Title: Hospital surgical volumes and mortality after coronary artery bypass

grafting: using international comparisons to determine a safe threshold

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Hospital surgical volumes and mortality after coronary artery bypass grafting: using international comparisons to determine a safe threshold

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Abstract

Objective: To estimate a safe minimum hospital volume for hospitals performing coronary artery bypass graft (CABG) surgery.

Data source: Hospital data on all publicly funded CABG in five European countries, 2007-2009 (106,149 patients).

Design: Hierarchical logistic regression models to estimate the relationship between hospital volume and mortality, allowing for case-mix. Segmented regression analysis to estimate a threshold.

Findings: The 30-day in-hospital mortality rate was 3.0% overall, 5.2% (95% CI 4.0-6.4) in low volume hospitals and 2.1% (95% CI 1.8-2.3) in high volume hospitals. There is a significant curvilinear relationship between volume and mortality, flatter above 415 cases per hospital per year.

Conclusions: There is a clear relationship between hospital CABG volume and mortality in Europe, implying a 'safe' threshold volume of 415 cases per year.

Introduction

The association between hospital volume and mortality after coronary artery bypass graft (CABG) surgery has been explored within countries since the 1970s, when a negative association was first described (Luft, Bunker & Enthoven 1979). A statistically significant and clinically relevant relationship between hospital volume and mortality has subsequently been found for many different forms of complex surgery in both cardiac and non-cardiac specialties. Relationships are generally attenuated but not eliminated after detailed adjustment for case-mix (Sowden, Deeks & Sheldon 1995, Halm, Lee & Chassin 2002, Shahian 2004).

This evidence, mostly from US studies, has generated debate about 'safe' hospital volumes of surgery. The 'Leapfrog Group', a US consortium of health care purchasers, recommended an annual minimum hospital volume of 450 CABG cases (Leapfrog Group 2008, Finks, Osborne and Birkmeyer 2011). Others suggest this is too high (Shahian and Normand 2003) and that 125-150 procedures a year can be sufficient (Shahian 2004, ACCF/AHA 2011), reflecting recent evidence that mandatory public reporting of CABG mortality has reduced or even eliminated the volume-outcome relationship in the USA (Marcin et al 2008). There is little evidence of this in other countries, many of which do not have mandatory public reporting of CABG mortality.

Some European countries – including England, The Netherlands and Sweden – have responded to evidence of a volume-mortality relationship by centralising CABG facilities (Banta & Bos 1991), but elsewhere hospital volumes remain low. This difference may help to explain observed cross country differences in mortality after cardiac surgery within Europe (Bridgewater et al 2010, Gutacker et al. 2015b). There remains uncertainty around a minimum 'safe' hospital CABG volume to inform policy

decisions in Europe and elsewhere about whether, and if so how far, to centralise CABG services.

We use comprehensive data on CABG in five countries to describe the relationship between hospital volume and short-term mortality, and to estimate a 'safe' minimum hospital volume.

Data and Methods

Study population

The population was drawn from the European Collaboration for Healthcare Optimisation (ECHO) project, including comprehensive record-level patient data on all patients treated in public hospitals from a number of European countries (Bernal-Delgado et al 2015). This study uses data from Denmark, England, Portugal, Slovenia and Spain, 2007 to 2009. We followed the US AHRQ indicator IQI#12 (AHRQ 2015), which includes all patients who have a CABG procedure. This is comparable with existing guidelines of 'safe' volume (e.g. Leapfrog Group 2008) which apply to all procedures, not to isolated CABG. Concomitant procedures are included in the risk-adjustment model. As a sensitivity analysis we included only patients with isolated CABG.

Patients were excluded if they were younger than 40 or had missing information for any of the variables used for casemix-adjustment (n=21). Hospital years were excluded if they included less than 50 patients (< 1% of the sample).

