

Letter to the Editor: The Pundit Speaks

By Randolph M. Howes, M.D., Ph.D.

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“Acid Reflux Drugs May Cause or Prevent Esophageal Cancer”

Heartburn or acid reflux (gastroesophageal reflux) affects about 20 percent of Americans. Millions of U.S. residents take proton pump inhibitors (PPIs), which include lansoprazole (**Prevacid**), and esomeprazole (**Nexium**) and omeprazole (**Prilosec**), both manufactured by AstraZeneca. Over-the-counter PPIs are most often used for heartburn and indigestion and many people end up taking the drugs for months or years. PPIs are some of the most widely prescribed drugs in the U.S., with \$14 billion in annual sales. But, significant side effects have been reported with increasing frequency, such as alterations of absorption of vitamins and minerals, metabolic effects on bone density, alterations of drug interactions, alterations of intended effect, infection risk, hypersensitivity response with consequent organ damage, vitamin B12 deficiency and susceptibility to hip, wrist or spinal fractures, increased the risk of heart attack, kidney failure, dementia and death. Because stomach acid kills bacteria, people who take PPIs are also more prone to foodborne infections, such as **Salmonella**. However, some authors are skeptical of some of the other reported side effects. Some of the reported side effects, such as vitamin B12 and iron deficiency (both of which ultimately result from a decrease in stomach acid), are real. But, authors forcefully conclude: "The low-quality evidence surrounding chronic kidney disease, myocardial infarction, bone fracture, and dementia is not at all compelling. Hence, currently available data do not support altering evidence-based PPI use on the basis of these hypothetical risks." A 2018 study published in *Cancer Epidemiology* reported that long-term maintenance therapy with proton-pump inhibitors (PPIs) was shown to be associated with an increased risk for esophageal cancer, even in patients taking PPIs for indications not previously associated with this cancer risk. This is not the first time that long-term PPI therapy has been implicated in increased cancer risk. Most recently, *Medscape Medical News* reported a Hong Kong study showing that long-term PPI therapy doubled gastric cancer risk after *Helicobacter pylori* eradication. However, other investigators caution that this study is not conclusive proof and it "potentially does more harm than good." The greatest cancer risk was seen with short-term PPI use, he pointed out. In patients who had been receiving PPIs for 5 years or longer, the association was not significant and seems to be the reverse of what you would observe if PPIs cause esophageal cancer. So, most practitioners follow published guidelines for prescribing PPIs. It is advised that PPI maintenance therapy be administered in the lowest effective dose, including on-demand or intermittent therapy.

In the America that I love, acid reflux is an unpleasant condition that may cause esophageal cancer. the American College of Gastroenterology recommends maintenance PPI therapy for patients with GERD, who continue to have symptoms after PPI therapy is discontinued.

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