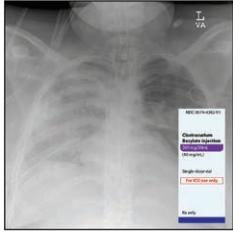


## Key Papers from the Most Recent Literature Relevant to Anesthesiologists



### Early neuromuscular blockade in the acute respiratory distress syndrome. *N Engl J Med* 2019; 380:1997–2008.

Early continuous neuromuscular blockade in mechanically ventilated patients with acute respiratory distress syndrome (ARDS) is commonly used but its benefits remain unclear. This study randomized 1,006 patients with moderate-to-severe ARDS to a 48-h continuous infusion of cisatracurium plus deep sedation or to usual care (no routine neuromuscular blockade and lighter sedation). The authors used the same mechanical ventilation strategies in both groups. Within 48 h of randomization, 488 intervention patients (97.4%) started a continuous infusion of cisatracurium and 86 control patients (17.0%) received a neuromuscular blocking agent. At 90 days, nearly identical numbers of patients in both groups had died: 213 (42.5%) in the experimental group and 216 (42.8%) in the control group. This was a between-group difference of  $-0.3$  points; 95% CI,  $-6.4$  to  $5.9$ ;  $P = 0.93$ . Accordingly, the study was stopped at the second interim analysis due to futility. Interestingly, intervention patients were less physically active yet had more cardiovascular events than control patients during their hospitalization. (Article Selection: Laszlo Vutskits. Image: J. P. Rathmell.)

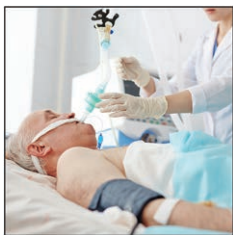
**Take home message:** There were no differences in 90-day mortality among patients with moderate-to-severe ARDS who were treated with early, continuous neuromuscular blockade and those who were treated with a usual care approach that included lighter sedation targets.



### Maternity leave in residency: A multicenter study of determinants and wellness outcomes. *Acad Med* 2019 May 14 [Epub ahead of print].

Recent studies demonstrate that the maternity leaves for resident physicians has not increased since the mid-1990s, with an average leave of less than 8 weeks. This study explored the factors that governed maternity leave among resident physicians and how maternity leave length affected resident well-being. The authors sent surveys to 1,500 female residents at six institutions in 25 specialties. Questions covered family member demographics and leave logistics, including how time off was categorized (paid vs. unpaid, vacation or sick time, etc.). The authors selected many study outcomes, including leave length, breastfeeding duration, screening for burnout, and depression and satisfaction. The survey's response rate was 52%, with 804 respondents. Only 16% of respondents were mothers; half had their first child during residency. Among 77 reported leaves, one third of women took only 6 weeks. Use of vacation time (81%, 62) and sick leave (64%, 49) were common. Respondents most frequently limited their leave so as to avoid extending their residency requirements (27%, 59). Half of the mothers were able to avoid lengthening training and half experienced burnout independent of leave length. (Article Selection: Franklyn Cladis. Image: ©gettyimages.)

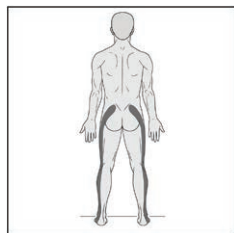
**Take home message:** There is significant variability in administration of resident maternity leave. Targets for intervention include policy clarification, improving program support, and consideration of parent wellness upon return to work.



### SCAI clinical expert consensus statement on the classification of cardiogenic shock: This document was endorsed by the American College of Cardiology (ACC), the American Heart Association (AHA), the Society of Critical Care Medicine (SCCM), and the Society of Thoracic Surgeons (STS) in April 2019. *Catheter Cardiovasc Interv* 2019; 94:29–37.

Despite varied percutaneous mechanical circulatory support options, outcomes for myocardial infarction complicated by cardiogenic shock have remained static for 30 yr. To date, there has not been a robust classification scheme to categorize cardiogenic shock. The Society for Cardiovascular Angiography and Interventions assembled a broad group of experts to develop a proposed classification schema. They devised a system describing stages of cardiogenic shock with increasing severity from A to E that was endorsed by the American College of Cardiology, the American Heart Association, the Society of Critical Care Medicine, and the Society of Thoracic Surgeons in April 2019. Stages C and beyond indicate the presence of hypoperfusion. In stage D the initial interventions have not restored adequate perfusion despite at least 30 min of observation. In stage E the patient is highly unstable and often experiences cardiovascular collapse. (Article Selection: Martin J. London. Image: ©gettyimages.)

