Systematic Review and Meta-analysis

Systematic review and a meta-analysis of hospital and surgeon volume/outcome relationships in colorectal cancer surgery

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Background: Numerous hospitals worldwide are considering setting minimum volume standards for colorectal surgery. This study aims to examine the association between hospital and surgeon volume on outcomes for colorectal surgery.

Methods: Two investigators independently reviewed six databases from inception to May 2016 for articles that reported outcomes according to hospital and/or surgeon volume. Eligible studies included those in which assessed the association hospital or surgeon volume with outcomes for the surgical treatment of colon and/or rectal cancer. Random effects models were used to pool the hazard ratios (HRs) for the association between hospital/surgeon volume with outcomes.

Results: There were 47 articles pooled (1,122,303 patients, 9,877 hospitals and 9,649 surgeons). The meta-analysis demonstrated that there is a volume-outcome relationship that favours high volume facilities and high volume surgeons. Higher hospital and surgeon volume resulted in reduced 30-day mortality (HR: 0.83; 95% CI: 0.78–0.87, P<0.001 & HR: 0.84; 95% CI: 0.80–0.89, P<0.001 respectively) and intra-operative mortality (HR: 0.82; 95% CI: 0.76–0.86, P<0.001 & HR: 0.50; 95% CI: 0.40–0.62, P<0.001 respectively). Post-operative complication rates depended on hospital volume (HR: 0.89; 95% CI: 0.81–0.98, P<0.05), but not surgeon volume except with respect to anastomotic leak (HR: 0.59; 95% CI: 0.37–0.94, P<0.01). High volume surgeons are associated with greater 5-year survival and greater lymph node retrieval, whilst reducing recurrence rates, operative time, length of stay and cost. The best outcomes occur in high volume hospitals with high volume surgeons, followed by low volume hospitals with high volume surgeons.

Conclusions: High volume by surgeon and high volume by hospital are associated with better outcomes for colorectal cancer surgery. However, this relationship is non-linear with no clear threshold of effect being identified and an apparent ceiling of effect.

Keywords: Colorectal cancer; volume-outcome; hospital volume; surgeon volume; meta-analyses

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Introduction

In 1979, Luft *et al.* called for regionalisation of certain types of surgery after demonstrating a relationship between surgical volume and outcome (1). Although this was an intuitive observation implementation of the recommendations has been controversial. As recently as 2015 a consortia of hospitals in the US have pledged to meet minimum volume standards for certain surgery types including rectal cancer surgery (2).

Volume-outcome relationships have been studied with respect to surgeon volume, hospital volume and the interaction between each of these variables. In cancer surgery volume-outcome relationships may focus on measures of surgical safety such as morbidity and mortality, value and performance measures such as length of stay, and quality measures related to the oncologic outcome such as disease free and overall survival. An association between volume and outcomes has been reported for oesophagectomy (3,4), pancreatectomy (4) and hepatic resections (3).

Demonstrating surgeon or hospital volume-outcome relationships in colorectal cancer surgery has been unclear due to inconsistent results (5-8). Potential reasons for variation in the results could relate to the setting of the studies such as Medicare or Department of Veterans Affairs only, and geographical variation between states, countries and continents. In addition there might be variance depending on the site of surgery i.e. colon versus rectum, and type of surgery, open, laparascopic or more recently robotic.

This review and meta-analysis aims to pool the current worldwide literature for the association between colorectal surgery outcomes with hospital volume and surgeon volume. This review will clarify several controversial issues including: (I) whether a hospital volume-outcome relationship exists in colorectal cancer resection; (II) whether a surgeon volume-outcome relationship exists; and (III) clarifying the association between high-hospital-volume-low-surgeon-volume versus low-hospital-volume-high-surgeon-volume.

Methods

Literature search

The present systematic review and meta-analysis was performed according to the meta-analysis of Observational Studies in Epidemiology (MOOSE) (9), PRISMA guidelines (10) and recommendations (9). Electronic searches were performed using Embase, Ovid Medline, PubMed, Cochrane Central Register of Controlled Trials (CCTR), Cochrane Database of Systematic Reviews (CDSR) and ACP Journal Club and Database of Abstracts of Review of Effectiveness (DARE) from their dates of inception to May 2016. To achieve maximum sensitivity of the search strategy and identify all studies, the following terms were combined as either keywords of MeSH terms: "volume", "outcome", "colorectal surgery", "colon surgery", "rectal surgery", "morbidity", "mortality", "complications", "hospital" and/or "surgeon". The reference lists of all retrieved articles were reviewed for further identification of potentially relevant studies. All identified articles were systematically assessed using the inclusion and exclusion criteria. Retrieval of the full articles of all available studies were conducted, including direct contact with authors.

Selection criteria

Eligible studies for the present systematic review and meta-analysis included those in which: (I) the subject of the study is the surgical treatment of colon, rectal or colorectal cancer; (II) hospital volume or surgeon volume is an independent variable tested; and (III) outcome parameters include post-operative mortality or survival. Studies that did not include mortality or complications as endpoints were excluded. When institutions published duplicate studies with accumulating numbers of patients or increased lengths of follow-up, only the most complete reports were included for quantitative assessment at each time interval. All publications were limited to those involving human subjects. There was no language restriction. Abstracts, unpublished studies, case reports, conference presentations, editorials, reviews and expert opinions were excluded.

