SCIENCE, MEDICINE, AND THE ANESTHESIOLOGIST

ANESTHESIOLOGY

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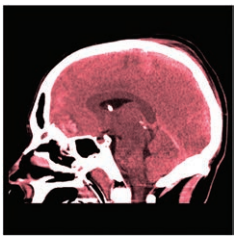
Key Papers from the Most Recent Literature Relevant to Anesthesiologists

Efficacy of low-dose amitriptyline for chronic low back pain: A randomized clinical trial. JAMA Intern Med 2018; 178:1474–81.

Low-dose tricyclic antidepressants have been used to treat chronic low back pain but questions remain about their efficacy. This study examined the efficacy of two low-dose antidepressants in reducing pain and disability in a randomized, double-blind trial. Patients received either low-dose amitriptyline (25 mg/d) or benztropine mesylate (1 mg/d) for 6 months. The primary outcome was pain intensity using the visual analog scale and Descriptor Differential Scale. Of the 146 participants, 118 (81%) completed 6-month follow-up. Treatment with low-dose amitriptyline did not result in greater pain reduction than benztropine mesylate at 6 (adjusted difference, –7.81; 95% CI, –15.7 to 0.10) or 3 months (adjusted difference, –1.05; 95% CI, –7.87 to 5.78), independent of baseline pain. Similarly, there was no statistically significant difference in disability between the groups at 6 months (adjusted difference, –0.98; 95% CI, –2.42 to 0.46). In contrast, there was a statistically significant improvement in disability in the low-dose amitriptyline group at 3 months (adjusted difference, –1.62; 95% CI, –2.88 to –0.36), suggesting that amitriptyline may be an effective treatment for chronic low back pain. *(Article Selection: J. David Clark. Image: ©gettyimages.)*

Take home message: Low-dose amitriptyline may reduce disability in patients with chronic low back pain but may not be superior to benztropine mesylate for reducing pain.



Effect of early sustained prophylactic hypothermia on neurologic outcomes among patients with severe traumatic brain injury: The POLAR randomized clinical trial. JAMA 2018; 320:2211–20.

Prophylactic hypothermia has been suggested to improve long-term neurologic outcomes among patients with traumatic brain injury. This study compared early prophylactic hypothermia with normothermic management of patients after traumatic brain injury in a randomized, controlled, multicenter trial in 6 countries. Patients randomized to the prophylactic hypothermia group were treated with hypothermia (33° to 35°C) for at least 72 h and up to 7 days after injury they had elevated intracranial pressures, followed by gradual rewarming. The normothermia group targeted temperature at 37°C. All other care was at the discretion of the treating physician. The primary outcome was favorable neurologic outcomes obtained by blinded assessors 6 months after injury. Favorable outcomes occurred in 117 patients (48.8%) in the hypothermia group and 111 (49.1%) in the normothermia group (risk difference, 0.4% [95% CI, –9.4 to 8.7%]; relative risk with hypothermia, 0.99 [95% CI, 0.82 to 1.19]; $P = 0.94$). In the hypothermia and normothermia groups, there were no differences in the rate of pneumonia or increased intracranial bleeding. The findings of this study do not support early prophylactic hypothermia for the treatment of traumatic brain injury patients. *(Article Selection: Martin J. London. Image: J. P. Rathmell.)*

Take home message: Induced hypothermia in the setting of traumatic brain injury may not lead to favorable outcomes when compared to maintenance of normothermia.

Haloperidol and ziprasidone for treatment of delirium in critical illness. N Engl J Med 2018 Oct 22 [Epub ahead of print].

The effect of antipsychotic medications on the development of delirium in intensive care unit patients remains controversial. This double-blinded study randomized patients with acute respiratory failure or shock who developed delirium to intravenous haloperidol (maximum dose, 20 mg daily), ziprasidone (maximum dose, 40 mg daily), or placebo. The primary outcomes were days alive without delirium or coma. Of the 566 patients that developed delirium, 184 received placebo, 192 received haloperidol, and 190 received ziprasidone. The median number of days alive without delirium or coma was 8.5 (95% CI, 5.6 to 9.9) in the placebo group, 7.9 (95% CI, 4.4 to 9.6) in the haloperidol group, and 8.7 (95% CI, 5.9 to 10.0) in the ziprasidone group ($P = 0.26$ for overall effect across groups). The use of haloperidol or ziprasidone had no significant effect on the primary endpoint (odds ratios, 0.88 [95% CI, 0.64 to 1.21] and 1.04 [95% CI, 0.73 to 1.48], respectively). *(Article Selection: Martin J. London. Image: J. P. Rathmell.)*

Take home message: This study suggests that the use of haloperidol or ziprasidone in intensive care unit patients with delirium may not significantly alter the duration of delirium.

