**Supplemental Table S1. Defined Daily Doses of PPIs and creation of episodes of use given various scenarios for consecutive prescriptions of the different PPIs in the dataset**

To measure the exposure to PPIs, we calculated the medication dose for each prescription fill by multiplying the medication strength by the number of units dispensed. This product was converted to a defined daily dose (DDD) by dividing by the defined daily dose by WHO for use in adults for Gastroesophageal reflux disease (GERD) (omeprazole: 20mg, pantoprazole: 40mg, lansoprazol: 30mg, rabeprazole: 20mg, esomeprazole: 30mg, dexlansoprazole: 30mg).

| **PPI prescription scenario \*** | **Illustration using pantoprazole and lansoprazole as examples** | **Decision for creating episodes of use** |
| --- | --- | --- |
| First prescription starts with at least DDD ≥ 56 | Pantoprazole 56 DDDs | A prescription with 56 DDDs, eligible as a PPI initiator  56 DDDs days |
| Second prescription starts and ends after the first one  No overlap of coverage dates  Interval (days) between the two prescriptions ≤ DDD of first prescription + 30 days | Interval (<=30 days)  28 DDDs  28 DDDs  Pantoprazole 28 DDDs  Lansoprazole 28 DDDs | Consecutive episode of use (56 DDDs), eligible as a PPI initiator  56 DDDs days |
| Second prescription starts and ends after the first one  No overlap of coverage dates  Interval between the two prescriptions > DDD of first prescription + 30 days | 28 DDDs  28 DDDs  Pantoprazole 28 DDDs  Lansoprazole 28 DDDs  Interval = 36 days | Episode of use (28 DDDs), not eligible as a PPI initiator  28 DDDs days |
| Second prescription starts and ends after the first one  Overlap of coverage dates  Different PPIs | 28 DDDs  28 DDDs  Pantoprazole 28 DDDs  Lansoprazole 28 DDDs | Consecutive episode of use (56 DDDs), eligible as a PPI initiator  28 DDDs  28 DDDs |
| Second prescription within coverage dates of the first one  Different PPIs | 14 DDDs  Lansoprazole 14 DDDs  Pantoprazole 28 DDDs  28 DDDs | Consecutive episode of use (42 DDDs), not eligible as a PPI initiator  14 DDDs  28 DDDs |
| Two prescriptions have same start date but different end date  Different PPIs | Lansoprazole 56 DDDs  Pantoprazole 28 DDDs | Retain the prescription with larger DDDs, eligible as a PPI initiator  Lansoprazole 56 DDDs |

**Supplemental Figure S1. Cohort dataset creating flowchart**

Population insured by AOK

between 2008-2018

(N=6,097,740)

Excluded (N= 2,770,652)

- PPI use, but not fulfilling 56 DDD condition

(N= 2,192,879)

- Washout period <1 year (N= 275,151)

- Age < 40 years (N= 112,310)

- Follow-up period < 1year (N= 91,943)

- Prevalent dementia (N= 98,313)

- Individuals with missing value (N= 56)

PPI initiators

(n= 674,544)

Noninitiators

(n= 2,023,632)

- 1:3 Exposure density sampling of Noninitiators for analysis

Total person-trials

(n= 99,786,708 trials

from 3,327,088 individuals )

Eligible individuals were those aged 40 years or older with at least one year of continuously insured records before and after study entry, who did not meet the exclusion criteria. PPI use was assessed using prescriptions dispensed by community pharmacies applying 365 days of washout period.

**Supplemental Table S2. Outcome: Categorized Codes for Dementia**

|  |  |
| --- | --- |
| **Description** | **ICD-10 Codes** |
| Unspecified dementia | F03, G31.1, G31.9 |
| Delirium in dementia | F05.1 |
| Alzheimer’s disease | F00, G30 |
| Frontotemporal dementia | G31.0 |
| Vascular dementia | F01 |
| Lewy-body-Dementia | F02.8+G31.82 |

