

## Additional file – Tables A1 to A6

**Table A1** Population characteristics of analyzed participants in comparison to the initial study population for the Munich and Wesel study centers

	Study population analyzed (N=1326)	Study population excluded (N=6477) <sup>A</sup>	p-value*
	Mean (SD) or n/N (%)		
Sex			
male	678/1326 (51)	3267/6316 (52)	0.72
female	648/1326 (49)	3049/6316 (48)	
Age at lung function measurement, years	15.2 (0.3)	15.3 (0.3)	< 0.01
Height at lung function measurement, cm	171.5 (8.2)	171.6 (8.5)	0.86
<b>Study specific</b>			
Study			
GINIplus control	508/1326 (38)	3231/6477 (50)	< 0.01
GINIplus intervention	457/1326 (34)	1795/6477 (28)	
LISAplus	361/1326 (27)	1451/6477 (22)	
Study center			
Munich	840/1326 (63)	3573/6477 (55)	< 0.01
Wesel	486/1326 (37)	2904/6477 (45)	
<b>Early life events</b>			
Parental atopy, yes	780/1326 (59)	3194/6276 (51)	< 0.01
Parental education			
low (< 10 years of school)	69/1326 (5)	827/6413 (13)	< 0.01
medium (= 10 years of school)	354/1326 (27)	1775/6413 (28)	
high (> 10 years of school)	903/1326 (68)	3811/6413 (59)	
Maternal age at delivery >31 years, yes	662/1326 (50)	2897/6461 (45)	< 0.01
Maternal smoking during pregnancy, yes	159/1326 (12)	1069/5657 (19)	< 0.01
Early second-hand smoke exposure at home (up to age 4), yes	433/1326 (33)	2117/4448 (48)	< 0.01
Season of birth, winter	339/1326 (26)	1702/6477 (26)	0.61
Birth weight, g	3482.7 (442.0)	3463.7 (461.3)	0.17
Exclusive breastfeeding > 4 months, yes	804/1326 (61)	2498/4957 (50)	< 0.01
Peak weight velocity, kg/month	1.06 (0.22)	1.09 (0.23)	< 0.01
Peak height velocity, cm/month	3.62 (0.42)	3.67 (0.42)	< 0.01
Lung infections (up to age 3), yes	414/1326 (31)	1371/4230 (32)	0.44

	Study population analyzed (N=1326)	Study population excluded (N=6477) <sup>A</sup>	p-value*
	Mean (SD) or n/N (%)		
<b>Environmental and lifestyle factors at age 15</b>			
Short-term air pollution at lung function measurement			
NO <sub>2</sub> (µg/m <sup>3</sup> )	20.4 (6.9)	20.4 (6.7)	0.83
PM <sub>2.5</sub> mass (µg/m <sup>3</sup> )	14.6 (7.3)	15.7 (7.2)	< 0.01
PM <sub>10</sub> mass (µg/m <sup>3</sup> )	18.9 (7.8)	20.1 (7.8)	< 0.01
Long-term air pollution at participant's home address			
NO <sub>2</sub> (µg/m <sup>3</sup> )	21.2 (4.8)	22.0 (4.4)	< 0.01
PM <sub>2.5</sub> mass (µg/m <sup>3</sup> )	14.8 (2.1)	15.5 (2.2)	< 0.01
PM <sub>10</sub> mass (µg/m <sup>3</sup> )	22.1 (3.2)	22.9 (3.3)	< 0.01
Regular indoor second-hand smoke exposure <sup>1</sup> , yes	266/1326 (20)	438/2242 (20)	0.74
Active smoking, yes	71/1326 (5)	165/2246 (7)	0.02
Serum vitamin D concentration <sup>2</sup> , nmol/l	68.4 (25.3)	66.3 (24.1)	0.07
Body mass index, kg/m <sup>2</sup>	20.7 (3)	21.2 (3.5)	< 0.01
<b>Allergic diseases at age 15</b>			
Asthma, yes	83/1326 (6)	145/2938 (5)	0.09
Rhinitis, yes	251/1326 (19)	491/2839 (17)	0.21
Sensitization to			
Aeroallergens, yes	602/1326 (45)	560/1199 (47)	0.54
Food allergens, yes	148/1326 (11)	144/1199 (12)	0.55

<sup>A</sup>Only participants from the Munich and Wesel study centers. \*t-test, Wilcoxon rank-sum test or Pearson's chi-square test. <sup>1</sup>at least once a week or more. <sup>2</sup>season-adjusted 25(OH)D concentration.