Effect of immediate vs delayed pushing on rates of spontaneous vaginal delivery among nulliparous women receiving neuraxial analgesia: A randomized clinical trial. JAMA 2018; 320:1444–54.

Questions remain about whether early or delayed second stage pushing affect spontaneous vaginal delivery rates and maternal and neonatal morbidity. This study evaluated whether immediate or delayed pushing results in higher rates of spontaneous vaginal delivery (primary outcome) or lower rates of maternal and neonatal morbidities (secondary outcomes). Nulliparous women at 37+ weeks' gestation admitted for spontaneous or induced labor with neuraxial analgesia were randomized at complete cervical dilation to either a control group (n = 1,200) that began pushing immediately or a delayed group (n = 1,204) instructed to wait 60 min before pushing. There were no differences in the rate of spontaneous vaginal delivery between the two groups (85.9% in the immediate group *vs.* 86.5% in the delayed group; absolute difference, –0.6% [95% CI, –3.4 to 2.1%]; relative risk, 0.99 [95% CI, 0.96 to 1.03]). The duration of the second stage of labor was significantly shorter in the immediate group compared with the delayed group (102.4 *vs.* 134.2 minutes, respectively; $P < 0.001$). *(Article Selection: Laszlo Vutskits. Image: J. P. Rathmell.)*

Take home message: This study suggests that the timing of pushing during the second stage of labor in nulliparous women receiving neuraxial anesthesia had no effect on the rate of spontaneous vaginal delivery.

<zdoi;10.1097/ALN.0000000000002556>

Effect of early surgery vs physical therapy on knee function among patients with nonobstructive meniscal tears: The ESCAPE randomized clinical trial. JAMA 2018; 320:1328–37.

Despite studies demonstrating that arthroscopic partial meniscectomy may not be more effective than physical therapy for the treatment of meniscal tears, it continues to be frequently performed. This study assessed whether physical therapy is noninferior to arthroscopic partial meniscectomy for improving patient-reported knee function. Participants were randomly assigned to arthroscopic partial meniscectomy (n = 159) or physical therapy (n = 162). The primary outcome was change in patient-reported knee function at 24-month follow-up. The noninferiority margin was an 8-point difference between groups with a 1-sided α of 0.025. In the physical therapy group, 47 participants (29%) had arthroscopic partial meniscectomy during the 24-month follow-up period. During a 24-month follow-up period, knee function improved in the arthroscopic partial meniscectomy group by 26 points (95% CI, 23 to 29) and in the physical therapy group by 20 points (95% CI, 18 to 23). The overall between-group difference was 3.6 points, suggesting that physical therapy is noninferior to arthroscopic partial meniscectomy for treatment of meniscal tears. *(Article Selection: J. David Clark. Image: ©gettyimages.)*

Take home message: Among patients with meniscal tears, physical therapy appears to be noninferior to arthroscopic partial meniscectomy for improving patient-reported knee function and may be considered as a surgical alternative.

The artificial intelligence clinician learns optimal treatment strategies for sepsis in intensive care. Nat Med 2018; 24:1716–20.

