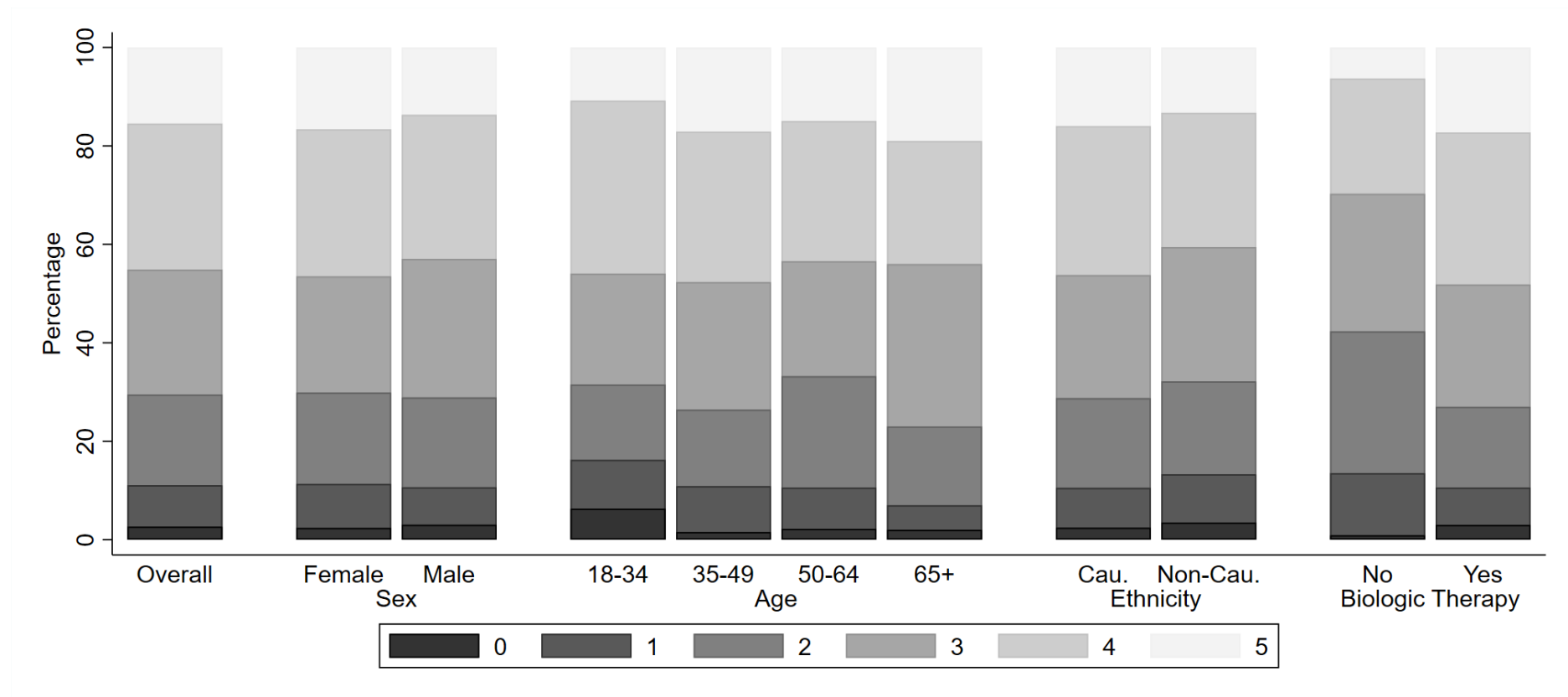


Supplement

Table E1 - Data completeness

Characteristic	Baseline	Follow-up
Age at assessment	1,140 (100%)	N/A
Gender	1,140 (100%)	N/A
Ethnicity	1,136 (99.6%)	N/A
BMI	1,135 (99.6%)	903 (79.2%)
Smoking status	1,116 (97.9%)	N/A
FEV₁	1,124 (98.6%)	955 (83.8%)
FVC	1,113 (97.6%)	911 (79.9%)
FEV₁/FVC	1,113 (97.6%)	910 (79.8%)
ACQ6	987 (86.6%)	929 (81.5%)
Exacerbations (Prior year)	1,120 (98.3%)	1,101 (96.6%)
ED Attendance (Prior year)	1,120 (98.3%)	1,089 (95.5%)
Hospital Admissions (Prior year)	1,127 (98.9%)	1,090 (95.6%)
Blood Eosinophil Count	1,119 (98.2%)	705 (61.8%)
FeNO	898 (78.8%)	583 (51.1%)
IGE	1,100 (96.5%)	N/A
mOCS	1,134 (99.5%)	1,138 (99.8%)
mOCS dose	637 (99.7%)	585 (99.7%)
ICS dose	1,062 (93.2%)	N/A
Biologic Therapy	NA	1,140 (100%)

Figure E1 – Bar chart depicting the representative proportion of patients that achieved improvement across five patient outcomes*



***Outcomes included:** ACQ improvement of 0.5 or greater or Well Controlled (ACQ \leq 0.75), an exacerbation reduction \geq 50% or No Exacerbations, a 50% or greater reduction in unscheduled care (ED attendance/hospitalisation) or No Unscheduled Secondary Care, an FEV₁ increase of 100ml or greater, an OCS dose reduction of 50% or greater (or not receiving OCS at follow-up appointment).

