Prevalence, prescriptions, outcomes and costs of type 2 diabetic patients with or without prior coronary artery disease or stroke. A longitudinal 5-year claims-data analysis of over 7 million inhabitants

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Supplementary Material

Supplementary Table 1 – Criteria to identify patients with diabetes mellitus during the accrual period (2015). At least one criterion had to be documented within the different administrative records.

Administrative database	Description
Hospitalizations	At least a hospitalization with one of the following main/secondary diagnoses (ICD-9-CM code): **250.00** - Diabetes mellitus without mention of complication, type II or unspecified type, not stated as uncontrolled **250.02** - Diabetes mellitus without mention of complication, type II or unspecified type, uncontrolled **250.10** - Diabetes with ketoacidosis, type II or unspecified type, not stated as uncontrolled **250.12** - Diabetes with ketoacidosis, type II or unspecified type, uncontrolled **250.20** - Diabetes with hyperosmolarity, type II or unspecified type, not stated as uncontrolled **250.22** - Diabetes with hyperosmolarity, type II or unspecified type, uncontrolled **250.30** - Diabetes with other coma, type II or unspecified type, not stated as uncontrolled **250.32** - Diabetes with other coma, type II or unspecified type, uncontrolled **250.40** - Diabetes with renal manifestations, type II or unspecified type, not stated as uncontrolled **250.42** - Diabetes with renal manifestations, type II or unspecified type, uncontrolled **250.50** - Diabetes with ophthalmic manifestations, type II or unspecified type, not stated as uncontrolled **250.52** - Diabetes with ophthalmic manifestations, type II or unspecified type, uncontrolled **250.60** - Diabetes with neurological manifestations, type II or unspecified type, not stated as uncontrolled **250.62** - Diabetes with neurological manifestations, type II or unspecified type, uncontrolled **250.70** - Diabetes with peripheral circulatory disorders, type II or unspecified type, not stated as uncontrolled **250.72** - Diabetes with peripheral circulatory disorders, type II or unspecified type, uncontrolled **250.80** - Diabetes with other specified manifestations, type II or unspecified type, not stated as uncontrolled **250.82** - Diabetes with other specified manifestations, type II or unspecified type, uncontrolled **250.90** - Diabetes with unspecified complication, type II or unspecified type, not stated as uncontrolled **250.92** - Diabetes with unspecified complication, type II or unspecified type, uncontrolled
Disease exemption	**013** - Diabetes Mellitus (only for patients aged ≥35 and older, receiving the exemption for the first time)
Pharmaceuticals	Prescription of at least a specific drug (ATC code): **A10B** – Blood glucose lowering drugs, excl. insulins

Supplementary Table 2. Criteria to identify patients with coronary artery disease (CAD, including revascularization procedures), stroke and percutaneous coronary intervention (PCI) during the 3-year observation (2013-2015). At least one code had to be documented within the different administrative records.

Coronary artery diseases
Angina pectoris was identified through <u>at least one hospitalization</u> with the following main/secondary diagnosis (ICD-9-CM code): • **413.x** - Angina pectoris
Myocardial infarction (MI), identified through <u>at least one hospitalization</u> with one of the following main/secondary diagnoses (ICD-9-CM code): • **410.x -** Acute myocardial infarction • **412** - Old myocardial infarction
Other acute and subacute forms of ischemic heart disease, identified through <u>at least one hospitalization</u> with the following main/secondary diagnosis (ICD-9-CM code): • **411.x -** Other acute and subacute forms of ischemic heart disease
Other forms of chronic ischemic heart disease, identified through <u>at least one</u> of the following criteria: • <u>Hospitalization</u> with the main/secondary diagnosis **414.x** - Other forms of chronic ischemic heart disease; • <u>Exemption</u> code **002.414 –** Diseases of the circulatory system
Revascularization procedures, identified through <u>at least one hospitalization</u> with one of the following main/secondary diagnoses (ICD-9-CM code): • **36.0 –** Removal of obstruction of the coronary artery and insertion of stent • **36.10 -** Aortocoronary bypass for heart revascularization, not otherwise specified • **36.11 -** (Aorto)coronary bypass of one coronary artery • **36.12 -** (Aorto)coronary bypass of two coronary arteries • **36.13 -** (Aorto)coronary bypass of three coronary arteries • **36.14 -** (Aorto)coronary bypass of four or more coronary arteries • **36.15 -** Single internal mammary-coronary artery bypass • **36.16 -** Double internal mammary-coronary artery bypass • **36.17-** Abdominal-coronary artery bypass • **36.2 -** Heart revascularization by arterial implant • **36.3x -** Other transmyocardial revascularization • **36.9x -** Other operations on vessels of heart • **00.66 -** Percutaneous transluminal coronary angioplasty [PTCA]

