The authors systematically reviewed the association between provider case volume and mortality in 101 publications involving greater than 1 million patients with esophageal, gastric, hepatic, pancreatic, colon, or rectal cancer, of whom more than 70,000 died. The majority of studies addressed the relation between hospital surgical case volume and short-term perioperative mortality. Few studies addressed surgeon case volume or evaluated long-term survival outcomes. Common methodologic limitations were failure to control for potential confounders, post hoc categorization of provider volume, and unit of analysis errors. A significant volume effect was evident for the majority of gastrointestinal cancers; with each doubling of hospital case volume, the odds of perioperative death decreased by 0.1 to 0.23. The authors calculated that between 10 and 50 patients per year, depending on cancer type, needed to be moved from a “low-volume” hospital to a “high-volume” hospital to prevent 1 additional volume-associated perioperative death. Despite this, approximately one-third of all analyses did not find a significant volume effect on mortality. The heterogeneity of results from individual studies calls into question the validity of case volume as a proxy for care quality, and leads the authors to conclude that more direct quality measures and the validity of their use to inform policy should also be explored. CA Cancer J Clin 2009;59:192-211. ©2009 American Cancer Society, Inc.

Introduction

Among the many reasons put forward for the regionalization of cancer services (particularly surgical services) is the widely held assumption that high-volume providers achieve better outcomes than low-volume providers. Since Luft et al described an inverse relation between surgical volume and mortality in 1979,1 healthcare decision-makers have been interested in the potential for regionalization of surgical services to improve patient outcomes, particularly mortality and morbidity, at lower cost. Subsequently, a plethora of research studies have examined the relation between surgical volume and outcome, and several policy strategies, particularly those designed to restrict specialty surgery to accredited high-volume providers, have been debated.

Arguments both for and against selective referral to high-volume surgical providers for specific cancer types (volume-based referral) make some sense. Advocates of volume-based referral point out the intrinsic logic that “practice makes perfect,” and use the analogy of surgical training in which, to achieve expected standards, surgical specialization is often encouraged and residents are required to perform a minimum number of relevant...
procedures.\textsuperscript{2,3} It is often implied that care by low-volume providers may be harmful for patients and may be an inefficient use of healthcare resources.

Those critical of volume-based referral argue that providers should be judged on their own outcomes and that case volume, as a proxy for quality, is an imprecise measure of individual provider performance. In this sense, volume-based referral may disenfranchise low-volume providers who provide high-quality services, just as it may provide an advantage for high-volume, low-quality providers. Such referral may not take into account a high-volume provider practicing in more than one low-volume center. Furthermore, referral to distant high-volume centers may be inconvenient for patients, who might place a greater value on receiving local care from familiar providers compared with having a reduced operative risk.\textsuperscript{3-5}

Three policy-oriented questions are particularly important for informing this debate and decisions concerning the regionalization of cancer services: 1) What is the strength and robustness of the association, if any, between hospital or clinician case volume and patient outcomes? 2) Is the association clinically important? 3) Is there consistent evidence of a threshold volume effect, above which better outcomes are observed?

To answer these questions, we undertook a systematic review of research literature. Although several systematic reviews on the relation between provider volume and outcomes in cancer have been published to date,\textsuperscript{6-19} the majority are narrative, nonquantitative syntheses that fail to provide the key policy-oriented information concerning effect size or thresholds that will be influential in policy and practice debates regarding volume-based referral and volume-based service provision.

This article reports the findings for gastrointestinal cancers, which is a subset of a larger review we conducted of the volume effect on all cancer types, in which studies relating to gastrointestinal cancers comprised approximately 60% of all studies.\textsuperscript{20} By limiting this review to gastrointestinal cancers, we were able to concentrate on the appraisal and synthesis of studies and perform a meta-analysis while retaining in the review results from a breadth of clinicians, cancer types, and procedures.

**Methods**

Standard systematic review methods were used along with meta-analysis to combine the results of multiple studies and estimate overall effect sizes and threshold volumes.

**Search Methods for the Identification of Studies**

We conducted a comprehensive search to identify all relevant primary studies addressing the impact of provider (hospital or clinician) case volume on patient outcomes in the treatment of cancer. Search terms used for each of the databases are shown in Table 1. Because this topic is not typically well indexed in electronic literature databases, our search method also included systematic reviews of related topics so that reference lists could be hand-searched to identify primary studies that may not have been identified in our electronic searches. We also searched PubMed using the “related articles” function and conducted forward citation searches in the ISI Web of Knowledge database to identify primary studies published within the last 2 years that may not have been cited in any previously published systematic reviews.

**Study Selection**

Two researchers independently screened the title and abstracts of all citations identified from each of the searches and selected potentially relevant systematic reviews and primary studies. These were obtained in full text and were screened independently by both researchers to identify primary studies that fulfilled our selection criteria (Table 2). Any discrepancies regarding the inclusion or exclusion of a primary study in the review were settled through discussion until consensus was reached.

**Quality of Research Evidence**

One reviewer critically appraised all included studies to determine risk of bias and a second reviewer critically appraised a random sample of studies to check for agreement. Risk of bias was assessed by documentation of study type (randomized controlled trial, prospective or retrospective cohort study, analysis of routinely collected data), whether the analysis accounted for clustering effects, and whether important confounders were considered (see Table 3 for justification of these criteria).
Data Collection

Standardized instruments created specifically for this review were used to collect data from the included studies. A single reviewer examined and extracted relevant data from each article, and a second reviewer subsequently checked the data extraction from a random sample of studies to estimate reliability. To ensure clarity of reporting, manuscripts obtained were called “publications,” research materials within publications that addressed the association between volume and outcomes for a particular cancer surgery were called “studies,” and individual assessments of the association between either hospital or surgeon volume and either short-term or long-term outcomes were called “analyses.”

### TABLE 1. Search Strategies for Bibliographic Databases

| Database | Search Strategy |
|----------|-----------------|
| OVID PreMEDLINE, MEDLINE databases | 1. exp HOSPITALS/ or hospital$.mp. 2. "Specialties, Medical"/ 3. Health Facility Size/ 4. provider$.mp. 5. or/1-4 6. exp Surgical Procedures, Operative/ 7. "Surgery Department, Hospital"/ 8. (surgery or surgical or treat$ or therap$).mp. 9. exp RADIOTHERAPY/ or radiotherapy.mp. 10. or/6-9 11. "Statistics"/ 12. "Workload"/ 13. outcome$.mp. 14. volume$.mp. 15. (frequency or frequent).mp. 16. sn.fs. 17. (lvh and hvh).mp. 18. regionali$.mp. 19. (access$ adj5 indicat$).mp. 20. or/11-19 21. (speciali$ or specialt$).mp. 22. exp NEOPLASMS/ 23. cancer$.mp. 24. malignan$.mp. 25. exp Lymphoma/ or lymphoma$.mp. 26. exp Leukemia/ or leukemia$.mp. 27. myeloma$.mp. 28. (tumour$ or tumor$).mp. 29. oncolog$.mp. 30. or/22-29 31. 5 and 10 and 20 and 30 | 1. Systematic reviews ((((hospital* OR (health/exp AND facil$1) OR provider*)) AND (neoplasm* OR cancer* OR malignan* OR lymphoma* OR leukemia* OR myeloma* OR tumour* OR tumor* OR oncolog*) AND (volume OR turnover OR frequen* OR rate OR mortality OR regional* OR workload OR special*)) AND (meta analysis/lim OR systematic review/lim)) AND (embase/lim AND ((cancer/lim OR public health/lim OR [radiology and nuclear medicine]/lim OR [surgery]/lim) AND [humans]/lim)) 2. Primary studies (hv$ AND lv$) OR (((hospital* OR (health/exp AND facil$1) OR provider*)) AND (neoplasm* OR cancer* OR malignan* OR lymphoma* OR leukemia* OR myeloma* OR tumour* OR tumor* OR oncolog*) AND (surgery OR surgical OR radiotherapy) AND (volume OR turnover OR frequen* OR outcome* OR regional* OR workload* OR special*)) AND ((controlled clinical trial/lim OR [randomized controlled trial]/lim) AND ((cancer/lim OR public health)/lim OR [radiology and nuclear medicine]/lim OR [surgery]/lim) AND [humans]/lim AND [1979-2005/py]) |
We extracted as much data regarding the types of cancers and procedures as were available in the reports. We classified esophageal, gastric, hepatic, pancreatic, colon, and rectal cancers separately. We included a separate category termed “colorectal (not otherwise defined)” for studies of colorectal cancers that did not differentiate between colon and rectal cancers. From publications that included more than one type of cancer, we extracted results for each cancer type. The cutpoints used by the authors of the primary studies for defining low-volume and high-volume groups were documented along with how these cutpoints were determined.

