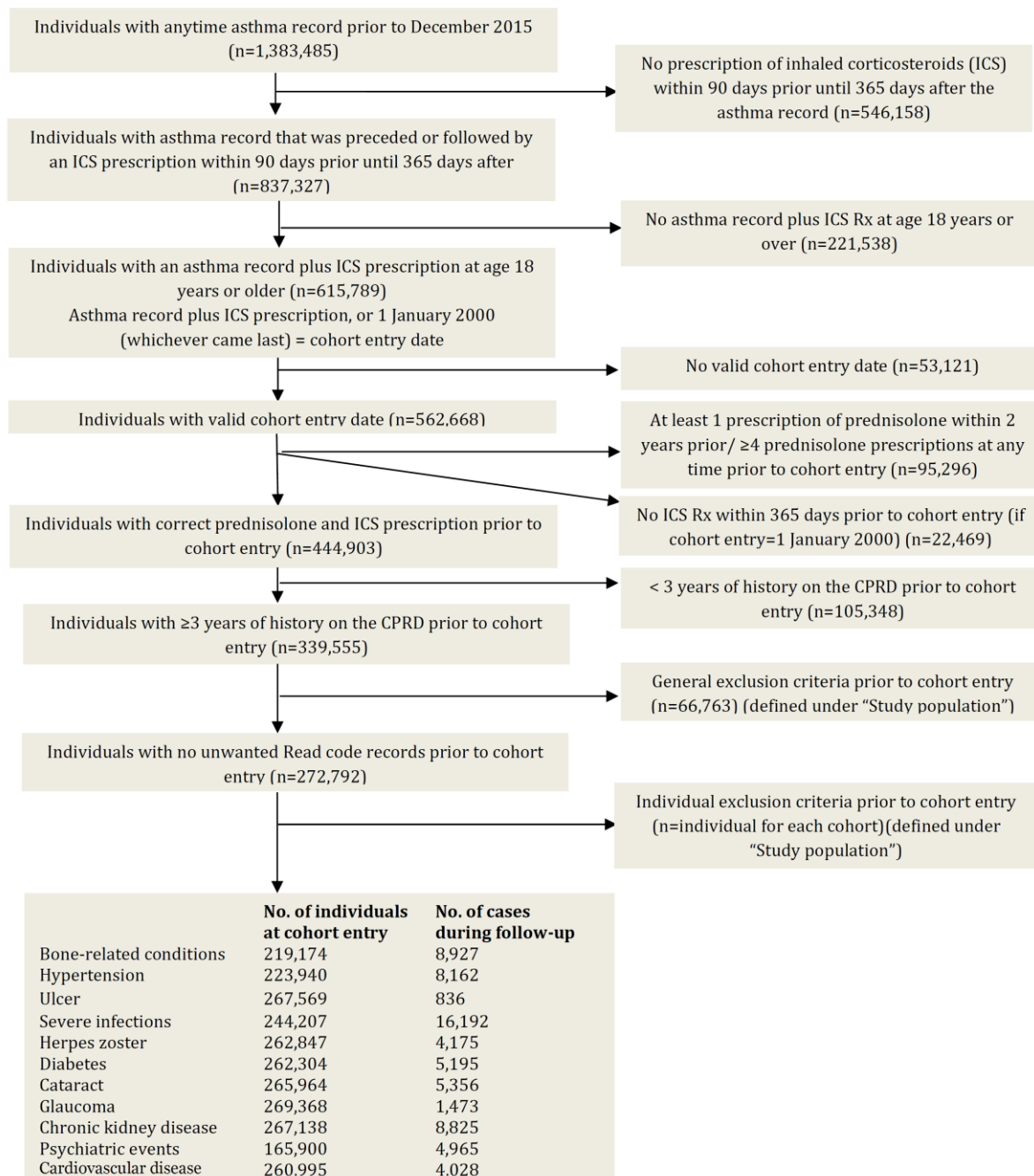


## Additional file 2

### Flowchart study population:



**Detailed information on characteristics and co-medication of cases and controls for each outcome at the index date:**

Characteristics and co-medication of cases with **bone-related conditions** and matched controls at the index date

