

|    | Node 1                 | Node 2                 | GOLD=0<br>P-value<br>(Control) | GOLD>=2<br>p-value<br>(Case) | Gold=2<br>p-value<br>(moderate) | GOLD>=3<br>p-value<br>(Severe) |
|----|------------------------|------------------------|--------------------------------|------------------------------|---------------------------------|--------------------------------|
| 1  | Emphysema              | Gas Trapping           | 1.07E-175                      | 0.00E+00                     | 8.89E-184                       | 3.45E-150                      |
| 2  | Gas Trapping           | BMI                    | 3.34E-30                       | 4.80E-48                     | 2.02E-23                        | 1.06E-31                       |
| 3  | Gas Trapping           | Age                    | 3.81E-28                       | 8.86E-36                     | 1.26E-16                        | 6.44E-16                       |
| 4  | Emphysema              | Airway Wall Area       | 8.66E-27                       | 5.53E-23                     | 1.14E-11                        | 2.45E-10                       |
| 5  | 6MWD                   | BMI                    | 6.15E-26                       | 9.97E-24                     | 2.86E-16                        | 1.37E-09                       |
| 6  | Airway Wall Area       | 6MWD                   | 2.72E-23                       | 3.87E-12                     | 6.46E-06                        | 2.85E-06                       |
| 7  | Age                    | Pack-years             | 3.18E-19                       | 5.11E-22                     | 5.08E-12                        | 2.73E-10                       |
| 8  | Gas Trapping           | 6MWD                   | 2.97E-18                       | 0.8002                       | 0.0042                          | 0.0032                         |
| 9  | Emphysema              | 6MWD                   | 2.10E-17                       | 0.0029                       | 0.1724                          | 0.0001                         |
| 10 | 6MWD                   | Pack-years             | 1.46E-15                       | 0.0004                       | 9.48E-06                        | 0.6282                         |
| 11 | FEV1% pred             | BMI                    | 5.43E-10                       | 6.23E-08                     | 3.27E-05                        | 0.7150                         |
| 12 | FEV1% pred             | Airway Wall Area       | 1.07E-08                       | 1.92E-58                     | 1.92E-14                        | 5.09E-14                       |
| 13 | Emphysema              | Age                    | 4.74E-07                       | 0.1503                       | 0.6508                          | 0.4983                         |
| 14 | Exacerbation Frequency | 6MWD                   | 4.65E-06                       | 2.46E-06                     | 1.34E-06                        | 0.0451                         |
| 15 | Emphysema              | Emphysema Distribution | 6.34E-06                       | 1.60E-05                     | 1.18E-12                        | 0.0315                         |
| 16 | FEV1% pred             | Emphysema              | 9.35E-06                       | 8.01E-08                     | 0.0069                          | 0.0051                         |
| 17 | Emphysema              | BMI                    | 1.48E-05                       | 0.0001                       | 0.7461                          | 0.0140                         |
| 18 | Emphysema Distribution | BMI                    | 1.64E-05                       | 0.5983                       | 4.51E-05                        | 0.1855                         |
| 19 | Emphysema Distribution | Airway Wall Area       | 1.97E-05                       | 0.8263                       | 0.3670                          | 0.8338                         |
| 20 | Emphysema Distribution | Pack-years             | 0.0002                         | 0.9547                       | 0.9462                          | 0.6874                         |
| 21 | Airway Wall Area       | BMI                    | 0.0003                         | 0.5511                       | 0.5282                          | 0.6508                         |
| 22 | FEV1% pred             | Pack-years             | 0.0005                         | 0.4973                       | 0.5306                          | 0.0635                         |
| 23 | Exacerbation Frequency | BMI                    | 0.0008                         | 0.0687                       | 0.0889                          | 0.5097                         |
| 24 | FEV1% pred             | Exacerbation Frequency | 0.0018                         | 1.81E-06                     | 0.0041                          | 0.0046                         |
| 25 | Gas Trapping           | Airway Wall Area       | 0.0063                         | 0.0406                       | 0.8633                          | 0.0033                         |
| 26 | Airway Wall Area       | Exacerbation Frequency | 0.0091                         | 0.0123                       | 0.0931                          | 0.0445                         |