Data extraction and appraisal

Two investigators independently conducted the study search [Y.R.H (BMed/MD, Honours), K.P. (MD, MPhil)]. The full articles of all relevant studies were extracted and evaluated for inclusion by both investigators. Discrepancies between the two reviewers were resolved by discussion and consensus with the two other authors [D.L.M (MD, PhD), W.L (MD)]. Study characteristics collected included year of publication, study period, primary country the study is based, population description, number of patients and number of hospitals. Outcomes extracted include 30-day mortality, in-hospital mortality, 5-year mortality, 5-year

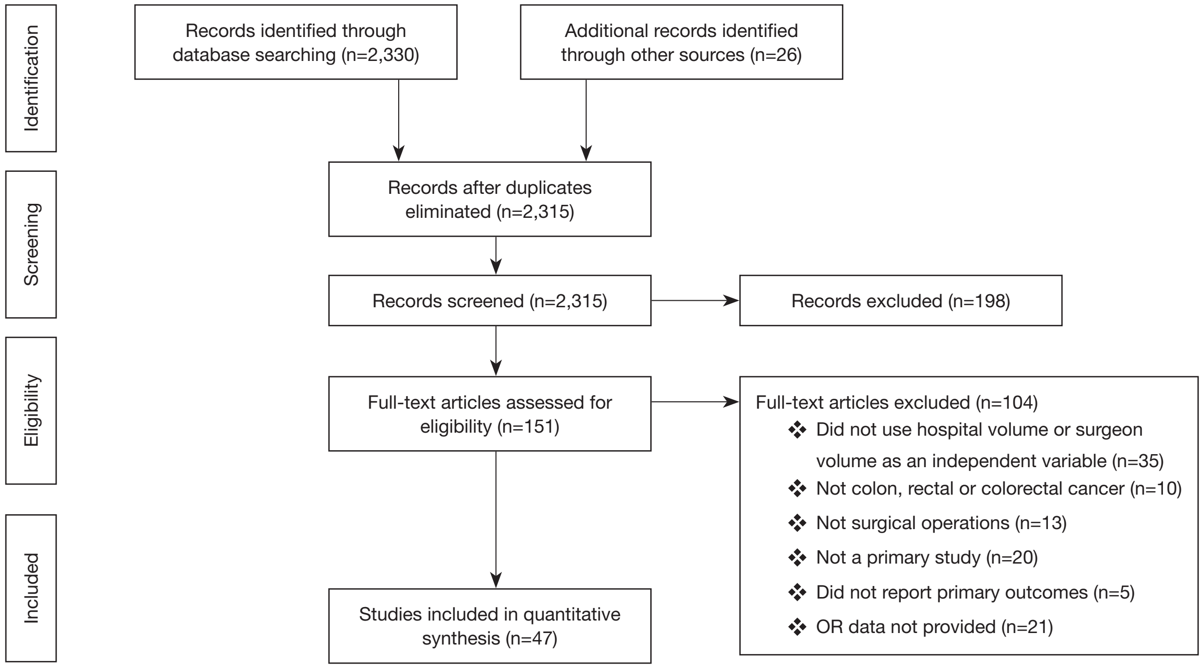

Figure 1 PRISMA flowchart for study selection

recurrence, local regional recurrence (LRR), postoperative complications, postoperative mortality, stoma rates, anastomic leak rates, and overall survival. Outcomes were extracted where possible as Hazard ratios (HR); 95% confidence interval (CI), and P values. Where possible, pooled outcomes were stratified by surgical procedure (rectal *vs.* colon *vs.* colorectal), and by the volume parameter (hospital procedure volume or surgeon volume).

Statistical analysis

Combined HRs for the association between hospital volume or surgeon volume with surgical outcomes were pooled under a random effects models. Heterogeneity analysis was performed using the Cochran Q test and I^2 index. Computations were performed using Comprehensive meta-Analysis v2 software (Biostat Inc, Englewood, New Jersey, USA).

Results

Methodologic characteristics of included studies

The initial search identified 2,330 potentially relevant articles to which the exclusion and inclusion criteria were applied (*Figure 1*). After exclusion of duplicate or irrelevant references, 2,315 potentially relevant articles were retrieved. After detailed evaluation of these articles, 151 studies remained for detailed assessment.After applying inclusion and exclusion criteria, 47 studies (*Table 1*) were included for the present systematic review and meta-analysis, of which: 18 only examined surgeon and/or hospital volume-outcome outcomes for rectal surgery, 15 for colon surgery, 13 for colorectal surgery, and 1 that reported outcomes for colon and rectal surgery separately (*Table 1*). Assessment of the quality of included studies are demonstrated in *Table S1*. Overall, 1,122,303 patients underwent colorectal surgery (in 9,877 hospitals by 9,649 surgeons).

The characteristics of each included study is summarized in *Table 1*. Each study stratified "high" and "low" volume groups to different cut-offs. A majority of studies determined their cut-offs based on their study sample and divided the numbers evenly between groups (i.e., median if two groups, quartiles if 4 groups). For "low" hospital volume, cut-offs ranged from 5 or less operation per 5 years (37) to 530 or less operations annually (11). For the "high" hospital volumes group, cut-off ranged from 6 or more annually (51) to 2,623 or more operations annually (11). For "low" surgeon volume, cut-offs ranged from 1 operation per 5 years (37), to 108 or less annually (11). For "high" surgeon volume, cut-offs ranged from 6–26 per 5 years (37), to 561 or more annually (11).

