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| **Table 1.** Clinical and demographic characteristics of each cohort and time point included in this study. | | | | | | | | | | | | |
| **Cohort** |  | **nPRS a** | **Median PRS**  **z-score (IQR) b** | **Time point c** | **nAssociation d** | **Sex (% male)** | **Smoking (%) e** | **Asthma (%) f** | **Mean age ± SD (years)** | **Mean FEV1 z-score ± SD g** | **Mean FVC**  **z-score ± SD g** | **Mean FEV1/FVC z-score ± SD g** |
|  |
| ALSPAC |  | 8,943 | 0·00  (-0·66 - 0·66) | 8 years | 4,871 | 50·4 | NA | 14·7 | 8·7 ± 0·3 | -0·1 ± 1·0 | -0·1 ± 1·0 | 0·0 ± 1·1 |  |
|  | 15 years | 3,332 | 48·1 | NA | 13·9 | 15·5 ± 0·3 | -0·7 ± 1·3 | -0·9 ± 1·2 | 0·4 ± 1·2 |  |
|  | 24 years | 2,590 | 39·7 | 19·6 | 17·5 | 24·5 ± 0·8 | -0·4 ± 1·0 | -0·2 ± 1·0 | -0·4 ± 0·9 |  |
| Ashford |  | 348 | -0·03  (-0·69 - 0·68) | 15 years | 322 | 50·6 | NA | 20·8 | 15·0 ± 0·0 | -0·7 ± 1·1 | -0·7 ± 1·1 | 0·0 ± 1·1 |  |
| BAMSE h |  | 463 i | -0·01  (-0·64 - 0·65) | 8 years | 335 | 54·6 | NA | 31·9 | 8·3 ± 0·5 | 0·4 ± 0·9 | 0·6 ± 0·9 | -0·5 ± 0·9 |  |
|  | 16 years | 305 | 52·8 | NA | 31·8 | 16·7 ± 0·4 | -0·2 ± 0·9 | 0·1 ± 0·9 | -0·5 ± 1·0 |  |
|  | 24 years | 282 | 50·7 | 17·5 | 22·7 | 22·5 ± 0·5 | -0·3 ± 0·8 | 0·0 ± 0·8 | -0·5 ± 0·9 |  |
|  | 2,173 j | 0·02  (-0·69 - 0·66) | 8 years | 1,230 | 48·5 | NA | 7·6 | 8·4 ± 0·5 | 0·5 ± 0·9 | 0·6 ± 0·9 | -0·3 ± 0·9 |  |
|  | 16 years | 1,185 | 44·6 | NA | 13·4 | 16·7 ± 0·4 | 0·0 ± 1·0 | 0·2 ± 0·9 | -0·3 ± 0·9 |  |
|  | 24 years | 1,044 | 43·3 | 18·4 | 10·2 | 22·6 ± 0·6 | -0·2 ± 0·9 | 0·0 ± 0·9 | -0·3 ± 0·9 |  |
| COPSAC2000 |  | 358 | 0·00  (-0·67 - 0·66) | 7 years | 292 | 50·3 | NA | 13·4 | 7·1 ± 0·4 | 0·0 ± 1·0 | 0·0 ± 1·0 | 0·0 ± 1·0 |  |
|  | 12 years | 293 | 48·5 | NA | 17·9 | 12·8 ± 0·6 | 0·0 ± 1·0 | 0·0 ± 1·0 | 0·0 ± 1·0 |  |
|  | 18 years | 317 | 47·9 | 17·3 | 29·7 | 17·7 ± 0·6 | 0·0 ± 1·0 | 0·0 ± 1·0 | 0·0 ± 1·0 |  |
| COPSAC2010 |  | 618 | -0·03  (-0·67 - 0·69) | 10 years | 530 | 52·3 | NA | 10·6 | 10·3 ± 0·4 | 0·0 ± 1·0 | 0·0 ± 1·0 | 0·0 ± 1·0 |  |
| Generation R |  | 5,756 | 0·00  (-0·68 - 0·67) | 9 years | 2,147 | 48·9 | NA | 3·5 | 9·6 ± 0·3 | 0·1 ± 1·0 | 0·2 ± 0·9 | -0·2 ± 0·9 |  |
|  | 13 years | 1,897 | 48·1 | NA | 5·3 | 13·6 ± 0·3 | -0·3 ± 1·0 | -0·2 ± 0·9 | -0·2 ± 0·9 |  |
| a Number of individuals with available genome-wide genotype data included in the estimation of the PRS for airflow limitation; b Median, quartile 1 and 3 of normalized PRS estimates into z-scores; c Average age of the individuals at the data collection follow-ups included in this study; d Number of individuals with available genotype data and spirometry measurements included in the association analyses; e Percentage of individuals with reported active smoking habits. Only shown for time points with participants aged 18 years and older with available data related to smoking habits; f Number of subjects with asthma at the time of data collection defined as doctor's diagnosis of asthma and any symptoms with breathing difficulties or occasional or regular use of asthma