People diagnosed with primary rectal cancer **Exclusion criteria** Patients not having resectional surgery and hospitals treating fewer than five cases (surgical or nonsurgical) in 2007	**Interventions** 'Caseload' was defined for both surgeon and hospital as the number of rectal cancers, regardless of the type of treatment, included in the audit.	**Details** Data collection: Data was collected from the Irish National Cancer Registry by 4 trained coders and entered into a database. Prognostic factors controlled for: Gender, age, stage and functional status at diagnosis Outcomes: Survival Follow up: Not reported Data analysis: The contribution of each variable to the model was tested using likelihood ratio testing. The impact of caseload and quality variables on survival was measured using Cox proportional hazard modelling, with a censoring date of 31 December 2008. Deaths due to all causes were included. Other factors were added stepwise and retained if they were significant ($P < 0.05$).	**Results** Complications: hospital vol. 1-2 vs 2-3 cases p.a. OR 1.02 (0.97 to 1.06) Complications: surgeon vol. 1-2 vs 2-3 cases p.a. OR 0.97 (0.91 to 1.03) Positive surgical margins: hospital vol. 1-2 vs 2-3 cases p.a. OR 0.99 (0.96 to 1.02) Positive surgical margins: surgeon vol. 1-2 vs 2-3 cases p.a. OR 0.99 (0.96 to 1.03)	**Limitations** Quality of the study assessed with the QUIPS checklist for prognostic factor studies 1. Study participation: High risk (patient characteristics not reported) 2. Study attrition: High risk (missing data was not accounted for) 3. Prognostic factor measurement: Low risk 4. Outcome measurement: High risk (did not adequately report primary outcome measurement) 5. Study confounding: Low risk 6. Statistical analysis reporting: Low risk **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study dates 1 January 2007 - 31 December 2007 **Source of funding** National Cancer Control Programme					
Full citation El Amrani, M., Clement, G., Lenne, X., Rogosnitzky, M., Theis, D., Pruvot, F. R., Zerbib, P., The Impact of Hospital Volume and Charlson Score on Postoperative Mortality of Proctectomy for Rectal Cancer: A Nationwide Study of 45,569 Patients, Ann SurgAnnals of surgery, 268, 854-860, 2018 **Ref Id** 918797 **Country/ies where the study was carried out** France **Study type** Cross-sectional observational study (cancer registry study)	**Sample size** N = 45,569 patients **Characteristics** 65% male, 76.5% were older than 60 years of age; Charlson score 0-2 (54%), 3 (14%), >=4 (32%); Surgery Proctectomy (98%), Coloproctectomy (1%) and Pelvectomy (1%) **Inclusion criteria** All patients undergoing proctectomy for rectal cancer in France between January, 2012 and December, 2016 were identified from the French national administrative prospective database for hospital care [Programme de Medicalisation des Systemes d'Information], which has discharge information from	**Interventions** Surgical procedures involving rectal surgery (proctectomy, coloproctectomy, and pelvectomy) by laparotomy or laparoscopic, for rectal cancer.	**Details** A multivariable logistic regression was performed to explain 90-day post-operative mortality with hospital volume, comorbidities, patient characteristics, and surgical conditions and complications. The variables included were: Charlson Comorbidity Score, sex, age, neoadjuvant chemotherapy, malnutrition, diabetes, obesity, metastasis, surgical procedure and approach (laparotomy or laparoscopy), and type of anastomosis. . Postoperative complications were identified as anastomotic fistula, septic complications, haemorrhage, and shock	**Results** Perioperative mortality: hospital vol. NR-10 vs 10-41 cases p.a. OR 0.69 (0.57 to 0.83) Perioperative mortality: hospital vol. 10-41 vs 41-NR cases p.a. OR 0.69 (0.57 to 0.83)	**Limitations** Quality of the study assessed with the QUIPS checklist for prognostic factor studies 1. Study participation: Low risk 2. Study attrition: Low risk 3. Prognostic factor measurement: Low risk 4. Outcome measurement: Low risk 5. Study confounding: Low risk 6. Statistical analysis reporting: Low risk **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Aim of the study To identify the impact of hospital volume according to Charlson Comorbidity Index on postoperative mortality after rectal cancer surgery **Study dates** 2012 to 2016 **Source of funding** Not reported	public and private French hospitals. **Exclusion criteria** Hospital episodes with incorrect patient identification; patients younger than 18 years and foreign patients were excluded from the analysis				
Full citation Elferink, M. A. G., Krijnen, P., Wouters, M. W. J. M., Lemmens, V. E. P. P., Jansen-Landheer, M. L. E. A., Van De Velde, C. J. H., Langendijk, J. A., Marijnen, C. A. M., Siesling, S., Tollenaar, R. A. E. M., Variation in treatment and outcome of patients with rectal cancer by region, hospital type and volume in the Netherlands, European Journal of Surgical Oncology, 36, S74-S82, 2010 **Ref Id**	**Sample size** n=16,039 **Characteristics** Male, n= 9384 Age at diagnosis, n < 60= 4209 60-74= 6966 75+= 4864 Clinical stage, n T0/IS-M0= 51 T1-M0=1384 T2/T3-M0=9393 T4-M0=1655 Tany-Nany-M1=2794 Unknown=762 Hospital of diagnosis, n General hospital=6721	**Interventions** Hospital volume was categorized into <25, 25-50 and >50 resections per year, including the resections of rectosigmoid tumours since rectosigmoid tumours are frequently resected by the same surgical technique as rectal tumours.	**Details** Data collection: Data was collected from the Netherlands Cancer Registry, pathological archive (PALGA), the Haematology Departments and the National Registry of Hospital Discharge Diagnosis by trained registers. Prognostic factors controlled for: age at diagnosis, gender, year of diagnosis, depth of invasion, nodal involvement, type of hospital of diagnosis, hospital volume and CCC-region on the odds of receiving preoperative radiotherapy (including preoperative chemoradiation) in patients with T2/T3-M0	**Results** Perioperative mortality: hospital vol. 9-25 vs 25-50 cases p.a. OR 0.7 (0.44 to 1.14) Perioperative mortality: hospital vol. 25-50 vs 50-92 cases p.a. OR 0.57 (0.24 to 1.34)	**Limitations** Quality of the study assessed with the QUIPS checklist for prognostic factor studies 1. Study participation: Low risk 2. Study attrition: Low risk 3. Prognostic factor measurement: Low risk 4. Outcome measurement: Low risk 5. Study confounding: Low risk 6. Statistical analysis reporting: Low risk **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
760755 **Country/ies where the study was carried out** the Netherlands **Study type** Retrospective population registry study **Aim of the study** The aim of the study was to assess treatment patterns and outcomes according to region, hospital type and volume among rectal cancer patients. **Study dates** 2001-2006 **Source of funding** Dutch Cancer Society	Teaching hospital for surgery=8326 University hospital=992 **Inclusion criteria** All patients with invasive rectal carcinoma, diagnosed between 2001 and 2006 **Exclusion criteria** Patients with diagnoses without histological confirmation, with diagnoses based only on autopsy findings, patients living abroad and patients with incomplete records		Outcomes: postoperative mortality (death within 30 days after surgery), survival Follow up: for survival - to death or to 1 January 2008. Data analysis: Logistic regression analysis was used to investigate the odds of postoperative mortality by age at diagnosis, gender, type of resection, type of hospital of surgery, hospital volume and CCC-region. Relative survival, an estimation of disease-specific survival, was calculated as the ratio of the observed rates in cancer patients to the expected rates in the general population using the Ederer method. p-value < 0.05 was statistically significant.		
Full citation Hagemans, J. A. W., Alberda, W. J., Verstegen, M., de Wilt, J. H. W., Verhoef, C., Elferink, M. A., Burger, J. W. A., Hospital volume and outcome in rectal cancer patients; results of a population-	**Sample size** 14050 patients with a cT1-3 tumour and 2104 patients with a cT4 tumour. Number of hospitals not reported. **Characteristics**	**Interventions** Rectal cancer surgery (low anterior-resection, abdominoperineal resection or proctocolectomy), with or without adjuvant therapy, with or without neoadjuvant therapy.	**Details** Cox-proportional hazards model was used for multivariable analysis of overall survival Available treatment related variables were: neoadjuvant treatment, adjuvant treatment, hospital volume based on number of rectal cancer resections per year, type of surgical procedure (low anterior-	**Results** Overall survival: hospital vol. 1-5 vs 5-10 cases p.a. HR 0.99 (0.81 to 1.22) Overall survival: hospital vol. 5-10 vs 10-NR cases	**Limitations** Quality of the study assessed with the QUIPS checklist for prognostic factor studies 1. Study participation: Low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
based study in the Netherlands, European Journal of Surgical Oncology., 2018 **Ref Id** 984250 **Country/ies where the study was carried out** The Netherlands **Study type** Cross sectional cancer registry study **Aim of the study** To evaluates the outcome of cT1-3 and cT4 rectal cancer according to hospital volume. **Study dates** 2005 to 2013 **Source of funding** Not reported	There were 14050 patients with cT1-3 rectal cancer: The majority had surgery in medium volume hospitals (62%), followed by high volume hospitals (21%) and low volume hospitals (17%). There were 2104 patients with cT4 rectal cancer: The majority of patients (60%) underwent surgery in low volume cT4 hospitals, followed by 25% in high volume hospitals and 15% in medium volume hospitals. **Inclusion criteria** Patients undergoing rectal cancer surgery (low anterior, resection, abdominoperineal resection or proctocolectomy) between 2005 and 2013 in the Netherlands were included from the National Cancer Registry. Hospitals were divided into low(1 to 20), medium(21 to 50) and high(>50 resections/year) volume for cT1-3 and low(1 to 4), medium(5 to 9) and high(10 resections/year) volume for cT4 rectal cancer. **Exclusion criteria** Patients with an unknown cT-stage were excluded from analysis, but were included in		resection, abdominoperineal resection or proctocolectomy). Involvement of circumferential resection margin (CRM) was available from 2008 onwards. Also included in the analysis were: age, gender, year of diagnosis, T-stage, N-stage, M-stage, tumour grade.	p.a. HR 0.87 (0.71 to 1.05)	2. Study attrition: Low risk 3. Prognostic factor measurement: Low risk 4. Outcome measurement: Low risk 5. Study confounding: Low risk 6. Statistical analysis reporting: Low risk **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	the determination of rectal cancer hospital volume.				
Full citation Harling, H., Bulow, S., Moller, L. N., Jorgensen, T., Burcharth, F., Baatrup, G., Christensen, H., Fenger, C., Gandrup, P., Jakobsen, A., Madsen, M. R., Nielsen, H. J., Rafaelsen, S., Rasmussen, O. O., Sorensen, J. B., Hospital volume and outcome of rectal cancer surgery in Denmark 1994-99, Colorectal Disease, 7, 90-95, 2005 **Ref Id** 865490 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**	**Sample size** See Cochrane review Archampong 2012 for study details **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results** Perioperative mortality: hospital vol. NR-15 vs 15-31 cases p.a. OR 1.02 (0.8 to 1.3) Perioperative mortality: hospital vol. 15-31 vs 31-NR cases p.a. OR 1.04 (0.81 to 1.33) Complications: hospital vol. NR-15 vs 15-31 cases p.a. OR 1.31 (0.71 to 2.39) Complications: hospital vol. 15-31 vs 31-NR cases p.a. OR 1.23 (0.8 to 1.85) Stoma rate: hospital vol. NR-15 vs 15-31 cases p.a. OR 0.44 (0.3 to 0.67)	**Limitations** Quality of the study assessed with the QUIPS checklist for prognostic factor studies 1. Study participation: Unclear risk (did not discuss methods to identify the sample sufficient to limit potential bias; did not report inclusion/exclusion criteria) 2. Study attrition: Low risk 3. Prognostic factor measurement: Low risk 4. Outcome measurement: Low risk 5. Study confounding: Low risk 6. Statistical analysis reporting: Low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				Stoma rate: hospital vol. 15-31 vs 31-NR cases p.a. OR 0.61 (0.34 to 1.09)	**Other information**
Full citation Hodgson, D. C., Zhang, W., Zaslavsky, A. M., Fuchs, C. S., Wright, W. E., Ayanian, J. Z., Relation of hospital volume to colostomy rates and survival for patients with rectal cancer, Journal of the National Cancer Institute, 95, 708-716, 2003 **Ref Id** 865543 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**	**Sample size** See Cochrane review Archampong 2012 for study details **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results** Perioperative mortality: hospital vol. 1-7 vs 7-14 cases p.a. OR 0.58 (0.26 to 1.26) Perioperative mortality: hospital vol. 7-14 vs 14-21 cases p.a. OR 0.83 (0.36 to 1.93) Perioperative mortality: hospital vol. 14-20 vs 20-28 cases p.a. OR 0.79 (0.39 to 1.61) Stoma rate: hospital vol. 1-7 vs 7-14 cases p.a. OR 0.98 (0.73 to 1.3) Stoma rate: hospital vol. 7-14 vs 14-21 cases	**Limitations** Quality of the study assessed with the QUIPS checklist for prognostic factor studies 1. Study participation: Low risk 2. Study attrition: Low risk 3. Prognostic factor measurement: Low risk 4. Outcome measurement: Low risk 5. Study confounding: Low risk 6. Statistical analysis reporting: Low risk **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				p.a. OR 0.9 (0.68 to 1.21) Stoma rate: hospital vol. 14-21 vs 21-28 cases p.a. OR 0.83 (0.66 to 1.03)	
Full citation Hohenberger, W., Merkel, S., Hermanek, P., Volume and outcome in rectal cancer surgery: The importance of quality management, International Journal of Colorectal Disease, 28, 197-206, 2013 **Ref Id** 865545 **Country/ies where the study was carried out** Germany **Study type** Prospective population registry study **Aim of the study** The aim of the study was to assess the effect of surgeon volume on short- and long-term outcomes of rectal cancer surgery	**Sample size** n= 1028 **Characteristics** Characteristics per hospital volume High, medium, low n= 800, 193, 35 Age, years, median (IQR)= 62.5 (18-94), 64 (27-89), 65 (45-86) Male, n= 528, 123, 22 ASA (unknown in 184 patients), n= ASA 1,2= 582, 114, 21 ASA 3,4= 96, 23, 9 **Inclusion criteria** "Solitary invasive rectal carcinoma (invasion at least of the submucosa), 16 cm or less from the anal verge; (2) no other previous or synchronous malignant tumour, except basal cell carcinoma of the skin; (3) carcinoma not arisen in familial	**Interventions** Surgeon caseload: High= ≥ 7/year Medium= 3-6/year Low= < 3/year	**Details** Data collection: Data was collected from the Erlangen Rectal Cancer Registry Prognostic factors controlled for: To control confounding and interactions in long-term results, a multivariate Cox regression analysis including factors with significant influence in univariate analysis was performed Outcomes: Postoperative mortality is defined as in-hospital death. Death by any cause was defined as an event for estimating observed overall survival. The circumferential resection margin was classified as pathologically positive if the minimal distance between tumour and margin was ≤1 mm. Locoregional recurrence was defined as the presence of any anastomotic, pelvic, or perineal tumour documented by clinical and/or pathological examination. Follow up: long-term results with appropriate follow-up time (5 years after primary surgery, 7 years after neoadjuvant radiochemotherapy [nRCT] followed by surgery). Median follow-up time	**Results** Perioperative mortality: surgeon vol. 1-3 vs 3-7 cases p.a. OR 0.15 (0.01 to 2.07) Perioperative mortality: surgeon vol. 3-7 vs 7-23 cases p.a. OR 1.11 (0.1 to 12.06) Complications: surgeon vol. 1-3 vs 3-7 cases p.a. OR 0.5 (0.05 to 4.94) Complications: surgeon vol. 3-7 vs 7-23 cases p.a. OR 1.67 (0.44 to 6.25) Positive surgical margins: surgeon vol. 1-3	**Limitations** Quality of the study assessed with the QUIPS checklist for prognostic factor studies 1. Study participation: Low risk 2. Study attrition: High risk (27% attrition for CRM outcome) 3. Prognostic factor measurement: Low risk 4. Outcome measurement: Low risk 5. Study confounding: Low risk 6. Statistical analysis reporting: Low risk **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study dates 1995-2010 **Source of funding** Not reported	adenomatous polyposis, ulcerative colitis, or Crohn's disease; (4) surgical treatment by (low) anterior resection, intersphincteric rectal resection with perianal anastomosis, Hartmann's procedure or abdominoperineal excision between 1995 and 2010 at the Department of Surgery, University Hospital Erlangen, Germany; (5) no distant metastases; (6) resection with curative intent (R0,1 at clinical and pathohistological examination); and (7) surgical treatment by certified surgeons (general and visceral surgery), mainly involved in major gastrointestinal surgery with a special interest in colorectal surgery." **Exclusion criteria** Patients who died postoperatively or with unknown tumour status		was 90 months (range 2–206) in the primary surgery group and 95 months (range 5–204) in the group who had nRCT. Data analysis: A logistic regression analysis was performed to consider factors influencing short-term results.The Kaplan–Meier method was used for analysis of survival and recurrences. The starting point was always defined as the date of start of treatment, either the date of primary surgery or start of radiochemotherapy	vs 3-7 cases p.a. OR 1.32 (0.15 to 11.81) Positive surgical margins: surgeon vol. 3-7 vs 7-23 cases p.a. OR 0.4 (0.18 to 0.89)	
Full citation Jonker, F. H. W., Hagemans, J. A. W., Burger, J. W. A., Verhoef, C., Borstlap, W. A. A., Tanis, P. J., Aalbers, A., Acherman, Y., Algie, G. D., Alting von Geusau, B., Amelung, F., *et al* The influence of hospital volume	**Sample size** n=2095 **Characteristics** Reported per hospital volume Low, medium, high n= 258, 1329, 508 Age, year, mean (SD)= 66.0 (12.3), 66.9 (11.1), 66.7 (11.2)	**Interventions** Annual hospital volume was defined as the total number of rectal cancer resections performed in 2011. This volume was classified as low (< 20), medium (20–50), or high (> 50).	**Details** Data collection: Hospitals registered in the Dutch Surgical Colorectal Audit were asked to participate. Eligible patients in the database were identified and their procedural, long-term surgical and oncological outcomes were extracted. Data entry was performed by surgical residents	**Results** Overall survival: hospital vol. NR-20 vs 20-51 cases p.a. HR 0.93 (0.68 to 1.27) Overall survival: hospital vol. 20-51 vs 51-NR	**Limitations** Quality of the study assessed with the QUIPS checklist for prognostic factor studies 1. Study participation: Low risk 2. Study attrition: Low risk 3. Prognostic factor measurement: Low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
on long-term oncological outcome after rectal cancer surgery, International Journal of Colorectal Disease, 1-7, 2017 **Ref Id** 747943 **Country/ies where the study was carried out** the Netherlands **Study type** Prospective cross-sectional study **Aim of the study** The aim of the study was to assess the effect of hospital volume on outcomes of rectal cancer **Study dates** 2011 **Source of funding** Not reported	Male, n= 153, 855, 309 ASA class 3/4, n= 39, 223, 81 Operative characteristics, n LAR= 113, 635, 50 APR= 79, 401, 159 Low Hartmann= 53, 261, 88 Different= 13, 32, 11 **Inclusion criteria** Patients who underwent a registered rectal cancer resection **Exclusion criteria** Not reported		supervised by a consultant surgeon. Prognostic factors controlled for: Not reported Outcomes: Disease free survival and overall survival Follow up: 3 years for survival outcomes Data analysis: Missing data were not defaulted to negative and denominators reflect only actual reported cases. Kaplan Meier survival analysis with log rank test was used to compare disease-free and overall survival rates at 3 years between volume groups. Multivariable Cox regression analysis was performed to determine independent predictors of long-term mortality. Hospital volume was included in this model besides all variables that were significant in univariable analysis ($p < 0.05$).	cases p.a. HR 1 (0.65 to 1.54)	4. Outcome measurement: Unclear risk (did not provide adequate descriptions of outcome measurement) 5. Study confounding: High risk (did not report which variables the study would adjust for) 6. Statistical analysis reporting: Low risk **Other information**
Full citation Jonker, F. H. W., Hagemans, J. A. W., Verhoef, C., Burger, J. W.	**Sample size** N cT1-3=14,651 N cT4= 1,511	**Interventions** Hospitals were divided into low (<20 cases/year), medium (21-50 cases/year) and high (>50 cases/year)	**Details** Data collection: Data, including patient and tumour characteristics, diagnostics, treatment and short term outcomes, were collected	**Results** Complications: hospital vol. NR-20 vs 20-51 cases p.a. OR	**Limitations** Quality of the study assessed with the QUIPS checklist for prognostic factor studies

