Supplementary Material

Table S1. The inclusion and exclusion criteria in SAAS

Inclusion criteria	- A diagnosis of new-onset asthma made by a respiratory specialist
	- Diagnosis confirmed by at least one of the following objective lung function measurements:
	  - FEV_1 reversibility in spirometry of at least 15% and 200 mL after 400 µg of salbutamol
	  - Diurnal variability (⩾20% on at least three days) or repeated reversibility (⩾15%/60 l/min on at least three occasions) during a two-week PEF monitoring
	  - A significant decrease in FEV1 (15%) or PEF (20%) in to exercise or allergen challenge test
	  - A significant reversibility in FEV_1 (at least 15% and 200 mL) or mean PEF (at least 20%) in response to a trial with oral or inhaled glucocorticoids
	- Symptoms of asthma
	- Age ≥15 years

Exclusion criteria	- Physical or mental inability to provide signed informed consent
	- Diagnosis of asthma below the age of 15 years
	- Of note:
	  - Patients with comorbidities, either other lung disease or any other significant disease, were not excluded
	  - Patients were not excluded because of smoking, alcohol use or any other lifestyle factor
	  - Respiratory symptoms or any other disease during childhood was not a reason to exclude patients but a diagnosis of asthma at age <15 years was an exclusion criteria

FEV_1= forced expiratory volume in one second. PEF= peak expiratory flow. SAAS= Seinäjoki Adult Asthma Study. Published earlier by Kankaanranta et al, 2015.[1]

Table S2. Baseline (1999-2002) characteristics in never-smokers, ex-smokers and current smokers.

	Never-smokers	Ex-smokers	Current smokers	p-value
N	84	57	33	
Age, years	44.5 ±13.9	49.9 ±12.3	41.1 ±13.5	0.014
Males	23 (27.4)	35 (61.4)	15 (45.5)	<0.001
BMI $kg \cdot m^{-2}$	27.1 (23.8-30.3)	27.4 (24.1-30.1)	26.6 (24.3-30.5)	0.805
Pack-years[#]	0	10 (4-20)	15 (6-23)	
DL % predicted	97.6 (89.3-114.0)	95.0 (88.0-109.0)	91.0 (83.0-103.0)	0.136
DL/VA % predicted	104.0 (91.0-115.8)	102.0 (85.0-114.0)	94.0 (87.0-105.0)	0.103
Blood eosinophils 10^9/l	0.30 (0.18-0.45)	0.24 (0.15-0.43)	0.22 (0.13-0.40)	0.717
Blood eosinophils ≥0.3 x10^9/l	41 (51.2)	23 (43.4)	15 (46.9)	0.669
Pre-bronchodilator lung function				
FEV_1 L	2.84 (2.21-3.29)	2.97 (2.35-3.42)	2.79 (2.39-3.62)	0.413
FEV_1 % predicted	83.5 (72.3-95.8)	80.0 (71.0-90.2)	80.0 (68.5-89.5)	0.448
FEV_1/FVC	0.750 (0.710-0.810)	0.760 (0.660-0.805)	0.740 (0.680-0.795)	0.375
FVC L	3.62 (2.98-4.27)	3.89 (3.53-4.44)	3.60 (3.12-4.81)	0.086
FVC % predicted	91.0 (80.0-101.8)	90.4 (75.9-99.0)	87.0 (79.5-96.0)	0.655
Post-bronchodilator lung function				
FEV_1 L	2.97 (2.46-3.36)	3.07 (2.61-3.53)	3.17 (2.55-3.78)	0.540
FEV_1 % predicted	90.0 (79.0-101.0)	85.0 (76.0-97.0)	84.0 (73.5-96.5)	0.284

