**Supplementary Tables**

Table S1. Smoking Status and Smoking Pack-years Definitions Used in the UK Biobank Study

Table S2. Risk of Incident COPD According to Glucosamine/[Chondroitin](C:/Program%20Files%20(x86)/Youdao/Dict/8.9.4.0/resultui/html/index.html#/javascript:;) Use

Table S3. Risk of Incident COPD According to Glucosamine/[Chondroitin](C:/Program%20Files%20(x86)/Youdao/Dict/8.9.4.0/resultui/html/index.html#/javascript:;) Use Within Each Smoking Category

Table S4. Risk of Incident COPD According to Glucosamine Use Within Each Smoking Category after excluding participants who use [chondroitin](C:/Program%20Files%20(x86)/Youdao/Dict/8.9.4.0/resultui/html/index.html#/javascript:;)

Table S5. Risk of Incident COPD According to Glucosamine Use Within Each Smoking Category after Excluding Participants Who Experienced an Outcome Event during the First Two Years of Follow-up

Table S6. Risk of Incident COPD According to Glucosamine Use Within Each Smoking Category after Excluding Participants Who Taken Aspirin or Non-aspirin NSAIDs At Baseline

Table S7. Risk of Incident COPD According to Aspirin or Non-aspirin NSAIDs Use

Table S8. Risk of Incident COPD According to Osteoarthritis

**Table S1. Smoking Status and Smoking Pack-years Definitions Used in the UK Biobank Study**

|  |  |  |
| --- | --- | --- |
|  | **Definition** | **UK Biobank Self Report Fields** |
| Smoking Status | UK Biobank touchscreen questionnaire at baseline: smoking status defined as never, previous, or current smoker | 1239, 1249, 2644, 20116 |
| Smoking Pack-years | UK Biobank touchscreen questionnaire at baseline: Pack-years = Number of cigarettes per day / 20 × (Age stopped smoking - Age start smoking) | 2867, 2887, 2897, 2907, 3436, 3486, 6183, 6194, 20161 |

**Table S2. Risk of Incident COPD According to Glucosamine/**[**Chondroitin**](C:/Program%20Files%20(x86)/Youdao/Dict/8.9.4.0/resultui/html/index.html#/javascript:;) **Use**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **glucosamine/chondroitin use** | **Total No. of participants** | **No. of COPD cases (%)** | **Person-**  **years** | **IRa** | **Model 1b** | |  | **Model 2c** | |  | **Model 3d** | |  | **Model 4e** | |
| **HR (95% CI)** | ***P* value** |  | **HR (95% CI)** | ***P* value** |  | **HR (95% CI)** | ***P* value** |  | **HR (95% CI)** | ***P* value** |
| Non-user | 390 963 | 7636(1.95) | 3 436 046 | 2.22 | 1.00 (reference) | - |  | 1.00 (reference) | - |  | 1.00 (reference) | - |  | 1.00 (reference) | - |
| User | 92 740 | 1380(1.49) | 818 644 | 1.69 | 0.73 (0.69 to 0.78) | <0.001 |  | 0.79 (0.75 to 0.84) | <0.001 |  | 0.78 (0.73 to 0.83) | <0.001 |  | 0.83 (0.77 to 0.88) | <0.001 |

Abbreviations: CI, confidence interval; COPD, Chronic Obstructive Pulmonary Disease; HR, hazard ratio; IR, incidence rate.

a Incidence rates are provided per 1000 person-years;

b Model 1: Cox proportional hazards regression adjusted for age and sex, ethnicity, education, household income, body mass index, physical activity, alcohol consumption, fruit consumption, vegetable consumption, passive smoking, occupational exposure, CVD, hypertension, diabetes, cancer, chronic pulmonary infections, rheumatoid arthritis, osteoarthritis, joint pain, asthma, arthritis, aspirin use, and Non-aspirin NSAIDs use;

c Model 2: Cox proportional hazards regression adjusted for Model 1 and smoking status, cholesterol lowering medication use, anti-hypertensive drug use, insulin use, vitamin use, minerals and other dietary supplements use, chondroitin use, and cortisone use;

d Model 3: Cox proportional hazards regression adjusted for Model 1 and smoking pack-years, cholesterol lowering medication use, anti-hypertensive drug use, insulin use, vitamin use, minerals and other dietary supplements use, chondroitin use, and cortisone use;

e Model 4: Cox proportional hazards regression adjusted for Model 2 and smoking pack-years.