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
A., The impact of hospital volume on perioperative outcomes of rectal cancer, European Journal of Surgical Oncology, 43, 1894-1900, 2017 **Ref Id** 771841 **Country/ies where the study was carried out** the Netherlands **Study type** Prospective cross-sectional study **Aim of the study** The aim of the study was to assess the effect of hospital volume on perioperative outcomes of cT1-3 and cT4 rectal cancers **Study dates** January 2009 to December 2015 **Source of funding** No funding	**Characteristics** cT1-3 Reported per hospital volume Low, medium, high n= 3210, 8730, 2711 Age, years, mean (SD)= 68.1 (10.7), 67.1 (10.7), 67.5 (10.4) Male, n= 2030, 5674, 1740 ASA class 3/4, n= 584, 1366, 459 Clinical tumour stage, n cT1= 160, 475, 173 cT2= 965, 2226, 908 cT3= 2085, 6029, 1630 Clinical lymph node stage, n cN0= 1585, 3889, 1180 cN1= 1043, 2784, 961 cN2= 426, 1677, 498 cM1= 102, 624, 156 cT4 Reported per hospital volume Low, medium, high Age, years, mean (SD)= 67.1 (11.0), 65.2 (12.0), 63.3 (11.1) Male sex, n= 376, 179, 231 ASA class 3/4, n= 149, 58, 58 Tumour characteristics cN0= 202, 46, 73 cN1= 278, 83, 135 cN2= 221, 188, 197 cM1= 89, 57, 76 **Inclusion criteria** All patients operated for rectal cancer, defined as a tumour within 15 cm of the anal verge, enrolled in the DSCA between	volume for cT1-3 rectal cancer, and for cT4 rectal cancer into low (1-4 cases/year), medium (5-9 cases/year) and high (≥ 10 cases/year) volume.	from the Dutch Surgical Colorectal Audit. All patient and hospital information were de-identified. Prognostic factors controlled for: See Data analysis Outcomes: Not reported Follow up: N/A Data analysis: Missing data were not defaulted to negative and denominators reflect only actual reported cases. Multivariable regression analysis was performed to investigate independent effects of hospital volume on a complicated course after resection of cT4 rectal cancer. Hospital volume and variables that were significant in univariate analysis ($p < 0.05$), were included in a multivariate logistic regression model to determine independent associations with this endpoint. p value < 0.05 was considered significant	1.09 (0.77 to 1.54) Complications: hospital vol. 20-51 vs 51-NR cases p.a. OR 1.19 (0.75 to 1.91)	1. Study participation: Low risk 2. Study attrition: Low risk 3. Prognostic factor measurement: Low risk 4. Outcome measurement: Low risk 5. Study confounding: Low risk 6. Statistical analysis reporting: Low risk **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	January 2009 and December 2015 **Exclusion criteria** Tumours >15 cm of the anal verge, tumours with unknown clinical tumour stage				
Full citation Kladny, J., Al-Amawi, T., Kozlowski, M., Wojtasik, P., Swider-Al-Amawi, M., Is the surgeon's experience an independent prognostic factor in rectal cancer?. [Polish, English], Polski Przeglad Chirurgiczny, 79, 733-742, 2007 **Ref Id** 865683 **Country/ies where the study was carried out** Poland **Study type** Prospective cohort study **Aim of the study** The aim of the study was to assess the effect of surgeons' caseloads on outcomes from treatment for rectal cancer	**Sample size** n=286 **Characteristics** No statistically significant differences were observed for age, sex and tumour location (most often tumour was located in lower part of the rectum in both groups Male, n= 155 **Inclusion criteria** Not reported **Exclusion criteria** Not reported	**Interventions** The number of surgeries performed for rectal cancer over the study period dictates the surgeon's experience level (more or less). When the surgeon performed at least 25 surgeries throughout the study period, we arbitrarily classified the surgeon as experienced.	**Details** Data collection: Patients were operated on in 8 surgical centres in Szczecin, Poland. Patients were enrolled in 2 different groups, defined by surgeon experience. Prognostic factors controlled for: age, centre, surgeon's caseload, perioperative complications, grade, metastases to regional lymph nodes, tumour localisation, adjuvant chemotherapy, inadvertent perforation of the tumour, local recurrence Outcomes: Mortality, post-operative complications, peri-operative mortality (within the first 30 days post-operation), 5 year overall survival Follow up: 5 year follow up for survival outcomes Data analysis: Survival analysis was performed using the Kaplan-Meier method, and the differences in survival were compared using the log-rank test. Multivariate analysis was performed using the Cox's hazard regression method.	**Results** Overall survival: surgeon vol. NR-5 vs 5-NR cases p.a. HR 0.62 (0.38 to 1)	**Limitations** Quality of the study assessed with the QUIPS checklist for prognostic factor studies 1. Study participation: Low risk 2. Study attrition: Low risk 3. Prognostic factor measurement: Low risk 4. Outcome measurement: Low risk 5. Study confounding: Low risk 6. Statistical analysis reporting: Unclear risk (results not clearly reported) **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study dates January 1993 to December 1997 **Source of funding** Not reported					
Full citation Kressner, M., Bohe, M., Cedermark, B., Dahlberg, M., Damber, L., Lindmark, G., Ovjerskog, B., Sjodahl, R., Johansson, R., Pahlman, L., The impact of hospital volume on surgical outcome in patients with rectal cancer, Diseases of the Colon and Rectum, 52, 1542-1549, 2009 **Ref Id** 865714 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates**	**Sample size** See Cochrane review Archampong 2012 for study details **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results** Perioperative mortality: hospital vol. NR-11 vs 11-26 cases p.a. OR 0.6 (0.4 to 0.9) Perioperative mortality: hospital vol. 11-26 vs 26-NR cases p.a. OR 1.17 (0.78 to 1.75)	**Limitations** Quality of the study assessed with the QUIPS checklist for prognostic factor studies 1. Study participation: Low risk 2. Study attrition: Low risk 3. Prognostic factor measurement: Low risk 4. Outcome measurement: Unclear risk (did not describe) 5. Study confounding: Low risk 6. Statistical analysis reporting: Low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Source of funding					**Other information**
Full citation Leonard, D., Penninckx, F., Kartheuser, A., Laenen, A., Van Eycken, E., Effect of hospital volume on quality of care and outcome after rectal cancer surgery, The British journal of surgery, 101, 1475-1482, 2014 **Ref Id** 865765 **Country/ies where the study was carried out** Belgium **Study type** Retrospective population registry study **Aim of the study** The aim of the study was to assess the relationship between hospital volume and quality of care in the treatment of rectal cancer	**Sample size** n=1469 **Characteristics** Age, years, median (IQR)= 68.3 (59.5-76.0) Male, n= 927 ASA grade ≥ 3= 289/1389 cTNM stage, n I= 192/1426 II= 249/1426 III= 985/1426 **Inclusion criteria** Patients with primary invasive adenocarcinoma of the rectum between 0 and 10 cm above the anal verge as determined by rigid or flexible endoscopy, who underwent elective total mesorectal excision (TME) **Exclusion criteria** Not reported	**Interventions** Hospital volume was calculated as the average annual number of radical resections for rectal cancer at any level in the interval 2006 to mid-2008	**Details** Data collection: Data were collected from the Belgian Cancer Registry and the Inter-Mutualistic Agency databases. Prognostic factors controlled for: patient or tumour characteristics associated with both volume and oncological outcome Outcomes: Local recurrence, overall recurrence, and overall survival. Follow up: 5 year follow up for overall outcomes Data analysis: The relationship between volume and quality indicators was analysed in patient data using logistic regression models or linear models for binary or continuous indicators respectively. Cox proportional hazard models were used for testing the association between volume and oncological outcomes (local recurrence, overall recurrence, survival). Hospital-level quality scores for the different rectal cancer management domains were based on a preselected set of quality indicators and calculated as the empirical Bayes estimates obtained from hierarchical (logistic) regression models.	**Results** Local recurrence: hospital vol. 1-2 vs 2-3 cases p.a. HR 1 (0.99 to 1.01) Local recurrence: hospital vol. 1-2 vs 2-3 cases p.a. HR 1 (0.99 to 1.01) Overall survival: hospital vol. 1-2 vs 2-3 cases p.a. HR 1 (0.99 to 1.01)	**Limitations** Quality of the study assessed with the QUIPS checklist for prognostic factor studies 1. Study participation: Low risk 2. Study attrition: High risk (13% attrition for 5 year outcomes) 3. Prognostic factor measurement: Low risk 4. Outcome measurement: Low risk 5. Study confounding: Low risk 6. Statistical analysis reporting: Low risk **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study dates 2006-2011 **Source of funding** Foundation against Cancer and INAMI-RIZIV					
Full citation Manchon-Walsh, P., Borras, J. M., Espinas, J. A., Aliste, L., Variability in the quality of rectal cancer care in public hospitals in Catalonia (Spain): Clinical audit as a basis for action, European Journal of Surgical OncologyEur J Surg Oncol, 37, 325-333, 2011 **Ref Id** 625551 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates**	**Sample size** See Cochrane review Archampong 2012 for study details **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results** Perioperative mortality: hospital vol. NR-12 vs 12-30 cases p.a. OR 0.93 (0.38 to 2.31) Perioperative mortality: hospital vol. 12-30 vs 30-NR cases p.a. OR 1.1 (0.5 to 2.39) Complications: hospital vol. NR-12 vs 12-30 cases p.a. OR 0.65 (0.49 to 0.88) Complications: hospital vol. 12-30 vs 30-NR cases p.a. OR 1.14 (0.9 to 1.44)	**Limitations** Quality of the study assessed with the QUIPS checklist for prognostic factor studies 1. Study participation: Low risk 2. Study attrition: Low risk 3. Prognostic factor measurement: Low risk 4. Outcome measurement: Unclear risk (did not describe how outcomes were assessed) 5. Study confounding: Low risk 6. Statistical analysis reporting: Low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Source of funding					**Other information**
Full citation Matthiessen, P, Hallböök, O, Rutegård, J, Sjödahl, R, Population-based study of risk factors for postoperative death after anterior resection of the rectum, British Journal of Surgery, 93, 498-503, 2006 **Ref Id** 865880 **Country/ies where the study was carried out** Sweden **Study type** Prospective population registry study **Aim of the study** The aim of the study was to assess risk factors for death within 30 days after anterior resection of the rectum **Study dates** 1987 to 1995	**Sample size** n=140 **Characteristics** Non-survivors, n=140 Male, n= 97 Age, years, median (IQR)= 76 (40-90) Dukes' stage, n A= 20 B= 48 C= 29 'D'= 26 Missing data= 6 **Inclusion criteria** Patients who underwent elective anterior resection of the rectum **Exclusion criteria** Not reported	**Interventions** Hospital caseload was divided arbitrarily into four categories, taking into consideration the existing differences in caseload in Sweden during the study period. Very low= < 6 Low= 6-11.9 Medium= 12-17.9 High= ≥ 18	**Details** Data collection: 140 patients who died with 30 days or within the initial hospital stay for elective anterior resection of the resection were assessed. These patients were compared with the randomly chosen control cohort selected from the remaining patients who underwent the same operation and who survived beyond 30 days and were discharged from the hospital. Patients were identified from the Swedish National Board of Health and Welfare hospital registry. Prognostic factors controlled for: age, Dukes' stage, BMI, duration of operation, intraoperative blood loss, level of anastomosis and hospital caseload Outcomes: Intraoperative bleeding, duration of operation, occurrence of intraoperative adverse events, level of anastomosis above the anal verge and construction of a temporary stoma at the primary operation), hospital-dependent risk factors (hospital caseload) and postoperative risk factors (clinical anastomotic leakage). Follow up: Not reported Data analysis: $\chi 2$ test and Mann–Whitney U test were used for comparison between groups. $\chi 2$ test for trend was used to determine the impact of hospital	**Results** Perioperative mortality: hospital vol. 1-6 vs 6-12 cases p.a. OR 0.82 (0.37 to 1.81) Perioperative mortality: hospital vol. 6-12 vs 12-18 cases p.a. OR 0.89 (0.42 to 1.89) Perioperative mortality: hospital vol. 12-18 vs 18-28 cases p.a. OR 0.63 (0.31 to 1.25)	**Limitations** Quality of the study assessed with the QUIPS checklist for prognostic factor studies 1. Study participation: High risk (11 patients did not have cancer) 2. Study attrition: High risk (Some data missing which could have biased results) 3. Prognostic factor measurement: Low risk 4. Outcome measurement: Low risk 5. Study confounding: Low risk 6. Statistical analysis reporting: Low risk **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Source of funding Research Committee, Orebro County Council, Sweden			caseload on postoperative mortality rate. Variables with P ≤ 0·100 in univariate analysis were included in the multivariate logistic regression analysis. In multivariate analysis P < 0·050 was considered significant.		11/140 patients did not have cancer
Full citation Meyerhardt, J. A., Tepper, J. E., Niedzwiecki, D., Hollis, D. R., Schrag, D., Ayanian, J. Z., O'Connell, M. J., Weeks, J. C., Mayer, R. J., Willett, C. G., MacDonald, J. S., Benson, Iii A. B., Fuchs, C. S., Impact of hospital procedure volume on surgical operation and long-term outcomes in high-risk curatively resected rectal cancer: Findings from the intergroup 0114 study, Journal of Clinical Oncology, 22, 166-174, 2004 **Ref Id** 749139 **Country/ies where the study was carried out** **Study type** **Aim of the study**	**Sample size** See Cochrane review Archampong 2012 for study details **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results** Stoma rate: hospital vol. 1-9 vs 9-17 cases p.a. OR 0.84 (0.65 to 1.09) Stoma rate: hospital vol. 9-17 vs 17-92 cases p.a. OR 0.65 (0.49 to 0.86) Local recurrence: hospital vol. 0-9 vs 9-17 cases p.a. HR 1.2 (0.87 to 1.67) Local recurrence: hospital vol. 9-17 vs 17-92 cases p.a. HR 0.76 (0.51 to 1.12) Local recurrence: hospital vol. 0-9 vs 9-17 cases	**Limitations** Quality of the study assessed with the QUIPS checklist for prognostic factor studies 1. Study participation: High risk (participants only somewhat representative of population) 2. Study attrition: High risk (participants lost to follow up likely to introduce outcome bias) 3. Prognostic factor measurement: Low risk 4. Outcome measurement: High risk (outcomes self-reported) 5. Study confounding: Low risk 6. Statistical analysis reporting: Low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study dates **Source of funding**				p.a. HR 1.2 (0.87 to 1.67) Local recurrence: hospital vol. 9-17 vs 17-92 cases p.a. HR 0.76 (0.51 to 1.12) Overall survival: hospital vol. 0-9 vs 9-17 cases p.a. HR 1 (0.81 to 1.24) Overall survival: hospital vol. 9-17 vs 17-92 cases p.a. HR 0.87 (0.7 to 1.06)	**Other information**
Full citation Ortiz, H., Codina, A., Ciga, M. A., Biondo, S., Enriquez-Navascues, J. M., Espin, E., Garcia-Granero, E., Roig, J. V., Effect of hospital caseload on long-term outcome after standardization of rectal cancer surgery in the Spanish Rectal Cancer Project, Cirugia espanola, 94, 442-52, 2016 **Ref Id** 761839	**Sample size** n= 2910 **Characteristics** Men, n= 1914 Age, years, n < 65= 1068 65-80= 1439 > 80= 403 ASA, n I= 172 II= 1589 III= 1059 IV= 90 Surgical technique, n AR= 2015 APR= 655	**Interventions** Groups were defined according to the mean number of patients treated annually (12–23, 24–35, and 36 patients). The hospital was considered a random confounding variable.	**Details** Data collection: This multicenter observational study was conducted with the prospective database of the Rectal Cancer Project (Association Espanola de Cirujanos). The data collected prospectively at the hospitals by surgeons in charge of the project were sent to a centralized registry, which made annual reports for each of the hospitals of the outcomes of their activity compared to the overall results of the participating hospitals Prognostic factors controlled for: age, categorized in 3 groups (<65, 65–80, >80 years); sex; severity of surgical risk (measured by the ASA	**Results** Local recurrence: hospital vol. 12-24 vs 24-36 cases p.a. HR 1.1 (0.63 to 1.92) Local recurrence: hospital vol. 24-36 vs 36-56 cases p.a. HR 0.76 (0.45 to 1.27)	**Limitations** Quality of the study assessed with the QUIPS checklist for prognostic factor studies 1. Study participation: Low risk 2. Study attrition: High risk (study did not account for patient attrition) 3. Prognostic factor measurement: Low risk 4. Outcome measurement: Low risk 5. Study confounding: Low risk 6. Statistical analysis reporting: Low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Country/ies where the study was carried out Spain **Study type** Prospective cohort study **Aim of the study** The aim of the study was to assess the effect of hospital caseload on long-term outcomes following standardisation of rectal cancer surgery **Study dates** March 2006 to March 2010 **Source of funding** FIS number PI11/00010 and the Healthcare Council of Navarra 20/11	Hartmann= 240 **Inclusion criteria** Patients who underwent one of three elective surgeries: anterior resection (AR), abdominoperineal resection (APR) and Hartmann's procedure. **Exclusion criteria** Patients treated with emergency surgery, those for whom no results were available for one of the variables of interest, and those with incongruent results.		anesthesia risk classification); tumour location, categorized in 3 groups (0–6, 7–12, 13–15 cm); type of mesorectal excision (partial or total); type of resection (AR, APR, Hartmann procedure); pathological tumour stage and lymphadenopathies; state of circumferential resection margins (CRM); intraoperative perforation; use of neoadjuvant therapy; and the hospital case load Outcomes: Local recurrence, metastasis that appeared during follow-up and overall survival Follow up: 5 years Data analysis: "To determine the variation of the outcome variables LR, M and OS among the hospitals included, a multi-level analysis was created, constructed of 3 models: a model of fixed effect that included the set confounding variables, a complete model that included the set of confounding variables and the random hospital variable, and a null model that only included the random hospital variable. In the first, a Cox regression was used, while in the latter two a multilevel Cox regression model was used. All the variables were included in the univariate, multivariate and multilevel studies."	Overall survival: hospital vol. 12-24 vs 24-36 cases p.a. HR 0.86 (0.65 to 1.13) Overall survival: hospital vol. 24-36 vs 36-56 cases p.a. HR 0.85 (0.64 to 1.13)	**Other information**
Full citation Ptok, H., Marusch, F., Kuhn, R., Gastinger, I., Lippert, H., Influence of	**Sample size** See Cochrane review Archampong 2012 for study details	**Interventions**	**Details**	**Results** Local recurrence: hospital vol. 10-20 vs 20-NR	**Limitations** Quality of the study assessed with the QUIPS

