

Online Supplement

Online Supplement 1: Definition of demographic and clinical outcomes in the OPCR

Variable	Description	Ascertainment Period
Exposures		
Socioeconomic Status	Assessed using quintiles of the 2011 Indices of Multiple Deprivation based on the location of the patient's general practice.	N/A
Outcomes		
Asthma Exacerbation	Read code indicating an 'Asthma Exacerbation' or 'Asthma Attack, prescription of acute oral corticosteroids (OCS), or a lower respiratory infection requiring antibiotics. We applied an algorithm based on number of days medication given, strength of tablet, diagnosis codes recorded during the prescribing visit, dosing instruction and frequency of OCS prescription to differentiate maintenance and acute OCS use. OCS prescribed during annual asthma reviews were excluded.	1 year from start of FUP
Asthma Review	Read code list recognised within the NHS Quality and Outcomes Framework: Asthma annual review (Read code: Xaleq), Asthma follow-up (Xaler), Asthma monitoring by nurse (Xalu5), Asthma monitoring by doctor (Xalu6), Asthma medication review (Xalfk) or Asthma monitoring check done (XE2Nb).	1 year from start of FUP
Blood Eosinophil Count	Blood eosinophil count measured in cells per litre ($10^9/L$).	1 year from start of FUP Last measurement recorded
Peak Flow	Percent predicted values were calculated using raw measurements and the formula specified by Knudson et al. ²⁸ We used a percent predicted peak flow value recorded directly in the medical records when no raw peak flow measure was available, or when the patient's height was unavailable.	1 year from start of FUP
Respiratory Referral	Patient has been reviewed by, or received a referral to, a respiratory specialist using a list of Read codes employed previously. ²⁹	1 year from start of FUP
Treatment Adherence	Assessed using the fixed medications possession ratio of inhaled corticosteroids during the exposure period. Good adherence was defined as an MPR of greater than or equal to 70%. Medication quantity and dosing instructions were imputed using the most common for that medication (by Read Code) when insufficient information was recorded in the primary care record. When the patient received more than one type of ICS prescription, we averaged the MPR across all relevant medications.	1 year from start of FUP
Uncontrolled Disease	Measured using the Royal College of Physicians 3 questions ³⁰ . Patients were classified as having poor control if 2 or 3 of the measures denote poor control	1 year from start of FUP

or if patients experience difficulty sleeping because of their asthma symptoms.

Covariates		
Alcohol Consumption	Using Read Codes and measured as units per week.	Last record before start of FUP
Atopic Asthma	Record of hay fever or eczema. ⁵⁷	Beginning of medical record to start of FUP
Body Mass Index	Using Read Codes and measured in kg/m ² .	Last record before start of FUP
Comorbidities	A large list of comorbidities were extracted including those comprising Charleston comorbidity score ³¹ , depression ³² , and those related to corticosteroid morbidity. ³³ Comorbidities with low prevalence (e.g. AIDs) were excluded and some categories were combined (e.g. mild/moderate liver disease was combined with severe liver disease to form a single category).	3 years before start of FUP
Ethnicity	Using Read codes which were assigned to UK census categories using code-lists employed elsewhere. ⁵⁸ In subgroup analysis ethnicity was dichotomised into White and Ethnic Minority Groups (comprising Asian, Black, Mixed, Other)	Entire Medical Record
Sex	Reported by the general practice for all patients	N/A
Smoking Status	Using Read Codes and categorised as Non-smoker, Current smoker, Ex-smoker.	Last record before start of FUP
Treatment Step	Asthma medications were identified using Read/SNOMED hierarchies, and patients were categorised according to GINA 2018 treatment step. ³⁴ Combination therapies (e.g. ICS/LABA, ICS/LABA/LAMA) were broken into their constituent parts and ICS dose was converted to a BDP equivalent. ³⁵ Step five was defined as more than 6 prescriptions of OCS in a year, spanning across at least two quarters. ³⁶	1 year before start of FUP
Year of birth	Reported by the general practice for all patients	N/A