**Table S3. Risk of Incident COPD According to Glucosamine/**[**Chondroitin**](C:/Program%20Files%20(x86)/Youdao/Dict/8.9.4.0/resultui/html/index.html#/javascript:;) **Use Within Each Smoking Category**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Subgroup** | **Total No. of participants** | **No. of**  **COPD cases (%)** | **Person-**  **years** | **IRa** | **HR (95% CI) b** | ***P* value** |
| **Smoking status and glucosamine** |  |  |  |  |  |  |
| **Never smoking** |  |  |  |  |  |  |
| Non-user | 216 346 | 1274 (0.59) | 1 919 916 | 0.66 | 1.00 (reference) | - |
| User | 51 509 | 312 (0.61) | 457 239 | 0.68 | 0.84 (0.73 to 0.95) | 0.008 |
| **Former smoking** |  |  |  |  |  |  |
| Non-user | 130 962 | 3258 (2.49) | 1 143 736 | 2.85 | 1.00 (reference) | - |
| User | 35 309 | 742 (2.10) | 310 270 | 2.39 | 0.83 (0.76 to 0.90) | 0.006 |
| **Current smoking** |  |  |  |  |  |  |
| Non-user | 43 655 | 3104 (7.11) | 372 394 | 8.34 | 1.00 (reference) | - |
| User | 5922 | 326 (5.50) | 51 126 | 6.38 | 0.72 (0.64 to 0.81) | <0.001 |
| **Smoking pack-years and glucosamine** |  |  |  |  |  |  |
| **Never smoking (0)** |  |  |  |  |  |  |
| Non-user | 217 294 | 1342 (0.62) | 1 927 799 | 0.70 | 1.00 (reference) | - |
| User | 51 695 | 320 (0.62) | 458 857 | 0.70 | 0.82 (0.72 to 0.94) | 0.003 |
| **Hardly ever smoking (0.1–10.0)** |  |  |  |  |  |  |
| Non-user | 29 603 | 335 (1.13) | 261 699 | 0.63 |  | - |
| User | 7726 | 80 (1.04) | 68 510 | 1.07 | 0.77 (0.59 to1.00) | 0.048 |
| **Light smoking (10.1–20.0)** |  |  |  |  |  |  |
| Non-user | 31 655 | 727 (2.30) | 277 578 | 2.62 |  | - |
| User | 7486 | 128 (1.71) | 65 884 | 1.94 | 0.69 (0.56 to 0.84) | <0.001 |
| **Moderate smoking (20.1–30.0)** |  |  |  |  |  |  |
| Non-user | 23 354 | 1058 (4.53) | 202 209 | 5.23 | 1.00 (reference) | - |
| User | 4914 | 155 (3.15) | 43 028 | 3.60 | 0.65 (0.55 to 0.78) | <0.001 |
| **Heavy smoking (>30.0)** |  |  |  |  |  |  |
| Non-user | 32 118 | 3315 (10.32) | 266 394 | 12.45 | 1.00 (reference) | - |
| User | 5724 | 496 (8.67) | 47 966 | 10.32 | 0.84 (0.76 to 0.93) | <0.001 |

Abbreviations: IR, incidence rate; HR, hazard ratio; CI, confidence interval; COPD, Chronic Obstructive Pulmonary Disease.

a Incidence rates are provided per 1000 person-years.

b Cox proportional hazards regression adjusted for age, sex, ethnicity, education, household income, body mass index, physical activity, alcohol consumption, fruit consumption, vegetable consumption, passive smoking, occupational exposure, CVD, hypertension, diabetes, cancer, chronic pulmonary infections, rheumatoid arthritis, osteoarthritis, joint pain, asthma, arthritis, cholesterol lowering medication use, blood pressure medication use, insulin use, aspirin use, Non-aspirin NSAIDs use, vitamin use, minerals and other dietary supplements use, and cortisone use.

