ANESTHESIOLOGY

Levels of Evidence Supporting the North American and European Perioperative Care Guidelines for Anesthesiologists between 2010 and 2020: A Systematic Review

Andres Laserna, M.D., Daniel A. Rubinger, M.D., Julian E. Barahona-Correa, M.D., Noah Wright, D.O., Mark R. Williams, M.D., Julie A. Wyrobek, M.D., Linda Hasman, M.S.L.S., Stewart J. Lustik, M.D., M.B.A., Michael P. Eaton, M.D., Laurent G. Glance, M.D.

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ABSTRACT

Background: Although there are thousands of published recommendations in anesthesiology clinical practice guidelines, the extent to which these are supported by high levels of evidence is not known. This study hypothesized that most recommendations in clinical practice guidelines are supported by a low level of evidence.

Methods: A registered (Prospero CRD42020202932) systematic review was conducted of anesthesia evidence-based recommendations from the major North American and European anesthesiology societies between January 2010 and September 2020 in PubMed and EMBASE. The level of evidence A, B, or C and the strength of recommendation (strong or weak) for each recommendation was mapped using the American College of Cardiology/American Heart Association classification system or the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system. The outcome of interest was the proportion of recommendations supported by levels of evidence A, B, and C. Changes in the level of evidence over time were examined. Risk of bias was assessed using Appraisal of Guidelines for Research and Evaluation (AGREE) II.

Results: In total, 60 guidelines comprising 2,280 recommendations were reviewed. Level of evidence A supported 16% (363 of 2,280) of total recommendations and 19% (288 of 1,506) of strong recommendations. Level of evidence C supported 51% (1,160 of 2,280) of all recommendations and 50% (756 of 1,506) of strong recommendations. Of all the guidelines, 73% (44 of 60) had a low risk of bias. The proportion of recommendations supported by level of evidence A *versus* level of evidence C (relative risk ratio, 0.93; 95% CI, 0.18 to 4.74; $P = 0.933$) or level of evidence B *versus* level of evidence C (relative risk ratio, 1.63; 95% CI, 0.72 to 3.72; $P = 0.243$) did not increase in guidelines that were revised. Year of publication was also not associated with increases in the proportion of recommendations supported by level of evidence A (relative risk ratio, 1.07; 95% CI, 0.93 to 1.23; $P = 0.340$) or level of evidence B (relative risk ratio, 1.05; 95% CI, 0.96 to 1.15; $P = 0.283$) compared to level of evidence C.

Conclusions: Half of the recommendations in anesthesiology clinical practice guidelines are based on a low level of evidence, and this did not change over time. These findings highlight the need for additional efforts to increase the quality of evidence used to guide decision-making in anesthesiology.

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- Anesthesia clinical practice guidelines make evidence-based recommendations intended to optimize patient outcomes. The extent to which these recommendations are supported by high-quality evidence is not known.

What This Article Tells Us That Is New

- In a systematic review of 2,280 recommendations in 60 guidelines published by major North American and European societies, half of the recommendations were supported by a low level of evidence.
- The proportion of recommendations supported by a high level of evidence did not increase between 2010 and 2020.

Perioperative mortality is the third leading cause of death in the United States after heart disease and cancer.[1] Over 60 years ago, Beecher reported that anesthesia caused 1 death per 1,560 operations.[2] Analyses based on contemporary data report that anesthesia-related mortality has dropped by nearly 99% to 8.2 deaths per million surgical discharges.[3] However, this contemporary analysis underestimates the impact of anesthetic care on outcomes because it only attributes deaths to anesthesia if they were caused by overdoses or adverse effects of anesthetics, malignant

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Submitted for publication June 10, 2020. Accepted for publication March 31, 2021. From the Departments of Anesthesiology and Perioperative Medicine (A.L., D.A.R., N.W., M.R.W., J.A.W., S.J.L., M.P.E., L.G.G.), Research and Clinical Information Sciences (L.H.), and Public Health Sciences (L.G.G.), University of Rochester Medical Center, Rochester, New York; Pontificia Universidad Javeriana, School of Medicine, Bogota, Colombia (J.E.B.-C.); and RAND Health, RAND, Boston, Massachusetts (L.G.G.).

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hyperthermia, or failed or difficult intubations.[3] This analysis ignores the role that anesthesiologists play in optimizing patient physiology to prevent complications such as myocardial infarctions, kidney injury, and strokes.[3]

Reducing preventable deaths and complications after surgery requires a better understanding of the gaps in the evidence base currently used by anesthesiologists to make clinical decisions. For nearly three decades, anesthesiology societies have published clinical practice guidelines on the perioperative management of patients undergoing surgery and other procedures. Anesthesiologists rely on these recommendations to guide decision-making because clinical practice guidelines represent the "epitome" of evidence-based medicine. These recommendations are based on the best available evidence and serve as the framework for best practices in perioperative care. However, clinical practice guidelines are only valid if the scientific basis for these guidelines is valid. In their landmark study published in 2009, Tricoci *et al.*[4] reported that only 11% of the American College of Cardiology/American Heart Association guidelines were based on the highest level of evidence, whereas nearly half were based only on expert opinion or case studies. This reliance on expert opinion is problematic because expert opinion, by definition, has not been scientifically validated. Ten years later, the extent to which cardiovascular guidelines rely on expert opinions has not changed significantly.[5] Similar findings have been reported for other medical and surgical subspecialties.[6–8] To date, the quality of the evidence supporting clinical practice guidelines in anesthesiology has not been reported.

We report the results of our systematic review of anesthesiology evidence-based clinical practice guidelines published by the major North American and European societies and anesthesiology subspecialty societies. Our primary objective is to evaluate the quality of the evidence underlying anesthesiology clinical practice guidelines. Our second objective is to examine the change in the quality of the evidence supporting these clinical practice guidelines over time. Our goal is to better understand the evidence base for anesthesia practice and help inform discussions on future steps needed to improve the quality of evidence underlying the perioperative care of surgical patients.

Materials and Methods

Protocol and Registration

We conducted our systematic review using the Cochrane method. We expanded our analysis to include guidelines published outside of the United States based on comments that we received during the editorial process. Our revised protocol was published in Prospero (CRD42020202932, June 9, 2020), an international registry of systematic reviews, after the initial peer review.[9] Our report adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.[10]

Eligibility Criteria

We reviewed perioperative clinical practice guidelines developed by the major anesthesiology societies in North America and Europe between January 1, 2010, and September 9, 2020. All documents that had a clear statement of being a clinical practice guideline and that graded the levels of evidence supporting their recommendations were included. We excluded guidelines related to intensive care and chronic pain. We excluded previous versions of published guidelines in our main analyses. We also excluded practice advisories because they represent a level of recommendation lower than that offered by clinical practice guidelines.[11]

Search Strategy

A librarian (L.H.) built a specific and sensitive search strategy, including the name of the major North American and European anesthesiology societies and the names of the leading subspecialty societies, followed by the names of the anesthesiology journals with the 10 highest impact factors (Scimago),[12] and finally connected with terms related to clinical practice guidelines and synonyms: ((‘American Society of Anesthesiologists’ OR ‘American Society of Regional Anesthesia and Pain Medicine’ OR ‘Society for Obstetric Anesthesia and Perinatology’ OR ‘Society of Cardiovascular Anesthesiologists’ OR ‘Society for Ambulatory Anesthesia’ OR ‘Society of Anesthesia and Sleep Medicine’ OR ‘Society of Critical Care Anesthesiologists’ OR ‘Society for Pediatric Anesthesia’ OR ‘Trauma Anesthesiology Society’ OR ‘Society for Neuroscience in Anesthesiology and Critical Care’ OR ‘Society for Airway Management’ OR ‘Society of Academic Associations of Anesthesiology and Perioperative Medicine’ OR ‘Society for the Advancement of Transplant Anesthesia’ OR ‘American Society for Enhanced Recovery’ OR ‘American Pain Society’ OR ‘European Society of Anaesthesiology’ OR ‘European Society of Regional Anaesthesia and Pain Therapy’ OR ‘European Society for Paediatric Anaesthesiology’ OR ‘European Association of Cardiothoracic Anesthesiology’ OR ‘Neuroanaesthesia and Critical Care Society’ OR ‘Obstetric Anaesthetists Association’ OR ‘Difficult Airway Society’ OR ‘ERAS Society’ OR ‘Association of Anaesthetists’ OR ‘Royal College of Anaesthetists’ OR ‘Canadian Anesthesiologists Society’ OR ‘Regional Anesthesia and Pain Medicine’:jt OR ‘Anesthesia and Analgesia’:jt OR ‘Anesthesiology’:jt OR ‘British Journal of Anaesthesia’:jt OR ‘Anaesthesia’:jt OR ‘European Journal of Anaesthesiology’:jt OR ‘Canadian Journal of Anesthesia’:jt OR ‘Paediatric Anaesthesia’:jt OR ‘Acta Anaesthesiologica Scandinavica’:jt OR ‘Anaesthesia Critical Care and Pain Medicine’:jt)) AND (‘practice guideline’ OR ‘guideline*’ OR ‘evidence based’ OR ‘task force’)

We used a time filter between January 1, 2010, and September 9, 2020. The decision to include or exclude each society for the search strategy was determined by three anesthesiologists (L.G.G., J.A.W., and M.R.W.).

Information Sources

We searched PubMed and EMBASE from January 1, 2010, to September 9, 2020, for clinical practice guidelines developed by the major anesthesiology societies in North America and Europe. No restriction on language was used. We also searched the web pages of these societies.

Study Selection

Two investigators independently screened the titles and abstracts of all references from the search results using the systematic review software Abstrackr.[13] The full texts of the relevant citations were reviewed and further screened for eligibility. Finally, based on the recommendations of the Cochrane Handbook for Systematic Reviews[14,15] and the PRISMA statement checklist,[10] disagreements about the references for data extraction were resolved by consensus. The analytic sample consisted of 60 guidelines with 2,280 recommendations.

Data Collection Process

Two investigators independently collected data from the included guidelines. The following items were retrieved: guideline title, sponsor (*e.g.*, American Society of Anesthesiologists), year of publication, update status, method used to grade evidence, funding source, population or focus of guideline, and the anesthesia subspecialty (if applicable). The extracted results were compared for concordance between reviewers, and disagreements were resolved by consensus. If a guideline was intended for a multidisciplinary audience (*i.e.*, 2010 guideline for diagnosis and management of patients with thoracic aortic disease[16] and 2011 guideline for coronary artery bypass graft surgery[17]), we only considered the recommendations directed toward anesthesiologists.

Extraction of Level of Evidence

The reviewed guidelines used different methodologies for evaluating the level of evidence. One third of the recommendations (796) were graded using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system. According to the GRADE system, level of evidence A is defined as "consistent evidence from well-performed randomized controlled trials or overwhelming evidence of some other form"; level of evidence B is defined as "evidence from randomized controlled trials with important limitations or very strong evidence of some other form"; and level of evidence C is defined as "evidence from observational studies, unsystematic clinical experience, or from randomized controlled trials with serious flaws"[18] (table 1). We categorized the other recommendations (1,484) using the American College of Cardiology/American Heart Association classification system: level of evidence A includes data from multiple randomized controlled trials or meta-analyses, level of evidence B represents data from a single randomized controlled study or observational studies, and level of evidence C is limited to data from case reports and expert opinion[4] (table 1). For those guidelines that did not explicitly classify the level of evidence using the American College of Cardiology/American Heart Association or GRADE classification system, two investigators independently classified the recommendations using the grading system (American College of Cardiology/American Heart Association or GRADE) that most closely approximated the grading system used in the guideline (table 1). Agreement between the evaluators was achieved by consensus as per the Cochrane Handbook for Systematic Reviews.[14]

Extraction of Strength of Recommendation

Recommendations (796) classified using the GRADE system were classified as either strong recommendations (benefits clearly outweigh risk and burdens or vice versa) or weak recommendations (benefits closely balanced with risks and burdens)[19] within the body of the documents. All other recommendations (1,484) were classified as strong or weak recommendations based on the American College of Cardiology/American Heart Association classification system (table 1) by three investigators (A.L., D.A.R., J.E.B.-C.), who independently reviewed the wording and categorized them as strong recommendations: class I (benefit clearly outweighs risk) or class III (no benefit, not helpful, harmful); or weak recommendations: class II (benefit closely balanced with risks).[20] Figure A1 shows the phrases used to map recommendations to the American College of Cardiology/American Heart Association strength of recommendations using either the GRADE or American College of Cardiology/American Heart Association classification system. For example, class I recommendations are those for which there is evidence and general agreement that the treatment is useful or effective. These are presented with terms such as "should," "is recommended," "is indicated," and "is useful/effective/beneficial." Agreement between the evaluators was achieved by consensus as per the Cochrane Handbook for Systematic Reviews.[14]

Risk of Bias in Individual Studies

All documents included were assessed independently by three reviewers using the Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument.[21] AGREE II is a framework for assessing the quality of guidelines that AGREE II defines "as the confidence the potential biases of guideline development have been addressed adequately."[21,22] Upon completing the 23 items of the AGREE II instrument, the reviewers made a judgment

Table 1. Definitions of Level of Evidence and Strength of Recommendations

	American College of Cardiology/American Heart Association	Grading of Recommendations Assessment, Development, and Evaluation (GRADE)[18,19]
Level of evidence		
A	Data derived from multiple randomized clinical trials or meta-analysis	Well performed randomized controlled trials or overwhelming evidence of some other form; further research unlikely to change our confidence in the estimate of benefit and risk
B	Data derived from a single randomized clinical trial or nonrandomized studies	Evidence from randomized controlled trials with important limitations (inconsistent results, methodologic flaws, indirect, or imprecise) or very strong evidence of some other form; further research (if performed) likely to have an impact on our confidence in the estimate of benefit and risk and may change the estimate
C	Only consensus opinion of experts, case studies or standard of care	Evidence from observational studies, unsystematic clinical experience, or from randomized controlled trials with serious flaws; any estimate of effect uncertain
Strength		
Strong	Class I = benefit clearly outweighs risk; recommendations use the terminology "should," "is recommended," "is indicated," "is useful," "is effective," or "is beneficial" Class III = no benefit, not helpful, or harmful; recommendations use the terminology "is not recommended," "is not indicated," should not be performed," should not be administered," "is not useful," "is not beneficial," "is not effective," "potentially harmful," or "causes harm"	Benefits clearly outweigh risk and burdens or vice versa. Should use the terminology "We recommend..." or "we do not recommend"
Weak	Class II = benefit outweighs risk but additional studies with focused objectives are needed; benefit closely balanced with risks Recommendations use the terminology "is reasonable," "can be useful," "can be effective," "can be beneficial," "is probably recommended," "is probably indicated," "may/might be considered," "may/might be reasonable," "usefulness/effectiveness is unknown," or "not well established"	Benefits closely balanced with risks and burdens Weak recommendations should use less definitive wording, such as "We suggest..."

about the quality of the guideline considering the criteria in the assessment process. A threshold of 70% in the overall assessment was used to identify highest quality guidelines with lowest risk of bias. This threshold was decided by consensus among the authors.[21,23]

Analysis

Descriptive Analysis. We first report the proportion of recommendations supported by levels of evidence A, B, and C. We then report the proportion of recommendations supported by levels of evidence A, B, and C stratified by the strength of the recommendation (strong *versus* weak), by classification system (GRADE, American College of Cardiology/American Heart Association), and by specialty (general, cardiovascular, obstetric, pediatric, acute pain, regional, and neuroanesthesia). For simplicity of presentation, the term "general" is used to define nonspecialty care. We used multinomial logistic regression modeling, only including intercept terms, to compare the proportion of recommendations supported by level of evidence A *versus* level of evidence C and the number supported by level of evidence B *versus* level of evidence C.

