## Uitgangsvraag 5: evidence tables

### Systematic reviews

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Method</th>
<th>Patient characteristics</th>
<th>Intervention(s)</th>
<th>Results primary outcome</th>
<th>Results secondary and other outcomes</th>
<th>Critical appraisal of review quality</th>
</tr>
</thead>
</table>
| Gruen 2009 | Design: SR and MA  
Source of funding: Victorian Government Department of Human Services - a National Health and Medical Research Council Career Development Award  
Search date: 1979-2005  
Searched databases: OVID PreMEDLINE, MEDLINE, Cochrane Library, AMI, EMBASE, EconLit, PubMed, ISI Web of Knowledge - also SRs of related topics so that reference lists could be hand-searched  
Included study designs: SR, MA, RCT; other controlled trials, comparative studies, and cohort studies  
Number of included studies: 28 on esophagus (patients: N=45822; hospitals: N=3405) | • Eligibility: esophageal cancer or those undergoing procedures usually undertaken to treat gastrointestinal cancers  
• Exclusion: non-English publications, publication types other than primary study, inappropriate study designs, studies not addressing relationship between volume and patient mortality, Sx performed for disease conditions other than cancer | Surgical interventions delivered by a high-volume clinician or in a high-volume hospital vs. Surgical interventions delivered by a low-volume clinician or in a low-volume hospital | Effect on mortality of doubling hospital case volume (N=24 studies): OR 0.81 (95%CI 0.77-0.84) (unadjusted) | Lower quartile mortality (max 3 cases/year): 16.7%  
Upper quartile mortality (min 18 cases/year): 6.7%  
Patients needed to be moved from a lower quartile hospital to an upper quartile hospital to prevent 1 volume-associated death (calculated by 100/[lower quartile mortality– upper quartile mortality]): NNT=10  
2 studies reported adjusted analyses (adjusted for age, stage of disease and comorbidities)  
• Bachmann 2002: 30-d surgical mortality, per increase of 10 cases in surgeon volume: OR 0.60 (0.36-0.99)  
Overall death rate: Per increase of 10 cases in hospital volume: HR 1.01 (0.96-1.05)  
Per increase of 10 cases in surgeon volume: HR 0.92 (0.85-0.99)  
• Birkmeyer 2003: Surgical mortality: Hospital volume low vs high: OR 1.67 (1.02-2.73)  
Surgeon volume low vs high: OR 1.80 (1.13-2.87) | Level of evidence: B  
• High quality SR: study quality assessed, data extraction clearly described, correctly performed statistics  
• Studies included: Bachmann MO, Br J Surg 2002  
Begg CB, JAMA 1998  
Birkmeyer JD, Ann Surg 2007  
Birkmeyer JD, Cancer 2006  
Birkmeyer JD, N Engl J Med 2002  
Birkmeyer JD, N Engl J Med 2003  
Dimick JB, Arch. Surg. 2003  
Finlayson EVA, Arch Surg 2006  
Gillison EW, Br J Surg 2002  
Hollenbeck BK, J Clin Oncol 2007  
Jensen LS, SJS 2007  
Kuo EY, Ann Thorac Surg 2001  
Patti MG, J Gastrointest Surg 1998  
Rouvelas I, Arch Surg 2007  
Swisher SG, J Thorac Cardiovasc Surg 2000  
Thompson AM, Br J Surg 2007  
Urbach DR, J Clin Epidemiol 2005  
Urbach DR, CMAJ 2003  
Urbach DR, Qual Saf Health Care 2004 |
Cohort studies

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Method</th>
<th>Patient characteristics</th>
<th>Intervention(s)</th>
<th>Results primary outcome</th>
<th>Results secondary and other outcomes</th>
<th>Critical appraisal of study quality</th>
</tr>
</thead>
</table>
| Al-Sarira 2007 | Design: Retrospective cohort study | • Eligibility criteria: patients undergoing esophagectomy and esophago-gastrectomy for esophageal and EGJ cancers  
• Exclusions: not reported  
• Patient characteristics: Age 64 years, 75% men stable over the period under study | Introduction of manual “Improving Outcomes in Upper Gastro-intestinal Cancers”  
Annual hospital volume grouped into 5 categories:  
Very high: ≥40  
High: 30–39  
Medium: 20–29  
Low: 10–19  
Very low: ≤9 | In hospital mortality, %  
Overall: Period 1: 11.7  
Period 3: 7.6  
p<0.001  
Very high:  
Period 1: 6.9  
Period 3: 4.5  
p=0.118  
High:  
Period 1: 9.0  
Period 3: 9.0  
p=0.845  
Medium:  
Period 1: 12.7  
Period 3: 6.0  
p<0.001  
Low:  
Period 1: 13.9  
Period 3: 8.3  
p<0.001  
Very low:  
Period 1: 13.0  
Period 3: 11.8  
p=0.801  
Number of hospitals performing esophagectomies/esophago-gastrectomies  
1997: 180  
2003: 111  
(decrease: mostly very low and low volume hospitals)  
Median annual hospital volume  
1997: 7  
2003: 11  
(p=0.030) | Prolonged hospital stay (longer than the 75th percentile)  
Overall: Period 1: 23.9% of patients  
Period 3: 23.9% of patients  
p=0.869  
Very high:  
Period 1: 17.6% of patients  
Period 3: 22.7% of patients  
p=0.040  
High:  
Period 1: 16.4% of patients  
Period 3: 25.2% of patients  
p=0.001  
Medium:  
Period 1: 20.0% of patients  
Period 3: 20.9% of patients  
p=0.913  
Low:  
Period 1: 26.3% of patients  
Period 3: 25.3% of patients  
p=0.212  
Very low:  
Period 1: 30.4% of patients  
Period 3: 25.3% of patients  
p=0.109 | Level of evidence: B  
• High quality retrospective cohort study; outcomes well defined but potential confounders not identified or taken into account in the analysis |
<table>
<thead>
<tr>
<th>Study ID</th>
<th>Method</th>
<th>Patient characteristics</th>
<th>Intervention(s)</th>
<th>Results primary outcome</th>
<th>Results secondary and other outcomes</th>
<th>Critical appraisal of study quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Branagan 2004</td>
<td>Design: Prospective cohort, compared to another prospective cohort</td>
<td>• Eligibility: patients undergoing esophageal cancer Sx</td>