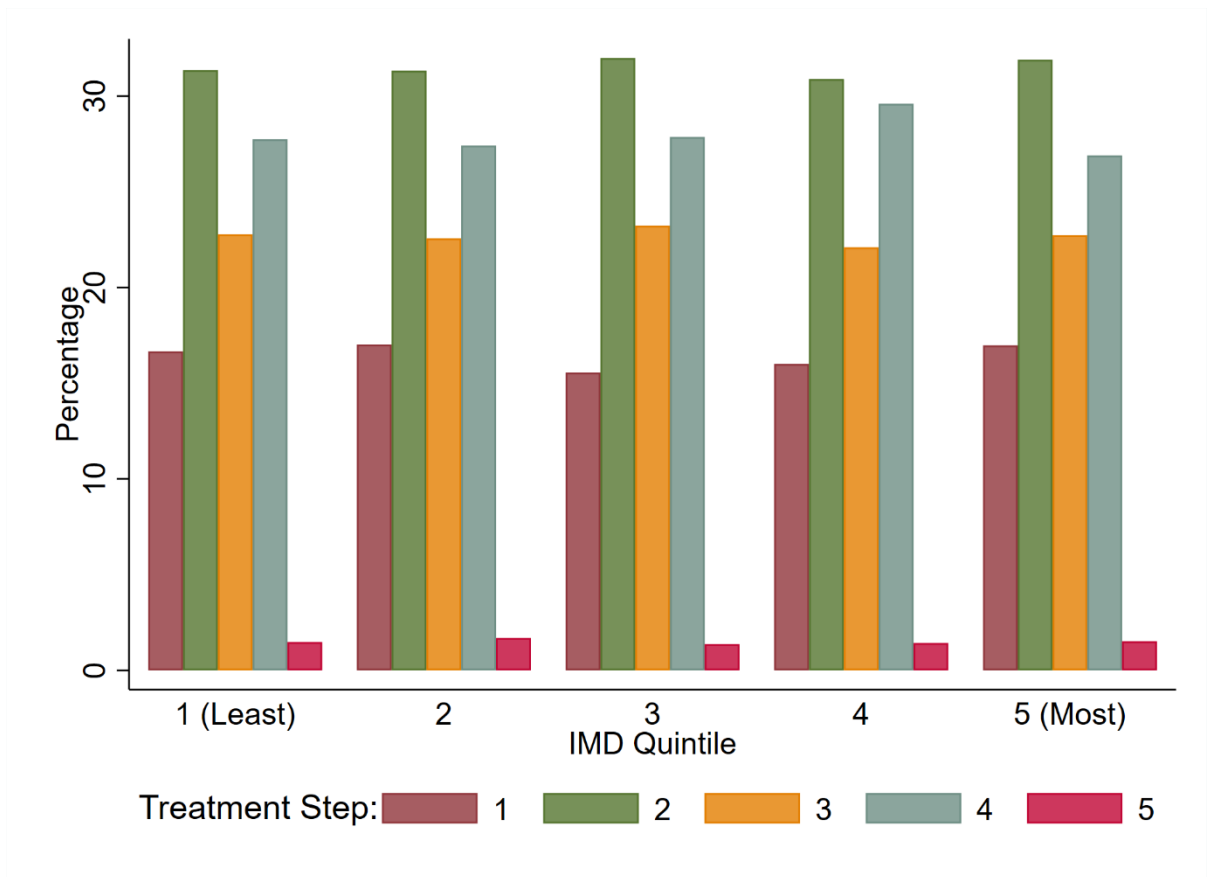
Online Supplement 2: Summary of asthma treatments by GINA (2018) Step^a

GINA (2018) treatment step	Asthma treatment
Step 1	only β -muscarinic antagonist OR only muscarinic agonist
Step 2	Low dose ICS without other controllers OR LTRA without other controllers OR Low dose theophylline all without other controllers
Step 3	Medium or high dose ICS without other controllers OR Low dose ICS/LABA OR Low dose ICS/LAMA OR Low dose ICS (without LABA/LAMA) and/or theophylline OR LABA and/or LAMA (without ICS) OR LTRA plus theophylline (without ICS)
Step 4	Medium or high dose ICS/LABA OR Medium or high dose ICS/LAMA OR Medium or high dose ICS plus LTRA and/or theophylline OR ≥ 3 controllers (without ICS)
Step 5	Maintenance OCS plus any other asthma treatment

^aICS: inhaled corticosteroid; LABA: long-acting $\beta 2$ -agonist; LAMA: long-acting muscarinic antagonist; LTRA: leukotriene receptor antagonist; OCS: oral corticosteroid. Low Dose ICS: $\leq 500\mu\text{g}$ Beclomethasone dipropionate [BDP] equivalent, Medium Dose ICS: 501-1000 BDP equivalent, High Dose ICS: >1000 BDP equivalent.

