**Supplementary File 2:** Supplementary results for

The mental health associations of vitiligo: a population-based cohort study in the UK

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**sFigure 1: Flow diagram showing the eligibility and final study population.**



\* People diagnosed with vitiligo during the study period were included in the pool of eligible unexposed people for matching, but if matched, were censored on the date of their vitiligo diagnosis. Such people were thus eligible to contribute to the study as matched controls until the date of their vitiligo diagnosis.

**sTable 2.1: Additional clinical characteristics of people newly diagnosed with vitiligo (cases) and matched controls without vitiligo.**

|  | **Vitiligo cases** | **Matched controls** | **SMDa** |
| --- | --- | --- | --- |
| n  | 7,224 | 28,880 |  |
| BMI median [IQR]  | 26 [23, 30] | 26 [23, 30] | 0.080 |
| **BMI category, n(%)** | **0.139** |
| <18.5 Underweight | 174 (2.4) | 670 (2.3) |  |
| 18.5-24.9 Healthy weight | 2,129 (29.5) | 7,544 (26.1) |  |
| 25-29.9 Overweight | 2,282 (31.6) | 8,511 (29.5) |  |
| 30-34.9 Class I obesity | 1,080 (15.0) | 4,316 (14.9) |  |
| 35-39.9 Class II obesity | 367 (5.1) | 1,674 (5.8) |  |
| >40 Class III obesity | 211 (2.9) | 1,013 (3.5) |  |
| Missing | 981 (13.6) | 5,152 (17.8) |  |
| **Smoking status, n(%)** | **0.193** |
| Non-smoker  | 2,357 (32.6) | 8,629 (29.9) |  |
| Current smoker  | 1,147 (15.9) | 5,881 (20.4) |  |
| Ex-smoker | 3,521 (48.7) | 12,862 (44.5) |  |
| Passive smoker | 30 (0.4) | 77 (0.3) |  |
| Missing smoking status | 169 (2.3) | 1,431 (5.0) |  |
| **Alcohol use, n(%)** | **0.114** |
| Non-drinker  | 2,438 (33.7) | 8,984 (31.1) |  |
| Safe use | 2,799 (38.7) | 11,101 (38.4) |  |
| Excess use | 970 (13.4) | 3,604 (12.5) |  |
| Alcoholism  | 116 (1.6) | 499 (1.7) |  |
| Missing use status | 901 (12.5) | 4,692 (16.2) |  |
| **Comorbidities, n(%)** |  |
| Angina | 136 (1.9) | 550 (1.9) | 0.002 |
| Asthma | 1,083 (15.0) | 4,331 (15.0) | <0.001 |
| Atrial fibrillation | 88 (1.2) | 412 (1.4) | 0.018 |
| Chronic kidney disease (stages 3-5) | 403 (5.6) | 1,477 (5.1) | 0.021 |
| Chronic liver disease | 127 (1.8) | 483 (1.7) | 0.007 |
| Chronic obstructive pulmonary disease  | 149 (2.1) | 604 (2.1) | 0.002 |
| Dementia | 51 (0.7) | 264 (0.9) | 0.023 |
| Heart failure | 61 (0.8) | 275 (1.0) | 0.011 |
| Hyperlipidaemia | 1,059 (14.7) | 3,960 (13.7) | 0.027 |
| Hypertension | 1,182 (16.4) | 4,514 (15.6) | 0.020 |
| Myocardial infarction | 88 (1.2) | 432 (1.5) | 0.024 |
| Stroke | 51 (0.7) | 299 (1.0) | 0.035 |
| Type 2 diabetes | 228 (3.2) | 899 (3.1) | 0.002 |

BMI = Body Mass Index (kg/m2), IQR = Interquartile range

a SMD Standard Mean Difference

**sTable 2.2:** **Prevalence of common mental health conditions in people newly diagnosed with vitiligo and matched controls, in sex, age, and ethnicity defined subgroups.** Data are number of people (% of people), with percentages representing the prevalence of each mental health condition in each subgroup.

