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Cardiovascular disease in Switzerland – health care, mortality and geographical pattern

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ABBREVATIONS

ACS	Acute coronary syndromes
AH	Avoidable hospitalisations
AMI	Acute myocardial infarction
CABG	Coronary artery bypass surgery
CHOP	Swiss operation procedure code
CPR	Cardiopulmonary resuscitation
CVD	Cardiovascular disease
DRG	Diagnosis Related Groups
EMS	Emergency medical services
EOLC	End of life care
HSA	Hospital service area or health service area
HSR	Health services research
ICD	International Classification of Diseases
MedStat	Geographical region defined for the hospital discharge and hospital statistics
NCDs	Non-communicable diseases
NSTEMI	Non-ST-segment elevation myocardial infarction
OECD	Organisation for Economic Co-operation and Development
PCI	Percutaneous coronary intervention
SEP	Swiss neighbourhood socioeconomic position index
SFSO	Swiss Federal Statistical Office
SNC	Swiss National Cohort
SNSF	Swiss National Science Foundation
STEMI	ST-segment elevation myocardial infarction
WHO	World Health Organization

SUMMARY

Switzerland is facing an aging population and a growing amount of patients with chronic diseases. It is crucial to display health care processes and pathways, to identify inequalities and obstacles, and to point out possibilities for improvements of the Swiss health care system (e.g. increase efficiency).

The introductory part of the thesis presents a brief description of the Swiss health care system, health services research and regional variation as well as an introduction of CVD and its epidemiological key figures, aetiology and treatments. This is followed by the description of the utilized methods and data, and the objectives of this thesis.

The subsequent sections present the four articles included in this thesis. The first article focuses on a small area analysis on regional variation of avoidable hospitalisations in Switzerland including density of primary care physicians and specialists, rurality and hospital supply factors as explanatory variables in the analysis. Lower rates of avoidable hospitalisations were found in areas with very high supply of primary care physicians, increased avoidable hospitalisation rates in areas with more specialists and in areas with higher proportion of rural residents.

The second article aims to examine whether emergency patients with acute ST-segment elevation myocardial infarction were adequately treated, i.e. according to the treatment guidelines, in Switzerland. Results show that older and female patients were less likely to receive revascularization which suggests that the treatment guidelines may not be uniformly applied in Switzerland.

Similar to the first article, also in the third article a small area analysis was performed but this time investigating regional variation in costs at the end of life. Strongest associations of cost was found with cause of death, age and language region of the decedents. The strong spatial variation of costs could only partly be explained by the included covariates.

Article four aims to examine the relationship of distance to different hospital types and mortality from AMI or stroke. We found that AMI mortality in the Swiss population 30 and older and stroke mortality in those 65 and above increased with distance to central and university hospitals, while adjusting for sociodemographic and economic characteristics of the population.

The presentation of the four articles is followed by a discussion, which summarizes the main findings and the strengths and limitations of the presented articles. The thesis concludes with a discussion about the challenges for policy, practice and future research.

1 Introduction

This thesis is a contribution to the field of cardiovascular disease (CVD) epidemiology and health services research (HSR) in Switzerland. The four articles presented in this thesis address different research questions and utilize a wide variety of methods and data, reflecting the multidisciplinary field of health services research.

This thesis first addresses the determinants of regional variations in avoidable hospitalisations in article 1. Avoidable hospitalisations are also called ambulatory-care sensitive conditions, indicating that appropriate ambulatory care can contribute to the prevention of avoidable hospitalisations. The thesis presents a study investigating avoidable hospitalisations including diabetes, hypertension and congestive heart failure. These conditions are risk factors for, or precursors or sequelae of, severe cardiovascular diseases such as acute myocardial infarction or stroke.

In article 2, the application of treatment guidelines in emergency patients with acute ST-segment elevation myocardial infarction (STEMI) is examined throughout Switzerland. The analysis included several characteristics of the patients and hospitals as possible factors to induce the treatment of STEMI patients.

At the end of life, health care costs often increase sharply. CVD is the number one cause of death in Switzerland and also plays a major role in the generated costs at the end of life. However, it remains unclear why health care costs differ between regions. An investigation of possible reasons for these differences is presented in the third article in this thesis.

A major research focus of HSR is access to health care. Time to treatment is an important factor to prevent severe health outcomes of life-threatening diseases such as acute myocardial infarction (AMI) and stroke. The fourth article of this thesis explores geographical access to Swiss hospitals and its influence on mortality due to AMI and stroke.

The following sections provide background information about the Swiss health care system, cardiovascular diseases, health services research, regional variations, the study designs and data used, and the objectives of this thesis.

1.1 Swiss health care system

The Swiss health care system is considered to be among the best health care systems worldwide, based on indicators including life expectancy, the number of health professionals and patient satisfaction. However, it also ranks as one of the most expensive health care systems among OECD (Organization for Economic Co-operation and Development) countries with 11.4% of its gross domestic product being spent on health care in 2009. Like other high-income countries, Switzerland is facing a massive demographic change in the form of a rapidly aging population. The consequence of this is a growing burden for the health care system and a resulting increase in costs. The OECD and WHO (World Health Organization) stated in their review of the Swiss health system in 2011 that a major challenge for Switzerland will be maintaining and improving the care of people suffering from chronic conditions (OECD/WHO, 2011).

Switzerland is a federal country with a decentralized structure, both governmentally and for health care. The 26 cantons each take on the responsibility for the planning and supply of health care services, subsidies of insurance premiums and financing of hospitals in their jurisdiction. The central government determines federal health legislation and regulates the health insurance market (including payment procedures and defining the health services to be covered by compulsory health insurance packages).

Basic health insurance is compulsory for all Swiss residents. Residents can choose from around 60 insurance companies. The insured can also choose the annual excess they will pay in the event of making a claim or claims. This excess is in the range of 300 to 2,500 Swiss Francs, with the monthly premium (ranging from 230 to 650 CHF) being lowered when a higher excess is selected. In addition to the excess, 10% of the yearly health expenditures are payable by the insured to a maximum of 700 Swiss Francs. In contrast to other countries, Swiss residents have the free choice of their physicians, hospital and other health care providers. However, individuals can choose insurance plans with managed care networks or GPs as gatekeepers where premiums are reduced.

Approximately 37% of all Swiss residents receive subsidies from their cantons for their health insurance to prevent premiums exceeding 8 – 10% of their household’s income. Around half of inpatient health care costs are also paid by the cantons, with the goal of providing equal access to high-quality health care.

The insurance providers are prevented by law from making a profit from compulsory insurance packages, but they can profit from additional private insurance packages e.g. covering dental care, single bed rooms in hospitals or complementary medicine (Biller-Andorno and Zeltner, 2015; Reinhardt, 2004).

Demographic changes and constantly rising health-care costs have created challenges for the Swiss health care system in the provision of sufficient health care professionals to deliver services for an elderly population and in preventing supply-induced overconsumption (Biller-Andorno and Zeltner, 2015). The fragmented health care system and the sheer number of health-care- and insurance-providers makes it challenging to collate data to provide insights into opportunities for improvement in Swiss health care. Nevertheless, the awareness of this great need for more information is increasing. The Swiss National Sciences Foundation just released a call for proposals to promote innovative health services research, examine the challenges of caring for chronically ill and improving the usability of health data (SNSF, 2015).

1.2 Health services research

The U.S. National Library of Medicine lists on their website HSR definitions of five American institutions from 1980 to 2000 and summarizes: "…, health services researchers investigate three major aspects of health care: access to care, the quality of care, and its cost. Health services researchers attempt to evaluate the effects and outcomes of the health care 'system' on people's health." (NIH, 2014)

In August 2015, the Swiss Federal Office of Public Health released a factsheet about HSR, stating that there is a backlog in Switzerland in HSR and results of HSR studies of other countries are not easily transferable to Switzerland. They define the aim of HSR in Switzerland as follows: to gain knowledge about how to optimize the structure of health care, how to increase the health care quality and efficiency, how to reduce over-, under- and wrong utilization of health-care services, and how patients' safety and navigation through the system can be improved (BAG, 2015).

1.3 Regional variation

A major research focus of HSR is the identification of regional variation in health care. The Dartmouth Institute for Health Policy & Clinical Practice in New Hampshire are pioneers in exploring regional variation using small area analysis in the US health-care system. For more than 20 years, they have explored efficiency and effectiveness of the US health care system in their Dartmouth atlases or reports of health care presenting maps and analyses of regional variation in costs, surgical procedures, end of life care or supply-sensitive care (The Dartmouth institute, 2016). The National Health Service England have published atlases of variation in health care for topics like diabetes, respiratory disease or diagnostic services since 2010 (NHS Right Care, 2016).

In Switzerland and elsewhere, considerable geographical and temporal variation in cardiovascular health care and mortality has been shown (David E.Wennberg and John D. Birkmeyer, 1999; Insam et al., 2014, 2013; Maeder et al., 2010; Marques-Vidal and Paccaud, 2012; Radovanovic et al., 2012). Variations can be shown in costs, treatment pattern, intensity of care, health outcome (e.g. mortality), re-hospitalisations as a measure of quality of care and health care expenditures, as well as utilization of health care providers (Agarwal et al., 2015; Busato et al., 2012; Panczak et al., 2012; Roussot et al., 2016). Several factors cause regional variation: differences in the prevalence of the underlying diseases, patient's medical conditions, demographic and socioeconomic characteristics, regional differences in capacity, quality and accessibility of supply, financial incentives related to different reimbursement systems, as well as patient or provider driven deviations from evidence-based practice. High variation can point to unnecessary care or underutilization of necessary care.

1.4 CVD – epidemiology, aetiology and treatment

Cardiovascular diseases belong to the non-communicable diseases (NCDs), also known as chronic diseases, with long duration and slow progression. The four main types of NCDs are CVD, cancers, chronic respiratory diseases and diabetes. Common potentially modifiable risk factors for dying from non-communicable diseases are physical inactivity, tobacco use, harmful use of alcohol and unhealthy diets. Globally, 17.5 million people die from CVD every year, making it the leading cause of death in the world (WHO, 2015a, 2008). CVD also causes the largest economic burden of disease worldwide. In 2004, the British National Health Service spent 21% of their health expenditures on CVD treatment alone (Luengo-Fernández et al., 2006).

Although over three quarters of CVD deaths take place in low- and middle-income countries and deaths from CVD decreased in high-income countries over the last decade, CVD is still the main cause of death in Switzerland (Bundesamt für Statistik, 2014; WHO, 2015b). In total, 21,674 persons died of CVD in 2013 (9,745 men and 11,929 women). 13,864 cases have been hospitalized because of AMI (65.5% men, 34.5% women) and 14,192 cases because of stroke (51.2% men, 48.8% women) (SFSO, 2015a).

Due to the huge burden of disease from CVD, various studies (Framingham Heart study, MONICA - Multinational Monitoring of trends and determinants in cardiovascular disease) were started to examine the determinants and risk factors, changes in prevalence and incidence of CVD, preventive factors and medication, the development of a risk score or the evaluation of different treatment procedures, which resulted in evidence based treatment guidelines (D'Agostino et al., 2013; Eriksson et al., 2012; Hense, 2000; Mendis; O'Gara et al., 2013; Peltonen et al., 1998; Steg et al., 2012; Windecker et al., 2014).

1.4.1 Aetiology of CVD

Cardiovascular disease comprises a group of disorders of the heart, blood vessels and vascular diseases of the brain. CVD due to atherosclerosis comprises ischemic heart disease or coronary artery disease (e.g. angina pectoris, heart attack), cerebrovascular disease (e.g. stroke) and diseases of the aorta and arteries, including hypertension and peripheral vascular disease. Other diseases belonging to CVD are rheumatic heart disease, congenital heart disease (malformations of heart structures), cardiomyopathies (disorders of the heart muscle) and cardiac arrhythmias (WHO, 2015b, 2011).

Atherosclerosis is a slow progressing pathological process in the walls of blood vessels, often beginning in childhood and adolescence. Several risk factors are known: tobacco use, physical inactivity, obesity, diabetes, unhealthy diet, harmful use of alcohol, hypertension, raised blood lipids, male gender, advancing age or genetic disposition. Atherosclerosis is an inflammatory process affecting medium- and large-sized blood vessels. Fatty material and cholesterol are deposited inside the lumen of the arteries. The continuing deposition of these plaques cause the lumen to become narrow and the blood flow is limited. Finally, the plaque can rupture and result in the formation of a thrombus. If the thrombus is large enough to block a coronary or a cerebral blood vessel than this results in a heart attack or ischemic stroke.

Another cause of stroke, although it is less frequent, is bleeding (haemorrhage) triggered by a rupture of a blood vessel due to an aneurysm or due to damage from high blood pressure. Also travelling blood clots can cause a stroke (Davis, 2005; WHO, 2011). Ischemic strokes are by far more frequent than haemorrhagic strokes, but this ratio differs by regions. Ischemic strokes account for approximately 80-90 % of all strokes (Andersen et al., 2009; Khaw and Kessler, 2006).

There are two different types of acute myocardial infarctions: non-ST-segment elevation myocardial infarction (NSTEMI or non-STEMI) and ST-segment elevation myocardial infarction (STEMI) referring to the different directions of ST-segment of an electrocardiogram. The ST elevation is due to the entire thickness of the myocardium having undergone necrosis, usually triggered by a total occlusion of the infarct-related artery. A non-occlusive thrombus causes NSTEMI (Kumar and Cannon, 2009a, 2009b), which is more frequent than STEMI. It’s estimated that each year worldwide more than 4 million people have a NSTEMI compared to more than 3 million having an acute STEMI (White and Chew, 2008). The change of the STEMI to NSTEMI ratio (declining STEMI and increasing NSTEMI diagnoses) in the past decades is most likely attributed to the changes in the diagnosis of AMI as well as the amelioration of troponin assays which lead to more diagnoses of NSTEMI instead of unstable angina (McManus et al., 2011; Tisminetzky et al., 2014). Together with unstable angina, STEMI and NSTEMI form the group of acute coronary syndromes (ACS).

1.4.2 Treatment of CVD

Emergency treatment depends on the type of AMI and stroke, the condition of the patient and the time from symptom onset and start of treatment. The earlier the treatment is initiated the more deaths and disability from heart attack and stroke can be prevented (Moser et al., 2006). AMI patients will have the greatest benefit from reperfusion therapy when it is performed within 2-3 hours from symptoms onset (Windecker et al., 2014). Stroke patients treated within 3 hours of stroke onset will have less disability after 3 months than patients with delayed care (Hacke et al., 2004). One component influencing the time to treatment is the travel distance to hospitals. The relationship of mortality from AMI or stroke with the distance to different types of hospital will be investigated in article 4.

In both AMI and stroke emergency treatment, it is of great importance to immediately reduce pain, remove the clot or blockage and prevent further heart attacks or strokes. The European Guidelines for management of acute STEMI patients recommend immediate angiography with primary percutaneous coronary intervention (PCI) if it can be performed in a timely manner (first medical contact to reperfusion therapy ≤ 90 min). Another option is pharmacological reperfusion with fibrinolytic therapy. Although primary PCI should be the primary choice of treatment, according to guidelines, performance of primary PCI is more difficult to implement than fibrinolysis as treatment in PCI-capable hospitals must be available in timely manner. If primary PCI is not possible to perform in time then fibrinolysis should be performed within 30 min of the first medical contact. Another treatment is coronary artery bypass surgery (CABG), which is an open heart surgery and much more invasive than the other two procedures. This procedure is not often performed in the acute phase of STEMI (Steg et al., 2012). In article 2 of the thesis the adherence to the treatment guidelines for STEMI is examined.

The treatment of NSTEMI is dependent on the risk profile of the patient. For low risk patients a conservative strategy (medical management, catheterization, revascularization if necessary) should be chosen, for high risk patients an early invasive strategy (cardiac catheterization, revascularization with PCI or CABG) is the treatment of choice (Hamm et al., 2011).

Ideally, stroke patients should be treated by stroke units, as they provide a reduction in mortality and improve the outcome of stroke in general (European Stroke Organisation Executive Committee, 2008; Steiner et al., 2006). Again, the treatment of ischemic or haemorrhagic stroke patients depends on the condition of the patient. The usual treatment for ischemic stroke is Aspirin given intravenously to prevent blood clots from forming and to prevent future strokes. The gold standard is an intravenous tissue plasminogen activator to break down the clots. Other treatments are mechanical clot removal, angioplasty and stents (European Stroke Organisation Executive Committee, 2008).

In the treatment of haemorrhagic stroke it is extremely important to lower the blood pressure in the brain, which is achieved through the administration of medications. Common treatments for ruptured intracranial aneurysms, a type of haemorrhagic stroke, are neurosurgical clipping and endovascular embolization (coiling) (Molyneux et al., 2002).

As stated previously, AMI and stroke, once they have occurred, are severe diseases and need immediate treatment. However, prevention of these conditions should be the major goal, as the majority of cases are due to modifiable risk factors. Appropriate treatment of known risk factors for AMI and stroke (e.g. hypertension or diabetes) by health care services are necessary for disease prevention, in addition to other interventions such as lifestyle changes.

1.5 Methods and data

In the following paragraphs I will present the study designs and the data sets that were used in this thesis.

1.5.1 Study designs

All study designs presented in this thesis are observational studies. In contrast to experimental studies, the investigator simply observes and does not intervene in observational studies.

Cross-sectional study

Cross-sectional studies measure exposures and outcomes simultaneously, i.e. it is a snapshot of the population's health status at a certain point in time. It is possible to identify prevalent cases, but not incident (new) cases. Therefore, this study design is also called a prevalence study. Cross-sectional studies are relatively easy and cheap to conduct and are often used for health services planning or to determine current health practices. Repeated cross-sectional studies are used to discover changes or trends in the outcome(s) or exposure(s) over time, which makes them ideal for monitoring purposes. Since information on both the exposures and outcomes are collected simultaneously, it is normally not possible to know whether the exposure preceded the outcome. Having no information about the temporal relationship of the exposure and outcome diminishes the possibility to infer causality quite substantially. Nevertheless, cross-sectional studies are used to generate research hypotheses, which then can then be applied to cohort or case-control studies to establish etiologic relationships (Carneiro and Howard, 2011; Gordis, 2009).

Cohort study

The word "cohort" is derived from the Latin word "cohors". One Roman legion consisted of 10 cohorts with a specific number of soldiers who would be traced during the battle (Song and Chung, 2010). The word "cohort" was first introduced into the epidemiology arena in a 1935 publication by Wade Hampton Frost (Doll, 2001; Song and Chung, 2010). The current definition of cohort in epidemiology is a "group of people with defined characteristics who are followed up to determine incidence of, or mortality from, some specific disease, all causes of death, or some other outcome." (Morabia, 2004)

A common characteristic of the study subjects can be their place of work or residence, their age or lifestyle choices (e.g. smoking habits), for example. Cohort studies are normally used to examine one or several common outcomes of interest. It is also possible to use a cohort design to study rare exposures, since the study population is selected by their exposure status. Investigator(s) select an exposed and an unexposed group of individuals who have not yet experienced the outcome of interest to form the study population. Participants are followed over time until the outcome occurs. The incidence of an outcome in the exposed group is then compared with the incidence of the outcome in the unexposed group in order to measure the effect of the exposure on the outcome of interest. The cohort study might include more than two groups (e.g. there may be groups representing no, little, moderate and high exposure). Cohort studies belong to longitudinal study designs which implies conducting several observations of the same subject over a period of time. The advantage is that the investigators can detect the developments or changes in characteristics of the study subjects (Carneiro and Howard, 2011; Gordis, 2009). Due to cohort studies identifying the exposure before the outcome, cohort studies meet the temporality criterion for causality and can therefore provide stronger scientific evidence of causality than cross-sectional studies (Song and Chung, 2010).

Cohort studies can be prospective or retrospective. Prospective cohort studies start, as described above, with the selection of the study population and finishes with the experience of the outcome or the predefined time frame. The disadvantages of this design are that they may be expensive to conduct, due to the large number of people followed over time, and that they often required long durations of follow-up. Furthermore, maintaining follow-up is difficult and loss to follow-up is a serious issue.

For retrospective cohort studies the investigator(s) identifies a historical cohort (e.g. all students of a school at January 1st, 2000) that don't have the outcome at the start date. Historical data is used to obtain the outcome and exposure (e.g. past records of yearly health examinations at school). The advantage of this study design is the reduction of the time required for the study, especially when studying diseases which take decades to develop. Often, routinely collected data are used in a retrospective cohort study and typically these data were not collected for the purpose of the study, and consequently important information about risk factors or confounders are not available (e.g. student was not present at all health examinations) or are of poor quality (e.g. incomplete health examination sheets) which can result in a biased cohort due to selection bias (Carneiro and Howard, 2011; Gordis, 2009; Song and Chung, 2010).

Article 4 of this thesis is presenting the investigation of a possible relationship of the distance to hospital and AMI or stroke mortality using the data of the Swiss National Cohort (SNC).

1.5.2 Data sources

In the following I give an overview of the data sets that were used to conduct the studies described in this thesis. Unlike Scandinavian countries, Switzerland does not have a universal personal identifier that can be used to link different data sets. Nevertheless, by using probabilistic and deterministic linkage techniques, various data sets without unique personal identifiers can be linked e.g. census data and death notifications (see the description of the Swiss National Cohort).

Hospital discharge statistics (medizinische Statistik der Krankenhäuser)

The Swiss Federal Statistical Office (SFSO) started the mandatory collection of hospital discharge statistics from all Swiss hospitals in 1998. This data is used to monitor the incidence and prevalence of the most important diseases, to provide basic medical data to investigate inter-cantonal care structures and to provide a data set for researchers and the public. Every record in the data set represents a hospitalisation and contains around 50 variables to describe the patient's characteristics (e.g. age, gender, and residential region called MedStat, see section 1.6.3) as well as information on where the patient was before admission (home, another hospital, nursing home, etc.), whether it was an emergency admission, how many hours the patient spent in an intensive care unit as well as the main diagnoses and comorbidities using ICD-10 codes (International Classification of Diseases, Injuries and Causes of Death, version 10), and the description of the treatment using CHOP codes (Swiss operation procedure code). Updated coding guidelines are published regularly, describing the procedure of the diagnosis and treatment coding. Before releasing the data to researchers, the hospital creates an encrypted and anonymous patient id using the patient's first name, surname, gender and date of birth. The hospitals send the data to the cantons, which are responsible for cleaning and checking the data. The cantons then transfer the data to the SFSO. The encrypted id enables the SFSO to identify the patient in different hospitals and over the years. Patients cannot be identified as a specific individual in the population (e.g. by name) through data in the SFSO.

Hospital statistics (Krankenhausstatistik)

Since 1997, all hospitals are obligated to send information about their technical infrastructure, staff and their ambulant and inpatient activities to the SFSO. For instance, they have to provide information about the type of hospital, number of CT scanners, MRI and angiography devices, number of beds, number of employees, their training and level of employment, number of discharges, finances and costs.

The hospital discharge and hospital statistics are used by the cantons for their health care planning and delivery of health services. The SFSO uses the data to inform the public about the health status of the population or trends in disease incidence. Research institutes also have access to the data, although not in the same detail as, for example, the cantons.

Hospital list of the Federal Office for Health (FOH)

The Federal Office for Health publishes key figures of all Swiss hospitals every year including their structure, staff, services, patients' characteristics and financial situation. This key figures data set is based on the hospital discharge statistics and the hospital statistics, but presents only a limited number of variables. Additionally, the addresses of the hospitals are provided in the dataset. Unfortunately, this list of addresses is not complete as companies that have several hospital locations report cumulated data for all their locations and only the address of the headquarters is stated. Therefore, I used data from the Federal Office of Topography (swisstopo) and TomTom to add the missing hospital locations.

The Swiss National Cohort (SNC)

The Swiss National Cohort, established in 2005, is an ongoing longitudinal study, based on census data from 1990 and 2000 on the resident population of Switzerland. Data from 6.87 million individuals from the 1990 census and 7.29 million individuals from the 2000 census are included. These data were linked to mortality and emigration records up to 2008 resulting in 1,052,527 linked deaths (see figure 1) (Spoerri et al., 2010).

Since 1850 censuses were conducted every ten years using questionnaires delivered to all residents of Switzerland. The census consists of three questionnaires to survey several variables: one for each person (for instance: date of birth, gender, marital status, citizenship, education, religious affiliation, number of children, languages, current employment situation, means of transport), one for each household (for instance: number of rooms, number of persons in the household) and for each building filled in by the owner of the building (for instance: type of building, number of floors, heating system, price of rent). The building questionnaires could then be linked to the federal registry of buildings which provided the geographical coordinates of each building. The dataset of the 2000 census includes 172 variables for each individual, 204 variables on household and 48 on building level (Spoerri et al., 2010).

The cause of death statistics have been collected in Switzerland since 1876 (Bundesamt für Statistik, 1996). The cause of death is coded according to the ICD (ICD-8 until 1994, ICD-10 since 1995). Aside from the cause of death, death certifications also record information on date of birth, gender, marital status, the place of residence and religion. The aim of the SNC is to examine all-cause and cause-specific mortality according to socioeconomic determinants.

Due to the lack of a unique person identifier and the anonymous death registration in Switzerland, the linkage used a combination of deterministic and probabilistic methods based on sex, gender, date of birth, marital status, nationality, religion and place of residence. For the linkage procedure the Generalized Record Linkage System package developed by Statistics Canada was used (Fair, 2004). Results of a pilot study in the canton of Zurich indicated that the linkage can be improved by including emigration records as well (Bopp and Gutzwiller, 2000).

Of the 1,122,376 deaths recorded in the mortality statistics, 93.8% could be linked to a census record from 1990 or 2000. The main characteristics of the unlinked deaths were: young (10-29 years), no Swiss nationality, female and single. Furthermore, 6.9% of the persons registered in the 1990 census couldn't be linked to a mortality, emigration or 2000 census record. The majority of these unlinked records are related to young individuals (10-29 years), which most likely refers to their higher mobility and residence in large cities (Spoerri et al., 2010) (see figure 1).

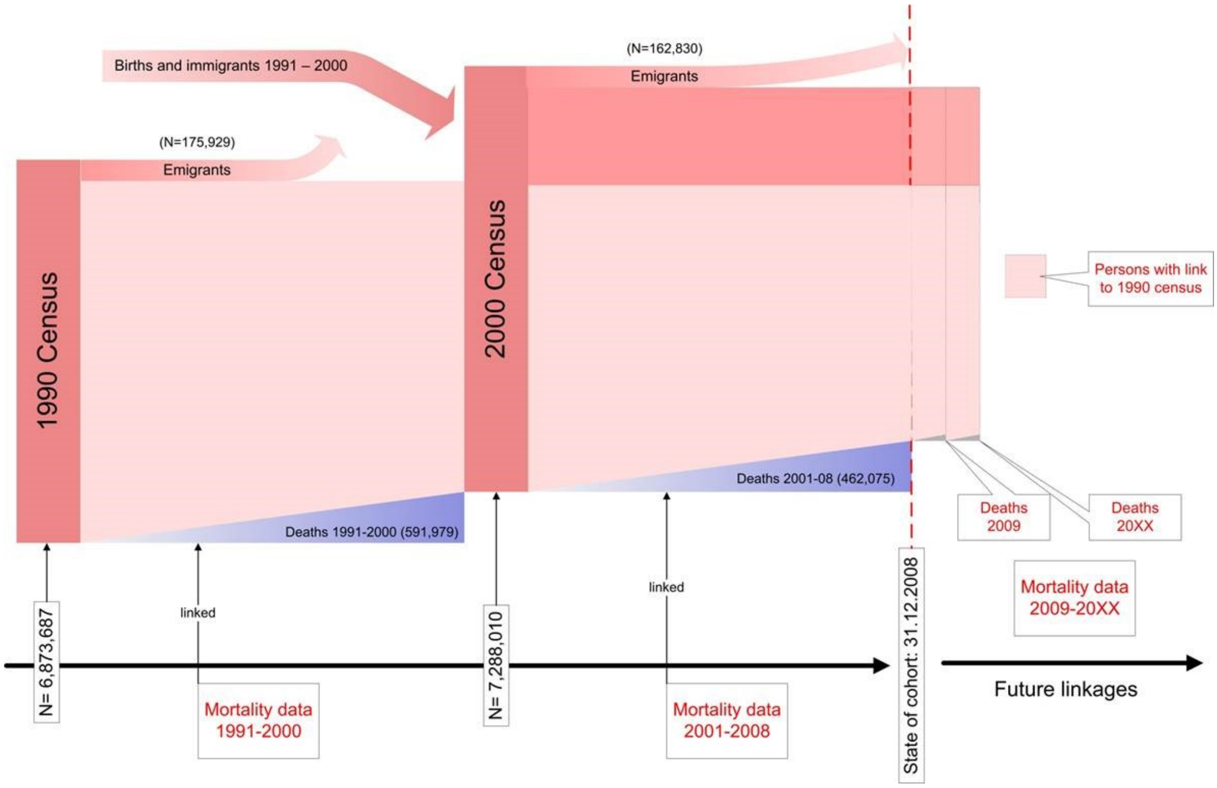

Figure 1: Structure of the Swiss National Cohort from Spoerri et al 2010.

The accuracy of the official mortality records differ according to the cause of death. Well-defined diagnoses are better reported than less well-defined diagnoses. The quality should be satisfactory for malignant neoplasms, cerebrovascular disease, ischemic heart disease and accidents, whereas for diseases of the nervous system, chronic respiratory diseases and other forms of heart disease the accuracy of the death certificates are less reliable (Bopp et al., 2009).

Another limitation is the lack of information about the income, capital or other assets of the individuals (Spoerri et al., 2010). Nevertheless, Panczak et al. were able to develop the Swiss neighborhood socioeconomic position index (SEP) based on the census data using the variables median rent, education and occupation of household heads and household crowding (Panczak et al., 2012). The development of the SEP broadened the possibility for subsequent studies to include the socioeconomic position of the neighborhood of the individual.

Similar to other countries, the census procedure has changed in Switzerland. Since 2010 the census is conducted every year using the data from registries (county and cantonal resident registries, federal registry of buildings) instead of sending questionnaires to the entire population. Just 5% of the residents have been interviewed in written or oral form each year to add information that is not recorded in the registries (e.g. work, mobility, education, language etc.). The registry data, the micro survey as well as the death and emigration records will be linked with each other and added to the current SNC data (BFS 2011).

The study design of the SNC is described in detail by Bopp et al and Spoerri et al (Bopp et al., 2009; Spoerri et al., 2010). Further information (e.g. the census questionnaires) can also find here: www.swissnationalcohort.ch. In article 4 of this thesis I used the SNC from 2000 to 2008 to examine the effect of distance to hospital on mortality due to AMI and stroke.

Additional data

In addition to the major data sets presented above, additional data that were used in this thesis were:

- SFSO census data from 2010, number of persons per community stratified by age and gender (SHAPE project)
- Community classification data set from the SFSO (Raumgliederung)
- A list of physicians and their specialisation, sector of employment (ambulatory, stationary, other), and postcode, from the Swiss Medical association
- Billing records of dead persons insured 12 months before their death from 6 major Swiss health insurances

1.6 Geographical units and their spatial congruence

Having several data sets with different geographical reference units (e.g. administrative areas, postcodes) is challenging, especially when they are not congruent with each other or change over time. In the following I give an overview and description of all used geographical units and how they relate to each other.

Communities

Communities are the smallest administrative units in Switzerland and are the basis of higher-level administrative units (districts, canton), regional planning regions and analytic regions (e.g. language regions, commuter regions, urban or rural classification). Community borders and numbers change as communities frequently merge, separate or otherwise restructure (reference date 31.12.2010: 2584 communities; reference date 31.12.2015: 2324 communities) (SFSO, 2016a).

Postcodes

A Swiss postcode is a series of four digits used in the address for the purpose of sorting mail. Normally, they are referring to a specific geographical area. There are also postcodes assigned to individual addresses or institutions. Postcodes are assigned by the Swiss Post and are subject to changes (implementation of new or abolition of old postcodes) due to population decrease or increase. Since postcodes are assigned independently of the community administrative units, they may not map perfectly to one another. As of 1st August 2015, there were 3,199 postcodes in Switzerland and 2,324 communities. Around 60% of these 3,199 postcodes mapped to one community or part of one community only. The remaining postcodes areas belonged to more than one community (see figure 2) (SFSO, 2015b; Swisstopo, 2016).

MedStat

The 705 Swiss MedStat regions are used in the hospital discharge and hospital statistics to determine the geographical region of the patients' place of residence and the location of the hospital. They were developed to prevent the identification of persons with rare diseases. MedStat regions consist of aggregated postcode areas resulting in more or less the same number of inhabitants per MedStat. Because postcodes are changing, the SFSO publishes a new table each year determining which postcode belongs to which MedStat region. The hospitals have to incorporate this updated list into their hospital information system to assign the patient to the correct MedStat region (SFSO, 2016b). In the article about avoidable hospitalisations we used the term aggregated zip-code areas instead of MedStat regions (see article 1).

