EVALUATION OF MORTALITY ASSOCIATED WITH PROTON PUMP INHIBITORS AND H2 BLOCKERS: A REAL WORLD EVIDENCE STUDY

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OBJECTIVES

Several studies suggest that taking proton pump inhibitors (PPIs) is associated with a number of serious adverse events that are associated with increased risk of death. The following analysis aims to estimate all-cause mortality among patients taking PPIs and histamine H2 antagonists (H2 blockers).

METHODS

Patients identified through a federated network of electronic medical records were required to have taken PPIs or H2 blockers. Among these two cohorts, patients were required to have two records of these treatments recorded in their medical history at least three months apart. Patients treated with PPIs were matched 1-to-1 with patients treated with H2 blockers on characteristics listed in Table 1, using a greedy-nearest-neighbor algorithm. The risk of mortality was measured in the one year, five years, and ten years following the index treatment. All criteria were defined using ICD9/10, CPT, and RxNorm terminology. Kaplan-Meier curves and risk ratios (95% CI) were used to compare the cohorts.

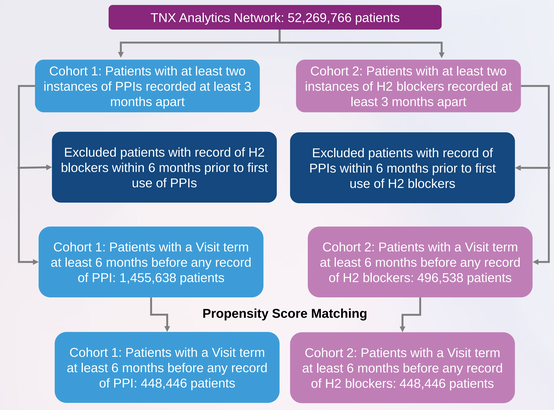

Figure 1. Patient flow diagram

Table 1. Baseline characteristics before and after propensity score matching

	Before Matching			After Matching		
	Cohort 1	Cohort 2	Stan. Mean Diff.	Cohort 1	Cohort 2	Stan. Mean Diff.
Age at Index, Mean (SD)	55 (18.7)	47 (22.5)	0.3760	48 (21.7)	48 (22.0)	0.0072
Current age, Mean (SD)	61 (18.7)	53 (22.6)	0.3931	54 (21.7)	54 (22.0)	0.0063
Female (%)	57.3	61.0	0.0752	61.1	60.9	0.0040
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified (%)	62.0	68.2	0.1306	63.0	68.2	0.1111
Diseases of the respiratory system (%)	38.3	42.4	0.0840	39.2	42.5	0.0657
Diseases of the nervous system (%)	36.9	39.6	0.0560	36.7	39.9	0.0666
Diseases of the genitourinary system (%)	34.2	39.9	0.1173	33.9	40.2	0.1323
Injury, poisoning and certain other consequences of external causes (%)	27.7	33.2	0.1198	27.9	33.4	0.1179
Diseases of esophagus, stomach and duodenum (%)	28.4	23.5	0.1120	24.2	23.8	0.0082
Other diseases of intestines (%)	19.7	20.7	0.0235	21.7	20.5	0.0312
Neoplasms (%)	22.3	25.3	0.0701	20.2	25.5	0.1267
Certain infectious and parasitic diseases (%)	18.7	23.1	0.1083	19.8	23.1	0.0802
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism (%)	19.4	20.7	0.0338	18.8	20.8	0.0508
External causes of morbidity (%)	13.5	17.0	0.0975	13.6	17.1	0.0977
Helicobacter pylori [H. pylori] as the cause of diseases classified elsewhere (%)	0.6	0.5	0.0205	0.4	0.5	0.0082

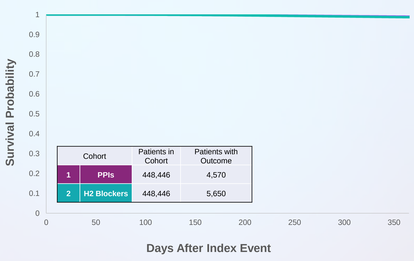

Figure 2. One-year overall survival

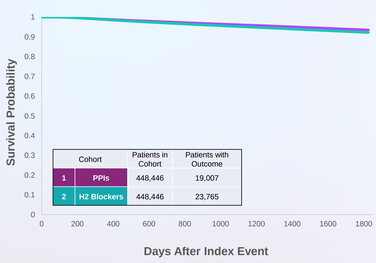

Figure 3. Five-year overall survival

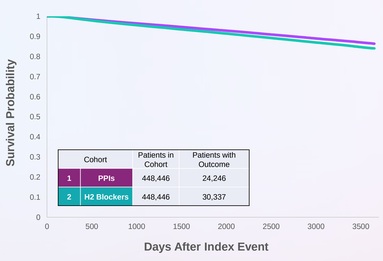

Figure 4. Ten-year overall survival

RESULTS

The mean age was 54.4 ± 18.8 (N=1,455,638) and 46.6 ± 22.7 (N=496,538) among PPI- and H2 blocker-treated patients. In the matched analysis (N=448,446), H2 blocker patients were 0.089 (0.778,0.841), 0.8 (0.785,0.815), and 0.799 (0.786,0.812) more likely to die than PPI patients in the one year, five years, and ten years following treatment. The survival probability was 0.25%, 1.34%, and 2.35% higher in PPI-treated patients than in H2-treated patients in the one year, five years, and ten years following treatment (all with p<0.05).

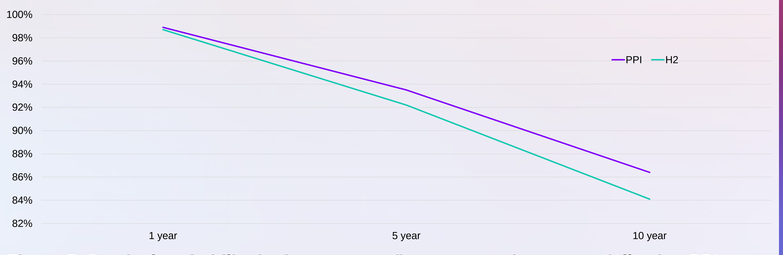

Figure 5. Survival probability in the one year, five years, and ten years following PPI or H2 blocker initiation

CONCLUSIONS

Results suggest that taking H2 blockers is associated with a small increased risk of mortality. This burden is observed in patients with and without an indication for PPI or H2 blocker use. PPIs were not associated with an increased risk of death, in contrast to other studies. This difference may be due to a broader and less selective patient population or use of different controls. Further research is needed to understand underlying causes of mortality.

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