**Table A2** Characteristics of lung function parameters of analyzed participants in comparison to all other subjects with valid lung function measurements at age 15 in the Munich and Wesel study centers

Spirometric parameter	Males		Females	
	Study population analyzed (N=678)	Study population excluded (N=470) <sup>A</sup>	Study population analyzed (N=648)	Study population excluded (N=562) <sup>A</sup>
	Mean (SD)		Mean (SD)	
FVC, l	4.50 (0.74)	4.53 (0.77)	3.64 (0.51)	3.65 (0.49)
FEV <sub>1</sub> , l	3.83 (0.64)	3.82 (0.67)	3.19 (0.42)	3.22 (0.42)
FEV <sub>1</sub> /FVC, %	85.33 (6.43)*	84.46 (6.37)	88.12 (6.02)	88.39 (5.99)
FEF <sub>25-75</sub> , l/s	4.12 (1.01)	4.03 (1.04)	3.70 (0.77)	3.77 (0.82)
PEF, l/s	7.73 (1.3)	7.64 (1.34)	6.54 (0.93)	6.55 (0.98)
FEF <sub>25</sub> , l/s	6.61 (1.27)	6.46 (1.32)	5.89 (0.92)	5.92 (0.99)
FEF <sub>50</sub> , l/s	4.71 (1.14)	4.58 (1.14)	4.19 (0.87)	4.29 (0.94)
FEF <sub>75</sub> , l/s	2.31 (0.78)	2.26 (0.80)	2.11 (0.63)	2.15 (0.64)

\*Significant difference in lung function parameter between participants analyzed and those excluded, stratified by sex (t-test,  $p < 0.05$ ). <sup>A</sup>Participants with valid lung function measurements at age 15 from the Munich and Wesel study centers.

FEV<sub>1</sub>: forced expiratory volume in 1 second. FVC: forced vital capacity. FEF<sub>25</sub>, FEF<sub>50</sub>, FEF<sub>75</sub>: forced expiratory flow rates at 25, 50 and 75% of exhaled FVC. FEF<sub>25-75</sub>: mean flow rate between 25 and 75% of FVC. PEF: peak expiratory flow. SD: standard deviation.

**Table A3** Coefficients (95% confidence intervals) of regression models with the lowest Mallows' Cp, determined by best subset selection in the total population

Spirometric parameter indicative of	Lung volume	Airways & volume	Airflow limitation	Airways	Function of larger conducting airways		peripheral airways	
	FVC, ml	FEV <sub>1</sub> , ml	FEV <sub>1</sub> /FVC, %	FEF <sub>25-75</sub> , ml/s	PEF, ml/s	FEF <sub>25</sub> , ml/s	FEF <sub>50</sub> , ml/s	FEF <sub>75</sub> , ml/s
Sex, male	<b>349 (291, 406)</b>	<b>217 (164, 270)</b>	<b>-2 (-2.8, -1.1)</b>	<b>118 (1, 234)</b>	<b>607 (473, 740)</b>	<b>274 (140, 409)</b>	<b>229 (99, 360)</b>	
Age, IQR years	<b>49 (27, 70)</b>	<b>34 (14, 54)</b>		31 (-10, 71)	45 (-4, 93)	<b>72 (22, 123)</b>	42 (-4, 88)	
Height, IQR cm	<b>646 (606, 687)</b>	<b>519 (483, 555)</b>	-0.4 (-1, 0.1)	<b>467 (389, 545)</b>	<b>709 (619, 799)</b>	<b>560 (469, 651)</b>	<b>482 (394, 571)</b>	<b>330 (274, 385)</b>
<b>Early life events</b>								
Parental atopy, yes			<b>-0.7 (-1.4, -0.1)</b>	-77 (-172, 18)	<b>-124 (-238, -10)</b>			-67 (-142, 9)
Parental education <sup>#</sup>								
high		<b>-51 (-100, -2)</b>		-90 (-193, 12)	<b>-154 (-282, -25)</b>	-118 (-243, 7)	-114 (-229, 2)	
low					-193 (-454, 67)			
Early second-hand smoke exposure at home (up to age 4), yes						<b>133 (7, 258)</b>		
Season of birth, winter	46 (-8, 100)							
Birth weight, IQR g	-33 (-66, 1)							
Peak weight velocity, IQR kg/month			<b>-0.7 (-1.2, -0.2)</b>	<b>-110 (-180, -40)</b>			<b>-120 (-200, -41)</b>	<b>-89 (-143, -35)</b>
Lung infections (up to age 3), yes		<b>-54 (-101, -6)</b>	<b>-1.0 (-1.7, -0.3)</b>	<b>-161 (-260, -62)</b>	<b>-131 (-249, -12)</b>	<b>-143 (-263, -23)</b>	<b>-169 (-281, -57)</b>	<b>-117 (-196, -38)</b>
<b>Environment &amp; lifestyle at age 15</b>								
Long term air pollution								
NO <sub>2</sub> , IQR µg/m <sup>3</sup>			-0.4 (-0.9, 0.1)					-43 (-98, 12)
PM <sub>2.5</sub> mass, IQR µg/m <sup>3</sup>	86 (-29, 201)							
Regular indoor second-hand smoke exposure <sup>1</sup> , yes		<b>-65 (-120, -10)</b>	<b>-0.8 (-1.6, 0)</b>	<b>-132 (-246, -17)</b>	<b>-177 (-315, -40)</b>	-137 (-278, 5)	-124 (-254, 6)	<b>-126 (-217, -35)</b>

