Use of proton pump inhibitors and risk of gastric cancer: a systematic review and meta-analysis

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I attest that I have no conflict of interests related to this study to disclose

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What is already known on this topic

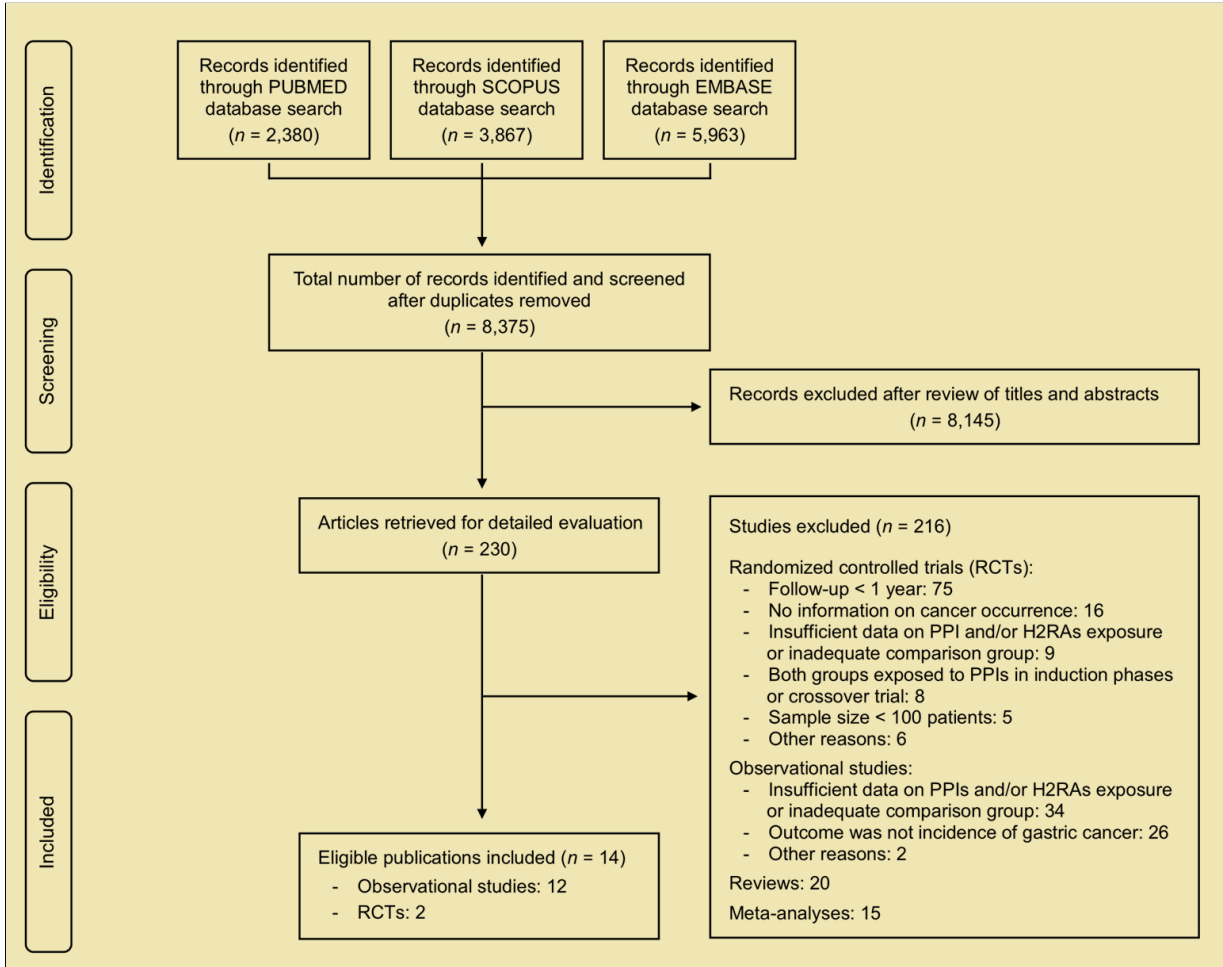
- Previous observational studies and meta-analyses suggest that exposure to **proton-pump inhibitors** (PPIs) is associated with **increased** risk of **gastric cancer**.
- Several methodological issues and biases may affect this area of research.
- The causal role of PPI use on the development of gastric cancer is still heavily debated in the medical community.

What we did

- Systematic search of Medline/PubMed, Embase and Scopus databases for randomized and observational studies of the association between PPIs and gastric cancer having considered **Histamine-2 receptor antagonists (H2RAs) users as controls**
- Stratified analyses and meta-regression were employed to explore heterogeneity.
- We used GRADE to evaluate certainty in the body of evidence.

