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| **Supplementary Table 3. Characteristics of the Pooled Study Population According to Proton Pump Inhibitor and Histamine-2 Receptor Antagonist Use (cDDD ≥ 180 days) a** |
| Characteristics | Full unweighted cohort | Propensity-score weighted cohort | Propensity score–matched cohort |
| Total(N=122118) | PPI users(N=66797) | H2RA users(N=55321) | SMD | Total(N=78766) | PPI users(N=39799) | H2RA users(N=38,967) | SMD | Total(N=77024) | PPI users(N=38512) | H2RA users(N=38512) | SMD |
| Sex |  |  |  | 0.2265 |  |  |  | -0.0002 |  |  |  | -0.0147 |
|  | Male | 66849 (54.7) | 39958 (59.8) | 26891 (48.6) |  | 42080 (53.4) | 21260 (53.4) | 20820 (53.4) |  | 41447 (53.81) | 20582 (53.4) | 20865 (54.2) |  |
|  | Female | 55269 (45.3) | 26839 (40.2) | 28430 (51.4) |  | 36686 (46.6) | 18539 (46.6) | 18147 (46.6) |  | 35577 (46.19) | 17930 (46.6) | 17647 (45.8) |  |
| Age (years) |  |  |  | -0.0674 |  |  |  | 0.0031 |  |  |  | 0.0064 |
|  | 40-49 | 8622 (7.1) | 4540 (6.8) | 4082 (7.4) |  | 5275 (6.7) | 2662 (6.7) | 2613 (6.7) |  | 5097 (6.62) | 2583 (6.7) | 2514 (6.5) |  |
|  | 50-59 | 42646 (34.9) | 24057 (36.0) | 18589 (33.6) |  | 27285 (34.6) | 13754 (34.6) | 13531 (34.7) |  | 26782 (34.77) | 13321 (34.6) | 13461 (35.0) |  |
|  | 60-69 | 41467 (34.0) | 23368 (35.0) | 18099 (32.7) |  | 26694 (33.9) | 13506 (33.9) | 13188 (33.8) |  | 26145 (33.94) | 13009 (33.8) | 13136 (34.1) |  |
|  | 70-79 | 23619 (19.3) | 12078 (18.1) | 11541 (20.9) |  | 15659 (19.9) | 7939 (20.0) | 7720 (19.8) |  | 15253 (19.80) | 7705 (20.0) | 7548 (19.6) |  |
|  | ≥80 | 5764 (4.7) | 2754 (4.1) | 3010 (5.4) |  | 3853 (4.9) | 1938 (4.9) | 1915 (4.9) |  | 3747 (4.86) | 1894 (4.9) | 1853 (4.8) |  |
| Calendar period |  |  |  | 0.2304 |  |  |  | -0.0099 |  |  |  | -0.0181 |
|  | 2004-2006 | 91302 (74.8) | 47174 (70.6) | 44128 (79.8) |  | 59708 (75.8) | 30230 (76.0) | 29478 (75.7) |  | 58140 (75.48) | 29251 (76.0) | 28889 (75.0) |  |
|  | 2007-2009 | 21634 (17.7) | 13245 (19.8) | 8389 (15.2) |  | 13958 (17.7) | 7023 (17.7) | 6935 (17.8) |  | 13805 (17.92) | 6775 (17.6) | 7030 (18.3) |  |
|  | 2010-2012 | 7179 (5.9) | 4850 (7.3) | 2329 (4.2) |  | 4215 (5.4) | 2107 (5.3) | 2108 (5.4) |  | 4157 (5.40) | 2011 (5.2) | 2146 (5.6) |  |
|  | 2013-2015 | 2003 (1.6) | 1528 (2.3) | 475 (0.9) |  | 885 (1.1) | 439 (1.1) | 446 (1.1) |  | 922 (1.20) | 475 (1.2) | 447 (1.2) |  |
| Medication start to 180 cDDD (months) b |  |  |  | 0.1826 |  |  |  | -0.0012 |  |  |  | -0.0253 |
|  | Median (IQR) | 83.9 (46.6, 116.8) | 87.5 (52.6, 119.4) | 78.6 (39.2, 113.3) |  | 86.4 (49.9, 118.4) | 85.7 (50.7, 118.3) | 87.11 (49.1, 118.5) |  | 86.97 (50.9, 118.8) | 85.7 (50.8, 118.4) | 88.3 (51.1, 119.2) |  |
