

# **Supplementary materials for the study ‘COVID-19 infection associated with increased risk of new-onset vascular dementia in adults $\geq 50$ years’**

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Table S1. Classification of certain diseases and their ICD-10 codes in the UK Biobank

| Type                           | ICD-10 codes |
|--------------------------------|--------------|
| <b>Cardiovascular diseases</b> |              |
| Heart failure                  | I50          |
| Coronary artery disease        | I20-25       |
| Cardiomyopathy                 | I42          |
| <b>Neurological diseases</b>   |              |
| Stroke                         | I63, I64     |
| Parkinson's disease            | G20          |
| Huntington's disease           | G10          |
| Multiple sclerosis             | G35          |
| Sleep disorders                | G47          |
| Intracranial injury            | S06          |
| <b>Mental illnesses</b>        |              |
| Depressive disorder            | F32, F33     |
| Schizophrenia                  | F20          |
| Bipolar disorder               | F31          |
| <b>Cancer</b>                  | C00-C97      |

ICD-10 diagnoses were taken from linked records with dates  $\leq$  index date; no fixed look-back limit was imposed.

Table S2. The ICD-10 codes of dementia in UK Biobank

| Type                    | ICD-10 codes   |
|-------------------------|--|
| Alzheimer's dementia    | F00, F00.0, F00.1, F00.2, F00.9, G30, G30.0, G30.1, G30.8, G30.9               |
| Vascular dementia       | F01, F01.0, F01.1, F01.2, F01.3, F01.8, F01.9, I67.3                           |
| Frontotemporal dementia | F02.0, G31.0   |
| Others                  | A81.0, F02, F02.1, F02.2, F02.3, F02.4, F02.8, F03, F05.1, F10.6, G31.1, G31.8 |

Table S3. Information on missing covariates among 54,757 UK Biobank participants

| <b>Covariates</b>          | <b>Number of missing</b> | <b>Missing rates (%)</b> |
|----------------------------|--------------------------|--------------------------|
| Ethnicity                  | 313                      | 0.57                     |
| Body mass index            | 430                      | 0.79                     |
| Townsend Deprivation Index | 69                       | 0.13                     |
| Metabolic equivalent task  | 13,646                   | 24.92                    |
| Smoking status             | 395                      | 0.72                     |
| Alcohol intake frequency   | 202                      | 0.37                     |
| Hypertension               | 107                      | 0.2                      |
| Diabetes mellitus          | 166                      | 0.3                      |

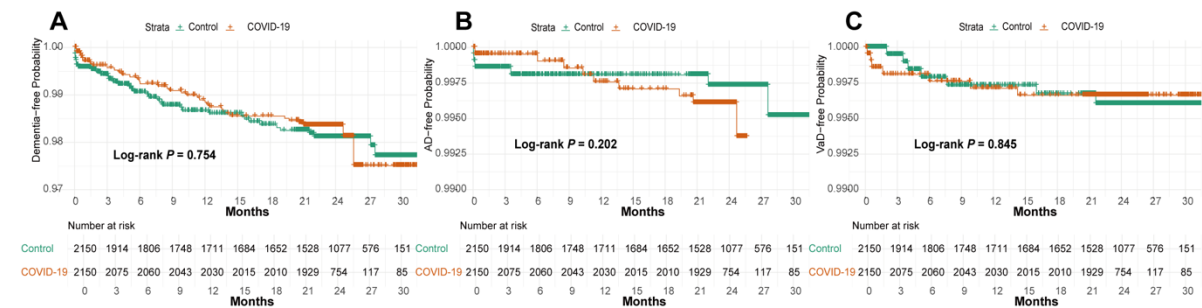
Table S4. Baseline characteristics of the 1:1 PSM dataset 2 in the UK Biobank