**Supplemental Table S3. Selected confounding factors**

|  |  |
| --- | --- |
| **Description** | **ICD-10 codes / ATC codes** |
| **Comorbidities** |  |
| Obesity | E66 |
| Diabetes | E10, E11, E12, E13, E14 |
| Hypertension | I10, I11, I12, I13, I15 |
| Cerebrovascular disease | I60, I61, I62, I63, I64, I65, I66, I67, I68, I69, G45, G46, H34.0 |
| Peripheral vascular disease | I70, I71, I73.1, I73.8, I73.9, I77.1, I79.0, I79.2, K55.1, K55.8, K55.9, Z95.8, Z95.9 |
| Coagulopathy | D65, D66, D67, D68, D69.1, D69.3, D69.4, D69.5, D69.6 |
| Chronic pulmonary disease | I27.8, I27.9, J40, J41, J42, J43, J44, J45, J46, J47, J60, J61, J62, J63, J64, J65, J66, J67, J68.4, J70.1, J70.3 |
| Heart disease | I09.9, I11.0, I13.0, I13.2, I25.5, I42.0, I42.5, I42.6, I42.7, I42.8, I42.9, I43, I50, P29.0, I44.1, I44.2, I44.3, I45.6, I45.9, I47, I49, R00.0, R00.1, R00.8, T82.1, Z45.0, Z95.0, A52.0, I05, I06, I07, I08, I09.1, I09.8, I34, I35, I36, I37, I38, I39, Q23.0, Q23.1, Q23.2, Q23.3, Z95.2, Z95.3, Z95.4, I26, I27, I28.0, I28.8, I28.9 |
| Cancer | C00, C01, C02, C03, C04, C05, C06, C07, C08, C09, C10, C11, C12, C13, C14, C15, C16, C17, C18, C19, C20, C21, C22, C23, C24, C25, C26, C30, C31, C32, C33, C34, C37, C38, C39, C40, C41, C43, C45, C46, C47, C48, C49, C50, C51, C52, C53, C54, C55, C56, C57, C58, C60, C61, C62, C63, C64, C65, C66, C67, C68, C73, C74, C75, C76, C81, C82, C83, C84, C85, C88, C90, C91, C92, C93, C94, C95, C96, C97, C77, C78, C80, C79.0, C79.1, C79.2, C79.5, C79.6, C79.8 |
| Diseases may cause dementia | F02.0, A81.0, G10, G20, G21, G22, B20, B21, B22, B24, E00, E01, E02, E03, E89.0, G40 |
| Inflammation, infection or injury in nervous system | S04, S06, S07, S09.0, S09.7, G00, G01, G02, G03, G04, G05, G06, G07, G08, G09, A17.0, A20.3, A39.0, A87, B01.1, B02.1, C69, C70, C71, C72, D31, D32, D33, D42, D43, D44, C47, C79.3, C79.4, C79.7, G35, E75, G31.8, A52.1, A69.2 |
| Depression | F20.4, F31.3, F31.4, F31.5, F32, F33, F34.1, F41.2, F43.2 |
| Abuse of substances or psychosis | F10.2, F11, F12, F13, F14, F15, F16, F17.2, F18, F19, Z71.5, Z72.2, F20, F22, F23, F24, F25, F28, F29, F30.2, F31.2 |
| **Gastrointestinal indications for PPI** |  |
| Gastroesophageal reflux disease (GERD), *Helicobacter Pylori*-infection, peptic ulcer, esophagitis, Zollinger-Ellison syndrome, and heartburn | K21, K20, K25, K26, K27, K28, B98.0, E16.4, R12 |
| **Drug use** |  |
| Antihypertensive drugs | C02, C03, C07, C08, C09 |
| Anti-inflammatory drugs | B01AC06, B01AC08, B01AC15, B01AC34, B01AC36, B01AC56, C01EB03, C01EB16, C10BX01, C10BX02, C10BX04, C01BX05, M01A, M01B, M01C, N02BA, N02BB, N02BG |
| Statins | C10AA |
| Antidiabetic drugs | A10 |
| Antidepressants | N06A |
| Psycholeptics | N05 |
| Corticosteroids | H02 |
| Anticholinergics | R06AX09, R06AA01, R06AB01, R06AA08, R06AB04, R06AA04, R06AX02, R06AB06, R06AB02, R06AB03, R06AA02, R06AA09, R06AX04, R06AD01, R06AX07, N06AA09, N06AA17, N06AA04, N06AA01, N06AA12, N06AA02, N06AA03, N06AA10, N06AB05, N06AA11, N06AA06, R06AE01, R06AE03, R06AA02, R06AE05, N04AC01, N04AA02, R06AA06, N04AA05, N04AA04, N04AA01, G04BD10, G04BD11, G04BD02, G04BD04, G04BD08, G04BD07, G04BD09, M03BX08, N04AB02, M03BC01, A03AA07, A03AX08, A03BA01, A03CA02, A03AB15, A03AB02, A03AB10, A03CB04, A03BA03, A03AB09, A03AB12, A03AB07, R06AX23, A03BB03, A03BB02, A03AA01, A03CA03, A03AB03, A03AB53, A03AB14, A03AB11, A03AB08, A03AA30, A03AB05, A03CA34, A04AD01, C01BA03 |
| Clopidogrel | B01AC04, B01AC34 |

