SUPPLEMENTARY MATERIAL

Contents

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Data Sources

The study consists of data from nationwide cohort studies including patients with heart failure (HF) from Belgium, Canada, Germany, Israel, Italy, Norway, Portugal, Spain, Sweden, Switzerland and United Kingdom to obtain a study population of appropriate coverage. Countries within the Europe and Canada region and associated data sources were selected based on quality, representativeness, and availability. Hence, within each country, all available sources were scrutinized and interrogated for the research purpose. The properties of registries vary country to country (e.g., access to primary- and hospital care [Belgium, Canada, Israel, Italy, Portugal, Spain and United Kingdom] versus hospital care only [Germany, Norway and Switzerland], full population data (Norway and Sweden), representative population data [all countries]. Each country is represented by a national scientific committee. Additionally, a single, pre-specified protocol was implemented within each country, ensuring that data collection procedures were consistent between nations despite inherent differences between the various healthcare registries. The initiative is sponsored by AstraZeneca. A description of the respective databases is provided below.

Belgium

The Belgian retrospective data analysis study "CORDIS-HF" was set-up in order to collect baseline descriptive data (demographics, medication use, medical history, lab values) and cardiovascular /renal outcomes from Belgian HF patients. The study used the electronic medical records obtained from HF patients in a representative cardiology centre in Belgium (Cardiovascular Centre OLV Hospital Aalst, Dr.Marc Vanderheyden).

LynxCare, a data processor according to the GDPR (acting solely on the instructions of the hospital), obtained the study data through their data mining and natural language processing solution 'CareMonitor' whereby structured, semi-structured and unstructured reports (e.g., free text in clinical notes) are automatically processed and pre-defined datapoints are extracted and coded. These pre-defined datapoints are detected by using computational linguistic techniques and comprehensive clinical ontologies, scientifically validated (like SNOMED CT). LynxCare is an accredited data partner of the European Health Data Network and stores the data compliant to the OMOP Common Database Model, enabling the participation in other international research. This process has proven a 90% accuracy on a patient level for the datapoints defined, contingent on the inclusion of the datapoint in the clinical file. The result of this study is a pseudonymized research database compliant with the European Health Data Network requirements to be used by the hospital for the duration of the project for answering study questions, improving clinical insights and outcomes for the patients and can be a source for future research projects (conditionally to subsequent EC approvals). For the hospital, the source data is visualised in a comprehensive dashboard and can be consulted on the database level. All extracted concepts can be easily verified using the traceback functionality that shows the initial source were the data is extracted from LynxCare.

Canada

We conducted a retrospective cohort analysis using administrative health databases housed at the Repository at the Manitoba Centre for Health Policy (MCHP) at the University of Manitoba. The Repository holds population-wide de-identified health information for Manitoba residents. All databases are de-identified but contain a scrambled personal health identification number (PHIN) that allows linking unique individuals across databases. Demographics and vital status information were obtained from the Manitoba Health Insurance Registry. Medication information was obtained from the Drug Program Information Network (DPIN) database. Diagnostic and procedural information from all hospitalizations was determined using the Hospital Discharge Abstracts (CIHI-DAD). Laboratory data was obtained from the Diagnostic Services of Manitoba database which captures laboratory measures from hospital and community laboratories in Manitoba.

This study was approved by the University of Manitoba Health Research Ethics Board (ethics file number HS223414 (H2019:454)). The results and conclusions are those of the authors and no official endorsement by Manitoba Health was intended or should be inferred. Data used in this study are from the Population Health Research Data Repository housed at the Manitoba Centre for Health Policy, University of Manitoba and were derived from data provided by Manitoba Health, Seniors, and Active Living, Vital Statistics, and Shared Health Diagnostic Services.