|  | **Recurrent Depressive Disorder** | **Depressive Episode** | **Anxiety Disorder** |
| --- | --- | --- | --- |
|  | **Vitiligo cases** | **Matched controls** | **Vitiligo cases** | **Matched controls** | **Vitiligo cases** | **Matched controls** |
| Total number of people | 7,224 | 28,880 | 7,224 | 28,880 | 7,224 | 28,880 |
| **Sex, n (%)** |
| Female  | 768 (20.1) | 3,032 (19.8) | 706 (18.4) | 2,820 (18.4) | 401 (10.5) | 1,436 (9.4) |
| Male  | 325 (9.6) | 1,273 (9.4) | 312 (9.2) | 1187 (8.7) | 168 (4.9) | 595 (4.4) |
| **Age Group (years), n (%)** |
| 18-49  | 633 (14.5) | 2,440 (14.0) | 604 (13.8) | 2,392 (13.7) | 341 (7.8) | 1,206 (6.9) |
| 50+  | 460 (16.1) | 1,865 (16.3) | 414 (14.5) | 1615 (14.1) | 228 (8.0) | 825 (7.2) |
| **Ethnicity, n (%)†** |
| White  | 632 (18.0) | 2,477 (17.7) | 556 (15.9) | 2,253 (16.1) | 318 (9.1) | 1,132 (8.1) |
| Non-white  | 461 (12.4) | 1,828 (12.3) | 462 (12.4) | 1,754 (11.8) | 251 (6.7) | 899 (6.0) |

†Ethnicity was missing for 1,966 (27.2%) cases and 8,769 (30.4%) controls and actively not stated for 199 (2.8%) cases and 949 (3.3%) controls.

**sTable 2.3: Associations between vitiligo and incident recurrent depressive disorder in age, sex and ethnicity defined subgroups.** Associations are expressed as hazard ratios and 95% confidence intervals

|  | **Number of people** | **Person-years at risk** | **Events** | **Unadjusted** | **Sex and age adjusted** | **Adjusted‡** |
| --- | --- | --- | --- | --- | --- | --- |
| **Sex** |
| Female controls | 9,928 | 18,223 | 212 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| Female cases | 3,060 | 5,624 | 72 | 1.10 (0.84, 1.44) | 1.12 (0.86, 1.46) | 1.13 (0.86, 1.48) |
| Male controls | 11,163 | 20,653 | 100 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| Male cases | 3,071 | 5,653 | 41 | 1.50 (1.04, 2.15)\* | 1.51 (1.05, 2.16)\* | 1.52 (1.06, 2.20)\* |
| **Age group** |
| 18-49 controls | 13,012 | 23,777 | 234 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| 18-49 cases | 3,733 | 6,794 | 75 | 1.12 (0.86, 1.45) | 1.11 (0.85, 1.44) | 1.14 (0.88, 1.48) |
| 50+ controls | 8,079 | 15,099 | 78 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| 50+ cases | 2,398 | 4,483 | 38 | 1.64 (1.11, 2.42)\* | 1.61 (1.09, 2.37)\* | 1.58 (1.07, 2.34)\* |
| **Ethnicity†** |
| White controls | 9,575 | 17,879 | 155 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| White cases | 2,872 | 5,355 | 58 | 1.25 (0.92, 1.69) | 1.23 (0.91, 1.66) | 1.26 (0.93, 1.70) |
| Non-white controls | 4,982 | 8,928 | 58 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| Non-white cases | 1,398 | 2,522 | 28 | 1.71 (1.09, 2.69)\* | 1.69 (1.08, 2.66)\* | 1.72 (1.06, 2.79)\* |

† Ethnicity was missing for 1,966 (27.2%) cases and 8,769 (30.4%) controls and actively not stated for 199 (2.8%) cases and 949 (3.3%) controls

‡ Adjusted for age, sex, ethnicity, social deprivation quintile, body mass index, smoking status, alcohol use, and comorbidities (hypertension, hyperlipidaemia, type 2 diabetes, atrial fibrillation, angina, myocardial infarction, heart failure, stroke, chronic kidney disease [stages 3-5], chronic obstructive pulmonary disease, asthma, chronic liver disease, and dementia).

