

Supplementary Material

1 Supplementary Tables

Supplementary Table 1. CaReDB characteristics.

| Characteristic | |
|--------------------------------|--|
| Geographic area | Campania, Italy |
| Population covered | ~5.8 million inhabitants |
| Age-span covered | Whole population |
| Time-span covered ^a | 2010–2019 |
| Scope | Drug utilisation and outcome research; real-world evidence for public health; pharmacoepidemiologic and pharmaco-economic analyses |
| Data sources | Specific fields in the data sources contributing to a database |
| Demographic information | Patient ID; sex; date of birth; municipality of residence; district; local health unit |
| Outpatient pharmacy records | Patient ID; drug code; prescription date; delivery date; quantity; ATC code; price; defined daily dose; drug distribution channel (file F, file D) |
| Hospital-discharge records | Patient ID; type of admission; date of admission; reasons for discharge; diagnoses (ICD-9 code); procedures (ICD-9 code); date of discharge; disease-related group |
| Type of codes for diagnoses | Hospital: ICD-9-CM |
| Type of codes for medications | ATC classification |

ATC=Anatomical Therapeutic Chemical; ICD-9-CM=International Classification of Diseases, 9th Revision, Clinical Modification.

^aTime-span covered was 2009–2018 for hospital-discharge records, and 2014–2019 for outpatient pharmacy records.

Supplementary Table 2. List of ATC codes used in the RxRiskV (mod).

| Disease | ATC code |
|------------------------------|--|
| Alcohol dependency | N07BB03, N07BB04, N07BB01 |
| Allergies | R01AC, R01AD, R06AD02, R06AD03, R06AD04, R06AD05, R06AD06, R06AD07, R06AD08, R06AD09, R06AD52, R06AD55, R06AE, R06AK, R06AX, excluding R06AX27 R06AX28 R06AX53 R06AX58 |
| Anti-coagulation therapy | B01AA03 B01AA04, B01AA07 – B01AA11, B01AB01, B01AB02, B01AB04–B01AB06, B01AB10, B01AE07, B01AF01, B01AF02 |
| Anti-platelet therapy | B01AC04 – B01AC19, B01AC30, B01AC22, B01AC23, B01AC24, B01AC27 |
| Anxiety | N05BA01 – N05BA12, N05BB01 |
| Arrhythmia | C01AA05, C01BA01–C01BD01, C07AA07 |
| Benign prostatic hypertrophy | G04CA01–G04CA04, G04CB01 |
| Bipolar disorder | N05AN01 |
| Chronic airways disease | R03AC, R03AK, R03AL01– |

| | |
|------------|---|
| | R03AL09, R03BA, R03AB, R03BC01, R03BC03, R03BX01, R03CA02, R03CB, R03CC, R03CC53, R03DA, R03DB, R03DC, R03DX05, R03BB |
| Dementia | N06DA02, N06DA03, N06DA04, N06DX |
| Depression | N06A |
| Epilepsy | N03AA01–N03AA04, N03AA30, N03AB01–N03AB05 N03AB52, N03AB54, N03AC01, N03AC02, N03AC03, N03AD01, N03AD02, N03AD03, N03AD51, N03AE01, N03AF01, N03AF02, N03AG01, N03AG02, N03AG03, N03AG04, N03AG05, N03AG06, N03AF03, N03AF04, N03AX |
| Glaucoma | S01EA01, S01EA02, S01EA03, S01EA04, S01EA05, S01EA51, S01EB01, S01EB02, S01EB03, S01EC03, S01EC04, S01EC54, S01ED01, S01ED02, S01ED03, S01ED04, S01ED05, S01ED06, S01ED51, S01ED52, S01ED54, S01EE01, S01EE02, S01EE03, |