<td>Centralization of esophageal cancer Sx into a single site vs. Esophageal cancer Sx in 4 hospitals before centralisation</td>
<td>Hospital deaths</td>
<td>Major postoperative complications</td>
<td>Level of evidence: B</td>
</tr>
<tr>
<td></td>
<td>Source of funding: Not reported</td>
<td>• Exclusions: not reported</td>
<td>Single site: 0 cases</td>
<td>Single site: 16 cases</td>
<td>Single site: 16 cases</td>
<td>• Cohort study with small sample size</td>
</tr>
<tr>
<td></td>
<td>Setting: 1 centre and 4 centres in the UK</td>
<td>• Patient characteristics: Mean age 62/66 Male: Female 25:8/34:6 ASA I 6/10; II 25/20; III 2/1 Site Upper third 1 /0 Middle third 0 /3 Lower third 18 /28 EGJ 14/9 Tumour stage Barrett’s 3 /0 II 4 /11 III 24 /17 Node stage 0 13/19 I 20/12 Not staged 0 /9</td>
<td>Hospital mortality</td>
<td>WOCA: 5 cases</td>
<td>Not significant</td>
<td>• Potential confounders are not taken into account for the analysis</td>
</tr>
<tr>
<td></td>
<td>Sample size: N=73 (cases: N=33; control group: N=40)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Lost to follow up not presented</td>
</tr>
<tr>
<td></td>
<td>Duration: From May 2002, for one year and from October 1999 to September 2000.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Adjusted analyses not including the same variables</td>
</tr>
<tr>
<td></td>
<td>• Intervention(s)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Setting: 11 hospitals + 1 university hospital in the Netherlands</td>
<td>• Exclusions: not reported</td>
<td>Risk of dying after Sx: Adjusted for stage, comorbidity, surgical approach, and neoadjuvant treatment) Adjusted HR compared to 1990–1994: 1995–1999 0.85 (0.63–1.16) 2000–2004 0.81 (0.44–0.86)</td>
<td>Risk of dying after Sx: Adjusted for stage, comorbidity, surgical approach, and surgical approach) Adjusted HR compared to 1990–1994: 1995–1999: 0.92 (0.66–1.29)</td>
<td>0.002</td>
<td>• Primary outcome not defined; Groups not comparable regarding stage and adjuvant treatment</td>
</tr>
<tr>
<td></td>
<td>Sample size: 555</td>
<td>• Patient characteristics: stable between periods, except for neoadjuvant therapy, surgical approach and anastomoses</td>
<td></td>
<td></td>
<td></td>
<td>• Lost to follow up not presented</td>
</tr>
<tr>
<td></td>
<td>Duration: 1990-2004</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Adjusted analyses not including the same variables</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study ID</td>
<td>Method</td>
<td>Patient characteristics</td>
<td>Intervention(s)</td>
<td>Results primary outcome</td>
<td>Results secondary and other outcomes</td>
<td>Critical appraisal of study quality</td>
</tr>
<tr>
<td>---------</td>
<td>--------</td>
<td>------------------------</td>
<td>-----------------</td>
<td>-------------------------</td>
<td>--------------------------------------</td>
<td>-----------------------------------</td>
</tr>
</tbody>
</table>
| Birkmeyer2005 | Design: retrospective cohort study  
Source of funding: National Cancer Institute and Agency for Healthcare Research and Quality  
Setting: 102 centers in the USA  
Sample size: 1987  
Cases: N=1173  
Controls: =814  
Duration: 1994-1999 | • Eligibility: Medicare recipients covered by the hospital care program and undergoing cancer related esophagectomy  
• Exclusion criteria: Medicare patients who were enrolled in risk-bearing health maintenance organizations (approximately 10% of Medicare enrollees) ; patients who were <65 or > 99 years  
• Patient characteristics:  
  Age >85 yrs (%) 1.4/1.6  
  % female 25.2/23.2  
  % black 6.2/6.1  
  Charlson comorbidity score (% ≥3) 43.4/41.0  
  Urban (%) 63.9/68.1  
  Low income (%) 17.9/20.6 | Cases: patients treated in 51 National cancer institute centers  
Controls: patients treated in 51 other hospitals with the highest volumes for each procedure. | Surgical mortality  
(before hospital discharge or within 30 days after the procedure)  
Adjusted OR 0.70 (0.51–0.97)  
(Adjusted for patient characteristics and residual procedure volume differences) | Long term survival (from date index surgical admission until death or the termination of the period of observation)  
Adjusted HR: 1.05 (0.92–1.20)  
(Adjusted for patient characteristics and residual procedure volume differences) | Level of evidence: B  
• High quality study with clearly defined primary outcome  
• Main confounders are taken into account |
| Kazui2007 | Design: Retrospective cohort study  
Source of funding: Not reported  
Setting: 551 nationwide Japanese hospitals  
Sample size: N=21020  
Cases N=4085  
Controls:  
1-4: N=3114;  
5-9:N=5290;  
10-14:N=3141;  
15-19:N=1538;  
20-29:N=2022  
30-39:N=1830  
Duration: Between 2000 and 2004 | • Eligibility: Patients undergoing esophageal cancer Sx | Cases: patients treated in institutions with an annual number of procedures of ≥40  
Controls: patients treated in institutions with an annual number of procedures of:  
30-39  
20-29  
15-19  
10-14  
5-9  
1-4 | In hospital mortality:  
≥40: reference group  
30-39: OR 0.96 (0.62-1.49)  
20-29: OR 1.20 (0.73-1.98)  
15-19: OR 1.61(0.94-2.76)  
10-14: OR 1.82 (1.22-2.70)  
5-9: OR 2.21 (1.53-3.21)  
1-4: OR 2.27 (1.54-3.33) | No other outcomes reported | Level of evidence: B  
• Large sample size  
• Potential confounders were not identified or taken into account in analysis |
<table>
<thead>
<tr>
<th>Study ID</th>
<th>Method</th>
<th>Patient characteristics</th>
<th>Intervention(s)</th>
<th>Results primary outcome</th>
<th>Results secondary and other outcomes</th>
<th>Critical appraisal of study quality</th>
</tr>
</thead>
</table>
| Gasper 2009 | Design: Retrospective cohort study  
Source of funding: Not reported  
