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## Supplemental information

# Cystatin C is associated with adverse COVID-19 outcomes in diverse populations

**Sam O. Kleeman, Mattia Cordioli, Paul R.H. J. Timmers, Atlas Khan, Pinkus Tober-Lau, Florian Kurth, Vadim Demichev, Hannah V. Meyer, James F. Wilson, Markus Ralser, Krzysztof Kiryluk, Andrea Ganna, Kenneth Baillie, and Tobias Janowitz**

# Supplemental material

## Supplemental Figures

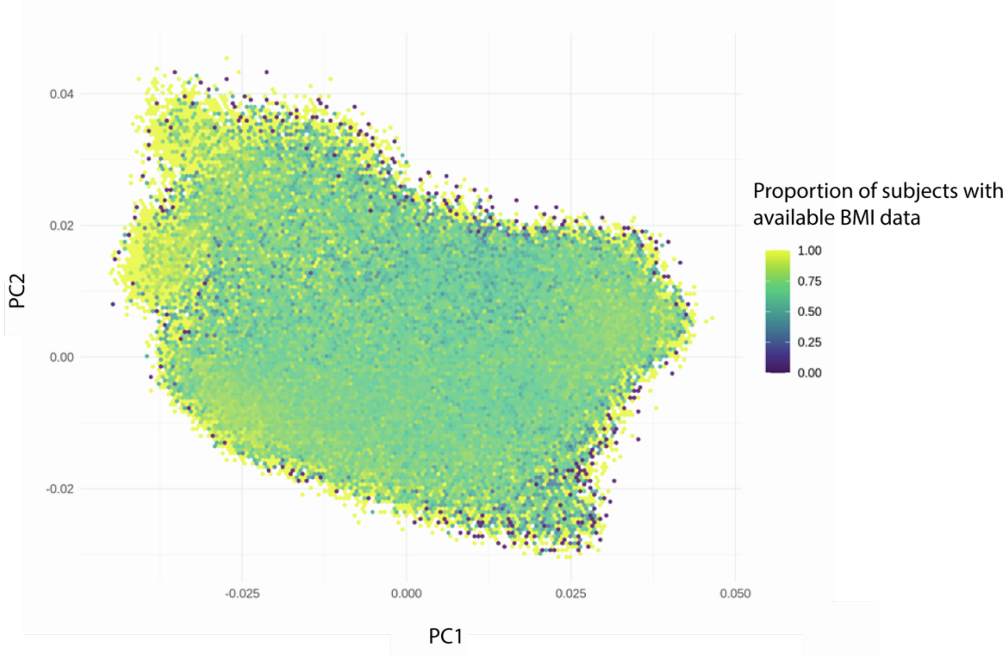

**Figure S1, Related to Figure 1:** Principal component analysis of linkage disequilibrium-pruned directly genotyped SNPs in FinnGen demonstrating no evidence of population stratification between FinnGen participants with BMI recorded versus not recorded. As individual-level PCA coordinates cannot be shared for FinnGen participants, data are displayed as a histogram where the color of each hexagon reflects the proportion of subjects with available BMI data.

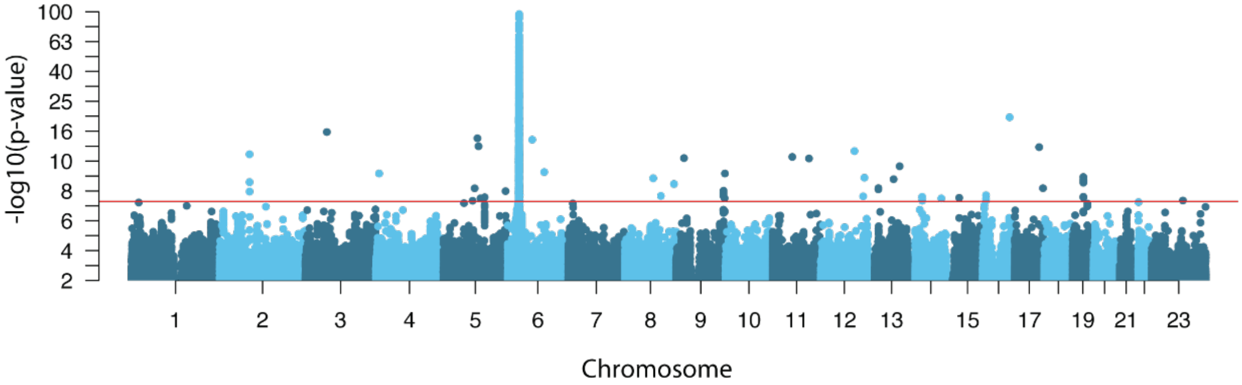

**Figure S2, Related to Figure 1:** Manhattan plot summarizing results of genome-wide association study for GWAS recorded/not recorded in FinnGen.

