**Epidemiology and Infection**

**Case–control association study between polygenic risk score and COVID-19 severity in a Russian population using low-pass genome sequencing**

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**Supplementary Tables**

**Supplementary Table 1:** Description of the distribution of myocardial infarction events in relation to COVID-19 severity and mortality outcomes.

| Myocardialinfarction | COVID-severity | COVID-mortality |
| --- | --- | --- |
| Cases | Controls | Cases | Controls |
| N | Mean age | N | Mean age | N | Mean age | N | Mean age |
| Comorbidity status | No | 275 | 61 | 584 | 54 | 102 | 68 | 757 | 54 |
| Yes | 44 | 73 | 79 | 69 | 31 | 76 | 92 | 69 |

**Supplementary Table 2:** Description of the distribution of heart failure events in relation to COVID-19 severity and mortality outcomes.

| Heart failure | COVID-severity | COVID-mortality |
| --- | --- | --- |
| Cases | Controls | Cases | Controls |
| N | Mean age | N | Mean age | N | Mean age | N | Mean age |
| Comorbidity status | No | 174 | 55 | 491 | 51 | 105 | 56 | 637 | 52 |
| Yes | 145 | 71 | 172 | 68 | 28 | 73 | 212 | 68 |

**Supplementary Table 3:** Description of the distribution of peripheral artery occlusive disease events in relation to COVID-19 severity and mortality outcomes.

| Peripheral arteryocclusive disease | COVID-severity | COVID-mortality |
| --- | --- | --- |
| Cases | Controls | Cases | Controls |
| N | Mean age | N | Mean age | N | Mean age | N | Mean age |
| Comorbidity status | No | 260 | 61 | 553 | 53 | 90 | 68 | 723 | 54 |
| Yes | 59 | 71 | 110 | 67 | 43 | 73 | 126 | 67 |

**Supplementary Table 4:** Description of the distribution of cerebrovascular disease events in relation to COVID-19 severity and mortality outcomes.

| Cerebrovasculardisease | COVID-severity | COVID-mortality |
| --- | --- | --- |
| Cases | Controls | Cases | Controls |
| N | Mean age | N | Mean age | N | Mean age | N | Mean age |
| Comorbidity status | No | 169 | 55 | 489 | 51 | 100 | 57 | 625 | 52 |
| Yes | 150 | 72 | 174 | 69 | 33 | 74 | 224 | 68 |

**Supplementary Table 5:** Description of the distribution of chronic obstructive pulmonary disease events in relation to COVID-19 severity and mortality outcomes.

| Chronic obstructivepulmonary disease | COVID-severity | COVID-mortality |
| --- | --- | --- |
| Cases | Controls | Cases | Controls |
| N | Mean age | N | Mean age | N | Mean age | N | Mean age |
| Comorbidity status | No | 283 | 62 | 615 | 55 | 110 | 70 | 788 | 55 |
| Yes | 36 | 68 | 48 | 66 | 23 | 70 | 61 | 65 |

**Supplementary Table 6:** Description of the distribution of diabetes events in relation to COVID-19 severity and mortality outcomes.

| Diabetes | COVID-severity | COVID-mortality |
| --- | --- | --- |
| Cases | Controls | Cases | Controls |
| N | Mean age | N | Mean age | N | Mean age | N | Mean age |
| Comorbidity status | No | 246 | 61 | 595 | 54 | 94 | 68 | 747 | 55 |
| Yes | 73 | 67 | 68 | 66 | 39 | 73 | 102 | 64 |

**Supplementary Table 7:** Description of the distribution of kidney damage events in relation to COVID-19 severity and mortality outcomes.

| Kidney damage | COVID-severity | COVID-mortality |
| --- | --- | --- |
| Cases | Controls | Cases | Controls |
| N | Mean age | N | Mean age | N | Mean age | N | Mean age |
| Comorbidity status | No | 264 | 61 | 624 | 55 | 89 | 69 | 799 | 55 |
| Yes | 55 | 71 | 39 | 70 | 44 | 72 | 50 | 70 |

**Supplementary Table 8:** Logistic regression results for the full model with COVID-19 severity as an outcome and PRS as a continuous variable.

