

SUPPLEMENTARY METHODS

S1. Detailed description of ER Regional Healthcare System databases used for the record-linkage process

1. **Drug prescription database (Assistenza Farmaceutica Territoriale (AFT).** It includes all drug prescriptions reimbursed by the National Health System, and provides information about purchase date, number of dosing units and type of drugs. Drugs are reported according to the Anatomical Therapeutic Chemical (ATC) classification.
2. **Regional inpatients register (Schede di Dimissione Ospedaliera, SDO).** It includes data on all patients discharged from private and public hospitals of ER Region. Diagnoses are coded according to the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM).
3. **Modena Local Health Unit registry.** It is part of the regional health registry and provides data of all Modena province residents. Moreover, it reports co-payment exemptions for morbidities, low-income and disability.
4. **Laboratory Information System (LIS).** This database encompasses the results of all laboratory tests performed in the Modena Province, including INR.
5. **PARMA® dataset.** The PARMA® management software (Werfen, Italy) has been developed to help physicians in patient management and drug dosing. Both AC and GP participating to the network management model utilize this software, sharing data about patients' clinical and demographic characteristics. Moreover, the PARMA® software directly receives the INR results from the LIS.
6. **Diabetes register of Modena province.**
7. **Mortality register of the Modena province.**

S2. Thromboembolism ICD9 codes

Ischemic Stroke/TIA: 433/434.x: Occlusion and stenosis of precerebral/cerebral arteries with cerebral infarction 435: Transient cerebral ischemia 436: Acute, but ill-defined, cerebrovascular disease
Systemic embolism (arterial thromboembolism): 444 Arterial embolism and thrombosis
Pulmonary embolism: 415.19 Other pulmonary embolism and infarction (non-iatrogenic)
Venous thromboembolism (excluding superficial vessels): 451.x: Phlebitis and thrombophlebitis of deep veins of lower extremities/ Phlebitis and thrombophlebitis of lower extremities, unspecified / Phlebitis and thrombophlebitis of unspecified site / Phlebitis and thrombophlebitis of iliac vein / Phlebitis and thrombophlebitis of deep veins of upper extremities / Phlebitis and thrombophlebitis of other sites 452: Portal vein thrombosis 453.x: Other venous embolism and thrombosis (excluded .1 Thrombophlebitis migrans)

S3 Major bleeding ICD9 codes

Intracranial bleeding:
430: Subarachnoid hemorrhage
431: Intracerebral hemorrhage
432.0: Nontraumatic extradural hemorrhage
432.1: Subdural hemorrhage
432.9: intracranial hemorrhage nos
852.0: Subarachnoid, subdural, and extradural hemorrhage, following injury without mention of open intracranial wound
853.0: Other and unspecified intracranial hemorrhage following injury without mention of open intracranial wound

Gastrointestinal bleeding:
456.0: Esophageal varices with bleeding
456.20: Esophageal varices in diseases classified elsewhere, with bleeding
530.7: Gastroesophageal laceration-hemorrhage syndrome (Mallory-Weiss)
285.1: Acute post-haemorrhagic anaemia
360.43: Hemophthalmia, except current injury
530.82: Esophageal hemorrhage
531.0x: Acute gastric ulcer with hemorrhage
531.2x: Acute gastric ulcer with hemorrhage and perforation
531.4x: Chronic or unspecified gastric ulcer with hemorrhage
531.6x: Chronic or unspecified gastric ulcer with hemorrhage and perforation
532.0x: Acute duodenal ulcer with hemorrhage
532.2x: Acute duodenal ulcer with hemorrhage and perforation
532.4x: Chronic or unspecified duodenal ulcer with hemorrhage
532.6x: Chronic or unspecified duodenal ulcer with hemorrhage and perforation
533.0x: Acute peptic ulcer, site unspecified, hemorrhage
533.2x: Acute peptic ulcer of unspecified site with hemorrhage and perforation
533.4x: Chronic or unspecified peptic ulcer of unspecified site with hemorrhage
533.6x: Chronic or unspecified peptic ulcer of unspecified site with hemorrhage and perforation
534.0X: Acute gastrojejunal ulcer with hemorrhage
534.2X: Acute gastrojejunal ulcer with hemorrhage and perforation
534.4X: Chronic or unspecified gastrojejunal ulcer with hemorrhage
534.6X: Chronic or unspecified gastrojejunal ulcer with hemorrhage and perforation
535.x1: Gastritis and/or duodenitis, with hemorrhage
537.83: Angiodysplasia of stomach and duodenum with hemorrhage
562.x2/.x3: Diverticulosis/Diverticulitis of small intestine/colon with hemorrhage
568.81: Hemoperitoneum
569.3: Hemorrhage of rectum and anus
578.0: Hematemesis
578.1: Blood in stool (Melena)
578.9: Hemorrhage of gastrointestinal tract, unspecified

Others:
285.1: Acute post-hemorrhagic anemia
360.43: Hemophthalmia, except current injury
362.81: Retinal hemorrhage
372.72: Conjunctival hemorrhage
379.23: Vitreous hemorrhage
459.0: Hemorrhage, unspecified
599.7: Hematuria
719.1x: Hemarthrosis
784.7: Epistaxis
786.3: Hemoptysis

SUPPLEMENTARY TABLES

Table S1. International Classification of Diseases (9th revision for hospital discharge diagnosis and surgery, 10th revision for death causes), Anatomical Therapeutic Chemical (ATC) Codes and Co-payment exemption codes used to identify comorbidity, outcomes, medications and co-medications.

