

Supplementary Table S1. Univariate analysis of demographic and clinical characteristics in 'Under 5s' cohort

Characteristic	N	100 person-years	Rate (95% CI) per 100 person years	Crude IRR (95% CI)
Gender				
Male	4997	111	45 (42.8-47.4)	Ref
Female	2577	66	39.2 (36.4-42.2)	0.84 (0.76-0.92)*
Age cat (years)				
1-1.9	884	20	43.9 (38-50.9)	Ref
2-2.9	3026	62	48.7 (45.4-52.3)	1.09 (0.9-1.32)"
3-3.9	2694	64	42.3 (39.6-45.2)	0.93 (0.77-1.13)"
4-4.9	970	31	31.5 (29-34.3)	0.6 (0.49-0.73)*
IMD				
1	1227	36	33.7 (30.7-37.2)	Ref
2	1550	34	45.3 (41-50.1)	1.26 (1.09-1.46)*
3	1306	31	42.3 (38.6-46.5)	1.23 (1.06-1.44)^
4	1744	38	45.7 (42-49.7)	1.3 (1.13-1.5)*
5	1743	37	47.3 (43.3-51.9)	1.3 (1.13-1.5)*
BMI				
Normal	3903	81	48.5 (45.9-51.4)	Ref
Overweight	483	10	47.7 (40.9-55.8)	1.06 (0.88-1.27)"
Obese	275	6	45 (37.3-54.8)	0.97 (0.77-1.22)"
Underweight	633	8	77.9 (66.2-92.3)	1.45 (1.19-1.78)*
BTS step				
BTS 1	1123	56	20.2 (18.4-22.2)	Ref
BTS 2	2808	68	41.3 (38.7-44.2)	2.17 (1.93-2.44)*
BTS 3	829	10	85.7 (75.6-97.7)	4.57 (3.76-5.55)*
BTS 4	1552	21	75.3 (68.4-83)	3.86 (3.33-4.47)*
BTS 5	88	1	106 (69-171.7)	4.36 (2.54-7.46)*
BTS 6	5	0	31.89 (13.27-76.6)	13.03 (0.58-294.9)"
Non BTS	277	5	55.8 (45.6-69.1)	3.04 (2.32-3.98)*
Atopy				
No	4941	129	38.5 (36.6-40.4)	Ref
Yes	2633	48	54.5 (50.7-58.8)	1.33 (1.21-1.47)*
Reflux				
No	7135	169	42.4 (40.6-44.2)	Ref
Yes	439	8	52.2 (43.4-63.3)	1.12 (0.9-1.38)"
Anxiety				
No	7416	174	42.6 (40.9-44.5)	Ref
Yes	158	3	56.9 (39.8-84.1)	1.22 (0.87-1.72)"
Season				
Winter	2018	9	219.3 (209.9-229)	Ref
Spring	1900	8	243.1 (232.4-254.3)	1.11 (1.1-1.12)*
Summer	1348	6	218.3 (207-230.3)	1.09 (1.08-1.1)*
Autumn	2308	11	206.6 (198.4-215.2)	1 (0.99-1.01)"

N exacerbations; rate: per 100 person years; p-values: * $p < 0.001$, ^ $p < 0.05$, “ $p > 0.05$; IMD, 1 is least deprived

Supplementary Table S2. Univariate analysis of demographic and clinical characteristics in '5 – 17s' cohort

