

# Short- and long-term neuropsychiatric outcomes in long COVID in South Korea and Japan

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**Supplement Figure 2:** Study design in Japan

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**Supplement Information.** External validation cohort in Japan

**Supplement Information.** The RECORD statement, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data

**Table S1.** Representative study population

| Category |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|----------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Disease  | <ul style="list-style-type: none"><li>▪ Exposure: SARS-CoV-2 or ARI</li><li>▪ Outcome: Neuropsychiatric disorders<ol style="list-style-type: none"><li>1. Anxiety disorder: F40-F48</li><li>2. Cognitive deficit: F01, F02, F03, F05, F06.8, G30, G31.0, G31.83, G31.84, G93.40, R40, R41, R48</li><li>3. Encephalitis: G04, G05, A86, A85.8</li><li>4. Epilepsy/seizures: G40, R56</li><li>5. Guillain-Barré syndrome: G61.0</li><li>6. Insomnia: F51.0, G47.0</li><li>7. Intracranial hemorrhage: I60-I62</li><li>8. Ischemic stroke: I63</li><li>9. Mood disorder: F30-39</li></ol></li></ul> |

|                                      |                                                                                                                                                                                                     |
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|                                      | 10. Myoneural junction/muscle disease: G70-G73<br>11. Nerve/nerve root/plexus disorders: G50-G59<br>12. Parkinsonism: G20, G21<br>13. Psychotic disorder: F20-F29                                   |
| Special considerations related to    |                                                                                                                                                                                                     |
| Sex                                  | The incidence of neuropsychiatric disorders affects females more than males.                                                                                                                        |
| Age                                  | The incidence of neuropsychiatric disorders is higher as age increases.                                                                                                                             |
| Socioeconomic status                 | Socioeconomic status is an important determinant affecting the severity of neuropsychiatric disorders.                                                                                              |
| Race and country                     | The incidence of neuropsychiatric disorders affects all races worldwide, with different social environment statuses among races.                                                                    |
| Geography of urban-rural interaction | Environmental factors may have a different impact on the outcome of neuropsychiatric disorders in urban and rural communities.                                                                      |
| Other considerations                 | Globally, neuropsychiatric disorders incidence varies widely within and among countries.<br>Furthermore, since the post-infectious response after respiratory infection is related to the incidence |

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and severity of neuropsychiatric disorders, it is necessary to compare similar respiratory infections such as the ARI to examine the direct and special association after SARS-CoV-2 infection.

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| Overall representativeness of this study | We used data from the Korean nationwide cohort (K-COV-N cohort; total n=10,145,517) and Japanese claim-based cohort (JMDC cohort; total n=12,218,680) to estimate risks of neuropsychiatric disorders following over one year after SARS-CoV-2 infection compared to noninfected controls and comparators (participants with ARI). We used two independent binational cohorts and sophisticated statistical techniques to strengthen and generalize our main findings. This is the most significant analysis to evaluate the incidence rate of neuropsychiatric disorders after SARS-CoV-2 infection and the first to focus on the vaccination protective effect of subsequent development of neuropsychiatric disorders. |
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ARI, another respiratory infection; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

**Table S2.** Sensitivity analyses and justification

| Sensitivity analysis (1 to 16)                                                   | Cohort                                                                                                      | Justification                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|----------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1. Incident neuropsychiatric disorders in COVID-19 versus the general population | Korean COVID-19 versus general population cohort after propensity score matching (missing indicator method) | <p>- Main results</p> <p>- Matching covariates were selected for age (20–39, 40–59, and <math>\geq 60</math> years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and <math>\geq 2</math>); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; and history of medication use for diabetes mellitus, dyslipidemia, and hypertension.</p> <p>- Adjusting covariates were selected for age (20–39, 40–59, and <math>\geq 60</math> years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and <math>\geq 2</math>); obesity (underweight [<math>&lt; 18.5 \text{ kg/m}^2</math>], normal [<math>18.5\text{--}23.0 \text{ kg/m}^2</math>], overweight [<math>23.0\text{--}25.0 \text{ kg/m}^2</math>], obese [<math>\geq 25.0 \text{ kg/m}^2</math>], and unknown); blood pressure (systolic blood pressure <math>&lt; 140 \text{ mmHg}</math> and diastolic blood pressure <math>&lt; 90 \text{ mmHg}</math>, systolic blood pressure <math>\geq 140 \text{ mmHg}</math> or diastolic blood pressure <math>\geq 90 \text{ mmHg}</math>, and unknown); fasting blood glucose (<math>&lt; 100</math>, <math>\geq 100 \text{ mg/dL}</math>, and unknown); serum total cholesterol (<math>&lt; 200</math>, <math>200\text{--}240</math>, <math>\geq 240 \text{ mg/dL}</math>, and unknown); glomerular filtration rate (<math>&lt; 60</math>, <math>60\text{--}90</math>, <math>\geq 90 \text{ mL/min/1.73 m}^2</math>, and unknown); smoking status (non-, ex-, current smoker, and unknown); alcohol consumption (drinks; <math>&lt; 1</math>, <math>1\text{--}2</math>, <math>3\text{--}4</math>, <math>\geq 5</math> days per week, and unknown); aerobic physical activity (sufficient, insufficient, and unknown); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and <math>\geq 2</math> times); outpatients contact in the year</p> |

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|                                                                                      |                                                                                                                  | before index date (0, 1-4, and $\geq 5$ times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no], fasting blood glucose missing indicator [yes or no], serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no], smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes or no]).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| 2. Incident neuropsychiatric disorders in COVID-19 versus contemporary control (ARI) | Korean COVID-19 versus ARI cohort after propensity score matching (missing indicator method)                     | - Contemporary control results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| 3. Incident neuropsychiatric disorders in COVID-19 versus general population         | Korean COVID-19 versus general population cohort after propensity score matching (complete case analysis method) | <p>- Matching covariates were selected for age (20–39, 40–59, and <math>\geq 60</math> years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and <math>\geq 2</math>); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; and history of medication use for diabetes mellitus, dyslipidemia, and hypertension.</p> <p>- Adjusting covariates were selected for age (20–39, 40–59, and <math>\geq 60</math> years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and <math>\geq 2</math>); obesity (underweight [<math>&lt; 18.5 \text{ kg/m}^2</math>], normal [<math>18.5\text{--}23.0 \text{ kg/m}^2</math>], overweight [<math>23.0\text{--}25.0 \text{ kg/m}^2</math>], and obese [<math>\geq 25.0 \text{ kg/m}^2</math>]); blood pressure (systolic blood pressure <math>&lt; 140 \text{ mmHg}</math> and diastolic blood pressure <math>&lt; 90 \text{ mmHg}</math>, systolic blood pressure <math>\geq 140 \text{ mmHg}</math> or diastolic blood pressure <math>\geq 90 \text{ mmHg}</math>); fasting blood glucose (<math>&lt; 100</math> and <math>\geq 100 \text{ mg/dL}</math>); serum total cholesterol (<math>&lt; 200</math>, <math>200\text{--}240</math>, and <math>\geq 240 \text{ mg/dL}</math>);</p> |

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|---------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                         |                                                                                                                                                                                                                                                                                                                     | glomerular filtration rate (< 60, 60–90, and $\geq$ 90 mL/min/1.73 m <sup>2</sup> ); smoking status (non-, ex-, and current smoker); alcohol consumption (drinks; < 1, 1–2, 3–4, and $\geq$ 5 days per week); aerobic physical activity (sufficient and insufficient); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and $\geq$ 2 times); and outpatients contact in the year before index date (0, 1–4, and $\geq$ 5 times); |
| 4. Incident neuropsychiatric disorders in COVID-19 versus contemporary control (ARI)                    | Korean COVID-19 versus ARI cohort after propensity score matching (complete case analysis method)                                                                                                                                                                                                                   | - Contemporary control results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| 5. Subgroup analysis of the risk of several neuropsychiatric diseases after SARS-CoV-2 infection or ARI | <p>1. Korean COVID-19 versus general population cohort after propensity score matching (missing indicator method)</p> <p>2. Korean COVID-19 versus general population cohort after propensity score matching (complete case analysis method)</p> <p>3. Korean COVID-19 versus ARI cohort after propensity score</p> | <p>- To investigate the likelihood of neuropsychiatric diseases after SARS-CoV-2 infection, compared with those after ARI</p> <p>- Several neuropsychiatric diseases: anxiety disorder, cognitive deficit, encephalitis, epilepsy/seizures, Guillain-Barré syndrome, insomnia, intracranial hemorrhage, ischemic stroke, mood disorder, myoneural junction/muscle disease, nerve/nerve root/plexus disorders, parkinsonism, and psychotic disorder</p>                                                                                                                                                                                   |

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matching (missing indicator method)

4. Korean COVID-19 versus ARI cohort after propensity score matching (complete case analysis method)

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6. Subgroup analysis of the risk of neuropsychiatric diseases development in COVID-19, stratified by COVID-19 severity, vaccination, and strains

1. Korean COVID-19 versus general population cohort after propensity score matching (missing indicator method)

2. Korean COVID-19 versus ARI cohort after propensity score matching (missing indicator analysis method)

- To investigate the association of neuropsychiatric disease incidence in COVID-19, stratified by COVID-19 severity (mild or moderate to severe), vaccination type and dose, and strains (delta or original).

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7. Attenuation time effect of neuropsychiatric diseases development after SARS-CoV-2 or ARI

1. Korean COVID-19 versus general population cohort after propensity score matching (missing indicator method)

2. Korean COVID-19 versus ARI cohort after propensity score matching (missing indicator analysis method)

- To investigate the attenuation time effect of neuropsychiatric diseases development after SARS-CoV-2 infection or ARI

|                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                  |
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| 8. Stratification analysis of the risk of neuropsychiatric disease development in COVID-19 or ARI                | <p>1. Korean COVID-19 versus general population cohort after propensity score matching (missing indicator method)</p> <p>2. Korean COVID-19 versus general population cohort after propensity score matching (complete case analysis method)</p> <p>3. Korean COVID-19 versus ARI cohort after propensity score matching (missing indicator method)</p> <p>4. Korean COVID-19 versus ARI cohort after propensity score matching (complete case analysis method)</p> | - To investigate the unintended mediation effects by sex, age, household income, Charlson comorbidity index, body mass index, smoking status, alcohol consumption, and aerobic physical activity |
| 9. Competitive analysis involving death and the development of neuropsychiatric diseases after SARS-CoV-2 or ARI | <p>1. Korean COVID-19 versus general population cohort after propensity score matching (missing indicator method)</p> <p>2. Korean COVID-19 versus ARI cohort after propensity score</p>                                                                                                                                                                                                                                                                            | - To investigate the competitive composite endpoints involving death and the development of neuropsychiatric diseases                                                                            |

|                                                                               | matching<br>method)                                                                                           | (missing<br>indicator<br>method)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
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| 10. Incident neuropsychiatric disorders in COVID-19 versus general population | Japanese COVID-19 versus general population cohort after propensity score matching (missing indicator method) | <p>- Main results (independent validation)</p> <p>- Matching covariates were selected for age (20–39, 40–59, and <math>\geq 60</math> years); sex; insurance status (insured or dependent); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; and history of medication use for diabetes mellitus, dyslipidemia, and hypertension.</p> <p>- Adjusting covariates were selected for age (20–39, 40–59, and <math>\geq 60</math> years); sex; insurance status (insured or dependent); body mass index (underweight [<math>&lt; 18.5</math> kg/m<sup>2</sup>]; normal [18.5–23.0 kg/m<sup>2</sup>], overweight [23.0–25.0 kg/m<sup>2</sup>], obese [<math>\geq 25.0</math> kg/m<sup>2</sup>], and unknown); blood pressure (systolic blood pressure <math>&lt; 140</math> mmHg and diastolic blood pressure <math>&lt; 90</math> mmHg, systolic blood pressure <math>\geq 140</math> mmHg or diastolic blood pressure <math>\geq 90</math> mmHg, and unknown); fasting blood glucose (<math>&lt; 100</math>, <math>\geq 100</math> mg/dL, and unknown); serum total cholesterol (<math>&lt; 200</math>, 200–240, <math>\geq 240</math> mg/dL, and unknown); glomerular filtration rate (<math>&lt; 60</math>, 60–90, <math>\geq 90</math> mL/min/1.73 m<sup>2</sup>, and unknown); smoking status (non-, current smoker, and unknown); alcohol consumption (rarely, sometimes, every day, and unknown); aerobic physical activity (sufficient, insufficient, unknown); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and <math>\geq 2</math> times); outpatients contact in the year before index date (0, 1–4, and <math>\geq 5</math> times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no], fasting blood glucose missing indicator [yes or no],</p> |

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|                                                                                       |                                                                                                                    | serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no], smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes or no]).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| 11. Incident neuropsychiatric disorders in COVID-19 versus contemporary control (ARI) | Japanese COVID-19 versus ARI cohort after propensity score matching (missing indicator method)                     | - Contemporary control results (independent validation)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| 12. Incident neuropsychiatric disorders in COVID-19 versus general population         | Japanese COVID-19 versus general population cohort after propensity score matching (complete case analysis method) | <p>- Main results (independent validation)</p> <p>- Matching covariates were selected for age (20–39, 40–59, and <math>\geq 60</math> years); sex; insurance status (insured or dependent); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; and history of medication use for diabetes mellitus, dyslipidemia, and hypertension.</p> <p>- Adjusting covariates were selected for age (20–39, 40–59, and <math>\geq 60</math> years); sex; insurance status (insured or dependent); body mass index (underweight [<math>&lt; 18.5</math> kg/m<sup>2</sup>], normal [18.5–23.0 kg/m<sup>2</sup>], overweight [23.0–25.0 kg/m<sup>2</sup>], and obese [<math>\geq 25.0</math> kg/m<sup>2</sup>]); blood pressure (systolic blood pressure <math>&lt; 140</math> mmHg and diastolic blood pressure <math>&lt; 90</math> mmHg and systolic blood pressure <math>\geq 140</math> mmHg or diastolic blood pressure <math>\geq 90</math> mmHg); fasting blood glucose (<math>&lt; 100</math> and <math>\geq 100</math> mg/dL); total serum cholesterol (<math>&lt; 200</math>, 200–240, and <math>\geq 240</math> mg/dL); glomerular filtration rate (<math>&lt; 60</math>, 60–90, and <math>\geq 90</math> mL/min/1.73 m<sup>2</sup>); smoking status (non- and current smoker); alcohol consumption (rarely, sometimes, and every day); aerobic physical activity (sufficient and insufficient); previous history of cardiovascular</p> |

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|                                                                                                                                                                 |                                                                                                                                                                                                                                  | disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and $\geq 2$ times); and outpatients contact in the year before index date (0, 1-4, and $\geq 5$ times).                                                                                                                  |
| 13. Incident neuropsychiatric disorders in COVID-19 versus contemporary control (ARI)                                                                           | Japanese COVID-19 versus ARI cohort after propensity score matching (complete case analysis method)                                                                                                                              | - Contemporary control results (independent validation)                                                                                                                                                                                                                                                                                                                                                                                         |
| 14. Competitive analysis involving death and the development of neuropsychiatric diseases after SARS-CoV-2 or ARI                                               | <p>1. Japanese COVID-19 versus general population cohort after propensity score matching (missing indicator method)</p> <p>2. Japanese COVID-19 versus ARI cohort after propensity score matching (missing indicator method)</p> | - To investigate the competitive composite endpoints involving death and the development of neuropsychiatric diseases                                                                                                                                                                                                                                                                                                                           |
| 15. Attenuation time effect of long-term sequelae risk of neuropsychiatric outcomes following COVID-19 or ARI diagnosis, stratified by COVID-19 or ARI severity | <p>1. Korean COVID-19 versus general population cohort after propensity score matching (missing indicator method)</p> <p>2. Korean COVID-19 versus ARI cohort after propensity score</p>                                         | <p>- To investigate the attenuation time effect of long-term sequelae risk of neuropsychiatric diseases development after SARS-CoV-2 infection or ARI, stratified by COVID-19 or ARI severity</p> <p>1. Mild COVID-19 versus general population</p> <p>2. Moderate to severe COVID-19 versus general population</p> <p>3. Mild COVID-19 versus ARI</p> <p>4. Moderate to severe COVID-19 versus ARI</p> <p>5. Mild COVID-19 versus mild ARI</p> |

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| <p>matching (missing indicator method)</p> <p>3. Japanese COVID-19 versus general population cohort after propensity score matching (missing indicator method)</p> <p>4. Japanese COVID-19 versus ARI cohort after propensity score matching (missing indicator method)</p> | <p>6. Moderate to severe COVID-19 versus moderate to severe ARI</p> |
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|                                                                           |                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|---------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p>16. Redefined cohort using alternative neuropsychiatric definition</p> | <p>1. Korean COVID-19 versus general population cohort after propensity score matching (missing indicator method)</p> <p>2. Japanese COVID-19 versus general population cohort after propensity score matching (missing indicator method)</p> | <p>- An alternative definition of neuropsychiatric outcomes was considered to mitigate detection bias.</p> <p>∫ Onset of neuropsychiatric outcomes were defined when a participant was diagnosed with a particular outcome three times or more within one year using the following ICD-10 codes.</p> <p>∫∫ Onset of neuropsychiatric outcomes were defined when a participant was diagnosed with a particular outcome four times or more within one year using the following ICD-10 codes.</p> |
|---------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

ARI, another respiratory infection; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

**Table S3.** Baseline covariates of participants in the entire unmatched South Korea and Japan cohorts

| Characteristics         | South Korea Entire cohort<br>(n =10,027,506) | Japan Entire cohort<br>(n= 12,218,680) |
|-------------------------|----------------------------------------------|----------------------------------------|
| Total, n                | 10,027,506                                   | 12,218,680                             |
| Age, years, mean (SD)   | 48.4 (13.4)                                  | 43.5 (14.7)                            |
| Age, years, n (%)       |                                              |                                        |
| 20 to 39                | 2,756,102 (27.5)                             | 5,298,703 (43.4)                       |
| 40 to 59                | 4,799,784 (47.9)                             | 4,935,219 (40.4)                       |
| ≥ 60                    | 2,471,620 (24.7)                             | 1,984,758 (16.2)                       |
| Sex, n (%)              |                                              |                                        |
| Male                    | 5,026,885 (50.1)                             | 6,334,565 (51.8)                       |
| Female                  | 5,000,621 (49.9)                             | 5,884,115 (48.2)                       |
| Insurance status, n (%) |                                              |                                        |
| Insured                 | -                                            | 8,524,220 (69.8)                       |
| Dependent               | -                                            | 3,694,460 (30.2)                       |
| SD, standard deviation  |                                              |                                        |

**Table S4.** Baseline characteristics for 1:2 propensity score-matched cohort (COVID-19 versus general) and 1:1 propensity score-matched cohort (COVID-19 versus ARI) in the entire unmatched validation cohort in Japan (total n= 12,218,680; missing indicator method)

| Matching covariates         | COVID-19 versus general |                       |        | COVID-19 versus ARI |                      |        |
|-----------------------------|-------------------------|-----------------------|--------|---------------------|----------------------|--------|
|                             | (n=2,059,727)           |                       |        | (n= 309,794)        |                      |        |
|                             | COVID-19<br>(n=790,176) | None<br>(n=1,269,551) | SMD    | ARI<br>(n= 154,897) | None<br>(n= 154,897) | SMD    |
| Total, n (%)                | 790,176 (38.4)          | 1,269,551 (61.6)      |        | 153,269 (50.0)      | 301,424 (50.0)       |        |
| Age, years, n (%)           |                         |                       | 0.147  |                     |                      | <0.001 |
| 20 to 39                    | 304,746 (38.6)          | 400,171 (31.5)        |        | 56,799 (36.7)       | 56,792 (36.7)        |        |
| 40 to 59                    | 406,366 (51.4)          | 724,098 (57.0)        |        | 77,956 (50.3)       | 77,942 (50.3)        |        |
| ≥ 60                        | 79,064 (10.0)           | 145,282 (11.4)        |        | 20,142 (13.0)       | 20,163 (13.0)        |        |
| Sex, n (%)                  |                         |                       | 0.038  |                     |                      | <0.001 |
| Male                        | 494,157 (62.5)          | 817,131 (64.4)        |        | 91,290 (58.9)       | 91,290 (58.9)        |        |
| Female                      | 296,019 (37.5)          | 452,420 (35.6)        |        | 63,607 (41.1)       | 63,607 (41.1)        |        |
| Insured or dependent, n (%) |                         |                       | <0.001 |                     |                      | <0.001 |
| Insured                     | 719,505 (91.1)          | 1,154,707 (91.0)      |        | 138,786 (89.6)      | 138,802 (89.6)       |        |

|                                                         |                |                |       |               |               |        |
|---------------------------------------------------------|----------------|----------------|-------|---------------|---------------|--------|
| Dependent                                               | 70,671 (8.9)   | 114,844 (9.1)  |       | 16,111 (10.4) | 16,095 (10.4) |        |
| History of cardiovascular disease, n (%)                | 49,963 (6.3)   | 58,408 (4.6)   | 0.076 | 5893 (3.8)    | 5889 (3.8)    | <0.001 |
| History of chronic kidney disease, n (%)                | 26,745 (3.4)   | 32,911 (2.6)   | 0.047 | 3031 (2.0)    | 3048 (2.0)    | <0.001 |
| History of chronic obstructive pulmonary disease, n (%) | 1810 (0.2)     | 1899 (0.1)     | 0.018 | 168 (0.1)     | 166 (0.1)     | <0.001 |
| Current medication for diabetes                         | 18,531 (2.4)   | 27,759 (2.2)   | 0.076 | 2564 (1.7)    | 2589 (1.7)    | <0.001 |
| Current medication for hyperlipidemia                   | 44,334 (5.6)   | 63,711 (5.0)   | 0.047 | 6515 (4.2)    | 6523 (4.2)    | <0.001 |
| Current medication for hypertension                     | 59,680 (7.6)   | 87,802 (6.9)   | 0.018 | 8847 (5.7)    | 8847 (5.7)    | <0.001 |
| <b>Unmatching covariates</b>                            |                |                |       |               |               |        |
| Body mass index, kg/m <sup>2</sup> , n (%)              |                |                | 0.026 |               |               | <0.001 |
| Underweight (<18.5)                                     | 418,173 (52.9) | 681,577 (53.7) |       | 84,163 (54.3) | 83,455 (53.9) |        |
| Normal (≥18.5 to <23.0)                                 | 149,986 (19.0) | 243,357 (19.2) |       | 29,002 (18.7) | 28,879 (18.6) |        |
| Overweight (≥23.0 to <25.0)                             | 170,346 (21.6) | 271,109 (21.4) |       | 32,216 (20.8) | 32,945 (21.3) |        |
| Obese (≥25.0)                                           | 50,512 (6.4)   | 72,043 (5.7)   |       | 9291 (6.0)    | 9411 (6.1)    |        |

|                                                                |                |                  |       |                |                |        |
|----------------------------------------------------------------|----------------|------------------|-------|----------------|----------------|--------|
| Unknown                                                        | 1159 (0.2)     | 1465 (0.1)       |       | 225 (0.2)      | 207 (0.1)      |        |
| Blood pressure, n (%)                                          |                |                  | 0.112 |                |                | 0.038  |
| SBP <140 mmHg and DBP <90 mmHg                                 | 686,599 (86.9) | 1,059,328 (83.4) |       | 134,241 (86.7) | 133,024 (85.9) |        |
| SBP ≥140mmHg or DBP ≥90 mmHg                                   | 45,835 (5.8)   | 98,169 (7.7)     |       | 9124 (5.9)     | 9662 (6.2)     |        |
| Unknown                                                        | 57,742 (7.3)   | 112,054 (8.8)    |       | 11,532 (7.4)   | 12,211 (7.9)   |        |
| Fasting blood glucose, mg/dL, n (%)                            |                |                  | 0.063 |                |                | 0.056  |
| <100                                                           | 509,964 (64.5) | 781,119 (61.5)   |       | 100,401 (64.8) | 97,939 (63.2)  |        |
| ≥100                                                           | 157,835 (20.0) | 280,019 (22.1)   |       | 30,602 (19.8)  | 31,028 (20.0)  |        |
| Unknown                                                        | 122,377 (15.5) | 208,413 (16.4)   |       | 23,894 (15.4)  | 25,930 (16.7)  |        |
| Serum total cholesterol, mg/dL, n (%)                          |                |                  | 0.102 |                |                | <0.001 |
| <200                                                           | 372,224 (47.1) | 552,219 (43.5)   |       | 71,985 (46.5)  | 71,408 (46.1)  |        |
| 200 to 240                                                     | 282,672 (35.8) | 469,729 (37.0)   |       | 55,772 (36.0)  | 56,132 (36.2)  |        |
| ≥240                                                           | 121,060 (15.3) | 221,317 (17.4)   |       | 24,493 (15.8)  | 24,565 (15.9)  |        |
| Unknown                                                        | 14,220 (1.8)   | 26,286 (2.1)     |       | 2647 (1.7)     | 2792 (1.8)     |        |
| Glomerular filtration rate, mL/min/1.73 m <sup>2</sup> , n (%) |                |                  | 0.046 |                |                | 0.021  |

|                                             |                |                |                |                |        |
|---------------------------------------------|----------------|----------------|----------------|----------------|--------|
| <60                                         | 3714 (0.5)     | 4252 (0.3)     | 741 (0.5)      | 616 (0.4)      |        |
| 60 to 90                                    | 70,603 (8.9)   | 122,887 (9.7)  | 14,191 (9.2)   | 14,585 (9.4)   |        |
| ≥90                                         | 429,143 (54.3) | 663,501 (52.3) | 83,735 (54.1)  | 82,804 (53.5)  |        |
| Unknown                                     | 286,716 (36.3) | 478,911 (37.7) | 56,230 (36.3)  | 56,892 (36.7)  |        |
| Smoking status, n (%)                       |                |                | 0.104          |                | <0.001 |
| Non-smoker                                  | 584,575 (74.0) | 897,530 (70.7) | 116,116 (75.0) | 116,352 (75.1) |        |
| Current smoker                              | 176,659 (22.4) | 334,576 (26.4) | 33,414 (21.6)  | 34,090 (22.0)  |        |
| Unknown                                     | 28,942 (3.7)   | 37,445 (3.0)   | 5367 (3.5)     | 4455 (2.9)     |        |
| Alcohol consumption; drinks per week, n (%) |                |                | 0.056          |                | 0.042  |
| Rarely                                      | 305,208 (38.6) | 497,749 (39.2) | 61,553 (39.7)  | 62,312 (40.2)  |        |
| Sometimes                                   | 266,138 (33.7) | 412,222 (32.5) | 51,254 (33.1)  | 51,269 (33.1)  |        |
| Everyday                                    | 160,466 (20.3) | 276,896 (21.8) | 30,770 (19.9)  | 31,343 (20.2)  |        |
| Unknown                                     | 58,364 (7.4)   | 82,684 (6.5)   | 11,320 (7.3)   | 9973 (6.4)     |        |
| Aerobic physical activity, n (%)            |                |                | 0.057          |                | 0.041  |
| Insufficient                                | 560,777 (71.0) | 885,853 (69.8) | 110,425 (71.3) | 110,444 (71.3) |        |

|                                                          |                |                  |                |                |        |
|----------------------------------------------------------|----------------|------------------|----------------|----------------|--------|
| Sufficient                                               | 157,268 (19.9) | 282,293 (22.2)   | 30,531 (19.7)  | 32,323 (20.9)  |        |
| Unknown                                                  | 72,131 (9.1)   | 101,405 (8.0)    | 13,941 (9.0)   | 12,130 (7.8)   |        |
| Hospital admissions in the year before index date, n (%) |                |                  | 0.142          |                | <0.001 |
| None                                                     | 779,617 (98.7) | 1,263,599 (99.5) | 152,727 (98.6) | 153,491 (99.1) |        |
| 1 time                                                   | 945 (0.1)      | 631 (0.1)        | 183 (0.1)      | 120 (0.1)      |        |
| ≥2 times                                                 | 9614 (1.2)     | 5321 (0.4)       | 1987 (1.3)     | 1286 (0.8)     |        |
| Outpatients contact in the year before index date, n (%) |                |                  | 0.585          |                | 0.397  |
| None                                                     | 157,974 (20.0) | 568,242 (44.8)   | 30,108 (19.4)  | 52,474 (33.9)  |        |
| 1-4 time                                                 | 163,949 (20.8) | 253,291 (20.0)   | 31,482 (20.3)  | 34,937 (22.6)  |        |
| ≥5 times                                                 | 468,253 (59.3) | 448,018 (35.3)   | 93,307 (60.2)  | 67,486 (43.6)  |        |

ARI, another respiratory infection; DBP, diastolic blood pressure; SBP, systolic blood pressure; SD, standard deviation; SMD, standardized mean difference.

An SMD < 0.1 indicates no significant imbalance. All SMD values were ≤0.076 in the 1:2 propensity score-matched cohorts, except for age (SMD=0.147).

**Table S5.** The hazard ratio (95% CI) for the **overall (short- and long-term) sequelae risk** of neuropsychiatric events following COVID-19 diagnosis of patients in the propensity score-matched cohorts in South Korea (missing indicator method)

|                                                   | COVID-19 versus general |                         |                         | COVID-19 versus ARI |                          |                         |
|---------------------------------------------------|-------------------------|-------------------------|-------------------------|---------------------|--------------------------|-------------------------|
|                                                   | (n=1,831,237)           |                         |                         | (n= 531,020)        |                          |                         |
|                                                   | HR (95% CI)             |                         |                         | HR (95% CI)         |                          |                         |
|                                                   | Events (%)              | Model 1 <sup>*</sup>    | Model 2 <sup>II</sup>   | Events (%)          | Model 1 <sup>*</sup>     | Model 2 <sup>II</sup>   |
| Any neuropsychiatric outcomes                     |                         |                         |                         |                     |                          |                         |
| Control (general population or patients with ARI) | 9393 (0.65)             | 1.0 (ref)               | 1.0 (ref)               | 8003 (3.01)         | 1.0 (ref)                | 1.0 (ref)               |
| Patients with COVID-19                            | 4628 (1.21)             | <b>1.89 (1.82-1.96)</b> | <b>1.83 (1.75-1.91)</b> | 4624 (1.74)         | <b>1.65 (1.59-1.72)</b>  | <b>1.56 (1.49-1.63)</b> |
| Anxiety disorder                                  |                         |                         |                         |                     |                          |                         |
| Control                                           | 2945 (0.20)             | 1.0 (ref)               | 1.0 (ref)               | 2968 (1.12)         | 1.0 (ref)                | 1.0 (ref)               |
| Patients with COVID-19                            | 1755 (0.46)             | <b>2.28 (2.15-2.42)</b> | <b>2.39 (2.23-2.57)</b> | 1756 (0.66)         | <b>1.63 (1.53-1.73)</b>  | <b>1.64 (1.53-1.76)</b> |
| Encephalitis                                      |                         |                         |                         |                     |                          |                         |
| Control                                           | 40 (0.0028)             | 1.0 (ref)               | 1.0 (ref)               | 22 (0.0083)         | 1.0 (ref)                | 1.0 (ref)               |
| Patients with COVID-19                            | 65 (0.027)              | <b>6.08 (4.10-9.01)</b> | <b>3.80 (2.34-6.18)</b> | 64 (0.024)          | <b>6.15 (3.67-10.32)</b> | <b>4.15 (2.30-7.50)</b> |

|                         |                           |                          |                         |             |                         |                         |
|-------------------------|---------------------------|--------------------------|-------------------------|-------------|-------------------------|-------------------------|
| Epilepsy/seizures       |                           |                          |                         |             |                         |                         |
| Control                 | 120 (0.083)               | 1.0 (ref)                | 1.0 (ref)               | 115 (0.043) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19  | 50 (0.013)                | <b>1.60 (1.15-2.22)</b>  | 1.00 (0.62-1.61)        | 50 (0.019)  | 1.18 (0.83-1.68)        | 0.74 (0.46-1.21)        |
| Guillain-Barré syndrome |                           |                          |                         |             |                         |                         |
| Control                 | 8 (5.5*10 <sup>-4</sup> ) | 1.0 (ref)                | 1.0 (ref)               | 12 (0.0045) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19  | 9 (0.0024)                | <b>4.28 (1.65-11.10)</b> | 1.66 (0.74-3.74)        | 9 (0.0034)  | 1.25 (0.70-2.22)        | 0.77 (0.38-1.58)        |
| Insomnia                |                           |                          |                         |             |                         |                         |
| Control                 | 1121 (0.077)              | 1.0 (ref)                | 1.0 (ref)               | 1629 (0.61) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19  | 827 (0.22)                | <b>2.81 (2.57-3.07)</b>  | <b>2.84 (2.56-3.15)</b> | 825 (0.31)  | <b>1.40 (1.28-1.53)</b> | <b>1.36 (1.23-1.51)</b> |
| Intracranial hemorrhage |                           |                          |                         |             |                         |                         |
| Control                 | 246 (0.017)               | 1.0 (ref)                | 1.0 (ref)               | 99 (0.0437) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19  | 65 (0.017)                | 1.00 (0.76-1.32)         | 0.89 (0.64-1.25)        | 65 (0.0254) | <b>2.30 (1.64-3.23)</b> | <b>1.91 (1.29-2.83)</b> |
| Ischemic stroke         |                           |                          |                         |             |                         |                         |
| Control                 | 448(0.034)                | 1.0 (ref)                | 1.0 (ref)               | 429 (0.16)  | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19  | 248 (0.065)               | <b>1.91 (1.64-2.33)</b>  | <b>1.75 (1.45-2.11)</b> | 249 (0.094) | <b>1.87 (1.58-2.21)</b> | <b>1.62 (1.33-1.97)</b> |

|                                   |              |                         |                         |             |                         |                         |
|-----------------------------------|--------------|-------------------------|-------------------------|-------------|-------------------------|-------------------------|
| Mood disorder                     |              |                         |                         |             |                         |                         |
| Control                           | 2534 (0.17)  | 1.0 (ref)               | 1.0 (ref)               | 2375 (0.89) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19            | 1423 (0.37)  | <b>2.15 (2.02-2.30)</b> | <b>1.99 (1.84-2.16)</b> | 1422 (0.54) | <b>1.79 (1.67-1.92)</b> | <b>1.57 (1.44-1.71)</b> |
| Nerve/nerve root/plexus disorders |              |                         |                         |             |                         |                         |
| Control                           | 26 (0.0018)  | 1.0 (ref)               | 1.0 (ref)               | 35 (0.013)  | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19            | 10 (0.0026)  | 1.46 (0.70-3.03)        | 1.24 (0.51-3.05)        | 10 (0.0038) | 0.87 (0.42-1.83)        | 0.81 (0.33-1.99)        |
| Myoneural junction/muscle disease |              |                         |                         |             |                         |                         |
| Control                           | 3107 (0.21)  | 1.0 (ref)               | 1.0 (ref)               | 1624 (0.61) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19            | 1135 (0.30)  | <b>1.39 (1.30-1.49)</b> | <b>1.47 (1.36-1.59)</b> | 1132 (0.43) | <b>2.27 (2.09-2.47)</b> | <b>2.33 (2.13-2.55)</b> |
| Parkinsonism                      |              |                         |                         |             |                         |                         |
| Control                           | 120 (0.083)  | 1.0 (ref)               | 1.0 (ref)               | 157 (0.059) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19            | 51 (0.013)   | <b>1.60 (1.15-2.22)</b> | 1.11 (0.73-1.70)        | 51 (0.019)  | 1.00 (0.71-1.40)        | 0.75 (0.49-1.15)        |
| Psychotic disorder                |              |                         |                         |             |                         |                         |
| Control                           | 111 (0.0077) | 1.0 (ref)               | 1.0 (ref)               | 184 (0.069) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19            | 56 (0.015)   | <b>1.92 (1.40-2.65)</b> | 1.03 (0.63-1.70)        | 56 (0.021)  | 0.89 (0.65-1.22)        | <b>0.45 (0.28-0.75)</b> |

ARI, another respiratory infection; CI, confidence interval; HR, hazard ratio.

\* **Model 1:** adjusted for age (20–39, 40–59, and  $\geq 60$  years) and sex.

<sup>II</sup> **Model 2:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and  $\geq 2$ ); obesity (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], obese [ $\geq 25.0 \text{ kg/m}^2$ ], and unknown); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$ , systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ , and unknown); fasting blood glucose ( $< 100$ ,  $\geq 100 \text{ mg/dL}$ , and unknown); serum total cholesterol ( $< 200$ ,  $200\text{--}240$ ,  $\geq 240 \text{ mg/dL}$ , and unknown); glomerular filtration rate ( $< 60$ ,  $60\text{--}90$ ,  $\geq 90 \text{ mL/min/1.73 m}^2$ , and unknown); smoking status (non-, ex-, current smoker, and unknown); alcohol consumption (drinks;  $< 1$ ,  $1\text{--}2$ ,  $3\text{--}4$ ,  $\geq 5$  days per week, and unknown); aerobic physical activity (sufficient, insufficient, and unknown); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); outpatients contact in the year before index date (0,  $1\text{--}4$ , and  $\geq 5$  times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no], fasting blood glucose missing indicator [yes or no], serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no],

smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes or no]).

Data in bold indicate significant differences ( $P < 0.05$ ).

