

GSK Medicine: Fluticasone propionate, beclomethasone, salmeterol, fluticasone propionate/salmeterol, fluticasone propionate/salmeterol/norflurane
Study No: WWE113672/WEUKBRE1157/EPI40472
Title: Assessment of the Risk of Pneumonia among COPD Patients on Seretide or Inhaled Corticosteroids in the UK primary care
Rationale: Pneumonia is both a serious and potentially life-threatening disease that is common in elderly patients and those subjects with risk factors for resistant pathogens. Given a signal detected in randomized clinical trials, it is important to ascertain whether the use of inhaled corticosteroids (ICS) or ICS with long acting beta agonists (LABA) in clinical practice is a risk factor for pneumonia in COPD or if specific doses of ICS are associated with increased risk of pneumonia. This study is a response to a regulatory commitment to the FDA.
Objectives: The objectives of the study were: 1) to quantify the occurrence of pneumonia among COPD patients in the four treatment groups ICS/LABA, ICS, LABA and short acting beta agonists (SABD); 2) to compare the risk of pneumonia (including repeated attack) in the three treatment groups ICS/LABA, ICS, LABA compared with SABD; 3) to quantify the occurrence of pneumonia among COPD patients in the four treatment groups : Futicasone Propionate/Salmeterol Xinafoate (FP/SAL) (including Seretide), FP, SAL and SABD; 4) to compare the risk of pneumonia (including repeated attack) in the three treatment groups FP/SAL (including Seretide), FP, SAL compared with SABD; and 5) to assess if there is a dose response relationship with respect to increased risk of pneumonia for patients exposed to ICS (class level) or FP only (drug level)
Indication:
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Research Methods:
Data Source: The General Practice Research Database (GPRD), containing computerized health care information entered by General Practitioners in the UK, was used as the source population. Over 400 General Practices have contributed medical history data since 1987 on over 6 million patients who are broadly representative of the total population. The database contains longitudinal data on patient characteristics, medical history (records of referrals to consultants and hospitalisations), and treatment history over a period of up to 15 years.
Study Design: We performed two different analyses in this study: a retrospective cohort study determining the hazard ratios of developing pneumonia in the treatment groups of interest, and a case-control study to assess the risk factors for pneumonia in exposure windows prior to the event.
Study Population: The study population consisted of a cohort of incident diagnosed COPD patients from up-to-standard practices in the UK General Practice Research Database (GPRD) between January 1, 1996 and December 31, 2002. Patients were followed up for as long as three years, ending December 31, 2005

Study Exposures, Outcomes: We defined exposure groups at both the class level and the drug level determined by physician ordered prescriptions. For the retrospective cohort analysis, the following exposure groups at the class level were defined: new regular users of ICS/LABA, ICS, LABA, or SABD; concomitant use of ICS and LABA (ICS/LABA); regular concomitant use of ICS and LABA; and new regular users of short-acting bronchodilator (SABD). For the case control study we defined exposure in the following time periods (0-6 months, >6-12 months, >12 – 18 months, >18 – 24 months) preceding the pneumonia date for cases and the matching date for the controls: For the drug level analysis, the following categories and hierarchy were applied:concomitant FP and SAL use, concomitant ICS and LABA use, FP use, ICS use, SAL Use, LABA Use, SABD Use (reference group),other respiratory treatment, no respiratory treatments

The outcome of interest is a physician-recorded diagnosis of pneumonia (based on GPRD Medical codes). Pneumonia was broadly defined as a viral, bacterial or fungal infection of lungs or pleura.

Study Results:

Demographics and Baseline Characteristics: The total size of the COPD cohort was 15,614 adults. Patients were most likely to be in the 60-79 year old age group and were evenly distributed by gender. Patients were most likely to be current smokers (46%) or former smokers (24%). Both at the class and drug level the crude incidence of pneumonia was slightly higher for the SABD group compared to other drug class groups, although the 95% Confidence Intervals overlapped for most categories.

Retrospective cohort analyses: At the class level there were no significant increases in pneumonia risk when comparing regular users of ICS/LABA (HR=0.99; 95%CI: 0.57, 1.74), ICS (HR=0.92; 95%CI: 0.54, 1.57), or LABA (HR=0.71; 95%CI: 0.27,1.84) separately to regular users of SABD. Older age, higher number of GP visits, history of lung cancer, history of pneumonia, and use of nebulisers at baseline were independently associated with a significant increased risk of pneumonia.