	International Classification of Diseases codes	Anatomical Therapeutic Chemical (ATC) codes	Co-payment exemption codes
History of:			
Deep vein thrombosis	4511, 4512, 4519, 4532, 4534, 45181, 45183, 45189		
Mitral stenosis	3940, 3942, 3960, 3961		
Pulmonary embolism	41519		
Heart valve surgery (excluding bio-prosthesis)	35 (excluding 21,23,25,27)		
Congestive heart failure/Left ventricular dysfunction	428	C03C	021
Cancer	140-208		048
Hypertension	401-405	see classes of antihypertensive drugs ^	031 A31
Diabetes mellitus #			
Myocardial infarction	410, 4110, 412, 42979		
Ischemic stroke/TIA	433-436		B02
Systemic embolism (arterial thromboembolism)	444		
Peripheral artery disease	4402,4403, 44381,44389, 4439		
Aortic plaque	4400		
Bleedings	Same codes as for outcomes but looking in the first four hospital discharge diagnoses		
Renal diseases	582,583,585,586		023
Liver diseases	570-573		008; 016
Outcomes			
Major bleeding: - Intracranial bleedings, - Gastrointestinal bleedings - Other bleedings	see list of major bleeding ICD9 codes		
Thromboembolic events: - Ischemic Stroke/TIA, - Arterial thromboembolism, - Pulmonary embolism, - Venous thromboembolism	see list of Ischemic Stroke/TIA, thromboembolism ICD9 codes		
Causes of death: - All natural causes - cerebrovascular diseases	ICD10 codes: A00-R999 I60-I69		
Medications			
TAO: Warfarin Acenocoumarol		B01AA03 B01AA07	
Coprescriptions in follow-up period*:			
Antiplatelet agents			
Aspirin		B01AC06	
Clopidogrel		B01AC04	
Ticlopidine		B01AC05	
Dipyridamole		B01AC07	
Prasugrel		B01AC22	
Ticagrelor		B01AC24	

Nonsteroidal anti-inflammatory drugs		M01A	
Heparins		B01AB01, B01AB05, B01AB07, B01AX05	B01AB04, B01AB06, B01AB08,
Statins		C10	
Protonic pump inhibitors (PPIs)		A02BC	

Each condition was deemed to be present if there were related ICD9CM or ATC or exemptions co-payment codes.

In order to find copatologies we looked for: ICD9CM codes in the main and subsequent 3 diagnosis of all hospitalizations occurred from 2008 until the study entry; ATC codes in prescriptions from 2010 until the study entry; co-payment exemption activated before the study entry.

Present in diabetes register in the same year of follow-up start or before. The Diabetes Register covers diabetics who are/were in charge by the Modena province Health Service by the 2010 year. A definite algorithm applied on seven routinely collected data sources (Hospital Discharge, Drug Dispensation, Biochemistry Laboratory, Disease-specific co-payment exemption, Centres for Diabetic Care, General Practitioners participating at the Diabetes Program and Mortality databases) identifies diabetics.

In order to find outcomes we looked only in the main diagnosis codes of all hospitalizations occurred during the follow-up periods.

*at least 2 prescriptions during follow-up period.

^ Classes of antihypertensive drugs:

I Alpha-adrenergic blockers: C02A, C02B, C02C, C02LE

II Non-loop diuretics: C02L, C03A, C03B, C03D, C03E, C07C, C07D, C08G, C09BA, C09DA, C09XA52, C09XA54

III Vasodilators: C02D

IV Beta-blockers: C07

V Calcium channel blockers: C07FB, C08, C09BB, C09DB

VI Renin-angiotensin system inhibitors: C09

Table S2. Balance in baseline characteristics between NAS and RGC cohorts, before and after CBPS-weighting

	All patients non-weighted standardized difference	CBPS-weighted standardized difference	Only naïve patients non-weighted standardized difference	CBPS-weighted standardized difference	Only experienced patients non-weighted standardized difference	CBPS-weighted standardized difference
Demographic characteristics						
Age at entry	0.1001 *	0.0000	0.0852	0.0000	0.0979	0.0000
Gender	0.0184	0.0000	0.0018	0.0000	0.0262	0.0000
Previous VKA use						
Naïve or Experienced	0.1167 *	0.0000				
Co-payment exemption						
for low income	0.0422	0.0000	0.0310	0.0000	0.0239	0.0000
for disability	0.0307	0.0000	0.0611	0.0000	0.0096	0.0000
Comorbidity						
Diabetes mellitus	0.0326	0.0000	0.0280	0.0000	0.0321	0.0000
Hypertension	0.0051	0.0000	0.0029	0.0000	0.0002	0.0000
Renal diseases	0.0624	0.0000	0.1130 *	0.0000	0.0332	0.0000
Liver diseases	0.0157	0.0000	0.0388	0.0000	0.0018	0.0000
Cancer	0.0691	0.0000	0.0733	0.0000	0.0625	0.0000
Myocardial infarction	0.0140	0.0000	0.0247	0.0000	0.0317	0.0000
Congestive heart failure	0.0652	0.0000	0.0517	0.0000	0.0456	0.0000
Mitral stenosis	0.0379	0.0000	0.0226	0.0000	0.0471	0.0000
Pulmonary embolism	0.0182	0.0000	0.0458	0.0000	0.0006	0.0000
Stroke/TIA	0.0127	0.0000	0.0101	0.0000	0.0296	0.0000
Aortic plaque / Arterial thromboembolism	0.0284	0.0000	0.0696	0.0000	0.0053	0.0000
Peripheral artery disease	0.0289	0.0000	0.0413	0.0000	0.0226	0.0000
Deep vein thromboembolism	0.0328	0.0000	0.0461	0.0000	0.0266	0.0000
Bleedings	0.0211	0.0000	0.0291	0.0000	0.0155	0.0000

* = effect size > 0.1 ; ** = effect size > 0.2 ; *** = effect size > 0.5 ; **** = effect size > 0.8