

THE LANCET Psychiatry

Supplementary appendix

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Supplement to: Lee SW, Yang JM, Moon SY, et al. Association between mental illness and COVID-19 in South Korea: a post-hoc analysis. *Lancet Psychiatry* 2021; published online Feb 19. [http://dx.doi.org/10.1016/S2215-0366\(21\)00043-2](http://dx.doi.org/10.1016/S2215-0366(21)00043-2).

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Method

We are honoured to have received the two letters received regarding our article, which investigated the potential association between pre-existing mental illness and positivity for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and clinical outcomes of COVID-19. The authors criticized the need for further analysis stratified by subtype of psychiatric disorders and region of residence: (1) upon reviewing recent studies by two groups, Hirakawa et al pointed out that our study lacked the subgroup analysis of mental illness subtype, in which the previously mentioned groups had reported the association between COVID-19 susceptibility and certain pre-existing psychiatric disorders (depression, anxiety, and substance misuse); and (2) in South Korea, residents of the Daegu/Gyeongbuk region experienced the highest number of COVID-19 cases (special pandemic control area) and two clusters of COVID-19 cases at a psychiatric hospital. Although we matched and adjusted for the region of residence (urban or rural area), Park et al suggested that our main results should be interpreted carefully given our dataset bias, which may have led to the unfavourable outcomes of COVID-19.

To clarify these issues, we performed the post-hoc analysis from the Korean nationwide cohort to address their questions. Data were obtained from the South Korean national health insurance claims database, which includes all individuals aged older than 20 years who underwent a SARS-CoV-2 test between 1 January and 15 May, 2020. Pre-existing psychiatric disorders were defined using the appropriate International Classification of Disease, Tenth Revision codes recorded at least twice within 1 year during the observational period (1 January 2017 to 15 May 2020): anxiety-related and stress-related disorders (F40–48); alcohol or drug misuse (F10–16, F18–19); mood disorders without psychotic symptoms (F32–34, F38–39, excluding F32.3 and F33.3); eating disorders (F50); and personality disorders (F60–63, F68–69). These pre-existing psychiatric disorders overlapped in some patients. The primary outcome was SARS-CoV-2 test positivity among all individuals who underwent SARS-CoV-2 testing. The secondary outcome was severe clinical outcomes of COVID-19, which comprised death, admission to the intensive care unit, or invasive ventilation.

Data were analysed using multivariate logistic regression models. Adjusted odds ratios (ORs) with 95% CIs were estimated after adjusting for the following covariates: age; gender; region of residence; history of diabetes, cardiovascular disease, cerebrovascular disease, chronic obstructive pulmonary disease, asthma, hypertension,

or chronic kidney disease; and Charlson comorbidity index.

Statistical analyses were performed in SAS, version 9.4 and R software, version 3.1.1. A two-sided $p < 0.05$ was considered significant. The study protocol was approved by the institutional review board of Sejong University (SJU-HR-E-2020-003).

Funding

This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (NRF2019R1G1A109977912). The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Acknowledgement

The authors appreciate healthcare professionals dedicated to treating COVID-19 patients in Korea, and the Ministry of Health and Welfare and the Health Insurance Review & Assessment Service of Korea for sharing invaluable national health insurance claims data in a prompt manner.

Table S1. Propensity score-matched adjusted ORs of mental illness with SARS-CoV-2 stratified by the Daegu/Gyeongbuk region (special pandemic control area) and other areas.

