## Centralisatie: 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>Critical appraisal of review quality</th>
</tr>
</thead>
</table>
| Markar 2012 | • Design: SR + MA  
• Source of funding: supported in part by the Ryan Hill Research Foundation  
• Search date: 1966-2011  
• Searched databases: Medline, Embase, meeting abstracts, reference lists, Current Controlled Trials Register  
• Included study designs: cohort studies  
• Number of included studies: N=9, 27,843 oesophagectomies | • Eligibility criteria: surgical treatment for oesophageal cancer, hospital volume as independent variable, resections since 2000, comparison of low- and high-volume hospitals, volume thresholds stated, primary data used  
• Exclusion criteria: studies that were not focused on oesophageal cancer and oesophageal cancer surgical treatment, and studies that failed to quantitatively define surgical volume for inclusion into high- and low-volume hospital groups (low and high) | Surgical treatment of oesophageal cancer in low-versus high-volume hospital  
Used thresholds: Low < 4 - 78  
High > 9 - 346 | In-hospital mortality (death during hospital admission): 6 trials  
• Overall: low 8.48% vs. high 2.82%  
• Pooled analysis: OR 0.29, 95%CI 0.16-0.53, p<0.0001; I² 95.2%  
30-day mortality (death within 30 days): 2 trials  
• Overall: low 2.09% vs. high 0.73%  
• Pooled analysis: OR 0.31, 95%CI 0.19-0.51, p<0.0001; no heterogeneity  
Length of hospital stay: 2 trials  
• WMD: -4.33, 95%CI -12.37 – 3.70, p=0.29; statistical heterogeneity | Risk of bias: high  
• Quality appraisal with Oxford checklists, but not reported |
| Wouters 2012 | • Design: SR + MA  
• Source of funding: nothing to disclose  
• Search date: 1/1995-7/2010  
• Searched databases: Medline, reference lists  
• Included study designs: all  
• Number of included studies: N=43 | • Eligibility criteria: surgical treatment for oesophageal cancer, primary data used, association between hospital or surgeon volume of oesophagectomies and clinical outcomes, not on results of single hospital or surgeon  
• Exclusion: lack of comparison between providers, no definition or cut-off for volume | Surgical treatment of oesophageal cancer in low-versus high-volume hospital  
Used thresholds: Low < 1 - 20  
High > 3 - 87 | Hospital volume  
Postoperative mortality: 16 trials  
• Pooled analysis: OR 2.30, 95%CI 1.89-2.80, p<0.001; I² 60%  
• Sensitivity analysis: larger effect in studies from the US (OR 2.56), studies based on clinical data (OR 2.56), studies that adjusted for urgency of operation (OR 2.84), studies that adjusted for tumour characteristics (OR 2.20)  
• Publication bias present  
Survival: 4 trials  
• Pooled analysis: HR 1.17, 95%CI 1.05-1.31, p=0.005, no heterogeneity | Risk of bias: high  
• Quality appraisal performed, but not reported  
• Only Medline + reference lists: publication statistically shown  
• Studies without a multivariate analysis and/or reporting of OR, HR or risk rates were excluded from the meta-analysis  
Surgeon volume  
Postoperative mortality: 3 trials  
• Pooled analysis: OR 1.55, 95%CI 0.88-2.75, p=0.13; I² 75%  
Survival: 2 trials  
• Pooled analysis: HR 1.16, 95%CI 0.94-1.45, p=0.17, I² 48% |
<table>
<thead>
<tr>
<th>Study ID</th>
<th>Method</th>
<th>Patient characteristics</th>
<th>Intervention(s)</th>
<th>Results primary outcome</th>
<th>Critical appraisal of study quality</th>
</tr>
</thead>
</table>
| Al-Refaie WB 2012 | • Design: retrospective cohort study  
• Source of funding: Supported by Enhancing Minority Participation in Clinical Trials (EMPaCT), funded by the National Institute on Minority Health and Health Disparities (NIMHD) and 2008 Veterans of Foreign Wars and Ladies Surgical Oncology Research Award; no CoI to declare  
• Setting: US, 20% stratified sample of US community hospitals  
• Sample size: N=3364 oesophagectomies  
Used thresholds: Low <13  
High >=13 | **In-hospital mortality:**  
