Table S1. APEX II Principal Investigators and participating centres.

Principal Investigator	**Centre**[†]	**City**
Dr A Menzies-Gow (co-Chief Investigator)	Royal Brompton Hospital	London
Dr R Niven (co-Chief Investigator)	Wythenshawe Hospital	Manchester
Dr D Saralaya/ Dr A Aziz	Bradford Royal Infirmary	Bradford
Dr R Chaudhuri	Gartnavel General Hospital	Glasgow
Dr M Masoli	Derriford Hospital	Plymouth
Dr C Bucknall	Stobhill ACH Hospital	Glasgow
Dr I Clifton	St. James's University Hospital	Leeds
Dr A Mansur	Birmingham Heartlands Hospital	Birmingham
Prof. N Barnes	The London Chest Hospital	London
Prof. L Heaney	Belfast City Hospital	Belfast
Dr R Kurukulaaratchy	Southampton General Hospital	Southampton
Prof. C Corrigan	Guys Hospital	London
Dr J Morjaria	Castle Hill Hospital	Hull
Dr A Hart-Thomas/ Dr A Graham	Huddersfield Royal Infirmary	Huddersfield
Dr S Hand	Prince Charles General Hospital	Merthyr Tydfil
Dr R Allcock	Queen Elizabeth II	Gateshead
Dr L Dobson	Torbay Hospital	Torquay
Dr R Gore	Lister Hospital	Stevenage
Dr N Segal	North Manchester General Hospital	Manchester
Dr S Ramamurthy	James Cook University Hospital	Middlesbrough
Dr M Nordstrum	St. Peter's Hospital	Chertsey
Dr G Davies	Singleton Hospital	Swansea

[†]10 centres included in the original APEX I study participated in APEX II. The additional centres were selected based on those providing secondary or specialist asthma management services that used omalizumab as part of normal clinical practice, that were interested in participating in the study and contributed to a geographical spread of centres throughout the UK to provide a representative study population

Table S2: Baseline patient characteristics

Variable	**Responders** (n=197)	**Non-responders** (n=42)	**CCS patients** (n=76)	**Non-CCS patients** (n=136)
Age (years)	44.0 (14.0)	46.5 (14.6)	46.5 (14.0)	43.0 (13.7)
Female	130 (66.0%)	28 (66.7%)	45 (59.2%)	94 (69.1)
Smoker				
Never	123 (62.4%)	30 (71.4%)	42 (55.3%)	90 (66.2%)
Ex	67 (34.0%)	8 (19.0%)	28 (36.8%)	41 (30.1%)
Current	3 (1.5%)	3 (7.1%)	3 (3.9%)	2 (1.5%)
Unknown	4 (2.0%)	1 (2.4%)	3 (3.9%)	3 (2.2%)
Weight (kg)	82.6 (19.9)	81.8 (21.1)	83.6 (21.0)	81.9 (18.9)
BMI (kg/m^2)	30.0 (6.5)[†]	30.0 (8.0)	30.1 (7.3)	29.9 (6.3)
Ethnicity				
White British	167 (84.8%)	39 (92.9%)	70 (92.1%)	112 (82.4%)
Pakistani	16 (8.1%)	2 (4.8%)	3 (3.9%)	12 (8.8%)
Other	14 (7.1%)	1 (2.4%)	3 (3.9%)	12 (8.8%)
Duration of asthma (years)[‡]	24.5 (14.6)	28.9 (16.7)	24.6 (15.3)	26.0 (14.8)
Age at asthma diagnosis (years)[‡]	19.7 (17.4)	18.8 (20.4)	23.2 (20.0)	17.2 (15.7)
Allergies				
House dust mite	134 (68.0%)	32 (76.2%)	54 (71.1%)	92 (67.6%)
Animal fur	129 (65.5%)	30 (71.4%)	46 (60.5%)	96 (70.6%)
Pollen	93 (47.2%)	24 (57.1%)	35 (46.1%)	68 (50.0%)
Mould	67 (34.0%)	15 (35.7%)	29 (38.2%)	44 (32.4%)
Plant material	62 (31.5%)	17 (40.5%)	27 (35.5%)	43 (31.6%)
None documented	6 (3.0%)	1 (2.4%)	2 (2.6%)	3 (2.2%)
Co-morbidities				
Perennial rhinitis	61 (31.0%)	11 (26.2%))	22 (28.9%))	44 (32.4%))
Seasonal rhinitis	42 (21.3%)	5 (11.9%)	10 (13.2%)	34 (25.0%)
Nasal polyps	29 (14.7%)	5 (11.9%)	13 (17.1%)	18 (13.2%)
Sinusitis	28 (14.2%)	5 (11.9%)	9 (11.8%)	18 (13.2%)
Anaphylaxis	18 (9.1%)	4 (9.5%)	7 (9.2%)	12 (8.8%)
Bronchiectasis	7 (3.6%)	1 (2.4%)	0 (0.0%)	7 (5.1%)
Diabetes	4 (2.0%)	0 (0.0%)	4 (5.3%)	1 (0.7%)
None	55 (27.9%)	14 (33.3%)	21 (27.6%)	35 (25.7%)

