Research Briefs

Too Few People Receive MAT for Opioid Addiction, Study Finds

Despite “compelling evidence” that medication-assisted treatment can help people recover from opioid addiction, methadone, buprenorphine, and naltrexone are woefully underused. A study co-funded by the National Institute on Drug Abuse (NIDA) found that in the first year following an overdose, fewer than one third of patients were provided any medication for opioid use disorder (OUD).

“A great part of the tragedy of this opioid crisis is that…we now possess effective treatment strategies that could address it and save many lives, yet tens of thousands of people die each year because they have not received these treatments,” said Dr. Nora Volkow, Director of NIDA.

The researchers analyzed data from 17,568 adults in Massachusetts who survived an opioid overdose between 2012 and 2014. Opioid overdose deaths declined by 59% among patients who received methadone and 38% for those who received buprenorphine over the 12 months of followup, compared with patients who did not receive treatment.

Another disturbing study finding: 34% of people who had had an overdose were nonetheless given one or more prescriptions for opioid painkillers over the next 12 months, and 26% were prescribed benzodiazepines.

Source: NIH, June 2018

Metformin, Long-Acting Insulin Don’t Help Slow Diabetes in Young People

The only two medicines currently approved for young people with type 2 diabetes—long-acting insulin and metformin—don’t slow the progression of diabetes in young people, according to a study funded in part by the National Institute of Diabetes and Digestive and Kidney Diseases.

A substudy of the Restoring Insulin Secretion (RISE) study, the RISE Pediatric Medication Study, looked at the effects of insulin and metformin in 91 patients aged 10 to 19. The participants were randomly assigned to one of two treatment groups. The first received three months of glargine, a long-acting insulin, followed by nine months of metformin. The second group received only metformin for 12 months. The participants were followed for three more months after treatment ended.

The pediatric study found that beta cell function declined in both groups during treatment and worsened after treatment ended.

Researchers also compared the pediatric participants with their adult counterparts in two other RISE trials and found that the young people had more insulin resistance and other signs of disease progression at the same stage in the disease. Moreover, at baseline, the younger patients responded to the severe insulin resistance with a greater insulin response than adults, which the researchers say may be a reason for their more rapid loss of beta cell function.

However, the study also found modest improvement in blood glucose with metformin in both groups. But metformin alone is not a long-term solution for many young people, said Dr. Kristen Nadeau, principal investigator for the pediatric study. Their findings underscore the “urgent and growing need,” she says, for more options.

Source: NIH, June 2018

NIAAA Ends Funding for Alcohol and CV Health Study

After just four months, the National Institute of Alcohol Abuse and Alcoholism is ending funding for the Moderate Alcohol and Cardiovascular Health (MACH) trial, citing concerns about the study design.

The MACH study was designed as a multicenter randomized trial to determine the effects of one serving of alcohol (approximately 15 grams) a day, compared with no alcohol intake, on the rate of new cases of cardiovascular disease and new cases of diabetes among participants free of diabetes at baseline. The study was launched because some epidemiological research had shown that moderate alcohol consumption had health benefits by reducing the risk for coronary artery disease, type 2 diabetes, and rheumatoid arthritis.

The study began enrollment in February 2018, and was suspended on May 10. NIAAA expected to commit $20 million to the project over 10 years, of which $4 million has been spent; remaining funding came from private donations of $67.7 million, of which $11.8 million has been spent.

In addition to the problems with the study design, a preliminary report from the NIH Office of Management Assessment determined that a small number of NIAAA employees violated NIH policies in soliciting gift funding and circumvented standard operating procedures.

Source: NIH, June 2018

Platelet Contamination Leads to Three Deaths

Platelet-transmitted bacterial infections persist as a cause of transfusion-associated morbidity and mortality, according to researchers writing in Mortality and Morbidity Weekly Report. They describe two separate clusters of platelet transfusion-associated bacterial sepsis reported in Utah and California, in which three patients died.

Contamination of blood products most commonly happens when skin microbiota are introduced during needle insertion. Because most platelets are stored at room temperature, bacteria can proliferate to clinically important levels by the time the unit is transfused, according to the Centers for Disease Control and Prevention (CDC). About one in 5,000 platelet collections are contaminated; one in 100,000 platelet transfusions results in bacterial sepsis.

In Utah, two patients received contaminated apheresis platelet units. One developed rigors 30 minutes after infusion, but...
transfusion-transmitted bacterial infection was not considered because of the patient’s complex medical history. He died four days later.