The association between hospital or surgeon case volume and 30-day or in-hospital mortality, survival, or long-term mortality was identified for each study. When it was reported, we documented results without adjustment in natural units (ie, deaths per study population) and the estimated effect sizes before and after adjustment for potential confounding factors, expressed as odds ratios (ORs), relative risks (RRs), or hazards ratios (HRs), with stated confidence intervals and measures of significance. We identified and noted the factors for which a statistical adjustment was made.

| TABLE 2. Criteria for the Inclusion and Exclusion of Studies |
|---------------------------------|---------------------------------|
| CHARACTERISTICS | INCLUSION | EXCLUSION |
| Participants | People with gastrointestinal cancer or those undergoing procedures usually undertaken to treat gastrointestinal cancers | |
| Intervention | Surgical interventions delivered by a high-volume clinician or in a high-volume hospital | |
| Comparators | Surgical interventions delivered by a low-volume clinician or in a low-volume hospital | |
| Outcomes | Short-term and long-term mortality | Narrative reviews, editorials, letters, articles identified as preliminary reports when results are published in later versions, articles in abstract form only, case reports, and collections of case reports in which results are only presented by individual study patient and not summarized |
| Study design | Systematic reviews, meta-analyses, and randomized controlled trials; other controlled trials, comparative studies, and cohort studies were assessed | |
| Publication | No language or publication date constraints were placed | |

| TABLE 3. Justification of Quality Criteria |
|---------------------------------|---------------------------------|
| CRITERIA | JUSTIFICATION |
| Adjustment for potential confounders: | If patients treated in high-volume settings are systematically different from those treated in low-volume settings in other ways (eg, older and with greater severity of disease, with greater numbers of comorbidities, or of lower socioeconomic status), this may impact on the results, with potential differences between high-volume and low-volume settings being attributable to these confounding factors rather than the different settings. Previous studies have demonstrated a strong association between age, comorbidity, and stage of disease and patient mortality (up to eight times greater than that of provider case volume). |
| - Age | |
| - Comorbidities such as cardiac disease, lung disease, and malnutrition | |
| - Stage and severity of cancer | |
| - Surgeon case volume for studies of the effect of hospital case volume and vice versa | |
| - Adjuvant and neoadjuvant treatment (for long-term outcomes) | |
| Accounting for clustering effects in the analysis | Unit-of-analysis error, or the failure to account for clustering effects, is a potential source of bias when groups of patients are treated by different providers. A clustering effect often exists in volume–outcome studies because patients attending the same hospital or being treated by the same physician are more similar to each other than those treated in different settings, and therefore cannot be assumed to be completely independent. Because the outcomes for these studies are collected at the patient level (mortality, length of stay, complications, etc), and the unit of comparison (volume) is collected at the level of the hospital or physician, it is important to either use an appropriate unit of analysis (ie, analysis performed at the same level as the unit of comparison) or to statistically adjust for the effect of clustering. Although failure to appropriately manage clustering in an analysis does not usually lead to erroneous point estimates of effect size, it does lead to overly narrow confidence intervals and hence the potential to claim a result is statistically significant when it may not be. |
Synthesis of Results

Our broad study selection criteria and range of cancer types led us to expect there would be heterogeneity of the included studies with respect to study design, method of reporting, and analysis, making statistical aggregation of the results challenging. We therefore planned to adopt a multilevel approach to reporting and synthesis, structured to avoid giving too much weight to studies with the greatest risk of bias:

1) All included studies were reported and characterized in terms of population, methods, and whether they reported significant or nonsignificant results for differences in mortality between high-volume and low-volume surgeons or high-volume and low-volume hospitals;
2) All raw unadjusted data were entered into a regression analysis to facilitate quantitative synthesis of all analyses to demonstrate, without adjusting for confounders, the crude mortality rate for different case volumes; and
3) We reported effect sizes (presented as ORs, RRs, or HRs) and measures of precision (such as confidence intervals or \( P \) values) only from studies that met the quality criteria outlined above for which we therefore had reasonable confidence in the estimated effect size and its precision.

Analysis of Unadjusted Data

It is inappropriate to combine the results of separate studies if they have used different methods to adjust for potential confounders. It may be possible to address inconsistencies in the way that data have been adjusted in separate studies by obtaining the raw data from the authors; however, this may not always be possible and was not a feasible approach for this review. An alternative approach is to combine the raw unadjusted data from the studies, with the limitation that differences in casemix will not be taken into account. Adopting this approach meant that studies could only be combined when they had provided sufficient data describing the provider volume cutoff points, the number of hospitals or surgeons in each volume category, and the number of patients treated in each category.

The unit of analysis was the volume category stratum reported in each analysis. For example, if an analysis followed the outcomes of three groups categorized as low-, medium-, and high-case volume, that analysis would contribute three data points to the overall meta-analysis. Mean values for separate volume strata were used when specified. If the mean was not specified, the midpoint of the upper and lower cutpoints of each strata were used as point estimates. If lower cutpoints were not reported, we determined the mean as half of the upper limit. If the upper cutpoint was missing, we found that 1.5 times the lower limit of that stratum most closely approximated situations in which values were known.

Addressing hospital volume and surgeon volume separately, and short-term and long-term mortality separately, we plotted mortality against case volume for each cancer type. We transformed volume to \( \log_{(base \ 2)} \) of volume because the data were skewed by many small volume categories and only a few very large volume categories, and also for practical reasons because the effect of changes in case volume could reasonably be assumed to be multiplicative, not additive, (eg, the difference in skill when going from 5 to 10 cases per year should be similar in effect to going from 25 to 50 cases per year). To verify the existence of a consistent change in risk in association with volume increase, we overlaid a “local regression” function (“lowess” in Stata statistical software [StataCorp, College Station, Tex])\(^2\) that is sensitive to nonlinear patterns.

We then used the Stata command “xtgee” to fit a logistic regression model defining deaths in each stratum as the outcome, \( \log_{2} \) (mean volume in stratum) as a single predictor, and the number of patients in each stratum as the denominator, and accounted for clustering by study, so that the meta-analysis took into account the nonindependence of different volume strata within the same study.\(^2\) This analysis provided an estimate of the OR of the increase (or decrease) in mortality for each unit increase in volume (expressed as \( \log_{2} \) [volume]). The model coefficient estimated the proportional change in the odds of mortality for each doubling of volume (eg, if \( OR = 0.9 \), then the odds decreased by 0.1 for each doubling of volume).

