SCIENCE, MEDICINE, AND THE ANESTHESIOLOGIST

ANESTHESIOLOGY

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Key Papers from the Most Recent Literature Relevant to Anesthesiologists

Modifiable risk factors, cardiovascular disease, and mortality in 155 722 individuals from 21 high-income, middle-income, and low-income countries (PURE): A prospective cohort study. Lancet 2019 Sep 3 [Epub ahead of print].

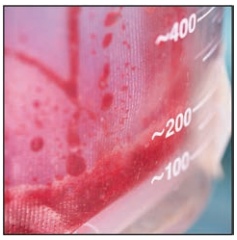
International estimations about the effect of modifiable risk factors on cardiovascular disease and mortality have often been based on multiple smaller studies. This international, prospective study examined associations between potentially modifiable risk factors for cardiovascular disease and mortality in 155,722 patients without a previous history of cardiovascular disease among 21 high-, middle-, and low-income countries between January 6, 2005, and December 4, 2016. The study noted that regardless of income status, low education (hazard ratio, 13; 95% CI, 11 to 14), tobacco use (hazard ratio, 11; 95% CI, 8 to 15), low grip strength (hazard ratio, 12; 95% CI, 7 to 16), poor diet (hazard ratio, 11; 95% CI, 8 to 15), hypertension (hazard ratio, 9; 95% CI, 8 to 10), household air pollution (hazard ratio, 7; 95% CI, 5 to 9), diabetes (hazard ratio, 6; 95% CI, 4 to 7), abdominal obesity (hazard ratio, 3; 95% CI, 1 to 4), depression (hazard ratio, 2; 95% CI, 1 to 4), and low physical activity (hazard ratio, 2; 95% CI, 1 to 3) were associated with overall death in high-, middle-, and low-income countries. *(Article Selection: Beatrice Beck-Schimmer. Photo: Adobe Stock. Illustration: M. Lane-Fall.)*

Take home message: Regardless of income, low education, tobacco use, grip strength, diet, hypertension, air pollution, diabetes, obesity, depression, and low physical activity are associated with a higher overall death rate internationally.

The contribution of obesity to prescription opioid use in the United States. Pain 2019; 160:2255–62.

Over the past couple of decades, obesity, chronic pain, and opioid use have increased. The purpose of this study was to investigate the relationships between obesity and prescription opioid use using National Health and Nutrition Examinations Surveys between 2003 and 2016. A total of 25,424 individuals between the ages of 35 and 79 yr with a body mass index between 15 and 80 kg/m^2 were included in this study. After adjusting for covariates, the use of prescription opioids for more than 90 days was progressively associated with higher body mass index when compared to those of normal weight. For patients with a body mass index between 30.0 and 34.9, the relative risk for persistent opioid use was 1.36 (95% CI, 1.06 to 1.75; $P = 0.02$), progressing for those with a body mass index between 35.0 and 39.9 to a relative risk of 1.89 (95% CI, 1.44 to 2.48; $P < 0.001$). Further progression was noted among those with a body mass index between 40 and 80, where the relative risk of chronic opioid use was 2.89 (95% CI, 2.12 to 3.88; $P < 0.001$). *(Article Selection: J. David Clark. Image: Adobe Stock.)*

Take home message: Increasing body mass index may be associated with an increased risk for chronic opioid use.



Window of opportunity to mitigate trauma-induced coagulopathy: Fibrinolysis shutdown not prevalent until 1 hour post-injury. Ann Surg 2019; 270:528–34.

The development of coagulopathy in the setting of trauma in children is associated with adverse outcomes. This prospective observational study was performed in children less than 18 yr old with a trauma exposure being admitted to a level 1 pediatric trauma center who had thromboelastography measured on arrival to the trauma center and where the time of injury was documented. The primary outcomes were in-hospital mortality, functional disability, massive transfusion, and the incidence of deep vein thrombosis in 285 patients. Normal fibrinolysis was noted in 51% of patients within 1 h of injury; however, between 1 and 3 h after injury, normal fibrinolysis was noted in only 38% of patients and this was reduced to 27% in those patients where the injury was noted to be more than 3 h before thromboelastographic measurement. Hyperfibrinolysis and shutdown of fibrinolysis were associated with mortality, massive transfusion, and the development of deep vein thrombosis. *(Article Selection: Deborah J. Culley. Image: Adobe Stock.)*

Take home message: Normal fibrinolysis is noted in 51% of pediatric trauma patients. Abnormal fibrinolysis after trauma is associated with adverse outcomes.