Statistical Analysis. Bivariate multinomial logistic regression was used to separately examine the association between the quality of evidence supporting clinical practice guidelines and (1) subspecialty, (2) strength of recommendation (strong *versus* weak), (3) region (the United States, Europe, or multinational), (4) methodology used for grading the quality of the evidence (American College of Cardiology/American Heart Association or GRADE), and (5) risk of bias (defined as an overall score of less than 70% or greater than or equal to 70% [where a higher score indicates a lower risk of bias] on AGREE II). The dependent variable was specified as a categorical indicator: level of evidence A, B, or C.

We then examined whether the quality of evidence supporting clinical practice guidelines changed over time using multinomial logistic regression. The analytic sample included all general guidelines that were revised (519 previous recommendations and 590 revised recommendations). We excluded subspecialty guidelines because very few subspecialty guidelines were updated. The dependent variable was specified as a categorical indicator variable: level of evidence A, B, or C. The key independent variable indicated whether a recommendation was included in the original guideline or the revised guideline. We estimated an unadjusted model in the main analysis. We then performed a sensitivity analysis in which we estimated a nonparsimonious multivariable model adjusting for subspecialty, strength of recommendation (strong *versus* weak), region (the United States, Europe, or multinational), and the methodology used for grading the quality of the evidence (American College of Cardiology/American Heart Association or GRADE). We did not adjust for AGREE II because it did not have a clinically meaningful effect size in the descriptive bivariate analyses. Next, we performed a secondary analysis based on the complete set of recommendations including previous versions of revised guidelines (2,280 recommendations from current guidelines and 580 recommendations from previous guidelines that had been revised). The key independent variable was the year in which a guideline was published, specified as a continuous variable. As above, we also performed a sensitivity analysis which adjusted for subspecialty, strength of recommendation (strong *versus* weak), region (the United States, Europe, or multinational), and the methodology used for grading the quality of the evidence (American College of Cardiology/American Heart Association or GRADE).

The use of multinomial logistic regression was not prespecified in our published protocol. We chose this approach instead of logistic regression to avoid the loss of information that would occur if we collapsed the three levels of evidence (levels of evidence A, B, and C) into two categories (level of evidence A and B *versus* level of evidence C). We selected multinomial logistic regression instead of ordered logistic regression because the parallel regression assumption in ordered logistic regression is rarely met.[24]

All analyses were performed using STATA 16.1 (StataCorp, USA). Because recommendations within the same guideline may not be independent, we used cluster robust variance estimators using the guideline as the unit of clustering.[25] Findings are reported as relative risk ratios. Two-sided P values of less than 0.05 are reported as statistically significant.

No statistical power calculation was conducted before the study. The sample size was based on the available data.

Results

Study Selection and Characteristics

We found 7,808 citations, of which we reviewed 271 in full text, and included 70 documents (60 guidelines with 2,280 recommendations) for data extraction (fig. A2; table 2). Overall, 29 guidelines were developed in the United States, 15 guidelines in Europe, and 16 in both. Sixteen of the guidelines were developed by or in collaboration with the American Society of Anesthesiologists (Schaumburg, Illinois) and ten of the guidelines were developed by or in collaboration with the European Society of Anesthesiology (Brussels, Belgium). Of the 2,280 recommendations, 60% were addressed toward general anesthesiology practice: 22% (511) to cardiovascular anesthesia, 6% (140) to regional anesthesia and acute pain, 5% (123) to obstetric anesthesia, 4% (93) to pediatric anesthesia, and 2% (51) to neuroanesthesia.

Level of Evidence Supporting Recommendations

We mapped the level of evidence in individual guidelines to that used by the American College of Cardiology/American Heart Association and GRADE systems (see table 1 for definitions). Level of evidence A supported 16% (363 of 2,280) of recommendations, level of evidence B supported 33% (757 of 2,280), and level of evidence C supported 51% (1,160 of 2,280). When assessing only strong recommendations, 19% (288 of 1,506) were supported by level of evidence A, 31% by level of evidence B (462 of 1,506), and 50% (756 of 1,506) by level of evidence C evidence (fig. 1). After stratifying this analysis by the classifying system (GRADE *versus* American College of Cardiology/American Heart Association), we found that the distribution of levels of evidence was qualitatively similar to the above (fig. 1).

Risk of Bias within Clinical Practice Guidelines

The scores of the AGREE II domains for each of the clinical practice guidelines are shown in table 2. Forty-four of the clinical practice guidelines (73%) exceeded the threshold score of 70% (table 3). Recommendations with a low risk of bias (AGREE II score greater than or equal to 70%) were not more likely to be supported by level of evidence A *versus* level of evidence C compared to recommendations with a higher risk of bias (relative risk ratio, 0.91; 95% CI, 0.32 to 2.57; $P = 0.857$; fig. 3a). Recommendations with a low risk of bias were also not more likely to be supported by level of evidence B *versus* level of evidence C compared to recommendations with a higher risk of bias (incidence-rate ratio, 1.05; 95% CI, 0.53 to 2.06; $P = 0.897$; fig. 3b).

Level of Evidence Supporting Recommendations Stratified by Subspecialty

Figure 2 depicts the distribution of levels of evidence across the different subspecialties stratified by the level of evidence classification system (GRADE *versus* American College of Cardiology/American Heart Association). Neuroanethesia (relative risk ratio, 0.06; 95% CI, 0.02 to 0.21; $P < 0.001$) and regional (relative risk ratio, 0.37; 95% CI, 0.20 to 0.68; $P = 0.001$) were less likely to be associated with level of evidence A *versus* level of evidence C compared to general (fig. 3, a and b). Recommendations in clinical practice guidelines for cardiovascular anesthesia were more likely to be associated with level of evidence B *versus* level of evidence C (relative risk ratio, 1.87; 95% CI, 1.02 to 3.43; $P = 0.043$) compared to general (fig. 3, a and b). Acute pain (relative risk ratio, 0.32; 95% CI, 0.11 to 0.97; $P = 0.044$), obstetrics (relative risk ratio, 0.29; 95% CI, 0.11 to 0.82; $P = 0.019$), and regional (relative risk ratio, 0.33; 95% CI, 0.22 to 0.49; $P < 0.001$) were less likely to be associated with level of evidence B *versus* level of evidence C compared to general (fig. 3, a and b).

Table 2. Descriptive Characteristics of Guidelines Included in the Analysis

Region	Society	Evidence Grading System	Comparable Grading System	Targeted Population	N	Authors and Year
Europe	ESA	ESC	ACC/AHA	Patients receiving regional anesthesia (and antithrombotic)	58	Gogarten *et al.* 2010[28]
Europe	ESA	SIGN	ACC/AHA	Perioperative patients	13	Smith *et al.* 2011[29]
Europe	ESC/ESA	AHA	ACC/AHA	Noncardiac surgery: cardiovascular assessment and management	121	Kristensen *et al.* 2014[30]
Europe	ESA	Level of evidence of the literature	ACC/AHA	Patients with postoperative delirium	40	Aldecoa *et al.* 2017[31]
Europe	ESA	GRADE	GRADE	Postoperative patients (severe bleeding)	161	Kozek-Langenecker *et al.* 2017[32]
Europe	ESC	ACC/AHA	ACC/AHA	Patients with cardiovascular diseases during pregnancy	13	Regitz-Zagrosek *et al.* 2018[33]
Europe	ESA	GRADE	GRADE	Perioperative venous thromboembolism prophylaxis	11	Ahmed *et al.* 2018[34]
				Perioperative venous thromboembolism prophylaxis	14	Faraoni *et al.* 2018[35]
				Perioperative venous thromboembolism prophylaxis	10	Jenny *et al.* 2018[36]
				Perioperative venous thromboembolism prophylaxis	10	Llau *et al.* 2018[37]
				Perioperative venous thromboembolism prophylaxis	18	Venclauskas *et al.* 2018[38]
				Perioperative venous thromboembolism prophylaxis	5	Comes *et al.* 2018[39]
				Perioperative venous thromboembolism prophylaxis	8	Afshari *et al.* 2018[40]
				Perioperative venous thromboembolism prophylaxis	36	Ahmed *et al.* 2018[41]
				Perioperative venous thromboembolism prophylaxis	4	Ducloy-Bouthors *et al.* 2018[42]
				Perioperative venous thromboembolism prophylaxis	7	Kozek-Langenecker *et al.* 2018[43]
				Perioperative venous thromboembolism prophylaxis	7	Venclauskas *et al.* 2018[44]
Europe	ESA/EBA	GRADE	GRADE	Adult patients undergoing procedural sedation and analgesia	27	Hinkelbein *et al.* 2018[45]
Europe	ESA	GRADE	GRADE	Patients undergoing elective noncardiac surgery	119	De Hert *et al.* 2018[18]
Europe	EACTS/EACTA/EBCP	ACC/AHA	ACC/AHA	Adult patient undergoing cardiac surgery with cardiopulmonary bypass	51	Wahba *et al.* 2019[46]
Europe	ESA	GRADE	GRADE	Patients requiring ultrasound-guided vascular access	35	Lamperti *et al.* 2020[47]
Europe	ESA/ESICM	GRADE	GRADE	Perioperatively hypoxemic patients	17	Leone *et al.* 2020[48]
Europe	EACTS/EACTA	ACC/AHA	ACC/AHA	Adult patients undergoing cardiac surgery	45	Boer *et al.* 2018[49]
Europe	APAGBI	SIGN (Scottish intercollegiate Guidelines Network	ACC/AHA	Perioperative pediatric patients	30	Morgan *et al.* 2018[50]
Europe	Difficult Airway Society	Center for Evidence based Medicine	ACC/AHA	Patients undergoing awake tracheal intubation	76	Ahmad *et al.* 2019[51]
United States	ASA	ASA category, level, direction	ACC/AHA	Surgical patients and potential surgical patients in the setting of cardiac surgery, noncardiac surgery, and postoperative critical care; guidelines do not apply to the assessment of nonsurgical patients or to postdischarge follow-up assessment of surgical patients	11	American Society of Anesthesiologists 2010[52]
United States	ACC/AHA/AATS/ ACR/ASA/SCA/SCAI/SIR/STS/SVM	ACC/AHA	ACC/AHA	Patients with diseases involving any or all parts of the thoracic aorta with the exception of aortic valve diseases; includes the abdominal aorta when contiguous thoracic aortic diseases are present	23	Hiratzka *et al.* 2010[16]
United States	ACC/AHA	ACC/AHA	ACC/AHA	Patients undergoing coronary artery bypass graft	82	Hillis *et al.* 2012[17]
United States	ASA	ASA category, level, direction	ACC/AHA	Adult (including geriatric) and pediatric patients undergoing either inpatient or outpatient surgery	37	American Society of Anesthesiologists 2012[53]
United States	ACC/AHA	ASA category, level, direction	ACC/AHA	Adult and pediatric patients requiring vascular cannulation	11	Troianos *et al.* 2012[54]
United States	ASA	ASA category, level, direction	ACC/AHA	Patients of all ages who have received general anesthesia, regional anesthesia, or moderate or deep sedation	39	Apfelbaum *et al.* 2013[55]
United States	ASA	ASA category, level, direction	ACC/AHA	Patients with difficult airways	31	Apfelbaum *et al.* 2013[56]
United States	ACC/AHA, ACS, ASA, ASE, ASNC, HRS, SCA, STS	ACC/AHA	ACC/AHA	Patients undergoing noncardiac surgery	71	Fleisher *et al.* 2014[57]

(*Continued*)

Table 2. (Continued)

Region	Society	Evidence Grading System	Comparable Grading System	Targeted Population	N	Authors and Year
United States	ASA	ASA category, level, direction	ACC/AHA	Patients with obstructive sleep apnea	45	American Society of Anesthesiologists 2014[58]
United States	ASA	ASA category, level, direction	ACC/AHA	Perioperative management of patients undergoing surgery or other invasive procedures in which significant blood loss occurs or is expected	49	American Society of Anesthesiologists 2015[59]
United States	Society of Thoracic Surgeons, Society of Cardiovascular Anesthesiologists, and American Society of ExtraCorporeal Technology	ACC/AHA	ACC/AHA	Patients undergoing cardiopulmonary bypass	9	Engelman *et al.* 2015[60]
United States	American Pain Society, American Society of Regional Anesthesia and Pain Medicine, and ASA	GRADE	GRADE	Postoperative patients (pain)	32	Chou *et al.* 2016[61]
United States	ASA	ASA category, level, direction	ACC/AHA	Anesthetic management of pregnant patients during labor, nonoperative delivery, operative delivery, and selected aspects of postpartum care and analgesia	77	American Society of Anesthesiologists 2016[62]
United States	ASA	ASA category, level, direction	ACC/AHA	Patients receiving epidural or spinal opioids in inpatient	39	American Society of Anesthesiology 2016[63]
United States	SAS	GRADE	GRADE	Adult surgical patients scheduled for elective surgery,	18	Chung *et al.* 2016[64]
United States	ASA	ASA category, level, direction	ACC/AHA	Healthy patients of all ages undergoing elective procedures	21	American Society of Anesthesiologists 2017[65]
United States	Society for Neuroscience in Anesthesiology and Critical Care	ACC/AHA	ACC/AHA	Perioperative care of adult patients with external ventricular and lumbar drains	35	Lele *et al.* 2017[66]
United States	ACC, AHA, AATS, ASE, SCAI, SCA, STS	ACC/AHA	ACC/AHA	Patients with valvular heart disease	4	Nishimura *et al.* 2017[67]
United States	ASRA, AAP ASA	USPSTF modified for ASIPP	GRADE	Patients requiring intravenous ketamine for acute pain management	14	Schwenk *et al.* 2018[68]
United States	STS/SCA/AmSECT	ACC/AHA	ACC/AHA	Patients undergoing cardiopulmonary bypass surgery	17	Shore-Lesserson *et al.* 2018[69]
United States	ASA	ASA category, level, direction	ACC/AHA	Adults and children requiring administration of moderate sedation and analgesia.	71	American Society of Anesthesiologists 2018[70]
United States	STS	ACC/AHA	ACC/AHA	Patients needing anticoagulation for cardiopulmonary bypass	17	Shore-Lesserson *et al.* 2018[71]
United States	SASM	GRADE	GRADE	Patients with obstructive sleep apnea	11	Memtsoudis *et al.* 2018[72]
United States	ASRA	Level of evidence and strength of recommendation	ACC/AHA	Patients requiring neuraxial and peripheral regional anesthetic/analgesic blockade	90	Horlocker *et al.* 2018[73]
United States	AACE/ACE, TOS, ASM&BS, OMA, ASA	AACE G4GAC: Evidence Rating	ACC/AHA	Patients undergoing bariatric procedures	46	Mechanick *et al.* 2019[74]
United States	ASRA	AAOS Clinical Practice Guidelines and Systematic reviews methodology	ACC/AHA	Patients undergoing orthopedic surgical procedures	8	Fillingham *et al.* 2019[75]
United States	ASA	ASA category, level, direction	ACC/AHA	Patients undergoing elective central venous access procedures	57	American Society of Anesthesiology 2019[76]
United States	ASER	ASA category, level, direction	ACC/AHA	Patient at risk of presenting with postoperative nausea and vomiting	96	Gan *et al.* 2020[77]
United States	Society for Neuroscience in Anesthesiology and Critical Care	ACC/AHA	ACC/AHA	Patients at high risk for stroke during or after noncardiac surgery	40	Vlisides *et al.* 2020[78]
US-EU	ERAS	GRADE	GRADE	Patients undergoing cystectomy	10	Cerantola *et al.* 2013[79]
US-EU	ERAS	GRADE	GRADE	Patients undergoing gastrectomy	24	Mortensen *et al.* 2014[80]
US-EU	ERAS	GRADE	GRADE	Patients undergoing liver surgery	10	Melloul *et al.* 2016[81]
US-EU	ERAS	GRADE	GRADE	Patients undergoing bariatric surgery	22	Thorell *et al.* 2016[82]

