

Supplemental table 1: Baseline demographic and health characteristics of the overall 2001 cohort of new users of acid suppression therapy, by type of acid suppressant at time of cohort entry, and those who were ever exposed to PPI.

		Overall cohort	New users of H2 Blockers at time of cohort entry	New users of PPI at time of cohort entry	Ever exposed to PPI ^a	P Value ^b
N		396884	208492	188392	293265	
Age (SD)		62.98 (13.05)	61.93 (13.24)	64.14 (12.74)	63.78 (12.81)	<0.001
eGFR in mL/min/1.73m ² (SD)		74.74 (22.43)	76.24 (22.04)	73.09 (22.73)	73.38 (22.61)	<0.001
Number of outpatient serum creatinine measurements (SD)		3.01 (3.40)	2.95 (3.23)	3.06 (3.58)	4.52 (5.51)	<0.001
Number of hospitalizations (SD)		0.37 (0.96)	0.36 (0.95)	0.38 (0.97)	0.51 (1.30)	<0.001
Race	White (%)	318534 (80.26)	164295 (78.80)	154239 (81.87)	236930 (80.79)	<0.001
	Black (%)	58355 (14.70)	32053 (15.37)	26302 (13.96)	42498 (14.49)	
	Other (%)	19995 (5.04)	12144 (5.82)	7851 (4.17)	13837 (4.72)	
Sex	Male (%)	377769 (95.18)	197685 (94.82)	180084 (95.59)	279023 (95.14)	<0.001
	Female (%)	19115 (4.82)	10807 (5.18)	8308 (4.41)	14242 (4.86)	
Diabetes mellitus (%)		92555 (23.32)	46562 (22.33)	45993 (24.41)	74344 (25.35)	<0.001
Hypertension (%)		231296 (58.28)	119554 (57.34)	111742 (59.31)	184529 (62.92)	<0.001
Chronic lung disease (%)		75810 (19.10)	39270 (18.84)	36540 (19.40)	64254 (21.91)	<0.001
Peripheral artery disease (%)		9141 (2.30)	4646 (2.23)	4495 (2.39)	8751 (2.98)	0.001
Cardiovascular disease (%)		122301 (30.82)	59814 (28.69)	62487 (33.17)	101220 (34.51)	<0.001
Cerebrovascular disease (%)		1529 (0.39)	776 (0.37)	753 (0.40)	1419 (0.48)	0.16
Dementia (%)		12031 (3.03)	6094 (2.92)	5937 (3.15)	10615 (3.62)	<0.001
Hyperlipidemia (%)		152040 (38.31)	78546 (37.67)	73494 (39.01)	130557 (44.52)	<0.001
Hepatitis C (%)		9332 (2.35)	4832 (2.32)	4500 (2.39)	8456 (2.88)	0.14
HIV (%)		209 (0.05)	105 (0.05)	104 (0.06)	183 (0.06)	0.51
Cancer (%)		46451 (11.70)	23312 (11.18)	23139 (12.28)	39473 (13.46)	<0.001
GERD (%)		110217 (27.77)	52586 (25.22)	57631 (30.59)	114132 (38.92)	<0.001

Upper GI tract bleeding (%)	11282 (2.84)	3352 (1.61)	7930 (4.21)	12458 (4.25)	<0.001
Ulcer disease (%)	35189 (8.87)	14152 (6.79)	21037 (11.17)	37472 (12.78)	<0.001
H. Pylori infection (%)	2599 (0.65)	477 (0.23)	2122 (1.13)	3795 (1.29)	<0.001
Barrett's esophagus (%)	0 (0.00)	0 (0.00)	0 (0.00)	245 (0.08)	NA
Achalasia (%)	188 (0.05)	41 (0.02)	147 (0.08)	245 (0.08)	<0.001
Stricture (%)	2218 (0.56)	415 (0.20)	1803 (0.96)	2953 (1.01)	<0.001
Esophageal adenocarcinoma (%)	223 (0.06)	79 (0.04)	147 (0.08)	262 (0.09)	<0.001
Years of follow up (IQR) ^c	5.65 (5.05 – 6.28)	3.35 (1.01 – 5.71) ^d	5.51 (5.01 – 6.08)	5.23 (3.22 – 5.90)	<0.001
Days of having related prescription during follow-up (IQR)	587 (168 – 1423) ^e	188 (90 – 561) ^d	621 (171 – 1496)	579 (172 – 1350)	<0.001
Death (%)	102802 (25.90)	31260 (14.99) ^d	51785 (27.49)	71565 (24.40)	<0.001
Incident death in 100 person years (95% CI)	5.08 (5.05 – 5.11)	4.40 (4.35 – 4.45) ^d	5.56 (5.51 – 5.61)	5.45 (5.41 – 5.49)	<0.001

- a. Includes patients exposed to PPI at T0 (n=275977) and during follow-up (n=33136). Variables were measured at time of PPI exposure.
- b. P value for difference between exposed to H2 at T0 and exposed to PPI at T0
- c. From T0 to first occurrence of death or September 30, 2013
- d. Outcome measured from T0 to first occurrence of exposure PPI, death or September 30, 2007
- e. Days of having PPI or H2 blockers

Abbreviations: CI, Confidence interval; eGFR, estimated Glomerular Filtration Rate; GERD, Gastroesophageal Reflux Disease; HIV, human immunodeficiency virus; IQR, interquartile range; NA, Not Applicable; SD, Standard deviation

Supplemental table 2: Duration of exposure to PPI and risk of death among new users of PPI in the 2001 cohort (n=101,109)

Duration (Days)	≤ 30	31 - 90	91 - 180	181 - 360	361 - 720
N (%)	15204 (15.04)	20409 (20.19)	17137 (16.95)	21586 (21.35)	26773 (26.48)
Hazard Ratio (95%CI)	1	1.04 (1.01, 1.07)	1.11 (1.08, 1.15)	1.18 (1.15, 1.22)	1.28 (1.24, 1.31)
<p>a. Within people exposure to PPI between 1 to 720 days</p> <p>b. Model controls for eGFR, age, race, gender, number of serum creatinine measurements, number of hospitalizations, diabetes mellitus, hypertension, cardiovascular disease, peripheral artery disease, cerebrovascular disease, chronic lung disease, hepatitis C, HIV, dementia, cancer, GERD, upper GI tract bleeding, ulcer disease, H. Pylori infection, Barrett's esophagus, achalasia, stricture and esophageal adenocarcinoma</p> <p>c. Time zero defined as date when the patients last PPI prescription end</p>					