

## Childhood pneumonia increases risk for chronic obstructive pulmonary disease: the COPDGene Study

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### Supplemental Material

#### Tables

| Table s1 Chest CT Parameters for Subjects With and Without History of Childhood Pneumonia |                     |       |        |                        |       |        |                     |
|---|---------------------|-------|--------|------------------------|-------|--------|---------------------|
| Chest CT Parameters   | Childhood Pneumonia |       |        | No Childhood Pneumonia |       |        | p Value             |
|   | N                   |       | SD     | N                      |       | SD     |                     |
| Wall Area %, Segmental  | 792                 | 61.9% | (3.3)  | 8693                   | 61.4% | (3.3)  | <0.001 <sup>a</sup> |
| Wall Area %, Subsegmental   | 286                 | 64.8% | (2.6)  | 2923                   | 64.3% | (2.6)  | 0.003 <sup>a</sup>  |
| SRWA-Pi10   | 768                 | 3.70  | (0.14) | 8526                   | 3.68  | (0.13) | 0.01 <sup>b</sup>   |
| Emphysema % (-950 HU)   | 789                 | 7.2%  | (9.7)  | 8679                   | 6.1%  | (9.6)  | <0.001 <sup>b</sup> |
| Gas Trapping %, expiratory scan (-856HU)  | 609                 | 27.0% | (21.4) | 6810                   | 22.1% | (20.3) | <0.001 <sup>b</sup> |
| Total Lung Capacity (L)   | 789                 | 5.7   | (1.4)  | 8679                   | 5.5   | (1.4)  | 0.004 <sup>a</sup>  |

Abbreviations: CT = computed tomography; HU = Hounsfield units. SRWA-Pi10 = square root wall area of a hypothetical airway with 10mm internal perimeter. Univariate analysis with: <sup>a</sup> t-test; <sup>b</sup> Wilcoxon rank sum test.

| <b>Table s2 Effect of Childhood Pneumonia with Childhood Asthmatics Removed</b> |   |                |                       |
|---|---|----------------|-----------------------|
| <b>Outcomes in N = 9,405 subjects, after removal of childhood asthmatics *</b>  | <b>Impact of Childhood Pneumonia<sup>b</sup></b>          |                |                       |
| Childhood pneumonia N = 717 (7.6%); No childhood pneumonia N = 8688 (92.4%)     | <b>OR (95% CI) or <math>\beta</math> (SE)<sup>c</sup></b> | <b>p Value</b> |                       |
| <b>RESPIRATORY SYMPTOMS AND DISEASE</b>   |   |                |                       |
| Chronic bronchitis  | 1.34  | (1.12, 1.61)   | 0.002 <sup>d,f</sup>  |
| COPD, GOLD 2-4  | 1.24  | (1.03, 1.50)   | 0.02 <sup>d</sup>     |
| Had a severe COPD exacerbation in past year                                     | 1.20  | (0.94, 1.51)   | 0.14 <sup>d,g</sup>   |
| Number of COPD exacerbations in past year                                       | 0.16  | 0.03           | <0.001 <sup>d,g</sup> |
| SGRQ Score, Total <sup>a</sup>  | 2.00  | 0.71           | 0.005 <sup>d,h</sup>  |
| MMRC Dyspnea Scale (0-4) <sup>a</sup>   | 0.14  | 0.05           | 0.003 <sup>d,h</sup>  |
| <b>LUNG FUNCTION</b>  |   |                |                       |
| FEV <sub>1</sub> post-BD (% predicted) <sup>a</sup>                             | -5.52   | 0.52           | <0.001 <sup>e</sup>   |
| FVC post-BD (% predicted) <sup>a</sup>  | -3.31   | 0.70           | <0.001 <sup>e</sup>   |
| FEV <sub>1</sub> /FVC post-BD (ratio x 100) <sup>a</sup>                        | -1.70   | 0.006          | 0.003 <sup>d,h</sup>  |
| <b>CHEST CT PARAMETERS</b>  |   |                |                       |
| Wall Area %, Segmental <sup>a</sup>   | 0.31  | 0.12           | 0.01 <sup>d,j</sup>   |
| Wall Area %, Subsegmental <sup>a</sup>  | 0.41  | 0.17           | 0.01 <sup>d,j</sup>   |
| SRWA-Pi10 <sup>a</sup>  | 0.01  | 0.005          | 0.04 <sup>d,j</sup>   |
| Emphysema % (-950 HU) <sup>a</sup>  | 0.14  | 0.35           | 0.69 <sup>d,j</sup>   |
| Gas Trapping %, expiratory scan (-856HU) <sup>a</sup>                           | 1.79  | 0.78           | 0.02 <sup>d,j</sup>   |
| Total Lung Capacity (L) <sup>a</sup>  | 0.008   | 0.04           | 0.84 <sup>d,j</sup>   |