Estimates of Effect From Adjusted Results

We reported adjusted results only for those studies that had included age, stage of disease, comorbidities, and both hospital and surgeon volume in the model, and in which an appropriate analysis was performed that took into account the effect of clustering of cases by provider surgeon or institution.
Results

Identification of Studies
Table 4 lists the search dates, the electronic databases searched, and the number of retrieved articles resulting from each search. A flow diagram outlining the overall search strategy and the identification of primary publications included in this systematic review is shown in Figure 1.

We identified 101 primary publications reporting 137 studies of the effect of hospital or clinician volume on the mortality outcomes of patients undergoing cancer surgery. Some publications included studies of more than one cancer type. Overall, studies addressed surgery for the following gastrointestinal cancers: esophageal cancer (28 studies), gastric cancer (22 studies), liver cancer (11 studies), pancreatic cancer (34 studies), and colorectal cancer (42 studies).

Definitions of Volume Categories
In nearly all the studies, high-volume and low-volume categories for providers were not defined a priori. Volume category cutoffs were most often determined post hoc through ranking providers (hospital or clinician) according to the number of procedures performed and then dividing the cohort into halves, tertiles, quartiles, or quintiles. Figure 2 shows how the lowest and highest volume categories were defined, revealing substantial overlap between studies. Some studies defined a given volume of cases as low volume, whereas other studies defined the same volume as high volume.

Characteristics of Included Studies
All included studies were observational studies and there were no controlled trials. The vast majority were analyses of data that are routinely and previously collected from hospital administrative databases, cancer registries, and a range of other specialist databases to report on patient mortality outcomes.

Tables 5 to 11 outline the characteristics of studies included in this review: provider volume assessed (hospital or clinician), outcomes reported (short-term or long-term mortality), significance of findings (as reported by the authors), adjustment made for potential confounding factors (demographics, comorbidities, clinical stage, treatment received, and both hospital and surgeon case volume), and whether the analysis accounted appropriately for the effects of clustering. The 137 studies of individual cancer types that were included reported 203 analyses of whether hospital or surgeon volume affected short-term or long-term mortality.

A total of 112 analyses (55%) attempted to determine the effect of hospital volume on short-term mortality (defined variously as either in-hospital, 30-day, surgical, or inpatient mortality). Thirty-seven analyses (18%) searched for an effect of hospital volume on long-term mortality, 38 analyses (19%) examined the effect of surgeon volume on short-term mortality, and 16 analyses (8%) attempted to determine an effect of surgeon volume on long-term mortality.

Although most studies made adjustments for some characteristics that could potentially act as confounders, only 20 (15%) included age, stage of disease, comorbidities, and both hospital and surgeon case volume as potentially confounding factors for each other. Seventy-six studies (55%) accounted for clustering of participants. Eleven studies (8%) had both adjusted for the specified confounding factors and accounted for clustering of participants.

Of 126 studies investigating the effect of hospital volume for a cancer type, 86 (68%) reported a significant association between hospital volume and either short-term or long-term mortality or both (including 17 of 27 studies of the esophagus, 14 of 20 studies of the stomach, 11 of 11 studies of the liver, 24 of 31 studies of the pancreas, 10 of 17 studies of the colon, 3 of 9 studies of the rectum, and 7 of 14 studies of the colo-

### TABLE 4. Search Results From Electronic Databases

| DATABASE                        | DATES COVERED | DATE SEARCHED | CITATIONS RETRIEVED |
|---------------------------------|---------------|---------------|---------------------|
| OVID PreMEDLINE and MEDLINE     | 1966-2007     | May 2007      | 3,112               |
| EMBASE                          | 1968-2007     | May 2007      | 2,390               |
| AMI                             | 1979-2007     | May 2007      | 519                 |
| Cochrane Library                | Issue 2, 2007 |               | 80                  |
| EconLit                         | 1979-2007     | May 2007      | 4                   |
| PubMed                          | 2005-2007     | June 2007     | 420                 |
| ISI Web of Knowledge            | July 2007     |               | 214                 |
| Total (after removal of duplicate citations) |                |               | 4,731               |

AMI, Australasian Medical Index; EMBASE, Excerpta Medica database.
rectal (not otherwise defined). Forty studies (32%) reported no significant association between hospital volume and short-term or long-term mortality (including 10 of 27 studies of the esophagus, 6 of 20 studies of the stomach, none of the 11 studies of the liver, 6 of 11 studies of the pancreas, 6 of 6 studies of the colon, 2 of 4 studies of the rectum, and 3 of 9 studies of the colon and rectum [not otherwise defined]). Sixteen (39%) studies reported a significant association between hospital volume and long-term but not short-term mortality (including 0 of 6 studies of the esophagus, 3 of 5 studies of the stomach, 0 of 0 studies of the liver, 5 of 11 studies of the pancreas, 0 of 6 studies of the colon, 2 of 4 studies of the rectum, and 6 of 9 studies of the colon and rectum [not otherwise defined]). Two studies of esophageal cancer surgery reported a significant association between surgeon volume and short-term mortality but not long-term mortality. In contrast, three studies of colorectal cancer surgery and one of pancreatic cancer surgery reported no significant impact of surgeon volume on short-term mortality, but a statistically significant relation between surgeon volume and long-term mortality was reported.

**Raw Unadjusted Mortality**

We were able to extract raw (unadjusted) data from 105 of the 112 analyses of the effect of hospital volume on perioperative mortality for meta-analysis. We did not undertake meta-analysis of the effect of hospital volume on long-term mortality, surgeon volume on perioperative mortality, or surgeon volume on long-term mortality because there were only small numbers of analyses available from which to obtain data.

In Figure 3, the mortality rate for each strata in each study was plotted against the midpoint of volume for that strata in each study. From the super-
imposed regression function, a consistent relation between unadjusted mortality rate and hospital case volume was evident for all cancer types except rectal cancer throughout the range of volume categories. No definite threshold point was apparent across the range of tumor types; however, the slope describing the relation between volume and outcome decreased for both esophageal and colon cancer surgery at a point lying within the range between 16 and 32 cases per year, suggesting that a potential threshold effect may be present.

Using the pooled unadjusted data, the ORs of mortality for each doubling of provider volume by-cancer type are shown in Table 12, and range from 0.77 for liver cancer to 0.90 for colon cancer surgery. All reported ORs were statistically significant. The number of patients that needed to be moved from a center treating the lowest quartile of case volume per year to a center treating the highest quartile of case volume per year in each cancer type to prevent 1 additional volume-associated death ranged from 10 (esophageal cancer) to 50 (stomach cancer). The estimates based on unadjusted data are conservative; all studies in which analyses were performed to adjust for potential confounders such as age, stage of disease, and comorbidities found that the effect of case volume was smaller after adjustment than it was when these confounders were not taken into account.

### Adjusted Mortality

In Table 13, the adjusted results are presented from the 11 studies reported in 8 publications (including 2 esophageal, 2 gastric, 2 pancreatic, 3 colon, 1 rectal, and 1 colorectal study) that controlled for age, stage of disease, comorbidity, and hospital and surgeon volume, as well as accounting for the effects of clustering.

All 11 studies reported at least 1 statistically significant association between case volume and mortality. Ten analyses reported an adjusted effect estimate for hospital volume. Five of these reported on perioperative mortality, of which four reported statistically significant results.

Six analyses reported long-term survival outcomes, five of which reported statistically significant results.

Nine analyses reported an adjusted effect estimate for surgeon volume. Seven of these studies reported on perioperative mortality, four of which reported statistically significant results, and six reported long-term survival outcomes, four of which reported statistically significant results.

Four studies reported on stratified combinations of low-volume and high-volume hospitals and surgeons for gastric, colon, and rectal cancer surgery. These analyses found a statistically significant short-term and long-term mortality benefit for higher volume combinations (of surgeons and hospitals).