	<b>No. of Cases (%) (N=8,907)</b>	<b>No. of Controls (%) (N=35,445)</b>	<b>Crude OR</b>	<b>95% CI</b>
Male	2,752 (30.9)	10,956 (30.9)	NA	NA
Female	6,155 (69.1)	24,489 (69.1)	NA	NA
<b>Age</b>				
18-39	2,321 (26.1)	9,263 (26.1)	NA	NA
40-59	2,713 (30.5)	10,858 (30.6)	NA	NA
60-79	2,947 (33.1)	11,781 (33.2)	NA	NA
≥80	926 (10.4)	3,543 (10.0)	NA	NA
<b>Smoking status</b>				
non	4,495 (50.5)	18,672 (52.7)	1.00	reference
current	1,438 (16.1)	5,020 (14.2)	1.20	1.12-1.29
ex	2,767 (31.1)	10,935 (30.9)	1.05	0.99-1.10
unknown	207 (2.3)	818 (2.3)	1.06	0.90-1.25
<b>Alcohol consumption (average units per week)</b>				
none	4,231 (47.5)	16,714 (47.2)	1.00	reference
<14	2,786 (31.3)	11,351 (32.0)	0.98	0.92-1.03
≥14	862 (9.7)	3,150 (8.9)	1.09	1.00-1.19
unknown	1,028 (11.5)	4,230 (11.9)	0.96	0.88-1.04
<b>Body mass index, kg/m<sup>2</sup></b>				
<18.5	197 (2.2)	612 (1.7)	1.17	0.99-1.38
18.5-24.9	3,006 (33.8)	10,850 (30.6)	1.00	reference
25-29.9	2,633 (29.6)	10,971 (31.0)	0.86	0.81-0.91
≥30	2,138 (24.0)	9,327 (26.3)	0.82	0.77-0.87
unknown	933 (10.5)	3,685 (10.4)	0.93	0.85-1.02
<b>Concomitant<sup>a</sup> drug use</b>				
SABA	7,646 (85.8)	29,977 (84.6)	1.10	0.92-1.32
SAMA	331 (3.7)	1,154 (3.3)	1.17	1.03-1.32
ICS (mono preparations)	6,353 (71.3)	25,892 (73.1)	0.96	0.86-1.08
ICS+LABA	3,048 (34.2)	11,350 (32.0)	1.13	1.07-1.20
Asthma add-on therapy <sup>b</sup>	420 (4.7)	1,511 (4.3)	1.13	1.01-1.26
Platelet aggregation inhibitors	1,226 (13.8)	4,343 (12.3)	1.18	1.09-1.27
Anticoagulants	862 (2.4)	239 (2.7)	1.10	0.95-1.27
Proton pump inhibitors	2,042 (22.9)	6,769 (19.1)	1.34	1.26-1.43
Immunosuppressants <sup>c</sup>	25 (0.3)	69 (0.2)	1.45	0.92-2.30
Bisphosphonates	231 (2.6)	287 (0.8)	3.30	2.76-3.94
Vitamin D	468 (5.3)	1,030 (2.9)	1.90	1.69-2.13
<b>Charlson Comorbidity Index</b>				
Median (25% perc./75% perc./range)	1 (1/1/8)	1 (1/1/10)	NA	NA
<b>Charlson Comorbidity Index (categories)</b>				
0	161 (1.8)	745 (2.1)	1.00	reference
1-3	8,369 (94.0)	33,443 (94.4)	1.18	1.01-1.37
4-6	349 (3.9)	1,185 (3.3)	1.38	1.14-1.67
7-10	28 (0.3)	72 (0.2)	1.80	1.18-2.74
<b>Number of prescriptions ICS prior</b>				
Median (25% perc./75% perc./range)	30 (12/58/383)	29 (12/56/361)	NA	NA

Characteristics and co-medication of cases with **hypertension** and matched controls at the index date

	No. of Cases (%) (N=8,148)	No. of Controls (%) (N=32,431)	Crude OR	95% CI
Male	3,469 (42.6)	13,790 (42.5)	NA	NA
Female	4,679 (57.4)	18,641 (57.5)	NA	NA
<b>Age</b>				
18-39	533 (6.5)	2,138 (6.6)	NA	NA
40-59	3,607 (44.3)	14,400 (44.4)	NA	NA
60-79	3,582 (44.0)	14,316 (44.1)	NA	NA
≥80	426 (5.2)	1,577 (4.9)	NA	NA
<b>Smoking status</b>				
non	3,966 (48.7)	16,377 (50.5)	1	reference
current	994 (12.2)	4,265 (13.1)	0.96	0.89-1.04
ex	3,015 (37.0)	10,923 (33.7)	1.15	1.08-1.21
unknown	173 (2.1)	866 (2.7)	0.81	0.68-0.96
<b>Alcohol consumption (average units per week)</b>				
none	3,766 (46.2)	13,661 (42.1)	1	reference
<14	2,750 (33.8)	11,578 (35.7)	0.86	0.82-0.91
≥14	1,171 (14.4)	4,026 (12.4)	1.06	0.98-1.14
unknown	461 (5.7)	3,166 (9.8)	0.53	0.47-0.58
<b>Body mass index, kg/m<sup>2</sup></b>				
<18.5	51 (0.6)	360 (1.1)	0.87	0.65-1.17
18.5-24.9	1,754 (21.5)	10,967 (33.8)	1	reference
25-29.9	2,844 (34.9)	11,424 (35.2)	1.57	1.47-1.68
≥30	2,970 (36.5)	6,635 (20.5)	2.92	2.72-3.12
unknown	529 (6.5)	3,045 (9.4)	1.05	0.95-1.17
<b>Concomitant<sup>a</sup> drug use</b>				
SABA	6,832 (83.9)	26,526 (81.8)	1.18	1.00-0.39
SAMA	312 (3.8)	1,181 (3.6)	1.06	0.93-1.21
ICS (mono preparations)	6,140 (75.4)	24,504 (75.6)	1.08	0.95-1.23
ICS+LABA	2,469 (30.3)	9,604 (29.6)	1.04	0.98-1.11
Asthma add-on therapy <sup>b</sup>	346 (4.3)	1,304 (4.0)	1.06	0.94-1.20
Platelet aggregation inhibitors	723 (8.9)	2,297 (7.1)	1.31	1.19-1.43
Anticoagulants	110 (1.4)	474 (1.5)	0.91	0.74-1.13
Proton pump inhibitors	1,714 (21.0)	5,681 (17.5)	1.27	1.20-1.36
Immunosuppressants <sup>c</sup>	15 (0.2)	80 (0.3)	0.74	0.43-1.29
Bisphosphonates	188 (2.3)	911 (2.8)	0.80	0.68-0.94
Vitamin D	287 (3.5)	1,168 (3.6)	0.96	0.84-1.10
<b>Charlson Comorbidity Index</b>				
Median (25% perc./75% perc./range)	1 (1/1/8)	1 (1/1/7)	NA	NA
<b>Charlson Comorbidity Index (categories)</b>				
0	219 (2.7)	844 (2.6)	1.00	reference
1-3	7,794 (95.7)	31,216 (96.3)	0.97	0.85-1.11
4-6	131 (1.6)	367 (1.1)	1.39	1.10-1.74
7-8	X	X	NA	NA

Characteristics and co-medication of cases with **peptic or esophageal ulcer** and matched controls at the index date

