

SUPPLEMENTARY MATERIAL**Real-World Effectiveness of Newly Initiated Systemic Therapy for Atopic Dermatitis in the United States: A Claims Database Analysis**

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Supplementary Table S1. Follow-up all-cause medical visits among patients new to systemic atopic dermatitis treatment

Medical visits	Overall <i>N</i> = 3249	Dupilumab <i>n</i> = 2455	SIS <i>n</i> = 794
Follow-up period (excluding index date), mean $\pm$ SD [median], days	472.3 $\pm$ 213.7 [433.0]	460.9 $\pm$ 211.0 [412.0]	507.5 $\pm$ 218.1 [477.0]
Inpatient visits			
Patients who had ≥ 1 visit, <i>n</i> (%)	218 (6.7)	141 (5.7)	77 (9.7)
Visits per year, mean $\pm$ SD [median], <i>n</i>	0.1 $\pm$ 0.3 [0.0]	0.1 $\pm$ 0.3 [0.0]	0.1 $\pm$ 0.5 [0.0]
Emergency room visits			
Patients who had ≥ 1 visit, <i>n</i> (%)	944 (29.1)	692 (28.2)	252 (31.7)
Visits per year, mean $\pm$ SD [median], <i>n</i>	0.5 $\pm$ 1.7 [0.0]	0.5 $\pm$ 1.1 [0.0]	0.6 $\pm$ 2.9 [0.0]
Outpatient visits			
Patients who had ≥ 1 visit, <i>n</i> (%)	3234 (99.5)	2441 (99.4)	793 (99.9)
Visits per year, mean $\pm$ SD [median], <i>n</i>	18.3 $\pm$ 20.8 [11.9]	17.3 $\pm$ 20.7 [10.3]	21.6 $\pm$ 21.0 [15.6]
Other visits			
Patients who had ≥ 1 visit, <i>n</i> (%)	510 (15.7)	385 (15.7)	125 (15.7)
Visits per year, mean $\pm$ SD [median], <i>n</i>	0.2 $\pm$ 0.8 [0.0]	0.2 $\pm$ 0.9 [0.0]	0.2 $\pm$ 0.7 [0.0]
Incident staphylococcal and GAS (including streptococcal skin) infection, <i>n</i> (%)	30 (0.9)	18 (0.7)	12 (1.5)

US AD RWE (IQVIA Claims)

Incident staphylococcal and GAS-related medical visits, <i>n</i> (%)	25 (0.8)	14 (0.6)	11 (1.4)
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GAS group A streptococci, *SD* standard deviation, *SIS* systemic immunosuppressant

Supplementary Table S2. Follow-up costs (per patient per year) among patients new to systemic atopic dermatitis treatment

Category	Cost, mean $\pm$ SD [median]		
	Overall <i>N</i> = 3249	Dupilumab <i>n</i> = 2455	SIS <i>n</i> = 794
All-cause healthcare costs			
Total (medical + pharmacy) costs	\$34,483 $\pm$ 32,484 [34,706]	\$37,733 $\pm$ 28,413 [37,151]	\$24,433 $\pm$ 41,107 [12,032]
Total medical costs	\$7407 $\pm$ 22,618 [1836]	\$6038 $\pm$ 18,233 [1617]	\$11,640 $\pm$ 32,293 [2597]
Inpatient visit costs	\$1727 $\pm$ 11,788 [0]	\$1262 $\pm$ 8756 [0]	\$3164 $\pm$ 18,143 [0]
ER visit costs	\$524 $\pm$ 2345 [0]	\$472 $\pm$ 1946 [0]	\$682 $\pm$ 3283 [0]
Outpatient visit costs	\$5133 $\pm$ 15,702 [1,558]	\$4281 $\pm$ 12,627 [1366]	\$7769 $\pm$ 22,521 [2218]
Other visit costs	\$24 $\pm$ 128 [0]	\$23 $\pm$ 138 [0]	\$25 $\pm$ 90 [0]
Pharmacy costs	\$27,075 $\pm$ 21,950 [30,327]	\$31,695 $\pm$ 19,606 [34,107]	\$12,793 $\pm$ 22,662 [3624]
AD-related healthcare costs^a			
Total (medical + pharmacy) costs	\$24,738 $\pm$ 16,214 [28,866]	\$29,946 $\pm$ 12,048 [33,054]	\$8633 $\pm$ 16,848 [1233]
Total medical costs	\$894 $\pm$ 7564 [141]	\$554 $\pm$ 3954 [143]	\$1945 $\pm$ 13,584 [137]
Inpatient visit costs	\$419 $\pm$ 2172 [136]	\$311 $\pm$ 1670 [139]	\$751 $\pm$ 3247 [131]
ER visit costs	\$0 $\pm$ 3 [0]	\$0 $\pm$ 3 [0]	\$0 $\pm$ 2 [0]
Outpatient visit costs	\$461 $\pm$ 7172 [0]	\$232 $\pm$ 3580 [0]	\$1170 $\pm$ 13,053 [0]
Other visit costs	\$14 $\pm$ 235 [0]	\$11 $\pm$ 202 [0]	\$24 $\pm$ 314 [0]

US AD RWE (IQVIA Claims)

Pharmacy costs	\$23,843 ± 14,983 [28,311]	\$29,392 ± 11,629 [32,656]	\$6689 ± 10,539 [837]
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AD atopic dermatitis, *ER* emergency room, *SD* standard deviation, *SIS* systemic immunosuppressant

^aInfection-related costs were identified using claims with *ICD-9/10-CM* codes for infection (*ICD-9-CM*: 001-139; *ICD-10-CM*: A00-B99) in any diagnosis position