Setting: multicenter study in California, USA  
Sample size: N=2404  
period B: N=1194  
period C: N=1210  
Duration: Between 1995 and 2004 | • Eligibility: patients who had resections for cancer of the esophagus  
Cases: patients treated in period A (1990-1994)  
Adjusted OR stratified by annual hospital volume  
Period A: reference  
Period B:  
<6: 1.95 (1.03–3.69)  
6-10: 1.01 (0.50–2.06)  
11-20: 1.59 (0.84–3.03)  
21-30: 1.29 (0.58–2.86)  
>30: 1.0  
Period C:  
<6: 1.65 (1.01–2.69)  
6-10: 1.45 (0.78–2.68)  
11-20: 1.19 (0.57–2.47)  
21-30: 0.94 (0.45–1.98)  
>30: 1.0  
(Adjusted for age, gender, race, insurance type, comorbidities, location of the tumor) | Number of hospitals: number of patients  
Period A:  
<6: 72%-29%  
6-10: 16%-21%  
11-20: 7%-19%  
21-30: 3%-14%  
>30: 2%-17%  
Period B:  
<6: 64%-23%  
6-10: 19%-20%  
11-20: 12%-24%  
21-30: 2%-8%  
>30: 3%-25%  
Period C:  
<6: 64.5%-21%  
6-10: 15.8%-14%  
11-20: 10.4%-18%  
21-30: 4.9%-14%  
>30: 4.4%-34% | Moderate quality study  
Clearly defined primary outcome  
Potential confounders are taken into account |
| Gomi 2003 | Design: Retrospective cohort study  
Source of funding: Not reported  
Setting: 76 randomly selected institutions in Japan  
Sample size: N=220  
A1:N=87  
A2:N=72  
B:N=61  
Duration: between September 1998 and March 2001 | • Eligibility: thoracic esophageal cancer treated during 1995–1997, any pathologic type, and ≥60 initial Karnofsky performance status who had undergone preoperative or postoperative RT  
Exclusions: presence of distant metastasis or other active malignancies.  
Patient characteristics: median age 62.3 years  
male 88.1%  
KPS 60–70: 17.5%  
SCC 99.5%  
Tumour location: upper: 11.8%  
middle: 61.3%  
lower: 24.5%  
Stage III: 41.7%  
In non-academic  
52.6%  
vs. academic 37.7%,  
A1= academic institutions (mainly cancer centers and university hospitals)  
≥300 patients annually;  
Control groups:  
A2= academic institutions (university hospitals)  
treating <300 patients annually  
B= non-academic institutions (national hospitals, public general hospitals, and private hospitals) | Overall 2-year survival rate  
A1: 77.9%  
A2: 61.6%  
C: 40.0%  
Difference A1 vs. non-academic: p=0.001  
Overall survival:  
Multivariate analysis:  
Type of institution (p=0.0373, RR=0.588)  
Clinical stage (p=0.0268, RR=0.566)  
Presence of macroscopic residual tumor (p=0.0040, RR=0.461)  
Photon energy (p=0.0215, RR=0.536)  
Use of chemotherapy (p=0.0118, RR=1.910) | Low quality cohort study  
Unclear which variables were included in multivariate analyses  
Lost of follow up not presented  
Small sample size | Level of evidence: B  
Level of evidence: B |
<table>
<thead>
<tr>
<th>Study ID</th>
<th>Method</th>
<th>Patient characteristics</th>
<th>Intervention(s)</th>
<th>Results primary outcome</th>
<th>Results secondary and other outcomes</th>
<th>Critical appraisal of study quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goodney 2003</td>
<td>Design: Retrospective cohort study</td>
<td>Eligibility: Medicare recipients covered by the hospital care program and undergoing cancer related esophagectomy</td>
<td>Exposure: annual hospital volume (average number of procedures annually)</td>
<td>Post-operative length of stay (period from the index procedure to hospital discharge); stratified by average number of procedures annually</td>
<td>30-day readmission rate (readmission to any hospital within 30 days of discharge after the index procedure); stratified by annual hospital volume quintile</td>
<td>Level of evidence: B</td>
</tr>
<tr>
<td>Ioka 2007</td>
<td>Design: Retrospective cohort study</td>
<td>Eligibility: Patients with esophagus cancer</td>
<td>Patients treated in high volume hospital vs. Patients treated in: Medium volume hospital Low volume hospital Very low volume hospital</td>
<td>5-year survival High: reference Medium volume: Adjusted HR 1.3 (1.2-1.5) Low volume: Adjusted HR 1.3 (1.2-1.5) Very low volume: Adjusted HR 1.6 (1.4-1.9) (adjusted for sex, age and cancer stage)</td>
<td>Overall 1-year survival: 69% Overall 5-year survival: 28.8% no significant difference amongst surgeons when adjusted for pathological staging (log-rank P=0.17)</td>
<td>Level of evidence: B</td>
</tr>
<tr>
<td>Jeganathan 2009</td>
<td>Design: retrospective cohort study</td>
<td>Eligibility: patients diagnosed with esophageal cancer who were surgically treated with curative intent at a tertiary referral centre with a total thoracic esophagectomy</td>
<td>Patients operated by consultants vs. Patients operated by trainees</td>
<td>In hospital mortality Consultants: 4.3% Trainees: 4.4% p=0.61 Case volume per surgeon: p=0.24</td>
<td>Overall 1-year survival: 69% Overall 5-year survival: 28.8% no significant difference amongst surgeons when adjusted for pathological staging (log-rank P=0.17)</td>
<td>Level of evidence: B</td>
</tr>
<tr>
<td>Study ID</td>
<td>Method</td>
<td>Patient characteristics</td>
<td>Intervention(s)</td>
<td>Results primary outcome</td>
<td>Results secondary and other outcomes</td>
<td>Critical appraisal of study quality</td>
</tr>
<tr>
<td>----------</td>
<td>--------</td>
<td>-------------------------</td>
<td>----------------</td>
<td>------------------------</td>
<td>-------------------------------------</td>
<td>----------------------------------</td>
</tr>
<tr>
<td>Leigh 2009</td>
<td>• Design: Retrospective cohort study • Sources of funding: English NHS National Coordinating Centre for Research Capacity Development - Hanson Trust Research fellowship • Setting: nationwide data from the UK • Sample size: N=9034 Hospitals ≥100 operations: N=3791; Hospitals &lt;100 operations: N=5243 • Duration: April 1998 to March 2003</td>