	Variable	No mental illness	Other mental illness	Severe mental illness
Patients who were tested for SARS-CoV-2				
Daegu/Gyeongbuk region (n = 15,756)				
Event number of the total number	COVID-19	944/7878 (12.0%)	699/6217 (11.2%)	209/1661 (12.6%)
Minimally adjusted OR†	COVID-19	1 (ref)	0.92 (0.82-1.02)	1.07 (0.91-1.25)
Fully adjusted OR‡	COVID-19	1 (ref)	0.94 (0.85-1.05)	1.05 (0.90-1.23)
Other areas (n = 78,148)				
Event number of the total number	COVID-19	507/39,074 (1.3%)	351/29,912 (1.2%)	111/9162 (1.2%)
Minimally adjusted OR†	COVID-19	1 (ref)	0.91 (0.79-1.05)	0.92 (0.75-1.14)
Fully adjusted OR‡	COVID-19	1 (ref)	0.93 (0.81-1.06)	0.94 (0.76-1.17)
Patients who tested positive for SARS-CoV-2				

Daegu/Gyeongbuk region (n = 1718)

Event number of the total number	Severe clinical outcomes of COVID-19*	86/859 (10.0%)	63/613 (10.3%)	39/246 (15.9%)
Minimally adjusted OR†	Severe clinical outcomes of COVID-19*	1 (ref)	1.12 (0.78-1.62)	1.93 (1.23-3.03) §
Fully adjusted OR‡	Severe clinical outcomes of COVID-19*	1 (ref)	1.05 (0.72-1.52)	2.55 (1.59-4.10) §

Other areas (n = 848)

Event number of the total number	Severe clinical outcomes of COVID-19*	14/424 (3.3%)	11/299 (3.7%)	9/125 (7.2%)
Minimally adjusted OR†	Severe clinical outcomes of COVID-19*	1 (ref)	1.19 (0.53-2.67)	2.35 (0.97-5.69)
Fully adjusted OR‡	Severe clinical outcomes of COVID-19*	1 (ref)	1.11 (0.50-2.46)	2.66 (1.08-6.57) §

Data are represented as OR (95% CI) unless specified.

SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. OR=odds ratio.

* Severe clinical outcomes of COVID-19 comprised admission to the intensive care unit, invasive ventilation, or death.

† Minimally adjusted for age and gender.

‡ Fully adjusted for age; gender; region of residence; history of diabetes, cardiovascular disease, cerebrovascular disease, chronic obstructive pulmonary disease, asthma, hypertension, or chronic kidney disease; and Charlson comorbidity index.

§ Significant differences ($p < 0.05$).

Table S2. Propensity score-matched characteristics of patients tested for SARS-CoV-2 and with mental illness stratified by Daegu/Gyeongbuk region (special pandemic control area) and other areas.

Characteristic	Daegu/Gyeongbuk region		SMD [‡]	Other areas		SMD [‡]
	No mental illness	Mental illness		No mental illness	Mental illness	
Total, n (%)	7878	7878		39,074	39,074	
Age, years (SD)	61.5 (17.6)	60.7 (17.4)	0.051	60.0 (19.3)	59.5 (19.5)	0.023
Sex, n (%)			0.018			0.028
Male	3484 (44.2)	3414 (43.3)		17,633 (45.1)	17,082 (43.7)	
Female	4394 (55.8)	4464 (56.7)		21,441 (54.9)	21,992 (56.3)	
History of diabetes mellitus, n (%)	2270 (28.8)	2322 (29.5)	0.016	11,856 (30.3)	11,610 (29.7)	0.015
History of cardiovascular disease, n (%)	1675 (21.3)	1798 (22.8)	0.042	10,674 (27.3)	10,843 (27.8)	0.011
History of cerebrovascular disease, n (%)	1417 (18.0)	1622 (20.6)	0.074	6799 (17.4)	7323 (18.7)	0.039
History of COPD, n (%)	1219 (15.5)	1269 (16.1)	0.019	5444 (13.9)	5650 (14.5)	0.017
History of asthma, n (%)	1494 (19.0)	1575 (20.0)	0.028	9075 (23.2)	9081 (23.2)	<0.001
History of hypertension, n (%)	3910 (49.6)	3820 (48.5)	0.025	19,928 (51.0)	19,409 (49.7)	0.029
History of chronic kidney disease, n (%)	841 (10.7)	863 (11.0)	0.010	4548 (11.6)	4587 (11.7)	0.003
Charlson comorbidity index, n (%)			0.005			0.021
0	2386 (30.3)	2117 (26.9)		11,364 (29.1)	10,973 (28.1)	
1	1404 (17.8)	1493 (19.0)		6052 (15.5)	6207 (15.9)	
≥ 2	4088 (51.9)	4268 (54.2)		21,658 (55.4)	21,894 (56.0)	

Data are represented as n (%), unless specified.