Stroke
At least one hospitalization with one of the following main/secondary diagnoses (ICD-9-CM code): • **433.x1 -** Occlusion and stenosis of artery with cerebral infarction • **434.x1 -** Cerebral thrombosis/embolism/artery occlusion with cerebral infarction • **436.x -** Acute, but ill-defined, cerebrovascular disease
Percutaneous coronary intervention (PCI)
At least one hospitalization with one of the following main/secondary diagnoses (ICD-9-CM code): • **36.0 –** Removal of obstruction of the coronary artery and insertion of stent • **36.3x -** Other transmyocardial revascularization • **36.9x -** Other operations on vessels of heart • **00.66 -** Percutaneous transluminal coronary angioplasty [PTCA]

Supplementary Table 3. Criteria to identify patients with comorbidities during the accrual period. At least one criterion had to be satisfied within the different administrative records.

Dyslipidaemia	
Administrative database	**Description**
Hospitalization	At least a hospitalization with one of the following main/secondary diagnoses (ICD-9-CM code): **272.x -** Disorders of lipoid metabolism
Disease exemption	**025 -** Type IIa and IIb heterozygous familial hypercholesterolemia – Polygenic hypercholesterolemia – Familial combined hypercholesterolemia – Type III hyperlipoproteinemia
Pharmaceutical	Prescription of at least 3 packs of specific drugs: **C10A -** Lipid modifying agents, plain **C10B -** Lipid modifying agents, combinations **and/or** at least a prescription with the exemption code 025
Severe liver diseases	
Administrative database	**Description**
Hospitalizations	At least a hospitalization with one of the following main/secondary diagnoses (ICD-9-CM code): **070.x -** Viral hepatitis **571.x -** Chronic liver disease and cirrhosis **572.x -** Liver abscess and sequelae of chronic liver disease **573.x -** Other disorders of liver **V42.7 -** Liver replaced by transplant
Exemption for disease	**016** – Chronic hepatitis (active) **008** – Liver cirrhosis, biliary cirrhosis
Pharmaceutical	At least a prescription of a specific drug: **J05AP** - Antivirals for treatment of HCV infections **and/or** at least a prescription with the exemption code **016 or 008**
Atrial fibrillation	
Administrative database	**Description**
Hospitalizations	**427.3 -** Atrial fibrillation and flutter

Heart failure	
Administrative database	**Description**
Hospitalizations	At least a hospitalization with one of the following main/secondary diagnoses (ICD-9-CM code): **402.01** – Malignant hypertensive heart disease with heart failure **402.11** – Benign hypertensive heart disease with heart failure **402.91** – Unspecified hypertensive heart disease with heart failure **404.01** – Hypertensive heart and chronic kidney disease, malignant, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified **404.03** – Hypertensive heart and chronic kidney disease, malignant, with heart failure and with chronic kidney disease stage V or end stage renal disease **404.11** – Hypertensive heart and chronic kidney disease, benign, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified **404.13** – Hypertensive heart and chronic kidney disease, benign, with heart failure and chronic kidney disease stage V or end stage renal disease **404.91** – Hypertensive heart and chronic kidney disease, unspecified, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified **404.93** - Hypertensive heart and chronic kidney disease, unspecified, with heart failure and chronic kidney disease stage V or end stage renal disease **428.x –** Heart failure
Disease exemption	**021.428** - Heart failure
Pharmaceutical	At least a prescription with the exemption code **021**
Depression	
Administrative database	**Description**
Hospitalizations	At least a hospitalization with one of the following main/secondary diagnoses (ICD-9-CM code): **296.2x** - Major depressive disorder single episode **296.3x -** Major depressive disorder recurrent episode **296.5x** - Bipolar disorder, most recent episode (or current) depressed **296.82** - Atypical depressive disorder **298.0x** - Depressive type psychosis **300.4** - Dysthymic disorder **301.12** - Chronic depressive personality disorder