<td>• Eligibility: Patients treated with esophagectomy for esophageal cancer or esophago-gastric cancer • Exclusions: not reported • Patient characteristics: Mean age 64.2/63.5 % male 72.9/74.0 Deprivation score 21.4/21.2 % EGJ, lower third 80.7/80.6 % esophago-gastrectomy 61.0/76.3 (p&lt;0.001)</td>
<td>Patients treated in low volume hospitals (&lt;100/5 year) vs Patients treated in high volume hospitals (≥100/5 year)</td>
<td>30-day mortality, low volume vs high volume Adjusted OR: 1.62 (1.38-1.91)</td>
<td>30 day mortality, general surgical patients vs cardiothoracic Sx patients Adjusted OR: 1.62 (1.34-1.96) 90-day mortality, low volume vs high volume Adjusted OR: 1.55 (1.35-.77) (Adjusted for age, sex, socio-economic deprivation score)</td>
<td>Level of evidence: B • Primary outcome not well defined • Cancer stage as confounders not taken into account</td>
</tr>
<tr>
<td>Meguid 2009</td>
<td>• Design: Retrospective cohort study • Sources of funding: Ruth L. Kirschstein National Research Service Award • Setting: data collected from the Nationwide Inpatient Sample file (US) • Sample size: N=4080 • Duration: 1998-2003</td>
<td>• Eligibility: patients from the NIS database ≥17 years of age admitted with the diagnosis of esophageal cancer • Exclusions: not reported • Patient characteristics: 79.6% male, median age 64 years, 83.9% were white, median Charlson Comorbidity Index 3 (IQR 2-8)</td>
<td>Hospital volume above or below volume threshold (≥15)</td>
<td>Mortality Rate: Centers ≥ Volume Threshold: 5.30% Centers &lt; Volume Threshold: 10.16% p&lt;0.01 Threshold modeling adjusted for patient age, gender, race and Charlson Index of comorbidities, procedure year, and hospital teaching status</td>
<td></td>
<td>Level of evidence: B • Primary outcome not well defined • Unclear whether difference in mortality rates took account of confounders</td>
</tr>
<tr>
<td>Study ID</td>
<td>Method</td>
<td>Patient characteristics</td>
<td>Intervention(s)</td>
<td>Results primary outcome</td>
<td>Results secondary and other outcomes</td>
<td>Critical appraisal of study quality</td>
</tr>
<tr>
<td>----------</td>
<td>--------</td>
<td>-------------------------</td>
<td>----------------</td>
<td>-------------------------</td>
<td>-------------------------------------</td>
<td>----------------------------------</td>
</tr>
<tr>
<td>Milne 2000</td>
<td>Design: Retrospective cohort study</td>
<td>• Eligibility: Patients with biopsy proven esophageal cancer</td>
<td>Treated by 1 general surgeon within the General district hospital vs Treated by 2 cardiothoracic surgeons in the regional cardiothoracic unit</td>
<td>Survival at 3 months General surgeon: 63% Specialist surgeons: 62%</td>
<td>Survival at 1 year Exposure: 24% Controls: 25% Survival at 2 years Exposure: 12% Controls: 8% Survival at 3 years Exposure: 7% Controls: 6% No statistical significant difference at any time point between the two groups</td>
<td>Level of evidence: B Primary outcome not defined Comparison between both groups does not indicate stage Confounders not taken into account Small sample size</td>
</tr>
<tr>
<td>Migliore 2007</td>
<td>Design: retrospective cohort study</td>
<td>• Eligibility: patients, who underwent esophagectomy for malignant disease with palliative or curative intent</td>
<td>Patients treated by a high-volume surgeon (mean ≥ 6 cases/year) vs Patients treated by a low-volume surgeon (mean &lt; 6 cases/year)</td>
<td>In hospital mortality, low vs high volume Adjusted OR: 4.60 (1.55-13.60) p=0.006 (Adjusted for age, tumour stage and type)</td>
<td>Overall survival, median High volume: 16.8 months (13.8-19.8) Low volume: 13.9 months (11.0-17.0) p=0.48</td>
<td>Level of evidence: B Small sample size Potential confounders identified and taken into account</td>
</tr>
<tr>
<td>Rouvelas 2007</td>
<td>Design: Prospective cohort study</td>
<td>• Eligibility: Swedish residents diagnosed with esophageal or cardia cancer treated with esophagectomy</td>
<td>Patients treated by low-volume surgeons (LVS) (&lt;2 esophagectomies annually) vs Patients treated by medium-volume surgeons (MVS) performed (2-6 esophagectomies annually) vs Patients treated by high-volume surgeons (HVS) (&gt;6 esophagectomies annually)</td>
<td>30-days post operative mortality Adjusted OR LVS: reference MVS: 0.39 (0.09-1.70) HVS: 0.42 (0.10-1.80) (Adjusted for age, sex, co-morbidity, tumour stage, location, histology, preoperative oncological treatment, and curative intention)</td>
<td>90-days post operative mortality Adjusted OR LVS: reference MVS: 0.48 (0.16-1.38) HVS: 0.86 (0.31-2.38) (Adjusted for age, sex, co-morbidity, tumor stage, location, histology, preoperative oncological treatment, and curative intention)</td>
<td>Level of evidence: B Potential confounders identified and taken into account</td>
</tr>
<tr>
<td>Study ID</td>
<td>Method</td>
<td>Patient characteristics</td>
<td>Intervention(s)</td>
<td>Results primary outcome</td>
<td>Results secondary and other outcomes</td>
<td>Critical appraisal of study quality</td>
</tr>
<tr>
<td>----------</td>
<td>--------</td>
<td>-------------------------</td>
<td>-----------------</td>
<td>------------------------</td>
<td>---------------------------------------</td>
<td>----------------------------------</td>
</tr>
<tr>
<td>Rutegard 2008</td>
<td>Design: Prospective cohort study</td>
<td>• Eligibility: patients newly diagnosed with esophageal or cardia cancer who underwent macroscopically and microscopically radical resection</td>
<td>Low volume hospitals (LVH) (0–9 operations annually) vs High volume hospitals (HVH) (≥ 9 operations annually)</td>