| 27 | FEV1% pred             | 6MWD                   | 0.0107                         | 3.73E-45                     | 4.64E-07                        | 5.46E-25                       |
| 28 | Emphysema Distribution | 6MWD                   | 0.0160                         | 0.0134                       | 0.0182                          | 0.1041                         |
| 29 | Emphysema Distribution | Gas Trapping           | 0.0347                         | 2.07E-05                     | 1.55E-08                        | 0.0329                         |
| 30 | Emphysema Distribution | Age                    | 0.0424                         | 0.0284                       | 0.0174                          | 0.1697                         |
| 31 | Airway Wall Area       | Age                    | 0.0516                         | 0.0285                       | 0.0001                          | 0.2416                         |
| 32 | FEV1% pred             | Emphysema Distribution | 0.0822                         | 0.7740                       | 0.7391                          | 0.7008                         |
| 33 | Airway Wall Area       | Pack-years             | 0.0890                         | 0.8360                       | 0.7846                          | 0.9626                         |
| 34 | 6MWD                   | Age                    | 0.1041                         | 8.28E-07                     | 0.0037                          | 8.24E-06                       |
| 35 | BMI                    | Age                    | 0.1110                         | 2.12E-06                     | 0.0007                          | 0.0643                         |
| 36 | FEV1% pred             | Gas Trapping           | 0.2125                         | 4.48E-133                    | 6.79E-15                        | 6.53E-34                       |
| 37 | Exacerbation Frequency | Age                    | 0.2707                         | 1.90E-05                     | 0.0190                          | 0.0003                         |
| 38 | Emphysema              | Pack-years             | 0.2911                         | 0.0238                       | 0.0542                          | 0.0076                         |
| 39 | Emphysema              | Exacerbation Frequency | 0.3110                         | 0.7687                       | 0.2180                          | 0.5722                         |
| 40 | Gas Trapping           | Exacerbation Frequency | 0.5458                         | 0.0773                       | 0.2741                          | 0.4850                         |
| 41 | Exacerbation Frequency | Pack-years             | 0.6904                         | 0.3498                       | 0.6985                          | 0.2569                         |
| 42 | Emphysema Distribution | Exacerbation Frequency | 0.7295                         | 0.8128                       | 0.7598                          | 0.9829                         |
| 43 | FEV1% pred             | Age                    | 0.7375                         | 2.62E-10                     | 0.6621                          | 2.36E-10                       |
| 44 | BMI                    | Pack-years             | 0.8928                         | 0.0722                       | 0.7600                          | 0.0799                         |
| 45 | Gas Trapping           | Pack-years             | 0.9744                         | 0.0045                       | 0.2041                          | 0.2517                         |

**Table S1:** p-values for all edges for different COPD status groups

|    | Node 1                 | Node 2                 | GOLD=0<br>PCOR<br>(Control) | GOLD>=2<br>PCOR<br>(Case) | GOLD=2<br>PCOR<br>(moderate) | GOLD>=3<br>PCOR<br>(severe) |
|----|------------------------|------------------------|-----------------------------|---------------------------|------------------------------|-----------------------------|
| 1  | Emphysema              | Gas Trapping           | 0.45                        | 0.64                      | 0.65                         | 0.63                        |
| 2  | Gas Trapping           | BMI                    | -0.19                       | -0.27                     | -0.25                        | -0.31                       |
| 3  | Gas Trapping           | Age                    | 0.18                        | 0.23                      | 0.21                         | 0.22                        |
| 4  | Emphysema              | Airway Wall Area       | -0.18                       | -0.18                     | -0.17                        | -0.17                       |
| 5  | 6MWD                   | BMI                    | -0.17                       | -0.19                     | -0.21                        | -0.17                       |
| 6  | Airway Wall Area       | 6MWD                   | -0.16                       | -0.13                     | -0.11                        | -0.13                       |
| 7  | Age                    | Pack-years             | 0.15                        | 0.18                      | 0.17                         | 0.17                        |
| 8  | Gas Trapping           | 6MWD                   | -0.14                       | 0.00                      | -0.07                        | 0.08                        |
