**Appendix**

**Supplementary Table 1**. Diagnoses and their ICD-8 and ICD-10 diagnosis codes in a study of patients with chronic myeloproliferative neoplasms, comorbidity, and risk of vascular disease.

| **Disease** | **ICD-8** | **ICD-10** |
| --- | --- | --- |
| **Exposure** |  |  |
| Essential thrombocythemia (ET) | 287.29 | D473, D752 |
| Polycythemia vera (PV) | 208.99 | D459 |
| Myelofibrosis (MF) / Myeloproliferative neoplasm unspecified (MPN-U) | 209 | D471, D474 |
| **Outcome** |  |  |
| *Arterial diseases* |  |  |
| Acute myocardial infarction (MI) | 410 | I21-I23 |
| Overall Stroke | 431-434 | I61, I63, I64 |
| Ischemic stroke | 433-434 | I63 |
| Peripheral arterial disease lower extremity (PAD) | 440.20 | I702 |
|  |  |  |
| *Venous diseases* |  |  |
| Pulmonary embolus or deep venous thrombosis lower extremity (VTE) | 450.99, 451.00, 451.08, 451.09, 451.99 | I26, I80.1-I80.9 |
| Splancnic vein thrombosis (SVT) | 452.99, 453.01, 444.29, 289.44, 453.03 | I81, I82.0, K550H |
| **Covariates** |  |  |
| *Charlsons comorbidity category* |  |  |
| Myocardial infarction | 410 | I21-I23 |
| Congestive heart failure | 427.09;427.10; 427.11;427.19; 428.99; 782.49 | I50, I11.0, I13.0, I13.2 |
| Peripheral vascular disease | 440; 441; 442; 443; 444 (excl 444.29); 445 | I70; I71; I72; I73; I74; I77 |
| Cerebrovascular disease  | 430-438 | I60-I69; G45; G46 |
| Dementia | 290.09-290.19; 293.09 | F00-F03; F05.1; G30 |
| Chronic pulmonary disease | 490-493; 515-518 | J40-J47; J60-J67; J68.4; J70.1; J70.3; J84.1; J92.0; J96.1; J98.2; J98.3 |
| Connective tissue disease | 712; 716; 734; 446; 135.99 | M05; M06; M08; M09;M30;M31; M32; M33; M34; M35; M36; D86 |
| Ulcer disease | 530.91; 530.98; 531-534 | K22.1; K25-K28 |
| Mild liver disease | 571; 573.01; 573.04 | B18; K70.0-K70.3; K70.9; K71; K73; K74; K76.0 |
| Diabetes type I Diabetes type II  | 249.00;249.06; 249.07; 249.09 250.00;250.06; 250.07; 250.09 | E10.0, E10.1; E10.9E11.0; E11.1; E11.9 |
| Hemiplegia | 344 | G81; G82 |
| Moderate to severe renal disease | 403; 404; 580-583;584;590.09; 593.19; 753.10-753.19; 792 | I12; I13; N00-N05; N07; N11; N14; N17-N19; Q61 |
| Diabetes with end-organ damage  | 249.01-249.05; 249.08250.01-250.05; 250.08 | E10.2-E10.8E11.2-E11.8 |
| Any tumour | 140-194 | C00-C75 |
| Leukemia | Excluded | Excluded |
| Lymphoma | 200-203;275.59 | C81-C85; C88; C90; C96 |
| Metastatic solid tumour | 195-198; 199 | C76-C80 |
| AIDS | 079.83 | B21-B24 |
|  |  |  |
| *Other cardiovascular risk factors* |  |  |
| Hypertension | 400-404 | I10-I15, I67.4 |
| Hyperlipidemia | 27200, 27201 | E780-E785  |
| Obesity | 277 | E65-E68 |
|  |  |  |
| *Other comorbidity groups* |  |  |
| Chronic obstructive pulmonary disease | 490-492 | J40-J44 |
|  |  |  |
| Alcohol-related diagnoses  | 291.19, 291.29, 291.39, 291.99, 303.09, 303.19, 303.20, 303.28, 303.29, 303.90, 303.99, 571.09, 571.92, 571.99, 571.90, 571.91, 571.10, 303.91 | P043, F10, T51, Z71.4, Z72.1, X65, E51.2, K70, K29.2, K76.0, K86.0, G62.1, G72.1, G31.2, G40.5B, G72.1, I42.6, K74.3, K74.4, K74.5, K74.6, E24.4, E52.9A, O35.4 |