Abbreviations: COPD = chronic obstructive pulmonary disease; GOLD = Global Initiative for Chronic Obstructive Lung Disease; SGRQ = St. George's Respiratory Questionnaire; MMRC = Modified Medical Research Council; FEV<sub>1</sub> = forced expiratory volume in the first second; FVC = forced vital capacity; post-BD = post bronchodilator; CT = computed tomography; HU = Hounsfield units. SRWA-Pi10 = square root wall area of a hypothetical airway with 10mm internal perimeter.

\* From original 10,156 subjects, 723 were removed with childhood asthma and 28 were removed for unclassifiable asthma status.

<sup>a</sup> Subjects included are fewer than total subjects due to subject survey response being missing or unclassifiable. <sup>b</sup> Each row represents a separate regression model. Included subjects in each model are those with classifiable data for the parameter.

<sup>c</sup> Odds ratio (OR), 95% confidence interval (CI) for logistic regression; beta coefficient ( $\beta$ ), standard error (SE) for linear regression.

<sup>d</sup> Covariates for analysis = age at enrollment in years + gender + race + pack-years. <sup>e</sup> Only covariate is pack-years.

Additional covariates: <sup>f</sup> current smoker; <sup>g</sup> current smoker + FEV<sub>1</sub> % predicted; <sup>h</sup> FEV<sub>1</sub> % predicted; <sup>i</sup> height; <sup>j</sup> body mass index + CT scanner model.

| <b>Table s3 Effect of Childhood Pneumonia in Childhood Asthmatics Only</b>   |   |              |                     |
|--|---|--------------|---------------------|
| <b>Outcomes in N = 723 subjects, only those with childhood asthma</b><br>Childhood pneumonia N = 137 (18.9%); No childhood pneumonia N = 586 (81.1%) | <b>Impact of Childhood Pneumonia<sup>b</sup></b>          |              |                     |
|  | <b>OR (95% CI) or <math>\beta</math> (SE)<sup>c</sup></b> |              | <b>p Value</b>      |
| <b>RESPIRATORY SYMPTOMS AND DISEASE</b>  |   |              |                     |
| Chronic bronchitis   | 1.14  | (0.13, 3.56) | 0.56 <sup>d,f</sup> |
| COPD, GOLD 2-4   | 1.85  | (1.10, 3.18) | 0.02 <sup>d</sup>   |
| Number of COPD exacerbations in past year  | 0.05  | 0.12         | 0.70 <sup>d,g</sup> |
| Had a severe COPD exacerbation in past year  | 1.22  | (0.76, 1.94) | 0.41 <sup>d,g</sup> |
| SGRQ Score, Total <sup>a</sup>   | -0.44   | 2.02         | 0.83 <sup>d,h</sup> |
| MMRC Dyspnea Scale (0-4) <sup>a</sup>  | -0.12   | 0.13         | 0.33 <sup>d,h</sup> |
| <b>LUNG FUNCTION</b>   |   |              |                     |
| FEV <sub>1</sub> post-BD (% predicted) <sup>a</sup>  | -6.24   | 2.35         | 0.008 <sup>e</sup>  |
| FVC post-BD (% predicted) <sup>a</sup>   | -4.66   | 1.79         | 0.009 <sup>e</sup>  |
| FEV <sub>1</sub> /FVC post-BD (ratio x 100) <sup>a</sup>   | -0.01   | 0.01         | 0.64 <sup>d,i</sup> |
| <b>CHEST CT PARAMETERS</b>   |   |              |                     |
| Wall Area %, Segmental <sup>a</sup>  | 0.39  | 0.33         | 0.25 <sup>d,j</sup> |
| Wall Area %, Subsegmental <sup>a</sup>   | 0.32  | 0.48         | 0.51 <sup>d,j</sup> |
| SRWA-Pi10 <sup>a</sup>   | 0.02  | 0.02         | 0.27 <sup>d,j</sup> |
| Emphysema % (-950 HU) <sup>a</sup>   | 0.42  | 0.77         | 0.58 <sup>d,j</sup> |
| Gas Trapping %, expiratory scan (-856HU) <sup>a</sup>  | 0.76  | 1.93         | 0.70 <sup>d,j</sup> |
| Total Lung Capacity (L) <sup>a</sup>   | -0.08   | 0.01         | 0.43 <sup>d,j</sup> |