medications in the last 12 months, or self-reports; g Obtained from applying the Global Lung Function Initiative equations on pre-bronchodilator spirometry measurements; h The PRS was separately estimated in each of the genotyping Waves of the BAMSE cohort (Wave 1, n=463; Wave 2, n=2,173); i Genotyping Wave 1 (n=463); j Genotyping Wave 2 (n=2,173); k Subjects were classified into groups of similar age for this study;  l Participants have been grouped based on the time point when the pulmonary function test was conducted.  FEV1: forced expiratory volume in one second; FVC: forced vital capacity; IQR: interquartile range; NA: not available; PFT: pulmonary function test visit; PRS: polygenic risk score; SD: standard deviation. | | | | | | | | | | | | |  |

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| **Table 1 (continuation).** Clinical and demographic characteristics of each cohort and time point included in this study. | | | | | | | | | | | | | |
| **Cohort** |  | **nPRS a** | **Median PRS**  **z-score (IQR) b** | **Time point c** | **nAssociation d** | **Sex (% male)** | **Smoking (%) e** | **Asthma (%) f** | **Mean age ± SD (years)** | **Mean FEV1**  **z-score ± SD g** | **Mean FVC**  **z-score ± SD g** | **Mean FEV1/FVC**  **z-score ± SD g** |
|  | |
| GINIplus/LISA North |  | 792 | -0·03  (-0·69 - 0·70) | 10 years | 374 | 52·9 | NA | 7·5 | 10·3 ± 0·2 | 0·1 ± 0·8 | -0·4 ± 0·8 | 0·9 ± 1·0 |  | |
|  | 15 years | 496 | 48·6 | NA | 5·1 | 15·2 ± 0·3 | -0·7 ± 0·9 | -0·6 ± 0·9 | -0·2 ± 0·9 |  | |
| GINIplus/LISA South |  | 1,511 | 0·00  (-0·71 - 0·67) | 6 years | 106 | 48·1 | NA | 5·3 | 6·1 ± 0·1 | -0·1 ± 0·9 | -0·6 ± 0·9 | 1·3 ± 0·8 |  | |
|  | 15 years | 843 | 49·5 | NA | 7·5 | 15·3 ± 0·3 | -0·4 ± 0·9 | -0·5 ± 0·9 | 0·0 ± 1·0 |  | |
| HUNT |  | 69,717 | 0·00  (-0·67 - 0·68) | 20-30 years k | 2,848 | 43·3 | 31·9 | 37·2 | 26·0 ± 3·1 | -0·2 ± 1·0 | 0·2 ± 0·9 | -0·5 ± 0·9 |  | |
|  | 31-40 years k | 3,107 | 45·1 | 33·7 | 40·8 | 36·4 ± 2·9 | -0·2 ± 1·1 | 0·1 ± 1·0 | -0·5 ± 1·0 |  | |
|  | 41-50 years k | 4,142 | 46 | 35·4 | 38·1 | 46·0 ± 2·9 | -0·2 ± 1·2 | 0·0 ± 1·0 | -0·4 ± 1·0 |  | |
|  | >50 years k | 9,027 | 47·4 | 27·2 | 36·2 | 63·4 ± 8·9 | -0·6 ± 1·4 | -0·3 ± 1·1 | -0·6 ± 1·2 |  | |
| INMA |  | 2,034 | -0·04  (-0·67 - 0·66) | 4 years | 559 | 51·7 | NA | NA | 4·5 ± 0·1 | -0·6 ± 1·2 | -0·6 ± 1·3 | 0·0 ± 1·0 |  | |
|  | 7 years | 925 | 50·4 | NA | NA | 7·4 ± 0·6 | 0·2 ± 1·0 | 0·4 ± 0·9 | -0·4 ± 1·0 |  | |
|  | 10 years | 65 | 58·5 | NA | NA | 10·6 ± 0·2 | -0·2 ± 1·0 | 0·1 ± 1·0 | -0·5 ± 0·9 |  | |
|  | 11 years | 792 | 51 | NA | NA | 11·2 ± 0·6 | -0·2 ± 1·0 | 0·0 ± 1·0 | -0·3 ± 1·0 |  | |
|  | 14 years | 188 | 51·6 | NA | NA | 14·6 ± 0·2 | 0·1 ± 1·0 | 0·0 ± 1·0 | 0·1 ± 0·9 |  | |
|  | 18 years | 87 | 35·6 | 20·7 | NA | 17·7 ± 0·3 | -0·4 ± 1·0 | -0·2 ± 1·0 | -0·3 ± 1·0 |  | |
| IoWBC |  | 956 | -0·01  (-0·72 - 0·70) | 10 years | 754 | 49·3 | NA | 23·3 | 10·0 ± 0·2 | 0·3 ± 1·0 | 0·2 ± 0·9 | 0·3 ± 1·0 |  | |
|  | 18 years | 669 | 46·2 | 25·2 | 20·2 | 17·7 ± 0·5 | 0·1 ± 1·0 | 0·1 ± 0·9 | 0·0 ± 1·1 |  | |