Of the nine analyses that examined and reported separately the effects of hospital and surgeon volume, four reported surgeon volume to have a greater effect than hospital volume, whereas three demonstrated a greater effect for hospital volume compared with surgeon volume, and in two analyses the effects of hospital volume and surgeon volume were found to be similar.

### Discussion

The findings of this review provide mixed support for the use of provider case volume as a proxy for quality of care and subsequent improved outcomes in the...
care of patients with gastrointestinal cancer. A quantifiable and statistically significant relationship appears to exist between hospital case volume and short-term mortality, based on an analysis pooling data from 101 publications from 12 countries spanning more than 20 years and including at least 1,112,340 patients, of whom at least 71,673 had died at the time of last follow-up. Despite this, approxi-

**TABLE 5. Included Studies by Anatomic Site: Esophagus**

| STUDY               | COUNTRY | PATIENTS | HOSPITALS | SURGEONS | HOSPITAL VOLUME | SURGEON VOLUME | ADJUSTMENT (D C S T V) | APPROPRIATE UNIT OF ANALYSIS |
|---------------------|---------|----------|-----------|----------|----------------|---------------|-----------------------|-------------------------------|
| Dimick 2001        | US      | 1,136    | 62        | —        | Sig            | —             | D+ C S T              | No                            |
| Dimick 2003        | US      | 8,657    | NR        | —        | Sig            | —             | D+ C S T              | No                            |
| Kuo 2001           | US      | 1,193    | 64        | —        | Sig            | —             | D+ C S              | Yes                           |
| Patti 1998         | US      | 1,561    | 273       | —        | Sig            | —             | D+ C S              | No                            |
| Swisher 2000       | US      | 340      | 25        | —        | Sig            | —             | D C S                | No                            |
| van Lanschot 2001  | Netherlands | 1,792 | 60        | —        | Sig            | —             | NR                   | No                            |
| Begg 1998          | US      | 503      | 190       | —        | Sig            | —             | D C S                | No                            |
| Birkmeyer 2002     | US      | 6,337    | 1,868     | —        | Sig            | —             | D+ C S T             | Yes                           |
| Finlayson 2003     | US      | 5,282    | 603       | —        | Sig            | —             | D+ C S T             | Yes                           |
| Urbach & Baxter 2004 | Canada | 613     | 47        | —        | NS             | —             | D C                  | No                            |
| Patti 1998         | US      | 1,561    | 273       | —        | Sig            | —             | D+ C S              | No                            |
| Lin 2006           | Taiwan  | 6,674    | 111       | —        | Sig            | —             | D C                  | Yes                           |
| Hollenbeck 2007    | US      | 4,020    | NR        | —        | Sig            | —             | D+ C S              | Yes                           |
| Birkmeyer 2006     | US      | 6,440    | 2,934     | —        | Sig            | —             | D+ C S T             | Yes                           |
| McCulloch 2003     | UK      | 365      | 24        | —        | Sig            | —             | D C S T              | Yes                           |
| Gordon 1999        | US      | 518      | 51        | —        | Sig            | —             | D+ C S              | Yes                           |
| Wenner 2005        | Sweden  | 1,429    | 74        | —        | Sig            | Sig           | D T                  | Yes                           |
| Rouvelas 2007      | Sweden  | 1,119    | 53        | —        | NS             | NS           | D C S T              | NR                            |
| Thompson 2007      | UK      | 1,490    | 53        | —        | NS             | NS           | D C S T              | No                            |
| Birkmeyer 2007     | US      | 822      | 206       | —        | Sig            | —             | D+ C S T             | Yes                           |
| Dimick 2005        | US      | 1,946    | NR        | 1,118    | Sig            | Sig          | D+ C S T             | Yes                           |
| Urbach & Austin 2005 | Canada | 613     | 58        | 93       | NS             | Sig           | D C                  | Yes                           |
| Ho 2006            | US      | 10,023   | NR        | —        | NS             | Sig           | D+ C S V             | Yes                           |
| Bachmann 2002      | US      | 322      | 23        | —        | NS             | NS           | D C S T V             | No                            |
| Gillison 2002      | UK      | 1,125    | 19        | 64       | NS             | NS           | D S                  | No                            |
| Birkmeyer 2003     | US      | NR       | NR        | NR       | Sig            | Sig          | D+ C S V             | Yes                           |

D indicates statistical analysis adjusted for patient age and sex; C, data were adjusted for comorbidities; S, data were adjusted for stage of disease (eg, tumor stage or emergent admission); T, data were adjusted for treatment received or type of procedure; V, both hospital and surgeon volume variables were considered in the analysis (eg, hospital volume data were adjusted for surgeon volume or surgeon volume data were adjusted for hospital volume); —, not done or not applicable; Sig, reported statistically significant difference for improved mortality outcomes at high-volume providers \( P < .05 \); D+, data were adjusted for additional demographic characteristics including age and sex; NR, not reported or unclear from the published data; NS, not significant.
mately one-third of all included analyses did not find any statistically significant association between hospital or clinician volume and short-term or long-term mortality.

Studies regarding this topic exhibit considerable heterogeneity with regard to design, quality, and results that limit the potential to generalize about any consistent effect of case volume on outcomes from gastrointestinal cancer surgery. The overall quality of this body of literature is in part limited by the quality of data available for review from administrative databases, upon which analyses are usually undertaken. The most significant limitations have been the degree to which the studies have adjusted for other variables known to influence outcome, especially age, comorbidities, and stage of disease, and due to the variability in definitions of high and low volume. Only approximately 8% of analyses accounted sufficiently for potential confounders in estimating the size of a volume effect, and conducted an appropriate analysis that correctly accounted for the clustered nature of the sample in estimating confidence intervals.

Acknowledging these important limitations, we can however make some conclusions that are likely to be useful for decision-making. The first relates to the strength and robustness of the association between

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**TABLE 6. Included Studies by Anatomic Site: Stomach**

| STUDY                | COUNTRY    | PATIENTS | HOSPITALS | SURGEONS | HOSPITAL VOLUME | SURGEON VOLUME | ADJUSTMENT | APPROPRIATE UNIT OF ANALYSIS |
|---------------------|------------|----------|-----------|----------|-----------------|----------------|------------|------------------------------|
| Birkmeyer 200231    | US         | 31,944   | 3,423     | —        | Sig             | —              | D+ C S     | Yes                          |
| Birkmeyer 200332    | US         | 9,403    | 2,934     | —        | Sig             | —              | D+ C S T   | Yes                          |
| Damhuis 200243      | Netherlands| 1,978    | 22        | —        | NS              | —              | D S        | No                           |
| Finlayson 200343     | US         | 16,081   | 911       | NS       | Sig             | —              | D+ C       | Yes                          |
| Gordon 199945       | US         | 705      | 51        | NS       | Sig             | —              | D+ C S     | Yes                          |
| Jensen 200737       | Denmark    | 537      | NR        | NS       | Sig             | —              | NR         | NR                           |
| Lin 200639          | Taiwan     | 1,138    | 174       | Sig      | —               | —              | D C        | Yes                          |
| Luft 198744         | US         | 24,072   | 864       | Sig      | —               | —              | D+ C T     | NR                           |
| McCulloch 200342     | UK         | 590      | 24        | Sig      | —               | —              | D C S T    | Yes                          |
| Reid-Lombardo 200755| US         | 3,277    | 691       | Sig      | —               | —              | D C S      | No                           |
| Smith JK 200756     | US         | 13,354   | NR        | Sig      | —               | —              | D C S T    | Yes                          |
| Smith DL 200747     | US         | 1,864    | 214       | Sig      | —               | —              | D+ C S T   | Yes                          |
| Wenner 200544       | Sweden     | 416      | 74        | Sig      | —               | —              | D S        | Yes                          |
| Thompson 200746     | UK         | 499      | 39        | NS       | NS              | —              | D C S T    | No                           |
| Birkmeyer 200747    | US         | 3,234    | 407       | Sig      | —               | —              | D+ C S T   | Yes                          |
| Enzinger 200748     | US         | 448      | 306       | NS       | —               | —              | D+ S T     | Yes                          |
| Nomura 200339       | Japan      | 28,608   | NR        | Sig      | —               | —              | D          | No                           |
| Callahan 200340     | US         | 6,434    | 213       | 1,387    | Sig             | Sig           | D+ C S V   | Yes                          |
| Hannan 200241       | US         | 3,711    | 207       | 1,114    | Sig             | Sig           | D+ C S V   | No                           |
| Bachmann 200242     | UK         | 405      | 23        | Sig      | NS              | NS            | D C S T V  | Yes                          |
| Fujita & Yamazaki 200262| Japan | 136 | NR      | 21        | —               | —              | D+ C S     | No                           |
| de Gara 200339      | Canada     | 577      | NR        | 84       | —               | —              | NS         | NR                           |