At the drug level there were no significant increases in pneumonia risk associated with regular use of FP/SAL (HR=0.96; 95%CI: 0.51, 1.79), FP (HR=1.01; 95%CI: 0.38, 2.70), or SAL (HR=0.78; 95%CI: 0.40, 1.52) compared with regular use of SABD. Older age, higher number of GP visits, and presence of a metastatic solid tumor at baseline were independently associated with a significant increased risk of pneumonia.

Nested Case Control Analysis: In examining risks associated with the current drug class exposure (0 to 6 months preceding the event), there was no increase in pneumonia risk observed for ICS/LABA (OR= 1.11; 95%CI: 0.70, 1.75), ICS (OR=0.78; 95%CI: 0.52, 1.17), or LABA (OR=0.93; 95%CI: 0.45, 1.92) use relative to SABD. Furthermore, in examining risks associated with the current drug exposure (0 to 6 months preceding the event), the risk of pneumonia was not associated with FP/SAL (OR= 1.15; 95%CI: 0.68, 1.95), FP (OR=0.95; 95%CI: 0.37, 2.47), or SAL (OR=0.88; 95%CI: 0.36, 2.13) relative to SABD.

Dose Response Analysis: In both analyses increasing average daily dose of ICS was not significantly associated with pneumonia risk. In both analyses of exposure at the drug level, there was no significant association between pneumonia risk and increasing average daily dose of ICS.

Crude Incidence Rates of Pneumonia

Regular User Category	No. Events	Person Years	Incidence Rate*	95% Confidence Interval	
Class Level					
ICS/LABA	122	7585.89	1.61	1.35	1.92

ICS	44	2776.99	1.58	1.18	2.13
LABA	5	426.48	1.17	0.49	2.82
SABD	23	1214.74	1.89	1.26	2.85
Drug Level					
FP/SAL	71	4266.38	1.66	1.32	2.10
FP	7	379.99	1.84	0.88	3.86
SAL	25	1973.47	1.27	0.86	1.87
SABD	23	1214.74	1.89	1.26	2.85

* per 100 person-years

Demographic Characteristics of the COPD Cohort: Drug Class

Covariate	ICS/LABA		ICS		LABA		SABD		Total	
	N	%	N	%	N	%	N	%	N	%
Gender										
Female	1,989	49	878	48	123	42	403	48	3,393	48
Male	2,101	51	942	52	167	58	436	52	3,646	52
Age at COPD index										
45-59	1,039	25	381	21	44	15	163	19	1,627	23
60-69	1,375	34	590	32	102	35	248	30	2,315	33
70-79	1,336	33	628	35	103	36	289	34	2,356	33
≥80	340	8	221	12	41	14	139	17	741	11
Smoking Status at COPD Index										
Non Smoker	888	22	367	20	44	15	142	17	1,441	20
Ex Smoker	1,058	26	439	24	71	24	153	18	1,721	24
Smoker	1,806	44	823	45	152	52	455	54	3,236	46
Unknown	338	8	191	10	23	8	89	11	641	9
No. of COPD Hospitalizations										
≥1	279	7	86	5	6	2	33	4	404	6
No. of GP Visits										
1 to 5	582	14	422	23	65	22	217	26	1,286	18
6 to 10	1,030	25	513	28	87	30	243	29	1,873	27
11 to 15	992	24	350	19	47	16	163	19	1,552	22
16 to 20	655	16	217	12	39	13	84	10	995	14
21 to 25	358	9	140	8	25	9	43	5	566	8
26+	454	11	155	9	24	8	79	9	712	10
Comorbidities										

