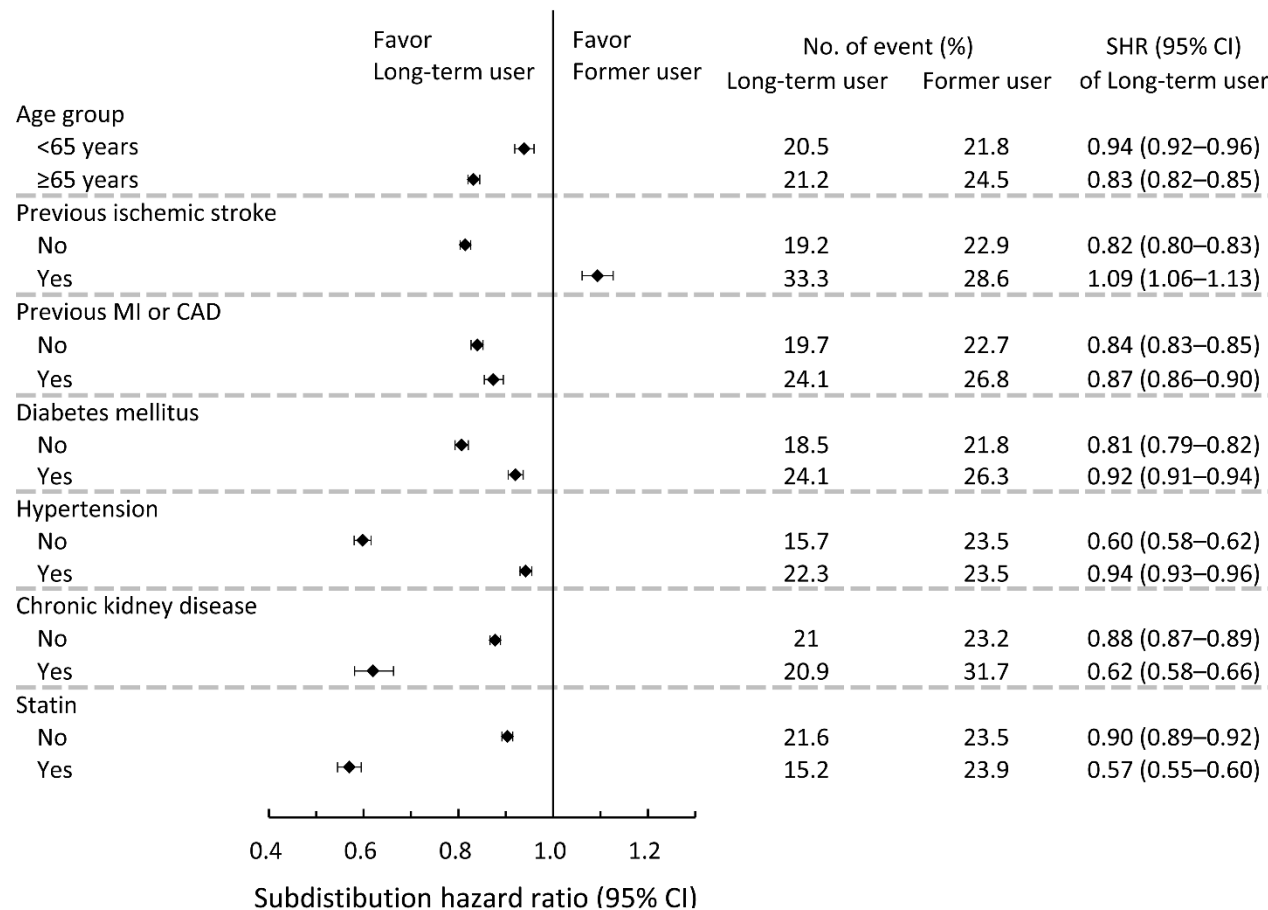**Supplementary files**

**Supplemental Figure S1.** Pre-specified subgroup analyses comparing the risk of 2-year recurrent ischemic stroke between long-term colchicine users and former colchicine users in the study cohort after IPTW.