|  | 26 years | 432 | 44·2 | NA | NA | 26·4 ± 0·4 | 0·0 ± 1·0 | 0·4 ± 1·0 | -0·7 ± 0·9 |  | |
| a Number of individuals with available genome-wide genotype data included in the estimation of the PRS for airflow limitation; b Median, quartile 1 and 3 of normalized PRS estimates into z-scores; c Average age of the individuals at the data collection follow-ups included in this study; d Number of individuals with available genotype data and spirometry measurements included in the association analyses; e Percentage of individuals with reported active smoking habits. Only shown for time points with participants aged 18 years and older with available data related to smoking habits; f Number of subjects with asthma at the time of data collection defined as doctor's diagnosis of asthma and any symptoms with breathing difficulties or occasional or regular use of asthma medications in the last 12 months, or self-reports; g Obtained from applying the Global Lung Function Initiative equations on pre-bronchodilator spirometry measurements; h The PRS was separately estimated in each of the genotyping Waves of the BAMSE cohort (Wave 1, n=463; Wave 2, n=2,173); i Genotyping Wave 1 (n=463); j Genotyping Wave 2 (n=2,173); k Subjects were classified into groups of similar age for this study;  l Participants have been grouped based on the time point when the pulmonary function test was conducted.  FEV1: forced expiratory volume in one second; FVC: forced vital capacity; IQR: interquartile range; NA: not available; PFT: pulmonary function test visit; PRS: polygenic risk score; SD: standard deviation. | | | | | | | | | | | | | |  | |

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| **Table 1 (continuation).** Clinical and demographic characteristics of each cohort and time point included in this study. | | | | | | | | | | | | |
| **Cohort** |  | **nPRS a** | **Median PRS**  **z-score (IQR) b** | **Time point c** | **nAssociation d** | **Sex (% male)** | **Smoking (%) e** | **Asthma (%) f** | **Mean age ± SD (years)** | **Mean FEV1 z-score ± SD g** | **Mean FVC**  **z-score ± SD g** | **Mean FEV1/FVC**  **z-score ± SD g** |
|  |
| Lifelines |  | 859 | 0·01  (-0·71 - 0·66) | 18-30 years k | 859 | 44·1 | 35 | 12·2 | 27·1 ± 2·6 | -0·4 ± 0·9 | -0·2 ± 0·9 | -0·4 ± 1·0 |  |
|  | 3,005 | -0·01  (-0·66 - 0·65) | 31-40 years k | 3,005 | 40·9 | 26·7 | 9·1 | 36·4 ± 2·8 | -0·4 ± 0·9 | -0·2 ± 0·9 | -0·4 ± 1·0 |  |
| MAAS |  | 852 | 0·01  (-0·67 - 0·70) | 8 years | 640 | 53 | NA | 12·2 | 8·0 ± 0·2 | 0·1 ± 1·0 | 0·3 ± 1·0 | -0·4 ± 1·0 |  |
|  | 16 years | 502 | 51 | NA | 14·3 | 16·1 ± 0·6 | -0·3 ± 1·0 | -0·4 ± 1·0 | 0·2 ± 1·1 |  |
|  | 19 years | 436 | 48 | 13·3 | 7·3 | 19·4 ± 0·8 | -0·3 ± 1·0 | -0·3 ± 0·9 | 0·0 ± 1·1 |  |
| PIAMA |  | 1,526 | -0·03  (-0·68 - 0·68) | 8 years | 907 | 50·4 | NA | 10 | 8·1 ± 0·3 | 0·5 ± 0·9 | 0·3 ± 0·9 | 0·3 ± 1·1 |  |
|  | 12 years | 1,018 | 48·3 | NA | 9·2 | 12·6 ± 0·4 | -0·6 ± 0·9 | -0·4 ± 0·9 | -0·4 ± 0·9 |  |
|  | 16 years | 653 | 47·9 | NA | 8·3 | 16·4 ± 0·2 | -0·3 ± 0·9 | 0·0 ± 0·8 | -0·5 ± 1·0 |  |