| Income |  |  |  | 0.0011 |  |  |  | 0.0018 |  |  |  | 0.0024 |
|  | 1-3 (low) | 32457 (27.1) | 17706 (27.1) | 14751 (27.2) |  | 21370 (27.1) | 10790 (27.1) | 10580 (27.2) |  | 20857 (27.1) | 10422 (27.1) | 10435 (27.1) |  |
|  | 4-7 (mid) | 37309 (31.2) | 20369 (31.2) | 16940 (31.2) |  | 24418 (31.0) | 12330 (31.0) | 12088 (31.0) |  | 23852 (31.0) | 11902 (30.9) | 11950 (31.0) |  |
|  | 8-10 (high) | 49864 (41.7) | 27236 (41.7) | 22628 (41.7) |  | 32978 (41.9) | 16679 (41.9) | 16299 (41.8) |  | 32315 (41.9) | 16188 (42.0) | 16127 (41.9) |  |
| BMI (kg/m2) |  |  |  | 0.0198 |  |  |  | 0.0012 |  |  |  | 0.0016 |
|  | Mean (SD) | 24.08 (3.2) | 24.11 (3.2) | 24.1 (3.2) |  | 24.10 (2.6) | 24.1 (2.5) | 24.10 (2.7) |  | 24.1 (3.2) | 24.1 (3.2) | 24.1 (3.2) |  |
|  | Median (IQR) | 23.9 (21.9, 26.0) | 24.0 (22.0, 26.1) | 23.9 (21.9, 26.0) |  | 24.0 (22.0, 26.0) | 24.0 (22.0, 26.0) | 24.0 (22, 3) |  | 24 (22, 26) | 24 (22, 26) | 24 (22, 26) |  |
| Smoking |  |  |  | 0.1851 |  |  |  | -0.0012 |  |  |  | -0.0086 |
|  | Never  | 74786 (61.4) | 37923 (56.9) | 36863 (66.8) |  | 49339 (62.6) | 24929 (62.6) | 24410 (62.6) |  | 48025 (62.4) | 24103 (62.6) | 23922 (62.1) |  |
|  | Former | 22201 (18.2) | 13665 (20.5) | 8536 (15.5) |  | 14131 (17.9) | 7158 (18.0) | 6973 (17.9) |  | 13929 (18.1) | 6915 (18.0) | 7014 (18.2) |  |
|  | Current | 24822 (20.4) | 15058 (22.6) | 9764 (17.7) |  | 15297 (19.4) | 7713 (19.4) | 7584 (19.5) |  | 15070 (19.6) | 7494 (19.5) | 7576 (19.7) |  |
| Alcohol |  |  |  | 0.1333 |  |  |  | -0.0026 |  |  |  | -0.0106 |
|  | None | 80879 (66.4) | 42323 (63.5) | 38556 (69.9) |  | 52593 (66.8) | 26584 (66.8) | 26009 (66.8) |  | 51229 (66.5) | 25698 (66.7) | 25531 (66.3) |  |
|  | 1-2 times/week | 23097 (19.0) | 13550 (20.3) | 9547 (17.3) |  | 14921 (18.9) | 7550 (19.0) | 7371 (18.9) |  | 14724 (19.1) | 7344 (19.1) | 7380 (19.2) |  |
|  | ≥3 times/week | 17843 (14.7) | 10781 (16.2) | 7062 (12.8) |  | 11252 (14.3) | 5665 (14.2) | 5587 (14.3) |  | 11071 (14.4) | 5470 (14.2) | 5601 (14.5) |  |
| GERD |  |  |  | 0.2774 |  |  |  | -0.0044 |  |  |  | -0.0214 |
|  | Yes | 45457 (37.2) | 28870 (43.2) | 16587 (30.0) |  | 28383 (36.0) | 14301 (35.9) | 14082 (36.1) |  | 28096 (36.5) | 13850 (36.0) | 14246 (37.0) |  |
|  | No | 76661 (62.8) | 37927 (56.8) | 38734 (70.0) |  | 50383 (64.0) | 25498 (64.1) | 24885 (63.9) |  | 48928 (63.5) | 24662 (64.0) | 24266 (63.0) |  |
| Ulcer |  |  |  | 0.091 |  |  |  | -0.001 |  |  |  | -0.0025 |
|  | Yes | 67927 (55.6) | 38522 (57.7) | 29405 (53.2) |  | 42874 (54.4) | 21654 (54.4) | 21220 (54.5) |  | 42070 (54.6) | 21011 (54.6) | 21059 (54.7) |  |
|  | No | 54191 (44.4) | 28275 (42.3) | 25916 (46.9) |  | 35892 (45.6) | 18145 (45.6) | 17747 (45.5) |  | 34954 (45.4) | 17501 (45.4) | 17453 (45.3) |  |