# Supplemental Tables

**Table S1, Related to Figure 1:** Summary statistics from logistic regression between Z-scored CyC-production PGS in four cohorts (UK Biobank, FinnGen, GenOMICC and Columbia COVID-19 Biobank). Tables summarizes the features of each regression, including case/control cohorts, numbers of cases/controls, patient ancestry, number of SNPs matched between the CyC-production PGS and the relevant cohort, the covariates included in the analysis and the summary statistics for the mild-moderate control and population control analyses. Black cells refer to missing data.

**Non BMI-adjusted analyses**

| | | | | | | | | | | Mild-moderate COVID-19 controls | | | Population controls | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Case cohort** | **Control cohort** | **n_cases_hosp** | **n_cases_critical** | **n_cases_death** | **n_controls_mildmod** | **n_controls_pop** | **Ancestry** | **Matched SNPs** | **Covariates** | **Hospitalization** | **Critical illness** | **Death** | **Hospitalization** | **Critical illness** | **Death** |
| UKB | UKB | 245 | 43 | 109 | 1513 | 48208 | EUR | 1031527 | PC1-10, sex, year of birth, recruitment centre,array | OR 1.21 (95% CI 1.04-1.40), p=0.01297 | OR 2.15 (95% CI 1.55-3.03), p=7.17e-6 | OR 1.16 (95% CI 0.93-1.46), 0.183 | OR 1.24 (95% CI 1.09-1.41), p=0.000766 | OR 2.13 (95% CI 1.58-2.87), p=7.12e-7 | OR 1.20 (95% CI 1.00-1.45), p=0.0529 |
| GenOMICC | UKB | | 2018 | | 11837 | 318280 | EUR | 980733 | PC1-10, age, sex, Townsend deprivation index, local authority | | OR 1.16 (95% CI 1.11-1.21), p=4.69e-8 | | | OR 1.20 (95% CI 1.16-1.25),p=2.49e-16 | |
| FinnGen | FinnGen | 319 | 165 | | 2835 | 305996 | EUR | 1016675 | PC1-4, age, sex | OR 1.09 (95% CI 0.96-1.25), p=0.164 | OR 1.22 (95% CI 1.02-1.46), p=0.0298 | | OR 1.04 (95% CI 0.93-1.16), p=0.538 | OR 1.10 (95% CI 0.94-1.28), p=0.233 | |
| Columbia | Columbia | 201 | 93 | | | 2341 | AFR | 957602 | PC1-3, sex | | | | OR 1.20 (95% CI 1.05-1.34), p=0.0175 | OR 1.44 (95% CI 1.22-1.65), p=0.000956 | |
| Columbia | UKB | 184 | 84 | | | 2334 | AFR | 957602 | PC1-8, age, sex | | | | OR 1.16 (95% CI 0.98-1.33), p=0.102 | OR 1.31 (95% CI 1.02-1.57), p=0.053 | |

**BMI-adjusted analyses**

| | | | | | | | | | | Mild-moderate COVID-19 controls | | | Population controls | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Case cohort** | **Control cohort** | **n_cases_hosp** | **n_cases_critical** | **n_cases_death** | **n_controls_mildmod** | **n_controls_pop** | **Ancestry** | **Matched SNPs** | **Covariates** | **Hospitalization** | **ICU admission** | **Death** | **Hospitalization** | **ICU admission** | **Death** |
| UKB | UKB | 245 | 43 | 109 | 1513 | 48208 | EUR | 1031527 | PC1-10, sex, year of birth, recruitment centre,array, BMI | OR 1.14 (95% CI 0.98-1.33), p=0.0918 | OR 2.02 (95% CI 1.45-2.85), p=4.17e-5 | OR 1.07 (95% CI 0.86-1.35), p=0.531 | OR 1.15 (95% CI 1.01-1.31), p=0.0277 | OR 1.94 (95% CI 1.44-2.63), p=1.55e-5 | OR 1.12 (95% CI 0.93-1.36), p=0.23 |
| FinnGen | FinnGen | 239 | 123 | | 1939 | 220475 | EUR | 1016675 | PC1-4, age, sex, BMI | OR 0.99 (95% CI 0.84-1.16), p=0.898 | OR 1.01 (95% CI 0.82-1.25), p=0.163 | | OR 0.97 (95% CI 0.85-1.10), p=0.639 | OR 1.08 (95% CI 0.90-1.29), p=0.397 | |