Sepsis is the main cause of mortality in hospitals, but the best treatment strategy for sepsis remains uncertain and there are concerns that the administration of intravenous fluids and vasopressors may be suboptimal and likely harmful in some patients. The authors developed the Artificial Intelligence Clinician, a computational model using reinforcement learning, which extracted implicit knowledge from a training dataset of 17,083 patients hospitalized with sepsis (88.4% of eligible patients). The testing dataset consisted of data from 79,073 admissions (73.6% of eligible patients). The authors extracted a set of 48 variables from each dataset, including demographics, vital signs, laboratory values, and intravenous fluids and vasopressors. On average, the Artificial Intelligence Clinician recommended lower doses of intravenous fluids and higher doses of vasopressors than the clinicians actually used. Overall, mortality in the validation cohort was lowest in patients for whom clinicians' actual doses matched the Artificial Intelligence decisions. The authors concluded that their model provides individualized and clinically interpretable treatment decisions for sepsis that could improve patient outcomes. *(Article Selection: Beatrice Beck-Schimmer. Image: ©gettyimages.)*

Take home message: Artificial Intellegence "clinicians" may eventually be useful in aiding in treatment decisions for sepsis.

Association between temporal changes in neonatal mortality and spontaneous and clinician-initiated deliveries in the United States, 2006–2013. JAMA Pediatr 2018; 172:949–57.

During the past decade, the number of preterm and postterm deliveries have decreased but little is known about whether this is associated with decreases in neonatal mortality. This study estimated changes in gestational age distribution among spontaneous and clinician-initiated deliveries and associated changes in neonatal mortality using a retrospective cohort analysis of 22 million births. Among clinician-initiated deliveries (43.3% of total), the proportion of births at 34 to 36 and 37 to 38 weeks declined and the proportion at 39 to 40 weeks increased. Among spontaneous deliveries, overall neonatal mortality rates declined from 1.8 to 1.3 per 1,000 live births, mainly at 20 to 27 weeks (adjusted annual decline, 1%; 95% CI, –2% to –1%) and 28 to 31 weeks (adjusted annual decline, 6%; 95% CI, –8% to –5%). Among clinician-initiated deliveries, overall mortality rates remained unchanged (2.1 to 2.2 per 1,000 live births). However, mortality rates declined (0.6 to 0.5 per 1,000 live births) at 39 to 40 weeks by 1% (95% CI, –3% to –0.4%) annually. *(Article selection: Laszlo Vutskits. Image: ©gettyimages.)*

Take home message: This study suggests that the reduction of spontaneous deliveries between 20 to 31 weeks is associated with a decrease in neonatal mortality. In addition, there was a decrease in neonatal mortality in clinician-initiated deliveries between 30 and 40 weeks.

Pantoprazole in patients at risk for gastrointestinal bleeding in the ICU. N Engl J Med 2018 Oct 24 [Epub ahead of print].

Patients in the intensive care unit frequently receive prophylaxis for gastrointestinal ulcerations although the risk–benefit ratio remains unclear. The authors of this prospective, randomized, multicenter trial assigned 3,282 adults with unplanned intensive care unit admission to receive 40 mg of intravenous pantoprazole or placebo daily during the intensive care unit stay. The primary outcome was death within 90 days after randomization. At 90 days, 510 patients (31.1%) in the pantoprazole group and 499 (30.4%) in the placebo group had died (relative risk, 1.02; 95% CI, 0.91 to 1.13; $P = 0.76$). During the intensive care unit stay, at least one clinically important event (significant gastrointestinal bleeding, pneumonia, *Clostridium difficile* infection, or myocardial ischemia) had occurred in 21.9% of pantoprazole patients and 22.6% of those on placebo (relative risk, 0.96; 95% CI, 0.83 to 1.11). In the pantoprazole group, 2.5% of patients had clinically important gastrointestinal bleeding, as compared with 4.2% on placebo. *(Article selection: Laszlo Vutskits. Image: ©gettyimages.)*

Take home message: This study suggests that the administration of pantoprazole to patients admitted to an intensive care had no effect on mortality or clinically important advents events for at least 90 days after admission to the intensive care unit.

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Predicting performance of first-year residents: Correlations between structured interview, licensure exam, and competency scores in a multi-institutional study. Acad Med 2018 Aug 28 [Epub ahead of print].