| Charlson Comorbidity Index |  |  |  | 0.1186 |  |  |  | -0.0005 |  |  |  | -0.0033 |
|  | Mean (SD) | 2.42 (1.9) | 2.53 (2.0) | 2.3 (1.9) |  | 2.4 (1.6) | 2.4 (1.5) | 2.38 (1.6) |  | 2.4 (1.9) | 2.4 (1.9) | 2.4 (1.9) |  |
|  | Median (IQR) | 2 (1, 3) | 2 (1, 3) | 2 (1, 3) |  | 2 (1, 3) | 2 (1, 3) | 2 (1, 3) |  | 2 (1, 3) | 2 (1, 3) | 2 (1, 3) |  |
| *H. pylori* treatment |  |  |  | 0.361 |  |  |  | 0.0025 |  |  |  | 0.0078 |
|  | Yes | 28095 (23.0) | 19843 (29.7) | 8252 (14.9) |  | 15637 (19.9) | 7922 (19.9) | 7715 (19.8) |  | 15717 (20.4) | 7919 (20.6) | 7798 (20.2) |  |
|  | No | 94023 (77.0) | 46954 (70.3) | 47069 (85.1) |  | 63129 (80.15) | 31877 (80.1) | 31252 (80.2) |  | 61307 (79.6) | 30593 (79.4) | 30714 (79.8) |  |
| No. of EGD tested |  |  |  | 0.6376 |  |  |  | 0.0238 |  |  |  | 0.0373 |
|  | Mean (SD) | 3.2 (2.7) | 4.0 (2.9) | 2.34 (2.10) |  | 2.8 (1.7) | 2.8 (1.6) | 2.8 (1.9) |  | 2.9 (2.21) | 2.9 (2.2) | 2.9 (2.2) |  |
|  | Median (IQR) | 3 (1, 4) | 3 (2, 5) | 2 (1, 3) |  | 2 (1, 4) | 2 (1, 4) | 2 (1, 4) |  | 2 (1, 4) | 2 (1, 4) | 2 (1, 4) |  |
| Aspirin |  |  |  | 0.0124 |  |  |  | 0.0005 |  |  |  | 0.0011 |
|  | User  | 22751 (18.6) | 12590 (18.9) | 10161 (18.4) |  | 14925 (19.0) | 7545 (19.0) | 7380 (18.9) |  | 14610 (19.0) | 7313 (19.0) | 7297 (18.95) |  |
|  | Non-user | 99367 (81.4) | 54207 (81.2) | 45160 (81.6) |  | 63841 (81.0) | 32254 (81.0) | 31587 (81.1) |  | 62414 (81.0) | 31199 (81.0) | 31215 (81.05) |  |
| Metformin |  |  |  | 0.0447 |  |  |  | -0.0012 |  |  |  | -0.0082 |
|  | User  | 15122 (12.4) | 8716 (13.1) | 6406 (11.6) |  | 9737 (12.4) | 4912 (12.3) | 4825 (12.4) |  | 9570 (12.4) | 4733 (12.3) | 4837 (12.56) |  |
|  | Non-user | 106996 (87.6) | 58081 (86.9) | 48915 (88.4) |  | 69029 (87.6) | 34887 (87.7) | 34142 (87.6) |  | 67454 (87.6) | 33779 (87.7) | 33675 (87.44) |  |
| Statin |  |  |  | 0.1356 |  |  |  | 0.0009 |  |  |  | -0.0107 |
|  | User  | 29670 (24.3) | 17978 (26.9) | 11692 (21.1) |  | 19253 (24.4) | 9736 (24.5) | 9517 (24.4) |  | 19068 (24.8) | 9445 (24.5) | 9623 (24.99) |  |
|  | Non-user | 92448 (75.7) | 48819 (73.1) | 43629 (78.9) |   | 59513 (75.6) | 30063 (75.5) | 29450 (75.6) |  | 57956 (75.2) | 29067 (75.5) | 28889 (75.01) |  |
| BMI, body mass index; cDDD, cumulative defined daily dose; 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 ≥ 180 cDDD-days, and combined use, PPI ≥ 180 cDDD-days and H2RA < 180 cDDD-days or PPI ≥ 180 cDDD-days and H2RA ≥ 180 cDDD-days. H2RA long-term use was defined as only H2RA use, H2RA ≥180 cDDD-days, and combined use of H2RA ≥ 180 cDDD-days and PPI < 180 cDDD-days.b Baseline characteristics of the patients are presented in eTable 1.  |