



Risk of bacterial pneumonia in patients with proton pump inhibitors versus histamine-2 receptor antagonist: A Korean single center-based long-term cohort study using OMOP-CDM Common Data Model

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Background

There are concerns about the infectious complication of gastric acid suppressive agent, further, the stronger acid suppression may enhance infectious complications. We aimed to compare the risk of bacterial pneumonia between proton pump inhibitors (PPIs) and histamine-2 receptor antagonis (H2RAs).

Methods

Using 30-year database of Kangdong Sacred Heart Hospital converted to the Observational Medical Outcomes Partnership (OMOP)-Common Data Model (CDM) Including 1,650,000 patients, we identified patients who were treated with PPIs and H2RAs \geq 30 days from January 1, 2004 through December 31, 2018. Inclusion criteria was adults $>$ 18 years without previous pneumonia within 6 months of index date and tuberculosis history.

Propensity score matching (PSM)-based analysis with covariates including age, index year, drugs and conditions in prior 1 year of index date were used to control confounders. Primary outcome was diagnosis of bacterial pneumonia after starting PPI or H2RA for more than 30 days. The version of ATLAS was 2.5 and we analyzed via Feedernet platform in which empirical calibration plot could not be provided currently.

Results

description	treatedPersons	comparatorPersons
Original cohorts	18622	4156
Removed subs in both cohorts	18622	4156
Removed subjects in both cohorts	18622	4156
No prior outcome	18211	4076
Matched on propensity score	1700	1700

Figure 1. Attrition diagram of study population

Results

A total of 18622 patients with PPI and 4156 patients with H2RA were included and 3400 patients were included after PSM matching. The cumulative 6-month, 1-year, 2-year and 3 year incidence was 0.33%, 0.59%, 0.84% and 1.01% among patients prescribed PPIs and 0.37%, 0.64%, 1.03% and 1.25% in patients with H2RAs. After propensity score matching, in PPI group, there were more events of pneumonia compared to H2RA group [0.025% (44/1700) vs. 0.014% (25/1700), HR; 1.64, 95% CI; 0.855-3.271, P=0.14].

Table 1. Demographics and clinical characteristics of KDH database

Characteristic	Value
No. of patients	1,689,604
Age	
0-5	153,994
6-12	64,673
13-18	44,267
19-24	85,057
25-44	347,345
45-64	256,304
65-80	94,693
>80	19,963
Gender	
male	828,079 (48)
female	861,525 (51)
No. of visit	
Outpatient	726,364 (42.99)
Emergency	402,247 (23.81)
Inpatient	362,212 (21.44)
Emergency room and inpatient	111,378 (6.59)
Condition	
No. of types	4,626
No. of conditions/patient	5.2 \pm 5.9
Drug exposure	
No. of types	3,075
No. of prescriptions/patient	6.9 \pm 7.8

Results

Table 2. Clinical characteristics of study population before and after propensity matching

Study population	Before Propensity matching		After Propensity matching	
	PPI N=18622	H2RA N=4156	PPI N=1700	H2RA N=1700
Age, n (%)				
18-29	953 (5.2)	227 (5.5)	93 (5.4)	88 (5.1)
30-39	1456 (7.8%)	365 (8.7%)	137 (8.1)	135 (7.8)
40-49	2506 (13.5)	649 (15.7)	256 (15)	253 (14.9)
50-59	4887 (26.3)	897 (21.6)	386 (22.7)	398 (23.4)
60-69	4331 (23.2)	897 (21.6)	368 (21.6)	355 (20.9)
70-79	3065 (16.3)	727 (17.4)	303 (17.7)	297 (17.4)
80-89	1278 (6.8)	349 (8.4)	142 (8.3)	150 (8.8)
90-99	146 (0.76)	40 (0.96)	15 (0.88)	22 (1.3)
Gender				
Male n (%)	8627 (46.3)	1778 (42.8)	782 (46)	780 (45.9)
Comorbidities, n (%)				
asthma	233 (1.3)	150 (3.6)	43 (2.5)	37 (2.2)
COPD	156 (0.8)	70 (1.7)	19 (1.1)	20 (1.2)
bronchiectasis	39 (0.2)	32 (0.8)	1 (0.1)	7 (0.4)
DM	856 (4.6)	127 (3.1)	78 (4.5)	55 (3.2)
GERD	3014 (16.2)	246 (5.9)	150 (8.8)	167 (9.8)
Medication, n (%)				
Aspirin	614 (3.3)	23 (0.6)	17 (1)	21 (1.2)
theophylline	73 (0.4)	118 (2.8)	19 (1.1)	14 (0.8)
corticosteroid	1927 (12.2)	410 (9.8)	126 (7.4)	131 (7.6)
ketoprofen	5328 (28.6)	927 (22.3)	348 (20.4)	355 (20.8)
IV cefazedone	3259 (17.5)	189 (4.5)	95 (5.5)	102 (6)
Charlson index – Romano adaptation	17389 (93.4)	4226 (101.7)	1861 (109.5)	1671 (98.3)

