

*Supplementary Material*

# Healthcare system encounters before COPD diagnosis: a registry-based longitudinal cohort study

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- 1. List of medications classified as other respiratory medications.**
- 2. Parameter estimates from the sensitivity analysis of the subset of participants with spirometry-confirmed moderate to severe COPD near the time of diagnosis.**
- 3. Parameter estimates from the subset of participants with no missing data.**
- 4. Parameters estimates from a new cohort of participants in which comparator subjects never developed COPD during follow-up.**

**e-Table 1:** Drug Identification Number (DIN) and category names for medications dispensed at pharmacist visits and classified as ‘other respiratory medications.’

DIN	Category	DIN	Category
14923	Bronchodilators-Theophylline	1926608	Bronchodilators-Theophylline
156701	Bronchodilators-Theophylline	1926616	Bronchodilators-Theophylline
178497	Bronchodilators-Theophylline	1926640	Bronchodilators-Theophylline
261203	Bronchodilators-Theophylline	1966219	Bronchodilators-Theophylline
346071	Bronchodilators-Theophylline	1966227	Bronchodilators-Theophylline
405310	Bronchodilators-Theophylline	1966235	Bronchodilators-Theophylline
441724	Bronchodilators-Theophylline	1966243	Bronchodilators-Theophylline
441732	Bronchodilators-Theophylline	1966251	Bronchodilators-Theophylline
451282	Bronchodilators-Theophylline	1966278	Bronchodilators-Theophylline
458708	Bronchodilators-Theophylline	1966286	Bronchodilators-Theophylline
458716	Bronchodilators-Theophylline	2014165	Bronchodilators-Theophylline
460982	Bronchodilators-Theophylline	2014181	Bronchodilators-Theophylline
460990	Bronchodilators-Theophylline	2014270	Bronchodilators-Theophylline
461008	Bronchodilators-Theophylline	2014289	Bronchodilators-Theophylline
466409	Bronchodilators-Theophylline	2230085	Bronchodilators-Theophylline
476366	Bronchodilators-Theophylline	2230086	Bronchodilators-Theophylline
476390	Bronchodilators-Theophylline	2230087	Bronchodilators-Theophylline
476412	Bronchodilators-Theophylline	261238	Cromolyn Sodium
488070	Bronchodilators-Theophylline	534609	Cromolyn Sodium
497193	Bronchodilators-Theophylline	555649	Cromolyn Sodium
497207	Bronchodilators-Theophylline	638641	Cromolyn Sodium
503436	Bronchodilators-Theophylline	2046113	Cromolyn Sodium
511692	Bronchodilators-Theophylline	2049082	Cromolyn Sodium
532223	Bronchodilators-Theophylline	2219468	Cromolyn Sodium
536709	Bronchodilators-Theophylline	2231431	Cromolyn Sodium
556742	Bronchodilators-Theophylline	2231671	Cromolyn Sodium
565377	Bronchodilators-Theophylline	605255	Cromolyn Sodium Nasal Solution
575151	Bronchodilators-Theophylline	1950541	Cromolyn Sodium Nasal Solution
582654	Bronchodilators-Theophylline	2231326	Cromolyn Sodium Nasal Solution
582662	Bronchodilators-Theophylline	2231390	Cromolyn Sodium Nasal Solution
589942	Bronchodilators-Theophylline	38121	Ephedrine
589950	Bronchodilators-Theophylline	438847	Ephedrine