	No. of Cases (%) (N=835)	No. of Controls (%) (N=3,328)	Crude OR	95% CI
Male	332 (39.8)	1,316 (39.5)	NA	NA
Female	503 (60.2)	2,012 (60.5)	NA	NA
<b>Age</b>				
18-39	87 (10.4)	343 (10.3)	NA	NA
40-59	239 (28.6)	966 (29.0)	NA	NA
60-79	359 (43.0)	1,435 (43.1)	NA	NA
≥80	150 (18.0)	584 (17.6)	NA	NA
<b>Smoking status</b>				
non	363 (43.5)	1,616 (48.6)	1.00	reference
current	141 (16.9)	379 (11.4)	1.70	1.35-2.13
ex	316 (37.8)	1,264 (38.0)	1.11	0.93-1.32
unknown	15 (1.8)	69 (2.1)	0.95	0.53-1.70
<b>Alcohol consumption (average units per week)</b>				
none	440 (52.7)	1,537 (46.2)	1.00	reference
<14	246 (29.5)	1,163 (35.0)	0.73	0.62-0.87
≥14	97 (11.6)	350 (10.5)	0.96	0.74-1.25
unknown	52 (6.2)	278 (8.4)	0.64	0.47-0.88
<b>Body mass index, kg/m<sup>2</sup></b>				
<18.5	17 (2.0)	37 (1.1)	1.98	1.09-3.58
18.5-24.9	242 (29.0)	1,032 (31.0)	1.00	reference
25-29.9	294 (35.2)	1,120 (33.7)	1.13	0.93-1.37
≥30	230 (27.5)	863 (25.9)	1.16	0.94-1.42
unknown	52 (6.2)	276 (8.3)	0.79	0.57-1.10
<b>Concomitant<sup>a</sup> drug use</b>				
SABA	691 (82.8)	2,755 (82.8)	0.94	0.59-1.49
SAMA	50 (6.0)	185 (5.6)	1.10	0.79-1.53
ICS (mono preparations)	604 (72.3)	2,522 (75.8)	1.00	0.67-1.51
ICS+LABA	283 (33.9)	993 (29.8)	1.26	1.06-1.51
Asthma add-on therapy <sup>b</sup>	47 (5.6)	106 (3.2)	1.83	1.29-2.61
Platelet aggregation inhibitors	245 (29.3)	641 (19.3)	2.05	1.69-2.50
Anticoagulants	57 (6.8)	123 (3.7)	1.96	1.41-2.73
Proton pump inhibitors	388 (46.5)	708 (21.3)	3.93	3.29-4.70
Immunosuppressants <sup>c</sup>	X	7 (0.2)	NA	NA
Bisphosphonates	51 (6.1)	125 (3.8)	1.74	1.23-2.46
Vitamin D	71 (8.5)	175 (5.3)	1.78	1.32-2.41
<b>Charlson Comorbidity Index</b>				
Median (25% perc./75% perc./range)	1 (1/2/12)	1 (1/1/9)	NA	NA
<b>Charlson Comorbidity Index (categories)</b>				
0	16 (1.9)	77 (2.3)	1.00	reference
1-3	743 (89.0)	3,072 (92.3)	1.20	0.71-2.03
4-6	71 (8.5)	169 (5.1)	2.14	1.19-3.84
7-12	5 (0.6)	10 (0.3)	2.54	0.93-6.99
<b>Number of prescriptions ICS prior</b>				
Median (25% perc./75% perc./range)	35 (15/66/312)	33 (14/64/281)	NA	NA

Characteristics and co-medication of cases with **severe infections** and matched controls at the index date

	No. of Cases (%) (N=16,160)	No. of Controls (%) (N=64,316)	Crude OR	95% CI
Male	5,223 (32.3)	20,709 (32.2)	NA	NA
Female	10,937 (67.7)	43,607 (67.8)	NA	NA
<b>Age</b>				
18-39	4,976 (30.8)	19,901 (30.9)	NA	NA
40-59	5,084 (31.5)	20,337 (31.6)	NA	NA
60-79	4,629 (28.6)	18,499 (28.8)	NA	NA
≥80	1,471 (9.1)	5,579 (8.7)	NA	NA
<b>Smoking status</b>				
non	7,457 (46.1)	33,128 (51.1)	1.00	reference
current	2,981 (18.5)	9,512 (14.8)	1.41	1.34-1.48
ex	5,479 (33.9)	20,441 (31.8)	1.19	1.14-1.24
unknown	243 (1.5)	1,235 (1.9)	0.86	0.74-0.99
<b>Alcohol consumption (average units per week)</b>				
none	8,050 (49.8)	29,212 (45.4)	1.00	reference
<14	5,012 (31.0)	21,137 (32.9)	0.86	0.82-0.89
≥14	1,450 (9.0)	6,400 (10.0)	0.81	0.76-0.86
unknown	1,648 (10.2)	7,567 (11.8)	0.77	0.73-0.82
<b>Body mass index, kg/m<sup>2</sup></b>				
<18.5	345 (2.1)	1,115 (1.7)	1.33	1.18-1.51
18.5-24.9	4,730 (29.3)	20,861 (32.4)	1.00	reference
25-29.9	4,883 (30.2)	19,793 (30.8)	1.10	1.05-1.15
≥30	4,964 (30.7)	16,182 (25.2)	1.38	1.32-1.45
unknown	1,238 (7.7)	6,365 (9.9)	0.82	0.76-0.88
<b>Concomitant<sup>a</sup> drug use</b>				
SABA	14,133 (87.5)	54,432 (84.6)	1.37	1.19-1.58
SAMA	694 (4.3)	1,598 (2.5)	1.84	1.68-2.02
ICS (mono preparations)	11,211 (69.4)	46,924 (73.0)	0.90	0.83-0.97
ICS+LABA	6,145 (38.0)	20,649 (32.1)	1.38	1.33-1.44
Asthma add-on therapy <sup>b</sup>	942 (5.8)	2,509 (3.9)	1.56	1.45-1.69
Platelet aggregation inhibitors	2,570 (15.9)	6,938 (10.8)	1.84	1.74-1.94
Anticoagulants	632 (3.9)	1,299 (2.0)	2.04	1.85-2.26
Proton pump inhibitors	4,458 (27.6)	11,064 (17.2)	2.13	2.03-2.22
Immunosuppressants <sup>c</sup>	61 (0.4)	84 (0.1)	2.95	2.12-4.11
Bisphosphonates	592 (3.7)	1,545 (2.4)	1.62	1.46-1.79
Vitamin D	974 (6.0)	2,469 (3.8)	1.71	1.58-1.86
<b>Charlson Comorbidity Index</b>				
Median (25% perc./75% perc./range)	1 (1/1/9)	1 (1/1/9)	NA	NA
<b>Charlson Comorbidity Index (categories)</b>				
0	334 (2.1)	1,469 (2.3)	1.00	reference
1-3	14,927 (92.4)	60,848 (94.6)	1.09	0.98-1.22
4-6	839 (5.2)	1,921 (3.0)	2.01	1.77-2.30
7-9	60 (0.4)	78 (0.1)	3.62	2.65-4.94
<b>Number of prescriptions ICS prior</b>				
Median (25% perc./75% perc./range)	26 (10/54/335)	25 (10/51/528)	NA	NA