| Characteristics                   | Covid-19<br>(n=2,150) | Non-COVID respiratory<br>conditions (n=2,150) | SMD  |
|-----------------------------------|-----------------------|---|------|
| Age                               | 71.40 ± 7.45          | 71.37 ± 7.34                                  | 0.00 |
| Male, N (%)                       | 1,127 (52.42%)        | 1,115 (51.86%)                                | 0.01 |
| White, N (%)                      | 2,029 (94.37%)        | 2,036 (94.70%)                                | 0.01 |
| Townsend deprivation index        | -1.11 ± 3.19          | -1.06 ± 3.28                                  | 0.02 |
| BMI                               | 28.17 ± 4.62          | 28.06 ± 5.03                                  | 0.02 |
| MET                               | 2812.12 ± 2806.70     | 2723.22 ± 2720.51                             | 0.03 |
| DM, N (%)                         | 168 (7.81%)           | 185 (8.60%)                                   | 0.03 |
| Hypertension, N (%)               | 1282 (59.63%)         | 1342 (62.42%)                                 | 0.06 |
| CVD, N (%)                        | 324 (15.07%)          | 501 (23.30%)                                  | 0.21 |
| ND, N (%)                         | 158 (7.35%)           | 250 (11.63%)                                  | 0.15 |
| MI, N (%)                         | 116 (5.40%)           | 222 (10.33%)                                  | 0.18 |
| Cancer, N (%)                     | 437 (20.33%)          | 692 (32.19%)                                  | 0.27 |
| Vaccinations, N (%)               |                       |   | 0.10 |
| <i>No</i>                         | 1523 (70.84%)         | 1581 (73.53%)                                 |      |
| <i>1 dose</i>                     | 383 (17.81%)          | 306 (14.23%)                                  |      |
| <i>2 doses</i>                    | 244 (11.35%)          | 263 (12.23%)                                  |      |
| Smoking status, N (%)             |                       |   | 0.21 |
| <i>Never</i>                      | 821 (38.19%)          | 717 (33.35%)                                  |      |
| <i>Previous</i>                   | 1139 (52.98%)         | 1099 (51.12%)                                 |      |
| <i>Current</i>                    | 190 (8.84%)           | 334 (15.53%)                                  |      |
| Alcohol intake frequency, N (%)   |                       |   | 0.08 |
| <i>Never</i>                      | 203 (9.44%)           | 198 (9.21%)                                   |      |
| <i>Special occasions only</i>     | 225 (10.47%)          | 238 (11.07%)                                  |      |
| <i>One to three times a month</i> | 218 (10.14%)          | 225 (10.47%)                                  |      |
| <i>Once or twice a week</i>       | 578 (26.88%)          | 529 (24.60%)                                  |      |
| <i>Three or four times a week</i> | 496 (23.07%)          | 472 (21.95%)                                  |      |
| <i>Daily or almost daily</i>      | 430 (20.00%)          | 488 (22.70%)                                  |      |

BMI, Body mass index; MET, Metabolic equivalent task; DM, Diabetes mellitus; CVD, Cardiovascular diseases; ND, Neurological diseases; MI, Mental illnesses; SMD, standardized mean difference; PSM, propensity score match.

In this study, neurological diseases are defined as including stroke, Parkinson's disease, Huntington's disease, multiple sclerosis, sleep disorders, and intracranial injury. Mental illnesses are defined as including depression, schizophrenia, and bipolar disorder. Cardiovascular diseases encompass heart failure, coronary artery disease, and cardiomyopathy.

Figure S1. Kaplan-Meier survival curves for dementia-free probability between participants with COVID-19 and participants with contemporary non-COVID respiratory tract diseases, stratified by (A) all-cause dementia, (B) AD, and (C) VaD



AD: Alzheimer's dementia; VaD: Vascular dementia.

In this figure, "control" represents participants with matched contemporary non-COVID respiratory tract diseases.

Table S5. Hazard ratios for the risk of new-onset all-cause dementia across all subgroups, comparing the COVID-19 group with the matched contemporary non-COVID-19 group and the contemporary non-COVID respiratory tract diseases group

| Type                            | COVID-19 group (n=16,017) vs. Contemporary non-COVID-19 group (n=16,017) |                  |          |                          | COVID-19 group (n=2,150) vs. Contemporary respiratory tract diseases group (n=2,150) |                  |          |                          |
|---------------------------------|--|------------------|----------|--------------------------|--|------------------|----------|--------------------------|
| Subgroups                       | Cases  | HR (95% CI)      | <i>p</i> | <i>P</i> for interaction | Cases  | HR (95% CI)      | <i>p</i> | <i>P</i> for interaction |
| <b>Sex</b>                      |  |                  |          | 0.028                    |  |                  |          | 0.79                     |
| Women                           | 142  | 1.27 (0.91-1.77) | 0.155    |                          | 32   | 0.67 (0.33-1.37) | 0.269    |                          |
| Men                             | 194  | 1.52 (1.14-2.02) | 0.004    |                          | 41   | 1.20 (0.64-2.23) | 0.566    |                          |
| <b>Age</b>                      |  |                  |          | <0.001                   |  |                  |          | 0.025                    |
| <65years                        | 23   | 0.55 (0.23-1.30) | 0.173    |                          | 3  | 0.60 (0.05-6.94) | 0.683    |                          |
| ≥65 years                       | 313  | 1.59 (1.27-2.00) | <0.001   |                          | 70   | 0.94 (0.58-1.51) | 0.792    |                          |
| <b>Ethnicity</b>                |  |                  |          | 0.03                     |  |                  |          | 0.916                    |
| Non-White                       | 19   | 1.99 (0.76-5.24) | 0.163    |                          | 3  | 0.43 (0.04-4.79) | 0.496    |                          |
| White                           | 317  | 1.39 (1.11-1.74) | 0.004    |                          | 70   | 0.96 (0.60-1.54) | 0.863    |                          |
| <b>BMI</b>                      |  |                  |          | 0.335                    |  |                  |          | 0.977                    |
| <30 kg/m <sup>2</sup>           | 223  | 1.44 (1.11-1.89) | 0.007    |                          | 53   | 0.99 (0.57-1.70) | 0.968    |                          |
| ≥30 kg/m <sup>2</sup>           | 113  | 1.34 (0.92-1.94) | 0.126    |                          | 20   | 0.78 (0.32-1.91) | 0.593    |                          |
| <b>Alcohol intake frequency</b> |  |                  |          | 0.017                    |  |                  |          | 0.615                    |
| Less than weekly                | 146  | 1.35 (0.97-1.87) | 0.075    |                          | 27   | 1.16 (0.53-2.51) | 0.711    |                          |
| Weekly or more                  | 190  | 1.46 (1.09-1.95) | 0.011    |                          | 46   | 0.83 (0.46-1.48) | 0.524    |                          |
| <b>Smoking status</b>           |  |                  |          | 0.116                    |  |                  |          | 0.336                    |
| Never                           | 124  | 1.54 (1.07-2.20) | 0.019    |                          | 27   | 1.45 (0.66-3.19) | 0.361    |                          |
| Ever                            | 212  | 1.34 (1.02-1.76) | 0.036    |                          | 46   | 0.72 (0.40-1.30) | 0.275    |                          |
| <b>Hypertension</b>             |  |                  |          | <0.001                   |  |                  |          | 0.067                    |
| No                              | 88   | 1.10 (0.72-1.68) | 0.646    |                          | 17   | 0.91 (0.34-2.42) | 0.849    |                          |
| Yes                             | 248  | 1.60 (1.24-2.07) | <0.001   |                          | 56   | 0.95 (0.56-1.62) | 0.863    |                          |
| <b>Diabetes mellitus</b>        |  |                  |          | <0.001                   |  |                  |          | 0.088                    |