Supplementary Table S3. Baseline demographics and clinical characteristics among patients new to systemic atopic dermatitis treatment

Patient Characteristics	Overall <i>N</i> = 3249	Index treatment	
		Dupilumab <i>n</i> = 2455	SIS <i>n</i> = 794
Demographics			
Age on index, mean $\pm$ SD, years**	40.6 $\pm$ 16.1	39.8 $\pm$ 15.5	43.4 $\pm$ 17.4
Age categories on index, <i>n</i> (%)			
12–17 years	203 (6.2)	97 (4.0)	106 (13.4)
$\geq$ 18 years	3046 (93.8)	2358 (96.0)	688 (86.6)
Female, <i>n</i> (%)	1761 (54.2)	1321 (53.8)	440 (55.4)
Region, <i>n</i> (%)			
South	1510 (46.5)	1169 (47.6)	341 (42.9)
Northeast	688 (21.2)	521 (21.2)	167 (21.0)
Midwest	700 (21.5)	544 (22.2)	156 (19.6)
West	351 (10.8)	221 (9.0)	130 (16.4)
Payer type, <i>n</i> (%)			
Commercial: fully insured	1811 (55.7)	1333 (54.3)	478 (60.2)
Commercial: self-insured	1417 (43.6)	1104 (45.0)	313 (39.4)
Medicaid	14 (0.4)	13 (0.5)	1 (0.1)
Medicare	5 (0.2)	3 (0.1)	2 (0.3)
Unknown	2 (0.1)	2 (0.1)	0 (0.0)
Year of index date, <i>n</i> (%)			
2017	953 (29.3)	673 (27.4)	280 (35.3)
2018	1570 (48.3)	1193 (48.6)	377 (47.5)
2019	726 (22.3)	589 (24.0)	137 (17.3)
Clinical characteristics			

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Comorbidities, <i>n</i> (%)			
Atopic march conditions	1155 (35.5)	917 (37.4)	238 (30.0)
Allergic rhinitis	865 (26.6)	696 (28.4)	169 (21.3)
Asthma	673 (20.7)	547 (22.3)	126 (15.9)
Food allergies	46 (1.4)	37 (1.5)	9 (1.1)
Psychological conditions	902 (27.8)	653 (26.6)	249 (31.4)
Anxiety	438 (13.5)	328 (13.4)	110 (13.9)
Depression	365 (11.2)	257 (10.5)	108 (13.6)
Sleep disorders	343 (10.6)	233 (9.5)	110 (13.9)
Uncomplicated hypertension	600 (18.5)	399 (16.3)	201 (25.3)
Infection	583 (17.9)	396 (16.1)	187 (23.6)
Viral infection	293 (9.0)	215 (8.8)	78 (9.8)
Fungal infection	191 (5.9)	116 (4.7)	75 (9.4)
Bacterial infection	125 (3.8)	78 (3.2)	47 (5.9)
AD-related condition	523 (16.1)	335 (13.6)	188 (23.7)
Conjunctivitis	238 (7.3)	188 (7.7)	50 (6.3)
Autoimmune disorder	248 (7.6)	110 (4.5)	138 (17.4)
Allergic urticaria	46 (1.4)	28 (1.1)	18 (2.3)
Esophagitis	35 (1.1)	27 (1.1)	8 (1.0)
Nasal polyps	11 (0.3)	9 (0.4)	2 (0.3)
Chronic inflammatory condition**	355 (10.9)	159 (6.5)	196 (24.7)
Psoriasis	245 (7.5)	136 (5.5)	109 (13.7)
Rheumatoid arthritis	76 (2.3)	17 (0.7)	59 (7.4)
Inflammatory bowel disease	44 (1.4)	9 (0.4)	35 (4.4)
Crohn's disease	30 (0.9)	6 (0.2)	24 (3.0)
Ulcerative colitis	22 (0.7)	3 (0.1)	19 (2.4)

US AD RWE (IQVIA Claims)

Psoriatic arthritis	16 (0.5)	5 (0.2)	11 (1.4)
Ankylosing spondylitis	3 (0.1)	0 (0.0)	3 (0.4)
Cancer	66 (2.0)	51 (2.1)	15 (1.9)
Any malignancy, including leukemia and lymphoma	62 (1.9)	48 (2.0)	14 (1.8)
Metastatic solid tumor	4 (0.1)	3 (0.1)	1 (0.1)
Solid tumor without metastasis	54 (1.7)	44 (1.8)	10 (1.3)
Lymphoma	11 (0.3)	6 (0.2)	5 (0.6)
Metastatic cancer	3 (0.1)	2 (0.1)	1 (0.1)
Treatments used at baseline, <i>n</i> (%)			
SCS**	1646 (50.7)	1186 (48.3)	460 (57.9)
Prednisone**	1437 (44.2)	1030 (42.0)	407 (51.3)
Methylprednisolone	373 (11.5)	275 (11.2)	98 (12.3)
Dexamethasone	29 (0.9)	24 (1.0)	5 (0.6)
Prednisolone	15 (0.5)	11 (0.4)	4 (0.5)
Other	13 (0.4)	8 (0.3)	5 (0.6)
Phototherapy	200 (6.2)	150 (6.1)	50 (6.3)
Topical corticosteroid	2474 (76.1)	1850 (75.4)	624 (78.6)
Low potency	514 (15.8)	384 (15.6)	130 (16.4)
Medium potency	1618 (49.8)	1212 (49.4)	406 (51.1)
High potency*	1483 (45.6)	1092 (44.5)	391 (49.2)
Unknown potency	61 (1.9)	51 (2.1)	10 (1.3)
Tacrolimus ointment**	557 (17.1)	482 (19.6)	75 (9.4)
Crisaborole**	349 (10.7)	289 (11.8)	60 (7.6)
Pimecrolimus cream**	329 (10.1)	288 (11.7)	41 (5.2)
No pharmacologic treatment	340 (10.5)	265 (10.8)	75 (9.4)