**Supplementary Table 2.** Five-year risk of vascular event in percent, risk differences, and hazard ratios (HRs) in patients with essential thrombocythemia (ET), polycythemia vera (PV), and myelofibrosis (MF) or unclassified myeloproliferative neoplasm (MPN-U), compared to members of age- and sex-matched general population comparison cohorts. The risks and HRs are stratified by type of vascular event and ET, PV, or MF/MPN-U diagnosis year for patients and index year for members of the comparison cohorts. The HRs are adjusted for age, sex, prevalent vascular diagnosis, chronic obstructive pulmonary disease, and alcohol-related diagnoses.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **ET** |  |  | **PV** |  |  | **MF/MPN-U** |  |
|  | **ET cohort 5-year risk (95% CI)** | **ET comparison cohort 5-year risk (95% CI)** | **Risk difference (95% CI)** | **Adjusted HR (95% CI)** | **PV cohort 5-year risk (95% CI)** | **PV comparison cohort 5-year risk (95% CI)** | **Risk difference (95% CI)** | **Adjusted HR (95% CI)** | **MF/MPN-U cohort 5-year risk (95% CI)** | **MF/MPN-U comparison cohort 5-year risk (95% CI)** | **Risk difference (95% CI)** | **Adjusted HR (95% CI)** |
| **Myocardial infarction**  |  |  |  |  |  |  |  |  |  |  |  |
|  | Overall | 3.3 (2.6-4.0) | 2.5 (2.4-2.7) | 0.7 (-0.1-1.6) | 1.3 (1.0-1.6) | 4.4 (3.9-5.0) | 3.3 (3.1-3.4) | 1.2 (0.5-1.8) | 1.3 (1.1-1.5) | 3.6 (3.0-4.2) | 3.7 (3.5-3.9) | -0.1 (-0.9-0.7) | 1.5 (1.2-1.9) |
|  | 1980-89 | 6.1 (1.1-18) | 4.6 (2.7-7.2) | 1.5 (-5.4-8.4) | 2.0 (0.4-10.7) | 5.5 (4.6-6.6) | 3.9 (3.9-4.2) | 1.6 (0.4-2.9) | 1.3 (1.0-1.7) | 4.6 (3.2-6.3) | 4.2 (3.7-4.7) | 0.4 (-1.5-2.2) | 2.1 (1.4-3.1) |
|  | 1990-99 | 3.8 (2.6-5.4) | 2.3 (2.0-2.7) | 1.5 (-0.1-3.0) | 1.6 (1.0-2.5) | 4.5 (3.6-5.5) | 3.5 (3.2-3.7) | 1.1 (-0.1-2.2) | 1.3 (1.0-1.7) | 2.6 (1.8-3.8) | 3.6 (3.3-4.0) | -1.0 (-2.2-0.2) | 1.2 (0.8-1.8) |
|  | 2000-13 | 3.0 (2.3-3.9) | 2.6 (2.4-2.8) | 0.4 (-0.5-1.4) | 1.1 (0.9-1.5) | 3.4 (2.6-4.2) | 2.5 (2.3-2.7) | 0.9 (-0.1-1.8) | 1.2 (0.9-1.5) | 3.7 (2.8-4.7) | 3.5 (3.2-3.8) | 0.2 (-1.4-2.3) | 1.6 (1.3-2.1) |
| **Stroke (any type)**  |  |  |  |  |  |  |  |  |  |  |  |
|  | Overall | 6.9 (6.0-7.9) | 4.0 (3.7-4.2) | 2.9 (1.8-4.1) | 1.6 (1.4-1.9) | 7.7 (7.1-8.5) | 3.4 (3.3-3.6) | 4.3 (3.5-5.2) | 2.2 (1.9-2.4) | 5.6 (4.9-6.5) | 4.6 (4.4-4.9) | 1.0 (0.0-2.0) | 1.7 (1.4-2.0) |
|  | 1980-89 | 0.0 | 2.4 (1.1-4.5) |  |  | 4.5 (3.7-5.6) | 1.6 (1.4-1.8) | 3.0 (1.9-4.0) | 2.5 (1.9-3.3) | 1.9 (1.1-3.2) | 1.9 (1.6-2.3) | 0.0 (-1.2-1.3) | 1.9 (1.0-3.5) |
|  | 1990-99 | 6.0 (4.4-7.9) | 3.9 (3.5-4.4) | 2.1 (0.1-4.1) | 1.4 (1.0-2.0) | 9.4 (8.1-11) | 4.1 (3.8-4.4) | 5.3 (3.7-6.8) | 2.4 (2.0-2.9) | 5.0 (3.8-6.4) | 5.0 (4.5-5.4) | 0.0 (-1.6-1.7) | 1.5 (1.1-2.0) |
|  | 2000-13 | 7.3 (6.2-8.5) | 4.0 (3.7-4.3) | 3.3 (1.9-4.7) | 1.7 (1.4-2.1) | 9.2 (7.9-11) | 4.4 (4.1-4.7) | 4.8 (3.3-6.3) | 1.9 (1.6-2.2) | 7.5 (6.3-8.9) | 5.6 (5.2-5.9) | 2.0 (0.4-3.6) | 1.8 (1.5-2.2) |
| **Ischemic stroke** |  |  |  |  |  |  |  |  |  |  |  |
|  | Overall | 3.7 (3.0-4.5) | 2.0 (1.9-2.2) | 1.7 (0.8-2.5) | 1.8 (1.4-2.3) | 3.9 (3.4-4.5) | 1.6 (1.5-1.7) | 2.3 (1.7-2.9) | 2.3 (2.0-2.7) | 2.3 (1.8-2.9) | 2.2 (2.1-2.4) | 0.1 (-0.5-0.7) | 1.5 (1.1-1.9) |
|  | 1980-89 | 0.0 | 0.0 |  |  | 3.0 (2.3-3.9) | 0.9 (0.8-1.1) | 2.1 (1.3-2.9) | 2.6 (1.8-3.7) | 0.7 (0.3-1.6) | 1.2 (1.0-1.5) | -0.5 (-1.2-0.2) | 1.0 (0.4-2.7) |
|  | 1990-99 | 3.1 (2.0-4.5) | 1.3 (1.1-1.6) | 1.8 (0.4-3.1) | 2.5 (1.5-4.2) | 3.6 (2.8-4.5) | 1.4 (1.2-1.5) | 2.2 (1.3-3.1) | 2.9 (2.2-3.8) | 1.8 (1.1-2.7) | 1.5 (1.3-1.8) | 0.3 (-0.6-1.2) | 1.9 (1.1-3.2) |