|  | coef | std err | z | P>|z| | [0.025 | 0.975] |
| --- | --- | --- | --- | --- | --- | --- |
| intercept | -1.528 | 0.148 | -10.338 | 4.75E-25 | -1.818 | -1.238 |
| age | 0.2727 | 0.104 | 2.618 | 8.85E-03 | 0.069 | 0.477 |
| sex | 0.5924 | 0.156 | 3.8 | 1.45E-04 | 0.287 | 0.898 |
| PRS | 0.4359 | 0.078 | 5.572 | 2.52E-08 | 0.283 | 0.589 |
| Myocardial infarction | -0.4745 | 0.245 | -1.939 | 5.25E-02 | -0.954 | 0.005 |
| Heart failure | 0.5087 | 0.209 | 2.439 | 1.47E-02 | 0.1 | 0.917 |
| Peripheral artery occlusive disease | -0.8205 | 0.237 | -3.461 | 5.39E-04 | -1.285 | -0.356 |
| Cerebrovascular disease | 0.534 | 0.201 | 2.661 | 7.80E-03 | 0.141 | 0.927 |
| Chronic obstructive pulmonary disease | 0.1994 | 0.256 | 0.778 | 4.37E-01 | -0.303 | 0.702 |
| Diabetes | 0.6888 | 0.209 | 3.295 | 9.84E-04 | 0.279 | 1.098 |
| Kidney damage | 0.7153 | 0.257 | 2.787 | 5.32E-03 | 0.212 | 1.218 |
| PC1 | 0.0283 | 0.098 | 0.289 | 7.73E-01 | -0.164 | 0.22 |
| PC2 | 0.1347 | 1.268 | 0.106 | 9.15E-01 | -2.35 | 2.619 |
| PC3 | -0.4851 | 1.264 | -0.384 | 7.01E-01 | -2.963 | 1.992 |
| PC4 | 0.208 | 0.575 | 0.361 | 7.18E-01 | -0.92 | 1.336 |
| PC5 | 0.2596 | 0.412 | 0.63 | 5.29E-01 | -0.548 | 1.067 |
| PC6 | 0.2689 | 0.272 | 0.987 | 3.24E-01 | -0.265 | 0.803 |
| PC7 | -0.0691 | 0.086 | -0.803 | 4.22E-01 | -0.238 | 0.1 |
| PC8 | -0.0737 | 0.073 | -1.004 | 3.15E-01 | -0.218 | 0.07 |
| PC9 | 0.0865 | 0.09 | 0.959 | 3.37E-01 | -0.09 | 0.263 |
| PC10 | 0.0432 | 0.077 | 0.562 | 5.74E-01 | -0.107 | 0.194 |

\*- coef: the coefficient of the variable (log[odd ratio]);

- std err: the standard error of the coefficient;

- Z: the z value for the estimated coefficient and the standard error;

- P>|z|: the p-value associated with the value in the z value column;

- [0.025, 0.975]: 95% confident interval (CI) for the coefficient.

**Supplementary Table 9:** Logistic regression results for the full model with COVID-19 severity as an outcome and PRS as a binary variable.