Case-mix adjustment

Expected deaths were predicted accounting for age group (40-55, 56-60, 61-65, 66-70, 71-75, 76-80 and >81), sex, age-sex interactions, year of hospitalisation and indicators for 31 Elixhauser co-morbid conditions (Elixhauser et al 1998, Quan et al 2005, Gutacker et al. 2015a). Mean number of comorbidities coded at each hospital was included to account for possible differences in coding intensity. Models included those measures of severity of the underlying condition, that are available in administrative data (Higgins et al. 1992, Pagano & Gale 2014): primary diagnosis of acute myocardial infarction (AMI), classified as ST-segment elevation (STEMI), non-STEMI or unclear, replacement of a heart valve, implantation of a cardiac or circulatory assistance device, and whether the intervention was major structural surgery. We did not include emergency admission as an explanatory variable because of differences in clinical pathways for similar patients across countries, and because it is highly collinear with a primary diagnosis of AMI.

Clinical outcomes

The clinical outcome was in-hospital 30-day all-cause mortality. Patients who were discharged or still in hospital 30 days after admission were classed as survivors.

Volume thresholds

We use two thresholds for overall hospital case volume derived from literature: low (<125 cases per year) (ACCF 2011), medium (125-449 cases per year) and high (≥450 cases per year) (Leapfrog Group 2015). Using pooled data from all five countries we estimated statistically the threshold where the relationship between volume of cases and outcome changed.

Statistical analysis

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Expected deaths were predicted using hierarchical logit models accounting for case-mix. Three approaches were used to identify a volume-outcome relationship. First, a smoothed (locally weighted) regression line was fitted through the points and confidence intervals calculated. Second, thresholds for overall hospital case volume derived from literature were used to compare average adjusted mortality rates for different hospitals. Third, using pooled data a threshold was determined where the relationship between volume and outcome appeared to change, using segmented regression analysis. All analyses were carried out using Stata version 12.

Sensitivity analysis

We conducted four sensitivity analyses. Firstly, we restricted the population to patients with no other surgical procedure (isolated CABG). Next, we excluded patients who were transferred out of the hospital where the surgery took place to another hospital as this may underestimate mortality rates. This was most pronounced in Denmark, where around 48% were transferred for rehabilitation, compared with 0-6.5% in the other countries. Our analyses provide two bounds of likely mortality rates – including transfers out gives the lowest possible estimate, assuming all who are transferred out survive. As deaths are likely to occur in the first (specialist) hospital, excluding transfers out may over-estimate mortality rates. Third, to mitigate between-country data differences (e.g. coding secondary diagnoses), we re-estimated adjusting only for age, sex and year, with and without transfers. Finally, we estimate a threshold using data from Spain and England only, which as the largest healthcare systems in our analysis constitute the majority of observations.

Results

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106,149 patients were included in the baseline analysis, with an overall mortality rate of 3.0%. The mean age and proportion male was similar across the countries. The main difference in patient characteristics (Table 1) was the recorded number of co-morbidities, notably lower in Denmark. Proportions of patients also varied by AMI type and in overall patients who were diagnosed with AMI, from 5.6% in England to 11.6% in Spain. There was substantial variation in the volume of cases across the five countries (Table 2).

[Table 1 about here]

[Table 2 about here]

Figure 1 illustrates CABG volume in each country and unadjusted mortality rates (see Appendix Figure A1, for individual countries). Hospital volume was lowest and unadjusted mortality rates highest in Spain. The case-mix adjusted relationship between volume and outcome is illustrated in Figure 2 (left panel), showing a clear downward curvilinear relationship. (See Appendix for effects of case-mix covariates on outcome). Volume explains almost half of the variation in adjusted mortality rates (R^2= 0.43). Figure 2 (middle panel) illustrates the volume thresholds suggested by US literature. The average adjusted mortality rate in lower volume hospitals was 5.2% (95% CI 4.0-6.4), falling to 1.9% (1.7-2.2) in higher volume hospitals, or 2.1% (1.8-2.3) after weighting for hospital size (Table 3).

[Figure 1 about here]

[Figure 2 about here]

[Table 3 about here]

The centre-volume threshold that best separated hospitals where volume affects mortality rates negatively from those were no volume effects are apparent was

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estimated at 415 procedures per hospital per year (Figure 2, right panel). Mortality rates declined by -1.1 percentage points (95% CI -1.7 to -0.4) per 100 additional operations below this threshold and were not affected by volume above the threshold (-0.05 percentage points per 100 operations; 95% CI -0.16 to 0.06).