Characteristics and co-medication of cases with **herpes zoster** and matched controls at the index date

	No. of Cases (%) (N=4,163)	No. of Controls (%) (N=16,605)	Crude OR	95% CI
Male	1,414 (34.0)	5,621 (33.9)	NA	NA
Female	2,749 (66.0)	10,984 (66.2)	NA	NA
<b>Age</b>				
18-39	729 (17.5)	2,923 (17.6)	NA	NA
40-59	1,353 (32.5)	5,402 (32.5)	NA	NA
60-79	1,717 (41.2)	6,884 (41.5)	NA	NA
≥80	364 (8.7)	1,396 (8.4)	NA	NA
<b>Smoking status</b>				
non	2,118 (50.9)	8,403 (50.6)	1.00	reference
current	525 (12.6)	2,234 (13.5)	0.93	0.83-1.03
ex	1,466 (35.2)	5,624 (33.9)	1.04	0.96-1.12
unknown	54 (1.3)	344 (2.1)	0.60	0.44-0.81
<b>Alcohol consumption (average units per week)</b>				
none	1,931 (46.4)	7,996 (48.2)	1.00	reference
<14	1,410 (33.9)	5,388 (32.5)	1.09	1.01-1.17
≥14	445 (10.7)	1,654 (10.0)	1.13	1.00-1.27
unknown	377 (9.1)	1,567 (9.4)	1.00	0.88-1.14
<b>Body mass index, kg/m<sup>2</sup></b>				
<18.5	63 (1.5)	203 (1.2)	1.21	0.90-1.61
18.5-24.9	1,304 (31.3)	5,060 (30.5)	1.00	reference
25-29.9	1,339 (32.2)	5,377 (32.4)	0.97	0.88-1.05
≥30	1,130 (27.1)	4,528 (27.3)	0.97	0.88-1.06
unknown	327 (7.9)	1,437 (8.7)	0.87	0.76-1.01
<b>Concomitant<sup>a</sup> drug use</b>				
SABA	3,452 (82.9)	13,901 (83.7)	0.88	0.70-1.11
SAMA	156 (3.8)	620 (3.7)	1.01	0.84-1.22
ICS (mono preparations)	3,004 (72.2)	12,224 (73.6)	0.99	0.85-1.17
ICS+LABA	1,416 (34.0)	5,250 (31.6)	1.15	1.07-1.25
Asthma add-on therapy <sup>b</sup>	215 (5.2)	703 (4.2)	1.24	1.06-1.46
Platelet aggregation inhibitors	650 (15.6)	2,337 (14.1)	1.16	1.05-1.29
Anticoagulants	149 (3.6)	491 (3.0)	1.22	1.01-1.48
Proton pump inhibitors	1,050 (25.2)	3,517 (21.2)	1.32	1.21-1.44
Immunosuppressants <sup>c</sup>	17 (0.4)	37 (0.2)	1.84	1.04-3.26
Bisphosphonates	151 (3.6)	542 (3.3)	1.13	0.93-1.36
Vitamin D	210 (5.0)	840 (5.1)	0.99	0.85-1.17
<b>Charlson Comorbidity Index</b>				
Median (25% perc./75% perc./range)	1 (1/1/10)	1 (1/1/8)	NA	NA
<b>Charlson Comorbidity Index (categories)</b>				
0	88 (2.1)	385 (2.3)	1.00	reference
1-3	3,877 (93.1)	15,595 (93.9)	1.10	0.88-1.36
4-6	187 (4.5)	595 (3.6)	1.38	1.06-1.79
7-10	11 (0.3)	30 (0.2)	1.60	0.85-3.04
<b>Number of prescriptions ICS prior</b>				
Median (25% perc./75% perc./range)	29 (12/57/269)	29 (12/56/528)	NA	NA

Characteristics and co-medication of cases with **type 2 diabetes mellitus** and matched controls at the index date

