Long-Term Proton Pump Inhibitor (PPI) Use: What the Real Evidence Shows

What Are Proton Pump Inhibitors

Proton pump inhibitors (PPIs) are medications that reduce stomach acid production. Common PPIs include omeprazole, esomeprazole, lansoprazole, pantoprazole, and rabeprazole. These medications are among the most effective treatments for gastroesophageal reflux disease (GERD), Barrett's esophagus, and peptic ulcers.

Why You May Need Long-Term PPI Therapy

Your healthcare provider may recommend long-term PPI therapy if you have:

- Severe erosive esophagitis (damage to the esophagus from acid)

- Barrett's esophagus (a condition that can increase cancer risk)

- Chronic GERD symptoms that return when medication is stopped

- A history of bleeding ulcers

- Certain other conditions requiring ongoing acid suppression (Zollinger_Ellison Syndrome, eosinophilic esophagitis, chronic NSAID use, pancreatic enzyme replacement)

What You May Have Heard About PPI Risks

Some news reports or articles in the lay press have stated that long-term PPI use is linked to serious health problems such as kidney disease, bone fractures, dementia, heart attacks, infections, vitamin deficiencies, and stomach cancer.

What Research Actually Shows

Most reported risks of PPIs are based on low-quality observational studies that cannot prove cause and effect. These include:

Observational studies that look at patterns in large groups of people but cannot prove that PPIs actually cause the problems they're associated with. These studies have major flaws:

- People who take PPIs long-term are often sicker to begin with, which may explain why they have more health problems

- The studies cannot account for all the differences between people who take PPIs and those who don't

- Many of these associations are weak and inconsistent

Randomized controlled trials (the gold standard of medical research). Multiple trials, including the largest which followed over 17,000 patients taking PPIs for up to 5 years, found **no significant increase in kidney disease, bone fractures, dementia, heart disease, pneumonia, stomach cancer, or death** compared to placebo. The only finding was a small increase in intestinal infections (Clostridioides difficile and small intestinal bacterial overgrowth). The relative risk of these infections is considered low.

What Medical Experts Say

The American Gastroenterological Association (AGA) and American College of Gastroenterology (ACG)—the leading expert organizations for digestive diseases—have carefully reviewed all available evidence. Their conclusions are:

- The quality of evidence linking PPIs to serious harms is **very low** for most reported risks

- High-quality studies have **not confirmed** most of the feared associations

- **The well-established benefits of PPIs far outweigh their theoretical risks** for people who need them

- Most associations found in observational studies are likely due to confounding factors and biases, not the PPIs themselves

The Bottom Line

For people with appropriate medical reasons to take PPIs, the proven benefits are substantial and the risks are minimal. PPIs effectively control symptoms, heal esophageal damage, and may help prevent serious complications like esophageal strictures and esophageal cancer.

While we cannot completely rule out the possibility that PPIs might carry a very small risk of certain conditions, the current evidence does not support stopping a medication that is providing clinical benefit. Like any medication, providers should aim to use the lowest effective dose and periodically reassess the need for therapy.