\*p<0.05 \*\*p<0.01 \*\*\*p<0.001

**sTable 2.4: Associations between vitiligo and incident depressive episodes in age, sex and ethnicity defined subgroups.** Associations are expressed as hazard ratios and 95% confidence intervals

|  | **Number of people** | **Person-years at risk** | **Events** | **Unadjusted** | **Sex and age adjusted** | **Adjusted‡** |
| --- | --- | --- | --- | --- | --- | --- |
| **Sex** |
| Female controls | 10,307 | 18,886 | 311 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| Female cases | 3,122 | 5,727 | 99 | 1.05 (0.84, 1.32) | 1.06 (0.85, 1.33) | 1.08 (0.86, 1.35) |
| Male controls | 11,295 | 20,861 | 190 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| Male cases | 3,084 | 5,665 | 58 | 1.12 (0.84, 1.51) | 1.13 (0.84, 1.52) | 1.17 (0.87, 1.57) |
| **Age group** |
| 18-49 controls | 13,138 | 23,966 | 372 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| 18-49 cases | 3,762 | 6,833 | 112 | 1.06 (0.85, 1.30) | 1.05 (0.85, 1.29) | 1.07 (0.86, 1.32) |
| 50+ controls | 8,464 | 15,780 | 129 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| 50+ cases | 2,444 | 4,558 | 45 | 1.21 (0.86, 1.70) | 1.19 (0.85, 1.67) | 1.20 (0.85, 1.68) |
| **Ethnicity†** |
| White controls | 10,024 | 18,655 | 264 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| White cases | 2,948 | 5,472 | 86 | 1.11 (0.87, 1.42) | 1.10 (0.86, 1.40) | 1.13 (0.88, 1.44) |
| Non-white controls | 5,065 | 9,072 | 96 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| Non-white cases | 1,416 | 2,558 | 36 | 1.33 (0.91, 1.95) | 1.32 (0.90, 1.94) | 1.56 (1.03, 2.37)\* |

† Ethnicity was missing for 1,966 (27.2%) cases and 8,769 (30.4%) controls and actively not stated for 199 (2.8%) cases and 949 (3.3%) controls

‡ Adjusted for age, sex, ethnicity, social deprivation quintile, body mass index, smoking status, alcohol use, and comorbidities (hypertension, hyperlipidaemia, type 2 diabetes, atrial fibrillation, angina, myocardial infarction, heart failure, stroke, chronic kidney disease [stages 3-5], chronic obstructive pulmonary disease, asthma, chronic liver disease, and dementia).

\*p<0.05 \*\*p<0.01 \*\*\*p<0.001

**sTable 2.5: Associations between vitiligo and incident anxiety disorder in age, sex and ethnicity defined subgroups.** Associations are expressed as hazard ratios and 95% confidence intervals

|  | **Number of people** | **Person-years at risk** | **Events** | **Unadjusted** | **Sex and age adjusted** | **Adjusted‡** |
| --- | --- | --- | --- | --- | --- | --- |
| **Sex** |
| Female controls | 12,481 | 23,092 | 263 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| Female cases | 3,427 | 6,339 | 69 | 0.96 (0.73, 1.25) | 0.96 (0.74, 1.26) | 1.00 (0.77, 1.30) |
| Male controls | 12,353 | 22,946 | 119 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| Male cases | 3,228 | 5,957 | 53 | 1.72 (1.24, 2.37)\*\* | 1.72 (1.25, 2.38)\*\* | 1.79 (1.29, 2.48)\*\*\* |
| **Age group** |
| 18-49 controls | 15,051 | 27,704 | 281 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| 18-49 cases | 4,025 | 7,363 | 90 | 1.21 (0.95, 1.53) | 1.20 (0.95, 1.52) | 1.23 (0.97, 1.56) |
| 50+ controls | 9,783 | 18,335 | 101 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| 50+ cases | 2,630 | 4,934 | 32 | 1.18 (0.79, 1.75) | 1.17 (0.78, 1.74) | 1.24 (0.83, 1.85) |
| **Ethnicity†** |
| White controls | 11,760 | 22,012 | 205 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| White cases | 3,186 | 5,940 | 67 | 1.21 (0.92, 1.60) | 1.21 (0.91, 1.59) | 1.25 (0.95, 1.65) |
| Non-white controls | 5,518 | 9,984 | 74 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| Non-white cases | 1,463 | 2,667 | 23 | 1.16 (0.73, 1.86) | 1.17 (0.73, 1.86) | 1.28 (0.78, 2.10) |

† Ethnicity was missing for 1,966 (27.2%) cases and 8,769 (30.4%) controls and actively not stated for 199 (2.8%) cases and 949 (3.3%) controls

‡ Adjusted for age, sex, ethnicity, social deprivation quintile, body mass index, smoking status, alcohol use, and comorbidities (hypertension, hyperlipidaemia, type 2 diabetes, atrial fibrillation, angina, myocardial infarction, heart failure, stroke, chronic kidney disease [stages 3-5], chronic obstructive pulmonary disease, asthma, chronic liver disease, and dementia).