IPTW, inverse probability of treatment weights.

| | Favor Long-term user | Favor Former user | No. of event (%) Long-term user | Former user | SHR (95% CI) of Long-term user |
|---|---|---|---|---|---|
| **Age group** | | | | | |
| <65 years | | | 20.5 | 21.8 | 0.94 (0.92–0.96) |
| ≥65 years | | | 21.2 | 24.5 | 0.83 (0.82–0.85) |
| **Previous ischemic stroke** | | | | | |
| No | | | 19.2 | 22.9 | 0.82 (0.80–0.83) |
| Yes | | | 33.3 | 28.6 | 1.09 (1.06–1.13) |
| **Previous MI or CAD** | | | | | |
| No | | | 19.7 | 22.7 | 0.84 (0.83–0.85) |
| Yes | | | 24.1 | 26.8 | 0.87 (0.86–0.90) |
| **Diabetes mellitus** | | | | | |
| No | | | 18.5 | 21.8 | 0.81 (0.79–0.82) |
| Yes | | | 24.1 | 26.3 | 0.92 (0.91–0.94) |
| **Hypertension** | | | | | |
| No | | | 15.7 | 23.5 | 0.60 (0.58–0.62) |
| Yes | | | 22.3 | 23.5 | 0.94 (0.93–0.96) |
| **Chronic kidney disease** | | | | | |
| No | | | 21 | 23.2 | 0.88 (0.87–0.89) |
| Yes | | | 20.9 | 31.7 | 0.62 (0.58–0.66) |
| **Statin** | | | | | |
| No | | | 21.6 | 23.5 | 0.90 (0.89–0.92) |
| Yes | | | 15.2 | 23.9 | 0.57 (0.55–0.60) |

0.4    0.6    0.8    1.0    1.2

Subdistibution hazard ratio (95% CI)

**Supplemental Table S1**. Baseline characteristics of patients after IPTW

| Variable | Non-chronic use category | | Chronic use category | | MASD |
|---|---|---|---|---|---|
| | Non-user ($n = 355{,}498$) | New user ($n = 912$) | Former user ($n = 4737$) | Long-term user ($n = 4354$) | |
| Age, years | $68.6 \pm 11.8$ | $69.6 \pm 10.3$ | $68.9 \pm 11.1$ | $68.9 \pm 11.1$ | 0.08 |
| Age group, year | | | | | |
| 40-64 years | 36.8 | 30.5 | 35.0 | 33.6 | 0.14 |
| 65-74 years | 30.1 | 35.8 | 31.5 | 32.6 | 0.12 |
| ≥75 years | 33.1 | 33.7 | 33.5 | 33.8 | 0.02 |
| Male sex | 57.6 | 60.2 | 61.8 | 61.9 | 0.09 |
| Hospital level | | | | | |
| Medical center (teaching hospital) | 28.8 | 26.7 | 29.6 | 34.2 | 0.16 |
| Regional / district hospital | 71.2 | 73.3 | 70.4 | 65.8 | 0.16 |
| Comorbidity | | | | | |
| Previous ischemic stroke | 9.7 | 14.4 | 10.2 | 12.8 | 0.16 |
| Previous hemorrhagic stroke | 1.10 | 0.49 | 0.76 | 2.11 | 0.16 |
| Gout | 7.0 | 9.5 | 7.9 | 10.8 | 0.15 |
| Diabetes mellitus | 38.3 | 43.8 | 37.9 | 43.8 | 0.12 |
| Hypertension | 75.0 | 81.8 | 77.6 | 80.0 | 0.16 |
| Previous myocardial infarction | 2.0 | 2.3 | 1.9 | 3.0 | 0.08 |
| Coronary artery disease | 19.4 | 24.2 | 19.3 | 29.5 | 0.26 |
| Chronic kidney disease | 2.8 | 4.8 | 3.2 | 3.1 | 0.12 |
| COPD | 8.8 | 12.2 | 10.0 | 12.7 | 0.14 |
| Dyslipidemia | 33.0 | 28.4 | 34.8 | 36.7 | 0.18 |
| Previous malignancy | 4.3 | 5.7 | 4.4 | 4.9 | 0.07 |