COPD, chronic obstructive pulmonary disease; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SMD, standardized mean difference.

Table S3. Propensity score-matched characteristics of patients positive for SARS-CoV-2 and with mental illness stratified by Daegu/Gyeongbuk region (special pandemic control area) and other areas.

Characteristic	Daegu/Gyeongbuk region		SMD [‡]	Other areas		SMD [‡]
	No mental illness	Mental illness		No mental illness	Mental illness	
Total, n (%)	859	859		424	424	
Age, years (SD)	61.2 (16.0)	60.5 (15.9)	0.036	51.6 (16.7)	51.1 (16.8)	0.034
Sex, n (%)			0.036			0.038
Male	331 (38.5)	346 (40.3)		159 (37.5)	167 (39.4)	
Female	528 (61.5)	513 (59.7)		265 (62.5)	257 (60.6)	
History of diabetes mellitus, n (%)	227 (26.4)	237 (27.6)	0.029	65 (15.3)	65 (15.3)	<0.001
History of cardiovascular disease, n (%)	111 (12.9)	128 (14.9)	0.062	24 (5.7)	35 (8.0)	0.092
History of cerebrovascular disease, n (%)	120 (14.0)	132 (15.4)	0.042	16 (3.8)	18 (4.3)	0.023
History of COPD, n (%)	72 (8.4)	87 (10.1)	0.062	18 (4.3)	16 (3.8)	0.023
History of asthma, n (%)	127 (14.8)	130 (15.1)	0.010	48 (11.3)	51 (12.0)	0.022
History of hypertension, n (%)	376 (43.8)	370 (43.1)	0.015	115 (27.1)	117 (27.6)	0.011
History of chronic kidney disease, n (%)	55 (6.4)	59 (6.9)	0.020	10 (2.4)	11 (2.6)	0.015
Charlson comorbidity index, n (%)			0.027			0.045
0	363 (42.3)	310 (36.1)		258 (60.9)	237 (55.9)	
1	117 (13.6)	157 (18.3)		60 (14.2)	77 (18.2)	
≥ 2	379 (44.1)	392 (45.6)		106 (25.0)	110 (25.9)	

Data are represented as n (%), unless specified.

COPD, chronic obstructive pulmonary disease; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SMD, standardized mean difference.

Figure S1. Summary of propensity score matched adjusted ORs for the risk of those with a mental illness testing positive for SARS-CoV-2 and the severe clinical outcomes of COVID-19 with mental illness (summary of an original and a post-hoc analysis).

SARS-CoV-2, severe acute respiratory syndrome 2.