D indicates statistical analysis adjusted for patient age and sex; C, data were adjusted for comorbidities; S, data were adjusted for stage of disease (eg, tumor stage or emergent admission); T, data were adjusted for treatment received or type of procedure; V, both hospital and surgeon volume variables were considered in the analysis (eg, hospital volume data were adjusted for surgeon volume or surgeon volume data were adjusted for hospital volume); —, not done or not applicable; Sig, reported statistically significant difference for improved mortality outcomes at high-volume providers (P < .05); D+, data were adjusted for additional demographic characteristics including age and sex; NS, not significant; NR, not reported or unclear from the published data.
case volume and cancer mortality, and whether hospital or surgeon volume is more important. In our meta-analysis combining the unadjusted results of 105 analyses, a statistically significant inverse relation between hospital volume and perioperative mortality was evident for each tumor type. Nonetheless, approximately one-third of analyses found no statistically significant association between hospital or surgeon volume and short-term or long-term mortality. Although some of these studies were small and may have been underpowered, several studies finding no volume effect included more than 1,000 patients, and as many as 120,000 patients. We therefore conclude that the inverse association noted between case volume and outcome is statistically significant (for hospital case volume and short-term mortality, at least), but not very robust. The small number of studies meeting our quality threshold support this assertion; most, but not all, found statistically significant inverse associations between hospital and/or surgeon case volume and short-term or long-term mortality.

With regard to whether hospital or surgeon volume is most important, the studies we identified predominantly addressed the relation between hospital case volume and short-term perioperative mortality. Much less attention has been given to the effect of surgeon case volume, and to survival and long-term mortality outcomes.

From the small number of higher-quality studies that examined for an effect of both hospital and surgical volume and accounted for important confounders, a lack of consistent results made us unable to consider the relative importance of surgeon volume and hospital volume as predictors of perioperative or long-term mortality. Surgeon volume and hospital volume are likely to affect outcomes through quite different mechanisms, with surgeon volume affecting preoperative and intraoperative decision-making, case selection, and surgical technique, whereas the effect of hospital volume involves systems and organizational features of care including the way in which teams work together and the institution of best-practice protocols, particularly in the postoperative period. They are also likely to be highly correlated because the presence of a high-volume surgeon will usually lead to a hospital being classified as high volume, and studies need to be specifically designed to separate the effects of each. Furthermore, the results of this review provide little guidance for the immediate resolution of the potential paradox of a low-volume surgeon operating in a high-volume hospital.

### Table 7. Included Studies by Anatomic Site: Liver

| Study          | Country | Patients | Hospitals | Surgeons | Hospital Volume | Surgeon Volume | Adjustment (D C S T V) | Appropriate Unit of Analysis |
|----------------|---------|----------|-----------|----------|-----------------|----------------|----------------------|-------------------------------|
| Begg 1998      | US      | 801      | 286       | —        | Sig             | —              | D C S                | No                            |
| Birkmeyer 2006 | US      | 829      | NR        | —        | Sig             | —              | D + C S T            | Yes                          |
| Choti 1998     | US      | 606      | NR        | —        | Sig             | —              | D + C S T            | No                            |
| Dimick 2003    | US      | 569      | 35        | —        | Sig             | —              | D + C S T            | No                            |
| Dimick 2004    | US      | 16,582   | NR        | —        | Sig             | —              | D + C S T            | No                            |
| Glasgow 1999   | US      | 507      | 138       | —        | Sig             | —              | D C S                | No                            |
| Gordon 1999    | US      | 293      | NR        | —        | Sig             | —              | D + C S T            | Yes                          |
| Hollenbeck 2007 | US      | 3,630    | NR        | —        | Sig             | —              | D + C S T            | Yes                          |
| Lin 2006       | Taiwan  | 1,872    | 82        | —        | Sig             | —              | D C                  | Yes                          |
| Fong 2005      | US      | 3,511    | 1,284     | —        | Sig              | Sig            | D C T                | Yes                          |
| Simunovic 2006 | Canada  | 362      | 41        | —        | NS              | Sig            | D + C S              | Yes                          |

D indicates statistical analysis adjusted for patient age and sex; C, data were adjusted for comorbidities; S, data were adjusted for stage of disease (eg, tumor stage or emergent admission); T, data were adjusted for treatment received or type of procedure; V, both hospital and surgeon volume variables were considered in the analysis (eg, hospital volume data were adjusted for surgeon volume or surgeon volume data were adjusted for hospital volume); —, not done or not applicable; Sig, reported statistically significant difference for improved mortality outcomes at high-volume providers ($P < .05$); NR, not reported or unclear from the published data; D +, data were adjusted for additional demographic characteristics including age and sex; NS, not significant.
| STUDY                | COUNTRY | PATIENTS | HOSPITALS | SURGEONS | HOSPITAL VOLUME | SURGEON VOLUME | ADJUSTMENT | APPROPRIATE UNIT OF ANALYSIS |
|---------------------|---------|----------|-----------|----------|----------------|----------------|-------------|-------------------------------|
| van Heek 2005       | Netherlands | NR | NR | — | — | — | — | D+ C S | Yes |
| Hollenbeck 2007     | US | 9,153 | NR | — | — | — | — | D+ C S | Yes |
| Lin 2007            | Taiwan | 1,766 | 86 | — | NS | — | D C | Yes |
| Birkmeyer 2002      | US | 10,530 | 1,868 | — | — | — | — | D+ C S | Yes |
| Gordon 1999         | US | 1,092 | NR | — | Sig | — | — | — | — |
| Ward 2004           | US | 39 | NR | — | NS | — | D C | No |
| Begg 1998           | US | 742 | NR | — | — | — | — | D C S | No |
| Finlayson 2003      | US | 3,414 | 483 | — | — | — | — | — |
| Glasgow & Mulvihill 1996 | US | 1,910 | NR | — | — | — | — | D+ C S | Yes |
| Gordon 1995         | US | 501 | 39 | — | — | — | — | — |
| Gordon 1998         | US | 795 | 43 | — | — | — | — | — |
| Gouma 2000          | Netherlands | 1,126 | NR | — | — | — | — | — |
| Ho & Heslin 2003    | US | 6,652 | 500 | — | — | — | — | D C | Yes |
| Imperato 1996       | US | 579 | 117 | — | — | — | — | D+ C | No |
| Kotwall 2002        | US | 24,926 | 720 | — | — | — | — | D C | Yes |
| Simonovic 1999      | Canada | 842 | 68 | — | — | — | — | D C S | No |
| Wade 1996           | US | 130 | NR | — | NS | — | — | D S | No |
| Jensen 2007         | Denmark | 581 | NR | — | — | — | — | — |
| Birkmeyer 2006      | US | 5,607 | 2,934 | — | — | — | — | D+ C S T | Yes |
| Fong 2005           | US | 2,592 | 1,101 | — | — | — | — | — |
| Birkmeyer 1999      | US | 5,01 | 39 | — | — | — | — | D C S | No |
| Birkmeyer 2000      | US | 1,236 | 48 | 373 | — | — | — | D+ C S V | No |
| Urbach & Baxter 2004 | Canada | 686 | 59 | 124 | NS | — | — | — |
| Urbach & Austin 2005 | Canada | 223 | 26 | 91 | NS | — | — | — |
| Edge 1993           | US | 223 | 26 | 91 | NS | — | — | — |
| Bachmann 2003       | UK | 261 | 23 | — | — | NS | Sig | NS | D C S T V | Yes |
| University of Leeds 2000 | UK | 3,262 | 58 | 318 | NS | Sig | NS | Sig | D+ T | No |
| Cheng 2007          | China | 295 | 9 | — | — | NS | — | D C | No |
| Birkmeyer 2003      | US | NR | NR | NR | — | — | Sig | — | D+ C S V | Yes |
| Rosemurgy 2010      | US | 698 | NR | 282 | — | — | Sig | — | NR | No |