599905	Bronchodilators-Theophylline	876534	Ephedrine
627410	Bronchodilators-Theophylline	893323	Ephedrine
631698	Bronchodilators-Theophylline	893331	Ephedrine
631701	Bronchodilators-Theophylline	2012111	Ephedrine
692689	Bronchodilators-Theophylline	2100231	Ephedrine
692697	Bronchodilators-Theophylline	2100258	Ephedrine
692700	Bronchodilators-Theophylline	2126400	Ephedrine
722065	Bronchodilators-Theophylline	2126419	Ephedrine
792934	Bronchodilators-Theophylline	2219743	Ephedrine
868450	Bronchodilators-Theophylline	2229678	Ephedrine
1926586	Bronchodilators-Theophylline	2229698	Ephedrine
1926594	Bronchodilators-Theophylline	2229711	Ephedrine
2236722	Ephedrine	30910	Oral Glucocorticoid Steroid
2237085	Ephedrine	30929	Oral Glucocorticoid Steroid
2242639	Ephedrine	30988	Oral Glucocorticoid Steroid
2242961	Ephedrine	36129	Oral Glucocorticoid Steroid
2243148	Ephedrine	36366	Oral Glucocorticoid Steroid
466417	Epinephrine	156876	Oral Glucocorticoid Steroid
525103	Epinephrine	176834	Oral Glucocorticoid Steroid
1927582	Epinephrine	210188	Oral Glucocorticoid Steroid
2017555	Epinephrine	232378	Oral Glucocorticoid Steroid
307548	Guaifenesin/ Theophylline	252417	Oral Glucocorticoid Steroid
317225	Guaifenesin/ Theophylline	271373	Oral Glucocorticoid Steroid
334510	Guaifenesin/ Theophylline	271381	Oral Glucocorticoid Steroid
356123	Guaifenesin/ Theophylline	280437	Oral Glucocorticoid Steroid
476374	Guaifenesin/ Theophylline	285471	Oral Glucocorticoid Steroid
545090	Guaifenesin/ Theophylline	295094	Oral Glucocorticoid Steroid
640093	Guaifenesin/ Theophylline	312770	Oral Glucocorticoid Steroid
721301	Guaifenesin/ Theophylline	354309	Oral Glucocorticoid Steroid
792942	Guaifenesin/ Theophylline	489158	Oral Glucocorticoid Steroid
828718	Guaifenesin/ Theophylline	508586	Oral Glucocorticoid Steroid
828726	Guaifenesin/ Theophylline	550957	Oral Glucocorticoid Steroid
828742	Guaifenesin/ Theophylline	598194	Oral Glucocorticoid Steroid
2449781	Humanized monoclonal antibody	607517	Oral Glucocorticoid Steroid
2456419	Humanized monoclonal antibody	610623	Oral Glucocorticoid Steroid
577308	Ketotifen AL	868426	Oral Glucocorticoid Steroid
600784	Ketotifen AL	868434	Oral Glucocorticoid Steroid
2020017	Ketotifen AL	868442	Oral Glucocorticoid Steroid
2176084	Ketotifen AL	1946897	Oral Glucocorticoid Steroid

2218305	Ketotifen AL	1964070	Oral Glucocorticoid Steroid
2221330	Ketotifen AL	1964968	Oral Glucocorticoid Steroid
2230730	Ketotifen AL	1964976	Oral Glucocorticoid Steroid
2231679	Ketotifen AL	2063190	Oral Glucocorticoid Steroid
2231680	Ketotifen AL	2194082	Oral Glucocorticoid Steroid
2236606	Leukotriene receptor antagonist	2194090	Oral Glucocorticoid Steroid
2238216	Leukotriene receptor antagonist	2237044	Oral Glucocorticoid Steroid
2238217	Leukotriene receptor antagonist	2237045	Oral Glucocorticoid Steroid
2243602	Leukotriene receptor antagonist	2237046	Oral Glucocorticoid Steroid
2247997	Leukotriene receptor antagonist	2239534	Oral Glucocorticoid Steroid
2260565	Omalizumab	2240684	Oral Glucocorticoid Steroid
15016	Oral Glucocorticoid Steroid	2240685	Oral Glucocorticoid Steroid
15024	Oral Glucocorticoid Steroid	2240687	Oral Glucocorticoid Steroid
16438	Oral Glucocorticoid Steroid	2250055	Oral Glucocorticoid Steroid
16446	Oral Glucocorticoid Steroid	2260298	Oral Glucocorticoid Steroid
16462	Oral Glucocorticoid Steroid	2260301	Oral Glucocorticoid Steroid
21695	Oral Glucocorticoid Steroid	2261081	Oral Glucocorticoid Steroid
28185	Oral Glucocorticoid Steroid	2279363	Oral Glucocorticoid Steroid
2311267	Oral Glucocorticoid Steroid	2230210	Systemic Glucocorticoid Steroid
3859	Synthetic Derivative of Adrenaline	2230211	Systemic Glucocorticoid Steroid
254134	Synthetic Derivative of Adrenaline	2231893	Systemic Glucocorticoid Steroid
1923870	Synthetic Derivative of Adrenaline	2231894	Systemic Glucocorticoid Steroid
1928449	Synthetic Derivative of Adrenaline	2231895	Systemic Glucocorticoid Steroid
2017652	Synthetic Derivative of Adrenaline	2232748	Systemic Glucocorticoid Steroid
2017660	Synthetic Derivative of Adrenaline	2232750	Systemic Glucocorticoid Steroid
16241	Systemic Glucocorticoid Steroid	2237835	Systemic Glucocorticoid Steroid
28096	Systemic Glucocorticoid Steroid	2241229	Systemic Glucocorticoid Steroid
30600	Systemic Glucocorticoid Steroid	2245400	Systemic Glucocorticoid Steroid
30619	Systemic Glucocorticoid Steroid	2245406	Systemic Glucocorticoid Steroid
30627	Systemic Glucocorticoid Steroid	2245407	Systemic Glucocorticoid Steroid
30635	Systemic Glucocorticoid Steroid	2245408	Systemic Glucocorticoid Steroid