**Table S4. Risk of Incident COPD According to Glucosamine Use Within Each Smoking Category after excluding participants who use** [**chondroitin**](C:/Program%20Files%20(x86)/Youdao/Dict/8.9.4.0/resultui/html/index.html#/javascript:;)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Subgroup** | **Total No. of participants** | **No. of**  **COPD cases (%)** | **Person-**  **years** | **IRa** | **HR (95% CI) b** | ***P* value** |
| **Smoking status and glucosamine** | | | | | | |
| **Never smoking** |  |  |  |  |  |  |
| Non-user | 216 346 | 1274 (0.59) | 1 919 916 | 0.66 | 1.00 (reference) | - |
| User | 48 085 | 292 (0.61) | 426 258 | 0.69 | 0.84 (0.73 to 0.96) | 0.009 |
| **Former smoking** |  |  |  |  |  |  |
| Non-user | 130 962 | 3258 (2.49) | 1 143 736 | 2.85 | 1.00 (reference) | - |
| User | 33 054 | 706 (2.14) | 290 012 | 2.43 | 0.84 (0.77 to 0.92) | 0.006 |
| **Current smoking** |  |  |  |  |  |  |
| Non-user | 43 655 | 3104 (7.11) | 372 394 | 8.34 | 1.00 (reference) | - |
| User | 5628 | 303 (5.38) | 48 543 | 6.24 | 0.71 (0.63 to 0.80) | <0.001 |
| **Smoking pack-years and glucosamine** |  |  |  |  |  |  |
| **Never smoking (0)** |  |  |  |  |  |  |
| Non-user | 217 294 | 1342 (0.62) | 1 927 799 | 0.70 | 1.00 (reference) | - |
| User | 48 261 | 298 (0.62) | 427 786 | 0.70 | 0.84 (0.72 to 0.94) | 0.003 |
| **Hardly ever smoking (0.1–10.0)** |  |  |  |  |  |  |
| Non-user | 29 603 | 335 (1.13) | 261 699 | 1.28 | 1.00 (reference) | - |
| User | 7204 | 75 (1.04) | 63 783 | 1.18 | 0.78 (0.60, 1.02) | 0.072 |
| **Light smoking (10.1–20.0)** |  |  |  |  |  |  |
| Non-user | 31 655 | 727 (2.28) | 277 578 | 2.62 | 1.00 (reference) | - |
| User | 6990 | 121(1.83) | 61 412 | 1.97 | 0.70 (0.57 to 0.86) | <0.001 |
| **Moderate smoking (2.1–30.0)** |  |  |  |  |  |  |
| Non-user | 23 354 | 1058 (4.53) | 202 209 | 5.23 | 1.00 (reference) | - |
| User | 4633 | 147 (3.17) | 40 500 | 3.63 | 0.66 (0.55 to 0.79) | <0.001 |
| **Heavy smoking (>30.0)** |  |  |  |  |  |  |
| Non-user | 32 118 | 3315 (10.32) | 266 292 | 12.45 | 1.00 (reference) | - |
| User | 5425 | 470 (8.68) | 45 516 | 10.33 | 0.85 (0.77 to 0.94) | 0.002 |

Abbreviations: IR, incidence rate; HR, hazard ratio; CI, confidence interval; COPD, Chronic Obstructive Pulmonary Disease.

a Incidence rates are provided per 1000 person-years.

b Cox proportional hazards regression adjusted for age, sex, ethnicity, education, household income, body mass index, physical activity, alcohol consumption, fruit consumption, vegetable consumption, passive smoking, occupational exposure, CVD, hypertension, diabetes, cancer, chronic pulmonary infections, rheumatoid arthritis, osteoarthritis, joint pain, asthma, arthritis, cholesterol lowering medication use, blood pressure medication use, insulin use, aspirin use, Non-aspirin NSAIDs use, vitamin use, minerals and other dietary supplements use, and cortisone use.

**Table S5. Risk of Incident COPD According to Glucosamine Use Within Each Smoking Category after Excluding Participants Who Experienced an Outcome Event during the First Two Years of Follow-up**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Subgroup** | **Total No. of participants** | **No. of**  **COPD cases (%)** | **Person-**  **years** | **IRa** | **HR (95% CI) b** | ***P* value** |
| **Smoking status and glucosamine** | | | | | | |
| **Never smoking** |  |  |  |  |  |  |
| Non-user | 215 586 | 1122 (0.52) | 1 919 670 | 0.58 | 1.00 (reference) | - |
| User | 51 262 | 268 (0.52) | 456 371 | 0.59 | 0.82 (0.71 to 0.95) | 0.008 |
| **Former smoking** |  |  |  |  |  |  |
| Non-user | 129 795 | 2805 (2.16) | 1142 898 | 2.45 | 1.00 (reference) | - |
| User | 35008 | 631 (1.8) | 309 482 | 2.04 | 0.83 (0.76 to 0.91) | <0.001 |
| **Current smoking** |  |  |  |  |  |  |
| Non-user | 42 871 | 2684 (6.26) | 371 640 | 7.22 | 1.00 (reference) | - |
| User | 5845 | 287 (4.91) | 50 944 | 5.63 | 0.71 (0.61 to 0.81) | <0.001 |
| **Smoking pack-years and glucosamine** |  |  |  |  |  |  |
| **Never smoking (0)** |  |  |  |  |  |  |
| Non-user | 216 510 | 1178 (0.54) | 1 927 525 | 0.61 | 1.00 (reference) | - |
| User | 51 446 | 275 (0.53) | 457 988 | 0.6 | 0.82 (0.71 to 0.94) | 0.005 |
| **Hardly ever smoking (0.1–10.0)** |  |  |  |  |  |  |
| Non-user | 29 453 | 293 (0.99) | 261 581 | 1.12 | 1.00 (reference) | - |
| User | 7692 | 66 (0.86) | 68 416 | 0.96 | 0.74 [0.56, 0.99] | 0.040 |
| **Light smoking (10.1–20.0)** |  |  |  |  |  |  |
| Non-user | 31 422 | 646 (2.06) | 277 427 | 2.33 | 1.00 (reference) | - |
| User | 7431 | 116 (1.56) | 65 713 | 1.77 | 0.69 (0.56 to 0.85) | <0.001 |
| **Moderate smoking (20.1–30.0)** |  |  |  |  |  |  |
| Non-user | 23 049 | 911 (3.95) | 201 976 | 4.51 | 1.00 (reference) | - |
| User | 4863 | 142 (2.92) | 42 867 | 3.31 | 0.70 (0.58 to 0.84) | <0.001 |
| **Heavy smoking (>30.0)** |  |  |  |  |  |  |
| Non-user | 31 252 | 2832 (10.61) | 265 445 | 10.67 | 1.00 (reference) | - |
| User | 5591 | 411 (7.35) | 47 850 | 8.59 | 0.82 (0.73 to 0.91) | <0.001 |