|  | 2000-13 | 4.0 (3.2-4.9) | 2.3 (2.1-2.5) | 1.7 (0.7-2.7) | 1.7 (1.3-2.2) | 5.1 (4.2-6.1) | 2.6 (2.3-2.8) | 2.6 (1.4-3.7) | 1.8 (1.5-2.3) | 3.3 (2.5-4.3) | 3.1 (2.9-3.4) | 0.2 (-0.9-1.3) | 1.5 (1.1-2.0) |
| **Peripheral arterial disease lower extremity** |  |  |  |  |  |  |  |  |  |  |
|  | Overall | 4.3 (3.6-5.1) | 1.5 (1.4-1.7) | 2.8 (2.0-3.7) | 2.1 (1.7-2.8) | 5.0 (4.4-5.6) | 1.5 (1.4-1.6) | 3.5 (2.8-4.1) | 2.8 (2.4-3.2) | 3.8 (3.2-4.5) | 1.7 (1.6-1.9) | 2.1 (1.4-2.9) | 2.5 (1.9-3.2) |
|  | 1980-89 | 3.0 (0.2-13) | 0.3 (0.0-1.6) | 2.7 (-0.4-5.8) | 0 | 4.1 (3.2-5.0) | 0.8 (0.7-1.0) | 3.2 (2.3-4.2) | 3.8 (2.7-5.4) | 1.2 (0.6-2.2) | 1.2 (0.9-1.4) | 0.0 (-0.8-0.9) | 2.0 (0.7-5.2) |
|  | 1990-99 | 5.0 (3.6-6.8) | 1.6 (1.3-1.9) | 3.5 (1.8-5.2) | 1.9 (1.1-3.0) | 6.9 (5.8-8.2) | 2.2 (2.0-2.4) | 4.8 (3.5-6.1) | 3.0 (2.3-3.7) | 5.0 (3.8-6.4) | 2.2 (1.9-2.5) | 2.8 (1.3-4.3) | 4.6 (2.7-7.9) |
|  | 2000-13 | 4.1 (3.3-5.0) | 1.5 (1.4-1.7) | 2.6 (1.6-3.5) | 2.3 (1.7-3.1) | 3.9 (3.1-4.8) | 1.6 (1.4-1.7) | 2.4 (1.4-3.3) | 2.1 (1.6-2.8) | 4.1 (3.2-5.2) | 1.6 (1.4-1.8) | 2.5 (1.5-3.6) | 2.5 (1.8-3.5) |
| **Venous tromboembolism** |  |  |  |  |  |  |  |  |  |  |  |
|  | Overall | 2.9 (2.3-3.6) | 1.3 (1.2-1.5) | 1.6 (0.9-2.3) | 2.1 (1.6-2.8) | 5.1 (4.6-5.7) | 1.3 (1.2-1.4) | 3.9 (3.2-4.5) | 3.7 (3.2-4.4) | 3.6 (3.0-4.3) | 1.4 (1.2-1.5) | 2.2 (1.5-2.9) | 3.7 (2.9-4.7) |
|  | 1980-89 | 3.0 (0.2-13) | 1.2 (0.4-2.9) | 1.8 (-1.8-3.7) | 3.1 (0.3-32) | 6.0 (5.0-7.1) | 1.1 (0.9-1.2) | 4.9 (3.7-6.1) | 5.6 (4.1-7.5) | 3.5 (2.3-5.1) | 1.3 (1.0-1.6) | 2.3 (0.8-3.7) | 6.1 (3.5-11) |
|  | 1990-99 | 1.5 (0.8-2.7) | 1.0 (0.8-1.2) | 0.6 (-0.4-1.5) | 1.8 (0.9-3.6) | 4.7 (3.8-5.7) | 1.2 (1.0-1.3) | 3.5 (2.5-4.6) | 4.5 (3.4-6.0) | 2.8 (1.9-4.0) | 1.2 (1.0-1.4) | 1.7 (0.6-2.8) | 3.1 (1.9-4.9) |
|  | 2000-13 | 3.4 (2.6-4.2) | 1.4 (1.3-1.6) | 1.9 (1.1-2.8) | 2.2 (1.7-3.0) | 4.8 (3.9-5.8) | 1.6 (1.4-1.8) | 3.2 (2.1-4.2) | 2.6 (2.0-3.3) | 4.0 (3.1-5.0) | 1.5 (1.3-1.7) | 2.5 (1.4-3.5) | 3.5 (2.5-4.8) |
| **Splanchnic venous thrombosis** |  |  |  |  |  |  |  |  |  |  |
|  | Overall | 0.6 (0.3-0.9) | 0.0 (0.0-0.1) | 0.6 (0.3-0.8) | 25 (2.8->100) | 0.6 (0.4-0.8) | 0.0 (0.0-0.0) | 0.6 (0.4-0.8) | >100 | 0.5 (0.3-0.8) | 0.0 (0.0-0.1) | 0.5 (0.3-0.7) | 13 (3.3-51) |
|  | 1980-89 | 0 | 0 |  |  | 0.3 (0.1-0.6) | 0.0 (0.0-0.1) | 0.3 (0.1-0.4) | >100 | 0.3 (0.0-1.0) | 0.0 (0.0-0.1) | 0.3 (0.0-0.5) | >100 |
|  | 1990-99 | 0.4 (0.1-1.2) | 0 |  |  | 0.4 (0.2-0.8) | 0.0 (0.0-0.0) | 0.4 (0.2-0.7) | 5.5 (0.3-99) | 0.3 (0.1-0.8) | 0.0 (0.0-0.1) | 0.3 (0.1-0.5) | 0 |
|  | 2000-13 | 0.6 (0.4-1.1) | 0.0 (0.0-0.0) | 0.6 (0.3-0.9) | 25 (2.8->100) | 1.0 (0.6-1.4) | 0.0 (0.0-0.1) | 0.9 (0.6-1.3) | >100 | 0.7 (0.4-1.2) | 0.0 (0.0-0.1) | 0.7 (0.3-1.0) | 11 (2.4-4) |

**Supplementary Table 3**. Incidences per 1,000 patient-years for vascular event during the first 5 years following diagnosis in patients with essential thrombocythaemia (ET), polycythaemia vera (PV), and myelofibrosis (MF) or unclassified myeloproliferative neoplasm (MPN-U), compared to members of age- and sex-matched general population comparison cohorts. The incidences are stratified by type of vascular event and ET, PV, or MF/MPN-U diagnosis year for patients and index year for members of the comparison cohorts.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **ET cohort incidence (95% CI)** | **ET comparison cohort incidence (95% CI)** |  | **PV cohort incidence (95% CI)** | **PV comparison cohort incidence (95% CI)** |  | **MF/MPN-U cohort incidence (95% CI)** | **MF/MPN-U comparison cohort incidence (95% CI)** |
| **Myocardial infarction**  |  |  |  |  |  |  |  |
