Journal Harvest

From the World Medical Literature: journal articles, conference summaries and published guidelines

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Dear readers,
Here are some summaries of the interesting articles, guidelines, and conference news that are recently published and are related to clinical practice. I hope that this material will help you offer the maximum care for patients. I hope you enjoy reading this journal picks.

Reducing the stress on clinicians working in the ICU

Stress of clinicians, physicians, & nurses working in the intensive care unit (ICU) is well known. For example, an estimated 39% of ICU nurses exhibit symptoms of posttraumatic stress disorder. This problem is not limited to nurses; physicians, medical trainees, and others who work in the ICU environment experience similar levels of psychological distress.
This is a randomized clinical trial among 198 ICU nurses from 8 adult ICUs in France testing the effect of a multicomponent educational intervention compared with a control group. Participants randomized to the intervention group were assigned to groups of 6 nurses and received 5 days of simulation-based education covering technical, interprofessional, and clinical reasoning skills. The primary outcome was job strain at 6-month follow-up operationalized as high psychological distress and low decision latitude assessed using the Job Content Questionnaire; secondary outcomes included other dimensions of job strain, absenteeism, and staff turnover at 6 and 12 months. The authors found that the presence of job strain was 13% in the intervention group vs 67% in the control group at 6-month follow-up, and the presence of isostrain (high levels of job strain in combination with low levels of social support) was 7% in the intervention group vs 55% in the control group. Moreover, absenteeism and turnover at 6 months were significantly lower in the intervention group. Comments: Stress & burnout among healthcare staff is becoming a real problem that might lead to serious consequences like suicide. In this study, multicomponent educational intervention has shown significant reduction of such problem. This intervention should be widely adopted to rectify this serious problem.

Effect of Aspirin on all- cause mortality in the healthy elderly

The ASPREE trial showed that aspirin did not prevent disability-free survival, but did increase major bleeding compared with placebo. The goal of the trial was to evaluate low-dose aspirin compared with placebo among healthy elderly patients. Questions raised: Is there any evidence to support the use of aspirin for primary prevention of
cardiovascular or other chronic disease in healthy older adults?
Several large, randomized trials have secondary prevention of cardiovascular disease among shown the efficacy of aspirin for the persons with a history of coronary heart disease or stroke. The evidence supporting a benefit of aspirin therapy in the primary prevention of cardiovascular or other chronic disease is less conclusive despite favorable trends suggesting that aspirin use reduces the incidence of cardiovascular events and possibly reduces the incidence of cancer and cancer-related mortality, particularly from colorectal cancer.

Does the daily use of 100 mg of aspirin prolong a healthy lifespan in older adults without cardiovascular disease, dementia, or physical disability?
In the ASPREE trial, the daily use of 100 mg of enteric-coated aspirin did not differ significantly from placebo in influencing the rates of disability-free survival at a median of 4.7 years. The primary end point of death, dementia, or physical disability occurred in 921 participants in the aspirin group (21.5 events per 1000 person-years) and in 914 in the placebo group (21.2 events per 1000 person-years). The between-group difference was not significant (hazard ratio, 1.01; 95% confidence interval [CI], 0.92 to 1.11; P=0.79). Among participants who had a primary end-point event, death was the most common first event (in 911 participants [50% of the events] at a mean age of 77.5 years), dementia was the next most common (in 549 participants [30% of the events] at a mean age of 77.7 years), and persistent physical disability was the least common.

**Vitamin D Supplements no help for preventing fractures and falls**

**Source:** Lancet Diabetes & Endocrinology article, 2018

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Vitamin D supplementation doesn't seem to prevent fractures or falls, according to a large meta-analysis in the Lancet Diabetes & Endocrinology. This is largely consistent with current guidelines from the U.S. Preventive Services Task Force on vitamin D supplementation for fall and fracture prevention.

Researchers analyzed 81 randomized trials that compared vitamin D supplementation (with or without calcium) to placebo, control, or lower-dose vitamin D among 54,000 adults. Vitamin D supplementation had no significant effect on fractures, hip fractures specifically, or falls. Supplementation's effects on bone mineral density were inconsistent and not clinically meaningful.