Less than a day after the first patient’s infusion, the second patient received the other platelet unit. No immediate symptoms of sepsis followed but later that day, routine laboratory testing revealed new intravascular hemolysis. She died 11 hours after transfusion.

In California, a patient developed vomiting, tachycardia, and hypotension within 15 minutes of an infusion that came from an apheresis blood donation. Although the transfusion was stopped, he died within five hours. A second patient developed septic shock approximately nine hours after infusion but recovered.

Subsequent investigation found that both the Utah and California collection facilities followed current practices. However, the CDC report highlights that, even when procedures are followed appropriately, the risk remains. The CDC says evidence-based strategies such as pathogen inactivation, rapid detection devices, and modified screening of bacterial culture protocols can help mitigate that risk.

Source: MMWR, June 2018

New Evidence May Explain How Viruses Act in Alzheimer’s Disease

Hundreds of reports since the 1980s have associated Alzheimer’s disease (AD) with bacteria and viruses. But they couldn’t explain the connection. Now, new research suggests that viral species, particularly herpesviruses, play a role in AD biology.

The hypotheses that link viruses to brain disease aren’t new, Richard Hodes, MD, Director of the National Institute on Aging, says, but this is the first study to provide “strong evidence” based on unbiased approaches and large datasets.

The study, funded by NIA, was originally intended to find out whether drugs used to treat other diseases can be repurposed for treating AD. Researchers analyzed large datasets from postmortem brain samples to map and compare biological networks underlying AD. They found that the disease biology is impacted by a “complex constellation” of factors, including the ways the interrelated systems of DNA, RNA, proteins, and metabolites interact with molecular, genetic, and clinical aspects of AD.

Among their key findings: Human herpesvirus 6A and 7 were more abundant in AD samples than in non-Alzheimer’s samples. They also found multiple points of overlap between virus-host interactions and genes associated with Alzheimer’s risk.

The research “reinforces the complexity of Alzheimer’s disease,” Hode says, and “highlights the importance of sharing data freely and widely with the research community.”

Source: NIH, June 2018

Mapping Socioeconomic Data of the Neighborhood

Where you live can determine how safe you are (or feel), where you shop, the kind of food you can buy, and other factors that affect your health. And for some people, social factors, like their neighborhood, can disproportionately affect health.

“Socioeconomic disadvantage is one of the fundamental factors that result in health disparities,” says Eliseo Pérez-Stable, MD, Director of the National Institute on Minority Health and Health Disparities.

Such a tool is available now: Developed by Amy Kind, MD, PhD, at the University of Wisconsin, the Neighborhood Atlas is an online platform that allows researchers to visualize socioeconomic data at local levels. Users can download maps indexed with data ranked according to 17 measures, including income, education, employment, and housing quality.

The Atlas is built to merge with other data sources to foster a better understanding of how disadvantaged neighborhoods influence health, Kind says. For instance, researchers and health and social service providers can use the data to understand the risk factors for diseases, study the impact of health policies, and better align resources. Kind adds that the Atlas and the data can be harnessed to advance disparities-focused research, and to improve translational, clinical and community research by showing ways to aid design, recruitment, retention, and outreach.

Source: NIH, June 2018

Helping Workers Beat the Heat

The “heat index” combines humidity and air temperature to quantify what conditions feel like to the human body. It’s an approximate guide, meant for the general public, and assumes that a person is wearing light clothing and walking in a shaded area with a light breeze—it doesn’t account for direct sunlight, stagnant air, work clothing, or strenuous activity.

A better way to gauge whether workers are safe in the heat, says the National Institute for Occupational Safety and Health, is to follow recommended occupational exposure limits for heat stress, which specify the maximum combination of environmental heat (measured as the wet bulb globe temperature [WBGT] and metabolic heat). Because WBGT incorporates four environmental factors—air temperature, relative humidity, wind speed, and radiation—it is the recommended workplace environmental heat metric. But how well does it work in real (hot) life?

CDC researchers reviewed 25 cases of outdoor occupational heat-related illness investigated by the Occupational Safety and Health Administration between 2011 and 2016. For each incident, OSHA assessed personal risk factors and estimated WBGT, workload, and the worker’s acclimatization status (that is, how new he/she was to the job’s environment).

Fourteen of the cases were fatal. Heat stress exceeded
exposure limits in all 14 deaths and eight of 11 nonfatal illnesses. Each incident occurred during outdoor work. Of the 25 workers, 12 had at least one predisposing personal risk factor. Workload was moderate to very heavy in 13 of the fatal cases; the fourteenth worker was unacclimatized.