	FEV_1/FVC	0.790 (0.754-0.840)	0.786 (0.720-0.820)	0.776 (0.730-0.830)	0.165
	FVC L	3.63 (3.21-4.31)	3.95 (3.51-4.68)	3.98 (3.40-4.94)	0.033
	FVC % predicted	93.0 (82.0-104.0)	94.4 (81.0-100.4)	88.0 (84.3-99.0)	0.929
FEV_1/FVC ratio<0.7		8 (9.8)	12 (23.5)	7 (21.9)	0.073
Atopy [¶]		31 (40.8)	17 (31.5)	11 (37.9)	0.554
ICS bud eq/day [a]		586 (328-852)	688 (497-1024)	664 (333-1199)	0.549

[#] of ever-smokers (ex- and current smokers) ;

[¶] as defined by positive skin-prick tests. ICS: inhaled corticosteroids

[a] daily dispensed ICS doses as 1000µg budesonide equivalent.

Data are presented as n (%), mean ± SD or median (interquartile range).

Total n=174

BMI: body mass index; DL: diffusing capacity of the lung; VA: alveolar volume FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity.

Table S3. The change in lung function from baseline to the maximum lung function point ($Max_{0\text{-}2.5}$) normalized with time from baseline to the $Max_{0\text{-}2.5}$ point in the groups of never-smokers, ex-smokers and current smokers.

	Never-smokers	Ex-smokers	Current-smokers	p-value
	n=79	n=53	n=32	
ΔFEV_1 mL/year	368.7 (89.3-795.5)	238.1 (39.2-1051.6)	473.1 (154.2-1368.3)	0.454
ΔFEV_1 % pred /year	12.1 (3.8-25.6)	8.4 (1.3-32.2)	14.6 (7.6-41.0)	0.487
ΔFVC mL/year	343.4 (0.0-976.2)	275.4 (-55.6-1118.0)	534.9 (261.2-1456.3)	0.137
ΔFVC % pred / year	10.0 (1.3-21.5)	5.5 (-0.5-21.4)	17.8 (5.9-32.9)	0.056
ΔFEV_1/FVC	0.026 (-0.027-0.076)	0.032 (-0.028-0.110)	0.033 (-0.034-0.069)	0.875

Data are shown as median (interquartile range).

Higher than 5 L changes in Δ FEV_1 have been excluded from the analysis.

Total n=164

FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity.

Table S4. The change in lung function from baseline to the maximum lung function point ($Max_{0\text{-}2.5}$) normalized with the time from baseline to the $Max_{0\text{-}2.5}$ and with the daily dose of 1000 µg budesonide equivalent in the groups of never-smokers, ex-smokers and current smokers.

	Never-smokers	Ex-smokers	Current-smokers	p-value
	n=74	n=49	n=29	
Δ FEV_1 mL/year/ 1000 µg	504.1 (155.3-1417.5)	335.9 (18.6-1529.3)	625.0 (268.4-1481.2)	0.622
Δ FEV_1 % pred/ year/ 1000 µg	15.9 (5.8-39.1)	11.8 (2.0-47.7)	18.7 (8.6-44.8)	0.632
Δ FVC mL/ year / 1000 µg	408.8 (-3.2-1222.8)	346.4 (-145.2-1658.6)	781.3 (242.7-2099.9)	0.199
Δ FVC % pred /year/ 1000 µg	12.0 (1.9-31.0)	6.9 (-2.2-34.8)	26.5 (4.8-59.1)	0.129
Δ FEV_1/FVC /year / 1000 µg	0.041 (-0.032-0.124)	0.044 (-0.037-0.151)	0.032 (-0.073-0.114)	0.827

Data are shown as median (interquartile range).

Higher than 5 L changes in Δ FEV_1 have been excluded from the analysis.

Total n=152

FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity.