|  | coef | std err | z | P>|z| | [0.025 | 0.975] |
| --- | --- | --- | --- | --- | --- | --- |
| intercept | -1.5995 | 0.15 | -10.652 | 1.71E-26 | -1.894 | -1.305 |
| 10% with the highest PRS values | 1.0795 | 0.234 | 4.604 | 4.14E-06 | 0.62 | 1.539 |
| age | 0.2693 | 0.103 | 2.607 | 9.13E-03 | 0.067 | 0.472 |
| sex | 0.5403 | 0.154 | 3.498 | 4.69E-04 | 0.238 | 0.843 |
| Myocardial infarction | -0.439 | 0.243 | -1.808 | 7.06E-02 | -0.915 | 0.037 |
| Heart failure | 0.5703 | 0.209 | 2.732 | 6.30E-03 | 0.161 | 0.979 |
| Peripheral artery occlusive disease | -0.8748 | 0.236 | -3.702 | 2.14E-04 | -1.338 | -0.412 |
| Cerebrovascular disease | 0.5203 | 0.2 | 2.6 | 9.32E-03 | 0.128 | 0.913 |
| Chronic obstructive pulmonary disease | 0.2688 | 0.255 | 1.053 | 2.92E-01 | -0.232 | 0.769 |
| Diabetes | 0.6799 | 0.209 | 3.26 | 1.11E-03 | 0.271 | 1.089 |
| Kidney damage | 0.689 | 0.255 | 2.697 | 6.99E-03 | 0.188 | 1.19 |
| PC1 | 0.0189 | 0.097 | 0.195 | 8.45E-01 | -0.171 | 0.209 |
| PC2 | 0.5335 | 1.262 | 0.423 | 6.73E-01 | -1.941 | 3.008 |
| PC3 | -0.8582 | 1.255 | -0.684 | 4.94E-01 | -3.318 | 1.602 |
| PC4 | 0.2265 | 0.534 | 0.424 | 6.72E-01 | -0.821 | 1.274 |
| PC5 | 0.266 | 0.385 | 0.691 | 4.90E-01 | -0.489 | 1.021 |
| PC6 | 0.2517 | 0.272 | 0.926 | 3.54E-01 | -0.281 | 0.784 |
| PC7 | -0.0536 | 0.087 | -0.619 | 5.36E-01 | -0.223 | 0.116 |
| PC8 | -0.0635 | 0.073 | -0.874 | 3.82E-01 | -0.206 | 0.079 |
| PC9 | 0.0825 | 0.09 | 0.92 | 3.58E-01 | -0.093 | 0.258 |
| PC10 | 0.0402 | 0.076 | 0.527 | 5.98E-01 | -0.109 | 0.19 |

**Supplementary Table 10:** Logistic regression results for the covariates-only model with COVID-19 severity as an outcome and PRS as a continuous variable.

|  | coef | std err | z | P>|z| | [0.025 | 0.975] |
| --- | --- | --- | --- | --- | --- | --- |
| intercept | -1.4475 | 0.142 | -10.183 | 2.37E-24 | -1.726 | -1.169 |
| age | 0.2555 | 0.101 | 2.518 | 1.18E-02 | 0.057 | 0.454 |
| sex | 0.5502 | 0.153 | 3.601 | 3.17E-04 | 0.251 | 0.85 |
| Myocardial infarction | -0.4594 | 0.24 | -1.911 | 5.60E-02 | -0.931 | 0.012 |
| Heart failure | 0.5499 | 0.206 | 2.671 | 7.56E-03 | 0.146 | 0.953 |
| Peripheral artery occlusive disease | -0.8703 | 0.234 | -3.72 | 1.99E-04 | -1.329 | -0.412 |
| Cerebrovascular disease | 0.4791 | 0.197 | 2.427 | 1.52E-02 | 0.092 | 0.866 |
| Chronic obstructive pulmonary disease | 0.2227 | 0.254 | 0.878 | 3.80E-01 | -0.274 | 0.72 |
| Diabetes | 0.6505 | 0.206 | 3.152 | 1.62E-03 | 0.246 | 1.055 |
| Kidney damage | 0.7441 | 0.253 | 2.936 | 3.33E-03 | 0.247 | 1.241 |
| PC1 | 0.0041 | 0.096 | 0.042 | 9.66E-01 | -0.184 | 0.192 |
| PC2 | 0.8017 | 1.253 | 0.64 | 5.22E-01 | -1.654 | 3.257 |
| PC3 | -1.0564 | 1.244 | -0.849 | 3.96E-01 | -3.494 | 1.381 |
| PC4 | 0.1782 | 0.456 | 0.391 | 6.96E-01 | -0.715 | 1.071 |
| PC5 | 0.2402 | 0.33 | 0.727 | 4.67E-01 | -0.407 | 0.887 |
| PC6 | 0.2175 | 0.232 | 0.939 | 3.48E-01 | -0.237 | 0.671 |
| PC7 | -0.0609 | 0.09 | -0.674 | 5.00E-01 | -0.238 | 0.116 |
| PC8 | -0.0629 | 0.072 | -0.869 | 3.85E-01 | -0.205 | 0.079 |
| PC9 | 0.1129 | 0.088 | 1.277 | 2.02E-01 | -0.06 | 0.286 |
| PC10 | 0.0453 | 0.075 | 0.602 | 5.47E-01 | -0.102 | 0.193 |