|                                |     |                  |       |        |    |                  |       |        |
|--------------------------------|-----|------------------|-------|--------|----|------------------|-------|--------|
| No                             | 265 | 1.36 (1.06-1.73) | 0.014 |        | 63 | 0.98 (0.60-1.62) | 0.952 |        |
| Yes                            | 71  | 1.68 (1.04-2.71) | 0.033 |        | 10 | 0.69 (0.19-2.44) | 0.563 |        |
| <b>Cardiovascular diseases</b> |     |                  |       | <0.001 |    |                  |       | 0.218  |
| No                             | 215 | 1.36 (1.03-1.78) | 0.028 |        | 50 | 0.80 (0.46-1.41) | 0.445 |        |
| Yes                            | 121 | 1.79 (1.25-2.57) | 0.002 |        | 23 | 1.59 (0.69-3.63) | 0.273 |        |
| <b>Neurological diseases</b>   |     |                  |       | <0.001 |    |                  |       | <0.001 |
| No                             | 231 | 1.36 (1.05-1.77) | 0.02  |        | 50 | 0.97 (0.55-1.7)  | 0.914 |        |
| Yes                            | 105 | 1.85 (1.26-2.73) | 0.002 |        | 23 | 1.18 (0.51-2.7)  | 0.703 |        |
| <b>Mental illnesses</b>        |     |                  |       | 0.001  |    |                  |       | 0.954  |
| No                             | 269 | 1.35 (1.06-1.71) | 0.016 |        | 66 | 0.89 (0.55-1.45) | 0.643 |        |
| Yes                            | 67  | 2.10 (1.29-3.42) | 0.003 |        | 7  | 1.55 (0.33-7.21) | 0.574 |        |
| <b>Cancer</b>                  |     |                  |       | 0.047  |    |                  |       | 0.362  |
| No                             | 254 | 1.38 (1.08-1.77) | 0.011 |        | 56 | 1.55 (0.33-7.21) | 0.412 |        |
| Yes                            | 82  | 1.70 (1.10-2.63) | 0.017 |        | 17 | 1.51 (0.58-3.91) | 0.4   |        |
| <b>Vaccination</b>             |     |                  |       | <0.001 |    |                  |       | 0.005  |
| No                             | 324 | 1.46 (1.17-1.82) | 0.001 |        | 71 | 0.97 (0.61-1.56) | 0.905 |        |
| Yes                            | 12  | 1.34 (0.43-4.22) | 0.617 |        | 2  | 0 (0-inf)        | 0.999 |        |

HR: Hazard Ratio; CI: Confidence Interval; BMI: body mass index.

The subgroup categorized by 'Physical activity' was not analysed due to a high value missing rate (n= 13,646, 24.92%).

'Cases' refer to the total number of incident dementia events observed in both the COVID-19 group and the comparator group.

Table S6. Hazard ratios for the risk of new-onset Alzheimer's dementia across all subgroups, comparing the COVID-19 group with the matched contemporary non-COVID-19 group and the contemporary non-COVID respiratory tract diseases group