Table 1 Study characteristics

Study	Year	Location	Study period	Cancer	Patient (N)	Hospital (N)	Surgeon (N)	Hospital volume (/year)		Surgeon volume (/year)	
								Low	High	Low	High
Liu (11)	2015	Taiwan	2005–2011	CR	61,728	-		<530	≥2,623	<108	≥561
Leonard (12)	2014	Belgium	2006–2011	R	1,469	68		<11	≥11		
Kolfschoten (6)	2014	Netherlands	2010	CR	8,911	89		<50	≥50	-	-
Richardson (13)	2013	Canada	2006–2006	R	377	-	25			1-5	9-14
Hohenberger (14)	2013	Germany	1995–2010	R	1,028	1	24	-	-	<3	7–23
Mroczkowski (15)	2011	Germany	2000–2004	C	31,261	345		<30	>60		
Borowski (16)	2010	Northern England	1998–2002	CR	8,219	17		<87	≥110	<26	>40
Yasunaga (17)	2009	Japan	2006–2007	C	1,212	247		<10	≥40	30–99	≥200
Yasunaga (18)	2009	Japan	2006–2007	R	2,285	371		<10	≥30	<50	≥500
Kressner (7)	2009	Sweden	1995–2003	R	10,425	91		<11	>25	-	
Boudourakis (19)	2009	USA	1999–2005	C	9,567	-		-	-	<12	>20
Truong (20)	2008	USA	1994–2004	CR	8,567	-		<33	>56	-	
Ptok (21)	2007	Germany	2000–2001	R	1,557	-		<10	≥20	-	
Bilingsley (22)	2007	USA	1992–1996	C	22,672	661	2677	<59	>150	<10	≥27
Ho (23)	2006	USA	1988–2000	CR*	C: 175,205; R: 58,568						
Matthiessen (24)	2006	Sweden	1987–1995	R	6,833	NA	NA				
Rogers (8)	2006	USA	1996–1999	CR	28,644	NA	NA	<84	>219	<13	>40
Renzulli (25)	2006	Switzerland		CR	915			<27	≥27	<6	≥6
Wibe (26)	2005	Norway	1993–1999	R	3,388	54	NA	<10	≥30		
McGrath (27)	2005	Australia	2000–2011	CR	1,911						
Kuhry (28)	2005	Western Europe	1997–2003	C	536	29	NA				
Harling (5)	2005	Denmark	1994–1999	R	5,021	50	NA	<15	>30		
Engel (29)	2005	Germany	1996–1998	R	884	39	NA	<10	>30		
Urbach (30)	2004	Canada	1994–1999	CR	18,898	134	NA				
Meyerhardt (31)	2004		1990–1992	R	1,330	646	NA				

Table 1 (*continued*)

Table 1 (*continued*)

Study	Year	Location	Study period	Cancer	Patient (N)	Hospital (N)	Surgeon (N)	Hospital volume (/year)		Surgeon volume (/year)	
								Low	High	Low	High
McArdle & Hole (32)	2004	UK	1991–1992	CR	3,200						
Zingmond (33)	2003	USA	1996–2000	CR	56,621	101	NA	≤20	>75		
Schrag (34)	2003	USA	1991–1996	C	24,166					<10	17–27
Meyerhardt (35)	2003	USA	1988–1992	C	3,759			<47	≥85		
Hodgson (36)	2003	USA	1994–1997	R	7,257			<7	>20		
Schrag (37)	2002	USA	1992–1996	R	2,815	420	1,141	5 yrs: <6	5 yrs: 21–57	5 yrs: 1	5 yrs: 6–26
Callahan (38)	2003	USA	1998–2001	C	48,582	223	2,651	<192	≥552	<28	≥79
Finlayson (4)	2003	US	1995–1997	C	120,270	1,082	NA	<61	>116		
Martling (39)	2002	Sweden	1995–1997	R	652	NA	46			<12	≥12
Ko (40)	2002	USA	1996	C	22,408						
Hannan (41)	2002	USA	1994–1997	C	22,128	229	2,052	<84	254–619	<12	35–262
Birkmeyer (42)	2002	US	1994–1999	C	304,285	4,587	NA	<33	>124		
Marusch (43)	2001	Germany	1999	R	1,463	75		<20	>40		
Simunovic (44)	2000	Canada	1990	C	1,072	124	NA				
Parry (45)	1999	USA	1993	CR	C: 548; R: 379			≤30	≥56	<7	≥19
Harmon (46)	1999	USA	1992–1996	CR	9,739	50	812	<40	≥70	≤5	>10
Khuri (47)	1999	USA	1991–1993	C	13,310	125	NA				
Gordon (48)	1999	USA	1989–1997	C	1,015	NA	NA				
Kee (49)	1999	Belfast	1990–1994	CR	3,135						
Porter (50)	1998	Canada	1983–1990	R	683	5	52			<21	≥21
Simons (51)	1997	USA	1988–1992	R	2,006	NA	NA	<5	≥5		
Holm (52)	1997	Sweden	NR	R	1,399	14	169	≤5	>10	<4	≥4

*, Reported outcomes separately for colon and rectal surgeries. C, colon; R, rectum; CR, colorectal; N, number.

Mortality: 30-day, in-hospital and intra-operative

The association between mortality with hospital volume and surgeon volume is summarised in *Table 2* and *Table 3* respectively. Thirty day mortality was significantly lower in hospitals with higher procedure volume compared to lower volumes (HR: 0.83; 95% CI: 0.78–0.87, P<0.001). Subgroup analysis demonstrated that this association remained significant for rectal surgery alone (HR: 0.81; 95% CI: 0.74–0.89) and colon surgery alone (HR: 0.67; 95% CI: 0.59–0.77) (*Table 2*).

Similarly, surgeons with a higher procedure volume had a significantly lower 30-day mortality for colorectal surgery than surgeons with a lower volume (HR: 0.84; 95% CI: 0.80–0.89) (*Table 3*). Subgroup analysis demonstrated this association remained significant for colon surgery and colorectal surgery, but not for rectal surgery (*Table 3*).

In-hospital mortality was significantly lower in high volume hospitals compared to low volume hospitals (HR: 0.93; 95% CI: 0.89–0.97, P<0.001) (*Table 2*). Similarly, high volume surgeons had significantly lower in-hospital mortality than low volume surgeons (HR: 0.98; 95% CI: 0.96–0.99, P<0.001) (*Table 3*).

Intra-operative mortality was reported by two studies which demonstrated significantly lower rates in high volume hospitals (HR: 0.82; 95% CI: 0.76–0.86, P<0.001) (*Table 2*), and high level surgeons (HR: 0.50; 95% CI: 0.40–0.62, P<0.001) (*Table 3*) compared to their respective low counterparts.

Detailed post-operative mortality for each surgeon and/or hospital volume group is listed in *Table S2*.

