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PERFORMANCE AND EFFICIENCY

EuroHOPE Stroke: Material, Methods and Indicators

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Introduction and objectives

The principal aim of the EuroHOPE Stroke project is to compare performance in the care of stroke patients between countries, within countries (regions and hospitals), and over time, using patient level data. This comparison is made for various purposes. We investigate to what extent and how the developed methodology could be used for the purpose of implementing European-wide benchmarking of outcomes, quality and costs. This will enable decision-makers and health professionals to learn from the best practices. We investigate the relationship between outcomes/quality and costs/resources between European countries, regions within countries, and types of healthcare organizations, applying a multilevel approach. Finally, we explore the reasons behind the differences in outcomes and costs. In particular, our focus will be on policy driven factors such as treatment practices (stroke centres, thrombolysis and other procedures, use of medications – also as defined in evidence-based recommendations), waiting times, organisation of services, and financing.

This paper defines specific protocols for international comparisons that are based on the data of hospital discharge registers, mortality registers, and other available registers (such as medication use, specialty visits, etc.). The protocol has been used in preparing both the **national stroke databases for each country and for an international comparative stroke database,** which was produced from the national stroke databases. The comparative database has been used for basic reporting on care of stroke patients, and for research on the reasons behind differences in performance.

This protocol defines how we have produced indicators at national and (within country) regional levels. The basic report includes basic information on patients (number of patients, demographic characteristics, co-morbidity), indicators on content of care (use of services and procedures, costs, treatment practices, process indicators), and outcomes. The current discussion paper belongs to the Stroke subproject of the EuroHOPE project. The following institutions in the six countries participate in the Stroke subproject: National Institute for Health and Welfare (Helsinki, Finland); Centre for Research on Health and Social Care Management, Università Commerciale Luigi Bocconi (Milan, Italy); Semmelweis University, Health Services Management Training Centre (Budapest, Hungary); National Institute of Public Health and the Environment (Bilthoven, the Netherlands); Ragnar Frisch Centre for Economic Research (Oslo, Norway); University of Edinburgh (Scotland, UK); Medical Management Centre, LIME, Karolinska Institutet (Stockholm, Sweden).

This paper is a joint work established (in alphabetical order) by Helen Banks, Eva Belicza, Anne Douglas, Peter Engelfriet, Richard Heijink, Unto Häkkinen, Antti Malmivaara, Emma Medin, Atte Meretoja, Dino Numerato, Mikko Peltola, Clas Rehnberg and Timo T. Seppälä. Antti Malmivaara is the primary author.

Definition of stroke

Definition of stroke: Stroke is defined by the WHO as: "Rapidly developed clinical signs of focal (or global in case of subarachnoid haemorrhage) disturbance of cerebral function, lasting more than 24 hours or leading to death before that, with no apparent cause other than of vascular origin."

Stroke includes ischemic stroke (ICD-9 codes 433-434 / ICD 10-code I63), intracerebral haemorrhage (431/I61), subarachnoid haemorrhage (430/I60), and ill-defined stroke (436/I64).

National Databases

Every country has established a **national stroke database**. From national discharge registers patients were included that had been admitted to hospital inpatient care because of a diagnosis of stroke: ischemic stroke (ICD-9 codes 433-434 / ICD 10-code I63), intracerebral haemorrhage (431/I61), subarachnoid haemorrhage (430/I60), and ill-defined stroke (436/I64).

At present the international database includes ischemic stroke patients (ICD-9 codes 433-434 / ICD 10-code I63) admitted **during the years 2006-2008** and was formed by combining patient level data from each country's national registers.

Using anonymised personal identification numbers we have linked patient information from the following sources:

- Hospital discharge registers
- Outpatient services in specialty care / hospitals
- Drug utilisation registers
- National cause-of-death registers

International database for calculating indicators

For an explanation regarding the approach used in this part of the study, please see Häkkinen et al. (2013).

Registry data on hospital discharges, prescription drugs and causes of death were acquired in the six participating European countries. The discussion paper describes in detail how the 2007 cohort dataset was created. The 2006 and 2008 cohort datasets were created using similar logic.

Using hospital discharge data, for the 2007 cohort, all patients admitted between 1st January 2007 and 31st December 2007 with a diagnosis of one of the stroke subtypes of cerebral infarction (WHO International Classification of Diseases, 9th edition codes 433-434; 10th edition code I63), intracerebral haemorrhage (431; I61), subarachnoid haemorrhage (430; I60), or ill-defined stroke (436; I64) were identified. The hospital discharge records and other data sources mentioned above for the identified patients were gathered for the period between 1.1.2006 and 31.12.2008; for each patient the period of continuous hospital care (hospital episode) was constructed starting from the first admission (index admission) in 2007 because of stroke by combining all consecutive hospital stays for each patient. Patients with a stroke admission during the previous 365 days before the index admission were excluded.

