

Centralisatie: evidence tables

Systematic reviews

Study ID	Method	Patient characteristics	Intervention(s)	Results primary outcome	Critical appraisal of review quality
Markar 2012	<ul style="list-style-type: none"> 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; 27843 oesophagectomies 	<ul style="list-style-type: none"> 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) 	<p>Surgical treatment of oesophageal cancer in low- versus high-volume hospital</p> <p>Used thresholds: Low < 4 - 78 High > 9 - 346</p>	<p>In-hospital mortality (death during hospital admission): 8 trials</p> <ul style="list-style-type: none"> 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% <p>30-day mortality (death within 30 days): 2 trials</p> <ul style="list-style-type: none"> Overall: low 2.09% vs. high 0.73% Pooled analysis: OR 0.31, 95%CI 0.19-0.51, p<0.0001; no heterogeneity <p>Length of hospital stay: 2 trials</p> <ul style="list-style-type: none"> WMD: -4.33, 95%CI -12.37 – 3.70, p=0.29; statistical heterogeneity <p>Postoperative complications: 3 trials</p> <ul style="list-style-type: none"> Pooled analysis: OR 0.62, 95%CI 0.37-1.05, p=0.08; statistical heterogeneity 	<p>Risk of bias: high</p> <ul style="list-style-type: none"> Quality appraisal with Oxford checklists, but not reported
Wouters 2012	<ul style="list-style-type: none"> 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 	<ul style="list-style-type: none"> 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 	<p>Surgical treatment of oesophageal cancer in low- versus high-volume hospital</p> <p>Used thresholds: Low < 1 - 20 High > 3 - 87</p>	<p>Hospital volume</p> <p>Postoperative mortality: 16 trials</p> <ul style="list-style-type: none"> 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 <p>Survival: 4 trials</p> <ul style="list-style-type: none"> Pooled analysis: HR 1.17, 95%CI 1.05-1.31, p=0.005, no heterogeneity <p>Surgeon volume</p> <p>Postoperative mortality: 3 trials</p> <ul style="list-style-type: none"> Pooled analysis: OR 1.55, 95%CI 0.88-2.75, p=0.13; I² 75% <p>Survival: 2 trials</p> <ul style="list-style-type: none"> Pooled analysis: HR 1.16, 95%CI 0.94-1.45, p=0.17, I² 48% 	<p>Risk of bias: high</p> <ul style="list-style-type: none"> 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

Cohort studies

Study ID	Method	Patient characteristics	Intervention(s)	Results primary outcome	Critical appraisal of study quality
Al-Refae WB 2012	<ul style="list-style-type: none"> 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 Col to declare Setting: US, 20% stratified sample of US community hospitals Sample size: N=3364 oesophagectomies Period: 2003-2008 	<ul style="list-style-type: none"> Eligibility criteria: patients with principal diagnosis of primary oesophageal cancer (ICD-9-CM) with surgery 	<p>Surgical treatment of oesophageal cancer in low-volume (N=2364) versus high-volume hospital (N=1000)</p> <p>Used thresholds: Low <13 High >13</p>	<p>In-hospital mortality:</p> <ul style="list-style-type: none"> OR 1.86, 95%CI 1.80-2.47 <p>Prolonged length of stay (stay beyond 75th percentile):</p> <ul style="list-style-type: none"> OR 1.30, 95%CI 1.11-1.56 	<p>Risk of bias: high</p> <ul style="list-style-type: none"> Population-based study (representative sample) Unclear which factors included in multivariate analyses for postoperative outcomes
Anderson O 2011	<ul style="list-style-type: none"> Design: retrospective cohort study Source of funding: no funding, no Col Setting: population-based cohort, South-East England Sample size: N=1584 oesophagectomies Period: 1998-2008 	<ul style="list-style-type: none"> Eligibility criteria: patients diagnosed with oesophageal cancer (ICD-10) and treated operatively (OPCS-4) 	<p>Surgical treatment of oesophageal cancer in low-volume versus high-volume hospital</p> <p>Used thresholds: 1-10, 11-20, 21-30, >30</p>	<p>0-30 days survival:</p> <ul style="list-style-type: none"> Significant variation between volume groups: p=0.008 HR 1-10 vs. >30: 0.66, p=0.001 <p>31-365 days survival:</p> <ul style="list-style-type: none"> Significant variation between volume groups: p<0.001 HR 1-10 vs. >30: 0.705, p=0.215 <p>366 days – 11-year survival:</p> <ul style="list-style-type: none"> No significant variation between volume groups: p=0.824 HR 1-10 vs. >30: 1.024, p=1.13 	<p>Risk of bias: low</p> <ul style="list-style-type: none"> 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.