<td>HRQOL at 6 months Mean score Per hospital: LVH: 60 (57–64) HVH: 60 (57–63) p≥0.05 Per surgeon LVS: 62 (58–65) HVS: 59 (56–62) p≥0.05</td>
<td></td>
<td>Level of evidence: B</td>
</tr>
<tr>
<td></td>
<td>Sources of funding: Swedish cancer society</td>
<td>• Exclusions: not reported</td>
<td>Low volume surgeons (LVS) (0–6 operations annually) vs High volume surgeons (HVS) (&gt; 6 operations annually)</td>
<td>Level of evidence: B • Small sample size • Potential confounders identified and taken into account • Well defined outcome • Measure of outcome is reliable</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Setting: multicentre study in Sweden</td>
<td>• Patient characteristics: Age (yr): &lt;60: 25.7%; 60–70: 33.5%; &gt;70 40.8%; Male 80.7% Comorbidity: None 32.7%, 1 or 2 62.6%; 3 or more 4.6% Tumour stage: Stage 0–I 18.7%; Stage II 29.1%; Stage III 40.5%; Stage IV 11.2%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rutegard 2009</td>
<td>Design: prospective cohort study</td>
<td>• Eligibility: patients diagnosed with esophageal or cardia cancer who underwent surgical resection</td>
<td>Patients treated by high volume surgeons (HVS) (&gt;6 operations annually) vs Patients treated by medium volume surgeons (MVS) (2-6 operations annually) vs patients treated by low volume surgeons (LVS) (&lt;2 operations annually)</td>
<td>Primary surgical complications (considered to be more closely linked with the individual surgeon’s efforts) HVS: reference MVS: OR 0.66 (0.38–1.17) LVS: OR 0.49 (0.19–1.24) (Adjusted for age, sex, tumor stage, location, histology, comorbidity, surgical approach, neoadjuvant therapy, macroscopic radicality, and examined lymph nodes)</td>
<td>Secondary surgical complications (less markedly related to the individual surgeon’s operative performance) HVS: reference MVS: OR 0.83 (0.39–1.74) LVS: OR 1.41 (0.65–3.08) (Adjusted for age, sex, tumor stage, location, histology, comorbidity, surgical approach, neoadjuvant therapy, macroscopic radicality)</td>
<td>Level of evidence: B</td>
</tr>
<tr>
<td></td>
<td>Sources of funding: Swedish cancer society</td>
<td>• Exclusions: not reported</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Setting: multicentre study in Sweden</td>
<td>• Patient characteristics: Age (yr): &lt;60: 25.7%; 60–70: 33.5%; &gt;70 40.8%; Male 80.7% Comorbidity: None 32.7%, 1 or 2 62.6%; 3 or more 4.6% Tumour stage: Stage 0–I 18.7%; Stage II 29.1%; Stage III 40.5%; Stage IV 11.2%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study ID</td>
<td>Method</td>
<td>Patient characteristics</td>
<td>Intervention(s)</td>
<td>Results primary outcome</td>
<td>Results secondary and other outcomes</td>
<td>Critical appraisal of study quality</td>
</tr>
<tr>
<td>----------</td>
<td>-------------------------------------</td>
<td>-----------------------------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------------</td>
<td>----------------------------------------</td>
</tr>
<tr>
<td>Smith 2008</td>
<td>Design: Retrospective cohort study</td>
<td>Tumour location: Cardia 46.2%, Lower esophagus 38.0%; Upper or middle esophagus 15.8%; SCC 24.2%; Neoadjuvant treatment 11.2%; Macroscopically radical 90.4%</td>
<td>Tumour location: Cardia 46.2%, Lower esophagus 38.0%; Upper or middle esophagus 15.8%; SCC 24.2%; Neoadjuvant treatment 11.2%; Macroscopically radical 90.4%</td>
<td>Overall complications (included those related to cardiac, pulmonary, thrombotic, hemorrhagic, iatrogenic, and wound infectious events)</td>
<td>In hospital mortality: General surgeon: 3.6%; Thoracic surgeon: 2.9%; p=0.31</td>
<td>Level of evidence: B; Primary outcome not defined; Confounders not taken into account; Groups not comparable regarding race, comorbidity and surgical approach</td>
</tr>
<tr>
<td>Stitzenberg 2009</td>
<td>Design: Retrospective cohort study</td>
<td></td>
<td>Eligibility: Patients who underwent partial or total esophagectomy for esophageal cancer</td>
<td>Patients treated by a general surgeon vs. Patients treated by a thoracic surgeon</td>
<td>Having Sx at a LVH over time Per year OR: 0.87(0.85 -0.90)</td>
<td>In hospital mortality 1996: 8.15%; 2006: 3.12%; p=0.038</td>
</tr>
<tr>
<td>Study ID</td>
<td>Method</td>
<td>Patient characteristics</td>
<td>Intervention(s)</td>
<td>Results primary outcome</td>
<td>Results secondary and other outcomes</td>
<td>Critical appraisal of study quality</td>
</tr>
<tr>
<td>----------</td>
<td>--------</td>
<td>-------------------------</td>
<td>-----------------</td>
<td>-------------------------</td>
<td>--------------------------------------</td>
<td>-----------------------------------</td>
</tr>
<tr>
<td>Sundelof 2008</td>
<td>Design: Retrospective cohort study (subset of earlier case-control study)</td>
<td>Eligibility: incident cases of ACA of the esophagus and gastric cardia and half of those with SCC of the esophagus in the native Swedish population, &lt;80 years of age, diagnosed between 1994 and 1997, and had undergone a surgical resection</td>
<td>High volume hospital (HVH) (annual number of the resections ≥ 10) vs Low volume hospitals (LVH)</td>
<td>5 year survival, stratified by volume hospital</td>
<td>Operating time (min), median (range)</td>
<td>Level of evidence: B</td>
</tr>
<tr>
<td></td>
<td>Sources of funding: National Cancer Institute, Cancerfonden</td>
<td>Exclusions: not reported</td>
<td>High volume surgeon (HVS) (annual number of the resections ≥ 10) vs Low volume surgeons (LVS)</td>
<td>HR, 95%CI: HVH: reference LVH: 1.3 (1.0–1.9) p=0.02</td>
<td>HVH: 525 (150–830) LVH 360 (145–780) p&lt;0.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Setting: Nationwide study in Sweden</td>