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
hospital volume on the frequency of abdominoperineal resections and long-term oncological outcomes in low rectal cancer, European Journal of Surgical Oncology, 33, 854-861, 2007 **Ref Id** 866091 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**	**Characteristics** **Inclusion criteria** **Exclusion criteria**			cases p.a. HR 0.72 (0.55 to 0.94)	checklist for prognostic factor studies 1. Study participation: Low risk 2. Study attrition: Low risk 3. Prognostic factor measurement: Low risk 4. Outcome measurement: Low risk 5. Study confounding: Low risk 6. Statistical analysis reporting: Low risk **Other information**
Full citation Richardson, D. P., Porter, G. A., Johnson, P. M., Surgeon knowledge contributes to the relationship between surgeon volume and patient outcomes in rectal cancer, Annals of Surgery, 257, 295-301, 2013	**Sample size** n= 521 **Characteristics** Patients treated by high-volume surgeons, n=182 Age, years, mean (range)= 65.6 (27.4-93.0) Male, %= 64	**Interventions** Surgeon volume calculated as average number of cases per year High-volume= average 12 cases/year Low-volume= average 2 cases/year	**Details** Data collection: data were retrospectively collected from the Nova Scotia Cancer Registry. Prognostic factors controlled for: age, sex, body mass index, Charlson comorbidity score, tumour height, use of neoadjuvant therapy, and TNM stage Outcomes: total mesorectal excision (TME), lymph node	**Results** Stoma rate: surgeon vol. 1-6 vs 6-14 cases p.a. OR 0.53 (0.3 to 0.93) Local recurrence: surgeon vol. 1-6	**Limitations** Quality of the study assessed with the QUIPS checklist for prognostic factor studies 1. Study participation: Low risk 2. Study attrition: Low risk 3. Prognostic factor measurement: Low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Ref Id 762692 **Country/ies where the study was carried out** Canada **Study type** Retrospective population registry study **Aim of the study** The aim of the study was to assess whether surgeon knowledge affects the relationship between surgeon procedure volume and patient outcomes in rectal cancer. **Study dates** July 1, 2002- June 30, 2006 **Source of funding** Canadian Institutes of Health Research, American Society of Colon and Rectal Surgeons	Charlson score, mean (range)= 1.63 (0-13) Surgical procedures, n Radical excision=167 Transanal excision= 7 Endoscopic excision= 7 Patients treated by low-volume surgeons, n=195 Age, years, mean (range)= 67.4 Male, %= 64 Charlson score, mean (range)= 1.57 (0-10) Surgical procedures, n Radical excision=175 Transanal excision= 8 Endoscopic excision=12 **Inclusion criteria** All patients with a new diagnosis of adenocarcinoma of the rectum between July 1, 2002, and June 30, 2006, who were residents of Nova Scotia, Canada, and underwent resection with curative intent **Exclusion criteria** Patients who were younger than 18 years or if they underwent primary treatment for rectal cancer outside of the province		harvest, permanent colostomy use, local recurrence, disease-specific survival and overall survival Follow up: minimum 3 years Data analysis: "Logistic regression analysis was used to determine the univariate and multivariate associations for dichotomous patient outcomes (permanent colostomy rate, use of TME, and adequate lymph node harvest). Kaplan-Meier survival curves and Cox proportional hazards regression were used to examine local recurrence, disease-specific survival, and overall survival. Specifically, the association between surgeon procedure volume and each of our 6 outcomes was examined using appropriate multivariate techniques."	vs 6-14 cases p.a. HR 0.54 (0.29 to 0.99) Overall survival: surgeon vol. 1-6 vs 6-14 cases p.a. HR 0.85 (0.59 to 1.22)	4. Outcome measurement: Low risk 5. Study confounding: Low risk 6. Statistical analysis reporting: Low risk **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Simunovic, M., To, T., Baxter, N., Balshem, A., Ross, E., Cohen, Z., McLeod, R., Engstrom, P., Sigurdson, E., Hospital procedure volume and teaching status do not influence treatment and outcome measures of rectal cancer surgery in a large general population, Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract, 4, 324-330, 2000 **Ref Id** 866215 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**	**Sample size** See Cochrane review Archampong 2012 for study details **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results** Perioperative mortality: hospital vol. NR-12 vs 12-18 cases p.a. OR 1 (0.41 to 2.44) Perioperative mortality: hospital vol. 12-18 vs 18-NR cases p.a. OR 1.11 (0.5 to 2.5) Overall survival: hospital vol. 12-18 vs 18-NR cases p.a. HR 0.91 (0.67 to 1.43)	**Limitations** Quality of the study assessed with the QUIPS checklist for prognostic factor studies 1. Study participation: Low risk 2. Study attrition: Low risk 3. Prognostic factor measurement: Low risk 4. Outcome measurement: Low risk 5. Study confounding: Low risk 6. Statistical analysis reporting: Low risk **Other information**
Full citation	**Sample size**	**Interventions**	**Details**	**Results**	**Limitations**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Syk, E., Glimelius, B., Nilsson, P. J., Factors influencing local failure in rectal cancer: Analysis of 2315 patients from a population-based series, Diseases of the Colon and Rectum, 53, 744-752, 2010 **Ref Id** 761994 **Country/ies where the study was carried out** Sweden **Study type** **Aim of the study** The aim of the study was to assess the risk factors for local failure **Study dates** January 1995 to December 2004 **Source of funding** No funding	n= 2282 **Characteristics** Male, n= 1326 Age, years, n < 71= 1183 > 71= 1099 T-stage, n T1-2= 657 T3-4= 1558 Missing= 67 N-stage, n N0= 1179 N1= 536 N2= 401 NX= 165 **Inclusion criteria** Patients with rectal cancer who underwent abdominal resections **Exclusion criteria** Not reported	Hospital caseload was determined by an arbitrary division where the 3 hospitals with the largest case load were compared with the remaining 6 hospitals High-volume hospital, median (IQR)= 294.5 (239-617) Low-volume hospital, median (IQR)= 64 (52-92)	Data collection: data were collected from the Regional Oncologic Center. For all patients with a reported local failure, medical records from the time of primary operation and date of diagnosis of the recurrence were collected and reviewed. Prognostic factors controlled for: gender, age, study period, tumour location, tumour size, T-stage, N-stage differentiation, radiotherapy, type of surgery, TME, intraoperative perforation of rectum, residual status, and case load Outcomes: local failure Follow up: date of operation to date of diagnosis of the recurrence or death, or until January 1, 2005 Data analysis: Explorative analyses of discriminators for hospitals with high and low failure rates were done with logistic regression analysis. Univariate analyses were done with the X^2 test.	Overall survival: hospital vol. 5-30 vs 30-62 cases p.a. HR 0.62 (0.45 to 0.87)	Quality of the study assessed with the QUIPS checklist for prognostic factor studies 1. Study participation: Low risk 2. Study attrition: Low risk 3. Prognostic factor measurement: Low risk 4. Outcome measurement: Low risk 5. Study confounding: Low risk 6. Statistical analysis reporting: Low risk **Other information**
Full citation	**Sample size**	**Interventions**	**Details**	**Results**	**Limitations** Quality of the study assessed with the QUIPS