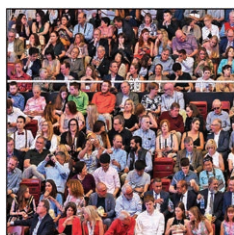
**Take home message:** The proposed classification system is clinically applicable across the spectrum of care but has not been validated to test its utility.



### Expenditures and health care utilization among adults with newly diagnosed low back and lower extremity pain. *JAMA Netw Open* 2019; 2:e193676.

Low back pain and lower extremity pain continue to be among the most common reasons that patients seek medical care, yet little is known about healthcare utilization among patients who do not receive spinal surgery. This retrospective cohort study used a large commercial database to assess use of healthcare resources and associated costs for low back pain management. The authors examined data from nearly 2.5 million opiate-naïve U.S. adults who had newly diagnosed low back pain or lower extremity pain during a 7-yr period. The primary outcome was total cost of care within the first 6 and 12 months after diagnosis, stratified by whether patients did or did not receive spinal surgery. More than half of the patients (55.7%) received no interventions. Only 1.2% of patients received surgery, but they accounted for 29.3% of the total 12-month costs (\$784 million). In contrast, total costs were \$1.8 billion for the vast majority of patients who did not receive surgery. The care given to the nonsurgical cohort was often inconsistent with clinical guidelines: approximately one third of patients received imaging within 30 days of diagnosis, whereas another third were imaged before physical therapy. (Article Selection: J. David Clark. Image: G. Nelson.)

**Take home message:** Surgery is rarely performed among patients with newly diagnosed low back pain or lower extremity pain but is associated with a significant increase in the cost of care, as was early imaging in patients who do not undergo surgery. These avoidable costs in the setting of newly diagnosed low back pain or lower extremity pain may result in excessive expenditures in the healthcare systems.



### Gender inequality and restrictive gender norms: Framing the challenges to health. *Lancet* 2019; 393:2440–54.

Unlike sex, the concept of gender in humans is more complex than suggested by the traditional duality of male and female, man and woman. This article, the first in a series of five, examines how health and well-being are influenced by gender inequality and restrictive gender norms. The authors build a conceptual framework to explain the development of biologically male or female humans into gendered beings and how poor health can develop through the structural pathways of sexism, patriarchy, racism, classism, and homophobia. They posit that gender bias in health care and medical research has serious implications for population health. Noting that decades of work to eliminate gender discrimination in global health have yielded only modest successes, they argue that a cohesive plan and widespread political commitment will be needed to meet the Sustainable Development Goals put forth by the United Nations. (Article Selection: Beatrice Beck-Schimmer. Image: J. P. Rathmell.)

**Take home message:** Gender bias in health care may have sobering implications for population health.



### Leadership development in postgraduate medical education: A systematic review of the literature. *Acad Med* 2019; 94:440–9.

Leadership skills have become a core competency for all physicians. To identify the level of leadership training during postgraduate medical education, the authors conducted a review of peer-reviewed articles from four relevant databases to examine specific interventions and found 21 relevant manuscripts that were analyzed by education setting, curriculum, level of training, type of instructor, educational methods, leadership framework and outcomes. The authors used Kirkpatrick Effectiveness scores and Best Evidence in Medical Education Quality of Evidence scores to assess the quality of the interventions. Seventeen of the 21 studies used a classroom setting and 13 used clinical faculty as instructors. Thirteen articles described isolated curricula that ranged in length from 3 h to 5 yr. Small group discussions (15 articles) and didactic teaching (14 articles) were the most commonly used educational methods. Study authors evaluated learner surveys for 17 articles and found that the average Kirkpatrick Effectiveness score was 1.0, whereas the average Best Evidence in Medical Education Quality of Evidence score was 2. (Article Selection: Cathleen Peterson-Layne. Image: J. P. Rathmell.)

**Take home message:** Interventions for leadership development during residency focus primarily on cognitive leadership domains. A more comprehensive approach that includes character development and emotional intelligence are encouraged.

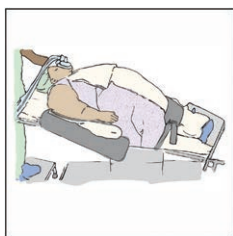


### A systematic review of the relative frequency and risk factors for prolonged opioid prescription following surgery and trauma among adults. *Ann Surg* 2019 Jun 10 [Epub ahead of print].