|  | Overall |  7.9 (6.3-9.6) | 5.4 (5.1-5.7) |  | 10.6 (9.6-11.6) | 7.5 (7.3-7.7) |  | 11.0 (9.2-12.7) | 8.4 (8.1-8.7) |
|  | 1980-89 | 15.4 (-2.0-32.7) | 7.5 (4.3-10.6) |  | 13.7 (11.4-15.9) | 8.8 (8.4-9.3) |  | 18.9 (12.6-25.1) | 9.7 (8.8-10.5) |
|  | 1990-99 | 7.8 (5.4-10.3) | 5.1 (4.6-5.7) |  | 11.2 (9.3-13.2) | 7.9 (7.4-8.3) |  | 8.2 (5.5-10.9) | 9.2 (5.7-12.6) |
|  | 2000-13 | 6.9 (5.4-8.5) | 5.5 (5.1-5.9) |  | 7.4 (5.9-9.0) | 5.7 (5.3-6.1) |  | 11.7 (9.1-14.4) | 7.5 (7.0-8.1) |
| **Stroke (any type)**  |  |  |  |  |  |  |  |
|  | Overall | 17.0 (14.5-19.4) | 8.8 (8.2-9.3) |  | 19.0 (17.7-20.3) | 9.2 (9.0-9.5) |  | 17.3 (15.1-19.5) | 11.6 (11.2-11.9) |
|  | 1980-89 | 5.0 (-4.8-14.9) | 5.3 (2.6-8.0) |  | 12.3 (10.2-14.4) | 4.4 (4.0-4.7) |  | 9.1 (4.8-13.5) | 6.0 (5.3-6.6) |
|  | 1990-99 | 16.0 (12.4-19.5) | 9.4 (8.6-10.2) |  | 23.9 (21.1-26.8) | 10.4 (9.9-10.9) |  | 16.1 (12.3-20.0) | 12.6 (11.8-13.4) |
|  | 2000-13 | 16.8 (14.4-19.3) | 8.7 (8.1-9.2) |  | 19.9 (17.3-22.5) | 9.9 (9.3-10.4) |  | 21.7 (18.0-25.4) | 12.5 (11.8-13.2) |
| **Ischemic stroke** |  |  |  |  |  |  |  |
|  | Overall | 8.6 (7.3-9.9) | 5.0 (4.7-5.3) |  | 9.3 (8.4-10.2) | 4.7 (4.5-4.8) |  | 8.0 (6.5-9.5) | 5.8 (5.5-6.1) |
|  | 1980-89 | 0.0 | 3.2 (1.1-5.2) |  | 6.9 (5.3-8.4) | 2.2 (1.9-2.4) |  | 3.8 (1.0-6.5) | 2.8 (2.3-3.3) |
|  | 1990-99 | 8.1 (5.6-10.6) | 3.8 (3.3-4.3) |  | 9.4 (7.6-11.1) | 4.0 (3.7-4.4) |  | 6.8 (4.4-9.3) | 4.7 (4.2-5.2) |
|  | 2000-13 | 8.9 (7.2-10.7) | 5.3 (4.9-5.7) |  | 11.6 (9.7-13.6) | 6.1 (5.6-6.1) |  | 9.9 (7.4-12.3) | 7.3 (6.7-7.8) |
| **Peripheral arterial disease, lower extremity** |  |  |  |  |  |  |
|  | Overall | 8.5 (7.2-9.8) | 2.9 (2.7-3.2) |  | 11.1 (10.1-12.1) | 3.4 (3.3-3.6) |  | 11.6 (9.8-13.4) | 3.8 (3.5-4.0) |
|  | 1980-89 | 5.3 (-5.1-15.7) | 1.0 (-0.1-2.2) |  | 10.2 (8.3-12.1) | 2.2 (2.0-2.4) |  | 5.4 (2.0-8.7) | 2.7 (2.3-3.2) |
|  | 1990-99 | 9.4 (6.7-12.1) | 3.4 (2.9-3.8) |  | 15.0 (12.7-17.2) | 4.5 (4.1-4.8) |  | 15.0 (11.3-18.7) | 4.7 (4.2-5.2) |
|  | 2000-13 | 8.8 (7.1-10.6) | 3.0 (2.7-3.3) |  | 8.8 (7.1-10.5) | 3.3 (3.0-3.6) |  | 12.3 (9.5-15.0) | 3.6 (3.2-4.0) |
| **Venous thromboembolism** |  |  |  |  |  |  |  |
|  | Overall | 7.1 (5.9-8.3) | 3.1 (2.9-3.3) |  | 11.3 (10.3-12.3) | 3.0 (2.9-3.2) |  | 11.5 (9.7-13.2) | 3.4 (3.2-3.6) |
|  | 1980-89 | 10.5 (-4.1-25.2) | 2.1 (0.4-3.8) |  | 13.6 (11.4-15.9) | 2.3 (2.0-2.5) |  | 14.7 (9.2-20.3) | 3.0 (2.5-3.5) |
|  | 1990-99 | 5.0 (3.0-6.9) | 2.2 (1.8-2.5) |  | 11.0 (9.1-12.9) | 2.7 (2.5-3.0) |  | 10.2 (7.1-13.2) | 2.9 (2.5-3.3) |
|  | 2000-13 | 8.2 (6.5-9.8) | 3.3 (3.0-3.6) |  | 11.6 (9.6-13.5) | 3.7 (3.3-4.0) |  | 13.0 (10.1-15.8) | 3.7 (3.3-4.1) |
| **Splanchnic venous thrombosis** |  |  |  |  |  |  |
|  | Overall | 0.9 (0.5-1.4) | 0.0 (0.0-0.0) |  | 1.0 (0.7-1.3) | 0.0 (0.0-0.1) |  | 1.4 (0.7-2.0) | 0.0 (0.0-0.1) |
|  | 1980-89 | 0 | 0 |  | 0.5 (0.1-0.9) | 0.0 (0.0-0.1) |  | 1.1 (-0.4-2.6) | 0.0 (0.0-0.1) |
|  | 1990-99 | 0.8 (0.0-1.6) | 0.0 (0.0-0.0) |  | 0.8 (0.3-1.3) | 0.0 (0.0-0.0) |  | 0.7 (-0.1-1.5) | 0.0 (0.0-0.1) |
|  | 2000-13 | 1.2 (0.6-1.9) | 0.0 (0.0-0.0) |  | 2.0 (1.2-2.8) | 0.1 (0.0-0.1) |  | 2.2 (1.0-3.3) | 0.1 (0.0-0.1) |