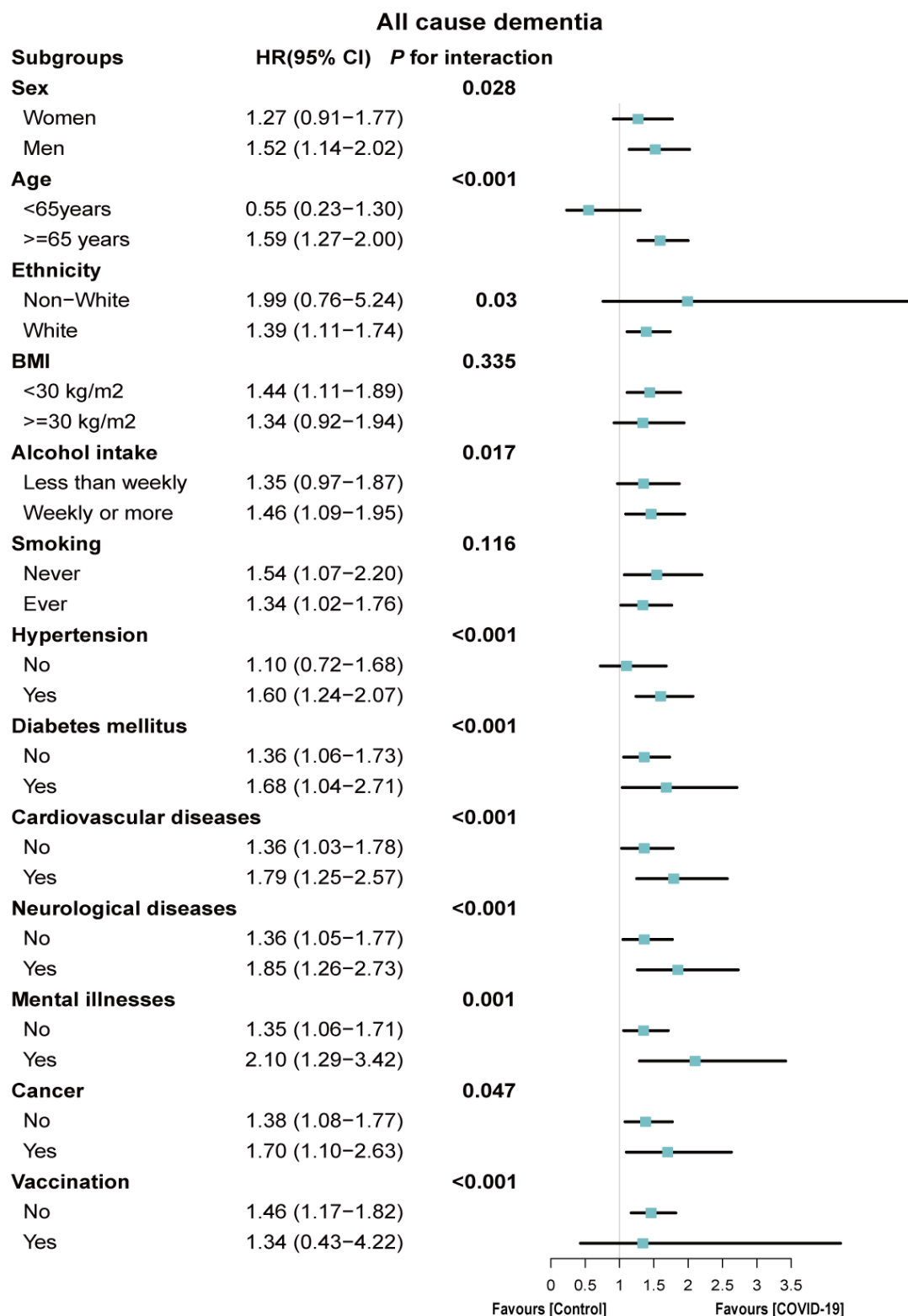
| Type                            | COVID-19 group (n=16,017) vs. Contemporary non-COVID-19 group (n=16,017) |                  |          |                          | COVID-19 group (n=2,150) vs. Contemporary respiratory tract diseases group (n=2,150) |                  |          |                          |
|---------------------------------|--|------------------|----------|--------------------------|--|------------------|----------|--------------------------|
| Subgroups                       | Cases  | HR (95% CI)      | <i>p</i> | <i>P</i> for interaction | Cases  | HR (95% CI)      | <i>p</i> | <i>P</i> for interaction |
| <b>Sex</b>                      |  |                  |          | 0.607                    |  |                  |          | 0.445                    |
| Women                           | 49   | 1.01 (0.58-1.78) | 0.959    |                          | 5  | 1.95 (0.29-13.2) | 0.496    |                          |
| Men                             | 53   | 1.17 (0.68-2.00) | 0.580    |                          | 11   | 1.97 (0.56-6.98) | 0.293    |                          |
| <b>Age</b>                      |  |                  |          | <0.001                   |  |                  |          | 0.996                    |
| <65years                        | 7  | 1.44 (0.32-6.51) | 0.637    |                          | 1  | inf (0-inf)      | 0.999    |                          |
| ≥65 years                       | 95   | 1.12 (0.75-1.68) | 0.571    |                          | 15   | 1.66 (0.57-4.84) | 0.356    |                          |
| <b>Ethnicity</b>                |  |                  |          | 0.381                    |  |                  |          | 0.998                    |
| Non-White                       | 7  | 1.24 (0.28-5.52) | 0.781    |                          | 0  | inf (0-inf)      | 0.781    |                          |
| White                           | 95   | 1.09 (0.73-1.63) | 0.688    |                          | 16   | 1.96 (0.68-5.62) | 0.210    |                          |
| <b>BMI</b>                      |  |                  |          | 0.385                    |  |                  |          | 0.838                    |
| <30 kg/m <sup>2</sup>           | 66   | 1.13 (0.69-1.83) | 0.634    |                          | 13   | 2.52 (0.75-8.50) | 0.137    |                          |
| ≥30 kg/m <sup>2</sup>           | 36   | 1.03 (0.54-1.99) | 0.925    |                          | 3  | 0.69 (0.06-8.42) | 0.772    |                          |
| <b>Alcohol intake frequency</b> |  |                  |          | 0.017                    |  |                  |          | 0.615                    |
| Less than weekly                | 46   | 0.90 (0.50-1.62) | 0.728    |                          | 4  | 6.64 (0.6-72.86) | 0.122    |                          |
| Weekly or more                  | 56   | 1.28 (0.75-2.16) | 0.367    |                          | 12   | 1.39 (0.43-4.51) | 0.578    |                          |
| <b>Smoking status</b>           |  |                  |          | 0.116                    |  |                  |          | 0.336                    |
| Never                           | 37   | 0.96 (0.50-1.82) | 0.892    |                          | 5  | 1.24 (0.21-7.42) | 0.815    |                          |
| Ever                            | 65   | 1.18 (0.72-1.92) | 0.512    |                          | 11   | 2.46 (0.68-8.99) | 0.172    |                          |
| <b>Hypertension</b>             |  |                  |          | <0.001                   |  |                  |          | 0.067                    |
| No                              | 28   | 1.36 (0.64-2.89) | 0.427    |                          | 5  | 8.65 (0.9-83.59) | 0.062    |                          |
| Yes                             | 74   | 1.05 (0.66-1.65) | 0.850    |                          | 11   | 1.12 (0.34-3.67) | 0.854    |                          |
| <b>Diabetes mellitus</b>        |  |                  |          | <0.001                   |  |                  |          | 0.088                    |