The heat index ranged from 83° to 110° F, with a median of 91°. Notably, four nonfatal illnesses and four deaths occurred when the heat index was between 85° and 90° F. (The researchers also cite other cases of serious illness when the heat index was below 90°, including 14% of moderate-to-severe heat-related illnesses at a U.S. military training installation.)

The sensitivity of the NIOSH exposure limits was 100% for detection of fatal heat stress and 73% for nonfatal cases. The study findings suggest that the recommended limits are safe for most workers. However, because working in high heat can be risky, the CDC advises that when the heat index is 85° F or higher, employers should take additional precautions, such as:

- designating someone to monitor heat conditions;
- providing extra protection to new workers;
- scheduling frequent breaks in a cooler location and supplying water; and
- adjusting schedules and workload to stay below established heat stress limits.

Source: MMWR, July 2018

**Senior Centers Can Be Foundation for Prevention Programs**

There’s no need to start a whole new program devoted to teaching people how to prevent chronic disease—if you already have the infrastructure of a state aging service. These services, which include senior centers that offer exercise and recreation, already have the staff and volunteers to deliver programs, track attendance, and record outcomes, say researchers from the University of Pittsburgh.

To assess how well such infrastructure can support prevention efforts, the University of Pittsburgh CDC Prevention Research Center partnered with the Pennsylvania Department of Aging APPRISE program to deliver the 10 Keys to Healthy Aging program.

APPRISE is a Medicare counseling program offered at senior centers as part of the state health insurance program. The 10 Keys Program is a series of workshops that cover the U.S. Preventive Services Task Force guidelines and other evidence-based recommendations. The "keys" are risk-prevention strategies for behavioral change in areas including blood pressure control, glucose control, smoking cessation, immunizations, and screening.

The program grew from 93 participants in pilot year 2013 to 694 in 2016. During the study period, 1,534 people attended at least one workshop; 1,044 (68%) completed eight or more Keys workshops, and 736 completed both the pretest and posttest. The program was effective, the researchers say: Correct answers on the prevention knowledge quiz rose from 61.5% to 78.5%. In monthly follow-up with 147 respondents over six months, maintenance of prevention behaviors was strong in the areas of physical activity and hypertension management, and significantly higher for people who completed more Keys workshops.

Source: CDC, July 2018

**Weight, Age, and Breast Cancer Risk: An Unexpected Finding**

Young women may not want to hear it, but fat could be their friend. Researchers from the Premenopausal Breast Cancer Collaborative Group have found that women aged 18 to 24 with high body fat have a lower risk of developing breast cancer before menopause.

The researchers pooled data from 19 different studies, involving nearly 800,000 women from around the world. Overall, 1.7% of the women developed breast cancer. The researchers found that the relative risk of premenopausal breast cancer dropped 12% to 23% for each five-unit increase in body mass index, depending on age. They saw the strongest effect at ages 18 to 24: Very obese women in this age group were 4.2 times less likely to develop premenopausal breast cancer than women with low BMI at the same age.

Just why high BMI might protect against breast cancer in some women is unclear. Breast cancer is relatively rare before menopause, although previous studies have suggested that the risk factors might be different for younger versus older women. For instance, it’s well known that women who gain weight, particularly after menopause, have a higher risk. The fact that this study found that the risk actually decreased in younger women points to the possibility that different biologic mechanisms are at work, researchers say.

Nonetheless, the researchers caution that young women should not intentionally gain weight to offset the risk.

Source: NIH, June 2018

**Psoriasis, Etanercept, and Myelodysplasia: Looking for Connections**

Patients with psoriasis may be more susceptible to myelodysplasia—but is that because of the autoimmunity or the treatment?

Doctors from Menoufia University and Cairo University, Egypt, and Al Hada Armed Forces Hospital, Saudi Arabia, report on a patient who developed myelodysplasia with excess blasts one year after he started on the tumor necrosis factor-blocker etanercept for psoriasis. The patient, a 76-year-old man, arrived at the emergency unit with ecchymosis and recurrent epistaxis. He had a critically low platelet count, anemia and normal leukocyte count. The reticulocyte index, serum ferritin and folate levels indicated ineffective erythropoiesis.
Bone marrow aspirate and biopsy confirmed a diagnosis of myelodysplastic syndrome.

His doctors stopped the etanercept and administered two cycles of azacitidine and folic acid supplementation, but the response was minimal and his platelet count worsened. While waiting for the third cycle, the patient was readmitted to the emergency department with lower gastrointestinal bleeding, epistaxis, and shock. He died of cardiopulmonary arrest.