(*Continued*)

Table 2. (Continued)

Region	Society	Evidence Grading System	Comparable Grading System	Targeted Population	N	Authors and Year
US-EU	ERAS	GRADE	GRADE	Patient undergoing lung surgery	27	Batchelor *et al.* 2018[83]
US-EU	ERAS	GRADE	GRADE	Patients undergoing cesarean section	4	Wilson *et al.* 2018[84]
US-EU	ERAS	GRADE	GRADE	Patients undergoing cesarean section	5	Caughey *et al.* 2018[85]
US-EU	ERAS	AHA	ACC/AHA	Patients undergoing cardiac surgery	11	Engelman *et al.* 2019[86]
US-EU	ERAS	GRADE	GRADE	Patients undergoing colorectal surgery	18	Gustafsson *et al.* 2019[87]
US-EU	ERAS	GRADE	GRADE	Patients undergoing esophagectomy	27	Low *et al.* 2019[88]
US-EU	ERAS	GRADE	GRADE	Patients undergoing gynecologic oncology surgery	16	Nelson *et al.* 2019[89]
US-EU	ERAS	GRADE	GRADE	Patients undergoing cesarean section	4	Macones *et al.* 2019[90]
US-EU	ERAS	GRADE	GRADE	Neonates undergoing intestinal surgery	10	Brindle *et al.* 2020[91]
US-EU	ERAS	GRADE	GRADE	Patients undergoing cytoreductive surgery	25	Hübner *et al.* 2020[92]
US-EU	ERAS	GRADE	GRADE	Patients undergoing vulvovaginal surgery	18	Altman *et al.* 2020[93]
US-EU	ERAS	GRADE	GRADE	Patients undergoing pancreatoduodenectomy surgery	12	Melloul *et al.* 2020[94]

AACE, American Association of Clinical Endocrinologists; AAOS, American Academy of Orthopaedic Surgeons; AAP, American Academy of Pediatrics; AATS, American Association for Thoracic Surgery; ACC, American College of Cardiology; ACR, American College of Radiology; AHA, American Heart Association; AmSECT, American Society of Extracorporeal Technology; APAGBI, Association of Pediatric Anaesthetists of Great Britain and Ireland; ASA, American Society of Anesthesiologists; ASE, American Society of Echocardiography; ASER, American Society for Enhanced Recovery; ASM&BS; American Society of Metabolic and Bariatric Surgery; ASNC, American Society of Nuclear Cardiology; ASRA, American Society of Regional Anesthesia and Pain Medicine; EACTS, European Association for Cardio-Thoracic Surgery; EACTA, European Association of Cardiothoracic Anaesthesiologists; EBA, European Board of Anesthesiology; EBCP, European Board of Cardiovascular Perfusion; ERAS, Enhanced Recovery after Surgery; ESA, European Society of Anesthesiology; ESC, European Society of Cardiology; ESICM, European Society of Intensive Care Medicine; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; HRS, Heart Rhythm Society; OMA, Obesity Medicine Association; SASM, Society of Anesthesia and Sleep Medicine; SCA, Society of Cardiovascular Anesthesiologists; SCAI, Society of Cardiovascular Angiography and Interventions; SIGN, Scottish intercollegiate Guidelines Network; SIR, Society of Interventional Radiology; STS, Society of Thoracic Surgeons; SVM, Society for Vascular Medicine; US-EU, United States and Europe; USPSTF, U.S. Preventive Services Task Force.

Strength of Recommendation

Compared to weak recommendations, strong recommendations were not significantly more likely to be associated with level of evidence A *versus* level of evidence C (relative risk ratio, 2.05; 95% CI, 0.93 to 4.55; $P = 0.077$), or level of evidence B *versus* level of evidence C (relative risk ratio, 0.84; 95% CI, 0.54 to 1.29; $P = 0.419$).

Regional Differences

There were 29 U.S. guidelines, 15 European guidelines (25 documents), and 16 multinational Enhanced Recovery after Surgery guidelines (the United States and Europe; fig. A1). Recommendations that were jointly developed in the United States and Europe were more likely to be supported by (1) level of evidence A *versus* level of evidence C (relative risk ratio, 4.63; 95% CI, 2.09 to 10.3; $P < 0.001$) and (2) level of evidence B *versus* level of evidence C (relative risk ratio, 3.06; 95% CI, 1.57 to 5.96; $P = 0.001$) compared to U.S. guidelines.

Methodology Used to Grade Level of Evidence: American College of Cardiology/American Heart Association *versus* GRADE

Using GRADE to classify level of evidence was not significantly associated with level of evidence A *versus* level of evidence C (relative risk ratio, 0.98; 95% CI, 0.41 to 2.36; $P = 0.961$) or level of evidence B *versus* level of evidence C (relative risk ratio, 1.45; 95% CI, 0.79 to 2.65; $P = 0.231$) compared to the American College of Cardiology/American Heart Association methodology.

Temporal Trends

Recommendations in revised guidelines were not more likely to be supported by level of evidence A *versus* level of evidence C (relative risk ratio, 0.93; 95% CI, 0.18 to 4.74; $P = 0.933$) compared to recommendations in the original guidelines. Recommendations in revised guidelines were also not more likely to be associated with level of evidence B *versus* level of evidence C (relative risk ratio, 1.63; 95% CI, 0.72 to 3.72; $P = 0.243$). In the sensitivity analysis in which we adjusted for recommendation strength, region, and methodology, recommendations in the revised guidelines were also not more likely to be supported by level of evidence A *versus* level of evidence C (relative risk ratio, 1.08; 95% CI, 0.24 to 4.88; $P = 0.921$) or level of evidence B *versus* level of evidence C (relative risk ratio, 2.08; 95% CI, 0.92 to 4.69; $P = 0.077$) compared to recommendations in the original guidelines (fig. 4). In the secondary analysis based on the complete set of recommendations (including previous versions of revised guidelines), the publication year was not associated with the level of evidence supporting the recommendations for either level of evidence A *versus*

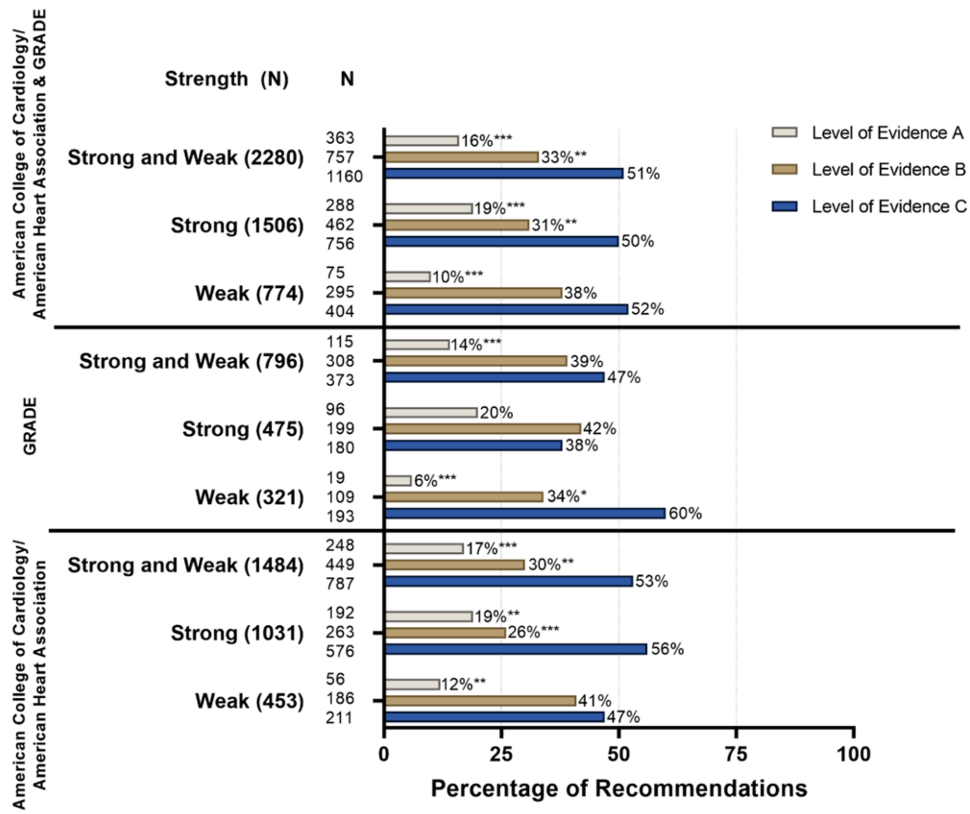

Fig. 1. Level of evidence for recommendations stratified by the grading system and strength of the recommendation. Each *bar* represents the percentage of recommendations supported by levels of evidence A, B, or C. Because all percentages were rounded to whole numbers, the sum of will not be exactly 100% in all cases. The *P* values for level of evidence A *versus* level of evidence C, and level of evidence B *versus* level of evidence C are based on multinomial logistic regression with intercept term only. $*P < 0.05$; $**P < 0.01$; $***P < 0.001$. *N* = number of recommendations. In the American College of Cardiology/American Heart Association, level of evidence A includes evidence from multiple randomized controlled trials or meta-analysis, level of evidence B includes evidence from a single randomized controlled trial or observational studies, and level of evidence C includes evidence from case reports and expert opinion.[4,20] In the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system, level of evidence A includes well performed randomized controlled trials or overwhelming evidence of some other form, level of evidence B includes evidence from randomized controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise) or very strong evidence of some other form, and level of evidence C includes evidence from observational studies, unsystematic clinical experience, or randomized controlled trials with serious flaws.[18,19]

level of evidence C (relative risk ratio, 1.07; 95% CI, 0.93 to 1.23; $P = 0.340$) or level of evidence B *versus* level of evidence C (relative risk ratio, 1.05; 95% CI, 0.96 to 1.15; $P = 0.283$). The results of the sensitivity analysis in which we adjusted for recommendation strength, region, and methodology are shown in figure A3 (a and b).

Discussion

In this systematic review of clinical practice guidelines developed by anesthesiology societies from the United States and Europe, only 16% of all recommendations were supported by a high level of evidence (level of evidence A). In total, 51% of recommendations were supported by a low level of evidence (level of evidence C). More strikingly, 50% of all strong recommendations were also only supported by a low level of evidence. The proportion of recommendations supported by level of evidence A or B did not increase over time compared to level of evidence C. Finally, recommendations in multinational guidelines were four times more likely to be supported by level of evidence A than recommendations in U.S. guidelines.

Previous studies have also evaluated the level of evidence supporting recommendations in clinical practice guidelines published by other medical organizations such as the American Heart Association, the American College of Cardiology, the European Society of Cardiology (Sophia Antipolis, France), the Society for Critical Care Medicine (Mount Prospect, Illinois), and the American College of Obstetricians and Gynecologists (Washington, D.C.).[5–8,95,96] In common with anesthesiology, most of the

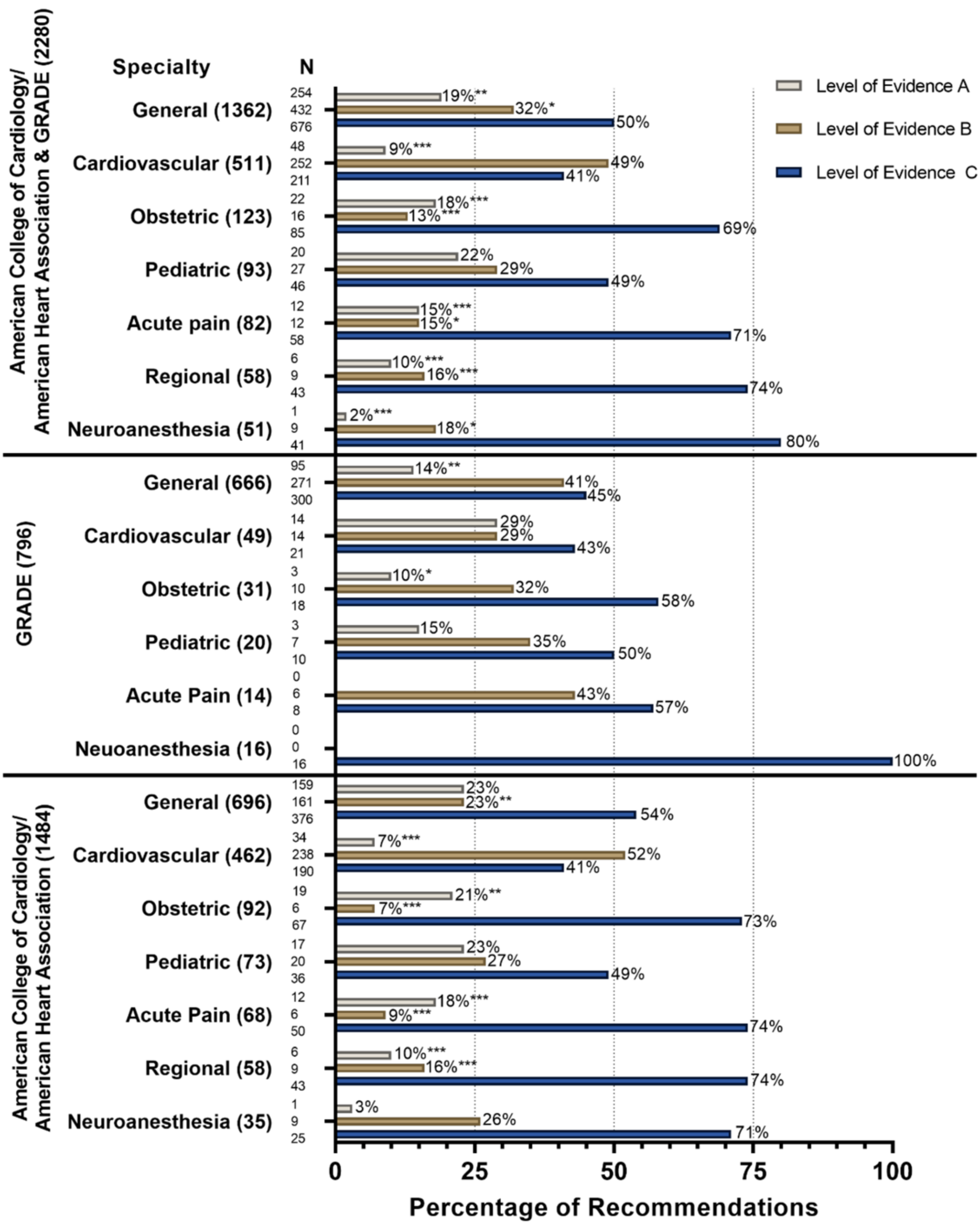

Fig. 2. Level of evidence for recommendations stratified by subspecialty. Each *bar* represents the percentage of recommendations supported by levels of evidence A, B, or C. N = number of recommendations. The *P* values for level of evidence A *versus* level of evidence C, and level of evidence B *versus* level of evidence C are based on multinomial logistic regression with intercept term only.*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$. In the American College of Cardiology/American Heart Association system, level of evidence A includes evidence from multiple randomized controlled trials or meta-analysis, level of evidence B includes evidence from a single randomized controlled trial or observational studies, and level of evidence C includes evidence from case reports and expert opinion.[4,20] In the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system, level of evidence A includes well performed randomized controlled trials or overwhelming evidence of some other form, level of evidence B includes evidence from randomized controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise) or very strong evidence of some other form, and level of evidence C includes evidence from observational studies, unsystematic clinical experience, or from randomized controlled trials with serious flaws.[18,19] All percentages were rounded to whole numbers; therefore the addition of the individual percentages can give more or less than 100%.