In 2008, the SFSO changed the formation of the MedStat regions, i.e. different postcodes to before were aggregated to new MedStat regions. Old names were used for new regions at new locations. The new MedStat regions are not compatible with MedStat regions before 2008. Unfortunately, my investigations showed that not all hospitals updated the postcode-MedStat list instantly but one or two years later. Consequently, we found huge variation in the number of hospitalisations per MedStat region in the hospital discharge statistics from 2008 to 2010 due to the wrong assignment of the MedStat region (Berlin et al., 2014b). Therefore, we decided to exclude 6 cantons from the analysis of the study of avoidable hospitalisations (see article 1) (Berlin et al., 2014a), changed the focus from small area analysis in the treatment article to the difference between the volume of cases of hospitals (see article 2) and limited our analysis in the end of life and treatment articles to the data from 2010 and/or 2011 (see article 2 and 3).

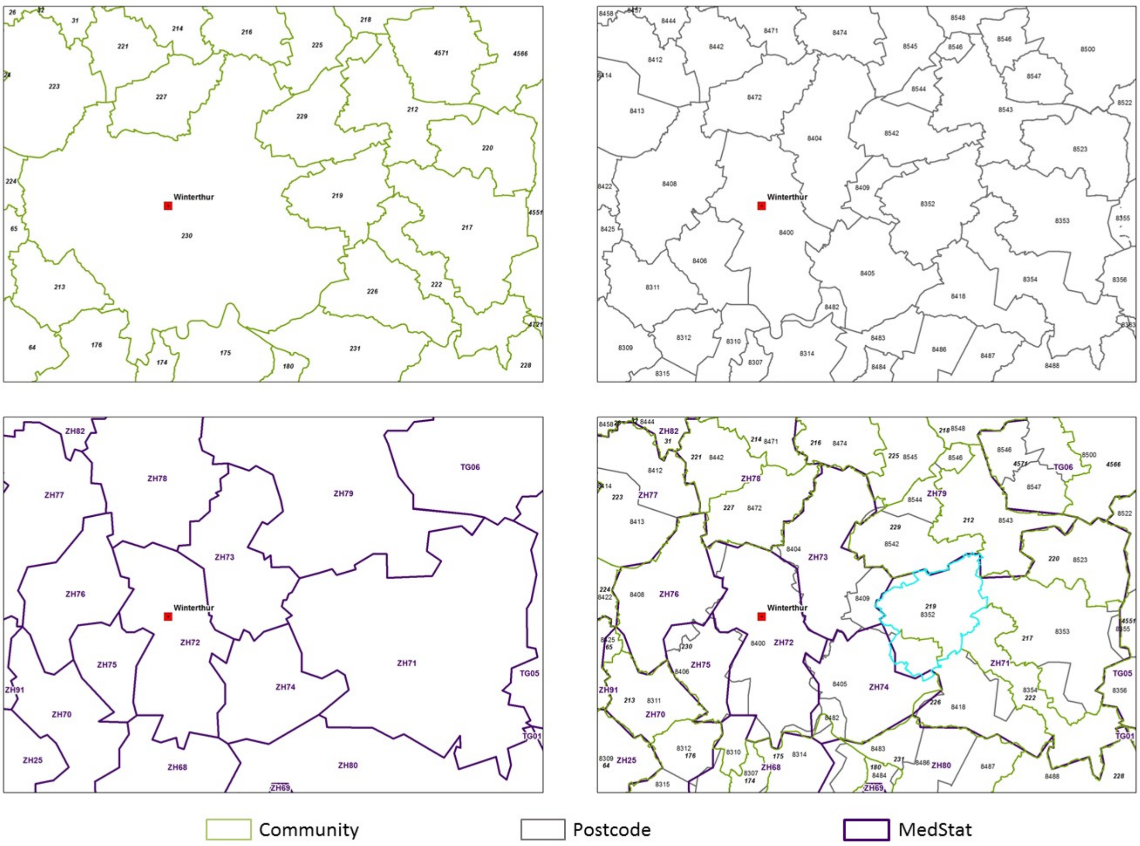

Figure 2: Communities, postcodes and MedStat regions and their spatial congruence. The four maps presenting the same geographical extent of the area around the city Winterthur.

Hospital service areas

Hospital service areas (HSAs) are created on the basis of the hospital discharge statistics and represent utilisation-based areas. HSAs were constructed by cross-tabulating the sum of the discharges of every MedStat region of the patients to the MedStat region of all possible hospitals. The hospital MedStat region with the highest number of discharges from a specific residential MedStat region was the main hospital provider region for the population of that particular residential MedStat region. Some assignments had to be adjusted manually e.g. when the patients went to two or more hospital regions equally often, i.e. the number of discharges was almost similar.

In summary, one HSA consists of one or more MedStat regions and can also be seen as the major catchment area of the hospitals. In areas with a low hospital density the HSAs can be geographically large. It is also possible to construct disease-specific HSAs by only using the discharges with this specific disease. More details about the construction of HSAs is described elsewhere (Klauss et al., 2005; Wennberg and Gittelsohn, 1973). Hospital service areas may also be called health service areas, as we did in article 1.

Geographical coordinates

The Swiss building and flat register (www.housing-stat.ch) provides, besides other variables, the geographical coordinates of all buildings used for living. The data of the registry were linked to the census data of 2000 and are therefore also included in the SNC data set.

1.7 Objective of this thesis

The overall aim of this thesis is to make a substantial contribution to the investigation of the determinants of regional variation in CVD health care and mortality in Switzerland.

Specific objectives included:

1) To examine regional variation in avoidable hospitalisations and to identify factors that affect them, such as medical resources, reimbursement systems or rurality (Article 1).
2) To analyze differences in evidence-based treatment of STEMI cases by hospital volume (Article 2).
3) To investigate the variation in costs for end-of-life care and detect the factors influencing the variation across regions (Article 3).
4) To explore the influence of distance from place of residence to different hospital types on AMI and stroke mortality (Article 4).

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2 Manuscripts

2.1 Article 1: Avoidable hospitalisations

Title:

Avoidable hospitalizations in Switzerland: a small area analysis on regional variation, density of physicians, hospital supply and rurality

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RESEARCH ARTICLE Open Access

Avoidable hospitalizations in Switzerland: a small area analysis on regional variation, density of physicians, hospital supply and rurality

Claudia Berlin[1], André Busato[1,2^], Thomas Rosemann[2], Sima Djalali[2] and Maud Maessen[1*]

Abstract

Background: Avoidable hospitalizations (AH) are hospital admissions for diseases and conditions that could have been prevented by appropriate ambulatory care. We examine regional variation of AH in Switzerland and the factors that determine AH.

Methods: We used hospital service areas, and data from 2008–2010 hospital discharges in Switzerland to examine regional variation in AH. Age and sex standardized AH were the outcome variable, and year of admission, primary care physician density, medical specialist density, rurality, hospital bed density and type of hospital reimbursement system were explanatory variables in our multilevel poisson regression.

Results: Regional differences in AH were as high as 12-fold. Poisson regression showed significant increase of all AH over time. There was a significantly lower rate of all AH in areas with more primary care physicians. Rates increased in areas with more specialists. Rates of all AH also increased where the proportion of residences in rural communities increased. Regional hospital capacity and type of hospital reimbursement did not have significant associations. Inconsistent patterns of significant determinants were found for disease specific analyses.

Conclusion: The identification of regions with high and low AH rates is a starting point for future studies on unwarranted medical procedures, and may help to reduce their incidence. AH have complex multifactorial origins and this study demonstrates that rurality and physician density are relevant determinants. The results are helpful to improve the performance of the outpatient sector with emphasis on local context. Rural and urban differences in health care delivery remain a cause of concern in Switzerland.

Keywords: Ambulatory care, Health services, Small area variation analysis, Hospitalization

Background

Increasing utilization and rising health care costs threaten the financial sustainability of many western health care systems. Governments and researchers have a growing interest in identifying ineffective and unnecessary health care. Avoidable hospitalizations (AH), also referred to as hospitalizations for ambulatory care sensitive conditions (ACSC) are hospital admissions for diseases and conditions that might have been avoided if better ambulatory care were available [1]. AH are indicators of access and quality of ambulatory care and have been used to monitor health system performance in several countries, including the United States, Canada, Brazil, several European countries, New Zealand and Australia [2-11]. Comparisons between countries that show AH rates for different health care systems may point out strengths and weaknesses of each system.

Structural deficits of care provision such as inequitable access across different societal groups, e.g. urban rural differences, racial and ethnic minorities or different levels of health insurance coverage were identified mainly in the US literature as important predictors of AH's [12,13]; but AH can also be seen as an indicator of process quality resulting in medical procedures not warranted by effective needs [14]. We are in favor of this process based view as it seems to be more relevant for the Swiss health system

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which is characterized by high density of supply and generally unlimited access to care [15].

For Switzerland, comprehensive data on AH in different regions and its causal factors are currently unavailable [11]. Switzerland is an interesting country to study AH, because it spends more on health care per capita (5270 USD) than any other country except the United States (8233 USD) and Norway (5388 USD) [16]. Switzerland is also an OECD country with among the highest per capita availability of physicians and nurses and it has one of the world's highest life expectancies [17].

Health care services in Switzerland are reimbursed by private insurances with compulsory basic health plans that cover a comprehensive catalogue of goods and services for all Swiss inhabitants. There are practically no uninsured patients and limited access to health care is rarely a factor in AH. However, Swiss health care is also characterized by considerable fragmentation due to cantonal autonomy [18] and heterogeneity regarding the distribution of physicians, hospitals and medical facilities, so regional variation of AH rates is to be expected. This project was initiated by the Swiss Federal Office of Public Health (SFOPH) with the goal of documenting regional variation in AH, and identifying relevant determinants of AH rates in Switzerland.

Methods

Design of the study

The study is designed as a retrospective analysis of all hospitalizations in Switzerland for the years 2008–2010. In 2002, the OECD initiated the Health Care Quality Indicator Project to measure and compare the quality of health care provision across countries and to develop a set of health care quality indicators [15,19,20]. Within this framework, the OECD uses AH as a measure of quality for prevention and management of chronic diseases in primary care. For comparability reasons, these indicators, including hospitalizations with a principal ICD10 code of asthma, chronic obstructive pulmonary disease (COPD), diabetes complications, congestive heart failure (CHF), and hypertension [19], are used to define AH for this study. Based on OECD eligibility criteria, we included only patients aged 15 and up (15+) and patients not transferred from other hospitals. Detailed ICD codes and additional information on inclusion and exclusion criteria of these conditions as defined by the OECD are given in the Additional file 1.

Data

We used data from multiple sources. Inpatient care data, including patient demographics, regional data of patient residency, characteristics of hospitalizations (length of stay, type of discharge, referral pathways, health insurance status) and diagnostic and treatment data (ICD10, procedure codes and All Patient Diagnosis Related Groups (APDRG's)) were extracted from the "Medizinische Statistik der Krankenhäuser", housed at the Swiss Federal Statistical Office (SFSO) [21]. These data cover all hospitalizations of acute care hospitals in Switzerland. One patient can be hospitalised multiple times (multiple cases). Anonymized unique patient identifiers allow tracking patients across hospitals in case of multiple hospitalizations. Data on structural attributes of acute care hospitals (localization, type, size and specialization of hospitals) are also available from the SFSO (Krankenhausstatistik).

Demographic data at the community level, including age and gender distribution, were available from the SFSO (census data) [22]. In 2010, a new federal population census was introduced by the SFSO (SHAPE project) and the population aged 15+ was used to build the denominator to calculate regional rates of AH for 2010. SHAPE data were also used to directly standardize rates by sex and age groups.

Geographic unit

Utilization-based health service areas (HSA) of acute care hospitals were the unit of geographic analyses. HSA's were constructed by analysing discharge data of all acute care hospitals in Switzerland for the period of 2008–2010 [23,24]. We used HSA's and aggregated zip-code areas of patient residence as the smallest geographic unit (MedStat areas). HSA's were constructed by cross-tabulating the sum of discharges of every zip-code cluster with all possible hospital regions, and then these regions were merged into an HSA by assigning to the hospital region in which the highest number of patients were treated [25]. Using HSA's has the advantage of describing where patients actually receive care, without regard to cantonal or other administrative borders [21,23,24,26,27]. This approach is well established and has become an indispensable source of information for current US healthcare reformers [28].

In 2008, the SFSO modified the concept of MedStat areas to make them compatible with other geographic classification systems. However, these changes were not equally implemented in the data collection procedures of all Swiss cantons during the course of the study. In consequence, geographic classification of hospitals and of patient residence was inconsistent in some cantons. Data from cantons Appenzell Innerrhoden, Appenzell Ausserrhoden, Schaffhausen, St. Gallen, Thurgau and Zurich were therefore discarded from the small area analysis.

Statistical procedures

All hospitalizations corresponding to the list of AH published by the OECD were included [15]. Statistical analysis of the data was performed in two steps. The first included a descriptive nationwide analysis of AH; the second step identified determinants of regional differences of AH-rates in cantons with eligible data. Descriptive procedures documented overall rates, demographic characteristics, comorbid conditions of patients (Charlson index [29]), length of stay, APDRG cost-weights, and inpatient mortality of all AH in Switzerland. APDRG cost weights that accounted for outliers of length of stay were calculated according to version 6.0 of the specifications of APDRG-Suisse [30].

Regional rates of AH were calculated at the level of zip-code clusters; the number of AH admittances in the numerator and the total regional population aged 15+ were the denominator. Direct standardization of rates by sex and age was performed at the level of zip-code clusters and used the total 15+ Swiss population of 2010 as the reference.

For geographic analyses we summarized the data at two levels (utilization-based health service areas [n = 59] and aggregated zip-code clusters [n = 436]) and developed statistical models to explore the relationship between rates of AH and characteristics of regional supply of medical care. For each zip code cluster, we determined the density of primary care physicians and of specialists in own practice (physicians per 10000 population). Physician groups were defined based on definitions established by the Swiss Medical association [31]. We also calculated the proportion of the population living in rural communities [32]. At the level of HSA's we calculated the number of acute care hospital beds per 10000 people as a measure of regional hospital supply.

We used a multilevel poisson regression model with the natural logarithm of the age and sex standardized number of AH as the outcome. We used the log number of the population of zip-code clusters as a fixed offset term in the regression equation. We added information on regional supply of ambulatory care and of population characteristics at the level of zip-code clusters, and added predictors at the level of HSA to estimate effects related to hospital supply. The final set of explanatory variables was obtained after a series of preliminary analyses that explored bivariate associations between the outcome and various measures of physician's supply, including full time equivalents, and other methods to classify patient residency geographically. We eventually included explanatory variables which explained the largest variability of AH admissions.

These are the explanatory variables included in the final model:

Level 1 (436 zip code areas)
- Year (2008, 2009, 2010)
- Number of primary care physicians per 10000 population
- Number of specialists per 10000 population (all medical specialists with office based practice)
- Proportion of the population living in rural areas
- Type of hospital reimbursement system (APDRG vs. other systems)

Level 2 (59 utilization based health service areas)
- Number of hospital beds per 10000 population

We added random intercepts at the level of HSA's and zip-code clusters to allow for unexplained variation around the respective means. We used the same model to analyse effects associated with the overall rate, and for condition specific rates of AH's. In order to explore linear relationships between continuous explanatory variables and AH, we additionally defined a second model and replaced the continuous data with quintiles of the respective variables. Differences to the first quintile were documented as incidence risk ratios. SAS 9.3 (proc GLIMMIX) was used for multilevel modeling and ArcGis 10 to create maps, the level of significance was set to $p < 0.05$ throughout the study.

Results

Characteristics of avoidable hospitalizations

For 2008–2010, 3470812 hospitalizations of patients were documented in the discharge data of the "Medizinische Statistik der Krankenhäuser". Of these, 92804 hospitalizations fulfilled the OECD inclusion criteria and had an ICD10 diagnose that corresponded with a AH. The overall rate of AH for the 15+ population during this period was 467 hospitalizations per 100000. The respective rates were 455 for women and 483 for men. From 2008 to 2010, we observed an increase of 2.7%. Annual rates for 2008–2010 were 463, 467 and 476 per 100000. In 2010, AH accounted for 3.1% of all hospital stays (n = 31805) and generated 180–200 Mio CHF of direct hospital costs (depending on annual cantonal APDRG base rates). The proportion of patients with additional health insurance in the study population was 15.2% — slightly below the Swiss average of 16.6% of all hospitalized patients. 74.3% of the AH were classified as emergencies, i.e. with a need for treatment within 12 hours, and 11.8% of patients were re-hospitalized within 3 months. On average, patients with a rehospitalization had 2.7 hospitalizations during the study period (2.3 for hypertension, 2.6 for Asthma, CHF and Diabetes and 3.0 for COPD). Inpatient mortality of AH was 5.1%. Characteristics of disease specific AH are given in Table 1.

Hospital characteristics

We used the specification of the SFSO to categorize hospitals into five hospital groups based on annual number of all hospitalizations. Characteristics of AH across these groups are given in Table 2. It is important to note the differences between low-volume clinics, usually located in

Table 1 Major characteristics of avoidable hospitalizations across ICD10 groups in Switzerland 2008-2010

ICD10 Group	Rate*	Avg. age of patients	Avg. length of stay (days)	Emergency admissions	In-hospital deaths	3-month Rehospitalization§
Asthma	18.6	54.1	6.8	84.0%	0.5%	5.6%
CHF†	211.0	78.8	12.2	78.1%	9.0%	11.5%
COPD‡	110.0	71.3	11.3	73.7%	3.6%	14.9%
Diabetes	70.7	62.6	12.2	63.7%	1.0%	7.5%
Hypertension	58.3	70.1	6.3	71.4%	0.4%	3.5%
All Avoidable hospitalizations	468.6	72.5	11.0	74.3%	5.1%	10.4%

*Rate per 100000 total population.
†Congestive heart failure.
‡Chronic obstructive pulmonary disease.
§Percentage of patient rehospitalized within 3 months after the initial hospitalization.

peripheral areas, and high volume clinics, located in urban areas. There was almost twice the proportion of AH in low-volume clinics (4% vs. 2%); average length of stay was six days longer; patients were older; and, in-hospital mortality was higher. In high volume clinics, APDRG cost-weights per case were almost double those of low volume clinics.

Regional differences

The 59 HSA's included in the study covered 87.0% of the area of Switzerland and 69.2% of the Swiss population in 2010. Key characteristics of these areas are given in Table 3. Depending on year, we observed up to 12-fold regional differences of age and sex standardized rates of AH across HSA's. As an example, geographic patterns are documented for 2010 in Figure 1. The three year averages of AH rates of HSA's showed only a 3.6-fold regional variation (range: 274–982 admittances per 100000 population). Rate ratios to the mean of the three year averages were used to document the regional variation of AH across disease groups (Figure 2). This data implies particularly high levels of variation for asthma and hypertension and less variation for congestive heart failure, COPD and diabetes.

The results of multilevel modelling are summarized in Table 4. The data show a significant increase in all AH over time, and significantly lower rates for all AH areas with more primary care physicians. Rates were increased in areas with more specialists, and also increased rates in areas with a higher proportion of rural residents. There was an insignificant association of all AH for regional hospital capacity (hospital beds per 10000 population) and for type of hospital reimbursement (APDRG vs. other). Quintiles of supply and population data show a 0.91 times lower incidence of AH in areas with more than 8.1 primary care physicians per 10000 compared to areas with less than 3.8 physicians ($p < 0.05$); there was a 1.15 times higher incidence in areas with more than 4.2 specialists in comparison to areas with zero specialists ($p < 0.05$) and a 1.12 times greater incidence in areas where more than 42% of the population lived in rural communities (reference: areas with zero rural residents, $p < 0.05$) (Table 4).

Inconsistent patterns of significant incidence ratios across different disease groups were observed for regional care supply. For asthma, a higher number of primary care physicians was partially associated with fewer AH, but increased rates of AH were observed for diabetic patients in areas with more primary care physicians. We observed more consistent significant associations of AH with regional specialist supply; higher supply was associated with higher rates irrespective of disease group. Inconsistent and

Table 2 Characteristics of avoidable hospitalizations across different acute care hospital groups

Hospital group*	% avoidable hospitalizations† (%)	Patient age (mean)	Length of stay (days)	Charlson index (mean)	Cost weights‡ (mean)	3-month Rehospitalization (%)	In-hospital Mortality (%)
Centrally provided treatments 1 (>30'000 admittances/year)	2.1	68.2	10.5	0.23	2.33	9.8%	4.1%
Centrally provided treatments 2 (9'000-30'000 admittances/year)	2.9	73.0	10.6	0.29	1.12	9.8%	5.5%
Basic care 1 (6'000-9'000 admittances/year)	3.0	70.8	10.0	0.31	1.14	9.4%	5.1%
Basic care 2 (3'000-6'000 admittances/year)	2.2	70.4	10.8	0.21	1.29	10.0%	4.2%
Basic care 3 (<3000 admittances/year)	4.0	74.0	16.8	0.20	1.26	13.2%	6.3%

*Based on definitions of the Swiss Federal Statistical office.
†Proportion of avoidable hospitalizations among all hospitalizations.
‡Average APDRG cost weights per avoidable hospitalization.

Table 3 Regional variation, characteristics of 59 health service areas (averages of 2008–2010)

Characteristic	Average	Min	Max	HILO ratio‡
Population size	94301	1614	507789	314.6
Population density*	303.4	26.4	1863.0	70.6
Number of hospitals	2.4	1	12	12.0
Hospital beds per 10000	41.1	13.5	414.0	30.7
Primary care physicians per 10000	6.5	1.9	10.9	5.7
Specialists per 10000	2.1	0.0	6.2	?
-Rate of avoidable hospitalizations†				
- Asthma	21.5	2.2	79.5	36.1
- congestive heart failure	236.2	146.0	569.2	3.9
- COPD	122.0	55.4	252.9	4.6
- Diabetes	74.1	30.4	136.3	4.5
- Hypertension	59.9	18.4	207.0	11.3
- all ICD10 groups	495.2	274.5	982.4	3.6

*Population per km^2 surface below 2000 meters altitude.
†Age and sex standardized rate per 100000 population.
‡Ratio of highest vs. lowest values.

partially non-linear relationships across disease groups were also seen for significant associations of AH with more rural populations (Table 4).

Discussion

Our study highlights up to 12-fold regional differences of AH over a period of three years. Research on medical practice variation shows that regional differences of this extent are mainly associated with the medical care system including provider factors and less to regional variation in the incidence of the underlying disease categories [8,9,33]. Comparative data across countries for avoidable hospitalizations are available from the OECD for Asthma, COPD and uncontrolled diabetes [17]. These data show low overall rates of avoidable hospitalizations for all three conditions in Switzerland implying a high quality of primary care. However, patterns of variation observed in our data point to difficulties of the Swiss health system to provide effective and equitable medical care to all societal groups.

Theoretically, hospital admissions for ACSC can be prevented by effective ambulatory care, irrespective of disease prevalence. However in practice, even the best ambulatory care may not be able to prevent these hospitalizations. Some factors are beyond the scope of ambulatory care providers, for example: different propensity of patients to seek care; advanced stage and complexity of some conditions; lack of compliance with preventive measures; financial constraints; and, poor access to transportation. To some degree, regional differences of AH rates will continue to reflect differences in prevalence of the underlying disease. However, studies which took regional variation of health status into account still found an independent association between AH and care supply [34,35]. It is therefore unlikely that adjacent geographical areas have a high enough difference in prevalence to produce up to 12-fold regional differences of AH. Our results also showed that, irrespective of condition, the majority of

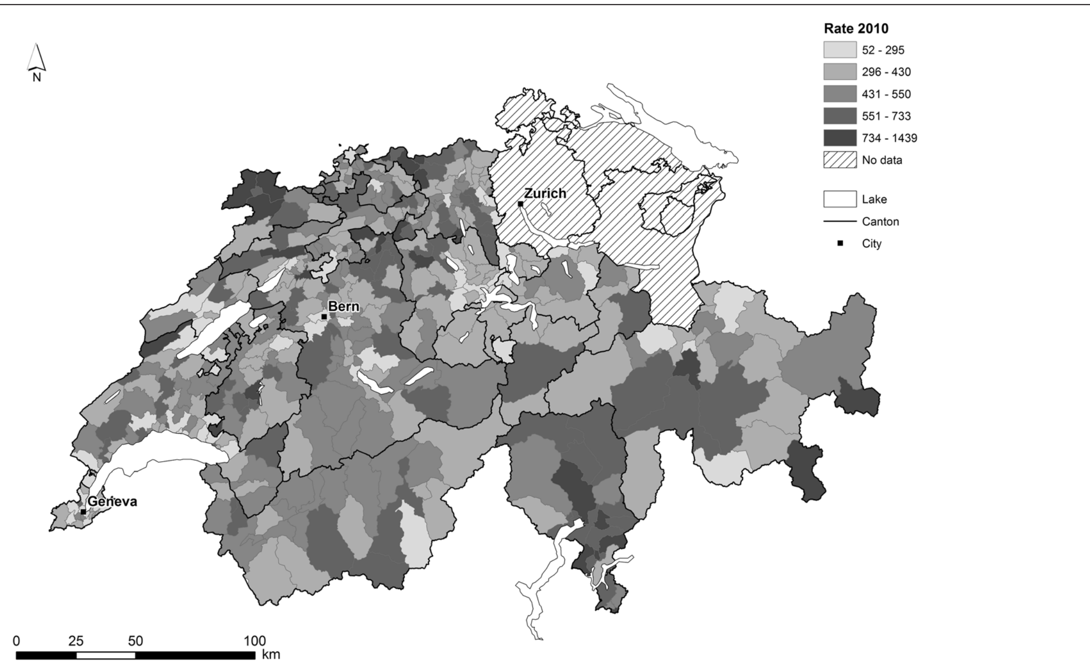

Figure 1 **Age and sex standardized rates per 100000 inhabitants of avoidable hospitalizations for 2010 of 436 zip-code clusters.**

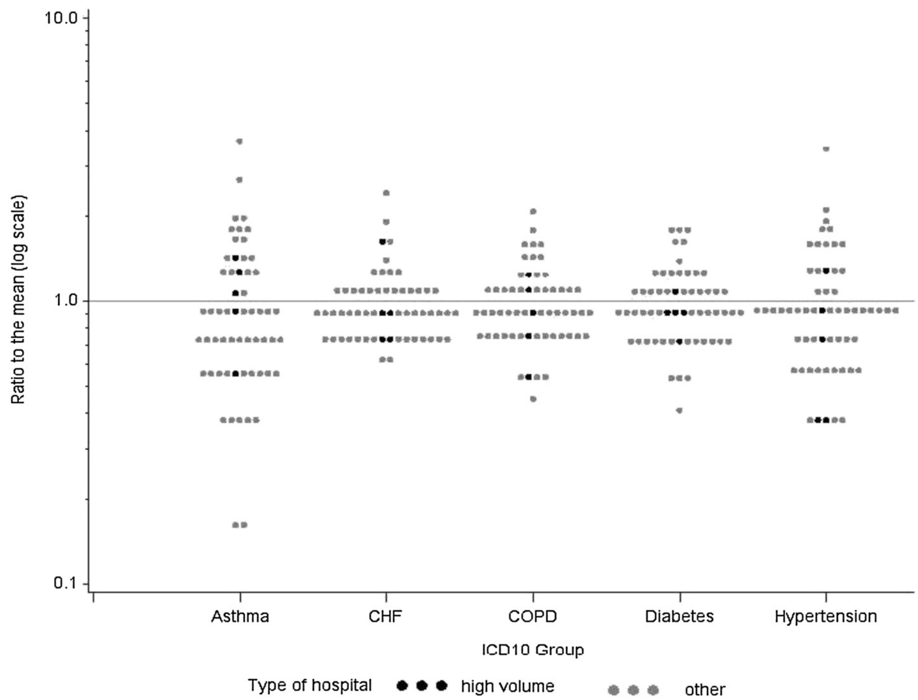

Figure 2 Regional variation (59 HSA's) of disease specific avoidable hospitalization rates*. *Each dot represents a HSA, rates are plotted as a ratio to the mean on a log scale. black dots denote HSA's with at least on high volume clinic.

AH were categorized as emergencies. These findings may raise questions about how avoidable these hospitalizations are, but they may also suggest inappropriate use of costly emergency services and indicate non-optimal quality and efficacy of outpatient care in Switzerland. Our data allow no further analysis of potential causes of emergency admissions as the data obtained from the Federal Statistical Office contain no variables on type of physicians referring patients to a hospital.

Characteristics of supply

Regional variation in the data suggest distinct differences between the decisions of primary care physicians and specialists to admit patients to hospitals, even demographic characteristics of patients and higher rates of AH in predominantly rural populations are both accounted for. An explanation of the patterns would require further comparison of physician practice styles. Risk ratios show that patients living in areas with a high density of primary care physicians are less likely to be admitted to hospitals for conditions that can be treated in ambulatory care. But it is important to note that we observed mostly non-linear relationships between AH and primary care supply. Our results show that AH can only be reduced in areas with very high density of primary care physicians. We also found differences across major disease groups indicating that primary care physicians may have varying ability to treat health problems and to prevent exacerbations, depending on the conditions they treat.

Our general findings are consistent with multiple studies performed in many countries, with a variety of health care delivery systems [35-37]. The data highlight the importance of primary care as an effective first-contact access to health care irrespective of the characteristics of the health system in which care takes place.

In contrast to the data on primary care physicians, we observed a consistent pattern of higher risks of AH in areas with a high density of specialists who work in own practices. Specialist practices in Switzerland are almost exclusively located near hospitals (not shown). We cannot confirm other research that established an association between AH and regional hospital beds supply [38]. Our findings suggest that primary care physicians and specialists have different priorities when they refer patients to hospitals, irrespective of regional hospital capacity.

It may be that specialists are treating more patients with more severe conditions which are more likely to require hospitalization. Our analyses, however, used age and sex standardized population-based rates on a small area scale as an outcome, and it is unlikely that populations in areas with high specialist density are characterized by a higher burden of disease. Specialists working in own practice are often affiliated with local hospitals

Table 4 Incidence rate ratios of health system characteristics associated with avoidable hospitalizations

Characteristic	All avoidable hospitalizations	Asthma	CHF	COPD	Diabetes	Hypertension
Intercept	0.005*	0.000*	0.002*	0.001*	0.001*	0.001*
Year 2008†	-	-	-	-	-	-
Year 2009	1.155*	0.979	0.923*	1.011	0.954	1.066*
Year 2010	1.168*	1.105*	0.940*	1.042*	0.904*	1.016
Primary care physicians per 10000	0.986*	0.989	0.998	1.006	1.015*	1.003
Q1‡	-	-	-	-	-	-
Q2	1.033	0.827*	1.060	1.043	1.174*	1.064
Q3	1.028	0.819*	0.996	1.049	1.152*	1.043
Q4	1.043	0.769*	1.021	1.046	1.132*	1.065
Q5	0.905*	0.883	1.002	1.029	1.189*	1.020
Specialists per 10000	1.017*	1.048*	1.017*	1.017*	1.019*	1.013
Q1‡	-	-	-	-	-	-
Q2	1.019	1.162	0.961	0.996	1.073	1.018
Q3	1.066*	1.044	1.008	1.031	1.126*	0.985
Q4	1.067*	1.262*	1.040	1.101*	1.063	1.005
Q5	1.152*	1.330*	1.132*	1.125*	1.162*	1.131
Proportion of residents in rural communities	1.113*	0.799	1.207*	1.061	0.981	0.888
Q1‡	-	-	-	-	-	-
Q2	0.987	0.918	1.023	0.895*	0.999	0.887
Q3	1.038	0.842	1.044	1.148*	0.990	0.967
Q4	1.037	0.771*	1.047	1.006	1.055	0.972
Q5	1.115*	0.859	1.171*	1.022	1.009	0.897
Hospital beds per 10000	1.000	1.001	0.999	1.001	1.000	0.998
Q1‡	-	-	-	-	-	-
Q2	1.008	1.144	1.040	0.959	1.134	0.918
Q3	1.023	1.076	1.027	1.069	1.141	0.804*
Q4	1.026	1.023	1.032	1.073	1.141	0.838*
Q5	1.024	1.062	1.001	1.069	1.070	0.877
Type of hospital reimbursement	0.949	1.414*	1.005	0.909	0.932	0.662*

*Significant incidence risk ratio, $p < 0.05$.
†Year 2008 as the reference.
‡Incidence risk ratio from a model with annual quintiles of continuous explanatory variables with the first quintile as the reference, quintiles are varying across years therefore no threshold levels are given in the table.

and, to some degree, hospital admissions may be influenced by financial incentives [39].

We observed distinct differences between patient characteristics and outcome indicators for high- and low volume clinics. AH in low-volume clinics were characterized by older patients with fewer comorbid conditions, higher 3-month rehospitalization rates, and higher in-patient mortality. These results appear contradictory and raise questions about the validity of diagnostic data; it is unlikely that older patients have lower burden of disease and fewer comorbid conditions. We speculate that this may be explained by different procedures for coding diagnoses across hospitals. Larger hospitals usually have dedicated staff for his task, while coding in smaller hospitals is normally done by clinicians.