In case a patient had many different stroke subtypes or ill-defined stroke diagnoses during the episode of care, the most 'severe' diagnosis was chosen. For that purpose, the following hierarchy was defined (from most to least severe): subarachnoid haemorrhage, intracerebral haemorrhage, cerebral infarction, and ill-defined stroke. The most severe diagnosis was chosen as the stroke subtype characterizing the episode of care.

Patients were followed for up for 365 days from the index admission for inpatient and outpatient care in hospitals, medication purchases and vital status. In addition, the hospital admissions and use of prescribed medicines in the 365 days prior to the index admission were used in assessing the presence of comorbid diseases among the patients.

We measured the length of stay (LoS) in acute care during the episode of care from the index day at the start of the admission to the last day of acute hospital care during the period of continuous hospital treatment (LoS = last date in acute treatment – index date +1). We defined acute hospital care as treatment given in a hospital's intensive care unit, stroke ward, neurological ward, or in other acute care settings (all other medical and surgical specialties). In addition, we calculated several other LoS measures including the length of the first admission, the total length of the continuous episode of care, the number of days in rehabilitation during the first continuous episode of care, and the number of days in hospital during the entire follow-up year. All LoS measures were truncated at 365 days if the length of stay was longer. In each country, the patients with LoS of the continuous hospital treatment episode longer than the 99th percentile, patients under 18 years of age, tourists, visitors and other residents with incomplete personal identification numbers were excluded.

Data restrictions

At present the international database includes ischemic stroke patients (ICD-9 codes 433-434 / ICD 10-code I63) admitted to hospital during the years 2006-2008**.**

The following patients were excluded:

- diagnosis of stroke (ICD-9 codes 430, 431, 433, 434 / ICD 10-code I60, I61 I63 I64) in the hospital discharge registry during the 365 days preceding a stroke admission.
- In each country, the patients with LoS of the continuous hospital treatment longer than the 99th percentile in that country
- patients under 18 years of age
- tourists, visitors, and patients who did not have a national patient identification number. In Italy, the patients whereby of the first index admission started outside their regions of residence (the Lazio region for the Provinces of Roma, Rieti, Latina, Frosinone, and Viterbo and the Piedmont region for the city of Turin), were excluded.

The main analysis will be done using the patient data collected from the National discharge registers as described above. Specific information on registers in each country is provided in Appendix 1. Appendix 2 describes country-specific definitions that have been used in preparing and analysing the data.

Definition of a hospital

A hospital is a health care institution providing treatment by specialized staff and equipment for a number of medical conditions. In EuroHOPE, we speak of hospitals meaning institutions providing somatic (non-psychiatric) inpatient care for patients staying overnight (for at least one night, "inpatients"), and very often also health care services (for diagnosis, treatment, or therapy) for patients without staying overnight ("outpatients"). A hospital may be a single building or a number of buildings on a campus. Also, in some countries a hospital can consist on many buildings in a certain geographical area. For example, in Finland after reorganization of Helsinki University Hospital, it includes after 2006 several building in the municipalities in the capital area.

Definition of the first hospital episode

The total hospital episode was defined as the entire treatment pathway from the beginning of the disease (i.e. acute stage of the disease) to the end of the episode (see below), irrespective of any organisational boundaries (Figure 1).

The first hospital episode: hospital inpatient treatment beginning on the index day (admission to hospital), also including possible discharge(s) to other hospital(s) and terminating on the first discharge to home or an institution, one year of continuous inpatient care, or in-hospital death (Figure 1). If the patient was immediately transferred to an inpatient rehabilitation center this was included (if data from this center was available) in the first hospital episode (Häkkinen et al. 2013).