Results

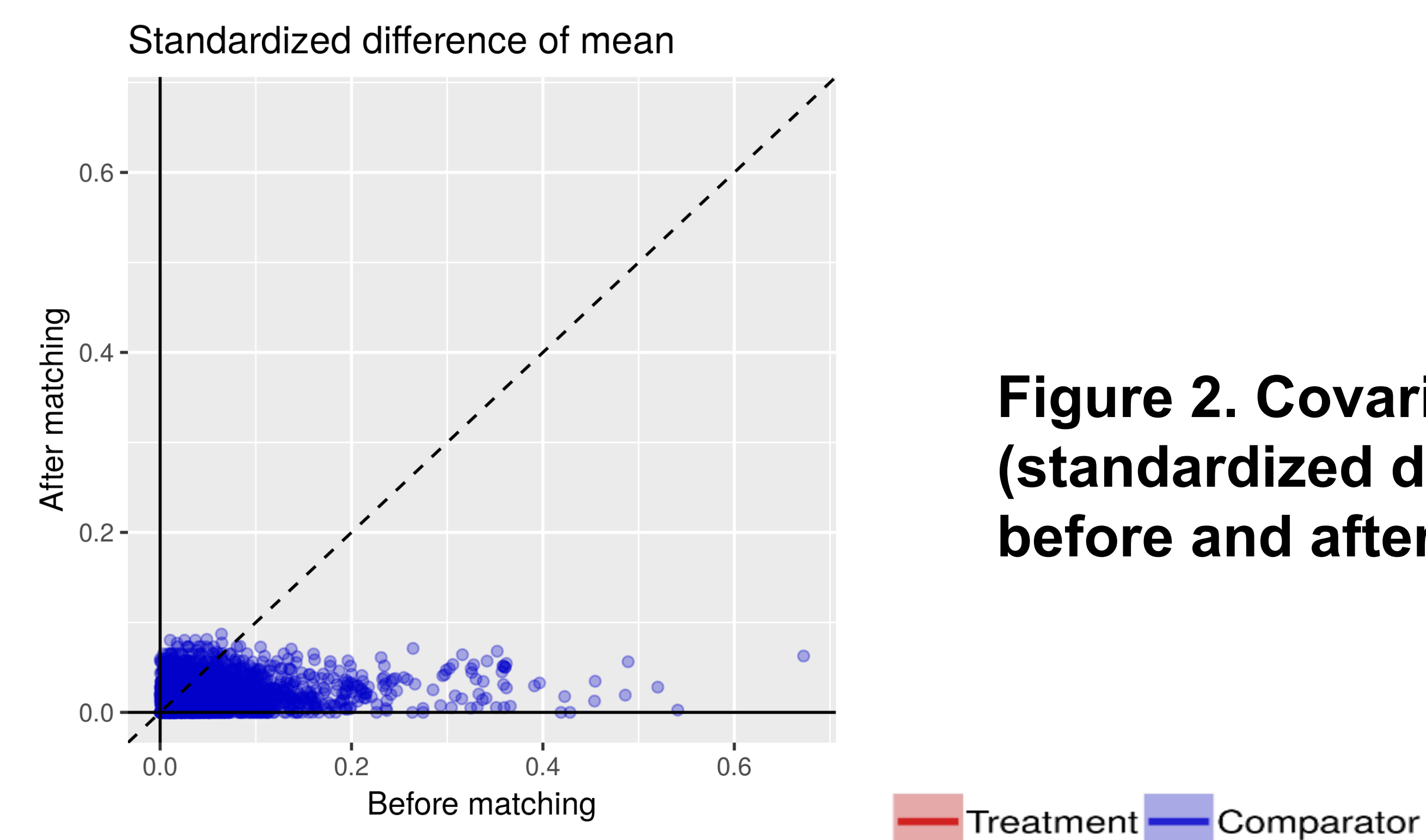


Figure 2. Covariate balance (standardized difference of mean) before and after matching)