Supplementary Material

| | |
|-----------------------|--|
| | S01EE04, S01EX01, S01EX02 |
| GORD and peptic ulcer | A02B |
| Heart disease | C07AA01, C07AA02, C07AA03, C07AA05, C07AA06, C07AA07, C07AA12, C07AA14, C07AA15, C07AA16, C07AA17, C07AA19, C07AA23, C07AA27, C07AA57, C07AB, C07AG01, C07AG02, C07BA02, C07BA05, C07BA06, C07BA07, C07BA12, C07BA68, C07BB02, C07BB03, C07BB04, C07BB06, C07BB07, C07BB52, C07BG01, C07CA02, C07CA03, C07CA17, C07CA23, C07CB02, C07CB03, C07CB53, C07CG01, C07DA06, C07DB01, C07FA05, C07FB02, C07FB03, C07FB07, C08CA01, C08CA02, C08CA03, C08CA04, C08CA05, C08CA06, C08CA07, C08CA08, C08CA09, C08CA10, C08CA11, C08CA12, C08CA13, C08CA14, C08CA15, C08CA55, C08CX01, C08DA01, C08DA02, C08DA51, C08DB01 |
| Hepatitis-C virus | J05AB54 |

| | |
|------------------------------|---|
| Human immunodeficiency virus | J05AE01–J05AE08, J05AF01– J05AF11, J05AG01, J05AG02, J05AG03 J05AR01–J05AR06, J05AX07 |
| Hyperkaliemia | V03AE01 |
| Hyperlipidemia | C10AA, C10AB, C10AC, C10AD, C10AX, C10BA, C10BX |
| Hypertension | C03AA, C03AB, C03AH, C03AX01, C02CA04, C03BA02, C03BA03, C03BA04, C03BA05, C03BA07, C03BA08, C03BA09, C03BA10, C03BA11, C03DB01, C03DB02, C03EA, C09BA02, C09BA03, C09BA04, C09BA05, C09BA06, C09BA07, C09BA08, C09BA09, C09BB, C09DB, C09DA01, C09DA02, C09DA03, C09DA04, C09DA06, C09DA07, C09DA08, C02AB01, C02AB02, C02AC01, C02AC02, C02AC04, C02AC05, C02DB02, C02DB03, C02DB04, C02DC01, C02DD01, C02DG01, C02KA01, C02KB01, C02KC01, C02KD01, C02KX01, C09XA |

Supplementary Material

| | |
|--------------------------------|---|
| Hyperuricemia/gout | M04AA01, M04AA02, M04AA03, M04AA51, M04AB01, M04AB02, M04AB03, M04AB04, M04AB05, M04AC01 |
| Hypothyroidism | H03AA01, H03AA02 |
| Inflammatory arthritis | M04AA01, M04AA02, M04AA03, M04AA51, M04AB01, M04AB02, M04AB03, M04AB04, M04AB05, M04AC01 |
| Inflammatory bowel disease | A07EC01, A07EC02, A07EC03, A07EC04 |
| Inflammatory/pain | M01AB, M01AC01, M01AC02, M01AC04, M01AC05, M01AC06, M01AE, M01AG, M01AH, N02BE51, N02BA01, N02BG06 |
| Ischaemic heart disease/angina | C01DA02, C01DA04, C01DA05, C01DA07, C01DA08, C01DA09, C01DA13, C01DA14, C01DX14, C01DX16, C01EB15, C01EB17, C01EB18 |
| Malignancies | L01AA01, L01AA02, L01AA03, L01AA05, L01AA06, L01AA07, L01AA08, L01AB, L01AC, L01AD, L01AG01, L01AX |

| | |
|----------------|--|
| | <p>L01BA01, L01BA03, L01BA04, L01BB02, L01BB03, L01BB04, L01BB05, L01BB06, L01BB07, L01BC, L01CA, L01CB, L01CC01, L01CD L01CX01 L01DA01 L01DB, L01DC, L01XA, L01XB01, L01XC, L01XD01, L01XD03, L01XD04 L01XD05 L01XD06 L01XE, L01XX, L02BA01, L02BA02, L02BG02, L02BG03, L02BG04, L02BG06, L02BB01, L02BB03, L02AE02, L02AE04, L02AB01</p> |
| Migraine | <p>N02CA01, N02CA02, N02CA04, N02CA07, N02CA51 N02CA52, N02CA72 N02CB01, N02CC01, N02CC02, N02CC03, N02CC04, N02CC05, N02CC06, N02CC07, N02CX01</p> |
| Osteoporosis | <p>M05BA, M05BB, M05BX03, G03XC01, A12AX92, H05AA02</p> |
| Pain (opiates) | <p>N02AA, N02AB, N02AC01, N02AC03, N02AC04, N02AC05, N02AC52, N02AC54, N02AC74, N02AD01, N02AD02, N02AE01,</p> |