• OR 1.86, 95%CI 1.80-2.47  
**Prolonged length of stay (stay beyond 75th percentile):**  
• OR 1.30, 95%CI 1.11-1.56 | Risk of bias: high  
• Population-based study (representative sample)  
• Unclear which factors included in multivariate analyses for postoperative outcomes |
| Anderson O 2011 | • Design: retrospective cohort study  
• Source of funding: no funding, no CoI  
• Setting: population-based cohort, South-East England  
• Sample size: N=1584 oesophagectomies  
• Period: 1998-2008 | • Eligibility criteria: patients diagnosed with oesophageal cancer (ICD-10) and treated operatively (OPCS-4) | Surgical treatment of oesophageal cancer in low-volume versus high-volume hospital  
Used thresholds: 1-10, 11-20, 21-30, >30 | **0-30 days survival:**  
• Significant variation between volume groups: p=0.008  
• HR 1-10 vs. 11-20: 0.66, p=0.001  
**31-365 days survival:**  
• Significant variation between volume groups: p<0.001  
• HR 1-10 vs. >30: 0.705, p=0.215  
**366 days – 11-year survival:**  
• No significant variation between volume groups: p=0.824  
• HR 1-10 vs. >30: 1.024, p=1.13 | Risk of bias: low  
• Population-based study  
• Probably overlap with Coupland 2012  
• Factors included in multivariate analysis: age, gender, socio-economic status, stage, neoadjuvant chemotherapy, morphology  

*Opmerking [JV1]: Excluderen: geen aparte resultaten voor oesofagus.*
<table>
<thead>
<tr>
<th>Study ID</th>
<th>Method</th>
<th>Patient characteristics</th>
<th>Intervention(s)</th>
<th>Results primary outcome</th>
<th>Critical appraisal of study quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilimoria KY 2010</td>
<td>Design: retrospective cohort study</td>
<td>• Eligibility criteria: patients undergoing cancer-directed surgery for oesophageal cancer</td>
<td>Surgical treatment of oesophageal cancer in ‘specialised centres’ (28.9%) versus ‘other academic institutions’ (28.0%) versus ‘community hospitals’ (43.1%)</td>
<td>60-day mortality: • Adjusted HR (vs. community hospitals): o Specialized centers: • High-risk patients: 0.48 (95%CI 0.33-0.69) • Low-risk patients: 0.46 (95%CI 0.32-0.67) o Other academic hospitals: • High-risk patients: 0.87 (95%CI 0.66-1.16) • Low-risk patients: 0.84 (95%CI 0.62-1.14) Number of potentially avoided deaths if regionalized: • Complete regionalization to specialized centres: 176 • Selective referral of high-risk patients: 176</td>
<td>Risk of bias: low  • Population-based study  • Specialized centre = National Cancer Institute-designated cancer centres and cancer site-specific highest-volume quintile hospitals  • Other academic institutions = lower-volume, non-National Cancer Institute-designated academic centres  • High risk = 75+ or Charlson score of at least 2  • Factors included in multivariate analysis: gender, age, race, stage, income, comorbidities, extent of resection</td>
</tr>
<tr>
<td>Boddy AP 2012</td>
<td>Design: retrospective cohort study</td>
<td>• Eligibility criteria: patients with oesophageal cancer undergoing resection</td>
<td>Centralisation: - Pre: 1996-2006, resections in 4 hospitals (Gloucester, Cheltenham, Worcester, Hereford) - Post: 2006-2010, resections in 1 hospital (Gloucester)</td>
<td>30-day mortality: • Prior to 2006: 11.1%; since 2006: 4.3%; p=0.076 90-day mortality: • Prior to 2006: 13.8%; since 2006: 10.3%; p=0.539 Median survival: • Prior to 2006: 1.1 years; since 2006: 2.1 years; p=0.028</td>
<td>Risk of bias: high  • Small sample size  • Patients who did not have a date of death on the hospital systems but had no local postoperative follow-up were considered lost to follow up  • Factors included in multivariate analysis: time period, surgeon, TNM stage, patient age and cancer site; however, also gastric cancer patients included</td>
</tr>
<tr>
<td>Cheung MC 2010</td>
<td>Design: retrospective cohort study</td>