| 9  | Emphysema              | 6MWD                   | 0.14                        | -0.06                     | 0.03                         | -0.11                       |
| 10 | 6MWD                   | Pack-years             | -0.13                       | -0.07                     | -0.11                        | -0.01                       |
| 11 | FEV1% pred             | BMI                    | -0.10                       | -0.10                     | -0.11                        | 0.01                        |
| 12 | FEV1% pred             | Airway Wall Area       | -0.10                       | -0.29                     | -0.19                        | -0.21                       |
| 13 | Emphysema              | Age                    | 0.08                        | -0.03                     | 0.01                         | -0.02                       |
| 14 | Exacerbation Frequency | 6MWD                   | -0.08                       | -0.09                     | -0.12                        | -0.06                       |
| 15 | Emphysema              | Emphysema Distribution | 0.08                        | 0.08                      | 0.18                         | 0.06                        |
| 16 | FEV1% pred             | Emphysema              | 0.07                        | -0.10                     | -0.07                        | -0.08                       |
| 17 | Emphysema              | BMI                    | 0.07                        | -0.07                     | 0.01                         | -0.07                       |
| 18 | Emphysema Distribution | BMI                    | -0.07                       | -0.01                     | -0.10                        | 0.04                        |
| 19 | Emphysema Distribution | Airway Wall Area       | 0.07                        | 0.00                      | 0.02                         | -0.01                       |
| 20 | Emphysema Distribution | Pack-years             | 0.06                        | 0.00                      | 0.00                         | -0.01                       |
| 21 | Airway Wall Area       | BMI                    | 0.06                        | 0.01                      | 0.02                         | 0.01                        |
| 22 | FEV1% pred             | Pack-years             | -0.06                       | -0.01                     | 0.02                         | -0.05                       |
| 23 | Exacerbation Frequency | BMI                    | 0.06                        | 0.03                      | 0.04                         | 0.02                        |
| 24 | FEV1% pred             | Exacerbation Frequency | -0.05                       | -0.09                     | -0.07                        | -0.08                       |
| 25 | Gas Trapping           | Airway Wall Area       | -0.05                       | -0.04                     | 0.00                         | -0.08                       |
| 26 | Airway Wall Area       | Exacerbation Frequency | 0.04                        | 0.05                      | 0.04                         | 0.06                        |
| 27 | FEV1% pred             | 6MWD                   | 0.04                        | 0.26                      | 0.13                         | 0.28                        |
| 28 | Emphysema Distribution | 6MWD                   | -0.04                       | -0.05                     | -0.06                        | -0.04                       |
| 29 | Emphysema Distribution | Gas Trapping           | -0.04                       | -0.08                     | -0.14                        | -0.06                       |
| 30 | Emphysema Distribution | Age                    | -0.03                       | -0.04                     | -0.06                        | -0.04                       |
| 31 | Airway Wall Area       | Age                    | -0.03                       | -0.04                     | -0.10                        | 0.03                        |
| 32 | FEV1% pred             | Emphysema Distribution | -0.03                       | 0.01                      | 0.01                         | 0.01                        |
| 33 | Airway Wall Area       | Pack-years             | -0.03                       | 0.00                      | -0.01                        | 0.00                        |
| 34 | 6MWD                   | Age                    | 0.03                        | -0.09                     | -0.07                        | -0.12                       |
| 35 | BMI                    | Age                    | 0.03                        | 0.09                      | 0.09                         | 0.05                        |
| 36 | FEV1% pred             | Gas Trapping           | -0.02                       | -0.43                     | -0.20                        | -0.32                       |
| 37 | Exacerbation Frequency | Age                    | 0.02                        | -0.08                     | -0.06                        | -0.10                       |
| 38 | Emphysema              | Pack-years             | 0.02                        | -0.04                     | 0.05                         | -0.07                       |