Spirometric parameter indicative of	Lung volume	Airways & volume	Airflow limitation	Airways	Function of larger conducting airways		peripheral airways	
	FVC, ml	FEV <sub>1</sub> , ml	FEV <sub>1</sub> /FVC, %	FEF <sub>25-75</sub> , ml/s	PEF, ml/s	FEF <sub>25</sub> , ml/s	FEF <sub>50</sub> , ml/s	FEF <sub>75</sub> , ml/s
Serum vitamin D concentration <sup>2</sup> , IQR nmol/L	<b>63 (32, 94)</b>	<b>31 (3, 60)</b>	<b>-0.6 (-1, -0.2)</b>					
Body mass index, IQR kg/m <sup>2</sup>	<b>226 (197, 254)</b>	<b>142 (116, 169)</b>	<b>-1.2 (-1.6, -0.8)</b>	<b>93 (38, 149)</b>	<b>261 (195, 327)</b>	<b>227 (161, 294)</b>	<b>149 (86, 211)</b>	
<b>Allergic diseases at age 15</b>								
Asthma, yes	<b>-119 (-216, -22)</b>	<b>-178 (-269, -88)</b>	<b>-2 (-3.4, -0.6)</b>	<b>-346 (-538, -154)</b>	-198 (-434, 38)	<b>-398 (-627, -168)</b>	<b>-405 (-620, -190)</b>	<b>-193 (-346, -40)</b>
Rhinitis, yes					119 (-28, 265)			
Aeroallergen sensitization, yes			0.6 (-0.1, 1.3)	78 (-17, 172)				70 (-5, 144)
<b>Study specific</b>								
Study group <sup>#</sup>								
GINIplus (intervention)	49 (-7, 105)							
LISAplus	<b>97 (34, 160)</b>	45 (-6, 97)				121 (-9, 252)		
Study center, Wesel	<b>-145 (-276, -15)</b>	<b>-138 (-188, -87)</b>	<b>-1.3 (-2.1, -0.6)</b>	<b>-266 (-368, -164)</b>	<b>-325 (-446, -204)</b>	<b>-334 (-462, -206)</b>	<b>-282 (-396, -168)</b>	<b>-179 (-263, -95)</b>

Significant associations are shown in bold (p<0.05). Estimates for continuous variables are presented per interquartile range (IQR) increase (IQR: age (0.26 years), height (11 cm), birth weight (587.5 g), peak weight velocity (0.28 kg/month), long term NO<sub>2</sub> (6.64 µg/m<sup>3</sup>), long term PM 2.5 mass (4.00 µg/m<sup>3</sup>), vitamin D concentration (32.35 nmol/l), body mass index (3.56 kg/m<sup>2</sup>).

<sup>#</sup>Factor entered using dummy coding. <sup>1</sup>at least once a week or more. <sup>2</sup>season-adjusted 25(OH)D concentration.