D indicates statistical analysis adjusted for patient age and sex; C, data were adjusted for comorbidities; S, data were adjusted for stage of disease (eg, tumor stage or emergent admission); T, data were adjusted for treatment received or type of procedure; V, both hospital and surgeon volume variables were considered in the analysis (eg, hospital volume data were adjusted for surgeon volume or surgeon volume data were adjusted for hospital volume); NR, not reported or unclear from the published data; —, not done or not applicable; Sig, reported statistically significant difference for improved mortality outcomes at high-volume providers (P < .05); D+, data were adjusted for additional demographic characteristics including age and sex; NS, not significant.
or a high-volume surgeon operating in several low-volume centers. Nor does it resolve the issue of whether outcomes are better for surgeons who restrict their practice to being high volume for a few complex procedures, or those who are high volume but undertake a wide range of procedures spanning several different cancer types.34

Our second conclusion relates to the magnitude of any association, and therefore its clinical importance. Using unadjusted (raw) mortality rates, which are prone to bias if casemix differs between low-volume and high-volume providers, we found that the magnitude of a volume effect is relatively consistent across tumor types, with the odds of perioperative death being within the range of 0.77 to 0.90 for each doubling of hospital case volume. Our estimate of the number of patients that needed to be moved from a low-volume service provider to a high-volume service provider to save 1 volume-associated life ranged from 10 to 50 patients for the different tumors, as estimated on the basis of a move from the lowest quartile to the highest quartile volume hospitals. The actual case volume this represented differed for each tumor type, but this form of data presentation may be a helpful guide when quantifying the potential benefits of regionalization. Although the estimated number needed to move may appear to be small, for some relatively uncommon cancers such as pancreatic and esophageal cancer, it may take many years in 1 health district to accrue sufficient cases for volume-based referral to make a measurable difference in mortality (eg, in places in which low-volume providers treat 1 to 2 cases per year, it may take 5 to 10 years of referring patients to high-volume centers to prevent 1 volume-associated death). This is likely to be an overestimate of the effect size because those studies that adjusted for

### TABLE 9. Included Studies by Anatomic Site: Colon

| STUDY                | COUNTRY | PATIENTS        | HOSPITALS | SURGEONS | HOSPITAL VOLUME | SURGEON VOLUME | ADJUSTMENT | APPROPRIATE UNIT OF ANALYSIS |
|----------------------|---------|-----------------|-----------|----------|----------------|---------------|------------|-------------------------------|
| Birkmeyer 200231     | US      | 304,285         | 4,587     | —        | Sig            | —             | —          | D+ C S T                      |
| Birkmeyer 200332     | US      | 120,270         | 1,082     | Sig      | —             | NS            | —          | D+ C S T                      |
| Gordon 199947        | US      | 1,015           | 51        | NS       | —             | Sig           | —          | D+ C S S                      |
| Khuri 199990         | US      | 13,310          | 125       | NS       | —             | Sig           | —          | D+ C S S                      |
| Riley & Lubitz 198591| US      | 22,560          | 6,403     | Sig      | —             | —             | —          | D+ S                          |
| Lin 200639           | Taiwan  | 13,054          | 178       | Sig      | —             | —             | —          | D+ C T S                      |
| Marusch 200152       | Germany | 2,293           | 75        | NS       | —             | —             | —          | —                            |
| Luft 198754          | US      | 36,860          | 898       | Sig      | —             | Sig           | —          | D+ C T NR                     |
| Simunovic 200658     | Canada  | 8,398           | 151       | NS       | —             | NS            | —          | D+ C S S                      |
| Birkmeyer 200747     | US      | 43,656          | 845       | Sig      | —             | —             | —          | D+ C S T                      |
| Meyerhardt 200355    | US      | 3,161           | 1,078     | Sig      | —             | —             | —          | D+ S                          |
| Callahan 200360      | US      | 48,582          | 223       | 2,651    | Sig            | Sig           | —          | D+ C S V                      |
| Hannan 198944        | US      | 10,297          | 250       | 1,997    | Sig            | Sig           | —          | D+ C S V                      |
| Hannan 200241        | US      | 22,128          | 229       | 2,052    | Sig            | Sig           | —          | D+ C S V                      |
| Ko 200245            | US      | 22,408          | >900      | Sig      | —             | Sig           | —          | D+ C S V                      |
| Billingsley 200756   | US      | 21,533          | 661       | 2,678    | NS             | Sig           | —          | D+ C S T V                    |
| Schrag 200057        | US      | 24,166          | 579       | 2,682    | Sig            | Sig           | NS         | D+ C S V                      |

D indicates statistical analysis adjusted for patient age and sex; C, data were adjusted for comorbidities; S, data were adjusted for stage of disease (eg, tumor stage or emergent admission); T, data were adjusted for treatment received or type of procedure; V, both hospital and surgeon volume variables were considered in the analysis (eg, hospital volume data were adjusted for surgeon volume or surgeon volume data were adjusted for hospital volume); —, not done or not applicable; Sig, reported statistically significant difference for improved mortality outcomes at high-volume providers ($P < .05$); D+, data were adjusted for additional demographic characteristics including age and sex; NS, not significant; NR, not reported or unclear from the published data.
### TABLE 10. Included Studies by Anatomic Site: Rectum

| STUDY        | COUNTRY  | PATIENTS | HOSPITALS | SURGEONS | HOSPITAL VOLUME | SURGEON VOLUME | ADJUSTMENT       | APPROPRIATE UNIT OF ANALYSIS |
|--------------|----------|----------|-----------|----------|-----------------|----------------|-----------------|-----------------------------|
|              |          |          |           |          | SHORT TERM       | LONGER TERM     | (DCSTV)         |                              |
|              |          |          |           |          |                 |                 |                 |                              |
| Matthiessen 200699 | Sweden   | 6,833    | 85        | —        | NS              | —               | —               | D C S T                     | NR                          |
| Marusch 2001100   | Germany  | 1,463    | 75        | —        | Sig             | —               | —               | No                          |
| Harling 2005101   | Denmark  | 4,922    | 53        | —        | NS              | NS             | —               | D S T                       | Yes                         |
| Hodgson 2003102   | Canada   | 7,257    | 367       | —        | Sig             | Sig            | —               | D + C S                     | Yes                         |
| Simons 1997103    | US       | 2,006    | 125       | —        | Sig             | —               | NR              | No                          |
| Engel 2005104     | Germany  | 884      | 39        | —        | NS              | —               | —               | D S T                       | NR                          |
| Meyerhardt 2004105 | US       | 1,330    | 646       | —        | NS              | —               | D + C S T       | Yes                         |
| Holm 1997106      | Sweden   | 1,399    | 14        | 149      | NS              | NS             | NS              | D S T                       | No                          |
| Schrag 2002107    | US       | 2,815    | 420       | 1,141    | NS              | NS             | Sig             | D + C S V                   | Yes                         |
| Ng 2006108        | UK       | 207      | NR        | NR       | —               | NS             | NS              | No                          |
| Porter 1998109    | Canada   | 683      | 5         | 52       | NS              | NS             | Sig             | D S                         | No                          |