Sensitivity analyses

Sensitivity analyses did not alter the main finding of a relationship between centre volume of cases and mortality rates (see Appendix Figures A2-A6). The threshold centre-volume inferred by the data under the different assumptions (excluding other procedures and transfers and simplifying risk-adjustment) did differ, ranging between 291 and 519 procedures per year. Analysis based on Spanish and English data only (Figure A7) suggested a threshold of 512 procedures per year.

Discussion

We found substantial differences in short-term mortality following CABG surgery in hospitals across five European countries. Patients treated in lower volume hospitals had significantly higher 30-day in-patient mortality rates. Below 415 cases per hospital per year, mortality rates increased at a greater rate. Between-country variations in volume are clearly associated with international differences in mortality rates, of which hospital volume explains a large proportion after adjustment for case-mix.

Our findings are consistent with earlier studies, primarily from the USA. More recent US studies have however focused on the importance of public reporting of CABG surgery performance, which appears to have attenuated the volume-outcome effect. For example, Marcin et al (2008), found a small but consistent volume-outcome

relationship during a time when public reporting was voluntary, but that this disappeared once reporting was mandated.

A relationship between volume and outcome could be the result of hospital-level processes, individual surgeon experience (Birkmeyer et al 2003) or both. Moreover, hospital volume of cases may be a marker for hospital quality (Peterson et al 2004) or possibly a more direct determinant of mortality. Our study includes five different European healthcare systems, with different levels of concentration of cardiac surgery services, a key institutional feature influencing CABG outcomes. The mix of organizational systems increases the external validity of the results.

Our study confirms the presence of a strong centre-volume outcome relationship using comprehensive data on all publicly funded patients and hospitals across five countries. Low and medium volume hospitals have substantially and statistically significantly higher adjusted mortality than high volume hospitals. The reduction in mortality risk of moving from "medium" to "high" volume appears greater than the reduction from moving from the "low" to "medium" category.

The data-driven estimate of the threshold volume, 415 cases per year, is similar to the 450 recommended by the US Leapfrog group (2008), lower than the 600 implemented by the Netherlands in the 1990s (Banta & Bos 1991) but substantially higher than the 125-150 recommended in recent US guidelines (ACCF 2011). The ACCF guidelines, however, reflect transparency about cardiac surgery performance, which is not publicly available in many countries outside the US (although it is available in the UK).

This analysis demonstrates the importance of international comparisons using administrative data and a pooled benchmark. This research, with a related study

(Gutacker et al 2015b), shows that restricting benchmarks to a region or even a country may provide false reassurance if there are systematic differences between countries. A threshold would not be adequately informed by any single country's data, and no one of these countries would have provided a sufficient sample to determine a volume-outcome relationship – Spanish hospitals are all (relatively) low-volume, English hospitals are all relatively high volume and the other three countries have only 3–6 medium volume hospitals conducting CABG surgery.

Our findings raise important policy questions about the concentration of services, particularly in countries with low volume hospitals, such as Spain. The Spanish health care system is decentralised in its decision-making: hospitals are organised by autonomous communities and districts. Political opposition to centralisation of services may contribute to explaining the relatively low hospital volume. In contrast, in England, networks of care, higher volume centres and transparent reporting of hospital and surgeon mortality rates has driven quality improvements (Bridgewater et al 2007).

There may be geographical, political or practical difficulties that prevent substantial changes in service delivery in some communities in the short to medium term. In the absence of immediate policies to centralise cardiac surgical provision, it is important to consider how best to improve mortality rates in low-volume units. Our analysis does not permit direct exploration of this, but potential quality improvement processes include participation in registries and associated initiatives (Bridgewater et al 2010, Shahian et al 2009) public reporting initiatives and improved transparency (Steinbrook 2006, Grant et al. 2013), and regional partnerships and quality improvement collaboratives (O'Connor et al 1996, Finks, Osborne and Birkmeyer 2011). Public reporting in the US appears to have reduced or even eliminated the

previous volume-outcome relationship, and this may be more achievable than centralisation of services in a devolved health care system like Spain.