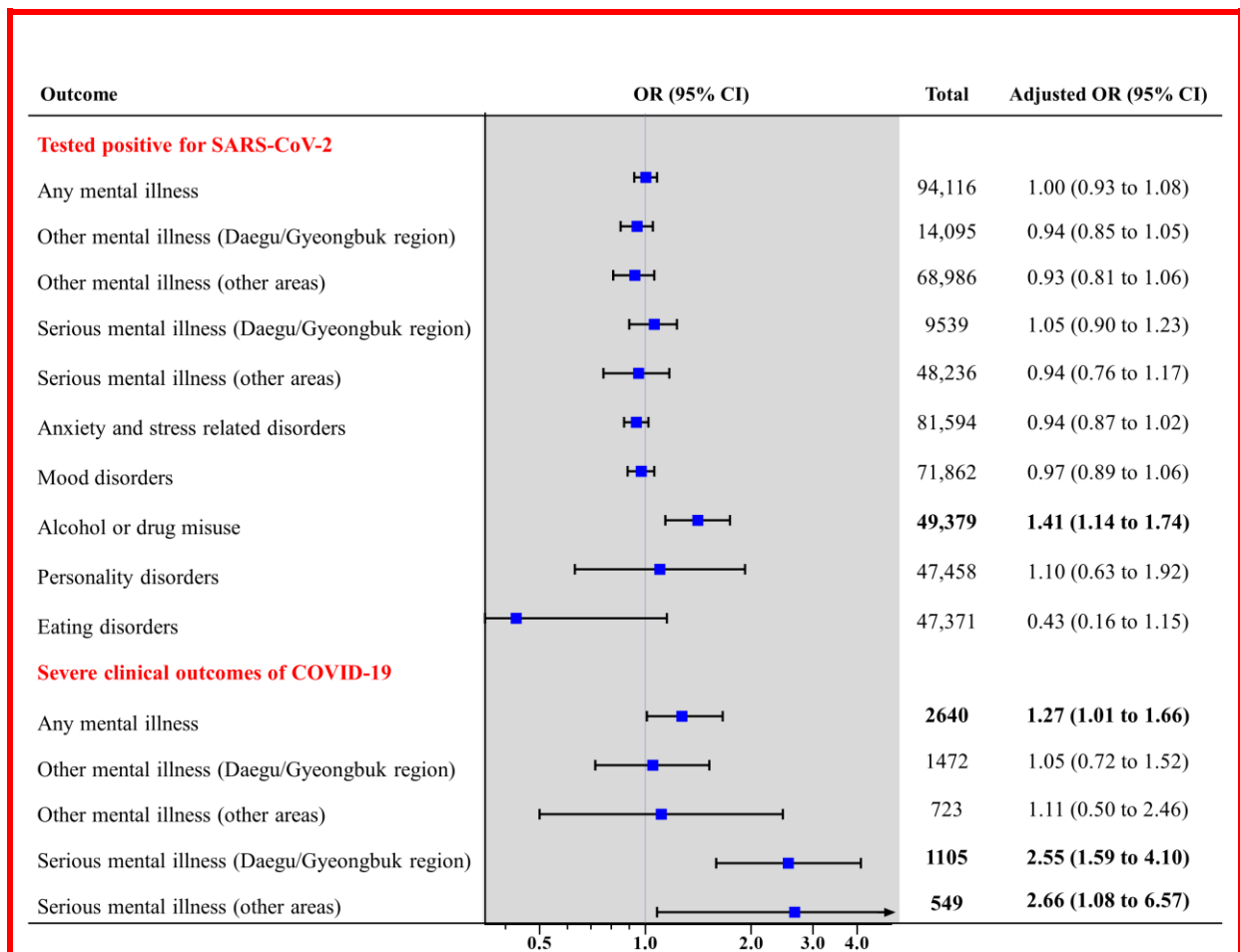


Figure S2. Density of propensity scores before and after matching among all patients who were tested for SARS-CoV-2 in Daegu/Gyeongbuk cohort (n = 15,756).

SARS-CoV-2, severe acute respiratory syndrome 2.

