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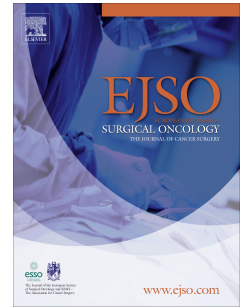


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Volume and outcome in colorectal cancer surgery

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Abstract**Aims**

There is a growing consensus to concentrate high-risk surgical procedures to high-volume surgeons in high-volume hospitals. However, there is fierce debate about centralizing more common malignancies such as colorectal cancer. The objective of this review is to conduct a meta-analysis using the best evidence available on the volume-outcome relationship for colorectal cancer treatment.

Methods

A systematic search was performed to identify all relevant articles studying the relation between hospital and/or surgeon volume and clinical outcomes for colorectal cancer. Using strict inclusion criteria, 23 articles were selected concerning colon cancer, rectal cancer or both diseases together as 'colorectal cancer'. Pooled estimated effect sizes were calculated using the casemix adjusted outcomes of the highest volume group opposed to the lowest volume group.

Results

High volume hospitals have a significantly lower postoperative mortality in half of the pooled results. Non significant results show a trend in favour of high volume hospitals. All results showed a significantly better long term survival in high volume hospitals. High volume surgeons have a lower postoperative mortality, although evidence is sparse. All analyses showed a significantly better long term survival in favour of high volume surgeons.

Conclusions

The results show a clear and consistent relation between high volume providers and improved long term survival. This applies to both high volume hospitals and high volume surgeons. Most results show a relation between high volume providers and a reduced postoperative mortality, but evidence is less convincing.

In the ideal world, extensive population based audit registrations with casemix adjusted feedback should make rigid minimal volume standards obsolete. Until then, using volume criteria for hospitals and surgeons treating colorectal cancer can improve mortality and especially long term survival.

Introduction

Since the relation between surgical volume and mortality was first described in the late seventies, many publications have reconfirmed a positive volume-outcome relationship, especially for high-risk surgical procedures such as esophagectomies or pancreatectomies¹⁻³. All striving for the best possible care, there is an ongoing and sometimes fierce debate between doctors, politicians and patients about centralizing surgical care to high volume centres. This led to a growing consensus to concentrate high-risk, relatively low incidence surgical procedures in high-volume hospitals⁴. However, the expertise for diagnosis and treatment of common types of cancer should preferably be widespread and easily accessible for all patients. After lung- and breast cancer, colorectal cancer is the third most common malignancy worldwide, with 1.15 million new cases every year⁵. Referring all colorectal cancer patients to a limited number of high volume centres will inevitably decrease accessibility for patients and their family. Not only for the operation, but also for (neo)adjuvant treatment and many years of follow-up. Because several studies on this topic do not correct adequately for casemix variation or have other methodological flaws, results can easily be misinterpreted. Fundamental decisions such as centralisation of colorectal cancer care should be made relying on the best available evidence. The objective of this review is to contribute to the debate by conducting a meta-analysis using the best available evidence about the volume-outcome relationship for colorectal cancer treatment.

Methods

Systematic Search Strategy

A specialised librarian performed a systematic search in Medline and Embase to identify all relevant studies describing the association between hospital or surgeon volume and clinical outcomes. Because volume is not well indexed, a combination of MESH terms and free text words was used (table 1). In addition, reference lists of relevant articles were hand-searched to identify additional articles and the “related articles” function in Pubmed was used. The last search was performed on February 1st 2010.

Study selection

The first two authors of this article independently screened titles and abstracts of all retrieved articles, using the following inclusion criteria:

- The subject of the study is the surgical treatment of colon cancer, rectal cancer or both.
- Hospital and/or surgeon volume is an independent variable.
- The outcome parameter is postoperative mortality and/or survival.

- The study does not describe a single hospital or surgeon.
- The study uses primary data (e.g. editorials, systematic reviews, are excluded).

After the first selection, articles were assessed in full text and further selected using the following criteria:

- If multiple publications are based on the same database, the study with the highest methodological quality was selected. In case of similar quality, the publication with the most recent study period was selected.
- Due to considerable changes in clinical and surgical practise, data older than 20 years was considered obsolete. Because the first selection for this review took place in 2008, studies older than 1988 were excluded.
- Multivariate analysis had to be corrected for at least age and gender.
- Volume had to be defined as a distinct number or cut-off value. Studies that defined volume as 'specialization' were excluded.