Hospital data also show higher proportions of AH and considerable longer hospital stays in low volume clinics. Consistent with our geographic analysis of rurality, and with other research [40], these results suggest potential effects scarcity of outpatient resources in proximity to low-volume clinics. However, we cannot exclude in this setting that supply sensitive effects of such hospitals are also promoting AH in order to legitimate the viability of low-volume hospitals. Due to lack of data, we cannot discriminate between the two mechanisms.

Patient characteristics

Our data showed more AH in men and confirmed gender associated differences documented in other research [20,41]. Our evidence on the socio-economic status of patients was in conflict with other research [37,42]. Some characteristics of Swiss health care are therefore important to note. All Swiss residents are required to purchase compulsory health insurance, covering a comprehensive catalogue of goods and services. Residents may also have supplementary health insurance contracts that typically provide superior levels of accommodation, give more choice of in-hospital physicians in hospitals and may provide cash benefits for sickness absence [18]. Data from the 2007 Swiss health survey shows that supplementary health insurance is typically purchased by those with high income [43]. Type of insurance coverage is thus a good proxy for the socio-economic status of patients. Our data on health insurance status of patients hospitalized for ACSC show 1.4% less patients with supplementary coverage compared to the overall Swiss average of 16.6% of patients with supplementary coverage. The results do not support the evidence that AH is influenced by a socioeconomic gradient in the setting of Swiss health care.

As in previous research [40,44], regional variation in our data indicates positive associations between AH and rurality of patient residence. Appropriate allocation of resources in rural areas is of concern to health care planners. However, we cannot distinguish between the effects of limited access to care and patient level factors that have been observed among rural residents in previous research, such as lower propensity to seek care [7]. More data is required to explain this regional variation within Swiss health care, and until it is collected and analyzed, specific policy recommendations cannot be made.

Strengths and limitations

Although we used hierarchical mixed models with random effects at the level of HSA's and zip-code clusters, which should address some concerns about unmeasured variables, it is important to recognize that health care delivery in the out-patient sector is highly complex. Statistical modelling is difficult because factors like physician behaviour, perceptions of quality of the interaction between patients and physicians, social status of patients and cultural norms including differential propensity among subpopulations to seek care are not fully understood [45]. The search for determinants is further complicated by a scarcity of data that measures the impact of different forms of care delivery on patient health at the health system level.

We were also limited by the lack of ambulatory care sensitive conditions specifically validated as indicators of quality of care for Switzerland. When using administrative data it is not always possible to directly discriminate between AH and necessary hospitalizations. A major limitation is that we have no knowledge about the patient's history of disease before the admission to the hospital: We don't know whether the patient's disease or symptoms of the disease were diagnosed, appropriate treated and monitored by ambulatory care before [1]. So we cannot determine with certainty that the hospitalization was clinically preventable or necessary. Although this misclassification on clinical level is unfortunate, we believe that the AH selection of the OECD can still be useful as a health indicator from a health service perspective.

The concept of avoidable hospitalizations is based on specific diagnoses that should not be treated in hospitals. Database information allows therefore only indirect identification of avoidable hospitalizations. We used the criteria of the OECD initiated Health Care Quality Indicator Project as the case definition of AH, but clinical criteria and appropriateness of hospitalization remains subject of constant debate. It will continue to be, as long as the concept of AH is not validated by patient-level outcomes. The concept of AH does not take into account the potential benefits for patients of a theoretically avoidable hospital stay. But as long as valid data regarding the outcome of hospitalizations on patient health remain unavailable, AH is currently the best approach for estimating the appropriateness of care.

We used administrative hospital data not specifically designed for this type of research, which caused a number of problems. Our results indicate that completeness and accuracy of coding diagnoses may differ between hospitals and that accuracy of geographic data of hospital location and patient residence were compromised in some cantons. This forced us to exclude data from six cantons for small area analysis. These difficulties directly reflect effects of federalism and cantonal autonomy in Swiss health care and point to an urgent need to improve the quality of nationwide health data collection.

Finally, we used age and sex standardized rates of AH for the whole population as the outcome in this study. This outcome may underestimate the overall burden of ACSC, and rates adjusted to the underlying disease prevalence should be used instead [46]. Unfortunately, small area data for disease prevalence are not available, and an expensive data collection processes would be required to obtain such data. However regional differences of rates of AH can also be interpreted as differential ability of a health system to meet region-specific burdens of ACSC; a prevalence adjusted analysis would obliterate such differences.

The major strength of this study is its nationwide approach; it gives insight into AH rates that transcend cantonal administrative boundaries. It proves that small area analysis in a complex setting is feasible, and has opened the door to further monitoring of regional variations of health interventions, which will support evidence-based policy making in Swiss health care. Another strength is our use of OECD definitions for AH and reported disease specific characteristics. This well established approach improves the generalizability of our data and allows comparative analyses across multiple health systems [15].

Conclusions

We identified significant determinants of AH in the Swiss health system that are important for health care planning. We uncovered disease specific characteristics of AH, indicating that disease specific health policy may be effective. However, we are limited by the quality of the data we used; more valid data must be collected by hospitals and ambulatory care providers. Our results may be used to improve the performance of the outpatient sector, particularly in local regional contexts. Rural and urban differences remain a cause of concern. Future research should assess specific physician characteristics that contribute to AH, with the goal of reducing the number of unnecessary procedures.

Additional file

Additional file 1: These tables represent the in- and exclusion criteria for avoidable hospitalizations based of on the criteria from the OECD Health Care Quality Indicator Project.

Abbreviations

AH: Avoidable hospitalizations; ACSC: Ambulatory care sensitive conditions; COPD: Chronic obstructive pulmonary disease; CHF: Congestive heart failure; SFOPH: Swiss Federal Office of Public Health; OECD: Organization for economic co-operation and development; SHAPE: System of household and personal statistics; HSA: Health service areas; ICD10: The International Classification of Diseases version 10; APDRG: All patient diagnosis related groups; CHF: Swiss Franc.

Competing interests

All authors declare that they have no competing interests.

Authors' contributions

CB analysed the validity of the geographic data, produced the geographical map and interpreted the results. AB, deceased on 12th November 2013, designed the original study project and performed the data analyses. MM helped drafting the manuscript and interpreting and prioritising the results. All authors contributed to revising the manuscript and approved the final manuscript.

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Additional file

These tables represent the in- and exclusion criteria for avoidable hospitalizations based of on the criteria from the OECD Health Care Quality Indicator Project.

Asthma admission rate

Numerator: All non-maternal hospital discharges (age 15+) with a principal diagnosis code of asthma in a specified year.

Asthma diagnosis codes:

ICD-9-CM	ICD-10-WHO
49300 Ext Asthma W/O Stat Ash	J450 Predominantly allergic asthma
49301 Ext Asthma W Status Ash	J451 Nonallergic asthma
49302 Ext Asthma W Acute Exac Oct00-	J458 Mixed asthma
49310 Int Asthma W/O Stat Asth	J459 Asthma, unspecified
49311 Int Asthma W Status Asth	J46 Status asthmaticus
49312 Int Asthma W Acute Exac Oct00-	
49320 Ch Ob Asth W/O Stat Asth	
49321 Ch Ob Asthma W Stat Asth	
49322 Ch Obs Asth W Acute Exac Oct00-	
49381 Exercse Ind Bronchospasm Oct03-	
49382 Cough Variant Asthma Oct03-	
49390 Asthma W/O Status Asthm	
49391 Asthma W Status Asthmat	
49392 Asthma W Acute Exacerbtn Oct00-	

Exclude cases:

- transferring from another institution

- pregnancy, childbirth, and puerperium

- newborn and other neonates

- with any diagnosis code of cystic fibrosis and anomalies of the respiratory system

- same day/day only admissions (admissions with a length of stay less than 24 hours. In those countries where a timestamp of admission or discharge is not available cases with a length of stay of 0 days shall be excluded.

Exclude diagnostic codes cystic fibrosis and anomalies of the respiratory system:

ICD-9-CM	ICD-10-WHO
27700 Cystic Fibros W/O Ileus	E840 Cystic fibrosis with pulmonary manifestations
27701 Cystic Fibros W Ileus	E841 Cystic fibrosis with intestinal manifestations
27702 Cystic Fibros W Pul Man	E848 Cystic fibrosis with other manifestations
27703 Cystic Fibrosis W Gi Man	E849 Cystic fibrosis, unspecified
27709 Cystic Fibrosis Nec	P27.0 Wilson-Mikity syndrome
74721 Anomalies Of Aortic Arch	P27.1 Bronchopulmonary dysplasia originating in the perinatal period
7483 Laryngotrach Anomaly Nec	P27.8 Other chronic respiratory diseases originating in the perinatal period
7484 Congenital Cystic Lung	P27.9 Unspecified chronic resp disease originating in the perinatal period
7485 Agenesis Of Lung	Q25.4 Other congenital malformations of aorta
74860 Lung Anomaly Nos	Q31.1 Congenital subglottic stenosis
74861 Congen Bronchiectasis	Q31.2 Laryngeal hypoplasia

74869 Lung Anomaly Nec	Q31.3 Laryngocele
7488 Respiratory Anomaly Nec	Q31.5 Congenital laryngomalacia
7489 Respiratory Anomaly Nos	Q31.8 Other congenital malformations of larynx
7503 Cong Esoph Fistula/Atres	Q31.9 Congenital malformation of larynx, unspecified
7593 Situs Inversus	Q32.0 Congenital tracheomalacia
7707 Perinatal Chr Resp Dis	Q32.1 Other congenital malformations of trachea
	Q32.2 Congenital bronchomalacia
	Q32.3 Congenital stenosis of bronchus
	Q32.4 Other congenital malformations of bronchus
	Q33.0 Congenital cystic lung
	Q33.1 Accessory lobe of lung
	Q33.2 Sequestration of lung
	Q33.3 Agenesis of lung
	Q33.4 Congenital bronchiectasis
	Q33.5 Ectopic tissue in lung
	Q33.6 Hypoplasia and dysplasia of lung
	Q33.8 Other congenital malformations of lung
	Q33.9 Congenital malformation of lung, unspecified
	Q34.0 Anomaly of pleura
	Q34.1 Congenital cyst of mediastinum
	Q34.8 Other specified congenital malformations of respiratory system
	Q34.9 Congenital malformation of respiratory system, unspecified
	Q39.0 Atresia of oesophagus without fistula
	Q39.1 Atresia of oesophagus with tracheo-oesophageal fistula
	Q39.2 Congenital tracheo-oesophageal fistula without atresia
	Q39.3 Congenital stenosis and stricture of oesophagus
	Q39.4 Oesophageal web
	Q39.8 Other congenital malformations of oesophagus
	Q89.3 Situs inversus

Denominator: 100,000 Population (age 15+ years).

COPD admission rate

Numerator: All non-maternal hospital discharges (age 15+) with a principal diagnosis code for Chronic Obstructive Pulmonary Disease (COPD) in a specified year.

COPD diagnosis codes:

ICD-9-CM	ICD-10-WHO
490 BRONCHITIS NOS*	J40 Bronchitis*
4660 AC BRONCHITIS*	J410 Simple chronic bronchitis
4910 Simple Chr Bronchitis	J411 Mucopurulent chronic bronchitis
4911 Mucopurul Chr Bronchitis	J418 Mixed simple and mucopurulent chronic bronchitis
49120 Obs Chr Brnc W/O Act Exa	J42 Unspecified chronic bronchitis
49121 Obs Chr Brnc W Act Exa	J430 MacLeod's syndrome
4918 Chronic Bronchitis Nec	J431 Panlobular emphysema
4919 Chronic Bronchitis Nos	J432 Centrilobular emphysema
4920 Emphysematous Bleb	J438 Other emphysema
4928 Emphysema Nec	J439 Emphysema, unspecified
494 Bronchiectasis Oct00-	J440 COPD with acute lower respiratory infection
4940 Bronchiectas W/O Ac Exac Oct00-	J441 COPD with acute exacerbation, unspecified
4941 Bronchiectasis W Ac Exac Oct00-	J448 Other specified chronic obstructive pulmonary disease
496 Chr Airway Obstruct Nec	J449 Chronic obstructive pulmonary disease, unspecified J47 Bronchiectasis
**Qualifies only if accompanied by secondary diagnosis of 491.xx, 492.x, 494.x or 496 (i.e., any other code on this list).*	**Qualifies only if accompanied by secondary diagnosis of J41, J43, J44, J47*

Exclude cases:

- transferring from another institution
- pregnancy, childbirth, and puerperium
- newborn and other neonates)
- same day/day only admissions (admissions with a length of stay less than 24 hours. In those countries where a timestamp of admission or discharge is not available cases with a length of stay of 0 days shall be excluded.

Denominator: 100,000 Population (age 15+ years).

Diabetes lower extremity amputation rate

Numerator: All non-maternal discharges (age 15+) with procedure code for lower extremity amputation in any field and diagnosis code of diabetes in any field in a specified year.

Diabetes lower extremity amputation diagnostic codes:

ICD-9-CM	ICD-10-WHO
Procedure codes for lower-extremity amputation	*Procedure codes for lower-extremity amputation*
8410 Lower Limb Amputat Nos	Not specified
8411 Toe Amputation	
8412 Amputation Through Foot	
8413 Disarticulation Of Ankle	
8414 Amputat Through Malleoli	
8415 Below Knee Amputat Nec	
8416 Disarticulation Of Knee	
8417 Above Knee Amputation	
8418 Disarticulation Of Hip	
8419 Hindquarter Amputation	

Diagnosis Codes For Diabetes:	*Diagnosis codes for diabetes:*
25000 Dmii Wo Cmp Nt St Uncntr	E10.0 Insulin-dependent diabetes mellitus with coma
25001 Dmi Wo Cmp Nt St Uncntrl	E10.1 Insulin-dependent diabetes mellitus with ketoacidosis
25002 Dmii Wo Cmp Uncntrld	E10.2 Insulin-dependent diabetes mellitus with renal complications
25003 Dmi Wo Cmp Uncntrld	E10.3 Insulin-dependent diabetes mellitus with ophthalmic complications
25010 Dmii Keto Nt St Uncntrld	E10.4 Insulin-dependent diabetes mellitus with neurological complications
25011 Dmi Keto Nt St Uncntrld	E10.5 Insulin-dependent DM with peripheral circulatory complications
25012 Dmii Ketoacd Uncontrold	E10.6 Insulin-dependent DM with other specified complications
25013 Dmi Ketoacd Uncontrold	E10.7 Insulin-dependent diabetes mellitus with multiple complications
25020 Dmii Hprsm Nt St Uncntrl	E10.8 Insulin-dependent diabetes mellitus with unspecified complications
25021 Dmi Hprsm Nt St Uncntrld	E10.9 Insulin-dependent diabetes mellitus without complications
25022 Dmii Hprosmlr Uncontrold	E11.0 Non-insulin-dependent diabetes mellitus with coma
25023 Dmi Hprosmlr Uncontrold	E11.1 Non-insulin-dependent diabetes mellitus with ketoacidosis
25030 Dmii O Cm Nt St Uncntrld	E11.2 Non-insulin-dependent diabetes mellitus with renal complications
25031 Dmi O Cm Nt St Uncntrl	E11.3 Non-insulin-dependent DMwith ophthalmic complications
25032 Dmii Oth Coma Uncontrold	E11.4 Non-insulin-dependent DM with neurological complications
25033 Dmi Oth Coma Uncontrold	E11.5 Non-insulin-dependent DM with peripheral circulatory complications

25040 Dmii Renl Nt St Uncntrld	E11.6 Non-insulin-dependent DM with other specified complications
25041 Dmi Renl Nt St Uncntrld	E11.7 Non-insulin-dependent diabetes mellitus with multiple complications
25042 Dmii Renal Uncntrld	E11.8 Non-insulin-dependent DM with unspecified complications
25043 Dmi Renal Uncntrld	E11.9 Non-insulin-dependent diabetes mellitus without complications
25050 Dmii Ophth Nt St Uncntrl	E13.0 Other specified diabetes mellitus with coma
25051 Dmi Ophth Nt St Uncntrld	E13.1 Other specified diabetes mellitus with ketoacidosis
25052 Dmii Ophth Uncntrld	E13.2 Other specified diabetes mellitus with renal complications
25053 Dmi Ophth Uncntrld	E13.3 Other specified diabetes mellitus with ophthalmic complications
25060 Dmii Neuro Nt St Uncntrl	E13.4 Other specified diabetes mellitus with neurological complications
25061 Dmi Neuro Nt St Uncntrld	E13.5 Other specified DM with peripheral circulatory complications
25062 Dmii Neuro Uncntrld	E13.6 Other specified diabetes mellitus with other specified complications
25063 Dmi Neuro Uncntrld	E13.7 Other specified diabetes mellitus with multiple complications
25070 Dmii Circ Nt St Uncntrld	E13.8 Other specified diabetes mellitus with unspecified complications
25071 Dmi Circ Nt St Uncntrld	E13.9 Other specified diabetes mellitus without complications
25072 Dmii Circ Uncntrld	
25073 Dmi Circ Uncntrld	
25080 Dmii Oth Nt St Uncntrld	
25081 Dmi Oth Nt St Uncntrld	
25082 Dmii Oth Uncntrld	
25083 Dmi Oth Uncntrld	
25090 Dmii Unspf Nt St Uncntrl	
25091 Dmi Unspf Nt St Uncntrld	
25092 Dmii Unspf Uncntrld	
25093 Dmi Unspf Uncntrld	

	Diagnosis codes for diabetes (continued):
	E14.0 Unspecified diabetes mellitus with coma
	E14.1 Unspecified diabetes mellitus with ketoacidosis
	E14.2 Unspecified diabetes mellitus with renal complications
	E14.3 Unspecified diabetes mellitus with ophthalmic complications
	E14.4 Unspecified diabetes mellitus with neurological complications
	E14.5 Unspecified DM with peripheral circulatory complications
	E14.6 Unspecified diabetes mellitus with other specified complications

	E14.7 Unspecified diabetes mellitus with multiple complications
	E14.8 Unspecified diabetes mellitus with unspecified complications
	E14.9 Unspecified diabetes mellitus without complications

Exclude cases:

- transferring from another institution
- pregnancy, childbirth, and puerperium)
- newborn and other neonates)
- with trauma diagnosis code in any field
- same day/day only admissions (admissions with a length of stay less than 24 hours. In those countries where a timestamp of admission or discharge is not available cases with a length of stay of 0 days shall be excluded.

Exclude trauma diagnosis codes:

ICD-9-CM	ICD-10-WHO
8950 Amputation Toe	S78.0 Traumatic amputation at hip joint
8951 Amputation Toe-Complicat	S78.1 Traumatic amputation at level between hip and knee
8960 Amputation Foot, Unilat	S78.9 Traumatic amputation of hip and thigh, level unspecified
8961 Amput Foot, Unilat-Compl	S88.0 Traumatic amputation at knee level
8962 Amputation Foot, Bilat	S88.1 Traumatic amputation at level between knee and ankle
8963 Amputat Foot, Bilat-Comp	S88.9 Traumatic amputation of lower leg, level unspecified
8970 Amput Below Knee, Unilat	S98.0 Traumatic amputation of foot at ankle level
8971 Amputat Bk, Unilat-Compl	S98.1 Traumatic amputation of one toe
8972 Amput Above Knee, Unilat	S98.2 Traumatic amputation of two or more toes
8973 Amput Abv Kn, Unil-Compl	S98.3 Traumatic amputation of other parts of foot
8974 Amputat Leg, Unilat Nos	S98.4 Traumatic amputation of foot, level unspecified
8975 Amput Leg, Unil Nos-Comp	T05.3 Traumatic amputation of both feet
8976 Amputation Leg, Bilat	T05.4 Traumatic amputation of 1 foot and other leg [any level, except foot]
8977 Amputat Leg, Bilat-Compl	T05.5 Traumatic amputation of both legs [any level]
	T13.6 Traumatic amputation of lower limb, level unspecified

Denominator: 100,000 Population (age 15+ years).

Diabetes Short-term Complications Admission Rate

Numerator: All non-maternal/non-neonatal hospital discharges (age 15+) with a principal diagnosis code for Diabetes short-term complications (i.e. ketoacidosis, hyperosmolarity, coma) in a specified year.

Diabetes short-term diagnostic codes:

ICD-9-CM	ICD-10-WHO
25010 Dm Keto T2, Dm Cont	E100 Insulin-dependent diabetes mellitus with coma

25011 Dm Keto T1, Dm Cont	E101 Insulin-dependent diabetes mellitus with ketoacidosis
25012 Dm Keto T2, Dm Uncont	E110 Non-insulin-dependent diabetes mellitus with coma
25013 Dm Keto T1, Dm Uncont	E111 Non-insulin-dependent diabetes mellitus with ketoacidosis
25020 Dm W/ Hyprosm T2, Dm Cont	E130 Other specified diabetes mellitus with coma
25021 Dm W/ Hyprosm T1, Dm Cont	E131 Other specified diabetes mellitus with ketoacidosis
25022 Dm W/ Hyprosm T2, Dm Uncnt	E140 Unspecified diabetes mellitus with coma
25023 Dm W/ Hyprosm T1, Dm Uncnt	E141 Unspecified diabetes mellitus with ketoacidosis
25030 Dm Coma Nec Typ Ii, Dm Cnt	
25031 Dm Coma Nec T1, Dm Cont	
25032 Dm Coma Nec T2, Dm Uncont	
25033 Dm Coma Nec T1, Dm Uncont	

Exclude cases:

- transferring from another institution
- pregnancy, childbirth, and puerperium)
- newborn and other neonates)
- with trauma diagnosis code in any field
- same day/day only admissions (admissions with a length of stay less than 24 hours. In those countries where a timestamp of admission or discharge is not available cases with a length of stay of 0 days shall be excluded.

Denominator: 100,000 Population (age 15+ years).

CHF admission rate

Numerator: All non-maternal/non-neonatal hospital discharges (age 15+) with principal diagnosis code for Congestive Heart Failure (CHF) in a specified year.

CHF diagnostic codes:

ICD-9-CM	ICD-10-WHO
39891 Rheumatic Heart Failure	I11.0 Hypertensive heart disease with (congestive) heart failure
40201 Mal Hypert Hrt Dis W Chf	I13.0 Hypertensive heart and renal disease with (congestive) heart failure
40211 Benign Hyp Hrt Dis W Chf	I13.2 Hypertensive heart and renal disease with both (congestive) heart failure and renal failure
40291 Hyperten Heart Dis W Chf	I50.0 Congestive heart failure
40401 Mal Hyper Hrt/Ren W Chf	I50.1 Left ventricular failure
40403 Mal Hyp Hrt/Ren W Chf/Rf	I50.9 Heart failure, unspecified
40411 Ben Hyper Hrt/Ren W Chf	
40413 Ben Hyp Hrt/Ren W Chf/Rf	
40491 Hyper Hrt/Ren Nos W Chf	
40493 Hyp Ht/Ren Nos W Chf/Rf	
4280 Congestive Heart Failure	
4281 Left Heart Failure	
42820 Systolic Hrt Failure Nos Oct02-	
42821 Ac Systolic Hrt Failure Oct02-	
42822 Chr Systolic Hrt Failure Oct02-	
42823 Ac On Chr Syst Hrt Fail Oct02-	
42830 Diastolc Hrt Failure Nos Oct02-	
42831 Ac Diastolic Hrt Failure Oct02-	
42832 Chr Diastolic Hrt Fail Oct02-	
42833 Ac On Chr Diast Hrt Fail Oct02-	
42840 Syst/Diast Hrt Fail Nos Oct02-	
42841 Ac Syst/Diastol Hrt Fail Oct02-	
42842 Chr Syst/Diastl Hrt Fail Oct02-	
42843 Ac/Chr Syst/Dia Hrt Fail Oct02-	
4289 Heart Failure Nos	

Exclude cases:

- transferring from another institution
- pregnancy, childbirth, and puerperium)
- newborn and other neonates)
- with cardiac procedure codes in any field
- with trauma diagnosis code in any field
- same day/day only admissions (admissions with a length of stay less than 24 hours. In those countries where a timestamp of admission or discharge is not available cases with a length of stay of 0 days shall be excluded.

Denominator: 100,000 Population (age 15+ years).

Hypertension Admission Rate

Numerator: All non-maternal hospital discharges (age 15+) with principal diagnosis code for Hypertension in a specified year.

Hypertension diagnostic codes:

ICD-9-CM	ICD-10-WHO
4010 Malignant Hypertension	I10 Essential (primary) hypertension
4019 Hypertension Nos	I119 Hypertensive heart disease without (congestive) heart failure
40200 Mal Hyperten Hrt Dis Nos	I129 Hypertensive renal disease without renal failure
40210 Ben Hyperten Hrt Dis Nos	I139 Hypertensive heart and renal disease, unspecified
40290 Hypertensive Hrt Dis Nos	
40300 Mal Hyp Ren W/O Ren Fail	
40310 Ben Hyp Ren W/O Ren Fail	
40390 Hyp Ren Nos W/O Ren Fail	
40400 Mal Hy Ht/Ren W/O Chf/Rf	
40410 Ben Hy Ht/Ren W/O Chf/Rf	
40490 Hy Ht/Ren Nos W/O Chf/Rf	

Exclude cases:
- transferring from another institution
- pregnancy, childbirth, and puerperium)
- newborn and other neonates)
- with cardiac procedure codes in any field

- with cardiac procedure codes in any field

- same day/day only admissions (admissions with a length of stay less than 24 hours. In those countries where a timestamp of admission or discharge is not available cases with a length of stay of 0 days shall be excluded.

Denominator: 100,000 Population (age 15+ years).

2.2 Article 2: Revascularization treatment of STEMI patients

Title:

Revascularization treatment of emergency patients with acute ST-segment elevation myocardial infarction in Switzerland:

Results from a nationwide, cross-sectional study in Switzerland for 2010-2011

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RESEARCH ARTICLE

Revascularization Treatment of Emergency Patients with Acute ST-Segment Elevation Myocardial Infarction in Switzerland: Results from a Nationwide, Cross-Sectional Study in Switzerland for 2010-2011

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Abstract

Background

Cardiovascular diseases are the leading cause of death worldwide and in Switzerland. When applied, treatment guidelines for patients with acute ST-segment elevation myocardial infarction (STEMI) improve the clinical outcome and should eliminate treatment differences by sex and age for patients whose clinical situations are identical. In Switzerland, the rate at which STEMI patients receive revascularization may vary by patient and hospital characteristics.

Aims

To examine all hospitalizations in Switzerland from 2010–2011 to determine if patient or hospital characteristics affected the rate of revascularization (receiving either a percutaneous coronary intervention or a coronary artery bypass grafting) in acute STEMI patients.

Data and Methods

We used national data sets on hospital stays, and on hospital infrastructure and operating characteristics, for the years 2010 and 2011, to identify all emergency patients admitted with the main diagnosis of acute STEMI. We then calculated the proportion of patients who were treated with revascularization. We used multivariable multilevel Poisson regression to determine if receipt of revascularization varied by patient and hospital characteristics.

collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: The authors have declared that no competing interests exist.

Results

Of the 9,696 cases we identified, 71.6% received revascularization. Patients were less likely to receive revascularization if they were female, and 80 years or older. In the multivariable multilevel Poisson regression analysis, there was a trend for small-volume hospitals performing fewer revascularizations but this was not statistically significant while being female (Relative Proportion = 0.91, 95% CI: 0.86 to 0.97) and being older than 80 years was still associated with less frequent revascularization.

Conclusion

Female and older patients were less likely to receive revascularization. Further research needs to clarify whether this reflects differential application of treatment guidelines or limitations in this kind of routine data.

Introduction

Mortality for cardiovascular diseases (CVDs) has continually decreased in developed countries, but CVDs are still the leading cause of death in Switzerland for both sexes [1]. More rapid and improved treatment of acute myocardial infarction (AMI) has substantially reduced CVD mortality [2]. International guidelines recommend, for optimal treatment, that AMI patients receive evidence-based therapies [3–5]. Treatment guidelines differ by type of AMI: ST-elevation myocardial infarction (STEMI) is differentiated from non-ST-elevation myocardial infarction (NSTEMI). If treatment guidelines are consistently followed, they should reduce or eliminate sex- or age-based treatment differences for patients whose clinical situations are identical.

In Switzerland, however, there is evidence that AMI patients are treated inconsistently, and that guidelines are more likely to be followed for men than for women. Radovanovic et al analyzed patients of the Swiss AMI registry (AMIS) between 1997–2011 and saw that percutaneous coronary interventions (PCI) had increased in STEMI patients overall. But, since 2006, they found that over 80% of male patients received PCI, while only 70% of women were treated with PCI [6]. Women were less likely to receive primary reperfusion (thrombolysis and PCI) and medications according to evidence-based guidelines [6,7]. Other studies documented that AMI treatment in Switzerland varied by region, hospital characteristics (presence or absence of 24 hour/7day cardiac catheterization facility), age, and number of comorbidities [7–9].

We used nation-wide hospital data of patients admitted to all Swiss hospitals in 2010 and 2011, with the goal of including all patients with acute STEMI as their main diagnosis because well-established treatment guidelines exist for these patients [3]. Our goal was to investigate the effect of patient and hospital characteristics on receipt of revascularization in acute STEMI patients accounting for hospital transfers and use of treatment information over the whole course of treatment.

Data and Methods

Ethics

Ethical approval was not required for this analysis of data, which are available to research institutions according to the ordinance on federal statistical monitoring activities and surveys.

Data sets

We used two national data sets from the Swiss Federal Statistical Office (SFSO) that provided information about inpatient care and hospital infrastructure in 2010 and 2011. The first data set, *Medizinische Statistik der Krankenhäuser*, focuses on hospital stays (HS) and includes mandatory information on all patients hospitalized for at least a day, recording age, sex, place of residence, date of admission and discharge (month) of the patient, as well as main and concomitant diagnoses, and treatment provided. The second data set, *Krankenhausstatistik*, focuses on hospital characteristics (HC) and contains information on hospital infrastructure for all hospitals in Switzerland, including type of hospital, number of beds, number of physicians and nurses, number of angiography devices, CT or MRI machines, presence of an emergency room. The information in these data sets can be cross-referenced by hospital-ID. To ensure data is protected, the patient residence and the geographical location of the hospital are aggregated into zip code areas consolidated into 705 medical statistics (Medstat) regions.

Ethical approval was not required for this analysis of data, which are available to research institutions according to the ordinance on federal statistical monitoring activities and surveys.

We used the community classification data set (*Raumgliederung*) from the SFSO (reference date December 31st, 2010) to determine the level of urbanization of Medstat regions. The variable urban/rural region in the community classification data set included four categories: (1) main city of an agglomeration; (2) other agglomeration community; (3) isolated city; and, (4) rural community. One Medstat region usually contains more than one community. If at least one community in the Medstat region was classified as 1, 2 or 3, we coded the whole Medstat region as urban. Otherwise we coded it as rural.

Construction of course of treatment

The years 2010–2011 included a total of 2,708,942 hospital stays (2010: 1.345.245; 2011: 1,363,697; Fig 1). We excluded 44,338 records for which date of entry, date of exit, hospital-ID or patient-ID were missing. Of that, the majority (99.7%) had no date of exit because these patients were hospitalized over New Year. So they had an incomplete record the year they entered the hospital and a complete record the year they were discharged. So we excluded them to eliminate duplicates and just use complete records. To protect patient anonymity, the treating hospital uses a Hash code (derived from the patient's name, gender and date of birth) to create a patient ID, which can be used to track patients with multiple hospital stays, either in the same, or in another hospital.

Patients with several hospital stays recorded close together may have been referred between hospitals to treat the same condition. For example, STEMI patients would be recorded twice in the HS data if they were treated in one hospital for a day, and then transferred to spend several days in another hospital for further treatment. To avoid double counting of patients, we reconstructed each of these short courses of treatment, searching for sequential hospitalizations in the HS record by patient-ID, sequence number, days to next hospitalization ($< = 1$), and month of entry. A case may thus contain several hospital stays. For the years 2010 and 2011, we constructed 2,418,502 full cases.