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Wibe, A., Eriksen, M. T., Syse, A., Tretli, S., Myrvold, H. E., Soreide, O., Effect of hospital caseload on long-term outcome after standardization of rectal cancer surgery at a national level, British Journal of Surgery, 92, 217-224, 2005 **Ref Id** 762233 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**	See Cochrane review Archampong 2012 for study details **Characteristics** **Inclusion criteria** **Exclusion criteria**			Local recurrence: hospital vol. 1-10 vs 10-20 cases p.a. HR 0.68 (0.48 to 0.98) Local recurrence: hospital vol. 10-20 vs 20-30 cases p.a. HR 1.23 (0.92 to 1.64) Local recurrence: hospital vol. 20-30 vs 30-34 cases p.a. HR 0.63 (0.45 to 0.83) Overall survival: hospital vol. 1-10 vs 10-20 cases p.a. HR 0.83 (0.69 to 1) Overall survival: hospital vol. 10-20 vs 20-30 cases p.a. HR 1.1 (1 to 1.21) Overall survival: hospital vol. 20-30 vs 30-34 cases p.a. HR 0.91 (0.77 to 1)	checklist for prognostic factor studies 1. Study participation: Low risk 2. Study attrition: Low risk 3. Prognostic factor measurement: Low risk 4. Outcome measurement: Low risk 5. Study confounding: Low risk 6. Statistical analysis reporting: Low risk **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Yeo, H. L., Abelson, J. S., Mao, J., O'Mahoney, P. R. A., Milsom, J. W., Sedrakyan, A., Surgeon annual and cumulative volumes predict early postoperative outcomes after rectal cancer resection, Annals of Surgery, 265, 151-157, 2017 **Ref Id** 866434 **Country/ies where the study was carried out** USA **Study type** Retrospective population registry study **Aim of the study** The aim of the study was to assess if surgeon volumes affected postoperative outcomes in patients with rectal cancer **Study dates** 2000-2013	**Sample size** n= 14,833 **Characteristics** Low cumulative/low annual, low cumulative/high annual, high cumulative/low annual, high cumulative/high annual Patients, n= 6382, 910, 631, 6910 Age, years, n < 65= 2771, 407, 291, 3596 65-75= 1695, 238, 172, 1738 ≥ 75= 1916, 265, 168, 1576 Procedure type, n= APR= 1653, 208, 170, 1775 LAR= 4477, 645, 411, 4215 LAR with diversion= 221, 51, 45, 870 **Inclusion criteria** Patients undergoing major rectal resection, including rectosigmoid tumours, as their principal procedure during hospitalization between 2000 and 2013 **Exclusion criteria** Patients who underwent surgery but whose discharge record did not report a particular surgeon. Additionally, surgeons who were not recorded to have	**Interventions** Surgeons were categorized into high cumulative (HC) and low cumulative (LC) and high annual (HA) and low annual (LA) volume based on median surgeon volumes, as has been done in prior volume outcome studies. Additionally, the total number and percent of all procedures performed from 2000 to 2013 was stratified by surgeon annual and cumulative volume. Cumulative volume: LC= 0-23 HC= ≥ 24 Annual volume: LA= 0-4 HA= ≥ 5	**Details** Data collection: Data were collected from the NYS Department of Health Statewide Planning and Research Cooperative System database, which collected patient, treatment and provider information. Prognostic factors controlled for: patient demographics, surgery year, surgery approach and type, tumour characteristics (benign/malignant and location), comorbidities, emergency surgery and hospital volume. Outcomes: Primary outcomes: acute myocardial infarction, stroke, pulmonary embolism, and shock. Secondary outcomes: prolonged length of stay, surgical complications (including iatrogenic/bleeding complications), anastomotic leak, nonroutine discharges, total charges, 30-day readmissions, and 30-day return to operating room) Follow up: N/A Data analysis: Unadjusted outcomes were presented as percentages of occurrence with graphs. A general linear mixed model, accounting for hospital clustering and surgeon clustering as random effects, was adopted to compare outcomes across groups, using LC/LA volume surgeons as the reference group. Further comparisons of procedures performed by HC/HA volume surgeons with both HC/LA volume	**Results** Complications: surgeon vol. 1-5 vs 5-NR cases p.a. OR 0.71 (0.6 to 0.84)	**Limitations** Quality of the study assessed with the QUIPS checklist for prognostic factor studies 1. Study participation: Low risk 2. Study attrition: Unclear risk (some missing demographic data, i.e. procedure type) 3. Prognostic factor measurement: Low risk 4. Outcome measurement: Low risk 5. Study confounding: Low risk 6. Statistical analysis reporting: Low risk **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Source of funding Not reported	conducted any surgery, rectal or otherwise, during at least 4 years out of the 5-year period were excluded.		surgeons and LC/HA volume surgeons, using HC/LA volume surgeons and LC/HA volume surgeons as the reference level for each comparison		
Full citation Yun, Y. H., Kim, Y. A., Min, Y. H., Park, S., Won, Y. J., Kim, D. Y., Choi, I. J., Kim, Y. W., Park, S. J., Kim, J. H., Lee, D. H., Yoon, S. J., Jeong, S. Y., Noh, D. Y., Heo, D. S., The influence of hospital volume and surgical treatment delay on long-term survival after cancer surgery, Annals of oncology, 23, 2731-2737, 2012 **Ref Id** 459466 **Country/ies where the study was carried out** South Korea **Study type** Retrospective population registry study **Aim of the study** The aim of the study was to assess the effect of hospital volume and delay of	**Sample size** Total sample size= 147,682 n rectal cancer= not reported **Characteristics** (For all patients in study cohort, not just patients with rectal cancer) Male age, years, mean (range)= 60.0 (20.0-98.0) Female age, years, mean (range)= 54.4 (20.0-100.0) **Inclusion criteria** Patients 20 years of age or older who had been diagnosed with cancer of the stomach, colon, rectum, pancreas, lung or breast **Exclusion criteria** Patients with multiple cancers or who did not undergo cancer surgery as their first line of treatment. Patients who had only radiotherapy, only chemotherapy, or radio and chemotherapy without cancer surgery	**Interventions** Hospital volume defined by number of operations/year with cut-off points (tertiles) of low, medium, and high. Hospital volume: Low= < 23 High= ≥23	**Details** Data collection: data were collected from the Korea Central Cancer Registry and the National Health Insurance claim database. Cancer conditions were classified according to the International Classification of Diseases for Oncology, 3rd edition and then converted to the ICD-10 Data from the two databases were merged using a unique patient identifier. Prognostic factors controlled for: age, sex, Charlson scale, hospital type, insurance, radiotherapy, chemotherapy, type of medical care institution, year of diagnosis and hospital volume Outcomes: Overall survival and treatment delay Follow up: 5 years Data analysis: For multivariate multiple logistic regression, we used categorical indicator factors that showed significant association in univariate analysis. We carried out multivariable Cox proportional hazards modeling to assess the effects of waiting time and hospital volume for each procedure in each treatment year on overall survival	**Results** Overall survival: hospital vol. NR-23 vs 23-NR cases p.a. HR 0.72 (0.66 to 0.79)	**Limitations** Quality of the study assessed with the QUIPS checklist for prognostic factor studies 1. Study participation: High risk (no demographic details provided for the sample) 2. Study attrition: Low risk 3. Prognostic factor measurement: Low risk 4. Outcome measurement: Low risk 5. Study confounding: Low risk 6. Statistical analysis reporting: High risk (Hazard ratios reported without p-value, unable to determine n in sample of patients with rectal cancer) **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
surgery on the long-term survival of postoperative cancer patients. **Study dates** 2001-2005 **Source of funding** National Cancer Center (1010081)					

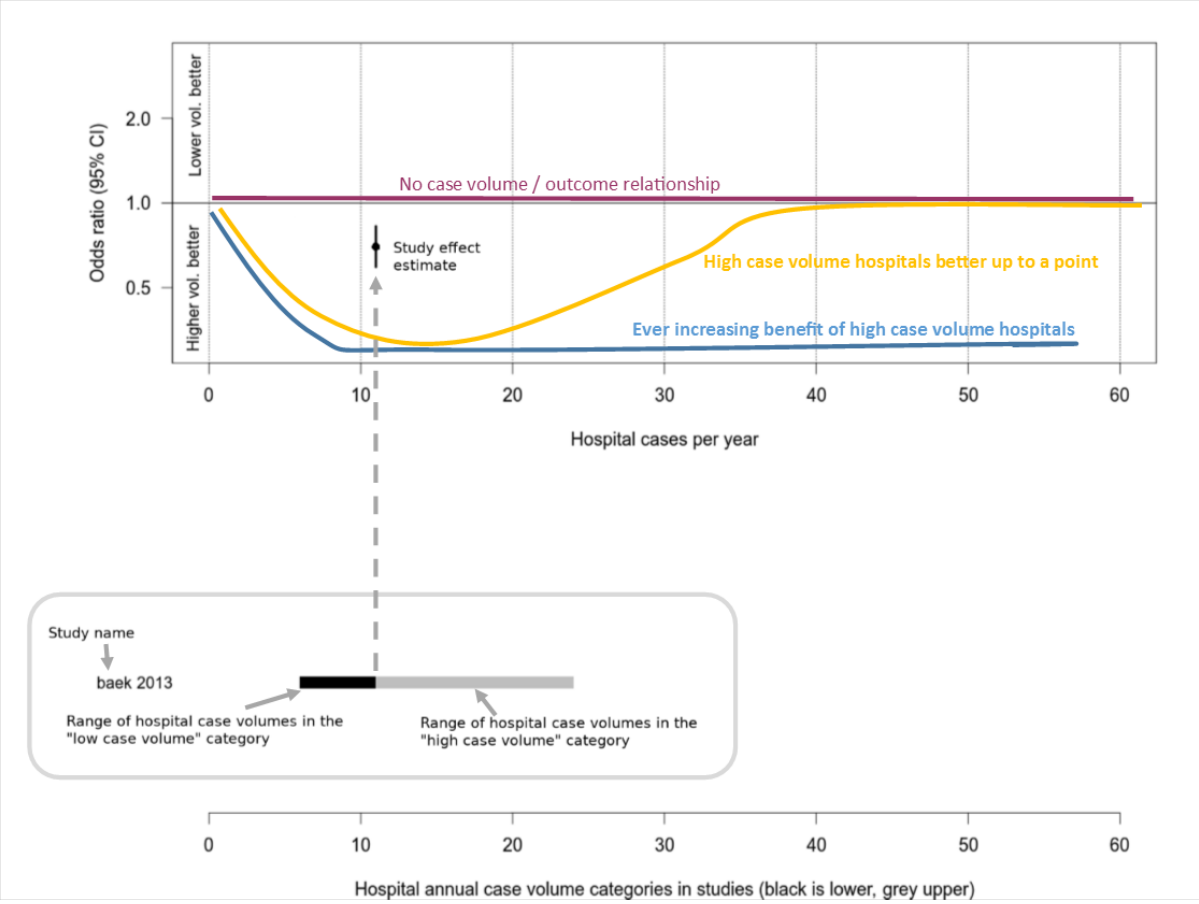
AJCC: American Joint Committee of Cancer; APR: abdominoperineal resection; AR: anterior resection; ASA: American Society of Anaestheologists; BMI: body mass index; CCC: Comprehensive Cancer Centre; CHARMS: Checklist for critical appraisal and data extraction for systematic Reviews of prediction Modelling Studies; CRM: circumferential resection margin; DSCA: Dutch Surgical Colorectal Audit; HA: high annual; HC: high cumulative; HR: hazard ratio; HV: high volume; HVH: high volume hospital; HVS: high volume surgeon; ICD(-9/-10); International Statistical Classification of Diseases and Related Health Problems (9th revision/10th revision); IQR: inter-quartile range; LA: low annual; LAR: low anterior resection: LC: low cumulative; LV: low volume; MV: medium volume; N: number; NBOCA: National Bowel Cancer Audit; NR: not reported; nRCT: neoadjuvant radiochemotherapy; OR: odds ratio p.a.: per annum; QUIPS: Quality in Prognosis Studies; R0: total resection: R1: microscopic tumour tissue remaining in rection margins; R2: macroscopic tumour tissue remaining in resection margins; TME: total mesorectal excision; TNM: Tumour, Node, Metastases stage; UICC: Union for International Cancer Control; VHV: very high volume

Appendix E – Forest plots

Forest plots for review question: Is there a relationship between surgical volumes and outcomes in the treatment of rectal cancer (primary and recurrent disease)?

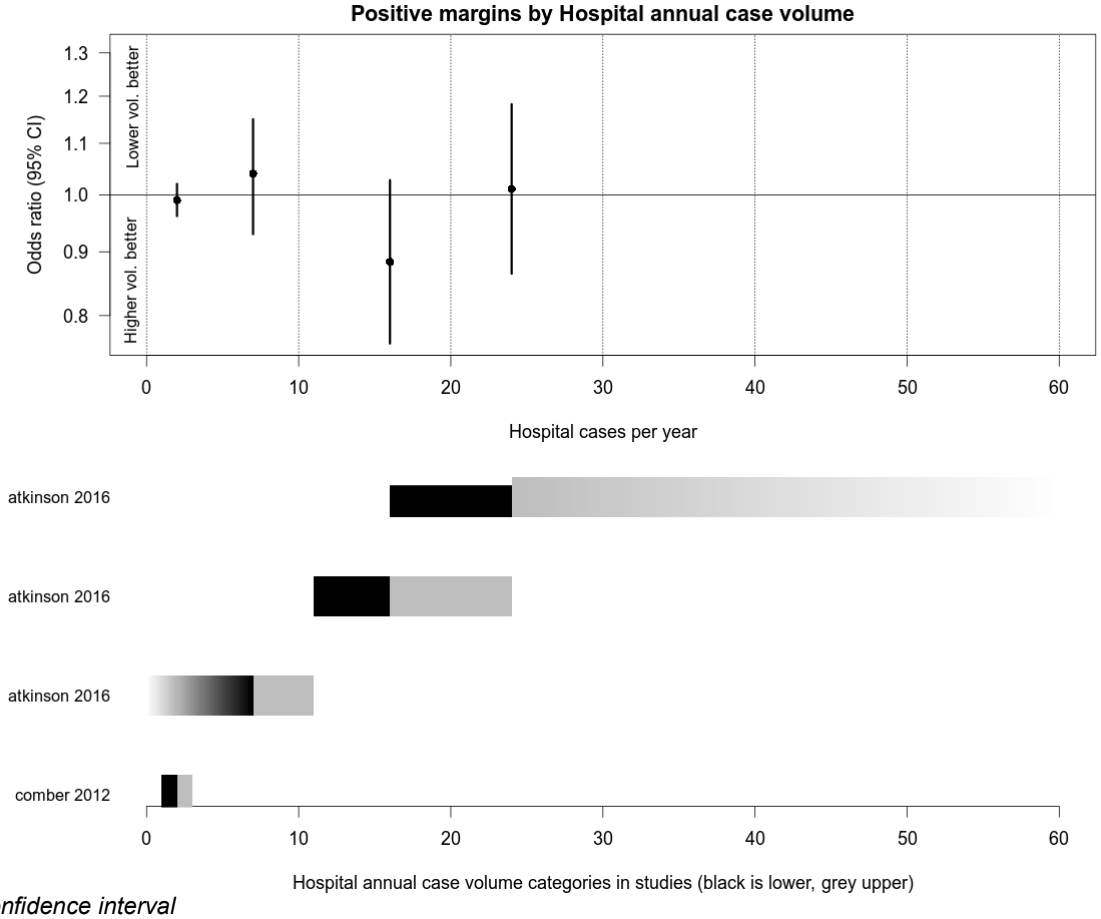
This section includes forest plots only for outcomes that are meta-analysed. Outcomes from single studies are not presented here.

