

Key Papers from the Most Recent Literature Relevant to Anesthesiologists



Recurrence of breast cancer after regional or general anaesthesia: A randomised controlled trial. *Lancet* 2019; 394:1807–15.

The stress response to surgery, volatile anesthetics, and opioid analgesics have been associated with impairments in the host defense against cancer recurrence. This study tested the hypothesis that breast cancer recurrence would be lower in patients treated with regional analgesia and propofol anesthesia when compared to opioid analgesia and sevoflurane analgesia in a prospectively randomized, international study. A total of 2,132 women were enrolled in the study. Among these women, 1,043 were assigned to regional analgesia with propofol anesthesia and 1,065 were assigned to opioid analgesia and sevoflurane anesthesia; 24 patients were excluded before surgery. Tumor recurrences were reported to occur in 10% of patients in each group at a median follow-up of 36 months (interquartile range, 24 to 49 months; hazard ratio, 0.97; 95% CI, 0.74 to 1.28; $P = 0.84$). Similarly, there were no differences between the groups for the secondary pain outcomes for up to 1 yr after surgery. (Article Selection: Beatrice Beck-Schimmer. Image: Adobe Stock.)

Take home message: This study suggests that there are no differences in breast cancer recurrence among patients treated with opioid analgesia and sevoflurane anesthesia when compared to those treated with regional analgesia and propofol anesthesia.



Randomized trial of medical versus surgical treatment for refractory heartburn. *N Engl J Med* 2019; 381:1513–23.

Proton pump inhibitor refractory heartburn is common and has multiple etiologies. This study enrolled 336 patients with refractory heartburn and treated them for 2 weeks with 20 mg of omeprazole twice daily and used multiple medical evaluations to identify whether they had reflux-related heartburn. Prerandomization procedures excluded the majority of the patients ($n = 288$ patients) and the remaining 78 patients with reflux-related heartburn were randomized to surgical treatment (laparoscopic Nissen fundoplication, $n = 27$); active medical treatment with omeprazole, baclofen, and \pm desipramine ($n = 25$); or control medical treatment with omeprazole and a placebo ($n = 26$). The primary outcome was treatment success defined as at least a 50% decrease in the Gastroesophageal Reflux Disease Health-Related Quality of Life score at 1 yr. The success rate with surgery was 68% and was superior to both active medical treatment (28% success rate, $P = 0.007$) and control medical management (12% success rate, $P < 0.001$). Interestingly, there were no differences between active and control medical management ($P = 0.17$), perhaps because of the small number of patients enrolled in each group. (Article Selection: Laszlo Vutskits. Image: Adobe Stock.)

Take home message: Surgical management of refractory reflux-related heartburn may be superior to medical management.



Paracetamol is ineffective for acute low back pain even for patients who comply with treatment: Complier average causal effect analysis of a randomized controlled trial. *Pain* 2019; 160:2848–54.

The 2014 Paracetamol for Acute Low Back Pain (PACE) trial suggested that paracetamol had no effect on acute low back pain in a placebo-controlled randomized controlled trial. Unfortunately, noncompliance (70%) was identified as a potential confounder in the study. This study used the same dataset to determine whether there were similar effects in the treatment of acute low back pain among compliant patients when compared to those who were not compliant in taking paracetamol.

The primary outcome was pain intensity measured on a numeric pain rating scale. There were no differences in the numeric pain rating scale between patients who were compliant in taking paracetamol when compared to those who were not compliant using multiple models (propensity-weighted complier average causal effect, 0.07; 95% CI, -0.37 to 0.50 ; $P = 0.76$; joint modelling complier average causal effect, 0.23; 95% CI, -0.16 to 0.62 ; $P = 0.24$; intention-to-treat 0.11; 95% CI, -0.20 to 0.42 ; $P = 0.49$; per protocol 0.29; 95% CI, -0.07 to 0.65 ; $P = 0.12$). (Article Selection: J. David Clark. Image: Adobe Stock.)

Take home message: This study suggests that paracetamol is ineffective in treating low back pain even among patients who are compliant in taking the medication.