	No. of Cases (%) (N=5,189)	No. of Controls (%) (N=20,715)	Crude OR	95% CI
Male	2,070 (39.9)	8,256 (39.9)	NA	NA
Female	3,119 (60.1)	12,459 (60.1)	NA	NA
<b>Age</b>				
18-39	653 (12.6)	2,609 (12.6)	NA	NA
40-59	1,927 (37.1)	7,728 (37.3)	NA	NA
60-79	2,252 (43.4)	8,984 (43.4)	NA	NA
≥80	357 (6.9)	1,394 (6.7)	NA	NA
<b>Smoking status</b>				
non	2,313 (44.6)	10,373 (50.1)	1.00	reference
current	751 (14.5)	2,619 (12.6)	1.29	1.18-1.42
ex	2,054 (39.6)	7,318 (35.3)	1.27	1.19-1.36
unknown	71 (1.4)	405 (2.0)	0.76	0.58-0.99
<b>Alcohol consumption (average units per week)</b>				
none	2,936 (56.6)	9,296 (44.9)	1.00	reference
<14	1,497 (28.9)	7,079 (34.2)	0.66	0.62-0.71
≥14	519 (10.0)	2,490 (12.0)	0.63	0.57-0.71
unknown	237 (4.6)	1,850 (8.9)	0.39	0.33-0.45
<b>Body mass index, kg/m<sup>2</sup></b>				
<18.5	15 (0.3)	266 (1.3)	0.72	0.42-1.23
18.5-24.9	464 (8.9)	6,267 (30.3)	1.00	reference
25-29.9	1,294 (24.9)	7,241 (35.0)	2.47	2.21-2.77
≥30	3,180 (61.3)	5,312 (25.6)	8.88	7.96-9.89
unknown	236 (4.6)	1,629 (7.9)	1.81	1.52-2.15
<b>Concomitant<sup>a</sup> drug use</b>				
SABA	4,485 (86.4)	17,037 (82.2)	1.32	1.05-1.65
SAMA	239 (4.6)	676 (3.3)	1.49	1.27-1.74
ICS (mono preparations)	3,647 (70.3)	15,030 (72.6)	1.02	0.88-1.18
ICS+LABA	1,879 (36.2)	6,805 (32.9)	1.19	1.11-1.28
Asthma add-on therapy <sup>b</sup>	259 (5.0)	931 (4.5)	1.13	0.98-1.30
Platelet aggregation inhibitors	998 (19.2)	2,541 (12.3)	1.92	1.76-2.10
Anticoagulants	249 (4.8)	569 (2.8)	1.84	1.58-2.15
Proton pump inhibitors	1,514 (29.2)	4,218 (20.4)	1.74	1.61-1.87
Immunosuppressants <sup>c</sup>	21 (0.4)	44 (0.2)	1.91	1.13-3.20
Bisphosphonates	119 (2.3)	639 (3.1)	0.72	0.58-0.88
Vitamin D	238 (4.6)	929 (4.5)	1.03	0.89-1.20
<b>Charlson Comorbidity Index</b>				
Median (25% perc./75% perc./range)	1 (1/1/6)	1(1/1/7)	NA	NA
<b>Charlson Comorbidity Index (categories)</b>				
0	122 (2.4)	511 (2.5)	1.00	reference
1-3	4,963 (95.6)	19,932 (96.2)	1.05	0.87-1.26
4-6	104 (2.0)	268 (1.3)	1.65	1.25-2.17
7	X	X	NA	NA
<b>Number of prescriptions ICS prior</b>				
Median (25% perc./75% perc./range)	31 (13/59/372)	29 (12/55/604)	NA	NA

Characteristics and co-medication of cases with **cataract** and matched controls at the index date

	<b>No. of Cases (%) (N=5,327)</b>	<b>No. of Controls (%) (N=21,019)</b>	<b>Crude OR</b>	<b>95% CI</b>
Male	1,659 (31.1)	6,507 (31.0)	NA	NA
Female	3,668 (68.9)	14,512 (69.0)	NA	NA
<b>Age</b>				
18-39	50 (0.9)	195 (0.9)	NA	NA
40-59	536 (10.1)	2,157 (10.3)	NA	NA
60-79	3,240 (60.8)	12,975 (61.7)	NA	NA
≥80	1,501 (28.2)	5,692 (27.1)	NA	NA
<b>Smoking status</b>				
non	2,524 (47.4)	10,739 (51.1)	1.00	reference
current	382 (7.2)	1,454 (6.9)	1.12	0.99-1.27
ex	2,333 (43.8)	8,388 (39.9)	1.19	1.12-1.27
unknown	88 (1.7)	438 (2.1)	0.84	0.66-1.07
<b>Alcohol consumption (average units per week)</b>				
none	2,892 (54.3)	11,123 (52.9)	1.00	reference
<14	1,623 (30.5)	6,480 (30.8)	0.97	0.90-1.03
≥14	475 (8.9)	1,865 (8.9)	0.98	0.87-1.10
unknown	337 (6.3)	1,551 (7.4)	0.83	0.73-0.94
<b>Body mass index, kg/m<sup>2</sup></b>				
<18.5	90 (1.7)	266 (1.3)	1.34	1.05-1.72
18.5-24.9	1,588 (29.8)	6,316 (30.1)	1.00	reference
25-29.9	1,898 (35.6)	7,572 (36.0)	1.00	0.93-1.08
≥30	1,425 (26.8)	5,394 (25.7)	1.06	0.98-1.15
unknown	326 (6.1)	1,471 (7.0)	0.88	0.76-1.00
<b>Concomitant<sup>a</sup> drug use</b>				
SABA	4,394 (82.5)	16,904 (80.4)	1.27	1.05-1.55
SAMA	338 (6.4)	1,274 (6.1)	1.07	0.94-1.21
ICS (mono preparations)	3,756 (70.5)	15,278 (72.7)	0.90	0.78-1.04
ICS+LABA	1,877 (35.2)	6,878 (32.7)	1.15	1.07-1.23
Asthma add-on therapy <sup>b</sup>	233 (4.4)	765 (3.6)	1.23	1.06-1.43
Platelet aggregation inhibitors	1,623 (30.5)	5,193 (24.7)	1.39	1.30-1.50
Anticoagulants	343 (6.4)	1,104 (5.3)	1.23	1.08-1.39
Proton pump inhibitors	1,720 (32.3)	5,870 (27.9)	1.27	1.18-1.36
Immunosuppressants <sup>c</sup>	25 (0.5)	34 (0.2)	2.89	1.70-4.90
Bisphosphonates	370 (7.0)	1,302 (6.2)	1.14	1.01-1.29
Vitamin D	540 (10.4)	1,842 (8.8)	1.18	1.06-1.31
<b>Charlson Comorbidity Index</b>				
Median (25% perc./75% perc./range)	1 (1/2/10)	1 (1/2/9)	NA	NA
<b>Charlson Comorbidity Index (categories)</b>				
0	78 (1.5)	387 (1.8)	1.00	reference
1-3	4,670 (87.7)	19,255 (91.6)	1.23	0.98-1.53
4-6	546 (10.3)	1,327 (6.3)	2.09	1.64-2.65
7-10	33 (0.6)	50 (0.2)	3.40	2.21-5.21
<b>Number of prescriptions ICS</b>				
Median (25% perc./75% perc./range)	41 (21/72/296)	40 (20/69/350)	NA	NA