Germany

The "HELIOS-HF" study database includes HF patient information from administrative data covering approximately 86 Helios group hospitals. The Helios hospital group operates metropolitan and regional acute care hospitals ranging from basic to maximum care, outpatient clinics, and prevention centres across Germany (https://www.helios-gesundheit.de/). Patients have free choice of healthcare providers independent of insurance status. Helios hospitals provide inpatient care to about 1.2 million patients annually that corresponds to about 7% of all hospitalizations in Germany. The German Diagnosis Related Groups (G-DRG) system is used for hospital

reimbursement in Germany since 2004 and is subject to encoded diagnoses (International Statistical Classification of Diseases, German Modification; ICD-10 GM) and procedures (German procedure classification; OPS). This obligatory documentation and accounting system is specified and regulated in detail by mandatory coding instructions and requires the coding of a main diagnosis for all in-hospital cases reflecting the underlying cause for hospital admission. Up to 15% of the codes are controlled – and corrected if required – by specialized physicians ("Medizinischer Dienst der Krankenversicherung") independently from health insurances and hospitals. Administrative data provides information on basic characteristics (age, gender), the encoded main and secondary diagnoses at hospital discharge, type of hospital admission and type of hospital discharge. EMR data contains additional information (including used medication and laboratory results) for the sub-cohort of patients from the Heart Center Leipzig. The data are arranged on a case-by-case basis and can only be assigned to the specific patient within one unique hospital. There are no cross-links between hospitals regarding cases of individual patients.

Israel

Data from the Maccabi Healthcare Services (MHS) were used for this study. MHS is the second largest primary healthcare insurer and provider in Israel. This health maintenance organization (HMO) serves 25% of the total population in Israel, with approximately 2.2 million members. Since 1999, information on member–MHS interactions have been recorded in a large central computerized database. The database includes beyond demographic and administrative data, information on hospitalizations, emergency department, physician, outpatient specialist, and home healthcare visits. Additionally, purchases of medications and other aids, laboratory tests, imaging, and paramedical services such as nursing care, physiotherapy, social workers, and dietary consultations, patients' socioeconomic status and health care utilization are all captured. Comorbidities are gathered in MHS chronic disease registries (diabetes mellitus, hypertension, chronic kidney disease, chronic obstructive pulmonary disease, and specific cardiovascular disease registry). Specific diagnoses including cerebrovascular accident, transient ischemic attack, myocardial infarction, peripheral vascular disease and atrial fibrillation were also available. Israel is well-represented by this database, though Maccabi patients are slightly younger, less heterogeneous, and have a slightly better higher income compared to the country as a whole.[1]

Italy

The database held by ReS Foundation (Fondazione ReS Ricerca e Salute) captures different administrative data sources, including Hospital Discharge Records (inpatient data, including causes of hospitalisation and associated costs), drug prescription, outpatient visits, and exemption codes for chronic diseases. Such data are reimbursement claims for the National Health System, which provides every resident in Italy with a public health insurance. The database is covering over 7 million patients aged 18 or older retrieved from several Regions across the whole Country, corresponding to more than 10% of the total Italian population. Subjects in the ReS database have been shown to have similar characteristics compared to demographics of the National Institute of Statistics (ISTAT) regarding the general census population.

Norway

The study database includes patient information from three linked national Norwegian registries with full coverage of the Norwegian population: the Norwegian Prescription Database (July 2004 to April 2020) covering all filled drug prescriptions using ATC codes; the Norwegian Cause of Death Registry (1958 to April 2020[2]; and the Norwegian Patient Register covering all open patient clinic visit diagnoses and all hospital discharge diagnoses for the years 2008 to 2020. Diagnoses are recorded according to the ICD-system. Data linkage was performed by the Norwegian Institute of Public Health.

The study was approved by the Regional Ethics Committee, Helse Sør-Øst (reference numbers 2015/1337/REK sør-øst A and 11744) and was authorized by the Norwegian Data Inspectorate (Datatilsynet). The linked database was separately managed by Statisticon AB (Uppsala, Sweden).