Data from Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, Updated; 2018.³⁴

Online Supplement 3: Treatment step (GINA 2018) by indices of multiple deprivation quintile



Online Supplement 4: Proportion of patients with complete data for variables included within the analysis

Variable	Overall (N [%])	IMD Quintile (N [%])				
		5 (Least Deprived)	4	3	2	1 (Most Deprived)
Exposures						
Socioeconomic Status	127,040 (100.0%)	28,215 (100.0%)	26,900 (100.0%)	24,332 (100.0%)	31,059 (100.0%)	16,534 (100.0%)
Outcomes						
Asthma Exacerbations	127,040 (100.0%)	28,215 (100.0%)	26,900 (100.0%)	24,332 (100.0%)	31,059 (100.0%)	16,534 (100.0%)
Asthma Review	127,040 (100.0%)	28,215 (100.0%)	26,900 (100.0%)	24,332 (100.0%)	31,059 (100.0%)	16,534 (100.0%)
Blood Eosinophil Count	45,761 (36.0%)	9,991 (35.4%)	9,530 (35.4%)	8,571 (35.2%)	11,175 (36.0%)	6,494 (39.3%)
Peak Flow	71,291 (56.1%)	15,227 (54.0%)	15,446 (57.4%)	13,655 (56.1%)	18,003 (58.0%)	8,960 (54.2%)
Respiratory Referral	127,040 (100.0%)	28,215 (100.0%)	26,900 (100.0%)	24,332 (100.0%)	31,059 (100.0%)	16,534 (100.0%)
Treatment Adherence	102,712 (80.9%)	23,107 (81.9%)	21,697 (80.7%)	19,660 (80.8%)	25,026 (80.6%)	13,222 (80.0%)
Uncontrolled Disease	40,078 (31.5%)	9,345 (33.1%)	8,471 (31.5%)	7,221 (29.7%)	10,299 (33.2%)	4,742 (28.7%)
Covariates						
Alcohol Consumption	69,202 (54.5%)	14,739 (52.2%)	14,542 (54.1%)	13,237 (54.4%)	18,178 (58.5%)	8,506 (51.4%)
Atopic Asthma	127,040 (100.0%)	28,215 (100.0%)	26,900 (100.0%)	24,332 (100.0%)	31,059 (100.0%)	16,534 (100.0%)
Body Mass Index	102,386 (80.6%)	21,533 (76.3%)	21,486 (79.9%)	19,154 (78.7%)	26,096 (84.0%)	14,117 (85.4%)
Comorbidities	127,040 (100.0%)	28,215 (100.0%)	26,900 (100.0%)	24,332 (100.0%)	31,059 (100.0%)	16,534 (100.0%)
Ethnicity	85,616 (67.4%)	18,744 (66.4%)	17,918 (66.6%)	16,396 (67.4%)	21,533 (69.3%)	11,025 (66.7%)
Sex	127,040 (100.0%)	28,215 (100.0%)	26,900 (100.0%)	24,332 (100.0%)	31,059 (100.0%)	16,534 (100.0%)
Smoking Status	122,527 (96.4%)	27,681 (98.1%)	26,150 (97.2%)	22,698 (93.3%)	30,390 (97.8%)	15,608 (94.4%)
Treatment Step	103,518 (81.5%)	23,138 (82.0%)	21,770 (80.9%)	19,966 (82.1%)	25,400 (81.8%)	13,244 (80.1%)
Year of Birth	127,040 (100.0%)	28,215 (100.0%)	26,900 (100.0%)	24,332 (100.0%)	31,059 (100.0%)	16,534 (100.0%)

Online Supplement 5: Comparison of demographic and clinical information by indices of multiple deprivation restricted to patients from ethnic minority groups

