Repurposed Drugs Failed to Prevent Severe COVID-19
A trial that evaluated 3 existing generic medicati-ons—metformin, ivermectin, and fluvoxamine—for early outpatient treatment of SARS-CoV-2 infection among adults with overweight and obesity did not prevent progression to severe COVID-19.

The study randomly assigned 1431 participants to 1 of 6 trial groups: metformin plus fluvoxamine; metformin plus ivermectin; metformin plus placebo; placebo plus fluvoxamine; placebo plus ivermectin; and placebo plus placebo. Patients were enrolled in the study within 3 days of a confirmed infection and in fewer than 7 days after the onset of symptoms. The median age of participants was 46 years; 56% were women, 6% were pregnant, and 52% had been vaccinated against COVID-19.

As reported in the New England Journal of Medicine, none of the 3 drugs was effective at preventing the composite primary endpoint of hypoxemia, emergency department visit, hospitalization, or death compared with identically matched placebo. A primary event occurred in 25.5% of 1305 study participants with complete data. The adjusted odds ratio for a primary event was 0.84 with metformin, 1.05 with ivermectin, and 0.94 with fluvoxamine. The analysis found that metformin may prevent emergency department visits, hospitalizations, or death associated with COVID-19 but the researchers noted that additional trials are needed for definitive results. Other studies have suggested that metformin may have anti-inflammatory and antiviral activity and may prevent hyperglycemia during acute illness.

Standing Desks Reduced Office Workers’ Sitting Time
Office-based workers typically spend 73% of their workday and 66% of their waking day sitting. In a recent trial workers who used a standing desk cut the amount of time they spent sitting by an hour per day.

The 12-month trial involved 756 office workers in England who were randomly assigned to the SMART Work and Life (SWAL) intervention, the SWAL intervention with a height-adjustable standing desk, or a control group that worked as usual. The intervention enlisted fellow employees to champion the importance of reducing sitting to prevent adverse health effects and to serve as role models for sitting less than 50% of the day and moving every 30 minutes both at work and at home. Workplaces were also changed to encourage employees to move more, such as relocating printers farther away. Participants’ sitting time was measured with an accelerometer.

At 1 year, both intervention groups sat less per day than the control group, but the addition of a standing desk was 3 times more effective. The SWAL participants sat an average of about 22 minutes less per day than the control group while the SWAL-plus-desk group sat about 64 minutes less. These effects were consistent regardless of age or body mass index, the authors reported.

“Observational evidence has suggested that these changes are likely to be clinically relevant, with the potential to improve health outcomes,” the authors wrote in the BMJ. The interventions also resulted in small improvements in stress, well-being, and energy levels. Most participants replaced sitting with standing instead of increasing energy levels. Most participants replaced sitting with standing instead of increasing energy levels.

Ketamine Noninferior to Fentanyl for Surgical Abortion Sedation
A noninferiority trial found no difference in satisfaction between women who underwent sedation with intravenous (IV) ketamine or IV fentanyl during first-trimester surgical abortion. The current opioid crisis has prompted interest in finding a nonopioid agent for pain control during outpatient surgical abortion. Although IV fentanyl is the current standard sedation, ketamine is frequently used in trauma and for acute pain crises and is favored in outpatient settings because it does not cause respiratory and cardiovascular depression.

The trial randomly assigned 110 patients either to receive 200 to 500 μg/kg of IV ketamine over 2 minutes, repeated every 5 minutes until appropriate analgesia was achieved, or to receive 0.5 to 1 μg/kg of IV fentanyl over 2 minutes, repeated every 5 minutes. All patients received 2 mg of IV midazolam immediately before the procedure.

The study, which was published in Obstetrics & Gynecology, found that ketamine was noninferior to fentanyl for patient satisfaction with anesthesia. There was also no difference between the ketamine and fentanyl groups on average pain scores, additional pain medication given during the procedure, constipation, physician satisfaction, and time to discharge. One-third of the women who received ketamine had hallucinations during the procedure compared with 4% of the fentanyl group. The ketamine group was also more likely to receive ketorolac during the procedure and to use oxycode done after the procedure.

The authors concluded that ketamine “has the potential to affect the nation’s opioid crisis and improve the safety of moderate sedation during abortion procedures.” They added that ketamine might also be used for other outpatient gynecologic procedures and may be especially warranted for patients with opioid use disorders.

Mepolizumab Cuts Asthma Exacerbations Among High-risk Kids
Researchers found that mepolizumab, a humanized monoclonal antibody, significantly reduced the number of asthma exacerbations in urban Black and Hispanic children, a population that has the highest
risk of asthma-related morbidity and mortality. Therapy directed at the eosinophilic phenotype of asthma has proved to be successful in adults but hasn’t been well studied in children and diverse populations.

The study, conducted at 9 urban US medical centers, enrolled 290 children and adolescents who had exacerbation-prone asthma and blood eosinophils of at least 150 cells/μL and who lived in socioeconomically disadvantaged neighborhoods. The participants were randomly assigned to receive 1 of 2 mepolizumab doses based on age or placebo injections once every 4 weeks for 52 weeks. All participants also received guideline-based care.

The average number of asthma exacerbations that were treated with systemic corticosteroids during the study was 0.96 with mepolizumab and 1.30 with placebo, which is a more modest effect than previously observed among adults. There were no differences between the groups in other asthma outcomes: lung function, changes in asthma severity, or physician and patient assessments of response to therapy. Treatment-emergent adverse events occurred in 29% of the mepolizumab group compared with 11% of the placebo group. The findings appeared in The Lancet.

The investigators also identified mechanisms that cause response to mepolizumab therapy and the inflammatory pathways associated with eosinophils and the epithelium as drivers of asthma exacerbation.

-- Anita Slomski

Note: Source references are available through embedded hyperlinks in the article text online.