Disease exemption	**044.296.2 -** Psychosis (major depressive disorder single episode) **044.296.3 -** Psychosis (major depressive disorder recurrent episode) **044.296.5 -** Psychosis (bipolar disorder, most recent episode (or current) depressed) **044.296.8 -** Psychosis (manic depressive psychosis, other unspecified) **044.298.0 –** Psychosis (depressive type psychosis)
Pharmaceutical	At least a prescription of a specific drug: **N06A**– Antidepressants

Arterial hypertension	
Administrative database	**Description**
Hospitalizations	At least a hospitalization with one of the following main/secondary diagnoses (ICD-9-CM code): **401.x -** Essential hypertension **402.x -** Hypertensive heart disease **403.x -** Hypertensive chronic kidney disease **404.x -** Hypertensive heart and chronic kidney disease **405.x -** Secondary hypertension
Disease exemption	**031** – Arterial hypertension **A31** - Arterial hypertension without organ damage
Pharmaceutical	Prescription of at least 4 packs of one or more specific drugs: **C02A** – Antiadrenergic agents, centrally acting **C02C -** Antiadrenergic agents, peripherally acting **C03** - Diuretics **C07** – Beta blocking agents **C08** – Calcium channel blockers **C09A** – ACE-inibhitors, plain **C09B** – ACE-inhibitors, combinations **C09C** - Angiotensin II receptor blockers (ARBs), plain **C09D** - Angiotensin II receptor blockers (ARBs), combinations **C09X** – Renin-inhibitors **and/or** Prescription with the exemption code **031 or A31**

Neoplasia	
Administrative database	**Description**
Hospitalizations	At least a hospitalization with one of the following main/secondary diagnoses (ICD-9-CM code): **140.x - 208.x –** Tumours **V10.x** - Personal history of malignant neoplasm **V58.1x** - Encounter for antineoplastic chemotherapy and immunotherapy **and/or**

	At least a hospitalization with one of the following procedures: **00.10** - Implantation of chemotherapeutic agent **00.15** - High-dose infusion interleukin-2 [IL-2] **99.25** - Injection or infusion of cancer chemotherapeutic substance **99.28** - Injection or infusion of biological response modifier [BRM] as an antineoplastic agent
Outpatient specialist services	**99.25** - Injection or infusion of cancer chemotherapeutic substance **99.24.1** – Infusion of hormonal substances
Disease exemption	**048** – Neoplastic malignant diseases and neoplasm of uncertain behaviour
Pharmaceutical	At least a prescription of a specific drug: **L01** – Antineoplastic agents **and/or** Prescription with the exemption code **048**

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Chronic kidney diseases

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Administrative database	Description
Hospitalizations	At least a hospitalization with one of the following main/secondary diagnoses (ICD-9-CM code): **582.x** - Chronic glomerulonephritis **583.x** - Nephritis and nephropathy not specified as acute or chronic **584.x** - Acute kidney failure **585.x** - Chronic kidney disease (CKD) **586** - Renal failure, unspecified **587** - Renal sclerosis, unspecified **588** - Disorders resulting from impaired renal function **V56.x** - Encounter for dialysis and dialysis catheter care **V42.0** - Kidney replaced by transplant **and/or** At least a hospitalization with the following DRG code: **317** - Renal failure with dialysis **and/or** At least a hospitalization with one of the following procedures: **39.95.x** - Hemodialysis **55.6x** - Renal transplantation **54.98.x** - Peritoneal dialysis
Outpatient specialist services	**39.95 –** Hemodialysis **54.98 -** Peritoneal dialysis
Disease exemption	**023** – Chronic renal failure **061** – Chronic renal diseases
Pharmaceutical	Prescription with the exemption code **023 or 061**

	Chronic lung diseases
Administrative database	**Description**
Hospitalizations	<u>At least a hospitalization</u> with one of the following main/secondary diagnoses (ICD-9-CM code): **490.x** - Bronchitis, not specified as acute or chronic **491.x** - Chronic bronchitis **492.x -** Emphysema **493.x** - Asthma **494.x** - Bronchiectasis **496.x** - Chronic airway obstruction, not elsewhere classified **518.81**- **518.84** - Respiratory failure
Disease exemption	**024** – Chronic respiratory failure **007** - Asthma
Pharmaceutical	Prescription of <u>at least 3 packs</u> of drugs for obstructive airway diseases: **R03** – Drugs for obstructive airway diseases **and/or** Prescription with the exemption code **024 or 007**

Supplementary Table 4. Criteria to identify patients with stroke/transient ischemic attack, acute coronary syndrome or peripheral artery disease during the two-year follow-up. At least one code had to be documented within the different administrative records.