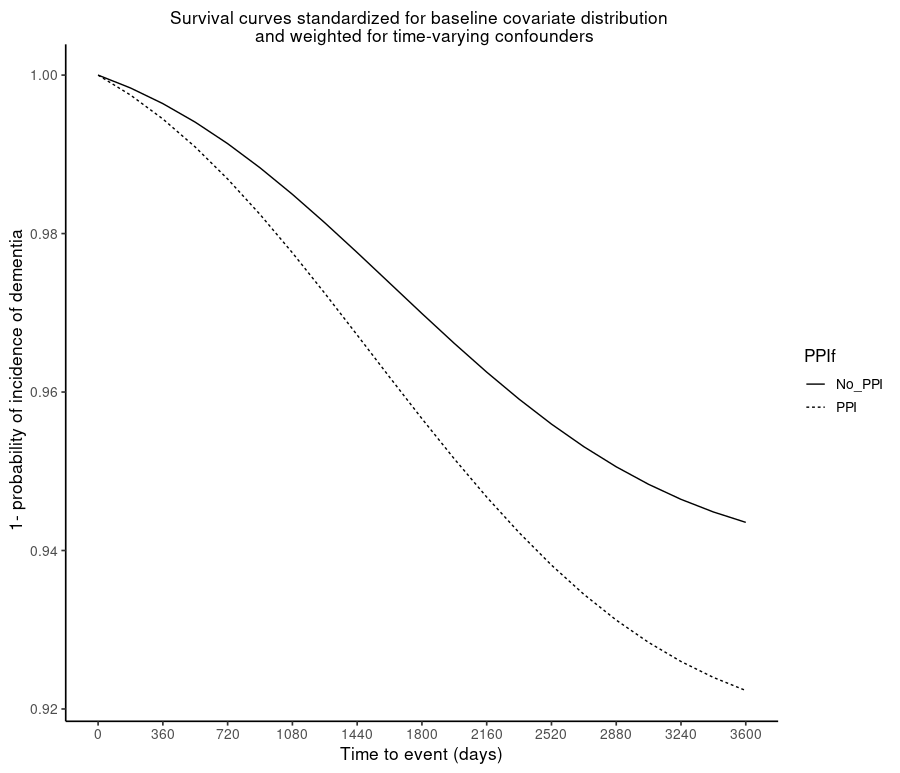
**Supplemental Table S4. Demographic and clinical characteristics of PPI initiators and non-initiators**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **PPI initiators** | |  | **Non-initiators** | |
|  | **n= 674,544** | |  | **n= 2,023,632** | |
|  | **n** | **(%)** |  | **n** | **(%)** |
| **Characteristics** |  |  |  |  |  |
| Age (years), mean (SD) | 62.8 (13.2) |  |  | 56.9 (12.4) |  |
| Women | 370,897 | 55.0 |  | 951,709 | 47.0 |
| German nationality | 577,458 | 85.6 |  | 1,525,175 | 75.4 |
| Hospitalizations in the year preceding cohort entry | 53,202 | 7.9 |  | 11,968 | 0.6 |
|  |  |  |  |  |  |
| **Comorbidities** |  |  |  |  |  |
| Obesity | 107,752 | 16.0 |  | 94,233 | 4.7 |
| Diabetes | 153,848 | 22.8 |  | 136,341 | 6.7 |
| Hypertension | 356,005 | 52.8 |  | 336,079 | 16.6 |
| Cerebrovascular disease | 75,552 | 11.2 |  | 47,363 | 2.3 |
| Peripheral vascular disease | 74,725 | 11.1 |  | 48,837 | 2.4 |
| Coagulopathy | 17,765 | 2.6 |  | 9,801 | 0.5 |
| Chronic pulmonary disease | 135,390 | 20.1 |  | 106,621 | 5.3 |
| Heart disease | 152,897 | 22.7 |  | 107,072 | 5.3 |
| Cancer | 65,582 | 9.7 |  | 42,338 | 2.1 |
| Diseases may cause dementia | 92,855 | 13.8 |  | 88,348 | 4.4 |