Table 3. Quality Assessment of Guidelines Using AGREE II

	Scope and Purpose	Stakeholder Involvement	Rigor of Development	Clarity of Presentation	Applicability	Editorial Independence	Overall	Recommended
2011 ACC/AHA guideline for coronary artery bypass graft surgery: report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines; developed in collaboration with the American Association for Thoracic Surgery, Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons[17]	100.0	64.87	91.7	98.1	77.8	100.0	94.4	Yes
2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines; developed in collaboration with the American College of Surgeons, American Society of Anesthesiologists, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, and Society for Cardiovascular Angiography and Interventions[57]	100.0	74.1	80.6	96.3	44.4	100.0	88.9	Yes
2014 ESC/ESA guidelines on noncardiac surgery: cardiovascular assessment and management: Joint Task Force on noncardiac surgery: cardiovascular assessment and management of the ESC and the ESA[30]	98.1	61.1	61.8	94.4	63.9	97.2	88.9	Yes
2018 ESC guidelines for the management of cardiovascular diseases during pregnancy[33]	96.3	63.0	70.8	96.3	59.7	97.2	83.3	Yes
2019 EACTS/EACTA/EBCP guidelines on cardiopulmonary bypass in adult cardiac surgery[46]	98.1	64.8	83.3	98.1	50.0	100.0	83.3	Yes
Clinical practice guidelines for the perioperative nutrition, metabolic, and nonsurgical support of patients undergoing bariatric procedures: 2019 Update: cosponsored by American Association of Clinical Endocrinologists/American College of Endocrinology, Obesity Society, American Society for Metabolic and Bariatric Surgery, Obesity Medicine Association, and American Society of Anesthesiologists[74]	96.3	72.2	70.1	94.4	48.6	80.6	66.7	Yes
Consensus guidelines for enhanced recovery after gastrectomy: ERAS Society recommendations[80]	88.9	50.0	66.0	94.4	33.3	80.6	66.7	Yes
Consensus guidelines for perioperative care in neonatal intestinal surgery: ERAS Society recommendations[91]	96.3	75.9	75.0	96.3	48.6	88.9	83.3	Yes
Consensus guidelines on the use of intravenous ketamine infusions for acute pain management from the American Society of Regional Anesthesia and Pain Medicine, the American Academy of Pain Medicine, and the American Society of Anesthesiologists[68]	90.7	59.3	68.1	90.7	38.9	80.6	66.7	Yes
Difficult Airway Society guidelines for awake tracheal intubation in adults[51]	96.3	83.3	84.0	83.3	55.6	100.0	77.8	Yes
European guidelines on perioperative venous thromboembolism prophylaxis[26]	96.3	51.9	63.2	88.9	27.8	97.2	77.8	Yes
European Society of Anesthesiology and European Board of Anesthesiology guidelines for procedural sedation and analgesia in adults[45]	98.1	55.6	78.5	90.7	30.6	100.0	72.2	Yes
European Society of Anesthesiology evidence-based and consensus-based guideline on postoperative delirium[31]	100.0	59.3	84.0	90.7	77.8	100.0	83.3	Yes
European Society of Anesthesiology guidelines on perioperative use of ultrasound-guided for vascular access (PERSEUS vascular access)[47]	96.3	59.3	88.2	98.1	68.1	100.0	88.9	Yes
Fourth consensus guidelines for the management of postoperative nausea and vomiting[77]	100.0	61.1	63.2	70.4	54.2	94.4	77.8	YWM
Guidelines for antenatal and preoperative care in cesarean delivery: Enhanced Recovery After Surgery Society recommendations (part 1)[84]	70.4	50.0	66.7	90.7	40.3	66.7	72.2	YWM
Guidelines for enhanced recovery after lung surgery: recommendations of the ERAS Society and the European Society of Thoracic Surgeons[83]	77.8	50.0	57.6	92.6	36.1	69.4	72.2	YWM
Guidelines for intraoperative care in cesarean delivery: Enhanced Recovery After Surgery Society recommendations (part 2)[85]	70.4	44.4	60.4	88.9	41.7	83.3	72.2	Yes
Guidelines for performing ultrasound-guided vascular cannulation: recommendations of the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists[54]	85.2	57.4	75.7	81.5	47.2	77.8	66.7	Yes
Guidelines for perioperative care after radical cystectomy for bladder cancer: ERAS Society recommendations[79]	79.6	55.6	66.7	87.0	40.3	100.0	72.2	Yes
Guidelines for perioperative care for liver surgery: ERAS Society recommendations[81]	77.8	53.7	72.9	88.9	26.4	77.8	66.7	Yes
Guidelines for perioperative care for pancreaticoduodenectomy: ERAS Society recommendations[94]	77.8	57.4	73.6	88.9	31.9	75.0	72.2	Yes
Guidelines for perioperative care in bariatric surgery: ERAS Society recommendations[82]	75.9	53.7	77.8	90.7	45.8	100.0	77.8	Yes

(*Continued*)

Table 3. (Continued)

	Scope and Purpose	Stakeholder Involvement	Rigor of Development	Clarity of Presentation	Applicability	Editorial Independence	Overall	Recommended
Guidelines for perioperative care in cardiac surgery: Enhanced Recovery After Surgery Society recommendations[86]	68.5	53.7	76.4	87.0	40.3	70.8	77.8	Yes
Guidelines for perioperative care in elective colorectal surgery: ERAS Society recommendations 2018[87]	77.8	55.6	68.1	85.2	47.2	75.0	72.2	YWM
Guidelines for perioperative care In Esophagectomy: ERAS Society recommendations[88]	74.1	53.7	63.9	87.0	50.0	75.0	66.7	Yes
Guidelines for perioperative care in gynecologic/oncology: ERAS Society recommendations–2019 update[89]	75.9	50.0	68.1	81.5	50.0	100.0	72.2	Yes
Guidelines for postoperative care in cesarean delivery: ERAS Society recommendations (part 3)[90]	83.3	46.3	59.0	87.0	48.6	55.6	66.7	Yes
Guidelines for vulvar and vaginal surgery: ERAS Society recommendations[93]	75.9	46.3	63.2	87.0	27.8	80.6	66.7	YWM
Management of postoperative pain: A clinical practice guideline from the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia[61]	85.2	61.1	95.8	90.7	43.1	100.0	77.8	YWM
Management of severe perioperative bleeding: Guidelines from the European Society of Anaesthesiology[32]	83.3	53.7	88.2	92.6	50.0	100.0	77.8	Yes
Noninvasive respiratory support in the hypoxemic perioperative/periprocedural patient: A joint ESA/ESICM guideline[48]	96.3	57.4	82.6	94.4	33.3	97.2	83.3	YWM
Perioperative care of patients at high risk for stroke during or after noncardiac, nonneurologic Surgery: 2020 guidelines from the Society for Neuroscience in Anesthesiology and Critical Care[78]	87.0	64.8	75.0	92.6	26.4	83.3	83.3	Yes
Perioperative fasting in adults and children: Guidelines from the European Society of Anesthesiology[29]	66.7	59.3	75.7	90.7	27.8	100.0	66.7	Yes
Perioperative management of adult patients with external ventricular and lumbar drains: Guidelines from the Society for Neuroscience in Anesthesiology and Critical Care[66]	87.0	64.8	71.5	92.6	20.8	80.6	77.8	Yes
Practice guidelines for central venous access 2020: An updated report by the American Society of Anesthesiologists Task Force on Central Venous Access[76]	90.7	61.1	78.5	92.6	52.8	94.4	77.8	YWM
Practice guidelines for management of the difficult airway: An updated report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway[56]	85.2	57.4	72.9	90.7	44.4	61.1	72.2	Yes
Practice guidelines for moderate procedural sedation and analgesia 2018: A report by the American Society of Anesthesiologists Task Force on Moderate Procedural Sedation and Analgesia, the American Association of Oral and Maxillofacial Surgeons, American College of Radiology, American Dental Association, American Society of Dentist Anesthesiologists, and Society of Interventional Radiology[70]	100.0	66.7	80.6	88.9	55.6	80.6	77.8	YWM
Practice guidelines for obstetric anesthesia: An updated report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia and the Society for Obstetric Anesthesia and Perinatology[62]	100.0	66.7	79.2	92.6	56.9	88.9	72.2	Yes
Practice guidelines for perioperative blood management: An updated report by the American Society of Anesthesiologists Task Force on Perioperative Blood Management[59]	100.0	66.7	81.3	96.3	61.1	88.9	83.3	Yes
Practice guidelines for perioperative transesophageal echocardiography: An updated report by the American Society of Anesthesiologists and the Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography[52]	100.0	66.7	79.2	88.9	50.0	55.6	72.2	YWM
Practice guidelines for postanesthetic care: An updated report by the American Society of Anesthesiologists Task Force on Postanesthetic Care[55]	100.0	66.7	78.5	90.7	45.8	55.6	72.2	YWM
Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: Application to healthy patients undergoing elective procedures: An updated report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters[65]	87.0	59.3	70.8	90.7	52.8	77.8	72.2	YWM
Practice guidelines for the perioperative management of patients with obstructive sleep apnea: An updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea[58]	100.0	66.7	79.9	92.6	44.4	88.9	77.8	Yes

(*Continued*)

Table 3. (Continued)

	Scope and Purpose	Stakeholder Involvement	Rigor of Development	Clarity of Presentation	Applicability	Editorial Independence	Overall	Recommended
Practice guidelines for the prevention, detection, and management of respiratory depression associated with neuraxial opioid administration: An updated report by the American Society of Anesthesiologists Task Force on Neuraxial Opioids and the American Society of Regional Anesthesia and Pain Medicine[63]	100.0	66.7	79.2	90.7	44.4	100.0	77.8	YWM
Prevention of perioperative venous thromboembolism in pediatric patients: Guidelines from the APAGBI[50]	92.6	64.8	77.1	94.4	16.7	97.2	72.2	YWM
Regional anesthesia and antithrombotic agents: recommendations of the ESA[28]	64.8	46.3	47.2	75.9	29.2	77.8	55.6	YWM
Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine evidence-based guidelines (fourth edition)[73]	83.3	57.4	59.7	88.9	31.9	66.7	61.1	Yes
Society of Anesthesia and Sleep Medicine guideline on intraoperative management of adult patients with obstructive sleep apnea[72]	94.4	59.3	81.3	88.9	47.2	100.0	83.3	Yes
Society of Anesthesia and Sleep Medicine guidelines on preoperative screening and assessment of adult patients with obstructive sleep apnea[64]	94.4	61.1	80.6	92.6	63.9	94.4	88.9	Yes
STS/SCA/AmSECT Clinical Practice guidelines: Anticoagulation during cardiopulmonary bypass[69]	88.9	63.0	75.0	90.7	48.6	66.7	72.2	Yes
The Society of Thoracic Surgeons, the Society of Cardiovascular Anesthesiologists, and the American Society of ExtraCorporeal Technology: Clinical practice guidelines for cardiopulmonary bypass–Temperature management during cardiopulmonary bypass[60]	85.2	51.9	73.6	92.6	37.5	66.7	66.7	Yes
The Society of Thoracic Surgeons, the Society of Cardiovascular Anesthesiologists, and the American Society of ExtraCorporeal Technology: Clinical practice guidelines for cardiopulmonary bypass–Temperature management during cardiopulmonary bypass[60]	85.2	53.7	73.6	79.6	37.5	66.7	66.7	Yes
Tranexamic acid in total joint arthroplasty: Endorsed clinical practice guides of the American Association of Hip and Knee Surgeons, American Society of Regional Anesthesia and Pain Medicine, American Academy of Orthopaedic Surgeons, and Hip Society[75]	92.6	55.6	73.6	87.0	31.9	100.0	66.7	Yes
2010 ACC/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease: Executive summary: A report of the ACC, AHA, AATS, ACR, ASA, SCA, SCAI, SIR, STS, and SVM[16]	100.0	66.7	87.5	94.4	70.8	95.8	94.4	Yes
2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: A report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines[67]	92.6	61.1	83.3	90.7	43.1	97.2	88.9	Yes
2017 EACTS/EACTA guidelines on patient blood management for adult cardiac surgery[49]	87.0	57.4	73.6	81.5	36.1	83.3	66.7	YWM
Guidelines for perioperative care in cytoreductive surgery with or without hyperthermic IntraPEritoneal chemotherapy: ERAS Society recommendations – Part I: Preoperative and intraoperative management[92]	74.1	53.7	63.9	87.0	50.0	75.0	66.7	Yes
Practice guidelines for acute pain management in the perioperative setting: An updated report by the ASA task force on acute pain management[53]	100.0	66.7	80.2	94.4	79.2	75.0	83.3	Yes
Preoperative evaluation of adults undergoing elective noncardiac surgery: Updated guideline from the ESA[18]	96.3	63.0	80.6	92.6	52.8	100.0	88.9	Yes
Median	90.7	59.3	75.0	90.7	45.8	88.9	72.2	
25th quartile	80.6	53.7	68.1	87.5	36.1	75.0	66.7	
75th quartile	98.1	64.8	80.6	92.6	52.8	100.0	83.3	

AATS, American Association for Thoracic Surgery; ACC, American College of Cardiology; ACR, American College of Radiology; AHA, American Heart Association; AmSECT, American Society of Extracorporeal Technology; APAGBI, Association of Pediatric Anaesthetists of Great Britain and Ireland; ASA, American Society of Anesthesiologists; EACTS, European Association for Cardio-Thoracic Surgery; EACTA, European Association of Cardiothoracic Anaesthesiologists; EBCP, European Board of Cardiovascular Perfusion; ERAS, Enhanced Recovery after Surgery; ESA, European Society of Anesthesiology; ESC, European Society of Cardiology; ESICM, European Society of Intensive Care Medicine; SCA, Society of Cardiovascular Anesthesiologists; SCAI, Society of Cardiovascular Angiography and Interventions; SIR, Society of Interventional Radiology; STS, Society of Thoracic Surgeons; SVM, Society for Vascular Medicine; YWM, yes with modifications.

recommendations from these medical specialties were also based on a low level of evidence instead of high-quality evidence. With the exception of the Infectious Disease Society of America (Arlington, Virginia), the reliance on expert opinion did not change over time.[95]

The large proportion of recommendations in anesthesia clinical practice guidelines based on low-quality evidence is a cause for concern. In the past, large clinical trials in perioperative medicine were uncommon compared to other fields such as cardiology.[97] However, the number of high-quality large clinical trials in perioperative medicine has increased markedly over the past 10 years. In particular, these clinical trials have focused on the use of aspirin, clonidine, and β-blockers in patients undergoing noncardiac surgery[98–100]; the safety of nitrous oxide[101]; the avoidance of general anesthesia in patients undergoing cancer surgery[102]; the safety of lower *versus* higher depth of anesthesia[103]; the use of the Bispectral Index to reduce awareness[104]; the cardioprotective effects of volatile anesthetics[105]; and transfusion triggers.[106] Despite this, there remain many important foundational questions that have yet to be answered. For example, although observational studies demonstrate a strong association between hypotension and end-organ damage,[100,107] we still lack a high level of evidence to support the specific mean arterial pressure target recently proposed in the Perioperative Quality Initiative consensus statement on intraoperative blood pressure.[108]

Our work and that of others demonstrate the extent to which clinical practice guidelines are based primarily on a