\*p<0.05 \*\*p<0.01 \*\*\*p<0.001

**sTable 2.6: Associations between vitiligo and risk of new onset secondary mental health conditions in vitiligo cases and matched controls**

|  | **Number****of people** | **Person-years****at risk** | **Events** | **Unadjusted HR** | **Sex and age adjusted HR** | **Fully adjusted HR†** |
| --- | --- | --- | --- | --- | --- | --- |
| **Adjustment disorder** |
| Matched controls  | 28,406  | 52,962  | 27  | 1.00 (ref)  | 1.00 (ref)  | 1.00 (ref)  |
| Vitiligo cases  | 7,162  | 13,330  | 7  | 1.03 (0.45, 2.37)  | 1.03 (0.45, 2.36)  | 1.04 (0.45, 2.39)  |
| **Substance abuse** |
| Matched controls  | 27,262  | 50,739  | 121  | 1.00 (ref)  | 1.00 (ref)  | 1.00 (ref)  |
| Vitiligo cases  | 7,029  | 13,072  | 35  | 1.12 (0.77, 1.64)  | 1.12 (0.77, 1.64)  | 1.21 (0.83, 1.77)  |
| **Self-harm** |
| Matched controls  | 28,481  | 53,137  | 17  | 1.00 (ref)  | 1.00 (ref)  | 1.00 (ref)  |
| Vitiligo cases  | 7,178  | 13,369  | 6  | 1.40 (0.55, 3.56)  | 1.41 (0.56, 3.59)  | 1.63 (0.63, 4.19)  |
| **Parasuicide** |
| Matched controls  | 28,402  | 52,962  | 12  | 1.00 (ref)  | 1.00 (ref)  | 1.00 (ref)  |
| Vitiligo cases  | 7,163  | 13,340  | <5  | NA | NA | NA |

† Adjusted for age, sex, ethnicity, social deprivation quintile, body mass index, smoking status, alcohol use, and comorbidities (hypertension, hyperlipidaemia, type 2 diabetes, atrial fibrillation, angina, myocardial infarction, heart failure, stroke, chronic kidney disease [stages 3-5], chronic obstructive pulmonary disease, asthma, chronic liver disease, and dementia).

\*p<0.05 \*\*p<0.01 \*\*\*p<0.001 (Note: no significant results)

# Sensitivity analysis

**sTable 2.7: Associations between vitiligo and incident mental health conditions in those diagnosed in the most recent 10-year period.** Associations are expressed as hazard ratios and 95% confidence intervals

|  | **Number of people**  | **Person-years at risk**  | **Events**  | **Unadjusted**  | **Sex and age adjusted**  | **Adjusted†**  |
| --- | --- | --- | --- | --- | --- | --- |
| **Recurrent Depressive Disorder** |
| Matched controls  | 13,330 | 23,912 | 157 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| Vitiligo cases  | 3,898 | 6,993 | 65 | 1.42 (1.06, 1.89)\* | 1.41 (1.05, 1.87)\* | 1.42 (1.06, 1.90)\* |
| **Depressive Episode** |
| Matched controls  | 13,564 | 24,282 | 295 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| Vitiligo cases  | 3,948 | 7,061 | 102 | 1.19 (0.95, 1.49) | 1.19 (0.95, 1.48) | 1.19 (0.94, 1.49) |
| **Anxiety Disorder** |
| Matched controls  | 15,593 | 28,145 | 239 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| Vitiligo cases  | 4,220 | 7,596 | 85 | 1.32 (1.03, 1.69)\* | 1.32 (1.03, 1.69)\* | 1.36 (1.06, 1.74)\* |

† Adjusted for age, sex, ethnicity, social deprivation quintile, body mass index, smoking status, alcohol use, and comorbidities (hypertension, hyperlipidaemia, type 2 diabetes, atrial fibrillation, angina, myocardial infarction, heart failure, stroke, chronic kidney disease [stages 3-5], chronic obstructive pulmonary disease, asthma, chronic liver disease, and dementia).