| Rotterdam Study |  | 11,496 | 0·00  (-0·68 - 0·69) | PFT 1  (50-98 years) l | 5,722 | 44·1 | 14·8 | 6 | 67·5 ± 9·3 | -0·1 ± 1·2 | -0·1 ± 1·1 | -0·1 ± 1·0 |  |
|  | PFT 2  (51-96 years) l | 3,317 | 44·3 | 10·4 | 7·2 | 70·7 ± 9·1 | -0·1 ± 1·1 | 0·0 ± 0·9 | -0·2 ± 0·9 |  |
|  | PFT 3  (70-100 years) l | 741 | 44·9 | 6·2 | 9·2 | 78·9 ± 5·2 | -0·1 ± 1·1 | 0·1 ± 0·9 | -0·6 ± 0·9 |  |
| SEATON |  | 552 | 0·05  (-0·68 - 0·71) | 10 years | 382 | 47·1 | NA | 13·4 | 10·3 ± 0·2 | -0·2 ± 1·1 | -0·3 ± 1·0 | 0·1 ± 1·0 |  |
|  | 15 years | 330 | 43 | NA | NA | 15·1 ± 0·3 | -0·4 ± 1·0 | -0·8 ± 1·0 | 0·8 ± 1·1 |  |
| a Number of individuals with available genome-wide genotype data included in the estimation of the PRS for airflow limitation; b Median, quartile 1 and 3 of normalized PRS estimates into z-scores; c Average age of the individuals at the data collection follow-ups included in this study; d Number of individuals with available genotype data and spirometry measurements included in the association analyses; e Percentage of individuals with reported active smoking habits. Only shown for time points with participants aged 18 years and older with available data related to smoking habits; f Number of subjects with asthma at the time of data collection defined as doctor's diagnosis of asthma and any symptoms with breathing difficulties or occasional or regular use of asthma medications in the last 12 months, or self-reports; g Obtained from applying the Global Lung Function Initiative equations on pre-bronchodilator spirometry measurements; h The PRS was separately estimated in each of the genotyping Waves of the BAMSE cohort (Wave 1, n=463; Wave 2, n=2,173); i Genotyping Wave 1 (n=463); j Genotyping Wave 2 (n=2,173); k Subjects were classified into groups of similar age for this study;  l Participants have been grouped based on the time point when the pulmonary function test was conducted.  FEV1: forced expiratory volume in one second; FVC: forced vital capacity; IQR: interquartile range; NA: not available; PFT: pulmonary function test visit; PRS: polygenic risk score; SD: standard deviation. | | | | | | | | | | | | |  |

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| **Table 2.** Results of the meta-analysis of association estimates of the PRS for airflow limitation with spirometry measurements by age group (up to 50 years). | | | | | | | | | | |
| **Age group** | **Sample size a** | **Nr. Cohorts b** | **Spirometry measurement c** |  | **β (95%CI) d** | ***p*-value e** | ***q*-value f** |  | ***I2* g** | ***p*-valueQ h** |
| *Preschool age (0-6 years)* | 665 | 2 | FEV1 |  | -0·09 (-0·17, 0·00) | 0·042 | 0·115 |  | 0 | 0·606 |
| FVC |  | -0·09 (-0·18, -0·01) | 0·031 | 0·115 |  | 0 | 0·436 |
| FEV1/FVC |  | 0·00 (-0·07, 0·08) | 0·914 | 1 |  | 13·63 | 0·282 |
| *School age (7-10 years)* | 13,387 | 11 | FEV1 |  | -0·07 (-0·09, -0·05) | 5·99 x 10-10 | **1·65 x 10-9** |  | 51·79 | 0·007 |
| FVC |  | 0·00 (-0·02, 0·01) | 0·752 | 1 |  | 0·80 | 0·220 |
| FEV1/FVC |  | -0·13 (-0·15, -0·11) | 1·28 x 10-53 | **7·04 x 10-53** |  | 0 | 0·932 |