Abbreviations: COPD = chronic obstructive pulmonary disease; GOLD = Global Initiative for Chronic Obstructive Lung Disease; SGRQ = St. George's Respiratory Questionnaire; MMRC = Modified Medical Research Council; FEV<sub>1</sub> = forced expiratory volume in the first second; FVC = forced vital capacity; post-BD = post bronchodilator; CT = computed tomography; HU = Hounsfield units. SRWA-Pi10 = square root wall area of a hypothetical airway with 10mm internal perimeter.

<sup>a</sup> Subjects included are fewer than total subjects due to subject survey response being missing or unclassifiable.

<sup>b</sup> Each row represents a separate regression model. Included subjects in each model are those with classifiable data for the parameter.

<sup>c</sup> Odds ratio (OR), 95% confidence interval (CI) for logistic regression; beta coefficient ( $\beta$ ), standard error (SE) for linear regression.

<sup>d</sup> Covariates for analysis = age at enrollment in years + gender + race + pack-years. <sup>e</sup> Only covariate is pack-years.

Additional covariates: <sup>f</sup> current smoker; <sup>g</sup> current smoker + FEV<sub>1</sub> % predicted; <sup>h</sup> FEV<sub>1</sub> % predicted; <sup>i</sup> height; <sup>j</sup> body mass index + CT scanner model.

| <b>Table s4 Recall Assessment in Subjects Who Did Not Report Known COPD or Emphysema Diagnosis</b> |  |   |   |              |                            |
|--|--|---|---|--------------|----------------------------|
|  | <b>Childhood<br/>Pneumonia</b><br>N = 374 (6.5%) | <b>No Childhood<br/>Pneumonia</b><br>N = 5369 (93.5%) | <b>Impact of Childhood<br/>Pneumonia<sup>b</sup></b><br><b>OR (95% CI) or <math>\beta</math> (SE)</b> |              | <b>p Value<sup>c</sup></b> |
| COPD, GOLD 2-4 (%) <sup>a</sup>  | 54 (14.4%)                                       | 698 (13.0%)   | 1.03  | (0.74, 1.41) | 0.85 <sup>d</sup>          |
| FEV <sub>1</sub> post-BD % predicted <sup>a</sup>  | 87%  | 89%   | -2.29   | (0.91)       | 0.01                       |
| FVC post-BD % predicted <sup>a</sup>   | 91%  | 93%   | -1.80   | (0.82)       | 0.03                       |
| FEV <sub>1</sub> /FVC post-BD (ratio x 100) <sup>a</sup>   | 0.74   | 0.75  | -0.004  | (0.005)      | 0.35 <sup>d,e</sup>        |

Abbreviations: COPD = chronic obstructive pulmonary disease; GOLD = Global Initiative for Chronic Obstructive Lung Disease;

FEV<sub>1</sub> = forced expiratory volume in the first second; FVC = forced vital capacity; post-BD = post bronchodilator.