30643	Systemic Glucocorticoid Steroid
30651	Systemic Glucocorticoid Steroid
30678	Systemic Glucocorticoid Steroid
30759	Systemic Glucocorticoid Steroid
30767	Systemic Glucocorticoid Steroid
36137	Systemic Glucocorticoid Steroid
213624	Systemic Glucocorticoid Steroid
664227	Systemic Glucocorticoid Steroid
716715	Systemic Glucocorticoid Steroid
732885	Systemic Glucocorticoid Steroid
732893	Systemic Glucocorticoid Steroid
751863	Systemic Glucocorticoid Steroid
783900	Systemic Glucocorticoid Steroid
872520	Systemic Glucocorticoid Steroid
872539	Systemic Glucocorticoid Steroid
874582	Systemic Glucocorticoid Steroid
878618	Systemic Glucocorticoid Steroid
878626	Systemic Glucocorticoid Steroid
888206	Systemic Glucocorticoid Steroid
888214	Systemic Glucocorticoid Steroid
888222	Systemic Glucocorticoid Steroid
888230	Systemic Glucocorticoid Steroid
1934325	Systemic Glucocorticoid Steroid
1934333	Systemic Glucocorticoid Steroid
1934341	Systemic Glucocorticoid Steroid
1977547	Systemic Glucocorticoid Steroid
2063697	Systemic Glucocorticoid Steroid
2063700	Systemic Glucocorticoid Steroid
2063719	Systemic Glucocorticoid Steroid
2063727	Systemic Glucocorticoid Steroid
2204266	Systemic Glucocorticoid Steroid
2204274	Systemic Glucocorticoid Steroid

**e-Table 2:** Parameter estimates and confidence intervals for the rate of outpatient visits among COPD patients who were prescribed long-acting muscarinic antagonist (LAMA) in the year before or after the index date (N=9,079). Patients in this subgroup had spirometry-confirmed moderate to severe COPD ( $FEV_1/FVC < 0.7$  and  $FEV_1 \leq 65\%$ ). COPD patients were matched to one non-COPD comparator subject.

	All-cause primary care visits		Respiratory related primary care visits		Specialist physician visits		Pharmacist visits	
	Rate Ratio	95% CI	Rate Ratio	95% CI	Rate Ratio	95% CI	Rate Ratio	95% CI
COPD (vs. comparator)	1.30	1.27-1.34	2.67	2.57-2.78	1.33	1.29-1.37	1.60	1.54-1.66
Period	1.07	1.06-1.08	1.18	1.17-1.19	1.08	1.08-1.09	1.07	1.06-1.08
Female (vs. male)	1.10	1.07-1.12	1.18	1.14-1.23	1.01	0.98-1.05	1.13	1.08-1.17
Age	1.02	1.02-1.02	1.00	1.00-1.00	1.02	1.02-1.03	1.01	1.01-1.01
SES								
1 (vs. 5)	1.12	1.08-1.17	1.13	1.06-1.20	0.99	0.95-1.04	1.32	1.24-1.41
2 (vs. 5)	1.08	1.04-1.12	1.12	1.06-1.20	0.97	0.93-1.02	1.13	1.07-1.18
3 (vs. 5)	1.04	1.00-1.08	1.10	1.04-1.18	0.97	0.92-1.01	1.08	1.03-1.14
4 (vs. 5)	1.04	1.00-1.08	1.02	0.96-1.09	1.01	0.96-1.07	1.07	1.03-1.13
Calendar year	1.00	0.99-1.00	0.96	0.95-0.96	1.01	1.01-1.02	1.02	1.01-1.02