Abbreviation: Cau (Caucasian)

Table E2 – Comparison of specialist referral benefit by demographic factors and biologic treatment status

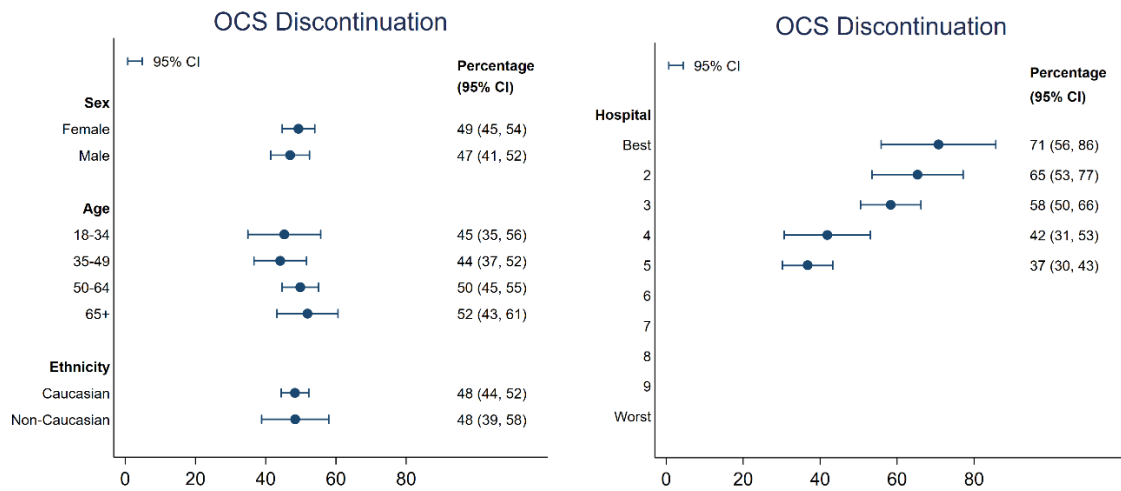
Exposure	ACQ6 Score ^a				Exacerbations ^b			
	Univariate	Multivariate (No biologic)	Multivariate	P- Value	Univariate	Multivariate (No biologic)	Multivariate	P- Value
Sex	N=1079	N=1075	N=1075		N=1140	N=1136	N=1136	
Female	Ref	Ref	Ref	.	Ref	Ref	Ref	.
Male	0.24 (0.06,0.42)	0.24 (0.05,0.42)	0.26 (0.08,0.44)	0.004	0.83 (0.75,0.91)	0.83 (0.75,0.91)	0.84 (0.76,0.93)	0.001
Age At First Assessment (Years) N=1079		N=1075	N=1075		N=1140	N=1136	N=1136	
18-34	Ref	Ref	Ref	.	Ref	Ref	Ref	.
35-49	-0.13 (-0.41,0.15)	-0.13 (-0.41,0.15)	-0.10 (-0.38,0.17)	0.457	0.82 (0.72,0.94)	0.82 (0.72,0.94)	0.83 (0.73,0.95)	0.008
50-64	-0.01 (-0.27,0.25)	-0.01 (-0.27,0.25)	0.02 (-0.23,0.28)	0.850	0.80 (0.71,0.91)	0.80 (0.71,0.91)	0.82 (0.72,0.92)	0.001
65+	0.14 (-0.17,0.45)	0.14 (-0.17,0.45)	0.18 (-0.13,0.48)	0.258	0.63 (0.54,0.75)	0.63 (0.54,0.75)	0.65 (0.55,0.77)	0.000
Ethnicity	N=1075	N=1075	N=1075		N=1136	N=1136	N=1136	
Caucasian	Ref	Ref	Ref	.	Ref	Ref	Ref	.
Non-Caucasian	-0.12 (-0.33,0.10)	-0.12 (-0.33,0.10)	-0.20 (-0.41,0.01)	0.063	1.05 (0.93,1.18)	1.05 (0.93,1.18)	1.02 (0.91,1.15)	0.732