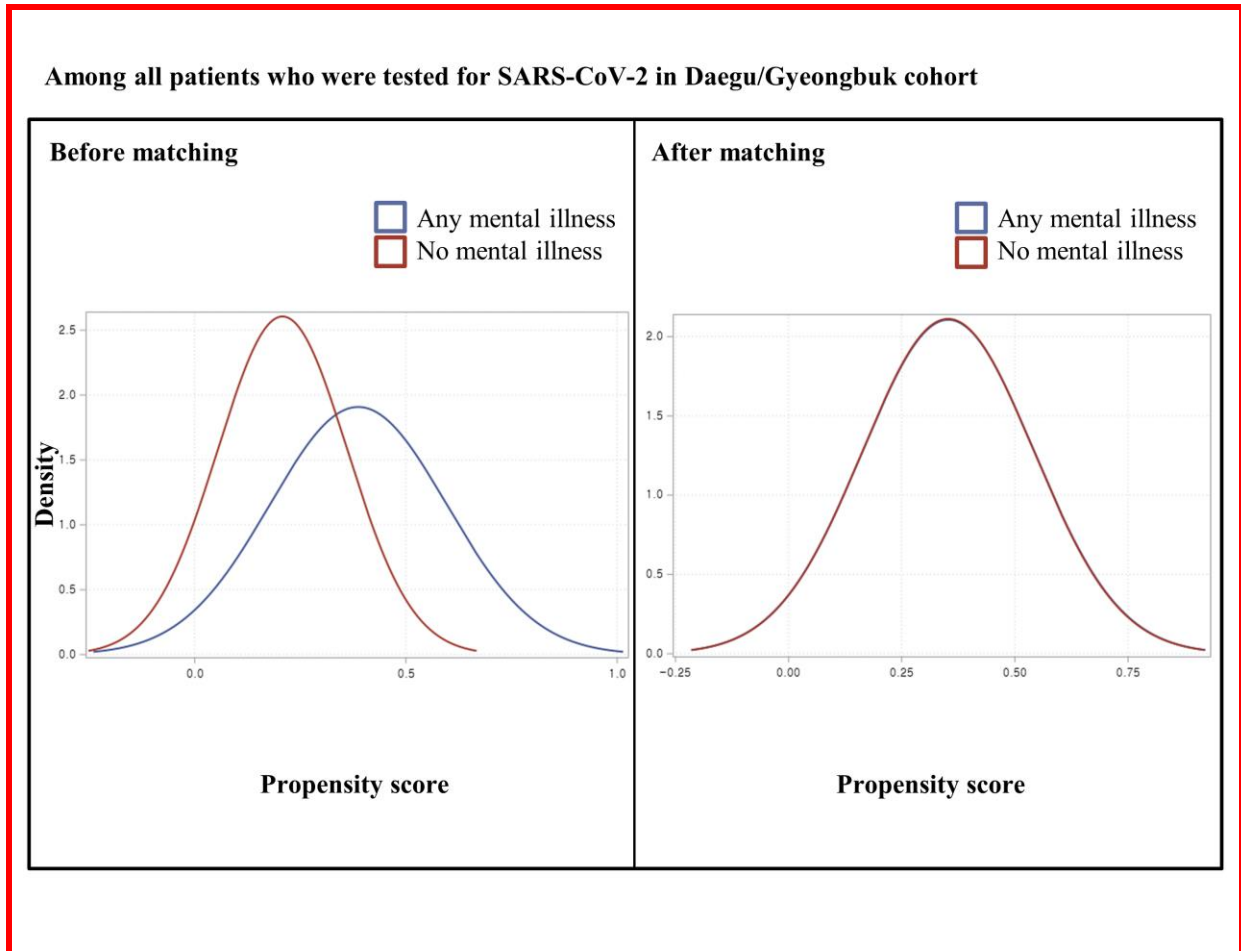


Figure S3. Density of propensity scores before and after matching among all patients who were tested for SARS-CoV-2 in other areas cohort (n = 78,148).

SARS-CoV-2, severe acute respiratory syndrome 2.