<td>Patient characteristics: Age at Sx (years) &lt;59 24%; 60-65 20%; 66-70 26%; &gt;70 30% Gender Male 83% Tumor location: Proximal/middle: 8% Distal esophagus 41% Cardia 51% Comorbidity None 60% Prior Sx within the operating field 14% Combined co-morbidity 3% Tumour stage: Stage 1 22% Stage 2 26% Stage 3 30% Stage 4 16% Grade of tumor differentiation High 7% Medium 33% Low 56% Treatment: Surgical resection only 77% Surgical resection and neoadjuvant therapy 23%</td>
<td></td>
<td>HR, 95%CI: HVS: reference LVS: 1.4 (1.0–2.0) p=0.07</td>
<td>HVS 546 (210–830) LVS 360 (145–780) p&lt;0.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sample size: N=232 High hospital: N=81 Low hospital: N=151 High surgeon: N=67 Low surgeon: N=165</td>
<td></td>
<td>30-day mortality, (%) HVH 0 LVH 3 p=0.30</td>
<td></td>
<td>Operative bleeding volume (ml), median (range) HVH: 1100 (250–5200) LVH: 1100 (200–6500) p=0.78</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Duration: December 1994-December 1997.</td>
<td></td>
<td>HVS 0 LVS 2 p=0.33</td>
<td></td>
<td>HVS 1000 (250–5200) LVS 1200 (200–6500) p=0.20</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>In-hospital mortality, (%) HVH 1 LVH 3 p=0.66</td>
<td></td>
<td>Postoperative complications, (%) HVH 28 LVH 6 p=0.31</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>HVS 0 LVS 2 p=0.33</td>
<td></td>
<td>HVS 30 LVS 35 p=0.54</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>HVS 1 LVS 2 p=1.00</td>
<td></td>
<td>Postoperative respirator support, (%) HVH 17 LVH 38 p&lt;0.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>HVS 24 LVS 34 p=0.16</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Days in ICU, median (range) HVH 1 (1–17) LVH 2 (1–72) p&lt;0.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>HVS 1 (1–17) LVS 2 (1–72) p&lt;0.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Days in hospital, median (range) HVH 19 (9–57) LVH 17.5 (7–102) p=0.28</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>HVS 18 (9–58) LVS 18 (7–102) p=0.42</td>
<td></td>
</tr>
<tr>
<td>Study ID</td>
<td>Method</td>
<td>Patient characteristics</td>
<td>Intervention(s)</td>
<td>Results primary outcome</td>
<td>Results secondary and other outcomes</td>
<td>Critical appraisal of study quality</td>
</tr>
<tr>
<td>----------</td>
<td>--------</td>
<td>--------------------------</td>
<td>-----------------</td>
<td>-------------------------</td>
<td>-------------------------------------</td>
<td>-----------------------------------</td>
</tr>
</tbody>
</table>
| Van Vliet 2008 | Design: retrospective cohort study  
Source of funding: Erasmus MC—University Medical Center Rotterdam  
Setting: 8 centres in the Netherlands  
Sample size: 8 (cases: N=2; controls: N=6)  
Duration: 1994-2003 | Eligibility: CT examinations (N=72) of patients diagnosed with esophageal or gastric cardia cancer (random selection) that were re-evaluated or repeated at the referral centre  
Patient characteristics:  
N stage: N0 41  
N1 31  
M stage: M0 35  
M1 37 | Radiologists from referral centers ('expert') (centers had a volume of >100 patients with esophageal or gastric cardia cancer per year) vs Radiologists from regional non-referral centers ('non-expert') (centers < 10 cases per year) | Radiologist experience (expert versus non-expert)  
Lymph node metastases  
All CT examinations  
OR 0.94 (0.50–1.77)  
Distant metastases  
All CT examinations  
OR 2.93 (1.36–6.29) (Adjusted for origin of CT examination)  
Quality of CT examination (referral center versus regional center)  
Lymph node metastases  
All CT examinations  
OR 1.06 (0.46–2.42)  
Distant metastases  
All CT examinations  
OR 0.85 (0.38–1.94) (Adjusted for radiologist experience and origin of CT examination) | Required secondary Sx (%):  
HVH 10  
LVS 13  
p=0.67  
HVH 9  
LVS 13  
p=0.50 | Level of evidence: B  
Primary outcome not defined  
Main confounders taken into account  
Partly overlap with Van Vliet AM J Gastroentero 2006 |
| Van Vliet 2006 | Design: Retrospective cohort study  
Source of funding: Erasmus MC—University Medical Center Rotterdam  
Setting: 62 centres in the Netherlands  
Sample size: N=573, repeated CT scan: 115  
re-evaluated CT scan: 235  
Duration: 1994-2003 | Eligibility: patients diagnosed with esophageal cancer; treated at the Erasmus MC Rotterdam, after first being diagnosed in a regional center  
Patient characteristics:  
Mean age ± SD (yr) 63 ± 10.4  
Male 77%  
Histology of tumour at biopsy (%)  
SCC 35%, ACA 57%  
Location of tumour (%)  
Cervical 1%, upper 1/3 thoracic 4%, central 1/3 thoracic 15%, lower 1/3 | Examinations evaluated at regional center vs Examinations evaluated at referral center | Repeated CT-scan (n = 115)  
Sensitivity (%)  
Regional lymph nodes  
Regional 26%  
Referral 52%  
p=0.002  
Distant metastases  
Regional 44%  
Referral 84%  
p=0.001  
Peri-esophageal lymph nodes  
Regional 26%  
Referral 48%  
p=0.022  
Celiac lymph nodes  
Regional 41%  
Repeate US Abdomen (n = 167)  
Sensitivity (%)  
Celiac lymph nodes  
Regional 7%  
Referral 44%  
p <0.001  
Liver metastases  
Regional 6%  
Referral 71%  
p=0.001  
Specificity (%)  
Celiac lymph nodes  
Regional 100%  
Referral 99%  
p=0.320 | Level of evidence: B  
Primary outcome not defined  
Potential confounders not taken into account  
Both groups comparable, CT scans repeated within median of 2 weeks=time bias  
<table>
<thead>
<tr>
<th>Study ID</th>
<th>Method</th>
<th>Patient characteristics</th>
<th>Intervention(s)</th>
<th>Results primary outcome</th>
<th>Results secondary and other outcomes</th>