Portugal

The Unidade de Saude Local de Matosinhos EPE (USLM-EPE) is an integrated public medical care centre comprising both primary, secondary and tertiary healthcare. It fully serves the population of Matosinhos region, a urban area, that amounts to approximately 175.000 patients. Data was collected and anonymised by the hospital IT department from multiple healthcare systems used to provide everyday care both in hospital and primary care. The study was approved by the Ethics Committee and the Data Protection Officer of USLM-EPE. This was a secondary data study and data were fully anonymized and dissociated from patients. Therefore, according to Portuguese regulation, there was no need for collecting informed consent from the patients.

Spain

Observational cohort study, comprising cross-sectional and longitudinal retrospective analyses using secondary data captured in electronic health records from seven Spanish regions. Data sources were provided by BIG-PAC®. BIG-PAC is an electronic database that integrates information from primary and specialist care medical records. This database has been validated as an information source for studies of epidemiology, therapeutic adaptation and health/non-healthcare resource use. It has been demonstrated its representativeness of the Spanish population. This study was approved by the Investigation Ethics Committee of Consorci Sanitari from Terrassa on 16th December 2019. This was a secondary data study and data were fully anonymized and dissociated from patients. Therefore, according to Spanish regulation, there was no need for providing informed consent.

Sweden

The study database includes patient information from three linked national Swedish registries with full coverage of the Swedish population: the Prescribed Drug Register (July 2005 to December 2018) covering all filled drug prescriptions using the Anatomical Therapeutic Chemical (ATC) codes; the Cause of Death Registry (1987 to 2018); and the National Patient Registry covering all open patient clinic visit diagnoses for 2001 to 2018 and all hospital discharge diagnoses for the years 1987–2018.[3] Diagnoses are recorded according to the ICD-system and has been shown to be of high validity.[4] All three registers are held by the Swedish National Board of Health and Welfare (NBHW), who also performed the data linkage by using unique personal identification numbers.[5]
The study was approved by the Stockholm Regional Ethics Committee (reference numbers 2020-05714 and 2013/2206-31), with data linkage performed by the Swedish National Board of Health and Welfare. The linked database was separately managed by Statisticon AB (Uppsala, Sweden).

Clinical and Laboratory data Sweden (CELOSIA HF dataset)

The study population in the CELOSIA HF dataset comprises all patients in Stockholm with a recorded diagnosis of heart failure in the Stockholm Regional Healthcare Data Warehouse (called VAL) between January 2013 to June 2018 (Stockholm with its 2.4 million citizens accounts for 24% of the Swedish population). VAL includes information on all contacts with healthcare financed by Region Stockholm and data from primary care, secondary care and hospitalizations are included. Diagnoses are recorded according to the ICD system. Data on prescription drugs are coded according to the ATC system. VAL also contains demographic information on patient age, sex, migration status and death. For the study population, we included data on diagnoses, clinical procedures, demographics, and drug utilization for the period of January 2003 to June 2018. From Electronic Health Records, we included data on clinical measurements and results from laboratory tests for the period of January 2003 to June 2018 (with limited data in the earlier years and increasing over time).

The study was approved by the Ethical Review Authority (reference number 2020-03850). The CELOSIA HF dataset was separately managed by Sence Research AB (Uppsala, Sweden).

Switzerland

All patients with heart failure who were admitted at Bern University Hospital (Inselspital), Switzerland- a large tertiary cardiology center- between January 2015 and January 2020, were eligible for the present study. The clinical data warehouse at the Inselspital contains administrative and medical data of all patients from the department of cardiology and the heart failure division. Among other data, demographic and clinical characteristics, information on hospitalizations, comorbidities, implantable cardiac devices, heart failure and diabetes medication, laboratory data, and survival status is obtained. Demographic and clinical characteristics included age, sex, body mass index, NYHA functional class and left ventricular ejection fraction. Comorbidities included were chronic kidney disease, type 2 diabetes mellitus; cardiac devices included implantable cardioverter defibrillator, pacemaker and cardiac resynchronization therapy. Laboratory data consisted of lipid profile, HbA1c, iron, estimated glomerular filtration, and N-terminal-pro hormone BNP. The presence of cardiac devices, mainly ICD and CRT, was extracted using Swiss surgical classification (CHOP) codes. Medication information was obtained using ATC codes. Survival status was assessed by linking with the national mortality record. Information about the diagnosis was obtained based on the International Statistical Classification of Diseases and Related Health Problems 10th version, ICD. Survival status was assessed by linking with the national mortality record.