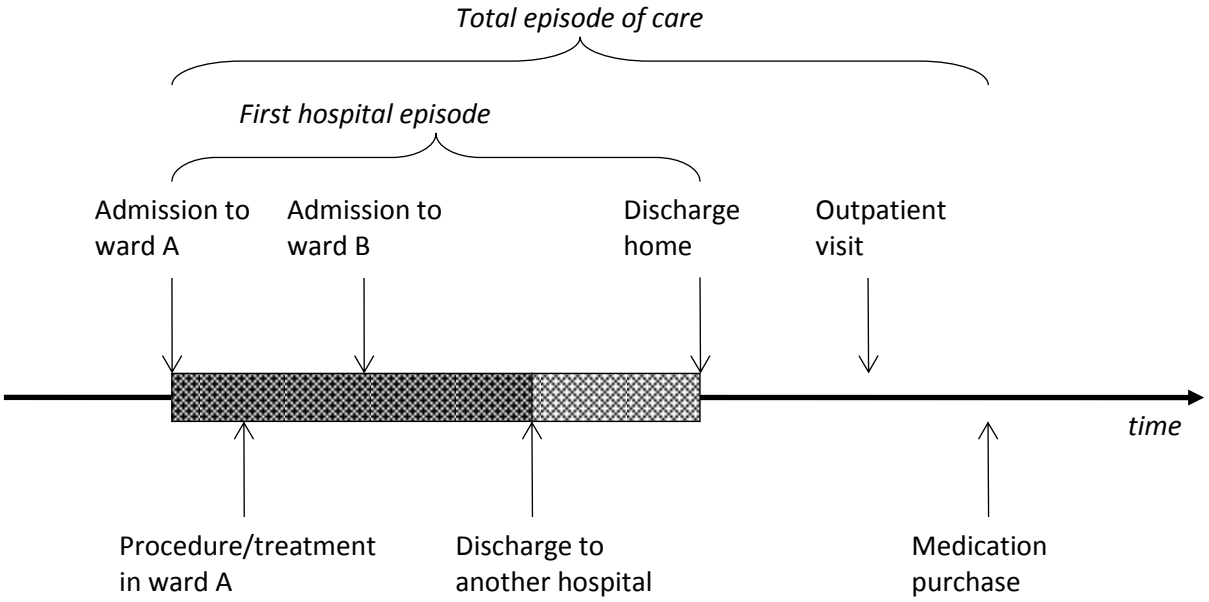

Figure 1. A schematic presentation of the follow-up of patients throughout the treatment pathway demonstrating the definitions of first hospital episode and the total episode of care.

Rehabilitation

In some countries (e.g. in Finland) it is difficult to separate rehabilitation given in a hospital from acute care as well as to separate rehabilitation from long-term care. Some countries (e.g. Hungary) have data on all inpatient rehabilitation. Other countries usually have data on inpatient rehabilitation given in hospitals but no data on rehabilitation given in specialized rehabilitation centres. Thus there are two alternatives: to include or exclude inpatient rehabilitation in first hospital episode.

We will include inpatient rehabilitation and thus keep our definition of ending the episode. In addition, in countries where rehabilitation is included in hospital inpatient data and can be separated from acute care this will be coded like mentioned earlier. In addition, an own class in the hospital hierarchy will be given for geriatric wards in hospitals. Furthermore, in a specific variable (HEPFUTR) recording the institution where the patient was transferred to at the end of the first hospital episode when it has ended to transfer into other institution than hospital, we separate long-term care and rehabilitation (in those countries where patient is transferred to inpatient rehabilitation, and this is not deterministically linkable).

Description of indicators

Baseline patient characteristics:

Age and gender

Comorbidities (see Appendix 2);

- Hypertension
- Coronary artery disease
- Atrial fibrillation
- Cardiac insufficiency (heart failure)
- Diabetes mellitus
- Atherosclerosis
- Cancer
- COPD and asthma
- Dementia
- Depression
- Parkinson's disease
- Mental disorders
- Renal insufficiency (failure)
- Alcoholism

The presence of co-morbidities was defined in two ways:

1. based on medication purchases*, and main or secondary diagnosis mentioned in the hospital discharge registry during the previous 365 days hospital inpatient utilisation) **
2. based only on main and secondary diagnoses during the previous 365 days hospital utilisation**

*The number and share of patients who purchased (or were prescribed/filled prescriptions for) drugs (outside hospitals) during the 365 days prior to the index date (including index date) based on the ATC (anatomic therapeutic classification) code (see below: the process indicators)

**In-patient hospital stay days during the one year period prior to stroke in acute care

Process indicators:

Length of stay of first hospital admission, days per patient

Length of stay of first hospital episode, days per patient

- Total
- Acute care
- Non-acute care
- Days per patient due to any cerebrovascular disorder

Total inpatient days per patient over the first year after stroke:

- Total

- Acute care
- Non-acute care
- Days per patient due to any cerebrovascular disorder

Number and share of patients with length of stay of the first hospital episode of 90 days or more

Number and share of patients treated during the first hospital episode in different types of stoke centres (Comprehensive stroke center (CSC), primary stroke center (PSC) or General hospital (GH)). This typology was not applied in the majority of the HDR databases of the EuroHOPE countries in the 2006-2008 period and therefore, an expert opinion was used to classify the level of the care during the first hospital episode.

Number and share of patients who received arteria carotis endarterectomy during the first hospital episode.

Number and share of patients who received thrombolysis during the first hospital episode.

Number and share of patients that have used drugs (outside hospitals) based on the ATC (anatomic therapeutic classification) code during the one year before and one year after hospitalisation.