US AD RWE (IQVIA Claims)

AD atopic dermatitis; *SCS* systemic corticosteroid, *S/S* systemic immunosuppressant

* $p < 0.05$

** $p < .001$

Supplementary Table S4. Baseline demographics, clinical characteristics, and site of care as predictors of indicators of non-response to index treatment: overall cohort

Baseline parameter	Hazard ratio (95% CI); <i>p</i> value ^a		
	Multivariable model 1 (clinically important variables)	Multivariable model 2 (variables with <i>p</i> < 0.25 in univariate analyses)	Multivariable model 3 (variables with <i>p</i> < 0.05 in univariate analyses)
Demographics			
Mean age on index,^b years	1.06 (1.02–1.09); 0.001*	1.05 (1.01–1.09); 0.024*	1.05 (1.01–1.10); 0.016*
Age categories on index			
12–17 (vs ≥ 18)	—	1.05 (0.82–1.35); 0.701	1.05 (0.82–1.34); 0.716
Female (vs male)	0.99 (0.89–1.11); 0.922	1.00 (0.89–1.12); 0.997	—
Region (vs West)			
South	1.44 (1.19–1.73); < 0.001**	1.43 (1.18–1.74); < 0.001**	1.38 (1.15–1.67); < 0.001**
Northeast	1.31 (1.06–1.62); 0.011*	1.31 (1.05–1.62); 0.016*	1.26 (1.02–1.56); 0.032*
Midwest	1.43 (1.17–1.75); < 0.001**	1.44 (1.17–1.77); < 0.001**	1.40 (1.14–1.72); 0.001*
Payer type (vs Medicaid/Medicare/unknown)			
Commercial: fully insured	—	0.84 (0.44–1.61); 0.608	—
Commercial: self-insured	—	0.82 (0.43–1.56); 0.543	—

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Insurance type^c (vs indemnity/traditional/CDHC/HSA/unknown)			
PPO	0.68 (0.44–1.04); 0.077	0.68 (0.43–1.07); 0.094	0.65 (0.42–1.00); 0.053
HMO	0.65 (0.40–1.03); 0.068	0.62 (0.38–1.03); 0.063	0.61 (0.38–0.98); 0.042*
POS	0.75 (0.46–1.22); 0.243	0.75 (0.44–1.25); 0.267	0.72 (0.44–1.19); 0.201
Site of care^d			
≥ 1 dermatologist visit (vs no visits)	1.12 (0.99–1.27); 0.071	1.10 (0.95–1.28); 0.202	1.16 (1.02–1.32); 0.026*
≥ 1 mental health professional visit (vs no visits)	—	0.92 (0.73; 1.16); 0.482	—
Prescribing provider specialty			
Dermatology specialist (vs not dermatology specialist)	—	1.04 (0.83–1.30); 0.738	—
Primary care specialist (vs not primary care specialist)	—	0.97 (0.77–1.22); 0.776	—
Allergy specialist (vs not allergy specialist)	—	0.86 (0.66–1.12); 0.259	—
Hospital physician (vs not hospital physician)	—	0.92 (0.67–1.26); 0.586	—
Pediatrician (vs not pediatrician)	—	1.07 (0.63–1.83); 0.802	—
Other	—	1.06 (0.84–1.33); 0.644	—
Comorbidities			
Charlson comorbidity			
Chronic pulmonary disease (vs no chronic pulmonary disease)	0.85 (0.57–1.29); 0.450	—	—

US AD RWE (IQVIA Claims)

Rheumatologic disease (vs no rheumatologic disease)	1.13 (0.84–1.52); 0.427	0.91 (0.54–1.53); 0.730	0.88 (0.53–1.46); 0.627
Mild liver disease (vs no mild liver disease)	—	1.38 (0.96–1.98); 0.080	3.09 (0.42–22.62); 0.268
Renal disease (vs no renal disease)	1.08 (0.71–1.67); 0.709	2.72 (0.45–16.57); 0.277	—
Peripheral vascular disease (vs no peripheral vascular disease)	—	0.86 (0.51–1.48); 0.592	—
Moderate or severe liver disease (vs no moderate or severe liver disease)	—	0.45 (0.06–3.72); 0.461	—
Dementia (vs no dementia)	—	4.63 (1.07–20.06); 0.041*	—
Elixhauser comorbidity			
Hypertension, uncomplicated (vs no uncomplicated hypertension)	—	1.02 (0.88–1.19); 0.782	0.99 (0.86–1.15); 0.909
Hypothyroidism (vs no hypothyroidism)	—	1.12 (0.91–1.39); 0.277	1.12 (0.91–1.38); 0.276
Rheumatoid arthritis/collagen vascular disease (vs no rheumatoid arthritis/collagen vascular disease)	—	1.48 (0.96–2.28); 0.079	1.57 (1.03–2.39); 0.037*
Cardiac arrhythmia (vs no cardiac arrhythmia)	—	1.19 (0.89–1.59); 0.250	1.01 (0.76–1.34); 0.933
Fluid and electrolyte disorder (vs no fluid and electrolyte disorder)	—	1.22 (0.85–1.75); 0.274	1.23 (0.86–1.74); 0.253
Deficiency anemia (vs no deficiency anemia)	—	1.07 (0.75–1.53); 0.706	1.05 (0.73–1.49); 0.805
Liver disease (vs no liver disease)	—	—	0.46 (0.06–3.28); 0.435
Other neurological disorder (vs no neurological disorder)	—	0.83 (0.52–1.33); 0.435	—

