

## Investigating the role of polygenic risk scores for comorbidities in COVID-19 susceptibility

Soo Min Song<sup>1</sup>, Taesung Park<sup>1,2\*</sup>

<sup>1</sup>*Interdisciplinary Program in Bioinformatics, Seoul National University, Seoul, Republic of Korea*

<sup>2</sup>*Department of Statistics, Seoul National University, Seoul, Republic of Korea*

\*Corresponding author: [tpark@stats.snu.ac.kr](mailto:tpark@stats.snu.ac.kr)

The COVID-19 pandemic has deeply impacted global health, causing severe illness and death worldwide. While clinical risk factors like age, sex, and comorbidities have been established as determinants of COVID-19 infection, the relationship between Polygenic Risk Scores (PRS) and COVID-19 mortality remains less explored. Therefore, we aim to investigate the potential association of polygenic susceptibilities related to comorbidities with COVID-19 mortality, adjusting for established risk factors. Utilizing data from the UK Biobank, a population-based prospective cohort study, our study focused on 2,157 participants who tested positive for COVID-19 and subsequently passed away. Through logistic regression analyses, we examined the relationship between PRS and COVID-19 mortality. We also developed prediction models to evaluate the predictive capacity of PRS when aligned with other variables. Our findings revealed significant associations between COVID-19 mortality and PRS for hypertension (OR: 0.91, 95%CI: 0.84-1.00, p-value: 0.039), ischaemic heart disease (OR: 1.09, 95%CI: 1.00–1.19, p-value: 0.043). Also, the prediction model with PRS showed higher performance than models without PRS. These findings contribute to our understanding of the multifactorial nature of COVID-19 mortality and highlight the potential utility of PRS in personalized risk assessment. Despite these insights, the study is constrained by particular demographic examined and the limited scope of genetic variants captured by the PRS. Further research is needed to validate these findings and refine risk assessment models.