Core competencies other than those in cognitive domains are not well measured during residency. This study examined whether scores on structured interview questions that measure noncognitive competencies predict subsequent first-year resident performance on Accreditation Council for Graduate Medical Education Milestones and whether structured interviews added incremental predictive validity over U.S. Medical Licensing Examination Clinical Knowledge scores. Eighteen behavioral description questions were used to measure noncognitive competencies like teamwork during the resident selection processes in 14 programs and evaluated the validity of structured interviews and U.S. Medical Licensing Examination scores in predicting first-year resident milestone performance in the Accreditation Council for Graduate Medical Education core competency domains. Structured interview scores predicted mid-year and year-end overall performance (r = 0.18 and 0.19, respectively; $P < 0.05$) and year-end performance on patient care, interpersonal and communication skills, and professionalism competencies (r = 0.23, r = 0.22, and r = 0.20, respectively; $P < 0.05$). Structured interview scores predicted year-end resident or fellow performance in areas involving patient care, interpersonal and communication skills, and professionalism. *(Article selection: Franklyn Cladis. Image: ©gettyimages.)*

Take home message: This study suggests that structured interview scores may predict first-year resident year-end performance in interpersonal and communication skills, patient care, and professionalism competency domains.

Frequency and associations of prescription nonsteroidal anti-inflammatory drug use among patients with a musculoskeletal disorder and hypertension, heart failure, or chronic kidney disease. JAMA Intern Med 2018; 178:1516–25.

Nephrology societies advise against nonsteroidal antiinflammatory drug (NSAID) use in patients with hypertension, heart failure, or chronic kidney disease. This study estimated the frequency of prescription NSAID use among patients that are at high-risk of complications using administrative claims databases to create a cohort of 2.4 million primary care visits for musculoskeletal disorders involving high-risk older adults. Of these, 224,825 (9.3%) were followed by prescription NSAID use. Multiple cardiovascular and renal safety-related outcomes occurred within 8 and 37 days, including cardiac and renal complications and death. The median physician-level prescribing rate was 11.0% (interquartile range, 6.7 to 16.7%) among 7,365 primary care physicians. In 35,552 exposed/nonexposed matched patient pairs, the rates of cardiac complications, renal complications, and death were not different between the exposed and nonexposed patients (absolute risk reduction, 0.0003; 95% CI, –0.001 to 0.002; $P = 0.74$). *(Article selection: J. David Clark. Image: J. P. Rathmell.)*

Take home message: Although the use of NSAID drugs is high among patients at risk of adverse outcomes, this study suggests that it is not associated with an increased risk of short-term adverse outcomes.

Effects of aspirin for primary prevention in persons with diabetes mellitus. N Engl J Med 2018; 379:1529–39.

The risk–benefit ratio of aspirin use to prevent cardiovascular events in patients with diabetes is uncertain. This study randomized 15,480 adults who had diabetes but no evidence of cardiovascular disease to receive aspirin (100 mg daily) or placebo. The primary outcomes were the development of a first major vascular or bleeding event. Serious vascular events occurred in a lower percentage of participants randomized to the aspirin group when compared to the control group (8.5% *vs.* 9.6%; rate ratio, 0.88; 95% CI, 0.79 to 0.97; $P = 0.01$). In contrast, major bleeding events were more likely in the aspirin group, (4.1% *vs.* 3.2%; rate ratio, 1.29; 95% CI, 1.09 to 1.52; $P = 0.003$) resulting in a counterbalance of the risk benefit ratio between the aspirin and placebo groups. *(Article selection: Laszlo Vutskits. Image: ©gettyimages.)*

Take home message: This study suggests that the risk of using aspirin to prevent serious vascular events in patients with diabetes may be counterbalanced by an increased risk of bleeding events.

Association of angiotensin-converting enzyme inhibitor or angiotensin receptor blocker use with outcomes after acute kidney injury. JAMA Intern Med 2018; 178:1681–90.