Single inhaler extrafine triple therapy in uncontrolled asthma (TRIMARAN and TRIGGER): Two double-blind, parallel-group, randomised, controlled phase 3 trials. Lancet 2019; 394:1737–49.

The effectiveness of single-inhaler therapy containing a corticosteroid, long-acting β_2 agonist and long-acting muscarinic antagonist when compared to single-inhaler therapy containing a corticosteroid and a long-acting β_2 agonist remains unknown. This article describes two parallel, double-blind randomized and active-controlled, international phase 3 trials involving 2,592 patients enrolled between 2016 and 2018. The primary endpoints for the studies were morning predose forced expiratory volume in 1 s at week 26 and the rate of moderate and severe exacerbations over 52 weeks in each study. After 26 weeks of treatment, forced expiratory volume in 1 s was improved in the group assigned to single-inhaler containing a corticosteroid, long-acting β_2 agonist and long-acting muscarinic antagonist in both study 1 (57 ml; 95% CI, 15 to 99; $P = 0.0080$) and study 2 (73 ml; 95% CI, 26 to 120; $P = 0.0025$) when compared to those treated with single-inhaler therapy containing only a corticosteroid and a long-acting β_2 agonist. However, there were no differences in moderate or severe exacerbations between the two treatment groups at 52 weeks. *(Article Selection: Beatrice Beck-Schimmer. Illustration: M. Lane-Fall.)*

Take home message: Treatment with single-inhaler therapy containing a corticosteroid, long-acting β_2 agonist and long-acting muscarinic antagonist when compared to single-inhaler therapy containing a corticosteroid and a long-acting β_2 alone may be associated with improved forced expiratory volume in 1 s but may not decrease the incidence of moderate to severe asthma exacerbations.

Recovery of physical activity after cesarean delivery and its relationship with pain. Pain 2019; 160:2350–7.

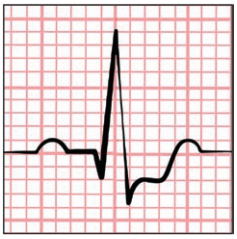
There are data demonstrating relationships between chronic pain and decreased physical activity, but less is known about the relationship between postoperative pain and physical activity after cesarean section. This study recruited 103 patients who had undergone elective cesarean delivery to evaluate the feasibility of measuring pain and hourly steps for 2 months after surgery. The primary outcome was the sum of daytime steps over time. The authors noted good compliance among the participants with 78% of the subjects having less than 7 days of missing data over the course of the 2-month study. The number of steps varied between participants but overall the number of daytime steps increased, and the number of nighttime steps decreased over the first 2 postoperative months, and both were highly correlated. On secondary analysis, the authors noted that the number of steps and pain were associated, with each single-point increase in pain being inversely associated with fewer steps (–119 steps; 95% CI, –2,214 to –224; $P = 0.01$). Although this difference is statistically significant, it remains unclear whether this is a clinically relevant difference. *(Article Selection: J. David Clark. Image: Adobe Stock.)*

Take home message: The number of steps taken after cesarean section decreases over the course of the subsequent two months.

Association of decreased postsurgical opioid prescribing with patients' satisfaction with surgeons. JAMA Surg 2019 Oct 16 [Epub ahead of print].

Opioids are commonly prescribed to treat pain in the postoperative period, but over-prescription of opioids is common. What is less clear is whether decreasing both the number of prescriptions and the number of pills per prescription is associated with changes in patient satisfaction with their surgeon. This retrospective study evaluated patient-reported surgeon satisfaction scores before and after an educational intervention to reduce opioid prescribing. Before the educational intervention, 90% of patients were provided with postoperative opioid prescriptions, which decreased to 73% after the educational intervention ($P < 0.001$). Similarly, the number of pills per prescription was reduced from 28 to 13 after the educational intervention ($P < 0.001$). There was a total of 996 patient-reported satisfaction scores. The surgeon satisfaction scores were 9.6 both before and after the education intervention ($P = 0.62$). *(Article Selection: Deborah J. Culley. Image: J. P. Rathmell.)*

Take home message: Decreasing opioid prescriptions in the postoperative period may not lead to lower surgeon satisfaction scores.