Abbreviations: IR, incidence rate; HR, hazard ratio; CI, confidence interval.

a Incidence rates are provided per 1000 person-years.

b Cox proportional hazards regression adjusted for age, sex, ethnicity, education, household income, body mass index, physical activity, alcohol consumption, fruit consumption, vegetable consumption, passive smoking, occupational exposure, CVD, hypertension, diabetes, cancer, chronic pulmonary infections, rheumatoid arthritis, osteoarthritis, joint pain, asthma, arthritis, cholesterol lowering medication use, blood pressure medication use, insulin use, aspirin use, Non-aspirin NSAIDs use, vitamin use, minerals and other dietary supplements use, chondroitin use, and cortisone use.

**Table S6. Risk of Incident COPD According to Glucosamine Use Within Each Smoking Category after Excluding Participants Who Taken Aspirin or Non-aspirin NSAIDs At Baseline**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Subgroup** | **Total No. of participants** | **No. of**  **COPD cases (%)** | **Person-**  **years** | **IRa** | **HR (95% CI) b** | ***P* value** |
| **Smoking status and glucosamine** | | | | | | |
| **Never smoking** |  |  |  |  |  |  |
| Non-user | 138 910 | 622 (0.45) | 1 233 241 | 0.50 | 1.00 (reference) | - |
| User | 30 147 | 126 (0.42) | 267 785 | 0.49 | 0.76 (0.62 to 0.93) | 0.008 |
| **Former smoking** |  |  |  |  |  |  |
| Non-user | 76 341 | 1370 (1.79) | 669 448 | 2.05 | 1.00 (reference) | - |
| User | 18 993 | 303 (1.60) | 167 326 | 1.81 | 0.85 (0.75 to 0.97) | 0.016 |
| **Current smoking** |  |  |  |  |  |  |
| Non-user | 24 540 | 1396 (6.26) | 211 009 | 6.62 | 1.00 (reference) | - |
| User | 3003 | 125 (4.91) | 26 081 | 4.79 | 0.63 (0.52 to 0.76) | <0.001 |
| **Smoking pack-years and glucosamine** |  |  |  |  |  |  |
| **Never smoking (0)** |  |  |  |  |  |  |
| Non-user | 139 443 | 646 (0.46) | 1 237 747 | 0.52 | 1.00 (reference) | - |
| User | 30 248 | 132 (0.44) | 268 665 | 0.49 | 0.77 (0.63 to 0.94) | 0.009 |
| **Hardly ever smoking (0.1–10.0)** |  |  |  |  |  |  |
| Non-user | 18 533 | 176 (0.97) | 163 869 | 1.09 | 1.00 (reference) | - |
| User | 4457 | 32 (0.72) | 39 544 | 0.81 | 0.62 (0.42 to 0.94) | 0.017 |
| **Light smoking (10.1–20.0)** |  |  |  |  |  |  |
| Non-user | 18 520 | 335 (1.81) | 162 688 | 2.06 | 1.00 (reference) | - |
| User | 3957 | 53 (1.34) | 34 857 | 1.52 | 0.62 (0.46 to 0.84) | 0.002 |
| **Moderate smoking (20.1–30.0)** |  |  |  |  |  |  |
| Non-user | 12 744 | 457 (3.59) | 110 816 | 4.12 | 1.00 (reference) | - |
| User | 2452 | 72 (2.94) | 21 466 | 3.35 | 0.75 (0.57 to 0.97) | 0.030 |
| **Heavy smoking (>30.0)** |  |  |  |  |  |  |
| Non-user | 16 042 | 1403 (8.75) | 134 604 | 10.42 | 1.00 (reference) | - |
| User | 2584 | 180 (6.97) | 21 875 | 8.23 | 0.79 (0.67 to 0.94) | 0.006 |