**Supplementary Table 11:** Logistic regression results for the PRS-only model with COVID-19 severity as an outcome and PRS as a continuous variable.

|  | coef | std err | z | P>|z| | [0.025 | 0.975] |
| --- | --- | --- | --- | --- | --- | --- |
| intercept | -0.7907 | 0.078 | -10.157 | 3.08E-24 | -0.943 | -0.638 |
| PRS | 0.3891 | 0.073 | 5.341 | 9.25E-08 | 0.246 | 0.532 |
| PC1 | -0.0102 | 0.092 | -0.111 | 9.12E-01 | -0.191 | 0.171 |
| PC2 | 0.4148 | 1.171 | 0.354 | 7.23E-01 | -1.88 | 2.709 |
| PC3 | -0.7998 | 1.176 | -0.68 | 4.97E-01 | -3.105 | 1.506 |
| PC4 | 0.1304 | 0.468 | 0.278 | 7.81E-01 | -0.788 | 1.048 |
| PC5 | 0.2196 | 0.336 | 0.653 | 5.14E-01 | -0.439 | 0.879 |
| PC6 | 0.307 | 0.296 | 1.037 | 3.00E-01 | -0.273 | 0.887 |
| PC7 | -0.0764 | 0.086 | -0.885 | 3.76E-01 | -0.246 | 0.093 |
| PC8 | -0.0735 | 0.078 | -0.947 | 3.43E-01 | -0.225 | 0.079 |
| PC9 | 0.0843 | 0.086 | 0.979 | 3.28E-01 | -0.085 | 0.253 |
| PC10 | -0.0401 | 0.072 | -0.555 | 5.79E-01 | -0.182 | 0.101 |

**Supplementary Table 12:** Logistic regression results for the full model with COVID-19 mortality as an outcome and PRS as a continuous variable.

|  | coef | std err | z | P>|z| | [0.025 | 0.975] |
| --- | --- | --- | --- | --- | --- | --- |
| intercept | -4.0733 | 0.301 | -13.552 | 7.67E-42 | -4.662 | -3.484 |
| age | 0.3928 | 0.173 | 2.276 | 2.28E-02 | 0.055 | 0.731 |
| sex | 0.6529 | 0.241 | 2.714 | 6.65E-03 | 0.181 | 1.124 |
| PRS | 0.4102 | 0.12 | 3.407 | 6.58E-04 | 0.174 | 0.646 |
| Myocardial infarction | -0.2595 | 0.291 | -0.892 | 3.72E-01 | -0.83 | 0.311 |
| Heart failure | 1.6768 | 0.295 | 5.693 | 1.25E-08 | 1.1 | 2.254 |
| Peripheral artery occlusive disease | -0.7706 | 0.28 | -2.755 | 5.87E-03 | -1.319 | -0.222 |
| Cerebrovascular disease | 0.9699 | 0.284 | 3.416 | 6.36E-04 | 0.413 | 1.526 |
| Chronic obstructive pulmonary disease | 0.6209 | 0.316 | 1.964 | 4.96E-02 | 0.001 | 1.241 |
| Diabetes | 0.4064 | 0.269 | 1.508 | 1.31E-01 | -0.122 | 0.935 |
| Kidney damage | 1.2328 | 0.29 | 4.246 | 2.17E-05 | 0.664 | 1.802 |
| PC1 | 0.0185 | 0.145 | 0.128 | 8.98E-01 | -0.266 | 0.303 |
| PC2 | 0.8495 | 2.147 | 0.396 | 6.92E-01 | -3.358 | 5.057 |
| PC3 | -1.7958 | 2.017 | -0.89 | 3.73E-01 | -5.75 | 2.158 |
| PC4 | 1.0886 | 1.083 | 1.005 | 3.15E-01 | -1.034 | 3.211 |
| PC5 | 0.6319 | 0.786 | 0.804 | 4.22E-01 | -0.909 | 2.173 |
| PC6 | 0.3957 | 0.52 | 0.761 | 4.47E-01 | -0.623 | 1.415 |
| PC7 | -0.0428 | 0.11 | -0.39 | 6.97E-01 | -0.258 | 0.172 |
| PC8 | 0.0004 | 0.149 | 0.002 | 9.98E-01 | -0.292 | 0.293 |
| PC9 | -0.0769 | 0.164 | -0.47 | 6.38E-01 | -0.398 | 0.244 |
| PC10 | 0.037 | 0.118 | 0.313 | 7.54E-01 | -0.195 | 0.269 |