D indicates statistical analysis adjusted for patient age and sex; C, data were adjusted for comorbidities; S, data were adjusted for stage of disease (eg, tumor stage or emergent admission); T, data were adjusted for treatment received or type of procedure; V, both hospital and surgeon volume variables were considered in the analysis (eg, hospital volume data were adjusted for surgeon volume or surgeon volume data were adjusted for hospital volume); —, not done or not applicable; NS, not significant; NR, not reported or unclear from the published data; Sig, reported statistically significant difference for improved mortality outcomes at high-volume providers (P < .05); D+, data were adjusted for additional demographic characteristics including age and sex.

### TABLE 11. Included Studies by Anatomic Site: Colon and Rectum (Not Specified as Either Colon or Rectum)

| STUDY       | COUNTRY   | PATIENTS | HOSPITALS | SURGEONS | HOSPITAL VOLUME | SURGEON VOLUME | ADJUSTMENT       | APPROPRIATE UNIT OF ANALYSIS |
|-------------|-----------|----------|-----------|----------|-----------------|----------------|-----------------|-----------------------------|
|             |           |          |           |          | SHORT TERM       | LONGER TERM     | (DCSTV)         |                              |
|             |           |          |           |          |                 |                 |                 |                              |
| Dimick 2003110 | US        | 20,862   | 842       | —        | Sig             | —               | —               | D + C S                     | Yes                         |
| Zhang 2007111 | US        | 38,237   | 383       | —        | Sig             | —               | —               | D + C S                     | NR                          |
| Engel 2005112 | Netherlands | 67,594  | 128       | —        | NS              | —               | —               | D                           | Yes                         |
| Simonovic 2000113 | Canada     | 1,072    | 124       | —        | NS              | NS             | —               | D C S                       | No                          |
| Rabeneck 2004114 | Canada     | 22,633   | 172       | —        | Sig             | —               | —               | D + C S T                   | No                          |
| Harmon 1999115 | US        | 9,739    | 50        | 812      | NS              | NS             | —               | D + C S T V                 | No                          |
| Ho 200650    | US        | 233,773  | 52        | 191      | NS              | NS             | —               | D + C S V                   | Yes                         |
| Parry 1999116 | UK        | 812      | 39        | 112      | NS              | NS             | NS              | D S T                       | No                          |
| Rogers 2006117 | US       | 28,644   | 397       | 2,993    | Sig             | Sig            | Sig             | D + C S T V                 | Yes                         |
| Kee 1999118  | UK        | 3,155    | 19        | 71       | Sig             | —               | NS              | D S V                       | No                          |
| Renzulli 2006119 | Switzerland | 915      | 26        | 132      | Sig             | —               | Sig             | D S T V                     | Yes                         |
| Galandiuk 2006120 | US       | 476      | 23        | 9        | —               | —               | NS              | —                           | No                          |
| Mella 1997121 | UK        | 3,221    | 52        | 161      | —               | NS              | NS              | —                           | No                          |
| McArdle & Hole 2004122 | UK  | 3,200    | 11        | 191      | —               | NS              | NS              | D + S                       | Yes                         |

D indicates statistical analysis adjusted for patient age and sex; C, data were adjusted for comorbidities; S, data were adjusted for stage of disease (eg, tumor stage or emergent admission); T, data were adjusted for treatment received or type of procedure; V, both hospital and surgeon volume variables were considered in the analysis (eg, hospital volume data were adjusted for surgeon volume or surgeon volume data were adjusted for hospital volume); —, not done or not applicable; NS, not significant; NR, not reported or unclear from the published data; Sig, reported statistically significant difference for improved mortality outcomes at high-volume providers (P < .05); D+, data were adjusted for additional demographic characteristics including age and sex.
A third conclusion of this review relates to whether a threshold volume effect is apparent. A threshold hospital volume above which mortality is much lower for a specified treatment was not apparent in our analysis of unadjusted data, although an inflection in the line of best fit was evident at 16 to 32 cases per year for esophageal and colon cancer surgery. Hospital volume appeared to be associated inversely with mortality across the volume spectrum in this analysis, and therefore the exact volume of cases that a hospital needs to manage to achieve acceptable outcomes remains a value judgment in most instances.

A limitation of this review is that it focused only on mortality outcomes because these are most widely reported in the literature. However, mortality is not the only important outcome measure in cancer studies and, increasingly, research is focusing on whether there is an association between provider case volume and nonmortality outcomes such as quality of life and disease recurrence, or tumor-specific outcomes such as colostomy use or wide local excision versus mastectomy in patients with breast cancer. The emergence of this information in volume-related research may be important for several reasons. First, these nonmortality outcomes are especially important to patients, as well as to payers and to clinicians, and this information may be helpful for informing the trade-off between mortality and patient choice to be treated close to home. Second, and importantly in

### TABLE 12. Summary Mortality Risk From Unadjusted Data

| TUMOR TYPE | STUDIES | HOSPITALS | PATIENTS | DEATHS | EFFECT ON MORTALITY OF DOUBLING HOSPITAL CASE VOLUME OR (95% CI) | UPPER LIMIT LOWER QUARTILE, CASES/YEAR | LOWER QUARTILE MORTALITY, % | LOWER LIMIT UPPER QUARTILE, CASES/YEAR | UP QUARTILE MORTALITY, % | NNT* |
|------------|---------|-----------|----------|--------|---------------------------------------------------------------|----------------------------------------|--------------------------------|-------------------------------|----------------|-----|
| Esophagus  | 24      | 3,405     | 45,822   | 4,177  | 0.81 (0.77-0.84)                                             | 3                                      | 16.7                          | 18                            | 6.7            | 10  |
| Stomach    | 14      | 5,058     | 179,540  | 16,369 | 0.88 (0.86-0.91)                                             | 6                                      | 8.8                           | 33                            | 6.8            | 50  |
| Liver      | 10      | 1,831     | 24,792   | 1,731  | 0.77 (0.72-0.83)                                             | 5                                      | 11.6                          | 34                            | 2.9            | 11  |
| Pancreas   | 30      | 7,282     | 64,215   | 7,092  | 0.78 (0.73-0.84)                                             | 3                                      | 12.8                          | 20                            | 5.3            | 13  |
| Colon†     | 13      | 7,309     | 575,235  | 31,896 | 0.90 (0.88-0.92)                                             | 18                                     | 9.8                           | 175                           | 3.6            | 16  |
| Rectum†    | 5       | 562       | 88,005   | 5,503  | 1.07 (1.01-1.14)                                             | 8                                      | 4.8                           | 46                            | 7.2            | —   |
| All colon, rectum, and colon and rectum (not otherwise defined) | 27 | 10,239 | 797,971 | 42,304 | 0.91 (0.89-0.93)                                             | 16                                     | 7.5                           | 135                           | 4.7            | 36  |

OR indicates odds ratio; 95% CI, 95% confidence interval; NNT, number needed to treat.