US AD RWE (IQVIA Claims)

Renal failure (vs no renal failure)	—	0.37 (0.06–2.45); 0.303	—
Hypertension, complicated (vs no complicated hypertension)	—	1.08 (0.63–1.86); 0.785	1.15 (0.73–1.81); 0.547
Coagulopathy (vs no coagulopathy)	—	1.41 (0.83–2.41); 0.203	1.47 (0.87–2.47); 0.149
Drug abuse (vs no drug abuse)	—	1.87 (1.04–3.38); 0.037*	1.81 (1.01–3.26); 0.048*
Lymphoma (vs no lymphoma)	—	0.97 (0.46–2.03); 0.933	—
Other comorbidities			
Atopic march condition (vs no atopic march condition)	1.09 (0.94–1.27); 0.244	0.80 (0.60–1.05); 0.101	0.81 (0.62–1.06); 0.130
Allergic rhinitis (vs no allergic rhinitis)	—	1.45 (1.15–1.84); 0.002*	1.35 (1.08–1.70); 0.009*
Asthma (vs no asthma)	—	0.73 (0.32–1.66); 0.459	0.63 (0.28–1.40); 0.254
Psychological condition (vs no psychological condition)	0.96 (0.85–1.08); 0.464	0.93 (0.75–1.17); 0.540	0.91 (0.73–1.12); 0.369
Anxiety (vs no anxiety)	—	1.03 (0.83–1.27); 0.800	1.03 (0.83–1.26); 0.805
Depression (vs no depression)	—	1.04 (0.84–1.29); 0.732	1.06 (0.86–1.30); 0.605
Sleep disorders (vs no sleep disorders)	—	0.99 (0.79–1.25); 0.954	1.02 (0.82–1.27); 0.848
Respiratory condition (vs no respiratory condition)	1.52 (1.00–2.30); 0.049*	0.84 (0.44–1.60); 0.600	0.82 (0.43–1.55); 0.542
Asthma (vs no asthma)	—	0.73 (0.32–1.66); 0.459	0.63 (0.28–1.40); 0.254
Chronic pulmonary disease, excluding asthma (vs no chronic pulmonary disease)	—	0.87 (0.54–1.39); 0.551	0.88 (0.55–1.40); 0.588
Chronic rhinosinusitis (vs no chronic rhinosinusitis)	—	1.64 (1.02–2.65); 0.042*	1.71 (1.07–2.76); 0.026*

US AD RWE (IQVIA Claims)

Infection (vs no infection)	—	0.86 (0.30–2.51); 0.785	0.94 (0.34–2.63); 0.913
Viral infection (vs no viral infection)	0.84 (0.67–1.06); 0.140	1.09 (0.76–1.57); 0.623	—
Fungal infection (v no fungal infection)	—	1.17 (0.81–1.68); 0.397	1.12 (0.86–1.45); 0.410
Bacterial infection (vs no bacterial infection)	—	0.96 (0.63–1.46); 0.849	—
AD-related condition (vs no AD-related condition)	1.15 (0.98–1.34); 0.084	1.42 (0.94–2.16); 0.095	1.13 (0.93–1.38); 0.227
Conjunctivitis (vs no conjunctivitis)	—	0.77 (0.52–1.15); 0.210	—
Autoimmune disorder (vs no autoimmune disorder)	—	0.65 (0.42–1.01); 0.056	0.81 (0.58–1.13); 0.213
Allergic urticaria (vs no allergic urticaria)	—	0.91 (0.56–1.47); 0.687	1.07 (0.72–1.59); 0.723
Esophagitis (vs no esophagitis)	—	1.22 (0.72–2.06); 0.459	1.37 (0.85–2.18); 0.192
Nasal polyps (vs no nasal polyps)	—	0.91 (0.38–2.18); 0.832	—
URTI (vs no URTI)	1.32 (1.15–1.51); < 0.001**	1.47 (0.79–2.74); 0.220	1.48 (0.82–2.69); 0.192
Inflammatory bowel disease (vs no inflammatory bowel disease)	1.42 (0.96–2.12); 0.083	2.02 (1.24–3.30); 0.005*	1.84 (1.14–2.99); 0.013*
Other chronic inflammatory condition (vs no chronic inflammatory condition)	0.90 (0.75–1.08); 0.253	0.94 (0.78–1.14); 0.531	0.92 (0.76–1.11); 0.381
Cardiovascular disease (vs no cardiovascular disease)	0.77 (0.52–1.15); 0.204	—	—
Heart failure (vs no heart failure)	—	—	—
Atrial fibrillation (vs no atrial fibrillation)	—	0.15 (0.04–0.57); 0.006*	—
Myocardial infarction (vs no myocardial infarction)	—	2.42 (1.03–5.65); 0.042*	—

US AD RWE (IQVIA Claims)