| *Puberty (11-15 years)* | 9,323 | 9 | FEV1 |  | -0·07 (-0·10, -0·05) | 2·58 x 10-7 | **7·10 x 10-7** |  | 36·29 | 0·092 |
| FVC |  | 0·00 (-0·02, 0·02) | 0·728 | 1 |  | 0 | 0·435 |
| FEV1/FVC |  | -0·14 (-0·16, -0·12) | 1·18 x 10-40 | **6·49 x 10-40** |  | 1·81 | 0·280 |
| *Post-puberty (16-17 years)* | 2,645 | 3 | FEV1 |  | -0·11 (-0·15, -0·08) | 1·03 x 10-9 | **2·83 x 10-9** |  | 0 | 0·575 |
| FVC |  | -0·01 (-0·05, 0·02) | 0·457 | 0·838 |  | 0 | 0·857 |
| FEV1/FVC |  | -0·15 (-0·19, -0·11) | 1·06 x 10-15 | **5·83 x 10-15** |  | 0 | 0·550 |
| *Adulthood (18-30 years)* | 9,132 | 8 | FEV1 |  | -0·12 (-0·14, -0·09) | 6·94 x 10-25 | **1·91 x 10-24** |  | 13 | 0·520 |
| FVC |  | -0·01 (-0·03, 0·01) | 0·280 | 0·513 |  | 0 | 0·715 |
| FEV1/FVC |  | -0·16 (-0·18, -0·14) | 1·06 x 10-57 | **5·83 x 10-57** |  | 2 | 0·908 |
| *Adulthood (31-40 years)* | 6,112 | 2 | FEV1 |  | -0·13 (-0·17, -0·10) | 4·65 x 10-12 | **1·28 x 10-11** |  | 54·48 | 0·138 |
| FVC |  | -0·03 (-0·05, 0·00) | 0·024 | **0·043** |  | 0 | 0·622 |
| FEV1/FVC |  | -0·17 (-0·19, -0·14) | 3·10 x 10-43 | **1·71 x 10-42** |  | 0·75 | 0·315 |
| *Adulthood (41-50 years) i* | 4,142 | 1 | FEV1 |  | -0·17 (-0·20, -0·13) | 1·63 x 10-20 | **4·48 x 10-20** |  | NA | NA |
| FVC |  | -0·07 (-0·10, -0·04) | 1·22 x 10-5 | **2·24 x 10-5** |  | NA | NA |
| FEV1/FVC |  | -0·16 (-0·19, -0·13) | 2·38 x 10-25 | **1·31 x 10-24** |  | NA | NA |
| a Number of individuals with available genotype data and spirometry measurements included in the association analyses; b Number of cohorts included in the meta-analysis per age group; c Z-score of pre-bronchodilator spirometry measurements obtained from applying the Global Lung Function Initiative equations; d Effect size as the change in z-score of lung function per one z-score increase in the PRS; e A random-effects model was applied to account for the heterogeneity across studies regardless of the significance of the Cochran Q-test and *I2* estimate; f Adjusted *p*-value accounting for the false discovery rate. The Benjamini & Yekutieli method was applied across spirometry measurements per age group; g Percentage of variation across cohorts due to heterogeneity; h P-value of the Cochran Q-test of heterogeneity; i Results shown correspond only to the association testing with spirometry measurements in the HUNT cohort given the absence of more cohorts with available spirometry data within that age range.  CI: confidence interval; FEV1: forced expiratory volume in one second; FVC: forced vital capacity.  Results are shown for the basic association model, including Principal Components of genetic ancestry and any cohort-specific variables as covariates.  Significant results (*q*-value ≤0·05) are highlighted in bold font. | | | | | | | | | | |

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| **Table 3.** Association results with spirometry measurements in HUNT participants aged >50 years from the basic regression model and sensitivity analyses accounting for smoking. | | | | | | |