Table S5. The change in lung function from baseline to the maximum lung function point ($Max_{0\text{-}2.5}$) normalized to correspond daily use of 1000 µg budesonide in the groups of never-smokers and ever-smokers

	Never-smokers	Ever-smokers	p-value
	N=82	N=87	
Δ FEV_1 mL/ 1000 µg bud eq	407.6 (144.4-1147.6)	414.8 (81.1-1054.1)	0.723
Δ FEV_1 % pred / 1000 µg bud eq	15.7 (7.5-33.5)	12.6 (4.6-27.3)	0.209
Δ FVC mL/ 1000 µg bud eq	347.9 (0.0-765.5)	363.0 (-38.0-1242.4)	0.510
Δ FVC % pred / 1000 µg bud eq	10.2 (2.0-24.5)	8.7 (1.2-24.5)	0.856
Δ FEV_1/FVC (/ 1000 µg bud eq)	0.045 (-0.027-0.115)	0.038 (-0.030-0.106)	0.809

Data are shown as median (interquartile range).

Higher than 5 L changes in Δ FEV_1 have been excluded from the analysis.

Total n=169

FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity.

Table S6. Baseline (1999-2002) characteristics in patients with smoking history <10 pack-years and patients with smoking history ≥10 pack-years.

	Pack-years < 10	Pack-years ≥ 10	p-value
N	116	53	
Age, years	42.5 ±13.9	52.4 ±10.3	< 0.001
Males	37 (31.9)	34 (64.2)	<0.001
BMI $kg \cdot m^{-2}$	26.6 (23.7-29.1)	28.7 (24.7-31.0)	0.031
Pack-years[#]	0	17 (15-28)	
DL % predicted	98.1 (89.8-112.8)	91.0 (77.0-105.0)	0.017
DLVA % predicted	104.5 (91.0-115.3)	90.0 (84.3-106.3)	0.003
Blood eosinophils 10^9/l	0.29 (0.17-0.42)	0.28 (0.15-0.42)	0.985
Blood eosinophils ≥0.3 x10^9/l	55 (49.5)	23 (46.9)	0.864
Pre-bronchodilator lung function			
FEV_1 L	2.96 (2.35-3.35)	2.75 (2.11-3.32)	0.105
FEV_1 % predicted	85.0 (73.8-94.8)	76.0 (63.9-83.5)	<0.001
FEV_1/FVC	0.760 (0.720-0.810)	0.720 (0.630-0.790)	0.003
FVC L	3.80 (3.15-4.49)	3.64 (3.19-4.42)	0.853
FVC % predicted	91.9 (83.0-101.8)	83.3 (75.5-93.5)	0.004
Post-bronchodilator lung function			
FEV_1 L	3.15 (2.58-3.69)	2.83 (2.37-3.34)	0.042
FEV_1 % predicted	90.0 (80.0-101.0)	79.5 (70.5-87.1)	<0.001
FEV_1/FVC	0.797 (0.760-0.843)	0.749 (0.650-0.799)	<0.001
FVC L	3.90 (3.25-4.52)	3.92 (3.36-4.62)	0.664
FVC % predicted	94.0 (85.0-104.0)	88.0 (79.8-98.1)	0.088
FEV_1/FVC ratio<0.7	10 (8.8)	16 (34.0)	<0.001
Atopy [¶]	44 (41.1)	14 (29.8)	0.209
ICS bud eq/day [a]	573 (312-809)	714 (555-953)	0.004

[#] of ever-smokers (ex- and current smokers)

[¶] as defined by positive skin-prick tests.

[a] daily dispensed ICS doses as 1000 µg budesonide equivalent.

Data are presented as n (%), mean ± SD or median (interquartile range).

Total n=174

BMI: body mass index; DL: diffusing capacity of the lung; VA: alveolar volume FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; ICS: inhaled corticosteroids.

Supplementary References:

1. Kankaanranta H, Ilmarinen P, Kankaanranta T, Tuomisto LE. Seinäjoki Adult Asthma Study (SAAS): a protocol for a 12-year real-life follow-up study of new-onset asthma diagnosed at adult age and treated in primary and specialised care. *NPJ Prim Care Respir Med.* 2015;25:15042. doi: 10.1038/npjpcrm.2015.42.