- diuretics (03*, C07BB*, C09BA*, C09DA),
- beta blockers (C07*)
- ACE-inhibitors (C09A* ja B*)
- AT II antagonists (C09C* ja D*)
- calcium blockers (C08*, C07FB*, C09BB*)
- insulin (A10A*)
- oral diabetes medication (A10B*)
- statins (C10AA*)
- clopidogrel (B01AC04)
- dipyridamol (B01AC07 , B01AC30)
- warfarin (B01AA03)
- antidepressants (N06A*)
- dementia medications (N06D*)
- antiepileptics (N03A*)

Outcome indicators:

- mortality at 30, 90, and 365 days from the index admission day.
- readmission (due to recurrence of stroke) to hospital within 30, 90 days and 365 days from the index admission.
- complications during the first hospital episode:
- pulmonary embolism
- acute myocardial infarction
- phlebitis and thrombophlebitis
- pneumonia

Adjusting for patient mix

One of the challenges when comparing health outcomes between countries is to adjust for differences in the patient mix. One country may have comparatively larger numbers of older, or severely ill, patients than another country. This is further complicated by the fact that countries may differ in the degree to which the relevant information is recorded, the availability of patient information, or variables being very differently

defined across countries. In order to have comparable performance indicators, the indicators have to be adjusted for confounding factors. EuroHOPE has tried to solve this problem by using all relevant registry data available for everyone with a specified health problem, that is, by collecting all available information on variables with a potential effect on health outcomes. Examples are disease specific comorbidities, length of hospital stay and medication use prior to the occurrence of the health problem studied. However, there is no way to solve the problem of the existence of differences between countries in registering this information.

For each outcome, three different risk adjusted outputs were produced: 1. adjusted for sex and age only, 2. adjusted for sex, age, disease-specific comorbidities based on primary and secondary diagnosis, LOS the year prior to index admission, and 3. identical to 2 except comorbidities are based on both primary and secondary diagnoses and medication purchases. **For detailed descriptions, see Appendix 3.**

Based on the experiences in the PERFECT project (Peltola et al., 2011), the observed/expected approach described by Ash et al. (2003) is used - this roughly corresponds to indirect standardization. Specifically, the method uses regression modelling for the risk adjustment. For mortality outcomes up to one year, logistic regression is used, while for the LOS outcomes, negative binomial regression is used. The method is described in greater detail in another manuscript (Moger and Peltola 2013).

Each country applied a standardized, centrally-constructed Stata syntax code to the national data for calculating the country and regional level indicators. The national files were processed in order to enable standardized reporting of the data from all countries with minimum workload and minimum possibility of human error in processing the data. This Stata do-file is available upon request from the researchers.

Case-mix standardisation will be used when comparing countries, regions, hospitals, or years. Variables which are considered potential prognostic factors (and thus confounders) are used for adjustment. These will be derived from primary and secondary diagnoses of previous discharge data and from data on previously prescribed medicines. We will use the following variables:

- age (in years, classified)
- gender
- comorbidity as defined in Appendix 2 (only the comorbid diseases with at least 1% prevalence in the study population in each country were included in the risk adjustment as confounding factors)
- number of in-patient hospital days during one year prior to stroke in acute care.

Levels of analysis

Indicators are produced at the national level and, within countries, also at the regional level, and later at the hospital level. Regional information is based on patients' place of residence. The definitions for regions have been made in each country according to the local preferences. The definitions for a region and for a hospital are described in Häkkinen et al. (2012).

Remarks on interpretation of indicators

We have described what should be taken into account in comparisons of indicators. The most important caveats are related to differences in coding practices, availability of data and differences in classifications. In particular the following issues were identified:

Please check and add other relevant issues if needed:

- Hospital definition: how to determine whether similar kind of institutions are included from all the countries, and the concordance of definitions of acute care and rehabilitation.
- Stroke hospitalisation rate for non-fatal cases only around 60% in the Netherlands and Scotland.
- Netherlands: the coverage of the hospital discharge register is not complete; approximately 35% of the hospitals do not report to the national register; thus not all cases are included, and some patients might be lost during follow-up or follow-up may be incomplete due to patients being transferred to a hospital that is not reporting to the national discharge register.
- Proportion of undefined stroke coding out of all strokes diagnoses in the EuroHOPE database is particularly common in Scotland (nearly 40%), but also common in the Netherlands and in the Lazio region of Italy.
- Netherlands: deterministic linkage was not possible as in the other participating countries; therefore age, sex and postal code of the patients were used in the matching of patient-level data in the Netherlands
- Italy: data regarding admissions previous to the index admission and the follow-up admissions are most likely not complete for the residents of the City of Turin.
- Differences in the availability of medication data: in Scotland the medication data is missing; in the Netherlands the medication data is on an aggregate level and the date of purchase is known only on a yearly basis.
- The regions do not necessarily correspond to internationally recognized, country-specific administrative divisions among the countries. In Italy the six EuroHOPE regions studied are geographical areas composed of the city of Turin and five Lazio region provinces: Latina, Frosinone, Rieti, Roma, and Viterbo.
- Sizes of regions (amount of population) vary, as does the number of stroke patients in a region per year. Therefore, we have provided confidence intervals for the indicators. Caution should be taken when comparing indicators of small regions having few stroke patients.