A large majority of surgical patients are prescribed opioids to manage postoperative pain. This systematic review examined the frequency of and risk factors for opioid prescriptions that persist for 3 to 6 months and more than 6 months after surgery. Studies published between January 1998 and April 2018 that investigated opioid prescribing more than 3 months after surgery and hospitalization and included data on preoperative opioid prescriptions were included in the analysis. Of the 10,003 articles that were screened, 35 were included in the study. The authors noted that the frequency of opioid

prescriptions was 4% at 3 to 6 months after surgery or trauma and 3% at more than 6 months after surgery or trauma in those that had no presurgical or pretrauma prolonged opioid prescribing. However, in those with prolonged preoperative or pretrauma opioid prescribing, 51% were prescribed opioids 3 to 6 months after surgery or trauma and 59% were prescribed opioids more than 6 months after surgery or trauma. Predictors for prolonged opioid prescribing after surgery or trauma in patients taking opioids preoperatively or pretrauma included income, tobacco, and antidepressant use. Among patients not taking opioids preoperatively or pretrauma, the use of benzodiazepines or muscle relaxants and alcohol or drug dependence were identified as predictors of long-term opioid use after surgery or trauma. (Article Selection: Deborah J. Culley. Image: ©gettyimages.)

**Take home message:** Preoperative or pretrauma opioid prescribing is a strong predictor of postoperative or posttrauma opioid prescribing more than 3 to 6 months after surgery or trauma.

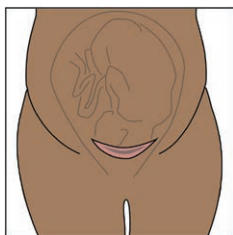


### Association of unrecognized obstructive sleep apnea with postoperative cardiovascular events in patients undergoing major noncardiac surgery. *JAMA* 2019; 321:1788–98.

Undiagnosed and untreated obstructive sleep apnea is known to increase cardiovascular risk, but it is less clear whether obstructive sleep apnea increases cardiovascular risks in the perioperative setting. This prospective cohort study examined the association between obstructive sleep apnea and 30-day risk of cardiovascular complications after major noncardiac surgery. The authors classified 1,218 participants as (1) not having obstructive sleep apnea, or (2) mild, (3) moderate, or (4) severe obstructive sleep apnea based on preoperative sleep monitoring. The primary outcome was a composite of

myocardial injury, cardiac death, heart failure, thromboembolism, atrial fibrillation, or stroke within 30 days of surgery. Nearly one third of patients with severe apnea met the primary outcome (30.1%, 41 of 136). Fewer patients experienced the primary outcome who had either moderate (22.1%, 52 of 235) or mild (19.0%, 86 of 452) obstructive sleep apnea. Only 14.2% of patients (56 of 395) without obstructive apnea experienced these complications. The authors found an association between apnea and the primary outcome; however, it was significant only in patients whose apnea was severe (adjusted hazard ratio, 2.23; 95% CI, 1.49 to 3.34;  $P = 0.001$ ). The authors found no significant interaction effects between the primary outcome and anesthesia type or the use of postoperative opioids or supplemental oxygen. (Article Selection: Laszlo Vutskits. Image: J. P. Rathmell.)

**Take home message:** High-risk patients undergoing major noncardiac surgery who have severe obstructive sleep apnea have an increased risk of postoperative cardiovascular complications.



### Maternal and perinatal mortality and complications associated with caesarean section in low-income and middle-income countries: A systematic review and meta-analysis. *Lancet* 2019; 393:1973–82.

Of the 300,000 women who die during childbirth globally each year, 99% are from low- and middle-income countries. This review examined the burden and risk factors for maternal and perinatal morbidity and mortality after caesarean sections in low- and middle-income countries. Based on 116 studies that included nearly 3 million caesarean sections, the authors found that the risk of maternal death in women who had a caesarean section in these low- to middle-income countries to be 8 per 1,000 procedures (95% CI, 7 to 9). Risk factors for mortality after caesarean section in low- and middle-income

countries included region (sub-Saharan Africa had the highest mortality rate, 10.9 per 1,000 procedures; 95% CI, 9.5 to 12.5) and income (low-income settings had the highest mortality rate, 13 per 1,000 procedures; 95% CI, 10 to 17); whereas those that were performed in private hospitals had the lowest mortality rate, 2.7 per 1,000 procedures (95% CI, 1 to 8). (Article Selection: Martin J. London. Image: J. P. Rathmell.)

**Take home message:** Maternal death after caesarean sections are excessively high in low- and middle-income countries.



### Effectiveness and safety of 5% lidocaine-medicated plaster on localized neuropathic pain after knee surgery: A randomized, double-blind controlled trial. *Pain* 2019; 160:1186–95.

