

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 pharmacoeconomic 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,

	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

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

	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
Migraine	N02CA01, N02CA02, N02CA04, N02CA07, N02CA51 N02CA52, N02CA72 N02CB01, N02CC01, N02CC02, N02CC03, N02CC04, N02CC05, N02CC06, N02CC07, N02CX01
Osteoporosis	M05BA, M05BB, M05BX03, G03XC01, A12AX92, H05AA02
Pain (opiates)	N02AA, N02AB, N02AC01, N02AC03, N02AC04, N02AC05, N02AC52, N02AC54, N02AC74, N02AD01, N02AD02, N02AE01,

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	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, N04BC09, 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	• 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
		410.x1, 427.5 412*	
		• Acute myocardial infarction 426.xx, 427.0, 427.1, 427.2, 427.3, 427.4, 427.6x, 427.8x, 427.9	
		• Arrhythmia 428.x, 785.5x, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93	
		• Congestive heart failure	
		429.2, 440.xx	38.12
		• Atherosclerosis	
	Peripheral vascular disease	• Peripheral vascular disease 250.7x, 441.xx, 442.xx, 443.xx, 444.xx, 447.1	38.13, 38.14, 38.16, 38.18, 39.25, 39.29, 39.50, 39.90, 99.10
		• 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.