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Appendix 1. National registers and data bases

Hospital discharges register for inpatient care

Finland	(1987-) 2000-
Hungary	2004-
Italy	2002- (1995-)
Netherlands	2000- (from 2005 incomplete) patient ID is questionable (age, sex, address, etc.)
Scotland	1980- (no private producers)
Sweden	(1987-) 2000-

Register on use of outpatient services in hospitals and/or other specialist units

Finland	(1998-) 2000-, data on diagnosis is not complete?
Hungary	2004-
Italy	2000- (some regions; domestic classification)
Netherlands	2005- (incomplete personal identifiers)
Scotland	Only Lothian county available
Sweden	2001-

Register of prescribed medicine

Finland	1995-
Hungary	2004-
Italy	2003- (linkable only through regions)
Netherlands	(1986-) 2000-semi-commercial drug database, coverage c. 12%
Scotland	Not linkable
Sweden	2005-

Cause of death register

Finland	National mortality register
Hungary	National mortality register
Italy	National mortality register
Netherlands	National mortality register
Scotland	National mortality register
Sweden	National mortality register

Appendix 2. Variable definitions.

Variable	Type	Definition	Classes/Coding
ID	Char	Patient ID	
C	Char	Country ID	FIN=Finland, SWE=Sweden, SCO=Scotland, HUN=Hungary, ITA=Italy, NOR=Norway, NL=Netherlands
GENERAL INFORMATION			
MALE	Num	Male	1/0
AGE	Num	Patient's age at first admission	In years
DIST	Char	Area (e.g. hospital district)	*See sheet DIST*
MUNI	Char	Municipality/Postal area	*See sheet DIST*
STROKECL	Char	Stroke classification according to severity of diagnosis	**SAV**: Subarachnoid haemorrhage (I60) **ICH**: Intracerebral haemorrhage (I61) **INF**: Cerebral infarction (I63) **OTH**: Other stroke (I64)
INFORMATION OF THE INDEX/FIRST ADMISSION ("FST")/FIRST HOSPITAL EPISODE ("HEP")			
YEAR	Num	Year of index admission	yyyy
INDATE	Char	Index day	dd/mm/yyyy
FSTDIAG	Char	Main diagnosis of the index admission	ICD-9/ICD-10 coding, w/o special marks (e.g. dots)
FSTEMGC	Num	The patient was admitted from emergency department	1/0
FSTSPTR	Num	A speciality transfer preceding index admission (patient was admitted from another ward of the same hospital)	1/0; missing, if no hospital transfers recorded
FSTLOS	Num	Length of the index admission By definition: (discharge day of the index admission - index day) + 1	
FSTHOSP	Char	ID of the index admission hospital	
HEPLOS	Num	Length of the first hospital episode By definition: (discharge day of first hospital episode - index day) + 1	
HEPADM	Num	Sum of hospital admissions within the first hospital episode	
HEPHOSP	Char	Hospital in charge during the first hospital episode	*See sheet Hospital hierarchy*

HEPCNTR	Char	Stroke center classification of HEPHOSP	**CSC/PSC/GH,** *See sheet Hospital hierarchy*
HEPFUTR	Char	Follow-up treatment: where did the patient go to when the first hospital episode ended	**0**: Home **1***: Hospital/retirement or nursing home/outpatient visit (See sheet *Hospital hierarchy*) (**1*S**: In treatment with a stroke main diagnosis) **2**: Dead **2***: Died in hospital * (**2*S**: Died in hospital * on an admission with a stroke main diagnosis) - missing, if HEPLOS>=365
MORTALITY			**MORTALITY:** *All variables get a missing value, if patient alive in the end of follow-up*
DTIME	Num	Time to death Define: (date of death - index day + 1)	
DPLACE	Char	Place of death	**1**: Healt care unit **2**: Home/apartment **3**: Other **4**: Abroad **9**: Unknown
DCAUSE	Char	Cause of death	ICD-10 coding
TREATMENT			
FROMT	Num	Where did the patient come from	**0:** Home **1**: Hospital **2:** Retirement/nursing home
STATE1-STATE365	Char	Patient's state during first, second, etc. day of the first year of follow-up - **4 characters**: 1. home/institution/dead, 2. hospital hierarchy, 3. stroke diagnosis indicator, 4. ward/unit type according to given classification - In case of overlapping admissions, the STATE variable is marked with the hospital being in the highest step of *hospital hierarchy* (defined by each country) - Admissions with treatment of stroke (main diagnosis code **I60, I61, I63, I64**) are marked with an additional symbol S	*See sheet Hospital hierarchy* **0:** Home **1*:** Hospital/retirement or nursing home/outpatient visit (See sheet *Hospital hierarchy*) (**1*S**: In treatment with an stroke main diagnosis) **2:** Dead 2*: Died in hospital * (**2*S**: Died in hospital * on an admission with a stroke main diagnosis)
LOSPY	Num	Days in hospital treatment during the previous year (last 365 days)	
LOSPY_11-18	Num	Days in hospital treatment during the previous year (last 365 days) in level 11-18 hospitals	Level 11-18 hospitals: *See sheet Hospital hierarchy*