| Inflammation, infection or injury of the nervous system | 18,310 | 2.7 |  | 13,813 | 0.7 |
| Depression | 152,131 | 22.6 |  | 115,990 | 5.7 |
| Abuse of substances or phychosis | 16,000 | 2.4 |  | 16,251 | 0.8 |
| **Gastrointestinal indications for PPI** |  |  |  |  |  |
| Gastritis/duodenitis | 163,685 | 24.3 |  | 30,431 | 1.5 |
| Gastroesophageal reflux disease | 153,637 | 22.8 |  | 26,748 | 1,3 |
| Peptic ulcer | 33,301 | 4.9 |  | 4,271 | 0.2 |
| Heartburn | 19,253 | 2.9 |  | 2,191 | 0,1 |
| Other esophageal diseases | 15,924 | 2.4 |  | 1,976 | 0.1 |
| *H. pylori* infection | 11,405 | 1.7 |  | 866 | 0,0 |
| Functional dyspepsia | 8,813 | 1.3 |  | 3,723 | 1.8 |
| Esophagitis | 4,415 | 0.7 |  | 619 | 0.0 |
| Zollinger-Ellison syndrome | 90 | 0.0 |  | 6 | 0.0 |
|  |  |  |  |  |  |
| **Drug use** |  |  |  |  |  |
| Antihypertensive drugs | 375,188 | 55.6 |  | 340,175 | 16.8 |
| Anti-inflammatory drugs | 334,716 | 49.6 |  | 200,353 | 9.9 |
| Statins | 137,488 | 20.4 |  | 101,273 | 5.0 |
| Antidiabetic drugs | 92,826 | 13.8 |  | 82,959 | 4.1 |
| Antidepressants | 68,568 | 10.2 |  | 45,502 | 2.2 |
| Psycholeptics | 62,812 | 9.3 |  | 38,919 | 1.9 |
| Corticosteroids | 57,267 | 8.5 |  | 21,817 | 1.1 |
| Anticholinergics | 44,144 | 6.5 |  | 30,722 | 1.5 |
| Clopidogrel | 21,259 | 3.2 |  | 6,220 | 0.3 |