Five-year survival

Five-year survival was significantly improved for high volume surgeons compared to low volume surgeons (HR: 0.79; 95% CI: 0.75–0.83, P<0.001) (*Table 3*). In comparison, 5-year survival was similar between low and high volume hospitals (HR: 0.99; 95% CI: 0.99–1.00). However, subgroup analysis demonstrated 5-year survival to be significantly better for high volume hospitals in the two studies which reported outcomes for colorectal surgery (HR: 0.91; 95% CI: 0.87–0.94, P<0.001) (*Table 2*). Detailed 5-year survival mortality for each surgeon and/or hospital volume group is listed in *Table S2*.

Local & 5-year recurrence

Local recurrence rates were reported in 5 studies (4 rectal and 1 colon surgery). Pooled results demonstrated local recurrence was significantly lower for high volume surgeons and high volume hospitals compared to low volume counterparts (HR: 0.71; 95% CI: 0.62–0.82, P<0.001 & HR: 0.55; 95% CI: 0.50–0.68, P<0.001 respectively) (*Tables 2,3*). Subgroup analysis demonstrated both associations were only significant for rectal surgery, not colon surgery. Five-year recurrence was similar for low and high volume hospitals (*Table 2*). No studies reported 5-year recurrence rates with surgeon procedure volume.

Post-operative complications

Compared to low-volume hospitals, high volume hospitals had significantly lower post-operative complications (HR: 0.89; 95% CI: 0.81–0.98, P<0.05) (*Table 2*). There was no significant difference in post-operative complications between high and low surgeon procedure volumes (HR: 0.85; 95% CI: 0.70–1.08) (*Table 3*).

Anastomotic leak

High procedure volume surgeons had significantly lower rates of anastomotic leak (HR: 0.59; 95% CI: 0.37–0.94, P<0.01) (*Table 3*). There were no differences in the incidence of anastomotic leaks between low and high volume hospitals (*Table 2*). However, subgroup analysis revealed that for rectal only resections, high volume hospitals had significantly lower rates of anastomotic leak compared to low volume hospitals (HR: 0.75; 95% CI: 0.58–0.97, P<0.05) (*Table 2*).

Trend between hospital/surgeon volume with 30-day mortality and 5-year survival

Rather than just "low" and "high" groups, a number of studies reported outcomes in three or more continuous volume groups to demonstrate a stepwise change in outcomes (*Table S2*). A total of 15 studies reported 30-day mortality rates for three or more consecutive increases in hospital volume. 30-day mortality was found to decrease with each stepwise increase in hospital volume in 87% (13/15) of studies (*Figure 2*). Furthermore, 5-year survival was found to increase with each stepwise increase in hospital volume in 91% (10/11) of studies (*Table S2*).

On the other hand, a total of 12 studies reported 30-mortality rates for three or more consecutive increases in surgeon volume. 30-day mortality was found to decrease

Table 2 Hospital procedure volume low *vs*. high: mortality, survival recurrence, complications, operating time, hospital stay, hospital expenses

Hospital volume-outcomes	Overall			Rectal only			Colon only			Colorectal		
	Study N [patient N]	HR[a]	(95% Ci)	Study N [patient N]	HR[a]	[95% Ci]	Study N [patient N]	HR[a]	(95% Ci)	Study N [patient N]	HR[a]	[95% Ci]
Mortality												
30-day	13 [140,118]	0.83	(0.78–0.87)***	4 [12,928]	0.81	(0.74–0.89)***	3 [73,820]	0.67	(0.59–0.77)***	6 [53,370]	0.89	(0.82–0.96)**
In-hospital	6 [390,520]	0.93	(0.89–0.97)***	1 [58,568]	0.92	(0.65–0.99)*	5 [331,952]	0.94	(0.89–0.98)***	–	–	–
Intra-operative	4 [375,304]	0.82	(0.76–0.86)***	–	–	–	2 [305,357]	0.80	(0.76–0.85)***	2 [69,947]	1.04	(0.86–1.27)
Survival												
5-year	8 [115,924]	0.99	(0.99–1.00)	3 [11,018]	1.00	(0.99–1.01)	2 [11,978]	1.09	(0.90–1.11)	2 [92,928]	0.91	(0.87–0.94)***
Recurrence												
5-year	4 [14,693]	1.00	(0.99–1.01)	4 [14,693]	1.00	(0.99–1.01)	–	–	–	–	–	–
Local	5 [9,934]	0.55	(0.50–0.68)***	4 [7,228]	0.53	(0.42–0.62)***	–	–	–	1 [2,706]	0.65	(0.42–1.02)
Complications												
Post-operative	5 [62,986]	0.89	(0.81–0.98)*	3 [5,153]	0.94	(0.74–1.21)	1 [1,212]	1.06	(0.36–3.12)	1 [56,621]	0.89	(0.80–0.98)*
Anastomotic leak	3 [23,665]	0.87	(0.69–1.09)	2 [15,446]	0.75	(0.58–0.97)*	–	–	–	1 [8,216]	1.40	(0.88–2.22)
Other												
Hospital stay	1 [61,728]	1.09	(0.81–1.48)	–	–	–	–	–	–	1 [61,728]	1.09	(0.81–1.48)
Operating time	1 [1,212]	1.28	(0.72–2.29)	–	–	–	1 [1,212]	1.28	(0.72–2.29)			
Hospital expenses	1 [61,728]	1.73	(1.33–2.25)***	–	–	–	–	–	–	1 [61,728]	1.73	(1.33–2.25)***

*, P value <0.05; **, P value <0.01; ***, P value <0.001. HR, hazard ratio; N, number; 95% CI, 95% confidence interval; [a], low (reference) *vs*. high hospital procedure volume.