FEV<sub>1</sub>: forced expiratory volume in 1 second. FVC: forced vital capacity. FEF<sub>25</sub>, FEF<sub>50</sub>, FEF<sub>75</sub>: forced expiratory flow rates at 25, 50 and 75% of exhaled FVC. FEF<sub>25-75</sub>: mean flow rate between 25 and 75% of FVC. PEF: peak expiratory flow.

**Table A4** Distribution of the frequency of inclusion of each factor in 1000 replication analyses (%)

Spirometric parameter	FVC	FEV <sub>1</sub>	FEV <sub>1</sub> /FVC	FEF <sub>25-75</sub>	PEF	FEF <sub>25</sub>	FEF <sub>50</sub>	FEF <sub>75</sub>
Sex, male	100	100	100	62	100	100	98	2
Age, years	100	98	14	35	51	90	54	23
Height, cm	100	100	42	100	100	100	100	100
<b>Early life events</b>								
Parental atopy, yes	10	26	54	38	72	11	31	36
Parental education <sup>#</sup>								
high	12	52	20	50	57	52	49	34
low	15	10	3	3	31	8	8	3
Maternal age at delivery >31 years, yes	7	3	20	17	12	8	13	16
Maternal smoking during pregnancy, yes	29	23	3	1	5	6	3	1
Early second-hand smoke exposure at home (up to age 4), yes	16	10	2	1	31	66	2	1
Season of birth, winter	43	18	1	2	10	9	2	10
Birth weight, g	44	8	5	4	18	11	20	10
Exclusive breastfeeding > 4 months, no	3	2	2	3	19	4	6	2
Peak weight velocity, kg/month	3	22	93	92	1	25	95	97
Peak height velocity, cm/month	23	18	3	4	12	3	4	11
Lung infections (up to age 3), yes	6	73	94	98	74	80	95	95
<b>Environment &amp; lifestyle at age 15</b>								
Short-term air pollution								
NO <sub>2</sub> (µg/m <sup>3</sup> )	2	4	17	24	7	4	41	13
PM <sub>2.5</sub> mass (µg/m <sup>3</sup> )	4	4	11	9	4	3	12	3
PM <sub>10</sub> mass (µg/m <sup>3</sup> )	9	1	39	12	3	2	17	10

Spirometric parameter	FVC	FEV <sub>1</sub>	FEV <sub>1</sub> /FVC	FEF <sub>25-75</sub>	PEF	FEF <sub>25</sub>	FEF <sub>50</sub>	FEF <sub>75</sub>
Long-term air pollution								
NO <sub>2</sub> (µg/m <sup>3</sup> )	6	19	31	27	19	6	28	24
PM <sub>2.5</sub> mass (µg/m <sup>3</sup> )	36	31	24	10	21	8	10	9
PM <sub>10</sub> mass (µg/m <sup>3</sup> )	8	4	8	9	16	3	13	20
Regular indoor second-hand smoke exposure <sup>1</sup> , yes	21	80	66	70	86	54	51	95
Active smoking, yes	9	12	7	7	21	8	6	9
Serum vitamin D concentration <sup>2</sup> , nmol/l	100	74	85	1	16	2	4	32
Body mass index, kg/m <sup>2</sup>	100	100	100	97	100	100	100	8
<b>Allergic diseases at age 15</b>								
Asthma, yes	79	99	84	97	39	97	99	79
Rhinitis, yes	7	5	6	8	31	3	10	5
Sensitization to								
Aeroallergens, yes	1	11	41	44	4	2	32	45
Food allergens, yes	3	2	4	4	3	8	5	2
<b>Study specific</b>								
Study group <sup>#</sup>								
GINIplus (intervention)	53	17	7	6	13	6	3	4
LISAplus	90	54	16	3	4	53	7	10
Study center, Wesel	82	99	63	86	99	99	83	78

Factors that were included in >70% of replication analyses are shaded in gray.

<sup>#</sup>Factor entered using dummy coding. <sup>1</sup>at least once a week or more. <sup>2</sup>season-adjusted 25(OH)D concentration. FEV<sub>1</sub>: forced expiratory volume in 1 second. FVC: forced vital capacity. FEF<sub>25</sub>, FEF<sub>50</sub>, FEF<sub>75</sub>: forced expiratory flow rates at 25, 50 and 75% of exhaled FVC. FEF<sub>25-75</sub>: mean flow rate between 25 and 75% of FVC. PEF: peak expiratory flow.

