**Supplementary Materials**

**Original Research**
**Bronchiectasis Occurs Independently of Chronic Obstructive Pulmonary Disease in Alpha-1 Antitrypsin Deficiency**

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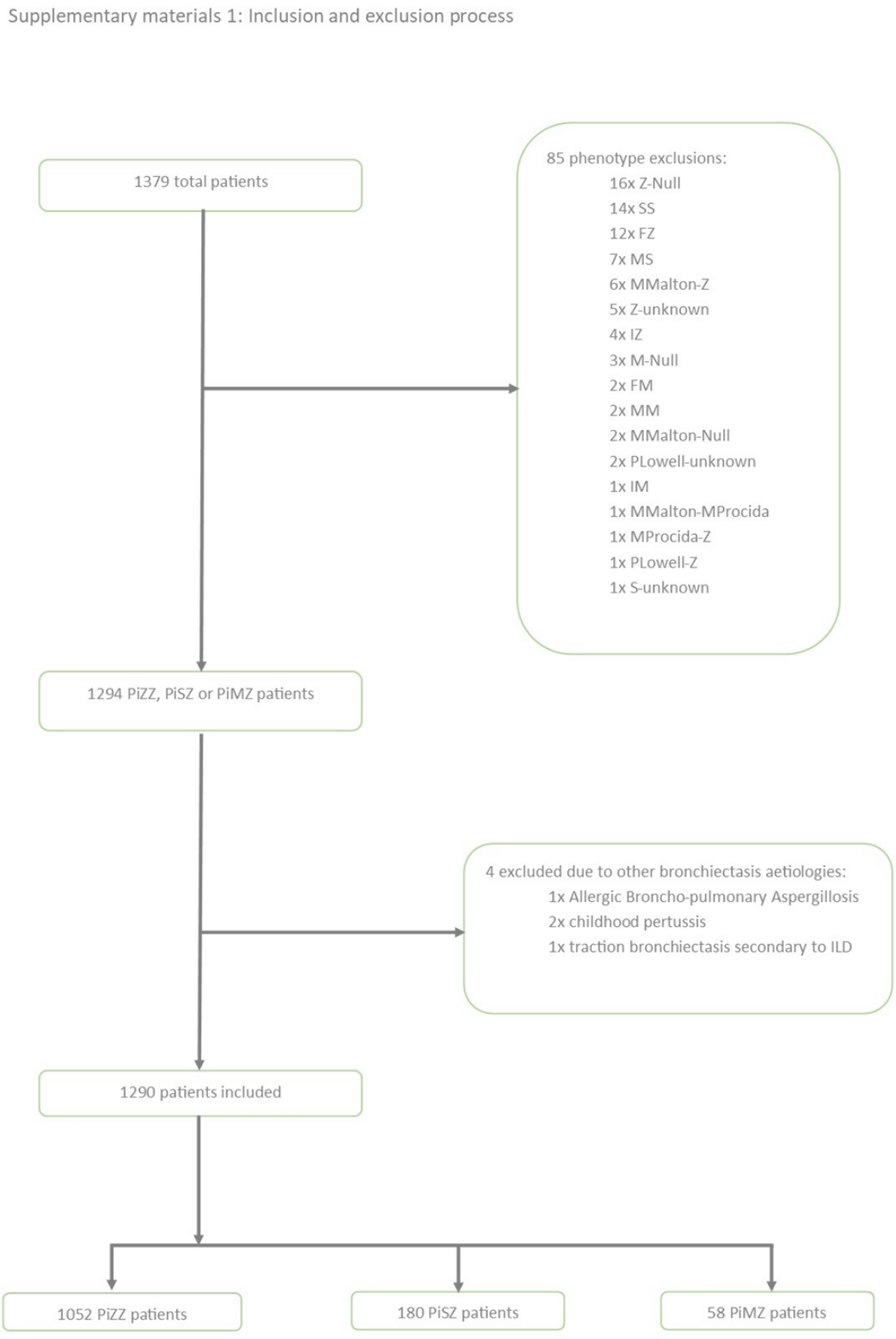