<th>Critical appraisal of study quality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>thoracic 39%, gastric cardia 41%</td>
<td>Referral 79% p=0.001</td>
<td>Regional 100% Referral 100% p=0.000</td>
<td>Repeated US Neck (n = 153) Sensitivity (%) Regional 28% Referral 84% p=0.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Liver metastases Regional 30% Referral 60% p=0.250</td>
<td>Specificity (%) Regional lymph nodes Regional 94% Referral 99% p=0.375</td>
<td>Specificity (%) Regional 100% Referral 100% p=1.000</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Distant metastases Regional 99% Referral 98 p= 1.000</td>
<td>Regional 100% Referral 100%</td>
<td>Repeated Chest x-Ray (n = 270) Sensitivity (%) Regional 9% Referral 64% p=0.031</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Peri-esophageal lymph nodes Regional 97% Referral 99% p= 1.000</td>
<td>Regional 99% Referral 99% p=0.625</td>
<td>Specificity (%) Regional 99% Referral 99% p=1.000</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Celiac lymph nodes Regional 96% Referral 99% p=0.625</td>
<td>Regional 100% Referral 97% p=0.083</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Liver metastases Regional 100% Referral 97% p=0.083</td>
<td>Re-evaluated CT-scan (n = 235) Sensitivity (%) Regional lymph nodes Regional 19% Referral 41% p &lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Distant metastases Regional 18% Referral 43% p &lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Peri-esophageal lymph nodes Regional 18% Referral 36% p &lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Celiac lymph nodes Regional 13%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study ID</td>
<td>Method</td>
<td>Patient characteristics</td>
<td>Intervention(s)</td>
<td>Results primary outcome</td>
<td>Results secondary and other outcomes</td>
<td>Critical appraisal of study quality</td>
</tr>
<tr>
<td>-----------</td>
<td>------------------------------------------------------------------------</td>
<td>------------------------------------------</td>
<td>--------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------</td>
<td>----------------------------------</td>
</tr>
<tr>
<td>Van Vliet 2006</td>
<td>Design: Retrospective cohort study, compared to literature data</td>
<td>Eligibility: patients diagnosed with esophageal cancer; who underwent endoscopic ultrasonography (EUS) at the Erasmus MC Rotterdam and underwent a resection without neoadjuvant chemotherapy and/or radiation therapy</td>
<td>EUS performed at a low volume center (the Erasmus MC Rotterdam: &lt;50 EUS/endoscopist/year) vs EUS performed at 3 high volume centers (&gt;50 EUS/ endoscopist/ year) (data identified by a literature search)</td>
<td>Referral 45% p &lt;0.001 Liver metastases Regional 8% Referral 31% p=0.250 Specificity (%) Regional lymph nodes Regional 92% Referral 90 p=0.804 Distant metastases Regional 97% Referral 95% p=0.375 Peri-esophageal lymph nodes Regional 91% Referral 91% p= 1.000 Celiac lymph nodes Regional 97% Referral 95% p=0.453 Liver metastases Regional 97% Referral 97% p= 1.000</td>
<td>k value= measure of agreement between the T stage determined by EUS and the postoperative T stage Low-volume center (EUS probe passage) 0.23 (0.14-0.33) Low-volume center (no EUS probe passage) -0.09 (-0.29-0.11) High-volume centers 0.58 (0.47-0.69) to 0.83 (0.77-0.89)</td>
<td>Level of evidence: C</td>
</tr>
<tr>
<td></td>
<td>• Source of funding: Erasmus MC—University Medical Center Rotterdam</td>
<td>• Patient characteristics: Mean age 64 y Male 83% Histology of tumour at biopsy: SCC 10%, ACA 87% Location of tumour Cervical -</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Setting: 8 centres in the Netherlands</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Sample size: N=244</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Duration: 1994-2003</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Eligibility: patients diagnosed with esophageal cancer; who underwent endoscopic ultrasonography (EUS) at the Erasmus MC Rotterdam and underwent a resection without neoadjuvant chemotherapy and/or radiation therapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study ID</td>
<td>Method</td>
<td>Patient characteristics</td>
<td>Intervention(s)</td>
<td>Results primary outcome</td>
<td>Results secondary and other outcomes</td>
<td>Critical appraisal of study quality</td>
</tr>
<tr>
<td>----------</td>
<td>--------</td>
<td>-------------------------</td>
<td>-----------------</td>
<td>-------------------------</td>
<td>--------------------------------------</td>
<td>----------------------------------</td>
</tr>
<tr>
<td>Verhoef 2007</td>
<td>Design: Prospective cohort study</td>
<td>• Eligibility: primary invasive esophageal cancer in the region of the Comprehensive Cancer Centre North-Netherlands</td>
<td>Non teaching hospital vs Teaching, non university hospital vs Treatment in university hospital</td>
<td>5 year survival University hospital: 49.2% Teaching non-university: 32.6% Non-teaching hospitals: 27.3% p=0.0039</td>
<td>Relative excess risk of death (RER) Adjusted RER Non teaching: reference Teaching: 1.32 (0.79–2.22) University: 0.57 (0.29–1.12) p=0.0126 (Adjusted for age, stage, and time since diagnosis) Multivariate analysis on RER (including age, stage, tumour location, hospital volume, frequency of referral, and time since diagnosis): stage: p&lt;0.0001 age: p=0.0467 hospital type: p=0.0126 hospital volume: p=0.112 Odds of operation: 1.89 (1.26–2.82) for non-teaching hospital vs. teaching non-university hospital (Adjusted for age, stage, and tumor location)</td>