**Table S6.** Stratification analysis for the **short-term risk** of incident neuropsychiatric events following COVID-19 diagnosis of patients in the propensity score-matched cohorts in South Korea (missing indicator method)

|                                                   | COVID-19 versus general |                         |                         | COVID-19 versus ARI |                         |                         |
|---------------------------------------------------|-------------------------|-------------------------|-------------------------|---------------------|-------------------------|-------------------------|
|                                                   | (n=1,831,237)           |                         |                         | (n=531,020)         |                         |                         |
|                                                   | HR (95% CI)             |                         |                         | HR (95% CI)         |                         |                         |
|                                                   | Events (%)              | Model 1*                | Model 2 <sup>II</sup>   | Events (%)          | Model 1*                | Model 2 <sup>II</sup>   |
| Any neuropsychiatric outcomes                     |                         |                         |                         |                     |                         |                         |
| Control (general population or patients with ARI) | 1920 (0.13)             | 1.0 (ref)               | 1.0 (ref)               | 793 (0.30)          | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                            | 1243 (0.32)             | <b>2.43 (2.26-2.61)</b> | <b>2.35 (2.16-2.56)</b> | 1119 (0.42)         | <b>1.42 (1.30-1.56)</b> | <b>1.36 (1.23-1.51)</b> |
| Male                                              |                         |                         |                         |                     |                         |                         |
| Control                                           | 906 (0.12)              | 1.0 (ref)               | 1.0 (ref)               | 382 (0.27)          | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                            | 571 (0.28)              | <b>2.40 (2.16-2.67)</b> | <b>2.44 (2.16-2.76)</b> | 522 (0.37)          | <b>1.40 (1.23-1.60)</b> | <b>1.40 (1.21-1.62)</b> |
| Female                                            |                         |                         |                         |                     |                         |                         |
| Control                                           | 1014 (0.15)             | 1.0 (ref)               | 1.0 (ref)               | 411 (0.33)          | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                            | 672 (0.37)              | <b>2.46 (2.23-2.71)</b> | <b>2.28 (2.03-2.56)</b> | 597 (0.47)          | <b>1.45 (1.28-1.64)</b> | <b>1.34 (1.16-1.55)</b> |

Age 20-39 years

|                        |            |                         |                         |            |                         |                         |
|------------------------|------------|-------------------------|-------------------------|------------|-------------------------|-------------------------|
| Control                | 550 (0.10) | 1.0 (ref)               | 1.0 (ref)               | 142 (0.18) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19 | 315 (0.22) | <b>2.20 (1.91-2.52)</b> | <b>2.11 (1.75-2.55)</b> | 292 (0.37) | <b>2.08 (1.70-2.54)</b> | <b>1.97 (1.55-2.51)</b> |

Age 40-59 years

|                        |            |                         |                         |            |                         |                         |
|------------------------|------------|-------------------------|-------------------------|------------|-------------------------|-------------------------|
| Control                | 712 (0.13) | 1.0 (ref)               | 1.0 (ref)               | 329 (0.28) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19 | 458 (0.32) | <b>2.48 (2.21-2.79)</b> | <b>2.61 (2.29-2.98)</b> | 422 (0.36) | <b>1.30 (1.12-1.50)</b> | <b>1.37 (1.17-1.60)</b> |

Age ≥ 60 years

|                        |            |                         |                         |            |                         |                         |
|------------------------|------------|-------------------------|-------------------------|------------|-------------------------|-------------------------|
| Control                | 658 (0.19) | 1.0 (ref)               | 1.0 (ref)               | 322 (0.47) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19 | 470 (0.49) | <b>2.57 (2.28-2.89)</b> | <b>2.26 (1.97-2.59)</b> | 405 (0.58) | <b>1.27 (1.10-1.47)</b> | <b>1.17 (0.99-1.38)</b> |

Low (0–39 percentile) income

|                        |            |                         |                         |            |                         |                         |
|------------------------|------------|-------------------------|-------------------------|------------|-------------------------|-------------------------|
| Control                | 884 (0.13) | 1.0 (ref)               | 1.0 (ref)               | 363 (0.31) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19 | 571 (0.33) | <b>2.42 (2.18-2.69)</b> | <b>2.30 (2.03-2.61)</b> | 513 (0.44) | <b>1.41 (1.23-1.61)</b> | <b>1.34 (1.15-1.56)</b> |

Middle (40–79 percentile) income

|                        |            |                         |                         |            |                         |                         |
|------------------------|------------|-------------------------|-------------------------|------------|-------------------------|-------------------------|
| Control                | 693 (0.13) | 1.0 (ref)               | 1.0 (ref)               | 287 (0.28) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19 | 417 (0.30) | <b>2.27 (2.01-2.57)</b> | <b>2.32 (2.02-2.67)</b> | 371 (0.36) | <b>1.29 (1.11-1.51)</b> | <b>1.32 (1.12-1.57)</b> |

High (80–100 percentile) income

|                                       |             |                         |                         |            |                         |                         |
|---------------------------------------|-------------|-------------------------|-------------------------|------------|-------------------------|-------------------------|
| Control                               | 343 (0.13)  | 1.0 (ref)               | 1.0 (ref)               | 143 (0.31) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                | 255 (0.37)  | <b>2.77 (2.36-3.26)</b> | <b>2.61 (2.16-3.15)</b> | 235 (0.53) | <b>1.73 (1.40-2.13)</b> | <b>1.61 (1.28-2.03)</b> |
| Charlson comorbidity index, 0 score   |             |                         |                         |            |                         |                         |
| Control                               | 1443 (0.11) | 1.0 (ref)               | 1.0 (ref)               | 659 (0.27) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                | 986 (0.29)  | <b>2.64 (2.43-2.86)</b> | <b>2.64 (2.40-2.91)</b> | 893 (0.36) | <b>1.37 (1.24-1.51)</b> | <b>1.32 (1.18-1.48)</b> |
| Charlson comorbidity index, 1 score   |             |                         |                         |            |                         |                         |
| Control                               | 312 (0.34)  | 1.0 (ref)               | 1.0 (ref)               | 75 (0.72)  | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                | 168 (0.56)  | <b>1.65 (1.36-1.99)</b> | <b>1.57 (1.26-1.96)</b> | 148 (1.41) | <b>1.98 (1.50-2.61)</b> | <b>1.93 (1.42-2.62)</b> |
| Charlson comorbidity index, ≥2 scores |             |                         |                         |            |                         |                         |
| Control                               | 165 (0.37)  | 1.0 (ref)               | 1.0 (ref)               | 59 (0.62)  | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                | 89 (0.65)   | <b>1.75 (1.35-2.27)</b> | <b>1.62 (1.18-2.22)</b> | 78 (0.82)  | 1.33 (0.95-1.87)        | 1.24 (0.83-1.83)        |
| BMI, < 25 kg/m <sup>2</sup>           |             |                         |                         |            |                         |                         |
| Control                               | 1186 (0.13) | 1.0 (ref)               | 1.0 (ref)               | 507 (0.31) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                | 476 (0.35)  | <b>2.59 (2.33-2.89)</b> | <b>2.59 (2.33-2.88)</b> | 423 (0.43) | <b>1.37 (1.21-1.56)</b> | <b>1.40 (1.23-1.60)</b> |
| BMI, ≥ 25 kg/m <sup>2</sup>           |             |                         |                         |            |                         |                         |
| Control                               | 734 (0.14)  | 1.0 (ref)               | 1.0 (ref)               | 286 (0.28) | 1.0 (ref)               | 1.0 (ref)               |

|                                       |             |                         |                         |            |                         |                         |
|---------------------------------------|-------------|-------------------------|-------------------------|------------|-------------------------|-------------------------|
| Patients with COVID-19                | 300 (0.31)  | <b>2.09 (1.83-2.40)</b> | <b>2.06 (1.80-2.36)</b> | 270 (0.38) | <b>1.30 (1.10-1.53)</b> | <b>1.31 (1.11-1.55)</b> |
| BMI, unknown                          |             |                         |                         |            |                         |                         |
| Control                               | 0 (0.00)    | 1.0 (ref)               | 1.0 (ref)               | 0 (0.00)   | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                | 467 (0.31)  | NA                      | NA                      | 426 (0.43) | NA                      | NA                      |
| Smoking status, non-smoker            |             |                         |                         |            |                         |                         |
| Control                               | 1233 (0.13) | 1.0 (ref)               | 1.0 (ref)               | 496 (0.30) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                | 530 (0.35)  | <b>2.43 (2.20-2.70)</b> | <b>2.39 (2.16-2.65)</b> | 465 (0.43) | <b>1.36 (1.20-1.54)</b> | <b>1.38 (1.22-1.57)</b> |
| Smoking status, ex- or current smoker |             |                         |                         |            |                         |                         |
| Control                               | 687 (0.13)  | 1.0 (ref)               | 1.0 (ref)               | 297 (0.29) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                | 246 (0.31)  | <b>2.30 (1.98-2.66)</b> | <b>2.30 (1.99-2.67)</b> | 228 (0.39) | <b>1.30 (1.09-1.54)</b> | <b>1.34 (1.12-1.59)</b> |
| Smoking status, unknown               |             |                         |                         |            |                         |                         |
| Control                               | 0 (0.00)    | 1.0 (ref)               | 1.0 (ref)               | 0 (0.00)   | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                | 467 (0.31)  | NA                      | NA                      | 426 (0.43) | NA                      | NA                      |
| Alcoholic drinks, < 1 per week        |             |                         |                         |            |                         |                         |
| Control                               | 1166 (0.14) | 1.0 (ref)               | 1.0 (ref)               | 530 (0.33) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                | 486 (0.36)  | <b>2.47 (2.22-2.74)</b> | <b>2.43 (2.19-2.71)</b> | 428 (0.44) | <b>1.27 (1.12-1.44)</b> | <b>1.30 (1.14-1.47)</b> |

Alcoholic drinks,  $\geq 1$  per week

|                        |            |                         |                         |            |                         |                         |
|------------------------|------------|-------------------------|-------------------------|------------|-------------------------|-------------------------|
| Control                | 754 (0.13) | 1.0 (ref)               | 1.0 (ref)               | 262 (0.25) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19 | 290 (0.30) | <b>2.27 (1.98-2.60)</b> | <b>2.28 (1.99-2.61)</b> | 265 (0.38) | <b>1.49 (1.25-1.77)</b> | <b>1.51 (1.27-1.79)</b> |

Alcoholic drinks, unknown

|                        |            |           |           |            |                  |           |
|------------------------|------------|-----------|-----------|------------|------------------|-----------|
| Control                | 0 (0.00)   | 1.0 (ref) | 1.0 (ref) | 1 (1.19)   | 1.0 (ref)        | 1.0 (ref) |
| Patients with COVID-19 | 467 (0.31) | NA        | NA        | 426 (0.43) | 0.41 (0.06-2.91) | NA        |

Aerobic physical activity, insufficient

|                        |            |                         |                         |            |                         |                         |
|------------------------|------------|-------------------------|-------------------------|------------|-------------------------|-------------------------|
| Control                | 968 (0.13) | 1.0 (ref)               | 1.0 (ref)               | 409 (0.30) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19 | 378 (0.32) | <b>2.29 (2.03-2.58)</b> | <b>2.27 (2.01-2.56)</b> | 336 (0.40) | <b>1.28 (1.10-1.48)</b> | <b>1.30 (1.13-1.50)</b> |

Aerobic physical activity, sufficient

|                        |            |                         |                         |            |                         |                         |
|------------------------|------------|-------------------------|-------------------------|------------|-------------------------|-------------------------|
| Control                | 950 (0.13) | 1.0 (ref)               | 1.0 (ref)               | 384 (0.30) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19 | 398 (0.35) | <b>2.49 (2.22-2.80)</b> | <b>2.47 (2.20-2.78)</b> | 357 (0.43) | <b>1.40 (1.21-1.62)</b> | <b>1.44 (1.24-1.66)</b> |

Aerobic physical activity, unknown

|                        |            |                         |           |            |           |           |
|------------------------|------------|-------------------------|-----------|------------|-----------|-----------|
| Control                | 2 (0.31)   | 1.0 (ref)               | 1.0 (ref) | 0 (0.00)   | 1.0 (ref) | 1.0 (ref) |
| Patients with COVID-19 | 467 (0.31) | <b>1.29 (0.32-5.19)</b> | NA        | 426 (0.43) | NA        | NA        |

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ARI, another respiratory infection; BMI, body mass index; CI, confidence interval; HR, hazard ratio.

\* **Model 1:** adjusted for age (20–39, 40–59, and  $\geq 60$  years) and sex.

<sup>II</sup> **Model 2:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and  $\geq 2$ ); obesity (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], obese [ $\geq 25.0 \text{ kg/m}^2$ ], and unknown); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$ , systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ , and unknown); fasting blood glucose ( $< 100$ ,  $\geq 100 \text{ mg/dL}$ , and unknown); serum total cholesterol ( $< 200$ ,  $200\text{--}240$ ,  $\geq 240 \text{ mg/dL}$ , and unknown); glomerular filtration rate ( $< 60$ ,  $60\text{--}90$ ,  $\geq 90 \text{ mL/min/1.73 m}^2$ , and unknown); smoking status (non-, ex-, current smoker, and unknown); alcohol consumption (drinks;  $< 1$ ,  $1\text{--}2$ ,  $3\text{--}4$ ,  $\geq 5$  days per week, and unknown); aerobic physical activity (sufficient, insufficient, and unknown); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); outpatients contact in the year before index date (0,  $1\text{--}4$ , and  $\geq 5$  times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no], fasting blood glucose missing indicator [yes or no], serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no], smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes or no]).

Data in bold indicate significant differences ( $P < 0.05$ ).

**Table S7.** Stratification analysis for the **long-term sequelae risk** of incident neuropsychiatric events following COVID-19 diagnosis of patients in the propensity score-matched cohorts in South Korea (missing indicator method)

|                                                   | COVID-19 versus general |                         |                         | COVID-19 versus ARI |                         |                         |
|---------------------------------------------------|-------------------------|-------------------------|-------------------------|---------------------|-------------------------|-------------------------|
|                                                   | (n=1,831,237)           |                         |                         | (n=531,020)         |                         |                         |
|                                                   | HR (95% CI)             |                         |                         | HR (95% CI)         |                         |                         |
|                                                   | Events (%)              | Model 1*                | Model 2 <sup>II</sup>   | Events (%)          | Model 1*                | Model 2 <sup>II</sup>   |
| Any neuropsychiatric outcomes                     |                         |                         |                         |                     |                         |                         |
| Control (general population or patients with ARI) | 9025 (0.62)             | 1.0 (ref)               | 1.0 (ref)               | 7839 (2.95)         | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                            | 4197 (1.10)             | <b>1.79 (1.72-1.85)</b> | <b>1.71 (1.64-1.79)</b> | 4211 (1.59)         | <b>1.71 (1.65-1.78)</b> | <b>1.60 (1.53-1.68)</b> |
| Male                                              |                         |                         |                         |                     |                         |                         |
| Control                                           | 4148 (0.54)             | 1.0 (ref)               | 1.0 (ref)               | 3509 (2.49)         | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                            | 1873 (0.93)             | <b>1.76 (1.67-1.86)</b> | <b>1.69 (1.58-1.80)</b> | 1878 (1.35)         | <b>1.72 (1.62-1.82)</b> | <b>1.62 (1.51-1.73)</b> |
| Female                                            |                         |                         |                         |                     |                         |                         |
| Control                                           | 4877 (0.72)             | 1.0 (ref)               | 1.0 (ref)               | 4330 (3.48)         | 1.0 (ref)               | 1.0 (ref)               |

|                                  |             |                         |                         |             |                         |                         |
|----------------------------------|-------------|-------------------------|-------------------------|-------------|-------------------------|-------------------------|
| Patients with COVID-19           | 2324 (1.28) | <b>1.81 (1.72-1.90)</b> | <b>1.73 (1.63-1.83)</b> | 2333 (1.85) | <b>1.72 (1.63-1.81)</b> | <b>1.60 (1.51-1.71)</b> |
| Aged 20-39 years                 |             |                         |                         |             |                         |                         |
| Control                          | 2547 (0.46) | 1.0 (ref)               | 1.0 (ref)               | 1553 (1.96) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19           | 1214 (0.85) | <b>1.84 (1.72-1.97)</b> | <b>1.71 (1.56-1.88)</b> | 1219 (1.54) | <b>2.53 (2.33-2.74)</b> | <b>2.35 (2.12-2.61)</b> |
| Aged 40-59 years                 |             |                         |                         |             |                         |                         |
| Control                          | 3388 (0.61) | 1.0 (ref)               | 1.0 (ref)               | 3151 (2.68) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19           | 1508 (1.05) | <b>1.74 (1.63-1.84)</b> | <b>1.78 (1.66-1.90)</b> | 1512 (1.29) | <b>1.40 (1.31-1.49)</b> | <b>1.44 (1.34-1.54)</b> |
| Aged ≥ 60 years                  |             |                         |                         |             |                         |                         |
| Control                          | 3090 (0.90) | 1.0 (ref)               | 1.0 (ref)               | 3135 (4.56) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19           | 1475 (1.54) | <b>1.80 (1.69-1.91)</b> | <b>1.65 (1.53-1.77)</b> | 1480 (2.13) | <b>1.70 (1.59-1.81)</b> | <b>1.55 (1.44-1.67)</b> |
| Low income (0–39 percentile)     |             |                         |                         |             |                         |                         |
| Control                          | 4194 (0.63) | 1.0 (ref)               | 1.0 (ref)               | 3781 (3.26) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19           | 1937 (1.11) | <b>1.77 (1.68-1.87)</b> | <b>1.66 (1.55-1.77)</b> | 1944 (1.66) | <b>1.62 (1.53-1.72)</b> | <b>1.51 (1.41-1.61)</b> |
| Middle income (40–79 percentile) |             |                         |                         |             |                         |                         |
| Control                          | 3133 (0.59) | 1.0 (ref)               | 1.0 (ref)               | 2692 (2.60) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19           | 1405 (1.01) | <b>1.73 (1.62-1.84)</b> | <b>1.74 (1.62-1.87)</b> | 1414 (1.36) | <b>1.69 (1.58-1.81)</b> | <b>1.68 (1.55-1.81)</b> |

High income (80–100 percentile)

|                        |             |                         |                         |             |                         |                         |
|------------------------|-------------|-------------------------|-------------------------|-------------|-------------------------|-------------------------|
| Control                | 1698 (0.66) | 1.0 (ref)               | 1.0 (ref)               | 1366 (2.97) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19 | 855 (1.24)  | <b>1.92 (1.77-2.09)</b> | <b>1.78 (1.61-1.96)</b> | 853 (1.93)  | <b>2.01 (1.84-2.20)</b> | <b>1.78 (1.60-1.98)</b> |

Charlson comorbidity index, 0 score

|                        |             |                         |                         |             |                         |                         |
|------------------------|-------------|-------------------------|-------------------------|-------------|-------------------------|-------------------------|
| Control                | 6674 (0.51) | 1.0 (ref)               | 1.0 (ref)               | 6571 (2.68) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19 | 3289 (0.97) | <b>1.94 (1.86-2.02)</b> | <b>1.89 (1.80-1.99)</b> | 3299 (1.34) | <b>1.63 (1.55-1.70)</b> | <b>1.53 (1.45-1.61)</b> |

Charlson comorbidity index, 1 score

|                        |             |                         |                         |            |                         |                         |
|------------------------|-------------|-------------------------|-------------------------|------------|-------------------------|-------------------------|
| Control                | 1533 (1.67) | 1.0 (ref)               | 1.0 (ref)               | 641 (6.15) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19 | 573 (1.91)  | <b>1.20 (1.09-1.32)</b> | <b>1.18 (1.06-1.32)</b> | 581 (5.55) | <b>2.26 (2.01-2.55)</b> | <b>2.21 (1.94-2.53)</b> |

Charlson comorbidity index,  $\geq 2$  scores

|                        |            |                         |                         |            |                         |                         |
|------------------------|------------|-------------------------|-------------------------|------------|-------------------------|-------------------------|
| Control                | 818 (1.82) | 1.0 (ref)               | 1.0 (ref)               | 627 (6.61) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19 | 335 (2.45) | <b>1.49 (1.31-1.70)</b> | <b>1.36 (1.16-1.59)</b> | 331 (3.50) | <b>1.61 (1.40-1.85)</b> | <b>1.46 (1.23-1.72)</b> |

BMI,  $< 25 \text{ kg/m}^2$

|                        |             |                         |                         |             |                         |                         |
|------------------------|-------------|-------------------------|-------------------------|-------------|-------------------------|-------------------------|
| Control                | 5641 (0.61) | 1.0 (ref)               | 1.0 (ref)               | 4973 (3.02) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19 | 1510 (1.11) | <b>1.76 (1.66-1.86)</b> | <b>1.77 (1.67-1.87)</b> | 1517 (1.56) | <b>1.56 (1.47-1.66)</b> | <b>1.57 (1.48-1.67)</b> |

BMI,  $\geq 25 \text{ kg/m}^2$

|                                       |             |                         |                         |             |                         |                         |
|---------------------------------------|-------------|-------------------------|-------------------------|-------------|-------------------------|-------------------------|
| Control                               | 3383 (0.65) | 1.0 (ref)               | 1.0 (ref)               | 2863 (2.84) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                | 1081 (1.13) | <b>1.64 (1.53-1.75)</b> | <b>1.62 (1.52-1.74)</b> | 1087 (1.55) | <b>1.66 (1.54-1.78)</b> | <b>1.65 (1.54-1.78)</b> |
| BMI, unknown                          |             |                         |                         |             |                         |                         |
| Control                               | 1 (0.63)    | 1.0 (ref)               | 1.0 (ref)               | 3 (6.12)    | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                | 1606 (1.07) | 1.57 (0.22-11.11)       | NA                      | 1607 (1.64) | 0.89 (0.29-2.76)        | 0.07 (0.01-0.47)        |
| Smoking status, non-smoker            |             |                         |                         |             |                         |                         |
| Control                               | 5774 (0.63) | 1.0 (ref)               | 1.0 (ref)               | 5154 (3.14) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                | 1772 (1.16) | <b>1.76 (1.67-1.85)</b> | <b>1.73 (1.64-1.83)</b> | 1782 (1.63) | <b>1.59 (1.51-1.69)</b> | <b>1.58 (1.50-1.68)</b> |
| Smoking status, ex- or current smoker |             |                         |                         |             |                         |                         |
| Control                               | 3251 (0.61) | 1.0 (ref)               | 1.0 (ref)               | 2682 (2.65) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                | 819 (1.03)  | <b>1.65 (1.52-1.78)</b> | <b>1.67 (1.54-1.80)</b> | 822 (1.41)  | <b>1.60 (1.47-1.74)</b> | <b>1.64 (1.51-1.78)</b> |
| Smoking status, unknown               |             |                         |                         |             |                         |                         |
| Control                               | 0 (0.00)    | 1.0 (ref)               | 1.0 (ref)               | 3 (3.41)    | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                | 1606 (1.07) | NA                      | NA                      | 1607 (1.64) | 1.63 (0.53-5.07)        | 0.07 (0.01-0.49)        |
| Alcoholic drinks, < 1 per week        |             |                         |                         |             |                         |                         |
| Control                               | 5548 (0.66) | 1.0 (ref)               | 1.0 (ref)               | 5229 (3.30) | 1.0 (ref)               | 1.0 (ref)               |

|                                         |             |                         |                         |             |                         |                         |
|-----------------------------------------|-------------|-------------------------|-------------------------|-------------|-------------------------|-------------------------|
| Patients with COVID-19                  | 1627 (1.21) | <b>1.76 (1.67-1.86)</b> | <b>1.75 (1.65-1.85)</b> | 1636 (1.69) | <b>1.55 (1.47-1.65)</b> | <b>1.55 (1.46-1.64)</b> |
| Alcoholic drinks, ≥1 per week           |             |                         |                         |             |                         |                         |
| Control                                 | 3476 (0.58) | 1.0 (ref)               | 1.0 (ref)               | 2607 (2.44) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                  | 964 (0.98)  | <b>1.64 (1.53-1.76)</b> | <b>1.65 (1.54-1.78)</b> | 968 (1.37)  | <b>1.68 (1.56-1.82)</b> | <b>1.69 (1.56-1.83)</b> |
| Alcoholic drinks, unknown               |             |                         |                         |             |                         |                         |
| Control                                 | 1 (0.20)    | 1.0 (ref)               | 1.0 (ref)               | 3 (3.57)    | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                  | 1606 (1.07) | 5.92 (0.83-42.02)       | NA                      | 1607 (1.64) | 1.56 (0.50-4.85)        | 0.07 (0.01-0.49)        |
| Aerobic physical activity, insufficient |             |                         |                         |             |                         |                         |
| Control                                 | 4678 (0.64) | 1.0 (ref)               | 1.0 (ref)               | 4105 (3.02) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                  | 1373 (1.18) | <b>1.75 (1.65-1.86)</b> | <b>1.76 (1.66-1.87)</b> | 1383 (1.64) | <b>1.65 (1.55-1.76)</b> | <b>1.66 (1.56-1.77)</b> |
| Aerobic physical activity, sufficient   |             |                         |                         |             |                         |                         |
| Control                                 | 4344 (0.61) | 1.0 (ref)               | 1.0 (ref)               | 3731 (2.88) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                  | 1217 (1.06) | <b>1.67 (1.57-1.78)</b> | <b>1.66 (1.55-1.77)</b> | 1220 (1.46) | <b>1.54 (1.44-1.64)</b> | <b>1.53 (1.43-1.64)</b> |
| Aerobic physical activity, unknown      |             |                         |                         |             |                         |                         |
| Control                                 | 3 (0.47)    | 1.0 (ref)               | 1.0 (ref)               | 3 (2.33)    | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                  | 1607 (1.07) | 2.85 (0.92-8.85)        | 2.57 (0.18-36.53)       | 1608 (1.64) | 2.50 (0.81-7.78)        | 0.07 (0.01-0.49)        |

ARI, another respiratory infection; BMI, body mass index; CI, confidence interval; HR, hazard ratio.

\* **Model 1:** adjusted for age (20–39, 40–59, and  $\geq 60$  years) and sex.

<sup>II</sup> **Model 2:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and  $\geq 2$ ); obesity (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], obese [ $\geq 25.0 \text{ kg/m}^2$ ], and unknown); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$ , systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ , and unknown); fasting blood glucose ( $< 100$ ,  $\geq 100 \text{ mg/dL}$ , and unknown); serum total cholesterol ( $< 200$ ,  $200\text{--}240$ ,  $\geq 240 \text{ mg/dL}$ , and unknown); glomerular filtration rate ( $< 60$ ,  $60\text{--}90$ ,  $\geq 90 \text{ mL/min/1.73 m}^2$ , and unknown); smoking status (non-, ex-, current smoker, and unknown); alcohol consumption (drinks;  $< 1$ ,  $1\text{--}2$ ,  $3\text{--}4$ ,  $\geq 5$  days per week, and unknown); aerobic physical activity (sufficient, insufficient, and unknown); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); outpatients contact in the year before index date (0,  $1\text{--}4$ , and  $\geq 5$  times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no], fasting blood glucose missing indicator [yes or no], serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no],

smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes or no]).

Data in bold indicate significant differences ( $P < 0.05$ ).

**Table S8.** Stratification analysis for the **overall (short- and long-term) risk** of incident neuropsychiatric events following COVID-19 diagnosis of patients in the propensity score-matched cohorts in South Korea (missing indicator method)

|                                                   | COVID-19 versus general<br>(n=1,831,237) |                         |                         | COVID-19 versus ARI<br>(n=531,020) |                         |                         |
|---------------------------------------------------|------------------------------------------|-------------------------|-------------------------|------------------------------------|-------------------------|-------------------------|
|                                                   | HR (95% CI)                              |                         |                         | HR (95% CI)                        |                         |                         |
|                                                   | Events (%)                               | Model 1 <sup>*</sup>    | Model 2 <sup>II</sup>   | Events (%)                         | Model 1 <sup>*</sup>    | Model 2 <sup>II</sup>   |
| Any neuropsychiatric outcomes                     |                                          |                         |                         |                                    |                         |                         |
| Control (general population or patients with ARI) | 9393 (0.65)                              | 1.0 (ref)               | 1.0 (ref)               | 8003 (3.01)                        | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                            | 4628 (1.21)                              | <b>1.89 (1.82-1.96)</b> | <b>1.83 (1.75-1.91)</b> | 4624 (1.74)                        | <b>1.65 (1.59-1.72)</b> | <b>1.56 (1.49-1.63)</b> |
| Male                                              |                                          |                         |                         |                                    |                         |                         |
| Control                                           | 5081 (0.75)                              | 1.0 (ref)               | 1.0 (ref)               | 4421 (3.55)                        | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                            | 2557 (1.41)                              | <b>1.91 (1.82-2.00)</b> | <b>1.84 (1.74-1.94)</b> | 2555 (2.03)                        | <b>1.65 (1.57-1.74)</b> | <b>1.56 (1.47-1.66)</b> |
| Female                                            |                                          |                         |                         |                                    |                         |                         |
| Control                                           | 2640 (0.48)                              | 1.0 (ref)               | 1.0 (ref)               | 1577 (1.99)                        | 1.0 (ref)               | 1.0 (ref)               |

|                                  |             |                         |                         |             |                         |                         |
|----------------------------------|-------------|-------------------------|-------------------------|-------------|-------------------------|-------------------------|
| Patients with COVID-19           | 1316 (0.92) | <b>1.92 (1.80-2.05)</b> | <b>1.82 (1.66-2.00)</b> | 1317 (1.67) | <b>2.47 (2.28-2.67)</b> | <b>2.33 (2.11-2.58)</b> |
| Aged 20-39 years                 |             |                         |                         |             |                         |                         |
| Control                          | 3528 (0.64) | 1.0 (ref)               | 1.0 (ref)               | 3224 (2.75) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19           | 1692 (1.18) | <b>1.87 (1.76-1.98)</b> | <b>1.92 (1.80-2.05)</b> | 1691 (1.45) | <b>1.38 (1.29-1.47)</b> | <b>1.42 (1.32-1.52)</b> |
| Aged 40-59 years                 |             |                         |                         |             |                         |                         |
| Control                          | 3225 (0.94) | 1.0 (ref)               | 1.0 (ref)               | 3202 (4.66) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19           | 1620 (1.69) | <b>1.88 (1.77-2.00)</b> | <b>1.74 (1.62-1.86)</b> | 1616 (2.33) | <b>1.58 (1.49-1.69)</b> | <b>1.47 (1.37-1.58)</b> |
| Aged ≥ 60 years                  |             |                         |                         |             |                         |                         |
| Control                          | 4373 (0.66) | 1.0 (ref)               | 1.0 (ref)               | 3847 (3.32) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19           | 2137 (1.22) | <b>1.87 (1.78-1.97)</b> | <b>1.76 (1.66-1.88)</b> | 2136 (1.82) | <b>1.58 (1.49-1.67)</b> | <b>1.47 (1.38-1.58)</b> |
| Low income (0–39 percentile)     |             |                         |                         |             |                         |                         |
| Control                          | 3253 (0.62) | 1.0 (ref)               | 1.0 (ref)               | 2752 (2.66) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19           | 1557 (1.12) | <b>1.84 (1.73-1.96)</b> | <b>1.87 (1.74-2.00)</b> | 1557 (1.49) | <b>1.63 (1.52-1.74)</b> | <b>1.63 (1.51-1.76)</b> |
| Middle income (40–79 percentile) |             |                         |                         |             |                         |                         |

|                                       |             |                         |                         |             |                         |                         |
|---------------------------------------|-------------|-------------------------|-------------------------|-------------|-------------------------|-------------------------|
| Control                               | 1767 (0.68) | 1.0 (ref)               | 1.0 (ref)               | 1404 (3.05) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                | 934 (1.36)  | <b>2.01 (1.86-2.18)</b> | <b>1.90 (1.73-2.09)</b> | 931 (2.11)  | <b>1.90 (1.74-2.07)</b> | <b>1.71 (1.55-1.90)</b> |
| High income (80–100 percentile)       |             |                         |                         |             |                         |                         |
| Control                               | 4312 (0.56) | 1.0 (ref)               | 1.0 (ref)               | 3582 (2.54) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                | 2071 (1.03) | <b>1.87 (1.77-1.97)</b> | <b>1.81 (1.70-1.93)</b> | 2069 (1.48) | <b>1.65 (1.56-1.75)</b> | <b>1.57 (1.47-1.68)</b> |
| Charlson comorbidity index, 0 score   |             |                         |                         |             |                         |                         |
| Control                               | 6964 (0.53) | 1.0 (ref)               | 1.0 (ref)               | 6706 (2.73) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                | 3642 (1.08) | <b>2.05 (1.97-2.14)</b> | <b>2.03 (1.93-2.13)</b> | 3641 (1.48) | <b>1.57 (1.50-1.64)</b> | <b>1.49 (1.42-1.57)</b> |
| Charlson comorbidity index, 1 score   |             |                         |                         |             |                         |                         |
| Control                               | 1585 (1.73) | 1.0 (ref)               | 1.0 (ref)               | 654 (6.27)  | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                | 625 (2.08)  | <b>1.26 (1.14-1.38)</b> | <b>1.23 (1.10-1.37)</b> | 628 (6.00)  | <b>2.23 (1.99-2.51)</b> | <b>2.19 (1.92-2.49)</b> |
| Charlson comorbidity index, ≥2 scores |             |                         |                         |             |                         |                         |
| Control                               | 844 (1.87)  | 1.0 (ref)               | 1.0 (ref)               | 643 (6.77)  | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                | 361 (2.64)  | <b>1.54 (1.36-1.74)</b> | <b>1.42 (1.22-1.65)</b> | 355 (3.75)  | <b>1.52 (1.32-1.74)</b> | <b>1.40 (1.19-1.65)</b> |
| BMI, < 25 kg/m <sup>2</sup>           |             |                         |                         |             |                         |                         |

|                                       |             |                         |                         |             |                         |                         |
|---------------------------------------|-------------|-------------------------|-------------------------|-------------|-------------------------|-------------------------|
| Control                               | 5856 (0.63) | 1.0 (ref)               | 1.0 (ref)               | 5083 (3.09) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                | 1699 (1.24) | <b>1.90 (1.80-2.01)</b> | <b>1.91 (1.81-2.02)</b> | 1698 (1.75) | <b>1.51 (1.43-1.60)</b> | <b>1.53 (1.44-1.62)</b> |
| BMI, ≥ 25 kg/m <sup>2</sup>           |             |                         |                         |             |                         |                         |
| Control                               | 3536 (0.68) | 1.0 (ref)               | 1.0 (ref)               | 2917 (2.89) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                | 1189 (1.25) | <b>1.72 (1.61-1.84)</b> | <b>1.71 (1.60-1.82)</b> | 1190 (1.69) | <b>1.59 (1.48-1.71)</b> | <b>1.59 (1.48-1.71)</b> |
| BMI, unknown                          |             |                         |                         |             |                         |                         |
| Control                               | 1 (0.63)    | 1.0 (ref)               | 1.0 (ref)               | 3 (6.12)    | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                | 1740 (1.16) | 1.73 (0.24-12.24)       | NA                      | 1736 (1.77) | 0.88 (0.29-2.75)        | 0.07 (0.01-0.46)        |
| Smoking status, non-smoker            |             |                         |                         |             |                         |                         |
| Control                               | 6020 (0.66) | 1.0 (ref)               | 1.0 (ref)               | 5255 (3.20) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                | 1987 (1.31) | <b>1.89 (1.79-1.99)</b> | <b>1.86 (1.77-1.96)</b> | 1987 (1.82) | <b>1.55 (1.47-1.64)</b> | <b>1.55 (1.47-1.64)</b> |
| Smoking status, ex- or current smoker |             |                         |                         |             |                         |                         |
| Control                               | 3373 (0.63) | 1.0 (ref)               | 1.0 (ref)               | 2745 (2.71) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                | 901 (1.13)  | <b>1.74 (1.62-1.88)</b> | <b>1.76 (1.63-1.89)</b> | 901 (1.54)  | <b>1.52 (1.40-1.64)</b> | <b>1.56 (1.44-1.69)</b> |

Smoking status, unknown

|                        |             |           |           |             |                  |                  |
|------------------------|-------------|-----------|-----------|-------------|------------------|------------------|
| Control                | 0 (0.00)    | 1.0 (ref) | 1.0 (ref) | 3 (3.41)    | 1.0 (ref)        | 1.0 (ref)        |
| Patients with COVID-19 | 1740 (1.16) | NA        | NA        | 1736 (1.77) | 1.62 (0.52-5.03) | 0.07 (0.01-0.49) |

Alcoholic drinks, < 1 per week

|                        |             |                         |                         |             |                         |                         |
|------------------------|-------------|-------------------------|-------------------------|-------------|-------------------------|-------------------------|
| Control                | 5776 (0.68) | 1.0 (ref)               | 1.0 (ref)               | 5339 (3.37) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19 | 1816 (1.35) | <b>1.88 (1.79-1.99)</b> | <b>1.87 (1.77-1.97)</b> | 1818 (1.87) | <b>1.50 (1.42-1.59)</b> | <b>1.50 (1.42-1.59)</b> |

Alcoholic drinks, ≥1 per week

|                        |             |                         |                         |             |                         |                         |
|------------------------|-------------|-------------------------|-------------------------|-------------|-------------------------|-------------------------|
| Control                | 3616 (0.60) | 1.0 (ref)               | 1.0 (ref)               | 2661 (2.49) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19 | 1072 (1.10) | <b>1.75 (1.64-1.88)</b> | <b>1.77 (1.65-1.89)</b> | 1070 (1.52) | <b>1.63 (1.51-1.76)</b> | <b>1.64 (1.52-1.77)</b> |

Alcoholic drinks, unknown

|                        |             |                   |           |             |                  |                  |
|------------------------|-------------|-------------------|-----------|-------------|------------------|------------------|
| Control                | 1 (0.20)    | 1.0 (ref)         | 1.0 (ref) | 3 (3.57)    | 1.0 (ref)        | 1.0 (ref)        |
| Patients with COVID-19 | 1740 (1.16) | 6.38 (0.90-45.24) | NA        | 1736 (1.77) | 1.55 (0.50-4.82) | 0.07 (0.01-0.49) |

Aerobic physical activity, insufficient

|         |             |           |           |             |           |           |
|---------|-------------|-----------|-----------|-------------|-----------|-----------|
| Control | 4849 (0.66) | 1.0 (ref) | 1.0 (ref) | 4189 (3.08) | 1.0 (ref) | 1.0 (ref) |
|---------|-------------|-----------|-----------|-------------|-----------|-----------|

|                                       |             |                         |                         |             |                         |                         |
|---------------------------------------|-------------|-------------------------|-------------------------|-------------|-------------------------|-------------------------|
| Patients with COVID-19                | 1522 (1.30) | <b>1.87 (1.77-1.98)</b> | <b>1.87 (1.77-1.99)</b> | 1522 (1.81) | <b>1.59 (1.49-1.69)</b> | <b>1.61 (1.51-1.71)</b> |
| Aerobic physical activity, sufficient |             |                         |                         |             |                         |                         |
| Control                               | 4541 (0.63) | 1.0 (ref)               | 1.0 (ref)               | 3811 (2.94) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                | 1365 (1.19) | <b>1.79 (1.69-1.90)</b> | <b>1.78 (1.67-1.89)</b> | 1365 (1.64) | <b>1.49 (1.39-1.59)</b> | <b>1.49 (1.40-1.59)</b> |
| Aerobic physical activity, unknown    |             |                         |                         |             |                         |                         |
| Control                               | 3 (0.47)    | 1.0 (ref)               | 1.0 (ref)               | 3 (2.33)    | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                | 1741 (1.16) | 3.08 (0.99-9.57)        | 2.67 (0.19-37.67)       | 1737 (1.77) | 2.48 (0.80-7.71)        | 0.07 (0.01-0.49)        |

ARI, another respiratory infection; BMI, body mass index; CI, confidence interval; HR, hazard ratio.

\* **Model 1:** adjusted for age (20–39, 40–59, and  $\geq 60$  years) and sex.

<sup>||</sup> **Model 2:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and  $\geq 2$ ); obesity (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], obese [ $\geq 25.0 \text{ kg/m}^2$ ], and unknown); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$ , systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ , and unknown); fasting blood glucose ( $<$

100,  $\geq 100$  mg/dL, and unknown); serum total cholesterol ( $< 200$ , 200–240,  $\geq 240$  mg/dL, and unknown); glomerular filtration rate ( $< 60$ , 60–90,  $\geq 90$  mL/min/1.73 m<sup>2</sup>, and unknown); smoking status (non-, ex-, current smoker, and unknown); alcohol consumption (drinks;  $< 1$ , 1–2, 3–4,  $\geq 5$  days per week, and unknown); aerobic physical activity (sufficient, insufficient, and unknown); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); outpatients contact in the year before index date (0, 1–4, and  $\geq 5$  times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no], fasting blood glucose missing indicator [yes or no], serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no], smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes or no]).

Data in bold indicate significant differences ( $P < 0.05$ ).

**Table S9.** Propensity-score-matched subgroup analysis of **long-term HR (95% CI)** of neuropsychiatric disorders following COVID-19 diagnosis stratified by COVID-19 severity in South Korea, with a two-sided test (missing indicator method)

|                                 | The severity of COVID-19 (adjusted HR <sup>II</sup> ) |                         |         |                             |         |
|---------------------------------|-------------------------------------------------------|-------------------------|---------|-----------------------------|---------|
|                                 | Non-infected controls                                 | Mild COVID-19           | P value | Moderate to severe COVID-19 | P value |
| Any neuropsychological outcomes | 1.0 (ref)                                             | <b>1.57 (1.50-1.65)</b> | <0.001  | <b>2.35 (2.19-2.52)</b>     | <0.001  |
| Anxiety disorder                | 1.0 (ref)                                             | <b>2.14 (1.99-2.31)</b> | <0.001  | <b>2.74 (2.41-3.12)</b>     | <0.001  |
| Cognitive deficit               | 1.0 (ref)                                             | 1.76 (0.84-3.69)        | 0.132   | <b>4.95 (2.38-10.31)</b>    | <0.001  |
| Encephalitis                    | 1.0 (ref)                                             | 1.04 (0.49-2.19)        | 0.922   | <b>4.81 (2.48-9.31)</b>     | <0.001  |
| Epilepsy/seizures               | 1.0 (ref)                                             | 0.66 (0.37-1.17)        | 0.157   | 1.82 (0.97-3.43)            | 0.063   |
| Guillain-Barré syndrome         | 1.0 (ref)                                             | 2.98 (0.84-10.56)       | 0.092   | <b>8.66 (2.51-29.86)</b>    | <0.001  |
| Insomnia                        | 1.0 (ref)                                             | <b>2.18 (1.93-2.46)</b> | <0.001  | <b>3.49 (2.93-4.15)</b>     | <0.001  |
| Intracranial hemorrhage         | 1.0 (ref)                                             | 0.24 (0.13-0.44)        | <0.001  | <b>2.36 (1.62-3.44)</b>     | <0.001  |

|                                   |           |                         |        |                         |        |
|-----------------------------------|-----------|-------------------------|--------|-------------------------|--------|
| Ischemic stroke                   | 1.0 (ref) | 0.69 (0.55-0.87)        | 0.001  | <b>1.44 (1.15-1.81)</b> | 0.002  |
| Mood disorder                     | 1.0 (ref) | <b>1.79 (1.64-1.95)</b> | <0.001 | <b>2.81 (2.45-3.23)</b> | <0.001 |
| Myoneural junction/muscle disease | 1.0 (ref) | 1.32 (0.48-3.58)        | 0.591  | 0.53 (0.07-4.34)        | 0.554  |
| Nerve/nerve root/plexus disorders | 1.0 (ref) | <b>1.39 (1.27-1.51)</b> | <0.001 | <b>1.84 (1.61-2.11)</b> | <0.001 |
| Parkinsonism                      | 1.0 (ref) | 0.99 (0.62-1.58)        | 0.953  | 1.36 (0.75-2.46)        | 0.307  |
| Psychotic disorder                | 1.0 (ref) | 0.69 (0.39-1.22)        | 0.201  | <b>2.32 (1.21-4.46)</b> | 0.011  |

---

ARI, another respiratory infection; BMI, body mass index; CI, confidence interval; HR, hazard ratio.

<sup>u</sup> **adjusted HR:** adjusted for age (20–39, 40–59, and ≥ 60 years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and ≥ 2); obesity (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], obese [ $\geq 25.0 \text{ kg/m}^2$ ], and unknown); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$ , systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ , and unknown); fasting blood glucose ( $< 100$ ,  $\geq 100 \text{ mg/dL}$ , and unknown); serum total cholesterol ( $< 200$ ,  $200\text{--}240$ ,  $\geq 240 \text{ mg/dL}$ , and unknown); glomerular filtration rate ( $< 60$ ,  $60\text{--}90$ ,

$\geq 90$  mL/min/1.73 m<sup>2</sup>, and unknown); smoking status (non-, ex-, current smoker, and unknown); alcohol consumption (drinks;  $< 1$ , 1–2, 3–4,  $\geq 5$  days per week, and unknown); aerobic physical activity (sufficient, insufficient, and unknown); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); outpatients contact in the year before index date (0, 1–4, and  $\geq 5$  times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no], fasting blood glucose missing indicator [yes or no], serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no], smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes or no]).

Data in bold indicate significant differences ( $P < 0.05$ ).