Figure 2: Guide to reading the forest plots for this review



CI: confidence interval

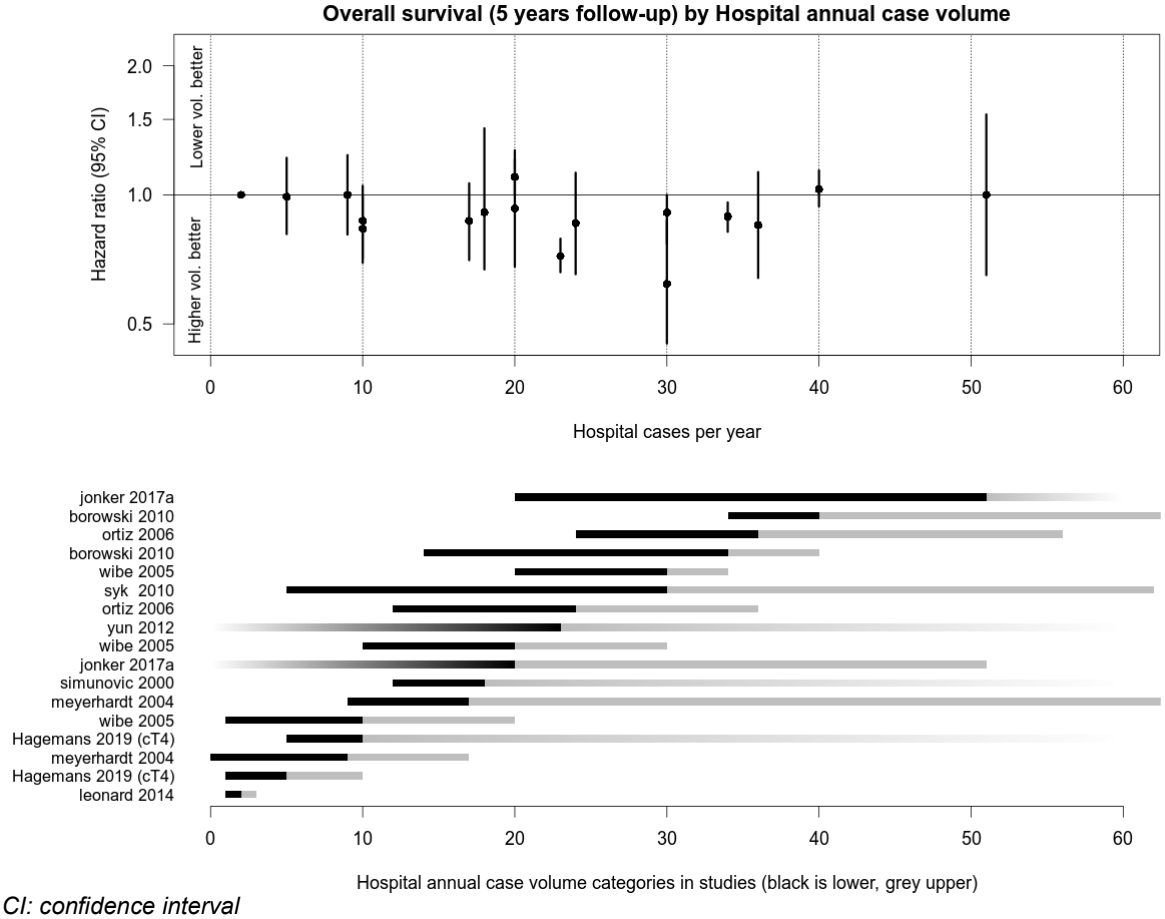
Figure 3: Outcomes by hospital volume of rectal cancer surgery – positive resection margin



CI: confidence interval

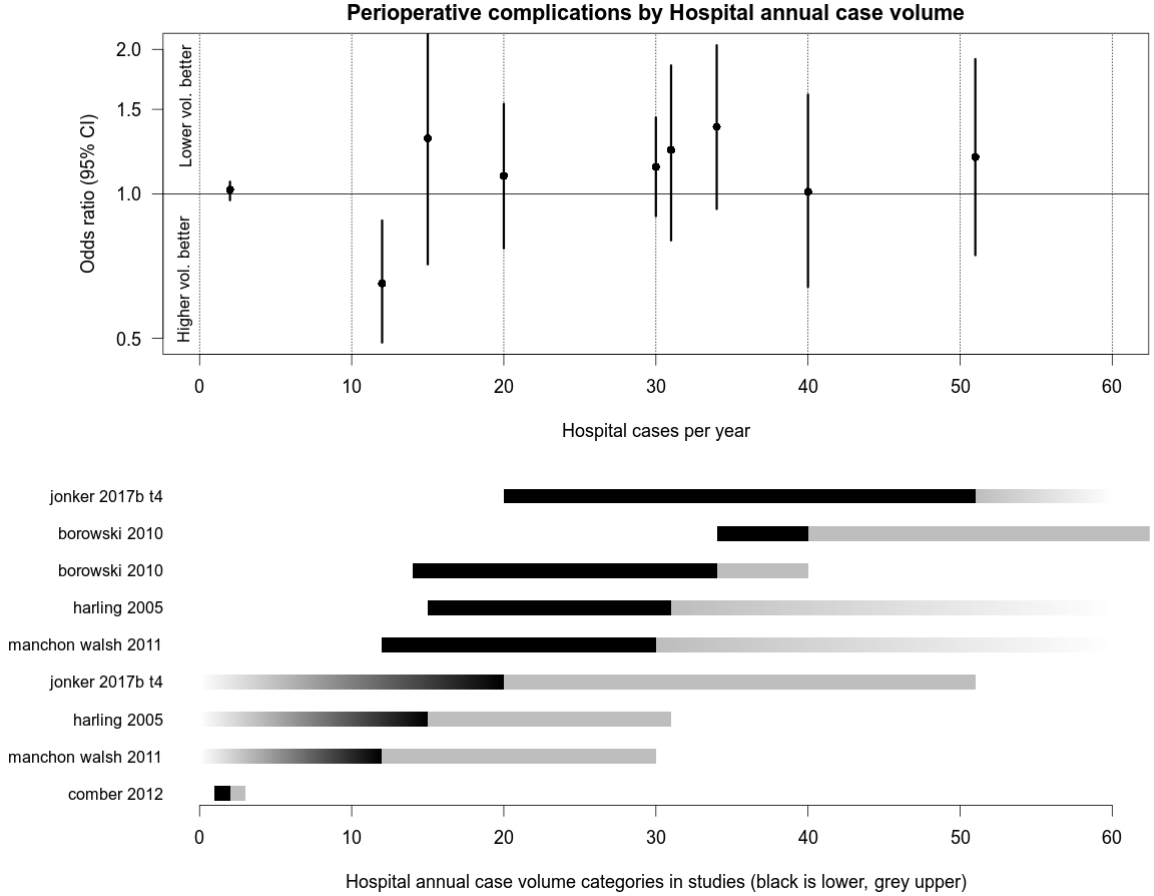
1

Figure 4: Outcome by hospital volume of rectal cancer surgery – Overall survival at 5 years



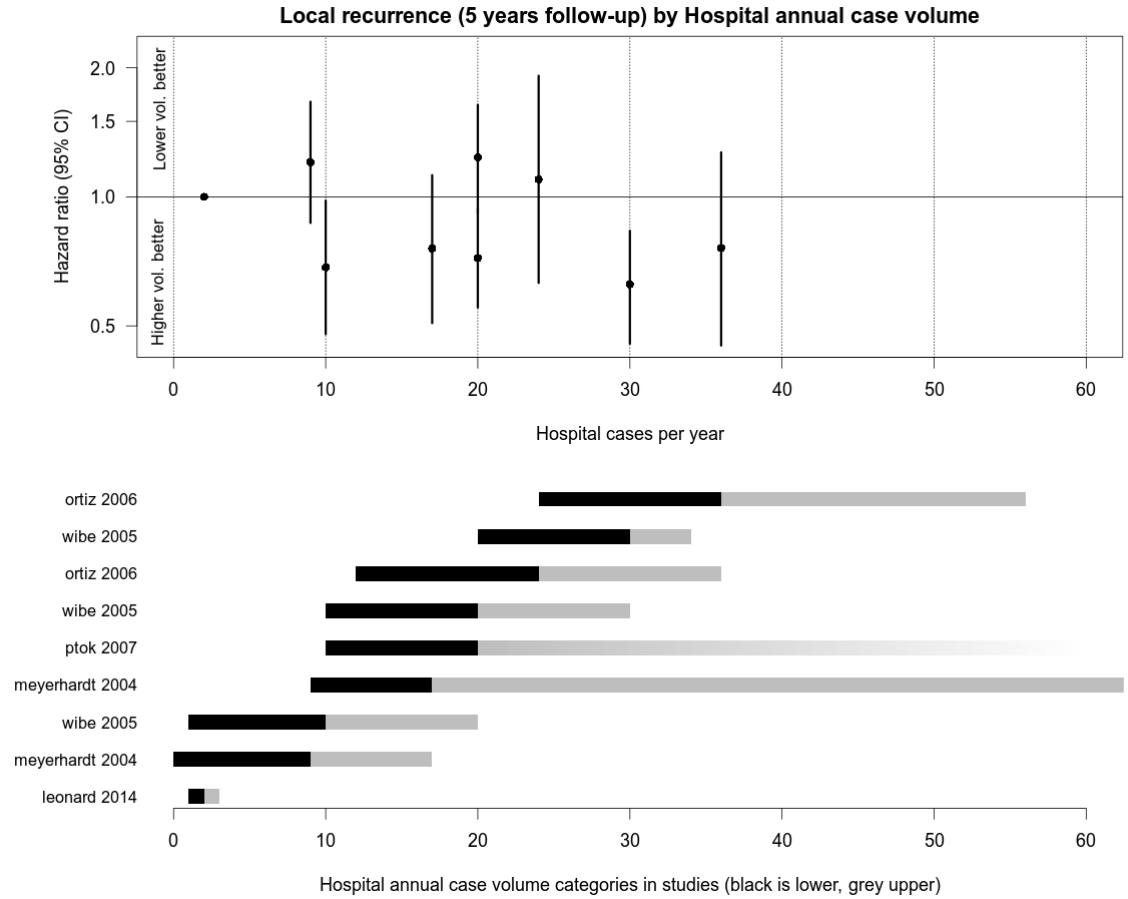
CI: confidence interval

Figure 5: Outcome by hospital volumes of rectal cancer surgery – Grade 3 or 4 complications



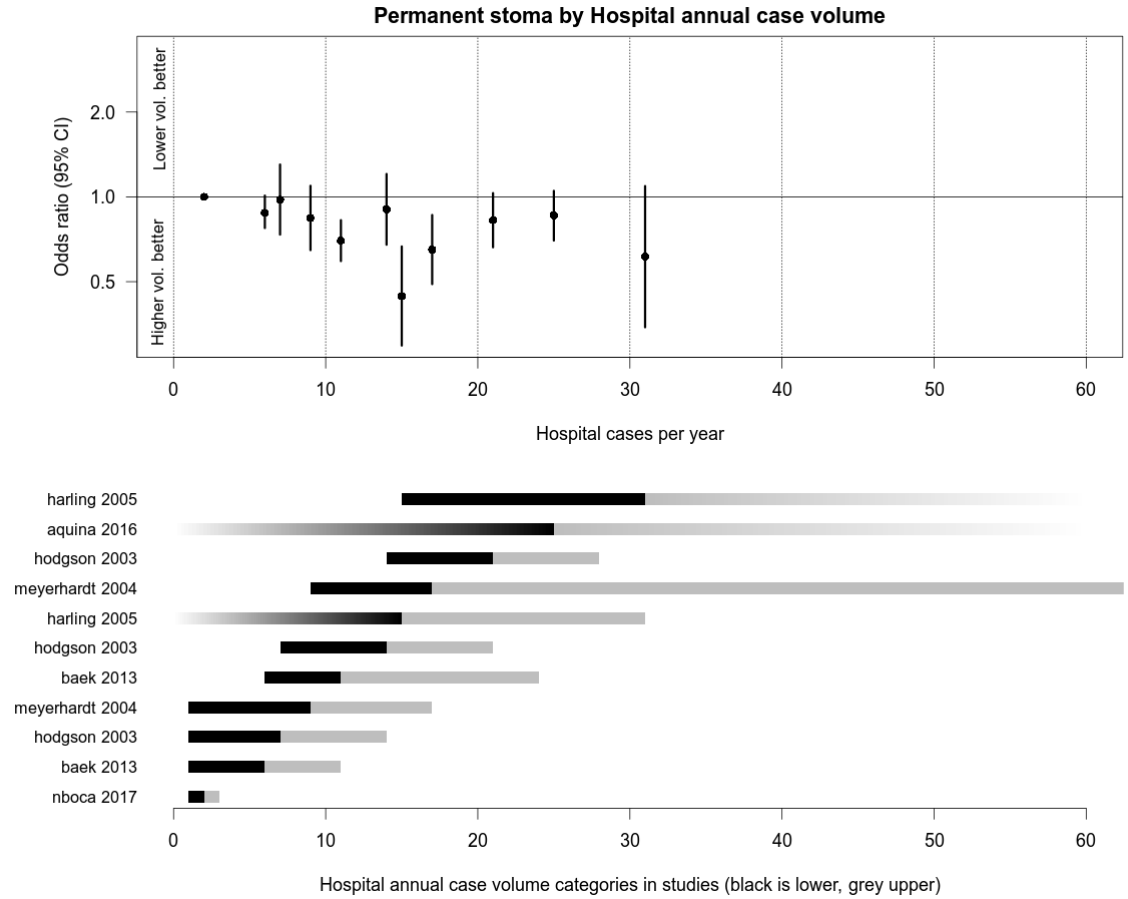
CI: confidence interval

Figure 6: Outcomes by hospital volume of rectal cancer surgery – Local recurrence