Characteristics and co-medication of cases with **glaucoma** and matched controls at the index date

	<b>No. of Cases (%) (N=1,467)</b>	<b>No. of Controls (%) (N=5,832)</b>	<b>Crude OR</b>	<b>95% CI</b>
Male	544 (37.1)	2,156 (37.0)	NA	NA
Female	923 (62.9)	3,676 (63.0)	NA	NA
<b>Age</b>				
18-39	42 (2.9)	171 (2.9)	NA	NA
40-59	302 (20.6)	1,206 (20.7)	NA	NA
60-79	832 (56.7)	3,335 (57.2)	NA	NA
≥80	291 (19.8)	1,120 (19.2)	NA	NA
<b>Smoking status</b>				
non	753 (51.3)	2,854 (48.9)	1.00	reference
current	132 (9.0)	543 (9.3)	0.92	0.75-1.14
ex	552 (37.6)	2,279 (39.1)	0.91	0.80-1.03
unknown	30 (2.0)	156 (2.7)	0.72	0.48-1.09
<b>Alcohol consumption (average units per week)</b>				
none	738 (50.3)	2,913 (50.0)	1.00	reference
<14	481 (32.8)	1,859 (31.9)	1.03	0.90-1.17
≥14	151 (10.3)	590 (10.1)	1.02	0.83-1.25
unknown	97 (6.6)	470 (8.1)	0.82	0.65-1.03
<b>Body mass index, kg/m<sup>2</sup></b>				
<18.5	21 (1.4)	68 (1.2)	1.22	0.74-2.01
18.5-24.9	447 (30.5)	1,756 (30.1)	1.00	reference
25-29.9	513 (35.0)	2,029 (34.8)	1.00	0.86-1.15
≥30	393 (26.8)	1,524 (26.1)	1.02	0.88-1.20
unknown	93 (6.3)	455 (7.8)	0.79	0.62-1.02
<b>Concomitant<sup>a</sup> drug use</b>				
SABA	1,181 (80.5)	4,748 (81.4)	0.81	0.58-1.11
SAMA	98 (6.7)	346 (5.9)	1.13	0.89-1.44
ICS (mono preparations)	1,083 (73.8)	4,270 (73.2)	1.00	0.75-1.33
ICS+LABA	451 (30.7)	1,876 (32.2)	0.94	0.82-1.08
Asthma add-on therapy <sup>b</sup>	67 (4.6)	211 (3.6)	1.26	0.95-1.68
Platelet aggregation inhibitors	373 (25.4)	1,268 (21.7)	1.28	1.11-1.47
Anticoagulants	69 (4.7)	249 (4.3)	1.08	0.82-1.43
Proton pump inhibitors	389 (26.5)	1,487 (25.5)	1.04	0.90-1.19
Immunosuppressants <sup>c</sup>	6 (0.4)	18 (0.3)	1.33	0.53-3.36
Bisphosphonates	61 (4.2)	294 (5.0)	0.81	0.60-1.07
Vitamin D	94 (6.4)	390 (6.7)	0.96	0.76-1.22
<b>Charlson Comorbidity Index</b>				
Median (25% perc./75% perc./range)	1 (1/2/8)	1 (1/2/10)	NA	NA
<b>Charlson Comorbidity Index (categories)</b>				
0	30 (2.0)	120 (2.1)	1.00	reference
1-3	1,333 (90.9)	5,368 (92.0)	1.00	0.69-1.44
4-6	99 (6.8)	326 (5.6)	1.20	0.79-1.83
7-10	5 (0.3)	18 (0.3)	1.13	0.44-2.92
<b>Number of prescriptions ICS prior</b>				
Median (25% perc./75% perc./range)	33 (15/60/241)	36 (16/66/351)	NA	NA

Characteristics and co-medication of cases with **chronic kidney disease** and matched controls at the index date