The physicians note that immune dysregulation and altered T-cell hemostasis are essential to the development of myelodysplastic syndrome. They also note that nonspecific activation and proliferation of T lymphocytes has been documented as promoting epidermal growth in genetically susceptible psoriasis patients.

Myelodysplastic syndrome has been associated with psoriasis in about 7% of cases, and researchers have found a higher incidence of leukemia and laryngeal cancer in families of psoriasis patients. There have also been reports of leukemia in psoriasis patients on systemic immunosuppressives. Etanercept has various hematological side effects, including pancytopenia and aplastic anemia.

However, only four cases of myelodysplastic syndrome (including this one) have been reported in psoriasis patients. Taken together, though, the cases add to the growing evidence that suggests a link between myelodysplastic syndrome and etanercept treatment for psoriasis. Those patients should be considered at dual risk from treatment and disease. The researchers recommend regular routine blood counts and discontinuing etanercept upon onset of any cytopenias.

Source: Indian Journal of Dermatology, July–August 2018

Implant Rupture After Radiation

The rupture rate for breast implants is about 10% at 10 years after insertion. That means women in their 70s and older have a greater risk of rupture. For women who had breast augmentation or reconstruction before the advent of fifth-generation implants, however, there are no specific recommendations regarding followup, and very little guidance in the literature about management for those who have had implants after radiation, say clinicians from Mayo Clinic.

They report on a 74-year-old patient who was treated for breast cancer in 1987 and 1988. She underwent lumpectomy, adjuvant unilateral radiation, a right simple mastectomy, left modified radical mastectomy, and implant-based reconstruction. Nearly 30 years later, she felt an asymmetry in one breast. MRI and ultrasound revealed that both implants had ruptured. It’s well known, the authors say, that complications of post-mastectomy radiotherapy include capsular contracture, infection, and loss of prosthesis in implant-based reconstruction. Studies have shown that fibrosis, a hallmark of chronic radiation therapy, can show up even several years after radiotherapy—underscoring the importance of long-term follow-up for these patients. Moreover, the fact that the consequences of silicone on irradiated mastectomy flaps is unknown posed a further challenge.

While the cause of their patient’s implant rupture is unknown, the clinicians say it is “very likely” that delayed-onset fibrosis and capsular contracture secondary to radiation played a role. Such complications, though rare, should be kept in mind, they advise, when evaluating patients who had radiation and implants.

Source: BMJ, June 4, 2018

Misdiagnosed Testicular Plasmacytoma

A 70-year-old man underwent salvage therapy for multiple myeloma. While on maintenance immunotherapy, he developed a sternal plasmacytoma. After the fifth cycle of treatment for that, he developed swelling, erythema, and pain in his right testis.

The main differential diagnoses for those symptoms are infections and tumors; infection is more common, so his clinicians at Indiana University School of Medicine presumed orchitis and started him on intravenous antibiotics. The pain resolved, but the swelling persisted after the antibiotic course. They turned to biochemical marker screening for germ cell tumors, but those were negative. Serial ultrasound imaging, which they had begun during his admission, remained unchanged.

Meanwhile, his chemotherapy was being held and he developed another sternal mass, prompting a fluorodeoxyglucose-PET/CT scan to evaluate for relapse of myeloma. The scan revealed an enlarged, diffusely hypermetabolic right testicle. Believing the symptoms were related to the myeloma and not orchitis, his doctors advised a radical orchietomy.

A biopsy after the surgery showed tumor cells consistent with testicular plasmacytoma.

While rare, testicular plasmacytoma is commonly associated with multiple myeloma, especially in the later stages, when cancer cells are more aggressive and not relying on bone marrow for survival, the clinicians say. Unlike myeloma, which typically spreads via blood to bone sites, testicular plasmacytoma may spread via lymphatic channels to the regional lymph nodes and subsequently to distant sites, they add, similarly to lymphoma or germ cell tumor.

It’s hard to diagnose, though. The clinicians say their patient’s case illustrates the challenges. Imaging studies such as ultrasound and CT scans are not specific. And although FDG-PET/CT imaging is a standard staging tool for myeloma and helpful in identifying plasmacytoma when evidenced as intramedullary or extramedullary hypermetabolic lesions, hypermetabolic lesions are not always malignant, they note. FDG-PET/CT can’t differentiate between orchitis and testicular plasmacytoma. Biopsy remains the diagnostic gold standard.

Source: BMJ, June 4, 2018