	5 (Least Deprived)	4	3	2	1 (Most Deprived)	P-value
Number Patients	476	958	619	1,016	1,288	
Age (years)	49.8 (16.2)	46.1 (15.2)	46.4 (16.4)	48.9 (17.1)	47.8 (16.1)	<0.001
<35	93 (19.5%)	246 (25.7%)	176 (28.4%)	241 (23.7%)	314 (24.4%)	
35-54	215 (45.2%)	466 (48.6%)	254 (41.0%)	416 (40.9%)	567 (44.0%)	
55-74	132 (27.7%)	200 (20.9%)	152 (24.6%)	273 (26.9%)	312 (24.2%)	
75+	36 (7.6%)	46 (4.8%)	37 (6.0%)	86 (8.5%)	95 (7.4%)	
Sex						0.739
Female	269 (56.5%)	547 (57.1%)	346 (55.9%)	584 (57.5%)	759 (58.9%)	
Male	207 (43.5%)	411 (42.9%)	273 (44.1%)	432 (42.5%)	529 (41.1%)	
Ethnicity						<0.001
Asian	304 (63.9%)	710 (74.1%)	449 (72.5%)	769 (75.7%)	933 (72.4%)	
Black	45 (9.5%)	104 (10.9%)	61 (9.9%)	143 (14.1%)	185 (14.4%)	
Mixed	48 (10.1%)	78 (8.1%)	59 (9.5%)	57 (5.6%)	55 (4.3%)	
Other	79 (16.6%)	66 (6.9%)	50 (8.1%)	47 (4.6%)	115 (8.9%)	
BMI (kg/m²)	27.7 (5.7)	27.3 (5.7)	27.5 (5.6)	28.2 (5.8)	28.7 (6.0)	<0.001
Alcohol Consumption (Weekly Units)	1.0 (0.0,5.0)	0.0 (0.0,2.0)	0.0 (0.0,2.0)	0.0 (0.0,0.0)	0.0 (0.0,0.0)	<0.001
Smoking Status						0.114
Never-Smoker	356 (75.3%)	738 (77.8%)	443 (74.3%)	757 (74.9%)	967 (75.3%)	
Ex-Smoker	79 (16.7%)	115 (12.1%)	83 (13.9%)	137 (13.6%)	162 (12.6%)	
Current Smoker	38 (8.0%)	96 (10.1%)	70 (11.7%)	117 (11.6%)	155 (12.1%)	
Comorbidities						
Allergic rhinitis	71 (14.9%)	210 (21.9%)	92 (14.9%)	184 (18.1%)	250 (19.4%)	0.001
Cancer	34 (7.1%)	69 (7.2%)	44 (7.1%)	73 (7.2%)	87 (6.8%)	0.993
Cataract	11 (2.3%)	19 (2.0%)	19 (3.1%)	35 (3.4%)	31 (2.4%)	0.279
Cerebrovascular disease	10 (2.1%)	11 (1.1%)	6 (1.0%)	17 (1.7%)	23 (1.8%)	0.416
Congestive heart disease	5 (1.1%)	7 (0.7%)	6 (1.0%)	10 (1.0%)	16 (1.2%)	0.832
Depression/Anxiety	47 (9.9%)	76 (7.9%)	48 (7.8%)	116 (11.4%)	109 (8.5%)	0.033
Diabetes	61 (12.8%)	109 (11.4%)	88 (14.2%)	191 (18.8%)	213 (16.5%)	<0.001
Eczema	53 (11.1%)	157 (16.4%)	79 (12.8%)	159 (15.6%)	204 (15.8%)	0.033
Glaucoma	6 (1.3%)	10 (1.0%)	9 (1.5%)	13 (1.3%)	17 (1.3%)	0.965
Hypertension	62 (13.0%)	126 (13.2%)	68 (11.0%)	154 (15.2%)	140 (10.9%)	0.023
Insomnia	7 (1.5%)	21 (2.2%)	12 (1.9%)	37 (3.6%)	40 (3.1%)	0.053