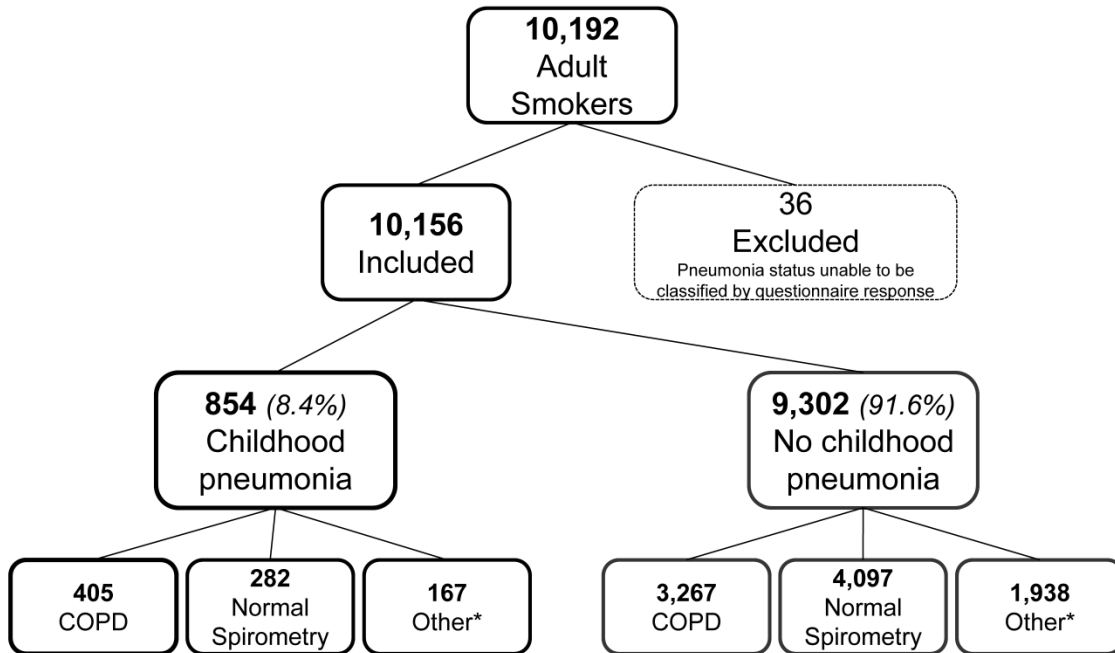
<sup>a</sup> Subjects included are fewer than total subjects due to subject survey response being missing or unclassifiable.

<sup>b</sup> Each row represents a separate regression model. Beta coefficient ( $\beta$ ) and standard error (SE) for linear regression.

<sup>c</sup> Covariate used for all analyses is pack years. <sup>d</sup> Additional covariates: gender + age at enrollment + race; <sup>e</sup> + height.