Previous international studies in this area have relied on clinical registry data (Bridgewater et al 2010). In most countries, however, registry data is collected voluntarily and remains vulnerable to selection bias, if hospitals and surgeons with low mortality rates are more likely to participate (Bufalino et al. 2011). This is the first international study of the CABG volume-mortality relationship to use comprehensive international comparisons of patient-level hospital administrative data. Our approach avoids selection bias, but has a more limited set of covariates for case mix adjustment.

Other limitations also remain. First, not all countries could provide mortality data outside hospital for an overall 30-day mortality rate. We used in-hospital 30-day mortality because the length of hospital stay varied across countries, making in-patient mortality rates a less than ideal basis for comparison (Spiegelhalter 2013). If high volume hospitals discharge patients earlier then our estimated association between volume and outcome may be biased downwards.

Second, there may be cross-country differences in coding. CABG is well-defined and patient characteristics and secondary diagnoses similar in four countries (Table 1), but apparent differences in comorbidity recording in Denmark may overestimate their adjusted mortality rates. There are also coding differences in concomitant procedures (e.g. apparently large numbers of heart valve replacements and cardiac assistance devices in Slovenia). Our sensitivity analyses, using only age and sex as risk-adjustment measures to avoid any hospital or country level differences in coding, and including isolated CABG only, do not change the main findings of the analysis (see

Appendix). A strong and significant association between volume and outcomes remains.

Finally, there may be hospital- or national-level differences in choice of treatments for similar conditions, in particular the choice between CABG surgery and percutaneous coronary interventions (PCIs) (Taggart 2009, Hlatky et al. 2009). Our dataset suggests that England (which dominates the high-volume segment) provides more CABG as a proportion of all revascularisation procedures than the other countries: 30 CABG procedures to 70 PCIs in England over the period compared with around 20:80 in Portugal and Denmark and 15:85 in Slovenia and Spain. This raises the question of differential selection between CABG and PCI procedures, but in initial explorations of PCI data in the ECHO data warehouse there was no negative correlation between hospital-level standardised mortality rates following CABG and PCI (R=0.045).

Overall, our findings demonstrate a strong and statistically significant relationship between hospital volume of CABG surgery and in-hospital 30-day mortality, and a threshold of 415 cases per hospital per year above which mortality rates are stable and on average much lower. All hospitals in Spain were below this threshold, whereas all hospitals in England were above it. Higher volume, higher throughput systems of care have the potential to reduce mortality rates further and there may be an international case to regionalise services where the hospital volume of CABG surgery is low.

Declaration of interests

None of the authors has any conflicts of interest with regard to this paper.

Contributorship

The statistical analysis was carried out by Nils Gutacker. Gutacker, Bloor, Cookson and Bernal-Delgado conceived and designed the study, and all contributed substantially to data acquisition, analysis and interpretation. Bloor wrote the first draft of the paper, with important contributions from all co-authors. Gale, Maynard, Pomar and Pagano contributed substantially to interpreting the data and critical revisions of the paper for important intellectual content. All authors have approved the version to be submitted, and agree to be accountable for all aspects of the work.

Table 1: Patient characteristics

	Denmark	England	Portugal	Slovenia	Spain	Total
	n=7,168	n=67,450	n=7,639	n=2,345	n=21,547	n=106,149
Age: mean (SD), years	67.1 (9.3)	67.4 (9.6)	66.3 (9.7)	67.6 (9.2)	67.7 (9.6)	67.4 (9.6)
Male (%)	79.2	78.8	76.5	74.1	78.1	78.4
Number of co-morbidities: mean (SD)	1.0 (1.2)	2.0 (1.4)	1.9 (1.4)	2.0 (1.4)	2.2 (1.4)	2.0 (1.4)
No co-morbidities (%)	44.5	12.7	16.3	12.1	10.0	14.6
1 co-morbidity (%)	27.0	27.9	28.1	29.9	24.0	27.5
2-3 co-morbidities (%)	24.1	45.5	43.4	45.2	49.7	44.8
4+ co-morbidities (%)	4.4	13.9	12.2	13.9	16.3	13.6
ST-elevation myocardial infarction (%)	0.8	1.8	2.9	3.5	4.6	2.4
Non ST-elevation myocardial infarction (%)	3.4	0.5	6.0	5.5	6.3	2.4
Unspecified myocardial infarction (%)	1.9	2.4	0.1	0.4	0.7	1.8
Heart valve surgery (%)	29.5	7.5	4.0	83.0	5.9	10.1
Cardiac assistance device surgery* (%)	3.3	9.2	4.2	42.4	3.9	8.1
Repair/revision or major structural surgery (%)	19.9	18.6	20.8	30.1	27.1	20.8