CI: Confidence interval

**Supplementary Table 4**. Five-year cumulative risks with 95% confidence intervals of vascular event in patients with essential thrombocythemia (ET), polycythemia vera (PV), and myelofibrosis (MF) or unclassified myeloproliferative neoplasm (MPN-U). The risks are stratified according to whether a previous or co-incident diagnosis of chronic pulmonary obstructive disease (COPD) had been made.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **ET without COPD**  | **ET with COPD**  | **PV without COPD**  | **PV with COPD**  | **MF/MPN-U without COPD**  | **MF/MPN-U with COPD**  |
| **Myocardial infarction**  |  |  |  |  |  |
|  |  | 3.2 (2.6-4.0) | 3.6 (1.7-6.7) | 4.4 (3.8-5.0) | 5.0 (3.4-7.0) | 3.4 (2.8-4.1) | 5.6 (3.2-9.0) |
| **Stroke (any type)**  |  |  |  |  |  |
|  |  | 6.4 (5.7-7.7) | 9.7 (6.2-14) | 7.9 (7.2-8.6) | 6.6 (4.7-8.8) | 5.6 (4.8-6.4) | 6.4 (3.7-10) |
| **Ischemic stroke** |  |  |  |  |  |
|  |  | 3.7 (3.0-4.5) | 4.2 (2.1-7.5) | 4.1 (3.6-4.7) | 2.2 (1.2-3.7) | 2.3 (1.8-2.9) | 2.7 (1.1-5.6) |
| **PAD** |  |  |  |  |  |
|  |  | 4.1 (3.3-4.9) | 7.5 (4.5-11) | 4.7 (4.2-5.3) | 7.1 (5.2-9.4) | 3.5 (2.9-4.2) | 8.7 (5.6-13) |
| **VTE** |  |  |  |  |  |
|  |  | 2.6 (2.0-3.0) | 6.3 (3.6-10) | 5.0 (4.4-5.6) | 6.9 (5.0-9.2) | 3.6 (3.0-4.3) | 3.5 (1.7-6.3) |

PAD: Peripheral arterial disease, lower extremity

VTE: Venous thromboembolism

**Supplementary Table 5.** Risk of vascular event in percent, risk differences, and hazard ratios (HRs) during the first year following diagnosis in patients with essential thrombocythemia (ET), polycythemia vera (PV), and myelofibrosis (MF) or unclassified myeloproliferative neoplasm (MPN-U), compared to members of age- and sex-matched general population comparison cohorts. The risks and HRs are stratified by type of vascular event and number of cardiovascular risk factors (CRF): hypertension, diabetes, obesity, hyperlipidemia, atrial fibrillation, or renal failure. The HRs are adjusted for age, sex, diagnosis year, prevalent vascular diagnosis, chronic obstructive pulmonary disease, and alcohol-related diagnoses.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **ET** |  |  | **PV** |  |  | **MF/MPN-U** |  |
|  | **ET cohort 1-year risk (95% CI)** | **ET comparison cohort 1-year risk (95% CI)** | **Risk difference (95% CI)** | **Adjusted HR (95% CI)** | **PV cohort 1-year risk (95% CI)** | **PV comparison cohort 1-year risk (95% CI)** | **Risk difference (95% CI)** | **Adjusted HR (95% CI)** | **MF/MPN-U cohort 1-year risk (95% CI)** | **MF/MPN-U comparison cohort 1-year risk (95% CI)** | **Risk difference (95% CI)** | **Adjusted HR (95% CI)** |
| **Myocardial infarction**  |  |  |  |  |  |  |  |  |  |  |  |
|  | CRF 0 | 0.9 (0.6-1.4) | 0.4 (0.3-0.5) | 0.5 (0.1-0.9) | 2.0 (1.2-3.3) | 1.3 (1.0-1.7) | 0.6 (0.5-0.7) | 0.7 (0.3-1.0) | 2.0 (1.5-2.7) | 1.0 (0.7-1.4) | 0.7 (0.7-0.9) | 0.2 (-0.2-0.7) | 1.6 (1.0-2.3) |
|  | CRF 1 | 1.7 (0.9-3.0) | 1.1 (0.8-1.5) | 0.6 (-0.6-1.7) | 1.8 (0.9-3.6) | 1.5 (0.9-2.2) | 1.5 (1.2-1.8) | 0.0 (-0.8-0.8) | 1.1 (0.6-1.7) | 1.5 (0.8-2.6) | 1.4 (1.1-1.8) | 0.1 (-1.0-1.2) | 1.4 (0.7-2.7) |
|  | CRF 2+ | 1.5 (0.4-3.5) | 2.0 (1.4-2.7) | -0.5 (-2.1-1.1) | 1.0 (0.4-2.9) | 2.4 (1.4-4.0) | 1.6 (1.2-2.2) | 0.8 (-0.7-2.3) | 1.6 (0.8-3.1) | 3.2 (1.6-5.6) | 2.0 (1.5-2.7) | 1.2 (-0.9-3.3) | 2.2 (1.1-4.2) |