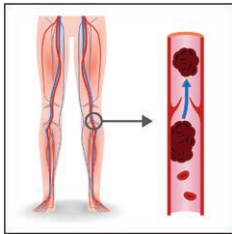


Conservative oxygen therapy during mechanical ventilation in the ICU. *N Engl J Med* 2019 Oct 14 [Epub ahead of print].

Patients undergoing mechanical ventilation in the intensive care unit are often placed on high levels of inspired oxygen despite concerns that high oxygen levels may be associated with systemic and pulmonary oxidative injury. This prospective, parallel-group, randomized clinical trial tested the hypothesis that conservative oxygen therapy (21% oxygen) would result in more ventilator-free days during the first 28 days after randomization than usual oxygen therapy in mechanically ventilated adults in the intensive care unit. A total of 965 patients were included in analysis: 481 in the usual-oxygen group and 481 in the conservative-oxygen group. Despite finding that the conservative-oxygen group spent less time with an oxygen

saturation level at or above 97%, there was no difference in the number of ventilator-free days between the groups (between-group difference -0.3 ; 95% CI, -2.1 to 1.6 ; $P = 0.80$). There were also no differences in mortality, subsequent employment status, and cognitive function (secondary outcomes). (Article Selection: Martin J. London. Image: Adobe Stock.)

Take home message: Conservative oxygen therapy in adult patients requiring mechanical ventilation in an intensive care unit may have no effect on the number of ventilator-free days in the 28 days after initiation of mechanical ventilation.



Prevention and management of venous thromboembolism. *JAMA* 2019 Sep 23 [Epub ahead of print].

The American Society of Hematology and McMaster University GRADE Centre have developed 2018 guidelines for the prevention and management of venous thromboembolism. The major recommendations suggest that venous thromboembolism prophylaxis is recommended in all acutely ill patients during hospitalization. They also identified that low-molecular-weight heparin and fondaparinux are the preferred agents for venous thromboembolism prophylaxis. Among patients at low-to-moderate risk of recurrent venous thromboembolism who require interruption of vitamin K antagonist therapy for invasive procedures, an interruption of anticoagulation is preferred to the use of low-molecular-weight heparin or unfractionated heparin. For pregnant women with an acute venous thromboembolism they suggest treatment with low-molecular-weight heparin over unfractionated heparin. To identify the presence of a pulmonary embolism the authors suggest the use of D-dimer as a strategy to exclude pulmonary embolism in patients at low risk, followed by the use of ventilation/perfusion scans or computed tomography pulmonary angiography for patients requiring additional testing. (Article Selection: Beatrice Beck-Schimmer. Image: Adobe Stock.)

Take home message: There are new guidelines for the prevention and management of venous thromboembolism based on patient demographics that are relevant to anesthesiologists.



Prevalence of survival without major comorbidities among adults born prematurely. *JAMA* 2019; 322:1580–8.

Although it is well known that preterm infants are at greater risk of developing cardiometabolic, respiratory, and neuropsychiatric disorders in adulthood, the prevalence of surviving into adulthood without a major comorbidity is unknown. This study investigated survival without comorbidity in adulthood among 22 to 27, 28 to 33, 34 to 36, and 37 to 38 weeks preterm infants when compared to full-term (39 to 41 weeks) infants using the Adolescent and Young Adult Health Outcomes and Patient Experience and Charlson Comorbidity indices. A total of 2,566,699 live births between 1973 and 1997 in Sweden were included in the study. Overall, the prevalence of live birth without significant comorbidity in adulthood based

on the Adolescent and Young Adult Health Outcomes and Patient Experience index was 0.35 (95% CI, 0.33 to 0.36) among 22 to 27 weeks, 0.76 among 28 to 33 weeks (95% CI, 0.75 to 0.77), 0.91 among 28 to 33 weeks (95% CI, 0.91 to 0.92), and 0.97 among 37 to 38 weeks (0.96 to 0.97) infants when compared to infants born at 39 to 41 weeks. Similar findings were noted on the Charlson Comorbidity index. (Article Selection: Laszlo Vutskits. Image: Adobe Stock.)

