**Supplemental Table 1.** Conditions excluded to rule out potential cases of secondary CAD (cold agglutinin syndrome)

|  |  |  |
| --- | --- | --- |
| **Disease** | **ICD-10** | **ICD-9** |
| Mycoplasma | A49.3 | 041.81 |
| Lymphoma |  |  |
| Follicular lymphoma | C82.X | 202.0x |
| Nonfollicular lymphoma | C83.X | 200.0x; 200.1x; 200.2x; 200.3x; 200.4x; 200.5x; 200.7x; 200.8x |
| Mature T-/NK-cell lymphoma | C84.X | 200.6x; 202.1x; 202.2x; 202.7x |
| Other and unspecified types of non-Hodgkin lymphoma | C85.X | 202.8x |
| Other types of T-/NK-cell lymphoma | C86.X | 202.8 |
| HIV infection resulting in Burkitt lymphoma | C83.7x (Burkitt lymphoma) with a code for HIV (B20; Z21; B97.35) | 200.2x (Burkitt lymphoma) with 042 or V08 or 079.53 (HIV) |
| HIV infection resulting in other types of non-Hodgkin lymphoma | C85.8x with a code for HIV (B20; Z21; B97.35) | 202.8x with 042 or V08 or 079.53 (HIV) |
| MALT lymphoma | C88.4 | 200.30 |
| Chronic lymphoid leukemia | C91.1 | 204.1x |
| Waldenström macroglobulinemia | C88.0 | 273.3 |
| Myeloma (any type of myeloma) | C90.X | 203.0x |
| Cytomegalovirus |  |  |
| Congenital cytomegalovirus | P35.1 | 771.1 |
| Cytomegaloviral mononucleosis |  | 078.5 |
| Cytomegaloviral disease | B25.X | 078.5 |
| Epstein-Barr virus infection |  |  |
| Infectious mononucleosis, unspecified | B27.9 | 075 |

CAD, cold agglutinin disease; HIV, human immunodeficiency virus; ICD-9, International Classification of Diseases, Ninth Revision; ICD-10, International Classification of Diseases, Tenth Revision; MALT, mucosa-associated lymphoid tissue; NK, natural killer.

**Supplemental Table 2.** Healthcare resource utilization of patients with presumed primary CAD and matched patients without CAD within 12 months after to the index date

|  |  |  |  |
| --- | --- | --- | --- |
|  | **CAD cohort**  **(n=272)** | **Non-CAD cohort**  **(n=2239)** | **P valuea** |
| **Hospital inpatient (N)** |  |  |  |
| Patients, n (%) | 98 (36.0) | 299 (13.4) | <0.0001b |
| Mean (SD) number of admissions | 0.76 (1.32) | 0.25 (0.88) | <0.0001c |
| 75th percentile (range) of admissions | 1 (0–8) | 0 (0–15) |  |
| Mean (SD) of mean length of stay, days | 2.27 (4.46) | 1.01 (5.59) | <0.0001d |
| 75th percentile (range) of mean length of stay, days | 4 (0–45) | 0 (0–205) |  |
| Mean (SD) total length of stay, days | 4.53 (9.95) | 1.66 (7.93) | <0.0001d |
| 75th percentile (95% CI) of total length of stay, days | 5 (3–7) | 0 (0–0) |  |
| Range of total length of stay, days | 0–66 | 0–205 |  |
| **Outpatient services** |  |  |  |
| Patients, n (%) | 257 (94.5) | 1654 (73.9) | <0.0001b |
| Mean (SD) number of visits | 16.44 (17.47) | 6.57 (10.29) | <0.0001c |
| 75th percentile (range) of visits | 23 (0–115) | 8 (0–121) |  |
| **Emergency room visits and services** |  |  |  |
| Patients, n (%) | 69 (25.4) | 369 (16.5) | 0.004b |
| Mean (SD) number of visits | 0.55 (1.25) | 0.30 (0.91) | <0.0001c |
| 75th percentile (range) of visits | 1 (0–10) | 0 (0–12) |  |
| **Transfusion use** |  |  |  |
| Patients, n (%) | 47 (17.3) | 49 (2.2) | <0.0001b |
| Mean (SD) number of transfusion days per patient | 0.61 (2.03) | 0.05 (0.46) | <0.0001c |
| Median (range) number of transfusion days per patient | 0 (0–20) | 0 (0–9) |  |

CAD, cold agglutinin disease; CI, confidence interval; SD, standard deviation.

aAdjusted for continuous Charlson Comorbidity Index score.

bConditional logistic regression.

cMixed Poisson model.

dLinear mixed model (log transformed).

**Supplemental Table 3.** Healthcare resource utilization of patients with presumed primary CAD and matched patients without CAD within 6 months prior to the index date

|  |  |  |  |
| --- | --- | --- | --- |
|  | **CAD cohort**  **(n=272)** | **Non-CAD cohort**  **(n=2239)** | **P valuea** |
| **Inpatient hospitalization** |  |  |  |
| Patients, n (%) | 59 (21.7) | 178 (7.9) | <0.0001b |
| Mean (SD) number of admissions | 0.33 (0.76) | 0.11 (0.41) | <0.0001c |
| 75th percentile (range) of admissions | 0 (0–4) | 0 (0–5) |  |
| Mean (SD) of mean length of stay in days | 1.64 (4.27) | 0.38 (1.68) | <0.0001d |
| 75th percentile (range) of mean length of stay, days | 0 (0–36) | 0 (0–30) |  |
| Mean (SD) total length of stay, days | 2.79 (9.59) | 0.48 (2.24) | <0.0001d |
| 75th percentile (95% CI) of total length of stay, days | 0 (0–1) | 0 (0–0) |  |
| Range of total length of stay, days | 0–109 | 0–39 |  |
| **Outpatient services** |  |  |  |
| Patient, n (%) | 233 (85.7) | 1298 (58.0) | <0.0001b |
| Mean (SD) number of visits | 6.37 (7.66) | 2.84 (4.88) | <0.0001c |
| 75th (range) percentile of admissions | 8 (0-44) | 4 (0-52) |  |
| **Emergency room visits and services** |  |  |  |
| Patients, n (%) | 45 (16.5) | 199 (8.9) | 0.002 b |
| Mean (SD) number of visits | 0.25 (0.76) | 0.13 (0.49) | 0.0002 c |
| 75th percentile (range) of admissions | 0 (0–8) | 0 (0–6) |  |
| **Transfusion use** |  |  |  |
| Patients, n (%) | 27 (9.9) | 16 (0.7) | <0.0001b |
| Mean (SD) number of transfusion days per patient | 0.25 (1.21) | 0.01 (0.13) | <0.0001c |
| Median (range) transfusion days per patient | 0 (0–16) | 0 (0–3) |  |

CAD, cold agglutinin disease; CI, confidence interval; SD, standard deviation.

aAdjusted for continuous Charlson Comorbidity Index score. bConditional logistic regression.   
cMixed Poisson model.   
dLinear mixed model (log transformed).