OPERATIONS			*See sheet Procedure codes*
TOPE	Num	Time between index day and first 'OPE' operation - Define: day of operation - index day - If operation day = missing, define: admission day of the operation admission - index day - See classes of 'OPE' below	In days; missing, if no operation has been done
NOPE	Num	Operation date NOT registered	1/0; missing, if no operation
OPE			
CEA		Thrombendarterectomy of arteries of aortic arch and branches	
IET		Thrombolytic treatment	
ANE		Ligature or endovascular occlusion of intracranial aneurysm	
HAE		Evacuation of traumatic intracerebral haematoma or spontaneous intracranial haematoma	
SHU		Shunt operations on ventricles of brain or intracerebral cysts	
OTH		Other operation of nervous system	
CT		Computed tomography (of the brain)	
COMPLICATIONS			*See sheet Procedure codes*
STRREC	Num	Stroke recurrence i.e. time between index day and first new stroke admission Define: admission day of new stroke admission - index day "First new stroke admission": - has a stroke main diagnosis (ICD-10: **I60, I61, I63, I64**) - doesn't belong to first hospital episode - starts at least 3 days after the end of first hospital episode (i.e. new stroke admission - first hospital episode discharge day > 3) OR starts from emergency department OR ends to death (i.e. discharge day of new stroke admission = time of death)	In days; missing, if no stroke recurrence
TCMP	Num	Time between index day and first 'CMP' complication - Define: admission day of an admission with 'CMP' main diagnosis - index day - See classes of 'CMP' below	In days; missing, if no complication is found
CMP			
EMB		Pulmonary embolism	
AMI		Acute myocardial infarction	
PHL		Phlebitis and thrombophlebitis	

PNE		Pneumonia	
COMORBIDITIES			
HEPCI	Num	Charlson index of the first hospital episode	
FSTCI	Num	Charlson index of the first admission	
TCOM_ICD	Num	Time to the latest 'COM' admission Define: index day - discharge day of the latest 'COM' admission - see classes of 'COM' below - check the main diagnosis only	In days; missing, if a previous 'COM'-episode doesn't exist
TCOM_SEC	Num	Time to the latest 'COM' admission Define: index day - discharge day of the latest 'COM' admission - see classes of 'COM' below - check the secondary diagnoses only	In days; missing, if a previous 'COM'-episode doesn't exist
TCOM_ATC	Num	Time to the latest purchase of medication for 'COM' Define: index day - day of purchase - see classes of 'COM' below	In days; missing, if no previous medication purchases for 'COM'
TC07_ATC	Num	Time to the latest purchase of beta-blockers Define: index day - day of purchase	In days; missing, if no previous medication purchases for beta-blockers - Used when defining comorbidity hypertension ("HTN")
TB01_ATC	Num	Time to the latest purchase of warfarin Define: index day - day of purchase	In days; missing, if no previous medication purchases for ACE anhibitors - ATC-class B01AA03
TC10_ATC	Num	Time to the latest purchase of statins Define: index day - day of purchase	In days; missing, if no previous medication purchases for statins - ATC-classes C10AA*
COM			
HTN		Hypertension	
CAD		Coronary artery disease	
AF		Atrial fibrillation	
CI		Cardiac insufficiency (heart failure)	
DM		Diabetes mellitus	
ATH		Atherosclerosis	
CA		Cancer	
CPD		COPD and asthma	
DEM		Dementia	
DEP		Depression	
PD		Parkinson's disease	
MD		Mental disorders	
RI		Renal insufficiency (failure)	
ALC		Alcoholism	