**Table S10.** Propensity-score-matched subgroup analysis of **long-term HR (95% CI)** of neuropsychiatric disorders following COVID-19 diagnosis stratified by COVID-19 vaccination in South Korea, with a two-sided test (missing indicator method)

|                                 | COVID-19 vaccination dosage (adjusted HR <sup>II</sup> ) |                          |         |                                   |         |                                            |         |
|---------------------------------|----------------------------------------------------------|--------------------------|---------|-----------------------------------|---------|--------------------------------------------|---------|
|                                 | Non-infected                                             | Patients with COVID-19   |         | Patients with COVID-19            |         | Patients with COVID-19                     |         |
|                                 | controls                                                 | but without vaccination  | P value | and vaccination<br>(dosage: once) | P value | and vaccination<br>(dosage: twice or more) | P value |
| Any neuropsychological outcomes | 1.0 (ref)                                                | <b>1.89 (1.80-1.98)</b>  | <0.001  | <b>1.30 (1.16-1.46)</b>           | <0.001  | 1.05 (0.93-1.17)                           | 0.006   |
| Anxiety disorder                | 1.0 (ref)                                                | <b>2.46 (2.28-2.66)</b>  | <0.001  | <b>1.48 (1.20-1.81)</b>           | <0.001  | <b>1.43 (1.18-1.72)</b>                    | <0.001  |
| Cognitive deficit               | 1.0 (ref)                                                | <b>4.19 (2.16-8.12)</b>  | <0.001  | 0.56 (0.07-4.32)                  | 0.581   | NA                                         | 0.934   |
| Encephalitis                    | 1.0 (ref)                                                | <b>2.74 (1.47-5.10)</b>  | 0.002   | 1.02 (0.23-4.48)                  | 0.975   | 0.97 (0.32-2.96)                           | 0.950   |
| Epilepsy/seizures               | 1.0 (ref)                                                | 0.99 (0.58-1.67)         | 0.939   | 0.92 (0.32-2.66)                  | 0.994   | 0.39 (0.09-1.64)                           | 0.924   |
| Guillain-Barré syndrome         | 1.0 (ref)                                                | <b>6.09 (2.10-17.71)</b> | <0.001  | NA                                | NA      | 2.38 (0.28-20.27)                          | 0.426   |

|                                   |           |                         |        |                          |       |                  |       |
|-----------------------------------|-----------|-------------------------|--------|--------------------------|-------|------------------|-------|
| Insomnia                          | 1.0 (ref) | <b>2.81 (2.50-3.15)</b> | <0.001 | 1.12 (0.78-1.61)         | 0.533 | 1.14 (0.83-1.57) | 0.422 |
| Intracranial hemorrhage           | 1.0 (ref) | 0.97 (0.67-1.39)        | 0.847  | 0.62 (0.23-1.69)         | 0.348 | 0.52 (0.21-1.30) | 0.163 |
| Ischemic stroke                   | 1.0 (ref) | 0.97 (0.80-1.19)        | 0.779  | 0.86 (0.54-1.35)         | 0.503 | 0.86 (0.59-1.25) | 0.423 |
| Mood disorder                     | 1.0 (ref) | <b>2.10 (1.92-2.29)</b> | <0.001 | <b>1.39 (1.11-1.73)</b>  | 0.004 | 1.24 (0.99-1.54) | 0.056 |
| Myoneural junction/muscle disease | 1.0 (ref) | 1.02 (0.35-3.04)        | 0.966  | <b>4.03 (1.06-15.32)</b> | 0.041 | NA               | 0.914 |
| Nerve/nerve root/plexus disorders | 1.0 (ref) | <b>1.59 (1.46-1.73)</b> | <0.001 | <b>1.39 (1.12-1.71)</b>  | 0.002 | 0.88 (0.70-1.10) | 0.269 |
| Parkinsonism                      | 1.0 (ref) | 1.18 (0.75-1.85)        | 0.486  | 1.27 (0.50-3.25)         | 0.612 | 0.58 (0.20-1.63) | 0.297 |
| Psychotic disorder                | 1.0 (ref) | 1.03 (0.60-1.78)        | 0.905  | 0.44 (0.10-1.90)         | 0.273 | 0.73 (0.25-2.15) | 0.573 |

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ARI, another respiratory infection; BMI, body mass index; CI, confidence interval; HR, hazard ratio.

<sup>a</sup>**Adjusted HR:** adjusted for age (20–39, 40–59, and ≥ 60 years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and ≥ 2); obesity (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ],

overweight [23.0–25.0 kg/m<sup>2</sup>], obese [ $\geq$  25.0 kg/m<sup>2</sup>], and unknown); blood pressure (systolic blood pressure < 140 mmHg and diastolic blood pressure < 90 mmHg, systolic blood pressure  $\geq$  140 mmHg or diastolic blood pressure  $\geq$  90 mmHg, and unknown); fasting blood glucose (< 100,  $\geq$  100 mg/dL, and unknown); serum total cholesterol (< 200, 200–240,  $\geq$  240 mg/dL, and unknown); glomerular filtration rate (< 60, 60–90,  $\geq$  90 mL/min/1.73 m<sup>2</sup>, and unknown); smoking status (non-, ex-, current smoker, and unknown); alcohol consumption (drinks; < 1, 1–2, 3–4,  $\geq$  5 days per week, and unknown); aerobic physical activity (sufficient, insufficient, and unknown); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq$ 2 times); outpatients contact in the year before index date (0, 1-4, and  $\geq$ 5 times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no], fasting blood glucose missing indicator [yes or no], serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no], smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes or no]).

Data in bold indicate significant differences ( $P < 0.05$ ).

**Table S11.** Time attenuation effect analysis of HR (95% CI) for **long-term sequelae risk** of neuropsychiatric outcomes following COVID-19 diagnosis in discovery and validation cohorts, stratified by COVID-19 or ARI severity, with a two-sided test (missing indicator method)

|                           | Mild COVID-19 versus general  |         |                                |         | Moderate to severe COVID-19 versus general |         |                                |         |
|---------------------------|-------------------------------|---------|--------------------------------|---------|--------------------------------------------|---------|--------------------------------|---------|
|                           | Discovery cohort <sup>*</sup> | P value | Validation cohort <sup>‡</sup> | P value | Discovery cohort <sup>*</sup>              | P value | Validation cohort <sup>‡</sup> | P value |
| Any neurological outcomes |                               |         |                                |         |                                            |         |                                |         |
| Within 6 months           | <b>1.66 (1.57-1.76)</b>       | <0.001  | <b>2.88 (2.80-2.97)</b>        | <0.001  | <b>2.45 (2.24-2.69)</b>                    | <0.001  | <b>11.71 (10.84-12.64)</b>     | <0.001  |
| Between 6 to 12 months    | <b>1.34 (1.21-1.49)</b>       | <0.001  | <b>2.25 (2.17-2.34)</b>        | <0.001  | <b>1.68 (1.40-2.03)</b>                    | <0.001  | <b>2.53 (2.14-2.99)</b>        | <0.001  |
| After 12 months           | 1.17 (0.67-2.02)              | 0.587   | <b>2.21 (2.09-2.34)</b>        | <0.001  | 1.69 (0.67-4.26)                           | 0.267   | <b>1.89 (1.42-2.52)</b>        | <0.001  |
|                           | Mild COVID-19 versus ARI      |         |                                |         | Moderate to severe COVID-19 versus ARI     |         |                                |         |
|                           | Discovery cohort <sup>*</sup> | P value | Validation cohort <sup>‡</sup> | P value | Discovery cohort <sup>*</sup>              | P value | Validation cohort <sup>‡</sup> | P value |
| Any neurological outcomes |                               |         |                                |         |                                            |         |                                |         |
| Within 6 months           | <b>1.54 (1.37-1.73)</b>       | <0.001  | <b>4.03 (3.86-4.20)</b>        | <0.001  | <b>2.48 (2.09-2.96)</b>                    | <0.001  | <b>10.70 (9.75-11.73)</b>      | <0.001  |
| Between 6 to 12 months    | <b>1.89 (1.57-2.28)</b>       | <0.001  | <b>4.47 (4.24-4.72)</b>        | <0.001  | <b>2.42 (1.77-3.30)</b>                    | <0.001  | <b>3.62 (2.98-4.40)</b>        | <0.001  |
| After 12 months           | <b>1.88 (1.36-2.60)</b>       | <0.001  | <b>3.20 (3.00-3.42)</b>        | <0.001  | <b>2.91 (1.72-4.93)</b>                    | <0.001  | <b>2.01 (1.43-2.82)</b>        | <0.001  |

|                           | Mild COVID-19 versus mild ARI |         |                         |         | Moderate to severe COVID-19 versus moderate to severe ARI |         |                         |         |
|---------------------------|-------------------------------|---------|-------------------------|---------|-----------------------------------------------------------|---------|-------------------------|---------|
|                           | Discovery cohort*             | P value | Validation cohort‡      | P value | Discovery cohort*                                         | P value | Validation cohort‡      | P value |
| Any neurological outcomes |                               |         |                         |         |                                                           |         |                         |         |
| Within 6 months           | <b>1.64 (1.45-1.85)</b>       | <0.001  | <b>4.05 (3.88-4.23)</b> | <0.001  | <b>1.40 (1.12-1.74)</b>                                   | 0.003   | <b>2.85 (1.87-4.35)</b> | <0.001  |
| Between 6 to 12 months    | <b>2.03 (1.68-2.45)</b>       | <0.001  | <b>4.47 (4.24-4.73)</b> | <0.001  | <b>1.50 (1.04-2.16)</b>                                   | 0.030   | <b>3.17 (1.17-8.59)</b> | <0.001  |
| After 12 months           | <b>2.00 (1.44-2.77)</b>       | <0.001  | <b>3.20 (3.00-3.42)</b> | <0.001  | 1.74 (0.98-3.07)                                          | 0.057   | 1.27 (0.49-3.27)        | 0.625   |

ARI, another respiratory infection; BMI, body mass index; CI, confidence interval; HR, hazard ratio.

\* **adjusted HR:** adjusted for age (20–39, 40–59, and ≥ 60 years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and ≥ 2); obesity (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], obese [ $\geq 25.0 \text{ kg/m}^2$ ], and unknown); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$ , systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ , and unknown); fasting blood glucose ( $< 100$ ,  $\geq 100 \text{ mg/dL}$ , and unknown); serum total cholesterol ( $< 200$ ,  $200\text{--}240$ ,  $\geq 240 \text{ mg/dL}$ , and unknown); glomerular filtration rate ( $< 60$ ,  $60\text{--}90$ ,  $\geq 90 \text{ mL/min/1.73 m}^2$ , and unknown); smoking status (non-, ex-, current smoker, and unknown); alcohol consumption (drinks;  $< 1$ ,  $1\text{--}2$ ,  $3\text{--}4$ ,  $\geq 5$  days per week, and unknown); aerobic physical activity (sufficient, insufficient, and unknown); previous history of cardiovascular disease,

chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); outpatients contact in the year before index date (0, 1-4, and  $\geq 5$  times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no], fasting blood glucose missing indicator [yes or no], serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no], smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes or no]).

‡ **adjusted HR:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; insurance status (insured or dependent); body mass index (underweight [ $< 18.5 \text{ kg/m}^2$ ]; normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], obese [ $\geq 25.0 \text{ kg/m}^2$ ], and unknown); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$ , systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ , and unknown); fasting blood glucose ( $< 100$ ,  $\geq 100 \text{ mg/dL}$ , and unknown); serum total cholesterol ( $< 200$ ,  $200\text{--}240$ ,  $\geq 240 \text{ mg/dL}$ , and unknown); glomerular filtration rate ( $< 60$ ,  $60\text{--}90$ ,  $\geq 90 \text{ mL/min/1.73 m}^2$ , and unknown); smoking status (non-, current smoker, and unknown); alcohol consumption (rarely, sometimes, every day, and unknown); aerobic physical activity (sufficient, insufficient, and unknown); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); outpatients contact in the year before

index date (0, 1-4, and  $\geq 5$  times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no], fasting blood glucose missing indicator [yes or no], serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no], smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes or no]).

Data in bold indicate significant differences ( $P < 0.05$ ).

**Table S12.** The hazard ratio (95% CI) for the competitive composite endpoints (death or neuropsychiatric event) following after SARS-CoV-2 infection in discovery and validation cohorts: **the short-, long- term, and overall (short- and long-term) sequelae risk**, with a two-sided test (missing indicator method)

|                           | COVID-19 versus general |         |                         |         | COVID-19 versus ARI     |         |                         |         |
|---------------------------|-------------------------|---------|-------------------------|---------|-------------------------|---------|-------------------------|---------|
|                           | Discovery cohort*       | P value | Validation cohort‡      | P value | Discovery cohort*       | P value | Validation cohort‡      | P value |
| Any neurological outcomes |                         |         |                         |         |                         |         |                         |         |
| Short-term                | <b>3.82 (3.61-4.05)</b> | <0.001  | <b>8.76 (8.33-9.20)</b> | <0.001  | <b>1.99 (1.85-2.13)</b> | <0.001  | <b>2.44 (2.34-2.55)</b> | <0.001  |
| Long-term                 | <b>2.24 (2.16-2.32)</b> | <0.001  | <b>2.67 (2.61-2.73)</b> | <0.001  | <b>1.70 (1.63-1.77)</b> | <0.001  | <b>4.28 (4.15-4.41)</b> | <0.001  |
| Overall                   | <b>2.32 (2.24-2.40)</b> | <0.001  | <b>3.34 (3.28-3.41)</b> | <0.001  | <b>1.67 (1.60-1.73)</b> | <0.001  | <b>3.75 (3.65-3.84)</b> | <0.001  |

ARI, another respiratory infection; CI, confidence interval; HR, hazard ratio.

\* **adjusted HR:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and  $\geq 2$ ); obesity (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], obese [ $\geq 25.0 \text{ kg/m}^2$ ], and unknown); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$ , systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ , and unknown); fasting blood glucose ( $<$

100,  $\geq 100$  mg/dL, and unknown); serum total cholesterol ( $< 200$ , 200–240,  $\geq 240$  mg/dL, and unknown); glomerular filtration rate ( $< 60$ , 60–90,  $\geq 90$  mL/min/1.73 m<sup>2</sup>, and unknown); smoking status (non-, ex-, current smoker, and unknown); alcohol consumption (drinks;  $< 1$ , 1–2, 3–4,  $\geq 5$  days per week, and unknown); aerobic physical activity (sufficient, insufficient, and unknown); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); outpatients contact in the year before index date (0, 1–4, and  $\geq 5$  times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no], fasting blood glucose missing indicator [yes or no], serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no], smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes or no]).

‡ **adjusted HR:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; insurance status (insured or dependent); body mass index (underweight [ $< 18.5$  kg/m<sup>2</sup>]; normal [18.5–23.0 kg/m<sup>2</sup>], overweight [23.0–25.0 kg/m<sup>2</sup>], obese [ $\geq 25.0$  kg/m<sup>2</sup>], and unknown); blood pressure (systolic blood pressure  $< 140$  mmHg and diastolic blood pressure  $< 90$  mmHg, systolic blood pressure  $\geq 140$  mmHg or diastolic blood pressure  $\geq 90$  mmHg, and unknown); fasting blood glucose ( $< 100$ ,  $\geq 100$  mg/dL, and unknown); serum total cholesterol ( $< 200$ , 200–240,  $\geq 240$  mg/dL, and unknown); glomerular filtration rate ( $< 60$ , 60–90,  $\geq 90$  mL/min/1.73 m<sup>2</sup>, and unknown); smoking status (non-, current smoker, and unknown); alcohol

consumption (rarely, sometimes, every day, and unknown); aerobic physical activity (sufficient, insufficient, and unknown); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); outpatients contact in the year before index date (0, 1-4, and  $\geq 5$  times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no], fasting blood glucose missing indicator [yes or no], serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no], smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes or no]).

Data in bold indicate significant differences ( $P < 0.05$ ).

**Table S13.** The hazard ratio (95% CI) for the **short- and long-term sequelae risk** of neuropsychiatric events following COVID-19 diagnosis of patients in the propensity score-matched cohorts in South Korea and Japan, using alternative cohort specifications (missing indicator method)

|                                                    | COVID-19 versus general (South Korea) |                         |                         | COVID-19 versus general (Japan) |                            |                          |
|----------------------------------------------------|---------------------------------------|-------------------------|-------------------------|---------------------------------|----------------------------|--------------------------|
|                                                    | Events (%)                            | HR (95% CI)             |                         | Events (%)                      | HR (95% CI)                |                          |
|                                                    |                                       | Model 1*                | Model 2 <sup>II</sup>   |                                 | Model 1*                   | Model 2 <sup>II</sup>    |
| Any neuropsychiatric outcomes                      |                                       |                         |                         |                                 |                            |                          |
| Short-term, diagnosed $\geq 3$ times <sup>I</sup>  |                                       |                         |                         |                                 |                            |                          |
| General population                                 | 937 (0.05)                            | 1.0 (ref)               | 1.0 (ref)               | 1427 (0.11)                     | 1.0 (ref)                  | 1.0 (ref)                |
| Patients with COVID-19                             | 575 (0.13)                            | <b>2.31 (2.08-2.57)</b> | <b>2.06 (1.81-2.34)</b> | 10,114 (1.25)                   | <b>12.14 (11.49-12.84)</b> | <b>9.67 (9.14-10.23)</b> |
| Long-term, diagnosed $\geq 3$ times <sup>I</sup>   |                                       |                         |                         |                                 |                            |                          |
| General population                                 | 4461 (0.26)                           | 1.0 (ref)               | 1.0 (ref)               | 9550 (0.74)                     | 1.0 (ref)                  | 1.0 (ref)                |
| Patients with COVID-19                             | 2283 (0.51)                           | <b>1.97 (1.87-2.07)</b> | <b>1.76 (1.66-1.88)</b> | 17,429 (2.16)                   | <b>2.99 (2.92-3.07)</b>    | <b>2.73 (2.66-2.80)</b>  |
| Short-term, diagnosed $\geq 4$ times <sup>II</sup> |                                       |                         |                         |                                 |                            |                          |
| General population                                 | 806 (0.05)                            | 1.0 (ref)               | 1.0 (ref)               | 1223 (0.09)                     | 1.0 (ref)                  | 1.0 (ref)                |
| Patients with COVID-19                             | 501 (0.11)                            | <b>2.35 (2.10-2.63)</b> | <b>2.07 (1.81-2.38)</b> | 8887 (1.08)                     | <b>12.43 (11.71-13.20)</b> | <b>9.69 (9.12-10.30)</b> |
| Long-term, diagnosed $\geq 4$ times <sup>II</sup>  |                                       |                         |                         |                                 |                            |                          |
| General population                                 | 3794 (0.22)                           | 1.0 (ref)               | 1.0 (ref)               | 7509 (0.57)                     | 1.0 (ref)                  | 1.0 (ref)                |
| Patients with COVID-19                             | 1952 (0.43)                           | <b>1.98 (1.88-2.09)</b> | <b>1.77 (1.65-1.89)</b> | 14,005 (1.70)                   | <b>3.04 (2.95-3.13)</b>    | <b>2.76 (2.68-2.84)</b>  |

ARI, another respiratory infection; CI, confidence interval; HR, hazard ratio.

¶ Onset of neuropsychiatric outcomes were defined when a participant was diagnosed with a particular outcome three times or more within one year using the following ICD-10 codes.

¶¶ Onset of neuropsychiatric outcomes were defined when a participant was diagnosed with a particular outcome four times or more within one year using the following ICD-10 codes.

\* **adjusted HR:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and  $\geq 2$ ); obesity (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], obese [ $\geq 25.0 \text{ kg/m}^2$ ], and unknown); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$ , systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ , and unknown); fasting blood glucose ( $< 100$ ,  $\geq 100 \text{ mg/dL}$ , and unknown); serum total cholesterol ( $< 200$ ,  $200\text{--}240$ ,  $\geq 240 \text{ mg/dL}$ , and unknown); glomerular filtration rate ( $< 60$ ,  $60\text{--}90$ ,  $\geq 90 \text{ mL/min/1.73 m}^2$ , and unknown); smoking status (non-, ex-, current smoker, and unknown); alcohol consumption (drinks;  $< 1$ ,  $1\text{--}2$ ,  $3\text{--}4$ ,  $\geq 5$  days per week, and unknown); aerobic physical activity (sufficient, insufficient, and unknown); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and

hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); outpatients contact in the year before index date (0, 1-4, and  $\geq 5$  times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no], fasting blood glucose missing indicator [yes or no], serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no], smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes or no]).

‡ **adjusted HR:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; insurance status (insured or dependent); body mass index (underweight [ $< 18.5 \text{ kg/m}^2$ ]; normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], obese [ $\geq 25.0 \text{ kg/m}^2$ ], and unknown); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$ , systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ , and unknown); fasting blood glucose ( $< 100$ ,  $\geq 100 \text{ mg/dL}$ , and unknown); serum total cholesterol ( $< 200$ ,  $200\text{--}240$ ,  $\geq 240 \text{ mg/dL}$ , and unknown); glomerular filtration rate ( $< 60$ ,  $60\text{--}90$ ,  $\geq 90 \text{ mL/min/1.73 m}^2$ , and unknown); smoking status (non-, current smoker, and unknown); alcohol consumption (rarely, sometimes, every day, and unknown); aerobic physical activity (sufficient, insufficient, and unknown); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); outpatients contact in the year before index date (0, 1-4, and  $\geq 5$  times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no],

fasting blood glucose missing indicator [yes or no], serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no], smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes or no]).

Data in bold indicate significant differences ( $P < 0.05$ ).

**Table S14.** Additional analysis of hazard ratio (95% CI) for the **long-term sequelae risk** of neuropsychiatric events following COVID-19 or ARI diagnosis of patients in the propensity score-matched discovery cohorts (missing indicator method)

|                                                   | COVID-19 versus ARI (n= 531,020) |               |                             |                         |                         |
|---------------------------------------------------|----------------------------------|---------------|-----------------------------|-------------------------|-------------------------|
|                                                   | Events (%)                       | Person-months | Incidence rate <sup>‡</sup> | HR (95% CI)             |                         |
|                                                   |                                  |               |                             | Model 1 <sup>*</sup>    | Model 2 <sup>  </sup>   |
| Any neuropsychiatric outcomes                     |                                  |               |                             |                         |                         |
| Control (general population or patients with ARI) | 7839 (2.95)                      | 63,571.4      | 4.04                        | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                            | 4211 (1.59)                      | 20,452.7      | 6.75                        | <b>1.71 (1.65-1.78)</b> | <b>1.60 (1.53-1.68)</b> |
| Anxiety disorder                                  |                                  |               |                             |                         |                         |
| Control                                           | 2899 (1.09)                      | 23,821.1      | 3.99                        | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                            | 1585 (0.60)                      | 7084.2        | 7.34                        | <b>1.69 (1.58-1.80)</b> | <b>1.69 (1.57-1.82)</b> |
| Cognitive deficit                                 |                                  |               |                             |                         |                         |
| Control                                           | 133 (0.050)                      | 960.4         | 4.54                        | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                            | 40 (0.015)                       | 219.5         | 5.97                        | 1.01 (0.70-1.45)        | 0.49 (0.28-0.85)        |

|                         |             |          |       |                         |                         |  |
|-------------------------|-------------|----------|-------|-------------------------|-------------------------|--|
| Encephalitis            |             |          |       |                         |                         |  |
| Control                 | 22 (0.0083) | 160.7    | 4.49  | 1.0 (ref)               | 1.0 (ref)               |  |
| Patients with COVID-19  | 44 (0.017)  | 142.3    | 10.14 | <b>5.30 (3.09-9.10)</b> | <b>2.74 (1.36-5.50)</b> |  |
| Epilepsy/seizures       |             |          |       |                         |                         |  |
| Control                 | 114 (0.043) | 843.6    | 4.43  | 1.0 (ref)               | 1.0 (ref)               |  |
| Patients with COVID-19  | 45 (0.017)  | 209.8    | 7.03  | 1.17 (0.81-1.68)        | 0.69 (0.41-1.16)        |  |
| Guillain-Barré syndrome |             |          |       |                         |                         |  |
| Control                 | 11 (0.0041) | 56.8     | 6.35  | 1.0 (ref)               | 1.0 (ref)               |  |
| Patients with COVID-19  | 9 (0.0033)  | 33.4     | 8.82  | 1.81 (0.72-4.59)        | 1.94 (0.72-5.25)        |  |
| Insomnia                |             |          |       |                         |                         |  |
| Control                 | 1592 (0.60) | 12,819.4 | 4.07  | 1.0 (ref)               | 1.0 (ref)               |  |
| Patients with COVID-19  | 706 (0.27)  | 3468.8   | 6.67  | <b>1.41 (1.28-1.55)</b> | <b>1.32 (1.18-1.48)</b> |  |
| Intracranial hemorrhage |             |          |       |                         |                         |  |
| Control                 | 98 (0.037)  | 897.6    | 3.58  | 1.0 (ref)               | 1.0 (ref)               |  |
| Patients with COVID-19  | 62 (0.023)  | 338.2    | 6.01  | <b>2.38 (1.69-3.35)</b> | <b>1.95 (1.31-2.90)</b> |  |

|                                   |             |          |      |                         |                         |  |
|-----------------------------------|-------------|----------|------|-------------------------|-------------------------|--|
| Ischemic stroke                   |             |          |      |                         |                         |  |
| Control                           | 427 (0.16)  | 63,571.4 | 3.83 | 1.0 (ref)               | 1.0 (ref)               |  |
| Patients with COVID-19            | 231 (0.087) | 20,452.7 | 6.55 | <b>1.92 (1.62-2.28)</b> | <b>1.63 (1.33-1.99)</b> |  |
| Mood disorder                     |             |          |      |                         |                         |  |
| Control                           | 2356 (0.89) | 23,821.1 | 3.82 | 1.0 (ref)               | 1.0 (ref)               |  |
| Patients with COVID-19            | 1342 (0.51) | 7084.2   | 6.94 | <b>1.84 (1.71-1.98)</b> | <b>1.62 (1.48-1.76)</b> |  |
| Myoneural junction/muscle disease |             |          |      |                         |                         |  |
| Control                           | 34 (0.013)  | 960.4    | 3.68 | 1.0 (ref)               | 1.0 (ref)               |  |
| Patients with COVID-19            | 9 (0.0033)  | 219.5    | 7.63 | 0.91 (0.42-1.96)        | 0.78 (0.30-2.04)        |  |
| Nerve/nerve root/plexus disorders |             |          |      |                         |                         |  |
| Control                           | 1577 (0.59) | 160.7    | 3.88 | 1.0 (ref)               | 1.0 (ref)               |  |
| Patients with COVID-19            | 1073 (0.40) | 142.3    | 5.67 | <b>2.41 (2.22-2.62)</b> | <b>2.47 (2.25-2.71)</b> |  |
| Parkinsonism                      |             |          |      |                         |                         |  |
| Control                           | 154 (0.058) | 843.6    | 3.95 | 1.0 (ref)               | 1.0 (ref)               |  |
| Patients with COVID-19            | 49 (0.018)  | 209.8    | 6.13 | 1.09 (0.78-1.53)        | 0.82 (0.54-1.26)        |  |

|                        |             |      |      |                  |                  |
|------------------------|-------------|------|------|------------------|------------------|
| Psychotic disorder     |             |      |      |                  |                  |
| Control                | 182 (0.069) | 56.8 | 3.72 | 1.0 (ref)        | 1.0 (ref)        |
| Patients with COVID-19 | 49 (0.018)  | 33.4 | 7.27 | 0.89 (0.64-1.23) | 0.46 (0.27-0.77) |

ARI, another respiratory infection; CI, confidence interval; HR, hazard ratio.

\* **Models 1:** adjusted for age (20–39, 40–59, and  $\geq 60$  years) and sex.

<sup>II</sup> **Model 2:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and  $\geq 2$ ); obesity (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], obese [ $\geq 25.0 \text{ kg/m}^2$ ], and unknown); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$ , systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ , and unknown); fasting blood glucose ( $< 100$ ,  $\geq 100 \text{ mg/dL}$ , and unknown); serum total cholesterol ( $< 200$ ,  $200\text{--}240$ ,  $\geq 240 \text{ mg/dL}$ , and unknown); glomerular filtration rate ( $< 60$ ,  $60\text{--}90$ ,  $\geq 90 \text{ mL/min/1.73 m}^2$ , and unknown); smoking status (non-, ex-, current smoker, and unknown); alcohol consumption (drinks;  $< 1$ ,  $1\text{--}2$ ,  $3\text{--}4$ ,  $\geq 5$  days per week, and unknown); aerobic physical activity (sufficient, insufficient, and unknown); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and

hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); outpatients contact in the year before index date (0, 1-4, and  $\geq 5$  times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no], fasting blood glucose missing indicator [yes or no], serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no], smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes or no]).

‡ **Incidence rate:** the number of events divided by 10 person-months. Data in bold indicate significant differences ( $P < 0.05$ ).

**Table S15.** Baseline characteristics for the 1:4 propensity score-matched cohort (COVID-19 versus general) and 1:1 propensity score-matched cohort (COVID-19 versus ARI) in the entire unmatched discovery cohort (total n=2,463,633; complete case analysis method)

| Matching covariates     | COVID-19 versus general |                     |        | COVID-19 versus ARI |                      |       |
|-------------------------|-------------------------|---------------------|--------|---------------------|----------------------|-------|
|                         | (n=591,174)             |                     |        | (n=227,786)         |                      |       |
|                         | COVID-19<br>(n=122,883) | None<br>(n=468,291) | SMD    | ARI<br>(n= 113,893) | None<br>(n= 113,893) | SMD   |
| Total, n (%)            | 122,883 (79.2)          | 468,291 (20.8)      |        | 113,893 (50.0)      | 113,893 (50.0)       |       |
| Age, years, n (%)       |                         |                     | 0.022  |                     |                      | 0.023 |
| 20 to 39                | 18,378 (15.0)           | 71,947 (15.4)       |        | 18,376 (16.1)       | 17,783 (15.6)        |       |
| 40 to 59                | 62,704 (51.0)           | 242,138 (51.7)      |        | 59,577 (52.3)       | 60,313 (53.0)        |       |
| ≥ 60                    | 41,801 (34.0)           | 154,206 (32.9)      |        | 35,940 (31.6)       | 35,797 (31.4)        |       |
| Sex, n (%)              |                         |                     | 0.010  |                     |                      | 0.003 |
| Male                    | 71,231 (58.0)           | 273,689 (58.4)      |        | 66,189 (58.1)       | 66,331 (58.2)        |       |
| Female                  | 51,652 (42.0)           | 194,602 (41.6)      |        | 47,704 (41.9)       | 47,562 (41.8)        |       |
| Household income, n (%) |                         |                     | <0.001 |                     |                      | 0.027 |

|                                                         |                |                |       |                |                |        |
|---------------------------------------------------------|----------------|----------------|-------|----------------|----------------|--------|
| Low (0–39 percentile)                                   | 49,095 (40.0)  | 186,771 (39.9) |       | 45,752 (40.2)  | 45,897 (40.3)  |        |
| Middle (40–79 percentile)                               | 47,630 (38.8)  | 182,357 (38.9) |       | 45,339 (39.8)  | 44,873 (39.4)  |        |
| High (80–100 percentile)                                | 26,158 (21.3)  | 99,163 (21.2)  |       | 22,802 (20.0)  | 23,123 (20.3)  |        |
| Region of residence, n (%)                              |                |                | 0.002 |                |                | <0.001 |
| Urban                                                   | 65,696 (53.5)  | 249,992 (53.4) |       | 59,242 (52.0)  | 59,241 (52.0)  |        |
| Rural                                                   | 57,187 (46.5)  | 218,299 (46.6) |       | 54,651 (48.0)  | 54,652 (48.0)  |        |
| Charlson comorbidity index, n (%)                       |                |                | 0.055 |                |                | <0.001 |
| 0                                                       | 106,493 (86.7) | 411,145 (87.8) |       | 103,703 (91.1) | 103,827 (91.2) |        |
| 1                                                       | 11,591 (9.4)   | 40,741 (8.7)   |       | 5892 (5.2)     | 5894 (5.2)     |        |
| ≥2                                                      | 4799 (3.9)     | 16,405 (3.5)   |       | 4298 (3.8)     | 4172 (3.7)     |        |
| History of cardiovascular disease, n (%)                | 6989 (5.7)     | 25,171 (5.4)   | 0.014 | 6014 (5.3)     | 5760 (5.1)     | 0.010  |
| History of chronic kidney disease, n (%)                | 2917 (2.4)     | 10,342 (2.2)   | 0.011 | 2290 (2.0)     | 2235 (2.0)     | 0.004  |
| History of chronic obstructive pulmonary disease, n (%) | 720 (0.6)      | 2188 (0.5)     | 0.016 | 626 (0.6)      | 517 (0.5)      | 0.014  |

|                                            |                |                |       |               |               |       |
|--------------------------------------------|----------------|----------------|-------|---------------|---------------|-------|
| Current medication for diabetes            | 28,812 (23.5)  | 107,045 (22.9) | 0.014 | 24,986 (21.9) | 24,664 (21.7) | 0.007 |
| Current medication for hyperlipidemia      | 26,175 (21.3)  | 97,421 (20.8)  | 0.012 | 22,677 (19.9) | 22,661 (19.9) | 0.076 |
| Current medication for hypertension        | 12,249 (10.)   | 44,149 (9.4)   | 0.028 | 9366 (8.2)    | 9347 (8.2)    | 0.008 |
| <b>Unmatching covariates</b>               |                |                |       |               |               |       |
| Body mass index, kg/m <sup>2</sup> , n (%) |                |                | 0.095 |               |               | 0.065 |
| Underweight (<18.5)                        | 2137 (1.7)     | 11,166 (2.4)   |       | 2040 (1.8)    | 2710 (2.4)    |       |
| Normal (18.5-23.0)                         | 35,940 (29.3)  | 154,436 (33)   |       | 33,731 (29.6) | 37,369 (32.8) |       |
| Overweight (23.0-25.0)                     | 30,198 (24.6)  | 114,882 (24.5) |       | 27,963 (24.6) | 27,806 (24.4) |       |
| Obese (≥25.0)                              | 54,608 (44.4)  | 187,807 (40.1) |       | 50,159 (44.0) | 46,008 (40.4) |       |
| Blood pressure, n (%)                      |                |                | 0.015 |               |               | 0.037 |
| SBP <140 mmHg and DBP <90 mmHg             | 103,139 (83.9) | 395,527 (84.5) |       | 95,968 (84.3) | 97,470 (85.6) |       |
| SBP ≥140mmHg or DBP ≥90 mmHg               | 19,744 (16.1)  | 72,764 (15.5)  |       | 17,925 (15.7) | 16,423 (14.4) |       |
| Fasting blood glucose, mg/dL, n (%)        |                |                | 0.024 |               |               | 0.020 |

|                                                                |               |                |               |               |        |
|----------------------------------------------------------------|---------------|----------------|---------------|---------------|--------|
| <100                                                           | 69,339 (56.4) | 258,623 (55.2) | 65,845 (57.8) | 64,749 (56.9) |        |
| ≥100                                                           | 53,544 (43.6) | 209,668 (44.8) | 48,048 (42.2) | 49,144 (43.2) |        |
| Serum total cholesterol, mg/dL, n (%)                          |               |                | 0.022         |               | 0.022  |
| <200                                                           | 66,655 (54.2) | 247,188 (52.8) | 61,112 (53.7) | 60,537 (53.2) |        |
| 200 to 240                                                     | 39,380 (32.1) | 152,196 (32.5) | 36,982 (32.5) | 37,067 (32.6) |        |
| ≥240                                                           | 16,848 (13.7) | 68,907 (14.7)  | 15,799 (13.9) | 16,289 (14.3) |        |
| Glomerular filtration rate, mL/min/1.73 m <sup>2</sup> , n (%) |               |                | 0.055         |               | <0.001 |
| <60                                                            | 4658 (3.8)    | 15,948 (3.4)   | 3948 (3.5)    | 3569 (3.1)    |        |
| 60 to 90                                                       | 57,817 (47.1) | 218,817 (46.7) | 53,224 (46.7) | 53,220 (46.7) |        |
| ≥90                                                            | 60,408 (49.2) | 233,526 (49.9) | 56,721 (49.8) | 57,104 (50.1) |        |
| Smoking status, n (%)                                          |               |                | 0.209         |               | 0.131  |
| Non-smoker                                                     | 77,203 (62.8) | 277,799 (59.3) | 71,456 (62.7) | 67,848 (59.6) |        |
| Ex-smoker                                                      | 25,954 (21.1) | 81,299 (17.4)  | 23,654 (20.8) | 21,142 (18.6) |        |
| Current smoker                                                 | 19,726 (16.1) | 109,193 (23.3) | 18,783 (16.5) | 24,903 (21.9) |        |

|                                                          |               |                |               |               |       |
|----------------------------------------------------------|---------------|----------------|---------------|---------------|-------|
| Alcohol consumption; drinks per week, n (%)              |               |                | 0.067         |               | 0.076 |
| <1                                                       | 71,079 (57.8) | 275,408 (58.8) | 65,344 (57.4) | 68,154 (59.8) |       |
| 1 to 2                                                   | 35,065 (28.5) | 132,292 (28.3) | 33,009 (29.0) | 31,342 (27.5) |       |
| 3 to 4                                                   | 12,357 (10.1) | 44,457 (9.5)   | 11,533 (10.1) | 10,500 (9.2)  |       |
| ≥5                                                       | 4382 (3.6)    | 16,134 (3.5)   | 4007 (3.5)    | 3897 (3.4)    |       |
| Aerobic physical activity, n (%)                         |               |                | 0.028         |               | 0.008 |
| Insufficient                                             | 59,543 (48.5) | 220,461 (47.1) | 55,273 (48.5) | 55,724 (48.9) |       |
| Sufficient                                               | 63,340 (51.5) | 247,830 (52.9) | 58,620 (51.5) | 58,169 (51.1) |       |
| Hospital admissions in the year before index date, n (%) |               |                | 0.553         |               | 0.480 |
| None                                                     | 79,070 (64.4) | 401,039 (85.6) | 77,402 (68.0) | 99,186 (87.1) |       |
| 1 time                                                   | 24,025 (19.6) | 23,808 (5.1)   | 20,748 (18.2) | 9790 (8.6)    |       |
| ≥2 times                                                 | 19,788 (16.1) | 43,444 (9.3)   | 15,743 (13.8) | 4917 (4.3)    |       |
| Outpatients contact in the year before index date, n (%) |               |                | 0.212         |               | 0.146 |

|          |               |                |               |               |
|----------|---------------|----------------|---------------|---------------|
| None     | 6820 (5.6)    | 55,513 (11.9)  | 6663 (5.9)    | 10,143 (8.9)  |
| 1-4 time | 25,734 (20.9) | 89,734 (19.2)  | 24,946 (21.9) | 29,034 (25.5) |
| ≥5 times | 70,329 (73.5) | 323,044 (69.0) | 82,284 (72.3) | 74,716 (65.6) |

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ARI, another respiratory infection; DBP, diastolic blood pressure; SBP, systolic blood pressure; SD, standard deviation; SMD, standardized mean difference.

An SMD < 0.1 indicates no significant imbalance. All SMD values were  $\leq 0.055$  in the 1:4 propensity score-matched cohort.

**Table S16.** Baseline characteristics for the 1:2 propensity score-matched cohort (COVID-19 versus general) and 1:1 propensity score-matched cohort (COVID-19 versus ARI) in the entire unmatched validation cohort (total n= 12,218,680; complete case analysis method)

| Matching covariates         | COVID-19 versus general |                     |       | COVID-19 versus ARI     |                    |        |
|-----------------------------|-------------------------|---------------------|-------|-------------------------|--------------------|--------|
|                             | (n=976,212)             |                     |       | (n= 148,096)            |                    |        |
|                             | COVID-19<br>(n=378,578) | None<br>(n=597,634) | SMD   | COVID-19<br>(n= 74,048) | ARI<br>(n= 74,048) | SMD    |
| Total, n (%)                | 378,578 (38.8)          | 597,634 (61.2)      |       | 74,048 (50.0)           | 74,048 (50.0)      |        |
| Age, years, n (%)           |                         |                     | 0.183 |                         |                    | <0.001 |
| 20 to 39                    | 116,026 (30.7)          | 136,675 (22.9)      |       | 20,818 (28.1)           | 20,798 (28.1)      |        |
| 40 to 59                    | 222,793 (58.9)          | 389,383 (65.2)      |       | 43,354 (58.6)           | 43,374 (58.6)      |        |
| ≥ 60                        | 39,759 (10.5)           | 71,576 (12.0)       |       | 9876 (13.3)             | 9876 (13.3)        |        |
| Sex, n (%)                  |                         |                     | 0.044 |                         |                    | <0.001 |
| Male                        | 239,693 (63.3)          | 391,016 (65.4)      |       | 44,550 (60.2)           | 44,530 (60.1)      |        |
| Female                      | 138,885 (36.7)          | 206,618 (34.6)      |       | 29,498 (39.8)           | 29,518 (39.9)      |        |
| Insured or dependent, n (%) |                         |                     | 0.004 |                         |                    | <0.001 |
| Insured                     | 332,033 (87.7)          | 525,001 (87.9)      |       | 63,731 (86.1)           | 63,711 (86.0)      |        |

|                                                         |                |                |        |               |               |        |
|---------------------------------------------------------|----------------|----------------|--------|---------------|---------------|--------|
| Dependent                                               | 46,545 (12.3)  | 72,633 (12.2)  |        | 10,317 (13.9) | 10,337 (14.0) |        |
| History of cardiovascular disease, n (%)                | 24,199 (6.4)   | 27,585 (4.6)   | 0.078  | 2700 (3.7)    | 2720 (3.7)    | 0.001  |
| History of chronic kidney disease, n (%)                | 13,899 (3.7)   | 16,006 (2.7)   | 0.057  | 1482 (2.0)    | 1462 (2.0)    | 0.002  |
| History of chronic obstructive pulmonary disease, n (%) | 889 (0.2)      | 931 (0.2)      | 0.018  | 71 (0.1)      | 71 (0.1)      | <0.001 |
| Current medication for diabetes                         | 8791 (2.3)     | 12,805 (2.1)   | 0.012  | 1133 (1.5)    | 1113 (1.5)    | 0.002  |
| Current medication for hyperlipidemia                   | 22,281 (5.9)   | 31,387 (5.3)   | 0.028  | 3154 (4.3)    | 3134 (4.2)    | 0.001  |
| Current medication for hypertension                     | 28137 (7.4)    | 40,219 (6.7)   | 0.027  | 3830 (5.2)    | 3850 (5.2)    | 0.001  |
| <b>Unmatching covariates</b>                            |                |                |        |               |               |        |
| Body mass index, kg/m <sup>2</sup> , n (%)              |                |                | <0.001 |               |               | 0.026  |
| Underweight (<18.5)                                     | 199,363 (52.7) | 318,201 (53.2) |        | 39,896 (53.9) | 39,607 (53.5) |        |
| Normal (≥18.5 to <23.0)                                 | 75,271 (19.9)  | 119,866 (20.1) |        | 14,675 (19.8) | 14,454 (19.5) |        |
| Overweight (≥23.0 to <25.0)                             | 82,252 (21.7)  | 129,232 (21.6) |        | 15,369 (20.8) | 15,943 (21.5) |        |
| Obese (≥25.0)                                           | 21,692 (5.7)   | 30335 (5.1)    |        | 4108 (5.6)    | 4044 (5.5)    |        |
| Blood pressure, n (%)                                   |                |                | 0.087  |               |               | 0.007  |
| SBP <140 mmHg and DBP <90 mmHg                          | 353,323 (93.3) | 543,745 (91.0) |        | 68,956 (93.1) | 68,827 (93.0) |        |
| SBP ≥140mmHg or DBP ≥90 mmHg                            | 25,255 (6.7)   | 53,889 (9.0)   |        | 5092 (6.9)    | 5221 (7.1)    |        |

|                                                                |                |                |       |               |               |
|----------------------------------------------------------------|----------------|----------------|-------|---------------|---------------|
| Fasting blood glucose, mg/dL, n (%)                            |                |                | 0.068 |               | 0.021         |
| <100                                                           | 287,799 (76.0) | 436,729 (73.1) |       | 56,465 (76.3) | 55,801 (75.4) |
| ≥100                                                           | 90,779 (24.0)  | 160,905 (26.9) |       | 17,583 (23.8) | 18,247 (24.6) |
| Serum total cholesterol, mg/dL, n (%)                          |                |                | 0.068 |               | <0.001        |
| <200                                                           | 175,790 (46.4) | 255,065 (42.7) |       | 33,604 (45.4) | 33,566 (45.3) |
| 200 to 240                                                     | 142,797 (37.7) | 233,789 (39.1) |       | 28,207 (38.1) | 28,341 (38.3) |
| ≥240                                                           | 59,991 (15.9)  | 108,780 (18.2) |       | 12,237 (16.5) | 12,141 (16.4) |
| Glomerular filtration rate, mL/min/1.73 m <sup>2</sup> , n (%) |                |                | 0.151 |               | <0.001        |
| <60                                                            | 2509 (0.7)     | 2965 (0.5)     |       | 488 (0.7)     | 418 (0.6)     |
| 60 to 90                                                       | 53,828 (14.2)  | 95,222 (15.9)  |       | 10,783 (14.6) | 11,097 (15.0) |
| ≥90                                                            | 322,241 (85.1) | 499,447 (83.6) |       | 62,777 (84.8) | 62,533 (84.5) |
| Smoking status, n (%)                                          |                |                | 0.196 |               | 0.017         |
| Non-smoker                                                     | 296,028 (78.2) | 441,390 (73.9) |       | 58,490 (79.0) | 58,315 (78.8) |
| Current smoker                                                 | 82,550 (21.8)  | 156,244 (26.1) |       | 15,558 (21.0) | 15,733 (21.3) |
| Alcohol consumption; drinks per week, n (%)                    |                |                | 0.057 |               | <0.001        |
| Rarely                                                         | 155,520 (41.1) | 243,073 (40.7) |       | 31,220 (42.2) | 30,969 (41.8) |

|                                                          |                |                |               |               |        |
|----------------------------------------------------------|----------------|----------------|---------------|---------------|--------|
| Sometimes                                                | 136,376 (36.0) | 207,038 (34.6) | 26,087 (35.2) | 26,229 (35.4) |        |
| Everyday                                                 | 86,682 (22.9)  | 147,523 (24.7) | 16,741 (22.6) | 16,850 (22.8) |        |
| Aerobic physical activity, n (%)                         |                |                | 0.196         |               | 0.017  |
| Insufficient                                             | 293,121 (77.4) | 447,169 (74.8) | 57,416 (77.5) | 56,678 (76.5) |        |
| Sufficient                                               | 85,457 (22.6)  | 150,465 (25.2) | 16,632 (22.5) | 17,370 (23.5) |        |
| Hospital admissions in the year before index date, n (%) |                |                | 0.142         |               | <0.001 |
| None                                                     | 373,805 (98.7) | 594,814 (99.5) | 73,083 (98.7) | 73,346 (99.1) |        |
| 1 time                                                   | 434 (0.1)      | 326 (0.1)      | 86 (0.1)      | 64 (0.1)      |        |
| ≥2 times                                                 | 4339 (1.2)     | 2494 (0.4)     | 879 (1.2)     | 638 (0.9)     |        |
| Outpatients contact in the year before index date, n (%) |                |                | 0.549         |               | 0.387  |
| None                                                     | 70,057 (18.5)  | 248,182 (41.5) | 13,445 (18.2) | 24,560 (33.2) |        |
| 1-4 time                                                 | 76,328 (20.2)  | 121,759 (20.4) | 14,756 (19.9) | 16,187 (21.9) |        |
| ≥5 times                                                 | 232,193 (61.3) | 227,693 (38.1) | 45,847 (61.9) | 33,301 (45.0) |        |

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ARI, another respiratory infection; DBP, diastolic blood pressure; SBP, systolic blood pressure; SD, standard deviation; SMD, standardized mean difference.

