Supplementary material

Supplementary Table 1. Disease and ATC codes in the study population.

|  |  |  |
| --- | --- | --- |
| Description | | Disease/ATC Codes |
| Inclusion Criteria | | |
|  | Organic sexual dysfunction | ICD-9-CM: 607.84; ICD-10-CM: N52 |
| Non-organic sexual dysfunction | ICD-9-CM: 302.70-302.72, 302.74-302.76, 302.79, V41.7; ICD-10-CM: F52.0, F52.1, F52.4, F52.6, F52.8, F52.9, R37 |
| Exclusion criteria | | |
|  | Patients with any cancer | ICD-9-CM codes: 140–239; ICD-10-CM codes: C00–D48 |
| Spinal cord injury | ICD-9-CM codes: 806, 952; ICD-10-CM codes: S14, S24, S34 |
| Pelvis fracture | ICD-9-CM code: 808; ICD-10-CM code: S32 |
| Multiple sclerosis | ICD-9-CM code: 340; ICD-10-CM code: G35 |
| Parkinson's disease | ICD-9-CM code: 332; ICD-10-CM codes: G20, G21 |
| Dementia | ICD-9-CM codes: 290, 294.1, 331.0; ICD-10-CM codes: F01, F02, F03, G30 |
| Schizophrenia | ICD-9-CM code: 295; ICD-10-CM codes: F20, F25 |
| Peyronie’s disease | ICD-9-CM code: 607.85; ICD-10-CM code: N48.6 |
| Primary outcomes | | |
| MACEs | | |
|  | Ischemic stroke | ICD-9-CM codes: 433-437; ICD-10-CM codes: G46.3–G46.8, I63, I65–I68 |
| Hemorrhagic stroke | ICD-9-CM codes: 430–432; ICD-10-CM codes: I60–I62 |
| Acute coronary syndrome | ICD-9-CM codes: 410, V45.81, V45.82; ICD-10-CM codes: I21, I22, Z95.1, Z95.5, Z98.61 |
| heart failure | ICD-9-CM code: 428; ICD-10-CM code: I50 |
| Malignant arrhythmia | ICD-9-CM codes: 426.0, 426.12, 426.13, 426.51, 426.52, 426.54, 427.1, 427.4, 427.5; ICD-10-CM codes: I44.1, I44.2, I45.3, I46, I47.0, I47.2, I49.0, I49.3 |
| Comorbidities | | |
|  | Hypertension | (ICD-9-CM codes: 401–405; ICD-10-CM codes: I10–I13, I15) |
| Diabetes mellitus | ICD-9-CM code: 250; ICD-10-CM codes: E08–E13 |
| Coronary artery disease | CD-9-CM codes: 410–414; ICD-10-CM codes: I20–I22, I24, I25 |
| Atherosclerosis | ICD-9-CM code: 440; ICD-10-CM code: I70 |
| Prostate diseases | ICD-9-CM codes: 600–602; ICD-10-CM codes: N40–N42 |
| Alcohol-related illness | ICD-9-CM codes: 291, 303, 305.0, 357.5, 425.5, 535.3, 571.0-571.3, 790.3, 980.0, V11.3, V79.1; ICD-10-CM codes: G31.2, G72.1, E24.4 F10, G62.1, I42.6, K29.2, K85.2, K86.0, K70, O99.31, R78.0, T51.0X1A–T51.0X4A, Z71.41 |
| Obesity | ICD-9-CM codes: 278.0, 278.1; ICD-10-CM codes: E65, E66 |
| Depression | ICD-9-CM codes: 296.2, 296.3, 296.82, 298.0, 300.4, 311; ICD-10-CM codes: F32, F33, F34.1 |
| Anxiety | ICD-9-CM code: 300.0; ICD-10-CM codes: F41.1, F41.3, F41.8, F41.9 |
| Hyperlipidemia | ICD-9-CM code: 272; ICD-10-CM code: E78 |
| Chronic kidney disease | ICD-9-CM code: 585; ICD-10-CM codes: N18.4–N18.6, N18.9 |
| Illicit drug dependence or abuse | ICD-9-CM codes: 304.0, 304.2–304.9, 305.2–305.9; ICD-10-CM codes: F11–F16, F18, F19 |