CI: confidence interval

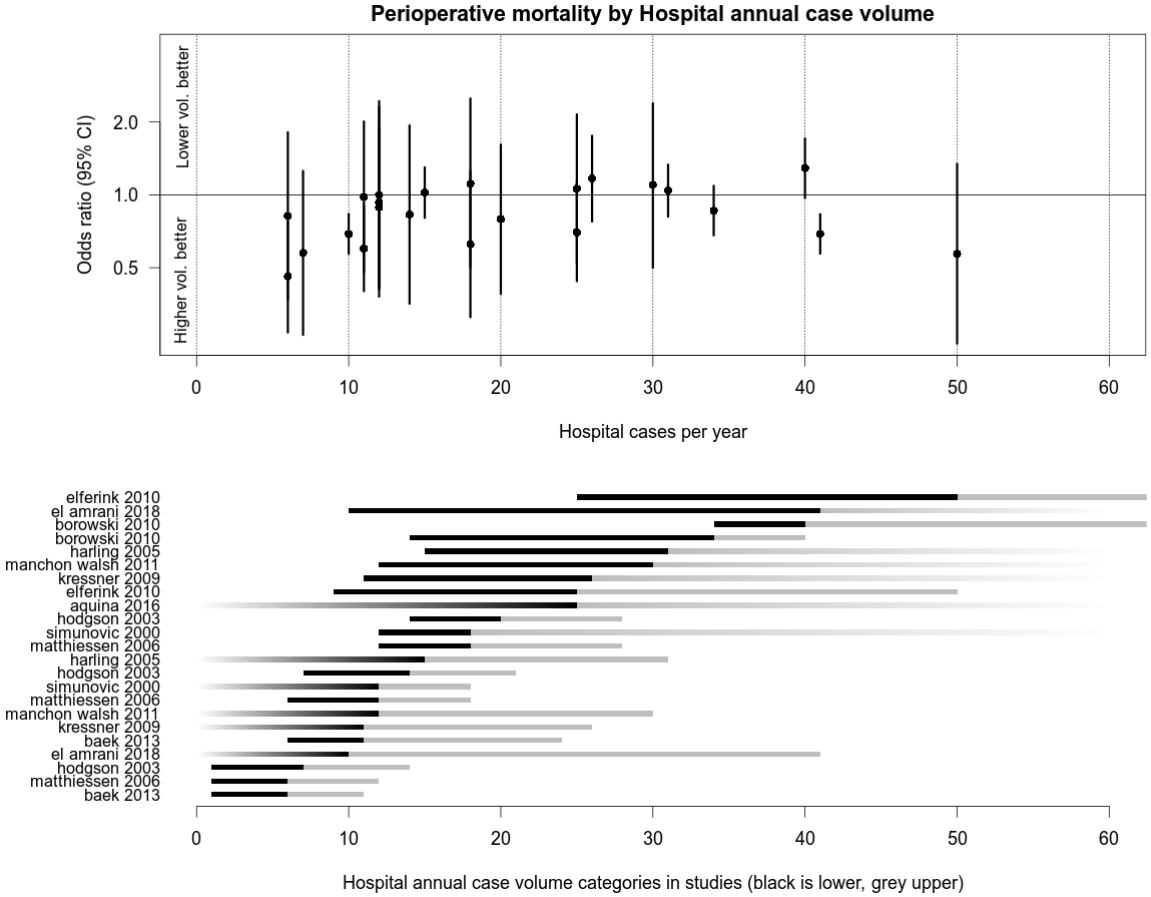
Figure 7: Outcomes by hospital volume of rectal cancer surgery – Permanent stoma



CI: confidence interval

1

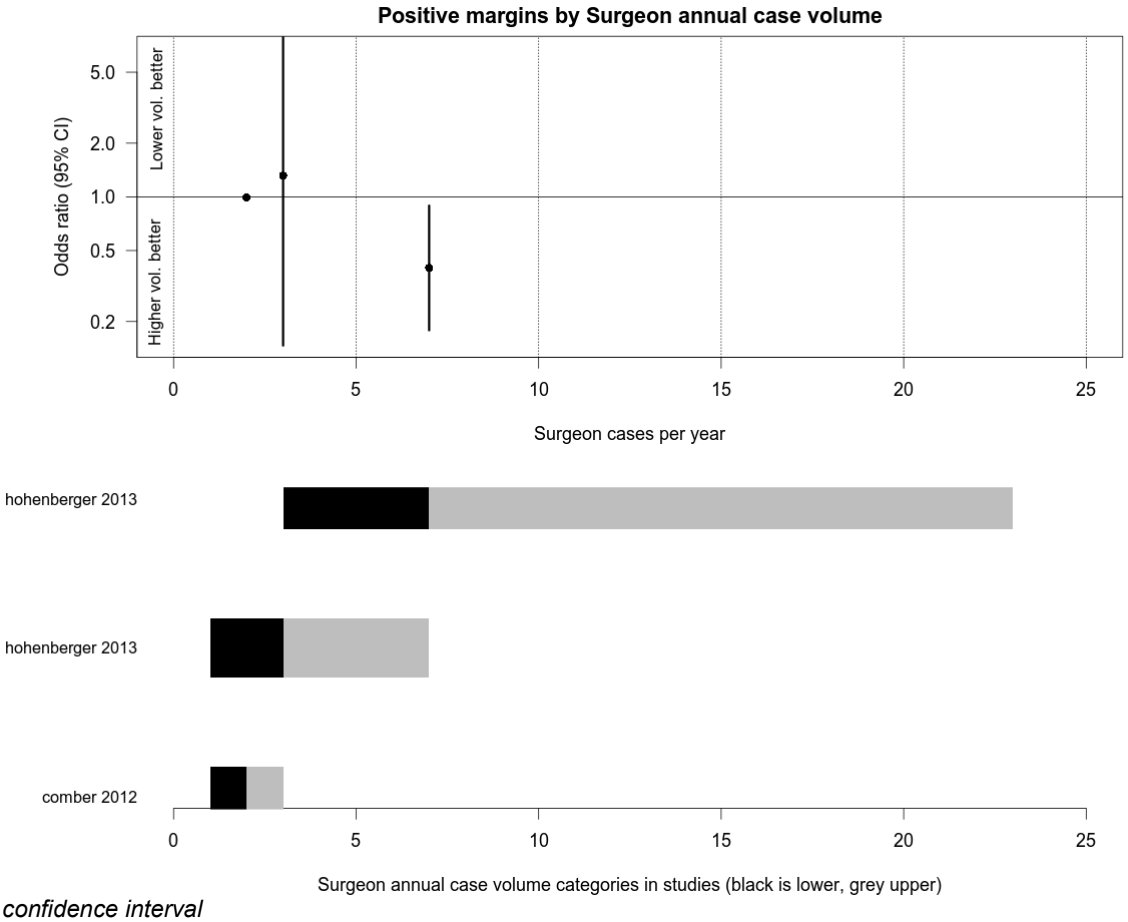
Figure 8: Outcomes by hospital volume of rectal cancer surgery – Perioperative mortality



CI: confidence interval

1

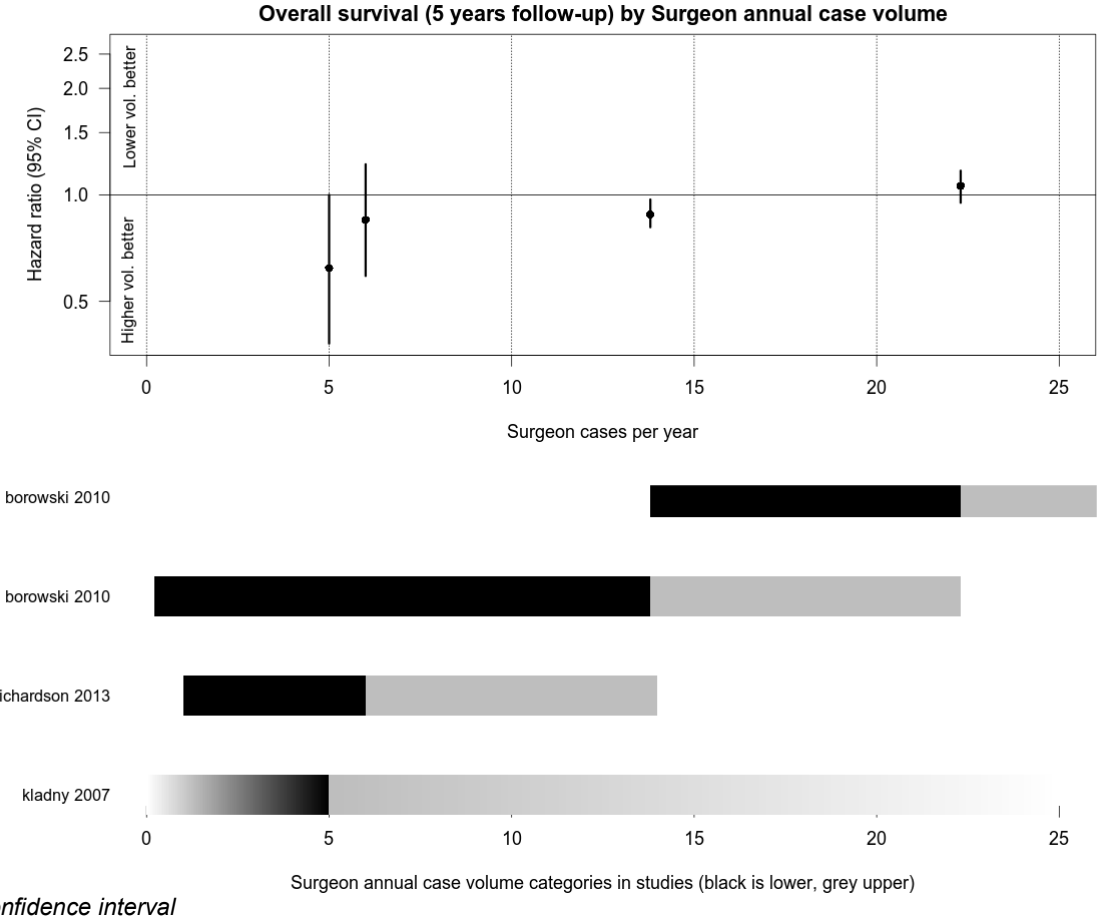
Figure 9: Outcomes by surgeon volume of rectal cancer surgery – Resection margins



CI: confidence interval

1

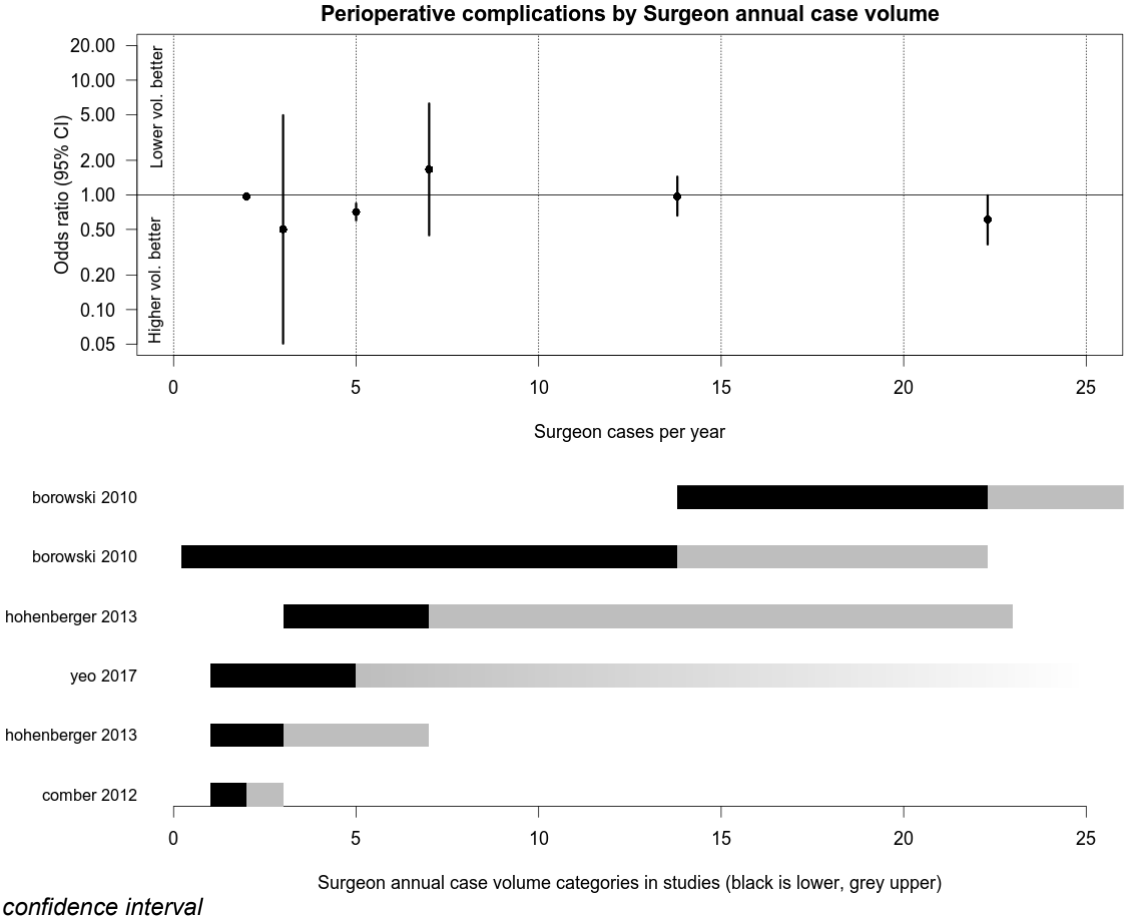
Figure 10: Outcomes by surgeon volume of rectal cancer surgery – Overall 5 year survival