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Bilimoria KY 2010	<ul style="list-style-type: none"> Design: retrospective cohort study Source of funding: Supported by the American College of Surgeons Clinical Scholars in Residence Program and a Priority Grant from North-Western University Setting: population-based study, US; 928 hospitals Sample size: N=6155 Period: 2003-2005 	<ul style="list-style-type: none"> Eligibility criteria: patients undergoing cancer-directed surgery for oesophageal cancer Exclusions: distant metastases, <18y, reporting hospital did not perform the index operation 	Surgical treatment of oesophageal cancer in 'specialized centres' (28.9%) versus 'other academic institutions' (28.0%) versus 'community hospitals' (43.1%)	<p>60-day mortality:</p> <ul style="list-style-type: none"> Adjusted HR (vs. community hospitals): <ul style="list-style-type: none"> Specialized centres: <ul style="list-style-type: none"> High-risk patients: 0.48 (95%CI 0.33-0.69) Low-risk patients: 0.46 (95%CI 0.32-0.67) Other academic hospitals: <ul style="list-style-type: none"> High-risk patients: 0.87 (95%CI 0.66-1.16) Low-risk patients: 0.84 (95%CI 0.62-1.14) <p>Number of potentially avoided deaths if regionalized:</p> <ul style="list-style-type: none"> Complete regionalization to specialized centres: 176 Selective referral of high-risk patients: 176 	<p>Risk of bias: low</p> <ul style="list-style-type: none"> 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
Boddy AP 2012	<ul style="list-style-type: none"> Design: retrospective cohort study Source of funding: none Setting: single centre, Gloucester, UK Sample size: N=224 resections for oesophageal cancer Period: 1996-2010 	<ul style="list-style-type: none"> Eligibility criteria: patients with oesophageal cancer undergoing resection Patient characteristics: male 77.7% vs. 87.9% (p=0.043), median age 63.6 vs. 62.9y (p>0.05) 	<p>Centralisation:</p> <ul style="list-style-type: none"> Pre: 1996-2006, resections in 4 hospitals (Gloucester, Cheltenham, Worcester, Hereford) Post: 2006-2010, resections in 1 hospital (Gloucester) 	<p>30-day mortality:</p> <ul style="list-style-type: none"> Prior to 2006: 11.1%; since 2006: 4.3%; p=0.076 <p>90-day mortality:</p> <ul style="list-style-type: none"> Prior to 2006: 13.8%; since 2006: 10.3%; p=0.539 <p>Median survival:</p> <ul style="list-style-type: none"> Prior to 2006: 1.1 years; since 2006: 2.1 years; p=0.028 	<p>Risk of bias: high</p> <ul style="list-style-type: none"> 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
Cheung MC 2010	<ul style="list-style-type: none"> Design: retrospective cohort study Source of funding: Supported in part by the James and Ester King Tobacco Research Grant; Col not reported Setting: population-based study, Florida, US Sample size: N=5041 Period: 1998-2002 	<ul style="list-style-type: none"> Eligibility criteria: patients with oesophageal cancer diagnosed ante-mortem; adenocarcinomas or SCC (ICD-O) Exclusions: non-Florida residents Patient characteristics: median age 68.6y, male 74.8%, adenocarcinoma 48.4% Group comparison: age 64.8 vs. 69.1y, p<0.001; regional disease 45.3% vs. 33.5%, p<0.001; undifferentiated tumours 3.8% vs. 1.3%, p=0.001 	Treatment at teaching facility (11 hospitals, N=669) versus non-teaching facility (N=4372)	<p>Median survival:</p> <ul style="list-style-type: none"> 12.5 versus 9.5 months, p<0.001 <ul style="list-style-type: none"> Adenocarcinoma: 16.1 vs. 10.0 months, p<0.001 SCC: 8.9 vs. 8.8 months, p=0.663 Surgery: 47.3 vs. 20.5 months, p<0.001 <p>90-day mortality:</p> <ul style="list-style-type: none"> 4.1 versus 11.2%, p<0.001 <ul style="list-style-type: none"> Adenocarcinoma: 3.4 vs. 11.3%, p<0.001 SCC: 5.5 vs. 13.1%, p=0.062 Surgery: 4.0 vs. 12.0%, p<0.001 <p>Multivariate analysis (worse survival):</p> <ul style="list-style-type: none"> Adenocarcinoma: low socio-economic status (HR 2.217, p=0.026), advanced stage (HR 3.18, p<0.001), and lack of resection (HR 1.95, p<0.001) or chemotherapy (HR 1.61, p<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<0.001), chemotherapy (HR 1.89, p<0.001) or radiotherapy (HR 1.16, p=0.048) 	<p>Risk of bias: low</p> <ul style="list-style-type: none"> 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