Selection of STEMI patients

The International Classification of Diseases, Injuries and Causes of Death (ICD) 10 codes were used to code main and secondary diagnoses in the HS data set. The ICD 10 code that starts with I21 is for acute transmural myocardial infarctions. To select AMI patients with STEMI specifically, we excluded cases with acute subendocardial myocardial infarction (I21.4) and unspecified acute myocardial infarction (I21.9). Cases with acute transmural myocardial

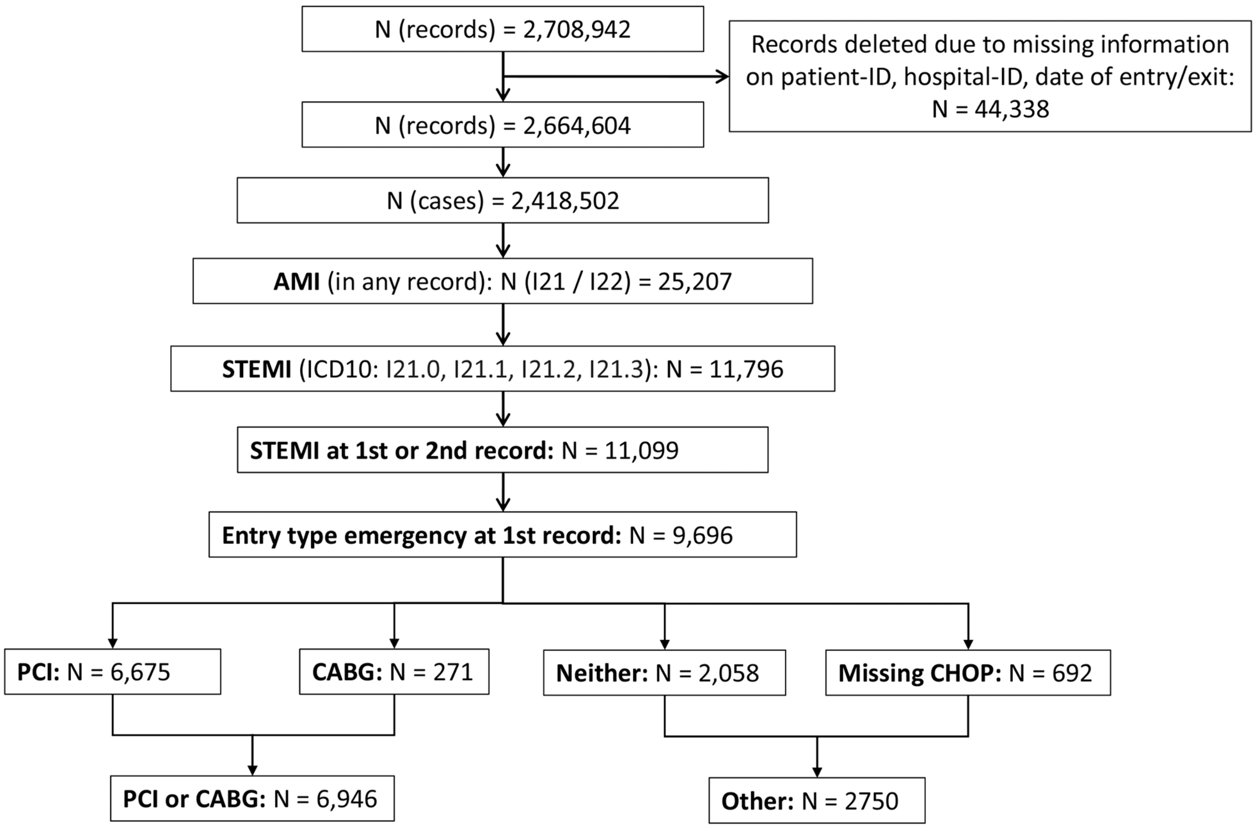

Fig 1. Flow chart of the selection process.

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infarction of anterior wall (I21.0), acute transmural myocardial infarction of inferior wall (I21.1), acute transmural myocardial infarction of other sites (I21.2) or acute transmural myocardial infarction of unspecified site (I21.3) were included. These four main diagnoses (I21.0, I21.1, I21.2, and I21.3) had to appear at the first or second hospitalization record. If mentioned on the second record we restricted the selection to cases matching predefined main diagnoses at the first record (see S1 Table). We chose these predefined diagnoses as they have similar symptoms like AMI and we wanted to identify just patients being hospitalized as an emergency with AMI. We only included cases if the first record was an emergency admission. This way we excluded patients with planned hospital stays, who were unlikely to have an acute STEMI. After applying these restrictions, we included 9,696 full treatment cases in our analysis.

Information on treatment received

To describe the treatments that STEMI patients received, we considered all records of treatment for each case. We coded information on treatment procedures in the HS data according to the Swiss operation classification system (CHOP), which was derived and modified from the American International Classification of Diseases, Ninth Revision, Clinical Modification: ICD-9-CM, volume 3, 1994. We also coded it according to classification in All Patient Diagnosis Related Groups (APDRG). We classified the 9,696 AMI cases into four groups, based on available treatment information: (1) codes that indicated a PCI; (2) codes that indicated a coronary artery bypass grafting (CABG); (3) codes that indicated treatments other than PCI or CABG; and, (4) patients with no available treatment codes (see S2 and S3 Tables for the exact CHOP and APDRG codes we used). We then created a variable that described if patients were treated with revascularization (PCI, CABG, or both) or not.

Patient characteristics

We assessed the following socio-demographic variables: sex, age (grouped 18–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84, 85+ years), and nationality (Swiss, foreign). As a proxy for the patient's socio-economic position, we used the patients insurance status (public, semi-private, or private), which indicates the type of insurance used for billing. Public insurance is mandatory, semi-private and private insurance are optional and paid for by patients in addition to paying public insurance. Semi private insurance is associated with a hospital stay in a two-bed room, private insurance with a stay in a single-bed room. We also used information on who referred the patient to the hospital (the patient or relatives, rescue service or a physician). To characterize the comorbidities of the patient, we used the maximum number of secondary diagnoses recorded either in the first or, if the patient was referred, the second record in the HS data (grouped into no, 1 to 2, 3 to 4, 5 to 6, and 7 or more secondary diagnoses).

Hospital characteristics

We used the following hospital level information: presence of an angiography device; full-time equivalent (FTE) of the physicians by 1,000 cases (grouped into tertiles); type of hospital region (urban or rural); language region of the hospital (German, French or Italian); and the number of hospital stays per year. As has been done previously [10], we divided hospitals into three groups: small-volume (<15,001 cases/year), medium-volume (15,001–30,000 cases/year) or high-volume (> 30,000 cases/year) volume.

Except for treatment information and comorbidities, we derived both patient and hospital characteristics from the first hospital stay of the short course of treatment. Coding guidelines for HS data imply that the referring hospital coded the treatment when it referred a patient to another hospital for ambulatory treatment, e.g., an ambulatory PCI. This explains why we focused on the first hospital, which also took the lead in providing treatment and made the decision to refer a patient to another hospital.

Statistical analysis

We calculated the number and percentage of patients who received revascularization and computed crude relative proportions with 95% confidence intervals (95% CI) when comparing groups of patients. We used Pearson Chi-square-test with a two-sided significance level $p<0.05$ to test for differences by patient or hospital characteristics. We then estimated relative proportions using multivariable multilevel Poisson regression to adjust for confounders and to identify characteristics independently associated with receiving revascularization [11]. We included patient characteristics (sex, age, nationality, bed category, maximum number of secondary diagnoses at first or second hospital, entry decision) and hospital characteristics (angiography device, fulltime equivalent of physicians per 1,000 cases, type of hospital region, language region, and hospital groups). We used multilevel Poisson regression as implemented in Stata, with the **xtpoisson** command, to account for the multilevel structure of the data (clustering of patients within the first contact hospital), and used Wald tests to examine the significance of association. In the analyses of variables with ordered levels we used the lowest level as the reference group and for dichotomous variables the level without the corresponding characteristic. We performed a sensitivity analysis by analyzing treatment with PCI alone, excluding CABG and found no major differences between the model with PCI alone and the model with

PCI/CABG, hence we used PCI/CABG in all further analyses. All analyses were performed using Stata version 13 (StataCorp, College Station, TX, USA).

Results

In Switzerland, in 2010 and 2011, 300 hospitals provided inpatient care, including specialized services for acute care, psychiatry, rehabilitation/geriatrics, or delivery/obstetrics. More than half these hospitals had an acute care division (2010: 179, 2011: 180). Of these 300 hospitals, 98 were the site of first contact in 2010, and 96 in 2011, for the 9,696 STEMI cases we included. In both years, 77 of the hospitals were located in an urban area. Of the first contact hospitals, 54 in 2010, and 56 in 2011, had at least one angiography device. Over both years, 35.4% of the included STEMI patients were initially treated in a small-volume hospital, 31.9% in a medium-volume hospital, and 32.6% in a high-volume hospital.

Study population

The 9,696 STEMI cases (total: 9,598 different persons) were, on average, 65.8 years old (range: 18–102 years); 70.8% were male, and the mean length of stay was 11.7 days. In the group treated with revascularization (6,946 of the 9,696, or 71.6% of all), mean age was 63.3 years, 75.6% were men, and average length of stay was 11.4 days. The 2,750 patients who did not receive revascularization were, on average, 72 years old; 58.7% were male, and mean length of stay was 12.5 days.

The proportion of cases who received revascularization was highest in the 50–54 age group (83.5%), and lowest in the 85+ years age group (29.6%). The proportion was highest in the private (76.8%), and lowest in the public insurance category (70.9%). It was highest in the high-volume hospital group (81.3%), and lowest in the small-volume hospital group (55.3%). In the Italian hospital language region, 80.6% of all hospitalized STEMI cases received revascularization, while in the French language region, 70.9% received the treatment (see Table 1).

Factors associated with receiving a revascularization

The results of the univariable Poisson regression analyses showed revascularization was less common in female patients, those older than 69 and those who were Swiss (see Table 1). Patients were more likely to receive revascularization if they were referred to the hospital by their physician, had any secondary diagnoses, were in the private insurance category, were first treated in a medium- or high-volume hospital, or were hospitalized in the Italian language region. The relative proportion of revascularization treatments increased with the number of FTE of physicians per 1,000 cases. Patients treated in an urban hospital, and in hospitals with an angiography device were more likely to receive revascularization.

In the multivariable multilevel Poisson regression analysis most of these associations disappeared, while following associations persisted: A negative association of revascularization with being female (RP = 0.91, 95% CI: 0.86 to 0.97) and with being 80 years and older (age group 80–84 years: RP = 0.80, 95% CI: 0.70 to 0.91; age group 85+ years: RP = 0.42, 95% CI: 0.36 to 0.49). Having more comorbidities did not reduce the likelihood for revascularization (see Fig 2 and S4 Table).

Furthermore, we present (Figs 3 and 4; S5 and S6 Tables) separate multilevel Poisson regression analyses for men and women, stratified by age (younger age group: 18–64 years, older age group: 65+ years).

Having comorbidities wasn't a limiting factor to receive revascularization for young or old men and old women. In the adjusted analyses, revascularization was lower for men and women over 80. Women in the older age group had more often revascularization (RP = 1.18, 95% CI:

Table 1. Socio-demographic, socioeconomic and healthcare-related factors of the study population and crude rates of receiving a revascularization, Switzerland 2010–2011.

	N (%)	PCI/CABG (%)	Unadjusted model crude relative proportions (95% CI)
Total	**9,696 (100.00%)**	**6,946 (71.64%)**	
Sex		**p<0.0000**	**p<0.0000**
Male	6,869 (70.84%)	5,254 (76.49%)	1.0
Female	2,827 (29.16%)	1,692 (59.85%)	0.78 (0.76,0.81)
Age groups		**p<0.0000**	**p<0.0000**
18 to 44 years	567 (5.85%)	454 (80.07%)	1.0
45 to 49 years	727 (7.50%)	594 (81.71%)	1.02 (0.97,1.08)
50 to 54 years	988 (10.19%)	825 (83.50%)	1.04 (0.99,1.10)
55 to 59 years	1,113 (11.48%)	888 (79.78%)	1.00 (0.95,1.05)
60 to 64 years	1,189 (12.26%)	946 (79.56%)	0.99 (0.94,1.04)
65 to 69 years	1,174 (12.11%)	952 (81.09%)	1.01 (0.96,1.06)
70 to 74 years	1,003 (10.34%)	756 (75.37%)	0.94 (0.89,0.99)
75 to 79 years	1,063 (10.96%)	727 (68.39%)	0.85 (0.81,0.91)
80 to 84 years	916 (9.45%)	521 (56.88%)	0.71 (0.66,0.76)
85+ years	956 (9.86%)	283 (29.60%)	0.37 (0.33,0.41)
Citizenship		**p<0.0000**	**p<0.0000**
Foreign	1,731 (17.85%)	1,331 (76.89%)	1.0
Swiss	7,965 (82.15%)	5,615 (70.50%)	0.92 (0.89,0.94)
Entry decision		**p<0.0386**	**p<0.0382**
Herself/Himself, relatives	2,415 (24.91%)	1,693 (70.10%)	1.0
Rescue services	3,730 (38.47%)	2,659 (71.29%)	1.02 (0.98,1.05)
Physician	3,551 (36.62%)	2,594 (73.05%)	1.04 (1.01,1.08)
Comorbidities		**p<0.0000**	**p<0.0000**
No	276 (2.85%)	91 (32.97%)	1.0
1–2	2,298 (23.70%)	1,757 (76.46%)	2.32 (1.96,2.75)
3–4	3,072 (31.68%)	2,384 (77.60%)	2.35 (1.99,2.79)
5–6	1,908 (19.68%)	1,415 (74.16%)	2.25 (1.90,2.67)
7+	2,142 (22.09%)	1,299 (60.64%)	1.84 (1.55,2.18)
Insurance status		**p<0.0030**	**p<0.0013**
Public	7,700 (79.41%)	5,462 (70.94%)	1.0
Half Private	1,401 (14.45%)	1,027 (73.30%)	1.03 (1.00,1.07)
Private	595 (6.14%)	457 (76.81%)	1.08 (1.03,1.13)
Hospital groups		**p<0.0000**	**p<0.0000**
Small (<15001 cases)	3,435 (35.43%)	1,900 (55.31%)	1.0
Medium (15001–30000 cases)	3,097 (31.94%)	2,475 (79.92%)	1.44 (1.40,1.50)
High (>30000 cases)	3,164 (32.63%)	2,571 (81.26%)	1.47 (1.42,1.52)
Language region		**p<0.0000**	**p<0.0000**
German	7,140 (73.64%)	5,085 (71.22%)	1.0
French	2,052 (21.16%)	1,455 (70.91%)	1.00 (0.96,1.03)
Italian	504 (5.20%)	406 (80.56%)	1.13 (1.08,1.18)
FTE physicians/1000 cases		**p<0.0000**	**p<0.0000**
1. tertile (<11.86)	3,236 (33.37%)	1,932 (59.70%)	1.0
2. tertile (11.86-<17.46)	3,300 (34.03%)	2,454 (74.36%)	1.25 (1.20,1.29)
3. tertile (17.46+)	3,151 (32.50%)	2,556 (81.12%)	1.36 (1.31,1.40)
n/a	9 (0.09%)	4 (44.44%)	

(*Continued*)

Table 1. (*Continued*)

	N (%)	PCI/CABG (%)	Unadjusted model crude relative proportions (95% CI)
Hospital region		**p<0.0000**	**p<0.0000**
Rural	504 (5.20%)	230 (45.63%)	1.0
Urban	9,192 (94.80%)	6,716 (73.06%)	1.60 (1.45,1.76)
Angiography device		**p<0.0000**	**p<0.0000**
No	1,290 (13.30%)	666 (51.63%)	1.0
Yes	8,406 (86.70%)	6,280 (74.71%)	1.45 (1.37,1.53)

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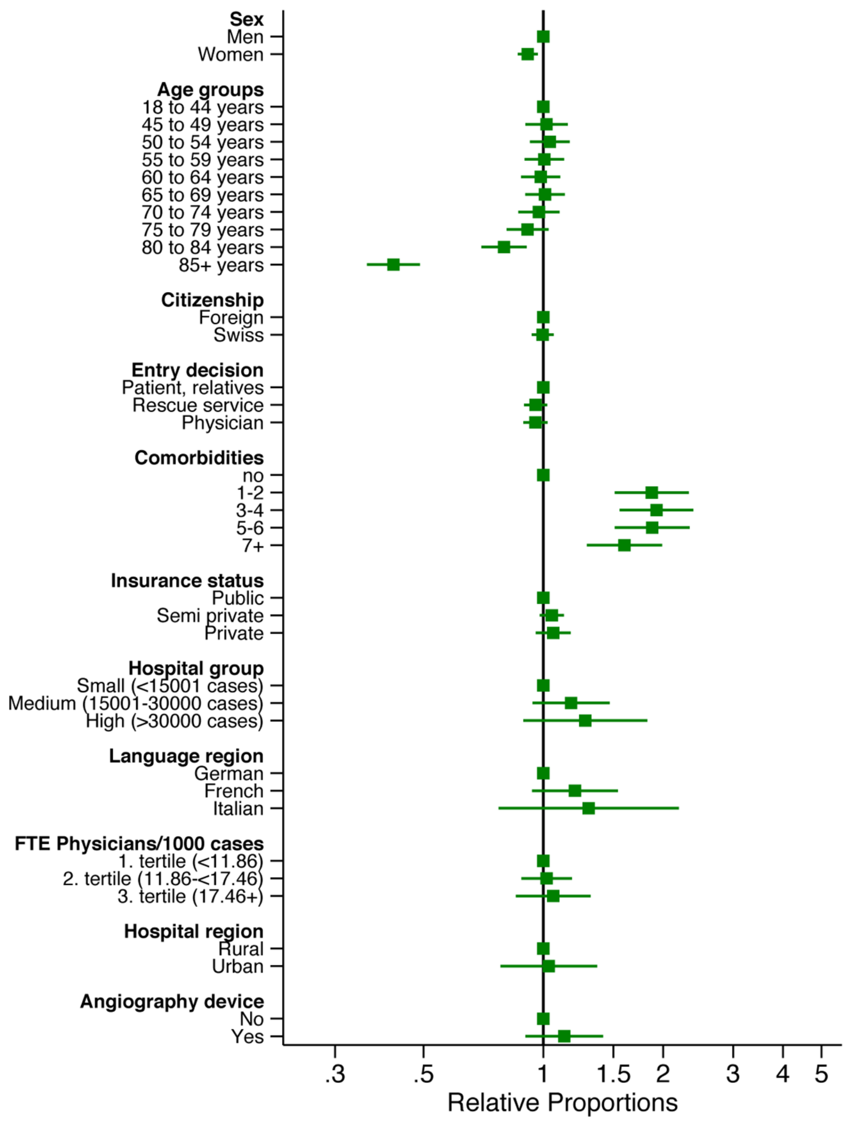

Fig 2. Results of multilevel Poisson regression for revascularization.

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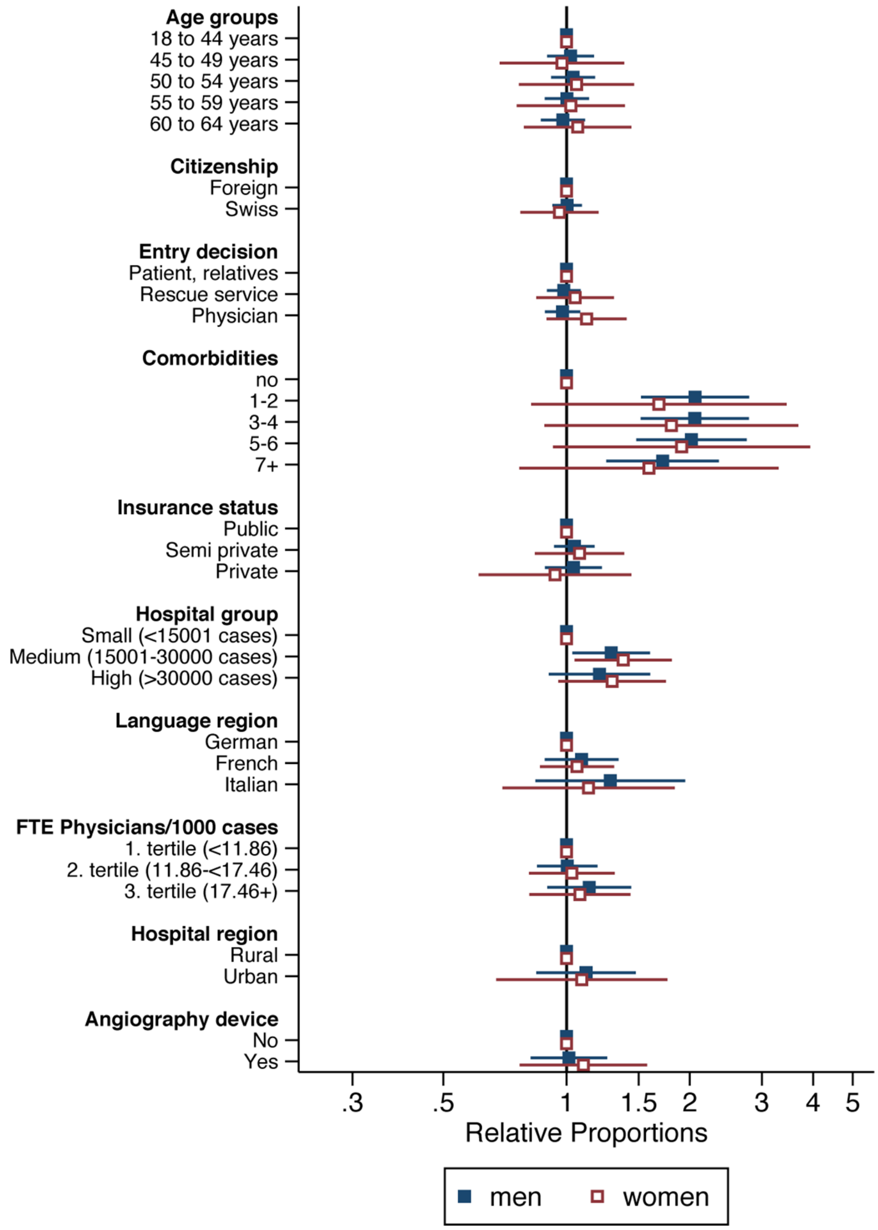

Fig 3. Results of multilevel Poisson regression for revascularization for male and female patients younger than 65 years.

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1.01 to 1.38) if their insurance status was semi-private. Young and old men as well as young women were more often treated with revascularization when admitted first to a medium size hospital (young men: RP = 1.29, 95% CI: 1.03 to 1.60; old men: RP = 1.32, 95% CI: 1.10 to 1.58; young women: RP = 1.38, 95% CI: 1.05 to 1.81).

In a sensitivity analysis we excluded cases which died the same day of admission, were 85 + years old or were admitted to hospitals with less than 3000 cases/year. This left 8,188 cases for the analysis. The stratified models showed that being hospitalized first in a small hospital led to less revascularization than an admission to a medium or high-volume hospital. The full model showed no significant association.

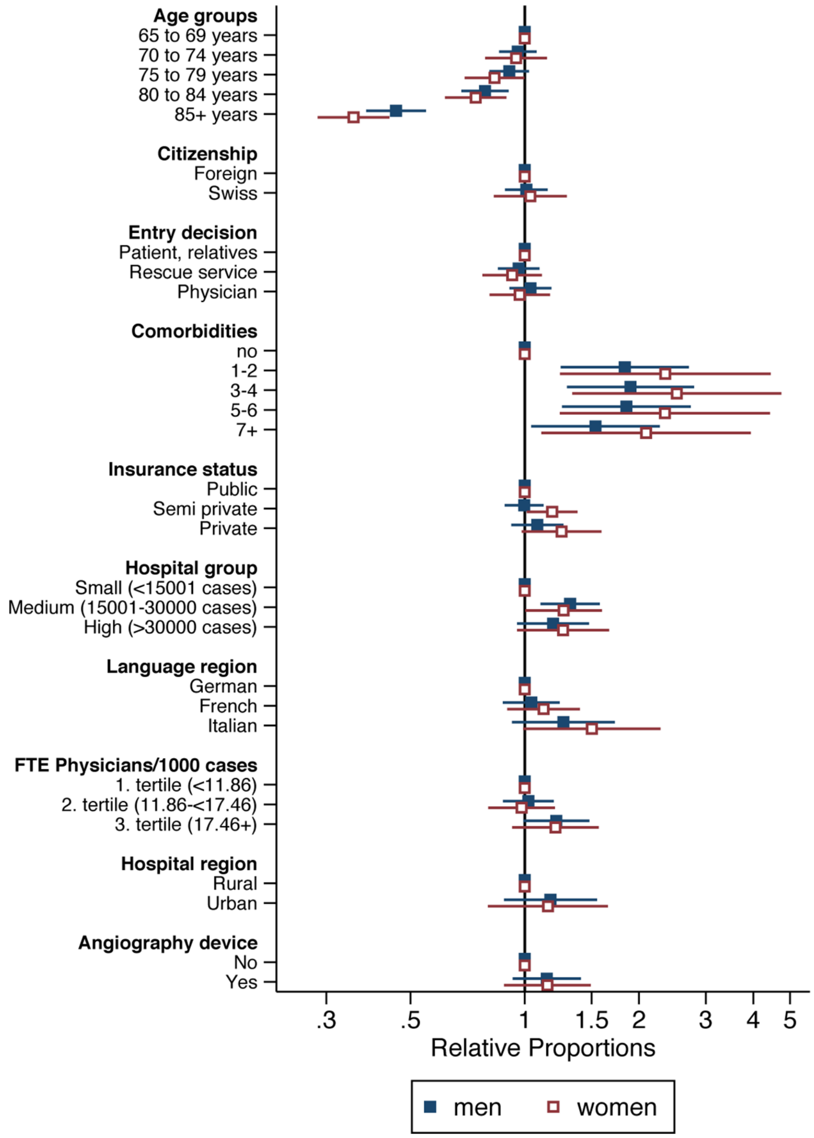

Fig 4. Results of multilevel Poisson regression for revascularization for male and female patients 65 years and older.

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Discussion

Main findings

In patients with acute ST-segment elevation myocardial infarction admitted as emergencies to Swiss hospitals in 2010 and 2011, close to three-quarters (71.6%) received revascularization. Women were less likely than men to be treated with PCI or CABG. Independent of other patient and hospital characteristics, patients 80 years and older underwent revascularization less frequently. In younger women, we observed no incremental association with number of comorbidities. Compared to patients with no comorbidities, having comorbidities was not a barrier to receive revascularization for old male and female patients as well as for young men. Patients admitted to a medium-sized (15001–30000 hospitalizations per year) hospital were more likely to receive a PCI or CABG. In a sensitivity analysis excluding patients died the day of admission, patients being 85 years and older or admitted to hospitals with less than 3000 cases/year we found a positive trend for revascularization when admitted to a medium or high-volume hospital compared to cases first hospitalized in a small hospital.

Limitations and strengths

Our study had some limitations. We used secondary data that was not collected for our study purpose, so we did not know why patients received no revascularization, or what kind of medication they received. For patients treated in more than one hospital, coding guidelines limit our ability to clearly determine which hospital provided which treatment [12]. We addressed this in two ways. First, for our analysis, we used the characteristics of the first hospital a patient went to. Second, we used treatment information across all hospitals in which a patient stayed during the course of treatment.

We chose the ICD-10 codes I21.0, I21.1, I21.2 and I21.3 to identify STEMI cases after consulting cardiologists and a coding expert from the Bern University hospital. ICD-10 codes do not distinguish between STEMI or NSTEMI cases [13,14]. Although they found difficulties in identifying the correct proportion of STEMI and NSTEMI on the bases of ICD-10 Alexandrescu et al. suggest to use I22.0, I22.1 and I22.8 additional to our chosen codes (I21.0-I21.3) to identify STEMI cases. When we included these ICD-10 codes, additional 44 cases were identified with almost identical results when included in the regression analyses.

We lacked specific information about the capability of a hospital to offer revascularization, and used the presence of an angiography device as a proxy without information about service hours of catheter labs (e.g. 24/7). Since treatments are coded, and diagnoses are made at the hospital where the patient is treated, coding practices may differ between hospitals e.g. due to variation in adherence to coding guidelines; this could introduce differential misclassification. The official coding guidelines are changed almost yearly. To limit the impact of changes, we restricted our analysis to 2010 and 2011. Although we used multilevel multivariable regression analyses, we cannot exclude residual confounding, bias due to variation of data collection procedures across hospitals, especially in information on prognostic factors of patients.

We examined the referral pattern per hospital group and the length of stay to consider difference in comorbidity coding. Of the 3,771 cases being transferred, 773 had no comorbidities coded in the first hospital. Considering the length of stay of these cases 88.4% (683) left the first hospital to another hospital the same day they were admitted. Therefore we believe that due to the short length of stay the registration of the comorbidities of the patient was poor in the first hospital. To overcome these differences in comorbidity coding we decided to use the maximum number of comorbidities at the first or second hospital. In a first analysis we used the number of comorbidities coded just by the first hospital. We found that having more than six comorbidities leads to less revascularization. We are convinced that the new variable of the maximum number of comorbidities is a better proxy for the real number of comorbidities of the patients. Nevertheless, this improvement is just referring to cases which were transferred.

Our study has several strengths. We analyzed standardized data of all hospitalized patients in all hospitals in Switzerland, so our results are valid for the whole country. The data set not only included patient characteristics and treatment provided, but also, via linkage to hospital characteristics data of the SFSO, it contained information on the personnel and technical infrastructure of Swiss hospitals. By constructing the course of treatment of emergency STEMI patients, we accounted for referrals and used the treatment information from all hospitals the patient visited during treatment. To our knowledge, previous Swiss studies did not take into account the treatments the patients received at all hospitals in case of hospital transfers [6–9,14]. The studies reporting on patients monitored in the AMIS registry restricted their analysis to patients exclusively treated at hospitals collaborating in the AMIS registry [6,7,9]. As 39% of all cases in our study were transferred at least once, it was important to consider all treatment information available over the whole course of treatment.

Comparison with other studies

Like other studies of AMI patients, the receipt of optimal revascularization varied by age and gender when we adjusted for age and other patient and hospital characteristics [6,15–18]. Studies in the US and UK observed higher rates of invasive cardiac procedures in hospitals with on-site revascularization facilities [19,20]. In our univariable analysis, patients in hospitals with an angiography device more often received revascularization, but in the multivariable analysis, this association was no longer statistically significant.

Tung, et al, showed more PCI use among physicians who had high overall case volume [21]. Although the total number of annual hospitalizations does not directly reflect the frequency with which a hospital performs PCI and CABG we found a trend for less revascularization when admitted first to a small-volume hospital but the association was not significant. Just in the stratified (by age and gender) sensitivity analysis (exclusion of cases admitted to hospitals with less than 3000 cases/year, 85 years and more of age or patients which died the day of admission) this trend was significant.

Insam and colleagues analyzed hospitalizations for AMI in Switzerland before 2009 to determine if clinical management of AMI varied across seven major regions. They observed significant geographical differences and explained that Swiss hospitals are largely autonomous in defining their standards of care [8,14], but did not account for urbanization. Like studies from Canada [22,23], we found no regional differences, either between the language regions or between urban and rural hospitals.

Conclusions

Older patients and women were less likely to receive revascularization. Further research needs to clarify whether this reflects differential application of treatment guidelines or limitations in this kind of routine data.

Supporting Information

S1 Table. Predefined main diagnosis at first hospitalization record if second hospitalization record is STEMI.
(DOCX)

S2 Table. CHOP and APDRG codes used to identify PCI treatment.
(DOCX)

S3 Table. CHOP and APDRG codes used to identify CABG treatment.
(DOCX)

S4 Table. Results of the multilevel Poisson regression for revascularization.
(DOCX)

S5 Table. Results of the multilevel Poisson regression for revascularization for male and female patients younger than 65 years.
(DOCX)

S6 Table. Results of the multilevel Poisson regression for revascularization for male and female patients 65 years and older.
(DOCX)

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Author Contributions

Conceived and designed the experiments: MZ PJ. Analyzed the data: CB MZ. Wrote the paper: CB MZ. Developed study design: MZ PJ. Selection of ICD-10, APDRG, CHOP codes for the study: OE PJ.