Take home message: The majority of preterm babies born in Sweden between 1973 and 1997 survived to adulthood without major comorbidities, but outcomes were worst for the most severely preterm infants.



Common types of gender-based microaggressions in medicine. *Acad Med* 2019 Oct 29 [Epub ahead of print].

Unconscious bias, covert prejudice, and hostility may result in subtle verbal or nonverbal behaviors also known as microaggressions. The goal of this study was to identify common microaggressions reported by faculty of medicine to identify whether gender demographic characteristics are related to the reported frequencies of microaggressions. The authors used a chain referral sampling method to confidentially collect real-life narratives related to microaggressions observed or experienced by faculty of medicine. From these narratives, 34 unique experiences were identified and scripted into 34 pairs of microaggression and control scenarios. Faculty from four medical schools were asked to evaluate each of the 68 videos

and score them from (A) has never happened nor is likely to ever happen to (D) affects every person sometime in their career. Although there were no differences between men and women in the scoring of the control videos, women reported more microaggressions portrayed in 33 of 34 microaggression videos when compared to men. Common themes identified in the 34 videos included sexism, parenting bias, ability bias, sexually inappropriate comments, relegation to mundane tasks, and feeling excluded or marginalized. (*Article Selection: Franklyn Cladis. Image: Adobe Stock.*)

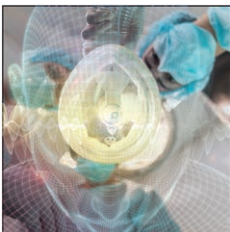
Take home message: Microaggressions in the workplace are more likely to be identified by women in a controlled context, but men may be less likely to recognize them when they occur.



Effect of the tailored, family-involved Hospital Elder Life Program on postoperative delirium and function in older adults: A randomized clinical trial. *JAMA Intern Med* 2019 Oct 21 [Epub ahead of print].

Postoperative delirium is a common finding in older surgical patients. The use of a traditional Hospital Elder Life Program (HELP) has been demonstrated to decrease the incidence of postoperative delirium but relies heavily on the use of volunteers. This study investigated the effect of a tailored, family-involved Hospital Elder Life Program (t-HELP) on the incidence of postoperative delirium in a two-arm, parallel-group, single-blinded, clinical trial in China. A total of 281 patients were included in the study and randomized to a nursing unit providing a tailored family-involved Hospital Elder Life Program ($n = 152$) or a control unit ($n = 129$) between April 3, 2016, and December 30, 2017. The primary outcome was the incidence of postoperative delirium. Postoperative delirium occurred in 2.6% of patients enrolled in the tailored, family-involved Hospital Elder Life Program and 19.4% in the control group with a relative risk of 0.14 (95% CI, 0.05 to 0.38). To prevent one case of delirium, the number needed to treat was 5.9 (95% CI, 4.2 to 11.1). (*Article Selection: Martin J. London. Image: Adobe Stock.*)

Take home message: A tailored, family-involved Hospital Elder Life Program may be used to prevent the development of postoperative delirium in elders.



Anaesthetic depth and complications after major surgery: An international, randomised controlled trial. *Lancet* 2019; 394:1907–14.

Observational studies have made associations between anesthetic depth and an increase in postoperative mortality. The aim of this study was to investigate all-cause 1-yr mortality in older patients having major surgery who were randomly assigned to light or deep general anesthesia. Patients 60 yr of age and older undergoing major surgery that was expected to last more than 2 h were enrolled. Enrollment was conducted at 73 institutions in seven countries ($n = 6,644$) over 5 yr and patients were randomized to receive deep (Bispectral Index target 35, $n = 3,328$) versus light (Bispectral Index target 50, $n = 3,316$) anesthesia. One-year mortality was 6.5% in the light group and 7.2% in the deep group (hazard ratio, 0.88;

95% CI, 0.73 to 1.07). There were also no differences between the groups in adverse events including primarily infections, vascular disorders, cardiac disorders, and neoplasms. (*Article Selection: Beatrice Beck-Schimmer. Image: Adobe Stock.*)

Take home message: This prospective randomized study found that there was no effect of deep relative to lighter general anesthesia on 1-yr mortality or other patient outcomes.