The study was approved for quality assurance by the Ethics Committee of the Canton Bern approved the study (KEK-Nr. Req-2020-00980). Data sharing is partly restricted as the original dataset contains de-identifying sets of coded diagnoses on patient level. Further data requests can be sent to Dr. Dominique Furrer (hc.lesni@rerruf.euqinimod), the director of the institutional data access at the Insel Data Science Center, University Hospital of Bern, Berne, Switzerland.

United Kingdom

Data Source: The Clinical Practice Research Datalink (CPRD) is a real-world research service supporting retrospective and prospective public health and clinical studies.[6] CPRD database contains de-identified patient data sourced from a sample of general practitioner (GP) practices that use either the Vision or EMIS software systems contributing to the CPRD GOLD or CPRD Aurum primary care databases, respectively.[7] These de-identified databases containing primary care data have been individually linked to secondary care and other health- and area-based datasets. The April 2020 release of both CPRD GOLD and CPRD Aurum were analysed. To avoid duplicate patient records, the 'Vison to EMIS Migrators' file was used to remove practices from CPRD GOLD where these overlap with the Aurum records. CPRD GOLD included 19 million individuals (with acceptable quality medical records) from 1987 onwards, from whom data were actively being collected for 3.1 million patients (4.7% of the population of UK). In addition, the CPRD GOLD database collects data from the four countries of the UK, with 22% of contributing practices located in England at the time of this study, 8% in Northern Ireland, 45% in Scotland and 25% in Wales. CPRD Aurum included 32 million individuals with complete reliable data spanning from 1 January 1995, from whom data were being actively collected for 11.1 million patients (17% of the population of UK). The CPRD Aurum database is more recently established, and at the time of this study (April 2020 release) drew on data collected from general practices in England mainly (99%), using the EMIS practice system. The databases include diagnoses, issued drug prescriptions, clinical measures taken within the general practice, lab tests and referrals to specialist care, and have been linked to national secondary care databases (e.g., Hospital Episode Statistics, HES with detailed hospitalisation information on hospital admissions episodes in UK) as well as deprivation and death registration (Office for National Statistics, ONS) data. The ONS mortality data was used to identify the specific cause of death outcomes. Hospitalisation information and specialist care notes are generally recorded by the general practitioner into the primary care patient records. Patients in CPRD are broadly representative of the UK general population.[7,8]

Study population: The study population comprised patients with heart failure diagnosis registered in CPRD GOLD and CPRD Aurum practices in the UK, including patients in research active practices and in those eligible for linkage to HES data. HF patients aged 18 years or older who had contributed data between 1 Jan 2007 and 30 April 2020 were included in this ecological study. Patients met the eligibility criteria for broad definition of prevalence estimates if they had a HF diagnosis (Read/SNOMED-CT) codes documented on or before the 1 January 2020 and were alive and registered in a CPRD practice on that date. Denominator data consisted of the count of all acceptable patients who were alive and registered at a CPRD contributing practice on 1 January 2020. Patients met the eligibility criteria for the strict definition of prevalence if they had an ICD-10 code for HF diagnosis documented on or before the 1 January 2019 and were alive and registered in a CPRD practice contributing linkage data to HES on that date. Denominator data consisted of the count of all acceptable patients who were alive and registered at a CPRD contributing practice with eligible linkage to HES on 1 January 2019. The latest available linked dataset for HES linkage at the time of this study (Set 18) was used for the analysis. A sub-cohort of patients with ICD-10 code in primary position for HF diagnosis in the HES-linked dataset and actively registered in the practices on 1 January 2018 was used to describe the 1-year year event rates. HES data were from practices in England only.