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Supporting Information

S1: Predefined main diagnosis at first hospitalization record if second hospitalization record is STEMI

ICD 10 code	Diagnosis
I20.0	Unstable angina
I20.1	Angina pectoris with documented spasm
I20.8	Other forms of angina pectoris
I20.9	Angina pectoris, unspecified
I24.8	Other forms of acute ischaemic heart disease
I24.9	Acute ischaemic heart disease, unspecified
I25.1	Atherosclerotic heart disease
I46.0	Cardiac arrest with successful resuscitation
I49.0	Other cardiac arrhythmias
R06.0	Dyspnoea
R07.1	Chest pain on breathing
R07.2	Precordial pain
R07.3	Other chest pain
R07.4	Chest pain, unspecified
R57.0	Cardiogenic shock
R57.9	Shock, unspecified

S2: CHOP and APDRG codes used to identify PCI treatment

CHOP code indicating PCI	Explanation
Z00.45	One stent inserted
Z00.46	Two stents inserted
Z00.47	Three stents inserted
Z00.48	Four or more stents inserted
Z00.66	Percutaneous transluminal coronary angioplasty [PTCA] or coronary atherectomy
Z36.0	Removal of coronary artery obstruction and insertion of stent(s)
Z36.06	Insertion of non-drug-eluting coronary artery stent(s)
Z36.07	Insertion of drug-eluting coronary artery stent(s)
APDRG code indicating PCI	**Explanation**
112	Percutaneous cardiovascular intervention without acute myocardial infarction, cardiac insufficiency/heart failure or shock
1112	Percutaneous cardiovascular intervention without acute myocardial infarction, cardiac insufficiency/heart failure or shock, with multiple interventions
808	Percutaneous cardiovascular intervention with acute myocardial infarction, cardiac insufficiency/heart failure or shock
1808	Percutaneous cardiovascular intervention with acute myocardial infarction, cardiac insufficiency/heart failure or shock, with multiple interventions

S3: CHOP and APDRG codes used to identify CABG treatment

CHOP code indicating CABG	Explanation
Z36.1	Bypass anastomosis for heart revascularization
Z36.10	Aortocoronary bypass for heart revascularization, not otherwise specified
Z36.11	(Aorto)coronary bypass of one coronary artery
Z36.12	(Aorto)coronary bypass of two coronary arteries
Z36.13	(Aorto)coronary bypass of three coronary arteries
Z36.14	(Aorto)coronary bypass of four or more coronary arteries
Z36.15	Single internal mammary-coronary artery bypass
Z36.16	Double internal mammary-coronary artery bypass
Z36.19	Other bypass anastomosis for heart revascularization
APDRG code indicating CABG	**Explanation**
106	Coronary bypass, with intracardiac catheter
107	Coronary bypass, without intracardiac catheter
546	Coronary bypass, with severe complications

S4: Results of the multilevel Poisson regression for revascularization

	All patients (95% CI)
Sex	**p<0.0023**
Male	1.0
Female	0.91 (0.86,0.97)
Age groups	**p<0.0000**
18 to 44 years	1.0
45 to 49 years	1.02 (0.90,1.15)
50 to 54 years	1.04 (0.93,1.16)
55 to 59 years	1.01 (0.90,1.13)
60 to 64 years	0.99 (0.88,1.10)
65 to 69 years	1.01 (0.90,1.13)
70 to 74 years	0.97 (0.86,1.10)
75 to 79 years	0.91 (0.81,1.03)
80 to 84 years	0.80 (0.70,0.91)
85+ years	0.42 (0.36,0.49)
Citizenship	**p<0.9026**
Foreign	1.0
Swiss	1.00 (0.93,1.06)
Entry decision	**p<0.3483**
Herself/Himself, relatives	1.0
Rescue services	0.96 (0.89,1.02)
Physician	0.96 (0.89,1.02)
Comorbidities	**p<0.0000**
No	1.0
1 - 2	1.87 (1.51,2.32)
3 - 4	1.92 (1.56,2.38)
5 - 6	1.88 (1.51,2.33)
7+	1.60 (1.29,1.99)
Insurance status	**p<0.2585**
Public	1.0
Half Private	1.05 (0.98,1.13)
Private	1.06 (0.96,1.17)
Hospital groups	**p<0.2157**
Small (<15001 cases)	1.0
Medium (15001-30000 cases)	1.17 (0.94,1.47)
High (>30000 cases)	1.27 (0.89,1.82)
Language region	**p<0.2404**
German	1.0
French	1.20 (0.94,1.54)
Italian	1.30 (0.77,2.19)
FTE physicians/1000 cases	**p<0.8691**
1. tertile (<11.86)	1.0
2. tertile (11.86-<17.46)	1.02 (0.88,1.18)
3. tertile (17.46+)	1.06 (0.85,1.31)
Hospital region	**p<0.8227**
Rural	1.0
Urban	1.03 (0.78,1.37)
Angiography device	**p<0.2886**
No	1.0
Yes	1.13 (0.90,1.41)

S5: Results of the multilevel Poisson regression for revascularization for male and female patients younger than 65 years

	Men (95% CI)	Women (95% CI)
Age groups	**p<0.8529**	**p<0.9728**
18 to 44 years	1.0	1.0
45 to 49 years	1.02 (0.90,1.17)	0.97 (0.69,1.38)
50 to 54 years	1.04 (0.92,1.17)	1.06 (0.77,1.46)
55 to 59 years	1.00 (0.88,1.14)	1.02 (0.76,1.39)
60 to 64 years	0.98 (0.87,1.11)	1.06 (0.79,1.44)
Citizenship	**p<0.9426**	**p<0.7214**
Foreign	1.0	1.0
Swiss	1.00 (0.92,1.09)	0.96 (0.77,1.20)
Entry decision	**p<0.9014**	**p<0.6067**
Herself/Himself, relatives	1.0	1.0
Rescue services	0.98 (0.90,1.08)	1.05 (0.84,1.31)
Physician	0.98 (0.89,1.08)	1.12 (0.89,1.40)
Comorbidities	**p<0.0000**	**p<0.3332**
No	1.0	1.0
1 - 2	2.06 (1.52,2.79)	1.68 (0.82,3.45)
3 - 4	2.06 (1.52,2.79)	1.80 (0.88,3.68)
5 - 6	2.02 (1.48,2.75)	1.91 (0.93,3.94)
7+	1.72 (1.25,2.36)	1.59 (0.77,3.29)
Insurance status	**p<0.7019**	**p<0.7939**
Public	1.0	1.0
Half Private	1.04 (0.93,1.17)	1.08 (0.84,1.38)
Private	1.04 (0.89,1.22)	0.94 (0.61,1.44)
Hospital groups	**p<0.0655**	**p<0.0703**
Small (<15001 cases)	1.0	1.0
Medium (15001-30000 cases)	1.29 (1.03,1.60)	1.38 (1.05,1.81)
High (>30000 cases)	1.20 (0.91,1.60)	1.29 (0.95,1.75)
Language region	**p<0.4001**	**p<0.7709**
German	1.0	1.0
French	1.09 (0.88,1.34)	1.06 (0.86,1.31)
Italian	1.28 (0.84,1.95)	1.13 (0.70,1.84)
FTE physicians/1000 cases	**p<0.5446**	**p<0.8723**
1. tertile (<11.86)	1.0	1.0
2. tertile (11.86-<17.46)	1.00 (0.85,1.19)	1.03 (0.81,1.31)
3. tertile (17.46+)	1.14 (0.90,1.44)	1.08 (0.81,1.43)
Hospital region	**p<0.4421**	**p<0.7278**
Rural	1.0	1.0
Urban	1.12 (0.84,1.48)	1.09 (0.67,1.76)
Angiography device	**p<0.9030**	**p<0.6044**
No	1.0	1.0
Yes	1.01 (0.82,1.26)	1.10 (0.77,1.57)

S6: Results of the multilevel Poisson regression for revascularization for male and female patients 65 years and older

	Men (95% CI)	Women (95% CI)
Age groups	**p<0.0000**	**p<0.0000**
65 to 69 years	1.0	1.0
70 to 74 years	0.96 (0.86,1.07)	0.95 (0.79,1.14)
75 to 79 years	0.91 (0.81,1.03)	0.83 (0.69,1.00)
80 to 84 years	0.79 (0.68,0.91)	0.74 (0.62,0.89)
85+ years	0.46 (0.38,0.55)	0.35 (0.28,0.44)
Citizenship	**p<0.8817**	**p<0.7658**
Foreign	1.0	1.0
Swiss	1.01 (0.89,1.15)	1.03 (0.83,1.29)
Entry decision	**p<0.4203**	**p<0.6750**
Herself/Himself, relatives	1.0	1.0
Rescue services	0.96 (0.85,1.09)	0.93 (0.77,1.11)
Physician	1.04 (0.91,1.18)	0.97 (0.81,1.17)
Comorbidities	**p<0.0001**	**p<0.0135**
No	1.0	1.0
1 - 2	1.83 (1.24,2.71)	2.35 (1.24,4.44)
3 - 4	1.90 (1.29,2.79)	2.52 (1.33,4.74)
5 - 6	1.85 (1.25,2.74)	2.34 (1.24,4.43)
7+	1.54 (1.04,2.27)	2.09 (1.11,3.94)
Insurance status	**p<0.6274**	**p<0.0359**
Public	1.0	1.0
Half Private	1.00 (0.89,1.12)	1.18 (1.01,1.38)
Private	1.08 (0.92,1.26)	1.25 (0.98,1.59)
Hospital groups	**p<0.0102**	**p<0.0873**
Small (<15001 cases)	1.0	1.0
Medium (15001-30000 cases)	1.32 (1.10,1.58)	1.27 (1.00,1.60)
High (>30000 cases)	1.19 (0.95,1.48)	1.26 (0.95,1.67)
Language region	**p<0.3227**	**p<0.1167**
German	1.0	1.0
French	1.04 (0.88,1.24)	1.12 (0.90,1.40)
Italian	1.26 (0.93,1.73)	1.50 (0.99,2.28)
FTE physicians/1000 cases	**p<0.1582**	**p<0.2855**
1. tertile (<11.86)	1.0	1.0
2. tertile (11.86-<17.46)	1.02 (0.88,1.19)	0.98 (0.80,1.20)
3. tertile (17.46+)	1.21 (0.99,1.48)	1.21 (0.93,1.57)
Hospital region	**p<0.2783**	**p<0.4489**
Rural	1.0	1.0
Urban	1.17 (0.88,1.55)	1.15 (0.80,1.66)
Angiography device	**p<0.2043**	**p<0.3051**
No	1.0	1.0
Yes	1.14 (0.93,1.41)	1.15 (0.88,1.49)

2.3 Article 3: The geography of end of life care cost

Title:

The geography of end of life care cost in Switzerland:

retrospective analysis using insurance claims data

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Medical Care

(submitted in February 2016)

Title: The geography of end of life care cost in Switzerland: retrospective analysis using insurance claims data

Brief title: The geography of end of life care cost

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Conflict of interest:

All authors declare that they have no competing interests.

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Keywords:

End-of-life, delivery of health care, health care cost, health insurance, small area analysis, regional variation, Switzerland

Abstract (250 words)

Background

Healthcare spending increases sharply at end of life (EOL). As the population ages, this places more and more pressure on the healthcare system. However, we know little about variation of EOL care between regions, or determinants of that care in Switzerland.

Methods

We used basic health insurance (BHI) claims of individuals who died between 2008 and 2010 to derive EOL care costs. We linked to the mortality database for information on cause of death and individual characteristics. We described characteristics of regions of residence, including healthcare supply measures. We used multilevel regression models to estimate differences in costs across regions and characteristics.

Results

Study population consisted of 111,275 individuals. Reimbursement by BHI was, on average, 33.1k (thousand) Swiss Francs (standard deviation 33.2k) during last year of life. Variance was reduced by 62-85% when we added individual and regional characteristics, with strong effect of language region. The highest cost ratios were observed for cause of death, particularly for cancer. These were followed by age and language region. Civil status and area-based socioeconomic position had smaller effects. Nationality, urbanicity and healthcare supply measures had little effect. We found spatial pattern in cost across regions: higher values clustered in the Eastern (French-speaking) part of the country, and around the cities of Bern, Basel and Zurich.

Conclusions

BHI data show that in Switzerland, EOL care cost depends mainly on the cause of death and age at death. Variation might indicate that that EOL care process seems to be organized differently between linguistic regions.

Introduction

Two factors characterize the Swiss healthcare system: high performance and high cost. An aging population and advances in medicine raise healthcare costs even higher. [1] Treatment patterns, intensity, and resulting costs depend both on medical condition, and on demographic and socioeconomic patient characteristics. [2] Since HCE are unevenly distributed across the life span [3], and end of life (EOL) is often associated with sharp increases in spending on health, the imbalance in spending may be attributable to rising costs and demands for resources placed on healthcare systems by EOL patients. [4–6]

A growing body of literature suggests that regional provider factors, such as financial incentives, and physicians' beliefs or practice norms result in different patterns of healthcare use and expense. [7–9] For instance, several Swiss studies found that in regions where density of physicians was higher, the cost of care also increased [10–14] suggesting supply-induced demand. Others pointed out that different reimbursement schemes affect cost-efficiency among hospitals that provide inpatient care. [15,16] These patterns do not necessarily match the preferences of patients and their families [17,18], it is not clear that more or more expensive services increase patient satisfaction or improve outcomes. [19,20]

Unfortunately, tracking variation in healthcare and identifying its causes, is non-trivial exercise. [21] It is particularly difficult in Switzerland, where strong federalism and regulated competition within the healthcare system, and a very culturally diverse population, can interact in various ways to cause myriad differences in healthcare utilization and costs among and across regions. [2,4,11,14,22] This may explain why only a handful of studies attempted to examine the importance of EOL care (EOLC) in the Swiss health system. Reich et al. [18] examined differences in healthcare utilization across place of death; Matter-Walstra et al. [2,23] looked at the delivery of care to cancer patients, and, von Wyl et al. [24] developed typology of cost trajectories in EOLC. All these studies had limited power to investigate small-area patterns across the country despite importance of such research for informing policy makers and clinicians. [6,11,25] In addition, some of these studies are limited because they used heterogeneous areas such as Swiss cantons that may not be best suited for regional analyses. [26,27]

We set out to study regional variation in cost of EOLC in Switzerland. We first constructed a nationally representative dataset of EOLC, allowing us to perform studies across small-areas. We then identified contextual factors and described how, and to what degree, context shaped variation in cost across regions.

Methods

Study setting

Switzerland is a small European federal republic of 26 cantons, stretched between the Alps, the Swiss Plateau and the Jura Mountains. Its consumer-driven healthcare system is chiefly financed by compulsory basic health insurance (BHI) and out-of-pocket payments. The package covers all essential benefits related to medical illness and pregnancy and deemed medically- and cost-appropriate. [see **Text 1, SDC** for more details].

Data sources

We harmonized and combined anonymized BHI claims of six large companies and used them as the primary data source for our study (**Table 1, SDC**). We included all individuals with BHI who died between 1.1.2008 and 31.12.2010. Information on sex, age, date of birth and death, and place of residence were available for each insuree. We aggregated all BHI claims within the last 12 months of life, and used the total amount reimbursed to derive overall EOLC cost.

The Swiss Federal Statistical Office's (SFSO) database of causes of death was probabilistically linked to insurance records using date of birth, date of death, sex, and community of residence to derive information on cause of death, nationality, civil status and religion. Based on SFSO data, we also assessed representativeness of the data. Characteristics of communities, supply of ambulatory, inpatient and non-acute care together with population denominator were derived from available sources (**Table 1, SDC**).

Analytical regions

We used 705 MedStat regions - basic unit of delivery of SFSO's health statistics, and aggregated them into 564 custom regions (hereinafter referred to as MedStat) that best approximated boundaries of Swiss communities. We then used SFSO's classification of communities (the lowest level of administrative division) to derive urbanicity and language region of MedStat. Swiss-SEP (area-based socioeconomic position) index [28] was derived as a median value of all neighbourhoods that overlapped MedStat and divided into quintiles. Utilization-based HSAs were created using methodology described in details elsewhere [26]. In short, we used individual-level discharges of all Swiss hospitals in 2010 to create matrix of patient flows and then aggregated them to form 71 units, where majority of residents were hospitalized [**Figure 1, SDC**].

Study population & measures

We excluded individuals below age 19, those who lived abroad, and those whose address was not known. We also excluded individuals who were not linked to mortality records, and those with no claims reimbursed by BHI during their last 12 months of life.

We aggregated age into 5-year bands. Civil status was categorized into 'single', 'married', 'widowed' and 'divorced'; nationality into 'Swiss' and 'foreigner' (including missing values); religion into 'Protestant', 'Catholic', 'No affiliation' and 'Other/Unknown'. Primary causes of death were simplified to eight categories, based on the main groupings of the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) classification (see **Table 1** for detailed codes).

Characteristics of regions of residence included urbanicity ('urban', 'peri-urban', 'rural') and language ('German', 'French', 'Italian'). Ambulatory care supply was measured by density of physicians per 10,000 inhabitants, acute care as number of utilized hospital beds per 10,000 inhabitants, and non-acute care as number of nursing home beds per 10,000 inhabitants 65 year old and older (all in quintiles).

Analyses

We calculated frequencies and described overall cost (mean, standard deviation [SD]) across characteristics. We used individual level data to fit multilevel regression models; MedStat regions were nested within HSAs. Main outcome was the log transformed overall EOLC cost. [29,30] In sensitivity analyses we used alternative measures of cost correcting for ambulatory care billed under the tariff system (TARMED): we used tariff points instead of CHF, and costs of inpatient care that included cantonal subsidies (based on first available data from 2012).

We assessed interaction of sex, and, within sex strata, also a binary age indicator (divided into 19-65 year-olds and those >66) with remaining variables. We considered four models, gradually increasing complexity by adjusting for more characteristics. Models were assessed according to the reduction of variance compared to unadjusted model. [31] For each region we calculated deviation from the national mean using the random part of the models.

Data management and analyses were done with Stata 14 (StataCorp LP, College Station, Texas, USA) and we used The Generalized Record Linkage System for record linkage. [32]

Ethics

Ethical approval was obtained from the Ethics Committee of the Canton of Bern.

Results

Study population

The initial dataset consisted of 119,613 individuals. We excluded 620 (0.5%) individuals younger than 19, 172 (0.1%) individuals who lived abroad, and 364 (0.3%) whose address was missing [**Figure 2, SDC**]. Remaining population was probabilistically linked to 2008-2010 mortality data with 95.6% success rate; 5,180 unlinked individuals were similar to the linked ones [**Table 2, SDC**] and were excluded. We also excluded 2,002 individuals who had no reimbursed claims [**Table 3, SDC**].The study population covered 61% of deaths in Switzerland between 2008-2010 [**Table 4, SDC**]. The sex, age nationality, civil status urbanicity, language region, Swiss-SEP and, most importantly, cause of death distributions were almost identical to overall mortality in that time period.

Final study population consisted of 111,275 individuals (**Table 1**). Of these, 85% were 66 years or older; women were older at the time of death. Main causes of death were CVD (36%) and cancer (26%). Cancer was more frequent among younger people and CVD more frequent among older. Relatively, older women more often died from mental and behavioural disorders, and older men more often from respiratory diseases. Young men were most likely to die of external causes. Study participants were almost all Swiss (92%), and either married (39%) or widowed (40%) at time of death. There were more foreigners and single individuals among younger age groups and older women were widows. There were few differences by religious affiliation, urbanicity and SEP.

EOL healthcare costs

Reimbursement by BHI was, on average, 33.1k (thousand) Swiss Francs (CHF; SD 33.2k) during last year of life [**Table 5, SDC**]. Average spending was higher among younger individuals, particularly women. For both sexes spending tended to first increase with age, and then decrease among the oldest age groups. Cancer deaths, especially among younger individuals, were the most expensive (range 40.4k to 66.4k CHF, depending on age). The next most expensive were diseases of the nervous system (particularly among younger individuals) and respiratory diseases (particularly for young women) - range of cost 30.4k – 46.0k CHF. CVD, external causes and, among younger individuals, mental and behavioural diseases, were on average, less expensive (range 13.5k - 26.3k CHF). Average EOL cost tended to be higher among foreigners, married persons, and those resident in French-speaking parts of Switzerland, and areas where SEP was higher but lower in areas with a higher density of nursing home beds.

Determinants of EOL healthcare costs

We found evidence of interaction of sex and age with other variables [**Table 6, SDC**]. We thus used separate models for younger (aged 19-65) and older (66 and above) men and women. Extending models by including more variables gradually reduced variance (**Table 2**). Model 2, which was adjusted for characteristics of individuals and their place of residence, reduced HSA level variance by 39% for younger men and 12% for older men, with smaller reductions for women (9% and 3%). When we also considered healthcare supply measures (Model 3) variance was 18% to 46% less than in the unadjusted model. Large effects appeared when we considered language region (Model 4): HSA level variance was less than half for all age and sex groups, when compared only to Model 3. Different variance patterns were observed on the MedStat level with slight reductions of variance for older individuals, drop for younger women and slight increase for younger men after first adjustment (model 2).

There was little change in the estimates of the covariates between Models 2 and 4 [**Tables 7-10, SDC**]. The fully adjusted model (4) showed wide variation of cost ratio across variables (**Table 5**). Cause of death had the strongest influence; cancer deaths were associated with the highest cost ratio, particularly for younger males and women. Costs were lower for cancer deaths among older men and older women. Death from diseases of the nervous system generated the second highest costs. The third costliest group varied based on age of death. For younger people, respiratory diseases were most expensive. For older people, mental and behavioural disorders were most expensive. Unsurprisingly, the cost was lowest for people who died from external causes. Age effect was weaker than cause of death and varied slightly between sexes. Young persons, and particularly men accumulated less costs. Costs increased among middle-aged individuals and then decrease again around age 70. We found moderate effects of increased cost among individuals from French- and Italian-speaking parts of Switzerland. We found small effects of decreased cost for people who were single, divorced, had no religious affiliation, and lived in areas of lowest SEP. Healthcare supply measures had little effect.

Geographical variation in EOL healthcare costs

There was considerable variation in spatial distribution of random effects (**Figure 1**). The highest cost was in the Western (French-speaking) parts of the country (regions around cities of Lausanne and Geneva), in canton Ticino (Italian-speaking) and near large German-speaking cities (Basel, Bern, Zurich). Costs associated with death among older people were higher in parts of canton Graubünden and Valais. The Alps and central and north-west regions had lower costs. Adjusting for individual, regional and supply care covariates (models 2 and 3) only slightly changed the random effects [**Figure 3** and **4, SDC**]. Adjusting for language region, however, had significant impact (**Figure 2**) and diminished the contrast between West, the South and rest of the country. The range of estimates significantly decreased: fewer regions fell into extreme classes of maps. Higher costs, mainly among older individuals, were still present around large cities (Bern, Zurich, Basel) and in parts of Canton Vaud. Among older women, pockets of increased cost were found in Eastern Valais and parts of Graubünden. The belt of lower costs stretched, in the north, between cantons Neuchatel and Thurgau (with the exception of Basel), and the western part of Valais (particularly for older women).

Discussion

Main findings

We studied geographical variation in EOLC cost in Switzerland and assessed possible determinants of cost across individual, regional and healthcare supply factors. We found strong associations of cost with cause of death and age of the decedent. When we included language region, variance was greatly reduced, and supply factors played virtually no role. The strong spatial patterning of cost between regions could be only explained by covariates.

Strengths

The biggest strength of the study is its sample size. This was the largest and most comprehensive dataset of EOLC ever assembled in Switzerland. Coverage and representativeness of the data allowed us to analyse, for the first time, small-area variation. Earlier Swiss studies used language regions [18,33] or cantons [10,11,14,23,34] to track variation in intensity and cost of care. But, as this study demonstrated, cantons are heterogeneous. Unlike other insurance-based EOLC studies from Switzerland [2,18,24], we included reliable cause of death information and socio-demographic characteristics recorded on the death certificate. By using BHI claims data, we were able to cover the full range of care providers and include cost from ambulatory, inpatient and non-acute settings. Finally, ancillary databases allowed us to describe communities and capture supply of healthcare. Supply measures, have been described using utilization-based areas which are better suited for this purpose than administrative units. [26,27]

Limitations

The study has some limitations. First, studies based on health insurance claims contain limited patient-level information. Quality or appropriateness of care are also difficult to measure from administrative data. We supplemented this data by linking to other sources, but important aspects of EOLC cost determinants may not be included; for instance, we could not include non-claims based measures of illness severity [35], patient and family preferences [36,37], functional impairment, or presence of relative nearby. [31] Second, overall cost is only one possible outcome in analyses of EOLC. [35,38,39], so our ongoing analyses will aim at disaggregating costs and exploring alternative measures of intensity of care. Third, focusing on the last 12 months of life is an arbitrary choice and, as in any retrospective design for a study of EOLC, we might have included costs unrelated to EOLC. [40] However, it is also one of the most frequently used time frames and facilitates comparability with other studies. A retrospective design efficiently identifies the members of EOLC studies so we could construct large representative datasets. Our study doesn't suffer from inaccurate prognostication of survival and incomplete enrolment of patients. Langton and colleagues [39] describe two retrospective and prospective cancer EOLC studies with comparable results. [41,42] Our own sensitivity analyses indicated that alternative, shorter time frames of six and one month provided similar results. Fourth, relying only on BHI claims could cause us to underestimate overall cost. Our estimates do not include costs covered by supplementary insurance, claims paid directly by patients or not delivered to insurers. [18,33] About 50% of inpatient cost are subsidized by cantons and BHI pays only about 18% of costs of nursing home stays (mainly for medical treatments). [24] However, our sensitivity analyses showed that while monetary cost understandably increases when we use cost corrected for cantonal subsidies of hospital care, the direction and strength of the associations remained unaffected.

Relation to other studies

Our reports of HCE during last 12 months of life is comparable with previous studies. Von Wyl et al. [24] estimated median cost to be 30.3k CHF (individuals aged 65 and over, last 12 months of life) and Reich et al. [18] to be 17.7k CHF (general population, last six months of life). These are considerably higher than among the general population in Switzerland: mean annual HCE is about 3,5k CHF [43]; for people aged 65 and over it is about 6.7k CHF per year. [33] Such a magnitude of difference with EOLC population was also reported in the U.S. [44], and points to importance of EOLC in delivery of care.

Cancer is the costliest cause of death in both Switzerland and the U.S. [44], and the highest cost trajectory of Swiss decedents identified by von Wyl et al. [24] found a high share of cancer patients. The high cost of cancer been linked to expensive new drugs and therapies. Decreases in the intensity and cost of EOLC with age were reported in Switzerland [4,23,24] and elsewhere. [5,31,39,44] Even among the general, older Swiss population, age was associated with decrease of HCE. [33] Less use of inpatient care (including Intensive Care Units) and/or less "aggressive" treatments for the elderly lower costs in older people, and this study may support these findings. The elderly also tend to die closer to diagnosis of serious illness, which lower expenses because time since diagnosis is often associated with intensity and cost of treatments. [40] Similarly, as in the U.S. [31] and the Netherlands [5], single and divorced individuals had slightly lower EOLC costs. Religious association seemed to play no role, which matches Kelley et al., [31] who found no association of EOLC cost with religiosity.

We found evidence for large geographic variation in cost, yet were unable to completely explain its causes. The influence of language region suggests that regional differences in provision and consumption of care could be factors. In Switzerland, we knew the differences across cantons in overall cost of care [10,14,25], overall number of hospitalizations [34], and intensity of EOLC of cancer patients. [2] Language region also played a role in treatment intensity in ambulatory settings. [12] These findings overlap with ours: costs were higher in many regions of French- and Italian-speaking Switzerland. More people died in the hospital in French- and Italian-speaking cantons, and since hospital deaths tend to cost more, this may be a partial explanation. [18,45] Doctors' EOL decisions also vary across cultural regions: Fisher, et al. demonstrated, for instance, that French-speaking physicians were more likely to manage pain and symptoms aggressively, but were less willing than their German-speaking colleagues to comply with patient wishes for non-treatment. [46] We found no association of the cost of EOLC with urbanization, but after we adjusted for urbanicity, we found increased EOL costs around the biggest cities. Others reported a lack of association of urbanicity with number of hospitalizations of cancer patients. [2]. Deaths at home, which are associated with lower cost, are more common in rural areas, which might explain part of the pattern. [18]

We found no association with healthcare supply measures. Density of physicians, which was associated with intensity and cost of general healthcare in Switzerland in earlier studies [11,12,14], was not a factor associated with EOLC cost. Both earlier studies, however, used aggregated data which might have biased their results. Similarly, hospital bed density was not associated with cost of care, resembling previous results from Switzerland [10], but not from the U.S. [8,19,37] Our results suggest that, after other characteristics are adjusted for, a larger supply of inpatient care does not raise EOLC cost by increasing use of hospitals.

Implications

Previous efforts have been made to track variation in EOLC cost across place of death [18] and across time. [24] This study adds regional analyses, which can be used to target interventions that will improve care. Policies that shape the cost of EOLC in Switzerland should focus more on individual-level characteristics of patients, but also account for regional differences in healthcare delivery and consumption. Supply of care does not seem to play a role in shaping EOLC costs. EOLC might not be the most efficient place for curbing the growing HCE [47], but we did identify significant variation that may indicate under- or overuse of services in EOLC. But if regions that spend more offer better quality of care and have higher patient satisfaction, the rest of the country should follow suit. If future research finds that this is not the case, then the areas highlighted by our findings should become the focus of regionally tailored interventions. Finally, regional findings may point to different patient preferences between regions. If serving these preferences, independent of medical needs, is considered a valid social goal [37], then substantial variation in cost of EOLC in Switzerland will persist.

Conclusion

BHI claims data show that in Switzerland EOLC cost depends on the cause of death and age of the decedents. Variation across language might indicate that care process for EOL seems to be organized differently between regions. However, supply of care does not seem to play a major role. In the light of the

2012 Swiss-wide changes to new inpatient reimbursement system, this study proves a benchmark for tracking the effects of these changes on EOLC.

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Table 1. Characteristics of the study population. Frequencies and percentages across sex and age. Abbreviations: 'CVD' –cardiovascular deaths, 'Mental & behav.' – mental and behavioural disorders. Swiss-SEP – Swiss neighbourhood index of socioeconomic position (see [28] for details). Causes of death are based on main groupings of the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) classification: 'cardiovascular diseases' (CVD; I00-I99); 'cancer' (C00-C99); 'mental and behavioural disorders' (F00-F99); 'diseases of the nervous system' (G00-G99); 'respiratory diseases' (J00-J99;, 'diseases of the digestive system' (K00-K99); 'external causes of death' (V00-V99, W00-W99, X00-X99 and Y00-Y99); and, 'other' (all remaining codes).

Characteristic	**Males, 19-65**		**Males, 66+**		**Females, 19-65**		**Females, 66+**		**Total**	
	No.	*Col %*	*No.*	*Col %*	*No.*	*Col %*	*No.*	*Col %*	*No.*	*Col %*
Age group										
19 - 25	253	2%			105	2%			358	0%
26 - 30	214	2%			126	2%			340	0%
31 - 35	262	3%			153	2%			415	0%
36 - 40	384	4%			252	4%			636	1%
41 - 45	671	6%			391	6%			1,062	1%
46 - 50	1,111	11%			702	11%			1,813	2%
51 - 55	1,606	15%			1,048	16%			2,654	2%
56 - 60	2,411	23%			1,468	23%			3,879	4%
61 - 65	3,672	35%			2,191	34%			5,863	5%
66 - 70			4,584	11%			2,801	5%	7,385	7%
71 - 75			5,713	14%			4,153	8%	9,866	9%
76 - 80			7,925	19%			6,607	13%	14,532	13%
81 - 85			9,496	23%			11,268	21%	20,764	19%
86 - 90			8,404	20%			13,527	26%	21,931	20%
91+			5,411	13%			14,366	27%	19,777	18%
Nationality										
Swiss	8,705	82%	38,063	92%	5,606	87%	50,065	95%	102,439	92%
Foreigner/Unknown	1,879	18%	3,470	8%	830	13%	2,657	5%	8,836	8%
Civil status										
Single	2,882	27%	3,365	8%	1,277	20%	5,701	11%	13,225	12%
Married	5,643	53%	24,809	60%	3,393	53%	9,671	18%	43,516	39%
Widowed	250	2%	10,546	25%	487	8%	33,388	63%	44,671	40%
Divorced	1,809	17%	2,813	7%	1,279	20%	3,962	8%	9,863	9%
Religion										
Protestant	3,731	35%	20,518	49%	2,422	38%	27,624	52%	54,295	49%
Catholic	3,825	36%	14,312	35%	2,296	36%	18,136	34%	38,569	35%
No affiliation	1,093	10%	2,137	5%	620	10%	1,661	3%	5,511	5%
Other/Unknown	1,935	18%	4,566	11%	1,098	17%	5,301	10%	12,900	12%
Cause of death										
CVD	2,178	21%	15,220	37%	786	12%	22,072	42%	40,256	36%

Cancer	4,234	40%	11,873	29%	3,450	54%	9,800	19%	29,357	26%
Mental & behav.	265	3%	2,048	5%	138	2%	4,532	9%	6,983	6%
Nervous system	305	3%	1,873	5%	260	4%	2,996	6%	5,434	5%
Respiratory	327	3%	3,310	8%	208	3%	3,152	6%	6,997	6%
Digestive	585	6%	1,503	4%	291	5%	2,128	4%	4,507	4%
External	1,628	15%	1,644	4%	663	10%	1,931	4%	5,866	5%
Other	1,062	10%	4,062	10%	640	10%	6,111	12%	11,875	11%
Urbanicity										
Urban	3,334	32%	12,752	31%	2,041	32%	18,462	35%	36,589	33%
Peri-urban	4,611	44%	18,114	44%	2,967	46%	21,852	41%	47,544	43%
Rural	2,639	25%	10,667	26%	1,428	22%	12,408	24%	27,142	24%
Language region										
German	7,150	68%	29,466	71%	4,496	70%	37,538	71%	78,650	71%
French	2,945	28%	9,912	24%	1,693	26%	12,212	23%	26,762	24%
Italian	489	5%	2,155	5%	247	4%	2,972	6%	5,863	5%
Swiss-SEP quintile										
1st (lowest)	787	7%	3,020	7%	403	6%	3,444	7%	7,654	7%
2nd	2,313	22%	9,167	22%	1,281	20%	11,042	21%	23,803	21%
3rd	3,027	29%	11,229	27%	1,751	27%	14,377	27%	30,384	27%
4th	3,587	34%	13,868	33%	2,335	36%	18,861	36%	38,651	35%
5th (highest)	870	8%	4,249	10%	666	10%	4,998	10%	10,783	10%
Total	10,584	100%	41,533	100%	6,436	100%	52,722	100%	111,275	100%

Table 2. Variance on MedStat and Hospital Service Area levels across four models. 'Change' indicates %change in relation to model 1. Abbreviation: HSA – Hospital Service Area.

