

**Supplementary Table 1.** Definition of autoimmune disease and nephrotic syndrome

<b>Disease</b>	<b>ICD-10 code</b>
Autoimmune disease	D51.0, D59.1, D69.3, E05.0, E06.3, E10, E27.1, G35, G61.0, H20, K50-K51, K73, K74.3, K90.0, L10, L12, L40 (excluding L40.4), L63, L80.9, M05-M06, M08, M30.1, M31.3, M33, M31.5-M31.6, M35.3, G70.0, M34, M32.1, M32.9, M35.0, M45.9 (13)
Nephrotic syndrome	N04

ICD-10, International Classification of Diseases, 10th revision.

**Supplementary Table 2.** Patient demographics and characteristics

	Full analysis population (N=2135)	Physician-referred (n=420)	Physician-referred frequent exacerbators (n=148)	Self-referred (n=1715)
Sex				
Female	1233 (57.8)	226 (53.8)	80 (54.1)	1007 (58.7)
Age (years) <sup>a</sup>	46.0 [11.8]	47.8 [12.4]	47.0 [11.8]	45.6 [11.6]
≥40 years	1513 (70.9)	312 (74.3)	111 (75.0)	1201 (70.0)
Comorbidity <sup>b</sup>				
Quan–Charlson comorbidity index score	2.5 [2.1]	3.0 [2.3]	2.9 [2.1]	2.4 [2.1]
Allergic rhinitis	1684 (78.9)	333 (79.3)	127 (85.8)	1351 (78.8)
Respiratory infection	1137 (53.3)	255 (60.7)	94 (63.5)	882 (51.4)
Pneumonia	724 (33.9)	197 (46.9)	66 (44.6)	527 (30.7)
Gastroesophageal reflux disease	622 (29.1)	148 (35.2)	70 (47.3)	474 (27.6)
Chronic paranasal sinusitis	596 (27.9)	125 (29.8)	66 (44.6)	471 (27.5)
Diabetes mellitus	585 (27.4)	143 (34.1)	49 (33.1)	442 (25.8)
COPD	510 (23.9)	129 (30.7)	47 (31.8)	381 (22.2)
Psychiatric disorder (depression, anxiety)	417 (19.5)	86 (20.5)	43 (29.1)	331 (19.3)
Sleep apnea	373 (17.5)	85 (20.2)	35 (23.7)	288 (16.8)
Cardiovascular disease (myocardial infarction, stroke, heart failure)	328 (15.4)	100 (23.8)	31 (21.0)	228 (13.3)
Atopic dermatitis	200 (9.4)	29 (6.9)	8 (5.4)	171 (10.0)
Osteoporosis	81 (3.8)	23 (5.5)	10 (6.8)	58 (3.4)

Data are n (%) or mean [standard deviation].

COPD, chronic obstructive pulmonary disease.

<sup>a</sup> Age at index date.

<sup>b</sup> Comorbidities before or on the index date. The counts duplicated among comorbidities.

**Supplementary Table 3.** Number of asthma exacerbations before and after referral to specialist in the physician-referred population

	Physician-referred (n=420)		P-value <sup>a</sup>
	Baseline period	Outcome period	
Asthma exacerbation (composite)			0.012
0 events	209 (49.8)	263 (62.6)	
1 event	112 (26.7)	73 (17.4)	
2 events	40 (9.5)	30 (7.1)	
3 events	19 (4.5)	16 (3.8)	
≥4 events	40 (9.5)	38 (9.1)	
Asthma-related hospitalization			0.459
0 events	385 (91.7)	392 (93.3)	
1 event	34 (8.1)	26 (6.2)	
2 events	1 (0.2)	2 (0.5)	
3 events	0	0	
≥4 events	0	0	
Injectable steroid use			0.074
0 events	272 (64.8)	308 (73.3)	
1 event	79 (18.8)	57 (13.6)	
2 events	30 (7.1)	17 (4.1)	
3 events	13 (3.1)	13 (3.1)	
≥4 events	26 (6.2)	25 (6.0)	
Oral corticosteroid burst			0.800
0 events	315 (75.0)	330 (78.6)	
1 event	71 (16.9)	46 (11.0)	
2 events	17 (4.1)	25 (6.0)	
3 events	7 (1.7)	9 (2.1)	
≥4 events	10 (2.4)	10 (2.4)	

Data are n (%).

<sup>a</sup> Two-sided P-value of Wilcoxon signed-rank test.

**Supplementary Table 4.** Numbers of asthma patients with an exacerbation before and after referral to a specialist in physician-referred patients with  $\geq 2$  asthma exacerbations

	Physician-referred frequent exacerbators (n=148)	
	Baseline period	Outcome period
Asthma exacerbation (composite)	148 (100.0)	88 (59.5)
Asthma-related hospitalization	26 (17.6)	17 (11.5)
Injectable steroid use	125 (84.5)	73 (49.3)
Oral corticosteroid burst	75 (50.7)	53 (35.8)

Data are n (%).

**Supplementary Table 5.** Numbers of asthma patients with an exacerbation before and after referral to a specialist in self-referred patients

	Self-referred patients (n=1715)	
	Baseline period	Outcome period
Asthma exacerbation (composite)	709 (41.3)	521 (30.4)
Asthma-related hospitalization	68 (4.0)	59 (3.4)
Injectable steroid use	511 (29.8)	389 (22.7)
Oral corticosteroid burst	344 (20.1)	257 (15.0)

Data are n (%).