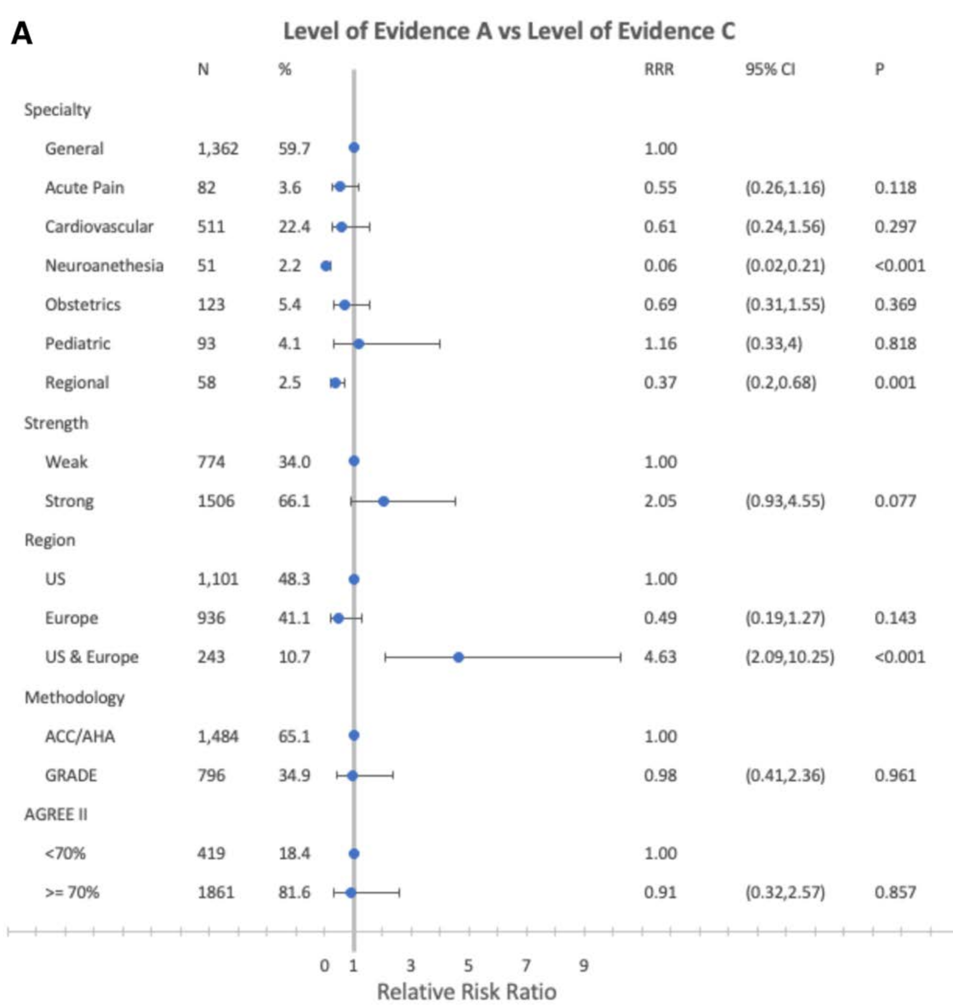

Fig. 3. (*A*) Results of bivariate analysis examining the association between recommendations supported by level of evidence A *versus* level of evidence C and specialty, strength of recommendation, and Appraisal of Guidelines for Research and Evaluation (AGREE) II score estimated using multinomial logistic regression. (*B*) Results of bivariate analysis examining the association between recommendations supported by level of evidence B *versus* level of evidence C and specialty, strength of recommendation, and AGREE II score estimated using multinomial logistic regression. (*Continued*)

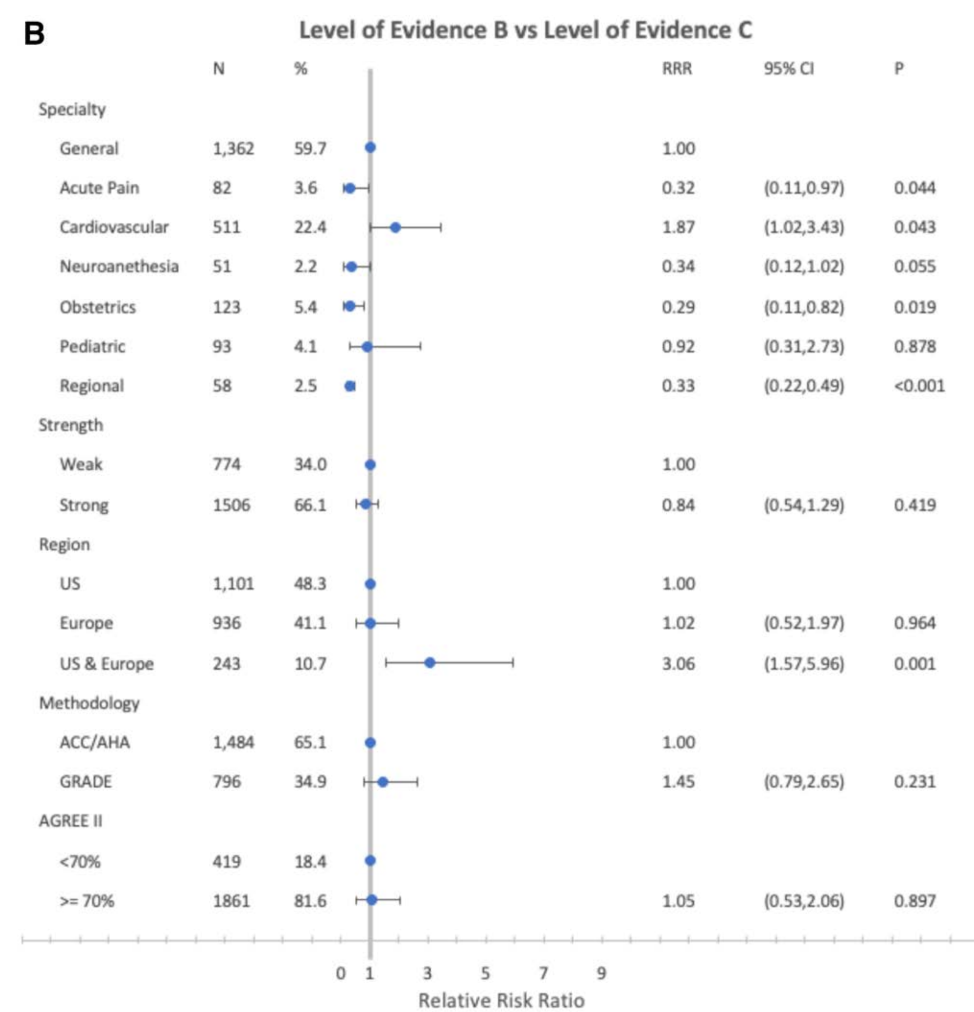

Fig. 3. (*Continued*)

low level of evidence. However, despite the recent increase in high-profile randomized clinical trials in perioperative medicine, randomized controlled trials will never replace lower levels of evidence because of cost considerations and time constraints.[109] Randomized controlled trials are expensive, usually taking several years to complete, and may lack external validity when study populations do not represent the population at large. Although drawing causal inferences from observational trials is generally discouraged because nonrandomized trials may not control for unknown prognostic factors,[110] there is frequently a good correlation between randomized and observational studies.[111,112]

In the absence of randomized clinical trials, many clinical questions may be addressed using well performed observational studies. Confounding bias, which is the main limitation of observational studies, can be reduced by using comprehensive databases that include most prognostic factors and (in some cases) through the use of statistical techniques such as propensity scoring, instrumental variable analysis, and inverse probability weighting. Well performed observational studies with very large effect sizes or large effect sizes can serve as level of evidence A or B, respectively, as defined by the GRADE methodology.[113] Our finding that over half of recommendations in clinical practice guidelines are based only on a low level of evidence should lead us to increase our efforts to conduct both robust randomized and observational studies. However, we should also recognize that some anesthesia best practices, such as pulse oximetry and capnography, are not supported by high levels of evidence but are nonetheless considered to be the foundation of anesthesia care. Finally, it is important to recognize that expert opinion can help guide clinical practice until the time when higher quality evidence becomes available.

Our study has several important limitations. First, our findings on the level of evidence supporting recommendations in anesthesiology clinical practice guidelines

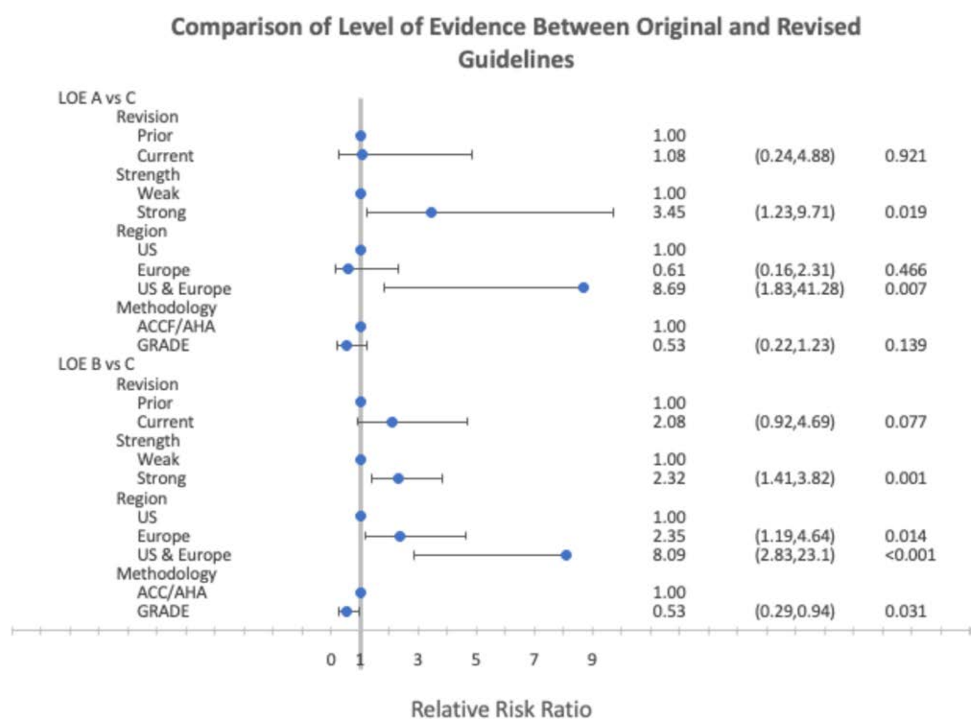

Fig. 4. Results of multivariable analysis of the level of evidence supporting recommendations in revised *versus* original guidelines controlling for strength of recommendation, region, and grading methodology using multinomial logistic regression.

developed by major anesthesiology societies in North America and Europe cannot be generalized to include all of the evidence base for anesthesiology and perioperative medicine. Second, anesthesiology clinical practice guidelines lacked a single uniform grading system for assigning levels of evidence and the strength of their recommendations. The American College of Cardiology/American Heart Association and GRADE systems use different criteria for the levels of evidence. For example, the American College of Cardiology/American Heart Association classifies recommendations as level of evidence C if they are based on expert opinion or case studies. GRADE, on the other hand, classifies evidence from observational studies or randomized controlled trials with serious flaws as level of evidence C. However, despite using two different classification systems, we still found that most guidelines were based on level of evidence C irrespective of which classification system was used. Third, for those guidelines that used grading systems that were similar but not identical to either the American College of Cardiology/American Heart Association or GRADE systems, we mapped their grading system to either American College of Cardiology/American Heart Association or GRADE to provide a standardized framework for categorizing the strengths of the recommendations and the levels of evidence. The risk of introducing bias in the mapping process was minimized by using multiple evaluators. Fourth, the American College of Cardiology/American Heart Association definitions for levels of evidence have changed slightly over time. We used the American College of Cardiology/American Heart Association level of evidence definitions presented in the seminal article by Tricoci *et al.*[4] because these definitions most closely approximated the approach used in guidelines that used a grading methodology similar to the American College of Cardiology/American Heart Association classification system. Finally, we excluded clinical practice guidelines that did not explicitly grade the levels of evidence to minimize the risk of misclassification of the levels of evidence. We also excluded consensus statements based on expert opinion only. Excluding the consensus statements may have led us to underestimate the proportion of recommendations based on level of evidence C.

Conclusions

In summary, less than one fifth of recommendations in anesthesiology clinical practice guidelines are supported by level of evidence A, and half of the recommendations are supported by level of evidence C. The quality of the evidence in anesthesiology clinical practice guidelines has not improved in the last 10 years. Given that death after surgery is a leading cause of death, our findings highlight the need to increase the number of well performed randomized and observational trials in perioperative medicine to lessen the reliance on low levels of evidence in anesthesia and perioperative medicine. To accomplish this, we need to increase National Institutes of Health investment in perioperative medicine and create a comprehensive research agenda to bring together anesthesiologists, surgeons, public health experts, and patients to improve perioperative outcomes.

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Competing Interests

The authors declare no competing interests.

Correspondence

Address correspondence to Dr. Glance: University of Rochester School of Medicine, Rochester, New York 14642. laurent_glance@urmc.rochester.edu. This article may be accessed for personal use at no charge through the Journal Web site, www.anesthesiology.org.

References

1. Bartels K, Karhausen J, Clambey ET, Grenz A, Eltzschig HK: Perioperative organ injury. ANESTHESIOLOGY 2013; 119:1474–89
2. Beecher HK, Todd DP: A study of deaths associated with anesthesia and surgery. Int Anesthesiol Clin 2007; 45:1–6
3. Li G, Warner M, Lang BH, Huang L, Sun LS: Epidemiology of anesthesia-related mortality in the United States, 1999–2005. ANESTHESIOLOGY 2009; 110:759–65
4. Tricoci P, Allen JM, Kramer JM, Califf RM, Smith SC Jr: Scientific evidence underlying the ACC/AHA clinical practice guidelines. JAMA 2009; 301:831–41
5. Fanaroff AC, Califf RM, Windecker S, Smith SC Jr, Lopes RD: Levels of evidence supporting American College of Cardiology/American Heart Association and European Society of Cardiology guidelines, 2008–2018. JAMA 2019; 321:1069–80
6. Sims CR, Warner MA, Stelfox HT, Hyder JA: Above the GRADE: Evaluation of guidelines in critical care medicine. Crit Care Med 2019; 47:109–13
7. Duarte-García A, Zamore R, Wong JB: The evidence basis for the American College of Rheumatology practice guidelines. JAMA Intern Med 2018; 178:146–8
8. Chauhan SP, Berghella V, Sanderson M, Magann EF, Morrison JC: American College of Obstetricians and Gynecologists practice bulletins: An overview. Am J Obstet Gynecol 2006; 194:1564–75
9. Laserna A, Rubinger D, Barahona JE, Williams MR, Wyrobek JA, Hasman L, Lustik SJ, Eaton MP, Glance LG: Levels of evidence supporting the North American and European perioperative care guidelines for anesthesiologists between 2010-2020. PROSPERO 2020:CRD42020202932. Available at: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020202932. Accessed July 1, 2020.
10. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group: Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. BMJ 2009; 339:b2535
11. Joshi GP, Benzon HT, Gan TJ, Vetter TR: Consistent definitions of clinical practice guidelines, consensus statements, position statements, and practice alerts. Anesth Analg 2019; 129:1767–70
12. SCImago: SJR: SCImago Journal and Country Rank [Portal]. Available at: https://www.scimagojr.com/journalrank.php?category=2703&area=2700&year=2019. Accessed September 1, 2020.
13. Abstrackr. Available at: http://abstrackr.cebm.brown.edu/. Accessed October 1, 2020.
14. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ WV: Cochrane Handbook for Systematic Reviews of Interventions, version 6.2. Cochrane, 2021. Available at: http://www.training.cochrane.org/handbook. Accessed October 1, 2020.
15. Boutron I, Page MJ, Higgins JP, Altman DG, Lundh A, Hróbjartsson A: Considering bias and conflicts of interest among the included studies, Cochrane Handbook for Systematic Reviews of Interventions. 2019. Available at: https://onlinelibrary.wiley.com/doi/abs/10.1002/9781119536604.ch7. Accessed September 1, 2020.
16. Hiratzka LF, Bakris GL, Beckman JA, Bersin RM, Carr VF, Casey DE Jr, Eagle KA, Hermann LK, Isselbacher EM, Kazerooni EA, Kouchoukos NT, Lytle BW, Milewicz DM, Reich DL, Sen S, Shinn JA, Svensson LG, Williams DM; American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines; American Association for Thoracic Surgery; American College of Radiology; American Stroke Association; Society

of Cardiovascular Anesthesiologists; Society for Cardiovascular Angiography and Interventions; Society of Interventional Radiology; Society of Thoracic Surgeons; Society for Vascular Medicine: 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the diagnosis and management of patients with thoracic aortic disease: Executive summary: A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. Anesth Analg 2010; 111:279–315