Sex	**Age**	**Level**	**Model**						
			1	*2*		*3*		*4*	
			Variance	*Variance*	*Change*	*Variance*	*Change*	*Variance*	*Change*
Males	*19-65*	*HSA*	0.028	0.017	-39%	0.015	-46%	0.005	-82%
		MedStat	0.003	0.007	133%	0.005	67%	0.005	67%
	66+	*HSA*	0.025	0.022	-12%	0.015	-40%	0.006	-76%
		MedStat	0.007	0.000	-100%	0.001	-86%	0.001	-86%
Females	*19-65*	*HSA*	0.034	0.031	-9%	0.024	-29%	0.008	-76%
		MedStat	0.008	0.004	-50%	0.004	-50%	0.004	-50%
	66+	*HSA*	0.040	0.039	-3%	0.033	-18%	0.014	-65%
		MedStat	0.006	0.005	-17%	0.005	-17%	0.006	0%

Table 3. Coefficients of multivariable, multilevel regression (model 4 - fully adjusted) across four subpopulations. Age and sex specific multilevel models using individual-patient data, adjusted for all variables present in the table, with 564 modified MedStat regions nested in 71 Hospital Service Areas (HAS). Estimates, presented as exponentiated coefficients, reflect cost ratio of end of life care cost during last 12 months of life, in comparison to reference category. Density of supply measures and Swiss-SEP index divided into quintiles of spatial units. Values of 'Constant' term were not exponentiated. P-values from the Wald test of the group parameters being jointly one. Abbreviations: 'Est.' – estimate; 'CI' confidence interval; 'ref.' – reference group; 'CVD' – cardiovascular deaths; 'Mental & behav.' – mental and behavioural disorders (see Table 1 for detailed ICD-10 codes); 'No affil.' – no religious affiliation; 'Swiss-SEP' – Swiss neighbourhood index of socioeconomic position (see [28] for details).

Variable	**Group**	**Males, <19-65**			**Males, 66+**			**Females, 19-65**			**Females, 66+**		
		Est.	*95% CI*	*p-value*	*Est.*	*95% CI*	*p-value*	*Est.*	*95% CI*	*p-value*	*Est.*	*95% CI*	*p-value*
Age	*19-25*	0.44	(0.37, 0.53)	<0.0001				0.82	(0.65, 1.04)	0.00			
	26-30	0.67	(0.55, 0.81)					0.85	(0.69, 1.06)				
	31-35	0.97	(0.81, 1.15)					0.92	(0.76, 1.11)				
	36-40	0.88	(0.76, 1.02)					1.20	(1.03, 1.40)				
	41-45	0.80	(0.72, 0.90)					1.18	(1.04, 1.34)				
	46-50	0.85	(0.78, 0.94)					1.09	(0.99, 1.20)				
	51-55	0.86	(0.79, 0.93)					1.04	(0.95, 1.13)				
	56-60	0.99	(0.92, 1.06)					0.96	(0.89, 1.04)				
	61-65	ref.	-					ref.	-				
	66-70				ref.	-	<0.0001				ref.	-	<0.0001
	71-75				1.02	(0.98, 1.06)					0.94	(0.90, 0.98)	
	76-80				0.99	(0.96, 1.03)					0.88	(0.85, 0.92)	
	81-85				0.94	(0.91, 0.98)					0.83	(0.80, 0.87)	
	86-90				0.92	(0.88, 0.96)					0.82	(0.79, 0.85)	
	91+				0.91	(0.87, 0.95)					0.82	(0.79, 0.86)	
Cause of death	*CVD*	ref.	-	<0.0001	ref.	-	<0.0001	ref.	-	<0.0001	ref.	-	<0.0001
	Cancer	6.17	(5.75, 6.62)		1.90	(1.85, 1.95)		4.67	(4.27, 5.11)		1.54	(1.51, 1.58)	
	Mental & behav.	0.98	(0.82, 1.16)		1.45	(1.39, 1.52)		1.10	(0.89, 1.36)		1.30	(1.26, 1.34)	
	Nervous system	3.38	(2.87, 3.98)		1.68	(1.60, 1.77)		2.69	(2.29, 3.16)		1.38	(1.33, 1.43)	
	Respiratory	2.67	(2.27, 3.12)		1.39	(1.34, 1.44)		2.45	(2.06, 2.93)		1.21	(1.17, 1.25)	
	Digestive	2.25	(1.99, 2.55)		1.35	(1.28, 1.43)		1.73	(1.48, 2.02)		1.16	(1.11, 1.21)	

	External	0.62	(0.56, 0.68)		0.93	(0.88, 0.98)		0.75	(0.66, 0.85)		0.96	(0.92, 1.00)	
	Other	1.79	(1.61, 1.98)		1.24	(1.19, 1.28)		1.74	(1.54, 1.97)		1.15	(1.12, 1.18)	
Civil status	*Single*	0.89	(0.83, 0.96)	0.00	0.87	(0.84, 0.90)	<0.0001	0.92	(0.85, 1.00)	0.14	0.92	(0.89, 0.95)	<0.0001
	Married	ref.	-		ref.	-		ref.	-		ref.	-	
	Widowed	0.96	(0.81, 1.14)		1.00	(0.97, 1.02)		0.93	(0.84, 1.04)		0.97	(0.95, 0.99)	
	Divorced	0.89	(0.82, 0.95)		0.89	(0.85, 0.93)		0.94	(0.87, 1.02)		0.96	(0.92, 0.99)	
Nationality	*Swiss*	ref.	-	0.07	ref.	-	0.08	ref.	-	0.03	ref.	-	0.31
	Foreigner/Unknown	1.07	(0.99, 1.15)		1.03	(1.00, 1.07)		1.11	(1.01, 1.21)		0.98	(0.94, 1.02)	
Religion	*Protestant*	ref.	-	0.18	ref.	-	<0.0001	ref.	-	<0.0001	ref.	-	<0.0001
	Catholic	1.01	(0.94, 1.08)		1.03	(1.01, 1.06)		1.00	(0.93, 1.07)		1.03	(1.01, 1.05)	
	No affil.	0.97	(0.88, 1.07)		1.04	(0.99, 1.09)		1.00	(0.91, 1.11)		0.97	(0.93, 1.02)	
	Other/Unknown	0.93	(0.85, 1.01)		0.91	(0.88, 0.94)		0.82	(0.75, 0.90)		0.94	(0.92, 0.97)	
Urbanicity	*Urban*	1.04	(0.94, 1.14)	0.77	1.01	(0.96, 1.05)	0.59	1.05	(0.95, 1.16)	0.63	1.02	(0.98, 1.07)	0.47
	Peri-urban	ref.	-		ref.	-		ref.	-		ref.	-	
	Rural	1.01	(0.92, 1.11)		0.98	(0.94, 1.02)		1.02	(0.93, 1.13)		0.99	(0.96, 1.03)	
Swiss-SEP	*1st (lowest)*	0.84	(0.74, 0.97)	0.00	0.92	(0.87, 0.98)	<0.0001	0.77	(0.66, 0.90)	0.00	0.97	(0.92, 1.03)	0.81
	2nd	0.91	(0.83, 1.00)		0.95	(0.92, 0.99)		0.85	(0.77, 0.94)		0.99	(0.95, 1.02)	
	3rd quintile	ref.	-		ref.	-		ref.	-		ref.	-	
	4th	1.10	(1.01, 1.19)		1.05	(1.01, 1.09)		1.04	(0.95, 1.13)		1.00	(0.96, 1.03)	
	5th (highest)	1.09	(0.97, 1.23)		1.11	(1.06, 1.18)		1.06	(0.94, 1.19)		1.02	(0.97, 1.07)	
Dens. of physicians	*1st (lowest)*	0.94	(0.85, 1.05)	0.56	0.98	(0.94, 1.03)	0.00	0.99	(0.88, 1.12)	0.13	1.01	(0.97, 1.06)	0.04
	2nd	0.93	(0.84, 1.03)		0.96	(0.92, 1.00)		1.11	(0.99, 1.24)		1.02	(0.98, 1.06)	
	3rd quintile	ref.	-		ref.	-		ref.	-		ref.	-	
	4th	0.99	(0.90, 1.09)		1.03	(0.99, 1.08)		1.11	(1.00, 1.23)		1.06	(1.02, 1.10)	
	5th (highest)	0.98	(0.88, 1.09)		1.05	(1.00, 1.10)		1.08	(0.97, 1.21)		1.04	(1.00, 1.09)	
Dens. of nursing home beds	*1st (lowest)*	0.98	(0.86, 1.12)	0.94	0.96	(0.88, 1.06)	0.59	0.98	(0.85, 1.13)	0.16	1.00	(0.90, 1.12)	0.86
	2nd	0.97	(0.86, 1.10)		0.96	(0.88, 1.05)		0.94	(0.82, 1.07)		0.97	(0.87, 1.08)	
	3rd quintile	ref.	-		ref.	-		ref.	-		ref.	-	
	4th	0.98	(0.87, 1.11)		0.94	(0.86, 1.03)		0.90	(0.79, 1.02)		0.98	(0.88, 1.09)	
	5th (highest)	0.94	(0.81, 1.08)		0.93	(0.85, 1.02)		0.84	(0.73, 0.98)		0.95	(0.85, 1.06)	
Dens. of hospital beds	*1st (lowest)*	1.05	(0.91, 1.21)	0.67	0.99	(0.90, 1.08)	0.94	1.03	(0.89, 1.19)	0.84	0.98	(0.88, 1.09)	0.92
	2nd	1.08	(0.96, 1.22)		1.03	(0.94, 1.12)		1.05	(0.92, 1.19)		1.03	(0.93, 1.15)	
	3rd quintile	ref.	-		ref.	-		ref.	-		ref.	-	
	4th	1.02	(0.92, 1.13)		1.01	(0.94, 1.10)		1.00	(0.90, 1.12)		1.00	(0.91, 1.11)	
	5th (highest)	1.07	(0.95, 1.21)		1.01	(0.92, 1.10)		1.07	(0.94, 1.21)		0.99	(0.89, 1.11)	
Language region	*German*	ref.	-	<0.0001	ref.	-	<0.0001	ref.	-	<0.0001	ref.	-	<0.0001
	French	1.33	(1.21, 1.47)		1.35	(1.26, 1.44)		1.28	(1.15, 1.42)		1.33	(1.24, 1.43)	
	Italian	1.24	(0.98, 1.57)		1.39	(1.14, 1.69)		1.16	(0.90, 1.50)		1.27	(1.01, 1.61)	
Constant		7.41	(6.30, 8.73)		14.78	(13.38, 16.32)		10.27	(8.56, 12.32)		19.42	(17.29, 21.80)	

Variance	*HSA level*	0.00	(0.00, 0.02)		0.01	(0.00, 0.01)		0.01	(0.00, 0.02)		0.01	(0.01, 0.02)		
	MedStat level	0.01	(0.00, 0.04)		0.00	(0.00, 0.01)		0.00	(0.00, 5.22)		0.01	(0.00, 0.01)		
	Residual	1.84	(1.79, 1.89)		1.06	(1.04, 1.07)		1.31	(1.26, 1.35)		0.86	(0.85, 0.87)		

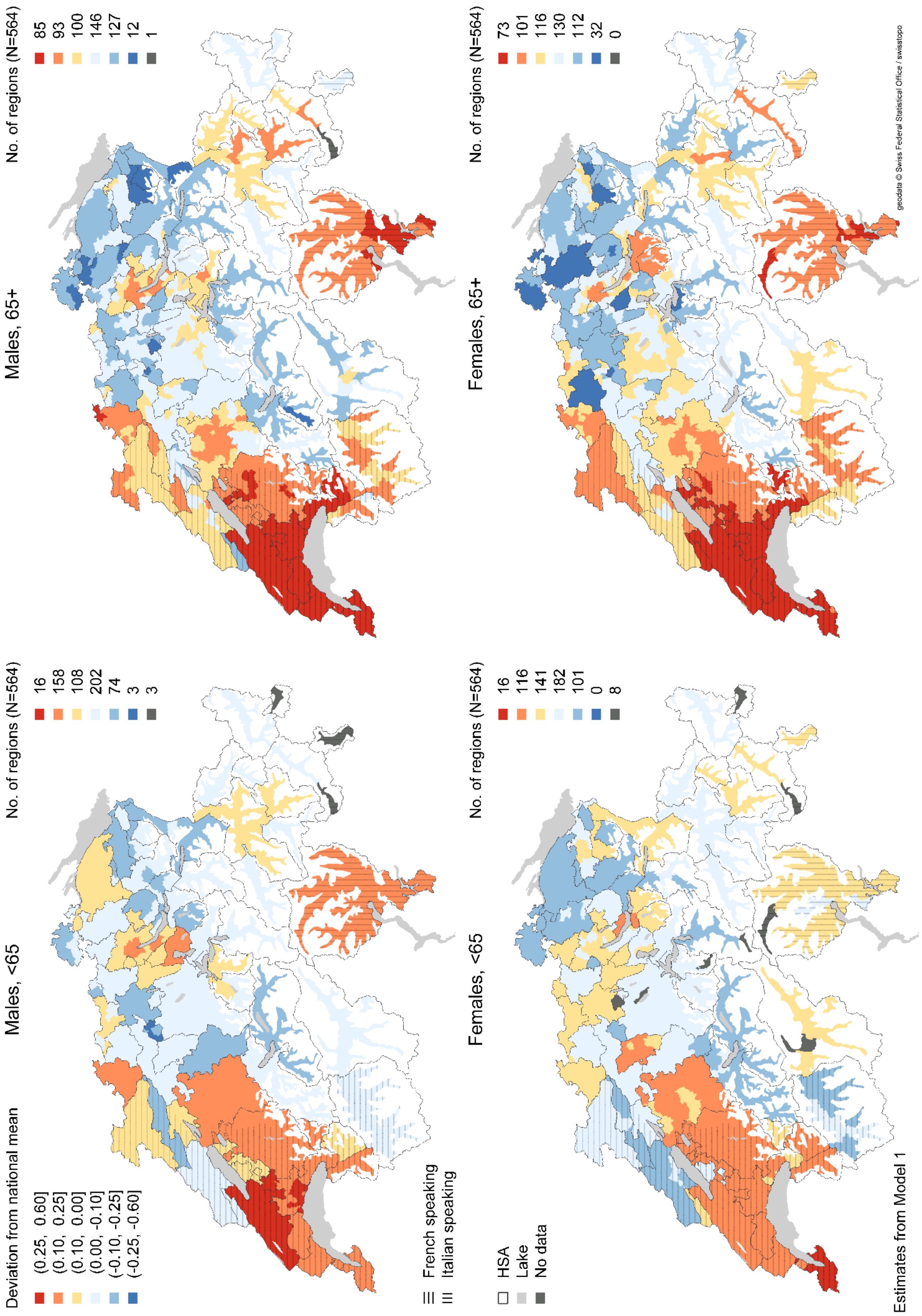

Figure 1. Spatial distribution of deviation from national mean (random effects) of model 1 (unadjusted) across 564 modified MedStat regions.

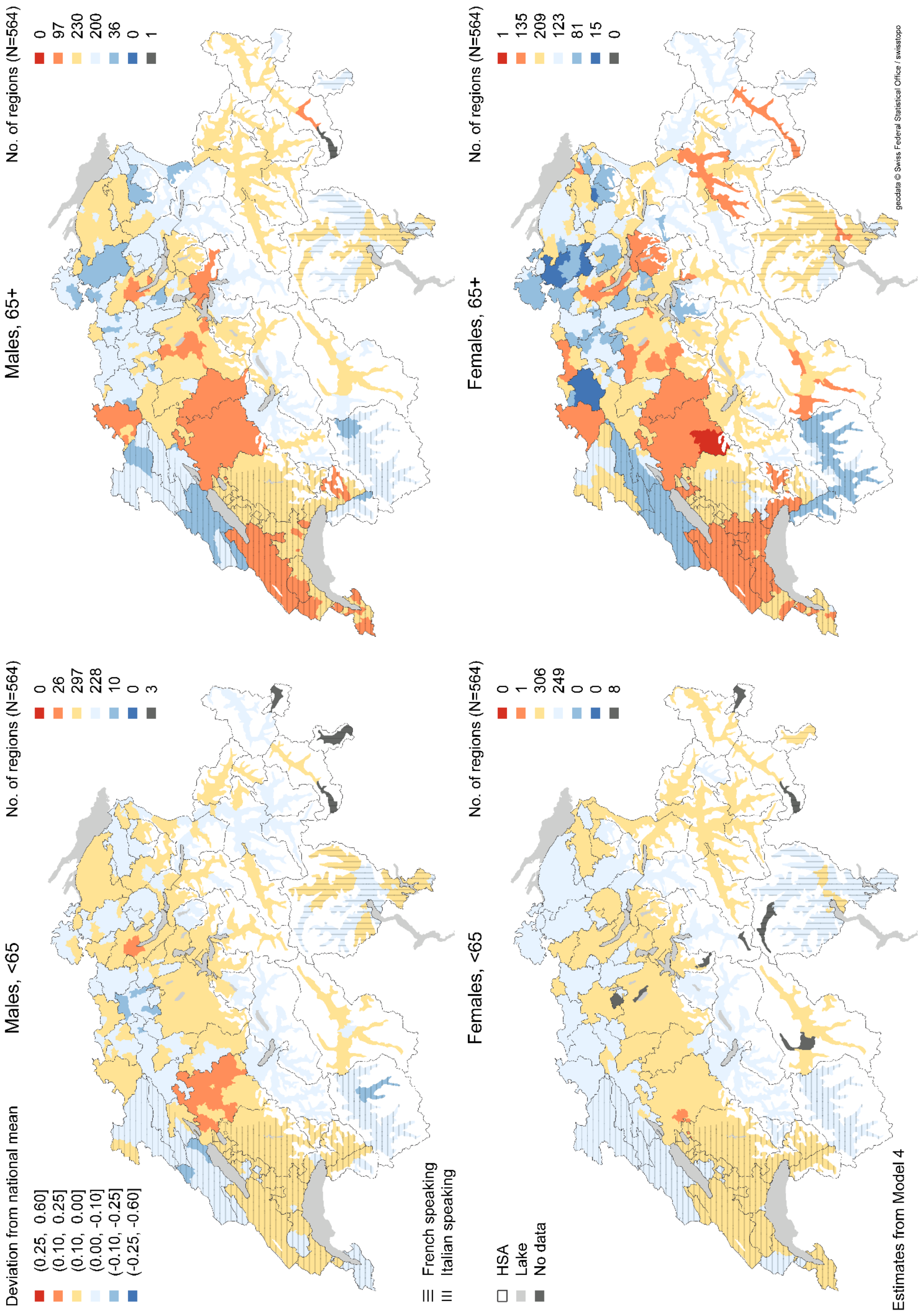

Figure 2. Spatial distribution of deviation from national mean (random effects) of model 4 (fully adjusted) across 564 MedStat regions. Class breaks of the colour scheme are the same as with model 1

Appendix

Text 1. Geography and healthcare system of Switzerland.

Switzerland has 8.2 million residents, of whom almost a quarter (23.8%) are foreigners. It has four official languages: German (declared as main language by 64% of residents), French (23%), Italian (8%) and Romansch (0.5%). 85% of population live in urban areas, with 39% concentrated in five largest cities. Despite a strong economy and high standard of living, there is substantial spatial variation in socioeconomic position and health outcomes across the country. [1,2]

The Swiss, consumer-driven healthcare system is chiefly financed by compulsory basic health insurance (BHI) and out-of-pocket payments. Citizens choose standardized BHI package offered to everyone on a private, highly regulated market of 60 (state as of 10.08.15) insurers, who deliver it on a non-profit basis. The package covers all essential benefits related to medical illness and pregnancy (including ambulatory and in-patient care, medications and medical aids) and deemed medically- and cost-appropriate. Approximately half of in-patient costs are co-financed and subsidised by the cantons. A separate insurance system covers accident-related costs. Residents choose a deductible in a range of 300 – 2,500 Swiss Francs (CHF: 1 CHF = 0.91 Euro = 0.98 U.S. Dollar, as of 27.01.16). Higher deductibles and managed care plans lower the cost of yearly premiums. Patients also make co-payments of 10% of their yearly healthcare costs, up to a limit of CHF 700. Social assistance subsidizes premium payments for low-income individuals. The basic insurance package can be supplemented with voluntary, private insurance to extend provider and treatment choices (e.g. complementary medicine, dental care) and providing additional benefits (e.g. private room during hospital stay). [3–5]

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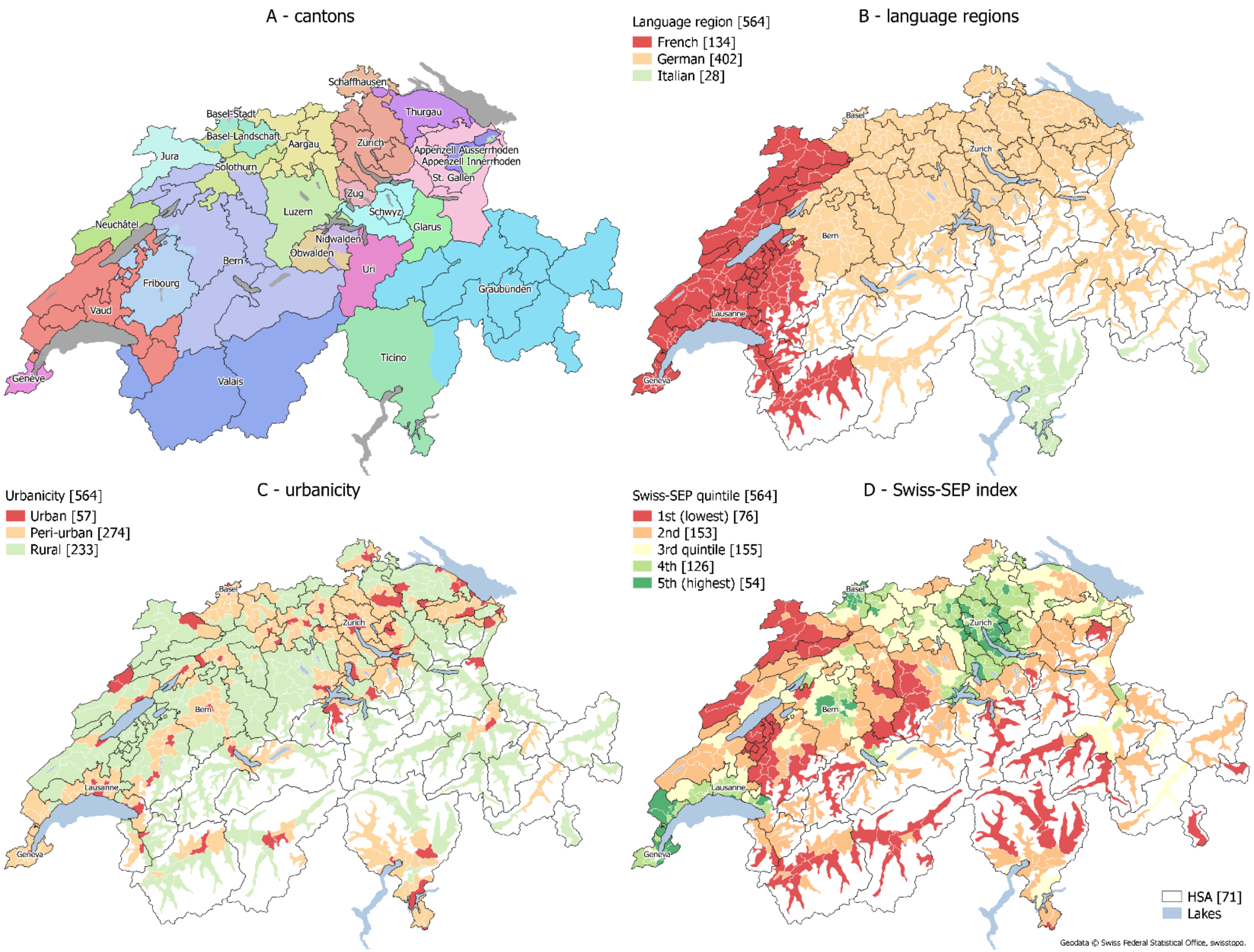
Table 1. Data sources of the study. Databases used in the analyses, together with their purpose, temporal coverage, resolutions and content. Causes of death in 'Mortality records' database are coded according to the International Classification of Diseases, Injuries, and Causes of Death, Tenth Revision (ICD-10). Abbreviations: SFSO - Swiss Federal Statistical Office; SMA- Swiss Medical Association (FMH).

Data	Source	Years	Purpose	Data resolution	Spatial resolution	Variables used
Health insurance claims	Six insurance companies	2008-10	Main dataset	Individual patients, health insurance claim	Postcode	Date of birth, date of death, sex and postcode of place of residence, reimbursed claim
Mortality records	SFSO	2008-10	Assessing representativeness, record linkage to claims for cause of death and characteristics of decedents	Individual patients	Community	date of birth, date of death, sex, community of residence, civil status, nationality, religion, main cause of death
Hospital discharges	SFSO	2010	Creating Hospital Service Areas	Individual hospital discharges	MedStat	Age, major diagnostic category, type of entry, region of patient's place of residence, region of hospitalization
Physicians database	SMA	2010	Supply of ambulatory care	Individual physicians	Postcode	Sector of employment (ambulatory, stationary, other), specialization
Characteristics of hospitals	SFSO	2010	Supply of acute care	Individual institutions	MedStat	Type of hospital, location of hospital, number of utilized beds, number of doctors and nurses (full time equivalent)
Characteristics of socio-medical institutions	SFSO	2010	Supply of non-acute care	Individual institutions	MedStat	Type of institution, location of institution, number of beds, number of nurses
Population	SFSO	2010	Population denominator for healthcare supply indicators	Individual patients	Community	Age, sex, community of residence
Characteristics of communities	SFSO	2008-10	Description of place of residence	Community	Community	Urbanicity, language region

Figure 1. Geographical regions of EOLC study. Swiss cantons (panel A), language regions (panel B), urbanicity (panel C) and Swiss-SEP index quintiles (panel D).



Panels B – D use 564 modified MedStat regions. All panels use overlay of 71 Hospital Service Areas.

Language region and urbanicity of the modified Medstat was derived from SFSO's classification of Swiss communities (*Gemeinde*). In cases when more than one community belonged to the region, and these differed in terms of urbanicity or language region we used majority (>50%) assignment as criterion. Communities where Romansh language was used were grouped together with German language. Swiss-SEP (area based socioeconomic position) index [28] was derived as median value of all neighbourhoods that overlapped with modified MedStat.

Boundaries of the 564 modified MedStat regions were adjusted to exclude the high altitude areas of Swiss Alps with very low density or no population.

71 HSAs were build using SFSO's individual-level discharges of all Swiss hospitals in 2010. We created matrix of counts derived from cross tabulation of regions of patient's place of residence with region of hospitalization. We excluded records with missing geographical codes, records of individuals younger than 19, records belonging to major diagnostic category 'Births' and records of individuals from prisons. Patients' flows derived from the matrix were then used to aggregate modified MedStat regions to larger units where majority of residents were hospitalized.

Figure 2. Flowchart of exclusion criteria for study population definition.

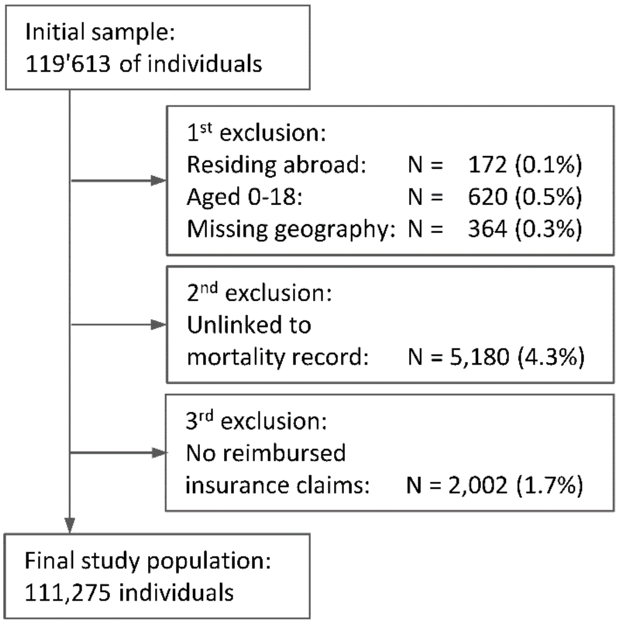


Table 2. Distribution of unlinked deaths across characteristics of the study population. Urbanicity, language region and Swiss-SEP index measured on the level of community (*Gemeinde*). Abbreviations: Swiss-SEP – Swiss neighbourhood index of socioeconomic position (see [28] for details).

Characteristic	**Linked**		**Unlinked**		**Total**	
	No.	*Col %*	*No.*	*Col %*	*No.*	*Col %*
Sex						
Male	53,316	47%	2,508	48%	55,824	47%
Female	59,961	53%	2,672	52%	62,633	53%
Age group						
19 - 30	810	1%	114	2%	924	1%
31 - 40	1,150	1%	119	2%	1,269	1%
41 - 50	3,072	3%	234	5%	3,306	3%
51 - 60	6,813	6%	380	7%	7,193	6%
61 - 70	13,533	12%	715	14%	14,248	12%
71 - 80	24,696	22%	1,048	20%	25,744	22%
81 - 90	43,160	38%	1,753	34%	44,913	38%
91+	20,043	18%	817	16%	20,860	18%
Urbanicity						
Urban	35,987	32%	1,813	35%	37,800	32%
Peri-urban	47,779	42%	2,117	41%	49,896	42%
Rural	29,510	26%	1,250	24%	30,760	26%
Language region						
German	80,129	71%	2,966	57%	83,095	70%
French	27,200	24%	1,909	37%	29,109	25%
Italian	5,947	5%	305	6%	6,252	5%
Swiss-SEP quintile						
1st (lowest)	8,902	8%	417	8%	9,319	8%
2nd	22,583	20%	1,038	20%	23,621	20%
3rd	30,902	27%	1,462	28%	32,364	27%
4th	38,126	34%	1,721	33%	39,847	34%
5th (highest)	12,764	11%	542	11%	13,306	11%
Total	113,277	100%	5,180	100%	118,457	100%

Table 3. Distribution of individuals without any reimbursed claims across characteristics of the study population. Abbreviations: 'CVD' –cardiovascular deaths, 'Mental & behav.' – mental and behavioural disorders (see text for ICD-10 codes). Swiss-SEP – Swiss neighbourhood index of socioeconomic position (see [28] for details).

Characteristic	Bills exist		No bills		Total	
	No.	*Col %*	*No.*	*Col %*	*No.*	*Col %*
Sex						
Male	52,117	47%	1,199	60%	53,316	47%
Female	59,158	53%	803	40%	59,961	53%
Age group						
19 - 30	698	1%	112	6%	810	1%
31 - 40	1,051	1%	99	5%	1,150	1%
41 - 50	2,875	3%	197	10%	3,072	3%
51 - 60	6,533	6%	280	14%	6,813	6%
61 - 70	13,248	12%	285	14%	13,533	12%
71 - 80	24,398	22%	298	15%	24,696	22%
81 - 90	42,695	38%	465	23%	43,160	38%
91+	19,777	18%	266	13%	20,043	18%
Nationality						
Swiss	102,439	92%	1,761	88%	104,200	92%
Foreigner	8,836	8%	241	12%	9,077	8%
Civil status						
Single	13,225	12%	514	26%	13,739	12%
Married	43,516	39%	607	30%	44,123	39%
Widowed	44,671	40%	563	28%	45,234	40%
Divorced	9,863	9%	318	16%	10,181	9%
Religion						
Protestant	54,295	49%	868	43%	55,163	49%
Catholic	38,569	35%	617	31%	39,186	35%
No affil.	5,511	5%	153	8%	5,664	5%
Other/Unknown	12,900	12%	364	18%	13,264	12%
Cause of death						
CVD	40,256	36%	674	34%	40,930	36%
Cancer	29,357	26%	124	6%	29,481	26%
Mental & behav.	6,983	6%	197	10%	7,180	6%
Nervous system	5,434	5%	106	5%	5,540	5%
Respiratory	6,997	6%	80	4%	7,077	6%
Digestive	4,507	4%	69	3%	4,576	4%
External	5,866	5%	429	21%	6,295	6%
Other	11,875	11%	323	16%	12,198	11%
Urbanicity						
Urban	36,589	33%	741	37%	37,330	33%
Peri-urban	47,544	43%	852	43%	48,396	43%
Rural	27,142	24%	409	20%	27,551	24%

Language region						
German	78,650	71%	1,425	71%	80,075	71%
French	26,762	24%	505	25%	27,267	24%
Italian	5,863	5%	72	4%	5,935	5%
Swiss-SEP quintile						
1st (lowest)	7,654	7%	121	6%	7,775	7%
2nd	23,803	21%	372	19%	24,175	21%
3rd	30,384	27%	506	25%	30,890	27%
4th	38,651	35%	785	39%	39,436	35%
5th (highest)	10,783	10%	218	11%	11,001	10%
Total	111,275	100%	2,002	100%	113,277	100%

Table 4. Representativeness of the study population across characteristics of overall Swiss mortality 2008-10.