\*p<0.05 \*\*p<0.01 \*\*\*p<0.001

**sTable 2.8: Associations between vitiligo and incident mental health conditions, excluding matched controls with no consultation in year prior to diagnosis.** Associations are expressed as hazard ratios and 95% confidence intervals. Only cases diagnosed after 2009 and matched controls are included.

|  | **Number of people**  | **Person-years at risk**  | **Events**  | **Unadjusted**  | **Sex and age adjusted**  | **Adjusted†**  |
| --- | --- | --- | --- | --- | --- | --- |
| **Recurrent Depressive Disorder** |
| Matched controls  | 11,557 | 22,008 | 154 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| Vitiligo cases  | 3,898 | 6,993 | 65 | 1.32 (0.99, 1.76) | 1.31 (0.98, 1.75) | 1.33 (0.99, 1.78) |
| **Depressive Episode** |
| Matched controls  | 11,817 | 22,407 | 285 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| Vitiligo cases  | 3,948 | 7,061 | 102 | 1.13 (0.90, 1.42) | 1.13 (0.90, 1.41) | 1.13 (0.90, 1.42) |
| **Anxiety Disorder** |
| Matched controls  | 13,698 | 26,080 | 226 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| Vitiligo cases  | 4,220 | 7,596 | 85 | 1.28 (1.00, 1.65) | 1.29 (1.00, 1.65)\* | 1.33 (1.03, 1.71)\* |

† Adjusted for age, sex, ethnicity, social deprivation quintile, body mass index, smoking status, alcohol use, and comorbidities (hypertension, hyperlipidaemia, type 2 diabetes, atrial fibrillation, angina, myocardial infarction, heart failure, stroke, chronic kidney disease [stages 3-5], chronic obstructive pulmonary disease, asthma, chronic liver disease, and dementia).

\*p<0.05 \*\*p<0.01 \*\*\*p<0.001

**sTable 2.9: A comparison of the baseline prevalence of primary and secondary mental health outcomes in people newly diagnosed with vitiligo and matched controls using the pre-specified definitions (replicated here for comparison) and diagnosis code only definitions.** Data are N (%) of the total number of patients with the condition in each subgroup.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Matched controls** | **Vitiligo cases** | **P value** |
|  | **n (%)** | **n (%)** |  |
| Total number of patients | 28,880 | 7,224 | - |
| **Primary mental health outcomes** |  |  |  |
| Recurrent depressive disorder  | 4,305 (14.9) | 1,093 (15.1) | 0.647 |
| Depressive episode  | 4,007 (13.9) | 1,018 (14.1) | 0.647 |
| Anxiety disorder | 2,031 (7.0) | 569 (7.9) | 0.014 |
| **Primary mental health outcomes defined using Diagnosis codes only†** |  |  |  |
| Recurrent depressive disorder  | 5596 (19.4) | 1403 (19.4) | 0.945 |
| Depressive episode  | 5596 (19.4) | 1403 (19.4) | 0.945 |
| Anxiety disorder | 3656 (12.7) | 976 (13.5) | 0.055 |

† Definitions not requiring the use of treatments i.e. based on diagnosis codes only.

**sTable 2.10: A comparison of the associations between vitiligo and risk of new onset common mental health conditions using the pre-specified definitions (replicated here for comparison) and diagnosis code only definitions.**