|                                |    |                  |       |        |    |                  |       |        |
|--------------------------------|----|------------------|-------|--------|----|------------------|-------|--------|
| No                             | 82 | 1.27 (0.82-1.96) | 0.286 |        | 15 | 2.41 (0.79-7.40) | 0.124 |        |
| Yes                            | 20 | 0.59 (0.24-1.49) | 0.265 |        | 1  | 0 (0-inf)        | 0.999 |        |
| <b>Cardiovascular diseases</b> |    |                  |       | <0.001 |    |                  |       | 0.218  |
| No                             | 71 | 1.17 (0.73-1.87) | 0.516 |        | 12 | 2.41 (0.68-8.51) | 0.171 |        |
| Yes                            | 31 | 1.10 (0.54-2.23) | 0.800 |        | 4  | 1.34 (0.19-9.54) | 0.769 |        |
| <b>Neurological diseases</b>   |    |                  |       | <0.001 |    |                  |       | <0.001 |
| No                             | 81 | 1.10 (0.71-1.71) | 0.666 |        | 12 | 2.16 (0.63-7.47) | 0.222 |        |
| Yes                            | 21 | 1.23 (0.52-2.91) | 0.639 |        | 4  | 1.94 (0.25-14.8) | 0.524 |        |
| <b>Mental illnesses</b>        |    |                  |       | 0.001  |    |                  |       | 0.954  |
| No                             | 83 | 1.02 (0.66-1.57) | 0.933 |        | 15 | 1.50 (0.52-4.33) | 0.450 |        |
| Yes                            | 19 | 1.82 (0.73-4.55) | 0.197 |        | 1  | inf (0-inf)      | 0.999 |        |
| <b>Cancer</b>                  |    |                  |       | 0.276  |    |                  |       | 0.784  |
| No                             | 81 | 1.18 (0.76-1.83) | 0.460 |        | 11 | 2.07 (0.57-7.54) | 0.272 |        |
| Yes                            | 21 | 0.86 (0.36-2.09) | 0.746 |        | 5  | 2.12 (0.35-12.7) | 0.412 |        |
| <b>Vaccination</b>             |    |                  |       | 0.002  |    |                  |       | 0.002  |
| No                             | 98 | 1.09 (0.73-1.62) | 0.681 |        | 16 | 1.93 (0.67-5.50) | 0.221 |        |
| Yes                            | 4  | 2.87 (0.30-27.6) | 0.361 |        | 0  | 0 (0-inf)        | 0.999 |        |

HR: Hazard Ratio; CI: Confidence Interval; BMI: body mass index.