- **2 randomized clinical trials** (498 patients; 1 gastric cancer)
- **12 Observational studies** (>6 million patients; 11,554 gastric cancers)
  - 6 studies provided a comprehensive adjustment of confounding
  - 3 studies provided partially-adjusted effect estimate
  - 2 studies provided crude/unadjusted relative risk estimate
  - 1 study excluded due to population overlap

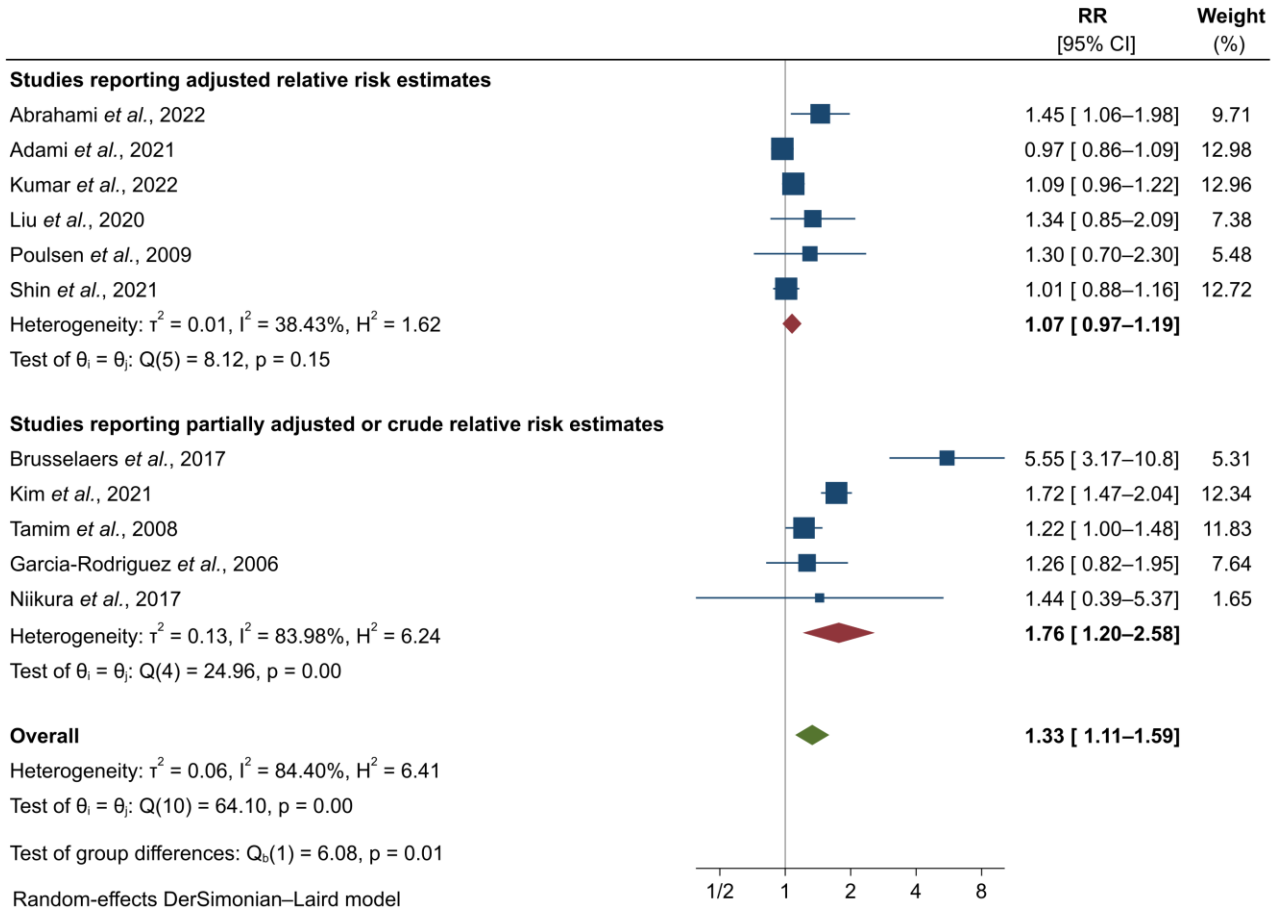
The **6 observational studies providing comprehensive adjustment of confounding** included about **2.5 million patients** receiving either PPIs or H2RAs and **7,372 gastric cancers**



- Meta-analysis of six observational studies providing a **comprehensive adjustment for confounding** did not show any association between PPIs and gastric cancer (**RR_{random}=1.07, 0.97−1.19**; RR_{fixed}=1.05, 0.98−1.12).
- Certainty in the random-effect estimate was low (observational studies) but the **results were consistent across sensitivity analyses**.
- No convincing evidence of a dose-response, or of increased risk with long-term use was found.
- Lack of or minimal adjustment for confounding was associated with larger effect sizes.

Interpretation:

- Patients using PPIs did not show a significantly differential risk of gastric cancer as compared to those using H2RAs when adjustment of confounding was comprehensive.
- The (nonsignificant) absolute increase corresponded to 2 more cases per 10,000 (from 1 less to 6 more) patients.



IMPLICATIONS FOR PRACTICE

Our findings are reassuring to all those patients who have an indication for long-term PPI use and need a persistent and effective acid gastric suppression to prevent serious health consequences.