Liver Disease	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (0.5%)	1 (0.1%)	0.014
Myocardial infarction	5 (1.1%)	1 (0.1%)	3 (0.5%)	6 (0.6%)	9 (0.7%)	0.181
Nasal polyps	7 (1.5%)	7 (0.7%)	4 (0.6%)	8 (0.8%)	15 (1.2%)	0.491
Oral candidiasis	7 (1.5%)	9 (0.9%)	13 (2.1%)	23 (2.3%)	30 (2.3%)	0.116
Osteoporosis	6 (1.3%)	11 (1.1%)	3 (0.5%)	13 (1.3%)	15 (1.2%)	0.621
Renal disease	9 (1.9%)	24 (2.5%)	12 (1.9%)	42 (4.1%)	36 (2.8%)	0.041
Rheumatological disease	6 (1.3%)	16 (1.7%)	15 (2.4%)	16 (1.6%)	22 (1.7%)	0.637
Atopic Disease	84 (17.6%)	281 (29.3%)	136 (22.0%)	237 (23.3%)	342 (26.6%)	<0.001
ICS Dose (BDP Equivalent)	500 (400,1000)	400 (400,1000)	500 (400,1000)	400 (400,1000)	400 (400,1000)	<0.001
LTRA	26 (5.5%)	35 (3.7%)	28 (4.5%)	66 (6.5%)	86 (6.7%)	0.013
SABA	402 (84.5%)	809 (84.4%)	532 (85.9%)	816 (80.3%)	1,115 (86.6%)	<0.001
Treatment Step (GINA 2018)						<0.001
1	81 (17.0%)	155 (16.2%)	108 (17.4%)	151 (14.9%)	267 (20.7%)	
2	143 (30.0%)	383 (40.0%)	196 (31.7%)	351 (34.5%)	435 (33.8%)	
3	113 (23.7%)	209 (21.8%)	136 (22.0%)	185 (18.2%)	270 (21.0%)	
4	137 (28.8%)	198 (20.7%)	174 (28.1%)	314 (30.9%)	302 (23.4%)	
5	2 (0.4%)	13 (1.4%)	5 (0.8%)	15 (1.5%)	14 (1.1%)	
Blood Eosinophils (10⁹/L)	0.28 (0.14,0.40)	0.22 (0.14,0.36)	0.27 (0.14,0.40)	0.23 (0.12,0.40)	0.25 (0.15,0.40)	0.140
Peak Flow (%)	85.5 (71.1,97.4)	83.3 (68.3,93.7)	84.4 (69.9,95.8)	78.5 (65.8,90.7)	78.5 (64.3,90.0)	<0.001
Treatment Adherent (MPR≥70%)	100 (25.8%)	158 (20.8%)	114 (22.9%)	224 (28.0%)	270 (28.2%)	0.002
Asthma Review	234 (49.2%)	352 (36.7%)	290 (46.8%)	485 (47.7%)	578 (44.9%)	<0.001
Uncontrolled Disease	65 (40.1%)	125 (47.0%)	132 (48.0%)	253 (54.8%)	233 (54.8%)	0.004
Any Exacerbations	80 (16.8%)	214 (22.3%)	115 (18.6%)	219 (21.6%)	334 (25.9%)	<0.001
Respiratory Referral	14 (2.9%)	29 (3.0%)	18 (2.9%)	58 (5.7%)	69 (5.4%)	0.002

Online Supplement 6: Sensitivity analysis comparing most to least indices of multiple deprivation quintile^a

	Multivariable			Multiple Imputation		+BMI, Smoking Adjustment	
	N	Ratio (95% CI)	P-value	Ratio (95% CI)	P-value	Ratio (95% CI)	P-value
Blood Eosinophils (10 ⁹ /L)	45,761	1.03 (1.00,1.06)	0.022	1.03 (1.01,1.05)	0.001	1.05 (1.02,1.08)	0.001
Peak Flow (%)	71,291	0.95 (0.94,0.97)	<0.001	0.95 (0.94,0.96)	<0.001	0.95 (0.94,0.97)	<0.001
Treatment Adherent	102,712	1.43 (1.17,1.76)	0.001	1.43 (1.21,1.69)	<0.001	1.42 (1.12,1.79)	0.003
Asthma Review	127,040	0.85 (0.55,1.34)	0.491	0.85 (0.55,1.34)	0.491	0.79 (0.49,1.28)	0.337
Respiratory Referral	127,040	1.02 (0.55,1.90)	0.947	1.02 (0.55,1.90)	0.947	0.87 (0.45,1.70)	0.694
Uncontrolled Disease	40,078	1.54 (1.16,2.05)	0.003	1.54 (1.37,1.72)	<0.001	1.39 (1.09,1.79)	0.009
Any Exacerbations	127,040	1.27 (1.13,1.42)	<0.001	1.27 (1.13,1.42)	<0.001	1.20 (1.07,1.35)	0.002

^aAdjusted for year, age (5 year groups) and sex