Characteristic	N	100 person-years	Rate (95% CI) per 100 person years	Crude IRR (95% CI)
Gender				
Male	22772	1555	14.7 (14.3-15.1)	Ref
Female	17198	1141	15.1 (14.6-15.7)	1 (0.95-1.04)"
Age cat (years)				
5-7	14755	772	19.2 (18.4-20)	Ref
8-10	12393	830	15 (14.3-15.7)	0.75 (0.71-0.79)*
11-13	8807	743	11.9 (11.4-12.5)	0.58 (0.55-0.62)*
14-17	4015	352	11.5 (10.8-12.1)	0.51 (0.48-0.54)*
IMD				
1	7827	624	12.6 (11.9-13.3)	Ref
2	7957	557	14.3 (13.6-15.1)	1.13 (1.06-1.21)*
3	7508	501	15 (14.2-15.9)	1.2 (1.12-1.28)*
4	8405	535	15.8 (15-16.6)	1.23 (1.15-1.32)*
5	8255	478	17.3 (16.4-18.3)	1.39 (1.3-1.49)*
Smoking				
Never	33471	2154	15.6 (15.2-16)	Ref
Current	856	64	13.4 (12.2-14.9)	0.96 (0.85-1.08)"
Ex	368	22	16.9 (13.8-20.9)	1.18 (0.97-1.43)"
BMI				
Normal	11209	709	15.9 (15.2-16.6)	Ref
Overweight	3232	186	17.4 (16.1-19)	1.15 (1.06-1.25)*
Obese	2251	126	18 (16.4-19.7)	1.13 (1.02-1.24)^
Underweight	16256	913	17.9 (17.1-18.6)	1.2 (1.14-1.27)*
BTS step				
BTS 1	8196	11000	7.3 (6.9-7.7)	Ref
BTS 2	11301	8000	14.1 (13.6-14.6)	2.05 (1.95-2.16)*
BTS 3	2740	1100	25.1 (23-27.6)	3.37 (3.07-3.71)*
BTS 4	10732	4200	25.3 (24.1-26.6)	3.76 (3.54-4)*
BTS 5	1858	359	51.8 (45.7-58.8)	7.21 (6.18-8.41)*
BTS 6	387	7	563.6 (424-772.1)	60.71 (23.13-159.36)*
Non BTS	1793	577	31.1 (27.5-35.2)	4.45 (3.93-5.04)*
Atopy				
No	24132	1824	13.3 (12.9-13.7)	Ref
Yes	15838	873	18.2 (17.5-18.9)	1.36 (1.3-1.42)*
Reflux				
No	38493	2637	14.6 (14.3-15)	Ref
Yes	1477	59	25.1 (21.1-30)	1.59 (1.39-1.83)*
Anxiety				
No	37510	2554	14.7 (14.4-15.1)	Ref
Yes	2460	143	17.3 (15.5-19.3)	1.09 (1-1.2)"

Depression				
No	38790	2636	14.8 (14.4-15.1)	Ref
Yes	1180	60	19.6 (17.2-22.5)	1.18 (1.03-1.34)^
COPD				
No	39781	2688	0 (0-0)	Ref
Yes	189	8	0 (0-0)	1.4 (0.97-2.02)"
Season				
Winter	10430	145	71.9 (70.6-73.3)	Ref
Spring	9877	126	78.2 (76.7-79.7)	1.12 (1.08-1.16)*
Summer	8589	113	76.2 (74.6-77.9)	1.08 (1.04-1.12)*
Autumn	11074	146	76 (74.6-77.4)	1.02 (0.99-1.05)"

N exacerbations; rate: per 100 person years; p-values: * p<0.001, ^ p<0.05, "p>0.05; IMD, 1 is least deprived

Supplementary Table S3. Univariate analysis of demographic and clinical characteristics in '18 – 54s' cohort