Data presented as mean (SD) or n (%); CCS: continuous corticosteroid

[†]One patient did not have height recorded

[‡]Duration of asthma not recorded for: 28 responders, 8 non-responders, 14 CCS, 18 non-CCS

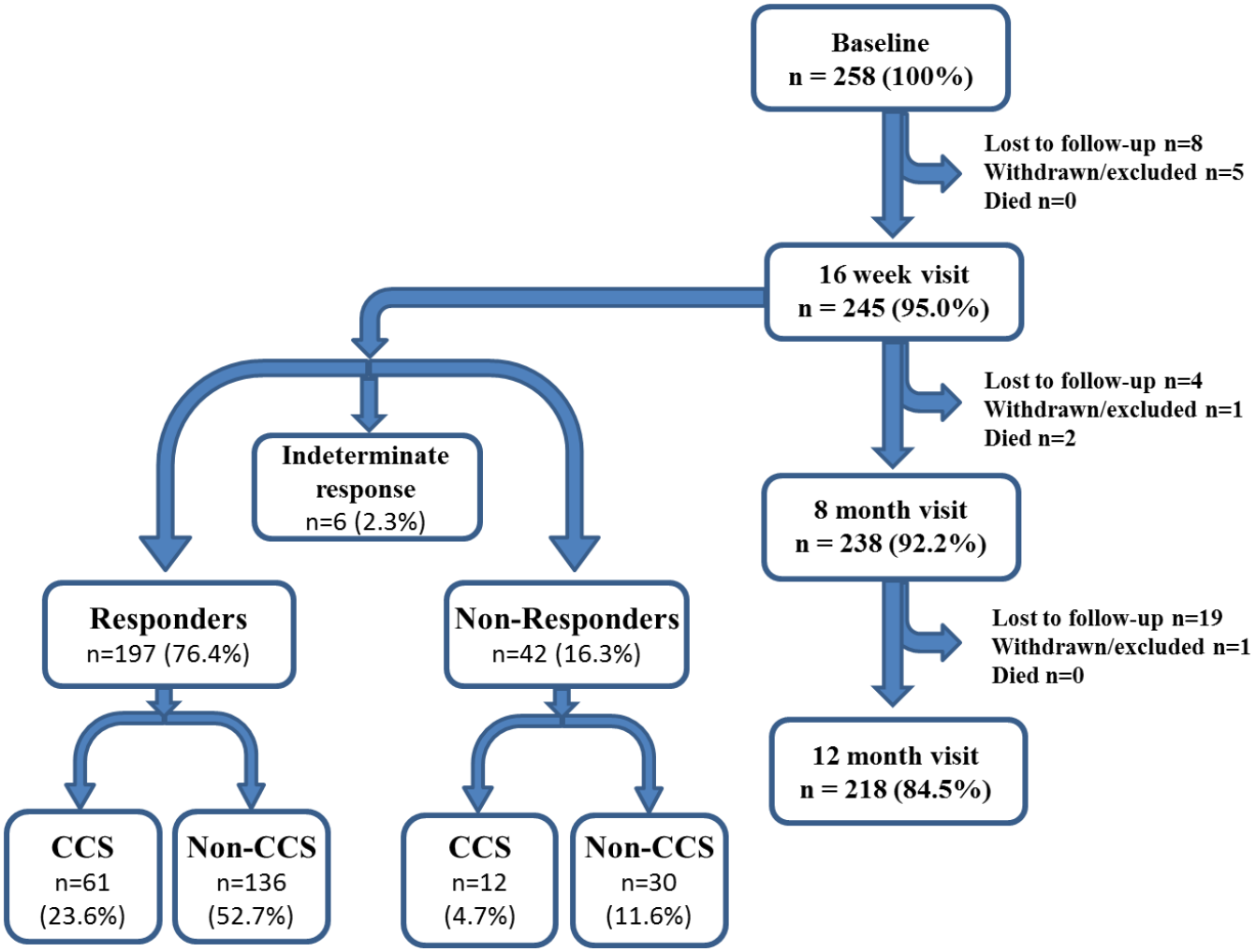

Figure S1. APEX II study participants.
Of the 258 patients recruited, 218 completed the 12 month visit following initiation of omalizumab. Response to omalizumab was assessed at the 16 week visit, with 197 patients being classified as responders at 16 weeks. Neither of the 2 deaths recorded was suspected to be related to omalizumab treatment. CCS: continuous corticosteroids.

Table S3. Reasons for discontinuing omalizumab

Reasons for discontinuing	All patients	
	n	**%**
Continuing at 12-month visit	179	69.4%
Discontinuing	67	26.0%
Excluded/withdrawn/died	9	3.5%
Not known	3	1.2%
Reasons for discontinuing:		
Lack of response	44	65.7%
Adverse event	4	6.0%
Patient choice	2	3.0%
Awaiting funding	1	1.5%
Non-compliant	2	3.0%
Lost to follow-up	14	20.9%

Figure S2. Impact of omalizumab on lung function: FEV1(L). Data presented as mean difference (95% confidence intervals [CI]) comparing assessments at 16 weeks, 8 months and 12 months post-omalizumab with baseline. Panel A: Intention to treat patients, paired t-test p<0.001 for each comparison; panel B: responder subgroup, paired t-test p<0.001 for each comparison; panel C: continuous corticosteroid subgroup, paired t-test p<0.001 for 16 weeks and 8 months comparisons and p<0.01 for 12 month comparisons.