Assessment of study quality & Data-extraction

Each study in the final selection was critically appraised following the STROBE criteria (www.strobe-statement.org) for study characteristics and methodological quality. For each volume group, crude and adjusted outcomes were recorded for postoperative mortality and survival. Parameters for adjusted outcomes were expressed as odds ratio's (OR), hazard ratio's (HR) or relative risks (RR) with confidence intervals (CI) and P-values. All items were scored in an Access 2003 database (Microsoft Corporation tm, Redmond WA, USA).

Statistical analysis

Data were analysed using Comprehensive Meta Analysis professional, version 2.2 (Biostat inc. Englewood, USA). Pooled estimated effect sizes were calculated using the adjusted outcomes of the highest volume group opposed to the lowest volume group (reference). In case the highest volume group was used as reference, results were re-calculated (1/effect size) to fit the statistical model. The random effect model was used to account for expected heterogeneity when pooling observational studies. Heterogeneity was quantified using the I^2 test. An $I^2 > 50$ was considered as notable heterogeneous. In case of heterogeneity, the impact of subgroups was explored with subgroup analyses for data source (administrative vs clinical), casemix adjustment (adjustment for comorbidity or severity) and country. For all pooled analyses involving three or more studies, publication bias was explored using an Egger's regression test.

Results

After combining the electronic library results and removing duplicates, 74 potentially relevant studies remained. Using the above described selection rounds, 23 studies were selected for the meta-analyses: 10 concerning colon cancer (table 2), 7 concerning rectal cancer (table 3) and 7 that analysed both diseases together as 'colorectal cancer' (table 4).

Colon Cancer

The following risk adjusted outcomes could be extracted from the 10 colon cancer studies:

A. the effect of hospital volume on postoperative mortality (n=6)

Five outcomes were expressed in Odds ratio's, with a pooled estimated effect of 0.88, 95% confidence interval 0.71-1.09, $I^2=87.1$. Subgroup analysis showed that omitting correction for comorbidity was a significant factor of heterogeneity, ($p=0.004$). When the analysis was repeated without the single study that did not correct for comorbidity [engel], the pooled estimated effect turned significant in favour of high volume hospitals: OR 0.82, 95% CI 0.68-0.99, $p=0.039$.

One outcome was expressed in a Hazard ratio of 0.813, 95% confidence interval 0.734-0.90. See figure 1a.

B. the effect of hospital volume on long term survival (n=4)

All four outcomes were expressed in Hazard ratio's, with a pooled estimated effect of 0.916, 95% confidence interval 0.872-0.962, $I^2=45.7$. See figure 1b.

C. the effect of surgeon volume on postoperative mortality (n=1)

One Odds ratio was available: 0.820, 95% confidence interval 0.675-0.997. See figure 1c.

D. the effect of surgeon volume on survival (n=1)

One Hazard ratio was available: 0.657, 95% confidence interval 0.532-0.811. See figure 1d.

Rectal Cancer

The following risk adjusted outcomes could be extracted from the 7 rectal cancer studies:

A. the effect of hospital volume on postoperative mortality (n=5)

Four outcomes were expressed in Odds ratio's, with a pooled estimated effect of 0.744, 95% confidence interval 0.496-1.116, $I^2 = 76.7$. One outcome was expressed in a Hazard ratio of 0.752, 95% confidence interval 0.621-0.910. See figure 2a.

B. the effect of hospital volume on survival (n=5)

All five outcomes were expressed in Hazard ratio's, with a pooled estimated effect of 0.838, 95% confidence interval 0.805-0.873, $I^2 = 0.0$. See figure 2b.

'Colorectal Cancer'

The following risk adjusted outcomes could be extracted from the 7 studies that analysed colon- and rectal cancer as one group:

A. the effect of hospital volume on postoperative mortality (n=2)

One Odds ratio was available: 0.781, 95% confidence interval 0.617-0.989 and one Risk ratio was available: 1.11, 95% confidence interval 0.886-1.393. See figure 3a.

B. the effect of hospital volume on survival (n=4)

All four outcomes were expressed in Hazard ratio's, with a pooled estimated effect of 0.912, 95% confidence interval 0.861-0.967, $I^2 = 37.7$. See figure 3b.

C. the effect of surgeon volume on postoperative mortality (n=2)

Both outcomes were expressed in Odds ratio's, with a pooled estimated effect of: 0.665, 95% confidence interval 0.528-0.836. See figure 3c.