| Variable | Non-chronic use category | | Chronic use category | | |
| --- | --- | --- | --- | --- | --- |
| | Non-user ($n = 355{,}498$) | New user ($n = 912$) | Former user ($n = 4737$) | Long-term user ($n = 4354$) | MASD |
| Carotid stenting or endarterectomy | 0.19 | 0.00 | 0.07 | 0.12 | 0.04 |
| CCI score | 2.5 ± 1.6 | 2.6 ± 1.5 | 2.4 ± 1.5 | 2.5 ± 1.4 | 0.09 |
| Estimated NIHSS | 6.6 ± 5.1 | 5.9 ± 4.3 | 6.4 ± 4.9 | 6.1 ± 4.3 | 0.14 |
| Estimated NIHSS group | | | | | |
| ≤5 | 68.8 | 75.9 | 69.9 | 70.3 | 0.15 |
| 6-13 | 19.3 | 15.6 | 19.6 | 20.0 | 0.11 |
| >13 | 11.9 | 8.4 | 10.5 | 9.8 | 0.11 |
| Anti-hypertensive agent | | | | | |
| ACEI/ARB | 46.4 | 50.9 | 48.7 | 50.9 | 0.09 |
| CCB | 42.3 | 47.9 | 46.5 | 40.9 | 0.14 |
| Alpha-blocker | 5.9 | 7.2 | 7.1 | 7.1 | 0.05 |
| Beta-blocker | 24.8 | 29.8 | 25.5 | 27.5 | 0.12 |
| Thiazide | 5.2 | 3.6 | 4.7 | 5.0 | 0.07 |
| Loop diuretics | 6.0 | 9.9 | 6.9 | 8.3 | 0.16 |
| Spironolactone | 0.98 | 0.95 | 0.69 | 0.34 | 0.07 |
| Others | 2.20 | 2.99 | 2.38 | 0.74 | 0.15 |
| Number of anti-hypertensive agents | | | | | |
| 0 | 28.8 | 23.1 | 26.2 | 27.9 | 0.15 |
| 1-2 | 54.9 | 54.5 | 56.0 | 54.7 | 0.03 |
| 3-4 | 15.5 | 22.1 | 17.0 | 16.9 | 0.16 |
| ≥5 | 0.77 | 0.33 | 0.90 | 0.47 | 0.05 |
| Average numbers of antihypertensive agents | 1.34 ± 1.16 | 1.53 ± 1.19 | 1.42 ± 1.18 | 1.41 ± 1.17 | 0.17 |