**Supplementary Table 6.** Prescriptions of asthma medication before and after referral to a specialist in physician-referred patients with  $\geq 2$  asthma exacerbations

	Physician-referred frequent exacerbators (n=148)	
	Baseline period	Outcome period
Drug for asthma		
SABA	85 (57.4)	60 (40.5)
ICS alone	34 (23.0)	25 (16.9)
LABA	40 (27.0)	17 (11.5)
LAMA	22 (14.9)	33 (22.3)
ICS/LABA	138 (93.2)	128 (86.5)
ICS/LABA/LAMA	0	2 (1.4)
OCS	104 (70.3)	72 (48.7)
LTRA	127 (85.8)	120 (81.1)
Theophylline	83 (56.1)	54 (36.5)
Biologics	2 (1.4)	4 (2.7)
OCS prescription		
Maintenance OCS	6 (4.1)	8 (5.4)
Any ICS prescription		
High dose	94 (63.5)	77 (52.0)
Middle dose	37 (25.0)	34 (23.0)
Low dose	17 (11.5)	24 (16.2)

Data are n (%).

ICS, inhaled corticosteroid; LABA, long-acting beta-agonist; LAMA, long-acting muscarinic antagonist; LTRA, LT receptor antagonist; OCS, oral corticosteroid; SABA, short-acting beta-agonist.

**Supplementary Table 7.** Prescription of asthma medication before and after referral to a specialist in self-referred patients

	Self-referred (n=1715)	
	Baseline period	Outcome period
Drug for asthma		
SABA	757 (44.1)	510 (29.7)
ICS alone	393 (22.9)	289 (16.9)
LABA	351 (20.5)	187 (10.9)
LAMA	82 (4.8)	120 (7.0)
ICS/LABA	1581 (92.2)	1425 (83.1)
ICS/LABA/LAMA	3 (0.2)	12 (0.7)
OCS	610 (35.6)	497 (29.0)
LTRA	1237 (72.1)	1092 (63.7)
Theophylline	592 (34.5)	435 (25.4)
Biologics	4 (0.2)	9 (0.5)
OCS prescription		
Maintenance OCS	12 (0.7)	26 (1.5)
Any ICS prescription		
High dose	824 (48.1)	628 (36.6)
Middle dose	534 (31.1)	484 (28.2)
Low dose	356 (20.8)	382 (22.3)

Data are n (%).

ICS, inhaled corticosteroid; LABA, long-acting beta-agonist; LAMA, long-acting muscarinic antagonist; LTRA, LT receptor antagonist; OCS, oral corticosteroid; SABA, short-acting beta-agonist.

**Supplementary Table 8.** Laboratory tests and medical procedures before and after referral to a specialist in physician-referred patients with  $\geq 2$  asthma exacerbations

	Physician-referred frequent exacerbators (n=148)	
	Baseline period	Outcome period
Spirometry	38 (25.7)	71 (48.0)
Spirometry		
0	110 (74.3)	77 (52.0)
1	4 (2.7)	1 (0.7)
2	23 (15.5)	42 (28.4)
3	1 (0.7)	6 (4.1)
$\geq 4$	10 (6.8)	22 (14.9)
Eosinophil count	77 (52.0)	91 (61.5)
Total IgE	34 (23.0)	64 (43.2)
RAST	29 (19.6)	49 (33.1)
FeNO	19 (12.8)	66 (44.6)
C-reactive protein	85 (57.4)	105 (71.0)

Data are n (%).

FeNO, fractional exhaled nitric oxide; IgE, immunoglobulin E; RAST, radioallergosorbent test.



**Supplementary Table 9.** Laboratory tests and medical procedures before and after referral in asthma patients self-referred to a specialist

	Self-referred (n=1715)	
	Baseline period	Outcome period
Spirometry	340 (19.8)	622 (36.3)
Spirometry		
0	1375 (80.2)	1093 (63.7)
1	26 (1.5)	44 (2.6)
2	193 (11.3)	352 (20.5)
3	8 (0.5)	33 (1.9)
≥4	113 (6.6)	193 (11.3)
Eosinophil count	541 (31.6)	698 (40.7)
Total IgE	203 (11.8)	365 (21.3)
RAST	162 (9.5)	300 (17.5)
FeNO	165 (9.6)	566 (33.0)
C-reactive protein	582 (33.9)	792 (46.2)

Data are n (%).

FeNO, fractional exhaled nitric oxide; IgE, immunoglobulin E; RAST, radioallergosorbent test.

**Supplementary Table 10.** Proportions of reverse referrals in asthma patients by subpopulation

	Physician-referred (n=420)	Physician-referred frequent exacerbators (n=148)	Self-referred (n=1715)
Reverse referral, n/N, % (95% CI)			
Overall	264/420, 62.9 (58.0–67.5)	82/148, 55.4 (47.0–63.6)	677/1715, 39.5 (37.2–41.8)
DPC hospital	219/326, 67.2 (61.8–72.3)	65/110, 59.1 (49.3–68.4)	396/742, 53.4 (49.7–57.0)
Non-DPC hospital	45/94, 47.9 (37.5–58.4)	17/38, 44.7 (28.6–61.7)	281/973, 28.9 (26.1–31.8)
Bed size, <20 beds	19/54, 35.2 (22.7–49.4)	8/25, 32.0 (15.0–53.5)	205/763, 26.9 (23.8–30.2)
Bed size, ≥20 beds	243/361, 67.3 (62.2–72.1)	73/120, 60.8 (51.5–69.6)	460/871, 52.8 (49.4–56.2)

DPC, diagnosis procedure combination.