Table 3 Surgeon procedure volume low *vs.* high: mortality, survival, recurrence, complications, 12 nodes examined, operating time, hospital stay, hospital expenses

Surgeon volume- outcomes	Overall			Rectal only			Colon only			Colorectal		
	Study N [patient N]	HR[a]	(95% CI)	Study N [patient N]	HR[a]	(95% CI)	Study N [patient N]	HR[a]	(95% CI)	Study N [patient N]	HR[a]	(95% CI)
Mortality												
30-day	15 [131,320]	0.84	(0.80–0.89)***	5 [7,246]	0.89	(0.75–1.04)	3 [60,258]	0.62	(0.53–0.72)***	7 [63,816]	0.88	(0.82–0.94)***
In-hospital	3 [256,181]	0.98	(0.96–0.99)***	1 [58,568]	0.87	(0.81–0.93)***	2 [197,613]	0.98	(0.97–0.99)**	–	–	–
Intra-operative	2 [69,947]	0.50	(0.40–0.62)***	–	–	–	–	–	–	2 [69,947]	0.50	(0.40–0.62)***
Survival												
5-year	4 [81,366]	0.79	(0.75–0.83)***	1 [8,219]	0.85	(0.73–0.83)***	1 [8,219]	0.84	(0.76–0.93)***	2 [64,928]	0.77	(0.72–0.82)***
Recurrence												
Local	6 [6,845]	0.71	(0.62–0.82)***	5 [4,139]	0.72	(0.62–0.83)***	–	–	–	1 [2,706]	0.64	(0.41–1.00)
Complications												
Post-operative	3 [4,896]	0.85	(0.70–1.08)	2 [3,684]	0.80	(0.62–1.03)	1 [1,212]	1.69	(0.73–3.93)	–	–	–
Anastomotic leak	1 [8,219]	0.59	(0.37–0.94)**	1 [8,219]	0.59	(0.37–0.94)**	–	–	–	–	–	–
Other												
Hospital stay	1 [61,728]	0.67	(0.46–0.99)*	–	–	–	–	–	–	1 [61,728]	0.67	(0.46–0.99)*
Operating time	1 [1,212]	0.17	(0.10–0.29)***	–	–	–	–	–	–	–	–	–
Hospital expenses	1 [61,728]	0.29	(0.18–0.44)***	–	–	–	–	–	–	1 [61,728]	0.29	(0.18–0.44)***
12 Nodes examined	1 [377]	3.66	(2.36–5.7)**	1 [377]	3.66	(2.36–5.7)**	–	–	–	–	–	–

*, P value <0.05; **, P value <0.01; ***, P value <0.001. HR, hazard ratio; N, number; 95% CI, 95% confidence interval; [a], low (reference) *vs.* high hospital procedure volume.

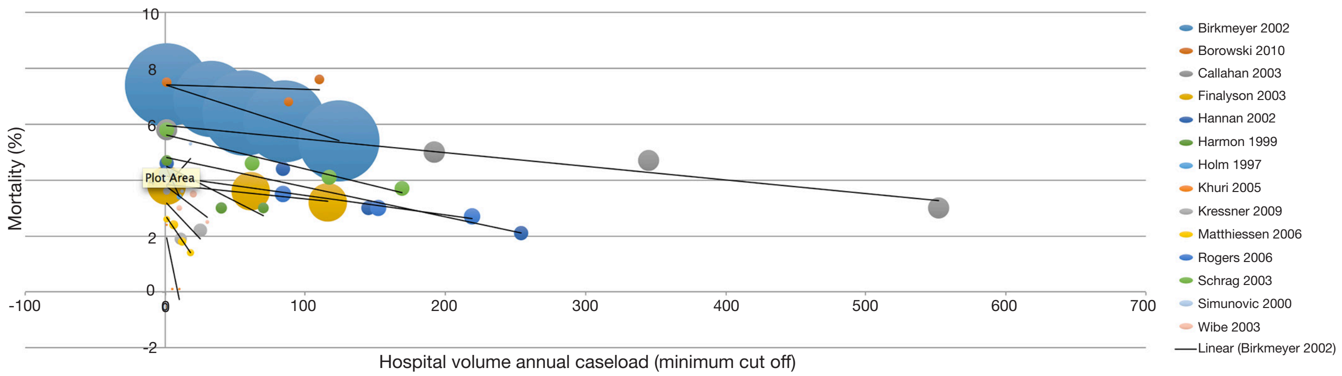

Figure 2 Bubble plot demonstrating relationship between hospital volume annual case load and mortality (%)