| Variable | Non-chronic use category | | Chronic use category | | MASD |
|---|---|---|---|---|---|
| | Non-user | New user | Former user | Long-term user | |
| | (n = 355,498) | (n = 912) | (n = 4737) | (n = 4354) | |
| Antidiabetic agent | | | | | |
| Biguanide (Metformin) | 21.8 | 23.5 | 20.3 | 22.1 | 0.08 |
| TZD | 3.2 | 3.8 | 3.0 | 3.7 | 0.05 |
| Sulfonylurea | 22.4 | 26.4 | 20.9 | 22.3 | 0.13 |
| DPP4i | 2.5 | 2.4 | 2.5 | 2.4 | 0.01 |
| Glinide | 3.4 | 4.5 | 4.0 | 4.7 | 0.08 |
| Alpha Glucosidase inhibitors | 3.9 | 5.3 | 2.7 | 5.6 | 0.15 |
| Insulin | 4.7 | 4.6 | 4.8 | 6.5 | 0.09 |
| Average number of antidiabetic agents | $0.62 \pm 1.02$ | $0.71 \pm 1.10$ | $0.58 \pm 0.99$ | $0.67 \pm 1.03$ | 0.12 |
| Other medications | | | | | |
| Aspirin | 17.5 | 21.4 | 17.2 | 27.6 | 0.27 |
| Clopidogrel | 1.3 | 1.1 | 1.5 | 2.2 | 0.10 |
| Cilostazol | 0.52 | 0.78 | 0.53 | 0.45 | 0.05 |
| Statin | 8.3 | 8.9 | 8.2 | 10.3 | 0.08 |
| Fibrate | 5.5 | 6.8 | 6.0 | 8.5 | 0.13 |
| NSAIDs including Cox-2 | 22.5 | 29.7 | 25.6 | 28.6 | 0.17 |
| Steroid | 2.5 | 4.5 | 3.3 | 2.0 | 0.16 |
| Gout medications | | | | | |
| Allopurinol | 1.5 | 1.8 | 1.7 | 2.3 | 0.06 |
| Benzbromarone | 2.4 | 3.1 | 2.7 | 3.7 | 0.09 |
| Sulfinpyrazone | 0.13 | 0.09 | 0.12 | 0.13 | 0.01 |
| Febuxostat | 0.004 | 0.000 | 0.006 | 0.002 | 0.01 |

| | Non-chronic use category | | Chronic use category | | |
| | Non-user | New user | Former user | Long-term user | |
| Variable | ($n$ = 355,498) | ($n$ = 912) | ($n$ = 4737) | ($n$ = 4354) | MASD |
|---|---|---|---|---|---|
| Follow-up year | 5.0 ± 3.6 | 5.1 ± 3.3 | 4.9 ± 3.5 | 4.9 ± 3.4 | 0.21 |

IPTW, inverse probability of treatment weighting; MASD, maximum absolute standardized difference; COPD, chronic obstruction pulmonary disease; CCI, Charlson comorbidity index; NIHSS, National Institute of Health Stroke Scale; ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; CCB, calcium channel blocker; TZD, thiazolidinedione; DPP4i, dipeptidyl peptidase-4 inhibitor; NASIDs, non-steroidal anti-inflammatory drug

Data were presented as frequency (percentage) or mean ± standard deviation.

**Supplemental table S2.** Long-term outcome of study patients before IPTW

| Variable | Non-chronic use category | | Chronic use category | |
|---|---|---|---|---|
| | Non-user ($n$ = 355,498) | New user ($n$ = 912) | Former user ($n$ = 4737) | Long-term user ($n$ = 4354) |
| 6 month | | | | |
| Primary outcome | | | | |
| Recurrence of ischemic stroke | 48,135 (13.5) | 122 (13.4) | 712 (15.0) | 642 (14.7) |
| Secondary outcome | | | | |
| Cardiovascular death | 9,481 (2.7) | 35 (3.8) | 160 (3.4) | 152 (3.5) |
| All-cause mortality | 17,325 (4.9) | 53 (5.8) | 260 (5.5) | 255 (5.9) |
| New-diagnosed atrial fibrillation | 11,716 (3.3) | 42 (4.6) | 188 (4.0) | 164 (3.8) |
| 2 year | | | | |
| Primary outcome | | | | |
| Recurrence of ischemic stroke | 74,581 (21.0) | 210 (23.0) | 1,089 (23.0) | 996 (22.9) |
| Secondary outcome | | | | |
| Cardiovascular death | 23,848 (6.7) | 79 (8.7) | 350 (7.4) | 382 (8.8) |
| All-cause mortality | 44,570 (12.5) | 129 (14.1) | 614 (13.0) | 657 (15.1) |
| New-diagnosed atrial fibrillation | 17,970 (5.1) | 67 (7.3) | 286 (6.0) | 265 (6.1) |

Data were presented as frequency (percentage).