Characteristic	N	100 person-years	Rate (95% CI) per 100 person years	Crude IRR (95% CI)
Gender				
Male	76254	3351	22.8 (22.3-23.3)	Ref
Female	168823	4240	39.9 (39.3-40.4)	1.67 (1.64-1.71)*
Age cat (years)				
18-24	28503	1334	21.4 (20.8-22)	Ref
25-34	57976	2115	27.5 (26.9-28.1)	1.22 (1.19-1.26)*
35-44	91169	2637	34.6 (33.9-35.3)	1.51 (1.47-1.55)*
45-54	67429	1505	44.9 (43.8-45.9)	1.97 (1.91-2.03)*
IMD				
1	39105	1729	22.7 (22.1-23.3)	Ref
2	46958	1648	28.6 (27.8-29.3)	1.23 (1.19-1.27)*
3	47393	1473	32.2 (31.4-33.1)	1.39 (1.35-1.44)*
4	55104	1497	36.9 (35.9-37.8)	1.58 (1.53-1.62)*
5	56391	1239	45.6 (44.5-46.7)	1.93 (1.87-1.99)*
Smoking				
Never	100753	3822	26.4 (25.9-26.9)	Ref
Current	80844	1933	41.9 (41-42.7)	1.57 (1.54-1.61)*
Ex	63469	1829	34.8 (34-35.6)	1.32 (1.29-1.35)*
BMI				
Normal	69182	2501	27.7 (27.1-28.3)	Ref
Overweight	66585	2161	30.9 (30.2-31.5)	1.12 (1.1-1.15)*
Obese	89918	1958	46 (45.1-46.9)	1.63 (1.59-1.67)*
Underweight	5084	136	37.4 (34-41.3)	1.33 (1.24-1.42)*
BTS step				
BTS 1	62730	35000	18.2 (17.8-18.6)	Ref
BTS 2	50228	18000	27.9 (27.4-28.5)	1.51 (1.47-1.55)*
BTS 3	24359	6400	38.8 (37.5-40.1)	2.05 (1.99-2.12)*
BTS 4	54192	11000	51.6 (50.3-52.9)	2.68 (2.61-2.75)*
BTS 5	39217	4900	80.7 (78.4-83.1)	4.1 (3.96-4.25)*
BTS 6	8450	200	421.3 (391.7-453.6)	20.88 (18.17-23.98)*
Non BTS	5369	798	69 (63.2-75.5)	3.54 (3.27-3.82)*
Atopy				
No	167639	5544	30.3 (29.9-30.7)	Ref
Yes	77438	2047	37.9 (37.1-38.7)	1.21 (1.18-1.23)*
Reflux				
No	208090	6939	30 (29.7-30.4)	Ref
Yes	36987	652	56.8 (54.9-58.8)	1.78 (1.72-1.84)*
Anxiety				
No	187540	6339	29.6 (29.2-30)	Ref
Yes	57537	1252	46 (44.9-47.2)	1.5 (1.46-1.54)*
Depression				

No	163724	5928	27.7 (27.3-28.1)	Ref
Yes	81353	1663	49 (48-50)	1.71 (1.68-1.75)*
COPD				
No	227779	7443	30.7 (30.3-31)	Ref
Yes	17298	148	116.9 (111.5-122.6)	3.4 (3.21-3.6)*
Season				
Winter	65630	817	80.3 (79.7-80.9)	Ref
Spring	59958	691	86.8 (86.1-87.5)	1.1 (1.09-1.12)*
Summer	56396	646	87.3 (86.5-88)	1.07 (1.06-1.09)*
Autumn	63093	757	83.4 (82.7-84)	1 (0.98-1.01)"

N exacerbations; rate: per 100 person years; p-values: * p<0.001, ^ p<0.05, "p>0.05; IMD, 1 is least deprived

Supplementary Table S4. Univariate analysis of demographic and clinical characteristics in '55+' cohort

Characteristic	N	100 person-years	Rate (95% CI) per 100 person years	Crude IRR (95% CI)
Gender				
Male	161258	1845	87.5 (85.8-89.2)	Ref
Female	273771	2785	98.3 (96.8-99.9)	1.11 (1.09-1.13)*
Age cat (years)				
55-64	151439	2012	75.3 (73.8-76.8)	Ref
65-74	161024	1576	102.2 (100.2-104.3)	1.36 (1.33-1.39)*
75-84	103650	869	119.3 (116.3-122.4)	1.63 (1.59-1.68)*
85+	18916	173	109.3 (103.6-115.3)	1.64 (1.57-1.71)*
IMD				
1	82641	1042	79.4 (77.1-81.7)	Ref
2	101774	1119	91 (88.8-93.3)	1.13 (1.1-1.16)*
3	89705	942	95.3 (92.7-97.9)	1.19 (1.16-1.23)*
4	84986	847	100.4 (97.7-103.1)	1.23 (1.2-1.27)*
5	75663	676	111.9 (108.8-115.1)	1.36 (1.32-1.41)*
Smoking				
Never	141855	1817	78.1 (76.5-79.9)	Ref
Current	64605	580	111.5 (108.3-114.8)	1.37 (1.33-1.41)*
Ex	228533	2233	102.4 (100.7-104.1)	1.29 (1.26-1.31)*
BMI				
Normal	114822	1189	96.6 (94.3-99.1)	Ref
Overweight	151104	1666	90.7 (88.9-92.6)	0.91 (0.89-0.94)*
Obese	144957	1521	95.3 (93.5-97.3)	0.96 (0.93-0.98)*
Underweight	9407	67	140.2 (129.1-152.5)	1.49 (1.39-1.6)*
BTS step				
BTS 1	55299	1100	50.1 (48.4-52)	Ref
BTS 2	64519	978	66 (64.1-68)	1.28 (1.24-1.31)*
BTS 3	43565	511	85.3 (82.5-88.2)	1.63 (1.58-1.69)*
BTS 4	110858	1000	108.3 (105.9-110.8)	2.06 (2-2.11)*
BTS 5	103228	778	132.7 (130-135.5)	2.47 (2.4-2.55)*
BTS 6	35276	59	601.9 (579.7-625.2)	11.52 (10.71-12.38)*
Non BTS	20206	167	120.7 (114.3-127.5)	2.25 (2.14-2.36)*
Atopy				
No	321078	3507	91.6 (90.3-92.9)	Ref
Yes	113951	1123	101.5 (99.1-104)	1.08 (1.05-1.1)*
Reflux				
No	339108	3775	89.9 (88.7-91.1)	Ref
Yes	95921	855	112.3 (109.4-115.2)	1.21 (1.18-1.24)*
Anxiety				
No	342657	3792	90.4 (89.2-91.7)	Ref
Yes	92372	839	110.2 (107.3-113.2)	1.2 (1.17-1.23)*
Depression				