MEDICATION PURCHASES			
TMED_PRE	Num	Time to the latest purchase of medication for 'MED' Define: index day - day of purchase - see classes of 'MED' below	In days; missing, if no previous medication purchases for 'MED' - day of purchase <= index day
TMED_POST	Num	Time to the first purchase of medication for 'MED' after index day Define: day of purchase - index day - see classes of 'MED' below	In days; missing, if no medication purchases for 'MED' after index day - day of purchase > index day
MED			
CLO		Clopidogrel	
DIP		Dipyridamole	
DIU		Diuretic	
BET		Beta blocker	
ACE		ACE inhibitor	
ARB		Angiotensin receptor blockers	
CCB		Calsium channel blockers	
INS		Insulin	
DM		Blood glucose lowering drugs, excluding insulins	
STA		Statin	
WAR		Warfarin	
DEP		Antidepressants	
DEM		Anti-dementia drugs	
EPI		Antiepileptics	
TREATMENT COSTS			
FSTCOST		Hospital costs of first admission	*Costs in national currency (not deflated)*
HEPCOST		Hospital costs of first hospital episode	*Costs in national currency (not deflated)*
COST365		Costs during 365 day from index day	*Costs in national currency (not deflated). For the hospital stays that are cut in the end of the follow-up, we only include the part of costs that have accumulated from the start of the hospital stay until the cut point. If the costs of such discharge are known only in total for the entire discharge, the total cost is divided by the number of inpatient days of this discharge, and then this average day cost is multiplied with the number of inpatient days that belong to the follow-up period.*
FSTCOSTAC		Hospital costs of first admission, acute care only	*Costs in national currency (not deflated) (by the 4th digit of STATE variables: 1,2,3,4 codes)*
HEPCOSTAC		Hospital costs of first hospital episode, acute care only	*Costs in national currency (not deflated) (by the 4th digit of STATE variables: 1,2,3,4 codes)*

COST365AC		Costs during 365 day from index day, acute care only	*Costs in national currency (not deflated) (by the 4th digit of STATE variables: 1,2,3,4 codes). For the hospital stays that are cut in the end of the follow-up, we only include the part of costs that have accumulated from the start of the hospital stay until the cut point. If the costs of such discharge are known only in total for the entire discharge, the total cost is divided by the number of inpatient days of this discharge, and then this average day cost is multiplied with the number of inpatient days that belong to the follow-up period.*
MEDICATION COSTS			
COST_MED		Costs of medicine MED purchases during one year of follow-up - see classes of 'MED' above	*Costs in national currency (not deflated)*

HOSPITAL HIERARCHY USED WHEN DEFINING THE HIGHESTLEVEL HOSPITAL THE PATIENT HAS BEEN TREATED IN DURING THE FIRST SEVEN (7) DAYS OF FOLLOW-UP

Level	Long name
CSC	Comprehensive stroke center
PCS	Primary stroke center
GH	General hospital

Hospital hierarchy used in STATE-variables
Note: Levels are fixed. Please spesify into field Availability whether the info can be obtained from you data (on some level).

2nd digit in STATE-variables:

Level	Hospital
1	University hospital
2	Specialized hospital
3	Central hospital or regional hospital
4	General hospital or local hospital
5	Rehabilitation
6	Geriatric and general care
7	Long term care
8	Psychiatric care
9	Outpatient services in hospitals

PROCEDURE CODES

OPE	Procedure	Codes	
CEA	Thrombendarterectomy of arteries of aortic arch and branches	3811, 3812, 3814	
IET	Thrombolytic treatment	0062, 9910	
ANE	Ligature or endovascular occlusion of intracranial aneurysm	3881, 3951, 3972	
HAE	Evacuation of traumatic intracerebral haematoma or spontaneous intracranial haematoma	0139	
SHU	Shunt operations on ventricles of brain or intracerebral cysts	023	
	Computed tomography (of the brain)		
OTH	Other operation of nervous system	059	
CMP	**Complications**	ICD-10	ICD-9
EMB	Pulmonary embolism	I26*	415.1
AMI	Acute myocardial infarction	I21*, I22*	410
PHL	Phlebitis and thrombophlebitis	I80*, I82*	451
PNE	Pneumonia	J12*, J13*, J14*, J15*, J16*, J17*, J18*, J69*	480-486

COMORBIDITIES

COM	Description	ICD-9	ICD-10	ATC-code
HTN	Hypertension	40*	I10*-I15*	C03*, C07* (with neither coronary artery disease nor atrial fibrillation), C08*, C09*
CAD	Coronary artery disease	410*-414*	I20*-I25*	N/A
AF	Atrial fibrillation	4273*	I48*	N/A
CI	Cardiac insufficiency (heart failure)	428*	I50*	N/A
DM	Diabetes mellitus	250*	E10*-E14*	A10A*, A10B*
ATH	Atherosclerosis	440*	I70*	N/A
CA	Cancer	140*-208*	C00*-C99*, D00*-D09*	L01* except L01BA01
CPD	COPD and asthma	4912*, 496*, 493*	J44*-J46*	R03*
DEM	Dementia	290*, 3310*	F00*-F03*, G30*	N06D*
DEP	Depression	2960*, 2961*	F32*-F34*	N06A*
PD	Parkinson's disease	332*	G20*	N04B*