An SMD < 0.1 indicates no significant imbalance. All SMD values were  $\leq 0.078$  in the 1:2 propensity score-matched cohorts, except age (SMD=0.183).

**Table S17.** Hazard ratio (95% CI) for the **short-term risk** of incident neuropsychiatric events following COVID-19 diagnosis of patients in the propensity score-matched discovery and validation cohorts (complete case analysis method)

| Discovery cohort                                  | COVID-19 versus general |                         |                         | COVID-19 versus ARI |                      |                       |
|---------------------------------------------------|-------------------------|-------------------------|-------------------------|---------------------|----------------------|-----------------------|
|                                                   | (n=591,174)             |                         |                         | (n= 227,786)        |                      |                       |
|                                                   | HR (95% CI)             |                         |                         | HR (95% CI)         |                      |                       |
|                                                   | Events (%)              | Model 1 <sup>*</sup>    | Model 2 <sup>II</sup>   | Events (%)          | Model 1 <sup>*</sup> | Model 2 <sup>II</sup> |
| Any neuropsychiatric outcomes                     |                         |                         |                         |                     |                      |                       |
| Control (general population or patients with ARI) | 688 (0.15)              | 1.0 (ref)               | 1.0 (ref)               | 356 (0.31)          | 1.0 (ref)            | 1.0 (ref)             |
| Patients with COVID-19                            | 428 (0.35)              | <b>2.36 (2.09-2.66)</b> | <b>2.34 (2.07-2.64)</b> | 377 (0.33)          | 1.07 (0.93-1.24)     | 1.08 (0.93-1.24)      |
| Anxiety disorder                                  |                         |                         |                         |                     |                      |                       |
| Control                                           | 175 (0.037)             | 1.0 (ref)               | 1.0 (ref)               | 137 (0.12)          | 1.0 (ref)            | 1.0 (ref)             |
| Patients with COVID-19                            | 173 (0.14)              | <b>3.76 (3.05-4.64)</b> | <b>3.74 (3.02-4.62)</b> | 153 (0.13)          | 1.12 (0.89-1.42)     | 1.13 (0.89-1.42)      |
| Encephalitis                                      |                         |                         |                         |                     |                      |                       |
| Control                                           | 0 (0.00)                | 1.0 (ref)               | 1.0 (ref)               | 0 (0.00)            | 1.0 (ref)            | 1.0 (ref)             |

|                         |                           |                         |                         |             |                         |                         |
|-------------------------|---------------------------|-------------------------|-------------------------|-------------|-------------------------|-------------------------|
| Patients with COVID-19  | 12 (0.0098)               | NA                      | NA                      | 11 (0.0097) | NA                      | NA                      |
| Epilepsy/seizures       |                           |                         |                         |             |                         |                         |
| Control                 | 10 (0.0020)               | 1.0 (ref)               | 1.0 (ref)               | 3 (0.0026)  | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19  | 4 (0.0033)                | 1.53 (0.48-4.88)        | 1.56 (0.48-5.01)        | 4 (0.0035)  | 1.33 (0.30-5.95)        | 1.47 (0.33-6.65)        |
| Guillain-Barré syndrome |                           |                         |                         |             |                         |                         |
| Control                 | 2 (4.2*10 <sup>-4</sup> ) | 1.0 (ref)               | 1.0 (ref)               | 0 (0.00)    | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19  | 2 (0.0016)                | 3.79 (0.53-26.92)       | 3.44 (0.46-25.50)       | 2 (0.0018)  | NA                      | NA                      |
| Insomnia                |                           |                         |                         |             |                         |                         |
| Control                 | 92 (0.020)                | 1.0 (ref)               | 1.0 (ref)               | 67 (0.059)  | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19  | 117 (0.10)                | <b>4.81 (3.66-6.32)</b> | <b>4.90 (3.72-6.45)</b> | 99 (0.087)  | <b>1.50 (1.10-2.04)</b> | <b>1.52 (1.11-2.08)</b> |
| Intracranial hemorrhage |                           |                         |                         |             |                         |                         |
| Control                 | 14 (0.0030)               | 1.0 (ref)               | 1.0 (ref)               | 2 (0.0018)  | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19  | 4 (0.0033)                | 1.08 (0.35-3.27)        | 1.04 (0.34-3.19)        | 3 (0.0026)  | 1.51 (0.25-9.00)        | 1.96 (0.30-12.90)       |
| Ischemic stroke         |                           |                         |                         |             |                         |                         |
| Control                 | 80 (0.017)                | 1.0 (ref)               | 1.0 (ref)               | 17 (0.015)  | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19  | 31 (0.025)                | 1.45 (0.96-2.20)        | 1.43 (0.94-2.17)        | 28 (0.025)  | 1.70 (0.93-3.12)        | 1.62 (0.88-2.98)        |

## Mood disorder

|                        |             |                         |                         |            |                  |                  |
|------------------------|-------------|-------------------------|-------------------------|------------|------------------|------------------|
| Control                | 116 (0.025) | 1.0 (ref)               | 1.0 (ref)               | 92 (0.081) | 1.0 (ref)        | 1.0 (ref)        |
| Patients with COVID-19 | 96 (0.078)  | <b>3.15 (2.40-4.12)</b> | <b>3.14 (2.39-4.13)</b> | 83 (0.073) | 0.91 (0.68-1.23) | 0.91 (0.68-1.23) |

## Nerve/nerve root/plexus disorders

|                        |             |                  |                  |            |                  |                  |
|------------------------|-------------|------------------|------------------|------------|------------------|------------------|
| Control                | 249 (0.053) | 1.0 (ref)        | 1.0 (ref)        | 61 (0.054) | 1.0 (ref)        | 1.0 (ref)        |
| Patients with COVID-19 | 58 (0.047)  | 0.88 (0.66-1.18) | 0.86 (0.65-1.15) | 51 (0.045) | 0.85 (0.59-1.24) | 0.85 (0.58-1.23) |

## Myoneural junction/muscle disease

|                        |                           |           |           |          |           |           |
|------------------------|---------------------------|-----------|-----------|----------|-----------|-----------|
| Control                | 2 (4.2*10 <sup>-4</sup> ) | 1.0 (ref) | 1.0 (ref) | 0 (0.00) | 1.0 (ref) | 1.0 (ref) |
| Patients with COVID-19 | 0 (0.00)                  | NA        | NA        | 0 (0.00) | NA        | NA        |

## Parkinsonism

|                        |             |                  |                  |            |                  |                  |
|------------------------|-------------|------------------|------------------|------------|------------------|------------------|
| Control                | 10 (0.0021) | 1.0 (ref)        | 1.0 (ref)        | 9 (0.0079) | 1.0 (ref)        | 1.0 (ref)        |
| Patients with COVID-19 | 3 (0.0024)  | 1.13 (0.31-4.10) | 1.00 (0.27-3.66) | 3 (0.0026) | 0.33 (0.09-1.23) | 0.34 (0.09-1.26) |

## Psychotic disorder

|                        |            |                  |                  |            |                  |                  |
|------------------------|------------|------------------|------------------|------------|------------------|------------------|
| Control                | 5 (0.0011) | 1.0 (ref)        | 1.0 (ref)        | 7 (0.0061) | 1.0 (ref)        | 1.0 (ref)        |
| Patients with COVID-19 | 2 (0.0016) | 1.52 (0.29-7.81) | 1.52 (0.29-7.94) | 2 (0.0018) | 0.29 (0.06-1.38) | 0.30 (0.06-1.44) |

| Validation cohort                                 | COVID-19 versus general |                           |                         | COVID-19 versus ARI |                          |                          |
|---------------------------------------------------|-------------------------|---------------------------|-------------------------|---------------------|--------------------------|--------------------------|
|                                                   | (n=976,212)             |                           |                         | (n= 148,096)        |                          |                          |
|                                                   | HR (95% CI)             |                           |                         | HR (95% CI)         |                          |                          |
|                                                   | Events (%)              | Model 3 <sup>*</sup>      | Model 4 <sup>‡</sup>    | Events (%)          | Model 3 <sup>*</sup>     | Model 4 <sup>‡</sup>     |
| Any neuropsychiatric outcomes                     |                         |                           |                         |                     |                          |                          |
| Control (general population or patients with ARI) | 804 (0.13)              | 1.0 (ref)                 | 1.0 (ref)               | 1538 (2.08)         | 1.0 (ref)                | 1.0 (ref)                |
| Patients with COVID-19                            | 5020 (1.33)             | <b>10.38 (9.63-11.18)</b> | <b>8.84 (8.20-9.53)</b> | 3782 (5.11)         | <b>2.46 (2.32-2.61)</b>  | <b>2.17 (2.04-2.30)</b>  |
| Anxiety disorder                                  |                         |                           |                         |                     |                          |                          |
| Control                                           | 327 (0.055)             | 1.0 (ref)                 | 1.0 (ref)               | 731 (0.99)          | 1.0 (ref)                | 1.0 (ref)                |
| Patients with COVID-19                            | 1099 (0.29)             | <b>5.29 (4.67-5.99)</b>   | <b>5.02 (4.43-5.68)</b> | 846 (1.14)          | <b>1.16 (1.05-1.28)</b>  | <b>1.13 (1.02-1.25)</b>  |
| Encephalitis                                      |                         |                           |                         |                     |                          |                          |
| Control                                           | 0 (0.00)                | 1.0 (ref)                 | 1.0 (ref)               | 2 (0.0027)          | 1.0 (ref)                | 1.0 (ref)                |
| Patients with COVID-19                            | 46 (0.012)              | NA                        | NA                      | 27 (0.036)          | <b>13.5 (3.21-56.76)</b> | <b>9.67 (2.27-41.23)</b> |
| Epilepsy/seizures                                 |                         |                           |                         |                     |                          |                          |
| Control                                           | 27 (0.0045)             | 1.0 (ref)                 | 1.0 (ref)               | 70 (0.095)          | 1.0 (ref)                | 1.0 (ref)                |

|                         |             |                            |                            |             |                            |                            |
|-------------------------|-------------|----------------------------|----------------------------|-------------|----------------------------|----------------------------|
| Patients with COVID-19  | 292 (0.08)  | <b>18.16 (12.24-26.93)</b> | <b>15.35 (10.31-22.87)</b> | 242 (0.33)  | <b>3.46 (2.65-4.51)</b>    | <b>2.84 (2.16-3.72)</b>    |
| Guillain-Barré syndrome |             |                            |                            |             |                            |                            |
| Control                 | 0 (0.00)    | 1.0 (ref)                  | 1.0 (ref)                  | 1 (0.0014)  | 1.0 (ref)                  | 1.0 (ref)                  |
| Patients with COVID-19  | 28 (0.0074) | NA                         | NA                         | 17 (0.023)  | <b>16.99 (2.26-127.54)</b> | <b>15.72 (2.08-118.92)</b> |
| Insomnia                |             |                            |                            |             |                            |                            |
| Control                 | 303 (0.051) | 1.0 (ref)                  | 1.0 (ref)                  | 707 (0.95)  | 1.0 (ref)                  | 1.0 (ref)                  |
| Patients with COVID-19  | 1848 (0.49) | <b>10.13 (8.97-11.44)</b>  | <b>8.08 (7.14-9.14)</b>    | 1317 (1.78) | <b>1.86 (1.70-2.04)</b>    | <b>1.62 (1.47-1.78)</b>    |
| Intracranial hemorrhage |             |                            |                            |             |                            |                            |
| Control                 | 22 (0.0037) | 1.0 (ref)                  | 1.0 (ref)                  | 38 (0.051)  | 1.0 (ref)                  | 1.0 (ref)                  |
| Patients with COVID-19  | 596 (0.16)  | <b>46.05 (30.09-70.48)</b> | <b>35.31 (23.01-54.19)</b> | 455 (0.61)  | <b>11.97 (8.60-16.67)</b>  | <b>8.36 (5.98-11.70)</b>   |
| Ischemic stroke         |             |                            |                            |             |                            |                            |
| Control                 | 50 (0.0084) | 1.0 (ref)                  | 1.0 (ref)                  | 115 (0.16)  | 1.0 (ref)                  | 1.0 (ref)                  |
| Patients with COVID-19  | 943 (0.25)  | <b>32.58 (24.52-43.30)</b> | <b>27.58 (20.72-36.72)</b> | 740 (1.00)  | <b>6.43 (5.28-7.83)</b>    | <b>5.56 (4.56-6.78)</b>    |
| Mood disorder           |             |                            |                            |             |                            |                            |
| Control                 | 247 (0.04)  | 1.0 (ref)                  | 1.0 (ref)                  | 350 (0.47)  | 1.0 (ref)                  | 1.0 (ref)                  |
| Patients with COVID-19  | 572 (0.15)  | <b>3.60 (3.10-4.18)</b>    | <b>3.37 (2.89-3.92)</b>    | 477 (0.64)  | <b>1.36 (1.19-1.56)</b>    | <b>1.33 (1.16-1.53)</b>    |

Nerve/nerve root/plexus disorders

|                        |                           |                           |                           |            |                         |                         |
|------------------------|---------------------------|---------------------------|---------------------------|------------|-------------------------|-------------------------|
| Control                | 5 (8.4*10 <sup>-4</sup> ) | 1.0 (ref)                 | 1.0 (ref)                 | 15 (0.020) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19 | 45 (0.012)                | <b>15.39 (6.11-38.77)</b> | <b>13.09 (5.15-33.30)</b> | 32 (0.043) | <b>2.13 (1.16-3.94)</b> | <b>1.85 (0.99-3.46)</b> |

Myoneural junction/muscle disease

|                        |             |                         |                         |            |                         |                         |
|------------------------|-------------|-------------------------|-------------------------|------------|-------------------------|-------------------------|
| Control                | 105 (0.018) | 1.0 (ref)               | 1.0 (ref)               | 93 (0.13)  | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19 | 414 (0.11)  | <b>6.51 (5.26-8.07)</b> | <b>6.26 (5.04-7.77)</b> | 293 (0.40) | <b>3.15 (2.50-3.98)</b> | <b>3.06 (2.41-3.87)</b> |

Parkinsonism

|                        |             |                          |                         |            |                         |                         |
|------------------------|-------------|--------------------------|-------------------------|------------|-------------------------|-------------------------|
| Control                | 7 (0.0012)  | 1.0 (ref)                | 1.0 (ref)               | 20 (0.027) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19 | 20 (0.0053) | <b>4.71 (1.99-11.14)</b> | <b>3.98 (1.65-9.64)</b> | 13 (0.018) | <b>0.65 (0.32-1.31)</b> | <b>0.61 (0.30-1.24)</b> |

Psychotic disorder

|                        |             |                          |                          |           |                         |                         |
|------------------------|-------------|--------------------------|--------------------------|-----------|-------------------------|-------------------------|
| Control                | 25 (0.0042) | 1.0 (ref)                | 1.0 (ref)                | 84 (0.11) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19 | 145 (0.038) | <b>9.46 (6.18-14.46)</b> | <b>6.76 (4.37-10.45)</b> | 98 (0.13) | <b>1.17 (0.87-1.56)</b> | <b>0.90 (0.67-1.22)</b> |

ARI, another respiratory infection; CI, confidence interval; HR, hazard ratio.

\* **Models 1 and 3:** adjusted for age (20–39, 40–59, and ≥ 60 years) and sex.

<sup>¶</sup> **Model 2:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and  $\geq 2$ ); obesity (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], and obese [ $\geq 25.0 \text{ kg/m}^2$ ]); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$ , systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ ); fasting blood glucose ( $< 100$  and  $\geq 100 \text{ mg/dL}$ ); serum total cholesterol ( $< 200$ ,  $200\text{--}240$ , and  $\geq 240 \text{ mg/dL}$ ); glomerular filtration rate ( $< 60$ ,  $60\text{--}90$ , and  $\geq 90 \text{ mL/min/1.73 m}^2$ ); smoking status (non-, ex-, and current smoker); alcohol consumption (drinks;  $< 1$ ,  $1\text{--}2$ ,  $3\text{--}4$ , and  $\geq 5$  days per week); aerobic physical activity (sufficient and insufficient); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); and outpatients contact in the year before index date (0,  $1\text{--}4$ , and  $\geq 5$  times).

<sup>‡</sup> **Model 4:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; insurance status (insured or dependent); body mass index (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], and obese [ $\geq 25.0 \text{ kg/m}^2$ ]); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$  and systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ ); fasting blood glucose ( $< 100$  and  $\geq 100 \text{ mg/dL}$ ); total serum cholesterol ( $< 200$ ,  $200\text{--}240$ , and  $\geq 240 \text{ mg/dL}$ ); glomerular filtration rate ( $< 60$ ,  $60\text{--}90$ , and  $\geq 90 \text{ mL/min/1.73 m}^2$ ); smoking status (non- and current smoker); alcohol consumption (rarely, sometimes, and every day); aerobic physical

activity (sufficient and insufficient); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); and outpatients contact in the year before index date (0, 1-4, and  $\geq 5$  times).

Data in bold indicate significant differences ( $P < 0.05$ ).

**Table S18.** Hazard ratio (95% CI) for the **long-term sequelae risk** of neuropsychiatric events following COVID-19 diagnosis of patients in the propensity score-matched discovery and validation cohorts (complete case analysis method)

| Discovery cohort                                  | COVID-19 versus general |                         |                         | COVID-19 versus ARI |                         |                         |
|---------------------------------------------------|-------------------------|-------------------------|-------------------------|---------------------|-------------------------|-------------------------|
|                                                   | (n=591,174)             |                         |                         | (n= 227,786)        |                         |                         |
|                                                   | HR (95% CI)             |                         |                         | HR (95% CI)         |                         |                         |
|                                                   | Events (%)              | Model 1 <sup>*</sup>    | Model 2 <sup>II</sup>   | Events (%)          | Model 1 <sup>*</sup>    | Model 2 <sup>II</sup>   |
| Any neuropsychiatric outcomes                     |                         |                         |                         |                     |                         |                         |
| Control (general population or patients with ARI) | 3226 (0.69)             | 1.0 (ref)               | 1.0 (ref)               | 3515 (3.09)         | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                            | 1433 (1.17)             | <b>1.72 (1.62-1.83)</b> | <b>1.71 (1.61-1.82)</b> | 1438 (1.26)         | <b>1.31 (1.23-1.40)</b> | <b>1.30 (1.22-1.39)</b> |
| Anxiety disorder                                  |                         |                         |                         |                     |                         |                         |
| Control                                           | 872 (0.19)              | 1.0 (ref)               | 1.0 (ref)               | 1237 (1.09)         | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                            | 559 (0.45)              | <b>2.48 (2.23-2.76)</b> | <b>2.48 (2.23-2.76)</b> | 559 (0.49)          | <b>1.41 (1.27-1.57)</b> | <b>1.42 (1.27-1.57)</b> |
| Cognitive deficit                                 |                         |                         |                         |                     |                         |                         |
| Control                                           | 10 (0.0021)             | 1.0 (ref)               | 1.0 (ref)               | 70 (0.061)          | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                            | 8 (0.0065)              | <b>3.01 (1.19-7.63)</b> | <b>2.93 (1.15-7.46)</b> | 8 (0.0070)          | <b>0.37 (0.18-0.78)</b> | <b>0.37 (0.18-0.79)</b> |

Encephalitis

|                        |                           |                           |                           |             |                  |                  |
|------------------------|---------------------------|---------------------------|---------------------------|-------------|------------------|------------------|
| Control                | 3 (6.4*10 <sup>-4</sup> ) | 1.0 (ref)                 | 1.0 (ref)                 | 11 (0.0097) | 1.0 (ref)        | 1.0 (ref)        |
| Patients with COVID-19 | 9 (0.0073)                | <b>11.49 (3.11-42.42)</b> | <b>10.29 (2.75-38.45)</b> | 9 (0.0079)  | 1.93 (0.78-4.79) | 1.92 (0.77-4.79) |

Epilepsy/seizures

|                        |             |                  |                  |             |                  |                  |
|------------------------|-------------|------------------|------------------|-------------|------------------|------------------|
| Control                | 34 (0.0073) | 1.0 (ref)        | 1.0 (ref)        | 51 (0.045)  | 1.0 (ref)        | 1.0 (ref)        |
| Patients with COVID-19 | 10 (0.0081) | 1.14 (0.56-2.30) | 1.20 (0.59-2.44) | 10 (0.0088) | 0.56 (0.28-1.13) | 0.56 (0.28-1.12) |

Guillain-Barré syndrome

|                        |                           |                   |                   |            |                   |                  |
|------------------------|---------------------------|-------------------|-------------------|------------|-------------------|------------------|
| Control                | 4 (8.5*10 <sup>-4</sup> ) | 1.0 (ref)         | 1.0 (ref)         | 2 (0.0018) | 1.0 (ref)         | 1.0 (ref)        |
| Patients with COVID-19 | 4 (0.0033)                | 3.84 (0.96-15.36) | 3.31 (0.81-13.53) | 4 (0.0035) | 3.43 (0.62-18.92) | 2.96 (0.52-16.7) |

Insomnia

|                        |             |                         |                         |            |                  |                  |
|------------------------|-------------|-------------------------|-------------------------|------------|------------------|------------------|
| Control                | 427 (0.091) | 1.0 (ref)               | 1.0 (ref)               | 750 (0.66) | 1.0 (ref)        | 1.0 (ref)        |
| Patients with COVID-19 | 253 (0.21)  | <b>2.28 (1.95-2.66)</b> | <b>2.33 (1.99-2.72)</b> | 259 (0.23) | 1.10 (0.95-1.28) | 1.12 (0.97-1.30) |

Intracranial hemorrhage

|                        |            |                  |                  |            |                         |                         |
|------------------------|------------|------------------|------------------|------------|-------------------------|-------------------------|
| Control                | 87 (0.019) | 1.0 (ref)        | 1.0 (ref)        | 44 (0.039) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19 | 22 (0.018) | 0.97 (0.61-1.55) | 0.96 (0.60-1.54) | 22 (0.019) | <b>1.90 (1.10-3.28)</b> | <b>1.83 (1.06-3.18)</b> |

|                                   |             |                         |                         |            |                         |                         |  |
|-----------------------------------|-------------|-------------------------|-------------------------|------------|-------------------------|-------------------------|--|
| Ischemic stroke                   |             |                         |                         |            |                         |                         |  |
| Control                           | 155 (0.026) | 1.0 (ref)               | 1.0 (ref)               | 222 (0.19) | 1.0 (ref)               | 1.0 (ref)               |  |
| Patients with COVID-19            | 76 (0.062)  | <b>1.88 (1.43-2.47)</b> | <b>1.84 (1.40-2.43)</b> | 78 (0.068) | 1.23 (0.94-1.62)        | 1.18 (0.90-1.55)        |  |
| Mood disorder                     |             |                         |                         |            |                         |                         |  |
| Control                           | 640 (0.14)  | 1.0 (ref)               | 1.0 (ref)               | 949 (0.83) | 1.0 (ref)               | 1.0 (ref)               |  |
| Patients with COVID-19            | 375 (0.31)  | <b>2.26 (1.99-2.57)</b> | <b>2.29 (2.01-2.60)</b> | 375 (0.33) | <b>1.27 (1.12-1.44)</b> | <b>1.27 (1.12-1.44)</b> |  |
| Myoneural junction/muscle disease |             |                         |                         |            |                         |                         |  |
| Control                           | 13 (0.0028) | 1.0 (ref)               | 1.0 (ref)               | 19 (0.017) | 1.0 (ref)               | 1.0 (ref)               |  |
| Patients with COVID-19            | 3 (0.0024)  | 0.89 (0.25-3.11)        | 0.90 (0.25-3.18)        | 3 (0.0026) | 0.59 (0.17-2.08)        | 0.55 (0.16-1.93)        |  |
| Nerve/nerve root/plexus disorders |             |                         |                         |            |                         |                         |  |
| Control                           | 1232 (0.26) | 1.0 (ref)               | 1.0 (ref)               | 774 (0.68) | 1.0 (ref)               | 1.0 (ref)               |  |
| Patients with COVID-19            | 437 (0.36)  | <b>1.37 (1.23-1.52)</b> | <b>1.33 (1.19-1.49)</b> | 438 (0.38) | <b>2.02 (1.78-2.28)</b> | <b>1.95 (1.72-2.21)</b> |  |
| Parkinsonism                      |             |                         |                         |            |                         |                         |  |
| Control                           | 49 (0.010)  | 1.0 (ref)               | 1.0 (ref)               | 72 (0.063) | 1.0 (ref)               | 1.0 (ref)               |  |
| Patients with COVID-19            | 15 (0.012)  | 1.17 (0.66-2.09)        | 1.06 (0.59-1.89)        | 15 (0.013) | 0.67 (0.38-1.18)        | 0.63 (0.36-1.13)        |  |

|                                                   |                         |                         |                         |                     |                         |                         |
|---------------------------------------------------|-------------------------|-------------------------|-------------------------|---------------------|-------------------------|-------------------------|
| Psychotic disorder                                |                         |                         |                         |                     |                         |                         |
| Control                                           | 32 (0.0068)             | 1.0 (ref)               | 1.0 (ref)               | 68 (0.060)          | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                            | 8 (0.0065)              | 0.96 (0.44-2.08)        | 0.95 (0.44-2.07)        | 8 (0.0070)          | <b>0.41 (0.20-0.88)</b> | <b>0.41 (0.19-0.87)</b> |
| <b>Validation cohort</b>                          |                         |                         |                         |                     |                         |                         |
|                                                   | COVID-19 versus general |                         |                         | COVID-19 versus ARI |                         |                         |
|                                                   | (n=976,212)             |                         |                         | (n=148,096)         |                         |                         |
|                                                   | HR (95% CI)             |                         |                         | HR (95% CI)         |                         |                         |
|                                                   | Events (%)              | Model 3 <sup>*</sup>    | Model 4 <sup>‡</sup>    | Events (%)          | Model 3 <sup>*</sup>    | Model 4 <sup>‡</sup>    |
| Any neuropsychiatric outcomes                     |                         |                         |                         |                     |                         |                         |
| Control (general population or patients with ARI) | 6610 (1.11)             | 1.0 (ref)               | 1.0 (ref)               | 3230 (4.36)         | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                            | 11,133 (2.94)           | <b>2.72 (2.64-2.81)</b> | <b>2.51 (2.44-2.59)</b> | 8510 (11.49)        | <b>4.38 (4.20-4.56)</b> | <b>4.13 (3.96-4.31)</b> |
| Anxiety disorder                                  |                         |                         |                         |                     |                         |                         |
| Control                                           | 2931 (0.49)             | 1.0 (ref)               | 1.0 (ref)               | 1529 (2.06)         | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19                            | 4570 (1.21)             | <b>2.40 (2.29-2.51)</b> | <b>2.32 (2.22-2.43)</b> | 3452 (4.66)         | <b>3.70 (3.48-3.94)</b> | <b>3.64 (3.42-3.88)</b> |
| Cognitive deficit                                 |                         |                         |                         |                     |                         |                         |
| Control                                           | 19 (0.0032)             | 1.0 (ref)               | 1.0 (ref)               | 12 (0.016)          | 1.0 (ref)               | 1.0 (ref)               |

|                         |             |                          |                          |             |                          |                         |
|-------------------------|-------------|--------------------------|--------------------------|-------------|--------------------------|-------------------------|
| Patients with COVID-19  | 53 (0.014)  | <b>4.76 (2.82-8.05)</b>  | <b>3.37 (1.95-5.81)</b>  | 55 (0.074)  | <b>6.25 (3.33-11.74)</b> | <b>4.50 (2.36-8.59)</b> |
| Encephalitis            |             |                          |                          |             |                          |                         |
| Control                 | 14 (0.0023) | 1.0 (ref)                | 1.0 (ref)                | 7 (0.0095)  | 1.0 (ref)                | 1.0 (ref)               |
| Patients with COVID-19  | 60 (0.016)  | <b>7.09 (3.96-12.70)</b> | <b>5.52 (3.03-10.04)</b> | 37 (0.050)  | <b>7.03 (3.11-15.86)</b> | <b>4.5 (1.94-10.40)</b> |
| Epilepsy/seizures       |             |                          |                          |             |                          |                         |
| Control                 | 215 (0.04)  | 1.0 (ref)                | 1.0 (ref)                | 97 (0.13)   | 1.0 (ref)                | 1.0 (ref)               |
| Patients with COVID-19  | 471 (0.12)  | <b>3.55 (3.02-4.18)</b>  | <b>2.73 (2.31-3.23)</b>  | 347 (0.47)  | <b>5.37 (4.26-6.76)</b>  | <b>4.18 (3.30-5.29)</b> |
| Guillain-Barré syndrome |             |                          |                          |             |                          |                         |
| Control                 | 7 (0.0012)  | 1.0 (ref)                | 1.0 (ref)                | 7 (0.0095)  | 1.0 (ref)                | 1.0 (ref)               |
| Patients with COVID-19  | 24 (0.0063) | <b>5.51 (2.37-12.81)</b> | <b>3.82 (1.59-9.14)</b>  | 14 (0.019)  | <b>2.56 (1.02-6.47)</b>  | <b>2.18 (0.85-5.60)</b> |
| Insomnia                |             |                          |                          |             |                          |                         |
| Control                 | 2678 (0.45) | 1.0 (ref)                | 1.0 (ref)                | 1368 (1.85) | 1.0 (ref)                | 1.0 (ref)               |
| Patients with COVID-19  | 4786 (1.26) | <b>2.86 (2.73-3.00)</b>  | <b>2.59 (2.47-2.72)</b>  | 3846 (5.19) | <b>4.53 (4.26-4.83)</b>  | <b>4.21 (3.94-4.49)</b> |
| Intracranial hemorrhage |             |                          |                          |             |                          |                         |
| Control                 | 115 (0.019) | 1.0 (ref)                | 1.0 (ref)                | 45 (0.061)  | 1.0 (ref)                | 1.0 (ref)               |
| Patients with COVID-19  | 303 (0.080) | <b>4.47 (3.60-5.54)</b>  | <b>3.64 (2.91-4.54)</b>  | 182 (0.25)  | <b>5.70 (4.09-7.93)</b>  | <b>4.46 (3.18-6.26)</b> |

## Ischemic stroke

|                        |             |                         |                         |            |                         |                         |
|------------------------|-------------|-------------------------|-------------------------|------------|-------------------------|-------------------------|
| Control                | 458 (0.077) | 1.0 (ref)               | 1.0 (ref)               | 187 (0.25) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19 | 828 (0.22)  | <b>3.09 (2.76-3.47)</b> | <b>2.75 (2.45-3.09)</b> | 506 (0.68) | <b>4.03 (3.40-4.79)</b> | <b>3.59 (3.01-4.27)</b> |

## Mood disorder

|                        |             |                         |                         |             |                         |                         |
|------------------------|-------------|-------------------------|-------------------------|-------------|-------------------------|-------------------------|
| Control                | 2174 (0.36) | 1.0 (ref)               | 1.0 (ref)               | 996 (1.35)  | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19 | 3324 (0.88) | <b>2.31 (2.19-2.44)</b> | <b>2.24 (2.12-2.37)</b> | 2690 (3.63) | <b>4.52 (4.19-4.87)</b> | <b>4.42 (4.10-4.77)</b> |

## Myoneural junction/muscle disease

|                        |             |                         |                         |            |                         |                         |
|------------------------|-------------|-------------------------|-------------------------|------------|-------------------------|-------------------------|
| Control                | 63 (0.011)  | 1.0 (ref)               | 1.0 (ref)               | 29 (0.039) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19 | 128 (0.034) | <b>3.43 (2.53-4.63)</b> | <b>2.88 (2.11-3.94)</b> | 82 (0.11)  | <b>4.27 (2.76-6.61)</b> | <b>3.63 (2.32-5.67)</b> |

## Nerve/nerve root/plexus disorders

|                        |             |                         |                         |            |                         |                         |
|------------------------|-------------|-------------------------|-------------------------|------------|-------------------------|-------------------------|
| Control                | 816 (0.14)  | 1.0 (ref)               | 1.0 (ref)               | 342 (0.46) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19 | 1100 (0.29) | <b>2.22 (2.03-2.44)</b> | <b>2.09 (1.91-2.30)</b> | 740 (1.00) | <b>3.58 (3.13-4.08)</b> | <b>3.41 (2.98-3.90)</b> |

## Parkinsonism

|                        |            |                         |                         |            |                         |                         |
|------------------------|------------|-------------------------|-------------------------|------------|-------------------------|-------------------------|
| Control                | 92 (0.015) | 1.0 (ref)               | 1.0 (ref)               | 30 (0.041) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19 | 78 (0.021) | <b>1.40 (1.04-1.90)</b> | <b>1.21 (0.89-1.66)</b> | 58 (0.078) | <b>3.25 (2.04-5.16)</b> | <b>2.77 (1.72-4.44)</b> |

## Psychotic disorder

|                        |             |                         |                         |            |                         |                         |
|------------------------|-------------|-------------------------|-------------------------|------------|-------------------------|-------------------------|
| Control                | 234 (0.039) | 1.0 (ref)               | 1.0 (ref)               | 101 (0.14) | 1.0 (ref)               | 1.0 (ref)               |
| Patients with COVID-19 | 446 (0.12)  | <b>3.02 (2.58-3.54)</b> | <b>2.44 (2.07-2.87)</b> | 345 (0.47) | <b>5.60 (4.45-7.04)</b> | <b>4.77 (3.78-6.02)</b> |

ARI, another respiratory infection; CI, confidence interval; HR, hazard ratio.

\* **Models 1 and 3:** adjusted for age (20–39, 40–59, and  $\geq 60$  years) and sex.

<sup>II</sup> **Model 2:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and  $\geq 2$ ); obesity (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], and obese [ $\geq 25.0 \text{ kg/m}^2$ ]); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$ , systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ ); fasting blood glucose ( $< 100$  and  $\geq 100 \text{ mg/dL}$ ); serum total cholesterol ( $< 200$ ,  $200\text{--}240$ , and  $\geq 240 \text{ mg/dL}$ ); glomerular filtration rate ( $< 60$ ,  $60\text{--}90$ , and  $\geq 90 \text{ mL/min/1.73 m}^2$ ); smoking status (non-, ex-, and current smoker); alcohol consumption (drinks;  $< 1$ ,  $1\text{--}2$ ,  $3\text{--}4$ , and  $\geq 5$  days per week); aerobic physical activity (sufficient and insufficient); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); and outpatients contact in the year before index date (0,  $1\text{--}4$ , and  $\geq 5$  times).

‡ **Model 4:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; insurance status (insured or dependent); body mass index (underweight [ $< 18.5$  kg/m<sup>2</sup>], normal [18.5–23.0 kg/m<sup>2</sup>], overweight [23.0–25.0 kg/m<sup>2</sup>], and obese [ $\geq 25.0$  kg/m<sup>2</sup>]); blood pressure (systolic blood pressure  $< 140$  mmHg and diastolic blood pressure  $< 90$  mmHg and systolic blood pressure  $\geq 140$  mmHg or diastolic blood pressure  $\geq 90$  mmHg); fasting blood glucose ( $< 100$  and  $\geq 100$  mg/dL); total serum cholesterol ( $< 200$ , 200–240, and  $\geq 240$  mg/dL); glomerular filtration rate ( $< 60$ , 60–90, and  $\geq 90$  mL/min/1.73 m<sup>2</sup>); smoking status (non- and current smoker); alcohol consumption (rarely, sometimes, and every day); aerobic physical activity (sufficient and insufficient); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); and outpatients contact in the year before index date (0, 1-4, and  $\geq 5$  times).

Data in bold indicate significant differences ( $P < 0.05$ ).

**Table S19.** Subgroup analysis (COVID-19 versus general population) of HR (95% CI) of neuropsychiatric outcomes following COVID-19 diagnosis stratified by vaccination, COVID-19 severity, and SARS-CoV-2 strain in the discovery cohort (complete case analysis method)

| Factors                       | Group                                               | Short-term neuropsychiatric risk |                         | Long-term neuropsychiatric sequelae |                         |
|-------------------------------|-----------------------------------------------------|----------------------------------|-------------------------|-------------------------------------|-------------------------|
|                               |                                                     | Events/total number              | Adjusted HR*            | Events/total number                 | Adjusted HR*            |
|                               |                                                     | (%)                              | (95% CI)                | (%)                                 | (95% CI)                |
| COVID-19 severity             | None                                                | 688/468,291 (0.15)               | 1.0 (ref)               | 3226/468,291 (0.69)                 | 1.0 (ref)               |
|                               | Mild COVID-19                                       | 290/106,052 (0.27)               | <b>1.93 (1.68-2.22)</b> | 1021/106,052 (0.96)                 | <b>1.54 (1.43-1.65)</b> |
|                               | Moderate to severe COVID-19                         | 138/16,831 (0.82)                | <b>4.29 (3.55-5.20)</b> | 412/16,831 (2.45)                   | <b>2.41 (2.16-2.67)</b> |
| SARS-CoV-2 vaccination dosage | None                                                | 688/468,291 (0.15)               | 1.0 (ref)               | 3226/468,291 (0.69)                 | 1.0 (ref)               |
|                               | COVID-19 without SARS-CoV-2 vaccination             | 283/52,844 (0.54)                | <b>3.75 (3.26-4.31)</b> | 1195/52,844 (2.26)                  | <b>1.92 (1.80-2.05)</b> |
|                               | COVID-19 after SARS-CoV-2 vaccination received once | 43/11,856 (0.36)                 | <b>2.48 (1.82-3.38)</b> | 117/11,856 (0.99)                   | <b>1.36 (1.13-1.64)</b> |

|                                |                                                              |                    |                         |                     |                         |
|--------------------------------|--------------------------------------------------------------|--------------------|-------------------------|---------------------|-------------------------|
|                                | COVID-19 after SARS-CoV-2 vaccination received twice or more | 102/58,183 (0.18)  | 1.13 (0.92-1.39)        | 121/58,183 (0.21)   | 0.93 (0.77-1.11)        |
| Type of SARS-CoV-2 vaccination | None                                                         | 688/468,291 (0.15) | 1.0 (ref)               | 3226/468,291 (0.69) | 1.0 (ref)               |
|                                | COVID-19 without SARS-CoV-2 vaccination                      | 283/52,844 (0.54)  | <b>3.74 (3.25-4.30)</b> | 1195/52,844 (2.26)  | <b>1.92 (1.80-2.05)</b> |
|                                | COVID-19 with mRNA SARS-CoV-2 vaccination                    | 61/33,153 (0.18)   | <b>1.39 (1.07-1.81)</b> | 106/33,153 (0.32)   | <b>1.24 (1.02-1.51)</b> |
|                                | COVID-19 with viral vector SARS-CoV-2 vaccination            | 76/28,873 (0.26)   | <b>1.46 (1.15-1.86)</b> | 126/28,873 (0.44)   | 1.03 (0.86-1.24)        |
|                                | COVID-19 with both types of SARS-CoV-2 vaccination           | 8/8013 (0.10)      | 0.67 (0.33-1.35)        | 6/8013 (0.075)      | 0.66 (0.30-1.48)        |
| Strain type (original)         | None‡                                                        | 306/150,911 (0.20) | 1.0 (ref)               | 2529/150,911 (1.68) | 1.0 (ref)               |
|                                | Original COVID-19                                            | 244/39,203 (0.62)  | <b>3.04 (2.56-3.60)</b> | 1133/39,203 (2.89)  | <b>1.74 (1.62-1.87)</b> |
| Strain type (delta)            | None‡                                                        | 382/317,380 (0.12) | 1.0 (ref)               | 697/317,380 (0.22)  | 1.0 (ref)               |
|                                | Delta COVID-19                                               | 184/83,680 (0.22)  | <b>1.80 (1.51-2.15)</b> | 300/83,680 (0.36)   | <b>1.62 (1.41-1.85)</b> |

HR, hazard ratio; CI, confidence interval; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

\* **adjusted HR:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and  $\geq 2$ ); obesity (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], and obese [ $\geq 25.0 \text{ kg/m}^2$ ]); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$ , systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ ); fasting blood glucose ( $< 100$  and  $\geq 100 \text{ mg/dL}$ ); serum total cholesterol ( $< 200$ ,  $200\text{--}240$ , and  $\geq 240 \text{ mg/dL}$ ); glomerular filtration rate ( $< 60$ ,  $60\text{--}90$ , and  $\geq 90 \text{ mL/min/1.73 m}^2$ ); smoking status (non-, ex-, and current smoker); alcohol consumption (drinks;  $< 1$ ,  $1\text{--}2$ ,  $3\text{--}4$ , and  $\geq 5$  days per week); aerobic physical activity (sufficient and insufficient); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); and outpatients contact in the year before index date (0,  $1\text{--}4$ , and  $\geq 5$  times).