AD treatment			
Index treatment			
Dupilumab (vs no dupilumab)	0.46 (0.41–0.52); < 0.001**	0.43 (0.33–0.57); < 0.001**	0.42 (0.32–0.54); < 0.001**
Methotrexate (vs no methotrexate)	—	0.86 (0.65–1.14); 0.303	0.84 (0.63–1.11); 0.214
Cyclosporine (vs no cyclosporine)	—	1.04 (0.77–1.42); 0.787	1.01 (0.75–1.37); 0.927
Azathioprine (vs no azathioprine)	—	0.84 (0.54–1.30); 0.429	0.82 (0.53–1.27); 0.383
Treatment during baseline			
Treatment for moderate-to-severe AD (vs no treatment for moderate-to-severe AD)			
SCS (vs no SCS)	1.67 (1.48–1.88); < 0.001**	1.05 (0.66–1.66); 0.842	1.05 (0.67–1.65); 0.816
Prednisone (vs no prednisone)	—	1.41 (1.08–1.83); 0.010*	1.43 (1.11–1.85); 0.005*
Methylprednisolone (vs no methylprednisolone)	—	1.42 (1.16–1.73); < 0.001**	1.42 (1.17–1.72); < 0.001**
Prednisolone (vs no prednisolone)	—	0.36 (0.13–1.03); 0.056	—
Other SCS (vs no other SCS)	—	2.30 (1.18–4.52); 0.015*	2.24 (1.16–4.33); 0.016*
Phototherapy (vs no phototherapy)	1.52 (1.20–1.93); < 0.001**	1.59 (1.17–2.15); 0.003*	1.65 (1.22–2.22); < 0.001**
Treatment for mild-to-moderate AD (vs no treatment for mild-to-moderate AD)			
Topical corticosteroid	0.87 (0.73–1.05); 0.152	—	—
Low potency (vs no low potency)	—	1.12 (0.97–1.30); 0.114	1.11 (0.96–1.28); 0.148

US AD RWE (IQVIA Claims)

Medium potency (vs no medium potency)	—	0.93 (0.83–1.04); 0.196	—
Unknown potency (vs no unknown potency)	—	0.81 (0.53–1.24); 0.339	—
Pimecrolimus cream (vs no pimecrolimus cream)	—	0.95 (0.79–1.14); 0.565	—
No pharmacological treatment (vs pharmacological treatment)	0.89 (0.68–1.17); 0.397	0.98 (0.79–1.22); 0.866	1.03 (0.83–1.26); 0.805
Medical Visits			
All-cause medical visits			
Inpatient visits			
≥ 1 visit (vs no visits)	—	0.81 (0.31–2.08); 0.658	1.03 (0.50–2.12); 0.937
Mean number of visits per year	1.10 (0.99–1.22); 0.064	1.26 (0.85–1.86); 0.242	1.15 (0.87–1.52); 0.335
ER visits			
≥ 1 visit (vs no visits)	—	1.03 (0.85; 1.25); 0.759	1.03 (0.86–1.24); 0.731
Mean number of visits per year	1.04 (1.02–1.06); < 0.001**	1.03 (0.99–1.07); 0.169	1.03 (0.99–1.07); 0.150
Outpatient visits			
Mean number of visits per year	1.00 (1.00–1.00); 0.077	1.00 (1.00–1.00); 0.968	1.00 (1.00–1.00); 0.900
Other visits			
≥ 1 visit (vs no visits)	—	1.05 (0.78–1.40); 0.769	1.08 (0.81–1.45); 0.609
Mean number of visits per year	1.04 (0.99–1.09); 0.092	1.04 (0.97–1.11); 0.292	1.03 (0.96–1.10); 0.475
AD-related medical visits			

US AD RWE (IQVIA Claims)

Inpatient visits			
Mean number of visits per year	1.02 (0.75–1.40); 0.884	1.34 (0.93–1.93); 0.115	1.24 (0.87–1.76); 0.227
ER visits			
≥ 1 visit (vs no visits)	—	1.02 (0.67–1.55); 0.920	1.02 (0.67–1.53); 0.940
Mean number of visits per year	0.92 (0.81–1.05); 0.220	—	—
Outpatient visits			
Mean number of visits per year	1.01 (1.00–1.02); 0.001*	1.01 (1.01–1.02); < 0.001**	1.01 (1.00–1.02); 0.001*
Infection-related medical visits			
Inpatient visits			
≥ 1 visit (vs no visits)	—	1.21 (0.18–8.32); 0.849	1.81 (0.35–9.43); 0.482
Mean number of visits per year	—	0.77 (0.35–1.70); 0.521	0.64 (0.33–1.23); 0.180
ER visits			
Mean number of visits per year	—	1.06 (0.82–1.39); 0.646	1.05 (0.81–1.36); 0.730
Outpatient visits (vs no outpatient visits)			
≥ 1 visit (vs no visits)	—	1.22 (0.63–2.36); 0.556	1.20 (0.63–2.29); 0.576
Mean number of visits per year	—	1.00 (0.97–1.03); 0.957	—
Asthma-related medical visits			
Inpatient visits			
≥ 1 visit (vs no visits)	—	3.09 (0.49–19.52); 0.230	0.98 (0.53–1.82); 0.960

US AD RWE (IQVIA Claims)

Mean number of visits per year	—	0.61 (0.28–1.33); 0.215	—
ER visits			
≥ 1 visit (vs no visits)	—	0.82 (0.34–1.97); 0.659	1.04 (0.45–2.44); 0.922
Mean number of visits per year	—	1.05 (0.80–1.39); 0.720	0.97 (0.75–1.27); 0.852
Outpatient visits			
≥ 1 visit (vs no visits)	—	1.33 (0.77–2.30); 0.308	1.52 (0.88–2.60); 0.130
Mean number of visits per year	—	1.00 (1.00–1.01); 0.389	1.00 (1.00–1.01); 0.302
CVD-related medical visits			
ER visits			
Mean number of visits per year	—	1.43 (0.87–2.36); 0.161	—
Eczema herpeticum–related medical visits			
Inpatient visits			
Mean number of visits per year	—	2.09 (0.73–6.00); 0.172	—
URTI-related medical visits			
ER visits			
≥ 1 visit (vs no visits)	—	0.64 (0.27–1.50); 0.308	0.68 (0.29–1.57); 0.366
Mean number of visits per year	—	1.14 (0.91–1.43); 0.268	1.12 (0.89–1.41); 0.323
Outpatient visits			
Patients who had ≥ 1 visit (vs no visits)	—	0.68 (0.36–1.26); 0.220	0.68 (0.37–1.24); 0.212