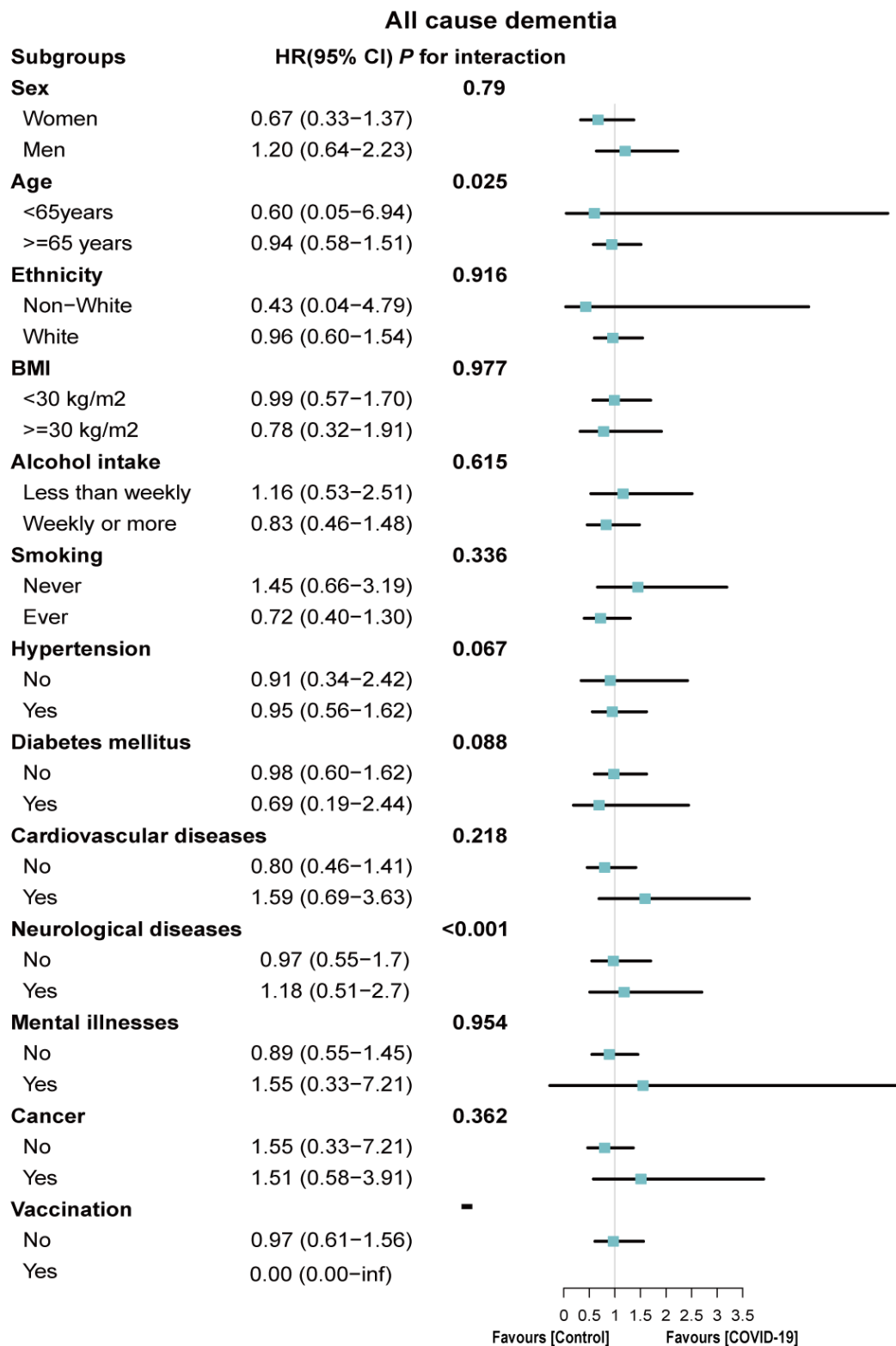
The subgroup categorized by 'Physical activity' was not analysed due to a high value missing rate (n= 13,646, 24.92%).

Figure S2. Association between COVID-19 infection and the risk of all-cause dementia across various subgroups, compared with the non-COVID-19 group



In this figure, “control” refers to the contemporary non-COVID-19 participants.

Figure S3. Association between COVID-19 infection and the risk of all-cause dementia across various subgroups, compared with the non-COVID-19 respiratory tract diseases group



In this figure, “control” refers to the contemporary non-COVID-19 respiratory tract diseases group.

Table S7. Association between COVID-19 and dementia risk compared to matched control groups, excluding participants with less than 3 months of follow-up

| Types              | COVID-19 group (n=15,961) vs.<br>Contemporary non-COVID-19<br>group (n=15,969) |                  |          | COVID-19 group (n=2,141) vs.<br>Contemporary respiratory tract<br>diseases group (n=2,150) |                   |          |
|--------------------|--|------------------|----------|--|-------------------|----------|
|                    | Cases  | HR (95% CI)      | <i>p</i> | Cases  | HR (95% CI)       | <i>p</i> |
| All-cause dementia | 232  | 1.52 (1.17-1.98) | 0.002    | 64   | 1.02 (0.59-1.78)  | 0.933    |
| AD                 | 64   | 1.30 (0.79-2.13) | 0.303    | 15   | 4.01 (1.00-15.88) | 0.051    |
| VaD                | 56   | 1.69 (1.01-2.89) | 0.048    | 10   | 0.43 (0.11-1.73)  | 0.235    |

AD: Alzheimer's dementia; VaD: Vascular dementia; HR: Hazard Ratio; CI: Confidence Interval

The analysis was conducted using propensity score matching, with matching performed based on age, sex, ethnicity, BMI, and vaccination status.