Exposure	Unscheduled Care Use ^b				OCS Discontinuation ^c			
	Univariate	Multivariate (No biologic)	Multivariate	P- Value	Univariate	Multivariate (No biologic)	Multivariate	P- Value
Sex	N=1139	N=1135	N=1135		N=637	N=635	N=635	
Female	Ref	Ref	Ref	.	Ref	Ref	Ref	.
Male	0.94 (0.79,1.12)	0.94 (0.79,1.12)	0.94 (0.79,1.12)	0.489	1.04 (0.69,1.56)	1.07 (0.71,1.62)	1.07 (0.71,1.62)	0.751
Age At First Assessment (Years) N=1139		N=1135	N=1135		N=637	N=635	N=635	
18-34	Ref	Ref	Ref	.	Ref	Ref	Ref	.
35-49	0.70 (0.57,0.85)	0.70 (0.57,0.85)	0.70 (0.58,0.86)	0.001	0.83 (0.41,1.66)	0.81 (0.40,1.63)	0.80 (0.39,1.62)	0.534
50-64	0.53 (0.44,0.65)	0.54 (0.44,0.65)	0.53 (0.44,0.65)	0.000	0.62 (0.33,1.17)	0.62 (0.33,1.19)	0.62 (0.32,1.18)	0.143
65+	0.45 (0.33,0.61)	0.45 (0.33,0.61)	0.46 (0.34,0.62)	0.000	0.68 (0.33,1.43)	0.68 (0.32,1.42)	0.67 (0.32,1.42)	0.297
Ethnicity	N=1135	N=1135	N=1135		N=635	N=635	N=635	
Caucasian	Ref	Ref	Ref	.	Ref	Ref	Ref	.
Non-Caucasian	1.23 (1.03,1.46)	1.23 (1.03,1.46)	1.21 (1.01,1.45)	0.034	0.87 (0.45,1.69)	0.89 (0.45,1.73)	0.90 (0.46,1.77)	0.761

Table E2 Footnote: Univariate analysis adjusts for hospital site, year of baseline assessment and time. Multivariate analysis (no biologic) adjusts for hospital site, year of baseline assessment, time, sex, age and ethnicity. Multivariate analysis adjusts for hospital site, year of baseline assessment, time, sex, age, ethnicity, and biologic therapy. All models included an interaction term between time and the variable of interest.

^a Mean difference; ^b Incidence rate ratio; ^c Odds ratio

Figure E2 – OCS discontinuation, defined as complete withdrawal of OCS or remaining on 5mg or less at annual review, stratified by patient demographic variables and hospital site



*All models are adjusted for sex, age category, ethnicity, biologic therapy, year of baseline assessment, hospital site, and base level of the relevant outcome of interest

**Analysis by site was restricted to hospitals with 30 or more patients per reported outcome.

***The terms best and worst refer to the magnitude of change for each outcome measured and are not consistent across panels.

Abbreviation: OCS (Oral corticosteroids)

Table E3 – Baseline patient characteristics stratified by age group at first assessment