	<b>No. of Cases (%) (N=8,778)</b>	<b>No. of Controls (%) (N=34,762)</b>	<b>Crude OR</b>	<b>95% CI</b>
Male	2,364 (26.9)	9,254 (26.6)	NA	NA
Female	6,414 (73.1)	25,508 (73.4)	NA	NA
<b>Age</b>				
18-39	170 (1.9)	668 (1.9)	NA	NA
40-59	1,062 (12.1)	4,260 (12.3)	NA	NA
60-79	5,158 (58.8)	20,727 (59.6)	NA	NA
≥80	2,388 (27.2)	9,107 (26.2)	NA	NA
<b>Smoking status</b>				
non	4,132 (47.1)	17,767 (51.1)	1.00	reference
current	622 (7.1)	2,710 (7.8)	0.99	0.90-1.09
ex	3,925 (44.7)	13,713 (39.5)	1.24	1.18-1.31
unknown	99 (1.1)	572 (1.7)	0.73	0.58-0.91
<b>Alcohol consumption (average units per week)</b>				
none	5,172 (58.9)	17,924 (51.6)	1.00	reference
<14	2,633 (30.0)	11,103 (31.9)	0.82	0.77-0.86
≥14	565 (6.4)	3,024 (8.7)	0.63	0.57-0.70
unknown	408 (4.7)	2,711 (7.8)	0.52	0.46-0.58
<b>Body mass index, kg/m<sup>2</sup></b>				
<18.5	104 (1.2)	532 (1.5)	1.00	0.80-1.24
18.5-24.9	2,061 (23.5)	10,893 (31.3)	1.00	reference
25-29.9	3,140 (35.8)	12,285 (35.3)	1.39	1.31-1.48
≥30	3,074 (35.0)	8,432 (24.3)	2.03	1.90-2.17
unknown	399 (4.6)	2,620 (7.5)	0.77	0.69-0.87
<b>Concomitant<sup>a</sup> drug use</b>				
SABA	7,241 (82.5)	28,138 (80.9)	0.94	0.82-1.09
SAMA	662 (7.5)	2,015 (5.8)	1.34	1.23-1.48
ICS (mono preparations)	6,390 (72.8)	25,978 (74.7)	0.79	0.70-0.88
ICS+LABA	2,981 (34.0)	10,886 (31.3)	1.14	1.08-1.20
Asthma add-on therapy <sup>b</sup>	346 (3.9)	1,320 (3.8)	1.04	0.92-1.17
Platelet aggregation inhibitors	3,188 (36.3)	7,773 (22.4)	2.21	2.09-2.33
Anticoagulants	710 (8.1)	1,352 (3.9)	2.22	2.02-2.45
Proton pump inhibitors	2,952 (33.6)	8,554 (24.6)	1.61	1.53-1.70
Immunosuppressants <sup>c</sup>	35 (0.4)	66 (0.2)	2.10	1.40-3.17
Bisphosphonates	548 (6.2)	2,153 (6.2)	1.00	0.90-1.10
Vitamin D	805 (9.2)	2,774 (8.0)	1.18	1.08-1.28
<b>Charlson Comorbidity Index</b>				
Median (25% perc./75% perc./range)	1 (1/2/8)	1 (1/1/8)	NA	NA
<b>Charlson Comorbidity Index (categories)</b>				
0	183 (2.1)	786 (2.3)	1.00	reference
1-3	8,004 (91.2)	33,166 (95.4)	1.04	0.90-1.21
4-6	572 (6.5)	798 (2.3)	3.14	2.63-3.73
7-9	19 (0.2)	12 (0.0)	7.43	4.07-13.55
<b>Number of prescriptions ICS prior</b>				
Median (25% perc./75% perc./range)	37 (17/66/412)	36 (17/64/363)	NA	NA

Characteristics and co-medication of cases with **affective disorders** and matched controls at the index date

	No. of Cases (%) (N=4,962)	No. of Controls (%) (N=19,809)	Crude OR	95% CI
Male	1,874 (37.8)	7,479 (37.8)	NA	NA
Female	3,088 (62.2)	12,330 (62.2)	NA	NA
<b>Age</b>				
18-39	2,586 (52.1)	10,316 (52.1)	NA	NA
40-59	1,665 (33.6)	6,657 (33.6)	NA	NA
60-79	579 (11.7)	2,328 (11.8)	NA	NA
≥80	132 (2.7)	508 (2.6)	NA	NA
<b>Smoking status</b>				
non	2,268 (45.7)	11,305 (57.1)	1.00	reference
current	1,247 (25.1)	3,129 (15.8)	2.01	1.86-2.18
ex	1,316 (26.5)	4,727 (23.9)	1.38	1.28-1.50
unknown	131 (2.6)	648 (3.3)	1.01	0.83-1.24
<b>Alcohol consumption (average units per week)</b>				
none	2,099 (42.3)	7,768 (39.2)	1.00	reference
<14	1,613 (32.5)	6,519 (32.9)	0.92	0.85-0.99
≥14	565 (11.4)	2,145 (10.8)	0.97	0.87-1.08
unknown	685 (13.8)	3,377 (17.1)	0.73	0.66-0.80
<b>Body mass index, kg/m<sup>2</sup></b>				
<18.5	127 (2.6)	387 (2.0)	1.43	1.16-1.76
18.5-24.9	1,627 (32.8)	7,197 (36.3)	1.00	reference
25-29.9	1,366 (27.5)	5,414 (27.3)	1.13	1.04-1.22
≥30	1,202 (24.2)	3,919 (19.8)	1.38	1.26-1.50
unknown	640 (12.9)	2,892 (14.6)	0.96	0.86-1.06
<b>Concomitant<sup>a</sup> drug use</b>				
SABA	4,403 (88.7)	17,039 (86.0)	1.81	1.35-2.44
SAMA	124 (2.5)	327 (1.7)	1.57	1.26-1.94
ICS (mono preparations)	3,692 (74.4)	15,096 (76.2)	0.94	0.81-1.10
ICS+LABA	1,602 (32.3)	5,709 (28.8)	1.23	1.14-1.32
Asthma add-on therapy <sup>b</sup>	236 (4.8)	718 (3.6)	1.34	1.15-1.56
Platelet aggregation inhibitors	304 (6.1)	805 (4.1)	1.73	1.48-2.01
Anticoagulants	64 (1.3)	166 (0.8)	1.58	1.17-2.12
Proton pump inhibitors	694 (14.0)	1,685 (8.5)	1.93	1.75-2.14
Immunosuppressants <sup>c</sup>	8 (0.2)	27 (0.1)	1.19	0.54-2.61
Bisphosphonates	64 (1.3)	180 (0.9)	1.45	1.07-1.95
Vitamin D	93 (1.9)	313 (1.6)	1.21	0.95-1.55
<b>Charlson Comorbidity Index</b>				
Median (25% perc./75% perc./range)	1 (1/1/10)	1 (1/1/8)	NA	NA
<b>Charlson Comorbidity Index (categories)</b>				
0	107 (2.2)	400 (2.0)	1.00	reference
1-3	4,772 (96.2)	19,214 (97.0)	0.93	0.77-1.13
4-6	80 (1.6)	191 (1.0)	1.60	1.18-2.17
7-10	X	X	NA	NA
<b>Number of prescriptions ICS prior</b>				
Median (25% perc./75% perc./range)	21 (8/45/358)	21 (8/44/348)	NA	NA

