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| **Supplementary Table 6. Characteristics of the Study Population According to Proton Pump Inhibitor and Histamine-2 Receptor Antagonist Use with an Index Date of 365 cDDD-days a** |
| Characteristics b | Full unweighted cohort | Propensity-score weighted cohort | Propensity score–matched cohort |
| Total(N=61,418) | PPI users(N=30,979) | H2RA users(N=30,439) | SMD | Total(N=39,696) | PPI users(N=20,084) | H2RA users(N=19.612) | SMD | Total(N=39,240) | PPI users(N=19,620) | H2RA users(N=19,620) | SMD |
| Sex |  |  |  | 0.1844 |  |  |  | 0.001 |  |  |  | -0.0018 |
|  | Male | 34200 (55.7) | 18651 (60.2) | 15549 (51.1) |  | 22010 (55.5) | 11141 (55.5) | 10869 (55.4) |  | 21928 (55.9) | 10955 (55.8) | 10973 (55.9) |  |
|  | Female | 27218 (44.3) | 12328 (39.8) | 14890 (48.9) |  | 17686 (44.6) | 8943 (44.5) | 8743 (44.6) |  | 17312 (44.1) | 8665 (44.2) | 8647 (44.1) |  |
| Age |  |  |  | -0.0959 |  |  |  | -0.0031 |  |  |  | 0.0049 |
|  | 40-49 | 2757 (4.5) | 1251 (4.0) | 1506 (5.0) |  | 1617 (4.1) | 821 (4.1) | 796 (4.1) |  | 1569 (4.0) | 791(4.0) | 778(4.0) |  |
|  | 50-59 | 18030 (29.4) | 9633 (31.1) | 8397 (27.6) |  | 11478 (28.9) | 5809 (28.9) | 5669 (28.9) |  | 11419 (29.1) | 5694(29.0) | 5725(29.2) |  |
|  | 60-69 | 21783 (35.5) | 11466 (37.0) | 10317 (33.9) |  | 14122 (35.6) | 7149 (35.6) | 6973 (35.6) |  | 13947 (35.5) | 6943(35.4) | 7004(35.7) |  |
|  | 70-79 | 14751 (24.0) | 6882 (22.2) | 7869 (25.9) |  | 9751 (24.6) | 4932 (24.6) | 4819 (24.6) |  | 9637 (24.6) | 4853(24.7) | 4784(24.4) |  |
|  | ≥80 | 4097 (24.0) | 1747 (5.7) | 2350 (7.7) |  | 2728 (6.9) | 1373 (6.8) | 1355 (6.9) |  | 2668 (6.8) | 1339(6.8) | 1329(6.8) |  |
| Calendar period |  |  |  | 0.195 |  |  |  | -0.0094 |  |  |  | -0.0162 |
|  | 2004-2006 | 46896 (76.4) | 22507 (72.7) | 24389 (80.12) |  | 30233 (76.2) | 15325 (76.3) | 14908 (76.0) |  | 29736 (75.8) | 14930 (76.1) | 14806 (75.5) |  |
|  | 2007-2009 | 10420 (17.0) | 5834 (18.8) | 4586 (15.07) |  | 6927 (17.5) | 3489 (17.4) | 3438 (17.5) |  | 6960 (17.7) | 3451 (17.6) | 3509 (17.9) |  |
|  | 2010-2012 | 3297 (5.4) | 2060 (6.7) | 1237 (4.06) |  | 2136 (5.4) | 1072 (5.3) | 1064 (5.4) |  | 2146 (5.5) | 1044 (5.3) | 1102 (5.6) |  |
|  | 2013-2015 | 805 (1.3) | 578 (1.9) | 227 (0.75) |  | 400 (1.0) | 198 (1.0) | 202 (1.0) |  | 398 (1.0) | 195 (1.0) | 203 (1.0) |  |
| Medication start to 365 cDDD (months) c |  |  |  | 0.3116 |  |  |  |  |  |  |  | -0.0427 |
|  | Median (IQR) | 92.1 (56.6, 122.3) | 98.7 (66.1, 126.7) | 84.05 (47.47, 116.91) |  | 95.9 (62.2, 124.5) | 96.4 (61.9, 124.8) | 95.3 (62.5, 124.2) | -0.0096 | 96.7 (63.2, 124.8) | 95.3 (62.4, 124.0) | 98.0 (64.0, 125.7) |  |