17. Hillis LD, Smith PK, Anderson JL, Bittl JA, Bridges CR, Byrne JG, Cigarroa JE, DiSesa VJ, Hiratzka LF, Hutter AM, Jessen ME, Keeley EC, Lahey SJ, Lange RA, London MJ, Mack MJ, Patel MR, Puskas JD, Sabik JF, Selnes O, Shahian DM, Trost JC, Winniford MD, American College of Cardiology Foundation, American Heart Association Task Force on Practice Guidelines: 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery. Anesth Analg 2012; 114:11–45
18. De Hert S, Staender S, Fritsch G, Hinkelbein J, Afshari A, Bettelli G, Bock M, Chew MS, Coburn M, De Robertis E, Drinhaus H, Feldheiser A, Geldner G, Lahner D, Macas A, Neuhaus C, Rauch S, Santos-Ampuero MA, Solca M, Tanha N, Traskaite V, Wagner G, Wappler F: Pre-operative evaluation of adults undergoing elective noncardiac surgery. Eur J Anaesthesiol 2018; 35:407–65
19. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, Schünemann HJ; GRADE Working Group: GRADE: An emerging consensus on rating quality of evidence and strength of recommendations. BMJ 2008; 336:924–6
20. Greenland P, Alpert JS, Beller GA, Benjamin EJ, Budoff MJ, Fayad ZA, Foster E, Hlatky MA, Hodgson JM, Kushner FG, Lauer MS, Shaw LJ, Smith SC Jr, Taylor AJ, Weintraub WS, Wenger NK, Jacobs AK; American College of Cardiology Foundation/American Heart Asscoiation Task Force on Practice Guidelines: 2010 ACCF/AHA guideline for assessment of cardiovascular risk in asymptomatic adults: Executive summary: A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation 2010; 122:2748–64
21. Brouwers MC, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, Fervers B, Graham ID, Grimshaw J, Hanna SE, Littlejohns P, Makarski J, Zitzelsberger L; AGREE Next Steps Consortium: AGREE II: Advancing guideline development, reporting and evaluation in health care. CMAJ 2010; 182:E839–42
22. AGREE Next Steps Consortium: The AGREE II Instrument, 2017. Available at: http://www.agreetrust.org. Accessed January 1, 2021.
23. Hoffmann-Eßer W, Siering U, Neugebauer EA, Brockhaus AC, Lampert U, Eikermann M: Guideline appraisal with AGREE II: Systematic review of the current evidence on how users handle the 2 overall assessments. PLoS One 2017; 12:e0174831
24. Long JS, Freese J: Stata Bookstore: Regression Models for Categorical Dependent Variables Using Stata, 3rd edition. College Station, Texas, Stata Press, 2014
25. Williams RL: A note on robust variance estimation for cluster-correlated data. Biometrics 2000; 56:645–6
26. Afshari A, Ageno W, Ahmed A, Duranteau J, Faraoni D, Kozek-Langenecker S, Llau J, Nizard J, Solca M, Stensballe J, Thienpont E, Tsiridis E, Venclauskas L, Samama CM; ESA VTE Guidelines Task Force: European guidelines on perioperative venous thromboembolism prophylaxis: Executive summary. Eur J Anaesthesiol 2018; 35:77–83
27. Duranteau J, Taccone FS, Verhamme P, Ageno W; ESA VTE Guidelines Task Force: European guidelines on perioperative venous thromboembolism prophylaxis: Intensive care. Eur J Anaesthesiol 2018; 35:142–6
28. Gogarten W, Vandermeulen E, Van Aken H, Kozek S, Llau JV, Samama CM; European Society of Anaesthesiology: Regional anaesthesia and antithrombotic agents: Recommendations of the European Society of Anaesthesiology. Eur J Anaesthesiol 2010; 27:999–1015
29. Smith I, Kranke P, Murat I, Smith A, O'Sullivan G, Søreide E, Spies C, in't Veld B; European Society of Anaesthesiology: Perioperative fasting in adults and children: Guidelines from the European Society of Anaesthesiology. Eur J Anaesthesiol 2011; 28:556–69
30. Kristensen SD, Knuuti J, Saraste A, Anker S, Bøtker HE, De Hert S, Ford I, Gonzalez-Juanatey JR, Gorenek B, Heyndrickx R, Hoeft A, Huber K, Iung B, Kjeldsen KP, Longrois D, Lüscher TF, Pierard L, Pocock S, Price S, Roffi M, Sirnes PA, Sousa-Uva M, Voudris V, Funck-Brentano C: 2014 ESC/ESA Guidelines on non-cardiac surgery: Cardiovascular assessment and management. Eur Heart J 2014; 35:2383–431
31. Aldecoa C, Bettelli G, Bilotta F, Sanders RD, Audisio R, Borozdina A, Cherubini A, Jones C, Kehlet H, MacLullich A, Radtke F, Riese F, Slooter AJ, Veyckemans F, Kramer S, Neuner B, Weiss B, Spies CD: European Society of Anaesthesiology evidence-based and consensus-based guideline on postoperative delirium. Eur J Anaesthesiol 2017; 34:192–214
32. Kozek-Langenecker SA, Ahmed AB, Afshari A, Albaladejo P, Aldecoa C, Barauskas G, De Robertis E, Faraoni D, Filipescu DC, Fries D, Haas T, Jacob M, Lancé MD, Pitarch

JVL, Mallett S, Meier J, Molnar ZL, Rahe-Meyer N, Samama CM, Stensballe J, Van der Linden PJF, Wikkelsø AJ, Wouters P, Wyffels P, Zacharowski K: Management of severe perioperative bleeding: Guidelines from the European Society of Anaesthesiology: First update 2016. Eur J Anaesthesiol 2017; 34:332–95
33. Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, Blomström-Lundqvist C, Cífková R, De Bonis M, Iung B, Johnson MR, Kintscher U, Kranke P, Lang IM, Morais J, Pieper PG, Presbitero P, Price S, Rosano GMC, Seeland U, Simoncini T, Swan L, Warnes CA; ESC Scientific Document Group: 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy. Eur Heart J 2018; 39:3165–241
34. Ahmed AB, Koster A, Lance M, Faraoni D; ESA VTE Guidelines Task Force: European guidelines on perioperative venous thromboembolism prophylaxis: Cardiovascular and thoracic surgery. Eur J Anaesthesiol 2018; 35:84–9
35. Faraoni D, Comes RF, Geerts W, Wiles MD; ESA VTE Guidelines Task Force: European guidelines on perioperative venous thromboembolism prophylaxis: Neurosurgery. Eur J Anaesthesiol 2018; 35:90–5
36. Jenny JY, Pabinger I, Samama CM; ESA VTE Guidelines Task Force: European guidelines on perioperative venous thromboembolism prophylaxis: Aspirin. Eur J Anaesthesiol 2018; 35:123–9
37. Llau JV, Kamphuisen P, Albaladejo P; ESA VTE Guidelines Task Force: European guidelines on perioperative venous thromboembolism prophylaxis: Chronic treatments with antiplatelet agents. Eur J Anaesthesiol 2018; 35:139–41
38. Venclauskas L, Llau JV, Jenny JY, Kjaersgaard-Andersen P, Jans Ø; ESA VTE Guidelines Task Force: European guidelines on perioperative venous thromboembolism prophylaxis: Day surgery and fast-track surgery. Eur J Anaesthesiol 2018; 35:134–8
39. Comes RF, Mismetti P, Afshari A; ESA VTE Guidelines Task Force: European guidelines on perioperative venous thromboembolism prophylaxis: Inferior vena cava filters. Eur J Anaesthesiol 2018; 35:108–11
40. Afshari A, Fenger-Eriksen C, Monreal M, Verhamme P; ESA VTE Guidelines Task Force: European guidelines on perioperative venous thromboembolism prophylaxis: Mechanical prophylaxis. Eur J Anaesthesiol 2018; 35:112–5
41. Ahmed A, Kozek-Langenecker S, Mullier F, Pavord S, Hermans C; ESA VTE Guidelines Task Force: European guidelines on perioperative venous thromboembolism prophylaxis: Patients with preexisting coagulation disorders and after severe perioperative bleeding. Eur J Anaesthesiol 2018; 35:96–107
42. Ducloy-Bouthors AS, Baldini A, Abdul-Kadir R, Nizard J; ESA VTE Guidelines Task Force: European guidelines on perioperative venous thromboembolism prophylaxis: Surgery during pregnancy and the immediate postpartum period. Eur J Anaesthesiol 2018; 35:130–3
43. Kozek-Langenecker S, Fenger-Eriksen C, Thienpont E, Barauskas G; ESA VTE Guidelines Task Force: European guidelines on perioperative venous thromboembolism prophylaxis: Surgery in the elderly. Eur J Anaesthesiol 2018; 35:116–22
44. Venclauskas L, Maleckas A, Arcelus JI; ESA VTE Guidelines Task Force: European guidelines on perioperative venous thromboembolism prophylaxis: Surgery in the obese patient. Eur J Anaesthesiol 2018; 35:147–53
45. Hinkelbein J, Lamperti M, Akeson J, Santos J, Costa J, De Robertis E, Longrois D, Novak-Jankovic V, Petrini F, Struys MMRF, Veyckemans F, Fuchs-Buder T, Fitzgerald R: European Society of Anaesthesiology and European Board of Anaesthesiology guidelines for procedural sedation and analgesia in adults. Eur J Anaesthesiol 2018; 35:6–24
46. Wahba A, Milojevic M, Boer C, De Somer FMJJ, Gudbjartsson T, van den Goor J, Jones TJ, Lomivorotov V, Merkle F, Ranucci M, Kunst G, Puis L, Alston P, Fitzgerald D, Nikolic A, Onorati F, Steen Rasmussen B, Svenmarker S: 2019 EACTS/EACTA/EBCP guidelines on cardiopulmonary bypass in adult cardiac surgery. Eur J Cardiothorac Surg 2020; 57:210–51
47. Lamperti M, Biasucci DG, Disma N, Pittiruti M, Breschan C, Vailati D, Subert M, Traškaitė V, Macas A, Estebe JP, Fuzier R, Boselli E, Hopkins P: European Society of Anaesthesiology guidelines on peri-operative use of ultrasound-guided for vascular access (PERSEUS vascular access). Eur J Anaesthesiol 2020; 37:344–76
48. Leone M, Einav S, Chiumello D, Constantin JM, De Robertis E, De Abreu MG, Gregoretti C, Jaber S, Maggiore SM, Pelosi P, Sorbello M, Afshari A; Guideline contributors: Noninvasive respiratory support in the hypoxaemic peri-operative/periprocedural patient: A joint ESA/ESICM guideline. Intensive Care Med 2020; 46:697–713
49. Boer C, Meesters MI, Milojevic M, Benedetto U, Bolliger D, Heymann C von, Jeppsson A, Koster A, Osnabrugge RL, Ranucci M, Ravn HB, Vonk ABA, Wahba A, Pagano D: 2017 EACTS/EACTA Guidelines on patient blood management for adult cardiac surgery. J Cardiothorac Vasc Anesth 2018; 32:88–120
50. Morgan J, Checketts M, Arana A, Chalmers E, Maclean J, Powis M, Morton N; Association of Paediatric Anaesthetists of Great Britain and Ireland Guidelines Working Group on Thromboprophylaxis in Children: Prevention of perioperative venous thromboembolism in pediatric patients: Guidelines from the Association of Paediatric Anaesthetists of Great Britain and Ireland (APAGBI). Paediatr Anaesth 2018; 28:382–91

51. Ahmad I, El-Boghdadly K, Bhagrath R, Hodzovic I, McNarry AF, Mir F, O'Sullivan EP, Patel A, Stacey M, Vaughan D: Difficult Airway Society guidelines for awake tracheal intubation (ATI) in adults. Anaesthesia 2020; 75:509–28
52. Practice guidelines for perioperative transesophageal echocardiography. Anesthesiology 2010; 112:1084–96
53. Practice guidelines for acute pain management in the perioperative setting. Anesthesiology 2012; 116:248–73
54. Troianos CA, Hartman GS, Glas KE, Skubas NJ, Eberhardt RT, Walker JD, Reeves ST: Guidelines for performing ultrasound guided vascular cannulation. Anesth Analg 2012; 114:46–72
55. Apfelbaum JL, Silverstein JH, Chung FF, Connis RT, Fillmore RB, Hunt SE, Nickinovich DG, Schreiner MS, Silverstein JH, Apfelbaum JL, Barlow JC, Chung FF, Connis RT, Fillmore RB, Hunt SE, Joas TA, Nickinovich DG, Schreiner MS; American Society of Anesthesiologists Task Force on Postanesthetic Care: Practice guidelines for postanesthetic care: An updated report by the American Society of Anesthesiologists Task Force on Postanesthetic Care. Anesthesiology 2013; 118:291–307
56. Apfelbaum JL, Hagberg CA, Caplan RA, Blitt CD, Connis RT, Nickinovich DG, Hagberg CA, Caplan RA, Benumof JL, Berry FA, Blitt CD, Bode RH, Cheney FW, Connis RT, Guidry OF, Nickinovich DG, Ovassapian A; American Society of Anesthesiologists Task Force on Management of the Difficult Airway: Practice guidelines for management of the difficult airway: An updated report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. Anesthesiology 2013; 118:251–70
57. Fleisher LA, Fleischmann KE, Auerbach AD, Barnason SA, Beckman JA, Bozkurt B, Davila-Roman VG, Gerhard-Herman MD, Holly TA, Kane GC, Marine JE, Nelson MT, Spencer CC, Thompson A, Ting HH, Uretsky BF, Wijeysundera DN: 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: Executive summary: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 2014; 130:2215–45
58. Practice guidelines for the perioperative management of patients with obstructive sleep apnea. Anesthesiology 2014; 120:268–86
59. Practice guidelines for perioperative blood management. Anesthesiology 2015; 122:241–75
60. Engelman R, Baker RA, Likosky DS, Grigore A, Dickinson TA, Shore-Lesserson L, Hammon JW: The Society of Thoracic Surgeons, the Society of Cardiovascular Anesthesiologists, and the American Society of ExtraCorporeal Technology: Clinical Practice Guidelines for Cardiopulmonary Bypass–Temperature Management During Cardiopulmonary Bypass. J Cardiothorac Vasc Anesth 2015; 29:1104–13
61. Chou R, Gordon DB, de Leon-Casasola OA, Rosenberg JM, Bickler S, Brennan T, Carter T, Cassidy CL, Chittenden EH, Degenhardt E, Griffith S, Manworren R, McCarberg B, Montgomery R, Murphy J, Perkal MF, Suresh S, Sluka K, Strassels S, Thirlby R, Viscusi E, Walco GA, Warner L, Weisman SJ, Wu CL: Management of postoperative pain: A clinical practice guideline from the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. J Pain 2016; 17:131–57
62. Practice guidelines for obstetric anesthesia. Anesthesiology 2016; 124:270–300
63. Practice guidelines for the prevention, detection, and management of respiratory depression associated with neuraxial opioid administration. Anesthesiology 2016; 124:535–52
64. Chung F, Memtsoudis SG, Ramachandran SK, Nagappa M, Opperer M, Cozowicz C, Patrawala S, Lam D, Kumar A, Joshi GP, Fleetham J, Ayas N, Collop N, Doufas AG, Eikermann M, Englesakis M, Gali B, Gay P, Hernandez AV, Kaw R, Kezirian EJ, Malhotra A, Mokhlesi B, Parthasarathy S, Stierer T, Wappler F, Hillman DR, Auckley D: Society of Anesthesia and Sleep Medicine guidelines on preoperative screening and assessment of adult patients with obstructive sleep apnea. Anesth Analg 2016; 123:452–73
65. Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: Application to healthy patients undergoing elective procedures. Anesthesiology 2017; 126:376–93
66. Lele AV, Hoefnagel AL, Schloemerkemper N, Wyler DA, Chaikittisilpa N, Vavilala MS, Naik BI, Williams JH, Venkat Raghavan L, Koerner IP; Representing SNACC Task Force for Developing Guidelines for Perioperative Management of External Ventricular and Lumbar Drains: Perioperative management of adult patients with external ventricular and lumbar drains: Guidelines from the society for neuroscience in anesthesiology and critical care. J Neurosurg Anesthesiol 2017; 29:191–210
67. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP, Fleisher LA, Jneid H, Mack MJ, McLeod CJ, O'Gara PT, Rigolin VH, Sundt TM, Thompson A: 2017 AHA/ACC Focused Update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 2017; 135:e1159–95
68. Schwenk ES, Viscusi ER, Buvanendran A, Hurley RW, Wasan AD, Narouze S, Bhatia A, Davis FN, Hooten WM,