| **Association model** | **Sample size a** |  | **Spirometry measurement b** | **β (95%CI) c** | ***p*-value** | ***q*-value d** |
| *Basic e* | 9,027 |  | FEV1 | -0·16 (-0·19, -0·13) | 5·80 x 10-31 | **1·60 x 10-30** |
|  | FVC | -0·07 (-0·09, -0·05) | 5·77 x 10-10 | **1·06 x 10-9** |
|  | FEV1/FVC | -0·17 (-0·19, -0·14) | 1·97 x 10-39 | **1·09 x 10-38** |
| *Sensitivity - Smoking status f* | 8,784 h |  | FEV1 | -0·16 (-0·19, -0·13) | 5·70 x 10-31 | **1·57 x 10-30** |
|  | FVC | -0·07 (-0·09, -0·05) | 9·77 x 10-10 | **1·79 x 10-9** |
|  | FEV1/FVC | -0·17 (-0·19, -0·14) | 3·79 x 10-40 | **2·08 x 10-39** |
| *Sensitivity - Smoking pack-years g* | 2,205 i |  | FEV1 | -0·19 (-0·24, -0·14) | 7·08 x 10-13 | **1·95 x 10-12** |
|  | FVC | -0·08 (-0·13, -0·04) | 2·46 x 10-4 | **4·52 x 10-4** |
|  | FEV1/FVC | -0·21 (-0·26, -0·16) | 3·00 x 10-16 | **1·65 x 10-15** |
| a Number of individuals with available genotype data and spirometry measurements included in the association analyses; b Z-score of pre-bronchodilator spirometry measurements obtained from applying the Global Lung Function Initiative equations; c Effect size as the change in z-score of lung function per one z-score increase in the PRS; d Adjusted *p*-value accounting for the false discovery rate. The Benjamini & Yekutieli method was applied across spirometry measurements per age group; e Basic association model, including ten PCs, the participation round, and the genotyping batch as covariates; f Sensitivity analyses accounting for active smoking. Ten PCs, the participation round, the genotyping batch, and smoking status were included as covariates; g Sensitivity analyses accounting for active smoking. Ten PCs, the participation round, the genotyping batch, and smoking pack-years were included as covariates. Tobacco pack-years were calculated by multiplying the number of smoking years by the number of daily cigarettes and dividing by 20 cigarettes often contained in a package; h Number of individuals with available genotype data, spirometry measurements, and smoking status information included in the association analyses; i Number of individuals with reported active smoking habits and available genotype data, spirometry measurements, smoking status information included in the association analyses.  CI: confidence interval; FEV1: forced expiratory volume in one second; FVC: forced vital capacity; PC: Principal Component of genetic ancestry.  Significant results (*q*-value ≤0·05) are highlighted in bold font. | | | | | | |

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| **Table 4.** Results of the meta-analyses accounting for active smoking status and habits in adults aged 18 to 50 years. | | | | | | | | | | | | |
|  |  |  | ***Smoking status a*** | | | |  | ***Smoking pack-years b*** | | | | |
| **Age group** |  | **Spirometry measurement c** | **Sample size d** | **β (95%CI) e** | ***p*-value f** | ***q*-value g** |  | **Sample size h** | **β (95%CI) e** | ***p*-value f** | ***q*-value g** |
| *Adulthood (18-30 years)* |  | FEV1 | 8,264 | -0·11  (-0·14, -0·09) | 1·30 x 10-20 | **3·58 x 10-20** |  | 1,417 | -0·13  (-0·18, -0·08) | 1·11 x 10-7 | **3·05 x 10-7** |