| Income |  |  |  | 0.0025 |  |  |  | 0.0009 |  |  |  | 0.0025 |
|  | 1-3 (low) | 16731 (28.0) | 8366 (27.8) | 8365 (28.25) |  | 11098 (28.0) | 5614(28.0) | 5484(28.0) |  | 10963 (27.9) | 5475(27.9) | 5488(28.0) |  |
|  | 4-7 (mid) | 18469 (31.0) | 9397 (31.3) | 9072 (30.64) |  | 12273 (30.9) | 6205(30.9) | 6068(30.9) |  | 12067 (30.8) | 6026(30.7) | 6041(30.8) |  |
|  | 8-10 (high) | 24470 (41.0) | 12295 (40.9) | 12175 (41.12) |  | 16325 (41.1) | 8265(41.2) | 8060(41.1) |  | 16210 (41.3) | 8119(41.4) | 8091(41.2) |  |
| BMI (kg/m2) |  |  |  | 0.033 |  |  |  | 0.001 |  |  |  | -0.002 |
|  | Mean (SD) | 24.1 (3.3) | 24.2 (3.3) | 24.08 (3.3) |  | 24.16 (2.7) | 24.15 (2.7) | 24.16 (2.7) |  | 24.15 (3.3) | 24.15 (3.2) | 24.15 (3.3) |  |
|  | Median (IQR) | 24 (21.9, 26.1) | 24 (22.0, 26.2) | 23.9 (21.8, 26.1) |  | 24 (22.0, 26.1) | 24 (21.9, 26.1) | 24 (22, 26.1) |  | 24 (22, 26.1) | 24 (22, 26.1) | 24 (22, 26.1) |  |
| Smoking |  |  |  | 0.147 |  |  |  | -0.001 |  |  |  | -0.003 |
|  | Never | 37101 (60.6) | 17430 (56.4) | 19671 (64.9) |  | 24167 (60.9) | 12227 (60.9) | 11940 (60.9) |  | 23741 (60.5) | 11884 (60.6) | 11857 (60.4) |  |
|  | Former | 11471 (18.7) | 6567 (21.3) | 4904 (16.2) |  | 7516 (18.9) | 3808 (19.0) | 3708 (18.9) |  | 7512 (19.1) | 3752 (19.1) | 3760 (19.2) |  |
|  | Current | 12653 (20.7) | 6902 (22.3) | 5751 (19.0) |  | 8013 (20.2) | 4049 (20.2) | 3964 (20.2) |  | 7987 (20.4) | 3984 (20.3) | 4003 (20.4) |  |
| Alcohol (times/week) |  |  |  | 0.123 |  |  |  | -0.003 |  |  |  | -0.010 |
|  | No  | 42157 (68.8) | 20341 (65.8) | 21816 (71.9) |  | 27203 (68.5) | 13771 (68.6) | 13432 (68.5) |  | 26823 (68.4) | 13455 (68.6) | 13368 (68.1) |  |
|  | 1-2  | 10542 (17.2) | 5832 (18.9) | 4710 (15.5) |  | 6945 (17.5) | 3515 (17.5) | 3430 (17.5) |  | 6943 (17.7) | 3455 (17.6) | 3488 (17.8) |  |
|  | ≥3  | 8537 (13.9) | 4734 (15.3) | 3803 (12.5) |  | 5548 (14.0) | 2798 (13.9) | 2750 (14.0) |  | 5474 (14.0) | 2710 (13.8) | 2764 (14.1) |  |
| GERD |  |  |  | 0.247 |  |  |  | -0.002 |  |  |  | -0.016 |
|  | Yes | 23290 (37.9) | 13575 (43.8) | 9715 (31.9) |  | 15134 (38.1) | 7646 (38.1) | 7488 (38.2) |  | 15104 (38.5) | 7474 (38.1) | 7630 (38.9) |  |
|  | No | 38128 (62.1) | 17404 (56.2) | 20724 (68.1) |  | 24562 (61.9) | 12438 (61.9) | 12124 (61.8) |  | 24136 (61.5) | 12146 (61.9) | 11990 (61.1) |  |
| Ulcer |  |  |  | 0.040 |  |  |  | 0.001 |  |  |  | 0.002 |
|  | Yes | 34792 (56.7) | 17853 (57.6) | 16939 (55.7) |  | 22135 (55.8) | 11202 (55.8) | 10933 (55.8) |  | 21991 (56.0) | 11006 (56.1) | 10985 (56.0) |  |
|  | No | 26626 (43.4) | 13126 (42.4) | 13500 (44.3) |  | 17561 (44.2) | 8882 (44.2) | 8679 (44.3) |  | 17249 (47.0) | 8614 (43.9) | 8635 (44.0) |  |
| Charlson Comorbidity Index |  |  |  | 0.072 |  |  |  | -0.001 |  |  |  | -0.002 |