Table S8. Association between COVID-19 and dementia risk compared to matched control groups using the Fine-Gray competing risk model.

| Types              | COVID-19 group (n=16,017) vs.<br>Contemporary non-COVID-19 group<br>(n=16,017) |                  |          | COVID-19 group (n=2,150) vs.<br>Contemporary respiratory tract<br>diseases group (n=2,150) |                  |          |
|--------------------|--|------------------|----------|--|------------------|----------|
|                    | Cases  | sHR (95% CI)     | <i>p</i> | Cases  | sHR (95% CI)     | <i>p</i> |
| All-cause dementia | 336  | 1.38 (1.11-1.71) | 0.004    | 73   | 1.04 (0.65-1.66) | 0.88     |
| AD                 | 102  | 1.07 (0.72-1.59) | 0.74     | 16   | 2.16 (0.71-6.63) | 0.18     |
| VaD                | 77   | 1.73 (1.08-2.76) | 0.022    | 14   | 1.00 (0.35-2.84) | 0.99     |

AD: Alzheimer's dementia; VaD: Vascular dementia; sHR: Subdistribution Hazard Ratio; CI: Confidence Interval

The analysis was conducted using propensity score matching, with matching performed based on age, sex, ethnicity, BMI, and vaccination status.

Table S9. Association between COVID-19 and dementia risk through the propensity score-matched approach with additional covariate adjustments

| Types              | COVID-19 group (n=16,017) vs.<br>Contemporary non-COVID-19 group<br>(n=16,017) |                  |          | COVID-19 group (n=2,150) vs.<br>Contemporary respiratory tract<br>diseases group (n=2,150) |                  |          |
|--------------------|--|------------------|----------|--|------------------|----------|
|                    | Cases  | HR (95% CI)      | <i>p</i> | Cases  | HR (95% CI)      | <i>p</i> |
| All-cause dementia | 336  | 1.58 (1.27-1.97) | <0.001   | 73   | 1.08 (0.68-1.74) | 0.736    |
| AD                 | 102  | 1.16 (0.79-1.72) | 0.452    | 16   | 2.19 (0.75-6.38) | 0.15     |
| VaD                | 77   | 2.05 (1.29-3.27) | 0.002    | 14   | 1.09 (0.37-3.24) | 0.872    |

AD: Alzheimer's dementia; VaD: Vascular dementia; HR: Hazard Ratio; CI: Confidence Interval

The analysis was conducted using propensity score matching, where matching was performed based on age, sex, ethnicity, BMI, and vaccinations. To further assess the impact of additional covariates, the models were additionally adjusted for MET, hypertension, diabetes mellitus, cardiovascular diseases, mental illnesses, neurological disorders, cancer, alcohol consumption frequency, and smoking status.



Table S10. Association between COVID-19 and dementia risk compared to control groups without propensity score matching, adjusted for covariates used in matching

| Types              | COVID-19 group (n=16,017) vs.<br>Contemporary non-COVID-19 group<br>(n=38,740) |                  |          | COVID-19 group (n=16,017) vs.<br>Contemporary respiratory tract<br>diseases group (n=2,150) |                  |          |
|--------------------|--|------------------|----------|---|------------------|----------|
|                    | Cases  | HR (95% CI)      | <i>p</i> | Cases   | HR (95% CI)      | <i>p</i> |
| All-cause dementia | 701  | 1.59 (1.34-1.88) | <0.001   | 229   | 1.34 (0.94-1.91) | 0.107    |
| AD                 | 218  | 1.30 (0.94-1.78) | 0.108    | 58  | 2.24 (0.95-5.26) | 0.065    |
| VaD                | 140  | 2.34 (1.64-3.33) | <0.001   | 55  | 1.88 (0.85-4.18) | 0.122    |

AD: Alzheimer's dementia; VaD: Vascular dementia; HR: Hazard Ratio; CI: Confidence Interval

The models were adjusted for the same covariates as in propensity score matching, including age, sex, ethnicity, BMI and vaccination status.

Table S11. Association between COVID-19 and dementia risk compared to control groups, with full covariate adjustment and without propensity score matching

| Types              | COVID-19 group (n=16,017) vs.<br>Contemporary non-COVID-19 group<br>(n=38,740) |                  |          | COVID-19 group (n=16,017) vs.<br>Contemporary respiratory tract<br>diseases group (n=2,150) |                  |          |
|--------------------|--|------------------|----------|---|------------------|----------|
|                    | Cases  | HR (95% CI)      | <i>p</i> | Cases   | HR (95% CI)      | <i>p</i> |
| All-cause dementia | 701  | 1.54 (1.3-1.83)  | <0.001   | 229   | 1.29 (0.90-1.84) | 0.169    |
| AD                 | 218  | 1.27 (0.92-1.74) | 0.143    | 58  | 2.15 (0.91-5.06) | 0.081    |
| VaD                | 140  | 2.23 (1.56-3.18) | <0.001   | 55  | 1.77 (0.8-3.92)  | 0.161    |

AD: Alzheimer's dementia; VaD: Vascular dementia; HR: Hazard Ratio; CI: Confidence Interval

The models were fully adjusted for age, sex, ethnicity, BMI, MET, hypertension, diabetes mellitus, cardiovascular diseases, mental illnesses, neurological disorders, cancer, alcohol consumption frequency, smoking status, and vaccination status.