*includes cardiac pacemaker and automatic implantable cardioverter defibrillator insertion during the same hospital stay

Table 2: Descriptive statistics

|	Denmark	England	Portugal	Slovenia	Spain	Total
Number of hospital years*	18	87	18	9	129	261
Total volume (2007-2009)*	7,168	67,450	7,639	2,345	21,547	106,149
Mean (median) volume per hospital per year	398 (410)	775 (709)	424 (429)	260 (205)	167 (152)	407 (279)
Minimum – maximum volume per hospital per year	239-544	466-1372	238-537	95-480	68-318	68-1372
Mean (SD) length of stay, days **	14.3 (8.4)	11.6 (7.2)	11.6 (6.8)	15.5 (8.6)	17.0 (8.3)	13.0 (7.8)
Transfers out, %	47.9	6.5	0.0	4.9	2.6	8.0
Mean (SD) 30-day in-hospital mortality rate %, *including* transfers**	2.8 (16.6)	2.2 (14.5)	2.3 (15.0)	3.5 (18.4)	4.9 (21.5)	3.0 (16.5)
Mean (SD) mortality rate % *excluding* transfers (sensitivity analysis)**	5.1 (22.1)	2.3 (15.0)	2.3 (15.0)	3.7 (18.8)	5.0 (21.8)	3.0 (17.1)

* hospital years with less than 50 patients were excluded
**mortality and length of stay are truncated at 30 days

Table 3: Adjusted 30-day in-hospital mortality rates in low, medium and high volume hospitals

Volume (cases per hospital per year)	**No. of hospitals**	**Adjusted mortality rates, mean (95% CI), unweighted**	**Adjusted mortality rates, mean (95% CI), weighted by hospital volume**
Low (<125)	15	5.2% (4.0 to 6.4)	5.1% (3.9 to 6.3)
Medium (125-449)	37	4.4% (3.6 to 5.1)	4.1% (3.3 to 4.8)
High (≥450)	35	1.9% (1.7 to 2.2)	1.9% (1.7 to 2.2)

Figure 1: Unadjusted 30-day in-hospital 30-day mortality rates and hospital annual volume by country