| Nicotine dependence | ICD-9-CM codes: 305.1, 989.84, V15.82; ICD-10-CM codes: F17.2, O99.33, T65.211A–T65.214A, T65.221A–T65.224A, T65.291A–T65.294A, Z71.6, Z72.0, Z87.891 |
| Medication | | |
|  | PDE5Is | ATC code: G04BE |
| Alprostadil | ATC code: G04BE01 |
| Sildenafil | ATC code: G04BE03 |
| Tadalafil | ATC code: G04BE08 |
| Vardenafil | ATC code: G04BE09 |
| Amide drugs |  |
| Lidocaine | ATC code: N01BB02 |
| Lidocaine and combinations | ATC code: N01BB52 |
| SSRIs | ATC codes: N06AB03, N06AB04, N06AB05, N06AB06, N06AB08, N06AB10 |
| Fluoxetine | ATC code: N06AB03 |
| Citalopram | ATC code: N06AB04 |
| Paroxetine | ATC code: N06AB05 |
| Sertraline | ATC code: N06AB06 |
| Fluvoxamine | ATC code: N06AB08 |
| Escitalopram | ATC code: N06AB10 |
| Nitrates | ATC codes: C01DA02, C01DA05, C01DA08, C01DA14 |
| Nitroglycerin | ATC code: C01DA02 |
| Pentaerithrityl tetranitrate | ATC code: C01DA05 |
| Isosorbide dinitrate | ATC code: C01DA08 |
| Isosorbide mononitrate | ATC code: C01DA14 |

ATC code: Anatomical Therapeutic Chemical Code; ICD-9-CM: International Classification of Disease, Ninth Revision, Clinical Modification; ICD-10-CM: International Classification of Disease, Tenth Revision, Clinical Modification; MACEs: major adverse cardiovascular events; PDE5Is: phosphodiesterase 5 inhibitors; SSRIs: selective serotonin reuptake inhibitors.

Supplementary Table 2. Stratification analysis of MACEs associated with TCM use.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Variable | | Non-TCM | | | TCM | | | | cHR | 95% CI | *p-*value | aHR | 95% CI | *p-*value |
| Event | PY | IR | Event | PY | IR | |
| Age, yr | | | | | | | | | | | | | | |
|  | 20–29 | 444 | 315,796.80 | 1.41 | 484 | 327,903.72 | | 1.48 | 1.04 | (0.92, 1.19) | 0.527 | 1.06 | (0.93, 1.20) | 0.404 |
| 30–39 | 1324 | 352,744.60 | 3.75 | 1380 | 373,336.55 | | 3.70 | 0.98 | (0.91, 1.05) | 0.566 | 0.98 | (0.91, 1.05) | 0.542 |
| 40–49 | 2913 | 347,491.21 | 8.38 | 3265 | 359,841.18 | | 9.07 | 1.07 | (1.02, 1.13)\*\* | 0.005 | 1.06 | (1.01, 1.12)\* | 0.014 |
| 50–59 | 3881 | 225,003.77 | 17.25 | 4430 | 232,971.76 | | 19.02 | 1.10 | (1.05, 1.15)\*\*\* | <0.001 | 1.09 | (1.04, 1.13)\*\*\* | <0.001 |
| 60–69 | 3571 | 95,375.33 | 37.44 | 4341 | 105,064.82 | | 41.32 | 1.10 | (1.05, 1.15)\*\*\* | <0.001 | 1.09 | (1.04, 1.14)\*\*\* | <0.001 |
| Comorbidities | | | | | | | | | | | | | | |
| Hypertension | | | | | | | | | | | | | | |
|  | No | 10,503 | 1,274,688.65 | 8.24 | 12,046 | 1,337,000.17 | | 9.01 | 1.09 | (1.06, 1.12)\*\*\* | <0.001 | 1.05 | (1.03, 1.08)\*\*\* | <0.001 |
| Yes | 1630 | 61,723.06 | 26.41 | 1854 | 62,117.86 | | 29.85 | 1.13 | (1.06, 1.21)\*\*\* | <0.001 | 1.14 | (1.07, 1.22)\*\*\* | <0.001 |