| **Stroke (any type)**  |  |  |  |  |  |  |  |  |  |  |  |
|  | CRF 0 | 1.5 (1.0-2.0) | 0.7 (0.6-0.8) | 0.8 (0.2-1.3) | 1.9 (1.3-2.8) | 2.4 (2.0-2.9) | 0.5 (0.5-0.6) | 1.9 (1.4-2.4) | 3.6 (2.9-4.6) | 1.6 (1.2-2.1) | 0.8 (0.7-1.0) | 0.8 (0.2-1.3) | 2.1 (1.5-2.9) |
|  | CRF 1 | 4.2 (2.8-6.0) | 1.3 (1.0-1.7) | 2.9 (1.1-4.6) | 3.3 (2.0-5.3) | 4.4 (3.4-5.6) | 2.0 (1.7-2.4) | 2.3 (1.0-3.7) | 2.6 (1.9-3.7) | 3.1 (2.0-4.6) | 2.3 (1.9-2.7) | 0.9 (-0.7-2.4) | 1.6 (1.0-2.6) |
|  | CRF 2+ | 5.1 (2.9-8.1) | 2.2 (1.6-3.0) | 2.9 (0.1-5.7) | 2.3 (1.2-4.3) | 5.2 (3.6-7.3) | 2.7 (2.1-3.5) | 2.5 (0.2-4.8) | 2.1 (1.3-3.3) | 4.4 (2.5-7.0) | 3.4 (2.6-4.2) | 1.0 (-1.6-3.6) | 1.7 (1.0-3.1) |
| **Ischemic stroke** |  |  |  |  |  |  |  |  |  |  |  |
|  | CRF 0 | 0.7 (0.5-1.2) | 0.4 (0.3-0.4) | 0.4 (0.0-0.8) | 1.9 (1.1-3.3) | 1.2 (0.9-1.5) | 0.3 (0.2-0.3) | 0.9 (0.6-1.2) | 3.7 (2.6-5.1) | 0.7 (0.4-1.1) | 0.4 (0.3-0.5) | 0.2 (-0.2-0.7) | 1.9 (1.1-3.0) |
|  | CRF 1 | 1.5 (0.7-2.7) | 0.7 (0.5-1.0) | 0.8 (-0.2-1.8) | 2.5 (1.1-5.4) | 2.0 (1.4-2.9) | 1.0 (0.8-1.3) | 1.0 (0.1-1.9) | 2.2 (1.4-3.6) | 1.2 (0.6-2.2) | 1.0 (0.8-1.3) | 0.2 (-0.7-1.1) | 1.4 (0.7-3.0) |
|  | CRF 2+ | 2.9 (1.4-5.4) | 1.0 (0.6-1.6) | 1.9 (0.0-3.8) | 2.7 (1.1-6.5) | 1.9 (1.0-3.3) | 1.2 (0.8-1.7) | 0.6 (-0.7-1.9) | 1.9 (0.9-3.9) | 1.6 (0.6-3.5) | 1.6 (1.1-2.2) | 0.0 (-1.5-1.4) | 1.3 (0.5-3.2) |
| **Peripheral arterial disease, lower extremity** |  |  |  |  |  |  |  |  |  |  |
|  | CRF 0 | 1.5 (1.1-2.1) | 0.3 (0.2-0.3) | 1.3 (0.8-1.8) | 3.2 (2.0-4.9) | 1.7 (1.3-2.1) | 0.3 (0.2-0.3) | 1.4 (1.0-1.9) | 3.6 (2.6-4.9) | 1.5 (1.1-2.0) | 0.3 (0.3-0.4) | 1.2 (0.7-1.6) | 3.2 (2.1-4.7) |
|  | CRF 1 | 4.0 (2.6-5.8) | 0.9 (0.7-1.3) | 3.0 (1.4-4.7) | 3.3 (1.9-5.6) | 1.6 (1.1-2.4) | 1.0 (0.8-1.3) | 0.6 (-0.2-1.4) | 1.6 (1.0-2.7) | 2.5 (1.5-3.9) | 0.9 (0.7-1.2) | 1.6 (0.4-2.9) | 2.4 (1.4-4.4) |
|  | CRF 2+ | 1.9 (0.7-4.2) | 1.2 (0.7-1.8) | 0.8 (-0.9-2.4) | 1.4 (0.4-3.8) | 3.8 (2.4-5.6) | 1.7 (1.2-2.3) | 2.1 (0.2-3.9) | 1.9 (1.1-3.3) | 4.5 (2.6-7.2) | 1.9 (1.4-2.6) | 2.5 (0.1-5.0) | 2.4 (1.3-4.5) |
| **Venous thromboembolism** |  |  |  |  |  |  |  |  |  |  |  |
|  | CRF 0 | 1.1 (0.7-1.6) | 0.2 (0.1-0.2) | 0.9 (0.4-1.3) | 5.0 (3.0-8.3) | 2.0 (1.6-2.5) | 0.2 (0.2-0.3) | 1.8 (1.4-2.2) | 6.9 (5.1-9.4) | 1.5 (1.1-2.0) | 0.3 (0.3-0.4) | 1.2 (0.7-1.6) | 4.5 (3.1-6.5) |
|  | CRF 1 | 1.5 (0.8-2.8) | 0.5 (0.3-0.8) | 1.0 (0.1-2.0) | 3.1 (1.4-6.9) | 1.7 (1.1-2.5) | 0.6 (0.4-0.8) | 1.2 (0.4-1.9) | 3.4 (1.9-5.9) | 1.2 (0.6-2.2) | 0.5 (0.4-0.8) | 0.6 (-0.2-1.4) | 2.4 (1.1-5.5) |
|  | CRF 2+ | 1.8 (0.7-4.0) | 0.9 (0.6-1.5) | 0.9 (-0.6-2.4) | 1.9 (0.7-5.2) | 1.5 (0.7-2.8) | 0.5 (0.3-0.9) | 1.0 (-0.1-2.0) | 2.2 (0.9-5.9) | 2.2 (1.0-4.3) | 0.8 (0.4-1.2) | 1.5 (-0.1-3.0) | 3.5 (1.4-8.7) |

CI: Confidence Interval

**Supplementary Table 6**. Five-year risk of vascular event in percent, risk differences, and hazard ratios (HRs) in patients with essential thrombocythemia (ET), polycythemia vera (PV), and myelofibrosis (MF) or unclassified myeloproliferative neoplasm (MPN-U), compared to members of age- and sex-matched general population comparison cohorts. The risks and HRs are stratified by type of vascular event and ET, PV, or MF/MPN-U diagnosis year for patients and index year for members of the comparison cohorts. The HRs are adjusted for age, sex, prevalent vascular diagnosis, chronic obstructive pulmonary disease, and alcohol-related diagnoses. Unlike results in supplementary Table 2, patients and members of the comparison cohort with the vascular event outcome prior to index date are excluded here.