**COPD:** Chronic Obstructive Pulmonary Disease, **SES:** Socioeconomic Status, **CI:** Confidence Interval

**e-Table 3:** Parameter estimates and confidence intervals for the rate of outpatient visits in the subset of COPD patients and comparator subjects with no missing data (N=110,556).

	All-cause primary care visits		Respiratory related primary care visits		Specialist physician visits		Pharmacist visits	
	Rate Ratio	95% CI	Rate Ratio	95% CI	Rate Ratio	95% CI	Rate Ratio	95% CI
COPD (vs. comparator)	1.40	1.39-1.41	2.16	2.14-2.19	1.35	1.34-1.36	1.61	1.60-1.63
Period	1.06	1.06-1.06	1.14	1.14-1.14	1.07	1.07-1.08	1.06	1.06-1.06
Female (vs. male)	1.15	1.15-1.16	1.27	1.25-1.28	1.08	1.07-1.09	1.18	1.17-1.20
Age	1.01	1.01-1.01	1.00	1.00-1.00	1.02	1.02-1.02	1.01	1.01-1.01
SES								
1 (vs. 5)	1.17	1.16-1.19	1.11	1.09-1.13	1.02	1.00-1.03	1.32	1.30-1.35
2 (vs. 5)	1.10	1.09-1.11	1.08	1.06-1.10	0.99	0.98-1.01	1.12	1.10-1.14
3 (vs. 5)	1.06	1.04-1.07	1.05	1.03-1.07	0.99	0.97-1.00	1.06	1.04-1.08
4 (vs. 5)	1.03	1.02-1.05	1.02	1.00-1.04	0.99	0.97-1.00	1.04	1.03-1.06
Calendar year	1.00	1.00-1.00	0.97	0.96-0.97	1.01	1.01-1.01	1.02	1.02-1.02

**COPD:** Chronic Obstructive Pulmonary Disease, **SES:** Socioeconomic Status, **CI:** Confidence Interval

**e-Table 4:** Parameter estimates and confidence intervals for the rate of outpatient visits in a cohort of 106,439 COPD/comparator pairs in which comparator subjects never developed COPD during follow-up.

	All-cause primary care visits		Respiratory related primary care visits		Specialist physician visits		Pharmacist visits	
	<i>Rate Ratio</i>	<i>95% CI</i>	<i>Rate Ratio</i>	<i>95% CI</i>	<i>Rate Ratio</i>	<i>95% CI</i>	<i>Rate Ratio</i>	<i>95% CI</i>
COPD (vs. comparator)	1.46	1.45-1.47	2.35	2.32-2.38	1.42	1.40-1.43	1.72	1.70-1.75
Period	1.06	1.06-1.06	1.13	1.13-1.14	1.07	1.07-1.08	1.06	1.05-1.06
Female (vs. male)	1.16	1.15-1.17	1.27	1.26-1.29	1.09	1.08-1.10	1.19	1.18-1.21
Age	1.01	1.01-1.01	1.00	1.00-1.00	1.02	1.02-1.02	1.01	1.01-1.01
SES								
1 (vs. 5)	1.15	1.13-1.16	1.09	1.07-1.11	1.01	1.00-1.02	1.29	1.26-1.31
2 (vs. 5)	1.09	1.07-1.10	1.08	1.06-1.10	0.99	0.97-1.00	1.11	1.09-1.13
3 (vs. 5)	1.04	1.03-1.05	1.04	1.02-1.06	0.99	0.97-1.00	1.06	1.04-1.08
4 (vs. 5)	1.02	1.01-1.04	1.01	0.99-1.03	1.00	0.98-1.01	1.03	1.01-1.05
Calendar year	1.01	1.00-1.01	0.97	0.97-0.97	1.01	1.01-1.01	1.02	1.02-1.03

**COPD:** Chronic Obstructive Pulmonary Disease, **SES:** Socioeconomic Status, **CI:** Confidence interval