<td>• Eligibility criteria: patients with oesophageal cancer diagnosed ante-mortem; adenocarcinomas or SCC (ICD-O)</td>
<td>Treatment at teaching facility (11 hospitals, N=669) versus non-teaching facility (N=4372)</td>
<td>Median survival: • 12.5 versus 9.5 months, p&lt;0.001 o Adenocarcinoma: 16.1 vs. 10.0 months, p&lt;0.001 o SCC: 8.9 vs. 8.8 months, p=0.663 o Surgery: 47.3 vs. 20.5 months, p&lt;0.001 90-day mortality: • 4.1 versus 11.2%, p&lt;0.001 o Adenocarcinoma: 3.4 vs. 11.3%, p&lt;0.001 o SCC: 5.5 vs. 13.1%, p=0.082 o Surgery: 4.0 vs. 12.0%, p&lt;0.001 Multivariate analysis (worse survival): • Adenocarcinoma: low socio-economic status (HR 2.217, p=0.026), advanced stage (HR 3.18, p&lt;0.001), and lack of resection (HR 1.95, p&lt;0.001) or chemotherapy (HR 1.61, p&lt;0.001); treatment at non-teaching facility (HR 1.35, p=0.003) • SCC: African Americans (HR 1.36, p=0.001), advanced stage (HR 2.47, p=0.001), lack of surgical resection (HR 1.58, p&lt;0.001), chemotherapy (HR 1.89, p&lt;0.001) or radiotherapy (HR 1.16, p=0.048)</td>
<td>Risk of bias: low  • Teaching facility = recognition as a teaching institution by the Association of American Medical Colleges  • Factors included in multivariate analysis: gender, age, race, ethnicity, smoking, alcohol, socio-economic status, tumour location, stage, grade, facility, treatment</td>
</tr>
<tr>
<td>Study ID</td>
<td>Method</td>
<td>Patient characteristics</td>
<td>Intervention(s)</td>
<td>Results primary outcome</td>
<td>Critical appraisal of study quality</td>
</tr>
<tr>
<td>----------</td>
<td>------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------------------------</td>
<td>-----------------------------------</td>
</tr>
</tbody>
</table>
| Coupland VH 2012 | • Design: retrospective cohort study  
• Source of funding: reported in article  
• Setting: population-based study, England, UK  
• Sample size: N=31632  
• Period: 2004-2008 | • Eligibility criteria: patients with oesophageal cancer (ICD-10 C15), no multiple tumours  
• Patient characteristics: not provided for oesophageal cancer alone; 5403 patients underwent surgery | Surgical treatment of oesophageal cancer in low-volume versus high-volume hospital  
Used thresholds: <10, 10-19, 20-29, 30-39, >40 | All-cause mortality at 5 years: adjusted HR compared with <10  
• 10-19: 0.94 (95%CI 0.84-1.05)  
• 20-29: 0.83 (0.74-0.94)  
• 30-39: 0.81 (0.70-0.93)  
• >40: 0.98 (0.85-1.13)  
• P for trend: 0.0638 | Risk of bias: low  
• Factors included in multivariate analysis: sex, age, socioeconomic deprivation, comorbidity, type of cancer |
| Dikken JL 2012a | • Design: retrospective cohort study  
• Source of funding: funded by the Signalling Committee on Cancer of the Dutch Cancer Society; no CoI to declare  
• Setting: population-based study, the Netherlands  
• Sample size: N=10025 oesophagectomies  
• Period: 1989-2009 | • Eligibility criteria: patients diagnosed with oesophageal cancer and undergoing resection  
• Exclusions: no hospital in registry, in situ or metastatic disease  
• Group comparability: >75y 12% vs. 11% vs. 11% vs. 9%, p=0.002; SCC 19% vs. 23% vs. 23% vs. 25%, p<0.001; stage III 34% vs. 35% vs. 36% vs. 38%, p=0.001 | Surgical treatment of oesophageal cancer in low-volume versus high-volume hospital  
Used thresholds: 1-5 (N=2914), 6-10 (N=2695), 11-20 (N=1494), >20 (N=2922) | 6-month mortality:  
• HR (vs. low-volume): high 0.48 (95%CI 0.38-0.61), medium 0.78 (0.62-0.97)  
3-year survival:  
• HR (vs. low-volume): high 0.77 (95%CI 0.70-0.85), medium 0.90 (0.81-0.99) | Risk of bias: low  
• Teaching hospital – offering a surgical residency programme  
• One specialized cancer centre was analysed as a university hospital  
• Factors included in multivariate analysis: annual hospital volume, year of diagnosis, sex, age, socioeconomic status, tumour stage, morphology, preoperative therapy use, postoperative therapy use (only for 3-year survival) and for clustering of deaths within hospitals |