‡ Comparators defined only 1:4 matched comparators in each patient group at the same index date to reduce an immortal bias.

Data in bold indicate significant differences ( $P < 0.05$ ).

**Table S20.** Time attenuation effect analysis of HR (95% CI) for **long-term sequelae risk** of neuropsychiatric outcomes following COVID-19 diagnosis in discovery and validation cohorts, with a two-sided test (complete case analysis method)

|                           | COVID-19 versus general |         |                         |         | COVID-19 versus ARI     |         |                         |         |
|---------------------------|-------------------------|---------|-------------------------|---------|-------------------------|---------|-------------------------|---------|
|                           | Discovery cohort*       | P value | Validation cohort‡      | P value | Discovery cohort*       | P value | Validation cohort‡      | P value |
| Any neurological outcomes |                         |         |                         |         |                         |         |                         |         |
| Within 6 months           | <b>1.79 (1.67-1.92)</b> | <0.001  | <b>2.89 (2.77-3.01)</b> | <0.001  | <b>1.18 (1.09-1.28)</b> | <0.001  | <b>3.96 (3.73-4.20)</b> | <0.001  |
| Between 6 to 12 months    | <b>1.51 (1.32-1.72)</b> | <0.001  | <b>2.11 (2.00-2.23)</b> | <0.001  | <b>1.28 (1.12-1.46)</b> | <0.001  | <b>4.44 (4.10-4.80)</b> | <0.001  |
| After 12 months           | 1.21 (0.59-2.48)        | 0.602   | <b>2.04 (1.88-2.22)</b> | <0.001  | 1.20 (0.96-1.49)        | 0.106   | <b>3.04 (2.77-3.35)</b> | <0.001  |

ARI, another respiratory infection; CI, confidence interval; HR, hazard ratio.

\* **adjusted HR:** adjusted for age (20–39, 40–59, and ≥ 60 years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and ≥ 2); obesity (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], and obese [ $\geq 25.0 \text{ kg/m}^2$ ]); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$ , systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ ); fasting blood glucose ( $< 100$  and  $\geq 100 \text{ mg/dL}$ ); serum total cholesterol ( $< 200$ ,  $200\text{--}240$ , and  $\geq 240 \text{ mg/dL}$ ); glomerular filtration rate ( $< 60$ ,  $60\text{--}90$ , and  $\geq 90 \text{ mL/min/1.73 m}^2$ ); smoking status (non-,

ex-, and current smoker); alcohol consumption (drinks; < 1, 1–2, 3–4, and  $\geq 5$  days per week); aerobic physical activity (sufficient and insufficient); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); and outpatients contact in the year before index date (0, 1–4, and  $\geq 5$  times).

‡ **adjusted HR:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; insurance status (insured or dependent); body mass index (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], and obese [ $\geq 25.0 \text{ kg/m}^2$ ]); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$  and systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ ); fasting blood glucose ( $< 100$  and  $\geq 100 \text{ mg/dL}$ ); total serum cholesterol ( $< 200$ ,  $200\text{--}240$ , and  $\geq 240 \text{ mg/dL}$ ); glomerular filtration rate ( $< 60$ ,  $60\text{--}90$ , and  $\geq 90 \text{ mL/min/1.73 m}^2$ ); smoking status (non- and current smoker); alcohol consumption (rarely, sometimes, and every day); aerobic physical activity (sufficient and insufficient); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); and outpatients contact in the year before index date (0, 1–4, and  $\geq 5$  times).

Data in bold indicate significant differences ( $P < 0.05$ ).

**Table S21.** Hazard ratio (95% CI) for the **short-term risk** of incident neuropsychiatric events following COVID-19 diagnosis of patients in the propensity score-matched discovery and validation cohorts, with a two-sided test (missing indicator method), presenting the P value from Table

2

| Discovery cohort              | COVID-19 versus general   |         |                           |         | COVID-19 versus ARI       |         |                           |         |
|-------------------------------|---------------------------|---------|---------------------------|---------|---------------------------|---------|---------------------------|---------|
|                               | (n=1,831,237)             |         |                           |         | (n= 531,020)              |         |                           |         |
|                               | Model 1 <sup>*</sup>      |         | Model 2 <sup>  </sup>     |         | Model 1 <sup>*</sup>      |         | Model 2 <sup>  </sup>     |         |
|                               | HR (95% CI)               | P value | HR (95% CI)               | P value | HR (95% CI)               | P value | HR (95% CI)               | P value |
| Any neuropsychiatric outcomes | <b>2.43 (2.26-2.61)</b>   | <0.001  | <b>2.35 (2.16-2.56)</b>   | <0.001  | <b>1.42 (1.30-1.56)</b>   | <0.001  | <b>1.36 (1.23-1.51)</b>   | <0.001  |
| Anxiety disorder              | <b>3.23 (2.87-3.65)</b>   | <0.001  | <b>3.40 (2.96-3.90)</b>   | <0.001  | <b>1.44 (1.24-1.66)</b>   | <0.001  | <b>1.45 (1.23-1.70)</b>   | <0.001  |
| Encephalitis                  | <b>19.82 (8.85-44.37)</b> | <0.001  | <b>12.34 (5.11-29.80)</b> | <0.001  | <b>17.83 (4.29-74.12)</b> | <0.001  | <b>12.95 (2.97-56.48)</b> | <0.001  |
| Epilepsy/seizures             | 1.91 (0.98-3.72)          | 0.058   | 1.82 (0.79-4.22)          | 0.162   | 1.86 (0.74-4.67)          | 0.185   | 1.73 (0.60-4.96)          | 0.310   |
| Guillain-Barré syndrome       | <b>7.47 (1.37-40.78)</b>  | 0.020   | <b>11.89 (2.09-67.55)</b> | 0.005   | 0.61 (0.15-2.54)          | 0.493   | 0.95 (0.22-4.06)          | 0.948   |
| Insomnia                      | <b>5.02 (4.22-5.98)</b>   | <0.001  | <b>5.36 (4.42-6.50)</b>   | <0.001  | <b>1.64 (1.34-2.00)</b>   | <0.001  | <b>1.73 (1.39-2.14)</b>   | <0.001  |
| Intracranial hemorrhage       | 0.66 (0.34-1.30)          | 0.233   | 0.59 (0.25-1.36)          | 0.215   | 1.00 (0.38-2.67)          | 0.995   | 1.11 (0.36-3.46)          | 0.855   |
| Ischemic stroke               | <b>1.84 (1.40-2.43)</b>   | <0.001  | <b>1.64 (1.17-2.29)</b>   | 0.004   | <b>2.20 (1.46-3.33)</b>   | <0.001  | <b>1.88 (1.18-2.99)</b>   | 0.008   |

|                                   |                            |         |                            |         |                           |         |                           |         |
|-----------------------------------|----------------------------|---------|----------------------------|---------|---------------------------|---------|---------------------------|---------|
| Mood disorder                     | <b>2.64 (2.29-3.03)</b>    | <0.001  | <b>2.49 (2.10-2.94)</b>    | <0.001  | <b>1.52 (1.27-1.81)</b>   | <0.001  | <b>1.31 (1.06-1.60)</b>   | 0.012   |
| Nerve/nerve root/plexus disorders | 0.92 (0.77-1.10)           | 0.350   | 0.97 (0.79-1.19)           | 0.788   | 1.09 (0.86-1.38)          | 0.563   | 1.16 (0.89-1.51)          | 0.904   |
| Myoneural junction/muscle disease | 0.42 (0.05-3.33)           | 0.413   | 0.64 (0.08-5.12)           | 0.675   | 0.49 (0.05-5.43)          | 0.481   | 0.86 (0.08-9.71)          | 0.266   |
| Parkinsonism                      | 1.45 (0.70-3.02)           | 0.322   | 0.91 (0.35-2.41)           | 0.850   | 0.63 (0.28-1.38)          | 0.248   | 0.44 (0.16-1.22)          | 0.115   |
| Psychotic disorder                | <b>4.17 (2.24-7.75)</b>    | <0.001  | 2.01 (0.80-5.06)           | 0.139   | 1.32 (0.69-2.54)          | 0.400   | 0.65 (0.25-1.67)          | 0.368   |
| <b>Validation cohort</b>          | COVID-19 versus general    |         |                            |         | COVID-19 versus ARI       |         |                           |         |
|                                   | (n=2,059,727)              |         |                            |         | (n= 309,794)              |         |                           |         |
|                                   | Model 3*                   |         | Model 4‡                   |         | Model 3*                  |         | Model 4‡                  |         |
|                                   | HR (95% CI)                | P value | HR (95% CI)                | P value | HR (95% CI)               | P value | HR (95% CI)               | P value |
| Any neuropsychiatric outcomes     | <b>10.16 (9.65-10.70)</b>  | <0.001  | <b>8.64 (8.20-9.10)</b>    | <0.001  | <b>2.70 (2.58-2.82)</b>   | <0.001  | <b>2.38 (2.28-2.49)</b>   | <0.001  |
| Anxiety disorder                  | <b>5.08 (4.67-5.52)</b>    | <0.001  | <b>4.76 (4.37-5.18)</b>    | <0.001  | <b>1.31 (1.22-1.40)</b>   | <0.001  | <b>1.27 (1.18-1.36)</b>   | <0.001  |
| Encephalitis                      | NA                         | 0.934   | NA                         | 0.922   | <b>14.99 (5.45-41.25)</b> | <0.001  | <b>11.76 (4.25-32.57)</b> | <0.001  |
| Epilepsy/seizures                 | <b>16.20 (12.57-20.87)</b> | <0.001  | <b>13.16 (10.18-17.02)</b> | <0.001  | <b>3.67 (3.04-4.44)</b>   | <0.001  | <b>2.96 (2.44-3.59)</b>   | <0.001  |
| Guillain-Barré syndrome           | NA                         | 0.943   | NA                         | 0.916   | <b>8.75 (3.11-24.62)</b>  | <0.001  | <b>7.61 (2.68-21.56)</b>  | <0.001  |
| Insomnia                          | <b>10.08 (9.25-10.97)</b>  | <0.001  | <b>8.01 (7.35-8.74)</b>    | <0.001  | <b>2.06 (1.93-2.21)</b>   | <0.001  | <b>1.79 (1.67-1.91)</b>   | <0.001  |

|                                   |                            |        |                            |        |                            |        |                          |        |
|-----------------------------------|----------------------------|--------|----------------------------|--------|----------------------------|--------|--------------------------|--------|
| Intracranial hemorrhage           | <b>62.62 (44.54-88.05)</b> | <0.001 | <b>47.66 (33.84-67.13)</b> | <0.001 | <b>13.81 (10.82-17.63)</b> | <0.001 | <b>9.89 (7.72-12.66)</b> | <0.001 |
| Ischemic stroke                   | <b>25.31 (21.17-30.26)</b> | <0.001 | <b>21.61 (18.05-25.87)</b> | <0.001 | <b>7.37 (6.36-8.54)</b>    | <0.001 | <b>6.40 (5.52-7.43)</b>  | <0.001 |
| Mood disorder                     | <b>3.44 (3.12-3.80)</b>    | <0.001 | <b>3.19 (2.89-3.53)</b>    | <0.001 | <b>1.65 (1.49-1.82)</b>    | <0.001 | <b>1.59 (1.44-1.76)</b>  | <0.001 |
| Myoneural junction/muscle disease | <b>16.71 (8.71-32.04)</b>  | <0.001 | <b>14.24 (7.37-27.49)</b>  | <0.001 | <b>2.59 (1.66-4.04)</b>    | <0.001 | <b>2.24 (1.42-3.52)</b>  | <0.001 |
| Nerve/nerve root/plexus disorders | <b>7.86 (6.67-9.27)</b>    | <0.001 | <b>7.52 (6.37-8.89)</b>    | <0.001 | <b>3.27 (2.75-3.89)</b>    | <0.001 | <b>3.17 (2.66-3.77)</b>  | <0.001 |
| Parkinsonism                      | <b>4.26 (2.43-7.47)</b>    | <0.001 | <b>3.73 (2.10-6.62)</b>    | <0.001 | 0.81 (0.49-1.31)           | 0.386  | 0.80 (0.48-1.31)         | 0.368  |
| Psychotic disorder                | <b>9.86 (7.41-13.13)</b>   | <0.001 | <b>6.83 (5.09-9.16)</b>    | <0.001 | <b>1.63 (1.32-2.01)</b>    | <0.001 | <b>1.27 (1.02-1.58)</b>  | 0.032  |

ARI, another respiratory infection; CI, confidence interval; HR, hazard ratio.

\* **Models 1 and 3:** adjusted for age (20–39, 40–59, and  $\geq 60$  years) and sex.

¶ **Model 2:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and  $\geq 2$ ); obesity (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], obese [ $\geq 25.0 \text{ kg/m}^2$ ], and unknown); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$ , systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ , and unknown); fasting blood glucose ( $< 100$ ,  $\geq 100 \text{ mg/dL}$ , and unknown); serum total cholesterol ( $< 200$ ,  $200\text{--}240$ ,  $\geq 240 \text{ mg/dL}$ , and unknown); glomerular filtration rate ( $< 60$ ,  $60\text{--}90$ ,

$\geq 90$  mL/min/1.73 m<sup>2</sup>, and unknown); smoking status (non-, ex-, current smoker, and unknown); alcohol consumption (drinks; < 1, 1–2, 3–4,  $\geq 5$  days per week, and unknown); aerobic physical activity (sufficient, insufficient, and unknown); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); outpatients contact in the year before index date (0, 1–4, and  $\geq 5$  times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no], fasting blood glucose missing indicator [yes or no], serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no], smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes or no]).

‡ **Model 4:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; insurance status (insured or dependent); body mass index (underweight [ $< 18.5$  kg/m<sup>2</sup>]; normal [18.5–23.0 kg/m<sup>2</sup>], overweight [23.0–25.0 kg/m<sup>2</sup>], obese [ $\geq 25.0$  kg/m<sup>2</sup>], and unknown); blood pressure (systolic blood pressure  $< 140$  mmHg and diastolic blood pressure  $< 90$  mmHg, systolic blood pressure  $\geq 140$  mmHg or diastolic blood pressure  $\geq 90$  mmHg, and unknown); fasting blood glucose ( $< 100$ ,  $\geq 100$  mg/dL, and unknown); serum total cholesterol ( $< 200$ , 200–240,  $\geq 240$  mg/dL, and unknown); glomerular filtration rate ( $< 60$ , 60–90,  $\geq 90$  mL/min/1.73 m<sup>2</sup>, and unknown); smoking status (non-, current smoker, and unknown); alcohol consumption (rarely, sometimes, every day, and unknown); aerobic physical activity (sufficient, insufficient, and unknown); previous history of

cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); outpatients contact in the year before index date (0, 1-4, and  $\geq 5$  times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no], fasting blood glucose missing indicator [yes or no], serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no], smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes or no]).

Data in bold indicate significant differences ( $P < 0.05$ ).

**Table S22.** Hazard ratio (95% CI) for the **long-term sequelae risk** of neuropsychiatric events following COVID-19 diagnosis of patients in the propensity score-matched discovery and validation cohorts, with a two-sided test (missing indicator method), presenting the P value from Table 3 and S14

| Discovery cohort              | COVID-19 versus general  |         |                          |         | COVID-19 versus ARI     |         |                         |         |
|-------------------------------|--------------------------|---------|--------------------------|---------|-------------------------|---------|-------------------------|---------|
|                               | (n=1,831,237)            |         |                          |         | (n= 531,020)            |         |                         |         |
|                               | Model 1*                 |         | Model 2 <sup>II</sup>    |         | Model 1*                |         | Model 2 <sup>II</sup>   |         |
|                               | HR (95% CI)              | P value | HR (95% CI)              | P value | HR (95% CI)             | P value | HR (95% CI)             | P value |
| Any neuropsychiatric outcomes | <b>1.79 (1.72-1.85)</b>  | <0.001  | <b>1.71 (1.64-1.79)</b>  | <0.001  | <b>1.71 (1.65-1.78)</b> | <0.001  | <b>1.60 (1.53-1.68)</b> | <0.001  |
| Anxiety disorder              | <b>2.13 (2.01-2.27)</b>  | <0.001  | <b>2.23 (2.08-2.40)</b>  | <0.001  | <b>1.69 (1.58-1.80)</b> | <0.001  | <b>1.69 (1.57-1.82)</b> | <0.001  |
| Cognitive deficit             | <b>6.00 (3.68-9.78)</b>  | <0.001  | <b>2.67 (1.39-5.15)</b>  | 0.003   | 1.01 (0.70-1.45)        | 0.963   | 0.49 (0.28-0.85)        | 0.011   |
| Encephalitis                  | <b>4.47 (2.90-6.89)</b>  | <0.001  | <b>2.15 (1.18-3.94)</b>  | 0.013   | <b>5.30 (3.09-9.10)</b> | <0.001  | <b>2.74 (1.36-5.50)</b> | 0.005   |
| Epilepsy/seizures             | <b>1.53 (1.08-2.16)</b>  | 0.016   | 0.90 (0.54-1.51)         | 0.701   | 1.17 (0.81-1.68)        | 0.406   | 0.69 (0.41-1.16)        | 0.165   |
| Guillain-Barré syndrome       | <b>4.30 (1.66-11.15)</b> | 0.003   | <b>4.63 (1.66-12.98)</b> | 0.004   | 1.81 (0.72-4.59)        | 0.210   | 1.94 (0.72-5.25)        | 0.191   |
| Insomnia                      | <b>2.47 (2.25-2.72)</b>  | <0.001  | <b>2.40 (2.15-2.69)</b>  | <0.001  | <b>1.41 (1.28-1.55)</b> | <0.001  | <b>1.32 (1.18-1.48)</b> | <0.001  |
| Intracranial hemorrhage       | 0.96 (0.72-1.27)         | 0.769   | 0.87 (0.61-1.23)         | 0.414   | <b>2.38 (1.69-3.35)</b> | <0.001  | <b>1.95 (1.31-2.90)</b> | <0.001  |
| Ischemic stroke               | <b>2.21 (1.88-2.60)</b>  | <0.001  | <b>2.00 (1.64-2.44)</b>  | <0.001  | <b>1.92 (1.62-2.28)</b> | <0.001  | <b>1.63 (1.33-1.99)</b> | <0.001  |

|                                   |                           |         |                          |         |                          |         |                          |         |
|-----------------------------------|---------------------------|---------|--------------------------|---------|--------------------------|---------|--------------------------|---------|
| Mood disorder                     | <b>2.07 (1.94-2.22)</b>   | <0.001  | <b>1.93 (1.77-2.09)</b>  | <0.001  | <b>1.84 (1.71-1.98)</b>  | <0.001  | <b>1.62 (1.48-1.76)</b>  | <0.001  |
| Nerve/nerve root/plexus disorders | <b>1.40 (1.30-1.50)</b>   | <0.001  | <b>1.47 (1.36-1.59)</b>  | <0.001  | <b>2.41 (2.22-2.62)</b>  | <0.001  | <b>2.47 (2.25-2.71)</b>  | <0.001  |
| Myoneural junction/muscle disease | 1.43 (0.66-3.07)          | 0.364   | 1.13 (0.43-2.98)         | 0.811   | 0.91 (0.42-1.96)         | 0.802   | 0.78 (0.30-2.04)         | 0.613   |
| Parkinsonism                      | <b>1.55 (1.11-2.17)</b>   | <0.001  | 1.08 (0.71-1.66)         | 0.715   | 1.09 (0.78-1.53)         | 0.613   | 0.82 (0.54-1.26)         | 0.375   |
| Psychotic disorder                | <b>1.72 (1.23-2.41)</b>   | 0.002   | 0.94 (0.56-1.59)         | 0.817   | 0.89 (0.64-1.23)         | 0.470   | 0.46 (0.27-0.77)         | 0.003   |
| <b>Validation cohort</b>          | COVID-19 versus general   |         |                          |         | COVID-19 versus ARI      |         |                          |         |
|                                   | (n=2,059,727)             |         |                          |         | (n= 309,794)             |         |                          |         |
|                                   | Model 3*                  |         | Model 4‡                 |         | Model 3*                 |         | Model 4‡                 |         |
|                                   | HR (95% CI)               | P value | HR (95% CI)              | P value | HR (95% CI)              | P value | HR (95% CI)              | P value |
| Any neuropsychiatric outcomes     | <b>2.89 (2.83-2.95)</b>   | <0.001  | <b>2.67 (2.61-2.73)</b>  | <0.001  | <b>4.53 (4.40-4.67)</b>  | <0.001  | <b>4.28 (4.15-4.41)</b>  | <0.001  |
| Anxiety disorder                  | <b>2.58 (2.50-2.67)</b>   | <0.001  | <b>2.50 (2.42-2.58)</b>  | <0.001  | <b>3.81 (3.65-3.98)</b>  | <0.001  | <b>3.74 (3.58-3.91)</b>  | <0.001  |
| Cognitive deficit                 | <b>5.44 (3.74-7.93)</b>   | <0.001  | <b>3.72 (2.51-5.52)</b>  | <0.001  | <b>5.12 (3.43-7.65)</b>  | <0.001  | <b>3.63 (2.40-5.50)</b>  | <0.001  |
| Encephalitis                      | <b>11.31 (6.89-18.56)</b> | <0.001  | <b>8.63 (5.21-14.30)</b> | <0.001  | <b>7.90 (4.28-14.59)</b> | <0.001  | <b>5.59 (2.99-10.46)</b> | <0.001  |
| Epilepsy/seizures                 | <b>3.95 (3.52-4.43)</b>   | <0.001  | <b>3.05 (2.71-3.44)</b>  | <0.001  | <b>5.14 (4.39-6.02)</b>  | <0.001  | <b>4.07 (3.46-4.78)</b>  | <0.001  |
| Guillain-Barré syndrome           | <b>4.83 (2.82-8.26)</b>   | <0.001  | <b>4.01 (2.32-6.95)</b>  | <0.001  | <b>3.91 (1.82-8.41)</b>  | <0.001  | <b>3.34 (1.53-7.29)</b>  | 0.003   |

|                                   |                  |        |                  |        |                  |        |                  |        |
|-----------------------------------|------------------|--------|------------------|--------|------------------|--------|------------------|--------|
| Insomnia                          | 3.06 (2.96-3.16) | <0.001 | 2.77 (2.68-2.86) | <0.001 | 4.84 (4.63-5.06) | <0.001 | 4.49 (4.29-4.69) | <0.001 |
| Intracranial hemorrhage           | 4.37 (3.77-5.08) | <0.001 | 3.54 (3.03-4.12) | <0.001 | 6.42 (5.07-8.13) | <0.001 | 5.04 (3.96-6.41) | <0.001 |
| Ischemic stroke                   | 3.29 (3.03-3.57) | <0.001 | 2.90 (2.67-3.16) | <0.001 | 4.03 (3.57-4.55) | <0.001 | 3.56 (3.15-4.03) | <0.001 |
| Mood disorder                     | 2.48 (2.39-2.58) | <0.001 | 2.40 (2.31-2.49) | <0.001 | 4.59 (4.36-4.82) | <0.001 | 4.50 (4.28-4.74) | <0.001 |
| Myoneural junction/muscle disease | 4.20 (3.36-5.26) | <0.001 | 3.35 (2.66-4.23) | <0.001 | 5.03 (3.63-6.96) | <0.001 | 3.93 (2.82-5.49) | <0.001 |
| Nerve/nerve root/plexus disorders | 2.33 (2.19-2.49) | <0.001 | 2.21 (2.07-2.36) | <0.001 | 3.77 (3.42-4.15) | <0.001 | 3.62 (3.29-4.00) | <0.001 |
| Parkinsonism                      | 1.86 (1.50-2.32) | <0.001 | 1.62 (1.30-2.03) | <0.001 | 3.73 (2.71-5.14) | <0.001 | 3.40 (2.45-4.71) | <0.001 |
| Psychotic disorder                | 3.32 (2.98-3.70) | <0.001 | 2.69 (2.41-3.01) | <0.001 | 5.48 (4.72-6.36) | <0.001 | 4.68 (4.03-5.45) | <0.001 |

ARI, another respiratory infection; CI, confidence interval; HR, hazard ratio.

\* **Models 1 and 3:** adjusted for age (20–39, 40–59, and  $\geq 60$  years) and sex.

|| **Model 2:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and  $\geq 2$ ); obesity (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], obese [ $\geq 25.0 \text{ kg/m}^2$ ], and unknown); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$ , systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ , and unknown); fasting blood glucose ( $<$

100,  $\geq 100$  mg/dL, and unknown); serum total cholesterol ( $< 200$ , 200–240,  $\geq 240$  mg/dL, and unknown); glomerular filtration rate ( $< 60$ , 60–90,  $\geq 90$  mL/min/1.73 m<sup>2</sup>, and unknown); smoking status (non-, ex-, current smoker, and unknown); alcohol consumption (drinks;  $< 1$ , 1–2, 3–4,  $\geq 5$  days per week, and unknown); aerobic physical activity (sufficient, insufficient, and unknown); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); outpatients contact in the year before index date (0, 1–4, and  $\geq 5$  times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no], fasting blood glucose missing indicator [yes or no], serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no], smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes or no]).

‡ **Model 4:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; insurance status (insured or dependent); body mass index (underweight [ $< 18.5$  kg/m<sup>2</sup>]; normal [18.5–23.0 kg/m<sup>2</sup>], overweight [23.0–25.0 kg/m<sup>2</sup>], obese [ $\geq 25.0$  kg/m<sup>2</sup>], and unknown); blood pressure (systolic blood pressure  $< 140$  mmHg and diastolic blood pressure  $< 90$  mmHg, systolic blood pressure  $\geq 140$  mmHg or diastolic blood pressure  $\geq 90$  mmHg, and unknown); fasting blood glucose ( $< 100$ ,  $\geq 100$  mg/dL, and unknown); serum total cholesterol ( $< 200$ , 200–240,  $\geq 240$  mg/dL, and unknown); glomerular filtration rate ( $< 60$ , 60–90,  $\geq 90$  mL/min/1.73 m<sup>2</sup>, and unknown); smoking status (non-, current smoker, and unknown); alcohol

consumption (rarely, sometimes, every day, and unknown); aerobic physical activity (sufficient, insufficient, and unknown); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); outpatients contact in the year before index date (0, 1-4, and  $\geq 5$  times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no], fasting blood glucose missing indicator [yes or no], serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no], smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes or no]).

Data in bold indicate significant differences ( $P < 0.05$ ).

**Table S23.** Subgroup analysis (COVID-19 versus general population) of HR (95% CI) of neuropsychiatric outcomes following COVID-19 diagnosis stratified by vaccination, COVID-19 severity, and SARS-CoV-2 strain in the discovery cohort, with a two-sided test (missing indicator method) , presenting the P value from Table 4

| Group                                                        | Short-term neuropsychiatric risk |         | Long-term neuropsychiatric sequelae |         |
|--------------------------------------------------------------|----------------------------------|---------|-------------------------------------|---------|
|                                                              | Adjusted HR* (95% CI)            | P value | Adjusted HR* (95% CI)               | P value |
| COVID-19 severity                                            |                                  |         |                                     |         |
| Mild COVID-19                                                | <b>2.01 (1.84-2.21)</b>          | <0.001  | <b>1.57 (1.50-1.65)</b>             | <0.001  |
| Moderate to severe COVID-19                                  | <b>4.18 (3.68-4.74)</b>          | <0.001  | <b>2.35 (2.19-2.52)</b>             | <0.001  |
| SARS-CoV-2 vaccination dosage                                |                                  |         |                                     |         |
| COVID-19 without SARS-CoV-2 vaccination                      | <b>3.53 (3.21-3.87)</b>          | <0.001  | <b>1.89 (1.80-1.98)</b>             | <0.001  |
| COVID-19 after SARS-CoV-2 vaccination received once          | <b>2.37 (1.96-2.87)</b>          | <0.001  | <b>1.30 (1.16-1.46)</b>             | <0.001  |
| COVID-19 after SARS-CoV-2 vaccination received twice or more | <b>1.21 (1.05-1.38)</b>          | 0.006   | 1.05 (0.93-1.17)                    | 0.427   |
| Type of SARS-CoV-2 vaccination                               |                                  |         |                                     |         |

|                                                    |                         |        |                         |        |
|----------------------------------------------------|-------------------------|--------|-------------------------|--------|
| COVID-19 without SARS-CoV-2 vaccination            | <b>3.50 (3.19-3.85)</b> | <0.001 | <b>1.89 (1.80-1.98)</b> | <0.001 |
| COVID-19 with mRNA SARS-CoV-2 vaccination          | <b>1.39 (1.19-1.63)</b> | <0.001 | <b>1.24 (1.10-1.39)</b> | <0.001 |
| COVID-19 with viral vector SARS-CoV-2 vaccination  | <b>1.66 (1.41-1.94)</b> | <0.001 | 1.12 (0.99-1.26)        | 0.073  |
| COVID-19 with both types of SARS-CoV-2 vaccination | 0.61 (0.37-1.02)        | 0.059  | 0.66 (0.38-1.14)        | 0.136  |
| <hr/> Strain type (original)                       |                         |        |                         |        |
| Original COVID-19                                  | <b>2.94 (2.61-3.30)</b> | <0.001 | <b>1.72 (1.64-1.81)</b> | <0.001 |
| <hr/> Strain type (delta)                          |                         |        |                         |        |
| Delta COVID-19                                     | <b>1.88 (1.66-2.12)</b> | <0.001 | <b>1.67 (1.53-1.84)</b> | <0.001 |

HR, hazard ratio; CI, confidence interval; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

\* **adjusted HR:** adjusted for age (20–39, 40–59, and ≥ 60 years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and ≥ 2); obesity (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], obese [ $\geq 25.0 \text{ kg/m}^2$ ], and unknown); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood

pressure < 90 mmHg, systolic blood pressure  $\geq$  140 mmHg or diastolic blood pressure  $\geq$  90 mmHg, and unknown); fasting blood glucose (< 100,  $\geq$  100 mg/dL, and unknown); serum total cholesterol (< 200, 200–240,  $\geq$  240 mg/dL, and unknown); glomerular filtration rate (< 60, 60–90,  $\geq$  90 mL/min/1.73 m<sup>2</sup>, and unknown); smoking status (non-, ex-, current smoker, and unknown); alcohol consumption (drinks; < 1, 1–2, 3–4,  $\geq$  5 days per week, and unknown); aerobic physical activity (sufficient, insufficient, and unknown); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq$ 2 times); outpatients contact in the year before index date (0, 1–4, and  $\geq$ 5 times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no], fasting blood glucose missing indicator [yes or no], serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no], smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes or no]).

‡ Comparators defined only 1:4 matched comparators in each patient group at the same index date to reduce an immortal bias.

Data in bold indicate significant differences ( $P < 0.05$ ).

**Table S24.** Time attenuation effect analysis of HR (95% CI) for **long-term sequelae risk** of neuropsychiatric outcomes after SARS-CoV-2 infection in discovery and validation cohorts, with a two-sided test (missing indicator method), presenting the P value from Table 5

|                           | COVID-19 versus general |         |                         |         | COVID-19 versus ARI     |         |                         |         |
|---------------------------|-------------------------|---------|-------------------------|---------|-------------------------|---------|-------------------------|---------|
|                           | Discovery cohort*       | P value | Validation cohort‡      | P value | Discovery cohort*       | P value | Validation cohort‡      | P value |
| Any neurological outcomes |                         |         |                         |         |                         |         |                         |         |
| Within 6 months           | <b>1.82 (1.74-1.92)</b> | <0.001  | <b>3.03 (2.94-3.12)</b> | <0.001  | <b>1.46 (1.38-1.54)</b> | <0.001  | <b>4.18 (4.01-4.36)</b> | <0.001  |
| Between 6 to 12 months    | <b>1.39 (1.26-1.53)</b> | <0.001  | <b>2.26 (2.18-2.35)</b> | <0.001  | <b>1.48 (1.34-1.63)</b> | <0.001  | <b>4.45 (4.22-4.70)</b> | <0.001  |
| After 12 months           | 1.38 (0.84-2.25)        | 0.203   | <b>2.21 (2.09-2.34)</b> | <0.001  | <b>1.50 (1.28-1.76)</b> | <0.001  | <b>3.17 (2.97-3.39)</b> | <0.001  |

ARI, another respiratory infection; CI, confidence interval; HR, hazard ratio.

\* **Adjusted HR:** adjusted for age (20–39, 40–59, and ≥ 60 years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and ≥ 2); obesity (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], obese [ $\geq 25.0 \text{ kg/m}^2$ ], and unknown); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$ , systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ , and unknown); fasting blood glucose ( $< 100$ ,  $\geq 100 \text{ mg/dL}$ , and unknown); serum total cholesterol ( $< 200$ ,  $200\text{--}240$ ,  $\geq 240 \text{ mg/dL}$ , and unknown); glomerular filtration rate ( $< 60$ ,  $60\text{--}90$ ,

$\geq 90$  mL/min/1.73 m<sup>2</sup>, and unknown); smoking status (non-, ex-, current smoker, and unknown); alcohol consumption (drinks; < 1, 1–2, 3–4,  $\geq 5$  days per week, and unknown); aerobic physical activity (sufficient, insufficient, and unknown); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); outpatients contact in the year before index date (0, 1–4, and  $\geq 5$  times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no], fasting blood glucose missing indicator [yes or no], serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no], smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes or no]).

‡ **Adjusted HR:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; insurance status (insured or dependent); body mass index (underweight [ $< 18.5$  kg/m<sup>2</sup>]; normal [18.5–23.0 kg/m<sup>2</sup>], overweight [23.0–25.0 kg/m<sup>2</sup>], obese [ $\geq 25.0$  kg/m<sup>2</sup>], and unknown); blood pressure (systolic blood pressure  $< 140$  mmHg and diastolic blood pressure  $< 90$  mmHg, systolic blood pressure  $\geq 140$  mmHg or diastolic blood pressure  $\geq 90$  mmHg, and unknown); fasting blood glucose ( $< 100$ ,  $\geq 100$  mg/dL, and unknown); serum total cholesterol ( $< 200$ , 200–240,  $\geq 240$  mg/dL, and unknown); glomerular filtration rate ( $< 60$ , 60–90,  $\geq 90$  mL/min/1.73 m<sup>2</sup>, and unknown); smoking status (non-, current smoker, and unknown); alcohol consumption (rarely, sometimes, every day, and unknown); aerobic physical activity (sufficient, insufficient, and unknown); previous history of

cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); outpatients contact in the year before index date (0, 1-4, and  $\geq 5$  times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no], fasting blood glucose missing indicator [yes or no], serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no], smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes or no]).

Data in bold indicate significant differences ( $P < 0.05$ ).

**Table S25.** The hazard ratio (95% CI) for the **overall (short- and long-term) sequelae risk** of neuropsychiatric events following COVID-19 diagnosis of patients in the propensity score-matched cohorts in South Korea, with a two-sided test (missing indicator method), presenting the P value from Table S5

| Discovery cohort              | COVID-19 versus general   |         |                           |         | COVID-19 versus ARI       |         |                           |         |
|-------------------------------|---------------------------|---------|---------------------------|---------|---------------------------|---------|---------------------------|---------|
|                               | (n=1,831,237)             |         |                           |         | (n= 531,020)              |         |                           |         |
|                               | Model 1*                  |         | Model 2 <sup>II</sup>     |         | Model 1*                  |         | Model 2 <sup>II</sup>     |         |
|                               | HR (95% CI)               | P value | HR (95% CI)               | P value | HR (95% CI)               | P value | HR (95% CI)               | P value |
| Any neuropsychiatric outcomes | <b>2.43 (2.26-2.61)</b>   | <0.001  | <b>2.35 (2.16-2.56)</b>   | <0.001  | <b>1.42 (1.30-1.56)</b>   | <0.001  | <b>1.36 (1.23-1.51)</b>   | <0.001  |
| Anxiety disorder              | <b>3.23 (2.87-3.65)</b>   | <0.001  | <b>3.40 (2.96-3.90)</b>   | <0.001  | <b>1.44 (1.24-1.66)</b>   | <0.001  | <b>1.45 (1.23-1.70)</b>   | <0.001  |
| Encephalitis                  | <b>19.82 (8.85-44.37)</b> | <0.001  | <b>12.34 (5.11-29.80)</b> | <0.001  | <b>17.83 (4.29-74.12)</b> | <0.001  | <b>12.95 (2.97-56.48)</b> | <0.001  |
| Epilepsy/seizures             | 1.91 (0.98-3.72)          | 0.058   | 1.82 (0.79-4.22)          | 0.162   | 1.86 (0.74-4.67)          | 0.185   | 1.73 (0.60-4.96)          | 0.310   |
| Guillain-Barré syndrome       | <b>7.47 (1.37-40.78)</b>  | 0.020   | <b>11.89 (2.09-67.55)</b> | 0.005   | 0.61 (0.15-2.54)          | 0.493   | 0.95 (0.22-4.06)          | 0.948   |
| Insomnia                      | <b>5.02 (4.22-5.98)</b>   | <0.001  | <b>5.36 (4.42-6.50)</b>   | <0.001  | <b>1.64 (1.34-2.00)</b>   | <0.001  | <b>1.73 (1.39-2.14)</b>   | <0.001  |
| Intracranial hemorrhage       | 0.66 (0.34-1.30)          | 0.233   | 0.59 (0.25-1.36)          | 0.215   | 1.00 (0.38-2.67)          | 0.995   | 1.11 (0.36-3.46)          | 0.855   |
| Ischemic stroke               | <b>1.84 (1.40-2.43)</b>   | <0.001  | <b>1.64 (1.17-2.29)</b>   | 0.004   | <b>2.20 (1.46-3.33)</b>   | <0.001  | <b>1.88 (1.18-2.99)</b>   | 0.008   |
| Mood disorder                 | <b>2.64 (2.29-3.03)</b>   | <0.001  | <b>2.49 (2.10-2.94)</b>   | <0.001  | <b>1.52 (1.27-1.81)</b>   | <0.001  | <b>1.31 (1.06-1.60)</b>   | 0.012   |

|                                   |                         |        |                  |       |                  |       |                  |       |
|-----------------------------------|-------------------------|--------|------------------|-------|------------------|-------|------------------|-------|
| Nerve/nerve root/plexus disorders | 0.92 (0.77-1.10)        | 0.350  | 0.97 (0.79-1.19) | 0.788 | 1.09 (0.86-1.38) | 0.563 | 1.16 (0.89-1.51) | 0.904 |
| Myoneural junction/muscle disease | 0.42 (0.05-3.33)        | 0.413  | 0.64 (0.08-5.12) | 0.675 | 0.49 (0.05-5.43) | 0.481 | 0.86 (0.08-9.71) | 0.266 |
| Parkinsonism                      | 1.45 (0.70-3.02)        | 0.322  | 0.91 (0.35-2.41) | 0.850 | 0.63 (0.28-1.38) | 0.248 | 0.44 (0.16-1.22) | 0.115 |
| Psychotic disorder                | <b>4.17 (2.24-7.75)</b> | <0.001 | 2.01 (0.80-5.06) | 0.139 | 1.32 (0.69-2.54) | 0.400 | 0.65 (0.25-1.67) | 0.368 |

| Validation cohort             | COVID-19 versus general    |         |                            |         | COVID-19 versus ARI        |         |                           |         |
|-------------------------------|----------------------------|---------|----------------------------|---------|----------------------------|---------|---------------------------|---------|
|                               | (n=2,059,727)              |         |                            |         | (n= 309,794)               |         |                           |         |
|                               | Model 3*                   |         | Model 4‡                   |         | Model 3*                   |         | Model 4‡                  |         |
|                               | HR (95% CI)                | P value | HR (95% CI)                | P value | HR (95% CI)                | P value | HR (95% CI)               | P value |
| Any neuropsychiatric outcomes | <b>10.16 (9.65-10.70)</b>  | <0.001  | <b>8.64 (8.20-9.10)</b>    | <0.001  | <b>2.70 (2.58-2.82)</b>    | <0.001  | <b>2.38 (2.28-2.49)</b>   | <0.001  |
| Anxiety disorder              | <b>5.08 (4.67-5.52)</b>    | <0.001  | <b>4.76 (4.37-5.18)</b>    | <0.001  | <b>1.31 (1.22-1.40)</b>    | <0.001  | <b>1.27 (1.18-1.36)</b>   | <0.001  |
| Encephalitis                  | NA                         | 0.965   | NA                         | 0.936   | <b>14.99 (5.45-41.25)</b>  | <0.001  | <b>11.76 (4.25-32.57)</b> | <0.001  |
| Epilepsy/seizures             | <b>16.20 (12.57-20.87)</b> | <0.001  | <b>13.16 (10.18-17.02)</b> | <0.001  | <b>3.67 (3.04-4.44)</b>    | <0.001  | <b>2.96 (2.44-3.59)</b>   | <0.001  |
| Guillain-Barré syndrome       | NA                         | 0.944   | NA                         | 0.975   | <b>8.75 (3.11-24.62)</b>   | <0.001  | <b>7.61 (2.68-21.56)</b>  | <0.001  |
| Insomnia                      | <b>10.08 (9.25-10.97)</b>  | <0.001  | <b>8.01 (7.35-8.74)</b>    | <0.001  | <b>2.06 (1.93-2.21)</b>    | <0.001  | <b>1.79 (1.67-1.91)</b>   | <0.001  |
| Intracranial hemorrhage       | <b>62.62 (44.54-88.05)</b> | <0.001  | <b>47.66 (33.84-67.13)</b> | <0.001  | <b>13.81 (10.82-17.63)</b> | <0.001  | <b>9.89 (7.72-12.66)</b>  | <0.001  |

|                                   |                            |        |                            |        |                         |        |                         |        |
|-----------------------------------|----------------------------|--------|----------------------------|--------|-------------------------|--------|-------------------------|--------|
| Ischemic stroke                   | <b>25.31 (21.17-30.26)</b> | <0.001 | <b>21.61 (18.05-25.87)</b> | <0.001 | <b>7.37 (6.36-8.54)</b> | <0.001 | <b>6.40 (5.52-7.43)</b> | <0.001 |
| Mood disorder                     | <b>3.44 (3.12-3.80)</b>    | <0.001 | <b>3.19 (2.89-3.53)</b>    | <0.001 | <b>1.65 (1.49-1.82)</b> | <0.001 | <b>1.59 (1.44-1.76)</b> | <0.001 |
| Myoneural junction/muscle disease | <b>16.71 (8.71-32.04)</b>  | <0.001 | <b>14.24 (7.37-27.49)</b>  | <0.001 | <b>2.59 (1.66-4.04)</b> | <0.001 | <b>2.24 (1.42-3.52)</b> | <0.001 |
| Nerve/nerve root/plexus disorders | <b>7.86 (6.67-9.27)</b>    | <0.001 | <b>7.52 (6.37-8.89)</b>    | <0.001 | <b>3.27 (2.75-3.89)</b> | <0.001 | <b>3.17 (2.66-3.77)</b> | <0.001 |
| Parkinsonism                      | <b>4.26 (2.43-7.47)</b>    | <0.001 | <b>3.73 (2.10-6.62)</b>    | <0.001 | 0.81 (0.49-1.31)        | 0.386  | 0.80 (0.48-1.31)        | 0.368  |
| Psychotic disorder                | <b>9.86 (7.41-13.13)</b>   | <0.001 | <b>6.83 (5.09-9.16)</b>    | <0.001 | <b>1.63 (1.32-2.01)</b> | <0.001 | <b>1.27 (1.02-1.58)</b> | 0.032  |

ARI, another respiratory infection; CI, confidence interval; HR, hazard ratio.