D. the effect of surgeon volume on survival (n=4)

All four outcomes were expressed in Hazard ratio's, with a pooled estimated effect of 0.869, 95% confidence interval 0.823-0.919, $I^2 = 0.0$. See figure 3d.

Interpretation

With this meta-analysis, an attempt is made to pool all available studies with a predefined statistical and methodological quality. With a final selection of 23 articles originating from many databases and several countries, it is inevitable to find a variety in endpoints, volume group cut-off

values and statistical effect measurements. Therefore, the results of this meta-analysis have to be interpreted with care.

Hospital volume

In table 5, the effects of high hospital volume on postoperative mortality and long term survival are summarized. The effects on postoperative mortality vary. Half of the results are significant in favour of high volume hospitals, evenly distributed over colon, rectal and colorectal cancer. Two-thirds of the non significant results show a trend in favour of high volume hospitals.

The effects on long term survival are more uniform. All pooled effects are homogeneous and show significant survival benefits for patients treated in high volume hospitals.

The median cut-off point of high volume hospitals is ≥ 126 annual procedures for colon cancer, ≥ 24 for rectal cancer and ≥ 55 for the combined 'colorectal' group.

None of the Egger's regression tests were significant for publication bias.

Surgeon volume

In table 6, the effects of high surgeon volume on postoperative mortality and long term survival are summarized. Except for long term survival after colorectal cancer, evidence is sparse and non existent for rectal cancer. Nevertheless, both effects for postoperative mortality are significant in favour of high volume surgeons.

Again, effects on long term survival are more convincing. Both effects show strongly significant long term survival benefits for patients treated by high volume surgeons.

The median cut-off point of high volume surgeons is ≥ 4 annual procedures for colon cancer and ≥ 17 for the combined 'colorectal' group.

None of the Egger's regression tests were significant for publication bias.

Discussion

There is a clear and consistent relationship between high volume providers and an improved long term survival. This counts for both high volume hospitals and high volume surgeons. For the relation between volume and postoperative mortality, evidence is less convincing. Nonetheless, with one non significant exception, all results point at a lower mortality in high volume settings.

Besides the ‘practice makes perfect’ theory, it is likely that volume is an indirect indicator for other important quality characteristics of health care providers. Certainly, the teamwork between the different consultants (gastro-enterology, surgery, radiology, radiotherapy, pathology) plays an important role. The existence of a good multidisciplinary infrastructure in which every patient is discussed in multidisciplinary meetings for an individual treatment regimen, seems an important factor for good outcomes²⁸. Quality of surgical wards and intensive care units are likely to be an important factor influencing outcome. While measuring these factors is difficult, hospital and surgeon volume are relatively easy to register.

Given the fact that high volume hospitals and surgeons perform better than their low volume equivalents, a logical reaction would be to define minimal volume standards for surgeons and hospitals. Unfortunately, it is not easy to define such standards based on the available evidence. The selected studies in this meta-analysis demonstrate a wide range of high and low volume definitions. Despite the definitions summarized in table 5, few surgeons will qualify themselves as ‘high-volume surgeons’ when they perform only 4 colon resections annually. On the other hand, median cut-off points calculated from several studies give better indications. For instance, the high volume hospital definitions of ≥ 126 for colon cancer and ≥ 24 for rectal cancer seem more realistic.

One could state that effect sizes around 0.9 in favour of high volume providers are not worth the negative consequences that come with centralization. On the other hand, with the high incidence of colorectal cancer, small improvements can save many lives. Besides, some expensive and widely adopted chemotherapy regimes have about the same effects.

Unfortunately, underperforming high volume providers do exist, as there are low volume providers with excellent outcomes. Rigid minimal volume standards leave underperforming high volume centres untouched and undeservedly close well performing low volume centres. Surgical audit with active feedback to health care providers might be a better instrument to improve quality of care.

Health care providers should ideally be provided with reliable and casemix adjusted feedback on their treatments. A comprehensive nationwide surgical audit provides insight in delivered quality of care, identifies and spreads best practice. Scandinavian experiences show how this can lead to spectacular improvements at very low costs^{29;30}.

In the ideal world, extensive population based audit registrations with casemix adjusted feedback should make rigid minimal volume standards obsolete. Until then, using volume criteria for hospitals and surgeons treating colorectal cancer can improve mortality and especially long term survival.