US AD RWE (IQVIA Claims)

Mean number of visits per year	—	1.12 (1.03–1.21); 0.006*	1.11 (1.03–1.20); 0.006*
Infection rates			
Patients with infection			
Any infection (vs no infection)	—	0.69 (0.21–2.30); 0.549	0.70 (0.21–2.29); 0.556
Mean number of infections per year			
Any infection	1.05 (0.99–1.12); 0.118	1.07 (0.98–1.17); 0.126	1.06 (0.99–1.14); 0.087

AD atopic dermatitis, CDHC consumer-directed healthcare; CI confidence interval, CVD cardiovascular disease, ER emergency room, HMO

health maintenance organization, HR hazard ratio, HSA, health savings account, POS point of service, PPO preferred provider organization, SCS

systemic corticosteroid, URTI upper respiratory tract infection

* $p < 0.05$

** $p < 0.001$

^aHRs, 95% CIs, and p values were estimated by fitting multivariate Cox regression with the indicator of non-response as the outcome

^bAge was included in the model as a continuous variable in 10-year increments

^cFully insured commercial insurance refers to employer insurance provided by a third party; self-insured commercial insurance refers to insurance for which the employer is the sponsor of the plan.

^dEvaluated in the baseline period, including the index date

Supplementary Table S5. Baseline demographic, clinical characteristics, and site of care as predictors of indicators of non-response to index treatment: dupilumab cohort

Baseline parameter	Hazard ratio (95% CI); <i>p</i> value ^a		
	Multivariable model 1 (clinically important variables)	Multivariable model 2 (variables with <i>p</i> < 0.25 in univariate analyses)	Multivariable model 3 (variables with <i>p</i> < 0.05 in univariate analyses)
Demographics			
Mean age on index,^b years	1.08 (1.04–1.13); < 0.001**	1.07 (1.02–1.13); 0.004*	1.08 (1.03–1.13); 0.002*
Female (vs male)	1.01 (0.89–1.16); 0.836	1.05 (0.92–1.21); 0.477	1.05 (0.92–1.21); 0.444
Region (vs West)			
South	1.40 (1.08–1.81); 0.011*	1.40 (1.07–1.83); 0.014*	1.44 (1.11–1.87); 0.006*
Northeast	1.40 (1.05–1.87); 0.020*	1.45 (1.09–1.95); 0.012*	1.47 (1.10–1.96); 0.009*
Midwest	1.27 (0.96–1.68); 0.094	1.26 (0.95–1.68); 0.108	1.31 (0.99–1.73); 0.060
Payer type^c			
Commercial: fully insured (vs not fully insured)	—	0.86 (0.43–1.72); 0.664	—
Commercial: self-insured (vs not self-insured)	—	0.80 (0.40–1.60); 0.532	—
Insurance type^c (vs indemnity/traditional/CDHC/HSA/unknown)			
PPO	0.80 (0.45–1.40); 0.429	0.64 (0.36–1.15); 0.137	0.66 (0.37–1.15); 0.142

US AD RWE (IQVIA Claims)

HMO	0.63 (0.34–1.17); 0.142	0.48 (0.25–0.90); 0.022*	0.52 (0.28–0.96); 0.038*
POS	1.02 (0.55–1.92); 0.939	0.87 (0.45–1.68); 0.674	0.90 (0.48–1.70); 0.752
Site of care^d			
≥ 1 dermatologist visit (vs no visits)	1.13 (0.97–1.32); 0.120	1.17 (1.00–1.38); 0.054	—
≥ 1 mental health professional visit (vs no visits)	—	1.16 (0.85–1.56); 0.350	—
Comorbidities			
Charlson comorbidity			
Chronic pulmonary disease (vs no chronic pulmonary disease)	0.83 (0.50–1.38); 0.477	—	—
Rheumatologic disease (vs no rheumatologic disease)	1.26 (0.73–2.17); 0.399	1.00 (0.42–2.42); 0.995	1.04 (0.44–2.48); 0.923
Mild liver disease (vs no mild liver disease)	—	1.56 (0.94–2.58); 0.086	1.50 (0.91–2.50); 0.114
Renal disease (vs no renal disease)	0.96 (0.54–1.72); 0.895	—	—
Elixhauser comorbidity			
Hypertension, uncomplicated (vs no uncomplicated hypertension)	—	1.05 (0.86–1.27); 0.647	1.04 (0.86–1.26); 0.655
Hypothyroidism (vs no hypothyroidism)	—	1.03 (0.77–1.37); 0.864	—
Rheumatoid arthritis/collagen vascular disease (vs no rheumatoid arthritis/collagen vascular disease)	—	1.57 (0.80–3.07); 0.189	1.33 (0.68–2.60); 0.410
Cardiac arrhythmia (vs no cardiac arrhythmia)	—	0.86 (0.58–1.28); 0.469	—

US AD RWE (IQVIA Claims)