\* **Model 1:** adjusted for age (20–39, 40–59, and  $\geq 60$  years) and sex.

<sup>II</sup> **Model 2:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and  $\geq 2$ ); obesity (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], obese [ $\geq 25.0 \text{ kg/m}^2$ ], and unknown); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$ , systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ , and unknown); fasting blood glucose ( $< 100$ ,  $\geq 100 \text{ mg/dL}$ , and unknown); serum total cholesterol ( $< 200$ ,  $200\text{--}240$ ,  $\geq 240 \text{ mg/dL}$ , and unknown); glomerular filtration rate ( $< 60$ ,  $60\text{--}90$ ,

$\geq 90$  mL/min/1.73 m<sup>2</sup>, and unknown); smoking status (non-, ex-, current smoker, and unknown); alcohol consumption (drinks; < 1, 1–2, 3–4,  $\geq 5$  days per week, and unknown); aerobic physical activity (sufficient, insufficient, and unknown); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); outpatients contact in the year before index date (0, 1–4, and  $\geq 5$  times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no], fasting blood glucose missing indicator [yes or no], serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no], smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes or no]).

Data in bold indicate significant differences ( $P < 0.05$ ).

**Table S26.** Stratification analysis for the **short-term risk** of incident neuropsychiatric events following COVID-19 diagnosis of patients in the propensity score-matched cohorts in South Korea, with a two-sided test (missing indicator method), presenting the P value from Table S6

|                                     | COVID-19 versus general |         |                         |         | COVID-19 versus ARI     |         |                         |         |
|-------------------------------------|-------------------------|---------|-------------------------|---------|-------------------------|---------|-------------------------|---------|
|                                     | (n=1,831,237)           |         |                         |         | (n=531,020)             |         |                         |         |
|                                     | Model 1*                |         | Model 2 <sup>II</sup>   |         | Model 1*                |         | Model 2 <sup>II</sup>   |         |
|                                     | HR (95% CI)             | P value | HR (95% CI)             | P value | HR (95% CI)             | P value | HR (95% CI)             | P value |
| Male                                | <b>2.40 (2.16-2.67)</b> | <0.001  | <b>2.44 (2.16-2.76)</b> | <0.001  | <b>1.40 (1.23-1.60)</b> | <0.001  | <b>1.40 (1.21-1.62)</b> | <0.001  |
| Female                              | <b>2.46 (2.23-2.71)</b> | <0.001  | <b>2.28 (2.03-2.56)</b> | <0.001  | <b>1.45 (1.28-1.64)</b> | <0.001  | <b>1.34 (1.16-1.55)</b> | <0.001  |
| Age 20-39 years                     | <b>2.20 (1.91-2.52)</b> | <0.001  | <b>2.11 (1.75-2.55)</b> | <0.001  | <b>2.08 (1.70-2.54)</b> | <0.001  | <b>1.97 (1.55-2.51)</b> | <0.001  |
| Age 40-59 years                     | <b>2.48 (2.21-2.79)</b> | <0.001  | <b>2.61 (2.29-2.98)</b> | <0.001  | <b>1.30 (1.12-1.50)</b> | <0.001  | <b>1.37 (1.17-1.60)</b> | <0.001  |
| Age ≥ 60 years                      | <b>2.57 (2.28-2.89)</b> | <0.001  | <b>2.26 (1.97-2.59)</b> | <0.001  | <b>1.27 (1.10-1.47)</b> | 0.002   | 1.17 (0.99-1.38)        | 0.063   |
| Low (0–39 percentile) income        | <b>2.42 (2.18-2.69)</b> | <0.001  | <b>2.30 (2.03-2.61)</b> | <0.001  | <b>1.41 (1.23-1.61)</b> | <0.001  | <b>1.34 (1.15-1.56)</b> | <0.001  |
| Middle (40–79 percentile) income    | <b>2.27 (2.01-2.57)</b> | <0.001  | <b>2.32 (2.02-2.67)</b> | <0.001  | <b>1.29 (1.11-1.51)</b> | <0.001  | <b>1.32 (1.12-1.57)</b> | <0.001  |
| High (80–100 percentile) income     | <b>2.77 (2.36-3.26)</b> | <0.001  | <b>2.61 (2.16-3.15)</b> | <0.001  | <b>1.73 (1.40-2.13)</b> | <0.001  | <b>1.61 (1.28-2.03)</b> | <0.001  |
| Charlson comorbidity index, 0 score | <b>2.64 (2.43-2.86)</b> | <0.001  | <b>2.64 (2.40-2.91)</b> | <0.001  | <b>1.37 (1.24-1.51)</b> | <0.001  | <b>1.32 (1.18-1.48)</b> | <0.001  |

|                                             |                         |        |                         |        |                         |        |                         |        |
|---------------------------------------------|-------------------------|--------|-------------------------|--------|-------------------------|--------|-------------------------|--------|
| Charlson comorbidity index, 1 score         | <b>1.65 (1.36-1.99)</b> | <0.001 | <b>1.57 (1.26-1.96)</b> | <0.001 | <b>1.98 (1.50-2.61)</b> | <0.001 | <b>1.93 (1.42-2.62)</b> | <0.001 |
| Charlson comorbidity index, $\geq 2$ scores | <b>1.75 (1.35-2.27)</b> | <0.001 | <b>1.62 (1.18-2.22)</b> | 0.003  | 1.33 (0.95-1.87)        | 0.098  | 1.24 (0.83-1.83)        | 0.295  |
| BMI, < 25 kg/m <sup>2</sup>                 | <b>2.59 (2.33-2.89)</b> | <0.001 | <b>2.59 (2.33-2.88)</b> | <0.001 | <b>1.37 (1.21-1.56)</b> | <0.001 | <b>1.40 (1.23-1.60)</b> | <0.001 |
| BMI, $\geq 25$ kg/m <sup>2</sup>            | <b>2.09 (1.83-2.40)</b> | <0.001 | <b>2.06 (1.80-2.36)</b> | <0.001 | <b>1.30 (1.10-1.53)</b> | 0.002  | <b>1.31 (1.11-1.55)</b> | 0.001  |
| BMI, unknown                                | NA                      | 0.954  | NA                      | 0.938  | NA                      | 0.935  | NA                      | 0.976  |
| Smoking status, non-smoker                  | <b>2.43 (2.20-2.70)</b> | <0.001 | <b>2.39 (2.16-2.65)</b> | <0.001 | <b>1.36 (1.20-1.54)</b> | <0.001 | <b>1.38 (1.22-1.57)</b> | <0.001 |
| Smoking status, ex- or current smoker       | <b>2.30 (1.98-2.66)</b> | <0.001 | <b>2.30 (1.99-2.67)</b> | <0.001 | <b>1.30 (1.09-1.54)</b> | 0.003  | <b>1.34 (1.12-1.59)</b> | 0.001  |
| Smoking status, unknown                     | NA                      | 0.956  | NA                      | 0.972  | NA                      | 0.964  | NA                      | 0.957  |
| Alcoholic drinks, < 1 per week              | <b>2.47 (2.22-2.74)</b> | <0.001 | <b>2.43 (2.19-2.71)</b> | <0.001 | <b>1.27 (1.12-1.44)</b> | <0.001 | <b>1.30 (1.14-1.47)</b> | <0.001 |
| Alcoholic drinks, $\geq 1$ per week         | <b>2.27 (1.98-2.60)</b> | <0.001 | <b>2.28 (1.99-2.61)</b> | <0.001 | <b>1.49 (1.25-1.77)</b> | <0.001 | <b>1.51 (1.27-1.79)</b> | <0.001 |
| Alcoholic drinks, unknown                   | NA                      | 0.974  | NA                      | 0.959  | 0.41 (0.06-2.91)        | 0.372  | NA                      | 0.985  |
| Aerobic physical activity, insufficient     | <b>2.29 (2.03-2.58)</b> | <0.001 | <b>2.27 (2.01-2.56)</b> | <0.001 | <b>1.28 (1.10-1.48)</b> | <0.001 | <b>1.30 (1.13-1.50)</b> | <0.001 |
| Aerobic physical activity, sufficient       | <b>2.49 (2.22-2.80)</b> | <0.001 | <b>2.47 (2.20-2.78)</b> | <0.001 | <b>1.40 (1.21-1.62)</b> | <0.001 | <b>1.44 (1.24-1.66)</b> | <0.001 |
| Aerobic physical activity, unknown          | 1.29 (0.32-5.19)        | 0.716  | NA                      | 0.953  | NA                      | 0.959  | NA                      | 0.984  |

ARI, another respiratory infection; BMI, body mass index; CI, confidence interval; HR, hazard ratio.

\* **Model 1:** adjusted for age (20–39, 40–59, and  $\geq 60$  years) and sex.

" **Model 2:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and  $\geq 2$ ); obesity (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], obese [ $\geq 25.0 \text{ kg/m}^2$ ], and unknown); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$ , systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ , and unknown); fasting blood glucose ( $< 100$ ,  $\geq 100 \text{ mg/dL}$ , and unknown); serum total cholesterol ( $< 200$ ,  $200\text{--}240$ ,  $\geq 240 \text{ mg/dL}$ , and unknown); glomerular filtration rate ( $< 60$ ,  $60\text{--}90$ ,  $\geq 90 \text{ mL/min/1.73 m}^2$ , and unknown); smoking status (non-, ex-, current smoker, and unknown); alcohol consumption (drinks;  $< 1$ ,  $1\text{--}2$ ,  $3\text{--}4$ ,  $\geq 5$  days per week, and unknown); aerobic physical activity (sufficient, insufficient, and unknown); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); outpatients contact in the year before index date (0,  $1\text{--}4$ , and  $\geq 5$  times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no], fasting blood glucose missing indicator [yes or no], serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no], smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes or no]).

Data in bold indicate significant differences ( $P < 0.05$ ).

**Table S27.** Stratification analysis for the **long-term sequelae risk** of incident neuropsychiatric events following COVID-19 diagnosis of patients in the propensity score-matched cohorts in South Korea, with a two-sided test (missing indicator method), presenting the P value from Table S7

|                                     | COVID-19 versus general |         |                         |         | COVID-19 versus ARI     |         |                         |         |
|-------------------------------------|-------------------------|---------|-------------------------|---------|-------------------------|---------|-------------------------|---------|
|                                     | (n=1,831,237)           |         |                         |         | (n=531,020)             |         |                         |         |
|                                     | Model 1*                |         | Model 2 <sup>II</sup>   |         | Model 1*                |         | Model 2 <sup>II</sup>   |         |
|                                     | HR (95% CI)             | P value | HR (95% CI)             | P value | HR (95% CI)             | P value | HR (95% CI)             | P value |
| Male                                | <b>1.76 (1.67-1.86)</b> | <0.001  | <b>1.69 (1.58-1.80)</b> | <0.001  | <b>1.72 (1.62-1.82)</b> | <0.001  | <b>1.62 (1.51-1.73)</b> | <0.001  |
| Female                              | <b>1.81 (1.72-1.90)</b> | <0.001  | <b>1.73 (1.63-1.83)</b> | <0.001  | <b>1.72 (1.63-1.81)</b> | <0.001  | <b>1.60 (1.51-1.71)</b> | <0.001  |
| Age 20-39 years                     | <b>1.84 (1.72-1.97)</b> | <0.001  | <b>1.71 (1.56-1.88)</b> | <0.001  | <b>2.53 (2.33-2.74)</b> | <0.001  | <b>2.35 (2.12-2.61)</b> | <0.001  |
| Age 40-59 years                     | <b>1.74 (1.63-1.84)</b> | <0.001  | <b>1.78 (1.66-1.90)</b> | <0.001  | <b>1.40 (1.31-1.49)</b> | <0.001  | <b>1.44 (1.34-1.54)</b> | <0.001  |
| Age ≥ 60 years                      | <b>1.80 (1.69-1.91)</b> | <0.001  | <b>1.65 (1.53-1.77)</b> | <0.001  | <b>1.70 (1.59-1.81)</b> | <0.001  | <b>1.55 (1.44-1.67)</b> | <0.001  |
| Low (0–39 percentile) income        | <b>1.77 (1.68-1.87)</b> | <0.001  | <b>1.66 (1.55-1.77)</b> | <0.001  | <b>1.62 (1.53-1.72)</b> | <0.001  | <b>1.51 (1.41-1.61)</b> | <0.001  |
| Middle (40–79 percentile) income    | <b>1.73 (1.62-1.84)</b> | <0.001  | <b>1.74 (1.62-1.87)</b> | <0.001  | <b>1.69 (1.58-1.81)</b> | <0.001  | <b>1.68 (1.55-1.81)</b> | <0.001  |
| High (80–100 percentile) income     | <b>1.92 (1.77-2.09)</b> | <0.001  | <b>1.78 (1.61-1.96)</b> | <0.001  | <b>2.01 (1.84-2.20)</b> | <0.001  | <b>1.78 (1.60-1.98)</b> | <0.001  |
| Charlson comorbidity index, 0 score | <b>1.94 (1.86-2.02)</b> | <0.001  | <b>1.89 (1.80-1.99)</b> | <0.001  | <b>1.63 (1.55-1.70)</b> | <0.001  | <b>1.53 (1.45-1.61)</b> | <0.001  |
| Charlson comorbidity index, 1 score | <b>1.20 (1.09-1.32)</b> | <0.001  | <b>1.18 (1.06-1.32)</b> | 0.004   | <b>2.26 (2.01-2.55)</b> | <0.001  | <b>2.21 (1.94-2.53)</b> | <0.001  |

|                                             |                         |        |                         |        |                         |        |                         |        |
|---------------------------------------------|-------------------------|--------|-------------------------|--------|-------------------------|--------|-------------------------|--------|
| Charlson comorbidity index, $\geq 2$ scores | <b>1.49 (1.31-1.70)</b> | <0.001 | <b>1.36 (1.16-1.59)</b> | <0.001 | <b>1.61 (1.40-1.85)</b> | <0.001 | <b>1.46 (1.23-1.72)</b> | <0.001 |
| BMI, < 25 kg/m <sup>2</sup>                 | <b>1.76 (1.66-1.86)</b> | <0.001 | <b>1.77 (1.67-1.87)</b> | <0.001 | <b>1.56 (1.47-1.66)</b> | <0.001 | <b>1.57 (1.48-1.67)</b> | <0.001 |
| BMI, $\geq 25$ kg/m <sup>2</sup>            | <b>1.64 (1.53-1.75)</b> | <0.001 | <b>1.62 (1.52-1.74)</b> | <0.001 | <b>1.66 (1.54-1.78)</b> | <0.001 | <b>1.65 (1.54-1.78)</b> | <0.001 |
| BMI, unknown                                | 1.57 (0.22-11.11)       | 0.654  | NA                      | 0.995  | 0.89 (0.29-2.76)        | 0.836  | 0.07 (0.01-0.47)        | 0.006  |
| Smoking status, non-smoker                  | <b>1.76 (1.67-1.85)</b> | <0.001 | <b>1.73 (1.64-1.83)</b> | <0.001 | <b>1.59 (1.51-1.69)</b> | <0.001 | <b>1.58 (1.50-1.68)</b> | <0.001 |
| Smoking status, ex- or current smoker       | <b>1.65 (1.52-1.78)</b> | 0.893  | <b>1.67 (1.54-1.80)</b> | 0.999  | <b>1.60 (1.47-1.74)</b> | 0.396  | <b>1.64 (1.51-1.78)</b> | 0.008  |
| Smoking status, unknown                     | NA                      | <0.001 | NA                      | <0.001 | 1.63 (0.53-5.07)        | <0.001 | 0.07 (0.01-0.49)        | <0.001 |
| Alcoholic drinks, < 1 per week              | <b>1.76 (1.67-1.86)</b> | <0.001 | <b>1.75 (1.65-1.85)</b> | <0.001 | <b>1.55 (1.47-1.65)</b> | <0.001 | <b>1.55 (1.46-1.64)</b> | <0.001 |
| Alcoholic drinks, $\geq 1$ per week         | <b>1.64 (1.53-1.76)</b> | <0.001 | <b>1.65 (1.54-1.78)</b> | <0.001 | <b>1.68 (1.56-1.82)</b> | <0.001 | <b>1.69 (1.56-1.83)</b> | <0.001 |
| Alcoholic drinks, unknown                   | 5.92 (0.83-42.02)       | 0.075  | NA                      | 0.994  | 1.56 (0.50-4.85)        | 0.439  | 0.07 (0.01-0.49)        | 0.008  |
| Aerobic physical activity, insufficient     | <b>1.75 (1.65-1.86)</b> | <0.001 | <b>1.76 (1.66-1.87)</b> | <0.001 | <b>1.65 (1.55-1.76)</b> | <0.001 | <b>1.66 (1.56-1.77)</b> | <0.001 |
| Aerobic physical activity, sufficient       | <b>1.67 (1.57-1.78)</b> | <0.001 | <b>1.66 (1.55-1.77)</b> | <0.001 | <b>1.54 (1.44-1.64)</b> | <0.001 | <b>1.53 (1.43-1.64)</b> | <0.001 |
| Aerobic physical activity, unknown          | 2.85 (0.92-8.85)        | 0.070  | 2.57 (0.18-36.53)       | 0.487  | 2.50 (0.81-7.78)        | 0.113  | 0.07 (0.01-0.49)        | 0.008  |

ARI, another respiratory infection; BMI, body mass index; CI, confidence interval; HR, hazard ratio.

\* **Model 1:** adjusted for age (20–39, 40–59, and  $\geq 60$  years) and sex.

<sup>||</sup> **Model 2:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and  $\geq 2$ ); obesity (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], obese [ $\geq 25.0 \text{ kg/m}^2$ ], and unknown); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$ , systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ , and unknown); fasting blood glucose ( $< 100$ ,  $\geq 100 \text{ mg/dL}$ , and unknown); serum total cholesterol ( $< 200$ ,  $200\text{--}240$ ,  $\geq 240 \text{ mg/dL}$ , and unknown); glomerular filtration rate ( $< 60$ ,  $60\text{--}90$ ,  $\geq 90 \text{ mL/min/1.73 m}^2$ , and unknown); smoking status (non-, ex-, current smoker, and unknown); alcohol consumption (drinks;  $< 1$ ,  $1\text{--}2$ ,  $3\text{--}4$ ,  $\geq 5$  days per week, and unknown); aerobic physical activity (sufficient, insufficient, and unknown); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); outpatients contact in the year before index date (0,  $1\text{--}4$ , and  $\geq 5$  times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no], fasting blood glucose missing indicator [yes or no], serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no], smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes or no]).

Data in bold indicate significant differences ( $P < 0.05$ ).

**Table S28.** Stratification analysis for the **overall (short- and long-term) risk** of incident neuropsychiatric events following COVID-19 diagnosis of patients in the propensity score-matched cohorts in South Korea, with a two-sided test (missing indicator method), presenting the P value from Table S8

|                                     | COVID-19 versus general |         |                         |         | COVID-19 versus ARI     |         |                         |         |
|-------------------------------------|-------------------------|---------|-------------------------|---------|-------------------------|---------|-------------------------|---------|
|                                     | (n=1,831,237)           |         |                         |         | (n=531,020)             |         |                         |         |
|                                     | Model 1 <sup>*</sup>    |         | Model 2 <sup>II</sup>   |         | Model 1 <sup>*</sup>    |         | Model 2 <sup>II</sup>   |         |
|                                     | HR (95% CI)             | P value | HR (95% CI)             | P value | HR (95% CI)             | P value | HR (95% CI)             | P value |
| Male                                | <b>1.91 (1.82-2.00)</b> | <0.001  | <b>1.84 (1.74-1.94)</b> | <0.001  | <b>1.65 (1.57-1.74)</b> | <0.001  | <b>1.56 (1.47-1.66)</b> | <0.001  |
| Female                              | <b>1.92 (1.80-2.05)</b> | <0.001  | <b>1.82 (1.66-2.00)</b> | <0.001  | <b>2.47 (2.28-2.67)</b> | <0.001  | <b>2.33 (2.11-2.58)</b> | <0.001  |
| Age 20-39 years                     | <b>1.87 (1.76-1.98)</b> | <0.001  | <b>1.92 (1.80-2.05)</b> | <0.001  | <b>1.38 (1.29-1.47)</b> | <0.001  | <b>1.42 (1.32-1.52)</b> | <0.001  |
| Age 40-59 years                     | <b>1.88 (1.77-2.00)</b> | <0.001  | <b>1.74 (1.62-1.86)</b> | <0.001  | <b>1.58 (1.49-1.69)</b> | <0.001  | <b>1.47 (1.37-1.58)</b> | <0.001  |
| Age ≥ 60 years                      | <b>1.87 (1.78-1.97)</b> | <0.001  | <b>1.76 (1.66-1.88)</b> | <0.001  | <b>1.58 (1.49-1.67)</b> | <0.001  | <b>1.47 (1.38-1.58)</b> | <0.001  |
| Low (0–39 percentile) income        | <b>1.84 (1.73-1.96)</b> | <0.001  | <b>1.87 (1.74-2.00)</b> | <0.001  | <b>1.63 (1.52-1.74)</b> | <0.001  | <b>1.63 (1.51-1.76)</b> | <0.001  |
| Middle (40–79 percentile) income    | <b>2.01 (1.86-2.18)</b> | <0.001  | <b>1.90 (1.73-2.09)</b> | <0.001  | <b>1.90 (1.74-2.07)</b> | <0.001  | <b>1.71 (1.55-1.90)</b> | <0.001  |
| High (80–100 percentile) income     | <b>1.87 (1.77-1.97)</b> | <0.001  | <b>1.81 (1.70-1.93)</b> | <0.001  | <b>1.65 (1.56-1.75)</b> | <0.001  | <b>1.57 (1.47-1.68)</b> | <0.001  |
| Charlson comorbidity index, 0 score | <b>2.05 (1.97-2.14)</b> | <0.001  | <b>2.03 (1.93-2.13)</b> | <0.001  | <b>1.57 (1.50-1.64)</b> | <0.001  | <b>1.49 (1.42-1.57)</b> | <0.001  |

|                                             |                         |        |                         |        |                         |        |                         |        |
|---------------------------------------------|-------------------------|--------|-------------------------|--------|-------------------------|--------|-------------------------|--------|
| Charlson comorbidity index, 1 score         | <b>1.26 (1.14-1.38)</b> | <0.001 | <b>1.23 (1.10-1.37)</b> | <0.001 | <b>2.23 (1.99-2.51)</b> | <0.001 | <b>2.19 (1.92-2.49)</b> | <0.001 |
| Charlson comorbidity index, $\geq 2$ scores | <b>1.54 (1.36-1.74)</b> | <0.001 | <b>1.42 (1.22-1.65)</b> | <0.001 | <b>1.52 (1.32-1.74)</b> | <0.001 | <b>1.40 (1.19-1.65)</b> | <0.001 |
| BMI, < 25 kg/m <sup>2</sup>                 | <b>1.90 (1.80-2.01)</b> | <0.001 | <b>1.91 (1.81-2.02)</b> | <0.001 | <b>1.51 (1.43-1.60)</b> | <0.001 | <b>1.53 (1.44-1.62)</b> | <0.001 |
| BMI, $\geq 25$ kg/m <sup>2</sup>            | <b>1.72 (1.61-1.84)</b> | <0.001 | <b>1.71 (1.60-1.82)</b> | <0.001 | <b>1.59 (1.48-1.71)</b> | <0.001 | <b>1.59 (1.48-1.71)</b> | <0.001 |
| BMI, unknown                                | 1.73 (0.24-12.24)       | 0.584  | NA                      | 0.993  | 0.88 (0.29-2.75)        | 0.831  | 0.07 (0.01-0.46)        | <0.001 |
| Smoking status, non-smoker                  | <b>1.89 (1.79-1.99)</b> | <0.001 | <b>1.86 (1.77-1.96)</b> | <0.001 | <b>1.55 (1.47-1.64)</b> | <0.001 | <b>1.55 (1.47-1.64)</b> | <0.001 |
| Smoking status, ex- or current smoker       | <b>1.74 (1.62-1.88)</b> | <0.001 | <b>1.76 (1.63-1.89)</b> | <0.001 | <b>1.52 (1.40-1.64)</b> | <0.001 | <b>1.56 (1.44-1.69)</b> | <0.001 |
| Smoking status, unknown                     | NA                      | 0.888  | NA                      | 0.999  | 1.62 (0.52-5.03)        | 0.430  | 0.07 (0.01-0.49)        | 0.008  |
| Alcoholic drinks, < 1 per week              | <b>1.88 (1.79-1.99)</b> | <0.001 | <b>1.87 (1.77-1.97)</b> | <0.001 | <b>1.50 (1.42-1.59)</b> | <0.001 | <b>1.50 (1.42-1.59)</b> | <0.001 |
| Alcoholic drinks, $\geq 1$ per week         | <b>1.75 (1.64-1.88)</b> | <0.001 | <b>1.77 (1.65-1.89)</b> | <0.001 | <b>1.63 (1.51-1.76)</b> | <0.001 | <b>1.64 (1.52-1.77)</b> | <0.001 |
| Alcoholic drinks, unknown                   | 6.38 (0.90-45.24)       | 0.064  | NA                      | 0.995  | 1.55 (0.50-4.82)        | 0.580  | 0.07 (0.01-0.49)        | 0.008  |
| Aerobic physical activity, insufficient     | <b>1.87 (1.77-1.98)</b> | <0.001 | <b>1.87 (1.77-1.99)</b> | <0.001 | <b>1.59 (1.49-1.69)</b> | <0.001 | <b>1.61 (1.51-1.71)</b> | <0.001 |
| Aerobic physical activity, sufficient       | <b>1.79 (1.69-1.90)</b> | <0.001 | <b>1.78 (1.67-1.89)</b> | <0.001 | <b>1.49 (1.39-1.59)</b> | <0.001 | <b>1.49 (1.40-1.59)</b> | <0.001 |
| Aerobic physical activity, unknown          | 3.08 (0.99-9.57)        | 0.051  | 2.67 (0.19-37.67)       | 0.468  | 2.48 (0.80-7.71)        | 0.116  | 0.07 (0.01-0.49)        | 0.008  |

ARI, another respiratory infection; BMI, body mass index; CI, confidence interval; HR, hazard ratio.

\* **Model 1:** adjusted for age (20–39, 40–59, and  $\geq 60$  years) and sex.

" **Model 2:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and  $\geq 2$ ); obesity (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], obese [ $\geq 25.0 \text{ kg/m}^2$ ], and unknown); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$ , systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ , and unknown); fasting blood glucose ( $< 100$ ,  $\geq 100 \text{ mg/dL}$ , and unknown); serum total cholesterol ( $< 200$ ,  $200\text{--}240$ ,  $\geq 240 \text{ mg/dL}$ , and unknown); glomerular filtration rate ( $< 60$ ,  $60\text{--}90$ ,  $\geq 90 \text{ mL/min/1.73 m}^2$ , and unknown); smoking status (non-, ex-, current smoker, and unknown); alcohol consumption (drinks;  $< 1$ ,  $1\text{--}2$ ,  $3\text{--}4$ ,  $\geq 5$  days per week, and unknown); aerobic physical activity (sufficient, insufficient, and unknown); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); outpatients contact in the year before index date (0,  $1\text{--}4$ , and  $\geq 5$  times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no], fasting blood glucose missing indicator [yes or no], serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no], smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes or no]).

Data in bold indicate significant differences ( $P < 0.05$ ).

**Table S29.** The hazard ratio (95% CI) for the **short- and long-term sequelae risk** of neuropsychiatric events following COVID-19 diagnosis of patients in the propensity score-matched cohorts in South Korea and Japan, using alternative cohort specifications, with a two-sided test (missing indicator method), presenting the P value from Table S13

|                                              | COVID-19 versus general (South Korea) |         |                         |         | COVID-19 versus general (Japan) |         |                          |         |
|----------------------------------------------|---------------------------------------|---------|-------------------------|---------|---------------------------------|---------|--------------------------|---------|
|                                              | Model 1 <sup>*</sup>                  |         | Model 2 <sup>  </sup>   |         | Model 1 <sup>*</sup>            |         | Model 2 <sup>  </sup>    |         |
|                                              | HR (95% CI)                           | P value | HR (95% CI)             | P value | HR (95% CI)                     | P value | HR (95% CI)              | P value |
| Any neuropsychiatric outcomes                |                                       |         |                         |         |                                 |         |                          |         |
| Short-term, diagnosed ≥3 times <sup>]</sup>  | <b>2.31 (2.08-2.57)</b>               | <0.001  | <b>2.06 (1.81-2.34)</b> | <0.001  | <b>12.14 (11.49-12.84)</b>      | <0.001  | <b>9.67 (9.14-10.23)</b> | <0.001  |
| Long-term, diagnosed ≥3 times <sup>]</sup>   | <b>1.97 (1.87-2.07)</b>               | <0.001  | <b>1.76 (1.66-1.88)</b> | <0.001  | <b>2.99 (2.92-3.07)</b>         | <0.001  | <b>2.73 (2.66-2.80)</b>  | <0.001  |
| Short-term, diagnosed ≥4 times <sup>]]</sup> | <b>2.35 (2.10-2.63)</b>               | <0.001  | <b>2.07 (1.81-2.38)</b> | <0.001  | <b>12.43 (11.71-13.20)</b>      | <0.001  | <b>9.69 (9.12-10.30)</b> | <0.001  |
| Long-term, diagnosed ≥4 times <sup>]]</sup>  | <b>1.98 (1.88-2.09)</b>               | <0.001  | <b>1.77 (1.65-1.89)</b> | <0.001  | <b>3.04 (2.95-3.13)</b>         | <0.001  | <b>2.76 (2.68-2.84)</b>  | <0.001  |

ARI, another respiratory infection; CI, confidence interval; HR, hazard ratio.

<sup>]</sup> Onset of neuropsychiatric outcomes were defined when a participant was diagnosed with a particular outcome three times of more within one year using the following ICD-10 codes.

]] Onset of neuropsychiatric outcomes were defined when a participant was diagnosed with a particular outcome four times or more within one year using the following ICD-10 codes.

\* **adjusted HR:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and  $\geq 2$ ); obesity (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], obese [ $\geq 25.0 \text{ kg/m}^2$ ], and unknown); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$ , systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ , and unknown); fasting blood glucose ( $< 100$ ,  $\geq 100 \text{ mg/dL}$ , and unknown); serum total cholesterol ( $< 200$ ,  $200\text{--}240$ ,  $\geq 240 \text{ mg/dL}$ , and unknown); glomerular filtration rate ( $< 60$ ,  $60\text{--}90$ ,  $\geq 90 \text{ mL/min/1.73 m}^2$ , and unknown); smoking status (non-, ex-, current smoker, and unknown); alcohol consumption (drinks;  $< 1$ ,  $1\text{--}2$ ,  $3\text{--}4$ ,  $\geq 5$  days per week, and unknown); aerobic physical activity (sufficient, insufficient, and unknown); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); outpatients contact in the year before index date (0,  $1\text{--}4$ , and  $\geq 5$  times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no], fasting blood glucose missing indicator [yes or no], serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no], smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes

or no])).

‡ **adjusted HR:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; insurance status (insured or dependent); body mass index (underweight [ $< 18.5 \text{ kg/m}^2$ ]; normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], obese [ $\geq 25.0 \text{ kg/m}^2$ ], and unknown); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$ , systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ , and unknown); fasting blood glucose ( $< 100$ ,  $\geq 100 \text{ mg/dL}$ , and unknown); serum total cholesterol ( $< 200$ ,  $200\text{--}240$ ,  $\geq 240 \text{ mg/dL}$ , and unknown); glomerular filtration rate ( $< 60$ ,  $60\text{--}90$ ,  $\geq 90 \text{ mL/min/1.73 m}^2$ , and unknown); smoking status (non-, current smoker, and unknown); alcohol consumption (rarely, sometimes, every day, and unknown); aerobic physical activity (sufficient, insufficient, and unknown); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); outpatients contact in the year before index date (0, 1–4, and  $\geq 5$  times); and missing indicators (obesity missing indicator [yes or no], blood pressure missing indicator [yes or no], fasting blood glucose missing indicator [yes or no], serum total cholesterol missing indicator [yes or no], glomerular filtration rate missing indicator [yes or no], smoking status missing indicator [yes or no], alcoholic drinks missing indicator [yes or no], and aerobic physical activity missing indicator [yes or no])).

Data in bold indicate significant differences ( $P < 0.05$ ).

**Table S30.** Hazard ratio (95% CI) for the **short-term risk** of incident neuropsychiatric events following COVID-19 diagnosis of patients in the propensity score-matched discovery and validation cohorts, with a two-sided test (complete case analysis method), presenting the P value from Table S17

| Discovery cohort              | COVID-19 versus general |         |                         |         | COVID-19 versus ARI     |         |                         |         |
|-------------------------------|-------------------------|---------|-------------------------|---------|-------------------------|---------|-------------------------|---------|
|                               | (n=591,174)             |         |                         |         | (n= 227,786)            |         |                         |         |
|                               | Model 1 <sup>*</sup>    |         | Model 2 <sup>II</sup>   |         | Model 1 <sup>*</sup>    |         | Model 2 <sup>II</sup>   |         |
|                               | HR (95% CI)             | P value | HR (95% CI)             | P value | HR (95% CI)             | P value | HR (95% CI)             | P value |
| Any neuropsychiatric outcomes | <b>2.36 (2.09-2.66)</b> | <0.001  | <b>2.34 (2.07-2.64)</b> | <0.001  | 1.07 (0.93-1.24)        | 0.354   | 1.08 (0.93-1.24)        | 0.329   |
| Anxiety disorder              | <b>3.76 (3.05-4.64)</b> | <0.001  | <b>3.74 (3.02-4.62)</b> | <0.001  | 1.12 (0.89-1.42)        | 0.322   | 1.13 (0.89-1.42)        | 0.311   |
| Encephalitis                  | NA                      | 0.974   | NA                      | 0.969   | NA                      | 0.990   | NA                      | 0.292   |
| Epilepsy/seizures             | 1.53 (0.48-4.88)        | 0.471   | 1.56 (0.48-5.01)        | 0.458   | 1.33 (0.30-5.95)        | 0.707   | 1.47 (0.33-6.65)        | 0.6170  |
| Guillain-Barré syndrome       | 3.79 (0.53-26.92)       | 0.183   | 3.44 (0.46-25.50)       | 0.227   | NA                      | 0.996   | NA                      | 0.998   |
| Insomnia                      | <b>4.81 (3.66-6.32)</b> | <0.001  | <b>4.90 (3.72-6.45)</b> | <0.001  | <b>1.50 (1.10-2.04)</b> | 0.011   | <b>1.52 (1.11-2.08)</b> | 0.009   |
| Intracranial hemorrhage       | 1.08 (0.35-3.27)        | 0.896   | 1.04 (0.34-3.19)        | 0.944   | 1.51 (0.25-9.00)        | 0.655   | 1.96 (0.30-12.90)       | 0.486   |
| Ischemic stroke               | 1.45 (0.96-2.20)        | 0.077   | 1.43 (0.94-2.17)        | 0.097   | 1.70 (0.93-3.12)        | 0.083   | 1.62 (0.88-2.98)        | 0.120   |
| Mood disorder                 | <b>3.15 (2.40-4.12)</b> | <0.001  | <b>3.14 (2.39-4.13)</b> | <0.001  | 0.91 (0.68-1.23)        | 0.546   | 0.91 (0.68-1.23)        | 0.537   |

|                                   |                  |       |                  |       |                  |       |                  |       |
|-----------------------------------|------------------|-------|------------------|-------|------------------|-------|------------------|-------|
| Nerve/nerve root/plexus disorders | 0.88 (0.66-1.18) | 0.996 | 0.86 (0.65-1.15) | 0.999 | 0.85 (0.59-1.24) | 0.396 | 0.85 (0.58-1.23) | 0.379 |
| Myoneural junction/muscle disease | NA               | 0.992 | NA               | 0.900 | NA               | NA    | NA               | NA    |
| Parkinsonism                      | 1.13 (0.31-4.10) | 0.856 | 1.00 (0.27-3.66) | 0.998 | 0.33 (0.09-1.23) | 0.100 | 0.34 (0.09-1.26) | 0.106 |
| Psychotic disorder                | 1.52 (0.29-7.81) | 0.620 | 1.52 (0.29-7.94) | 0.620 | 0.29 (0.06-1.38) | 0.118 | 0.30 (0.06-1.44) | 0.132 |

| Validation cohort             | COVID-19 versus general    |         |                            |         | COVID-19 versus ARI        |         |                            |         |
|-------------------------------|----------------------------|---------|----------------------------|---------|----------------------------|---------|----------------------------|---------|
|                               | (n=976,212)                |         |                            |         | (n= 148,096)               |         |                            |         |
|                               | Model 3*                   |         | Model 4‡                   |         | Model 3*                   |         | Model 4‡                   |         |
|                               | HR (95% CI)                | P value | HR (95% CI)                | P value | HR (95% CI)                | P value | HR (95% CI)                | P value |
| Any neuropsychiatric outcomes | <b>10.38 (9.63-11.18)</b>  | <0.001  | <b>8.84 (8.20-9.53)</b>    | <0.001  | <b>2.46 (2.32-2.61)</b>    | <0.001  | <b>2.17 (2.04-2.30)</b>    | <0.001  |
| Anxiety disorder              | <b>5.29 (4.67-5.99)</b>    | <0.001  | <b>5.02 (4.43-5.68)</b>    | <0.001  | <b>1.16 (1.05-1.28)</b>    | 0.004   | <b>1.13 (1.02-1.25)</b>    | 0.015   |
| Encephalitis                  | NA                         | 0.974   | NA                         | 0.973   | <b>13.5 (3.21-56.76)</b>   | <0.001  | <b>9.67 (2.27-41.23)</b>   | 0.002   |
| Epilepsy/seizures             | <b>18.16 (12.24-26.93)</b> | <0.001  | <b>15.35 (10.31-22.87)</b> | <0.001  | <b>3.46 (2.65-4.51)</b>    | <0.001  | <b>2.84 (2.16-3.72)</b>    | <0.001  |
| Guillain-Barré syndrome       | NA                         | 0.935   | NA                         | 0.947   | <b>16.99 (2.26-127.54)</b> | 0.006   | <b>15.72 (2.08-118.92)</b> | 0.008   |
| Insomnia                      | <b>10.13 (8.97-11.44)</b>  | <0.001  | <b>8.08 (7.14-9.14)</b>    | <0.001  | <b>1.86 (1.70-2.04)</b>    | <0.001  | <b>1.62 (1.47-1.78)</b>    | <0.001  |
| Intracranial hemorrhage       | <b>46.05 (30.09-70.48)</b> | <0.001  | <b>35.31 (23.01-54.19)</b> | <0.001  | <b>11.97 (8.60-16.67)</b>  | <0.001  | <b>8.36 (5.98-11.70)</b>   | <0.001  |

|                                   |                            |        |                            |        |                         |        |                         |        |
|-----------------------------------|----------------------------|--------|----------------------------|--------|-------------------------|--------|-------------------------|--------|
| Ischemic stroke                   | <b>32.58 (24.52-43.30)</b> | <0.001 | <b>27.58 (20.72-36.72)</b> | <0.001 | <b>6.43 (5.28-7.83)</b> | <0.001 | <b>5.56 (4.56-6.78)</b> | <0.001 |
| Mood disorder                     | <b>3.60 (3.10-4.18)</b>    | <0.001 | <b>3.37 (2.89-3.92)</b>    | <0.001 | <b>1.36 (1.19-1.56)</b> | <0.001 | <b>1.33 (1.16-1.53)</b> | <0.001 |
| Myoneural junction/muscle disease | <b>15.39 (6.11-38.77)</b>  | <0.001 | <b>13.09 (5.15-33.30)</b>  | <0.001 | <b>2.13 (1.16-3.94)</b> | 0.016  | <b>1.85 (0.99-3.46)</b> | 0.056  |
| Nerve/nerve root/plexus disorders | <b>6.51 (5.26-8.07)</b>    | <0.001 | <b>6.26 (5.04-7.77)</b>    | <0.001 | <b>3.15 (2.50-3.98)</b> | <0.001 | <b>3.06 (2.41-3.87)</b> | <0.001 |
| Parkinsonism                      | <b>4.71 (1.99-11.14)</b>   | <0.001 | <b>3.98 (1.65-9.64)</b>    | 0.002  | 0.65 (0.32-1.31)        | 0.227  | 0.61 (0.30-1.24)        | 0.169  |
| Psychotic disorder                | <b>9.46 (6.18-14.46)</b>   | <0.001 | <b>6.76 (4.37-10.45)</b>   | <0.001 | 1.17 (0.87-1.56)        | 0.300  | 0.90 (0.67-1.22)        | 0.510  |

ARI, another respiratory infection; CI, confidence interval; HR, hazard ratio.