The authors conclude: "There is little justification for the use of vitamin D supplements to maintain or improve musculoskeletal health, and clinical guidelines..."
should reflect these findings. The clear exception to this is for the prevention or treatment of the rare conditions of rickets and osteomalacia."

**New Lipid Guidelines**

**A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines**

Source: Grundy SM, et al.

Circulation December 2018

The American Heart Association (AHA) and American College of Cardiology, along with numerous other groups, released updated guidelines on cholesterol management on Saturday. The recommendations were presented at the AHA's annual meeting and published in Circulation.

Among the noteworthy points:

- Personalized risk assessment for statin therapy should now include "risk-enhancing factors" in addition to traditional risk factors like smoking and hypertension. Risk-enhancing factors include family history of premature atherosclerotic cardiovascular disease (ASCVD), LDL persistently at or above 160 mg/dL, chronic kidney disease, and prior preeclampsia, among others.

- For patients who've had multiple ASCVD events — or 1 ASCVD event plus several high-risk conditions — and whose LDL remains at or above 70 mg/dL despite maximal statin therapy, clinicians may consider adding ezetimibe to their regimen. If LDL still remains elevated, it is reasonable to add a PCSK9 inhibitor (evolocumab or alirocumab), "although the long-term safety (>3 years) is uncertain and cost effectiveness is low at mid-2018 list prices."

- Adding ezetimibe — and then a PCSK9 inhibitor — may also be considered for certain patients with severe primary hypercholesterolemia.

Additionally, the guidance offers recommendations on when to add coronary artery calcium measurement to risk assessment.

**Comment:**

These new guidelines wisely recommend that we should inform patients about their risk, talk with them about their options, and help them choose the best path for them. More importantly, it emphasizes the value of coronary calcium for risk assessment, expands the range of evidence-based medications, and pushes the importance of shared decision-making.

**More references:**

Lipid guideline executive summary in Circulation (Free PDF)

Full lipid guidelines (Free PDF)

Evidence review for guidelines (Free PDF)

**Blood group genotyping test goes beyond A, B, and O**

Source: FDA news:

doi:10.1001/jama.2018.17838

The FDA has approved a molecular assay that helps determine blood compatibility for transfusion patients by identifying genetic markers that code for red blood cell antigens.

The ID Core XT blood group genotyping kit can streamline blood compatibility testing and offers clinicians another alternative to antisera blood testing. They stated that that DNA testing holds great promise to provide more informative, accurate, and cost-effective methods that can enhance patient care.

Officials at the FDA said the kit is the second molecular blood typing test approved. The first was in 2014, but the ID Core XT test is the first to report genotypes rather than only phenotypes as final results.

Molecular red blood cell typing particularly benefits patients who need frequent transfusions and therefore are at higher risk of receiving incompatible donor blood, which can cause hemolytic reactions that may result in dyspnea, hypotension, tachycardia, or chest pain. For example, some patients with sickle cell disease require blood transfusions every 3 to 4 weeks for months or years.

Of the more than 300 antigens represented in 33 blood group systems, the ID Core XT kit is able to identify 37 antigens in 10 blood group
systems. Officials at the FDA said a study that compared ID Core XT with licensed serological reagents, the previously approved molecular test, and with DNA sequencing showed that each test performed similarly.

**Sodium glucose cotransporter 2 inhibitors and risk of serious adverse events: nationwide register based cohort study**  
**Source:** BMJ 2018;363:k4365 (free)

Sodium-glucose cotransporter 2 (SGLT2) inhibitors are associated with twice the risk for lower limb amputation and diabetic ketoacidosis relative to comparator diabetes drugs, an observational study in The BMJ suggests.