<td>Level of evidence: B • Potential confounders identified and taken into account • Different groups are not comparable</td>
</tr>
<tr>
<td>Wenger 2005</td>
<td>Design: Retrospective Cohort study</td>
<td>• Eligibility: patients newly diagnosed with esophageal or cardia cancer, treated with self-expanding metal stents</td>
<td>High-volume unit (&gt;10 procedures) Low-volume units (&lt;10 procedures)</td>
<td>Overall survival time p=0.001 in favour of being treated in low volume units</td>
<td>Overall complication rate High volume: 30% Low volume: 25% Not significant</td>
<td>Level of evidence: B • Clinical data of only 152 patients was available for analysis of complication rate • No comparison of demographics between the two groups is presented • Potential confounders are not identified or taken into account</td>
</tr>
<tr>
<td>Wouters 2008</td>
<td>Design: Retrospective cohort study</td>
<td>• Eligibility: surgically treated esophageal carcinomas</td>
<td>High volume center (mean volume: 56 surgeries annually) Low volume center (&lt;7 surgeries annually)</td>
<td>In hospital mortality Adjusted OR: 3.05 (1.82–5.11) (Adjusted for age and comorbidity)</td>
<td>Surgical complications LVH: 42% Lvh/H:37% p=0.01 General complications LVH: 96%</td>
<td>Level of evidence: B • Partly overlap with Wouters 2008 and Wouters J Surg Oncol 2009 • Primary outcome not defined</td>
</tr>
<tr>
<td>Study ID</td>
<td>Method</td>
<td>Patient characteristics</td>
<td>Intervention(s)</td>
<td>Results primary outcome</td>
<td>Results secondary and other outcomes</td>
<td>Critical appraisal of study quality</td>
</tr>
<tr>
<td>------------------</td>
<td>------------------------------------------------------------------------</td>
<td>-------------------------</td>
<td>--------------------------------------------------------------------------------</td>
<td>-------------------------</td>
<td>--------------------------------------</td>
<td>-----------------------------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Low volume hospitals (&lt;10 resections/year) vs Medium volume hospitals (10-20 resections/year) vs High volume hospitals (&gt;20 resections/year)</td>
<td>HVH: 37% p&lt;0.01</td>
<td>No complications</td>
<td>Both groups not comparable regarding stage and adjuvant treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>LVH: 26%</td>
<td>HVH: 44% p&lt;0.01</td>
<td>Lost of follow up not presented</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Overall survival after esophagus resection for stage I and II carcinoma: (in-hospital mortality excluded) log rank p value =0.04 in favour of HVH</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wouters 2009</td>
<td>Design: Nested case control study</td>
<td></td>
<td></td>
<td></td>
<td>Odds of dying before and after 2000 4.68 times (1.26-17.3; p&lt;0.02) in favour of after 2000</td>
<td>Level of evidence: B</td>
</tr>
<tr>
<td></td>
<td>Sources of funding: Not reported</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Setting: Nationwide study in the Netherlands</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sample size: N=4939 Low: N=1886; Medium: N=515; High: N=1629</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Duration: 1991-2005</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Eligibility: all esophageal resections for cancer that were performed in Dutch hospitals</td>
<td></td>
<td></td>
<td></td>
<td>In hospital mortality</td>
<td>Partly overlap with Wouters 2008 and Wouters Ann Surg Oncol 2009</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MVH: OR 1.01 (0.66-1.54)</td>
<td>Cancer stage not taken into account as potential confounder</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(p=0.98)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>HVH: OR 0.48 (0.30-0.77)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(p=0.003)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(Adjusted for age, gender, operation year, volume, and region)</td>
<td></td>
</tr>
<tr>
<td>Study ID</td>
<td>Method</td>
<td>Patient characteristics</td>
<td>Intervention(s)</td>
<td>Results primary outcome</td>
<td>Results secondary and other outcomes</td>
<td>Critical appraisal of study quality</td>
</tr>
<tr>
<td>---------</td>
<td>--------</td>
<td>-------------------------</td>
<td>----------------</td>
<td>-------------------------</td>
<td>--------------------------------------</td>
<td>---------------------------------</td>
</tr>
<tr>
<td>Wright 2009</td>
<td>Design: Retrospective cohort study</td>
<td>• Eligibility: patients treated with esophagectomies for primary esophageal cancer</td>
<td>Hospital volume</td>
<td>Morbidity, for a 10-unit decrease in volume: OR: 1.09 (0.98–1.20) p=0.10 (Adjusted for age, gender, race and comorbidities)</td>
<td></td>
<td>Level of evidence: B</td>
</tr>
</tbody>
</table>

- No comparison between high and low volume hospitals was presented
- Cancer stage as potential confounder not identified and taken into account

Abbreviations: 95%CI: 95 percent confidence intervals; ACA: adenocarcinoma; ASA: American Society of Anesthesiologists; CRT: chemoradiotherapy; EGJ: esophagogastric junction; HR: hazard ratio; HVH: high volume hospital; HVS: high volume surgeon; LVH: low volume hospital; LVS: low volume surgeon; MA: meta-analysis; MVH: medium volume hospital; MVS: LVH: low volume hospital; LVS: low volume surgeon; NS: not significant; OR: odds ratio; RCT: randomized controlled trial; RER: relative excess risk; RR: risk ratio; RT: radiotherapy; SCC: squamous cell carcinoma; SD: standard deviation; SR: systematic review; Sx: surgery; UK: United Kingdom; US: United States; WOCA: Wessex Oesophageal Cancer Audit.

Reference List