CI: confidence interval

1

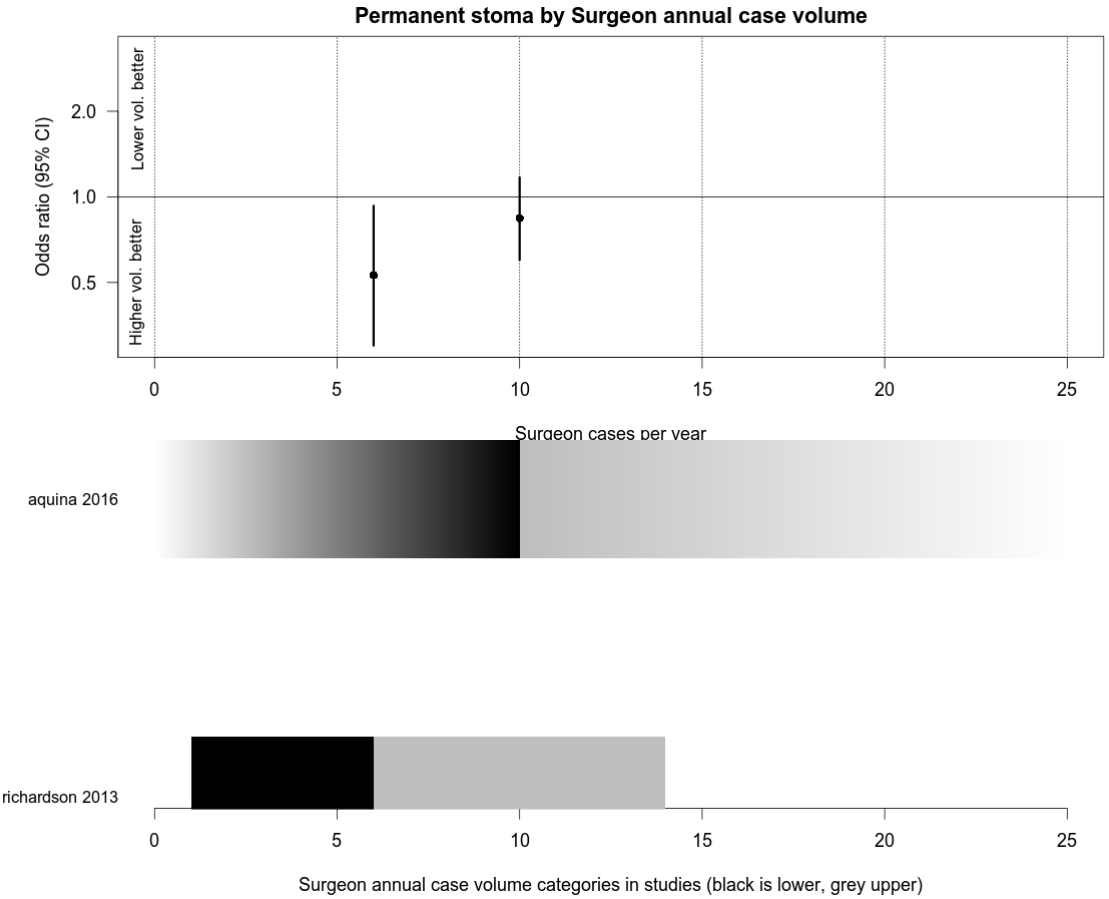
Figure 11: Outcomes by surgeon volume of rectal cancer surgery – Grade 3 or 4 complications



CI: confidence interval

1

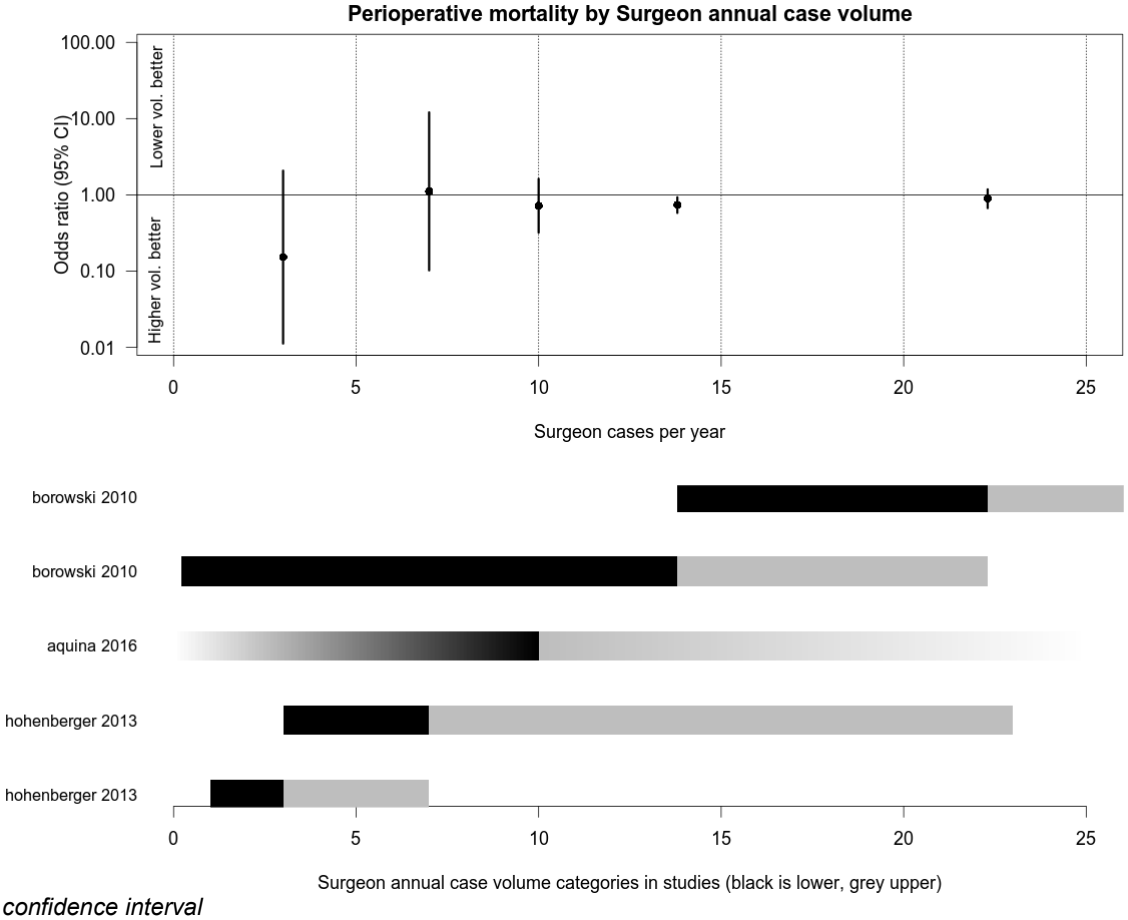
Figure 12: Outcomes by surgeon volume of rectal cancer surgery – Permanent stoma



CI: confidence interval

1

Figure 13: Outcomes by surgeon volume of rectal cancer surgery – Perioperative mortality



CI: confidence interval

1

1 Appendix F – GRADE tables

2 GRADE tables for review question: Is there a relationship between surgical volumes and outcomes in the treatment of rectal 3 cancer (primary and recurrent disease)?

4 Table 11: Clinical evidence profile for outcomes by hospital volume of rectal cancer surgery (higher volume versus lower volume)

Quality assessment							N participants	Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		Relative (95% CI)	Absolute		
Positive resection margins – higher versus lower volume (volume threshold between 1 to 9 cases per annum)											
2	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	113,694	OR ranged from 0.99 to 1.04 (median 1.02)	-	MODERATE	CRITICAL
Positive resection margins – higher versus lower volume (volume threshold between 10 to 19 cases per annum)											
1	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	113,113	OR 0.88 (0.75,1.03)	-	MODERATE	CRITICAL
Positive resection margins – higher versus lower volume (volume threshold between 20 to 29 cases per annum)											
1	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	113,113	OR 1.01 (0.86,1.18)	-	MODERATE	CRITICAL
Positive resection margins – per additional case											
1	observational	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	581	OR 0.99 (0.96,1.02)	-	VERY LOW	CRITICAL
Overall survival – higher versus lower volume (volume threshold between 1 to 9 cases per annum)											
3	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	4,903	HR ranged from 0.99 to 1 (median 1)	-	MODERATE	CRITICAL
Overall survival – higher versus lower volume (volume threshold between 10 to 19 cases per annum)											
4	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	7,894	HR ranged from 0.83 to 0.91 (median 0.87)	-	MODERATE	CRITICAL
Overall survival – higher versus lower volume (volume threshold between 20 to 29 cases per annum)											

Quality assessment							N participants	Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		Relative (95% CI)	Absolute		
4	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	10,405	HR ranged from 0.72 to 1.1 (median 0.89)	-	MODERATE	CRITICAL
Overall survival – higher versus lower volume (volume threshold between 30 to 39 cases per annum)											
4	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	16,021	HR ranged from 0.62 to 0.91 (median 0.87)	-	MODERATE	CRITICAL
Overall survival – higher versus lower volume (volume threshold between 40 to 49 cases per annum)											
1	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	7,441	HR 1.03 (0.94,1.13)	-	MODERATE	CRITICAL
Overall survival – higher versus lower volume (volume threshold between 50 to 59 cases per annum)											
1	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	2,095	HR 1.00 (0.65 to 1.54)	-	MODERATE	CRITICAL
Overall survival – per additional case											
1	observational	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	1,469	HR 1.00 (0.99 to 1.01)	-	HIGH	CRITICAL
Perioperative complications – Grade 3 or 4 complications – higher versus lower volume (volume threshold between 1 to 9 cases per annum)											
1	observational	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	581	OR 1.2 (0.97,1.06)	-	VERY LOW	CRITICAL
Perioperative complications – Grade 3 or 4 complications – higher versus lower volume (volume threshold between 10 to 19 cases per annum)											
2	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	6,852	OR ranged from 0.65 to 1.31 (median 0.98)	-	MODERATE	CRITICAL
Perioperative complications – Grade 3 or 4 complications – higher versus lower volume (volume threshold between 20 to 29 cases per annum)											
1	observational	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	1,511	OR 1.09 (0.77,1.54)	-	LOW	CRITICAL
Perioperative complications – Grade 3 or 4 complications – higher versus lower volume (volume threshold between 30 to 39 cases per annum)											
3	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	14,293	OR ranged from 1.14 to 1.38 (median 1.23)	-	MODERATE	CRITICAL
Perioperative complications – Grade 3 or 4 complications – higher versus lower volume (volume threshold between 40 to 49 cases per annum)											

Quality assessment							N participants	Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		Relative (95% CI)	Absolute		
1	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	7,441	OR 1.01 (0.64,1.6)	-	MODERATE	CRITICAL
Perioperative complications – Grade 3 or 4 complications – higher versus lower volume (volume threshold between 50 to 59 cases per annum)											
1	observational	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	1,511	OR 1.19 (0.75,1.91)	-	LOW	CRITICAL
Perioperative complications – Grade 3 or 4 complications – per additional case											
1	observational	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	581	OR 1.02 (0.97,1.07)	-	VERY LOW	CRITICAL
Perioperative complications – unplanned return to theatre – not reported											
0	-	-	-	-	-	-	-	-	-	-	CRITICAL
Local recurrence – higher versus lower volume (volume threshold between 1 to 9 cases per annum)											
2	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	2,799	HR ranged from 1 to 1.2 (median 1.1)	-	MODERATE	IMPORTANT
Local recurrence – higher versus lower volume (volume threshold between 10 to 19 cases per annum)											
2	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	4,718	HR ranged from 0.68 to 0.76 (median 0.72)	-	MODERATE	IMPORTANT
Local recurrence – higher versus lower volume (volume threshold between 20 to 29 cases per annum)											
3	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	7,855	HR ranged from 0.72 to 1.23 (median 1.1)	-	MODERATE	IMPORTANT
Local recurrence – higher versus lower volume (volume threshold between 30 to 39 cases per annum)											
2	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	6,298	HR ranged from 0.62 to 0.76 (median 0.69)	-	MODERATE	IMPORTANT
Local recurrence – per additional case											
1	observational	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	1,469	HR 0.99 (0.97 to 1.01)	-	MODERATE	CRITICAL
Overall quality of life – not reported											
0	-	-	-	-	-	-	-	-	-	-	IMPORTANT

Quality assessment							N participants	Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		Relative (95% CI)	Absolute		
Permanent stoma – higher versus lower volume (volume threshold between 1 to 9 cases per annum)											
4	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	19,922	OR ranged from 0.84 to 1 (median 0.93)	-	MODERATE	IMPORTANT
Permanent stoma – higher versus lower volume (volume threshold between 10 to 19 cases per annum)											
4	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	20,795	OR ranged from 0.44 to 0.9 (median 0.67)	-	MODERATE	IMPORTANT
Permanent stoma – higher versus lower volume (volume threshold between 20 to 29 cases per annum)											
2	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	15,055	OR ranged from 0.83 to 0.86 (median 0.84)	-	MODERATE	IMPORTANT
Permanent stoma – higher versus lower volume (volume threshold between 30 to 39 cases per annum)											
1	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	5,021	OR 0.61 (0.34,1.09)	-	MODERATE	IMPORTANT
Permanent stoma – per additional case											
1	observational	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	4,622	OR 1.00 (1.00 to 1.01)	-	HIGH	CRITICAL
Perioperative mortality – higher versus lower volume (volume threshold between 1 to 9 cases per annum)											
3	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	14,584	OR ranged from 0.46 to 0.82 (median 0.58)	-	MODERATE	IMPORTANT
Perioperative mortality – higher versus lower volume (volume threshold between 10 to 19 cases per annum)											
8	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	79,714	OR ranged from 0.6 to 1.11 (median 0.91)	-	MODERATE	IMPORTANT
Perioperative mortality – higher versus lower volume (volume threshold between 20 to 29 cases per annum)											
4	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	41,519	OR ranged from 0.7 to 1.17 (median 0.93)	-	MODERATE	IMPORTANT
Perioperative mortality – higher versus lower volume (volume threshold between 30 to 39 cases per annum)											

Quality assessment							N participants	Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		Relative (95% CI)	Absolute		
3	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	14,293	OR ranged from 0.86 to 1.1 (median 1.04)	-	MODERATE	IMPORTANT
Perioperative mortality – higher versus lower volume (volume threshold between 40 to 49 cases per annum)											
2	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	53,010	OR ranged from 0.69 to 1.29 (median 0.99)	-	MODERATE	IMPORTANT
Perioperative mortality – higher versus lower volume (volume threshold between 50 to 59 cases per annum)											
1	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	16,039	OR 0.57 (0.24,1.34)	-	MODERATE	IMPORTANT

CI: confidence interval; HR: hazard ratio; OR: odds ratio
HR or OR less than 1 favours higher case volume hospitals.
1 Quality of the evidence downgraded by 1 level because hospital case volume (a continuous outcome) has been dichotomised by these studies, so the statistical power to detect a relation between the case volume and patient outcome is reduced.
2 Quality of the evidence downgraded by 2 levels because patient characteristics not reported; study did not account for attrition; study did not describe outcome measurement.
3 Quality of the evidence downgraded by 1 level due to imprecisions (number of events < 300)

Table 12: Clinical evidence profile for outcomes by surgeon volume of rectal cancer surgery (higher volume versus lower volume)

Quality assessment							N participants	Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		Relative (95% CI)	Absolute		
Positive resection margins – higher versus lower volume (volume threshold < 5 cases per annum)											
2	observational	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	1,609	OR ranged from 0.99 to 1.32 (median 1.15)	-	LOW	CRITICAL
Positive resection margins – higher versus lower volume (volume threshold between 5 to 9 cases per annum)											

Quality assessment							N participants	Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		Relative (95% CI)	Absolute		
1	observational	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	1,028	OR 0.40 (0.18,0.89)	-	LOW	CRITICAL
Overall survival – higher versus lower volume (volume threshold between 5 to 9 cases per annum)											
2	observational	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	807	HR ranged from 0.62 to 0.85 (median 0.74)	-	LOW	CRITICAL
Overall survival – higher versus lower volume (volume threshold between 10 to 14 cases per annum)											
1	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	7,441	HR 0.88 (0.81,0.97)	-	MODERATE	CRITICAL
Overall survival – higher versus lower volume (volume threshold between 20 to 24 cases per annum)											
1	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	7,441	HR 1.06 (0.95 to 1.17)	-	MODERATE	CRITICAL
Perioperative complications – Grade 3 or 4 complications – higher versus lower volume (volume threshold < 5 cases per annum)											
2	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	1,609	OR ranged from 0.5 to 0.97 (median 0.74)	-	MODERATE	CRITICAL
Perioperative complications – Grade 3 or 4 complications – higher versus lower volume (volume threshold between 5 to 9 cases per annum)											
2	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	15,861	OR ranged from 0.71 to 1.67 (median 1.19)	-	MODERATE	CRITICAL
Perioperative complications – Grade 3 or 4 complications – higher versus lower volume (volume threshold between 10 to 14 cases per annum)											
1	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	7,441	OR 0.97 (0.66,1.44)	-	MODERATE	CRITICAL
Perioperative complications – Grade 3 or 4 complications – higher versus lower volume (volume threshold between 20 to 24 cases per annum)											
1	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	7,441	OR 0.61 (0.37 to 0.99)	-	MODERATE	CRITICAL
Perioperative complications – Grade 3 or 4 complications – per additional case											
1	observational	very serious[3]	no serious inconsistency	no serious indirectness	serious[2]	none	581	OR 0.97 (0.91 to 1.03)	-	VERY LOW	CRITICAL
Perioperative complications – unplanned return to theatre – higher versus lower volume (volume threshold between 5 to 9 cases per annum)											
1	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	14,833	OR 0.98 (0.82 to 1.17)	-	MODERATE	CRITICAL
Local recurrence – higher versus lower volume (volume threshold between 5 to 9 cases per annum)											