Characteristic	Study population		National mortality		Representativeness
	No.	*Col %*	*No.*	*Col %*	*% of national mortality (row %)*
Sex					
Male	*52'117*	*47%*	88'907	48%	60%
Female	*59'158*	*53%*	95'910	52%	63%
Age group					
19 - 30	698	*1%*	1'389	1%	58%
31 - 40	1'051	*1%*	2'026	1%	57%
41 - 50	2'875	*3%*	5'535	3%	56%
51 - 60	6'533	*6%*	11'658	6%	58%
61 - 70	13'248	*12%*	22'300	12%	61%
71 - 80	24'398	*22%*	40'165	22%	61%
81 - 90	42'695	*38%*	69'849	38%	62%
91+	19'777	*18%*	31'895	17%	63%
Nationality					
Swiss	102,439	92%	170'420	92%	61%
Foreigner	8,836	8%	14'397	8%	63%
Civil status					
Single	13,225	12%	22'839	12%	60%
Married	43,516	39%	73'095	40%	60%
Widowed	44,671	40%	72'432	39%	62%
Divorced	9,863	9%	16'451	9%	62%
Religion					
Protestant	54,295	49%	82'221	44%	67%
Catholic	38,569	35%	71'919	39%	54%
No affil.	5,511	5%	9'977	5%	57%
Other/Unknown	12,900	12%	20'700	11%	64%
Cause of death					
CVD	40,256	36%	66'472	36%	62%
Cancer	29,357	26%	48'207	26%	61%
Mental & behav.	6,983	6%	11'571	6%	62%
Nervous system	5,434	5%	9'237	5%	60%
Respiratory	6,997	6%	11'442	6%	62%
Digestive	4,507	4%	7'431	4%	62%
External	5,866	5%	10'597	6%	59%
Other	11,875	11%	19'860	11%	61%
Urbanicity					
Urban	36,589	33%	61'288	33%	59%
Peri-urban	47,544	43%	74'145	40%	64%
Rural	27,142	24%	49'384	27%	60%
Language region					
German	78,650	71%	133'177	72%	60%

French	26,762	24%	42'586	23%	64%
Italian	5,863	5%	9'054	5%	66%
Swiss-SEP quintile					
1st (lowest)	7,654	7%	16'291	9%	55%
2nd	23,803	21%	36'660	20%	62%
3rd	30,384	27%	47'931	26%	64%
4th	38,651	35%	63'707	34%	60%
5th (highest)	10,783	10%	20'228	11%	63%
Total	111,275	100%	184'817	100%	61%

Table 5. Mean cost and standard deviation [SD] of end of life care across study population characteristics. All costs given in thousands of Swiss Francs: 1 CHF = 0.91 Euro = 0.98 the U.S. Dollar, as of 27.01.16. Abbreviations: 'CVD' –cardiovascular deaths, 'Mental & behav.' – mental and behavioural disorders (see text for ICD-10 codes). Swiss-SEP – Swiss neighbourhood index of socioeconomic position (see [28] for details).

Characteristic	**Males 19-65**		**Males 66+**		**Females 19-65**		**Females 66+**		**Total**	
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*
Age group										
19 - 25	21.6	53.1			39.7	58.4			26.9	55.3
26 - 30	25.4	46.4			39.2	57.2			30.5	51.0
31 - 35	35.7	65.9			42.1	58.7			38.1	63.4
36 - 40	32.5	50.7			52.6	48.0			40.5	50.6
41 - 45	32.4	52.5			53.7	53.2			40.2	53.7
46 - 50	38.6	47.5			55.5	53.3			45.1	50.5
51 - 55	39.3	52.2			50.3	46.8			43.7	50.4
56 - 60	43.5	54.2			50.3	48.5			46.1	52.2
61 - 65	43.0	47.4			49.4	45.4			45.4	46.7
66 - 70			41.8	42.7			46.8	47.1	43.7	44.5
71 - 75			39.1	38.9			40.5	38.1	39.7	38.6
76 - 80			35.5	35.8			34.5	30.5	35.0	33.5
81 - 85			30.1	27.9			29.2	22.8	29.6	25.3
86 - 90			27.0	22.4			26.9	18.9	26.9	20.3
91+			25.0	19.2			25.8	15.9	25.6	16.9
Nationality										
Swiss	39.5	51.6	31.9	31.5	50.1	49.1	29.9	25.1	32.6	32.6
Foreigner	42.4	48.5	37.8	34.8	51.4	46.4	34.8	33.0	39.2	39.1
Civil status										
Single	29.9	44.3	28.7	26.4	43.3	47.5	28.9	23.3	30.5	32.8
Married	46.6	54.8	34.3	34.3	55.1	51.5	35.8	34.0	37.8	39.6
Widowed	40.1	52.1	28.7	25.5	46.5	45.0	28.3	21.9	28.7	23.5
Divorced	35.6	45.4	34.0	35.4	45.7	42.0	33.7	30.4	35.7	36.8
Religion										
Protestant	39.7	47.9	31.1	31.3	50.1	48.8	29.1	24.7	31.5	31.1
Catholic	41.5	53.1	32.9	30.6	50.8	48.0	31.1	25.2	34.0	33.0
No affil.	37.6	52.8	36.1	38.5	52.2	49.2	32.1	31.5	37.0	41.6
Other/Unknown	39.1	51.7	34.6	34.3	48.3	49.8	32.2	28.8	35.5	37.3
Cause of death										
CVD	21.2	40.2	25.7	28.3	26.3	42.5	25.7	21.3	25.5	26.0
Cancer	63.4	50.7	42.2	36.4	66.4	47.9	40.4	34.6	47.5	41.0
Mental & behav.	19.2	31.8	29.5	20.4	23.3	29.1	29.3	15.9	28.9	18.6
Nervous system	40.6	43.0	35.3	27.5	41.5	32.7	32.7	18.4	34.5	24.7
Respiratory	35.4	38.5	30.8	26.8	46.0	47.2	30.4	23.5	31.3	27.0
Digestive	31.6	50.2	32.0	31.3	33.4	39.3	30.0	27.1	31.1	33.2
External	13.5	26.2	24.8	28.2	19.9	24.7	25.5	23.9	21.3	26.4

Other	37.3	67.9	33.2	34.8	42.8	56.4	30.7	27.5	32.8	37.4
Urbanicity										
Urban	40.0	48.2	34.3	32.4	50.5	48.2	31.6	26.1	34.4	32.7
Peri-urban	41.1	52.9	33.3	33.6	52.1	50.4	30.2	26.2	33.8	34.8
Rural	38.2	51.3	28.5	27.5	46.2	45.7	27.9	23.3	30.1	30.6
Language region										
German	37.7	49.1	29.9	30.3	47.0	45.1	27.9	23.9	30.6	31.2
French	45.3	56.1	38.7	35.1	59.1	56.8	36.6	29.3	39.8	37.8
Italian	42.7	45.5	36.9	32.4	49.5	46.0	32.5	25.1	35.7	31.4
Swiss-SEP quintile										
1st (lowest)	37.0	44.1	29.8	26.7	43.6	43.1	29.6	21.7	31.2	28.4
2nd	37.8	44.4	29.7	27.6	45.8	43.9	28.7	22.3	30.9	29.0
3rd	39.9	54.2	31.7	30.5	49.9	46.2	29.4	25.7	32.5	33.1
4th	41.2	52.2	33.7	33.4	52.8	52.5	31.1	27.0	34.3	34.7
5th (highest)	44.2	56.7	37.3	40.4	55.0	52.4	32.2	28.7	36.6	38.5
Physicians / 10'000 (FMH)										
1st (lowest)	38.9	45.4	29.9	29.3	48.8	46.4	29.4	28.6	31.8	32.8
2nd	37.9	46.2	29.8	29.8	50.9	49.8	28.7	23.1	31.5	31.5
3rd quintile	38.9	55.3	29.1	28.7	45.1	44.6	27.4	23.0	30.2	31.6
4th	41.1	53.1	33.1	32.8	51.4	49.6	30.7	25.0	33.8	33.7
5th (highest)	40.9	51.4	34.7	33.5	51.8	49.9	31.4	26.3	34.6	33.9
Nursing home beds / 10'000 (65+)										
1st (lowest)	42.1	57.3	36.9	35.9	58.5	58.0	34.2	29.1	37.6	38.4
2nd	41.7	50.1	33.4	32.9	52.2	50.3	31.4	27.4	34.4	34.4
3rd quintile	41.4	56.9	32.9	30.1	49.3	47.0	29.7	24.6	33.1	32.9
4th	38.4	47.9	30.7	31.1	47.1	44.4	29.2	24.4	31.6	31.4
5th (highest)	35.4	41.0	28.9	27.7	46.2	45.9	26.7	21.0	29.3	28.0
Utilized beds (all) / 10'000										
1st (lowest)	38.8	65.0	27.4	27.0	45.0	43.7	26.4	24.3	29.1	33.3
2nd	37.5	45.2	29.4	29.0	47.0	45.6	27.8	21.9	30.4	29.6
3rd quintile	39.7	52.3	31.3	30.5	49.2	48.1	29.3	24.3	32.4	32.9
4th	41.2	50.0	35.6	35.2	53.5	51.4	32.7	28.3	35.8	35.4
5th (highest)	40.5	49.7	31.6	29.8	49.9	47.9	29.3	23.9	32.2	31.2
Total	40.0	51.1	32.4	31.9	50.3	48.7	30.2	25.6	33.1	33.2

Table 6.Significance of interaction parameters. P-values from test of interaction of sex (second column) and binary age indicator (19-65 vs. 66+; second and third columns) with the variables in rows. Multilevel models using individual patient data with log of overall cost as outcome with MedStat and Hospital Service Areas as extra levels, adjusted for all variables listed in the table.

Characteristics	**Interaction with sex**	**Interaction with age**	
		Males	*Females*
Age group	<0.0001	--	--
Nationality	0.784	0.584	0.066
Civil status	<0.0001	<0.0001	<0.0001
Religion	0.193	0.021	<0.0001
Cause of death	<0.0001	<0.0001	<0.0001
Urbanicity	<0.0001	0.806	0.001
Language region	0.08	0.015	0.002
Swiss-SEP quintile	<0.0001	0.141	<0.0001

Figure 3. Spatial distribution of deviation from national mean (random effects) of model 2 (adjusted) across 564 modified MedStat regions. Class breaks of the colour scheme are the same as with model 1 (Figure 1, main manuscript).

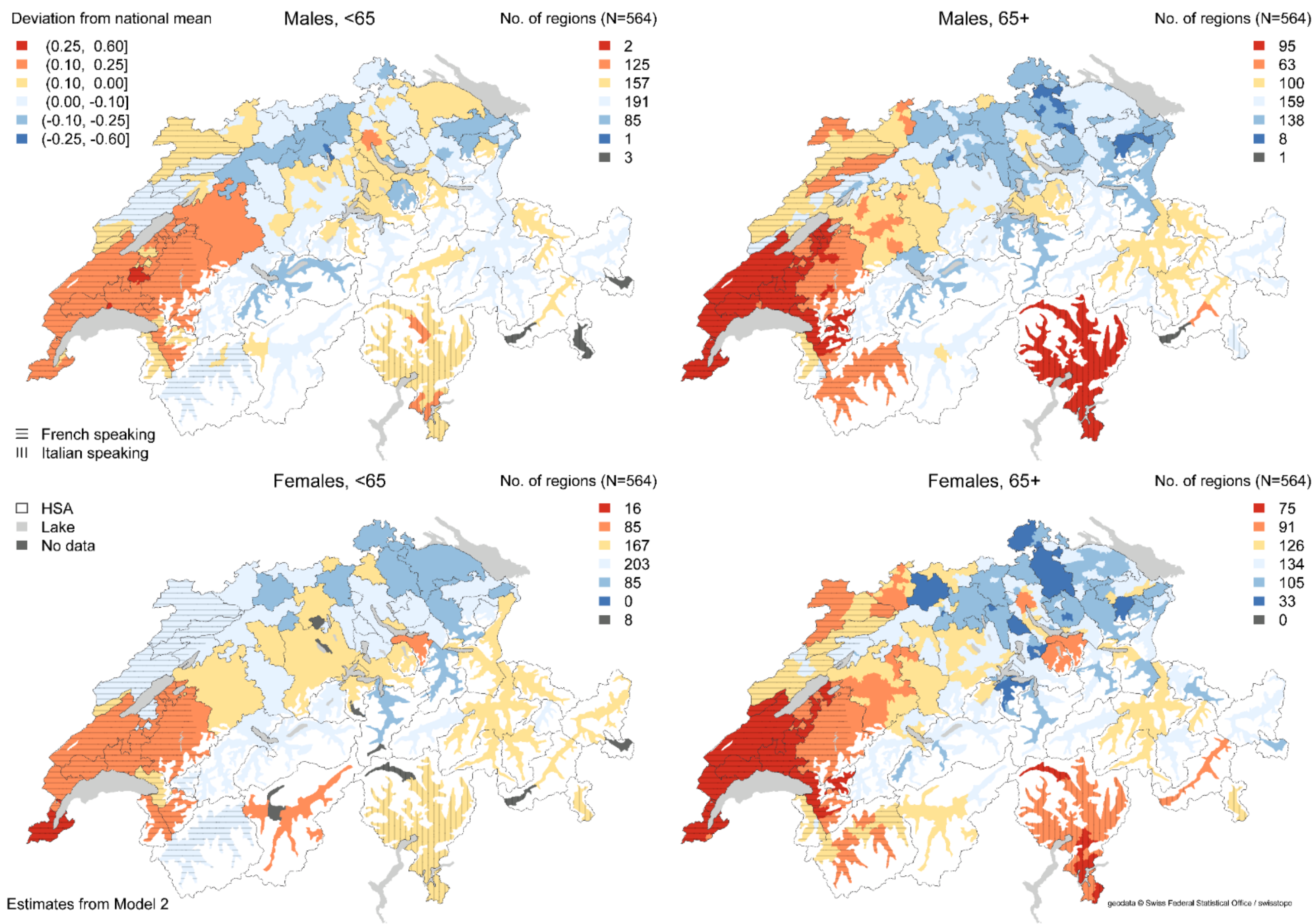


Figure 4. Spatial distribution of deviation from national mean (random effects) of model 3 (adjusted) across 564 modified MedStat regions. Class breaks of the colour scheme are the same as with model 1 (Figure 1, main manuscript).

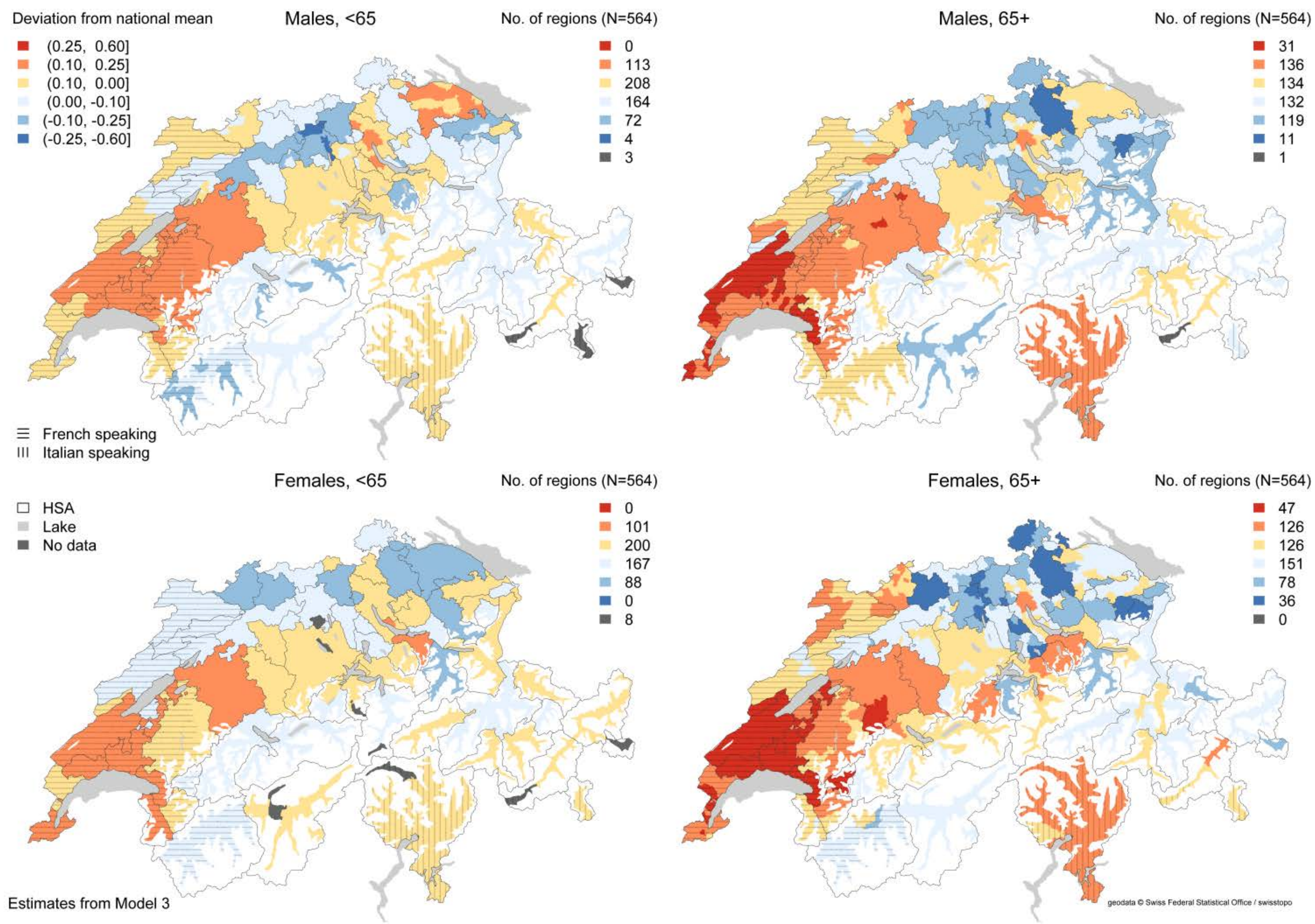


Table 7. Regression coefficients of multilevel models 1 (no covariates), 2 (adjusted for individual factors), 3 (adjusted for individual and regional factors) and 4 (adjusted for individual, regional factors and health supply measures) for males 19-65. Exponentiated coefficients of regressing log of overall cost of end of life care during the last 12 months of life. Density of supply measures and Swiss-SEP index divided into quintiles of spatial units. P-values from the Wald test of the group parameters being jointly one. Abbreviations: 'Est.' – estimate; 'CI' confidence interval; 'CVD' –cardiovascular deaths; 'Mental & behav.' – mental and behavioural disorders (see Table 1 for ICD-10 codes); 'No affil.' – no religious affiliation; 'Swiss-SEP' – Swiss neighbourhood index of socioeconomic position (see [28] for details).

Variable	Group	Model: 1		Model: 2			Model: 3	
		Est.	95% CI	Est.	95% CI	p-value	Est.	95% CI
Age	*19-25*			0.44	(0.36, 0.53)	<0.0001	0.44	(0.37, 0.53)
	26-30			0.67	(0.55, 0.82)		0.67	(0.55, 0.81)
	31-35			0.97	(0.82, 1.16)		0.97	(0.81, 1.16)
	36-40			0.88	(0.76, 1.02)		0.88	(0.76, 1.02)
	41-45			0.80	(0.72, 0.90)		0.81	(0.72, 0.90)
	46-50			0.85	(0.78, 0.94)		0.85	(0.78, 0.94)
	51-55			0.86	(0.79, 0.93)		0.86	(0.79, 0.93)
	56-60			0.99	(0.92, 1.06)		0.99	(0.92, 1.06)
	61-65			ref.	-		ref.	-
Cause of death	*CVD*			ref.	-	<0.0001	ref.	-
	Cancer			6.18	(5.76, 6.64)		6.18	(5.76, 6.64)
	Mental & behav.			0.98	(0.82, 1.16)		0.98	(0.82, 1.16)
	Nervous system			3.38	(2.87, 3.98)		3.38	(2.87, 3.98)
	Respiratory			2.68	(2.29, 3.14)		2.68	(2.29, 3.14)
	Digestive			2.25	(1.99, 2.55)		2.25	(1.99, 2.55)
	External			0.62	(0.57, 0.68)		0.62	(0.57, 0.68)
	Other			1.79	(1.62, 1.99)		1.79	(1.62, 1.98)
Civil status	*Single*			0.89	(0.83, 0.95)	0.00	0.89	(0.83, 0.95)
	Married			ref.	-		ref.	-
	Widowed			0.97	(0.82, 1.15)		0.97	(0.81, 1.15)
	Divorced			0.89	(0.83, 0.96)		0.89	(0.83, 0.96)
Nationality	*Swiss*			ref.	-	0.05	ref.	-
	Foreigner			1.08	(1.00, 1.16)		1.07	(1.00, 1.15)

Religion	*Protestant*			ref.	-	0.17	ref.	-
	Catholic			1.01	(0.94, 1.08)		1.01	(0.94, 1.08)
	No affil.			0.97	(0.88, 1.07)		0.97	(0.88, 1.07)
	Other/Unknown			0.93	(0.85, 1.01)		0.93	(0.85, 1.00)
Urbanicity	*Urban*			1.05	(0.98, 1.13)	0.23	1.05	(0.95, 1.16)
	Peri-urban			ref.	-		ref.	-
	Rural			0.97	(0.88, 1.06)		0.98	(0.89, 1.08)
Swiss-SEP	*1st (lowest)*			0.93	(0.81, 1.06)	0.31	0.92	(0.80, 1.05)
	2nd			0.95	(0.86, 1.04)		0.95	(0.86, 1.03)
	3rd quintile			ref.	-		ref.	-
	4th			1.05	(0.97, 1.15)		1.05	(0.97, 1.14)
	5th (highest)			1.05	(0.93, 1.19)		1.05	(0.92, 1.18)
Density of physicians	*1st (lowest)*						0.94	(0.85, 1.05)
	2nd						0.92	(0.83, 1.02)
	3rd quintile						ref.	-
	4th						0.99	(0.90, 1.09)
	5th (highest)						0.98	(0.88, 1.09)
Density of nursing home beds	*1st (lowest)*						1.06	(0.91, 1.23)
	2nd						0.99	(0.86, 1.15)
	3rd quintile						ref.	-
	4th						0.91	(0.79, 1.05)
	5th (highest)						0.92	(0.78, 1.09)
Density of hospital beds	*1st (lowest)*						0.90	(0.77, 1.05)
	2nd						0.99	(0.86, 1.14)
	3rd quintile						ref.	-
	4th						0.99	(0.87, 1.13)
	5th (highest)						0.96	(0.83, 1.12)
Language region	*German*							
	French							
	Italian							
Constant		15.53	(14.65, 16.47)	7.92	(7.14, 8.78)		8.59	(7.20, 10.25)
Variance	*HSA level*	0.03	(0.01, 0.06)	0.02	(0.01, 0.03)		0.01	(0.01, 0.03)
	MedStat level	0.00	(0.00, 0.80)	0.01	(0.00, 0.04)		0.00	(0.00, 0.05)
	Residual	2.78	(2.71, 2.86)	1.84	(1.79, 1.89)		1.84	(1.79, 1.89)

Table 8. Regression coefficients of multilevel models 1 (no covariates), 2 (adjusted for individual factors), 3 (adjusted for individual and regional factors) and 4 (adjusted for individual, regional factors and health supply measures) for males 66+. Exponentiated coefficients of regressing log of overall cost of end of life care during the last 12 months of life. Density of supply measures and Swiss-SEP index divided into quintiles of spatial units. P-values from the Wald test of the group parameters being jointly one. Abbreviations: 'Est.' – estimate; 'CI' confidence interval; 'CVD' –cardiovascular deaths; 'Mental & behav.' – mental and behavioural disorders (see Table 1 for ICD-10 codes); 'No affil.' – no religious affiliation; 'Swiss-SEP' – Swiss neighbourhood index of socioeconomic position (see [28] for details).

Variable	**Group**	**Model: 1**		**Model: 2**			**Model: 3**	
		Est.	**95% CI**	**Est.**	**95% CI**	**p-value**	**Est.**	**95% CI**
Age	*66-70*			ref.	-	<0.0001	ref.	-
	71-75			1.02	(0.98, 1.06)		1.02	(0.98, 1.06)
	76-80			1.00	(0.96, 1.03)		1.00	(0.96, 1.03)
	81-85			0.94	(0.91, 0.98)		0.94	(0.91, 0.98)
	86-90			0.92	(0.89, 0.96)		0.92	(0.88, 0.96)
	91+			0.91	(0.87, 0.95)		0.91	(0.87, 0.95)
Cause of death	*CVD*			ref.	-	<0.0001	ref.	-
	Cancer			1.90	(1.85, 1.95)		1.90	(1.85, 1.95)
	Mental & behav.			1.46	(1.39, 1.53)		1.46	(1.39, 1.53)
	Nervous system			1.68	(1.60, 1.77)		1.68	(1.60, 1.77)
	Respiratory			1.39	(1.34, 1.44)		1.39	(1.34, 1.45)
	Digestive			1.36	(1.28, 1.43)		1.36	(1.28, 1.43)
	External			0.93	(0.88, 0.98)		0.93	(0.88, 0.98)
	Other			1.24	(1.19, 1.28)		1.24	(1.19, 1.28)
Civil status	*Single*			0.87	(0.83, 0.90)	<0.0001	0.87	(0.83, 0.90)
	Married			ref.	-		ref.	-
	Widowed			1.00	(0.97, 1.02)		1.00	(0.97, 1.02)
	Divorced			0.89	(0.86, 0.93)		0.89	(0.86, 0.93)
Nationality	*Swiss*			ref.	-	0.06	ref.	-
	Foreigner			1.04	(1.00, 1.08)		1.03	(1.00, 1.07)
Religion	*Protestant*			ref.	-	<0.0001	ref.	-
	Catholic			1.03	(1.01, 1.06)		1.03	(1.01, 1.06)
	No affil.			1.04	(0.99, 1.09)		1.04	(0.99, 1.09)

	Other/Unknown			0.91	(0.88, 0.94)		0.91	(0.88, 0.94)
Urbanicity	*Urban*			1.05	(1.01, 1.09)	0.00	1.01	(0.97, 1.06)
	Peri-urban			ref.	-		ref.	-
	Rural			0.97	(0.93, 1.01)		0.98	(0.94, 1.02)
Swiss-SEP	*1st (lowest)*			0.93	(0.88, 0.99)	<0.0001	0.95	(0.89, 1.01)
	2nd			0.96	(0.92, 1.00)		0.96	(0.93, 1.01)
	3rd quintile			ref.	-		ref.	-
	4th			1.05	(1.01, 1.09)		1.04	(1.00, 1.08)
	5th (highest)			1.11	(1.05, 1.18)		1.10	(1.04, 1.16)
Density of physicians	*1st (lowest)*						0.98	(0.94, 1.03)
	2nd						0.96	(0.92, 1.00)
	3rd quintile						ref.	-
	4th						1.03	(0.98, 1.07)
	5th (highest)						1.04	(0.99, 1.09)
Density of nursing home beds	*1st (lowest)*						0.98	(0.86, 1.12)
	2nd						0.95	(0.83, 1.08)
	3rd quintile						ref.	-
	4th						0.86	(0.75, 0.98)
	5th (highest)						0.88	(0.77, 1.02)
Density of hospital beds	*1st (lowest)*						0.86	(0.76, 0.99)
	2nd						0.95	(0.84, 1.08)
	3rd quintile						ref.	-
	4th						1.01	(0.89, 1.14)
	5th (highest)						0.94	(0.83, 1.08)
Language region	*German*							
	French							
	Italian							
Constant		19.36	(18.45, 20.32)	15.52	(14.56, 16.55)		17.34	(15.19, 19.80)
Variance	*HSA level*	0.03	(0.02, 0.05)	0.03	(0.02, 0.05)		0.02	(0.02, 0.04)
	MedStat level	0.01	(0.01, 0.01)	0.00	(0.00, 0.01)		0.00	(0.00, 0.01)
	Residual	1.14	(1.12, 1.16)	1.06	(1.04, 1.07)		1.06	(1.04, 1.07)

Table 9. Regression coefficients of multilevel models 1 (no covariates), 2 (adjusted for individual factors), 3 (adjusted for individual and regional factors) and 4 (adjusted for individual, regional factors and health supply measures) for females 19-65. Exponentiated coefficients of regressing log of overall cost of end of life care during the last 12 months of life. Density of supply measures and Swiss-SEP index divided into quintiles of spatial units. P-values from the Wald test of the group parameters being jointly one. Abbreviations: 'Est.' – estimate; 'CI' confidence interval; 'CVD' –cardiovascular deaths; 'Mental & behav.' – mental and behavioural disorders (see Table 1 for ICD-10 codes); 'No affil.' – no religious affiliation; 'Swiss-SEP' – Swiss neighbourhood index of socioeconomic position (see [28] for details).

Variable	Group	Model: 1		Model: 2			Model: 3	
		Est.	95% CI	Est.	95% CI	p-value	Est.	95% CI
Age	*19-25*			0.82	(0.65, 1.04)	0.00	0.82	(0.65, 1.04)
	26-30			0.85	(0.68, 1.06)		0.86	(0.69, 1.06)
	31-35			0.92	(0.76, 1.12)		0.92	(0.75, 1.11)
	36-40			1.20	(1.03, 1.40)		1.20	(1.03, 1.40)
	41-45			1.18	(1.04, 1.33)		1.18	(1.04, 1.34)
	46-50			1.09	(0.98, 1.20)		1.09	(0.99, 1.21)
	51-55			1.04	(0.95, 1.13)		1.04	(0.96, 1.13)
	56-60			0.97	(0.89, 1.04)		0.97	(0.90, 1.04)
	61-65			ref.	-		ref.	-
Cause of death	*CVD*			ref.	-	<0.0001	ref.	-
	Cancer			4.68	(4.28, 5.12)		4.68	(4.28, 5.12)
	Mental & behav.			1.10	(0.89, 1.35)		1.10	(0.89, 1.35)
	Nervous system			2.71	(2.30, 3.18)		2.71	(2.31, 3.18)
	Respiratory			2.47	(2.07, 2.94)		2.46	(2.07, 2.94)
	Digestive			1.74	(1.49, 2.03)		1.74	(1.49, 2.03)
	External			0.75	(0.67, 0.85)		0.75	(0.66, 0.85)
	Other			1.75	(1.55, 1.97)		1.75	(1.55, 1.97)
Civil status	*Single*			0.93	(0.86, 1.00)	0.19	0.93	(0.85, 1.00)
	Married			ref.	-		ref.	-
	Widowed			0.94	(0.84, 1.05)		0.93	(0.83, 1.04)
	Divorced			0.95	(0.88, 1.02)		0.95	(0.88, 1.02)
Nationality	*Swiss*			ref.	-	0.02	ref.	-
	Foreigner			1.11	(1.02, 1.22)		1.11	(1.02, 1.21)

Religion	*Protestant*			ref.	-	<0.0001	ref.	-
	Catholic			1.00	(0.93, 1.08)		0.99	(0.92, 1.06)
	No affil.			1.00	(0.90, 1.11)		0.99	(0.90, 1.10)
	Other/Unknown			0.82	(0.75, 0.90)		0.82	(0.75, 0.89)
Urbanicity	*Urban*			1.07	(1.00, 1.15)	0.15	1.05	(0.95, 1.16)
	Peri-urban			ref.	-		ref.	-
	Rural			0.99	(0.90, 1.10)		1.01	(0.91, 1.11)
Swiss-SEP	*1st (lowest)*			0.84	(0.72, 0.98)	0.03	0.83	(0.71, 0.96)
	2nd			0.88	(0.80, 0.97)		0.88	(0.80, 0.97)
	3rd quintile			ref.	-		ref.	-
	4th			1.03	(0.94, 1.12)		1.01	(0.93, 1.10)
	5th (highest)			1.04	(0.92, 1.18)		1.03	(0.91, 1.16)
Density of physicians	*1st (lowest)*						1.00	(0.89, 1.13)
	2nd						1.11	(0.99, 1.24)
	3rd quintile						ref.	-
	4th						1.12	(1.01, 1.24)
	5th (highest)						1.09	(0.98, 1.22)
Density of nursing home beds	*1st (lowest)*						1.02	(0.87, 1.20)
	2nd						0.94	(0.82, 1.09)
	3rd quintile						ref.	-
	4th						0.83	(0.72, 0.96)
	5th (highest)						0.81	(0.69, 0.96)
Density of hospital beds	*1st (lowest)*						0.90	(0.77, 1.06)
	2nd						0.95	(0.82, 1.11)
	3rd quintile						ref.	-
	4th						0.96	(0.85, 1.10)
	5th (highest)						1.01	(0.87, 1.17)
Language region	*German*							
	French							
	Italian							
Constant		27.16	(25.64, 28.76)	11.00	(9.72, 12.44)		11.67	(9.65, 14.12)
Variance	*HSA level*	0.02	(0.01, 0.05)	0.02	(0.01, 0.04)		0.01	(0.01, 0.03)
	MedStat level	0.01	(0.00, 0.08)	0.00	(0.00, 7.e+186)		0.00	(0.00, 5280.80)
	Residual	1.83	(1.77, 1.90)	1.31	(1.27, 1.36)		1.31	(1.26, 1.36)

Table 10. Regression coefficients of multilevel models 1 (no covariates), 2 (adjusted for individual factors), 3 (adjusted for individual and regional factors) and 4 (adjusted for individual, regional factors and health supply measures) for females 66+. Exponentiated coefficients of regressing log of overall cost of end of life care during the last 12 months of life. Density of supply measures and Swiss-SEP index divided into quintiles of spatial units. P-values from the Wald test of the group parameters being jointly one. Abbreviations: 'Est.' – estimate; 'CI' confidence interval; 'CVD' –cardiovascular deaths; 'Mental & behav.' – mental and behavioural disorders (see Table 1 for ICD-10 codes); 'No affil.' – no religious affiliation; 'Swiss-SEP' – Swiss neighbourhood index of socioeconomic position (see [28] for details).