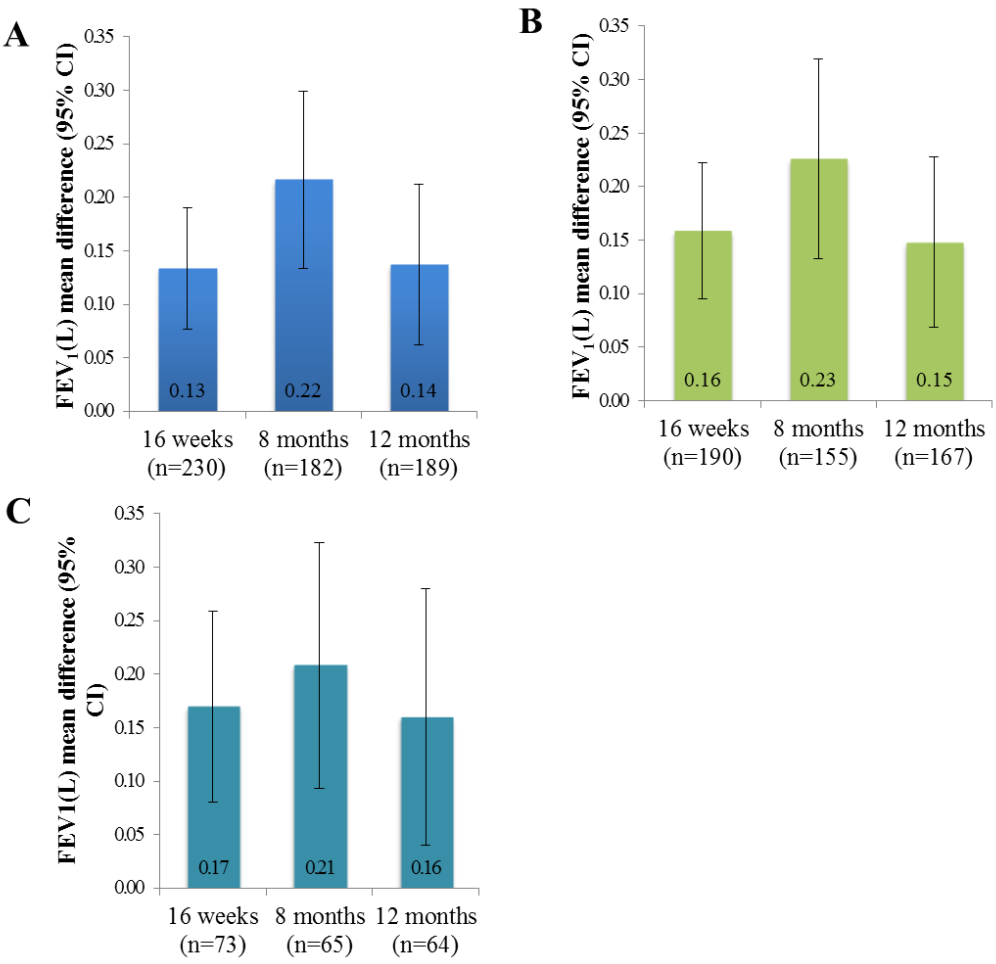

Table S4. Patient reported outcome measures in the responder subgroup of patients

	Post-omalizumab initiation visit		
	16 weeks	**8 months**	**12 months**
ACT score	n=179	n=153	n=162
Mean (SD) at baseline	9.85 (4.24)	9.79 (4.34)	9.93 (4.37)
Mean (SD) at visit	16.18 (5.35)	15.53 (5.68)	15.04 (5.63)
Mean difference (95% CI)	6.34 (5.60, 7.07)†	5.74 (4.90, 6.58)†	5.11 (4.23, 5.99)†
AQLQ score	n=157	n=130	n=137
Mean (SD) at baseline	3.21 (1.26)	3.12 (1.28)	3.15 (1.26)
Mean (SD) at visit	4.85 (1.50)	4.76 (1.51)	4.54 (1.50)
Mean difference (95% CI)	1.65 (1.43, 1.86)†	1.64 (1.41, 1.87)†	1.40 (1.16, 1.64)†
EQ-5D index	n=173	n=146	n=146
Mean (SD) at baseline	0.59 (0.25)	0.58 (0.26)	0.58 (0.24)
Mean (SD) at visit	0.74 (0.24)	0.70 (0.24)	0.71 (0.25)
Mean difference (95% CI)	0.15 (0.11, 0.18)†	0.12 (0.09, 0.16)†	0.13 (0.09, 0.16)†
EQ-5D VAS	n=160	n=142	n=140
Mean (SD) at baseline	54.6 (20.6)	53.7 (20.1)	54.1 (20.4)
Mean (SD) at visit	69.7 (20.4)	68.6 (21.6)	69.2 (19.9)
Mean difference (95% CI)	15.1 (11.9, 18.4)†	14.9 (11.3, 18.5)†	15.0 (11.3, 18.7)†

†$p<0.001$

ACT: Asthma Control Test; AQLQ: Asthma Quality of Life Questionnaire; EQ-5D VAS: EQ-5D visual analogue scale

Table S5. Patient reported outcome measures in the continuous corticosteroid subgroup of patients