| Diabetes mellitus | | | | | | | | | | | | | | |
|  | No | 11,045 | 1,303,546.43 | 8.47 | 12,668 | 1,365,122.49 | | 9.28 | 1.09 | (1.06, 1.12)\*\*\* | <0.001 | 1.06 | (1.04, 1.09)\*\*\* | <0.001 |
| Yes | 1088 | 32,865.28 | 33.10 | 1232 | 33,995.55 | | 36.24 | 1.09 | (1.01, 1.18)\* | 0.036 | 1.07 | (0.99, 1.16) | 0.092 |
| Coronary artery disease | | | | | | | | | | | | | | |
|  | No | 11,602 | 1,322,376.10 | 8.77 | 13,333 | 1,384,726.33 | | 9.63 | 1.10 | (1.07, 1.12)\*\*\* | <0.001 | 1.07 | (1.04, 1.09)\*\*\* | <0.001 |
| Yes | 531 | 14,035.61 | 37.83 | 567 | 14,391.70 | | 39.40 | 1.04 | (0.93, 1.17) | 0.493 | 1.06 | (0.94, 1.20) | 0.315 |
| Atherosclerosis | | | | | | | | | | | | | | |
|  | No | 12,044 | 1,334,014.33 | 9.03 | 13,814 | 1,396,514.99 | | 9.89 | 1.09 | (1.07, 1.12)\*\*\* | <0.001 | 1.07 | (1.04, 1.10)\*\*\* | <0.001 |
| Yes | 89 | 2397.39 | 37.12 | 86 | 2603.04 | | 33.04 | 0.89 | (0.66, 1.20) | 0.446 | 0.81 | (0.60, 1.10) | 0.181 |
| Prostate diseases | | | | | | | | | | | | | | |
|  | No | 11,168 | 1,298,049.39 | 8.60 | 12,792 | 1,359,466.17 | | 9.41 | 1.09 | (1.06, 1.12)\*\*\* | <0.001 | 1.06 | (1.04, 1.09)\*\*\* | <0.001 |
| Yes | 965 | 38,362.32 | 25.15 | 1108 | 39,651.86 | | 27.94 | 1.11 | (1.02, 1.21)\* | 0.017 | 1.10 | (1.01, 1.20)\* | 0.035 |
| Alcohol-related illnesses | | | | | | | | | | | | | | |
|  | No | 11,697 | 1,321,489.56 | 8.85 | 13,420 | 1,379,931.43 | | 9.73 | 1.10 | (1.07, 1.12)\*\*\* | <0.001 | 1.07 | (1.05, 1.10)\*\*\* | <0.001 |
| Yes | 436 | 14,922.15 | 29.22 | 480 | 19,186.60 | | 25.02 | 0.88 | (0.77, 1.00)\* | 0.050 | 0.87 | (0.77, 1.00)\* | 0.043 |
| Obesity | | | | | | | | | | | | | | |
|  | No | 12,116 | 1,334,575.86 | 9.08 | 13,883 | 1,397,430.08 | | 9.93 | 1.09 | (1.07, 1.12)\*\*\* | <0.001 | 1.07 | (1.04, 1.09)\*\*\* | <0.001 |
| Yes | 17 | 1835.85 | 9.26 | 17 | 1687.95 | | 10.07 | 1.15 | (0.58, 2.29) | 0.680 | 1.76 | (0.81, 3.83) | 0.152 |
| Depression | | | | | | | | | | | | | | |
|  | No | 11,868 | 1,318,038.92 | 9.00 | 13,587 | 1,378,644.68 | | 9.86 | 1.09 | (1.07, 1.12)\*\*\* | <0.001 | 1.06 | (1.04, 1.09)\*\*\* | <0.001 |
| Yes | 265 | 18,372.80 | 14.42 | 313 | 20,473.36 | | 15.29 | 1.07 | (0.90, 1.25) | 0.449 | 1.15 | (0.97, 1.35) | 0.107 |
| Anxiety | | | | | | | | | | | | | | |
|  | No | 11,497 | 1,295,854.92 | 8.87 | 13,177 | 1,356,949.94 | | 9.71 | 1.09 | (1.07, 1.12)\*\*\* | <0.001 | 1.06 | (1.04, 1.09)\*\*\* | <0.001 |
| Yes | 636 | 40,556.79 | 15.68 | 723 | 42,168.09 | | 17.15 | 1.10 | (0.99, 1.22) | 0.085 | 1.12 | (1.00, 1.24)\* | 0.041 |
| Hyperlipidemia | | | | | | | | | | | | | | |
|  | No | 11,265 | 1,287,898.96 | 8.75 | 12,903 | 1,352,494.85 | | 9.54 | 1.09 | (1.06, 1.12)\*\*\* | <0.001 | 1.05 | (1.03, 1.08)\*\*\* | <0.001 |