Figure 2: Adjusted 30-day in-hospital mortality rate and hospital annual volume, all five countries pooled. LOWESS plot (left panel), average mortality by volume group (middle panel), segmented regression line (right panel). Estimated threshold volume: 415 procedures per hospital per year
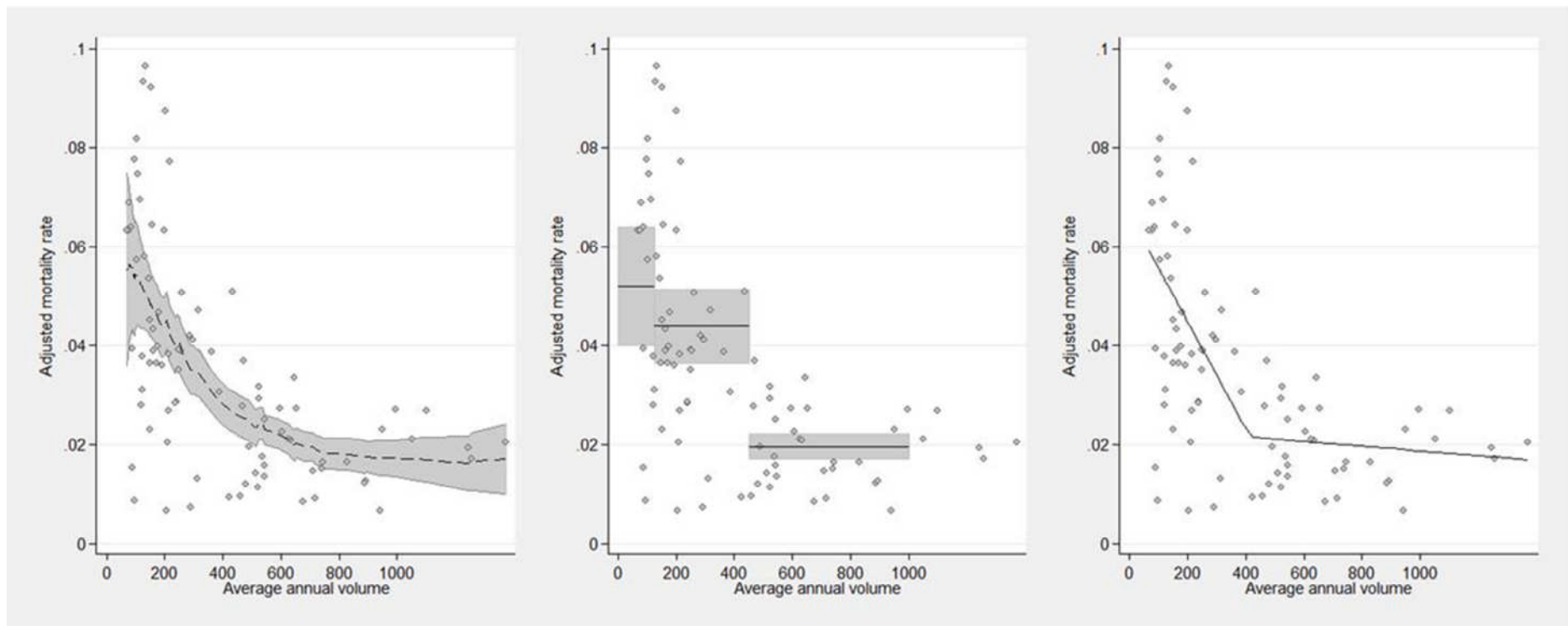
References

ACCF/AHA "Guideline for coronary artery bypass graft surgery: a report of the American College of Cardiology Foundation / American Heart Association task force on practice guidelines 2011". Available at http://www.guideline.gov/content.aspx?id=34979 (accessed 18th March 2015)

Agency for Healthcare Research and Quality. "In-patient Quality Indicators. IQI#12 Coronary Artery Bypass Graft (CABG) mortality rate". Available at: http://www.qualityindicators.ahrq.gov/Downloads/Modules/IQI/V42/TechSpecs/IQI%2012%20CABG%20Mortality.pdf (accessed 18th March 2015)

Banta D., M. Bos. 1991. "The relation between quantity and quality with coronary artery bypass graft (CABG) surgery". Health Policy; 18: 1-10

Bernal-Delgado, E., T. Christiansen, K. Bloor, C. Mateus, A,M. Yazbeck, J. Munck, & J. Bremner. 2015. "ECHO: health care performance assessment in several European health systems." European Journal of Public Health; 25(S1): 3-7.

Birkmeyer J.D., T.A. Stukel, A.E. Siewers, P.P Goodney, D.E. Wennberg and F.L. Lucas. 2003. "Surgeon Volume and Operative Mortality in the United States". New England Journal of Medicine; 349: 2117-2127.

Bridgewater, B, A.D. Grayson, N. Brooks, G. Grotte, B.M. Fabri, J. Au, T. Hooper, M. Jones, and B. Keogh. 2007. "Has the publication of cardiac surgery outcome data been associated with changes in practice in northwest England: an analysis of 25 730 patients undergoing CABG surgery under 30 surgeons over eight years." Heart; 93(6): 744-748.

Bridgewater B., J. Gummert J, P.K.H. Walton, R. Kinsman and European Association for Cardio-Thoracic Surgery. "EACTS Adult Cardiac Surgical Database Report 2010". Henley-on-Thames: Dendrite Clinical Systems Ltd. 2010.