Anxiety/Depression	347	8	165	9	22	8	83	10	617	9
Asthma	945	23	222	12	23	8	35	4	1,225	17
Cerebrovascular Disease	49	1	40	2	1	0	16	2	106	2
Congestive Heart Failure	151	4	97	5	11	4	44	5	303	4
Dementia	1	0	7	0	0	0	5	1	13	0
Diabetes	187	5	103	6	11	4	57	7	358	5
Diabetes with Complications	15	0	13	1	1	0	7	1	36	1
Hemiplegia/Paraplegia	6	0	3	0	0	0	2	0	11	0
Lung Cancer	7	0	4	0	1	0	4	0	16	0
Mild Liver Disease	0	0	1	0	0	0	0	0	1	0
Moderate/ Severe Liver Disease	4	0	1	0	3	1	1	0	9	0
Myocardial Infarction	39	1	25	1	3	1	14	2	81	1
Peptic Ulcer	60	1	32	2	1	0	20	2	113	2
Peripheral Vascular Disease	37	1	17	1	0	0	6	1	60	1
Pneumonia Broad	54	1	26	1	0	0	14	2	94	1
Renal Disease	11	0	10	1	3	1	6	1	30	0
Rheumatologic Disease	271	7	135	7	21	7	70	8	497	7
Solid Tumor/Met	41	1	24	1	7	2	17	2	89	1
Solid Tumor/Non Met	17	0	8	0	2	1	12	1	39	1
Baseline Treatment										
ICS	3,289	80	979	54	43	15	111	13	4,422	63
ICS and LABA	587	14	10	1	3	1	20	2	620	9
LABA	1,493	37	89	5	97	33	20	2	1,699	24
SABD	3,954	97	1,630	90	267	92	666	79	6,517	93
Nebuliser	485	12	119	7	17	6	28	3	649	9
Oral Steroids	2,154	53	585	32	84	29	161	19	2,984	42
Oxygen	128	3	46	3	9	3	13	2	196	3
Tiotropium	226	6	22	1	5	2	10	1	263	4
Other	72	2	16	1	2	1	6	1	96	1
Yrs from COPD to end of study										
1	44	1	10	1	0	0	7	1	61	1
2	176	4	120	7	12	4	69	8	377	5
3	546	13	253	14	44	15	165	20	1,008	14
4	774	19	325	18	68	23	187	22	1,354	19
5	749	18	326	18	63	22	138	16	1,276	18
6	584	14	239	13	42	14	98	12	963	14
7	448	11	217	12	30	10	74	9	769	11
8	390	10	168	9	19	7	59	7	636	9
9+	379	9	162	9	12	4	42	5	595	8
Yrs from COPD to therapy start										
1	1,663	41	772	42	77	27	378	45	2,890	41

2	718	18	450	25	88	30	208	25	1,464	21
3	618	15	276	15	48	17	127	15	1,069	15
4	431	11	157	9	32	11	50	6	670	10
5	279	7	81	4	30	10	41	5	431	6
6	196	5	46	3	8	3	18	2	268	4
7	101	2	22	1	3	1	10	1	136	2
8	65	2	12	1	3	1	5	1	85	1
9	19	0	4	0	1	0	2	0	26	0

Risk of Pneumonia by Drug Class

Covariates	Hazard Ratio	95% Confidence Interval		P Value
Drug Class				
SABD				
ICS/LABA	0.992	0.566	1.739	0.9770
ICS	0.918	0.537	1.569	0.7536
LABA	0.706	0.270	1.843	0.4771
Age				
45-69	Reference			
60-69	1.112	0.681	1.818	0.6706
70-79	1.232	0.753	2.016	0.4068
≥ 80	2.692	1.590	4.556	0.0002
SEX				
Male	Reference			
Female	0.825	0.621	1.095	0.1827
Smoking Status				
Non Smoker	Reference			
Ex Smoker	0.814	0.525	1.262	0.3573
Smoker	0.951	0.633	1.429	0.8087
Unknown	1.413	0.860	2.322	0.1722
Number of Days of COPD from Index				
183-274	Reference			
275-547	0.991	0.629	1.559	0.9672
548-913	1.083	0.674	1.739	0.7415
914-1360	0.915	0.556	1.507	0.7275
>1360	1.020	0.626	1.664	0.9355
Number of GP Visits				
≤8	Reference			
8 to 15	1.234	0.825	1.847	0.3056
>15	1.731	1.166	2.571	0.0065
No of COPD Hospitalizations				
No Hospitalizations	Reference			
	1.496	0.910	2.457	0.1119