Stroke/Transient Ischemic Attack
At least a hospitalization with one of the following main diagnoses (ICD-9-CM code):
433.x – Occlusion and stenosis of precerebral arteries
434.x - Occlusion of cerebral arteries
435.x - Transient cerebral ischemia
436.x - Acute, but ill-defined, cerebrovascular disease
437.x - Other and ill-defined cerebrovascular disease
Acute Coronary Syndrome
At least a hospitalization with one of the following main diagnoses (ICD-9-CM code):
410.x – Acute myocardial infarction
411.x - Other acute and subacute forms of ischemic heart disease
Peripheral Artery Disease
At least a hospitalization with one of the following main diagnoses (ICD-9-CM code):
250.7x - Diabetes with peripheral circulatory disorders
440.x – Atherosclerosis
441.x - Aortic aneurysm and dissection
442.x - Other aneurysm
443.x - Other peripheral vascular disease
444.x - Arterial embolism and thrombosis
447.1 - Stricture of artery
707.1x - Ulcer of lower limbs, except decubitus ulcer
785.4 – Gangrene
V49.6x - Upper limb amputation status
V49.7x - Lower limb amputation status
AND/OR

Hospitalization associated to one of the following DRG codes:

113 - Amputation due to circulatory diseases, except upper limb and toes amputations

114 – Upper limb and toes amputation due to circulatory diseases

AND/OR

Hospitalization with procedures on cardiovascular or musculoskeletal system, or on blood vessels

00.45 - Insertion of one vascular stent

00.55 - Insertion of drug-eluting non-coronary artery stent(s)

00.61 - Percutaneous angioplasty of extracranial vessel(s)

00.63 - Percutaneous insertion of carotid artery stent(s)

00.64 - Percutaneous insertion of other extracranial artery stent(s)

38.02 - Incision of vessels, other vessels of head and neck

38.12 - Endarterectomy, other vessels of head and neck

38.18 - Endarterectomy, lower limb arteries

38.32 - Resection of vessel with anastomosis, other vessels of head and neck

38.42 - Resection of vessel with replacement, other vessels of head and neck

38.62 - Other excision of vessels, other vessels of head and neck

38.82 - Other surgical occlusion of vessels, other vessels of head and neck

39.22 - Aorta-subclavian-carotid bypass

39.25 - Aorta-iliac-femoral bypass

39.29 - Other (peripheral) vascular shunt or bypass
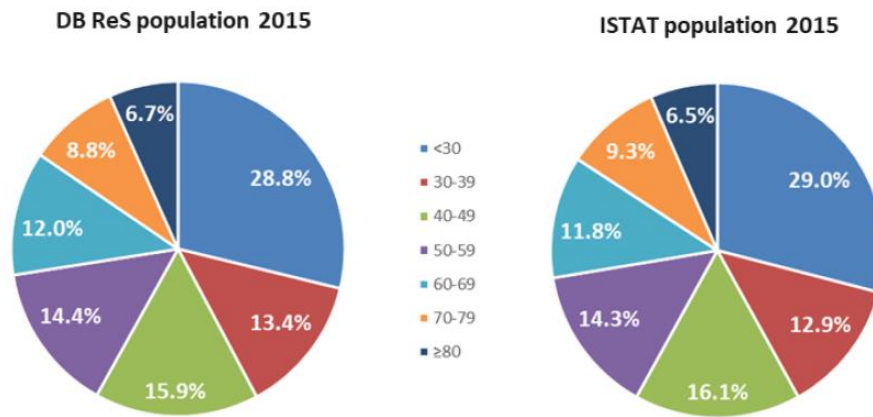
39.50 - Angioplasty of other non-coronary vessel

39.90 - Insertion of non-drug-eluting, non-coronary artery stent(s)

84.0x - Amputation of upper limb

84.1x - Amputation of lower limb

Supplementary Figure 1. The 2015 Italian population from the Ricerca e Salute (ReS) database (DB) and from the Italian Institute of Statistics (ISTAT) by age groups.

[1] http://demo.istat.it/