*H. pylori*, *Helicobacter Pylori*; PPI, proton pump inhibitor

Comorbidities and medication use are defined using data in the 180 days prior to and including the date of cohort entry.

**Supplemental Figure S2. Survival curves standardized for baseline covariate distribution and weighted for time-varying confounders and censoring**

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**Supplemental Table S5. Comparison of baseline confounders for initiators of PPIs and non-initiators with PPI on-label indications before/after application of weighting**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Unweighted population** | | | **Weighted population** | | | |
|
|  | **PPI Initiators**  **with indications**† | **Non-initiators**  **with indications** | **SD** | **PPI Initiators**  **with indications** | **Non-initiators**  **with indications** | | **SD** |
|  | 193,513 | 32,974 | 193,513 | 32,974 | |
| Age (years) | 61.3 (12.6) | 62.1 (12.4) | 0.063 | 61.4 (12.6) | 61.4 (12.6) | <0.001 | |
| Women (n, %) | 99,839 (51.6) | 17,302 (52.5) | 0.018 | 100,081 (51.7) | 17,054 (51.7) | <0.001 | |
| German nationality (n, %) | 163,209 (84.3) | 28,463 (86.3) | 0,056 | 163,760 (84.6) | 27,905 (84.6) | <0.001 | |
| Hospitalizations in the year preceding cohort entry | 21,235 (11.0) | 866 (2.6) | 0,336 | 18,886 (9.8) | 3,217 (9.8) | <0.001 | |
| Obesity | 32,730 (16.9) | 5,690 (17.3) | 0.009 | 32,821 (17.0) | 5,594 (17.0) | <0.001 | |
| Diabetes | 40,100 (20.7) | 7,202 (21.8) | 0.027 | 40,414 (20.9) | 6,887 (20.9) | <0.001 | |
| Hypertension | 104,304 (53.9) | 17,916 (54.3) | 0.009 | 104,410 (54.0) | 17,792 (54.0) | <0.001 | |
| Heart disease | 42,754 (22.1) | 7,210 (21.9) | 0.006 | 42,687 (22.1) | 7,274 (22.1) | <0.001 | |
| Peripheral vascular disease | 21,009 (10.9) | 3,504 (10.6) | 0.007 | 20,944 (10.8) | 3,568 (10.8) | <0.001 | |
| Coagulopathy | 5,385 (2.8) | 656 (2.0) | 0.052 | 5,147 (2.7) | 880 (2.7) | <0.001 | |
| Chronic pulmonary disease | 43,280 (22.4) | 7,599 (23.0) | 0.016 | 43,475 (22.5) | 7,406 (22.5) | <0.001 | |
| Cancer | 16,871 (8.7) | 2,586 (7.8) | 0.032 | 16,633 (8.6) | 2,833 (8.6) | <0.001 | |
| Depression | 47,068 (24.3) | 8,563 (26.0) | 0.038 | 47,535 (24.6) | 8,100 (24.6) | <0.001 | |
| Abuse of substances or phychosis | 4,600 (2.4) | 841 (2.6) | 0.011 | 4,648 (2.4) | 793 (2.4) | <0.001 | |
| Diseases may cause dementia | 29,376 (15.2) | 5,078 (15.4) | 0.006 | 29,436 (15.2) | 5,016 (15.2) | <0.001 | |
| Cerebrovascular disease | 20,851 (10.8) | 3,298 (10.0) | 0.025 | 20,633 (10.7) | 3,515 (10.7) | <0.001 | |
| Inflammation, infection or injury in nervous system | 4,844 (2.5) | 803 (2.4) | 0.004 | 4,825 (2.5) | 822 (2.5) | <0.001 | |
| Antihypertensive drugs | 96,809 (50.0) | 15,836 (48.0) | 0.040 | 96,217 (49.7) | 16,398 (49.7) | <0.001 | |
| Anti-inflammatory drugs | 73,500 (38.0) | 10,316 (31.3) | 0.141 | 71,610 (37.0) | 12,202 (37.0) | <0.001 | |
| Statins | 33,751 (17.4) | 5,180 (15.7) | 0.047 | 33,262 (17.2) | 5,668 (17.2) | <0.001 | |
| Antidiabetic drugs | 22,115 (11.4) | 3,780 (11.5) | 0.001 | 22,124 (11.4) | 3,769 (11.4) | <0.001 | |
| Antidepressants | 17,521 (9.1) | 2,737 (8.3) | 0.027 | 17,310 (8.9) | 2,950 (8.9) | <0.001 | |
| Psycholeptics | 14,215 (7.3) | 2,237 (6.8) | 0.022 | 14,057 (7.3) | 2,394 (7.3) | <0.001 | |
| Corticosteroids | 10,726 (5.5) | 1,307 (4.0) | 0.074 | 10,279 (5.3) | 1,752 (5.3) | <0.001 | |
| Anticholinergics | 11,543 (6.0) | 1,876 (5.7) | 0.012 | 11,465 (5.9) | 1,954 (5.9) | <0.001 | |
| Clopidogrel | 4,076 (2.1) | 394 (1.2) | 0.072 | 3,807 (2.0) | 652 (2.0) | 0.001 | |

PPI, proton pump inhibitor; SD, standardized difference

Data are mean (standard deviation) or n (percentages)

† PPI indications included gastroesophageal reflux disease (GERD), *Helicobacter Pylori*-infection, peptic ulcer, esophagitis, Zollinger Ellison-syndrome, and heartburn.