History of Pneumonia				
No history of Pneumonia				
	1.606	0.565	4.567	0.3744
Baseline Treatment				
No Use	Reference			
ICS	0.825	0.582	1.168	0.2784
ICS/LABA	1.396	0.841	2.319	0.1969
LABA	0.840	0.570	1.237	0.3770
SABD	0.894	0.507	1.577	0.6990
Nebuliser	1.649	1.101	2.469	0.0151
Oral Steroids	1.080	0.790	1.478	0.6290
Oxygen	1.161	0.559	2.410	0.6890
Tiotropium	0.774	0.301	1.993	0.5961
Comorbidities				
No Disease	Reference			
Anxiety/Depression	1.093	0.674	1.771	0.7183
Asthma	0.847	0.566	1.269	0.4211
Cerebrovascular Disease	1.190	0.481	2.941	0.7064
Congestive Heart Failure	1.034	0.559	1.912	0.9156
Dementia	0.000	0.000	0.000	<.0001
Diabetes	1.344	0.744	2.427	0.3268
Diabetes With Complications	1.048	0.185	5.931	0.9575
Hemiplegia/Paraplegia	2.966	0.566	15.555	0.1984
Lung Cancer	4.997	1.312	19.028	0.0184
Myocardial Infarction	0.399	0.060	2.653	0.3419
Peptic Ulcer	0.251	0.035	1.786	0.1673
Peripheral Vascular Disease	0.526	0.070	3.930	0.5315
Broad Pneumonia	2.338	0.972	5.625	0.0579
Renal Disease	0.000	0.000	0.000	<.0001
Rheumatologic Disease	1.026	0.596	1.765	0.9273
Solid Tumor Met	1.726	0.678	4.398	0.2525
Solid Tumor Non Met	0.000	0.000	0.000	<.0001

Demographic Characteristics of Case Control Analysis: Drug Class 6 Month

Covariates	Cases		Control		Total	
	N	%	N	%	N	%
Gender						
Male	311	51	1,474	52	1,785	51
Female	297	49	1,385	48	1,682	49
Age at Index						
45-59	85	14	379	13	464	13
60-69	132	22	686	24	818	24
70-79	265	44	1,303	46	1,568	45
≥80	126	21	491	17	617	18
Smoking status at COPD index						
Non Smoker	142	23	821	29	963	28
Ex Smoker	156	26	734	26	890	26
Smoker	244	40	1,024	36	1,268	37

Unknown	66	11	280	10	346	10
Number of GP Visits						
0 to 17	123	20	1,045	37	1,168	34
18-30	192	32	914	32	1,106	32
31+	293	48	900	31	1,193	34
No. of COPD Hospitalizations						
≥1	143	24	164	6	307	9
Length of Drug Exposure						
0-6 months						
ICS/LABA	204	34	895	31	1,099	32
ICS	180	30	934	33	1,114	32
LABA	22	4	119	4	141	4
Other	18	3	36	1	54	2
No Respiratory Therapy	66	11	380	13	446	13
SABD	118	19	495	17	613	18
6-12 months						
ICS/LABA	179	29	816	29	995	29
ICS	200	33	966	34	1,166	34
LABA	26	4	119	4	145	4
Other	12	2	28	1	40	1
No Respiratory Therapy	68	11	395	14	463	13
SABD	123	20	535	19	658	19
12-18 months						
ICS/LABA	160	26	740	26	900	26
ICS	214	35	1,001	35	1,215	35
LABA	31	5	109	4	140	4
Other	11	2	30	1	41	1
No Respiratory Therapy	73	12	380	13	453	13
SABD	119	20	599	21	718	21
18-24 months						
ICS/LABA	143	24	652	23	795	23
ICS	229	38	1,069	37	1,298	37
LABA	26	4	95	3	121	3
Other	11	2	32	1	43	1
No Respiratory Therapy	70	12	391	14	461	13
SABD	129	21	620	22	749	22
Comorbidities						
Anxiety/Depression	119	20	351	12	470	14
Asthma	114	19	545	19	659	19
Cerebrovascular Disease	46	8	87	3	133	4
Congestive Heart Failure	97	16	168	6	265	8
Dementia	13	2	24	1	37	1
Diabetes	57	9	225	8	282	8
Diabetes With Complications	8	1	36	1	44	1
Hemiplegia/Paraplegia	5	1	9	0	14	0
Lung Cancer	14	2	10	0	24	1
Moderate/Severe Liver Disease	4	1	2	0	6	0

