

Table 1 Characteristics of PPIs and non-PPIs users

	All (n=63 397)	PPIs users (n=3271)	Non-PPIs users (n=60 126)
Age at triple therapy (years)*	54.7 (46.0–65.4)	64.1 (53.6–75.3)	54.3 (45.7–64.7)
Male sex (n, %)	29 499 (46.5%)	1641 (50.2%)	27 858 (46.3%)
Duration of follow-up (years)*	7.6 (5.1–10.3)	7.4 (4.5–10.0)	7.6 (5.2–10.3)
Smoking (n, %)	1 629 (2.6%)	162 (5.0%)	1 467 (2.4%)
Alcohol (n, %)	552 (0.9%)	50 (1.5%)	502 (0.8%)
Dyspepsia (n, %)	4 145 (6.5%)	262 (8.0%)	3 883 (6.5%)
GORD (n, %)	3 278 (5.2%)	593 (18.1%)	2 685 (4.5%)
History of GU (n, %)	1 268 (2.0%)	153 (4.7%)	1 115 (1.9%)
History of DU (n, %)	1 897 (3.0%)	139 (4.2%)	1 758 (2.9%)
DM (n, %)	7 383 (11.6%)	772 (23.6%)	6 611 (11.0%)
Hypertension (n, %)	13 065 (20.6%)	1 334 (40.8%)	11 731 (19.5%)
Dyslipidaemia (n, %)	5 045 (8.0%)	579 (17.7%)	4 466 (7.4%)
Obesity	637 (1.0%)	61 (1.9%)	576 (1.0%)
IHD (n, %)	5 701 (9.0%)	906 (27.7%)	4 795 (8.0%)
AF (n, %)	2 404 (3.8%)	371 (11.3%)	2 033 (3.4%)
CHF (n, %)	2 512 (4.0%)	463 (14.2%)	2 049 (3.4%)
Stroke (n, %)	3 965 (6.3%)	561 (17.2%)	3 404 (5.7%)
CRF (n, %)	1 388 (2.2%)	236 (7.2%)	1 152 (1.9%)
Cirrhosis (n, %)	1 037 (1.6%)	98 (3.0%)	939 (1.6%)
Statins (n, %)	13 180 (20.8%)	1 351 (41.3%)	11 829 (19.7%)
Metformin (n, %)	7 935 (12.5%)	605 (18.5%)	7 330 (12.2%)
Aspirin (n, %)	8 965 (14.1%)	1 358 (41.5%)	7 607 (12.7%)
NSAIDs/COX-2 Inhibitors (n, %)	3 556 (5.6%)	391 (12.0%)	3 165 (5.3%)
Clopidogrel (n, %)	980 (1.5%)	200 (6.1%)	780 (1.3%)
H2RA (n, %)	21 729 (34.3%)	1 499 (45.8%)	20 230 (33.6%)

Categorical variables were expressed as number (%).

Drug use was defined as at least weekly use, and expressed as number (%).

*Age was expressed as median (years) with IQR.

AF, atrial fibrillation; CHF, congestive heart failure; COX-2, cyclooxygenase-2; CRF, chronic renal failure; DM, diabetes mellitus; DU, duodenal ulcer; GU, gastric ulcer; H2RA, histamine 2 receptor antagonist; IHD, ischaemic heart disease; NSAIDs, non-steroidal anti-inflammatory drugs; PPIs, proton pump inhibitors.