**Supplemental Table S6. Comparison of baseline confounders for initiators of PPIs and H2RA initiators before/after weighting**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Unweighted population** | | | **Weighted population** | | | |
|
|  | **PPI initiators** | **H2RA initiators** | **SD** | **PPI initiators** | **H2RA initiators** | | **SD** |
| n | 660,635 | 9,457 | 660,635 | 9,457 | |
| Age (years) | 62.7 (13.2) | 64.0 (12.7) | 0.098 | 62.8 (13.2) | 62.8 (13.2) | <0.001 | |
| Women (n, %) | 363,039 (55.0) | 5,277 (55.8) | 0.017 | 363,102 (55.0) | 5,198 (55.0) | <0.001 | |
| German nationality (n, %) | 565,858 (85.7) | 7,827 (82.8) | 0.079 | 565,601 (85.6) | 8,096 (85.6) | <0.001 | |
| Hospitalizations in the year preceding cohort entry | 52,029 (7.9) | 540 (5.7) | 0.086 | 51,795 (7.8) | 742 (7.8) | <0.001 | |
| Obesity | 105,262 (15.9) | 1,515 (16.0) | 0.002 | 105,298 (15.9) | 1,507 (15.9) | <0.001 | |
| Diabetes | 149,733 (22.7) | 2,357 (24.9) | 0.053 | 149,942 (22.7) | 2,146 (22.7) | <0.001 | |
| Hypertension | 349,135 (52.8) | 5,170 (54.7) | 0.037 | 349,312 (52.9) | 5,000 (52.9) | <0.001 | |
| Heart disease | 149,184 (22.6) | 2,194 (23.2) | 0.015 | 149,266 (22.6) | 2,137 (22.6) | <0.001 | |
| Peripheral vascular disease | 73,624 (11.1) | 1,155 (12.2) | 0.033 | 73,735 (11.2) | 1,055 (11.2) | <0.001 | |
| Coagulopathy | 17,369 (2.6) | 209 (2.2) | 0.027 | 17,330 (2.6) | 248 (2.6) | <0.001 | |
| Chronic pulmonary disease | 131,886 (20.0) | 2,046 (21.6) | 0.041 | 132,031 (20.0) | 1,890 (20.0) | <0.001 | |
| Cancer | 63,978 (9.7) | 747 (7.9) | 0.063 | 63,795 (9.7) | 913 (9.7) | <0.001 | |
| Depression | 155,240 (23.5) | 2,387 (25.2) | 0.041 | 155,384 (23.5) | 2,225 (23.5) | <0.001 | |
| Abuse of substances or psychosis | 28,558 (4.3) | 354 (3.7) | 0.029 | 28,499 (4.3) | 409 (4.3) | <0.001 | |
| Diseases may cause dementia | 90,815 (13.7) | 1,246 (13.2) | 0.017 | 90,774 (13.7) | 1,299 (13.7) | <0.001 | |
| Cerebrovascular disease | 73,665 (11.2) | 1,096 (11.6) | 0.014 | 73,704 (11.2) | 1,055 (11.2) | <0.001 | |
| Inflammation, infection or injury in nervous system | 17,779 (2.7) | 229 (2.4) | 0.017 | 17,755 (2.7) | 254 (2.7) | <0.001 | |
| Antihypertensive drugs | 366,129 (55.4) | 5,796 (61.3) | 0.119 | 366,680 (55.5) | 5,249 (55.5) | <0.001 | |
| Anti-inflammatory drugs | 327,375 (49.6) | 4,389 (46.4) | 0.063 | 327,112 (49.5) | 4,683 (49.5) | <0.001 | |
| Statins | 133,901 (20.3) | 2,327 (24.6) | 0.104 | 134,268 (20.3) | 1,923 (20.3) | <0.001 | |
| Antidiabetic drugs | 90,777 (14.3) | 1,440 (15.2) | 0.044 | 90,473 (13.7) | 1,295 (13.7) | <0.001 | |
| Antidepressants | 66,789 (10.1) | 1,078 (11.4) | 0.042 | 66,901 (10.1) | 958 (10.1) | <0.001 | |
| Psycholeptics | 60,922 (9.2) | 1,032 (10.9) | 0.056 | 61,087 (9.2) | 874 (9.2) | <0.001 | |
| Corticosteroids | 55,983 (8.5) | 726 (7.7) | 0.029 | 55,903 (8.5) | 801 (8.5) | <0.001 | |
| Anticholinergics | 42,744 (6.5) | 772 (8.2) | 0.065 | 42,917 (6.5) | 614 (6.5) | <0.001 | |
| Clopidogrel | 20,527 (3.1) | 717 (7.6) | 0.200 | 20,920 (3.2) | 300 (3.2) | <0.001 | |