Cohen SP: Consensus guidelines on the use of intravenous ketamine infusions for acute pain management from the American Society of Regional Anesthesia and Pain Medicine, the American Academy of Pain Medicine, and the American Society of Anesthesiologists. Reg Anesth Pain Med 2018; 43:456–66
69. Shore-Lesserson L, Baker RA, Ferraris V, Greilich PE, Fitzgerald D, Roman P, Hammon J: STS/SCA/AmSECT clinical practice guidelines: Anticoagulation during cardiopulmonary bypass. J Extra Corpor Technol 2018; 50:5–18
70. Practice guidelines for moderate procedural sedation and analgesia 2018. Anesthesiology 2018; 128:437–79
71. Shore-Lesserson L, Baker RA, Ferraris VA, Greilich PE, Fitzgerald D, Roman P, Hammon JW: The Society of Thoracic Surgeons, the Society of Cardiovascular Anesthesiologists, and the American Society of ExtraCorporeal Technology: Clinical practice guidelines–Anticoagulation during cardiopulmonary bypass. Anesth Analg 2018; 126:413–24
72. Memtsoudis SG, Cozowicz C, Nagappa M, Wong J, Joshi GP, Wong DT, Doufas AG, Yilmaz M, Stein MH, Krajewski ML, Singh M, Pichler L, Ramachandran SK, Chung F: Society of Anesthesia and Sleep Medicine guideline on intraoperative management of adult patients with obstructive sleep apnea. Anesth Analg 2018; 127:967–87
73. Horlocker TT, Vandermeuelen E, Kopp SL, Gogarten W, Leffert LR, Benzon HT: Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine evidence-based guidelines (fourth edition). Reg Anesth Pain Med 2018; 43:263–309
74. Mechanick JI, Apovian C, Brethauer S, Garvey WT, Joffe AM, Kim J, Kushner RF, Lindquist R, Pessah-Pollack R, Seger J, Urman RD, Adams S, Cleek JB, Correa R, Figaro MK, Flanders K, Grams J, Hurley DL, Kothari S, Seger MV, Still CD: Clinical practice guidelines for the perioperative nutrition, metabolic, and nonsurgical support of patients undergoing bariatric procedures – 2019 update: Cosponsored by American Association of Clinical Endocrinologists/American College of Endocrinology, the Obesity Society, American Society for Metabolic & Bariatric Surgery, Obesity Medicine Association, and American Society of Anesthesiologists. Surg Obes Relat Dis 2020; 16:175–247
75. Fillingham YA, Ramkumar DB, Jevsevar DS, Yates AJ, Bini SA, Clarke HD, Schemitsch E, Johnson RL, Memtsoudis SG, Sayeed SA, Sah AP, Della Valle CJ: Tranexamic acid in total joint arthroplasty: The endorsed clinical practice guides of the American Association of Hip and Knee Surgeons, American Society of Regional Anesthesia and Pain Medicine, American Academy of Orthopaedic Surgeons, Hip Society, and Knee Society. Reg Anesth Pain Med 2019; 44:7–11
76. Practice Guidelines for Central Venous Access 2020. Anesthesiology 2020; 132:8–43
77. Gan TJ, Belani KG, Bergese S, Chung F, Diemunsch P, Habib AS, Jin Z, Kovac AL, Meyer TA, Urman RD, Apfel CC, Ayad S, Beagley L, Candiotti K, Englesakis M, Hedrick TL, Kranke P, Lee S, Lipman D, Minkowitz HS, Morton J, Philip BK: Fourth consensus guidelines for the management of postoperative nausea and vomiting. Anesth Analg 2020; 131:411–48
78. Vlisides PE, Moore LE, Whalin MK, Robicsek SA, Gelb AW, Lele AV, Mashour GA: Perioperative care of patients at high risk for stroke during or after non-cardiac, non-neurological surgery: 2020 guidelines from the Society for Neuroscience in Anesthesiology and Critical Care. J Neurosurg Anesthesiol 2020; 32:210–26
79. Cerantola Y, Valerio M, Persson B, Jichlinski P, Ljungqvist O, Hubner M, Kassouf W, Muller S, Baldini G, Carli F, Naesheimh T, Ytrebo L, Revhaug A, Lassen K, Knutsen T, Aarsether E, Wiklund P, Patel HR: Guidelines for perioperative care after radical cystectomy for bladder cancer: Enhanced Recovery After Surgery (ERAS(®)) society recommendations. Clin Nutr 2013; 32:879–87
80. Mortensen K, Nilsson M, Slim K, Schäfer M, Mariette C, Braga M, Carli F, Demartines N, Griffin SM, Lassen K; Enhanced Recovery After Surgery (ERAS®) Group: Consensus guidelines for enhanced recovery after gastrectomy: Enhanced Recovery After Surgery (ERAS®) Society recommendations. Br J Surg 2014; 101:1209–29
81. Melloul E, Hübner M, Scott M, Snowden C, Prentis J, Dejong CH, Garden OJ, Farges O, Kokudo N, Vauthey JN, Clavien PA, Demartines N: Guidelines for perioperative care for liver surgery: Enhanced Recovery After Surgery (ERAS) Society recommendations. World J Surg 2016; 40:2425–40
82. Thorell A, MacCormick AD, Awad S, Reynolds N, Roulin D, Demartines N, Vignaud M, Alvarez A, Singh PM, Lobo DN: Guidelines for perioperative care in bariatric surgery: Enhanced Recovery After Surgery (ERAS) Society recommendations. World J Surg 2016; 40:2065–83
83. Batchelor TJP, Rasburn NJ, Abdelnour-Berchtold E, Brunelli A, Cerfolio RJ, Gonzalez M, Ljungqvist O, Petersen RH, Popescu WM, Slinger PD, Naidu B: Guidelines for enhanced recovery after lung surgery: Recommendations of the Enhanced Recovery After Surgery (ERAS®) Society and the European Society of Thoracic Surgeons (ESTS). Eur J Cardiothorac Surg 2019; 55:91–115
84. Wilson RD, Caughey AB, Wood SL, Macones GA, Wrench IJ, Huang J, Norman M, Pettersson K, Fawcett WJ, Shalabi MM, Metcalfe A, Gramlich L, Nelson G: Guidelines for antenatal and preoperative care in cesarean delivery: Enhanced Recovery After Surgery Society recommendations (Part 1). Am J Obstet Gynecol 2018; 219:523.e1–e15

85. Caughey AB, Wood SL, Macones GA, Wrench IJ, Huang J, Norman M, Pettersson K, Fawcett WJ, Shalabi MM, Metcalfe A, Gramlich L, Nelson G, Wilson RD: Guidelines for intraoperative care in cesarean delivery: Enhanced Recovery After Surgery Society recommendations (Part 2). Am J Obstet Gynecol 2018; 219:533–44
86. Engelman DT, Ben Ali W, Williams JB, Perrault LP, Reddy VS, Arora RC, Roselli EE, Khoynezhad A, Gerdisch M, Levy JH, Lobdell K, Fletcher N, Kirsch M, Nelson G, Engelman RM, Gregory AJ, Boyle EM: Guidelines for perioperative care in cardiac surgery: Enhanced Recovery After Surgery Society recommendations. JAMA Surg 2019; 154:755–66
87. Gustafsson UO, Scott MJ, Hubner M, Nygren J, Demartines N, Francis N, Rockall TA, Young-Fadok TM, Hill AG, Soop M, de Boer HD, Urman RD, Chang GJ, Fichera A, Kessler H, Grass F, Whang EE, Fawcett WJ, Carli F, Lobo DN, Rollins KE, Balfour A, Baldini G, Riedel B, Ljungqvist O: Guidelines for perioperative care in elective colorectal surgery: Enhanced Recovery After Surgery (ERAS®) Society recommendations: 2018. World J Surg 2019; 43:659–95
88. Low DE, Allum W, De Manzoni G, Ferri L, Immanuel A, Kuppusamy M, Law S, Lindblad M, Maynard N, Neal J, Pramesh CS, Scott M, Mark Smithers B, Addor V, Ljungqvist O: Guidelines for perioperative care in esophagectomy: Enhanced Recovery After Surgery (ERAS®) Society recommendations. World J Surg 2019; 43:299–330
89. Nelson G, Bakkum-Gamez J, Kalogera E, Glaser G, Altman A, Meyer LA, Taylor JS, Iniesta M, Lasala J, Mena G, Scott M, Gillis C, Elias K, Wijk L, Huang J, Nygren J, Ljungqvist O, Ramirez PT, Dowdy SC: Guidelines for perioperative care in gynecologic/oncology: Enhanced Recovery After Surgery (ERAS) Society recommendations–2019 update. Int J Gynecol Cancer 2019; 29:651–68
90. Macones GA, Caughey AB, Wood SL, Wrench IJ, Huang J, Norman M, Pettersson K, Fawcett WJ, Shalabi MM, Metcalfe A, Gramlich L, Nelson G, Wilson RD: Guidelines for postoperative care in cesarean delivery: Enhanced Recovery After Surgery (ERAS) Society recommendations (part 3). Am J Obstet Gynecol 2019; 221:247.e1–9
91. Brindle ME, McDiarmid C, Short K, Miller K, MacRobie A, Lam JYK, Brockel M, Raval MV, Howlett A, Lee KS, Offringa M, Wong K, de Beer D, Wester T, Skarsgard ED, Wales PW, Fecteau A, Haliburton B, Goobie SM, Nelson G: Consensus guidelines for perioperative care in neonatal intestinal surgery: Enhanced Recovery After Surgery (ERAS®) Society recommendations. World J Surg 2020; 44:2482–92
92. Hübner M, Kusamura S, Villeneuve L, Al-Niaimi A, Alyami M, Balonov K, Bell J, Bristow R, Guiral DC, Fagotti A, Falcão LFR, Glehen O, Lambert L, Mack L, Muenster T, Piso P, Pocard M, Rau B, Sgarbura O, Somashekhar SP, Wadhwa A, Altman A, Fawcett W, Veerapong J, Nelson G: Guidelines for perioperative care in Cytoreductive Surgery (CRS) with or without hyperthermic IntraPEritoneal chemotherapy (HIPEC): Enhanced Recovery After Surgery (ERAS®) Society recommendations – Part II: Postoperative management and special considerations. Eur J Surg Oncol 2020; 46:2311–23
93. Altman AD, Robert M, Armbrust R, Fawcett WJ, Nihira M, Jones CN, Tamussino K, Sehouli J, Dowdy SC, Nelson G: Guidelines for vulvar and vaginal surgery: Enhanced Recovery After Surgery Society recommendations. Am J Obstet Gynecol 2020; 223:475–85
94. Melloul E, Lassen K, Roulin D, Grass F, Perinel J, Adham M, Wellge EB, Kunzler F, Besselink MG, Asbun H, Scott MJ, Dejong CHC, Vrochides D, Aloia T, Izbicki JR, Demartines N: Guidelines for perioperative care for pancreatoduodenectomy: Enhanced Recovery After Surgery (ERAS) recommendations 2019. World J Surg 2020; 44:2056–84
95. Khan AR, Khan S, Zimmerman V, Baddour LM, Tleyjeh IM: Quality and strength of evidence of the Infectious Diseases Society of America clinical practice guidelines. Clin Infect Dis 2010; 51:1147–56
96. Alseiari M, Meyer KB, Wong JB: Evidence underlying KDIGO (Kidney Disease: Improving Global Outcomes) guideline recommendations: A systematic review. Am J Kidney Dis 2016; 67:417–22
97. Devereaux PJ, Chan MTV, Eisenach J, Schricker T, Sessler DI: The need for large clinical studies in perioperative medicine. Anesthesiology 2012; 116:1169–75
98. Devereaux PJ, Mrkobrada M, Sessler DI, Leslie K, Alonso-Coello P, Kurz A, Villar JC, Sigamani A, Biccard BM, Meyhoff CS, Parlow JL, Guyatt G, Robinson A, Garg AX, Rodseth RN, Botto F, Lurati Buse G, Xavier D, Chan MT, Tiboni M, Cook D, Kumar PA, Forget P, Malaga G, Fleischmann E, Amir M, Eikelboom J, Mizera R, Torres D, Wang CY, VanHelder T, Paniagua P, Berwanger O, Srinathan S, Graham M, Pasin L, Le Manach Y, Gao P, Pogue J, Whitlock R, Lamy A, Kearon C, Baigent C, Chow C, Pettit S, Chrolavicius S, Yusuf S; POISE-2 Investigators: Aspirin in patients undergoing noncardiac surgery. N Engl J Med 2014; 370:1494–503
99. Devereaux PJ, Sessler DI, Leslie K, Kurz A, Mrkobrada M, Alonso-Coello P, Villar JC, Sigamani A, Biccard BM, Meyhoff CS, Parlow JL, Guyatt G, Robinson A, Garg AX, Rodseth RN, Botto F, Lurati Buse G, Xavier D, Chan MT, Tiboni M, Cook D, Kumar PA, Forget P, Malaga G, Fleischmann E, Amir M, Eikelboom J, Mizera R, Torres D, Wang CY, Vanhelder T, Paniagua P, Berwanger O, Srinathan S, Graham M, Pasin L, Le Manach Y, Gao P, Pogue J, Whitlock R, Lamy A, Kearon C, Chow C, Pettit S, Chrolavicius S, Yusuf S; POISE-2 Investigators: Clonidine in patients undergoing noncardiac surgery. N Engl J Med 2014; 370:1504–13

100. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): A randomised controlled trial. Lancet 2008; 371:1839–47
101. Myles PS, Leslie K, Chan MTV, Forbes A, Peyton PJ, Paech MJ, Beattie WS, Sessler DI, Devereaux PJ, Silbert B, Schricker T, Wallace S: The safety of addition of nitrous oxide to general anaesthesia in at-risk patients having major non-cardiac surgery (ENIGMA-II): A randomised, single-blind trial. Lancet 2014; 384:1446–54
102. Sessler DI, Pei L, Huang Y, Fleischmann E, Marhofer P, Kurz A, Mayers DB, Meyer-Treschan TA, Grady M, Tan EY, Ayad S, Mascha EJ, Buggy DJ; Breast Cancer Recurrence Collaboration: Recurrence of breast cancer after regional or general anaesthesia: A randomised controlled trial. Lancet 2019; 394:1807–15
103. Short TG, Campbell D, Frampton C, Chan MTV, Myles PS, Corcoran TB, Sessler DI, Mills GH, Cata JP, Painter T, Byrne K, Han R, Chu MHM, McAllister DJ, Leslie K; Australian and New Zealand College of Anaesthetists Clinical Trials Network; Balanced Anaesthesia Study Group: Anaesthetic depth and complications after major surgery: An international, randomised controlled trial. Lancet 2019; 394:1907–14
104. Avidan MS, Jacobsohn E, Glick D, Burnside BA, Zhang L, Villafranca A, Karl L, Kamal S, Torres B, O'Connor M, Evers AS, Gradwohl S, Lin N, Palanca BJ, Mashour GA; BAG-RECALL Research Group: Prevention of intraoperative awareness in a high-risk surgical population. N Engl J Med 2011; 365:591–600
105. Landoni G, Lomivorotov VV, Nigro Neto C, Monaco F, Pasyuga VV, Bradic N, Lembo R, Gazivoda G, Likhvantsev VV, Lei C, Lozovskiy A, Di Tomasso N, Bukamal NAR, Silva FS, Bautin AE, Ma J, Crivellari M, Farag AMGA, Uvaliev NS, Carollo C, Pieri M, Kunstýř J, Wang CY, Belletti A, Hajjar LA, Grigoryev EV, Agrò FE, Riha H, El-Tahan MR, Scandroglio AM, Elnakera AM, Baiocchi M, Navalesi P, Shmyrev VA, Severi L, Hegazy MA, Crescenzi G, Ponomarev DN, Brazzi L, Arnoni R, Tarasov DG, Jovic M, Calabrò MG, Bove T, Bellomo R, Zangrillo A; MYRIAD Study Group: Volatile anesthetics *versus* total intravenous anesthesia for cardiac surgery. N Engl J Med 2019; 380:1214–25
106. Mazer CD, Whitlock RP, Fergusson DA, Belley-Cote E, Connolly K, Khanykin B, Gregory AJ, de Médicis É, Carrier FM, McGuinness S, Young PJ, Byrne K, Villar JC, Royse A, Grocott HP, Seeberger MD, Mehta C, Lellouche F, Hare GMT, Painter TW, Fremes S, Syed S, Bagshaw SM, Hwang NC, Royse C, Hall J, Dai D, Mistry N, Thorpe K, Verma S, Jüni P, Shehata N; TRICS Investigators and Perioperative Anesthesia Clinical Trials Group: Six-month outcomes after restrictive or liberal transfusion for cardiac surgery. N Engl J Med 2018; 379:1224–33
107. Wesselink EM, Kappen TH, Torn HM, Slooter AJC, van Klei WA: Intraoperative hypotension and the risk of postoperative adverse outcomes: A systematic review. Br J Anaesth 2018; 121:706–21
108. Sessler DI, Bloomstone JA, Aronson S, Berry C, Gan TJ, Kellum JA, Plumb J, Mythen MG, Grocott MPW, Edwards MR, Miller TE, Miller TE, Mythen MG, Grocott MP, Edwards MR; Perioperative Quality Initiative-3 workgroup; POQI chairs; Physiology group; Preoperative blood pressure group; Intraoperative blood pressure group; Postoperative blood pressure group: Perioperative quality initiative consensus statement on intraoperative blood pressure, risk and outcomes for elective surgery. Br J Anaesth 2019; 122:563–74
109. Frieden TR: Evidence for health decision making: Beyond randomized, controlled trials. N Engl J Med 2017; 377:465–75
110. Agoritsas T, Merglen A, Shah ND, O'Donnell M, Guyatt GH: Adjusted analyses in studies addressing therapy and harm: Users' guides to the medical literature. JAMA 2017; 317:748–59
111. Concato J, Shah N, Horwitz RI: Randomized, controlled trials, observational studies, and the hierarchy of research designs. N Engl J Med 2000; 342:1887–92
112. Ioannidis JPA, Contopoulos-Ioannidis DG, Haidich AB, Pappa M, Pantazis N, Kokori SI, Tektonidou MG, Contopoulos-Ioannidis DG, Ioannidis JPA, Lau J: Comparison of evidence of treatment effects in randomized and nonrandomized studies. JAMA 2001; 286:821–30
113. Brozek JL, Akl EA, Alonso-Coello P, Lang D, Jaeschke R, Williams JW, Phillips B, Lelgemann M, Lethaby A, Bousquet J, Guyatt GH, Schünemann HJ; GRADE Working Group: Grading quality of evidence and strength of recommendations in clinical practice guidelines: Part 1 of 3. An overview of the GRADE approach and grading quality of evidence about interventions. Allergy 2009; 64:669–77

Appendix

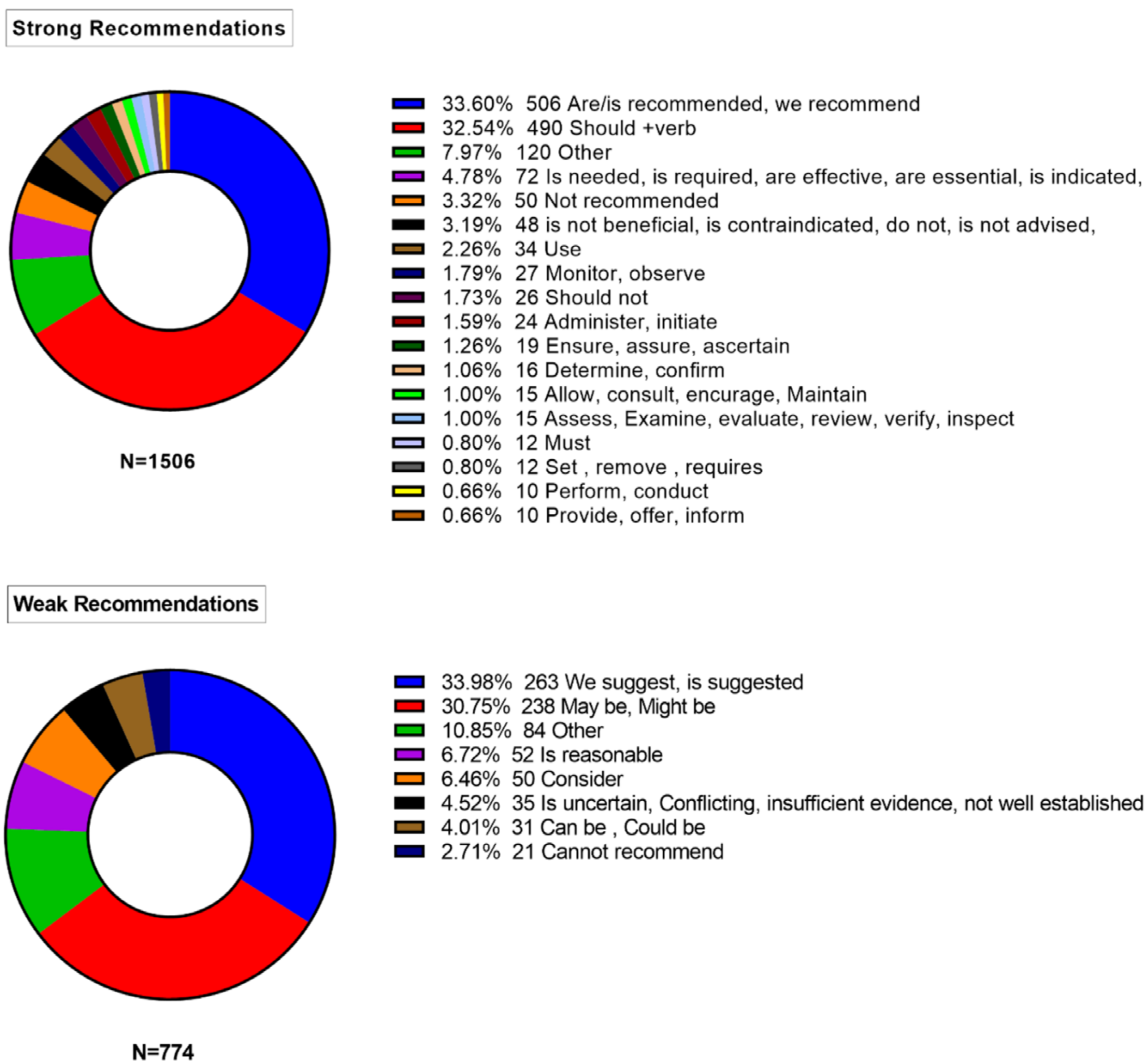

Fig. A1. Phrases used to map recommendations in guidelines to the American Heart Association Strength of Recommendation in guidelines that did not explicitly classify recommendations using the GRADE or American Heart Association classification systems.

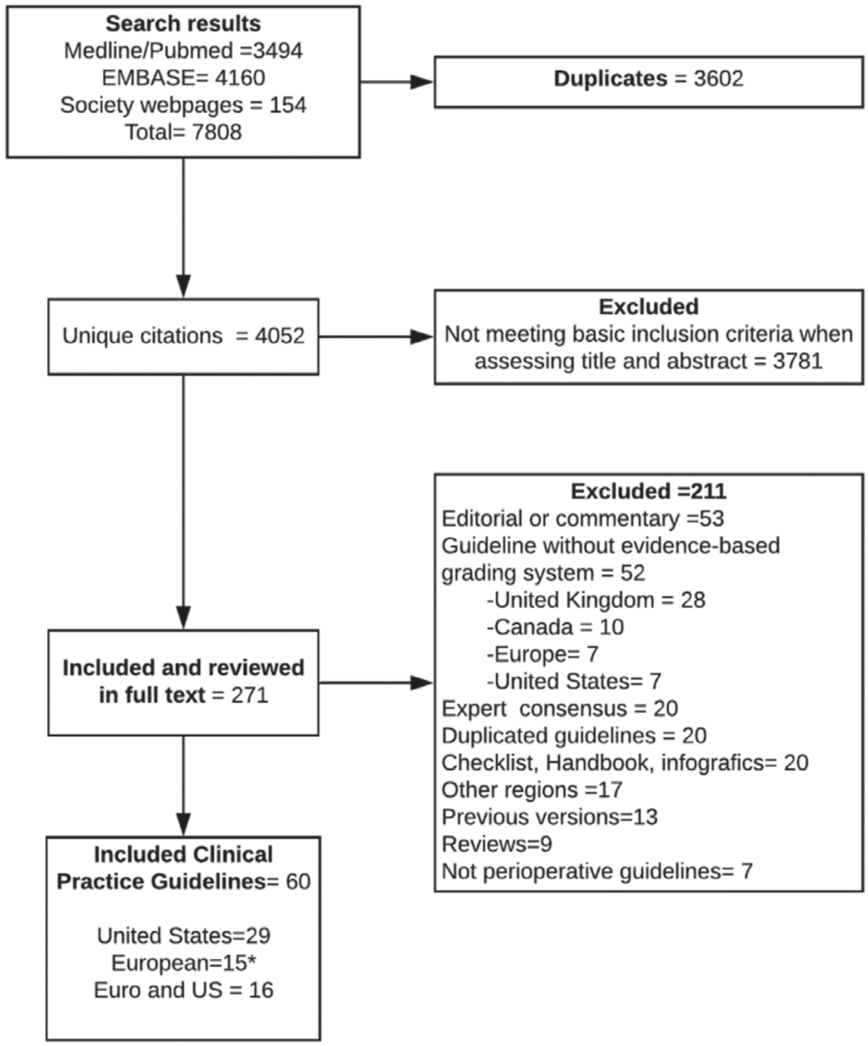

Fig. A2. PRISMA flow diagram. *One guideline[26] was published in 12 different articles. One of them was excluded because it was directed to intensive care,[27] and the remaining 11 documents were counted as a single guideline.

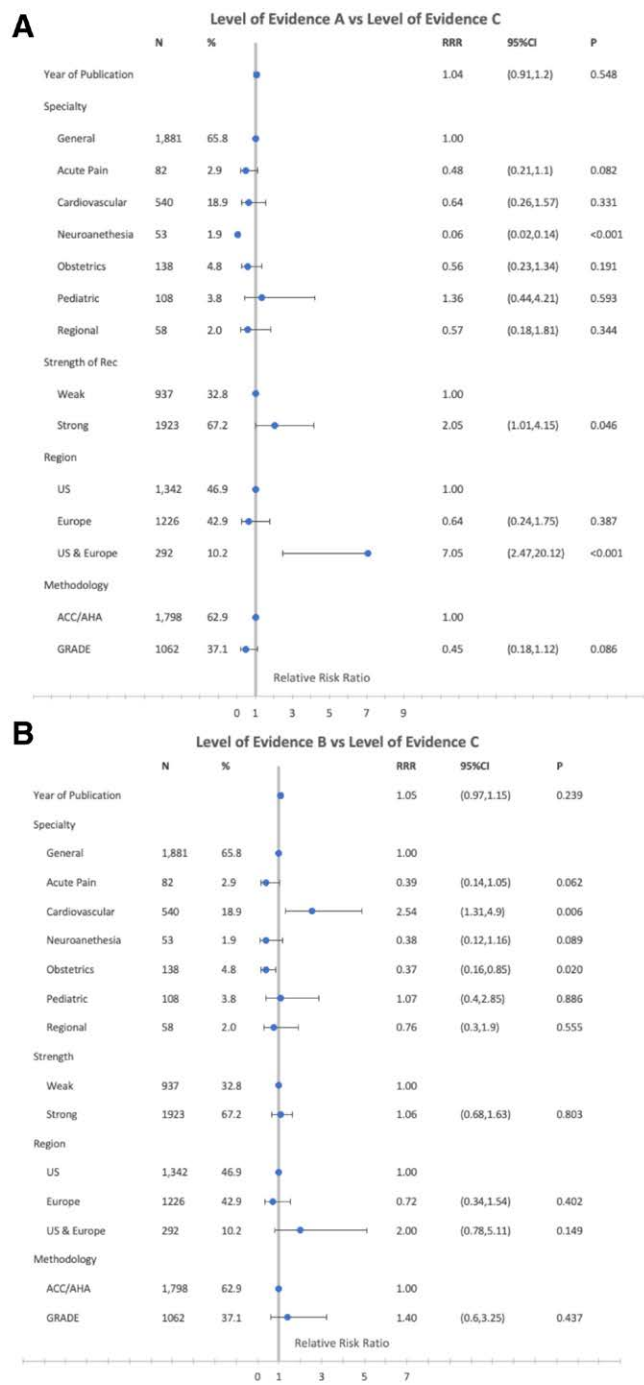

Fig. A3. (*A*) Results of multivariable analysis examining the association between recommendations supported by level of evidence A *versus* level of evidence C and year of publication, controlling for specialty, strength of recommendation, region, and grading methodology using multinomial logistic regression. This analysis included original and updated guidelines. (*B*) Results of multivariable analysis examining the association between recommendations supported by level of evidence B *versus* level of evidence C and year of publication, controlling for specialty, strength of recommendation, region, and grading methodology using multinomial logistic regression. This analysis included original and updated guidelines.