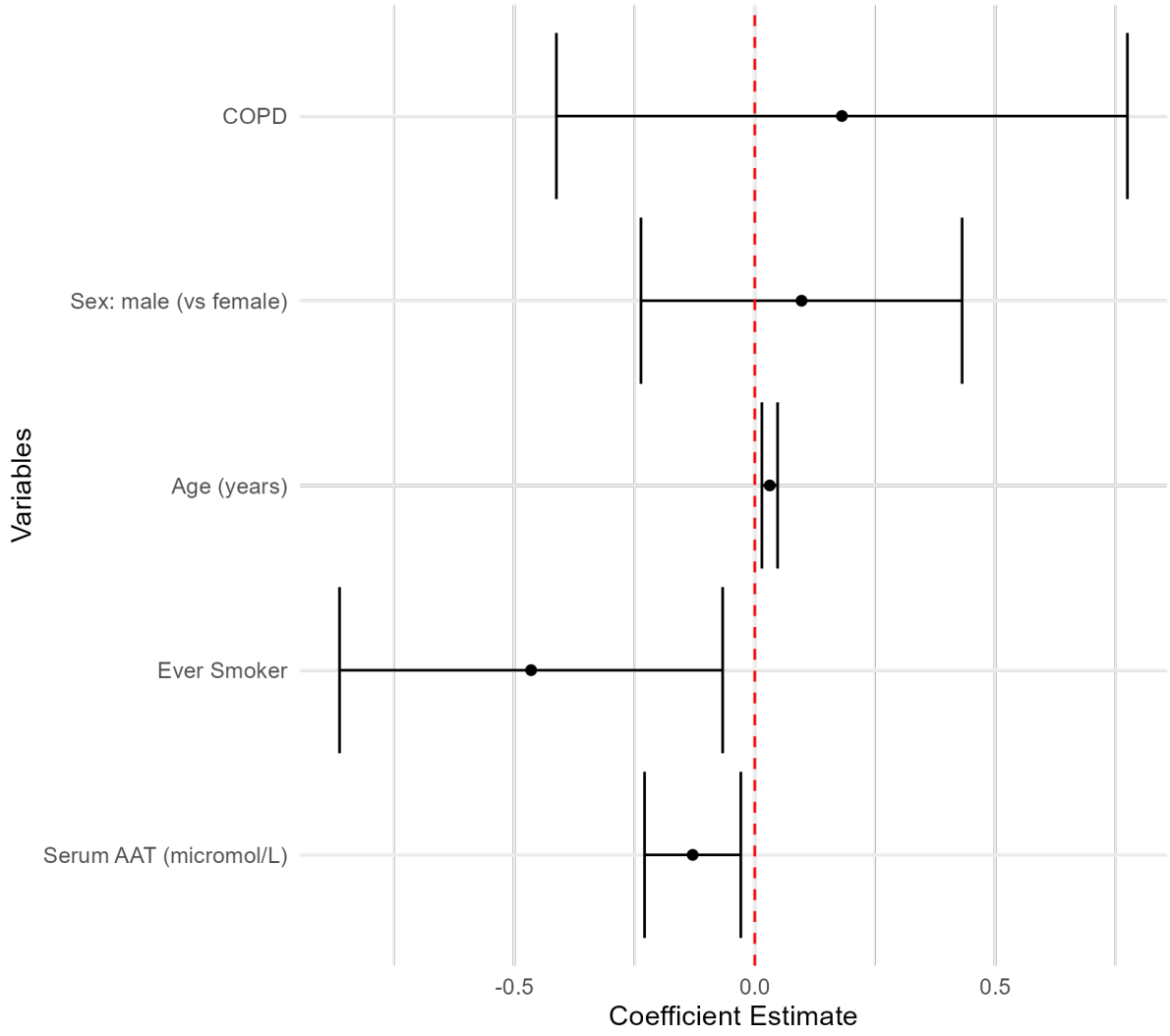
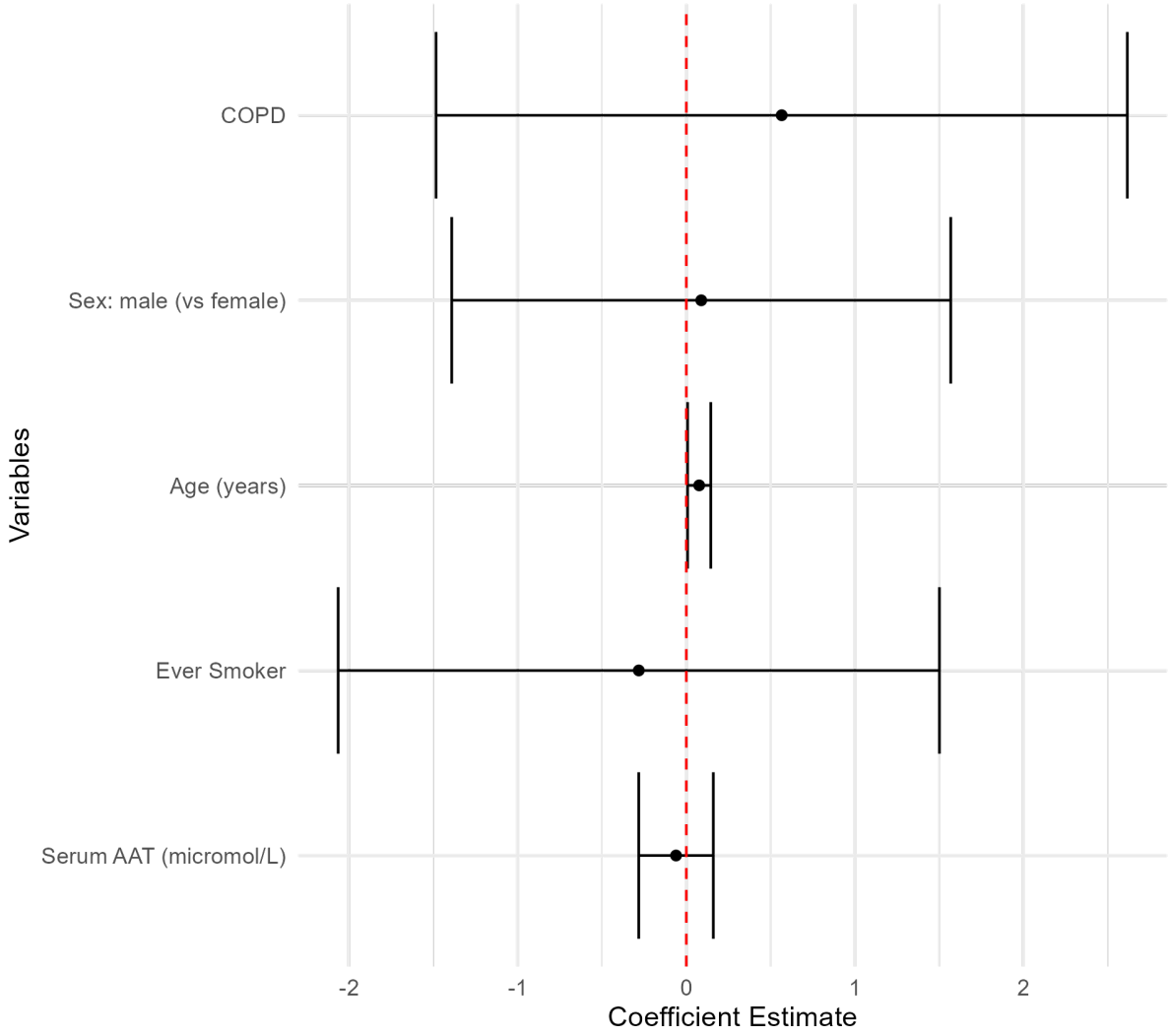
e-Figure 1: Inclusion/exclusion process