| 39 | Emphysema              | Exacerbation Frequency | 0.02                        | -0.01                     | 0.03                         | -0.02                       |
| 40 | Gas Trapping           | Exacerbation Frequency | 0.01                        | 0.03                      | 0.03                         | 0.02                        |
| 41 | Exacerbation Frequency | Pack-years             | -0.01                       | -0.02                     | -0.01                        | -0.03                       |
| 42 | Emphysema Distribution | Exacerbation Frequency | -0.01                       | 0.00                      | 0.01                         | 0.00                        |
| 43 | FEV1% pred             | Age                    | -0.01                       | 0.12                      | -0.01                        | 0.17                        |
| 44 | BMI                    | Pack-years             | 0.00                        | 0.03                      | 0.01                         | 0.05                        |
| 45 | Gas Trapping           | Pack-years             | 0.00                        | 0.05                      | 0.03                         | 0.03                        |

**Table S1 (cont.):** partial correlations for all edges for different COPD status groups

|    | Node 1                 | Node 2                 | Perm Pval<br>GOLD=0<br>(control) | Perm Pval<br>GOLD>=2<br>(case) | Perm Pval<br>GOLD=2<br>(moderate) | Perm Pval<br>GOLD>=3<br>(severe) |
|----|------------------------|------------------------|----------------------------------|--------------------------------|-----------------------------------|----------------------------------|
| 1  | Emphysema              | Gas Trapping           | 0                                | 0.9808                         | 0.3518                            | 0.8558                           |
| 2  | Gas Trapping           | BMI                    | 0                                | 0.0066                         | 0.531                             | 0.0024                           |
| 3  | Gas Trapping           | Age                    | 0                                | 0.7922                         | 0.2956                            | 0.9624                           |
| 4  | Emphysema              | Airway Wall Area       | 0.0024                           | 0.0036                         | 0.531                             | 0.7482                           |
| 5  | 6MWD                   | BMI                    | 0.6018                           | 0.7232                         | 0.4316                            | 0.2412                           |
| 6  | Airway Wall Area       | 6MWD                   | 0.5244                           | 0.0012                         | 0.4882                            | 0.9066                           |
| 7  | Age                    | Pack-years             | 0.0062                           | 0.978                          | 0.7298                            | 0.753                            |
| 8  | Gas Trapping           | 6MWD                   | 0                                | 0                              | 0.0072                            | 0.017                            |
| 9  | Emphysema              | 6MWD                   | 0.003                            | 0.0144                         | 0.7594                            | 0.0042                           |
| 10 | 6MWD                   | Pack-years             | 0.0006                           | 0.0628                         | 0.058                             | 0.0056                           |
| 11 | FEV1% pred             | BMI                    | 0.4118                           | 0.4066                         | 0.342                             | 8.00E-04                         |
| 12 | FEV1% pred             | Airway Wall Area       | 0                                | 0.9204                         | 0                                 | 2.00E-04                         |
| 13 | Emphysema              | Age                    | 0.0006                           | 0.302                          | 0.5702                            | 0.9808                           |
| 14 | Exacerbation Frequency | 6MWD                   | 0.8302                           | 0.5492                         | 0.1392                            | 0.0646                           |
| 15 | Emphysema              | Emphysema Distribution | 0.3376                           | 0.4012                         | 0                                 | 0.0274                           |
| 16 | FEV1% pred             | Emphysema              | 4.00E-04                         | 0.1792                         | 0                                 | 0.0044                           |
| 17 | Emphysema              | BMI                    | 0.0066                           | 0.0504                         | 0.0016                            | 0.5482                           |
| 18 | Emphysema Distribution | BMI                    | 0.3404                           | 0.2012                         | 0.035                             | 0.6342                           |