| Yes | 868 | 48,512.75 | 17.89 | 997 | 46,623.18 | | 21.38 | 1.19 | (1.09, 1.31)\*\*\* | <0.001 | 1.23 | (1.12, 1.35)\*\*\* | <0.001 |
| Chronic kidney disease | | | | | | | | | | | | | | |
|  | No | 11,783 | 1,330,895.80 | 8.85 | 13,550 | 1,392,297.74 | | 9.73 | 1.10 | (1.07, 1.12)\*\*\* | <0.001 | 1.07 | (1.05, 1.10)\*\*\* | <0.001 |
| Yes | 350 | 5515.91 | 63.45 | 350 | 6820.29 | | 51.32 | 0.84 | (0.72, 0.97)\* | 0.018 | 0.84 | (0.72, 0.98)\* | 0.026 |
| Illicit drug dependence or abuse | | | | | | | | | | | | | | |
|  | No | 12,100 | 1,334,489.02 | 9.07 | 13,868 | 1,397,289.46 | | 9.92 | 1.09 | (1.07, 1.12)\*\*\* | <0.001 | 1.07 | (1.04, 1.09)\*\*\* | <0.001 |
| Yes | 33 | 1922.69 | 17.16 | 32 | 1828.57 | | 17.50 | 1.05 | (0.64, 1.70) | 0.857 | 0.97 | (0.58, 1.63) | 0.904 |
| Nicotine dependence | | | | | | | | | | | | | | |
|  | No | 11,990 | 1,325,233.52 | 9.05 | 13,761 | 1,387,714.36 | | 9.92 | 1.09 | (1.07, 1.12)\*\*\* | <0.001 | 1.07 | (1.04, 1.09)\*\*\* | <0.001 |
| Yes | 143 | 11,178.19 | 12.79 | 139 | 11,403.67 | | 12.19 | 0.95 | (0.76, 1.21) | 0.698 | 1.02 | (0.80, 1.29) | 0.881 |
| Medication | | | | | | | | | | | | | | |
| PDE5Is | | | | | | | | | | | | | | |
|  | No | 12,125 | 1,336,025.10 | 9.08 | 13,897 | 1,398,748.53 | | 9.94 | 1.09 | (1.07, 1.12)\*\*\* | <0.001 | 1.07 | (1.04, 1.09)\*\*\* | <0.001 |
| Yes | 8 | 386.61 | 20.69 | 3 | 369.50 | | 8.12 | 0.41 | (0.11, 1.54) | 0.186 | 0.47 | (0.11, 2.12) | 0.328 |
| Amides | | | | | | | | | | | | | | |
|  | No | 12,126 | 1,335,875.07 | 9.08 | 13,890 | 1,398,535.78 | | 9.93 | 1.09 | (1.07, 1.12)\*\*\* | <0.001 | 1.07 | (1.04, 1.09)\*\*\* | <0.001 |
| Yes | 7 | 536.65 | 13.04 | 10 | 582.25 | | 17.17 | 1.31 | (0.50, 3.43) | 0.589 | 0.63 | (0.21, 1.92) | 0.421 |
| SSRIs | | | | | | | | | | | | | | |
|  | No | 11,937 | 1,306,785.02 | 9.13 | 13,654 | 1,368,197.88 | | 9.98 | 1.09 | (1.06, 1.12)\*\*\* | <0.001 | 1.06 | (1.04, 1.09)\*\*\* | <0.001 |
| Yes | 196 | 29,626.69 | 6.62 | 246 | 30,920.16 | | 7.96 | 1.19 | (0.98, 1.43) | 0.073 | 1.24 | (1.02, 1.50)\* | 0.028 |
| Nitrates | | | | | | | | | | | | | | |
|  | No | 9946 | 1,252,740.28 | 7.94 | 11,655 | 1,309,399.19 | | 8.90 | 1.12 | (1.09, 1.15)\*\*\* | <0.001 | 1.10 | (1.07, 1.12)\*\*\* | <0.001 |
| Yes | 2187 | 83,671.43 | 26.14 | 2245 | 89,718.84 | | 25.02 | 0.95 | (0.89, 1.00) | 0.066 | 0.93 | (0.88, 0.99)\* | 0.015 |

aHR: adjusted hazard ratio (adjusted for age, comorbidities and medication); cHR: crude hazard ratio; CI: confidence interval; IR: incidence rate; MACEs: major adverse cardiovascular events; PDE5Is: phosphodiesterase 5 inhibitors; PY: person-years; SSRIs: selective serotonin reuptake inhibitors; TCM: traditional Chinese medicine. \**p* < 0.05; \*\**p* < 0.01; \*\*\**p* < 0.001.