	Post-omalizumab initiation visit		
	16 weeks	**8 months**	**12 months**
ACT score	n=66	n=62	n=63
Mean (SD) at baseline	9.65 (4.46)	9.84 (4.85)	9.75 (4.66)
Mean (SD) at visit	14.18 (5.67)	14.00 (5.98)	13.59 (5.66)
Mean difference (95% CI)	4.53 (3.27, 5.79)†	4.16 (2.97, 5.36)†	3.84 (2.48, 5.21)†
AQLQ score	n=57	n=53	n=54
Mean (SD) at baseline	3.28 (1.41)	3.20 (1.40)	3.20 (1.34)
Mean (SD) at visit	4.46 (1.59)	4.41 (1.59)	4.29 (1.52)
Mean difference (95% CI)	1.19 (0.76, 1.61)†	1.21 (0.81, 1.60)†	1.09 (0.69, 1.48)†
EQ-5D index	n=66	n=60	n=59
Mean (SD) at baseline	0.56 (0.25)	0.55 (0.26)	0.56 (0.26)
Mean (SD) at visit	0.69 (0.24)	0.65 (0.25)	0.68 (0.27)
Mean difference (95% CI)	0.13 (0.08, 0.19)†	0.10 (0.05, 0.15)†	0.12 (0.06, 0.18)†
EQ-5D VAS	n=60	n=57	n=57
Mean (SD) at baseline	56.6 (20.3)	54.5 (19.4)	58.5 (20.2)
Mean (SD) at visit	64.7 (21.6)	65.2 (20.9)	67.7 (20.9)
Mean difference (95% CI)	8.1 (2.1, 14.0)‡	10.7 (5.5, 15.8)†	9.2 (3.0, 15.4)‡

†$p<0.001$; ‡$p<0.01$

ACT: Asthma Control Test; AQLQ: Asthma Quality of Life Questionnaire; EQ-5D VAS: EQ-5D visual analogue scale

Table S6. Resource utilisation in the responder subgroup

	Pre-omalizumab (n=184)	**Post-omalizumab** (n=184)	**Mean difference** (95% CI)
A&E visits/patient	1.19 (1.80)	0.31 (0.84)	-0.88 (-1.14, -0.62) p<0.001
Inpatient admissions/patient	1.24 (1.70)	0.53 (1.36)	-0.71 (-0.89, -0.52) p<0.001
Outpatient visits/patient†	4.62 (2.55)	1.31 (1.94)	-3.31 (-3.77, -2.85) p<0.001
Bed days/per patient	6.35 (9.47)	3.21 (8.65)	-3.14 (-4.26, -2.02) p<0.001
Day case visits/patient	0.03 (0.18)	0.03 (0.21)	0.00 (-0.04, 0.04) p>0.1

Data presented as mean (SD); †excluding visits for omalizumab administration

Table S7. Resource utilisation in the continuous corticosteroid subgroup

	Pre-omalizumab (n=76)	**Post-omalizumab** (n=76)	**Mean difference** (95% CI)
A&E visits/patient	0.92 (1.70)	0.21 (0.60)	-0.71 (-1.10, -0.32) p<0.001
Inpatient admissions/patient	0.88 (1.52)	0.46 (1.48)	-0.42 (-0.68, -0.16) p<0.01
Outpatient visits/patient†	4.33 (2.08)	1.55 (1.88)	-2.79 (-3.42, -2.16) p<0.001
Bed days/per patient	4.13 (7.04)	2.42 (7.76)	-1.71 (-3.32, -0.10) p<0.05
Day case visits/patient	0.01 (0.11)	0.01 (0.11)	0.00 (-0.04, 0.04) p>0.1

Data presented as mean (SD); †excluding visits for omalizumab administration

Table S8. Serious suspected-related adverse events reported

Adverse event	Number of Events	Events leading to discontinuation[†]
Accident (no other information available)	1	
Anaphylactic reaction	1	1
Arthralgia	2	1
Asthma	2	
Hypersensitivity	1	
Hypophagia	1	1
Malaise	1	
Nausea	1	1
Paraesthesia oral	2	1
Pruritus	1	1
Pruritus generalised	1	
Swollen tongue	1	
Urinary tract infection	1	
Urticaria	1	1
Vomiting	1	1
Wheezing	1	1
Total	**19**	**9**

[†]Events not mutually exclusive