| Dikken JL 2012b | • Design: retrospective cohort study  
• Source of funding: supported by a grant (P01AG019783-07S1) from the National Institute on Aging; CoI available  
• Setting: national Medicare data, US  
• Sample size: N=43756 oesophagectomies  
• Period: 1999-2008 | • Eligibility criteria: patients aged 65-99y who underwent oesophagectomy (ICD-9)  
• Group comparability: median age 63 vs. 64 vs. 65y, p=0.001; SCC 61% vs. 20.9 vs. 19.9%, p=0.001; stage III 39.0% vs. 33.4% vs. 34.4%, p=0.001 | Treatment at university hospital (9 hospitals, N=3559) versus non-university teaching hospital (N=3905) versus non-university non-teaching hospital (N=2561) | 3-month mortality:  
• Adjusted rate: 2.5 (95%CI 1.8-3.2) vs. 4.4 (3.5-5.2) vs. 4.1% (3.2-5.0), p=0.006  
3-year survival:  
• Adjusted rate: 46 (44-49) vs. 42 (40-44) vs. 43% (40-59), p=0.027 | Risk of bias: low  
• Market concentration: proportion of Medicare patients undergoing procedure in the top decile and top quintile of hospitals by volume for each year  
• Factors included in multivariate analysis: age, sex, race, admission acuity (elective, urgent, or emergency), coexisting conditions, socioeconomic status |
| Finks JF 2011 | • Design: retrospective cohort study  
• Source of funding: supported by a grant (P01AG019783-07S1) from the National Institute on Aging; CoI available  
• Setting: national Medicare data, US  
• Sample size: N=43756 oesophagectomies  
• Period: 1999-2008 | • Eligibility criteria: patients aged 65-99y who underwent oesophagectomy (ICD-9)  
• Group comparability: median age 63 vs. 64 vs. 65y, p=0.001; SCC 61% vs. 20.9 vs. 19.9%, p=0.001; stage III 39.0% vs. 33.4% vs. 34.4%, p=0.001 | Centralisation | Market concentration:  
• 1999-2000: 39%; 2007-2008: 44%  
• Median volume: 4 in 1999-2000 (1734 hospitals), 7 in 2007-2008 (1309 hospitals)  
Operative mortality (death before discharge or within 30 days after surgery):  
• 1999-2000: 10.0%; 2007-2008: 8.9%; p=0.001  
• Proportion of difference in mortality explained by increased hospital volume: 32% | Risk of bias: low  
• Market concentration: proportion of Medicare patients undergoing procedure in the top decile and top quintile of hospitals by volume for each year  
• Factors included in multivariate analysis: age, sex, race, admission acuity (elective, urgent, or emergency), coexisting conditions, socioeconomic status |
<table>
<thead>
<tr>
<th>Study ID</th>
<th>Method</th>
<th>Patient characteristics</th>
<th>Intervention(s)</th>
<th>Results primary outcome</th>
<th>Critical appraisal of study quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ghaferi AA 2011</td>
<td>Design: retrospective cohort study</td>
<td>• Eligibility criteria: patients aged 65-99y who underwent oesophagectomy (ICD-9-CM)</td>
<td>Surgical treatment of oesophageal cancer in low-volume versus high-volume hospital</td>
<td>Hospital mortality (death in-hospital or within 30 days after surgery): • Risk-adjusted rates: OR 3.7 (95% CI 2.74-4.98)</td>
<td>Risk of bias: low • Possible overlap with Finks 2011 • Factors included in multivariate analysis: age, sex, race, urgency of operation, and comorbidities</td>
</tr>
</tbody>
</table>
  o 1-4: 3.23 (95% CI 2.02-5.15) 
  o 5-9: 3.59 (2.28-5.65) 
  o 10-14: 2.31 (1.37-3.90) 
  o 15-19: 2.82 (1.37-5.81) 
  o 20-29: 1.65 (0.91-3.00) 
  o 30-39: 1.33 (0.77-2.29) | Risk of bias: High • Survey among JATS members: 91.1% response rate • Volume-outcome relation evaluated with Pearson’s correlation coefficient method • No risk-adjustment |

Abbreviations: 95%CI: 95 percent confidence intervals; CoI: conflict of interest; HR: hazard ratio; ICD: international classification of diseases; NS: not significant; OR: odds ratio; RCT: randomized controlled trial; SCC: squamous cell carcinoma; SD: standard deviation; SR: systematic review; UK: United Kingdom; US: United States; WMD: weighted mean difference.

References