Using 2013–2016 data from Swedish and Danish registries, researchers compared adverse event rates between 17,000 adults newly prescribed SGLT2 inhibitors and 17,000 matched patients who received glucagon-like peptide-1 (GLP-1)-receptor agonists. Overall, lower limb amputation occurred more often with SGLT2 inhibitors than GLP-1-receptor agonists (2.7 vs. 1.1 events per 1000 person-years), as did diabetic ketoacidosis (1.3 vs. 0.6).

In contrast, rates of bone fracture, acute kidney injury, serious urinary tract infection, venous thromboembolism, and acute pancreatitis did not differ between the groups.

Of note, dapagliflozin and empagliflozin accounted for 99% of SGLT2 inhibitor use in the study. A third SGLT2 inhibitor, canagliflozin, already has a boxed warning due to the amputation risk among patients with or at risk for cardiovascular disease.

**Comments:** This analysis study from two countries, has concluded that the use of SGLT2 inhibitors, as compared with GLP1 receptor agonists, was associated with an increased risk of lower limb amputation and diabetic ketoacidosis, but not with other serious adverse events. However, the mechanism of such side effects is yet to be identified.

A form of intermittent fasting known as the 16:8 diet helps obese individuals to lose weight and lower their blood pressure, according to a new study.

**The original study:** Effects of 8-hour time restricted feeding on body weight and metabolic disease risk factors in obese adults: A pilot study.  
Gabel, Kelsey et al. Nutrition and Healthy Aging, vol. 4, no. 4, pp. 345-353, 2018

What is known: Some of the new research is suggesting that not all IF approaches are the same, and some are actually very reasonable, effective, and sustainable, especially when combined with a nutritious plant-based diet. This study investigated the effects of 8-h time restricted feeding on body weight and metabolic disease risk factors in obese adults. Obese subjects (n=23) participated in an 8-h time restricted feeding intervention (ad libitum feeding between 10:00 to 18:00h, water fasting between 18:00 to 10:00h) for 12 weeks. Weight loss and other outcomes were compared to a matched historical control group (n=23).

Main findings: Body weight and energy intake decreased in the time restricted group (–2.6% ± 0.5; −341 ± 53kcal/d) relative to controls over 12 weeks (P<0.05). Systolic blood pressure decreased in the time restricted feeding group (−7 ± 2mm Hg) versus controls (P<0.05). Fat mass, lean mass, visceral fat mass, diastolic blood pressure, LDL cholesterol, HDL cholesterol, triglycerides, fasting glucose, fasting insulin, HOMA-IR, and homocysteine were not significantly different from controls after 12 weeks (no group×time interaction).

**Comments:** The findings of this study suggest that 8-h time restricted feeding produces mild caloric restriction and weight loss in obese adults, without intentional calorie counting. Another benefit is lowering of systolic BP. Of course further studies with larger number of participants is needed to confirm these findings.
The objective: High pre-pregnancy body mass index (ppBMI) has been linked to neurodevelopmental impairments in childhood. However, very few studies have investigated mechanisms in human cohorts. The study was conducted among 1361 mother–child pairs in Project Viva and examined associations of ppBMI categories with the Peabody Picture Vocabulary Test III [PPVT] and Wide Range Assessment of Visual Motor Abilities [WRAVMA] in early childhood (median 3.2y); and with the Kaufman Brief Intelligence test (KBIT) and WRAVMA in mid-childhood (7.7y). Also it examined the role of maternal inflammation in these associations using the following measures from the 2nd trimester of pregnancy: plasma C-reactive protein (CRP), dietary inflammatory index (DII), and plasma omega-6 (n-6): n-3 fatty acid ratio.

The main findings: Children of mothers with prenatal obesity (ppBMI ≥30 kg/m2) had WRAVMA scores that were 2.1 points lower (95% CI: −3.9, −0.2) in early childhood than children of normal weight mothers (ppBMI 18.5–<25 kg/m2), in a covariate adjusted model. This association was attenuated when we additionally adjusted for maternal CRP (β −1.8 points; 95% CI: −3.8, 0.2) but not for other inflammatory markers. PpBMI was not associated with other cognitive outcomes. It concluded that maternal inflammation may modestly mediate the association between maternal obesity and offspring visual motor abilities.