**Table A5** Coefficients (95% confidence intervals) of regression models of flow rates adjusted for covariates that remained stable in replication analyses

Spirometric parameter indicative of airway function of	larger conducting airways		peripheral airways	
	PEF, ml/s	FEF <sub>25</sub> , ml/s	FEF <sub>50</sub> , ml/s	FEF <sub>75</sub> , ml/s
Sex, male	602 (470, 735)	285 (150, 420)	227 (97, 358)	
Age, IQR years		63 (14, 112)		
Height, IQR cm	713 (623, 803)	555 (464, 646)	488 (399, 576)	328 (272, 383)
<b>Early life events</b>				
Parental atopy, yes	-123 (-236, -11)			
Peak weight velocity, IQR kg/month			-122 (-202, -43)	-82 (-136, -28)
Lung infections (up to age 3), yes	-140 (-258, -23)	-150 (-270, -29)	-171 (-283, -58)	-118 (-198, -39)
<b>Environment &amp; lifestyle at age 15</b>				
Regular indoor second-hand smoke exposure <sup>1</sup> , yes	-164 (-301, -27)			-130 (-220, -39)
Serum vitamin D concentration <sup>2</sup> , IQR nmol/l				
Body mass index, IQR kg/m <sup>2</sup>	265 (200, 331)	231 (165, 297)	149 (87, 212)	
<b>Allergic diseases at age 15</b>				
Asthma, yes		-391 (-621,-161)	-392 (-607,-177)	-171 (-323, -20)
<b>Study specific</b>				
Study center (Wesel vs Munich)	-314 (-430,-198)	-303 (-419,-186)	-266 (-375,-157)	-201 (-277,-125)

All associations were statistically significant ( $p < 0.05$ ). Estimates for continuous variables are presented per interquartile range (IQR) increase (IQR: age (0.26 years), height (11 cm), peak weight velocity (0.28 kg/month), vitamin D (32.35 nmol/l), body mass index (3.56 kg/m<sup>2</sup>)).

<sup>1</sup>at least once a week or more. <sup>2</sup>season-adjusted 25(OH)D concentration.

FEF<sub>25</sub>, FEF<sub>50</sub>, FEF<sub>75</sub>: forced expiratory flow rates at 25, 50 and 75% of exhaled forced vital capacity.  
PEF: peak expiratory flow.



**Table A6** Relative importance of variables in final regression models of flow rates (averaged R<sup>2</sup> contribution)

Spirometric parameter indicative of airway function of	larger conducting airways		peripheral airways	
	PEF	FEF <sub>25</sub>	FEF <sub>50</sub>	FEF <sub>75</sub>
<b>Total R<sup>2</sup> of the model</b>	0.38	0.24	0.18	0.13
Sex	32.9	21.8	18.2	
Age		2.6		
Height	55.0	54.8	55.5	68.3
<b>Early life events</b>				
Parental atopy	0.7			
Peak weight velocity			4.0	4.1
Lung infections (up to age 3)	0.4	1.3	3.3	5.1
<b>Environment &amp; lifestyle at age 15</b>				
Regular indoor second-hand smoke exposure <sup>1</sup>	0.6			5.1
Serum vitamin D concentration <sup>2</sup>				
Body mass index	8.2	12.1	6.9	
<b>Allergic diseases at age 15</b>				
Asthma		3.0	5.5	3.9
<b>Study specific</b>				
Study center (Wesel vs Munich)	2.1	4.4	6.7	13.5

  

< 1%	< 3%	< 5%	< 10%	< 15%	≥ 15%
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Relative importance of variables in regression models adjusted for covariates that remained stable in replication analyses are displayed as normalized percent of R<sup>2</sup> contribution averaged (unweighted) over variable orderings.

<sup>1</sup>at least once a week or more. <sup>2</sup>season-adjusted 25(OH)D concentration.

FEF<sub>25</sub>, FEF<sub>50</sub>, FEF<sub>75</sub>: forced expiratory flow rates at 25, 50 and 75% of exhaled forced vital capacity. PEF: peak expiratory flow.