Myocardial Infarction	25	4	49	2	74	2
Peptic Ulcer	34	6	93	3	127	4
Peripheral Vascular Disease	18	3	42	1	60	2
Renal Disease	20	3	49	2	69	2
Rheumatologic Disease	88	14	399	14	487	14
Solid Tumor/ Non Met	18	3	50	2	68	2
Solid Tumor/Met	29	5	87	3	116	3
Risk of Pneumonia by Drug Class: Case Control (6 Mo)						
Covariate	Odds Ratio	95% Confidence Interval			P Value	
Length of Drug Exposure						
0-6 months						
SABD	Reference					
ICS/LABA	1.106	0.700	1.747	0.6669		
ICS	0.778	0.518	1.169	0.2265		
LABA	0.930	0.452	1.915	0.8442		
Other	1.663	0.747	3.702	0.2126		
No Respiratory Therapy	0.848	0.536	1.343	0.4828		
6-12 months						
SABD	Reference					
ICS/LABA	0.776	0.445	1.354	0.3719		
ICS	0.927	0.590	1.458	0.7440		
LABA	0.625	0.277	1.407	0.2560		
Other	1.003	0.371	2.717	0.9946		
No Respiratory Therapy	0.710	0.443	1.138	0.1553		
12-18 months						
SABD	Reference					
ICS/LABA	1.079	0.613	1.901	0.7922		
ICS	1.333	0.851	2.087	0.2096		
LABA	1.666	0.790	3.512	0.1800		
Other	1.600	0.605	4.233	0.3439		
No Respiratory Therapy	1.331	0.825	2.148	0.2414		
18-24 months						
SABD	Reference					
ICS/LABA	1.155	0.713	1.870	0.5586		
ICS	1.019	0.701	1.481	0.9224		
LABA	1.156	0.560	2.386	0.6949		
Other	1.205	0.496	2.929	0.6811		
No Respiratory Therapy	0.861	0.559	1.325	0.4962		
Smoking Status						
No-Smoker	Reference					
Ex Smoker	1.292	0.981	1.702	0.0683		
Smoker	1.337	1.026	1.740	0.0313		
Unknown	1.298	0.908	1.857	0.1530		
No of COPD Hospitalizations						
No Hospitalization	Reference					
≥1	3.594	2.740	4.715	<0.0001		

No. of GP Visits						
0-17	Reference					
18 to 30	1.455	1.122	1.886	0.0047		
31+	1.867	1.422	2.450	<.0001		
Comorbidities						
No Disease	Reference					
Anxiety/Depression	1.198	0.914	1.571	0.1896		
Asthma	0.753	0.583	0.971	0.0288		
Cerebrovascular Disease	2.060	1.367	3.103	0.0005		
Congestive Heart Failure	2.299	1.697	3.114	<.0001		
Dementia	1.823	0.839	3.961	0.1292		
Diabetes	1.001	0.710	1.410	0.9957		
Lung Cancer	5.705	2.378	13.688	<.0001		
Myocardial Infarction	2.144	1.245	3.693	0.0059		
Peptic Ulcer	1.193	0.756	1.882	0.4494		
Peripheral Vascular Disease	1.855	0.994	3.461	0.0524		
Renal Disease	1.246	0.699	2.223	0.4562		
Rheumatologic Disease	0.810	0.611	1.075	0.1450		
Solid Tumor/ Met	1.099	0.673	1.795	0.7066		
Solid Tumor/ Non Met	1.351	0.704	2.591	0.3655		
Descriptive Characteristics for the Case Control Analysis: Drug Product (6 mo)						
Covariate	Cases		Control		Total	
	N	%	N	%	N	%
Gender						
Female	297	49	1,385	48	1,682	49
Male	311	51	1,474	52	1,785	51
Age at Index						
45-59	85	14	383	13	468	13
60-69	132	22	689	24	821	24
70-79	265	44	1,298	45	1,563	45
≥80	126	21	489	17	615	18
Smoking status at COPD index						
Non-Smoker	142	23	861	30	1,003	29
Ex Smoker	156	26	721	25	877	25
Smoker	244	40	1,010	35	1,254	36
Unknown	66	11	267	9	333	10
Number of GP Visits						
0 to 17	123	20	1,059	37	1,182	34
18-30	192	32	909	32	1,101	32
31+	293	48	891	31	1,184	34
No. of COPD Hospitalizations						
≥1	143	24	154	5	297	9
Length of Drug Exposure						
0-6 months						
Seretide	111	18	423	15	534	15
Other ICS/LABA	93	15	461	16	554	16
Fluticasone Propionate	21	3	82	3	103	3