Characteristics and co-medication of cases with **cardiovascular disease** and matched controls at the index date

	No. of Cases (%) (N=4,014)	No. of Controls (%) (N=15,945)	Crude OR	95% CI
Male	1,885 (47.0)	7,477 (46.9)	NA	NA
Female	2,129 (53.0)	8,468 (53.1)	NA	NA
<b>Age</b>				
18-39	66 (1.6)	265 (1.7)	NA	NA
40-59	977 (24.3)	3,913 (24.5)	NA	NA
60-79	2,274 (56.7)	9,087 (57.0)	NA	NA
≥80	697 (17.4)	2,680 (16.8)	NA	NA
<b>Smoking status</b>				
non	1,746 (43.5)	7,954 (49.9)	1.00	reference
current	544 (13.6)	1,495 (9.4)	1.70	1.51-1.90
ex	1,622 (40.4)	6,046 (37.9)	1.23	1.14-1.33
unknown	102 (2.5)	450 (2.8)	1.03	0.82-1.29
<b>Alcohol consumption (average units per week)</b>				
none	2,048 (51.0)	7,294 (45.7)	1.00	reference
<14	1,311 (32.7)	5,243 (32.9)	0.89	0.82-0.96
≥14	427 (10.6)	1,973 (12.4)	0.76	0.67-0.85
unknown	228 (5.7)	1,435 (9.0)	0.56	0.48-0.65
<b>Body mass index, kg/m<sup>2</sup></b>				
<18.5	39 (1.0)	192 (1.2)	0.96	0.68-1.37
18.5-24.9	994 (24.8)	4,744 (29.8)	1.00	reference
25-29.9	1,525 (38.0)	5,762 (36.1)	1.27	1.16-1.39
≥30	1,142 (28.5)	3,777 (23.7)	1.47	1.33-1.62
unknown	314 (7.8)	1,470 (9.2)	1.00	0.87-1.16
<b>Concomitant<sup>a</sup> drug use</b>				
SABA	3,368 (83.9)	12,932 (81.1)	1.05	0.85-1.29
SAMA	277 (6.9)	798 (5.0)	1.44	1.25-1.66
ICS (mono preparations)	3,053 (76.1)	12,403 (77.8)	0.89	0.75-1.07
ICS+LABA	1,213 (30.2)	4,337 (27.2)	1.22	1.12-1.32
Asthma add-on therapy <sup>b</sup>	160 (4.0)	542 (3.4)	1.19	0.99-1.43
Platelet aggregation inhibitors	1,394 (34.7)	2,091 (13.1)	4.00	3.67-4.36
Anticoagulants	200 (5.0)	462 (2.9)	1.79	1.51-2.13
Proton pump inhibitors	1,226 (30.5)	3,362 (21.1)	1.80	1.66-1.96
Immunosuppressants <sup>c</sup>	12 (0.3)	21 (0.1)	2.29	1.13-4.65
Bisphosphonates	167 (4.2)	627 (3.9)	1.08	0.90-1.29
Vitamin D	269 (6.7)	872 (5.5)	1.27	1.09-1.47
<b>Charlson Comorbidity Index</b>				
Median (25% perc./75% perc./range)	1 (1/2/7)	1 (1/1/8)	NA	NA
<b>Charlson Comorbidity Index (categories)</b>				
0	101 (2.5)	398 (2.5)	1.00	reference
1-3	3,651 (91.0)	14,974 (93.9)	0.97	0.80-1.19
4-6	249 (6.2)	562 (3.5)	1.77	1.39-2.24
7-8	13 (0.3)	11 (0.1)	4.62	2.21-9.68
<b>Number of prescriptions ICS prior</b>				
Median (25% perc./75% perc./range)	34 (14/63/257)	33 (14/60/408)	NA	NA

**Abbreviations for all characteristics and co-medication tables:** LABA, long-acting beta-adrenoceptor agonists; ICS, inhaled corticosteroids; SABA, short-acting beta-adrenoceptor agonists; SAMA, short-acting muscarinic antagonists; LAMA, long-acting muscarinic antagonists; NA, not applicable; X: cell contained <5 observations (due to confidentiality reasons, we are not allowed to display cells containing <5 observations); perc., percentile.

<sup>a</sup> Last prescription within 365 days before the index date; reference group: non-users of these drug groups.

<sup>b</sup> Theophylline, leukotriene receptor antagonists, or omalizumab.

<sup>c</sup> Selective immunosuppressants, tumor necrosis factor alpha inhibitors, interleukin inhibitors, calcineurin inhibitors, azathioprine, thalidomide, lenalidomide, or methotrexate.