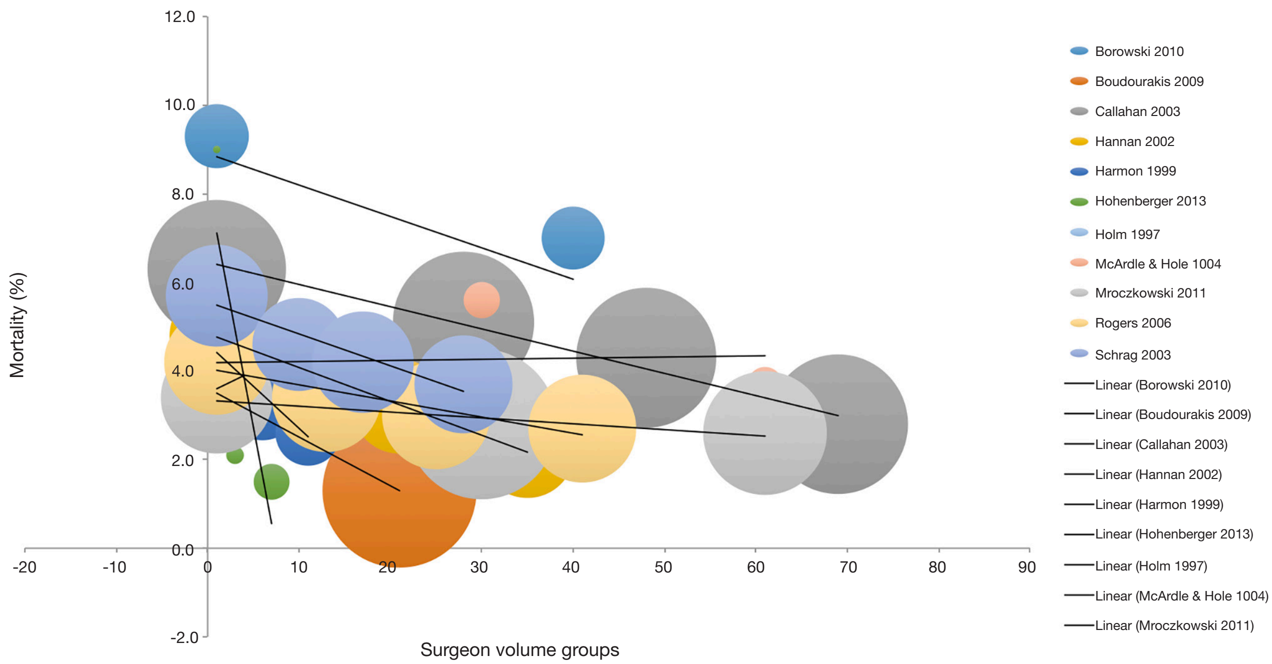

Figure 3 Bubble plot demonstrating relationship between surgeon volume groups and mortality (%)

with each stepwise increase in surgeon volume in 83% (10/12) of studies (*Table S2*, *Figure 3*). Furthermore, 5-year survival was found to increase with each stepwise increase in surgeon volume in 100% (6/6) of studies (*Table S2*).

Interaction between surgeon volume and hospital volume

Four studies (25,38,41,46) examined the interaction between surgeon and hospital volume on outcomes. High-hospital-high-surgeon-volume had the best 5-year survival [78% in Renzulli *et al.* (25)] and lowest mortality rates [(3.2% in Callahan *et al.* (38)]. Low-hospital-high-surgeon-volume had better 5-year survival than high-surgeon-low-surgeon-volume [76% *vs.* 68% in Renzulli *et al.* (25)], and lower mortality rates in Callahan and colleagues' study (14) (4.2% *vs.* 5.0%). However, one study (41) reported low-hospital-high-surgeon-volume had a higher mortality rate than high-surgeon-low-surgeon-volume (*Table S3*). Low-hospital-low-surgeon-volume had the highest mortality rate and lowest 5-year survival outcome in all four studies (*Table S3*).

Hospital stay

Liu *et al.* (11) [2015] identified hospital stay was significantly shorter with high volume surgeons whereby patients were more likely to be discharged within 14 days post-operatively (HR: 0.67; 95% CI: 0.46–0.99, P<0.05) (*Table 3*). Hospital volume was not associated with shorter hospital stay (*Table 2*).

Operating time

Yasunaga *et al*. (17) [2009] reported operating time was significantly reduced with high volume surgeons compared to low volume surgeons for colon surgery (HR: 0.17; 95% CI: 0.10–0.29, P<0.001) (*Table 3*). Hospital volume was not found to be associated with operating time (*Table 2*).

Hospital expenses

Liu *et al*. (11) [2015] defined hospital expenses as the total expenses during hospitalization and related expenditures for a definitive surgery. Interestingly, Liu and colleagues reported hospital expenses was higher with high volume hospitals (OR: 1.73; 95% CI: 1.33–2.25, P<0.001) (*Table 2*), but lower with high volume surgeons (OR: 0.29; 95% CI: 0.18–0.44, P<0.001) (*Table 3*).

Adequate lymph nodes resected

Richardson *et al*. (13) [2013] defined adequate lymph node resection as 12 lymph nodes in rectal surgery. The study reported high volume surgeons were more likely to have adequate lymph node resected compared to low volume surgeons (50% *vs*. 23% respectively, HR: 2.66; 95% CI: 2.36–5.70, P=0.01) (*Table 3*). No study examined the association between lymph node resection and hospital volume.

Discussion

This review and meta-analysis demonstrates that there is a volume-outcome relationship that favours high volume facilities and high volume surgeons. Higher hospital and surgeon volume resulted in reduced overall, in-hospital and intra-operative mortality. Post-operative complication rates depended on hospital not surgeon volume except with respect to anastomotic leak. Notably, high volume surgeons are associated with improved oncologic outcomes including greater lymph node retrieval, reduced recurrence rate and 5 year survival. Higher volume surgeons also improve value through reduced operative time, length of stay and cost. The best outcomes occur in high volume hospitals with high volume surgeons.

It is interesting that this meta-analysis demonstrates the rates of mortality are not the lowest in the studies with the highest hospital or surgeon annual case load. For example, studies where the highest volume had more than 100 operations annually than the lowest group had smaller reduction in mortality between groups than studies where the highest group had more than 20 operations annually than the lowest group. This makes it difficult to identify a clear threshold of effect, or a mathematical relationship between increasing volume and improvement in any of the outcome measures. A potential reason for this may be the highest volume hospitals have more surgeons, and therefore, each individual surgeon volume is low, whilst the smaller hospitals only have a few surgeons, and each individual surgeon volume is high. One study (41) reported low-hospital-high-surgeon-volume had a higher mortality rate than high-surgeon-low-surgeon-volume. However, three included studies demonstrated that low-hospital-high-surgeon-volume had better 5-year survival and lower risk of mortality than high-surgeon-low-surgeon-volume (25,38,46) (*Table S3*). This suggests that high surgeon volume is more critical than high hospital volume to optimise outcomes.

The mortality and 5-year survival varied between studies due to the different patient populations between and within the studies. The gold-standard for comparing surgical outcomes is to adjust for risk related to underlying patient characteristics that might influence the outcome (53). In the identified publications there was major variation in controlling for patient, cancer, hospital and surgeon characteristics. In addition, different risk measures such as Charlson score or ASA were used in different studies. Maruthappu *et al*. (53) has demonstrated overall poor methodological qualities for studies assessing individual surgical performance. Future studies should seek to control for patient characteristics and utilise risk stratification.

Numerous other factors may contribute to surgical outcomes. Some of these are directly related to volume, e.g., learning curve, and potentially explain the lack of continuous relationship between volume and outcome for surgeons or centres. It is worth noting that the annual volumes reported in this manuscript are often lower than those in studies of learning curve for colorectal surgery (54). This perhaps suggests that once initial learning curve is overcome then further improvement in outcomes is likely to be in small increments.