Bufalino, V.J., F.A. Masoudi, S. Stranne, K. Horton, N.M Albert, C. Beam, R.O. Bonow, R.L. Davenport, M. Girgus, G.C. Fonarow, H.M. Krumholz, M.W. Legnini, W.R. Lewis, G. Nichol, E.D. Peterson, W. Rosamund, J.S. Rumsfeld, L.H Schwamm, D.M Shahian, J.A. Spertus, P.K. Woodard, C.W. Yancy on behalf of the American Heart Association Advocacy Coordinating Committee. 2011. "The American Heart Association's Recommendations for Expanding the Applications of Existing and Future Clinical Registries A Policy Statement From the American Heart Association". Circulation; 123(19), 2167-2179.

Elixhauser A, C. Steiner, D.R. Harris, R.M. Coffey. 1998. "Comorbidity measures for use with administrative data". Medical Care; 36(1): 8-27.

Finks J.F., N.H. Osborne, J.D. Birkmeyer. 2011. "Trends in hospital volume and operative mortality for high-risk surgery". New England Journal of Medicine; 364: 2128-2137.

Grant S.W., G.L Hickey, R. Cosgriff, G. Cooper, J. Deanfield, J. Roxburgh, B. Bridgewater. 2013. "Creating transparency in UK adult cardiac surgery data". Heart; 99(15), 1067-1068.

Gutacker, N., K. Bloor, and R. Cookson. 2015a. "Comparing the performance of the Charlson/Deyo and Elixhauser comorbidity measures across five European countries and three conditions". European Journal of Public Health; 25(S1): 15-20.

Gutacker N., K. Bloor, R. Cookson, S. Garcia-Armesto, E. Bernal-Delgado. 2015b. "Comparing hospital performance within and across countries: an illustrative study of coronary artery bypass graft surgery in England and Spain". European Journal of Public Health; 25(S1): 28-34.

Halm E.A., C. Lee C, M.R. Chassin. 2002. "Is volume related to outcome in health care? A systematic review and methodologic critique of the literature". Annals of Internal Medicine; 137: 511-520.

Higgins T.L., F.G. Estafanous, F.D. Loop, G.J. Beck, J.M Blum, L. Paranandi. 1992. "Stratification of morbidity and mortality outcome by preoperative risk factors in coronary artery bypass patients. A clinical severity score". JAMA; 267: 2344-2348.

Hlatky MA, D.B Boothroyd, D.M. Bravata, E. Boersma, J. Booth, M.M. Brooks, D. Carrié, T.C. Clayton, N. Danchin, M. Flather, C.W. Hamm, W.A. Hueb, J. Kähler, S.F. Kelsey, S.B. King, A.S. Kosinski, N. Lopes, K.M. McDonald, A. Rodriguez, P. Serruys, U. Sigwart, R.H. Stables, D.K. Owens. 2009. "Coronary artery bypass surgery compared with percutaneous coronary interventions for multivessel disease: a collaborative analysis of individual patient data from ten randomised trials". Lancet; 373: 1190-1197.

Iglehart J.K. 2009 . "Prioritizing comparative-effectiveness research — IOM Recommendations". New England Journal of Medicine; 361(4): 325-328.

Leapfrog Group. "Factsheet: Evidence-based Hospital Referral (04/09/08)" http://www.leapfroggroup.org/media/file/Leapfrog-Evidence-Based_Hospital_Referral_Fact_Sheet.pdf (accessed 18th March 2015).

Luft H.S., J.P. Bunker, A.C. Enthoven. 1979. "Should operations be regionalized? The empirical relation between surgical volume and mortality." New England Journal of Medicine; 20(301): 1364-1369.

Marcin J.P., Z. Li, R.L. Kravits, J.J Dai, D.M. Rocke, P.S. Romano. 2008. "The CABG volume-outcome relationship: temporal trends and selection effects in California, 1998-2004". Health Services Research; 43(1): 174-192.