Therapeutic strategies that improve long-term outcomes in patients with acute kidney injury are not well described. This study evaluated whether the use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers is associated with better outcomes in patients with acute kidney injury. The authors used the Alberta Kidney Disease Network database to evaluate 46,253 patients with acute kidney injury and followed them for at least 2 yr. Propensity scores were used to construct a cohort of patients with and without prescriptions for an angiotensin-converting enzyme inhibitors or angiotensin receptor blockers. The primary outcome was mortality. Within 6 months of discharge, 22,193 (48.0%) of participants were prescribed an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker. Angiotensin-converting enzyme inhibitor or angiotensin receptor blocker use was associated with lower mortality in patients with acute kidney injury after 2 yr (adjusted hazard ratio, 0.85; 95% CI, 0.81 to 0.89). However, patients who received an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker had a higher risk of hospitalization for renal causes (adjusted hazard ratio, 1.28; 95% CI, 1.12 to 1.46). *(Article selection: Martin J. London. Image: J. P. Rathmell.)*

Take home message: This study suggests that angiotensin-converting enzyme inhibitor or angiotensin receptor blocker therapy may decrease mortality in patients with acute kidney injury but may increase the risk of subsequent hospitalization for renal causes.

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Association of prenatal maternal depression and anxiety symptoms with infant white matter microstructure. JAMA Pediatr 2018; 172:973–81.

Maternal anxiety and depression have been associated with long-term effects on child development. The effect of maternal symptoms of anxiety and depression on early brain development remains unclear. This study examined the association between third-trimester maternal anxiety and depression symptoms on offspring brain white matter at 1 month of age. The authors used diffusion tensor imaging and neurite orientation dispersion and density imaging to evaluate whether there was an association between maternal depression and anxiety and 1-month infant white matter microstructure. Among 101 mother-infant dyads, lower 1-month right frontal white matter microstructure (decreased neurite density and increased mean, radial, and axial diffusivity) was associated with higher prenatal maternal symptoms of anxiety and depression. In addition, there were suggestions of sex differences in these outcomes on univariate analysis that were no longer significant after accounting for multiple comparisons. *(Article selection: Laszlo Vutskits. Image: J. P. Rathmell.)*

Take home message: This study suggests that maternal prenatal anxiety and depression may be associated with white matter changes at 1 month of age in their offspring.

Twelve tips for using applied improvisation in medical education. Med Teach 2018; 40:351–6.

Learning how to teach complex interpersonal skills is an important component of resident education. This manuscript describes "best practices" in using applied improvisation as an instructional strategy, utilizing the concepts of improvisational theater to teach complex interpersonal skills that can be used to enhance medical education in teamwork, power structure, and patient-centeredness. It is most effective when directly connected to curricular content as the improvisational games are designed to teach a specific concept or illuminate a hidden concept that fuels reflective thinking to maximize learning outcomes. The practical tips described in this manuscript are aimed to help medical faculty that are new to improvisation to establish goals, choose appropriate games, understand the value of effective debriefing, consider novel evaluation strategies, and managing resistance to this type of learning. Some tips include understanding applied improvisation as both a mindset and an approach to training, establishing trust and safety, appropriate sequencing of improvisational games, and emphasizing the interdependence of the team. *(Article selection: Franklyn Cladis. Image: ©gettyimages.)*

Take home message: Applied improvisation may be used to enhance medical education in areas of teamwork and patient-centeredness.

Forecasting life expectancy, years of life lost, and all-cause and cause-specific mortality for 250 causes of death: Reference and alternative scenarios for 2016–40 for 195 countries and territories. Lancet 2018; 392:2052–90.

Past global health forecasts have highlighted the need for a more robust modeling to assess health care policy and potential health trajectories. This study provides a novel approach to modeling life expectancy, all-cause mortality and cause-of-death forecasts for 250 causes of death from 2016 to 2040 in 195 countries and territories. This study utilized a flexible forecasting platform from which reference forecasts and alternative health scenarios can be explored relative to a wide range of independent healthcare drivers. The reference forecast suggests overall improvements in health through 2040 in most countries, yet the range found across better and worse health scenarios renders a precarious vision of a world with accelerating progress from technical innovation but with the potential for worsening health outcomes in the absence of deliberate policy action. This study suggests that decision-makers should plan for a potential shift toward noncommunicable diseases and focus resources toward the modifiable risk factors that associated with substantial premature mortality. Prioritization of modifiable disease risk factors may lead to reduced avoidable mortality in the future. *(Article selection: Beatrice Beck-Schimmer. Image: J. P. Rathmell.)*

Take home message: Identification of modifiable risk factors for premature death and focusing resources on them now may lead to a reduction in avoidable mortality in the future.

<zdoi;10.1097/ALN.0000000000002556>