|  | Mean (SD) | 2.78 (2.1) | 2.85 (2.1) | 2.7 (2.0) |  | 2.76 (1.7) | 2.76 (1.7) | 2.76 (1.7) |  | 2.8 (2.1) | 2.77 (2.1) | 2.77 (2.0) |  |
|  | Median (IQR) | 2 (1, 4) | 2 (1, 4) | 2 (1, 4) |  | 2 (1, 4) | 2 (1, 4) | 2 (1, 4) |  | 2 (1, 4) | 2 (1, 4) | 2 (1, 4) |  |
| *H. pylori* treatment |  |  |  | 0.304 |  |  |  | 0.004 |  |  |  | 0.007 |
|  | Yes | 13936 (22.7) | 8958 (28.9) | 4978 (16.4) |  | 8599 (21.7) | 4367 (21.7) | 4232 (21.6) |  | 8663 (22.1) | 4358 (22.2) | 4305 (21.9) |  |
|  | No | 47482 (77.3) | 22021 (71.1) | 25461 (83.6) |  | 31097 (78.3) | 15717 (78.3) | 15380 (78.4) |  | 30577 (77.9) | 15262 (77.8) | 15315 (78.1) |  |
| Number of EGD tests |  |  |  | 0.627 |  |  |  | 0.022 |  |  |  | 0.052 |
|  | Mean (SD) | 3.86 (3.3) | 4.84 (3.7) | 2.85 (2.6) |  | 3.53 (2.2) | 3.51 (2.3) | 3.55 (2.0) |  | 3.62 (2.8) | 3.69 (2.8) | 3.55 (2.8) |  |
|  | Median (IQR) | 3 (2, 5) | 4 (2, 7) | 2 (1, 4) |  | 3 (2, 5) | 3 (2, 5) | 3 (2, 5) |  | 3 (2, 5) | 3 (2, 5) | 3 (2, 5) |  |
| Use of Aspirin |  |  |  | -0.035 |  |  |  | 0 |  |  |  | 0.006 |
|  | Yes | 14204 (23.1) | 6935 (22.4) | 7269 (23.9) |  | 9327 (23.5) | 4719 (23.5) | 4608 (23.5) |  | 9191 (23.4) | 4621 (23.6) | 4570 (23.3) |  |
|  | No | 47214 (76.9) | 24044 (77.6) | 23170 (76.1) |  | 30369 (76.5) | 15365 (76.5) | 15004 (76.5) |  | 30049 (76.6) | 14999 (76.5) | 15050 (76.7) |  |
| Use of Metformin |  |  |  | 0.029 |  |  |  | -0.003 |  |  |  | 0.001 |
|  | Yes | 9764 (15.9) | 5089 (16.4) | 4675 (15.4) |  | 6382 (16.1) | 3218 (16.0) | 3164 (16.1) |  | 6344 (16.2) | 3174 (16.2) | 3170 (16.2) |  |
|  | No | 51654 (84.1) | 25890 (83.6) | 25764 (84.6) |  | 33314 (83.9) | 16866 (84.0) | 16448 (83.9) |  | 32896 (83.8) | 16446 (83.8) | 16450 (83.8) |  |
| Use of Statin |  |  |  | 0.160 |  |  |  | -0.002 |  |  |  | -0.017 |
|  | Yes | 19927 (32.4) | 11194 (36.1) | 8733 (29.0) |  | 13307 (33.5) | 6726 (33.5) | 6581 (33.6) |  | 13253 (33.8) | 6548 (33.4) | 6705 (34.2) |  |
|  | No | 41491 (67.6) | 19785 (63.9) | 21706 (71.3) |  | 26389 (66.5) | 13358 (66.5) | 13031 (66.4) |  | 25987 (66.2) | 13072 (66.6) | 12915 (65.8) |  |
| BMI, body mass index; EGD, esophagogastroduodenoscopy; GERD, gastroesophageal reflux disease; *H. pylori*, *Helicobacter pylori*; IQR, interquartile range; SMD, Standardized mean difference; SD, standard deviationa PPI long-term use was defined as only PPI use, PPI ≥ 365 cDDD-days, and combined use, PPI ≥ 365 cDDD-days and H2RA < 365 cDDD-days or PPI ≥ 365 cDDD-days and H2RA ≥ 365 cDDD-days. H2RA long-term use was defined as only H2RA use, H2RA ≥365 cDDD-days, and combined use of H2RA ≥ 365 cDDD-days and PPI < 365 cDDD-days.b Baseline characteristics of the patients are presented in eTable 1.  |