Abbreviations: IR, incidence rate; HR, hazard ratio; CI, confidence interval.

a Incidence rates are provided per 1000 person-years.

b Cox proportional hazards regression adjusted for age, sex, ethnicity, education, household income, body mass index, physical activity, alcohol consumption, fruit consumption, vegetable consumption, passive smoking, occupational exposure, CVD, hypertension, diabetes, cancer, chronic pulmonary infections, rheumatoid arthritis, osteoarthritis, joint pain, asthma, arthritis, cholesterol lowering medication use, blood pressure medication use, insulin use, vitamin use, minerals and other dietary supplements use, chondroitin use, and cortisone use.

**Table S7. Risk of Incident COPD According to Aspirin or Non-aspirin NSAIDs Use**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Subgroup** | **Total No. of participants** | **No. of**  **COPD cases (%)** | **Person-**  **years** | **IRa** | **HR (95% CI) b** | ***P* value** |
| **Aspirin Use** |  |  |  |  |  |  |
| No | 417 216 | 6455 (1.55) | 3 678 792 | 1.75 | 1.00 (reference) | - |
| Yes | 66 487 | 2561 (3.85) | 525 898 | 4.45 | 1.04 (0.98 to 1.10) | 0.211 |
| **Non-aspirin NSAIDs** |  |  |  |  |  |  |
| No | 339 733 | 5678 (1.55) | 2 989 190 | 1.90 | 1.00 (reference) | - |
| Yes | 143 970 | 3338 (2.32) | 1 265 501 | 2.64 | 1.16 (1.08 to 1.24) | <0.001 |

Abbreviations: CI, confidence interval; COPD, Chronic Obstructive Pulmonary Disease; HR, hazard ratio; IR, incidence rate.

a Incidence rates are provided per 1000 person-years;

b Cox proportional hazards regression adjusted for age and sex, and ethnicity, education, household income, body mass index, physical activity, smoking status, alcohol consumption, fruit consumption, vegetable consumption, passive smoking, occupational exposure, CVD, hypertension, diabetes, cancer, chronic pulmonary infections, rheumatoid arthritis, osteoarthritis, joint pain, asthma, arthritis, cholesterol lowering medication use, anti-hypertensive drug use, insulin use, aspirin use, and Non-aspirin NSAIDs use, vitamin use, minerals and other dietary supplements use, glucosamine use, chondroitin use, and cortisone use.

**Table S8. Risk of Incident COPD According to Osteoarthritis**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Osteoarthritis** | **Total No. of participants** | **No. of COPD cases (%)** | **Person-**  **years** | **IRa** | **Model 1b** | |  | **Model 2c** | |
| **HR (95% CI)** | ***P* value** |  | **HR (95% CI)** | ***P* value** |
| No | 445 047 | 7551 (1.70) | 3 915 579 | 1.93 | 1.00 (reference) | - |  | 1.00 (reference) | - |
| Yes | 38 656 | 1465 (3.79) | 339 111 | 4.32 | 1.36 (1.29 to 1.44) | <0.001 |  | 1.35 (1.28 to 1.44) | <0.001 |

Abbreviations: CI, confidence interval; COPD, Chronic Obstructive Pulmonary Disease; HR, hazard ratio; IR, incidence rate.

a Incidence rates are provided per 1000 person-years;

b Model 1: Cox proportional hazards regression adjusted for Model 1 and ethnicity, education, household income, body mass index, physical activity, smoking status, alcohol consumption, fruit consumption, vegetable consumption, passive smoking, occupational exposure, CVD, hypertension, diabetes, cancer, chronic pulmonary infections, rheumatoid arthritis, joint pain, asthma, arthritis;

c Model 2: Cox proportional hazards regression adjusted for Model 2 and cholesterol lowering medication use, anti-hypertensive drug use, insulin use, aspirin use, and Non-aspirin NSAIDs use, vitamin use, minerals and other dietary supplements use, glucosamine use, chondroitin use, and cortisone use.