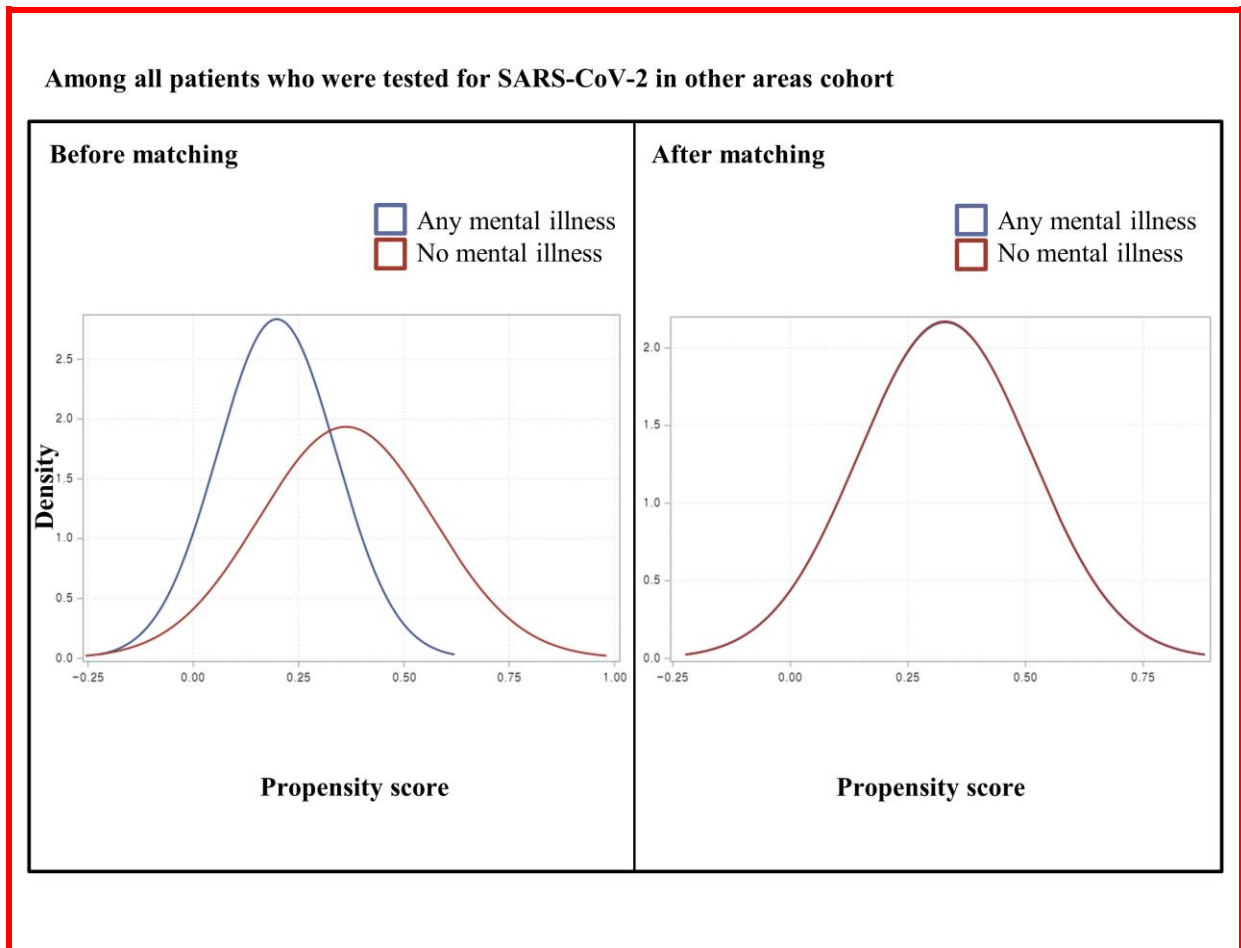


Figure S4. Density of propensity scores before and after matching among all patients who tested positive for SARS-CoV-2 in Daegu/Gyeongbuk cohort (n = 1718).

SARS-CoV-2, severe acute respiratory syndrome 2.

