

Supplementary material:

**Table S1a**

Included participants with asthma, baseline characteristics:

Variable:	V&V 18– 44 years of age	ECRHS-Uppsala 20–45 years of age	V&V 45–74 years of age	Rotterdam 70–95 years of age
Number of participants	176	90	65	166
Female n(%)	91 (52%)	50 (56%)	32 (49%)	102 (61%)
Age mean ±SD	31 ± 7.6	33 ± 7.0	54 ± 6.0	78 ± 4.9
Never smokers n(%)	57 (32%)	39 (43%)	31 (48%)	59 (36%)
Previous smokers n(%)	16 (9%)	23 (26%)	6 (9%)	101 (61%)
Current smokers n(%)	103 (59%)	28 (31%)	28 (43%)	6 (4%)
Pack-years median (IQR)†	4.8 (1.5– 11.2)	8.6 (4.7–15.7)	26.3 (13.2–41.2)	20.0 (9.0–32.1)
BMI mean ±SD	24.4 ± 3.9	23.8 ± 4.2	28.1 ± 4.9	28.2 ± 4.9
FEV <sub>1</sub> % of predicted mean ±SD	76% ± 16%	95% ± 15%	65% ± 23%	88% ± 19%
Blood eosinophils GM ±exp.SD	148 ± 2.9	247 ± 1.9	179 ± 2.4	216 ± 1.9
Blood eosinophils ≥300 cells /µL n (%)	36 (21%)	37 (41%)	17 (26%)	56 ( 34%)

**Table S1b**

Included participants without asthma, baseline characteristics:

Variable:	V&V 18–44 years of age	ECRHS-Uppsala 20–45 years of age	V&V 45–74 years of age	Rotterdam 70–95 years of age
Number of participants	4702	585	1738	1571
Female n(%)	2441 (52%)	291 (50%)	784 (45%)	860 (55%)
Age mean $\pm$ SD	30 $\pm$ 8.0	33 $\pm$ 7.4	53 $\pm$ 5.9	78 $\pm$ 5.1
Never smokers n(%)	1501 (32%)	300 (51%)	865 (50%)	530 (34%)
Previous smokers n(%)	474 (10%)	131 (22%)	140 (8%)	935 (60%)
Current smokers n(%)	2727 (58%)	154 (26%)	733 (42%)	105 (7%)
Pack-years median (IQR)†	4.2 (0.9-11.3)	11.1 (5.0-19.5)	23.2 (12.8-5.7)	16.5 (6.8-22.6)
BMI mean $\pm$ SD	24.6 $\pm$ 3.5	23.2 $\pm$ 3.3	27.4 $\pm$ 4.0	27.3 $\pm$ 4.0
FEV <sub>1</sub> % of predicted mean $\pm$ SD	86% $\pm$ 12%	103% $\pm$ 12%	80% $\pm$ 14.5%	98% $\pm$ 19%
Blood eosinophils GM $\pm$ exp.SD	96 $\pm$ 2.7	140 $\pm$ 2.1	107 $\pm$ 2.6	179 $\pm$ 1.9
Blood eosinophils $\geq$ 300 cells / $\mu$ L n (%)	375 (8%)	81 (14%)	141 (8%)	313 (20%)