Ethics: This overall study protocol was approved by the Independent Scientific Advisory Committee (ISAC) of CPRD; protocol reference number: 19_264AR3. This study is based in part on data from the Clinical Practice Research Datalink (CPRD) obtained under license from the UK Medicines and Healthcare Products Regulatory Agency. The data is provided by patients and collected by the National Health Service as part of patient care and support. This CPRD study also used data from the Office for National Statistics and Hospital Episode Statistics. The interpretation and conclusions contained in this study are those of the authors alone.

Table S1: Comorbidity definitions

Disease	ICD-8	ICD-9	ICD 10	Surgical code/medication
CVRD (includes all codes below)				
Myocardial infarction	410.9, 410.99	410	I21-I22, I25.2, I25.6	
CABG		414.02-07, V45.81-82		Surgical by-pass codes
PCI with stent				Peripheral intervention codes
Unstable angina		411	I20.0	
Angina pectoris	4193, 4139	413, 414.0	I20.1, I20.8, I20.9, I25.1, I25.5	Nitrates: C01DA
Heart failure (total)	425.99, 427.09–427.19, 427.99, 428.99	428	I50, I11.0, I13.0, I13.2	
Heart failure			I50	
Heart failure - hypertensive			I11.0, I13.0, I13.2	
CKD (total)	581.00–582.09, 583	585, 583.81, 250D	N17-N19, I12.0-I12.9, I13.1, I13.2, N08.3, E10.2, E11.2, E12.2, E13.2, E14.2, Z49, Z99.2	Dialysis and kidney transplantation codes
CKD - Acute			N17	
CKD - Chronic			N18	
CKD - Unspecified			N19	
CKD - Diabetic			E10.2, E11.2, E12.2, E13.2, E14.2, N08.3	
CKD - Hypertensive			I12.0-I12.9, I13.1, I13.2	
CKD - Dialysis			Z49, Z99.2	Daily codes
Atrial fibrillation	427.93, 427.94	427.3	I48	
Stroke		430-438, V125	I60-I66, G45	
Hemorrhagic	43000-43099, 43100, 43108–43190, 43198-43199	430-432	I60-I62	
Ischemic	43200–43299, 43309–43399, 43409-43499	433-434, 436	I63	
Transitory ischemic attack	43509-43599	V12.5, 435	G45	
Peripheral artery disease	440.20–440.30	440/441/444	I70.2, I73.9, I74.2-9	Revascularization codes, upper/lower extremities
Dialysis			Z49, Z99.2	
Cancer	140.0–204.4	140-239	C00-C99	

CVRD, cardiovascular renal disease. CABG, coronary artery bypass graft. PCI, percutaneous coronary intervention. CKD, chronic kidney disease.

Table S2: Index dates for the cohorts

	Cohort 1: Most contemporary baseline date	**Cohort 2:** 1-year event rate baseline date	**Cohort 3:** 5-year cost analysis baseline date
Belgium	2018-01-01	2018-01-01	n/a
Canada	2019-01-01	2018-01-01	2014-01-01
Germany	First HHF during 2019	n/a	n/a
Israel	2020-01-01	2019-01-01	n/a
Italy	2018-01-01	2018-01-01	2018-01-01
Norway	2020-01-01	2019-01-01	n/a
Portugal	2019-01-01	2018-01-01	2017-01-01
Spain	2019-01-01	2019-01-01	2015-01-01
Sweden	2019-01-01	2018-01-01	2014-01-01
Switzerland	First HHF during 2015-2019	n/a	n/a
UK	2020-01-01	2018-01-01	2014-01-01

Table S3: Outcomes

Variable	Definition	Comment
All-cause death	Death of any cause	
Cardiovascular death	Death with any "I" diagnosis as underlying cause of death	Only in countries with cause of death registry
Myocardial infarction	I21, I22	
Stroke	I60-I63	
Heart failure	I50, I11.0, I13.0, I13.2	
CKD	N17-N19, I12.0-I2.9, I13.1, I13.2, N08.3, E10.2, E11.2, E12.2, E13.2, E14.2, Z49, Z99.2 + procedure codes	
PAD	I70.2, I73.9, I74.2-9	

CKD, chronic kidney disease. PAD, peripheral artery disease.

