Abstract Submission form

*Title of Abstract Characters limits: 120	**DEVELOPMENT AND VALIDATION OF COMER - A DNA-METHYLATION-BASED RISK SCORE TO PREDICT COVID-19 INFECTION SEVERITY**
* Introduction	During COVID-19 pandemic, shortages in healthcare facilities prompted the need for early identification of high-risk patients.
*Objectives	We aimed to develop a novel score based on DNA methylation profiles to predict the severity of COVID-19 patients.
*Methods	From 2021 to 2022, we conducted a patient-level meta-analysis based on five public datasets of whole blood DNA methylation of COVID-19 patients and healthy controls. Four datasets were pooled and then randomly split into training and testing sets, while one independent cohort was left out for validation. Severe cases were defined as having COVID-GRAM[1] at least 40% or WHO COVID-19 Ordinal Scale[2] least 5 or being admitted to ICU. Briefly, EPIC DNA methylation data were processed with an in-house pipeline. From nearly 700,000 DNA methylation probes, multivariable linear regression and feature selection algorithms retained a set of three best probes, which formed the COVID-19 Methylation Risk Score (COMER score).
*Results	In a total of 1704 individuals, 1103, 471 and 130 participants were included in the training, testing and validation set respectively. Mean age of healthy controls, mild and severe patients were 47.8 ± 19.2, 61.1 ± 17.7 and 66.9 ± 17.7 years respectively. In the training set, biological pathway enrichment analysis revealed that the differentially expressed probes were enriched in virus-related pathways. Cg13452062, cg07189579 and cg22652934 probes, which formed the COMER score, regulate the gene IFI44L, NDRG1 and RUNX1 respectively. On testing set, COMER score was significantly higher in severe groups (p-value$<1\times10^{-14}$) with an AUC of 0.85. In the validation cohort, COMER score accurately predicted 51 out 66 severe cases and had an AUC of 0.83. COMER score also correlated with COVID-19 GRAM score (R-squared=0.52).
*Conclusion(s)	COMER score is a novel and potent tool for early prediction of COVID-19 infection severity. Further studies may investigate the

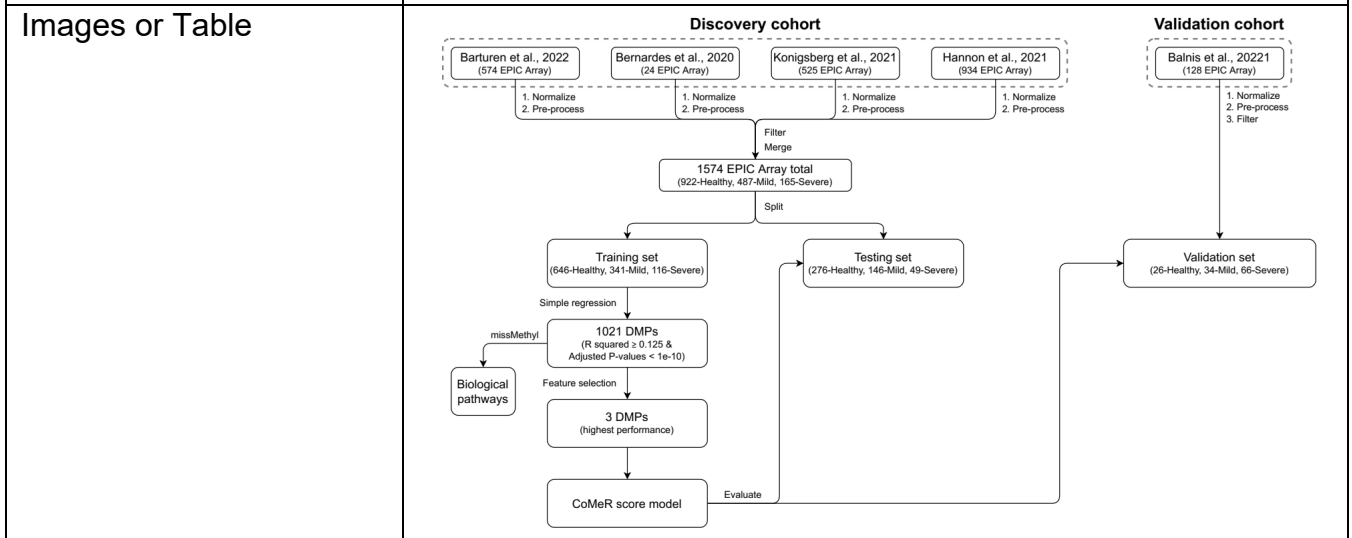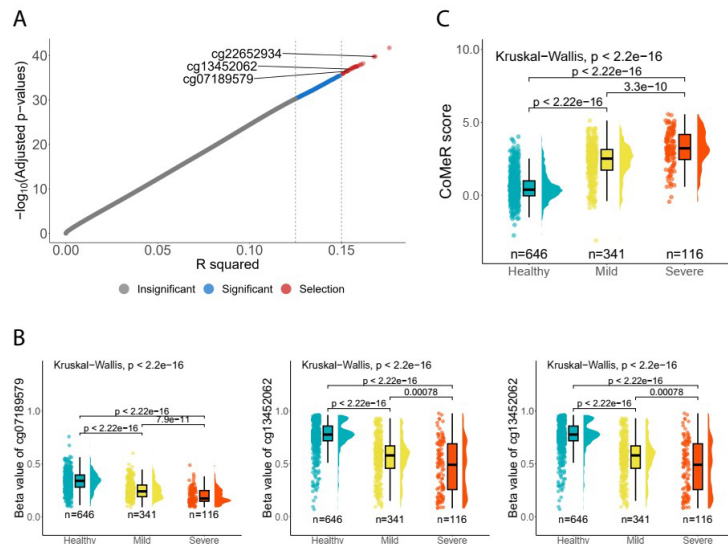|	
	benefits of a COMER-guided approach in COVID-19 management.
Reference(s)	1. Liang W, Liang H, Ou L, Chen B, Chen A, Li C, et al. Development and Validation of a Clinical Risk Score to Predict the Occurrence of Critical Illness in Hospitalized Patients With COVID-19. JAMA internal medicine. 2020;180(8):1081-9. 2. WHO. Novel Coronavirus COVID-19 Therapeutic Trial Synopsis. WHO R&D Blueprint. 2020.
Grant Acknowledgement	Nil
Images or Table	 Figure 1: Workflow Figure 2: COMER score and the three DNA methylation probes