**Supplementary Table 13:** Logistic regression results for the full model with COVID-19 mortality as an outcome and PRS as a binary variable.

|  | coef | std err | z | P>|z| | [0.025 | 0.975] |
| --- | --- | --- | --- | --- | --- | --- |
| intercept | -4.2696 | 0.316 | -13.493 | 1.71E-41 | -4.89 | -3.649 |
| 10% with the highest PRS values | 1.4697 | 0.342 | 4.299 | 1.72E-05 | 0.8 | 2.14 |
| age | 0.3729 | 0.172 | 2.164 | 3.04E-02 | 0.035 | 0.711 |
| sex | 0.611 | 0.241 | 2.535 | 1.12E-02 | 0.139 | 1.083 |
| Myocardial infarction | -0.2145 | 0.292 | -0.736 | 4.62E-01 | -0.786 | 0.357 |
| Heart failure | 1.7802 | 0.304 | 5.854 | 4.79E-09 | 1.184 | 2.376 |
| Peripheral artery occlusive disease | -0.8416 | 0.281 | -2.991 | 2.78E-03 | -1.393 | -0.29 |
| Cerebrovascular disease | 1.014 | 0.292 | 3.478 | 5.06E-04 | 0.443 | 1.586 |
| Chronic obstructive pulmonary disease | 0.6964 | 0.319 | 2.185 | 2.89E-02 | 0.072 | 1.321 |
| Diabetes | 0.4112 | 0.27 | 1.525 | 1.27E-01 | -0.117 | 0.94 |
| Kidney damage | 1.2124 | 0.291 | 4.163 | 3.14E-05 | 0.642 | 1.783 |
| PC1 | 0.0295 | 0.145 | 0.204 | 8.39E-01 | -0.255 | 0.314 |
| PC2 | 1.2105 | 2.166 | 0.559 | 5.76E-01 | -3.035 | 5.457 |
| PC3 | -2.1391 | 2.04 | -1.049 | 2.94E-01 | -6.137 | 1.859 |
| PC4 | 1.092 | 1.076 | 1.015 | 3.10E-01 | -1.017 | 3.201 |
| PC5 | 0.6214 | 0.779 | 0.798 | 4.25E-01 | -0.906 | 2.148 |
| PC6 | 0.4605 | 0.529 | 0.87 | 3.84E-01 | -0.577 | 1.498 |
| PC7 | -0.0315 | 0.111 | -0.282 | 7.78E-01 | -0.25 | 0.187 |
| PC8 | 0.0104 | 0.157 | 0.066 | 9.47E-01 | -0.298 | 0.319 |
| PC9 | -0.0644 | 0.162 | -0.397 | 6.91E-01 | -0.382 | 0.254 |
| PC10 | 0.0446 | 0.118 | 0.379 | 7.04E-01 | -0.186 | 0.275 |

**Supplementary Table 14:** Multivariate Cox regression results for the model with COVID-19 severity as an outcome and PRS as a continuous variable.