Table S12. Association between COVID-19 identified in inpatients and dementia risk through the propensity score-matched approach

| Types              | COVID-19 group (n=3,442) vs.<br>Contemporary non-COVID-19 group<br>(n=3,442) |                  |          | COVID-19 group (n=2,150) vs.<br>Contemporary respiratory tract<br>diseases group (n=2,150) |                  |          |
|--------------------|--|------------------|----------|--|------------------|----------|
|                    | Cases  | HR (95% CI)      | <i>p</i> | Cases  | HR (95% CI)      | <i>p</i> |
| All-cause dementia | 133  | 1.89 (1.33-2.66) | <0.001   | 88   | 1.58 (1.04-2.42) | 0.033    |
| AD                 | 28   | 0.99 (0.47-2.12) | 0.988    | 12   | 1.15 (1.15-3.57) | 0.809    |
| VaD                | 31   | 2.56 (1.23-5.36) | 0.012    | 23   | 2.67 (1.10-6.50) | 0.03     |

AD: Alzheimer's dementia; VaD: Vascular dementia; HR: Hazard Ratio; CI: Confidence Interval

The analysis was conducted using propensity score matching, where matching was performed based on age, sex, ethnicity, BMI, and vaccinations.

Table S13. Association between COVID-19 identified in inpatients and dementia risk through the propensity score match approach with additional covariate adjustments

| Types              | COVID-19 group (n=3,442) vs.<br>Contemporary non-COVID-19 group<br>(n=3,442) |                  |          | COVID-19 group (n=2,150) vs.<br>Contemporary respiratory tract<br>diseases group (n=2,150) |                  |          |
|--------------------|--|------------------|----------|--|------------------|----------|
|                    | Cases  | HR (95% CI)      | <i>p</i> | Cases  | HR (95% CI)      | <i>p</i> |
| All-cause dementia | 133  | 1.79 (1.26-2.54) | 0.001    | 88   | 1.30 (0.84-2.01) | 0.234    |
| AD                 | 28   | 0.88 (0.41-1.89) | 0.742    | 12   | 0.98 (0.31-3.11) | 0.969    |
| VaD                | 31   | 2.42 (1.15-5.10) | 0.019    | 23   | 1.79 (0.72-4.48) | 0.212    |

AD: Alzheimer's dementia; VaD: Vascular dementia; HR: Hazard Ratio; CI: Confidence Interval

The analysis was conducted using propensity score matching, where matching was performed based on age, sex, ethnicity, BMI, and vaccinations. To further assess the impact of additional covariates, the models were additionally adjusted for MET, hypertension, diabetes mellitus, cardiovascular diseases, mental illnesses, neurological disorders, cancer, alcohol consumption frequency, and smoking status.

Table S14. Association between COVID-19 (n=16,017) and dementia risk, compared to non-COVID respiratory infections (n=331)

| Type               | Model 1 |                   |          | Model 2 |                   |          |
|--------------------|---------|-------------------|----------|---------|-------------------|----------|
|                    | Cases   | HR (95% CI)       | <i>p</i> | Cases   | HR (95% CI)       | <i>p</i> |
| All-cause dementia | 199     | 1.33 (0.62-2.83)  | 0.461    | 199     | 1.30 (0.61-2.78)  | 0.497    |
| AD                 | 52      | N/A               | N/A      | 52      | N/A               | N/A      |
| VaD                | 49      | 2.47 (0.34-17.93) | 0.373    | 49      | 2.52 (0.35-18.38) | 0.362    |

AD: Alzheimer's dementia; VaD: Vascular dementia; HR: Hazard Ratio; CI: Confidence Interval

Model 1 was adjusted for age, sex, ethnicity, BMI, and vaccination status. Model 2 was additionally adjusted for MET, hypertension, diabetes mellitus, cardiovascular diseases, mental illnesses, neurological disorders, cancer, alcohol consumption frequency, and smoking status.

Table S15. Association between COVID-19 and dementia risk in participants without baseline neurological or psychiatric disorders, with full covariate adjustment

| Types    | COVID-19 group (n=13,662) vs.<br>Contemporary non-COVID-19 group<br>(n=31,994) |                  |          | COVID-19 group (n=13,662) vs.<br>Contemporary respiratory tract diseases<br>(n=1,725) |                   |          |
|----------|--|------------------|----------|---|-------------------|----------|
|          | Cases  | HR (95% CI)      | <i>p</i> | Cases   | HR (95% CI)       | <i>p</i> |
| Dementia | 422  | 1.45 (1.16-1.82) | 0.001    | 129   | 1.26 (0.78-2.02)  | 0.346    |
| AD       | 158  | 1.14 (0.77-1.68) | 0.512    | 38  | 1.87 (0.65-5.38)  | 0.081    |
| VaD      | 73   | 2.30 (1.40-3.77) | 0.001    | 27  | 3.54 (0.83-15.15) | 0.088    |

AD: Alzheimer's dementia; VaD: Vascular dementia; HR: Hazard Ratio; CI: Confidence Interval

The analysis excluded participants with any recorded diagnosis of major neurological or psychiatric disorders at baseline (e.g., stroke, Parkinson's disease, multiple sclerosis, depressive disorder, schizophrenia, or bipolar disorder). Models were fully adjusted for age, sex, ethnicity, BMI, MET, hypertension, diabetes mellitus, cardiovascular diseases, cancer, alcohol consumption frequency, smoking status, and COVID-19 vaccination status.