Supplementary Material

| | |
|---|--|
| | N02AF01, N02AF02, N02AG, N02AJ06, N02AJ08, N02AJ17, N02AX01, N02AX02, N02AX52, N02AX05 |
| Pancreatic insufficiency | A09AA02 |
| Parkinson's disease | N04AA01, N04AA02, N04AA03, N04AA04, N04AA05, N04AA08, N04AA09, N04AA10, N04AA11, N04AA12, N04AB01, N04AB02, N04AC01, N04AC30, N04BA01, N04BA02, N04BA03, N04BA04, N04BA05, N04BA06, N04BB01, N04BC01, N04BC02, N04BC03, N04BC04, N04BC05, N04BC06, N04BC07, N04BD01, N04BX01, N04BX02, N0BC09, N04BD02 |
| Psoriasis | D05BB01, D05BB02, D05AX |
| Psychotic illness | N05AA, N05AB, N05AC, N05AD, N05AE, N05AF, N05AG N05AH, N05AL, N05AN01, N05AX |
| Smoking cessation | N06AX12, N07BA01, N07BA03 |
| Corticosteroid-responsive disease – systemic corticosteroid use | H02AB, H02AA |
| Transplant | L04AA01, L04AA02, L04AA03, L04AA04, L04AA05, L04AA06, |

| | |
|--------------|---|
| | L04AA08, L04AA09, L04AA10, L04AA11, L04AA12, L04AA14, L04AA15, L04AA16, L04AA17, L04AA18, L04AA19, L04AA21, L04AD01, L04AD02, L04AX01 |
| Tuberculosis | J04AB04, J04AB05, J04AB30, J04AC01, J04AC51, J04AD01, J04AD02, J04AD03, J04AK01, J04AK02, J04AM02, J04AM05 |

Supplementary Table 3. ICD–9 codes for micro/macrovascular complications.

| Complication | Clinical condition | ICD-9-CM diagnosis | Procedure code | |
|----------------------|--|---|--|--|
| Macrovascular | Cardiovascular disease | <ul style="list-style-type: none"> Ischemic heart disease | 410.xx (excluding 410.x1) 411.xx, 413.xx, 414.xx | 36.0x, 36.1x, 36.2, 36.3, 36.9, 88.5x, 37.8x |
| | | <ul style="list-style-type: none"> Acute myocardial infarction | 410.x1, 427.5 412* | |
| | | <ul style="list-style-type: none"> Arrhythmia | 426.xx, 427.0, 427.1, 427.2, 427.3, 427.4, 427.6x, 427.8x, 427.9 | |
| | | <ul style="list-style-type: none"> Congestive heart failure | 428.x, 785.5x, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93 | |
| | | <ul style="list-style-type: none"> Atherosclerosis | 429.2, 440.xx | 38.12 |
| | | Peripheral vascular disease | <ul style="list-style-type: none"> Peripheral vascular disease | 250.7x, 441.xx, 442.xx, 443.xx, 444.xx, 447.1 |
| | <ul style="list-style-type: none"> Lower-limb complications | 040.0, 681.1x, 682.6, 682.7, 707.1x, 711.9, 713.5, 730.0, 730.0x 730.1x 730.2x 730.3x 785.4 | 84.10-84.19, 86.22 | |

| | | | |
|----------------------|-------------------------|--|--|
| | Cerebrovascular disease | 430.xx-438.xx | 38.11, 38.12 |
| Microvascular | Nephropathy | 250.4x, 403.xx, 404.xx, 581.81, 584.x, 585, 586, 593.9 | 38.95, 39.27, 39.42, 39.95, 54.93, 54.98 |
| | Neuropathy | 250.6x, 337.1, 354, 355, 357.2, 377.xx, 536.3, 596.54, 607.84, 713.5 | |
| | Retinopathy | 250.5x, 361.0x, 361.9, 362.0x, 362.1x, 362.83, 364.42, 365.44, 365.6x, 366.1x, 366.41, 369.xx, 377.xx, 379.2x, 369.0x- 369.9x, V431 | 13.xx, 14.33, 14.34, 14.35, 14.53, 14.54, 14.55, 14.73, 14.74 |

ICD-9-CM=International Classification of Disease, 9th edition, clinical modification.