No	329034	3673	89.6 (88.4-90.9)	Ref
Yes	105995	957	110.8 (108.1-113.6)	1.21 (1.19-1.24)*
COPD				
No	304241	3754	81.1 (79.9-82.3)	Ref
Yes	130788	876	149.3 (146.2-152.5)	1.78 (1.74-1.82)*
Season				
Winter	114083	866	131.7 (130.9-132.4)	Ref
Spring	112214	765	146.6 (145.7-147.5)	1.11 (1.10-1.12)*
Summer	102679	671	152.9 (152-153.9)	1.09 (1.08-1.10)*
Autumn	106053	749	141.6 (140.8-142.5)	1.00 (0.99-1.01)''

N exacerbations; rate: per 100 person years; p-values: * p<0.001, ^ p<0.05, ''p>0.05; IMD, 1 is least deprived

Table S5. Median time to first exacerbation by age group and BTS step

	Median time without an exacerbation (years)			
	Under 5s	5-17s	18-54s	55+
BTS 1	> 4	>8.5	>8.5	5.3
BTS 2	> 4	>8.5	5.9	3.4
BTS 3	2.4	7.4	4.4	2.5
BTS 4	2.8	8.4	3.6	2
BTS 5	1.3	3.8	2.1	1.4
BT S6	0.34	0.1	0.2	0.1

Log-rank test $p < 0.001$

Table S6. Sensitivity analysis demonstrating the small change in effect when using a higher prednisolone cut-off dose

55+	350mg cut-off			400mg cut-off		
	IRR	95% CI		IRR	95% CI	
BTS2	1.3	1.2	1.3	1.3	1.2	1.3
BTS3	1.6	1.5	1.6	1.6	1.5	1.6
BTS4	1.9	1.9	2.0	1.9	1.9	2.0
BTS5	2.3	2.2	2.3	2.3	2.2	2.3
BTS6	10.0	9.3	10.7	10.0	9.3	10.8
18 to 54s	350mg cut-off			400mg cut-off		
	IRR	95% CI		IRR	95% CI	
BTS2	1.4	1.4	1.5	1.4	1.4	1.5
BTS3	1.9	1.8	2.0	1.9	1.8	2.0
BTS4	2.4	2.3	2.5	2.4	2.3	2.5
BTS5	3.4	3.3	3.5	3.4	3.3	3.5
BTS6	16.1	14.1	18.3	16.5	14.5	18.9
5 to 17s	350mg cut-off			400mg cut-off		
	IRR	95% CI		IRR	95% CI	
BTS2	1.8	1.7	2.0	1.8	1.7	2.0
BTS3	3.1	2.8	3.4	3.1	2.8	3.4
BTS4	3.3	3.1	3.6	3.3	3.1	3.6
BTS5	6.3	5.3	7.4	6.3	5.3	7.4
BTS6	56.3	22.5	140.7	57.5	23.1	143.5

Results should be compared to figure 4 which used a 300mg cut-off for patients aged ≥ 5 years old.