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- Figure 1a. The effect of hospital volume on postoperative mortality for colon cancer treatment
- Figure 1b. The effect of hospital volume on long term survival for colon cancer treatment
- Figure 1c. The effect of surgeon volume on postoperative mortality for colon cancer treatment
- Figure 1d. The effect of surgeon volume on long term survival for colon cancer treatment
- Figure 2a. The effect of hospital volume on postoperative mortality for rectal cancer treatment
- Figure 2b. The effect of hospital volume on long term survival for rectal cancer treatment
- Figure 3a. The effect of hospital volume on postoperative mortality for colorectal cancer treatment
- Figure 3b. The effect of hospital volume on long term survival for colorectal cancer treatment
- Figure 3c. The effect of surgeon volume on postoperative mortality for colorectal cancer treatment
- Figure 3d. The effect of surgeon volume on long term survival for colorectal cancer treatment

Table 1: Terms used for the systematic search in the databases Medline and Embase

<p>Medline (Pubmed)</p> <p>("hospital volume" OR "surgeon volume" OR "surgical volume" OR workload OR caseload OR "procedure volume" OR "procedural volume")</p> <p>AND</p> <p>(surgical complications OR "Postoperative Complications"[Mesh] OR mortality OR (("Survival Rate"[Mesh] OR "Survival"[Mesh]) OR "Disease-Free Survival"[Mesh]) OR "Mortality"[Mesh] OR "Neoplasm Recurrence, Local"[Mesh] OR "Recurrence"[Mesh] OR treatment outcome[Mesh] OR "treatment outcome")</p> <p>AND</p> <p>("Surgical Procedures, Operative"[Mesh] OR surgery OR surgical OR surgeon)</p>
<p>Embase</p> <p>hospital volume.mp. OR surgeon volume.mp. OR workload.mp. OR Workload/ OR caseload.mp. OR procedure volume.mp.</p> <p>AND</p> <p>surgical complications.mp. OR postoperative complications.mp. OR exp Postoperative Complication/ OR Mortality/ OR mortality.mp. OR exp Survival Rate/ OR exp Survival/ OR survival.mp. OR exp Cancer Recurrence/ OR neoplasm recurrence.mp. OR treatment outcome.mp. OR exp Treatment Outcome/ OR surgical mortality.mp. OR exp Surgical Mortality/ OR exp recurrent disease/ or exp tumor recurrence/ OR exp cancer survival/ OR disease free survival.mp. or exp Disease Free Survival/</p> <p>AND</p> <p>surgery/ OR exp cancer surgery/ OR surgeon.mp. OR exp Surgeon/ OR surgical procedures.mp. or exp Surgical Technique/</p>

Table 2: selected publications colon cancer

Author	Year	Data source	Patients	Hospitals	Surgeons	Casemix correction
Bilimoria ⁶	2008	National Cancer Data Base (NCDB)	86451	1634	2678	A / G / C / S
Billingsley ⁷	2007	SEER-Medicare	22672	662		A / G / C / S / U
Birkmeyer ⁸	2007	SEER-Medicare	43656	845		A / G / C / S / U
Birkmeyer ³	2002	Medicare-MEDPAR	304285	4587		A / G / C / U
Engel ⁹	2005	Dutch National Medical Registry	67594	128		A / G / U
Finlayson ¹⁰	2003	Nationwide Inpatient Sample (NIS)	120270	1082		A / G / C / U
Lin ¹¹	2006	Taiwan National Health Insurance Research Database	13055	178	106	A / G / C / S
Meyerhardt ¹²	2003	Intergroup 0089	3161			A / G / C / S / U
Morris ¹³	2007	State of Western Australia	1467	27		A / G / S / U
Simunovic ¹⁴	2006	Ontario Cancer Registry	8398	151		A / G / C / S

Table 3: selected publications rectal cancer

Author	Year	Data source	Patients	Hospitals	Surgeons	Casemix correction
Bilimoria ⁶	2008	National Cancer Data Base (NCDB)	56795	1523		A / G / C / S
Harling ¹⁵	2005	Danish Rectal Cancer Registry	5021	53		A / G / S
Hodgson ¹⁶	2003	California Cancer Registry	7257	367		A / G / C / S
Kressner ¹⁷	2009	Swedish Rectal Cancer Registry	10425	91		A / G / S
Meyerhardt ¹⁸	2004	Intergroup 0114	1330	646		A / G / S / U
Simunovic ¹⁹	2000	Ontario Cancer Registry	1072	124		A / G / C
Wibe ²⁰	2005	Norwegian Rectal Cancer Project	3388	54		A / G / S