**Figures**

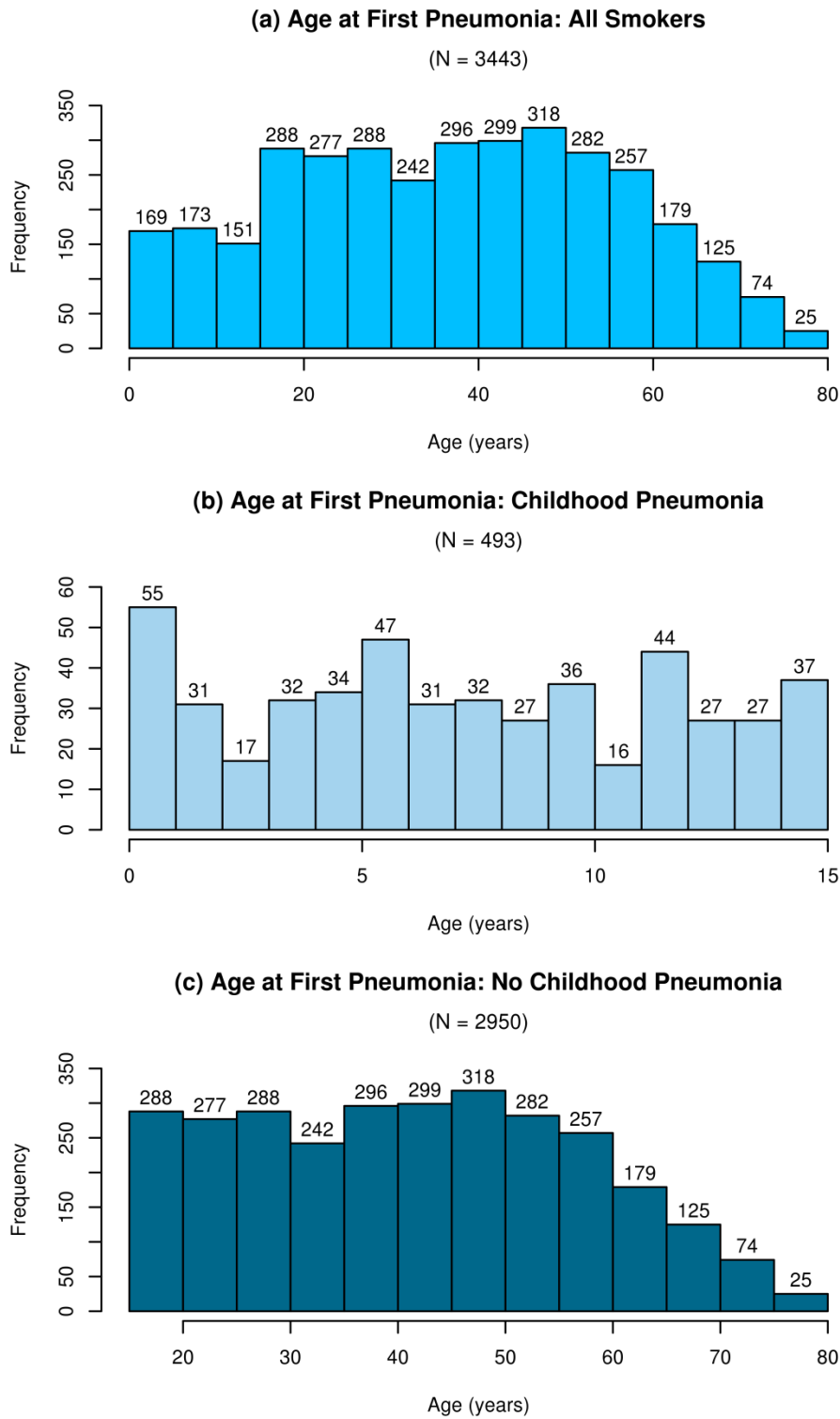
**Figure s1 Subject Classification**



**Figure s1** Classification of subjects in cohort based on childhood pneumonia status.

\*Includes subjects with GOLD Stage 1 ( $FEV_1/FVC < 0.7$  with  $FEV_1 \geq 80\%$  predicted) or Preserved Ratio Impaired Spirometry (PRISm,  $FEV_1/FVC \geq 0.7$  with  $FEV_1 < 80\%$  predicted)

**Figure s2 Pneumonia Age Distribution**



**Figure s2** Distribution of age of first pneumonia in entire cohort (a) in subjects with a history of childhood pneumonia (b) and in subjects without a history of childhood pneumonia (c). Includes all subjects who reported an age of first pneumonia.