H2RA, histamine 2 receptor antagonist; PPI, proton pump inhibitor; SD, standardized difference

Data are mean (standard deviation) or n (percentages)

**Supplemental Figure S3. Modified classification of dementia subtypes for additional analyses**

Since we assigned the subtypes by the first validated ICD-10 code for dementia, we further investigated whether the individuals with unspecified dementia were also diagnosed with other subtypes later on and whether our findings were affected by differently classified subtypes.

(a) Unspecified dementia

**Unspecified**

(b) Alzheimer’s disease (AD) (c) Vascular dementia (VaD)

**Unspecified**

**VaD**

**VaD**

**Unspecified**

**AD**

**AD**

(d) Mixed dementia

**Unspecified**

**AD**

**VaD**

**Unspecified**

**VaD**

**AD**

**AD**

**VaD**

**VaD**

**AD**

(e) Delirium in dementia (f) Frontotemporal dementia

**Unspecified**

**Delirium**

**Delirium**

**Unspecified**

**FD**

**FD**

(g) Lewy-body dementia

**Unspecified**

**Lewy-body**

**Lewy-body**

AD, alzheimer’s disease; VaD, vascular dementia

**Supplemental Figure S4. Incidence of dementia subtypes in whole study population, 2009-2018, by (a) original classification, (b) modified classification**

(a) Subtype distribution by original classification

(b) Subtype distribution by modified classification

AD, alzheimer’s disease; FD, Frontotemporal dementia; VaD, vascular dementia

**Supplemental Table S7. Effect of PPI initiation and time-updated use of PPI on the risk of dementia subtypes**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Number of events in  initiators | Number of events in  non-initiators | Initiation effect | | Time-updated use effect† | |
|  | HR (95% CI) | *P* | HR (95% CI) | *P* |
| Unspecified dementia | 14,068 | 12,495 | 1.56 (1.51-1.61) | <2e-16 | 1.57 (1.49-1.66) | <2e-16 |
| AD | 6,559 | 6,459 | 1.55 (1.47-1.62) | <2e-16 | 1.37 (1.26-1.49) | <2e-16 |
| VaD | 6,816 | 5,739 | 1,55 (1.48-1.63) | <2e-16 | 1.76 (1.62-1.91) | <2e-16 |
| Mixed dementia | 1,667 | 1,536 | 1.59 (1.45-1.76) | <2e-16 | 1.38 (1.19-1.63) | 1.5e-4 |

AD, Alzheimer’s disease; CI , confidence interval; HR, hazard ratio; PPI, proton pump inhibitor; VaD, vascular dementia

hazard ratios(HRs) were adjusted for age, sex, German nationality, hospitalizations in the year preceding cohort entry, history of obesity, diabetes, hypertension, heart disease, peripheral vascular disease, coagulopathy, chronic pulmonary disease, cancer, depression, Abuse of substances or phychosis, underlying diseases directly causing dementia, cerebrovascular disease, inflammation, infection or injury in nervous system, use of antidiabetics, antihypertensives, statins, clopidogrel, anticholinergics, anti-inflammatory drugs, corticosteroids, antidepressants and psycholeptics

† Using weighted pooled logistic regression with adjustment for all covariates listed above and follow-up time (180 day-interval) and its square term.