\* **Models 1 and 3:** adjusted for age (20–39, 40–59, and  $\geq 60$  years) and sex.

<sup>II</sup> **Model 2:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and  $\geq 2$ ); obesity (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], and obese [ $\geq 25.0 \text{ kg/m}^2$ ]); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$ , systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ ); fasting blood glucose ( $< 100$  and  $\geq 100 \text{ mg/dL}$ ); serum total cholesterol ( $< 200$ ,  $200\text{--}240$ , and  $\geq 240 \text{ mg/dL}$ ); glomerular filtration rate ( $< 60$ ,  $60\text{--}90$ , and  $\geq 90 \text{ mL/min/1.73 m}^2$ ); smoking status (non-,

ex-, and current smoker); alcohol consumption (drinks; < 1, 1–2, 3–4, and  $\geq 5$  days per week); aerobic physical activity (sufficient and insufficient); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); and outpatients contact in the year before index date (0, 1–4, and  $\geq 5$  times).

‡ **Model 4:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; insurance status (insured or dependent); body mass index (underweight [ $< 18.5$  kg/m<sup>2</sup>], normal [18.5–23.0 kg/m<sup>2</sup>], overweight [23.0–25.0 kg/m<sup>2</sup>], and obese [ $\geq 25.0$  kg/m<sup>2</sup>]); blood pressure (systolic blood pressure < 140 mmHg and diastolic blood pressure < 90 mmHg and systolic blood pressure  $\geq 140$  mmHg or diastolic blood pressure  $\geq 90$  mmHg); fasting blood glucose (< 100 and  $\geq 100$  mg/dL); total serum cholesterol (< 200, 200–240, and  $\geq 240$  mg/dL); glomerular filtration rate (< 60, 60–90, and  $\geq 90$  mL/min/1.73 m<sup>2</sup>); smoking status (non- and current smoker); alcohol consumption (rarely, sometimes, and every day); aerobic physical activity (sufficient and insufficient); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); and outpatients contact in the year before index date (0, 1–4, and  $\geq 5$  times).

Data in bold indicate significant differences ( $P < 0.05$ ).

**Table S31.** Hazard ratio (95% CI) for the **long-term sequelae risk** of neuropsychiatric events following COVID-19 diagnosis of patients in the propensity score-matched discovery and validation cohorts, with a two-sided test (complete case analysis method), presenting the P value from Table S18

| Discovery cohort              | COVID-19 versus general<br>(n=591,174) |         |                           |         | COVID-19 versus ARI<br>(n= 227,786) |         |                         |         |
|-------------------------------|----------------------------------------|---------|---------------------------|---------|-------------------------------------|---------|-------------------------|---------|
|                               | Model 1 <sup>*</sup>                   |         | Model 2 <sup>II</sup>     |         | Model 1 <sup>*</sup>                |         | Model 2 <sup>II</sup>   |         |
|                               | HR (95% CI)                            | P value | HR (95% CI)               | P value | HR (95% CI)                         | P value | HR (95% CI)             | P value |
| Any neuropsychiatric outcomes | <b>1.72 (1.62-1.83)</b>                | <0.001  | <b>1.71 (1.61-1.82)</b>   | <0.001  | <b>1.31 (1.23-1.40)</b>             | <0.001  | <b>1.30 (1.22-1.39)</b> | <0.001  |
| Anxiety disorder              | <b>2.48 (2.23-2.76)</b>                | <0.001  | <b>2.48 (2.23-2.76)</b>   | <0.001  | <b>1.41 (1.27-1.57)</b>             | <0.001  | <b>1.42 (1.27-1.57)</b> | <0.001  |
| Cognitive deficit             | <b>3.01 (1.19-7.63)</b>                | 0.020   | <b>2.93 (1.15-7.46)</b>   | 0.025   | <b>0.37 (0.18-0.78)</b>             | 0.009   | <b>0.37 (0.18-0.79)</b> | 0.010   |
| Encephalitis                  | <b>11.49 (3.11-42.42)</b>              | <0.001  | <b>10.29 (2.75-38.45)</b> | 0.001   | 1.93 (0.78-4.79)                    | 0.165   | 1.92 (0.77-4.79)        | 0.495   |
| Epilepsy/seizures             | 1.14 (0.56-2.30)                       | 0.725   | 1.20 (0.59-2.44)          | 0.618   | 0.56 (0.28-1.13)                    | 0.104   | 0.56 (0.28-1.12)        | 0.103   |
| Guillain-Barré syndrome       | 3.84 (0.96-15.36)                      | 0.057   | 3.31 (0.81-13.53)         | 0.096   | 3.43 (0.62-18.92)                   | 0.157   | 2.96 (0.52-16.7)        | 0.220   |
| Insomnia                      | <b>2.28 (1.95-2.66)</b>                | <0.001  | <b>2.33 (1.99-2.72)</b>   | <0.001  | 1.10 (0.95-1.28)                    | 0.191   | 1.12 (0.97-1.30)        | 0.134   |
| Intracranial hemorrhage       | 0.97 (0.61-1.55)                       | 0.904   | 0.96 (0.60-1.54)          | 0.874   | <b>1.90 (1.10-3.28)</b>             | 0.021   | <b>1.83 (1.06-3.18)</b> | 0.032   |

|                                   |                          |         |                          |         |                          |         |                          |         |
|-----------------------------------|--------------------------|---------|--------------------------|---------|--------------------------|---------|--------------------------|---------|
| Ischemic stroke                   | <b>1.88 (1.43-2.47)</b>  | 0.314   | <b>1.84 (1.40-2.43)</b>  | 0.321   | 1.23 (0.94-1.62)         | 0.126   | 1.18 (0.90-1.55)         | 0.233   |
| Mood disorder                     | <b>2.26 (1.99-2.57)</b>  | <0.001  | <b>2.29 (2.01-2.60)</b>  | <0.001  | <b>1.27 (1.12-1.44)</b>  | <0.001  | <b>1.27 (1.12-1.44)</b>  | <0.001  |
| Nerve/nerve root/plexus disorders | 0.89 (0.25-3.11)         | 0.852   | 0.90 (0.25-3.18)         | 0.868   | 0.59 (0.17-2.08)         | 0.415   | 0.55 (0.16-1.93)         | 0.351   |
| Myoneural junction/muscle disease | <b>1.37 (1.23-1.52)</b>  | <0.001  | <b>1.33 (1.19-1.49)</b>  | <0.001  | <b>2.02 (1.78-2.28)</b>  | <0.001  | <b>1.95 (1.72-2.21)</b>  | <0.001  |
| Parkinsonism                      | 1.17 (0.66-2.09)         | 0.595   | 1.06 (0.59-1.89)         | 0.855   | 0.67 (0.38-1.18)         | 0.166   | 0.63 (0.36-1.13)         | 0.121   |
| Psychotic disorder                | 0.96 (0.44-2.08)         | 0.918   | 0.95 (0.44-2.07)         | 0.894   | <b>0.41 (0.20-0.88)</b>  | 0.021   | <b>0.41 (0.19-0.87)</b>  | 0.020   |
| <b>Validation cohort</b>          | COVID-19 versus general  |         |                          |         | COVID-19 versus ARI      |         |                          |         |
|                                   | (n=976,212)              |         |                          |         | (n=148,096)              |         |                          |         |
|                                   | Model 3 <sup>*</sup>     |         | Model 4 <sup>‡</sup>     |         | Model 3 <sup>*</sup>     |         | Model 4 <sup>‡</sup>     |         |
|                                   | HR (95% CI)              | P value | HR (95% CI)              | P value | HR (95% CI)              | P value | HR (95% CI)              | P value |
| Any neuropsychiatric outcomes     | <b>2.72 (2.64-2.81)</b>  | <0.001  | <b>2.51 (2.44-2.59)</b>  | <0.001  | <b>4.38 (4.20-4.56)</b>  | <0.001  | <b>4.13 (3.96-4.31)</b>  | <0.001  |
| Anxiety disorder                  | <b>2.40 (2.29-2.51)</b>  | <0.001  | <b>2.32 (2.22-2.43)</b>  | <0.001  | <b>3.70 (3.48-3.94)</b>  | <0.001  | <b>3.64 (3.42-3.88)</b>  | <0.001  |
| Cognitive deficit                 | <b>4.76 (2.82-8.05)</b>  | <0.001  | <b>3.37 (1.95-5.81)</b>  | <0.001  | <b>6.25 (3.33-11.74)</b> | <0.001  | <b>4.50 (2.36-8.59)</b>  | <0.001  |
| Encephalitis                      | <b>7.09 (3.96-12.70)</b> | <0.001  | <b>5.52 (3.03-10.04)</b> | <0.001  | <b>7.03 (3.11-15.86)</b> | <0.001  | <b>4.50 (1.94-10.40)</b> | <0.001  |
| Epilepsy/seizures                 | <b>3.55 (3.02-4.18)</b>  | <0.001  | <b>2.73 (2.31-3.23)</b>  | <0.001  | <b>5.37 (4.26-6.76)</b>  | <0.001  | <b>4.18 (3.30-5.29)</b>  | <0.001  |

|                                   |                          |        |                         |        |                         |        |                         |        |
|-----------------------------------|--------------------------|--------|-------------------------|--------|-------------------------|--------|-------------------------|--------|
| Guillain-Barré syndrome           | <b>5.51 (2.37-12.81)</b> | <0.001 | <b>3.82 (1.59-9.14)</b> | 0.003  | <b>2.56 (1.02-6.47)</b> | <0.001 | <b>2.18 (0.85-5.60)</b> | <0.001 |
| Insomnia                          | <b>2.86 (2.73-3.00)</b>  | <0.001 | <b>2.59 (2.47-2.72)</b> | <0.001 | <b>4.53 (4.26-4.83)</b> | <0.001 | <b>4.21 (3.94-4.49)</b> | <0.001 |
| Intracranial hemorrhage           | <b>4.47 (3.60-5.54)</b>  | <0.001 | <b>3.64 (2.91-4.54)</b> | <0.001 | <b>5.70 (4.09-7.93)</b> | <0.001 | <b>4.46 (3.18-6.26)</b> | <0.001 |
| Ischemic stroke                   | <b>3.09 (2.76-3.47)</b>  | <0.001 | <b>2.75 (2.45-3.09)</b> | <0.001 | <b>4.03 (3.40-4.79)</b> | <0.001 | <b>3.59 (3.01-4.27)</b> | <0.001 |
| Mood disorder                     | <b>2.31 (2.19-2.44)</b>  | <0.001 | <b>2.24 (2.12-2.37)</b> | <0.001 | <b>4.52 (4.19-4.87)</b> | <0.001 | <b>4.42 (4.10-4.77)</b> | <0.001 |
| Myoneural junction/muscle disease | <b>3.43 (2.53-4.63)</b>  | <0.001 | <b>2.88 (2.11-3.94)</b> | <0.001 | <b>4.27 (2.76-6.61)</b> | <0.001 | <b>3.63 (2.32-5.67)</b> | <0.001 |
| Nerve/nerve root/plexus disorders | <b>2.22 (2.03-2.44)</b>  | <0.001 | <b>2.09 (1.91-2.30)</b> | <0.001 | <b>3.58 (3.13-4.08)</b> | <0.001 | <b>3.41 (2.98-3.90)</b> | <0.001 |
| Parkinsonism                      | <b>1.40 (1.04-1.90)</b>  | 0.029  | 1.21 (0.89-1.66)        | 0.224  | <b>3.25 (2.04-5.16)</b> | <0.001 | <b>2.77 (1.72-4.44)</b> | <0.001 |
| Psychotic disorder                | <b>3.02 (2.58-3.54)</b>  | <0.001 | <b>2.44 (2.07-2.87)</b> | <0.001 | <b>5.60 (4.45-7.04)</b> | <0.001 | <b>4.77 (3.78-6.02)</b> | <0.001 |

ARI, another respiratory infection; CI, confidence interval; HR, hazard ratio.

\* **Models 1 and 3:** adjusted for age (20–39, 40–59, and  $\geq 60$  years) and sex.

<sup>II</sup> **Model 2:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and  $\geq 2$ ); obesity (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], and obese [ $\geq 25.0 \text{ kg/m}^2$ ]); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $<$

90 mmHg, systolic blood pressure  $\geq 140$  mmHg or diastolic blood pressure  $\geq 90$  mmHg); fasting blood glucose ( $< 100$  and  $\geq 100$  mg/dL); serum total cholesterol ( $< 200$ ,  $200\text{--}240$ , and  $\geq 240$  mg/dL); glomerular filtration rate ( $< 60$ ,  $60\text{--}90$ , and  $\geq 90$  mL/min/1.73 m<sup>2</sup>); smoking status (non-, ex-, and current smoker); alcohol consumption (drinks;  $< 1$ ,  $1\text{--}2$ ,  $3\text{--}4$ , and  $\geq 5$  days per week); aerobic physical activity (sufficient and insufficient); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); and outpatients contact in the year before index date (0,  $1\text{--}4$ , and  $\geq 5$  times).

‡ **Model 4:** adjusted for age (20–39, 40–59, and  $\geq 60$  years); sex; insurance status (insured or dependent); body mass index (underweight [ $< 18.5$  kg/m<sup>2</sup>], normal [ $18.5\text{--}23.0$  kg/m<sup>2</sup>], overweight [ $23.0\text{--}25.0$  kg/m<sup>2</sup>], and obese [ $\geq 25.0$  kg/m<sup>2</sup>]); blood pressure (systolic blood pressure  $< 140$  mmHg and diastolic blood pressure  $< 90$  mmHg and systolic blood pressure  $\geq 140$  mmHg or diastolic blood pressure  $\geq 90$  mmHg); fasting blood glucose ( $< 100$  and  $\geq 100$  mg/dL); total serum cholesterol ( $< 200$ ,  $200\text{--}240$ , and  $\geq 240$  mg/dL); glomerular filtration rate ( $< 60$ ,  $60\text{--}90$ , and  $\geq 90$  mL/min/1.73 m<sup>2</sup>); smoking status (non- and current smoker); alcohol consumption (rarely, sometimes, and every day); aerobic physical activity (sufficient and insufficient); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); and outpatients contact in the year before index date (0,  $1\text{--}4$ , and  $\geq 5$  times).

Data in bold indicate significant differences ( $P < 0.05$ ).

**Table S32.** Subgroup analysis (COVID-19 versus general population) of HR (95% CI) of neuropsychiatric outcomes following COVID-19 diagnosis stratified by vaccination, COVID-19 severity, and SARS-CoV-2 strain in the discovery cohort, with a two-sided test (complete case analysis method), presenting the P value from Table S19

| Group                                                        | Short-term neuropsychiatric risk |         | Long-term neuropsychiatric sequelae |         |
|--------------------------------------------------------------|----------------------------------|---------|-------------------------------------|---------|
|                                                              | Adjusted HR* (95% CI)            | P value | Adjusted HR* (95% CI)               | P value |
| COVID-19 severity                                            |                                  |         |                                     |         |
| Mild COVID-19                                                | <b>1.93 (1.68-2.22)</b>          | <0.001  | <b>1.54 (1.43-1.65)</b>             | <0.001  |
| Moderate to severe COVID-19                                  | <b>4.29 (3.55-5.20)</b>          | <0.001  | <b>2.41 (2.16-2.67)</b>             | <0.001  |
| SARS-CoV-2 vaccination dosage                                |                                  |         |                                     |         |
| COVID-19 without SARS-CoV-2 vaccination                      | <b>3.75 (3.26-4.31)</b>          | <0.001  | <b>1.92 (1.80-2.05)</b>             | <0.001  |
| COVID-19 after SARS-CoV-2 vaccination received once          | <b>2.48 (1.82-3.38)</b>          | <0.001  | <b>1.36 (1.13-1.64)</b>             | <0.001  |
| COVID-19 after SARS-CoV-2 vaccination received twice or more | 1.13 (0.92-1.39)                 | 0.261   | 0.93 (0.77-1.11)                    | 0.412   |
| Type of SARS-CoV-2 vaccination                               |                                  |         |                                     |         |

|                                                    |                         |        |                         |             |
|----------------------------------------------------|-------------------------|--------|-------------------------|-------------|
| COVID-19 without SARS-CoV-2 vaccination            | <b>3.74 (3.25-4.30)</b> | <0.001 | <b>1.92 (1.80-2.05)</b> | <0.001      |
| COVID-19 with mRNA SARS-CoV-2 vaccination          | <b>1.39 (1.07-1.81)</b> | 0.013  | <b>1.24 (1.02-1.51)</b> | <b>0.03</b> |
| COVID-19 with viral vector SARS-CoV-2 vaccination  | <b>1.46 (1.15-1.86)</b> | 0.002  | 1.03 (0.86-1.24)        | 0.721       |
| COVID-19 with both types of SARS-CoV-2 vaccination | 0.67 (0.33-1.35)        | 0.261  | 0.66 (0.30-1.48)        | 0.315       |
| <hr/> Strain type (original)                       |                         |        |                         |             |
| Original COVID-19                                  | <b>3.04 (2.56-3.60)</b> | <0.001 | <b>1.74 (1.62-1.87)</b> | <0.001      |
| <hr/> Strain type (delta)                          |                         |        |                         |             |
| Delta COVID-19                                     | <b>1.80 (1.51-2.15)</b> | <0.001 | <b>1.62 (1.41-1.85)</b> | <0.001      |

HR, hazard ratio; CI, confidence interval; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

\* **adjusted HR:** adjusted for age (20–39, 40–59, and ≥ 60 years); sex; household income (low income, middle income, and high income); region of residence (urban and rural); Charlson comorbidity index (0, 1, and ≥ 2); obesity (underweight [ $< 18.5 \text{ kg/m}^2$ ], normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], and obese [ $\geq 25.0 \text{ kg/m}^2$ ]); blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $<$

90 mmHg, systolic blood pressure  $\geq 140$  mmHg or diastolic blood pressure  $\geq 90$  mmHg); fasting blood glucose ( $< 100$  and  $\geq 100$  mg/dL); serum total cholesterol ( $< 200$ , 200–240, and  $\geq 240$  mg/dL); glomerular filtration rate ( $< 60$ , 60–90, and  $\geq 90$  mL/min/1.73 m<sup>2</sup>); smoking status (non-, ex-, and current smoker); alcohol consumption (drinks;  $< 1$ , 1–2, 3–4, and  $\geq 5$  days per week); aerobic physical activity (sufficient and insufficient); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and  $\geq 2$  times); and outpatients contact in the year before index date (0, 1–4, and  $\geq 5$  times).

‡ Comparators defined only 1:4 matched comparators in each patient group at the same index date to reduce an immortal bias.

Data in bold indicate significant differences ( $P < 0.05$ ).

**Figure S1.** Study design in South Korea

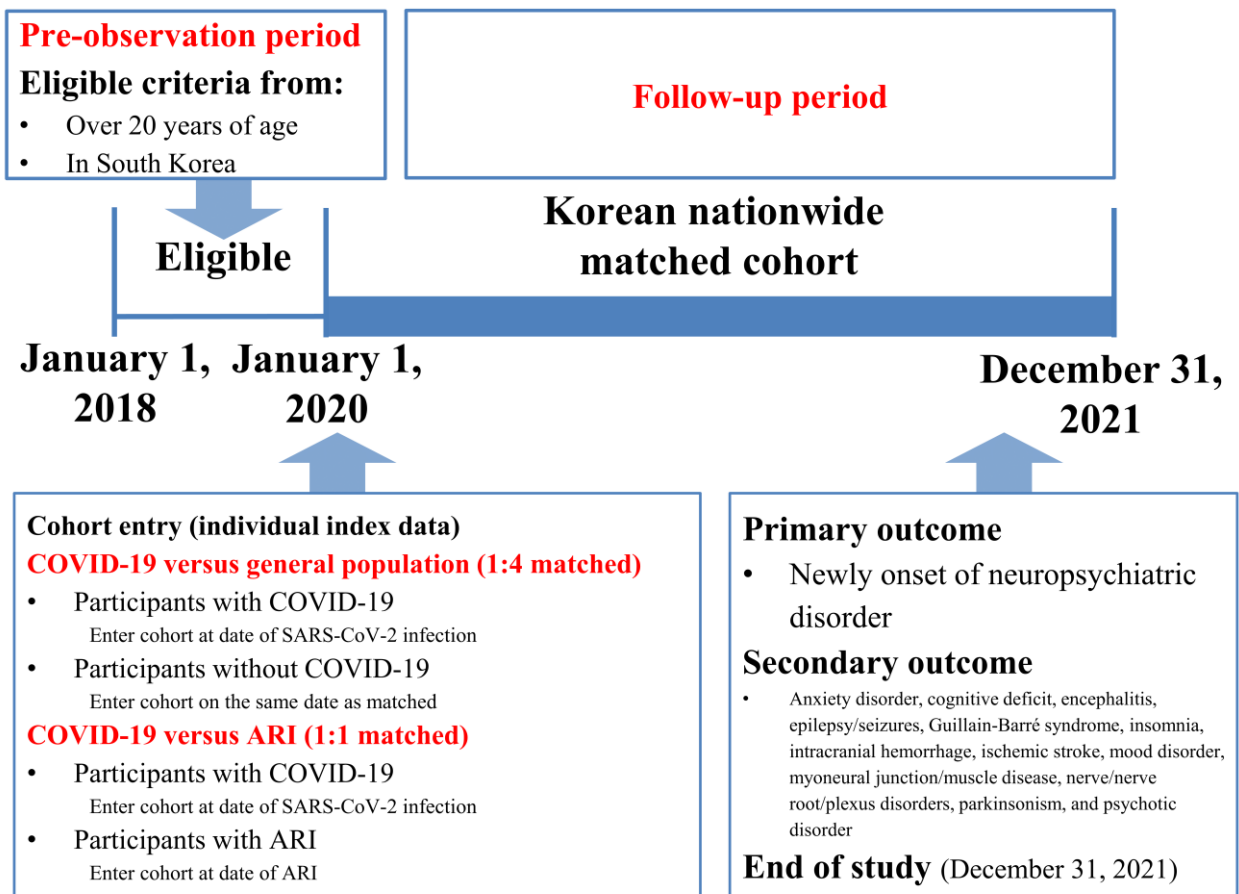


**Figure S2. Study design in Japan**

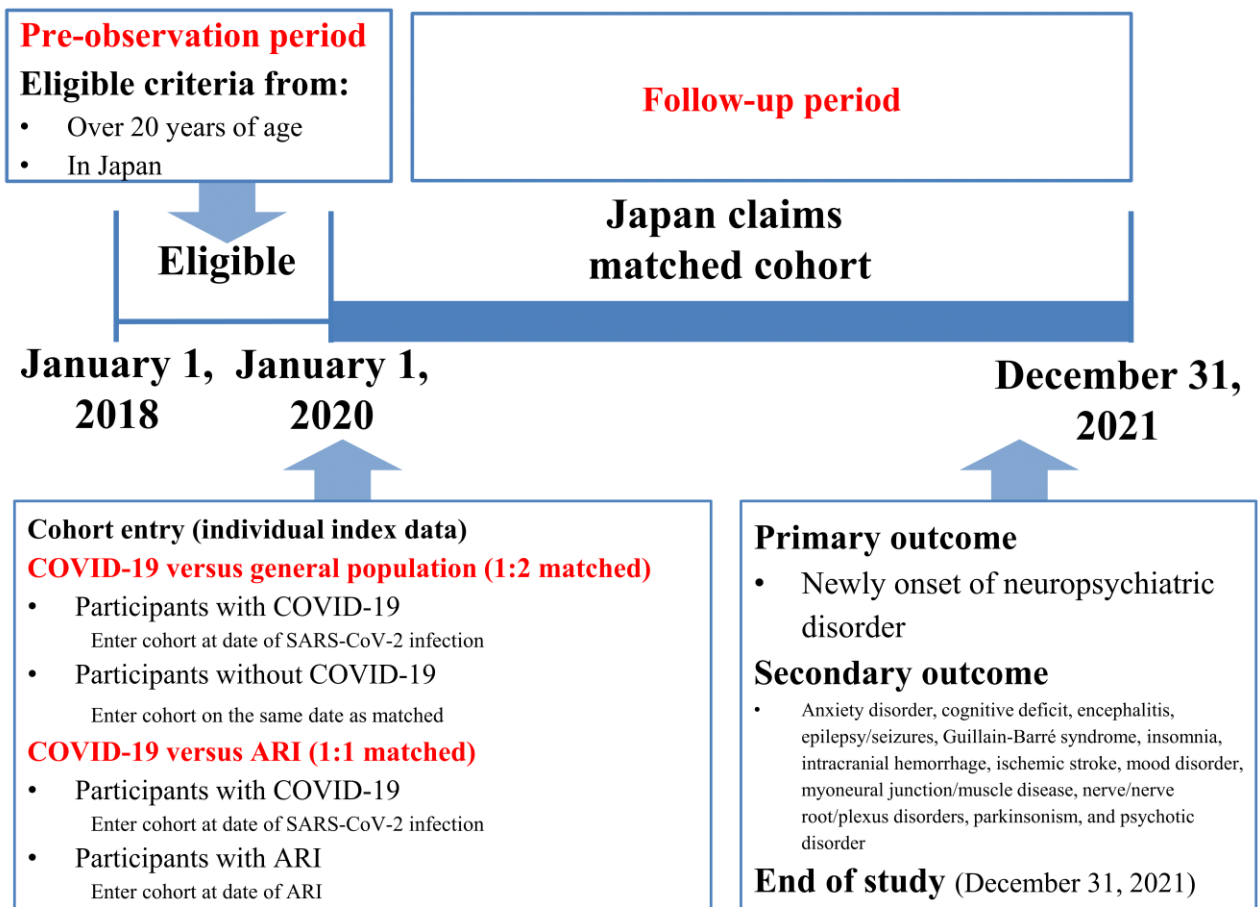


**Figure S3.** Study flow chart (detail version)

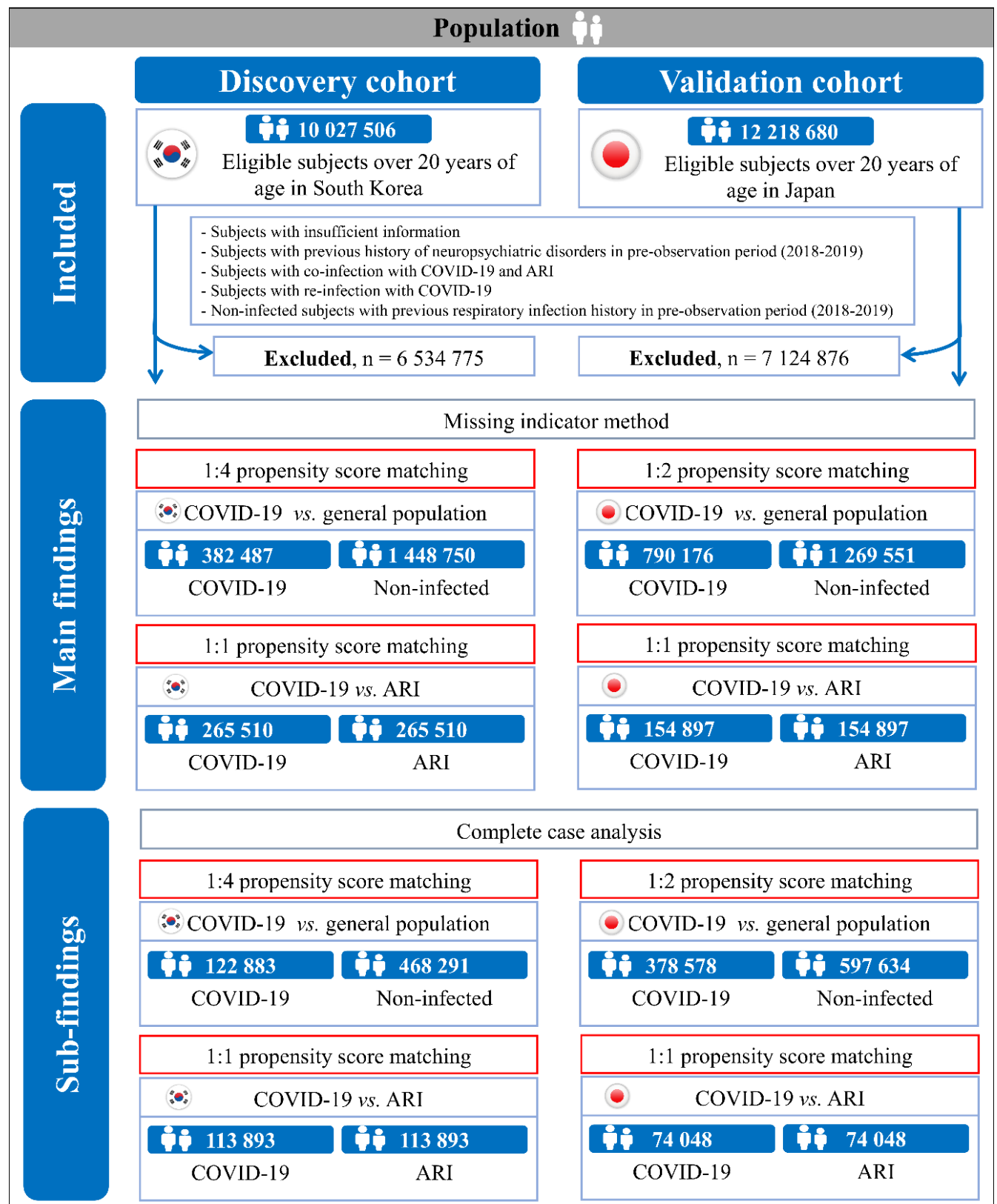


**Figure S4.** Density plot and box plot for before matching and after matching in patients with COVID-19 and non-COVID-19 in South Korea (missing indicator method)

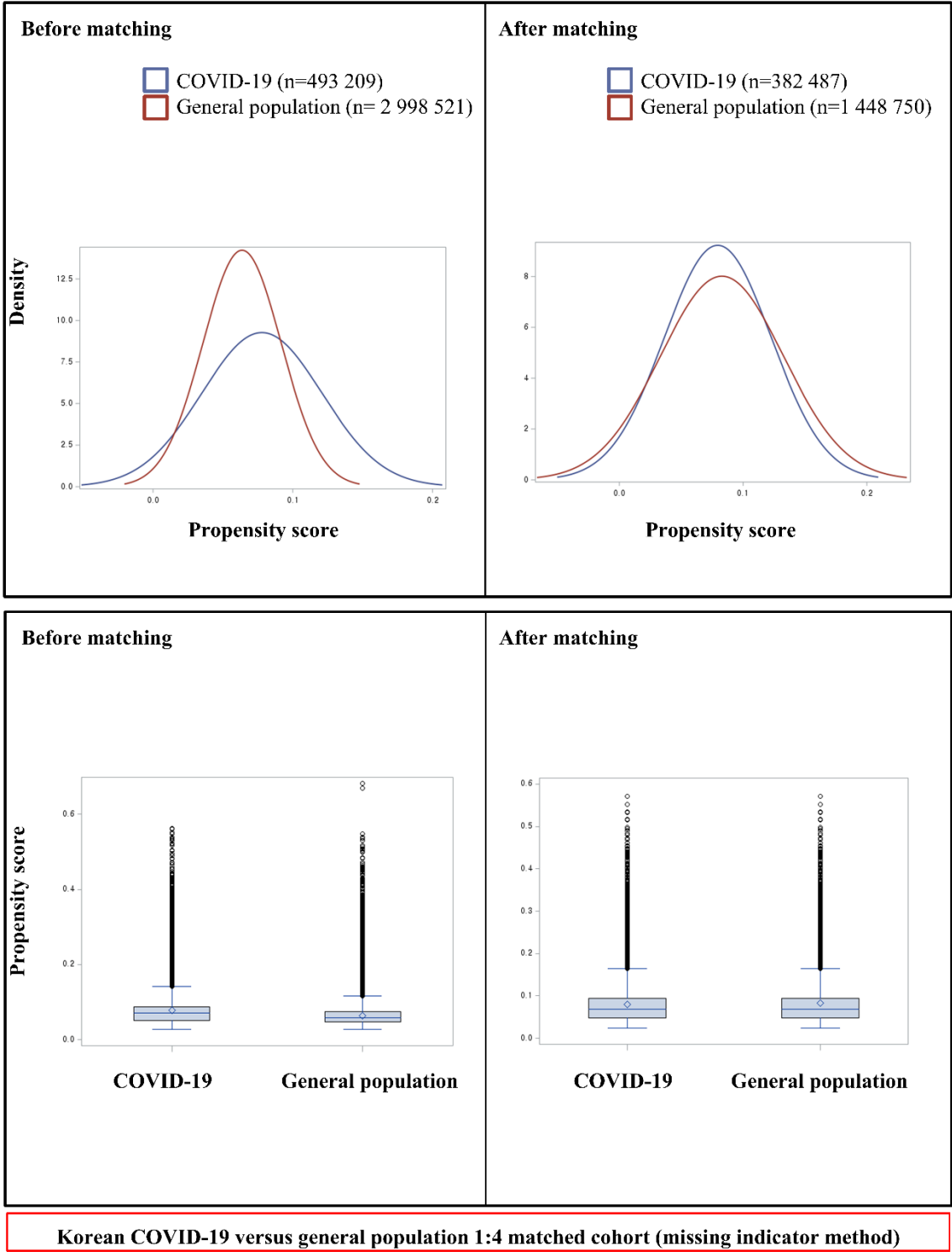


**Figure S5.** Density plot and box plot for before matching and after matching in patients with ARI and non-ARI in South Korea (missing indicator method)

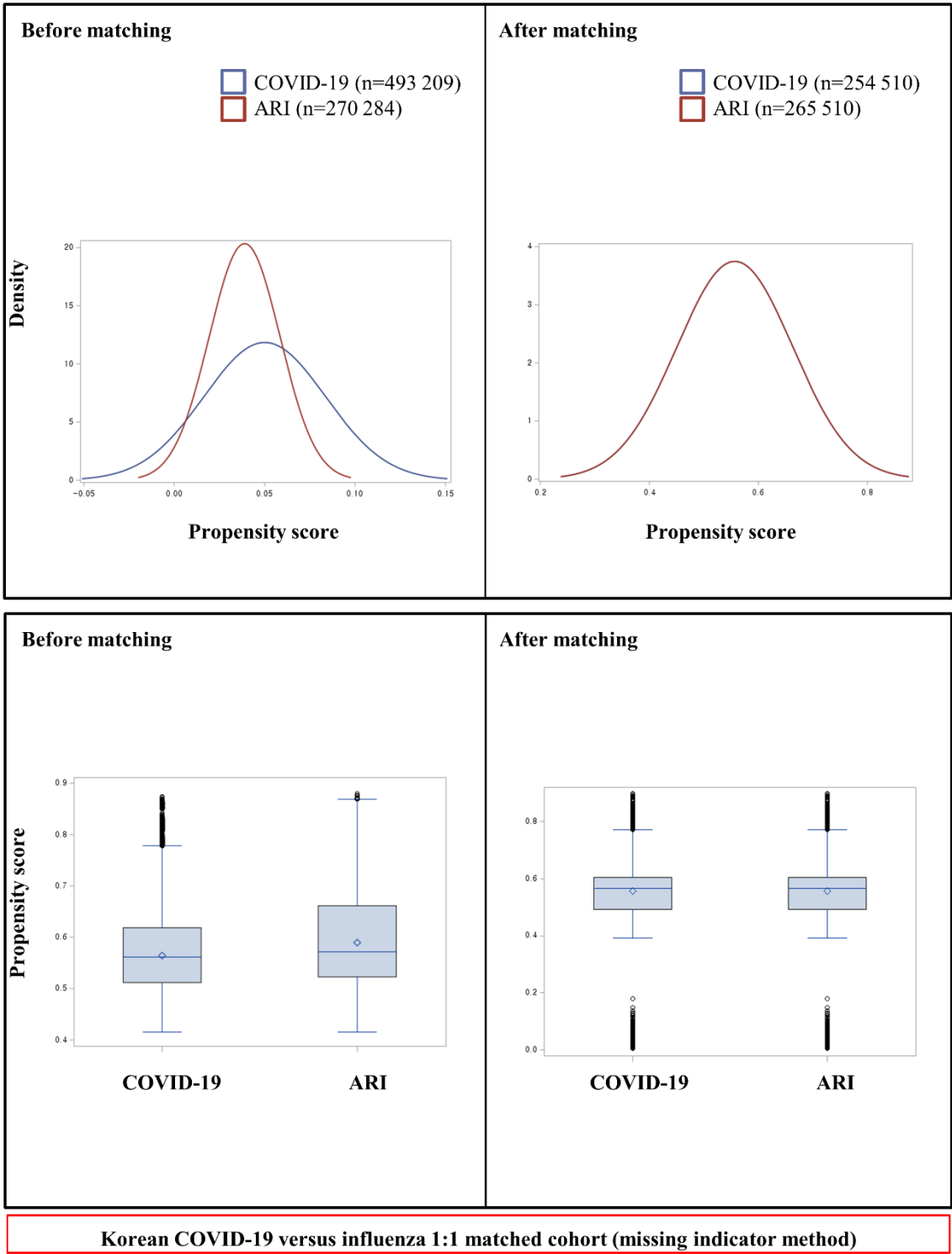


**Figure S6.** Density plot and box plot for before matching and after matching in patients with COVID-19 and non-COVID-19 in South Korea (complete case analysis method)

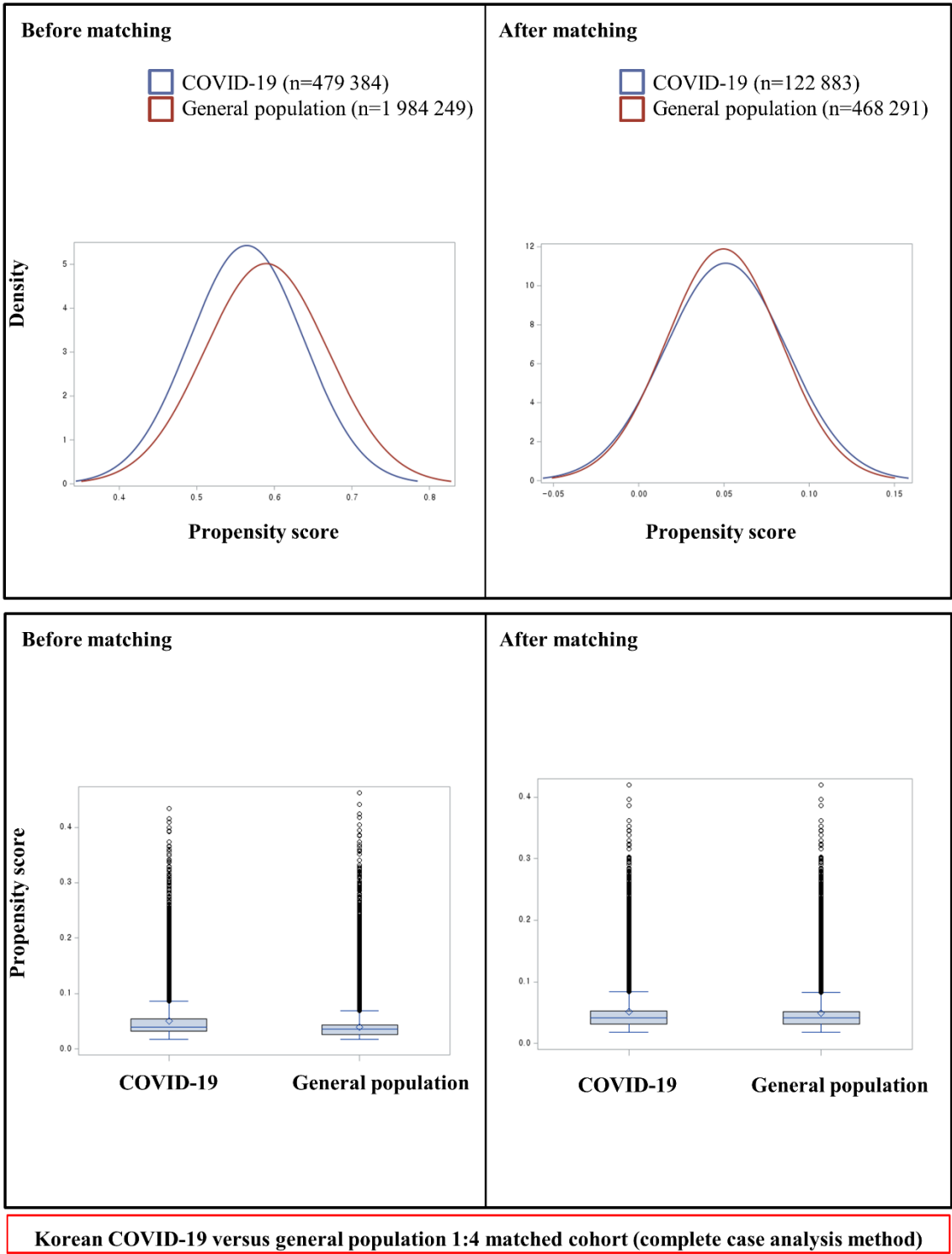


**Figure S7.** Density plot and box plot for before matching and after matching in patients with ARI and non- ARI in South Korea (complete case analysis method)