Table S4: Coverage of EF% and eGFR in data sources

Proportion of patients with registered ejection fraction (EF) or estimated glomerular filtration rate (eGFR) with available electronic medical records (EMR) containing laboratory data

	Population with available EMR	EF registration	%
Portugal	3681	2032	55 %
Israel	9759	4980	51 %
Spain	21851	19708	90 %
Sweden	28116	4294	15 %
Switzerland	14204	8374	59 %
Belgium	2379	2379	100 %
UK	165244	6073	4 %
Total	**245234**	**47840**	**20 %**

	Population with available EMR	eGFR registration	%
Portugal	3681	2537	69 %
Canada	29953	2338	8 %
UK	165244	116841	71 %
Israel	9759	9168	94 %
Belgium	2379	2222	93 %
Sweden	28116	15369	55 %
Total	**239132**	**148475**	**62 %**

Proportion of patients with registered ejection fraction (EF) or estimated glomerular filtration rate (eGFR) with *and without* available electronic medical records (EMR) containing laboratory data

	Total HF population	EF	%
Portugal	3681	2032	55 %
Israel	9759	4980	51 %
Spain	21851	19708	90 %
Sweden	180727	4294	2 %
Switzerland	14204	8374	59 %
Belgium	2379	2379	100 %
UK	165244	6073	4 %
Norway	76561	0	0 %
Italy	67396	0	0 %
Total	**541802**	**47840**	**9 %**

	Total HF population	eGFR	%
Portugal	3681	2537	69 %
Canada	29953	2338	8 %
UK	165244	116841	71 %
Israel	9759	9168	94 %
Belgium	2379	2222	93 %
Sweden	180727	15369	9 %
Norway	76561	0	0 %
Italy	67396	0	0 %
Total	**535700**	**148475**	**28 %**

Table S5: Baseline EF% and eGFR

	Belgium	Canada	Germany*	Israel	Portugal	Spain	Sweden	Switzerland	UK	Total	Random effects estimate (95%CI)	τ^2
Ejection fraction, mean (SD)	44 (14)	n/a	43 (15)	n/a	55 (12)	44 (11)	42 (12)	43 (16)	42 (14)	44 (13)	44.7 (41.3-48.1)	4.61
≥50%	891 (37)	n/a	1,041 (29)	2,536 (51)	1,516 (75)	8,123 (41)	1,704 (40)	3,322 (40)	1,498 (25)	20,631 (40)	42.1 (31.5-52.8)	15.31
>40 - <50%	445 (19)	n/a	1,029 (29)	888 (18)	256 (13)	1,553 (8)	1,103 (26)	1,057 (13)	1,599 (26)	7,930 (15)	18.8 (13.5-24.0)	7.51
≤40%	1,043 (44)	n/a	1,532 (43)	1,553 (31)	260 (13)	10,032 (51)	1,487 (35)	3,995 (48)	2,976 (49)	22,878 (44)	39.1 (30.3-47.8)	12.63
eGFR, mean (SD)	52 (23)	65 (25)	62 (24)	62 (25)	69 (24)	n/a	52 (19)	n/a	60 (19)	60 (21)	60.1 (54.5-65.7)	6.99
≥60	811 (36)	13,615 (58)	n/a	4,746 (52)	1,753 (69)	n/a	5,421 (35)	n/a	64,492 (55)	90,838 (54)	51.0 (40.6-61.5)	13.05
<60	1,411 (64)	9,766 (42)	n/a	4,422 (48)	784 (31)	n/a	9,948 (65)	n/a	52,349 (45)	78,680 (46)	49.0 (38.5-59.4)	13.05
45-59	481 (22)	4,716 (20)	n/a	1,882 (21)	377 (15)	n/a	4,510 (29)	n/a	27,905 (24)	39,871 (24)	21.8 (17.9-25.6)	4.74
30-44	470 (21)	3,205 (14)	n/a	1,502 (16)	228 (9)	n/a	3,311 (22)	n/a	17,580 (15)	26,296 (16)	16.1 (12.3-19.9)	4.70
15-29	380 (17)	1,272 (5)	n/a	710 (8)	122 (5)	n/a	1,773 (12)	n/a	5,665 (5)	9,922 (6)	8.5 (4.7-12.4)	4.83
<15	80 (4)	573 (2)	n/a	328 (4)	57 (2)	n/a	354 (2)	n/a	1,199 (1)	2,591 (2)	2.5 (1.7-3.3)	0.94