Table 4: selected publications colorectal cancer

Author	Year	Data source	Patients	Hospitals	Surgeons	Casemix correction
Borowski ²¹	2007	UK Northern Region Colorectal Cancer Audit Group	7411		140	A / G / C / S / U
Kee ²²	1999	Northern Ireland Colorectal Cancer Register	3135	19	71	A / G / S / U
McArdle ²³	2004	National Health Service central Scotland	2235	11	84	A / G / S / U
Parry ²⁴	1999	UK North Western Regional Cancer Registry	927	39	112	A / G / S / U
Rabeneck ²⁵	2004	Veteran Affairs Patient Treatment File	19231	172		A / G / C / S
Rogers ²⁶	2006	California Cancer Registry	28644	397	2993	A / G / C / S / U
Urbach ²⁷	2003	Canadian Institute for Health Information	18898	134		A / G / C

Casemix correction abbreviations: Age (A), Gender (G), Comorbidity (C), Severity (S) , Urgency (U)

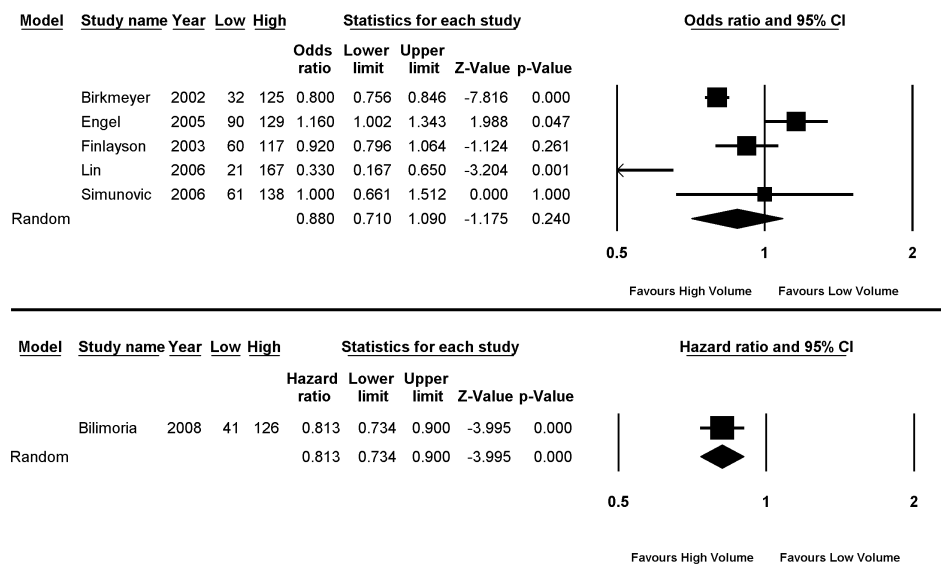
Table 5: Pooled effects Hospital volume

	Median cut-off (range)		Postoperative mortality					Long term survival				
	Low volume	High volume	Effect	95% CI	P-value	I ²	Egger	Effect	95% CI	P-value	I ²	Egger
Colon Cancer	45 (21-90)	126 (85-167)	OR 0.88 HR 0.813	0.710 - 1.090 0.734 - 0.900	0.24 <0.001	87.1 -	0.76 -	HR 0.916	0.872 - 0.962	<0.001	45.7	0.69
Rectal Cancer	9 (6-14)	24 (17-35)	OR 0.744 HR 0.752	0.496 - 1.116 0.621 - 0.910	0.152 0.003	76.7 -	0.32 -	HR 0.838	0.805 - 0.873	<0.001	0.0	0.62
Colorectal Cancer	24 (20-61)	55 (25-150)	OR 0.781 RR 1.111	0.617 - 0.989 0.886 - 1.393	0.041 0.361	- -	- -	HR 0.912	0.861 - 0.967	0.002	37.7	0.89