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Coupland VH 2012	<ul style="list-style-type: none"> Design: retrospective cohort study Source of funding: reported in article Setting: population-based study, England, UK Sample size: N=31632 Period: 2004-2008 	<ul style="list-style-type: none"> Eligibility criteria: patients with oesophageal cancer (ICD-10 C15), no multiple tumours Patient characteristics: not provided for oesophageal cancer alone: 5403 patients underwent surgery 	<p>Surgical treatment of oesophageal cancer in low-volume versus high-volume hospital</p> <p>Used thresholds: <10, 10-19, 20-29, 30-39, >40</p>	<p>All-cause mortality at 5 years: adjusted HR compared with <10</p> <ul style="list-style-type: none"> 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 	<p>Risk of bias: low</p> <ul style="list-style-type: none"> Factors included in multivariate analysis: sex, age, socio-economic deprivation, co-morbidity, type of cancer
Dikken JL 2012a	<ul style="list-style-type: none"> Design: retrospective cohort study Source of funding: funded by the Signalling Committee on Cancer of the Dutch Cancer Society; no Col to declare Setting: population-based study, the Netherlands Sample size: N=10025 oesophagectomies Period: 1989-2009 	<ul style="list-style-type: none"> 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 	<p>Surgical treatment of oesophageal cancer in low-volume versus high-volume hospital</p> <p>Used thresholds: 1-5 (N=2914), 6-10 (N=2695), 11-20 (N=1494), >20 (N=2922)</p>	<p>6-month mortality:</p> <ul style="list-style-type: none"> HR (vs. low-volume): high 0.48 (95%CI 0.38-0.61), medium 0.78 (0.62-0.97) <p>3-year survival:</p> <ul style="list-style-type: none"> HR (vs. low-volume): high 0.77 (95%CI 0.70-0.85), medium 0.90 (0.81-0.99) 	<p>Risk of bias: low</p> <ul style="list-style-type: none"> 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		<ul style="list-style-type: none"> Group comparability: median age 63 vs. 64 vs. 65y, p<0.001; SCC 26.1 vs. 20.9 vs. 19.9%, p<0.001; stage III 39.0 vs. 33.4 vs. 34.4%, p<0.001 	<p>Treatment at university hospital (9 hospitals, N=3559) versus non-university teaching hospital (N=3905) versus non-university non-teaching hospital (N=2561)</p>	<p>3-month mortality:</p> <ul style="list-style-type: none"> 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 <p>3-year survival:</p> <ul style="list-style-type: none"> Adjusted rate: 46 (44-49) vs. 42 (40-44) vs. 43% (40-59), p=0.027 	
Finks JF 2011	<ul style="list-style-type: none"> Design: retrospective cohort study Source of funding: Supported by a grant (P01AG019783-07S1) from the National Institute on Aging; Col available Setting: national Medicare data, US Sample size: N=43756 oesophagectomies Period: 1999-2008 	<ul style="list-style-type: none"> Eligibility criteria: patients aged 65-99y who underwent oesophagectomy (ICD-9) 	<p>Centralisation</p>	<p>Market concentration:</p> <ul style="list-style-type: none"> 1999-2000: 39%; 2007-2008: 44% Median volume: 4 in 1999-2000 (1734 hospitals), 7 in 2007-2008 (1309 hospitals) <p>Operative mortality (death before discharge or within 30 days after surgery):</p> <ul style="list-style-type: none"> 1999-2000: 10.0%; 2007-2008: 8.9%; p<0.001 Proportion of difference in mortality explained by increased hospital volume: 32% 	<p>Risk of bias: low</p> <ul style="list-style-type: none"> 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, socio-economic status