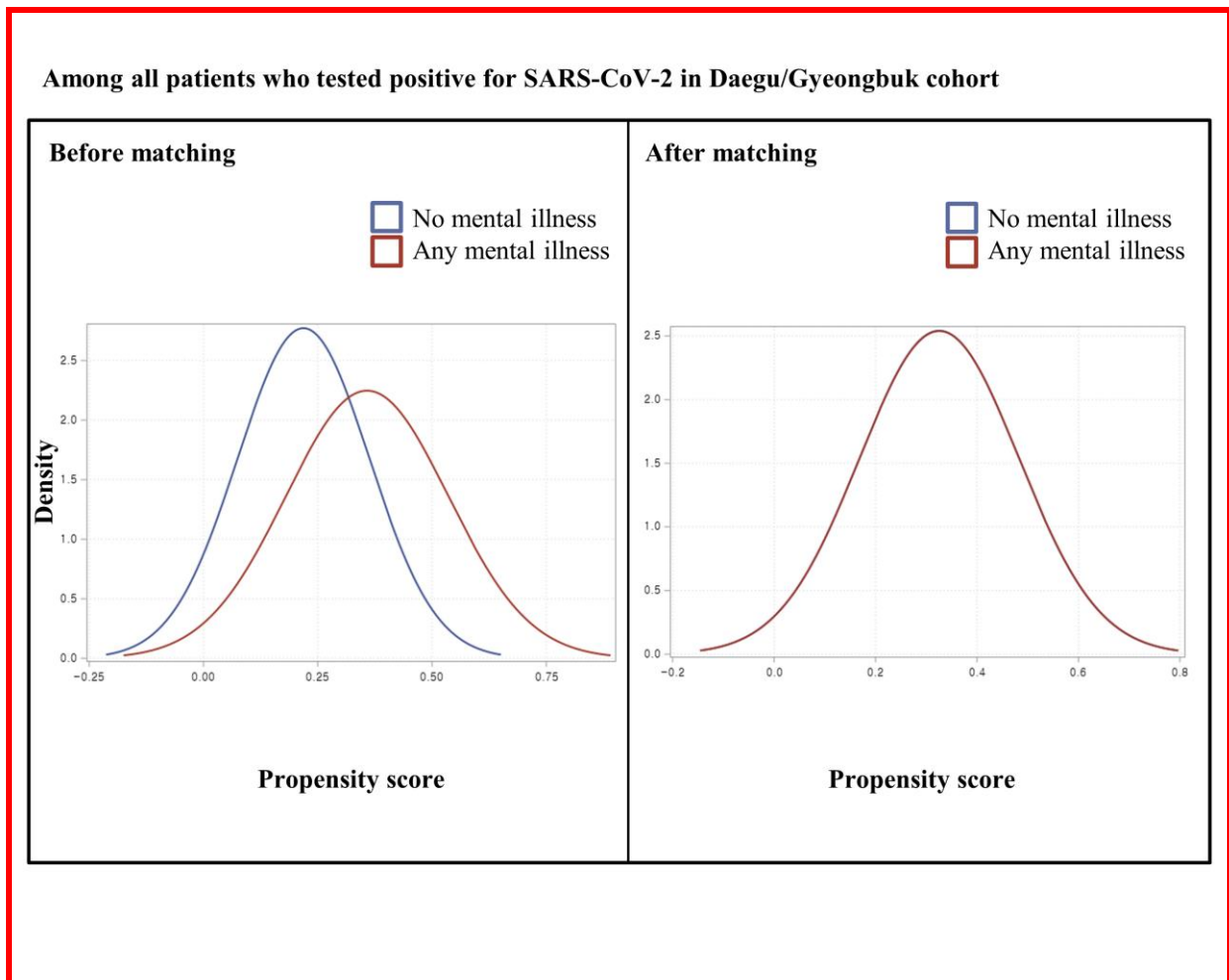


Figure S5. Density of propensity scores before and after matching among all patients who tested positive for SARS-CoV-2 in other areas cohort (n = 848).

SARS-CoV-2, severe acute respiratory syndrome 2.