Other ICS	159	26	834	29	993	29
Salmeterol	14	2	83	3	97	3
Other LABA	8	1	31	1	39	1
Other	18	3	47	2	65	2
No Respiratory Therapy	66	11	372	13	438	13
SABD	118	19	526	18	644	19
6-12 months						
Seretide	89	15	353	12	442	13
Other ICS/LABA	90	15	443	15	533	15
Fluticasone Propionate	22	4	78	3	100	3
Other ICS	178	29	867	30	1,045	30
Salmeterol	19	3	91	3	110	3
Other LABA	7	1	29	1	36	1
Other	12	2	38	1	50	1
No Respiratory Therapy	68	11	378	13	446	13
SABD	123	20	582	20	705	20
12-18 months						
Seretide	77	13	292	10	369	11
Other ICS/LABA	83	14	426	15	509	15
Fluticasone Propionate	23	4	85	3	108	3
Other ICS	191	31	930	33	1,121	32
Salmeterol	25	4	79	3	104	3
Other LABA	6	1	22	1	28	1
Other	11	2	34	1	45	1
No Respiratory Therapy	73	12	374	13	447	13
SABD	119	20	617	22	736	21
18-24 months						
Seretide	71	12	248	9	319	9
Other ICS/LABA	72	12	378	13	450	13
Fluticasone Propionate	21	3	86	3	107	3
Other ICS	208	34	993	35	1,201	35
Salmeterol	21	3	76	3	97	3
Other LABA	5	1	20	1	25	1
Other	11	2	38	1	49	1
No Respiratory Therapy	70	12	369	13	439	13
SABD	129	21	651	23	780	22
Comorbidities						
Anxiety/Depression	119	20	379	13	498	14
Asthma	114	19	557	19	671	19
Cerebrovascular Disease	46	8	93	3	139	4
Congestive Heart Failure	97	16	159	6	256	7
Dementia	13	2	22	1	35	1
Diabetes	57	9	241	8	298	9
Diabetes With Complications	8	1	36	1	44	1
Hemiplegia/Paraplegia	5	1	4	0	9	0
Lung Cancer	14	2	11	0	25	1
Moderate/Severe Liver Disease	4	1	6	0	10	0
Myocardial Infarction	25	4	56	2	81	2
Peptic Ulcer	34	6	89	3	123	4
Peripheral Vascular Disease	18	3	53	2	71	2
Renal Disease	20	3	44	2	64	2

Rheumatologic Disease	88	14	417	15	505	15
Solid Tumor/ Non Met	18	3	47	2	65	2
Solid Tumor/Met	29	5	97	3	126	4

Risk of Pneumonia by Dug Product: Case Control Analysis

Covariate	Odds Ratio	95% Confidence Interval		P Value
Length of Drug Exposure				
0-6 months				
SABD	Reference			
Seretide	1.154	0.684	1.946	0.5914
Other ICS/LABA	0.902	0.537	1.514	0.6960
Fluticasone Propionate	0.952	0.368	2.465	0.9191
Other ICS	0.740	0.490	1.119	0.1537
Salmeterol	0.879	0.363	2.126	0.7745
Other LABA	1.163	0.359	3.764	0.8015
Other	1.499	0.642	3.504	0.3495
No Respiratory Therapy	0.790	0.504	1.238	0.3042
6-12 months				
SABD	Reference			
Seretide	0.699	0.353	1.383	0.3042
Other ICS/LABA	0.913	0.490	1.704	0.7760
Fluticasone Propionate	1.160	0.391	3.445	0.7891
Other ICS	1.128	0.719	1.770	0.6006
Salmeterol	0.471	0.172	1.292	0.1436
Other LABA	0.728	0.198	2.678	0.6326
Other	0.783	0.280	2.193	0.6420
No Respiratory Therapy	0.803	0.497	1.297	0.3704
12-18 months				
SABD	Reference			
Seretide	1.114	0.530	2.345	0.7754
Other ICS/LABA	1.030	0.561	1.891	0.9235
Fluticasone Propionate	1.482	0.523	4.200	0.4594
Other ICS	1.181	0.757	1.842	0.4638
Salmeterol	2.567	1.083	6.082	0.0322
Other LABA	0.876	0.234	3.282	0.8444
Other	1.744	0.667	4.561	0.2570
No Respiratory Therapy	1.306	0.804	2.123	0.2813
18-24 months				
SABD	Reference			
Seretide	1.820	0.952	3.479	0.0700
Other ICS/LABA	1.210	0.707	2.071	0.4859
Fluticasone Propionate	0.907	0.362	2.269	0.8344
Other ICS	1.095	0.750	1.599	0.6372
Salmeterol	1.225	0.520	2.885	0.6423
Other LABA	2.415	0.649	8.995	0.1887
Other	1.328	0.544	3.240	0.5336
No Respiratory Therapy	1.072	0.695	1.654	0.7523
Smoking Status				