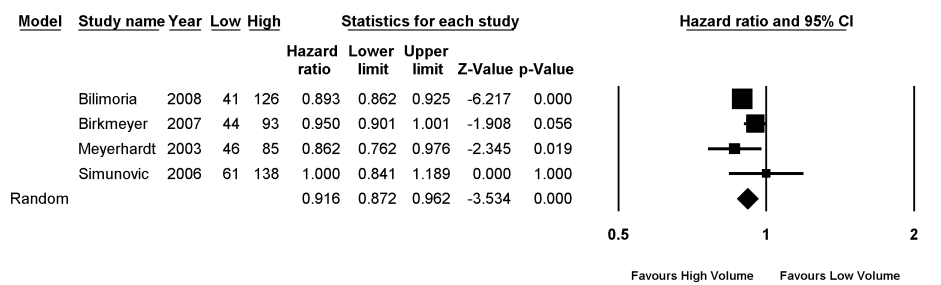
Table 6: Pooled effects Surgeon volume

	Median cut-off (range)		Postoperative mortality					Long term survival				
	Low volume	High volume	Effect	95% CI	P-value	I ²	Egger	Effect	95% CI	P-value	I ²	Egger
Colon Cancer	2 (1-2)	4 (3-5)	OR 0.820	0.675 - 0.997	0.046	-	-	HR 0.657	0.532 - 0.811	<0.001	-	-
Rectal Cancer	-	-	-	-	-	-	-	-	-	-	-	-
Colorectal Cancer	9 (3-19)	17 (11-38)	OR 0.665	0.528 - 0.836	<0.001	45.6	-	HR 0.869	0.823 - 0.919	<0.001	0.0	0.67

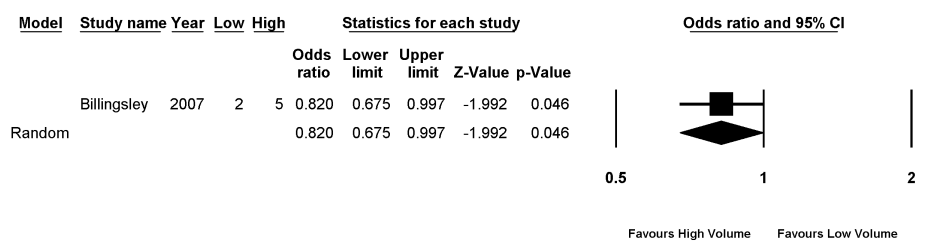
Colon Cancer Hospital Mortality



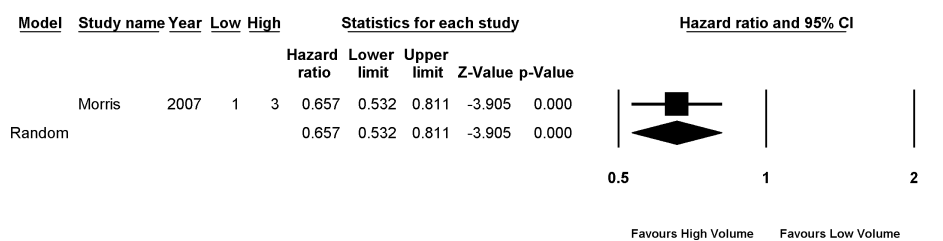
Colon Cancer Hospital Survival



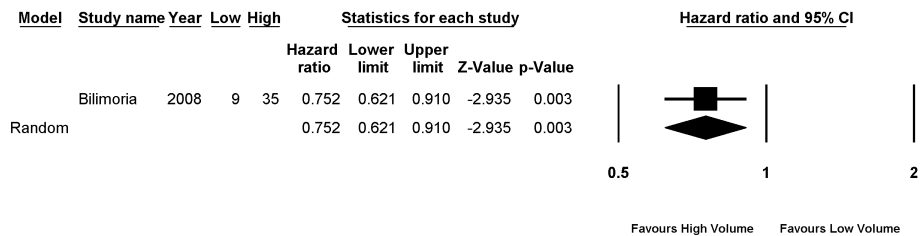
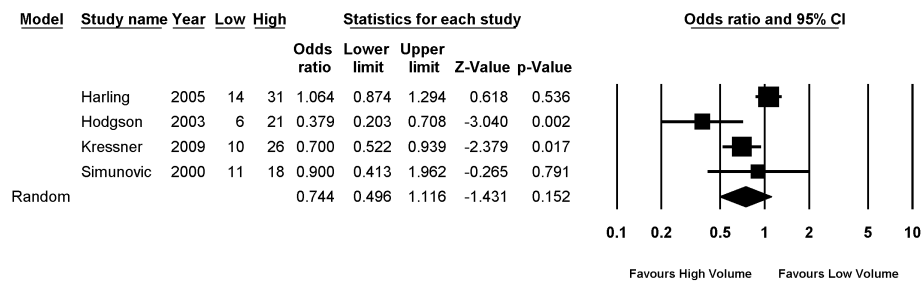
Colon Cancer Surgeon Mortality