Effect of postextubation high-flow nasal oxygen with noninvasive ventilation vs high-flow nasal oxygen alone on reintubation among patients at high risk of extubation failure. JAMA 2019 Oct 2 [Epub ahead of print].

Multiple studies have demonstrated that administration of high-flow nasal oxygen may prevent respiratory failure after extubation in the intensive care unit. This study investigated whether high-flow nasal oxygenation with noninvasive ventilation immediately after extubation reduces the risk of reintubation when compared with high-flow oxygenation alone in patients at high risk of extubation failure in the intensive care unit. This multicentered clinical trial randomized 641 patients over the age of 65 to high-flow nasal oxygen ($n = 302$) or high-flow nasal oxygen with noninvasive ventilation ($n = 339$) immediately

after extubation. The primary outcome was the percentage of patients reintubated at day 7. The reintubation rate for those randomized to high flow nasal oxygen alone was 18% (95% CI, 14 to 23%) and 12% for those receiving high-flow nasal oxygen with noninvasive ventilation (95% CI, 8 to 15%) with a difference of -6% (95% CI, -12 to -1%, $P = 0.02$). (Article Selection: Beatrice Beck-Schimmer and Laszlo Vutskits. Image: Adobe Stock.)

Take home message: In high-risk older patients in the intensive care unit, administration of high-flow nasal oxygen plus noninvasive ventilation may decrease the risk of reintubation when compared to high-flow nasal oxygen alone.



Risk of wrong-patient orders among multiple vs singleton births in the neonatal intensive care units of 2 integrated health care systems. JAMA Pediatr 2019 Aug 26 [Epub ahead of print].

Multiple-birth infants admitted to the neonatal intensive care unit often have similar patient identifiers that may place them at higher risk of wrong-patient orders when compared to single-birth infants. This retrospective study involved six neonatal intensive care units in two integrated healthcare systems. The primary outcome was wrong-patient electronic orders based on a Wrong-Patient-Retract-and-Reorder Measure defined by one or more orders retracted by a clinician within 10 min and then reordered by the same clinician to a new patient within 10 min. Among the 10,819 patients who were included

in the study the majority were single-birth infants (85%) and 14.5% were multiple-birth infants. In contrast, the wrong-patient order rate was higher with multiple-birth infants (66 per 100,000 orders) when compared to single-birth infants (42 per 10,000 orders) with an adjusted odds ratio of 1.75 (95% CI, 1.39 to 2.20; $P < 0.001$). (Article Selection: Laszlo Vutskits. Image: Adobe Stock.)

Take home message: The risk of wrong-patient orders in the neonatal intensive care unit may be higher with multiple births when compared to single births, which suggests that vigilance and organizational strategies should be used to prevent these errors.



Association of disposable perioperative jackets with surgical site infections in a large multicenter health care organization. JAMA Surg 2019 Oct 23 [Epub ahead of print].

Despite minimal evidence of benefit, the Association for Perioperative Nurses in 2015 recommended that long-sleeved disposable jackets should be worn by all nonscrubbed personnel in the operating room and perioperative areas to reduce the risk of surgical site infections. This study tested the hypothesis that the use of long-sleeved disposable perioperative jackets and the associated policy would not reduce the incidence of surgical site infection but that it would increase cost.

More than 60,000 patients were included in this retrospective study. The incidence of surgical site infection for clean wounds was 0.87% before and 0.83% after policy implementation (odds ratio, 0.96; 95% CI, 0.80 to 1.14; $P = 0.61$). During the policy implementation, 2,010,040 jackets were purchased at a cost of \$1,709,898. (Article Selection: Deborah J. Culley. Image: Adobe Stock.)

Take home message: The use of disposable perioperative jackets may not reduce the incidence of surgical site infections but does increase healthcare costs.