There has been a trend towards providing feedback to surgeons and physicians about their performance. It has been thought that feedback in its own right will lead to reflection and efforts to improve outcomes. This has been controversial particularly in the context where league tables are reported publically and linked to reimbursement. Recent studies comparing outcomes of hospitals participating in the American College of Surgeons' National Surgical Quality Improvement Program (NSQIP) to non-NSQIP hospitals found no difference in rate of improvement in outcomes or in morbidity/mortality rates for a variety of general surgical procedures (55). Notably, however, there was across the board improvement overtime in both groups. Some suggest it may reflect a generally increased interest in quality improvement (55). However, as reasons for this are speculative, future research in this area is necessary to determine the most appropriate methods improve patient outcomes.

Volume outcome relationships have been challenged in other settings. Kurlansky *et al*. (56) demonstrate that low volume centres and low volume surgeons can have good outcomes if they are compliant with evidence-based quality standards (56). It is recognised that quality improvement requires multi-factorial interventions such as appropriate feedback and education (57). It may be that high volume for individual surgeons or high volume hospitals may actually be a surrogate for quality interventions such as protocolisation of care pathways, however future research to confirm this is warranted.

This study has limitations that need to be considered when interpreting the results. Firstly, there is little overlap between the cut-off points that define low and high volume groups between studies. As each health district and country holds different health service to population ratios, what is considered "high volume" is substantially different to another. This makes it difficult to demonstrate a universal cut-off level for minimum amount of operations annually to optimise outcomes. However, with most studies, the increase in surgeon and hospital volume is associated with a trend for reduced adverse outcomes, irrespective of absolute volume load. Secondly, some of the studies from USA used databases such as Medicare, SEER-Medicare, NCDB and California Cancer Registry which have overlapping patients. This may result in some patients being included multiple times in this meta-analysis. The studies from other countries such as Taiwan and Germany do not have this limitation as they are from independent hospital databases. Finally, heterogeneity exists between the studies in terms of the types of colorectal surgeries performed, distribution of cancer stages among hospitals and surgeons of various volumes. It is possible that those surgeons and hospitals with the highest volume perform more complex, high-risk operations. This would under-estimate the benefit of a high volume load over small volume load. Nevertheless, even with increasing volume loads, and the potential increase in more complex operations performed, a majority of the studies demonstrate a decrease on adverse outcomes with increasing volumes.

In conclusion, this study confirms that surgeon and hospital volume impacts colorectal surgical outcomes but fails to demonstrate a linear relation between volume and outcome. This suggests that whilst centralisation of such services may represent good policy, volume alone will not guarantee good or improved outcomes. Low and high volume surgeons and centres should seek to address quality through multiple methods, not just by increasing volume. Further studies on volume should better describe the quality improvement context of the operator such as participation in improvement programs, performance feedback and compliance with guidelines.

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Footnote

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Table S1 30-day postoperative mortality and 5-year survival based on hospital and surgeon volume for each study

Study	Hospital volume/year					Surgeon volume/year				
	Hospital volume/ year	Post-op mortality	30-day post-op mortality trend with ↑hospital volume	5-year survival	5-year survival trend with ↑hospital volume	Surgeon volume/year	Post-op mortality	30-day Post-op Mortality trend with ↑surgeon volume	5-year survival	5-year survival trend with ↑surgeon volume
Liu 2015	≤530			29.1%		1–107			27%	
	531–1,311			32%	↑	108–321			30%	↑
	1,312–2,622			32.8%		322–560			34%	
	≥2,623			38.7%		≥561			41%	
Leonard 2014	≤10			78%	–					
	>10			78%						
Richardson 2013						1–5			64%	↑
						9–14			66%	
Hohenberger 2013						1–2	9%		70%	
						3–6	2.1%	↓	72.9%	↑
						7–23	1.5%		77%	
Mroczkowski 2011	≤29			51.1%		<30	3.4%			
	30–60			52.3%	↑	30–60	2.8%	↓		
	>60			56.3%		>60	2.6%			
Borowski 2010	<87	7.5%		47.8%		<26	9.3%	↓	39.3%	
	88–109	6.8%	↑	47.4%	↓	27–39	5.6%		50.1%	↑
	≥110	7.6%		46.8%		>40	7%		52.5%	
Boudourakis 2009						<12	3.5%	↓		
						>20	1.3%			
Kressner 2009	≤10	3.6%		51%						
	11–25	1.9%	↓	53%	↑					
	≥26	2.2%		51%						
Truong 2008	≤33			71.4%						
	33–36			75.6%	↑					
	57–84			77%						
Matthiessen 2006	1–5	2.6%								
	6–11.9	2.4%	↓							
	12–17.9	1.8%								
	18+	1.4%								
Renzulli 2006						1–5			60%	↑
						6–10			79%	
Rogers 2006	1–83	4.2%		51.3%		1–12	4.2%		52.9%	
	84–151	3.5%	↓	53%	↑	13–24	3.4%	↓	55%	↑
	152–219	3%		55%		25–40	3%		57%	
	≥220	2.7%		58.9%		>40	2.7%		59%	
Engel 2005	1–9			65%						
	10–30			65%	↑					
	≥31			68%						
Harling 2005	1–14			40%						
	15–30			42%	↑					
	≥30			42%						
Kuhry 2005	1–4	2.4%								
	5–10	0.1%	↓							
	>10	0.1%								
Wibe 2005	1–9	3.9%		57.8%						
	10–19	3%	↓	60.8%	↑					
	20–29	3.5%		64%						
	≥30	2.5%		64.4%						
McArdle & Hole 2004						<30	3.5%			
						30–60	5.6%	↑		
						>60	3.7%			
Callahan 2003	<192	5.8%				<28	6.3%			
	192–344	5%	↓			28–47	5.1%	↓		
	345–551	4.7%				48–78	4.3%			
	552–1,725	3%				79–251	2.8%			
Finlayson 2003	<61	3.8%	↓							
	61–116	3.6%								
	>116	3.2%								
Meyerhardt 2003	1–46			63.8%						
	47–84			67%	↑					
	≥85			67%						
Schrag 2003	1–61	5.8%				1–9	5.7%			
	62–116	4.6%	↓			10–16	4.6%	↓		
	117–167	4.1%				17–27	4.2%			
	169–383	3.7%				28–85	3.7%			
Birkmeyer 2002	<33	7.4%								
	33–56	6.9%								
	57–84	6.4%	↓							
	85–124	6.1%								
	>124	5.4%								
Hannan 2002	1–83	4.6%				1–11	4.8%			
	84–144	4.4%	↓			12–20	3.9%	↓		
	145–253	3%				21–34	3.2%			
	254+	2.1%				35+	2.2%			
Schrag 2002	1–5/5–yrs	3.9%				1/5–yrs	4.3%			
	6–11/5–yrs	4%	↓			2/5–yrs	3.7%	↓		
	12–20/5–yrs	2.4%				3–5/5–yrs	3.5%			
	21–57/5–yrs	3.3%				6–26/5–yrs	1.7%			
Simunovic 2000	1–11	4.1%								
	12–17	3.6%	↑							
	18+	5.3%								
Harmon 1999	<40	4.7%				1–5	4.5%			
	40–70	3%	↓			6–10	3.3%	↓		
	<70	3%				>10	2.6%			
Holm 1997	1–5	4.4%	↓			1–3	3.6%	↑		
	6–10	3.9%				>3	3.9%			
	>10	3.4%								
Simons 1997	1–5			50%	↑					
	≥6			70%						