Effect of remote ischaemic conditioning on clinical outcomes in patients with acute myocardial infarction (CONDI-2/ERIC-PPCI): A single-blind randomised controlled trial. Lancet 2019; 394:1415–24.

Remote ischemic conditioning has been associated with reductions in myocardial infarct size in patients with ST-elevation myocardial infarction treated with primary percutaneous coronary intervention. This study describes the results of a prospective, single-blinded, randomized control trial involving 5,401 patients to investigate whether ischemic conditioning could also reduce the incidence of cardiac death and hospital readmission for heart failure at 12 months. A total of 5,115 (2,569 controls, 2,546 remote ischemic conditioning) patients completed the study. The authors report that the risk of cardiac death or hospitalization for heart failure occurred in 8.6% of the control patients and 9.4% of patients who received remote ischemic conditioning (hazard ratio, 1.1; 95% CI, 0.91 to 0.32; $P = 0.32$). These data suggest that although remote ischemic conditioning may lead to smaller infarct size, it may not be associated with superior long-term outcomes. *(Article Selection: Beatrice Beck-Schimmer. Image: J. P. Rathmell.)*

Take home message: Although remote ischemic conditioning may decrease myocardial infarct size, it does not appear to be associated with improved long-term outcomes.

Early and late mortality following discharge from the ICU: A multicenter prospective cohort study. Crit Care Med 2019 Oct 11 [Epub ahead of print].

Although much effort is placed on increasing intensive care unit (ICU) survival, much less is known about mortality after discharge from an ICU. This multicenter, prospective cohort study recruited patients 18 yr old and older who survived their ICU stay and were discharged from the hospital. The investigators performed telephone interviews at 3, 6, and 12 months after discharge. A total of 1,454 patients were included in the follow-up analysis and another 100 were lost to follow-up. On multivariate analysis, mortality within 30 days of discharge was associated with age greater than 65 yr (hazard ratio, 1.65; 95% CI, 1.11 to 2.45; $P = 0.01$), high comorbidities (hazard ratio, 1.59; 95% CI, 1.07 to 2.37; $P = 0.02$), physical dependence (hazard ratio, 2.29; 95% CI, 1.57 to 3.33; $P < 0.001$), risk of death at ICU admission (hazard ratio, 1.008; 95% CI, 1.001 to 1.015; $P = 0.03$ per 1% increase in risk), ICU-acquired infections (hazard ratio, 2.25; 95% CI, 1.47 to 3.44; $P < 0.001$), and ICU readmission (hazard ratio, 3.76; 95% CI, 2.54 to 5.56; $P < 0.001$). Late mortality was associated with age greater than 65 yr (hazard ratio, 1.30; 95% CI, 1.02 to 1.64; $P = 0.03$), high comorbidities (hazard ratio, 2.28; 95% CI, 1.76 to 2.95; $P < 0.001$), physical dependence (hazard ratio, 2.00; 95% CI, 1.56 to 2.56; $P < 0.001$), risk of death at ICU admission (hazard ratio, 1.010; 95% CI, 1.007 to 1.015; $P < 0.001$ per 1% increase in risk), and ICU readmission. *(Article Selection: Deborah J. Culley. Image: J. P. Rathmell.)*

Take home message: There are a number of predictors of both early and late mortality after care in an ICU, including age, multiple comorbidities, physical dependence, risk of death at ICU admission, ICU readmission, and ICU-acquired infections.

Risk of pulmonary embolism more than 6 weeks after surgery among cancer-free middle-aged patients. JAMA Surg 2019 Oct 9 [Epub ahead of print].

Although the risk of pulmonary embolism is high in the perioperative period, it remains unclear how long after surgery this risk remains. This retrospective study used data from the French national inpatient database involving 60,703 patients who developed a pulmonary embolism included in the analysis. For all surgical procedures, the risk of pulmonary embolism increased beyond the first 6 weeks after surgery with odds ratios ranging from 5.24 (95% CI, 3.91 to 7.01) for vascular surgery to 8.34 (95% CI, 6.07 to 11.45) for fracture surgery. At 18 weeks postsurgery the risk of pulmonary embolism was increased for patients with fractures (odds ratio, 2.39; 95% CI, 1.65 to 3.46), hip or knee replacement (odds ratio, 2.26; 95% CI, 1.53 to 3.35), and vascular surgery (odds ratio, 2.64; 95% CI, 1.80 to 3.89). There was little evidence for risk of pulmonary embolism 18 weeks after surgery. *(Article Selection: Gregory Crosby. Image: ©gettyimages.)*

Take home message: This study suggests that the risk of pulmonary embolism persists for up to 18 weeks after a surgical procedure.