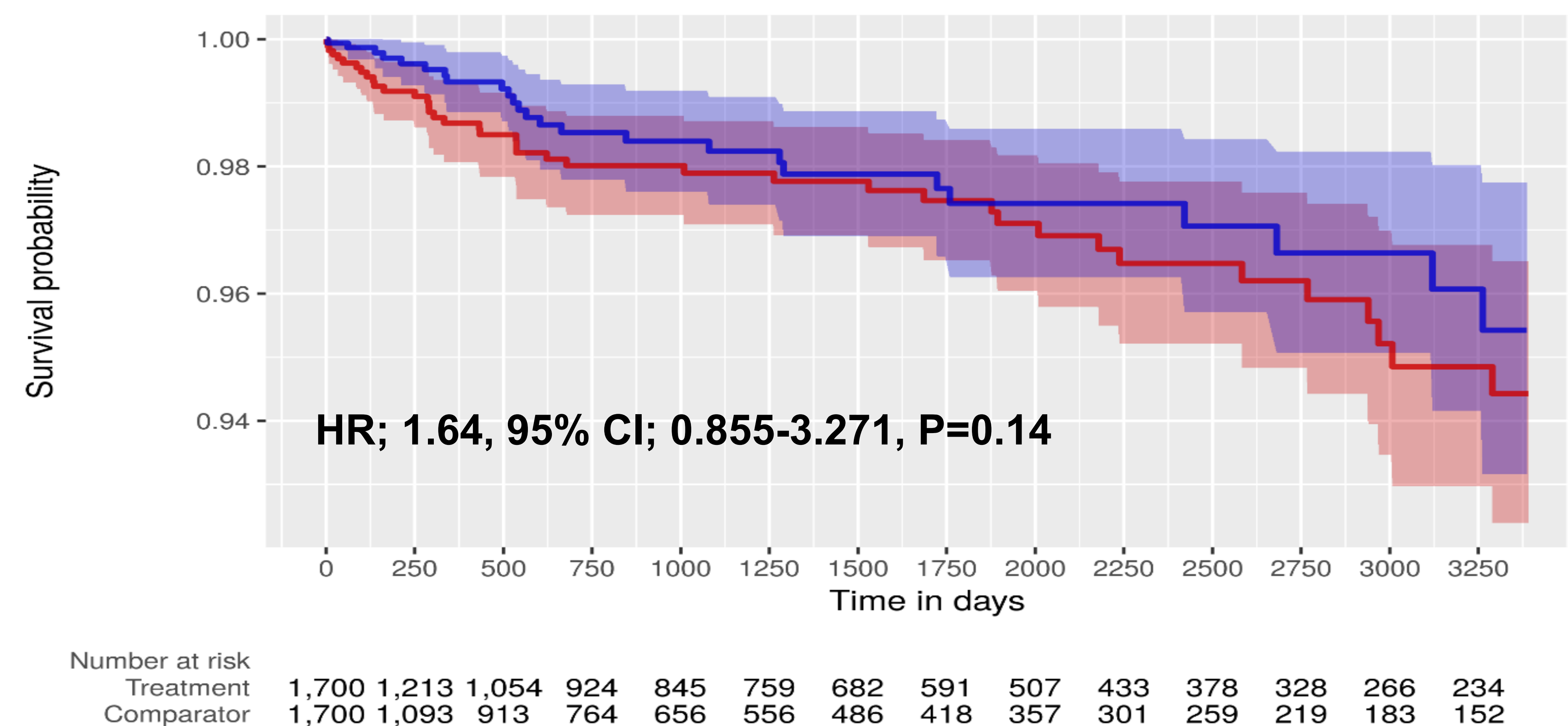


Figure 3. Kaplan meier curve of pneumonia development in PPI vs. H2RA group

Conclusions

We tried to evaluate the complications of acid suppressive agents based on OMOP-CDM-based hospital database. Although, the study did not demonstrate that stronger acid suppression may increase the risk of bacterial pneumonia., however, it could be applied to other infectious complications by common R code and it'll be able to used to find out safety of acid-suppressive agents..