|  | FVC | 8,264 | -0·01  (-0·03, 0·01) | 0·399 | 1 |  | 1,417 | -0·02  (-0·07, 0·03) | 0·376 | 0·689 |
|  | FEV1/FVC | 8,264 | -0·16  (-0·18, -0·13) | 6·28 x 10-43 | **3·45 x 10-42** |  | 1,417 | -0·16  (-0·21, -0·12) | 3·91 x 10-12 | **2·15 x 10-11** |
| *Adulthood (31-40 years)* |  | FEV1 | 6,015 | -0·13  (-0·16, -0·10) | 7·58 x 10-14 | **2·08 x 10-13** |  | 1,734 | -0·14  (-0·19, -0·10) | 5·54 x 10-9 | **1·52 x 10-8** |
|  | FVC | 6,015 | -0·03  (-0·05, 0·00) | 0·036 | 0·066 |  | 1,734 | -0·03  (-0·08, 0·01) | 0·146 | 0·268 |
|  | FEV1/FVC | 6,015 | -0·16  (-0·19, -0·14) | 1·01 x 10-42 | **5·56 x 10-42** |  | 1,734 | -0·17  (-0·22, -0·13) | 7·50 x 10-14 | **4·13 x 10-13** |
| *Adulthood (41-50 years) i* |  | FEV1 | 4,103 | -0·16  (-0·20, -0·13) | 9·99 x 10-20 | **2·75 x 10-19** |  | 1,392 | -0·12  (-0·18, -0·06) | 1·49 x 10-4 | **4·10 x 10-4** |
|  | FVC | 4,103 | -0·06  (-0·09, -0·03) | 3·36 x 10-5 | **6·16 x 10-5** |  | 1,392 | 0·00  (-0·05, 0·05) | 0·956 | 1 |
|  | FEV1/FVC | 4,103 | -0·16  (-0·19, -0·13) | 3·65 x 10-25 | **2·01 x 10-24** |  | 1,392 | -0·19  (-0·25, -0·14) | 1·99 x 10-11 | **1·09 x 10-10** |
| a Linear regressions were adjusted by the same covariates as in the basic association model, including PCs of genetic ancestry and any cohort-specific variables as covariates and additionally smoking status; b A covariate related to tobacco pack-years was added to the basic regression model. Tobacco pack-years were calculated by multiplying the number of smoking years by the number of daily cigarettes and divided by 20 cigarettes often contained in a package; c Z-score of pre-bronchodilator spirometry measurements obtained from applying the Global Lung Function Initiative equations; d Number of individuals with available genotype data, spirometry measurements, and smoking status information included in the association analyses; e Effect size of the association as the change in z-score of lung function per one z-score increase in the PRS; f A random-effects model was applied to account for the heterogeneity across studies regardless of the significance of the Cochran Q-test and *I2* estimate; g Adjusted *p*-value accounting for the false discovery rate. The Benjamini & Yekutieli method was applied across spirometry measurements per age group; h Number of individuals with reported active smoking habits and available genotype data, spirometry measurements, and smoking status information included in the association analyses; i Results shown correspond only to the association testing with spirometry measurements in the HUNT cohort given the absence of more cohorts with available spirometry data within that age range.  CI: confidence interval; FEV1: forced expiratory volume in one second; FVC: forced vital capacity.  Results are shown for sensitivity analyses exploring the potential modification of the association effect by active smoking in adults (≥18 years of age).  Significant results (*q*-value ≤0·05) are highlighted in bold font. | | | | | | | | | | | | |