| 19 | Emphysema Distribution | Airway Wall Area       | 0.001                            | 0.1576                         | 0.5056                            | 0.4982                           |
| 20 | Emphysema Distribution | Pack-years             | 0.0068                           | 0.0322                         | 0.2686                            | 0.9346                           |
| 21 | Airway Wall Area       | BMI                    | 0.0054                           | 0.2246                         | 0.943                             | 0.6908                           |
| 22 | FEV1% pred             | Pack-years             | 0                                | 0                              | 0.7616                            | 0.0814                           |
| 23 | Exacerbation Frequency | BMI                    | 0.1084                           | 0.8046                         | 0.7726                            | 0.3548                           |
| 24 | FEV1% pred             | Exacerbation Frequency | 0                                | 0                              | 0.4448                            | 0.7154                           |
| 25 | Gas Trapping           | Airway Wall Area       | 0.1062                           | 0.4174                         | 0.1552                            | 0.0236                           |
| 26 | Airway Wall Area       | Exacerbation Frequency | 0.5798                           | 0.813                          | 0.9082                            | 0.6548                           |
| 27 | FEV1% pred             | 6MWD                   | 0                                | 0                              | 0                                 | 0.054                            |
| 28 | Emphysema Distribution | 6MWD                   | 0.9604                           | 0.883                          | 0.5006                            | 0.5982                           |
| 29 | Emphysema Distribution | Gas Trapping           | 0                                | 0.4616                         | 0.092                             | 0.0376                           |
| 30 | Emphysema Distribution | Age                    | 0.29                             | 0.1616                         | 0.444                             | 0.513                            |
| 31 | Airway Wall Area       | Age                    | 0.0348                           | 0.2766                         | 0.025                             | 0.2118                           |
| 32 | FEV1% pred             | Emphysema Distribution | 0.6946                           | 0.0054                         | 0.6958                            | 0.4886                           |
| 33 | Airway Wall Area       | Pack-years             | 0.3906                           | 0.1888                         | 0.6044                            | 0.0746                           |
| 34 | 6MWD                   | Age                    | 0.1178                           | 0.0092                         | 0.4922                            | 0.0784                           |
| 35 | BMI                    | Age                    | 0.001                            | 0.0434                         | 0.78                              | 0.0986                           |
| 36 | FEV1% pred             | Gas Trapping           | 0                                | 0.281                          | 0                                 | 0.0124                           |
| 37 | Exacerbation Frequency | Age                    | 0.1034                           | 0.004                          | 0.439                             | 0.2154                           |
| 38 | Emphysema              | Pack-years             | 0.0684                           | 0.8348                         | 0.0966                            | 0.0244                           |
| 39 | Emphysema              | Exacerbation Frequency | 0.5656                           | 0.436                          | 0.1668                            | 0.9252                           |
| 40 | Gas Trapping           | Exacerbation Frequency | 0.0066                           | 0.5338                         | 0.6762                            | 0.4782                           |
| 41 | Exacerbation Frequency | Pack-years             | 0.406                            | 0.9026                         | 0.6628                            | 0.5014                           |
| 42 | Emphysema Distribution | Exacerbation Frequency | 0.8294                           | 0.7476                         | 0.8898                            | 0.0506                           |
| 43 | FEV1% pred             | Age                    | 0.0956                           | 0.0026                         | 0                                 | 0.0012                           |
| 44 | BMI                    | Pack-years             | 0.0798                           | 0.3096                         | 0.1924                            | 0.3502                           |
| 45 | Gas Trapping           | Pack-years             | 2.00E-04                         | 0.4822                         | 0.1962                            | 0.345                            |

**Table S1 (cont.):** permutation-based p-values for all edges for different COPD status groups