O'Connor, GT, Plume SK, Olmstead EM, Morton JR, Maloney CT, Nugent WC, Hernandez F, Clough R, Leavitt BJ, Coffin LH, Marrin CAS Wennberg D, Birkmeyer JD, Charlesworth DC, Malenka DJ, Quinton HB, Kasper JF, Hernandez F. Quinton H, Carey-Johnson D, Downs CM, Hessel JJ, Hoffman RM, Johnson ER, McKinnon H, Mingo C, Pedersen C, Perkins W, Rowe ML, Sargent K, Silver T, Ver Lee P, Waren C, Barber S, Brown P, Brandenburg RG, Colmanaro S, Gundel WD, Jackson RS, Johnson D, Laramee A, Paganelli WC, Pappalardo D, Raabe DS, Terrien C, Vaitkus P, Watkins M, Beggs V, Burke W, Catherwood E, Daeey LJ, Darcey C, Defoe G, Dodds T, Fillinger M, Friedman B, Hettleman B, Kneeland T, Maislen E, Niles N, O'Connor NJ, Robb J, Schults W; Sullivan WJ; Wahrenberger J Wolf B, Baribeau Y, Becker A, Berry CC, Berry K,. Bradley WA, Cuddy S, Dewey RC, Fedele F, Fink LI, Funk EJ, Garstka AE, Halstead D, Hearne MJ, Hunter JB, Kaplan AD, Lambert P, Lawrence PM, Lockhart J, McNeil K, Palank E, Porelle J, Pulsifer D, Robichaud J, Schnitz J, Shea S,. Westbrook BM, Wharton TP, Wheeler KW, White D, Keller RB, Soule DC; Abbott M, Adrian L, Alpern WD, Anderson E; Anderson RA, Banister L, Berg C, Blank S, Bredenberg CE, Brennan M, Brewster L, Burkey D, Cirillo A, Clark C, Cleaves J, Courtney D, Cutler J, Donegal D, Fallo P, Hanley D, Kane J, Katz S, Kellett MA, Kramer R, Lambrew CT, Larned S, Lutes CA, Nowicki ER, O'Meara JR, Osher H, Peasley P, Prouty C, Quinn RD, Redfield D, Reynolds K, Ryan T, Saunders

J, Schultz A, Seekins S, Stogsdill R, Sweeny PW, Tolan K, Tooker N, Tryzelaar JF, Turcotte M, Viger K, Westlund C, White RL, Whittet W, Zografos C. 1996. "A regional intervention to improve the hospital mortality associated with coronary artery bypass graft surgery". Journal of the American Medical Association; 275(11): 841-846.

Pagano D, C.P. Gale. "The death of administrative data for benchmarking cardiothoracic mortality?". 2014. Heart; 100(9): 680-682.

Peterson E.D., L.P Coombs, E.R. DeLong, C.K. Haan, T.B Ferguson. "Procedural volume as a marker of quality for CABG surgery". 2004. Journal of the American Medical Association; 291: 195-201.

Quan H, V. Sundararajan, P. Halfon, A. Fong, B. Burnand, J-C. Luthi, L.D. Saunders, C.A. Beck, T.E. Feasby, W.A. Ghali. 2005. "Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data". Medical Care; 43(11): 1130-1139.

Shahian D.M..2004. "Improving cardiac surgery quality – volume, outcome, process?" Journal of the American Medical Association; 291(2): 246-248.

Shahian D.M. and S-L. T. Normand. 2003. "The volume-outcome relationship: from Luft to Leapfrog". Ann Thorac Surg; 75: 1048-1058.

Shahian D.M., S.M. O'Brien, G. Filardo, V.A. Ferraris, C.K Haan, J.B. Rich, S-L.T. Normand, E.R. DeLong, C.M. Shewan, R.S. Dokholyan, E.D. Peterson, F.H. Edwards, R.P Anderson. 2009. "The Society of Thoracic Surgeons 2008 cardiac surgery risk models: part 1—coronary artery bypass grafting surgery". The Annals of Thoracic Surgery; 88(1): S2-S22.

Sowden A.J., J.J Deeks, T.A. Sheldon. 1995. "Volume and outcome in coronary artery bypass graft surgery: true association or artefact?" British Medical Journal; 311: 151.

Spiegelhalter, D. 2013. "Are you 45% more likely to die in a UK hospital rather than a US hospital?". British Medical Journal; 347: f5775.

Steinbrook, R. 2006. "Public report cards - cardiac surgery and beyond". New England Journal of Medicine; 355(18): 1847.

Taggart D. "PCI or CABG in coronary artery disease?" Lancet 2009; 373: 1150–1152.