Although 5% lidocaine plaster is generally recommended for localized neuropathic pain, evidence is lacking for use after total knee arthroplasty. This study examined the effectiveness of 5% lidocaine plaster on allodynia, hyperalgesia, and thermal stimuli in postsurgery knee localized neuropathic pain. The authors conducted a randomized, double-blind clinical trial among 36 patients at a single institution in France. Patients received either 5% lidocaine plaster or placebo plaster applied topically to the operative knee for 12 h daily over 3 months. At each visit the authors recorded neuropathic pain intensity and

other data points such as the size of the allodynic area. Dynamic mechanical allodynia declined by at least 30% over the course of 3 months in 96% of patients that received 5% lidocaine plaster (23 of 24) but in only 58% of the placebo group (7 of 12;  $P = 0.003$ ). More than 80% of patients that received 5% lidocaine plaster experienced a reduction of allodynia of at least 50% (20 of 24, 83%) versus 50% in the placebo group (6 of 12,  $P = 0.04$ ). During that same time, improvements were also seen in cold pain ( $P = 0.001$ ) and maximal mechanical pain ( $P = 0.007$ ) thresholds. (Article Selection: J. David Clark. Image: J. P. Rathmell.)

**Take home message:** Topical 5% lidocaine plaster may be useful in preventing allodynia after total knee arthroplasty.

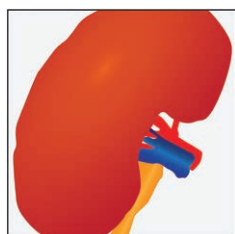


### Early sedation with dexmedetomidine in critically ill patients. *N Engl J Med* 2019; 380:2506–17.

Dexmedetomidine may shorten the time that intensive care unit (ICU) patients experience delirium or require mechanical ventilation. This open-label, randomized trial enrolled 4,000 newly ventilated, critically ill ICU patients to receive either dexmedetomidine as the sole or primary sedative or usual care consisting of propofol, midazolam, or other sedatives. The rate of death from any cause at 90 days was the primary outcome. Patients were randomized to treatment groups a median of 4.6 h after becoming eligible. In the group treated with dexmedetomidine, 29% died within 90 days (566 of 1,948) and this was identical to those patients in the control group (29%, 569 of 1,956; adjusted risk difference 0.0 points; 95% CI, -2.9 to

2.8). To achieve the prescribed level of sedation, patients in the dexmedetomidine group often received supplemental sedatives including propofol (64%), midazolam (3%), or both (7%) during the first 2 days after randomization compared to the use of propofol (60%), midazolam (12%), or both (20%) in the usual care group. Not surprisingly, bradycardia and hypotension were more common among patients who received dexmedetomidine. (Article Selection: Laszlo Vutskits. Image: J. P. Rathmell.)

**Take home message:** The use of dexmedetomidine in the ICU in patients requiring mechanical ventilation was associated with a similar 90-day death rate when compared to patients randomized to the usual care group.



### Clinical outcomes after ABO-incompatible renal transplantation: A systematic review and meta-analysis. *Lancet* 2019; 393:2059–72.

Due to the continuing organ shortage, ABO-incompatible renal transplantation has become increasingly common. Early and late noninferiority comparisons with ABO-compatible renal transplantation are needed. This review, which included an ABO-compatible control group, compared outcome differences between the two types of transplants. All-cause mortality and graft survival at 1, 3, 5, and 8+ yr posttransplantation were the primary endpoints. The authors analyzed 40 studies that included 49 patient groups. Of 65,063 patients who were eligible for analysis, 7,098 had undergone ABO-incompatible renal transplantation. At 1 yr, ABO-incompatible transplants were associated with significantly higher mortality (odds ratio

2.17; 95% CI, 1.63 to 2.90;  $P < 0.0001$ ). This was also true at the 3-yr (odds ratio 1.89; 95% CI, 1.46 to 2.45;  $P < 0.0001$ ) and 5-yr (odds ratio 1.47; 95% CI, 1.08 to 2.00;  $P = 0.010$ ) intervals. Death-censored graft survival was similarly lower among ABO-incompatible patients only at 1 yr (odds ratio 2.52; 95% CI, 1.80 to 3.54;  $P < 0.0001$ ) and 3 yr (odds ratio 1.59; 95% CI, 1.15 to 2.18;  $P = 0.0040$ ). At 5 and 8 yr posttransplant the results were inconclusive. (Article Selection: Martin J. London. Image: J. P. Rathmell.)

**Take home message:** ABO-incompatible renal transplantation procedures may be associated with excess mortality and loss of kidney grafts when compared with compatible renal transplantation within the first 3 yr after transplantation.