↑ Increase; ↓ Decrease; – no change (trend with increasing hospital/surgeon volume).

Table S2 Interaction between surgeon and hospital volume on outcomes

Study	Outcomes reported	Hospital–surgeon volume category			
		High hospital–high surgeon volume	Low hospital–high surgeon volume	High hospital–low surgeon volume	Low hospital–low surgeon volume
Renzulli 2006	Patient N	286	150	145	334
	5–year survival	78%	76%	68%	60%
	5–year survival absolute difference	(Reference)	–2%	–10%	–18%
Callahan 2003	Surgeon N	135	168	895	1453
	Patient N	14973	9289	9106	15160
	Observed mortality rate	3.2%	4.2%	5.0%	6.2%
	Mortality rate absolute increase	Reference	+1.0%	+1.8%	+3.0%
	Adjusted OR (95% CI)	1.00 (Reference)	1.19 (0.98–1.44)	1.54 (1.30–1.84)*	1.82 (1.53–2.17)*
Hannan 2002	Mortality rate absolute increase %	(Reference)	+1.2%	+0.7%	+2.3%
Harmon 1999	Relative risk of mortality	0.58*	0.63*	0.8*	1.00 (Reference)

*, Significant P value <0.05, N, number.

Table S3 Assessment of quality of included studies

Study		Research questions clearly stated	Study population/ database clearly specified	Study period >3 years	Provided size justification/ power description/adequate patient volume (>1,000)	Overall Hospital/ Surgeon volume reported	Adequate hospitals (>20)/surgeons (>20) included	Outcome measures clearly defined, reliable and implemented consistently	Outcomes adjusted for confounders	Overall quality rating
Liu	2015	•	•	•	•		•	•	•	A
Leonard	2014	•	•	•	•			•	•	A
Kolfschoten	2014	•	•		•	•	•	•	•	A
Richardson	2013	•	•			•		•	•	B
Hohenberger	2013	•	•	•	•	•		•		A
Mroczkowski	2011	•	•	•	•	•	•	•		A
Borowski	2010	•	•	•	•	•	•	•		A
Yasunaga	2009	•	•		•	•	•	•	•	A
Yasunaga	2009	•	•		•	•	•	•	•	A
Kressner	2009	•	•	•	•	•	•	•	•	A
Boudourakis	2009	•	•	•	•			•		B
Truong	2008	•	•	•	•			•		B
Ptok	2007	•	•		•			•		B
Bilingsley	2007	•	•	•	•	•	•	•	•	A
Ho	2006	•	•		•			•	•	B
Matthiessen	2006	•		•	•			•		B
Rogers	2006	•			•			•		C
Renzulli	2006	•		•				•		C
Wibe	2005	•	•	•	•	•	•	•		A
McGrath	2005	•	•	•	•			•		B
Kuhry	2005	•	•	•		•		•		B
Harling	2005	•	•	•	•	•	•	•	•	A
Engel	2005	•	•			•	•	•	•	A
Urbach	2004	•	•	•	•	•	•	•	•	A
Meyerhardt	2004	•	•		•	•		•	•	A
McArdle & Hole	2004	•	•		•			•		B
Zingmond	2003	•	•	•	•	•	•	•	•	A
Schrag	2003	•	•	•	•			•	•	A
Meyerhardt	2003	•	•	•	•			•	•	A
Hodgson	2003	•	•	•	•	•	•	•	•	A
Schrag	2002	•	•	•	•	•	•	•	•	A
Callahan	2003	•	•	•	•	•	•	•		A
Finlayson	2003	•	•		•	•	•	•		A
Martling	2002	•	•			•	•	•	•	A
Ko	2002	•	•		•			•		B
Hannan	2002	•	•	•	•	•	•	•		A
Birkmeyer	2002	•	•	•	•	•	•	•		A
Marusch	2001	•	•		•	•	•	•		A
Simunovic	2000	•	•		•	•	•	•		A
Parry	1999	•	•					•	•	B
Harmon	1999	•	•	•	•	•	•	•		A
Khuri	1999	•	•		•	•	•	•		A
Gordon	1999	•		•	•			•	•	B
Kee	1999	•		•	•			•		B
Porter	1998	•	•	•		•		•		B
Simons	1997	•	•	•	•			•		B
Holm	1997	•	•		•	•		•		B

A, good; B, fair; C, poor.