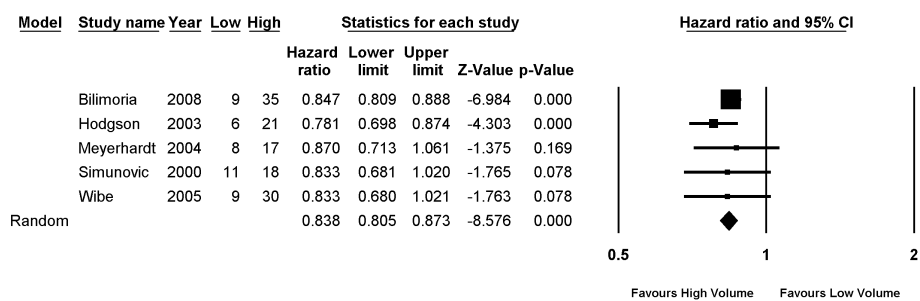
Colon Cancer Surgeon Survival



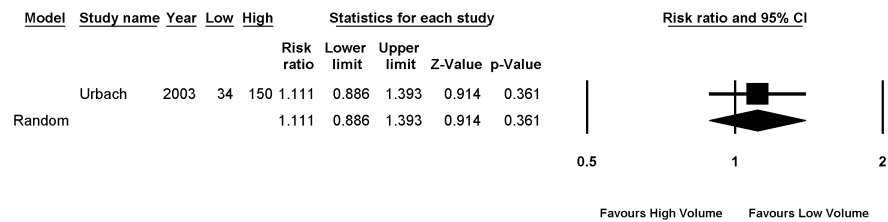
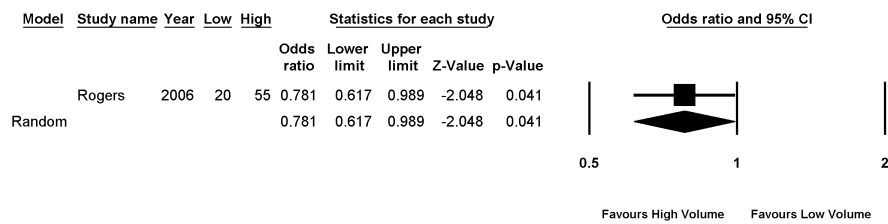
Rectal Cancer Hospital Mortality



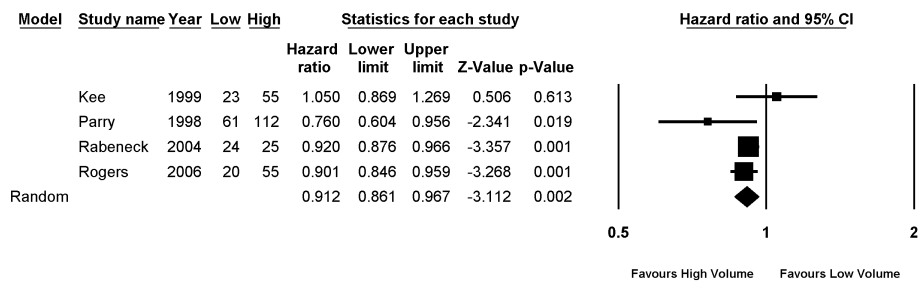
Rectal Cancer Hospital Survival



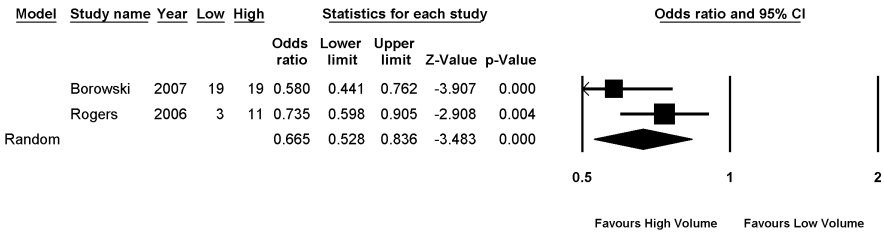
Colorectal Hospital Mortality



Colorectal Cancer Hospital Survival



Colorectal Surgeon Mortality



Colorectal Cancer Surgeon Survival

