the PRUDENT prescriber

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In this edition:

Opioids were No Better than Placebo at Relieving Acute Back Pain

In a study from Sydney Australia, 347 adults presenting to an emergency department with low back or neck pain of at least moderate severity for less than 12 weeks duration were randomized to an opioid (20 mg oral oxycodone per day) or an identical placebo. (Lancet June 28,2023) The primary outcome was pain severity at six weeks measured with the pain severity subscale of the brief pain inventory.

Results: Opioids were no more effective than placebo at reducing acute lower back or neck pain after six weeks of treatment. Adverse events were similar between groups. Twenty percent of participants who were treated with opioids were at risk of opioid misuse at one year compared to 10% of those who received a placebo.

MY TAKE

This is a relatively small study of short duration, but nonetheless adds support for not using opioids in acute back pain.

What's your "T" score? Testosterone Looks Safe, but is it Effective?

Eight years ago, the FDA mandated manufacturers of testosterone products conduct studies on cardiovascular safety. The previous research had been inconclusive. The June 16, 2023, New England Journal of Medicine reported on an industry funded randomized trial that involved 5200 men (average age 63) with known CV disease or multiple CV risk factors randomized to transdermal 1.62%, testosterone gel or placebo. Testosterone was dosed to a target level of 350-750 ng/dL.

Results: The incidence of the primary endpoint (CV related death, non-fatal MI, non-fatal stroke), was 7% in both the testosterone and placebo groups after 33 months of follow-up.

The study is reassuring, but it's a pretty short follow-up. And 40% of the participants dropped out of the study. The more pertinent question is whether or not testosterone is actually efficacious in this older population. The best previous study showed negligible to minimal improvement in symptoms..

Survey Shows Millions of People Forgo Medications to Decrease Their Pharmacy Bills

Wondering why your patients' blood pressure or blood sugars didn't come down? A report for the National Center for Health Statistics might have part of the answer. They demonstrated that 8.2% of US adults aged 18 to 64 years did not take their medicine as prescribed because of cost.

- People with disabilities were the most likely to report cutting back on medications due to cost. Twenty percent did not take their prescriptions as directed compared with 7.1% of people without disabilities.
- More women than men cut back on their prescriptions consistently.
- Black adults were more likely to report not taking medication to reduce cost than Asians and White adults.
- The survey revealed that to save money, patients reported skipping doses of their meds, taking less of their drugs than prescribed or delaying refills of their prescriptions.

And from the School of "Just when I thought I had seen everything" comes a Vibrating Capsule for Patients with Constipation

Yes, the FDA did approve Vibrant, a vibrating capsule for treating patients with chronic idiopathic constipation. The capsule contains a computer chip programed to make the capsule vibrate in cycles. Fifteen hours after swallowing the capsule, it begins mechanically stimulating the colonic wall.
The clinical trial that brought this to market studied 312 patients who had idiopathic constipation (1–2.5 spontaneous bowel movements weekly) and had not responded to standard treatments. Patients were randomized to swallow a vibrating capsule or a placebo, five nights weekly for eight weeks.

Results: 39% of patients taking the vibrating capsule versus 22% in the placebo group had an increase of one or more spontaneous bowel movements per week (NNT = 6). For an increase of two or more bowel movements weekly, the proportions in the two groups were 23% and 11%, respectively. (NNT= 9). No major side effects were reported.

The good news is that this intervention is cheap: $89 for a month's worth of 20+ vibrators.

Polypills: Still Not Ready for Primetime?

Polypills have been around for more than a decade in Europe but are still not on the market in the USA. In a recent published study (American Journal Cardiology, 2023, June 27; 201:211–218) the authors examine the use of polypills for cardiovascular disease, primary and secondary prevention. The study involved 11 RCTs with 25,389 patients. The follow-up ranged from 1 to 5.6 years.

Results: Polypill therapy was associated with a lower risk of Major Adverse Cardiac and Cerebral Events. MACCES were: 5.8% in the polypill arm versus 7.7% in the control arm. (NNT = 53)

- Polypill therapy was associated with a lower incidence of cardiovascular mortality, 2.1% versus 3% (N=111); myocardial infarction 2.3% versus 3.2% (NNT=111) and stroke 0.9% versus 1.6% (NNT=143).
- Polypill therapy is associated with a higher degree of adherence. There was no difference between groups in the incidence of serious adverse effects, 16.1%, versus 15.9%.
- The benefit was consistent for both primary and secondary prevention.

In most of the studies the pill included a statin, a blood pressure medicine and aspirin. As a public health intervention, those are reasonable NNTs. Will the polypill fly in the US where we tend to customize treatment for our patients?

Which Inhalers Are Most Effective for COPD?

COPD guidelines favor use of a long acting antimuscarinic antagonist (LAMA), plus a long-acting beta agonist (LABA) over inhalers that combine an inhaled corticosteroid (ICS) plus a LABA. Previous studies have shown that LAMA-LABA combinations are more effective in preventing COPD exacerbations.

A new observational study (JAMA Intern Med 2023 May 22) scoured an insurance data base for some 31,000 pairs of COPD patients who filled new prescriptions for LAMA-LABA or ICS-LABA during 2014 through 2019. LAMA-LABA treatment was associated with 8% fewer (NNT=12) moderate or severe COPD exacerbations plus 20% fewer (NNT=5) pneumonia hospitalizations.

Zuranolone approved for Postpartum Depression

Approximately one in seven women giving birth can develop postpartum depression, according to the American College of Obstetricians and Gynecologists (ACOG). Fifty percent of patients are not diagnosed due to gaps in screening or reporting.

The FDA has approved the medication zuranolone (trade name Zurzuvae) for the treatment of postpartum depression. It's the first FDA approved oral medication in the United States specifically for postpartum depression.

Zuranolone works by improving a woman's levels of alopregnalone, a neuroactive steroid that can increase during pregnancy and dip steeply afterward. Dosing is one 50 mg capsule a day with a fatty meal for 14 days.

Study: 196 women with severe postpartum depression (HAM-D score >26), were randomized to daily zuranolone 50 mg for 14 days versus a similar appearing placebo for 14 days. Breast feeding women were excluded. Eighty-seven percent of the women completed the 45-day study (American Journal of Psychiatry July 26,2023)

Results: The day after the women completed the 14-day treatment course, the researchers found that 57% reported a 50% or higher improvement in their depressive symptoms compared with 38% of those on placebo (NNT=5). At 45 days similarly 50% or greater improvement was seen in 62% of those taking zuranolone compared with 54% of those taking a placebo. (NNT = 12) Onset of symptom improvement was noted within three days.

Adverse Effects: The most common side effects include drowsiness, dizziness, diarrhea, fatigue, nasopharyngitis, and urinary tract infection. The drowsiness was of such magnitude that the FDA required a black-box warning patients not to drive within 12 hours of ingesting the medication.

MY TAKE

- This drug represents a promising response for an illness that has been poorly studied.
- Limitations to this study: short follow up of only 45 days and a relatively small "N."
- My biggest concern about this drug is that it was studied in women with severe postpartum depression. It seems likely that there will be indication creep and Zurzuvae will be used in women who are less depressed who will get fewer positive responses.
  The good news is that this is a "Z" drug with just not one "Z" but two "Zs."

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