Testing set
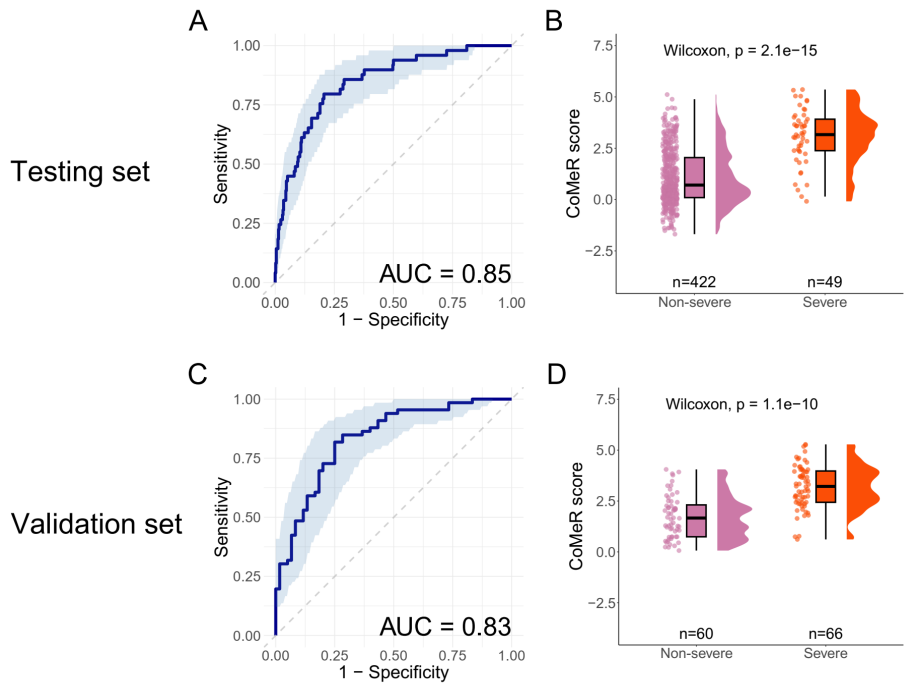
Validation set

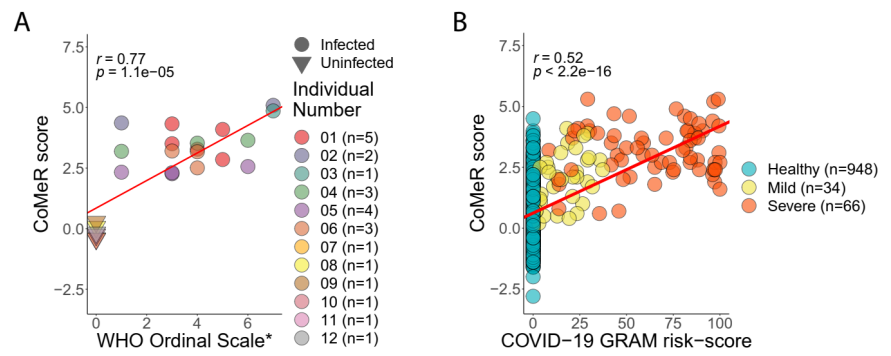Figure 3: COMER score performance on testing and validation set

Figure 4: COMER score correlates with COVID-GRAM score and WHO Ordinal scale