ベースラインの患者群では
ピロリ菌とは無関係の患者群も含まれています。
つまり抗血小板薬や抗凝固薬との併用での
PPI服用も含まれているようです。

Table 2 Characteristics of H2RA and non-H2RA users

	All (n=63 397)	H2RA users (n=21 729)	Non- H2RA users (n=41 668)
Age at triple therapy (years)*	54.7 (46.0–65.4)	60.0 (51.6–71.0)	52.0 (43.4–61.6)
Male sex (n, %)	29 499 (46.5%)	9 454 (43.5%)	20 045 (48.1%)
Duration of follow-up (years)*	7.6 (5.1–10.3)	7.2 (4.8–9.8)	7.8 (5.3–10.5)
Smoking (n, %)	1 629 (2.6%)	863 (4.0%)	766 (1.8%)
Alcohol (n, %)	552 (0.9%)	232 (1.1%)	320 (0.8%)
Dyspepsia (n, %)	4 145 (6.5%)	1 826 (8.4%)	2 319 (5.6%)
GORD (n, %)	3 278 (5.2%)	1 629 (7.5%)	1 649 (4.0%)
History of GU (n, %)	1 268 (2.0%)	446 (2.1%)	822 (2.0%)
History of DU (n, %)	1 897 (3.0%)	503 (2.3%)	1 394 (3.3%)
DM (n, %)	7 383 (11.6%)	3 885 (17.9%)	3 498 (8.4%)
Hypertension (n, %)	13 065 (20.6%)	7 137 (32.8%)	5 928 (14.2%)
Dyslipidaemia (n, %)	5 045 (8.0%)	2 939 (13.5%)	2 106 (5.1%)
Obesity	637 (1.0%)	351 (1.6%)	286 (0.7%)
IHD (n, %)	5 701 (9.0%)	3 560 (16.4%)	2 141 (5.1%)
AF (n, %)	2 404 (3.8%)	1 468 (6.8%)	936 (2.2%)
CHF (n, %)	2 512 (4.0%)	1 512 (7.0%)	1 000 (2.4%)
Stroke (n, %)	3 965 (6.3%)	2 466 (11.3%)	1 499 (3.6%)
CRF (n, %)	1 388 (2.2%)	814 (3.7%)	574 (1.4%)
Cirrhosis (n, %)	1 037 (1.6%)	425 (2.0%)	612 (1.5%)
Statins (n, %)	13 180 (20.8%)	7 401 (34.1%)	5 779 (13.9%)
Metformin (n, %)	7 935 (12.5%)	3 899 (17.9%)	4 036 (9.7%)
Aspirin (n, %)	8 965 (14.1%)	6 376 (29.3%)	2 589 (6.2%)
NSAIDs/COX-2 inhibitors (n, %)	3 556 (5.6%)	3 092 (14.2%)	464 (1.1%)
Clopidogrel (n, %)	980 (1.5%)	602 (2.8%)	378 (0.9%)
PPIs (n, %)	3 271 (5.2%)	1 499 (6.9%)	1 772 (4.3%)

Categorical variables were expressed as number (%).

Drug use was defined as at least weekly use and expressed as number (%).

*Age was expressed as median (years) with IQR.

AF, atrial fibrillation; CHF, congestive heart failure; COX-2, cyclooxygenase-2; CRF, chronic renal failure; DM, diabetes mellitus; DU, duodenal ulcer; GU, gastric ulcer; H2RA, histamine 2 receptor antagonist; IHD, ischaemic heart disease; NSAIDs, non-steroidal anti-inflammatory drugs; PPIs, proton pump inhibitors.

前の表と同様にH2ブロッカーに対するベースラインです。

Table 5 Comparison of incidence rates of gastric cancer in different cohorts according to PPIs uses and prior *Helicobacter pylori* (HP) eradication therapy

Before matching	Number of patients	Number of person-years	Number of GC cases	Incidence rate (per 10000 person-years)	Incidence rate ratio with 95% CI
Non-PPIs users with prior HP therapy	60 126	459 864	134	2.9	Ref
PPIs users with prior HP therapy	3271	23 395	19	8.1	2.81 (1.68 to 4.43)
PPIs users without prior HP therapy	142 460	705 094	59	0.8	0.29 (0.21 to 0.39)
After matching	Number of patients	Number of person-years	Number of GC cases	Incidence rate (per 10000 person-years)	Incidence rate ratio with 95% CI
PPIs users with prior HP therapy	3270	23 384	19	8.1	Ref
PPIs users without prior HP therapy*	13 080	93 500	9	1.0	0.12 (0.05 to 0.26)

*Matched with age (± 5 years), sex, duration of follow-up (± 2 years) and frequency of PPIs use (± 0.3) in a 1:4 ratio. GC, gastric cancer; PPIs, proton pump inhibitors.

除菌と無関係でPPIを服用した場合の危険率を1とすると、除菌後の服用では8となります。

Table 4 HRs and 95% CIs for the association between frequency and duration of PPIs use and risk of gastric cancer (propensity score adjustment with trimming)

PPIs frequency	Dose—response relationship (n=57 057, GC=139)									
	HR	95% CI			95% CI			p Value		
Non-user (<weekly use)	Ref	–			–			–		
Weekly to <daily	2.43	1.37 to 4.31			0.002			0.002		
Daily	4.55	1.12 to 18.52			0.034			0.034		
PPIs frequency	PPIs use ≥1 year (n=50 932, GC=112)			PPIs use ≥2 years (n=49 462, GC=88)			PPIs use ≥3 years (n=48 511, GC=69)			
	HR	95% CI	p Value	HR	95% CI	p Value	HR	95% CI	p Value	
Non-user (<weekly use)	Ref	–	–	Ref	–	–	Ref	–	–	
Weekly to <daily	1.81	0.90–3.64	0.098	0.98	0.31–3.17	0.979	0.58	0.08–4.23	0.590	
Daily	5.04	1.23–20.61	0.024	6.65	1.62–27.26	0.009	8.34	2.02–34.41	0.004	

Significant p Values were highlighted in bold.
GC, gastric cancer; PPIs, proton pump inhibitors.

PPIの服用が1年、2年、3年と長期になるに従って危険率は増加します。