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)

<u>S3 Major bleeding ICD9 codes</u>

Intractinul Decening: 430: Subarachnoid hemorrhage 431: Intracerebral hemorrhage 432: Intracerebral hemorrhage 432: Intracerebral hemorrhage 432: Intracerebral hemorrhage nos 852:0: Subarachnoid, subdural, and extradural hemorrhage, following injury without mention of open intracranial wound 635:30: Other and unspecified intracranial hemorrhage following injury without mention of open intracranial wound 635:30: Other and unspecified intracranial hemorrhage following injury without mention of open intracranial wound 635:30: Other and unspecified intracranial hemorrhage following injury without mention of open intracranial wound 635:30: Other and unspecified intracranial hemorrhage following injury without mention of open intracranial wound 635:30: Other and unspecified intracranial hemorrhage syndrome (Mallory-Weiss) 285:1: Acute post-haemorrhage earstion-hemorrhage syndrome (Mallory-Weiss) 285:1: Acute post-haemorrhage enteritor hemorrhage 53:10: Acute gastric ulcer with hemorrhage 53:10: Acute gastric ulcer with hemorrhage 53:10: Acute gastric ulcer with hemorrhage 53:10: Acute duodenal ulcer with hemorrhage and perforation 53:10: Acute duodenal ulcer with hemorrhage and perforation 53:22: Acute duodenal ulcer with hemorrhage and perforation 53:24: Chronic or unspecified duodenal ulcer with hemorrhage and perforation 53:34: Chronic or unspecified perit ulcer of unspecified site with hemorrhage 53:34: Chronic or unspecified perit ulcer of unspecified site with hemorrhage 53:34: Chronic or unspecified perit ulcer of unspecified site with hemorrhage 53:44: Chronic or unspecified perit ulcer of unspecified site with hemorrhage 53:44: Chronic or unspecified perit ulcer of unspecified site with hemorrhage 53:45: Acute gastrojugnal ulcer with hemorrhage 53:46: Chronic or unspecified perit ulcer of unspecified site with hemorrhage 53:83: Angedysplasi of Stanach and duodenum with hemorrhage 54:84: Chronic or unspecified gastrojeunal ulcer with hemorrhage 55:83: Acute gastrojeunal ulcer wi	
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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 #		<u> </u>		
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: - <i>Intracranial bleedings</i> , - 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:	ICD10 codes:			
- All natural causes	A00-R999			
- cerebrovascular diseases	160-169			
Medications				
TAO:				
Warfarin		B01AA03		
Acenocoumarol		B01AA07		
Coprescriptions in follow-up period*:				
Antiplatelet agents				
Aspirin		B01AC06		
Clopidogrel		B01AC04		
Ticlopidine		B01AC05		
Dipyridamole		B01AC07	1	
Prasugrel		B01AC22		
1 10005101		B01AC22 B01AC24		

Nonsteroidal anti- inflammatory drugs	M01A	
Heparins	B01AB01,B01AB04,B01AB05,B01AB06,B01AB07,B01AB08,B01AX05B01AX05	
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 followup 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

	All patients non-weighted standardized difference	CBPS-weighted standardized difference	Only naïve patient non-weighted standardized difference	s CBPS-weighted standardized difference	Only experience non-weighted standardized difference	d patients 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