e-Figure 2: Forest plot of logistic regression estimates of Bronchiectasis associations in PiZZ Alpha-1 Antitrypsin Deficiency



e-Figure 3: Forest plot of logistic regression estimates of Bronchiectasis associations in PiSZ Alpha-1 Antitrypsin Deficiency



**e-Table 1: Diagnostic accuracy of COPD**

| *n = 967* | FEV1/FVC ≤ 0.7 | FEV1/FVC > 0.7 |
|---|---|---|
| COPD diagnosis | 766 (79.2%) | 6 (0.6%) |
| No COPD diagnosis | 16 (1.7%) | 179 (19.6%) |

*COPD: Chronic Obstructive Pulmonary Disease*

**e-Table 2: Diagnostic accuracy of Bronchiectasis**

| *n = 290* | CT evidence | No CT evidence |
|---|---|---|
| Bronchiectasis diagnosis | 193 (66.5%) | 0 (0.0%) |
| No Bronchiectasis diagnosis | 22 (7.5%) | 75 (25.8%) |

**e-Table 3: CT characteristics of AATD patients stratified by phenotype and pre-existing clinical diagnosis**

| | PiZZ | | PiSZ | |
|---|---|---|---|---|
| | Bronchiectasis diagnosis | No previous bronchiectasis diagnosis | Bronchiectasis diagnosis | No previous bronchiectasis diagnosis |
| n | 174 | 81 | 9 | 12 |
| n lobes affected (%) | | | | |
| 0 | 0 (0.0) | 61 (75.3) | 0 (0.0) | 11 (91.7) |
| 1 | 24 (13.8) | 7 (8.6) | 5 (55.6) | 0 (0.0) |
| 2 | 95 (54.6) | 7 (8.6) | 3 (33.3) | 1 (8.3) |
| 3 | 9 (5.2) | 3 (3.7) | 1 (11.1) | 0 (0.0) |
| 4 | 12 (6.9) | 1 (1.2) | 0 (0.0) | 0 (0.0) |
| 5 | 5 (2.9) | 1 (1.2) | 0 (0.0) | 0 (0.0) |
| 6 | 29 (16.7) | 1 (1.2) | 0 (0.0) | 0 (0.0) |
| Cylindrical (%) | 168 (96.6) | 21 (25.9) | 9 (100.0) | 1 (8.3) |
| Varicose (%) | 45 (25.9) | 4 (4.9) | 0 (0.0) | 0 (0.0) |
| Cystic (%) | 15 (8.6) | 0 (0.0) | 0 (0.0) | 0 (0.0) |

**e-Table 4: CT characteristics of AATD with radiological evidence of bronchiectasis stratified by phenotype**

| | PiZZ | PiSZ | p |
|---|---|---|---|
| n | 198 | 10 | |
| n lobes affected (%) | | | **0.009** |
| 1 | 31 (15.7) | 5 (50.0) | |
| 2 | 104 (52.5) | 4 (40.0) | |
| 3 | 12 (6.1) | 1 (10.0) | |
| 4 | 13 (6.6) | 0 (0.0) | |
| 5 | 7 (3.5) | 0 (0.0) | |
| 6 | 31 (15.7) | 0 (0.0) | |
| Cylindrical (%) | 192 (97.0) | 10 (100.0) | 0.842 |
| Varicose (%) | 50 (25.3) | 0 (0.0) | 0.161 |
| Cystic (%) | 15 (7.6) | 0 (0.0) | 0.638 |

*AATD: Alpha-1 Antitrypsin Deficiency*

**e-Table 5: Bronchiectasis Severity Index Scores for AATD patients, stratified by phenotype**

| | **PiZZ** | **PiSZ** | **p** |
|---|---|---|---|
| n | 259 | 21 | |
| BSI (mean (SD)) | 4.78 (3.02) | 3.86 (2.69) | 0.176 |
| BSI Severity (%) | | | 0.236 |
| Mild | 135 (52.5) | 15 (71.4) | |
| Moderate | 90 (35.0) | 4 (19.0) | |
| Severe | 32 (12.5) | 2 ( 9.5) | |

*AATD: Alpha-1 Antitrypsin Deficiency; BSI: Bronchiectasis Severity Index*

**e-Table 6: Regression model estimates comparing lung function and exacerbation rate between bronchiectasis and non-bronchiectasis patients with AATD, stratified by phenotype**

| | **PiZZ** | | | | **PiSZ** | | | |
|---|---|---|---|---|---|---|---|---|
| *Outcome* | *n* | *est* | *CI* | *p* | *n* | *est* | *CI* | *p* |
| FEV1pp baseline | 973 | -0.49 | -3.78 – 2.79 | 0.768 | 140 | -10.25 | -23.22 – 2.72 | 0.121 |
| $FEV_1$pp/year decline | 687 | -0.02 | -0.33 – 0.29 | 0.903 | 85 | -0.44 | -1.78 – 0.90 | 0.518 |
| KCOpp/year decline | 525 | -0.23 | -0.70 - - 0.24 | 0.338 | 58 | -1.59 | -3.95 – 0.77 | 0.181 |
| TLCOpp/year decline | 498 | -0.12 | -0.57 – 0.32 | 0.577 | 60 | 1.54 | -0.85 – 3.94 | 0.202 |
| Exacerbation yearly rate | 979 | 0.99 | 0.61-1.59 | 0.963 | 141 | 0.63 | 0.05 – 7.89 | 0.721 |

*n = number of patients included in model; $FEV_1$ = Forced Expiratory Volume in 1 second; KCO = transfer coefficient of carbon monoxide; TLCO = transfer factor of the lung for carbon monoxide; pp = % predicted; multivariate estimates adjust for age, sex, phenotype, smoking history, and concurrent COPD diagnosis. Linear regression models used for $FEV_1$pp, KCOpp and TLCOpp; zero-inflated model used for exacerbation rate.*