*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]).

†Excludes studies in which patients with colon and rectal cancer were considered collectively and were not differentiated into specific tumor groups (1,369 hospitals, 107,750 patients, and 3,714 deaths).
## TABLE 13. Effect of Case Volume in Studies That Adjusted For Age, Stage of Disease, Comorbidities, and Both Hospital and Surgeon Volume, and That Also Accounted for Clustering in the Analysis

| STUDY (CANCER TYPE) | NO. OF HOSPITALS, SURGEONS, AND PATIENTS | MORTALITY OUTCOME | MORTALITY RANGE, % | HOSPITAL VOLUME | SURGEON VOLUME | COMBINED HOSPITAL AND SURGEON VOLUME |
|---------------------|------------------------------------------|-------------------|-------------------|-----------------|--------------|--------------------------------------|
|                      |                                          |                   |                   | VOLUME CATEGORIES | ADJUSTED EFFECT | VOLUME CATEGORIES | ADJUSTED EFFECT | VOLUME CATEGORIES | ADJUSTED EFFECT | |
|                      |                                          |                   |                   |                 | Increase of 10 cases |                 | Increase of 10 cases |                 | Increase of 10 cases |                 | |
|                      |                                          |                   |                   |                 | OR=0.60 (0.36-0.99, 95% CI) |                 | OR=0.92 (0.85-0.99, 95% CI) |                 | OR=1.80 (1.13-2.87, 95% CI) |                 | |
|                      |                                          |                   |                   |                 | Increase of 10 cases |                 | Increase of 10 cases |                 | Increase of 10 cases |                 | |
|                      |                                          |                   |                   |                 | OR=0.60 (0.36-0.99, 95% CI) |                 | OR=0.92 (0.85-0.99, 95% CI) |                 | OR=1.80 (1.13-2.87, 95% CI) |                 | |
|                      |                                          |                   |                   |                 | Increase of 10 cases |                 | Increase of 10 cases |                 | Increase of 10 cases |                 | |
|                      |                                          |                   |                   |                 | OR=0.60 (0.36-0.99, 95% CI) |                 | OR=0.92 (0.85-0.99, 95% CI) |                 | OR=1.80 (1.13-2.87, 95% CI) |                 | |
|                      |                                          |                   |                   |                 | Increase of 10 cases |                 | Increase of 10 cases |                 | Increase of 10 cases |                 | |
|                      |                                          |                   |                   |                 | OR=0.60 (0.36-0.99, 95% CI) |                 | OR=0.92 (0.85-0.99, 95% CI) |                 | OR=1.80 (1.13-2.87, 95% CI) |                 | |
|                      |                                          |                   |                   |                 | Increase of 10 cases |                 | Increase of 10 cases |                 | Increase of 10 cases |                 | |
|                      |                                          |                   |                   |                 | OR=0.60 (0.36-0.99, 95% CI) |                 | OR=0.92 (0.85-0.99, 95% CI) |                 | OR=1.80 (1.13-2.87, 95% CI) |                 | |
|                      |                                          |                   |                   |                 | Increase of 10 cases |                 | Increase of 10 cases |                 | Increase of 10 cases |                 | |
|                      |                                          |                   |                   |                 | OR=0.60 (0.36-0.99, 95% CI) |                 | OR=0.92 (0.85-0.99, 95% CI) |                 | OR=1.80 (1.13-2.87, 95% CI) |                 | |
|                      |                                          |                   |                   |                 | Increase of 10 cases |                 | Increase of 10 cases |                 | Increase of 10 cases |                 | |
|                      |                                          |                   |                   |                 | OR=0.60 (0.36-0.99, 95% CI) |                 | OR=0.92 (0.85-0.99, 95% CI) |                 | OR=1.80 (1.13-2.87, 95% CI) |                 | |
|                      |                                          |                   |                   |                 | Increase of 10 cases |                 | Increase of 10 cases |                 | Increase of 10 cases |                 | |
|                      |                                          |                   |                   |                 | OR=0.60 (0.36-0.99, 95% CI) |                 | OR=0.92 (0.85-0.99, 95% CI) |                 | OR=1.80 (1.13-2.87, 95% CI) |                 | |
|                      |                                          |                   |                   |                 | Increase of 10 cases |                 | Increase of 10 cases |                 | Increase of 10 cases |                 | |
|                      |                                          |                   |                   |                 | OR=0.60 (0.36-0.99, 95% CI) |                 | OR=0.92 (0.85-0.99, 95% CI) |                 | OR=1.80 (1.13-2.87, 95% CI) |                 | |
|                      |                                          |                   |                   |                 | Increase of 10 cases |                 | Increase of 10 cases |                 | Increase of 10 cases |                 | |
|                      |                                          |                   |                   |                 | OR=0.60 (0.36-0.99, 95% CI) |                 | OR=0.92 (0.85-0.99, 95% CI) |                 | OR=1.80 (1.13-2.87, 95% CI) |                 | |

*H indicates hospitals; S, surgeons; NR, not recorded; P, patients; HR, hazards ratio; OR, odds ratio; LVH, low-volume hospital; HVH, high-volume hospital; LVS, low-volume surgeon; HVS, high-volume surgeon; VLVH, very low-volume hospital; MHS, moderate-volume hospital; RR, relative risk; VLVS, very low-volume surgeon; MVS, moderate-volume surgeon; VHVS, very high-volume hospital; VHHS, very high-volume surgeon.

*Study sample represents a subset of the total number of patients treated, and should not be used to identify volume thresholds.
light of this review, nonmortality measures are often process measures (such as patients undergoing a particular operation or treatment) rather than outcome measures (such as mortality) and may provide alternative indicators of the quality of care.

The heterogeneity of results in this review calls into question the usefulness of case volume alone as a proxy for quality in healthcare decision-making. Overall, the studies in this review, when combined, demonstrate a quantifiable and statistically significant inverse association between case volume and mortality, yet on an individual study level such an association was not always evident. Thus, volume is only ever at best an imperfect proxy for healthcare quality. Well-chosen process measures and individual risk-adjusted outcome measures may also play a role in reflecting quality of care and predicting patient outcomes. Analyses incorporating such data may yield evidence to suggest what it is that high-volume providers do to obtain better outcomes. However, it is still unclear whether process-based outcome measures, such as those used in the Surgical Care Improvement Project (SCIP), and direct measurement of risk-adjusted outcomes, such as is used in the National Surgical Quality Improvement Program (NSQIP), offer more robust estimates of quality than case volume alone can provide from studies of previously collected administrative data.123

Findings of the current study regarding case volume can provide some guidance for service planning and volume-based referral. High-volume hospitals in general have lower perioperative mortality rates for most gastrointestinal cancer surgery. There is limited evidence that suggests the association may extend to long-term outcomes, and may apply to surgery case volume as well. On the basis of mortality outcomes alone, it appears prudent to support volume-based referral and high-volume centers. However, there are also clearly some low-volume providers who get good results, and therefore referral to relatively low-volume providers should be supported if good outcomes can be demonstrated by process measures or by risk-adjusted outcomes, or if there are compelling personal or medical reasons for the patient to be treated close to home.

Future research in this area should address long-term and nonmortality outcomes, not just surgical mortality, and further examine the relative contributions of hospital case volume, surgeon volume, and the volume characteristics of other providers involved in patient care, incorporating important study design criteria such as a priori consistent and meaningful definitions if categorizations of high and low volumes are used, adjustment for potential confounding factors, and appropriate consideration of unit of analysis. The generalizability of these findings to other types of cancer needs to be tested, and more economic analyses are needed to weigh the benefits of any improvement in outcome against measures of patient preference and service accessibility.

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