**Table S2.** Baseline characteristics for the longitudinal analysis

Variable	V&V 30–45 years of age	ECRHS-Uppsala 20–45 years of age	V&V 45–68 years of age
Number of participants	2909	487	736
Follow-up time, years, mean $\pm$ SD	15.1 $\pm$ 6.0	16.2 $\pm$ 5.7	15.9 $\pm$ 5.6
Female n(%)	1328 (46%)	233 (48%)	377 (51%)
Age in years mean $\pm$ SD	35.4 $\pm$ 4.5 range 30–45	34 $\pm$ 7.3 range: 20–45	50.5 $\pm$ 4.6 range:46–68
Never smokers n(%)	858 (29%)	247 (51%)	304 (41%)
Previous smokers n(%)	425 (15%)	116 (24%)	83 (11%)
Current smokers n(%)	1626 (56%)	124 (25%)	349 (47%)
Pack-years smoking, median (IQR)	9.2 (3.6–15.0)	9.0 (3.7–16.3)	20.0 (10.5–32.3)
Asthma n(%)	109 (3.8%)	70 (14%)	19 (2.6%)
ICS use	-	31 (6%)	-
ICS use, asthmatics n(%)		25 (36%)	
OCS use	-	2 (0.5%)	-
OCS use, asthmatics n(%)		2 (3%)	
BMI mean $\pm$ SD		23.4 $\pm$ 3.6	
FEV <sub>1</sub> % of predicted mean $\pm$ SD	85.3 $\pm$ 12.5	102 $\pm$ 12	80.5 $\pm$ 13.6
Blood eosinophils GM $\pm$ exp.SD	97.5 $\pm$ 2.6	155 $\pm$ 2.2	99.9 $\pm$ 2.8
Blood eosinophils $\geq$ 300 cells / $\mu$ L n(%)	231 (7.9%)	91 (19%)	56 (7.6%)
Blood eosinophils $\geq$ 300 cells / $\mu$ L in the group with asthma n(%)	22 (20%)	29 (41%)	3 (16%)

†Among the participants with a smoking history

Abbreviations: ECRHS: European Community Respiratory Health Survey, V&V: Vlagtwedde Vlaardingen study, FEV<sub>1</sub>: Forced Exhaled Volume during the first second, GM: geometric mean, IQR: inter quartile range, SD: standard deviation, ICS: inhaled corticosteroids, OCS: oral corticosteroids, BMI: body mass index

**Table S3.** Cross-sectional associations between Ln (B-Eos) and lung function

<b>Estimates for ln(blood eosinophils)</b>	V&V (n=4,881) β (95% CI)	ECRHS-Uppsala (n=676) β (95% CI)	V&V (n=1,803) β (95% CI)	RS (n=1,737) β (95% CI)
FEV <sub>1</sub> adjusted* (mL)	-24 (-37; -11)	-54 (-106; -2.0)	-51 (-74; -28)	-62.8 (-98.7, -26.8)
VC adjusted*† (mL)	-21 (-35; -7)	-35 (-94; 25)	-23 (-47; 1)	-19.6 (-61.9, 22.8)
FEV <sub>1</sub> /VC† adjusted (%)	-0.21 (-0.43; 0.01)	-0.59 (-1.26; 0.092)	-1.04 (-1.48;-0.61)	-1.6 (-2.2, -0.9)

\* adjusted for age, height, weight, sex, ex-smoking, current smoking, pack-years smoking

† VC stands for FVC (RD and ECRHS-Uppsala) or IVC (V&V)

**Table S4.** Longitudinal association between Ln(blood eosinophils) and lung function decline

Estimated for time*ln(blood eosinophils)	V&V <45 years old (n=2,909) $\beta$ (95% CI)	ECRHS-Uppsala (n=487) $\beta$ (95% CI)	V&V >45 years old (n=736) $\beta$ (95% CI)
FEV <sub>1</sub> adjusted* (mL/year)	0.73 (-0.23; 1.69)	-4.12 (-6.30; -1.95)	0.87 (-0.97; 2.70)
VC adjusted*† (mL/year)	0.57 (-0.37; 1.50)	-3.74 (-6.29; -1.20)	0.54 (-1.38; 2.45)
FEV <sub>1</sub> /VC percent/year adjusted*†	$3.8 \times 10^{-3}$ ( $2.3 \times 10^{-2}$ ; $1.6 \times 10^{-2}$ )	$-3.0 \times 10^{-2}$ ( $-7.1 \times 10^{-2}$ ; $1.0 \times 10^{-2}$ )	$2.7 \times 10^{-3}$ ( $-4.1 \times 10^{-2}$ ; $4.6 \times 10^{-2}$ )

\* adjusted for age, height, weight, sex, ex-smoking, current smoking, pack-years smoking, all in interaction with time † VC stands for FVC (ECRHS) or IVC (V&V)

Abbreviations: ln: natural logarithm, ECRHS: European Community Respiratory Health Survey, V&V: Vlagtwedde Vlaardingen study, FEV<sub>1</sub>: Forced Exhaled Volume during the first second, VC: Vital Capacity, FVC: Forced Vital Capacity, IVC: Inhaled Vital Capacity, ln: natural logarithm, CI: Confidence Interval