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **ET** |  |  | **PV** |  |  | **MF/MPN-U** |  |
|  | **ET cohort 5-year risk (95% CI)** | **ET comparison cohort 5-year risk (95% CI)** | **Risk difference (95% CI)** | **Adjusted HR (95% CI)** | **PV cohort 5-year risk (95% CI)** | **PV comparison cohort 5-year risk (95% CI)** | **Risk difference (95% CI)** | **Adjusted HR (95% CI)** | **MF/MPN-U cohort 5-year risk (95% CI)** | **MF/MPN-U comparison cohort 5-year risk (95% CI)** | **Risk difference (95% CI)** | **Adjusted HR (95% CI)** |
| **Myocardial infarction**  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | 2.6 (2.0-3.0) | 2.2 (2.0-2.4) | 0.4 (-0.3-1.2) | 1.3 (1.0-1.7) | 3.5 (3.0-4.0) | 2.9 (2.7-3.0) | 0.6 (0.0-1.2) | 1.2 (1.0-1.4) | 2.7 (2.2-3.3) | 3.2 (3.0-3.4) | -0.5 (-1.2-0.3) | 1.4 (1.1-1.8) |
| **Stroke (any type)**  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | 5.0 (4.2-5.9) | 3.5 (3.3-3.7) | 1.5 (0.5-2.6) | 1.5 (1.2-1.8) | 5.8 (5.1-6.4) | 3.0 (2.9-3.2) | 2.8 (2.0-3.5) | 2.2 (1.9-2.5) | 4.2 (3.5-5.0) | 4.1 (3.9-4.3) | 0.1 (-0.8-1.0) | 1.5 (1.2-1.8) |
| **Ischemic stroke** |  |  |  |  |  |  |  |  |  |  |  |
|  |  | 2.9 (2.3-3.7) | 1.9 (1.7-2.1) | 1.0 (0.3-1.8) | 1.6 (1.2-2.1) | 3.2 (2.8-3.7) | 1.5 (1.4-1.6) | 1.7 (1.2-2.3) | 2.3 (2.0-2.8) | 2.0 (1.5-2.5) | 2.1 (1.9-2.2) | -0.1 (-0.7-0.5) | 1.4 (1.0-1.8) |
| **Peripheral arterial disease, lower extremity** |  |  |  |  |  |  |  |  |  |  |
|  |  | 2.4 (1.9-3.1) | 1.2 (1.0-1.3) | 1.3 (0.6-1.9) | 2.3 (1.7-3.1) | 3.7 (3.2-4.2) | 1.2 (1.1-1.3) | 2.4 (1.9-3.0) | 2.9 (2.4-3.4) | 2.5 (1.9-3.0) | 1.3 (1.2-1.5) | 1.1 (0.5-1.8) | 2.6 (2.0-3.5) |
| **Venous thromboembolism** |  |  |  |  |  |  |  |  |  |  |  |
|  |  | 2.3 (1.8-3.0) | 1.3 (1.1-1.3) | 1.2 (0.6-1.9) | 2.0 (1.5-2.7) | 4.2 (3.6-4.7) | 1.1 (1.1-1.2) | 3.0 (2.4-3.6) | 4.0 (3.4-4.7) | 2.9 (2.4-3.5) | 1.2 (1.1-1.4) | 1.7 (1.0-2.3) | 3.7 (2.9-4.7) |
| **Splanchnic venous thrombosis** |  |  |  |  |  |  |  |  |  |  |
|  |  | 0.2 (0.1-0.4) | 0.0 (0.0-0.0) | 0.2 (0.0-0.3) | 25 (2.8->100) | 0.3 (0.2-0.4) | 0.0 (0.0-0.0) | 0.2 (0.1-0.4) | >100 (15->100) | 0.2 (0.1-0.4) | 0.0 (0.0-0.0) | 0.2 (0.1-0.3) | 13 (3.3-51) |

CI: Confidence Interval

**Supplementary Table 7.** Hazard ratios (HR) for vascular event in patients with essential thrombocythemia (ET), polycythemia vera (PV), and myelofibrosis (MF) or unclassified myeloproliferative neoplasm (MPN-U), compared to members of age- and sex-matched general population comparison cohorts. The HRs are stratified by level of comorbidity based on Charlson Comorbidity (CCI) scores and duration of follow-up and are adjusted for age, sex, diagnosis year, prevalent vascular diagnosis, chronic obstructive pulmonary disease, and alcohol-related diagnoses.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **ET** |  |  | **PV** |  |  | **MF/MPN-U** |  |
|  | **MI adjusted HR (95% CI)** | **Stroke adjusted HR (95% CI)** | **Ischemic stroke adjusted HR (95% CI)** | **VTE adjusted HR (95% CI)** | **MI adjusted HR (95% CI)** | **Stroke adjusted HR (95% CI)** | **Ischemic stroke adjusted HR (95% CI)** | **VTE adjusted HR (95% CI)** | **MI adjusted HR (95% CI)** | **Stroke adjusted HR (95% CI)** | **Ischemic stroke adjusted HR (95% CI)** | **VTE adjusted HR (95% CI)** |