 DOI: 10.1097/ALN.0000000000003082

Waste in the US health care system: Estimated costs and potential for savings. JAMA 2019 Oct 7 [Epub ahead of print].

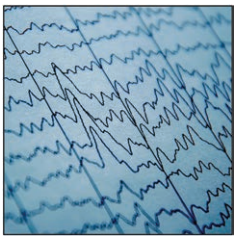
Approximately 30% of healthcare spending may be wasteful. To estimate current U.S. healthcare system waste, the authors searched peer-reviewed and "gray" literature focused on the waste domains identified by the Institute of Medicine, including failure of care delivery, coordination, overtreatment or low-value care, pricing failures, fraud and abuse, and administrative complexity. The authors found computed waste estimates of $102 to $166 billion for failure of care delivery, $27 to $78 billion for failure of care coordination, $76 to $101 billion for over-treatment or low-value care, $231 to $241 billion for pricing failures, $59 to $84 billion for fraud and abuse, and $266 billion for administrative complexity. Overall, the estimated cost of healthcare system waste in the United States ranged from $760 to $935 billion. Measures to address healthcare waste are projected to lead to $191 to $282 billion in healthcare saving per year. Interestingly, no studies identified intervention to address administrative complexity. *(Article Selection: Deborah J. Culley. Image: ©gettyimages.)*

Take home message: Approximately 25% of healthcare waste could be reduced by implementation of measures identified to eliminate waste.

Intraoperative methadone administration and postoperative pain control: A systematic review and meta-analysis. Pain 2019 Oct 10 [Epub ahead of print].

The management of postoperative pain is a complex process with a large percentage of patients reporting that their postoperative pain is inadequately managed. This systematic review and meta-analysis tested the hypothesis that administration of intraoperative methadone would result in lower postoperative pain scores (primary outcome), require less postoperative opioid administration, and that patients would be more satisfied with their postoperative analgesia without increasing the risk for postoperative complications. Ten studies including a total of 617 patients, among whom 319 received intraoperative methadone, were included in this analysis. Overall, compared to patients receiving other shorter duration opioids, patients that received intraoperative methadone reported lower pain scores at rest and with movement. In two studies, patients had greater satisfaction scores with analgesia in the methadone group when compared to those receiving shorter duration opioids. There were no differences in adverse outcomes between the groups. *(Article Selection: Deborah J. Culley. Image: ©gettyimages.)*

Take home message: Intraoperative methadone administration may result in lower pain scores and higher patient satisfaction scores without differences in adverse outcomes.



Association of residents' neural signatures with stress resilience during surgery. JAMA Surg 2019 Aug 7 [Epub ahead of print].

Intraoperative stress may lead to performance declines that threaten patient safety. It is well recognized that not all surgeons cope equally well to stress. This study evaluated prefrontal cortex activation between surgical residents with stable and declining performances under stress. The residents performed a suturing task at their own pace or when under time pressure that required them to suture at a rate of 2 min per knot. The primary outcome involved the comparison of performance stability described by a composite deterioration score and comparing it to changes in prefrontal cortex oxygenated hemoglobin levels. Prefrontal cortex oxygenated hemoglobin levels among residents with the most stable performance (quartile 1) were compared to those with evidence of significant decline (quartile 4). Those residents in quartile 1 demonstrated increases in hemoglobin oxygen saturation in the prefrontal cortex when under time pressure. In contrast, those in quartile 4 had decreases in hemoglobin oxygen saturation when suturing with and without time pressure despite no differences in Surgical Task Load Index or heart rate in either group ($P \leq 0.001$). *(Article Selection: Deborah J. Culley. Image: ©gettyimages.)*

Take home message: There may be differences in prefrontal oxygenation between surgical residents who perform well in the setting of stress when compared to those who perform poorly.