Fluid and electrolyte disorder (vs no fluid and electrolyte disorder)	—	1.01 (0.63–1.63); 0.954	1.00 (0.62–1.61); 0.996
Deficiency anemia (vs no deficiency anemia)	—	1.29 (0.81–2.05); 0.288	—
Other neurological disorder (vs no neurological disorder)	—	1.50 (0.85–2.65); 0.165	—
Drug abuse (vs no drug abuse)	—	1.70 (0.75–3.85); 0.203	1.51 (0.66–3.44); 0.325
Other comorbidities			
Atopic march conditions	1.18 (0.98–1.43); 0.088	0.80 (0.57–1.13); 0.205	0.78 (0.56–1.09); 0.149
Allergic rhinitis (vs no allergic rhinitis)	—	1.59 (1.20–2.10); 0.001*	1.56 (1.19–2.06); 0.002*
Asthma (vs no asthma)	—	0.94 (0.35–2.55); 0.908	0.89 (0.32–2.43); 0.815
Psychological condition (vs no psychological condition)	1.06 (0.92–1.23); 0.432	0.91 (0.69–1.20); 0.488	0.95 (0.72–1.24); 0.696
Anxiety (vs no anxiety)	—	1.04 (0.80–1.35); 0.775	1.04 (0.80–1.35); 0.756
Depression (vs no depression)	—	1.10 (0.83–1.45); 0.515	1.14 (0.88–1.48); 0.321
Sleep disorders (vs no sleep disorders)		1.17 (0.88–1.56); 0.280	1.15 (0.87–1.52); 0.318
Respiratory condition (vs no respiratory condition)	1.53 (0.91–2.57); 0.112	0.67 (0.31–1.41); 0.290	0.69 (0.32–1.46); 0.330
Asthma (vs no asthma)	—	0.94 (0.35–2.55); 0.908	0.89 (0.32–2.43); 0.815
Chronic pulmonary disease, excluding asthma (vs no chronic pulmonary disease)	—	1.13 (0.66–1.93); 0.656	1.04 (0.61–1.79); 0.875
Chronic rhinosinusitis (vs no chronic rhinosinusitis)	—	1.79 (1.07–3.01); 0.027*	1.82 (1.09–3.06); 0.023*
Infection (vs no infection)	0.81 (0.58–1.13); 0.214	—	—

US AD RWE (IQVIA Claims)

AD-related condition	1.18 (0.97–1.42); 0.092	1.35 (0.76–2.39); 0.304	0.98 (0.69–1.39); 0.913
Conjunctivitis (vs no conjunctivitis)	—	0.87 (0.50–1.50); 0.608	1.10 (0.76–1.61); 0.606
Autoimmune disorder (vs no autoimmune disorder)	—	0.61 (0.34–1.09); 0.094	—
Allergic urticaria (vs no allergic urticaria)	—	0.97 (0.50–1.86); 0.917	1.33 (0.77–2.31); 0.300
Esophagitis (vs no esophagitis)	—	1.38 (0.70–2.71); 0.348	1.63 (0.91–2.93); 0.103
Nasal polyps (vs no nasal polyps)	—	1.00 (0.37–2.72); 0.999	—
URTI (vs no URTI)	1.38 (1.16–1.63); < 0.001**	1.22 (0.53–2.83); 0.644	1.23 (0.55–2.75); 0.619
Inflammatory bowel diseases (vs no inflammatory bowel disease)	1.80 (0.83–3.92); 0.136	2.17 (0.91–5.17); 0.081	1.81 (0.81–4.07); 0.150
Other chronic inflammatory condition (vs no chronic inflammatory condition)	1.20 (0.92–1.55); 0.175	1.30 (0.99–1.69); 0.055	1.28 (0.98–1.66); 0.066
Obesity (vs no obesity)	—	1.01 (0.77–1.33); 0.960	1.03 (0.79–1.35); 0.808
Cardiovascular disease (vs no cardiovascular disease)	0.92 (0.57–1.51); 0.751	—	—
Myocardial infarction (vs no myocardial infarction)	—	1.76 (0.68–4.55); 0.241	—
Angina (vs no angina)	—	2.33 (0.52–10.33); 0.267	—
AD Treatments			
Treatment during baseline			
Treatment of moderate-to-severe AD (vs no treatment of moderate-to-severe AD)	—	1.15 (0.71–1.86); 0.564	1.11 (0.69–1.78); 0.676

US AD RWE (IQVIA Claims)

SCS (vs no SCS)	1.74 (1.50–2.01); < 0.001**	1.10 (0.63–1.92); 0.749	1.10 (0.64–1.90); 0.733
Prednisone (vs no prednisone)	—	1.41 (1.02–1.96); 0.038*	1.42 (1.04–1.95); 0.030*
Methylprednisolone (vs no methylprednisolone)	—	1.36 (1.06–1.74); 0.016*	1.33 (1.05–1.69); 0.018*
Prednisolone (vs no prednisolone)	—	0.22 (0.05–1.06); 0.060	—
Other SCS (no other SCS)	—	0.97 (0.37–2.52); 0.950	—
Phototherapy (vs no phototherapy)	1.37 (1.03–1.82); 0.032*	1.34 (0.91–1.96); 0.136	1.39 (0.95–2.02); 0.086
Treatment of mild-to-moderate AD (vs no treatment of mild-to-moderate AD)	0.88 (0.69–1.11); 0.274	—	—
Topical corticosteroid of unknown potency (vs known potency)	—	0.70 (0.42–1.18); 0.181	—
No pharmacological treatment (vs pharmacological treatment)	0.98 (0.69–1.38); 0.894	1.08 (0.84–1.40); 0.541	1.07 (0.83–1.38); 0.623
Dosage of index treatment			
Dupilumab			
300 mg/2 mL (vs 200 mg/1.4 mL)	2.84 (0.58–14.01); 0.200	—	—
Medical visits			
All-cause medical visits			
Inpatient visits			
≥ 1 visit (vs no visits)	—	2.03 (0.61–6.68); 0.246	—

US AD RWE (IQVIA Claims)