SD, Standard deviation. EF%, left ventricular ejection fraction. eGFR, estimated glomerular filtration rate, ml/min/1.73 m^2. *eGFR <60 ml/min/1.73 m^2. CKD, chronic kidney disease defined as eGFR <60 ml/min/1.73 m^2.
UK, United Kingdom.

Table S6: Detailed Hospital health care costs (US$) per patient.

	Year 1	Year 2	Year 3	Year 4	Year 5
Canada					
Cardiovascular and renal disease					
Cardiorenal disease					
Heart failure	3719	4563	5450	6464	7280
Chronic kidney disease	2104	3473	5299	7073	11023
Atherosclerotic cardiovascular disease					
Myocardial infarction	3908	4962	6150	7172	7913
Stroke	261	349	468	557	650
Peripheral artery disease	602	724	940	1108	1229
Italy					
Cardiovascular and renal disease					
Cardiorenal disease					
Heart failure	700	1038	n/a	n/a	n/a
Chronic kidney disease	100	195	n/a	n/a	n/a
Atherosclerotic cardiovascular disease					
Myocardial infarction	177	244	n/a	n/a	n/a
Stroke	128	226	n/a	n/a	n/a
Peripheral artery disease	101	193	n/a	n/a	n/a
Portugal					
Cardiovascular and renal disease					
Cardiorenal disease					
Heart failure	867	1597	2142	2626	3074
Chronic kidney disease	468	868	1196	1551	1914
Atherosclerotic cardiovascular disease					
Myocardial infarction	43	101	146	191	217
Stroke	510	885	947	1015	1050
Peripheral artery disease	94	138	180	225	271
Spain					
Cardiovascular and renal disease					
Cardiorenal disease					
Heart failure	2161	3982	5603	7028	8618
Chronic kidney disease	625	1173	1750	2258	2752
Atherosclerotic cardiovascular disease					
Myocardial infarction	107	203	289	366	457
Stroke	152	290	435	553	677
Peripheral artery disease	69	123	185	238	297
Sweden					
Cardiovascular and renal disease					
Cardiorenal disease					
Heart failure	2983	4933	6561	7954	9114
Chronic kidney disease	1250	2245	3119	3899	4586
Atherosclerotic cardiovascular disease					
Myocardial infarction	209	360	482	576	654
Stroke	298	487	643	772	879
Peripheral artery disease	274	461	607	742	848
United Kingdom					
Cardiovascular and renal disease					
Cardiorenal disease					
Heart failure	3303	6297	9060	12454	15831
Chronic kidney disease	2505	4841	7074	9872	12721
Atherosclerotic cardiovascular disease					
Myocardial infarction	1672	3184	4532	6144	7816
Stroke	245	440	633	899	1174
Peripheral artery disease	359	688	979	1355	1807

SD, Standard deviation. The holistic cardiorenal disease definition (heart failure or chronic kidney disease)[9] is important to better understand the interchangeable relationship between these conditions, [10,11] improve treatment strategies,[12] and reduce the burden on healthcare providers.[13,14]

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