| **CCI 0** |  |  |  |  |  |  |  |  |  |  |
|  | 0-1 yr | 1.5 (0.7-3.0) | 1.6 (0.9-2.6) | 1.5 (0.7-3.1) | 5.1 (2.6-10) | 2.0 (1.4-2.9) | 4.0 (3.0-5.3) | 3.9 (2.6-5.8) | 8.4 (5.9-12) | 1.7 (1.0-2.8) | 2.6 (1.8-3.9) | 1.7 (0.9-3.3) | 4.7 (2.9-7.7) |
|  | 1-2 yr | 0.8 (0.3-1.8) | 1.0 (0.5-2.0) | 0.8 (0.3-2.2) | 2.4 (1.1-5.2) | 1.6 (1.1-2.4) | 2.3 (1.6-3.3) | 3.3 (2.1-5.1) | 3.3 (2.1-5.3) | 0.9 (0.4-2.0) | 1.5 (0.9-2.6) | 0.2 (0.0-1.7) | 3.4 (1.7-6.5) |
|  | 2-3 yr | 0.9 (0.3-2.3) | 1.4 (0.8-2.7) | 1.9 (0.8-4.1) | 1.5 (0.5-4.3) | 1.0 (0.6-1.7) | 1.8 (1.2-2.8) | 2.8 (1.6-4.7) | 4.6 (3.0-7.0) | 2.1 (1.1-3.8) | 1.1 (0.6-2.3) | 0.5 (0.1-2.2) | 3.8 (1.8-8.0) |
|  | 3-4 yr | 2.1 (1.0-4.2) | 1.2 (0.6-2.3) | 1.1 (0.5-2.8) | 2.6 (1.2-5.6) | 1.4 (0.9-2.4) | 1.6 (1.0-2.5) | 1.9 (1.0-3.5) | 2.8 (1.6-5.0) | 0.9 (0.3-2.5) | 2.9 (1.7-4.9) | 2.3 (1.0-5.3) | 4.3 (1.8-10) |
|  | 4-5 yr | 0.9 (0.3-2.6) | 1.2 (0.6-2.5) | 2.1 (0.9-5.0) | 0.7 (0.2-2.8) | 1.3 (0.7-2.1) | 2.3 (1.6-3.4) | 1.9 (1.1-3.4) | 3.7 (2.2-6.1) | 2.0 (0.9-4.5) | 1.1 (0.5-2.6) | 2.2 (0.9-5.6) | 2.6 (0.9-7.4) |
| **CCI 1-2** |  |  |  |  |  |  |  |  |  |  |  |  |
|  | 0-1 yr | 1.7 (1.0-3.0) | 2.6 (1.8-3.9) | 2.4 (1.3-4.2) | 2.6 (1.4-4.9) | 1.1 (0.8-1.7) | 2.6 (2.0-3.4) | 2.5 (1.7-3.6) | 3.8 (2.5-5.7) | 1.2 (0.7-2.0) | 1.5 (1.0-2.3) | 1.8 (1.1-3.1) | 3.2 (2.0-5.4) |
|  | 1-2 yr | 1.1 (0.5-2.2) | 1.7 (1.1-2.9) | 1.8 (0.8-3.8) | 1.5 (0.6-3.9) | 1.6 (1.0-2.5) | 1.6 (1.1-2.3) | 1.9 (1.1-3.3) | 1.9 (1.1-3.2) | 1.0 (0.5-2.1) | 1.0 (0.5-1.8) | 1.1 (0.4-2.7) | 3.5 (1.8-7.2) |
|  | 2-3 yr | 0.9 (0.3-2.2) | 1.0 (0.5-1.9) | 1.3 (0.5-3.0) | 0.9 (0.3-2.9) | 0.7 (0.4-1.2) | 1.6 (1.1-2.4) | 1.1 (0.6-2.1) | 2.5 (1.5-4.3) | 1.8 (0.9-3.5) | 1.5 (0.9-2.8) | 0.7 (0.2-2.1) | 3.5 (1.3-9.0) |
|  | 3-4 yr | 1.4 (0.6-3.3) | 2.1 (1.2-3.6) | 2.3 (1.1-4.6) | 1.2 (0.3-4.0) | 1.1 (0.7-1.8) | 1.4 (0.9-2.3) | 1.5 (0.8-2.8) | 2.1 (1.2-3.8) | 1.1 (0.5-2.6) | 2.6 (1.5-4.8) | 3.0 (1.2-7.2) | 2.2 (0.9-5.8) |
|  | 4-5 yr | 1.5 (0.6-3.6) | 1.6 (0.8-3.2) | 2.0 (0.9-4.6) | 1.0 (0.2-4.3) | 0.8 (0.4-1.7) | 1.4 (0.8-2.3) | 1.9 (1.0-3.7) | 3.5 (1.7-7.1) | 1.2 (0.4-3.4) | 3.1 (1.7-5.8) | 3.1 (1.4-7.2) | 3.3 (1.1-9.9) |
| **CCI 3** |  |  |  |  |  |  |  |  |  |  |  |  |
|  | 0-1 yr | 1.5 (0.7-3.1) | 2.3 (1.3-4.1) | 2.6 (1.1-6.2) | 3.4 (1.5-7.6) | 1.9 (1.1-3.3) | 2.1 (1.3-3.2) | 1.4 (0.7-3.1) | 2.8 (1.4-5.9) | 2.2 (1.2-4.1) | 1.3 (0.8-2.4) | 0.8 (0.3-2.1) | 2.4 (1.1-5.4) |
|  | 1-2 yr | 2.8 (1.0-7.7) | 1.2 (0.6-2.5) | 1.2 (0.4-3.4) | 0.5 (0.1-2.2) | 1.1 (0.5-2.4) | 1.2 (0.6-2.2) | 1.3 (0.6-3.0) | 2.7 (1.1-6.6) | 2.5 (1.0-6.3) | 0.8 (0.3-1.9) | 1.0 (0.3-3.6) | 0.8 (0.2-3.7) |
|  | 2-3 yr | 0.4 (0.1-2.8) | 2.7 (1.1-6.0) | 4.5 (1.7-12) | 1.5 (0.3-7.9) | 1.6 (0.7-3.7) | 1.9 (0.9-3.9) | 2.3 (1.0-5.0) | 4.3 (1.7-11) | 1.7 (0.6-5.0) | 0.9 (0.3-3.0) | 1.4 (0.3-6.0) | 3.3 (0.8-15) |
|  | 3-4 yr | 0.7 (0.1-5.6) | 1.5 (0.6-4.0) | 0 | 6.8 (1.3-35) | 0.4 (0.1-1.7) | 0.8 (0.3-2.1) | 0.8 (0.2-3.8) | 0 | 2.2 (0.6-8.0) | 0.6 (0.1-2.5) | 0.6 (0.1-4.7) | 2.5 (0.5-13) |
|  | 4-5 yr | 0.6 (0.1-4.7) | 1.0 (0.2-4.4) | 1.2 (0.3-5.9) | 3.6 (0.2-78) | 0.4 (0.1-2.7) | 1.4 (0.5-3.4) | 0.8 (0.2-3.5) | 1.5 (0.5-4.8) | 2.0 (0.4-9.9) | 3.4 (1.2-9.4) | 3.4 (0.9-13) | 20 (1.8-213) |

MI: Myocardial infarction, VTE: Venous Thromboembolism, CI: Confidence Interval