Quality assessment							N participants	Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		Relative (95% CI)	Absolute		
1	observational	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	521	HR 0.54 (0.29 to 0.99)	-	LOW	IMPORTANT
Overall quality of life – not reported											
0	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Permanent stoma – higher versus lower volume (volume threshold between 5 to 9 cases per annum)											
1	observational	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	521	OR 0.53 (0.3,0.93)	-	LOW	IMPORTANT
Permanent stoma – higher versus lower volume (volume threshold between 10 to 14 cases per annum)											
1	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	7,798	OR 0.84 (0.6,1.17)	-	MODERATE	IMPORTANT
Perioperative mortality – higher versus lower volume (volume threshold 1 to 4 cases per annum)											
1	observational	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	1,028	OR 0.15 (0.01,2.07)	-	LOW	IMPORTANT
Perioperative mortality – higher versus lower volume (volume threshold between 5 to 9 cases per annum)											
1	observational	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	1,028	OR 1.11 (0.1,12.06)	-	LOW	IMPORTANT
Perioperative mortality – higher versus lower volume (volume threshold between 10 to 14 cases per annum)											
2	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	15,239	OR ranged from 0.72 to 0.74 (median 0.73)	-	MODERATE	IMPORTANT
Perioperative mortality – higher versus lower volume (volume threshold between 20 to 24 cases per annum)											
1	observational	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	7,441	OR 0.89 (0.67 to 1.18)	-	MODERATE	IMPORTANT

1 *CI: confidence interval; HR: hazard ratio; OR: odds ratio*
2 *HR or OR less than 1 favours higher case volume surgeons.*
3 *1 Quality of the evidence downgraded by 1 level because surgeon case volume (a continuous outcome) has been dichotomised by these studies, so the statistical power to*
4 *detect a relation between the case volume and patient outcome is reduced.*
5 *2 Quality of the evidence downgraded by 1 level due to imprecisions (number of events < 300)*
6 *3 Quality of the evidence downgraded by 2 levels because patient characteristics not reported; study did not account for attrition; study did not describe outcome measurement.*

Appendix G – Economic evidence study selection

Economic evidence study selection for review question: Is there a relationship between surgical volumes and outcomes in the treatment of rectal cancer (primary and recurrent disease)?

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 tables for review question: Is there a relationship between surgical volumes and outcomes in the treatment of rectal cancer (primary and recurrent disease)?

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

Appendix I – Economic evidence profiles

Economic evidence profiles for review question: Is there a relationship between surgical volumes and outcomes in the treatment of rectal cancer (primary and recurrent disease)?

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

Appendix J – Economic analysis

Economic evidence analysis for review question: Is there a relationship between surgical volumes and outcomes in the treatment of rectal cancer (primary and recurrent disease)?

No economic analysis was conducted for this review question.

1 Appendix K – Excluded studies

2 Excluded clinical studies for review question: Is there a relationship between 3 surgical volumes and outcomes in the treatment of rectal cancer (primary and 4 recurrent disease)?

5 **Table 13: Excluded studies and reasons for their exclusion**

Study	Reason for exclusion
Aquina, C. T., Rickles, A. S., Iannuzzi, J. C., Probst, C. P., Kelly, K. N., Zhang, L., Noyes, K., Monson, J. R. T., Fleming, F. J., Centres of excellence have lower ostomy-related complications, Colorectal Disease, 16, 42, 2014	Abstract
Archampong, D., Borowski, D. W., Dickinson, H. O., Impact of surgeon volume on outcomes of rectal cancer surgery: A systematic review and meta-analysis, Surgeon, 8, 341-352, 2010	All studies and outcomes reported in Cochrane systematic review (Archampong 2012)
Avdic, D., Lundborg, P., Vikstrom, J., Estimating returns to hospital volume: Evidence from advanced cancer surgery, Journal of Health Economics, 63, 81-99, 2019	Not rectal cancer
Boyle, E., Timmons, A., Al-Akash, M., Kennedy, A. M., O'Grady, H., Hill, A. D., Comber, H., Keane, F. B., The management of rectal cancer in Ireland in 2007 - room for improvement?, Surgeon, 9, 179-186, 2011	Outcomes not relevant
Brady, J. T., Xu, Z., Scarberry, K. B., Saad, A., Fleming, F. J., Remzi, F. H., Wexner, S. D., Winchester, D. P., Monson, J. R. T., Lee, L., Dietz, D. W., Evaluating the Current Status of Rectal Cancer Care in the US: Where We Stand at the Start of the Commission on Cancer's National Accreditation Program for Rectal Cancer, Journal of the American College of Surgeons, 226, 881-890, 2018	Outcomes not relevant
Chioreso, C., Del Vecchio, N., Schweizer, M. L., Schlichting, J., Gribovskaja-Rupp, I., Charlton, M. E., Association Between Hospital and Surgeon Volume and Rectal Cancer Surgery Outcomes in Patients With Rectal Cancer Treated Since 2000: Systematic Literature Review and Meta-analysis, Diseases of the Colon and Rectum, 61, 1320-1332, 2018	Systematic review - checked for relevant studies.
DaSilva, G., Bashankaev, B., Rosen, L., Narita, K., Cadeddu, F., Wexner, S. D., Low rates of abdominal-perineal resection for rectal cancer - Are they useful in predicting superior performance?, Colorectal Disease, 1), 26, 2010	Abstract
Debes, A. J., Storkson, R. H., Jacobsen, M. B., Curative rectal cancer surgery in a low-volume hospital: A quality assessment, European Journal of Surgical Oncology, 34, 382-389, 2008	No case mix adjustments
Deijen, C. L., Tsai, A., Koedam, T. W. A., Veltcamp Helbach, M., Sietses, C., Lacy, A. M., Bonjer, H. J., Tuynman, J. B., Clinical outcomes and case volume effect of transanal total mesorectal excision for rectal cancer: a systematic review, Techniques in Coloproctology, 20, 811-824, 2016	Studies included in systematic review not relevant
Drolet, S., Shaheen, A. A., Maclean, A. R., Dixon, E., Myers, R. P., Increased rate of sphincter preservation following rectal cancer resection in high volume hospitals, Gastroenterology, 1), S868, 2010	Abstract
Engel, J., Kerr, J., Eckel, R., Gunther, B., Heiss, M., Heitland, W., Siewert, J. R., Jauch, K. W., Holzel, D., Influence of hospital volume on local recurrence and survival in a population sample of rectal cancer patients, European Journal of Surgical Oncology, 31, 512-520, 2005	No case mix adjustments

Study	Reason for exclusion
Etzioni, D. A., Young-Fadok, T. M., Cima, R. R., Wasif, N., Madoff, R. D., Naessens, J. M., Habermann, E. B., Patient survival after surgical treatment of rectal cancer: Impact of surgeon and hospital characteristics, Cancer, 120, 2472-2481, 2014	Outcomes not relevant
Guller, U., Warschkow, R., Ackermann, C. J., Schmied, B. M., Cerny, T., Ess, S., Lower hospital volume is associated with higher mortality after oesophageal, gastric, pancreatic and rectal cancer resection, Swiss Medical Weekly, 147 (no pagination), 2017	Outcomes not relevant
Hatzidis,, Solomon,, Schnitzler,, Cartmill,, Loder,, Chapuis,, Does the caseload of the pathologist influence the minimum and extended data set of pathology variables reported for rectal adenocarcinoma?, Colorectal Disease, 2, 26-30, 2000	Outcomes not relevant
Hermanek, P., Hermanek, P. J., Role of the surgeon as a variable in the treatment of rectal cancer, Seminars in Surgical Oncology, 19, 329-335, 2000	Literature review of studies published pre-2000
Hoehn, R. S., Go, D. E., Hanseman, D. J., Shah, S. A., Paquette, I. M., Hospital safety-net burden does not predict differences in rectal cancer treatment and outcomes, Journal of Surgical Research, 221, 204-210, 2018	Outcomes not relevant
Huo, Y. R., Phan, K., Morris, D. L., Liauw, W., Systematic review and a meta-analysis of hospital and surgeon volume/outcome relationships in colorectal cancer surgery, Journal of Gastrointestinal Oncology, 8, 534-546, 2017	Studies in systematic review assessed individually
Khoury, W., Lavery, I., Kiran, R., Are there surgeon-related variations in outcomes for patients with rectal cancer undergoing resection at a tertiary center?, Diseases of the Colon and Rectum, 52 (4), 816, 2009	Abstract
Klingbeil, K., MacLean, A., Datta, I., Brar, M., Heine, J., Buie, D., Rectal cancer surgery by high volume surgeons results in improved oncologic outcomes and sphincter preservation, Diseases of the Colon and Rectum, 56 (4), e264-e265, 2013	Abstract
Lee, J., Doumouras, A., Springer, J., Eskicioglu, C., Amin, N., Caddedu, M., Hong, D., The influence of comparable procedure volumes on patient outcomes after laparoscopic rectal surgery, Diseases of the Colon and Rectum, 61 (5), e60, 2018	Abstract
Link, K. H., Coy, P., Roitman, M., Link, C., Kornmann, M., Staib, L., Minimum volume discussion in the treatment of colon and rectal cancer: A review of the current status and relevance of surgeon and hospital volume regarding result quality and the impact on health economics, Visceral Medicine, 33, 140-147, 2017	Literature review
Martling, A., Cedermark, B., Johansson, H., Rutqvist, L. E., Holm, T., The surgeon as a prognostic factor after the introduction of total mesorectal excision in the treatment of rectal cancer, British Journal of Surgery, 89, 1008-13, 2002	No case mix adjustments
Marusch, F., Koch, A., Schmidt, U., Pross, M., Gastinger, I., Lippert, H., Hospital caseload and the results achieved in patients with rectal cancer, British Journal of Surgery, 88, 1397-1402, 2001	No case mix adjustments
Murken, D., Concors, S. J., Aarons, C. B., Saur, N. M., Shanmugan, S. S., Paulson, E., Operative outcomes after robotic proctectomy for rectal cancer are influenced by center-level volume, Diseases of the Colon and Rectum, 61 (5), e229-e230, 2018	Abstract
Nugent, E., Neary, P., Rectal cancer surgery: volume-outcome analysis, International Journal of Colorectal DiseaseInt J Colorectal Dis, 25, 1389-96, 2010	Narrative review

Study	Reason for exclusion
Ortiz, H., Biondo, S., Codina, A., Ciga, M. A., Enriquez-Navascues, J. M., Espin, E., Garcia-Granero, E., Roig, J. V., Hospital variability in postoperative mortality after rectal cancer surgery in the Spanish Association of Surgeons project: The impact of hospital volume, Cirugia Espanola, 94, 22-30, 2016	Outcomes not relevant
Pawlak, M., Morawiec, Z., Dziki, L., Morawiec, J., Kolacinska, A., Dziki, A., Does the choice of hospital increase a chance of survival in rectal cancer?, Polski przeglad chirurgiczny, 84, 638-645, 2012	No case mix adjustments
Pucciarelli, S., Zorzi, M., Gennaro, N., Marchegiani, F., Barina, A., Rugge, M., Zuin, M., Perin, A., Maretto, I., Bergamo, F., Boso, C., Urso, E. D. L., Frambach, P., Corti, M. C., Relationship between hospital volume and short-term outcomes: A nationwide population-based study including 75,280 rectal cancer surgical procedures, Oncotarget, 9, 17149-17159, 2018	Outcomes not relevant
Ricciardi, R., Baxter, N., Read, T., Roberts, P., Marcello, P., Schoetz, D., Presence of specialty surgeons reduces the likelihood of colostomy formation after proctectomy for rectal cancer, Diseases of the Colon and Rectum, 53 (4), 616, 2010	Abstract
Salz, T., Sandler, R. S., The Effect of Hospital and Surgeon Volume on Outcomes for Rectal Cancer Surgery, Clinical Gastroenterology and Hepatology, 6, 1185-1193, 2008	Studies assessed in Cochrane review Archampong 2012
Schrag, D., Panageas, K. S., Riedel, E., Cramer, L. D., Guillem, J. G., Bach, P. B., Begg, C. B., Hospital and surgeon procedure volume as predictors of outcome following rectal cancer resection, Annals of Surgery, 236, 583-592, 2002	No case mix adjustments
Sineshaw, H. M., Jemal, A., Mitin, T., Changes in treatment patterns for patients with locally advanced rectal cancer in the United States over the past decade: An analysis from the National Cancer Data Base (NCDB), Journal of Clinical Oncology. Conference, 34, 2016	Abstract
Snijders, H., Henneman, D., Fiocco, M., Leersum, N. J., Tollenaar, R. A. E. M., Wouters, M. J. W. M., The limited relevance of case-mix adjustment when comparing anastomotic leakage rates between hospitals, European Journal of Surgical Oncology, 38 (9), 791, 2012	Abstract
Vignali, A., Kusamura, S., Staudacher, C., Learning curve and surgeon volume in laparoscopic TME. A single istitu-tional series of 245 cases, Diseases of the Colon and Rectum, 54 (5), e41, 2011	Abstract
Wyrwicz, L., Michalski, W., Rutkowski, A., Krynski, J., Zajac, L., Szczepkowski, M., Tarnowski, W., Kosakowska, E., Winiarek, M., Polkowski, W., Impact of surgical site experience on treatment outcomes of fixed-cT3 and cT4 rectal cancer patients in phase III study comparing preoperative radiochemotherapy and short-course radiotherapy with consolidation chemotherapy (Polish-II study), Annals of Oncology, 27, ii125-ii126, 2016	Abstract
Xu, Z., Becerra, A. Z., Justiniano, C. F., Boodry, C. I., Aquina, C. T., Swanger, A. A., Temple, L. K., Fleming, F. J., Is the distance worth it? Patients with rectal cancer traveling to high-volume centers experience improved outcomes, Diseases of the Colon and Rectum, 60, 1250-1259, 2017	Outcomes reported without p-values; reference groups not relevant; unable to assess data
Yasunaga, H., Matsuyama, Y., Ohe, K., Volume-outcome relationship in rectal cancer surgery: A new perspective, Surgery Today, 39, 663-668, 2009	No case mix adjustments

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Appendix L – Research recommendations

Research recommendations for review question: Is there a relationship between surgical volumes and outcomes in the treatment of rectal cancer (primary and recurrent disease)?

No research recommendations were made for this review question.