|  | coef | Hazard ratio (HR) | HR lower 95% | HR upper 95% | p | -log2(p) |
| --- | --- | --- | --- | --- | --- | --- |
| sex | 0.74 | 2.1 | 1.66 | 2.66 | <0.005 | 30.72 |
| PRS | 0.33 | 1.39 | 1.24 | 1.57 | <0.005 | 24.71 |
| Myocardial infarction | -0.77 | 0.46 | 0.33 | 0.66 | <0.005 | 16 |
| Heart failure | -0.43 | 0.65 | 0.49 | 0.86 | <0.005 | 8.38 |
| Peripheral artery occlusive disease | -0.12 | 0.88 | 0.64 | 1.22 | 0.46 | 1.13 |
| Cerebrovascular disease | -0.49 | 0.61 | 0.47 | 0.8 | <0.005 | 11.57 |
| Chronic obstructive pulmonary disease | -0.21 | 0.81 | 0.57 | 1.16 | 0.25 | 1.99 |
| Diabetes | 0.14 | 1.15 | 0.87 | 1.52 | 0.32 | 1.64 |
| Kidney damage | 0.04 | 1.04 | 0.75 | 1.45 | 0.8 | 0.32 |
| PC1 | 0.01 | 1.01 | 0.88 | 1.17 | 0.85 | 0.23 |
| PC2 | 0.2 | 1.22 | 0.16 | 9.33 | 0.85 | 0.24 |
| PC3 | -0.45 | 0.64 | 0.09 | 4.55 | 0.65 | 0.62 |
| PC4 | 0.59 | 1.8 | 0.68 | 4.79 | 0.24 | 2.07 |
| PC5 | 0.45 | 1.57 | 0.77 | 3.2 | 0.21 | 2.25 |
| PC6 | 0.22 | 1.25 | 0.78 | 1.99 | 0.35 | 1.5 |
| PC7 | -0.01 | 0.99 | 0.86 | 1.13 | 0.84 | 0.25 |
| PC8 | -0.05 | 0.95 | 0.85 | 1.06 | 0.36 | 1.48 |
| PC9 | 0.13 | 1.14 | 0.99 | 1.31 | 0.07 | 3.82 |
| PC10 | 0.04 | 1.04 | 0.93 | 1.17 | 0.49 | 1.04 |

**Supplementary Table 15:** Multivariate Cox regression results for the model with COVID-19 mortality as an outcome and PRS as a continuous variable.

|  | coef | Hazard ratio (HR) | HR lower 95% | HR upper 95% | p | -log2(p) |
| --- | --- | --- | --- | --- | --- | --- |
| sex | 0.9 | 2.47 | 1.68 | 3.63 | <0.005 | 17.75 |
| PRS | 0.37 | 1.44 | 1.19 | 1.75 | <0.005 | 12.29 |
| Myocardial infarction | -0.61 | 0.55 | 0.35 | 0.85 | 0.01 | 7 |
| Heart failure | 0.55 | 1.73 | 1.05 | 2.85 | 0.03 | 4.92 |
| Peripheral artery occlusive disease | -0.04 | 0.96 | 0.64 | 1.46 | 0.86 | 0.22 |
| Cerebrovascular disease | -0.01 | 0.99 | 0.63 | 1.57 | 0.98 | 0.03 |
| Chronic obstructive pulmonary disease | 0.2 | 1.22 | 0.76 | 1.97 | 0.42 | 1.26 |
| Diabetes | 0.12 | 1.13 | 0.75 | 1.7 | 0.55 | 0.86 |
| Kidney damage | 0.34 | 1.41 | 0.93 | 2.12 | 0.1 | 3.3 |
| PC1 | 0.01 | 1.01 | 0.8 | 1.26 | 0.96 | 0.05 |
| PC2 | -0.21 | 0.81 | 0.03 | 21.2 | 0.9 | 0.15 |
| PC3 | -0.24 | 0.78 | 0.04 | 15.96 | 0.87 | 0.19 |
| PC4 | 0.44 | 1.55 | 0.28 | 8.74 | 0.62 | 0.69 |
| PC5 | 0.22 | 1.24 | 0.34 | 4.54 | 0.74 | 0.43 |
| PC6 | 0.28 | 1.33 | 0.6 | 2.96 | 0.49 | 1.03 |
| PC7 | 0 | 1 | 0.84 | 1.2 | 0.98 | 0.02 |
| PC8 | -0.04 | 0.96 | 0.77 | 1.2 | 0.71 | 0.5 |
| PC9 | -0.01 | 0.99 | 0.76 | 1.29 | 0.97 | 0.05 |
| PC10 | 0.04 | 1.04 | 0.86 | 1.25 | 0.72 | 0.48 |