Mean number of visits per year	0.99 (0.85–1.16); 0.917	0.74 (0.44–1.25); 0.260	—
ER visits			
≥ 1 visit (vs no visits)	—	0.99 (0.77–1.28); 0.952	1.06 (0.83–1.35); 0.651
Mean number of visits per year	1.06 (1.02–1.11); 0.003*	1.02 (0.96–1.09); 0.527	1.02 (0.96–1.08); 0.532
Outpatient visits			
Mean number of visits per year	1.00 (1.00–1.01); 0.073	1.00 (1.00–1.00); 0.774	1.00 (1.00–1.00); 0.870
Other visits			
≥ 1 visit (vs no visits)	—	1.03 (0.72–1.48); 0.877	1.01 (0.70–1.44); 0.964
Mean number of visits per year	1.04 (0.98–1.10); 0.187	1.03 (0.95–1.12); 0.428	1.04 (0.96–1.13); 0.375
AD-related medical visits			
Inpatient visits			
Mean number of visits per year	1.10 (0.59–2.05); 0.760	—	—
ER visits (vs no ER visits)			
≥ 1 visit (vs no visits)	—	1.27 (0.73–2.22); 0.398	—
Mean number of visits per year	0.93 (0.77–1.13); 0.482	—	—
Outpatient visits			
Mean number of visits per year	1.01 (1.01–1.02); < 0.001**	1.02 (1.01–1.02); < 0.001**	1.02 (1.01–1.02); < 0.001**
Infection-related medical visits^e			
Inpatient visits			

US AD RWE (IQVIA Claims)

≥ 1 visit (vs no visits)	—	0.73 (0.27–2.02); 0.549	—
ER visits			
≥ 1 visit (vs no visits)	—	0.47 (0.10–2.35); 0.359	—
Mean number of visits per year	—	1.54 (0.93–2.54); 0.094	1.23 (0.95–1.60); 0.115
Staphylococcal and GAS-related (including streptococcal skin infections) medical visits			
Outpatient visits (vs no outpatient visits)			
≥ 1 visit (vs no visits)	—	1.51 (0.13–16.86); 0.739	—
Mean number of visits per year	—	0.97 (0.80–1.17); 0.748	—
Asthma-related medical visits			
Inpatient visits			
≥ 1 visit (vs no visits)	—	2.73 (1.08–6.95); 0.035*	1.52 (0.74–3.12); 0.256
ER visits			
≥ 1 visit (vs no visits)	—	0.74 (0.27–2.04); 0.560	0.81 (0.30–2.19); 0.685
Mean number of visits per year	—	1.09 (0.78–1.51); 0.624	1.02 (0.73–1.41); 0.919
Outpatient visits			
≥ 1 visit (vs no visits)	—	0.92 (0.46–1.84); 0.816	0.95 (0.48–1.88); 0.881
Mean number of visits per year	—	1.00 (1.00–1.01); 0.551	1.00 (1.00–1.01); 0.487
Herpes zoster–related medical visits			

US AD RWE (IQVIA Claims)

Other visits			
≥ 1 visit (vs no visits)	—	2.80 (0.65–11.97); 0.166	—
URTI-related medical visits			
ER visits			
≥ 1 visit (vs no visits)	—	0.65 (0.18–2.43); 0.525	0.77 (0.21–2.84); 0.697
Mean number of visits per year	—	1.35 (0.91–2.00); 0.133	1.21 (0.80–1.81); 0.365
Outpatient visits			
≥ 1 visit (vs no visits)	—	0.67 (0.28–1.62); 0.378	0.69 (0.30–1.59); 0.381
Mean number of visits per year	—	1.19 (1.06–1.33); 0.003*	1.19 (1.06–1.33); 0.003*
Infection rates			
Patients with infections			
Staphylococcal and GAS-related (including streptococcal skin) infection ^f (vs no infection)	—	0.34 (0.01–7.70); 0.496	—
Mean no. of infections per year			
All infection ^g	1.06 (0.95–1.17); 0.293	1.00 (0.94–1.06); 0.963	—
Staphylococcal and GAS-related (including streptococcal skin) infection ^f	—	1.01 (0.31–3.35); 0.981	—

AD atopic dermatitis, CDHC consumer-directed healthcare, CI confidence interval, ER emergency room, GAS group A streptococci, HMO health maintenance organization, HR hazard ratio, HSA health savings account, POS point of service, PPO preferred provider organization, SCS systemic corticosteroid, SIS systemic immunosuppressant, URTI upper respiratory tract infection

US AD RWE (IQVIA Claims)

* $p < 0.05$

** $p < 0.001$

^aHRs, 95% CIs, and p values were estimated by fitting multivariate Cox regression with the indicator of non-response as the outcome

^bAge was included in the model as a continuous variable in 10-year increments

^cFully insured commercial insurance refers to employer insurance provided by a third party; self-insured commercial insurance refers to insurance for which the employer is the sponsor of the plan

^dEvaluated in the baseline period, including the index date

^eInfection-related healthcare resource utilization was identified as claims with *ICD-9/10-CM* codes for infection (*ICD-9-CM*: 001-139; *ICD-10-CM*: A00-B99) in any diagnosis position

^fInfections were identified using claims with *ICD-9/10-CM* codes for infection (*ICD-9-CM*: 001-139; *ICD-10-CM*: A00-B99) in any diagnosis position

^gStaphylococcal and GAS infections were identified using claims with *ICD-9/10-CM* codes for staphylococcal or GAS-related infection (*ICD-9-CM*: 041.01, 041.1x; *ICD-10-CM*: B95.0, B95.6x-B95.8) in any diagnosis position