|  | **Number of people**  | **Person-years at risk**  | **Events**  | **Unadjusted**  | **Sex and age adjusted**  | **Adjusted†**  |
| --- | --- | --- | --- | --- | --- | --- |
| **RDD** |
| Matched controls  | 21,091  | 38,876  | 312  | 1.00 (ref)  | 1.00 (ref)  | 1.00 (ref)  |
| cases  | 6,131  | 11,277  | 113  | 1.25 (1.01, 1.55)\*  | 1.24 (1.00, 1.53)  | 1.25 (1.01, 1.56)\*  |
| **DE** |
| Matched controls  | 21,602  | 39,746  | 501  | 1.00 (ref)  | 1.00 (ref)  | 1.00 (ref)  |
| cases  | 6,206  | 11,392  | 157  | 1.09 (0.91, 1.31)  | 1.08 (0.91, 1.30)  | 1.11 (0.92, 1.32)  |
| **AD** |
| Matched controls  | 24,834  | 46,038  | 382  | 1.00 (ref)  | 1.00 (ref)  | 1.00 (ref)  |
| cases  | 6,655  | 12,297  | 122  | 1.20 (0.98, 1.47)  | 1.19 (0.97, 1.46)  | 1.23 (1.00, 1.51)\*  |
| **DE – Diagnosis codes only**‡ |
| Matched controls  | 19,082  | 35,078  | 475  | 1.00 (ref)  | 1.00 (ref)  | 1.00 (ref)  |
| cases  | 5,821  | 10,660  | 177  | 1.23 (1.03, 1.46)\*  | 1.22 (1.03, 1.45)\*  | 1.24 (1.04, 1.47)\*  |
| **AD - Diagnosis codes only**‡ |
| Matched controls  | 22,004  | 40,730  | 423  | 1.00 (ref)  | 1.00 (ref)  | 1.00 (ref)  |
| cases  | 6,248  | 11,505  | 150  | 1.26 (1.04, 1.51)\*  | 1.25 (1.04, 1.51)\*  | 1.26 (1.05, 1.52)\*  |
| **RDD - Diagnosis codes only**‡ |
| Matched controls  | 19,082  | 35,078  | 475  | 1.00 (ref)  | 1.00 (ref)  | 1.00 (ref)  |
| cases  | 5,821  | 10,660  | 177  | 1.23 (1.03, 1.46)\*  | 1.22 (1.03, 1.45)\*  | 1.24 (1.04, 1.47)\*  |

†Adjusted for age, sex, ethnicity, social deprivation quintile, body mass index, smoking status, alcohol use, and comorbidities (hypertension, hyperlipidaemia, type 2 diabetes, atrial fibrillation, angina, myocardial infarction, heart failure, stroke, chronic kidney disease [stages 3-5], chronic obstructive pulmonary disease, asthma, chronic liver disease, and dementia).
‡ Definitions not requiring the use of treatments i.e. based on diagnosis codes only.

\*p<0.05 \*\*p<0.01 \*\*\*p<0.001

**sTable 2.11: A comparison of the associations between vitiligo and risk of new onset common mental health conditions excluding patients previously diagnosed with any of RDD, DE and AD.**

|  | **Number of people**  | **Person-years at risk**  | **Events**  | **Unadjusted**  | **Sex and age adjusted**  | **Adjusted†**  |
| --- | --- | --- | --- | --- | --- | --- |
| **RDD** |
| Matched controls  | 20,155  | 37,209  | 292  | 1.00 (ref)  | 1.00 (ref)  | 1.00 (ref)  |
| cases  | 5,826  | 10,750  | 105  | 1.24 (1.00, 1.56)  | 1.23 (0.98, 1.54)  | 1.25 (1.00, 1.57)\*  |
| **DE** |
| Matched controls  | 20,416  | 37,655  | 376  | 1.00 (ref)  | 1.00 (ref)  | 1.00 (ref)  |
| cases  | 5,826  | 10,733  | 119  | 1.11 (0.90, 1.36)  | 1.11 (0.90, 1.36)  | 1.14 (0.93, 1.40)  |
| **AD** |
| Matched controls  | 21,757  | 40,414  | 221  | 1.00 (ref)  | 1.00 (ref)  | 1.00 (ref)  |
| cases  | 5,826  | 10,766  | 79  | 1.34 (1.04, 1.74)\*  | 1.34 (1.04, 1.74)\*  | 1.38 (1.07, 1.79)\*  |

†Adjusted for age, sex, ethnicity, social deprivation quintile, body mass index, smoking status, alcohol use, and comorbidities (hypertension, hyperlipidaemia, type 2 diabetes, atrial fibrillation, angina, myocardial infarction, heart failure, stroke, chronic kidney disease [stages 3-5], chronic obstructive pulmonary disease, asthma, chronic liver disease, and dementia).
\*p<0.05 \*\*p<0.01 \*\*\*p<0.001