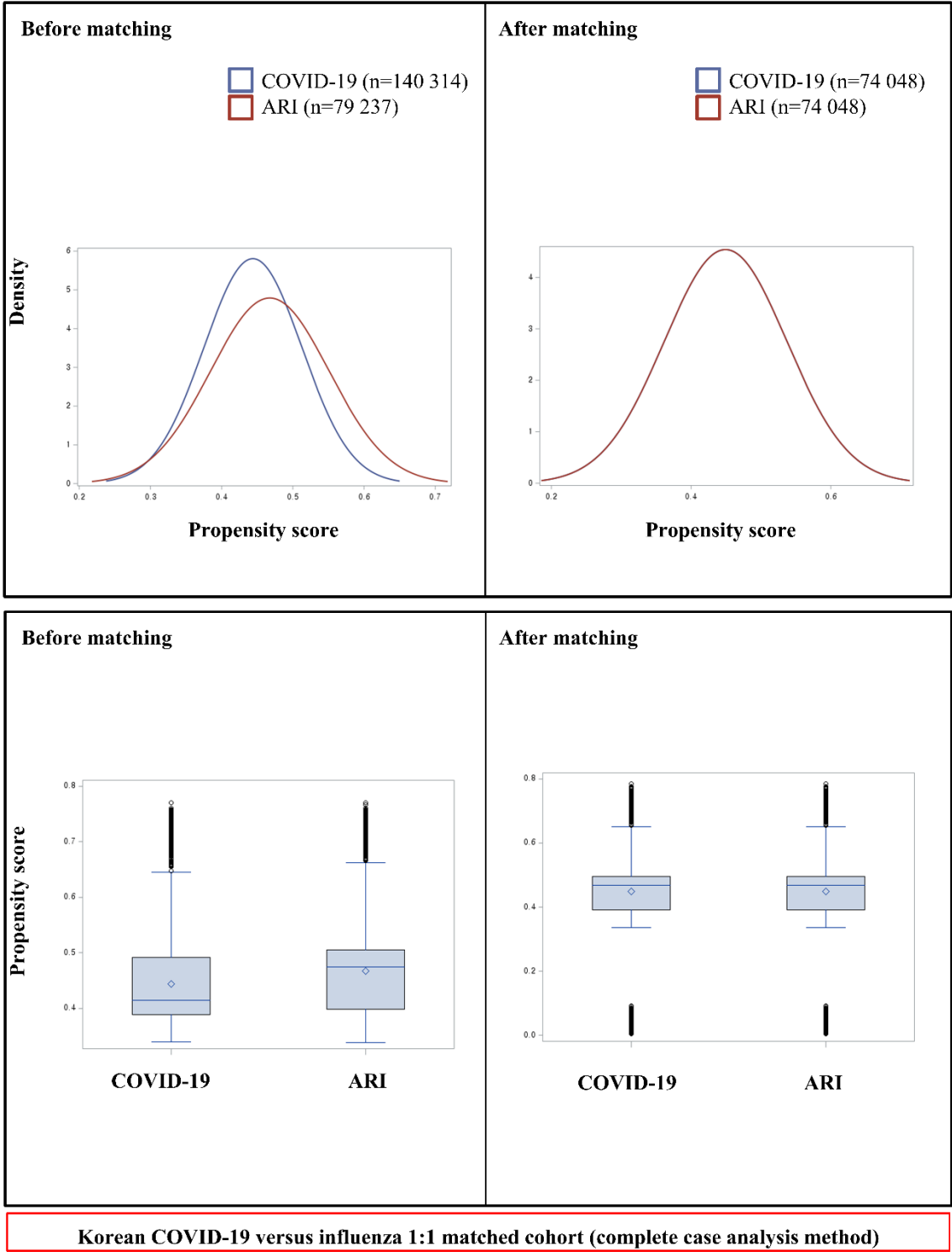


**Figure S8.** Density plot and box plot for before matching and after matching in patients with COVID-19 and non-COVID-19 in Japan (missing indicator method)

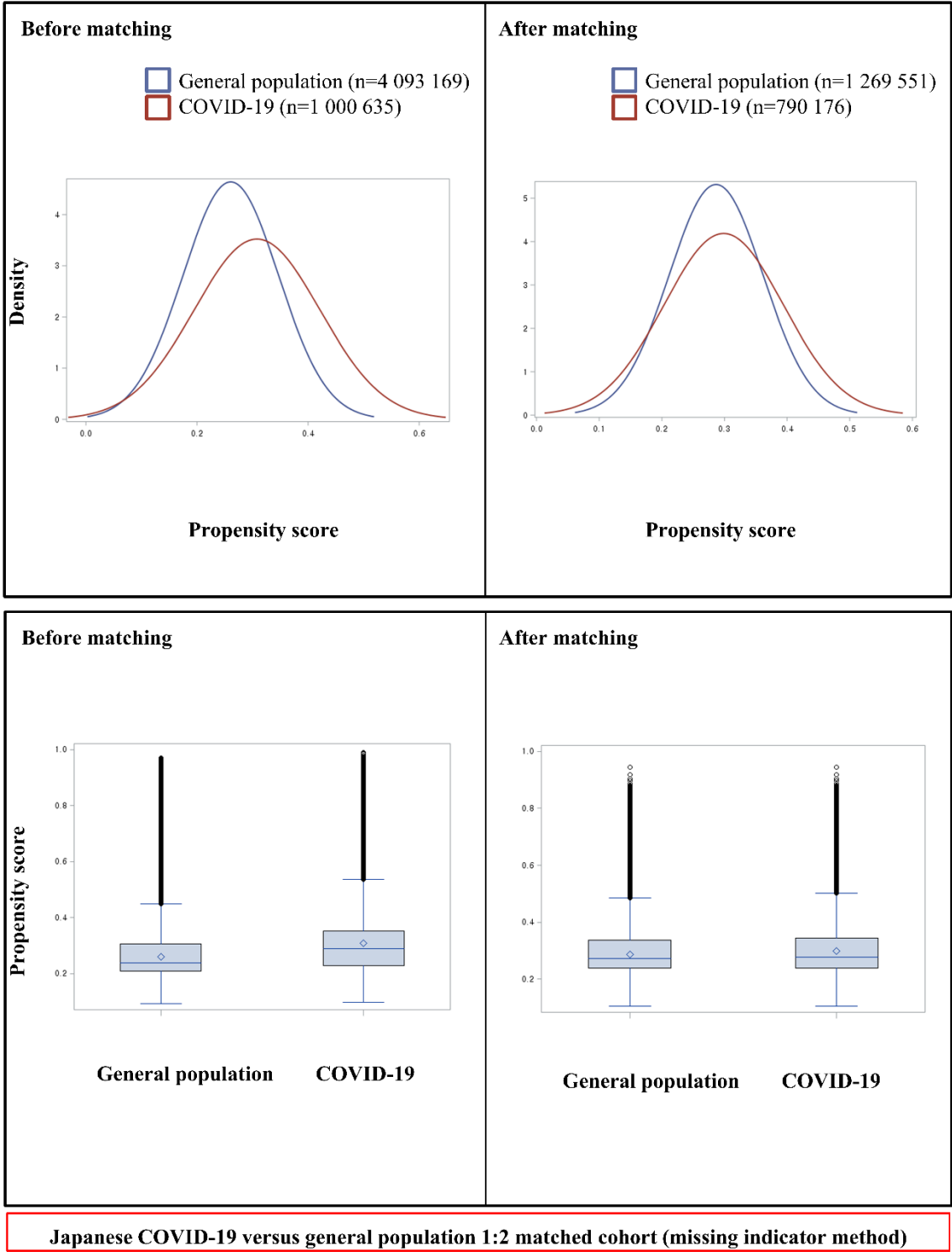


**Figure S9.** Density plot and box plot for before matching and after matching in patients with ARI and non-ARI in Japan (missing indicator method)

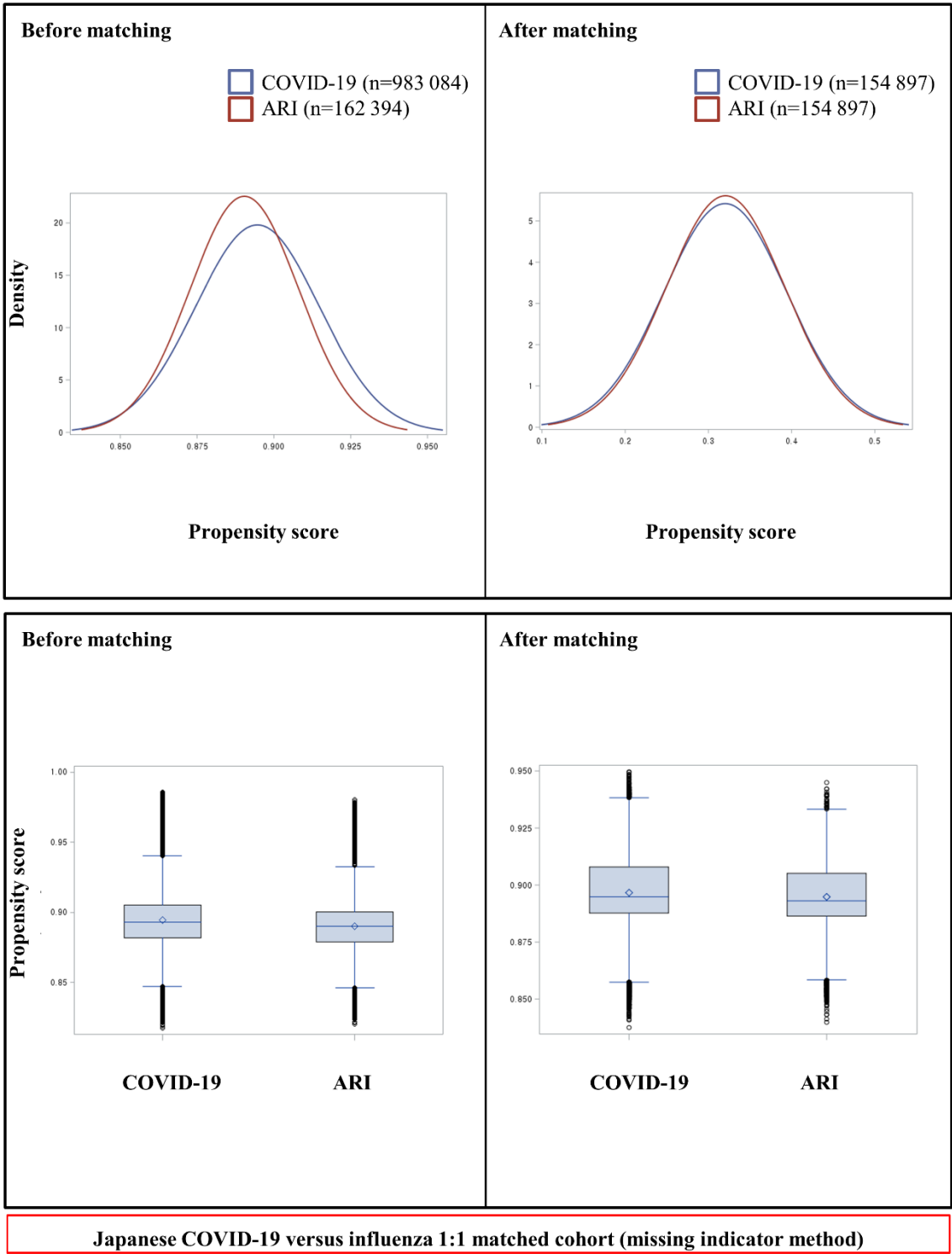


**Figure S10.** Density plot and box plot for before matching and after matching in patients with COVID-19 and non-COVID-19 in Japan (complete case analysis)

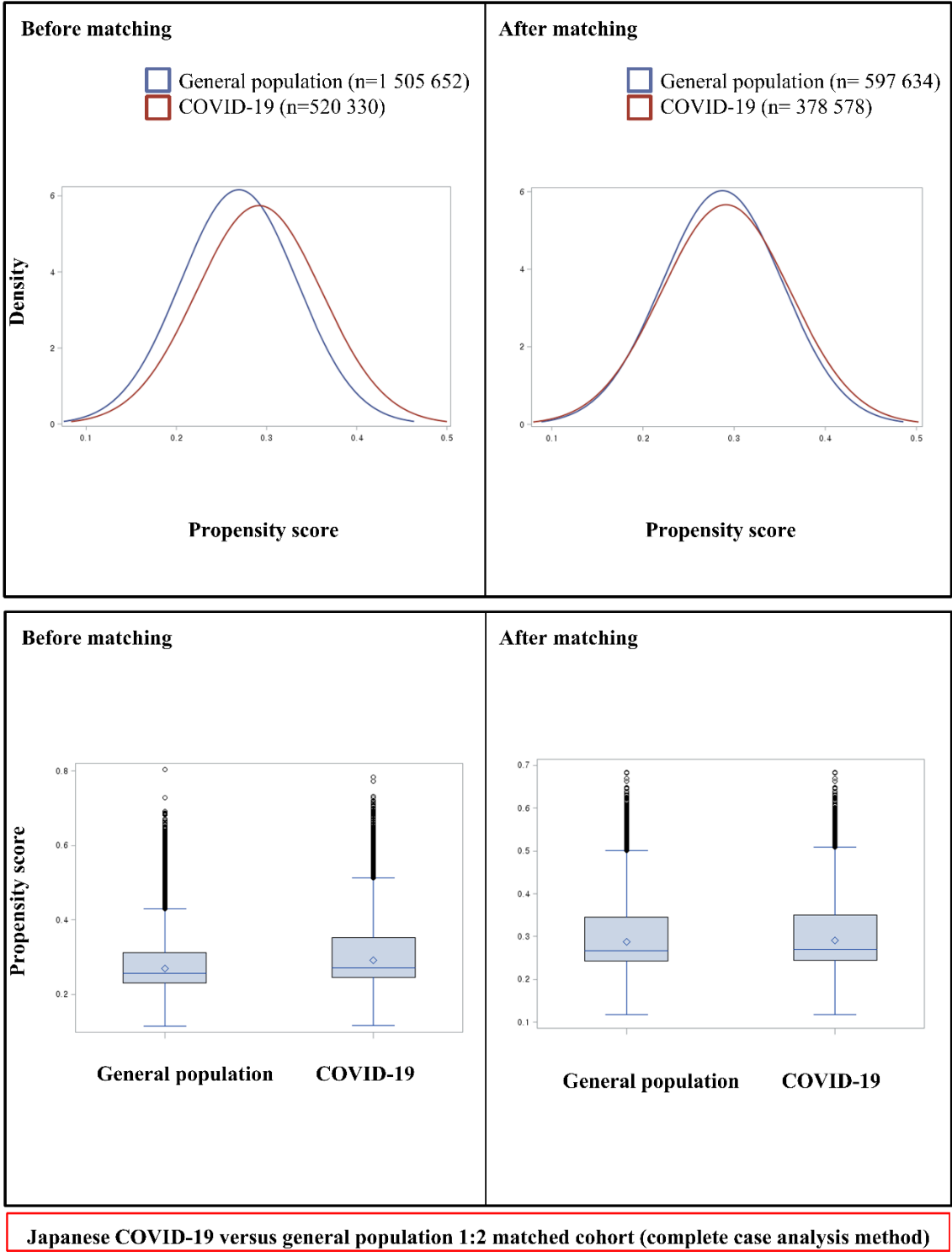
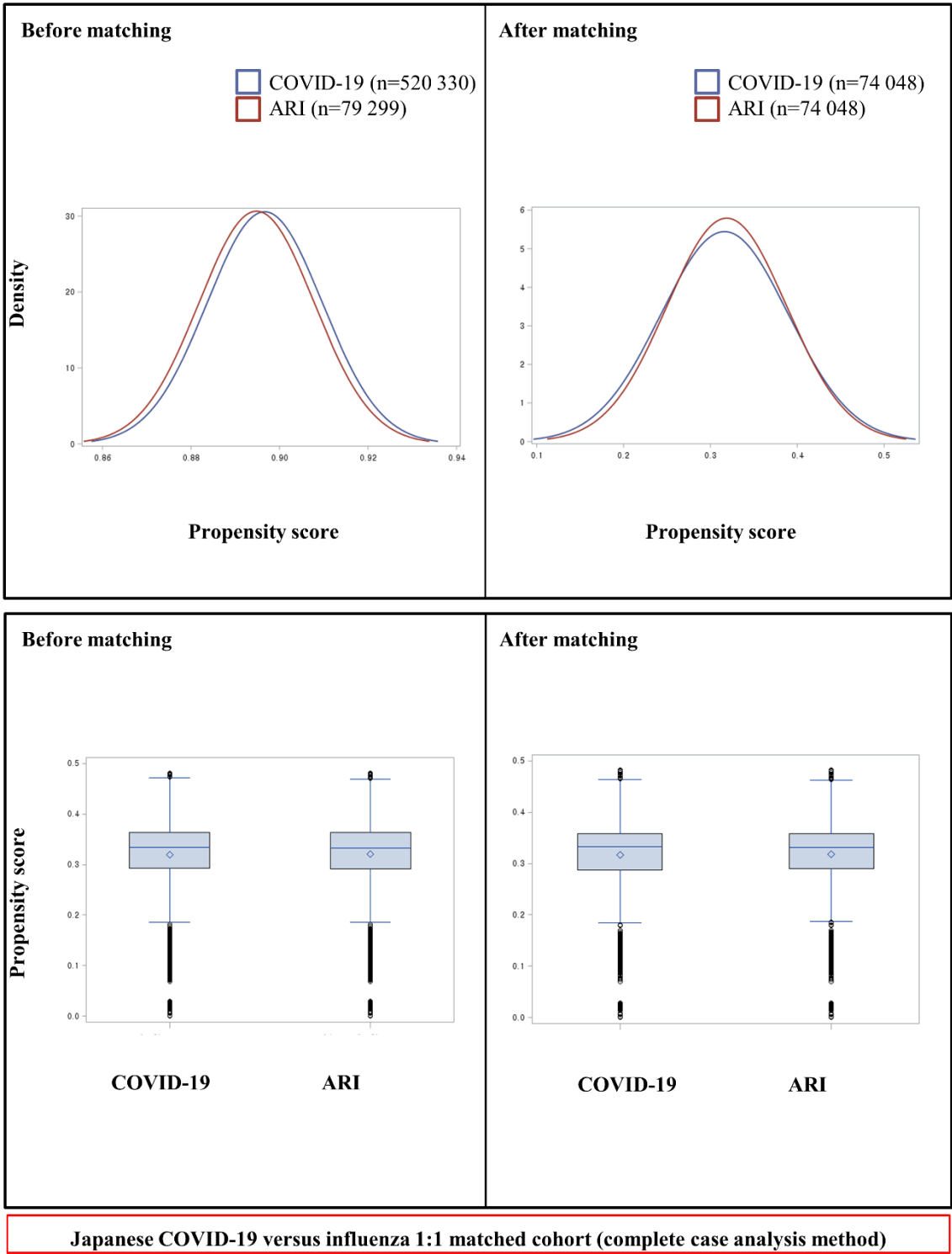


**Figure S11.** Density plot and box plot for before matching and after matching in patients with ARI and non- ARI in Japan (complete case analysis)



### **Supplement Information.** External Validation cohort in Japan

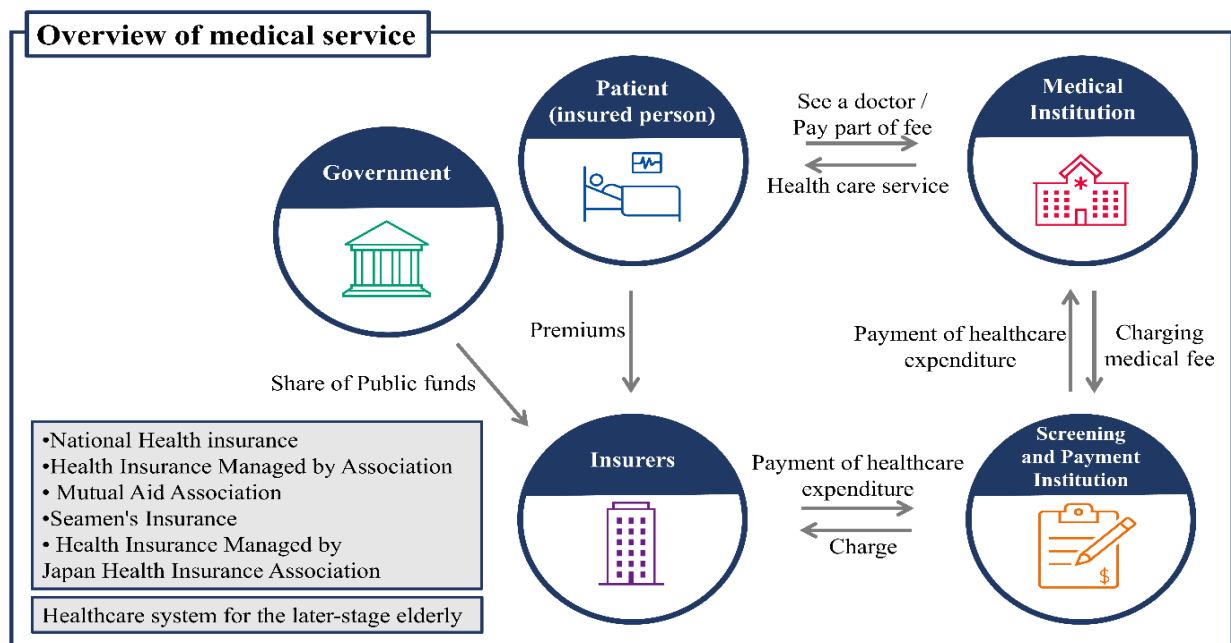
Japan has health insurance provided by the universal insurance system. The Japanese claim-based cohort (JMDC) has contracts with over 60 insurance providers and includes health insurance claim records data of insured individuals, primarily employees of relatively large companies in Japan.<sup>1,2</sup> JMDC has created a database, consisting of patient-level data (age, sex, and insurance status) and claims for inpatient and outpatient (disease class according to ICD-10 code, prescribed drugs based on Anatomical Therapeutic Chemical class, and drug dosage, and form), diagnosis or therapeutic procedure, institutional information (hospital character), and health checkup (i.e., body mass index, blood pressure, laboratory test, medication history, and self-administered questionnaire such as smoking status, alcohol consumption, and physical activity).<sup>3</sup>

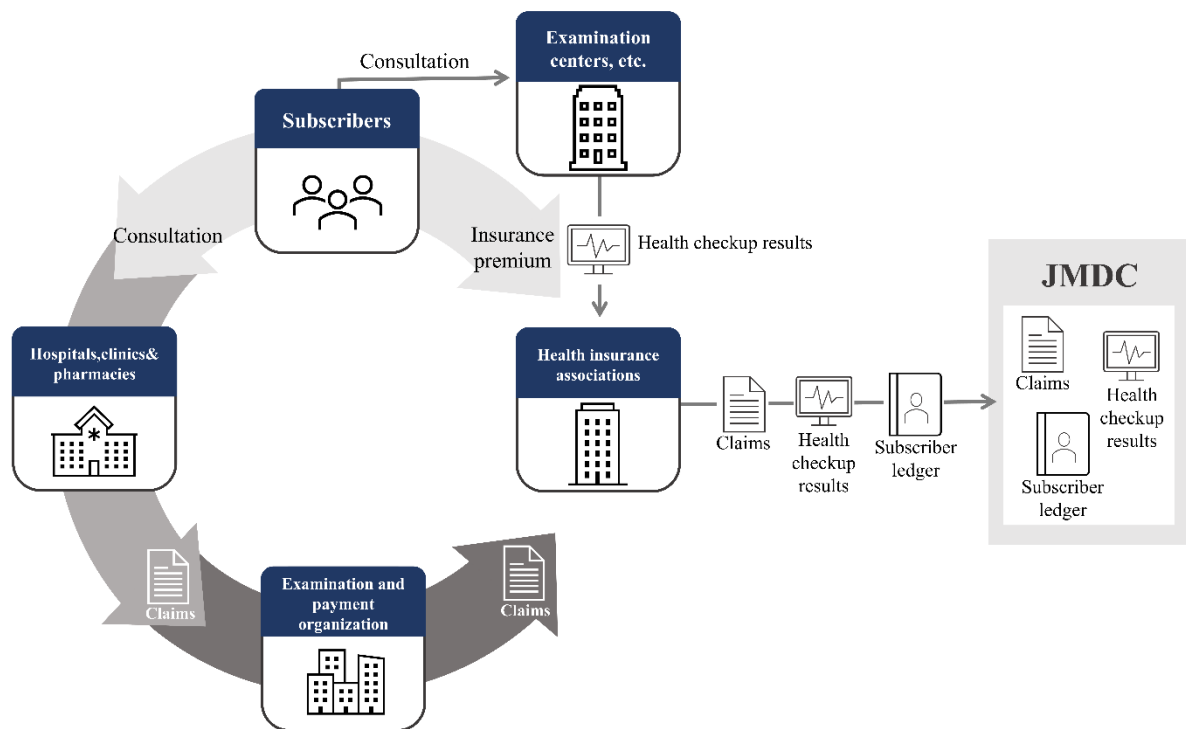
We utilized the ICD-10 codes, general health examination, exposure and outcomes, follow-up duration, and 1:2 propensity score matching for the Japanese claims-based cohort (JMDC cohort; total n=12,218,680) as we did for the South Korean cohort. However, as COVID-19 vaccination data were absent in the JMDC cohort, we decided to consider the JMDC solely to validate the primary findings obtained from South Korea. After conducting matching and addressing missing values (missing indicator method and the complete case method), we conducted separate Cox analyses for each cohort.

Participants who tested positive for COVID-19 were selected from January 1, 2020, to December 31, 2021. The Institutional Review Board of Kyung Hee University Hospital (KHUH 2022-06-042) and JMDC approved the current study. The requirement for informed consent was waived because this study used de-identified administrative data. This study followed the Reporting of studies Conducted using an Observational Routinely-collected

## health Data (RECORD) Statement

Among the participants in the JMDC cohort, we excluded the following: (1) those with insufficient socioeconomic status information or who died before; (2) those with a previous history of neuropsychiatric disorders (anxiety disorder, cognitive deficit, dementia, encephalitis, epilepsy/seizures, Guillain-Barre syndrome, insomnia, intracranial hemorrhage, ischemic stroke, mood disorder, myoneural junction/muscle disease, nerve/nerve root/plexus disorders, parkinsonism, and psychotic disorder) in the pre-observation period (2018–2019); and (3) those with co-infection with COVID-19 and another respiratory infection (ARI). Finally, in the general population group, patients with ARI between 2018 and 2019 were excluded (n=7,124,876).





## Exposures

COVID-19 prior exposure in the matched COVID-19 cohort was defined if the participants tested positive for the SARS-CoV-2 infection.<sup>4</sup> Moderate to severe COVID-19 was defined for patients admitted to the intensive care unit, or requiring oxygen therapy, extracorporeal membrane oxygenation, renal replacement, or cardio resuscitation. Others were defined as having mild COVID-19.<sup>4</sup>

ARI primary exposure in the matched ARI cohort was defined if the participants were diagnosed with J00 to J22 (J00-06, acute respiratory infection; J09-18, influenza and pneumonia; and J20-22, Other acute lower respiratory infections) using the International Classification of Disease 10th revision (ICD-10) codes twice or more within one year, during the COVID-19 pandemic (2020–2021). ARIs diagnosed in 2018–2019 were excluded from the study.

## ***Outcomes***

The primary outcome was the onset of neuropsychiatric outcomes, classified into 13 categories. The outcomes were defined if a participant was diagnosed with a particular outcome twice or more within one year using the following ICD-10 codes: (1) anxiety disorder, (2) cognitive deficit, (3) encephalitis, (4) epilepsy/seizures, (5) Guillain-Barre syndrome, (6) insomnia, (7) intracranial hemorrhage, (8) ischemic stroke, (9) mood disorder, (10) myoneural junction/muscle disease, (11) nerve/nerve root/plexus disorders, (12) parkinsonism, and (13) psychotic disorder. (Table S10) Participants were classified as having a neuropsychiatric outcome if they were diagnosed with any of these outcomes. The short-term risk of a neuropsychiatric event was defined as one of 13 neuropsychiatric outcomes that first occurred within 30 days after the SARS-CoV-2 diagnosing date. The long-term sequelae risk of neuropsychiatric events was defined as one of the 13 neuropsychiatric outcomes that occurred 30 days after the SARS-CoV-2 diagnosing date.

## ***Covariates***

Data on age, sex, household income, and region of residence were obtained from the insurance dataset. Adjusting covariates were selected for age (20–39, 40–59, and  $\geq 60$  years); sex; insurance status (insured or dependent); body mass index (underweight [ $< 18.5 \text{ kg/m}^2$ ]; normal [ $18.5\text{--}23.0 \text{ kg/m}^2$ ], overweight [ $23.0\text{--}25.0 \text{ kg/m}^2$ ], obese [ $\geq 25.0 \text{ kg/m}^2$ ], and unknown)<sup>5</sup>; blood pressure (systolic blood pressure  $< 140 \text{ mmHg}$  and diastolic blood pressure  $< 90 \text{ mmHg}$ , systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ , and unknown);

fasting blood glucose (< 100, ≥ 100 mg/dL, and unknown); serum total cholesterol (< 200, 200–240, ≥ 240 mg/dL, and unknown); glomerular filtration rate (< 60, 60–90, ≥ 90 mL/min/1.73 m<sup>2</sup>, and unknown); smoking status (non-, current smoker, and unknown); alcohol consumption (rarely, sometimes, every day, and unknown); aerobic physical activity (sufficient, insufficient, unknown); previous history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease; and history of medication use for diabetes mellitus, dyslipidemia, and hypertension; hospital admissions in the year before index date (0, 1, and ≥2 times); and outpatients contact in the year before index date (0, 1-4, and ≥5 times). Sufficient aerobic physical activity was defined if the participants engaged in aerobic physical activity amounting to ≥ 600 Metabolic Equivalent Task scores (MET-min/week) based on World Health Organization guidelines on physical activity.<sup>6</sup>

### ***Propensity score matching***

We selected general population or individuals diagnosed with ARI as a comparator to differentiate the incidence risk of neuropsychiatric disorders following SARS-CoV-2 infection from the casual manifestations of ARI or general population.

We performed exposure-driven propensity score matching to determine the robustness and generalizability of our main results and to balance the baseline covariates of the two groups from the predicted probability of (1) subjects with COVID-19 vs. general population and (2) subjects with COVID-19 vs. those with ARI. We generated 1:2 (COVID-19 vs. general population) or 1:1 (COVID-19 vs. ARI) matching cohorts using a ‘greedy nearest-neighbor’ algorithm (random selection without subject replacement within caliper widths [0.001 standard

deviations]).

Finally, we conducted a total of 8 rounds of exposure-driven propensity score matching to derive an adjusted logistic regression model from the predicted probabilities of the exposure group (SARS-CoV-2) vs. the general population or the external comparator (ARI); 1:4 COVID-19 vs. general population in South Korea using (1) the missing indicator method (382,487 vs. 1,448,750) and (2) the complete case analysis method (122,883 vs. 468,291); 1:1 COVID-19 vs. ARI in South Korea using (3) the missing indicator method (265,510 vs. 265,510) and (4) the complete case analysis method (113,893 vs. 113,893); 1:2 COVID-19 vs. general population in Japan using (5) the missing indicator method (790,176 vs. 1,269,551) and the complete case analysis method (378,578 vs. 597,634); and 1:1 COVID-19 vs. ARI Japan using (7) the missing indicator method (154,897 vs. 154,897) and (8) the complete case analysis method (74,048 vs. 74,048).

### ***Statistical analysis***

In validation cohorts, SARS-CoV-2 infection or ARI was defined as “primary exposure,” and the onset of neuropsychiatric outcome was defined as “primary outcome.” The date of first diagnosis of SARS-CoV-2 infection or ARI or matched data among non-infected participants was considered the “individual index date” to reduce immortal time bias. The follow-up ended on December 31, 2021, or at the participant’s death. Japan and Korean data are constructed without immigrants during the data construction process, analysis on immigration is omitted.

A Cox proportional hazard regression model (endpoint in short-term, long-term, and overall risk of neuropsychiatric events) with hazard ratios (HRs) and 95% confidence intervals (CIs) was estimated. Further, we analyzed the time attenuation effect after SARS-CoV-2 infection or

ARI (1–6, 6–12, and  $\geq 12$  months) to reduce reverse causation. For the matched COVID-19 cohort, we performed several analyses such as stratification by 13 neuropsychiatric diseases and COVID-19 severity (none, mild, and moderate to severe). We performed multiple subgroup analyses using sex, age group, household income, Charlson Comorbidity Index, BMI, smoking status, alcohol consumption, and aerobic physical activity. We conducted competing risk analysis (considering death and/or neuropsychiatric events) and utilized an alternative cohort with a more stringent definition (alternative neuropsychiatric definitions was defined using ICD-10 codes with  $\geq 3$  or  $\geq 4$  claims by a patient within 1 year).<sup>7</sup> To reduce unpredictable bias, we performed both the missing indicator method and complete case analysis models, but presented the final analysis result by adopting the missing indicator method. Statistical analyses were performed using SAS (version 9.4; SAS Institute Inc., Cary, NC, USA).<sup>8</sup> A two-tailed P-value of less than 0.05 was considered statistically significant.

**Supplement Information.** The RECORD statement, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data

|                           | Item No. | STROBE items                                                                                                                                                                               | Location in manuscript where items are reported | RECORD items                                                                                                                                                                                                                                                                                                                                                                                                                                | Location in manuscript where items are reported |
|---------------------------|----------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------|
| <b>Title and abstract</b> |          |                                                                                                                                                                                            |                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                 |
|                           | 1        | (a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found |                                                 | RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included.<br><br>RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract.<br><br>RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract. | Title Page                                      |
| <b>Introduction</b>       |          |                                                                                                                                                                                            |                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                 |
| Background rationale      | 2        | Explain the scientific background and rationale for                                                                                                                                        |                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                             | Introduction                                    |

|                |   |                                                                                                                                                                                                                                                                                                                                                 |  |                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                 |
|----------------|---|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------|
|                |   | the investigation being reported                                                                                                                                                                                                                                                                                                                |  |                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                 |
| Objectives     | 3 | State specific objectives, including any prespecified hypotheses                                                                                                                                                                                                                                                                                |  |                                                                                                                                                                                                                                                                                                                                                                                                                 | Introduction                                                    |
| <b>Methods</b> |   |                                                                                                                                                                                                                                                                                                                                                 |  |                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                 |
| Study Design   | 4 | Present key elements of study design early in the paper                                                                                                                                                                                                                                                                                         |  |                                                                                                                                                                                                                                                                                                                                                                                                                 | -Discovery cohort in South Korea<br>-Validation cohort in Japan |
| Setting        | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection                                                                                                                                                                                                                 |  |                                                                                                                                                                                                                                                                                                                                                                                                                 | -Discovery cohort in South Korea<br>-Validation cohort in Japan |
| Participants   | 6 | (a) <i>Cohort study</i> - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up<br><i>Case-control study</i> - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls |  | RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided.<br><br>RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed | -Discovery cohort in South Korea<br>-Validation cohort in Japan |

|                              |   |                                                                                                                                                                                                                                                                                                                                                                   |  |                                                                                                                                                                                                                                                                                      |                                                                            |
|------------------------------|---|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|
|                              |   | <p><i>Cross-sectional study</i> - Give the eligibility criteria, and the sources and methods of selection of participants</p> <p><i>(b) Cohort study</i> - For matched studies, give matching criteria and number of exposed and unexposed</p> <p><i>Case-control study</i> - For matched studies, give matching criteria and the number of controls per case</p> |  | <p>methods and results should be provided.</p> <p>RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.</p> |                                                                            |
| Variables                    | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.                                                                                                                                                                                                                         |  | RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.                                                                      | <p>-Outcomes</p> <p>-Covariates</p>                                        |
| Data sources/<br>measurement | 8 | <p>For each variable of interest, give sources of data and details of methods of assessment (measurement).</p> <p>Describe comparability of assessment methods if there is more than one group</p>                                                                                                                                                                |  |                                                                                                                                                                                                                                                                                      | <p>-Discovery cohort in South Korea</p> <p>-Validation cohort in Japan</p> |
| Bias                         | 9 | Describe any efforts to address potential sources of bias                                                                                                                                                                                                                                                                                                         |  |                                                                                                                                                                                                                                                                                      | Propensity score matching                                                  |

|                        |    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |  |  |                                                                 |
|------------------------|----|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|-----------------------------------------------------------------|
| Study size             | 10 | Explain how the study size was arrived at                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |  |  | -Discovery cohort in South Korea<br>-Validation cohort in Japan |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why                                                                                                                                                                                                                                                                                                                                                                                               |  |  | -Discovery cohort in South Korea<br>-Validation cohort in Japan |
| Statistical methods    | 12 | (a) Describe all statistical methods, including those used to control for confounding<br>(b) Describe any methods used to examine subgroups and interactions<br>(c) Explain how missing data were addressed<br>(d) <i>Cohort study</i> - If applicable, explain how loss to follow-up was addressed<br><i>Case-control study</i> - If applicable, explain how matching of cases and controls was addressed<br><i>Cross-sectional study</i> - If applicable, describe analytical methods taking account of sampling strategy |  |  | Statistical analysis                                            |

|                                  |    |                                                                                                                                                                                                                                                                                           |  |                                                                                                                                                                                                                                                                                                                    |                      |
|----------------------------------|----|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|
|                                  |    | (e) Describe any sensitivity analyses                                                                                                                                                                                                                                                     |  |                                                                                                                                                                                                                                                                                                                    |                      |
| Data access and cleaning methods |    | ..                                                                                                                                                                                                                                                                                        |  | <p>RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population.</p> <p>RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.</p>                                                | Statistical analysis |
| Linkage                          |    | ..                                                                                                                                                                                                                                                                                        |  | RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.                                                                                          | Statistical analysis |
| <b>Results</b>                   |    |                                                                                                                                                                                                                                                                                           |  |                                                                                                                                                                                                                                                                                                                    |                      |
| Participants                     | 13 | <p>(a) Report the numbers of individuals at each stage of the study (<i>e.g.</i>, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed)</p> <p>(b) Give reasons for non-participation at each stage.</p> |  | RECORD 13.1: Describe in detail the selection of the persons included in the study ( <i>i.e.</i> , study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram. | Results              |

|                  |    |                                                                                                                                                                                                                                                                                                                                                 |  |  |         |
|------------------|----|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|---------|
|                  |    | (c) Consider use of a flow diagram                                                                                                                                                                                                                                                                                                              |  |  |         |
| Descriptive data | 14 | (a) Give characteristics of study participants ( <i>e.g.</i> , demographic, clinical, social) and information on exposures and potential confounders<br>(b) Indicate the number of participants with missing data for each variable of interest<br>(c) <i>Cohort study</i> - summarise follow-up time ( <i>e.g.</i> , average and total amount) |  |  | Results |
| Outcome data     | 15 | <i>Cohort study</i> - Report numbers of outcome events or summary measures over time<br><i>Case-control study</i> - Report numbers in each exposure category, or summary measures of exposure<br><i>Cross-sectional study</i> - Report numbers of outcome events or summary measures                                                            |  |  | Results |
| Main results     | 16 | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision ( <i>e.g.</i> , 95% confidence interval). Make clear which confounders were                                                                                                                                                                 |  |  | Results |

|                   |    |                                                                                                                                                                                                                                          |  |                                                                                                                                                                                                                                                                                                          |                                      |
|-------------------|----|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|
|                   |    | adjusted for and why they were included<br>(b) Report category boundaries when continuous variables were categorized<br>(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period |  |                                                                                                                                                                                                                                                                                                          |                                      |
| Other analyses    | 17 | Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses                                                                                                                                        |  |                                                                                                                                                                                                                                                                                                          | Results                              |
| <b>Discussion</b> |    |                                                                                                                                                                                                                                          |  |                                                                                                                                                                                                                                                                                                          |                                      |
| Key results       | 18 | Summarise key results with reference to study objectives                                                                                                                                                                                 |  |                                                                                                                                                                                                                                                                                                          | Discussion                           |
| Limitations       | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias                                                                               |  | RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported. | Limitations                          |
| Interpretation    | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of                                                                                                                                   |  |                                                                                                                                                                                                                                                                                                          | Basic mechanisms in neuropsychiatric |

|                                                           |    |                                                                                                                                                               |  |                                                                                                                                                          |                                    |
|-----------------------------------------------------------|----|---------------------------------------------------------------------------------------------------------------------------------------------------------------|--|----------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|
|                                                           |    | analyses, results from similar studies, and other relevant evidence                                                                                           |  |                                                                                                                                                          | outcomes and COVID-19              |
| Generalisability                                          | 21 | Discuss the generalisability (external validity) of the study results                                                                                         |  |                                                                                                                                                          | Comparisons with previous research |
| <b>Other Information</b>                                  |    |                                                                                                                                                               |  |                                                                                                                                                          |                                    |
| Funding                                                   | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based |  |                                                                                                                                                          | Funding                            |
| Accessibility of protocol, raw data, and programming code |    | ..                                                                                                                                                            |  | RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code. | NA                                 |

\*Reference: Benchimol EI, Smeeth L, Guttman A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.

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