MD	Mental disorders	295*-298* expect 2960* and 2961*	F20*-F31*	N05A* except N05AB01 and N05AB04, and no dementia
RI	Renal insufficiency (failure)	585*	N18*	N/A
ALC	Alcoholism	291*, 304*, 305'	F10*-F19*	N/A

MEDICATION

MED	Long name	ATC classes
CLO	Clopidogrel	B01AC04
DIP	Dipyridamole	B01AC07, B01AC30
DIU	Diuretic	C03*, C07BB*, C09BA*, C09DA*
BET	Beta blocker	C07*
ACE	ACE inhibitor	C09A*, C09B*
ARB	Angiotensin receptor blockers	C09C*, C09D*
CCB	Calsium channel blockers	C08*, C07FB*, C09BB*
INS	Insulin	A10A*
DM	Blood glucose lowering drugs, excluding insulins	A10B*
STA	Statin	C10AA*
WAR	Warfarin	B01AA03
DEP	Antidepressants	N06A*
DEM	Anti-dementia drugs	N06D*
EPI	Antiepileptics	N03A*

Appendix 3. Adjustment for confounding (apply for between and within country comparisons).

The point estimates and confidence intervals for incidence, process variables and treatment outcomes are produced as follows:

1. **Unadjusted data**
    - Incidence of ischemic stroke
    - Age and gender
    - CT- imaging, thrombolysis and arteria carotis endarterectomy during the first hospital episode
    - Comorbidities based on main diagnosis or medicine purchase during the previous 365 days
    - Medication purchases 365 days prior the index date (including antithrombotic medication prior ischemic stroke)
    - Medication purchases 365 days after the index date (including antithrombotic medication after ischemic stroke)
    - Proportions treated at comprehensive stroke centers, primary stroke centers and general hospitals
2. **Data adjusted for age and gender only**
    - Complications (pulmonary embolism, acute myocardial infarction, phlebitis and thrombophlebitis, pneumonia)
    - Length of stay at hospital: first admission, hospital episode, total length of stay during one year after index admission due to ischemic stroke
    - Length of stay in acute hospital care: during the first hospital episode, and during one year after index admission due to ischemic stroke
    - Stroke recurrence at 30, 90 and 365 days after index admission due to ischemic stroke
    - All cause mortality at 30, 90 and 365 days after index admission due to ischemic stroke
3. **Adjusted for age, gender, number of hospital days during previous 365 days (LOS) prior to index admission, disease specific comorbidities based on primary and secondary diagnosis**[1]
    - Complications (pulmonary embolism, acute myocardial infarction, phlebitis and thrombophlebitis, pneumonia)
    - Length of stay at hospital: first admission, hospital episode, total length of stay during one year after index admission due to ischemic stroke
    - Length of stay in acute hospital care: during the first hospital episode, and during one year after index admission due to ischemic stroke
    - Stroke recurrence at 30, 90 and 365 days after index admission due to ischemic stroke
    - All cause mortality at 30, 90 and 365 days after index admission due to ischemic stroke

4. Mortality at 30, 90 and 365 days after index admission **Adjusted for age, gender, LOS the year prior to index admission, disease specific comorbidities based on primary and secondary diagnosis[1] & medication purchase[2].**
    - Complications (pulmonary embolism, acute myocardial infarction, phlebitis and thrombophlebitis, pneumonia)
    - Length of stay at hospital: first admission, hospital episode, total during one year after index admission due to ischemic stroke
    - Stroke recurrence at 30, 90 and 365 days after index admission due to ischemic stroke
    - All cause mortality at 30, 90 and 365 days after index admission due to ischemic stroke

[1]hypertension, coronary heart disease, atrial fibrillation, cardiac insufficiency, diabetes mellitus, atherosclerosis, cancer, chronic obstructive pulmonary disease and asthma, dementia, depression, Parkinson's disease, mental disorders, renal insufficiency, alcoholism.

[2]medication purchase (prescription and special reimbursement data): clopidogrel, dipyridamole, diuretic, beta blocker, ACE inhibitor, angiotensin receptor blockers, calsium channel blockers, insulin, blood glucose lowering drugs excluding insulin, statin, warfarin or dicoumarol, antidepressants, anti-dementia drugs.