Met opmaak: Inspringing: Links: 0,01 cm, Verkeerd-om: 0,25 cm

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Ghaferi AA 2011	<ul style="list-style-type: none"> Design: retrospective cohort study Source of funding: Agency for Healthcare Research and Quality & National Cancer Institute Setting: national Medicare data, US Sample size: N=3443 Period: 2005-2007 	<ul style="list-style-type: none"> Eligibility criteria: patients aged 65-99y who underwent oesophagectomy (ICD-9-CM) Group comparability: median age 74.9 vs. 73.6y (NS); male 65.8% vs. 73.3% (p<0.05); 3+ comorbidities 17.0% vs. 8.5% (p<0.05) 	<p>Surgical treatment of oesophageal cancer in low-volume versus high-volume hospital</p> <p>Used thresholds: very low 1-4 (N=1883), very high >15 (N=1560)</p>	<p>Hospital mortality (death in-hospital or within 30 days after surgery):</p> <ul style="list-style-type: none"> Risk-adjusted rates: OR 3.7 (95%CI 2.74-4.98) <p>Major complications (pulmonary failure, pneumonia, myocardial infarction, deep venous thrombosis/pulmonary embolism, acute renal failure, hemorrhage, surgical site infection, gastrointestinal bleeding):</p> <ul style="list-style-type: none"> Risk-adjusted rates: OR 1.35 (95%CI 1.11-1.65) <p>Failure to rescue (death in a patient with at least 1 major complication):</p> <ul style="list-style-type: none"> Risk-adjusted rates: OR 3.18 (95%CI 2.39-4.22) 	<p>Risk of bias: low</p> <ul style="list-style-type: none"> Possible overlap with Finks 2011 Factors included in multivariate analysis: age, sex, race, urgency of operation, and comorbidities
Sakata R 2012	<ul style="list-style-type: none"> Design: retrospective cohort study Source of funding: not reported Setting: member institutions of Japanese Association for Thoracic Surgery (JATS), Japan Sample size: N=24224 surgeries for oesophageal cancer (493 hospitals) Period: 2005-2009 	<ul style="list-style-type: none"> Eligibility criteria: patient with oesophageal cancer undergoing surgery 	<p>Surgical treatment of oesophageal cancer in low-volume versus high-volume hospital</p> <p>Used thresholds: 1-4 (N=3116), 5-9 (N=3131), 10-14 (N=2648), 15-19 (N=2071), 20-29 (N=2914), 30-39 (N=3215), 40+ (N=7129)</p>	<p>30-day mortality:</p> <ul style="list-style-type: none"> OR (vs. 40+): <ul style="list-style-type: none"> 1-4: 3.23 (95%CI 2.02-5.15) 5-9: 3.59 (2.28-5.65) 10-14: 2.31 (1.37-3.90) 15-19: 2.82 (1.37-5.81) 20-29: 1.65 (0.91-3.00) 30-39: 1.33 (0.77-2.29) 	<p>Risk of bias: high</p> <ul style="list-style-type: none"> 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; Col: 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

Al-Refaie WB, Muluneh B, Zhong W, Parsons HM, Tuttle TM, Vickers SM, et al. Who receives their complex cancer surgery at low-volume hospitals? J. Am. Coll. Surg. 2012;214(1):81-7.

Bilimoria KY, Bentrem DJ, Talamonti MS, Stewart AK, Winchester DP, Ko CY. Risk-based selective referral for cancer surgery: A potential strategy to improve perioperative outcomes. Ann. Surg. 2010;251(4):708-16.

Boddy AP, Williamson JML, Vipond MN. The effect of centralisation on the outcomes of oesophagogastric surgery - A fifteen year audit. Int. J. Surg. 2012;10(7):360-3.

Cheung MC, Koniaris LG, Yang R, Zhuge Y, Mackinnon JA, Byrne MM, et al. Do all patients with carcinoma of the esophagus benefit from treatment at teaching facilities? J. Surg. Oncol. 2010;102(1):18-26.

[Coupland VH, Lagergren J, Luchtenborg M, Jack RH, Allum W, Holmberg L, et al. Hospital volume, proportion resected and mortality from oesophageal and gastric cancer: A population-based study in England, 2004-2008. Gut. 2012; Oct 19. \[Epub ahead of print\]](#)

Dikken JL, Dassen AE, Lemmens VEP, Putter H, Krijnen P, Van Der Geest L, et al. Effect of hospital volume on postoperative mortality and survival after oesophageal and gastric cancer surgery in the Netherlands between 1989 and 2009. Eur. J. Cancer. 2012;48(7):1004-13.

Dikken JL, Wouters MWJM, Lemmens VEP, Putter H, van der Geest LGM, Verheij M, et al. Influence of hospital type on outcomes after oesophageal and gastric cancer surgery. Br J Surg. 2012;99(7):954-63.

Finks JF, Osborne NH, Birkmeyer JD. Trends in hospital volume and operative mortality for high-risk surgery. New Engl. J. Med. 2011;364(22):2128-37.

Ghaferi AA, Birkmeyer JD, Dimick JB. Hospital volume and failure to rescue with high-risk surgery. Med. Care. 2011;49(12):1076-81.

Markar SR, Karthikesalingam A, Thrumurthy S, Low DE. Volume-outcome relationship in surgery for esophageal malignancy: systematic review and meta-analysis 2000-2011. J Gastrointest Surg. 2012;16(5):1055-63.

Sakata R, Kuwano H, Yokomise H. Hospital volume and outcomes of cardiothoracic surgery in Japan: 2005-2009 National survey. Gen. Thorac. Cardiovasc. Surg. 2012;60(10):625-38.

Wouters MWJM, Gooiker GA, Van Sandick JW, Tollenaar RAEM. The volume-outcome relation in the surgical treatment of esophageal cancer: A systematic review and meta-analysis. Cancer. 2012;118(7):1754-63.

Met opmaak: Engels
(Groot-Brittannië)