Non Smoker	Reference			
Ex Smoker	1.379	1.047	1.818	0.0225
Smoker	1.502	1.156	1.951	0.0023
Unknown	1.624	1.135	2.325	0.0080
No. of GP Visits				
0-17	Reference			
18 to 30	1.529	1.173	1.994	0.0017
31+	1.987	1.515	2.606	<.0001
No. of Hospitalizations				
No Hospitalizations	Reference			
≥1	3.779	2.858	4.995	<.0001
Comorbidities				
No Disease	Reference			
Anxiety/Depression	1.164	0.891	1.521	0.2662
Asthma	0.819	0.635	1.058	0.1260
Cerebrovascular Disease	2.158	1.429	3.260	0.0003
Congestive Heart Failure	2.561	1.870	3.505	<.0001
Dementia	1.925	0.863	4.291	0.1094
Diabetes	0.901	0.639	1.271	0.5543
Lung Cancer	4.779	2.020	11.311	0.0004
Myocardial Infarction	1.803	1.039	3.129	0.0362
Peptic Ulcer	1.379	0.866	2.195	0.1754
Peripheral Vascular Disease	1.320	0.713	2.442	0.3773
Renal Disease	1.337	0.743	2.408	0.3324
Rheumatologic Disease	0.765	0.578	1.011	0.0601
Solid Tumor/ Non Met	1.492	0.779	2.857	0.2271
Solid Tumor/Met	0.949	0.588	1.532	0.8294
Results of Average Daily Dose Analysis				
Average Daily Dose of ICS	OR*	95% CI		P value
6 months				
Low	1.00	0.27	3.65	0.99
Medium	0.90	0.25	3.30	0.88
High	1.38	0.39	4.89	0.62
1 year				
Low	0.52	0.28	0.96	0.04
Medium	0.45	0.25	0.83	0.01
High	0.71	0.41	1.23	0.22
*reference group are the "very low" exposure				
Results of Average Daily Dose Analysis				
Average Daily Dose of FP	OR*	95% CI		P value
Prior 6 months				
150-250 mcg	1.26	0.37	4.29	0.71
250-500 mcg	1.00	0.38	2.61	1.00
500-750 mcg	1.04	0.43	2.50	0.93

750-1300 mcg	1.18	0.46	3.01	0.73
1300+ mcg	1.26	0.53	2.96	0.60
Prior 1 year				
150-250 mcg	1.04	0.42	2.60	0.94
250-500 mcg	0.91	0.39	2.13	0.82
500-825 mcg	1.29	0.57	2.93	0.54
825-1225 mcg	1.53	0.65	3.65	0.33
1225+ mcg	1.03	0.33	3.16	0.96
*reference group are the “1 – 150 mcg” exposure group. Patients with FP exposure only in the time period of interest were included in these analyses.				
Conclusion:				
In this analyses of a large, population-based COPD cohort from the UK, no significant increases in pneumonia incidence were observed to be associated with ICS use, with or without LABA, relative to SABD use. Further, in the case control analyses current ICS exposure compared with SABD was not associated with a significant increased pneumonia risk. Finally, no dose response relationship between average daily dose exposure to ICS or FP and increased pneumonia risk was detected.				
Publications: No publication				

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