	18-34	35-49	50-64	65+	P-value
Number of Patients	189	300	461	190	
Age At First Assessment (Years)	26.9 (4.6)	43.4 (4.2)	56.5 (4.2)	70.9 (6.9)	<0.001
Age of Onset (Years)	10.5 (8.3)	19.4 (13.6)	29.2 (18.5)	40.5 (22.5)	<0.001
Gender					<0.001
Female	142 (75.1%)	187 (62.3%)	270 (58.6%)	97 (51.1%)	
Male	47 (24.9%)	113 (37.7%)	191 (41.4%)	93 (48.9%)	
Ethnicity					0.007
Caucasian	152 (80.4%)	225 (75.3%)	366 (79.9%)	170 (89.5%)	
Non-Caucasian	37 (19.6%)	74 (24.7%)	92 (20.1%)	20 (10.5%)	
BMI (kg/m2)	29.9 (7.9)	31.1 (7.5)	31.2 (6.9)	29.6 (5.4)	0.013
Smoking Status					<0.001
Never smoked	137 (74.5%)	197 (67.0%)	293 (64.8%)	129 (69.4%)	
Ex-smoker	31 (16.8%)	85 (28.9%)	150 (33.2%)	55 (29.6%)	
Current smoker	16 (8.7%)	12 (4.1%)	9 (2.0%)	2 (1.1%)	
Atopic Disease	143 (75.7%)	187 (63.2%)	224 (49.0%)	74 (40.0%)	<0.001
FEV1 (ml)	2416.6 (801.6)	2159.6 (805.7)	1845.1 (711.5)	1709.3 (621.6)	<0.001
FEV1 (% Predicted)	70.3 (20.5)	67.1 (21.2)	64.3 (21.2)	67.7 (20.1)	0.008
FVC (ml)	3544.8 (934.2)	3348.7 (1061.6)	2979.5 (975.4)	2866.3 (954.6)	<0.001
FVC (% Predicted)	87.7 (16.5)	84.0 (19.1)	82.1 (18.9)	87.1 (19.9)	0.001
FEV1/FVC	67.6 (13.4)	64.7 (13.7)	62.7 (23.6)	60.7 (13.9)	0.002
ACQ6 Score	3.3 (2.3,4.3)	3.2 (2.2,4.2)	3.0 (1.8,3.8)	2.3 (1.3,3.2)	<0.001
Uncontrolled Asthma (ACQ6>1.5)	155 (90.6%)	214 (84.3%)	330 (82.9%)	112 (68.3%)	<0.001
EuroQoL Utility	0.73 (0.46,0.89)	0.74 (0.53,0.89)	0.70 (0.43,0.85)	0.78 (0.51,0.89)	0.483
Exacerbations (Prior Year)	6 (4,10)	5 (3,7)	4 (3,8)	5 (2,6)	<0.001
Any ED Attendance (Prior Year)	104 (55.9%)	129 (43.6%)	148 (33.0%)	54 (28.7%)	<0.001
Any Hospital Admissions (Prior Year)	96 (51.3%)	115 (38.9%)	156 (34.3%)	70 (37.0%)	0.008
Invasive Ventilations (Ever)	31 (16.8%)	31 (10.5%)	47 (10.4%)	8 (4.3%)	0.016
Eczema	11 (5.8%)	7 (2.3%)	6 (1.3%)	3 (1.6%)	0.006
Nasal Polyps	24 (12.7%)	54 (18.0%)	98 (21.3%)	35 (18.4%)	0.086
Gastro-oesophageal Reflux	29 (15.3%)	50 (16.7%)	87 (18.9%)	41 (21.6%)	0.375
Depression or Anxiety	23 (12.2%)	33 (11.0%)	48 (10.4%)	5 (2.6%)	0.004
Blood Eosinophil Count (N/109L)	0.40 (0.20,0.60)	0.41 (0.20,0.70)	0.33 (0.20,0.60)	0.31 (0.15,0.55)	0.009
Highest Blood Eosinophil Count (N/109L)	0.70 (0.40,1.10)	0.70 (0.40,1.18)	0.66 (0.40,1.00)	0.68 (0.44,1.10)	0.578
FeNO (ppb)	49 (21,87)	39 (20,75)	41 (25,69)	38 (19,63)	0.276
IGE (IU/mL)	204 (85,551)	152 (61,432)	147 (47,389)	145 (44,466)	0.013

mOCS	79 (41.8%)	156 (52.3%)	294 (64.2%)	110 (58.2%)	<0.001
mOCS (prednisolone equivalent/mg)	10 (10,20)	10 (10,20)	10 (8,15)	10 (5,10)	<0.001
ICS Dose (BDP equivalent/ug)	2000 (1600,2000)	2000 (1600,2000)	2000 (1600,2000)	2000 (1600,2000)	0.592
LAMA	111 (58.7%)	162 (54.4%)	254 (56.3%)	119 (63.3%)	0.098
Theophylline	45 (23.9%)	69 (23.2%)	129 (28.4%)	36 (18.9%)	0.075
Leukotriene Receptor Antagonists	107 (59.4%)	148 (50.7%)	224 (49.7%)	89 (47.6%)	0.095
Maintenance Macrolides	13 (7.2%)	12 (4.1%)	43 (9.4%)	14 (7.5%)	0.029
Nebuliser	42 (22.6%)	51 (17.0%)	102 (22.8%)	37 (19.8%)	0.029
Biologic Therapy	142 (75.1%)	242 (80.7%)	382 (82.9%)	161 (84.7%)	0.071
Biological Therapy Name					0.048
Mepolizumab	71 (52.6%)	151 (64.0%)	260 (69.9%)	109 (69.4%)	
Benralizumab	32 (23.7%)	49 (20.8%)	63 (16.9%)	33 (21.0%)	
Omalizumab	31 (23.0%)	36 (15.3%)	48 (12.9%)	15 (9.6%)	
Dupilumab	1 (0.7%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	

Footnote: Abbreviations: FEV1 (Forced expiratory volume in the first second), FVC (Forced vital capacity), ACQ6 (Asthma Control Questionnaire 6), ED (Emergency Department), FeNO (Fractional exhaled nitric oxide), IGE (Immunoglobulin E), mOCS (Maintenance oral corticosteroids), ICS (Inhaled corticosteroids), LAMA (Long-acting muscarinic antagonists), SABA (Short-acting beta-agonists)