Variable	Group	Model: 1		Model: 2			Model: 3	
		Est.	95% CI	Est.	95% CI	p-value	Est.	95% CI
Age	***66-70***			ref.	-	<0.0001	ref.	-
	71-75			0.94	(0.90, 0.98)		0.94	(0.90, 0.98)
	76-80			0.88	(0.85, 0.92)		0.88	(0.85, 0.92)
	81-85			0.83	(0.80, 0.87)		0.83	(0.80, 0.87)
	86-90			0.82	(0.79, 0.85)		0.82	(0.79, 0.85)
	91+			0.82	(0.79, 0.86)		0.82	(0.79, 0.86)
Cause of death	***CVD***			ref.	-	<0.0001	ref.	-
	Cancer			1.55	(1.51, 1.58)		1.55	(1.51, 1.58)
	Mental & behav.			1.30	(1.26, 1.34)		1.30	(1.26, 1.34)
	Nervous system			1.38	(1.33, 1.43)		1.38	(1.33, 1.43)
	Respiratory			1.21	(1.17, 1.25)		1.21	(1.17, 1.25)
	Digestive			1.16	(1.11, 1.21)		1.16	(1.11, 1.21)
	External			0.96	(0.92, 1.01)		0.96	(0.92, 1.01)
	Other			1.15	(1.12, 1.18)		1.15	(1.12, 1.18)
Civil status	***Single***			0.92	(0.89, 0.95)	<0.0001	0.92	(0.89, 0.95)
	Married			ref.	-		ref.	-
	Widowed			0.97	(0.95, 0.99)		0.97	(0.95, 0.99)
	Divorced			0.96	(0.92, 0.99)		0.96	(0.92, 0.99)
Nationality	***Swiss***			ref.	-	0.34	ref.	-
	Foreigner			0.98	(0.95, 1.02)		0.98	(0.94, 1.02)
Religion	***Protestant***			ref.	-	<0.0001	ref.	-
	Catholic			1.03	(1.01, 1.05)		1.03	(1.01, 1.05)
	No affil.			0.97	(0.92, 1.02)		0.97	(0.92, 1.02)

	Other/Unknown			0.94	(0.92, 0.97)		0.94	(0.92, 0.97)
Urbanicity	***Urban***			1.04	(1.01, 1.07)	0.03	1.03	(0.99, 1.07)
	Peri-urban			ref.	-		ref.	-
	Rural			0.99	(0.95, 1.03)		0.99	(0.96, 1.03)
Swiss-SEP	***1st (lowest)***			0.99	(0.93, 1.04)	0.88	0.99	(0.94, 1.05)
	2nd			0.99	(0.95, 1.02)		0.99	(0.96, 1.03)
	3rd quintile			ref.	-		ref.	-
	4th			1.00	(0.97, 1.04)		1.00	(0.96, 1.03)
	5th (highest)			1.02	(0.97, 1.07)		1.01	(0.96, 1.07)
Density of physicians	***1st (lowest)***						1.01	(0.97, 1.06)
	2nd						1.02	(0.98, 1.06)
	3rd quintile						ref.	-
	4th						1.05	(1.01, 1.10)
	5th (highest)						1.03	(0.99, 1.08)
Density of nursing home beds	***1st (lowest)***						1.04	(0.90, 1.21)
	2nd						0.98	(0.85, 1.14)
	3rd quintile						ref.	-
	4th						0.91	(0.78, 1.06)
	5th (highest)						0.92	(0.79, 1.08)
Density of hospital beds	***1st (lowest)***						0.86	(0.74, 0.99)
	2nd						0.96	(0.83, 1.11)
	3rd quintile						ref.	-
	4th						0.99	(0.86, 1.14)
	5th (highest)						0.94	(0.81, 1.09)
Language region	***German***							
	French							
	Italian							
Constant		20.27	(19.27, 21.32)	21.08	(19.69, 22.57)		22.24	(19.18, 25.79)
Variance	***HSA level***	0.04	(0.03, 0.06)	0.04	(0.03, 0.06)		0.03	(0.02, 0.05)
	MedStat level	0.01	(0.00, 0.01)	0.01	(0.00, 0.01)		0.01	(0.00, 0.01)
	Residual	0.90	(0.89, 0.91)	0.86	(0.85, 0.87)		0.86	(0.85, 0.87)

2.4 Article 4: AMI and stroke mortality vary by distance to hospital?

Title:

Do acute myocardial infarction and stroke mortality vary by distance to hospitals in Switzerland?

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Do acute myocardial infarction and stroke mortality vary by distance to hospitals in Switzerland?

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Abstract:

We examined the relationship between distance to different hospital types and mortality from acute myocardial infarction or stroke in the Swiss National Cohort. We performed Cox analyses using driving time and straight-line distance as distance measures, additionally adjusting for sociodemographic and economic variables. Compared to the lowest quintile of driving time to a university hospital, the acute myocardial infarction mortality was 27% and 14% higher in the highest quintile for the young and old population, whereas the stroke mortality was 15% higher in the third quintile and 7% higher in the fourth quintile in the fully adjusted model. Acute myocardial infarction mortality among those in the population 30 and older and stroke mortality in those 65 and above increase with distance to central and university hospitals.

Keywords: distance to hospital, acute myocardial infarction, stroke, mortality

Introduction

Life-threatening diseases such as acute myocardial infarction (AMI) or stroke need immediate medical intervention. Multiple factors can influence the time to treatment and thus survival. These include time from the event to the alert of emergency medical services (EMS), presence of a person to perform cardiopulmonary resuscitation, availability of an automated external defibrillator, and travel time to a hospital with necessary specialized treatment (e.g., thrombolysis or percutaneous coronary intervention (PCI)).

The European guidelines on myocardial revascularization indicate the greatest benefit from reperfusion therapy occurs 2–3 hours after onset [1]. In a Danish study of ST-segment elevation myocardial infarction (STEMI), patients for whom the time from first contact with the health care system to initiation of reperfusion therapy is no longer than 60 minutes have a long-term mortality rate of 15.4%; this rate doubles to 30.8% with a delay of 181 to 360 minutes [2]. The recommendations for STEMI and non-ST-segment elevation acute coronary syndrome (NSTE-ACS) differ according to available treatment and patient risk profile. STEMI patients should be treated without delay, whereas NSTE-ACS patients should receive revascularization within 24 hours, but in any event no later than 72 hours after onset. However, high risk NSTE-ACS patients should undergo urgent coronary angiography within 2 hours of onset. In STEMI patients, primary PCI without previous fibrinolysis is now recommended over fibrinolysis as the preferred reperfusion therapy if it can be provided in a timely manner by experienced operators. But if PCI cannot be performed within 120 minutes of contact with the health system patients should receive fibrinolysis followed by angiography [1].

The 2008 European guidelines for stroke treatment recommend intravenous thrombolysis within 3 hours of stroke onset [3]. The following year the treatment window was extended to 4.5 hours [4].

These windows for reperfusion therapy indicate prompt notification of the EMS and rapid transportation to the hospital. Geographical inequalities in the provision of health care may therefore influence the likelihood of dying from acute myocardial infarction or stroke.

In Switzerland, inhabitants of remote areas like peripheral valleys or mountainous regions often face long travel distances to the nearest hospital, which may not necessarily be a hospital specialized in AMI or stroke treatment with a catheter laboratory or a stroke unit). This will affect transport time, treatment, and survival. Switzerland has a high hospital density and efficient ambulance and air rescue services [5], which should reduce AMI and stroke mortality for people living farther from hospitals. However, no study has yet assessed the relation between AMI and stroke mortality, and distance to hospitals in Switzerland. We therefore used Swiss National Cohort (SNC) data to assess how AMI and stroke mortality in Switzerland relate to distance as driving time from home to different types of hospitals.

Data and methods

Swiss National Cohort

The Swiss National Cohort (SNC) is a longitudinal study that links census data for the entire population of Switzerland with mortality and emigration records. In addition to sociodemographic and economic variables, the SNC also includes the geographical coordinates of residences. But due to the lack of a unique person identifier and the anonymous death registry in Switzerland, we linked the records of the census of 1990 and 2000 to death and emigration records up to 2008 using deterministic and probabilistic linkage methods based on sex, date of birth, place of residence, nationality, and other variables. The SNC is explained in detail elsewhere [6,7].

Hospital information

Yearly the Federal Office for Health (FOH) derives key figures for Swiss hospitals from hospital characteristics and discharge statistics available from the Swiss Federal Statistical Office (SFSO, http://www.bag.admin.ch/kzss). However, those data do not provide addresses and further information for all individual hospitals when a single corporate entity operates more than one hospital in one town or canton. We therefore used additional data from the Federal Office of Topography (swisstopo) and TomTom to locate individual hospitals.

We derived the geographical coordinates of the FOH data set of 2008 using the STATA command **geocode3,** which retrieves coordinates via Google Geocoding API V3. To identify additional hospital locations we compared the coordinates of the FOH data set with the hospital coordinates that are provided by swisstopo, and the hospital coordinates provided by the TomTom MultiNet Shapefile 2011. We deleted duplicates and checked for further information about the hospitals via the Internet. We merged the data sets to create one data set with the following information on hospitals operating in 2008: type of hospital (acute care, acute care with emergency room 24/7 (ER), central hospital, and university hospital), and geographical coordinates.

Distance calculation using geographical information system

We calculated two related measures of the distance between residences and hospitals using ArcGIS 10.3: straight-line distance and driving time. Driving times for the road network of Switzerland were calculated using the TomTom MultiNet Shapefile (2011) and ArcGIS Network Analyst. To model the road options for ambulances we excluded ferries, car-train tunnels, and walkways, but included pedestrian areas. Because not all buildings are immediately adjacent to streets, we measured the straight-line distance to the next traversable street segment, assumed 15 km/h speed for traveling this distance, and adjusted driving distance and time accordingly. These data were then added to the SNC data base.

Selection of records

We excluded people younger than 30 at the 2000 census because CVD deaths are quite rare in this age group. We also excluded records having no or imprecise building coordinates that is necessary for the calculation of exact distance to hospital. These buildings also had no Swiss neighborhood index of socioeconomic position (SSEP) values [8] necessary for calculation of exact location. Persons with institutional residences, who are older and have poorer health, were also excluded because they have higher stroke or AMI risk than the general population. Only records with deaths that were identified by stringent probabilistic linkage were included. Individuals were followed from 5 December 2000 until death, emigration, or the end of the study period on 31 December 2008.

Primary cause of death was coded using the International Classification of Disease, Injuries and Causes of Death, 10th revision (ICD-10). Outcomes were deaths by AMI (I21, I22) and stroke (I60, I61, I63, I64).

We analyzed the association of driving time and straight-line distance with stroke and AMI mortality using three different Cox proportional hazard models. Each was age-adjusted via the time axis, which was individuals' age, and includes this information:

- Model 1: hospital distance (driving time or straight-line distance)
- Model 2: hospital distance, sex, nationality, civil status, religion, education, household type, and language region
- Model 3: hospital distance, sex, nationality, civil status, religion, education, household type, language region, SSEP, and urbanization

Analyses were stratified for younger (30-64 years) and older (≥ 65 years) persons because other SNC studies have shown differences in younger and older SNC subjects [9,10]. For further information about the categories of the variables included in the analyses see table 1. Driving time and straight-line distance to each of the four different hospital types (nearest acute hospital, acute hospital with ER, central hospital, or nearest university hospital) was divided into quintiles, the other four of which were compared to the lowest quintile in the Cox analyses. Figure 1 is illustrating the driving distance quintiles to university hospitals for all included buildings in Switzerland. Statistical analyses were done in Stata version 13 (Stata Corporation, College Station, TX, USA).

Overview of study population

In 2008, 173 hospitals were operating in Switzerland. Of these, 138 had an ED, 12 were central hospitals, and 5 university hospitals. The distance calculation used 1,293,780 buildings. Originally, 7,280,246 persons were included in the 2000 census. After excluding persons younger than 30, those living in nursing homes or institutions, and records without precise building coordinates, 4,490,439 persons remained in the study. Of these 48% were male, 76.9% were 30 to 64 years old, 79.3% lived in households with two or more persons, 69.3% were married, 25.7% lived in rural regions, and 72.2% resided in German-speaking Switzerland. 42.3% were Catholics, 17.9% did not have Swiss citizenship, and 22.2% had tertiary level education (see table 1).

Table 1 Characteristics of the study population

Characteristics	Study population		Stroke deaths				AMI deaths			
					Crude rate per 100,000				Crude rate per 100,000	
	Number	%	Number	%	Rate	95% CI	Number	%	Rate	95% CI
All	4,490,439	100	21,931	100	63.8	63-64.7	19,301	100	56.2	55.4-57
Gender										
Male	2,156,749	48	9,361	42.7	57.1	55.9-58.3	11,446	59.3	69.8	68.5-71.1
Female	2,333,690	52	12,570	57.3	70.0	68.8-71.2	7,855	40.7	43.7	42.8-44.7
Age (years)										
30 - 34	549,551	12.2	53	0.2	1.2	0.9-1.6	62	0.3	1.4	1.1-1.8
35 - 39	603,925	13.4	88	0.4	1.8	1.5-2.3	174	0.9	3.6	3.1-4.2
40 - 44	547,237	12.2	162	0.7	3.7	3.2-4.4	287	1.5	6.6	5.9-7.4
45 - 49	491,143	10.9	240	1.1	6.2	5.4-7	479	2.5	12.3	11.3-13.5
50 - 54	478,402	10.7	344	1.6	9.1	8.2-10.2	790	4.1	21.0	19.6-22.5
55 - 59	438,264	9.8	466	2.1	13.6	12.4-14.9	1,065	5.5	31.1	29.3-33.1
60 - 64	342,555	7.6	744	3.4	28.2	26.3-30.3	1,212	6.3	46.0	43.4-48.6
65 - 69	306,346	6.8	1,440	6.6	61.9	58.8-65.2	1,780	9.2	76.5	73-80.2
70 - 74	267,196	6	2,685	12.2	136.8	131.7-142	2,750	14.2	140.1	134.9-145.4
75 - 79	219,519	4.9	4,596	21	303.6	295-312.5	3,662	19	241.9	234.2-249.9
80 - 84	140,276	3.1	5,408	24.7	625.0	608.5-641.9	3,553	18.4	410.6	397.3-424.3
85 - 89	76,053	1.7	3,941	18	999.5	968.8-1031.2	2,554	13.2	647.8	623.1-673.4
90 - 94	25,576	0.6	1,516	6.9	1429.7	1359.5-1503.5	798	4.1	752.6	702.1-806.6
95+	4,396	0.1	248	1.1	1773.0	1565.5-2008	135	0.7	965.1	815.3-1142.5
Neighbourhood index of SEP										
Lowest quintile	898,100	20	4,511	20.6	66.2	64.3-68.1	4,240	22	62.2	60.3-64.1
Second quintile	898,083	20	4,786	21.8	69.9	68-71.9	4,336	22.5	63.4	61.5-65.3
Third quintile	898,089	20	4,577	20.9	66.6	64.7-68.6	4,119	21.3	59.9	58.1-61.8
Fourth quintile	898,081	20	4,210	19.2	61.0	59.2-62.8	3,599	18.6	52.1	50.4-53.9
Highest quintile	898,086	20	3,847	17.5	55.6	53.9-57.4	3,007	15.6	43.5	42-45.1
Type of household										
Single person household	927,282	20.7	9,048	41.3	132.5	129.8-135.2	6,846	35.5	100.2	97.9-102.6
Household with 2 or more persons	3,563,157	79.3	12,883	58.7	46.8	46-47.6	12,455	64.5	45.3	44.5-46.1
Marital status										
Single	646,207	14.4	1,925	8.8	38.4	36.7-40.2	1,692	8.8	33.8	32.2-35.4
Married	3,110,107	69.3	10,609	48.4	44.2	43.4-45	10,865	56.3	45.3	44.4-46.1
Widowed	356,153	7.9	8,151	37.2	337.5	330.3-344.9	5,405	28	223.8	217.9-229.9
Divorced	377,972	8.4	1,246	5.7	42.6	40.3-45.1	1,339	6.9	45.8	43.4-48.3
Urbanization										
urban	1,301,289	29	7,458	34	75.9	74.2-77.6	6,171	32	62.8	61.2-64.4
peri-urban	2,034,574	45.3	8,602	39.2	54.9	53.8-56.1	7,652	39.6	48.9	47.8-50
rural	1,154,576	25.7	5,871	26.8	66.2	64.6-67.9	5,478	28.4	61.8	60.2-63.5
Language region										
German	3,241,186	72.2	16,187	73.8	65.2	64.2-66.2	14,075	72.9	56.7	55.7-57.6
French	1,034,224	23	4,726	21.5	60.1	58.4-61.8	4,223	21.9	53.7	52.1-55.3
Italian	215,029	4.8	1,018	4.6	61.9	58.2-65.8	1,003	5.2	61.0	57.3-64.9
Religious affiliation										
Protestant Churches	1,664,535	37.1	10,755	49	84.6	83-86.2	8,841	45.8	69.5	68.1-71
Roman Catholic Church	1,900,346	42.3	8,481	38.7	58.3	57.1-59.6	7,844	40.6	54.0	52.8-55.2
No religious affiliation	521,035	11.6	1,140	5.2	28.3	26.7-30	1,274	6.6	31.6	29.9-33.4
Other/ unknown	404,523	9	1,555	7.1	50.5	48.1-53.1	1,342	7	43.6	41.3-46

Results

Over the eight years of the study period, 381,659 persons (8.5% of 4,490,439) died. 51.6% of the deceased were men. 142,926 died of CVD (48.9% male), 21,931 died of stroke (42.7% male), and 19,301 (59.3% male) died of AMI. The crude mortality rate per 100,000 persons was 416 for CVD, 64 for stroke, and 56 for AMI (see table 1).

The average driving time to an acute hospital was 6.5 min (maximum 65 min.) and 80.8% of persons in the SNC data set could access an acute hospital in less than 10 minutes. Just 1.3% had to travel 20 minutes or more. The average driving time to a university hospital was 29.7 min (maximum 178 min), while 58.2% had to travel 20 minutes or more (table 2, while the figures for straight-line distance are given in appendix 1).

Table 2 Number of persons in the SNC by driving time for the four different hospital types and average driving time

Driving time	Average driving time in min (max)	SNC persons Number	SNC persons in %
Acute hospital	**6.5 (65)**		
<5min		2,017,352	44.9
5 < 10min		1,610,354	35.9
10 < 15min		674,382	15.0
15 < 20min		132,161	2.9
20min+		56,190	1.3
Acute hospital with ER	**7 (65)**		
<5min		1,834,768	40.9
5 < 10min		1,672,327	37.2
10 < 15min		747,662	16.7
15 < 20min		162,452	3.6
20min+		73,230	1.6
Central hospital	**17.4 (119.6)**		
<5min		679,954	15.1
5 < 10min		795,805	17.7
10 < 15min		619,898	13.8
15 < 20min		755,915	16.8
20min+		1,638,867	36.5
University hospital	**29.7 (178.2)**		
<5min		502,197	11.2
5 < 10min		548,417	12.2
10 < 15min		372,887	8.3
15 < 20min		454,895	10.1
20min+		2,612,043	58.2

Cox analysis results

We ran 96 Cox analyses; 48 for driving time and 48 for straight-line distance. Figures 2–5 present the results of these analyses of AMI and stroke deaths for the 30–64 and 65 and older age groups. On the top of each figure the results of 12 separate analyses for the three models and the driving time to the four different hospital types are displayed. At the bottom of the figures the results of the analyses for straight-line distance is shown (see appendix tables 2–5 for the exact numbers of the driving time analyses and appendix tables 6—9 for the results of the straight-line distance analyses).

In younger persons, driving time to the nearest acute hospital and the nearest hospital with an ER was not associated with AMI mortality, but AMI mortality did increase with driving time to a central or university hospital (figure 2). In persons 65 and older, mortality increased with driving time to all four hospital types in model 1 (figure 3). After including sociodemographic variables (model 2) and additional SSEP and urbanization (model 3) the magnitude of the effects is weaker but still statistically significant for central and university hospitals (highest quintile of driving time to university hospital model 1: HR = 1.27, 95%CI: 1.21–1.34; model 2: HR = 1.19, 95%-CI: 1.13–1.26; model 3: HR = 1.15, 95%-CI: 1.08–1.21).

The impact of driving time on stroke mortality is less pronounced than it is for AMI mortality, especially in younger persons (figure 4). We found no significant relationship between stroke mortality and driving time (figure 4) except for driving time to a university hospital in model 1. In older persons (figure 5), model 1 showed significant associations between driving time to all types of hospital and stroke mortality. No relationship between driving time to acute hospitals and those with an ER was seen in models 2 and 3. Stroke mortality generally increased with driving time to central and university hospitals in all 3 models, though results were greatest in the fourth quintile (central hospital) or third quintile (university hospital). Compared to the lowest quintile of driving time to a university hospital in the fully adjusted model 3, the stroke mortality was 15% higher in the third quintile and 7% higher in the fourth quintile.

Discussion

Main findings

Risk of dying from AMI increased with distance (in driving time) from a central or university hospital for both those younger and older than 65 years in the Swiss National Cohort. For stroke mortality, though, a significant association with distance to the same hospitals was observed only in those 65 and older. However, we did not observe a clear dose-response relationship, as the strongest association was seen when comparing the third and fourth quantile to first quantile of distance. For those younger than 65, stroke mortality was not associated with distance from any type of hospital once the analyses adjusted for relevant individual and regional characteristics. Although we found statistically significant increased hazards for AMI and stroke mortality with increasing distance to central and university hospitals, the hazard ratios were relatively small and could be the result of residual confounding.

Possible mechanisms

Our study analyzed the outcome of death following AMI or stroke at any point along a rather complex chain of events and interventions: 1) experiencing the AMI/stroke, 2) someone noticing the AMI/stroke (the patient, if able, otherwise someone else), 3) alerting the EMS, 4) CPR and defibrillation if needed by AMI patients, 5) transport to a treatment facility, 6) treatment, 7) rehabilitation. Differences observed in AMI/stroke mortality by hospital distance could arise in any element of this chain.

The positive association of stroke mortality with distance in those over 65 might be explained by differences in the awareness and interpretability of stroke symptoms by patients themselves, or persons in the same household or workplace. Certainly alarm time might be longer for older people living alone than younger people living in family households. Another possibility is that elderly people, who are known to be at higher risk for stroke [11], might also be more susceptible to time delays due to comorbidities or physical or biochemical disturbances that may accompany a stroke. It also might be possible that, similar to trauma patients who have been observed to have lower trauma unit admission rates with higher age [12], stroke patients—especially from rural areas where the awareness of stroke symptoms might be lower—have lower primary stroke unit admission rates, and increased mortality. In any event, treatment of patients who live far from a hospital with a stroke unit might more effectively rely upon air transport by helicopter.

Early after occurrence, AMI (especially STEMI) can have poor survival, while mortality from stroke often occurs later due to secondary sequelae such as secondary cerebral bleeding in the infarct territory, haemodynamic instability, or pulmonary complications. Furthermore, stroke patients might suffer severe neurological impairment, increasing with increasing time to revascularization, but still survive. This might explain why the association between AMI and distance to hospital was more pronounced in all age groups compared to stroke patients.

Most studies focus on in-hospital mortality because these data are easy to access. Data about persons dying at the scene of the event, on the way to the hospital, or after discharge from hospital are more difficult to obtain.

Referral to and enrollment in a chronic disease management program for cardiac rehabilitation was less likely in patients in Ontario, Canada who lived 60 or more minutes from a cardiac rehabilitation site [13]. Therefore, it is important to distinguish health care utilization from emergency treatment in the association of accessibility of health care facilities and outcomes.

Investigating the association of distance to hospital and increased risk of death in patients with life-threatening emergencies, Nicholl et al. justified the exclusion of out-of-hospital cardiac arrests from their study because survival depends upon time from call to treatment by ambulance staff rather than time or distance from scene to hospital [14]. In contrast, Evenson et al. emphasize that in acute stroke care prehospital delay—the time from onset of symptoms to hospital arrival—contributes the major proportion of delay time [15]. Because the SNC lacks detailed information about circumstances and place of death (e.g., death before being reached, death during transport, death in nursing home or hospital), we could not perform sensitivity analyses by excluding prehospital deaths. What we did do, however, was exclude persons who lived in institutions at the 2000 census from all analyses because treatment decisions for such persons, most of whom are elderly, might differ from those still living at home by, e.g., the existence of do not resuscitate orders.

Study limitations

As noted above, the SNC does not contain information on the exact location of a person when he or she had a stroke or heart attack. Because the average ages of all persons dying from stroke and AMI were respectively 82 and 78 we assumed the vast majority of stroke or AMI events occurred at or close to home and reasonably, we believe, we used home to hospital distance in our analyses.

We located SNC participants at a place of residence in the 2000 census, which was also the basis for defining the neighborhood index of socioeconomic position [8]. However, over the years 2001 to 2008 residents could have moved (some surely did) and that information is not available in the SNC data. For those who died, the SNC also has information about the community (but not exact geocode) of the residence at death. Of the 381,659 people who died in our study population 19,785 (5.2%) did not die in the same community in which they lived at the census 2000 (1,089 in stroke cases, 908 in AMI cases).

Information on whether a patient was admitted, to which hospital, was not available. We partially addressed this problem by including the distance to different types of hospitals as patients will be admitted to different specialized hospitals depending on their diagnosis/symptoms.

Catheter laboratories and stroke units provide the best evidence-based treatments for AMI and stroke patients [1,3,16]. It would have been ideal to know the distance to hospitals that have catheter laboratories or stroke units. However, in Switzerland health care is mainly organized at the cantonal level with 26 cantons in charge of health care planning and organization. Information on which treatment services are available at each hospital does not exist in a national database, and this includes catheter labs and stroke units operating in the years 2000 to 2008. At the local level, rescue crews are supposed to know which hospitals on which day and hour can receive patients who are in need of specialized AMI or stroke treatments.

Strengths

This study benefits from data that form a true nationwide cohort with almost complete follow-up during the study period for persons 30 years or older at the 2000 census. All Swiss hospitals operating in 2008 were included and classified by type. Due to Swiss topography we decided to calculate driving time instead of only using straight-line distance because driving time is a more accurate measure of access in peripheral and rural areas [17]. However, in the mountains and other remote regions emergency medical transportation might be carried out by helicopter. Therefore, we also calculated straight-line distance to model helicopter flight times. We found results were comparable to driving time (see figures 2—5 or appendices 6–9).

Comparison with other studies

Several studies have found that AMI and stroke mortality increase with distance to hospital [18–22], whereas others have not found such an association [23–26].

However, studies investigating how mortality from AMI or stroke varies by distance to hospital differ by study design (cohort study, ecological study), subjects included (patients, population), selection of hospitals (federal hospitals), type of mortality (in-hospital, prehospital, posthospital, all-cause mortality) or geographical setting (city, urban and rural, county, state, country). Moreover, one expects that the role of hospital distance differs by size and geographical structure of the region or country (e.g., Canada versus Monaco). This complicates any comparison of results obtained in other regions or countries with those of our study of Switzerland.

Conclusions

AMI mortality increased with distance to central and university hospitals in the Swiss population both under and over 65 years of age, while stroke mortality increased in those 65 and older, although the strength of the observed associations was rather small. Even though hospital density in Switzerland is high, complex geography in more remote Swiss areas might make it difficult for EMS to guarantee adequate time from onset to intervention for acute events such as AMI and stroke.

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Ethical approval: For this type of study formal consent is not required.

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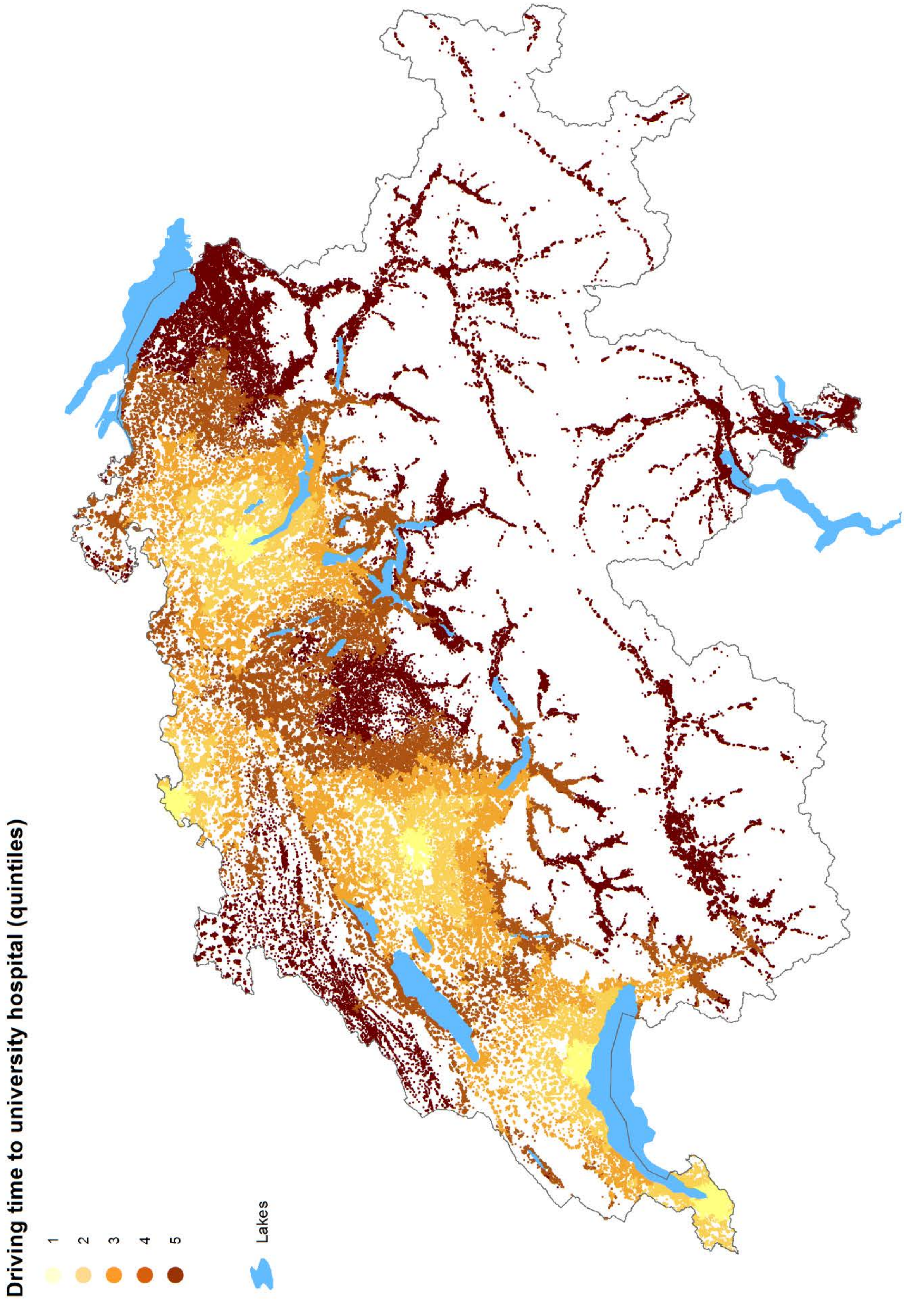

Fig. 1 Driving time quintiles to university hospitals displayed for each building

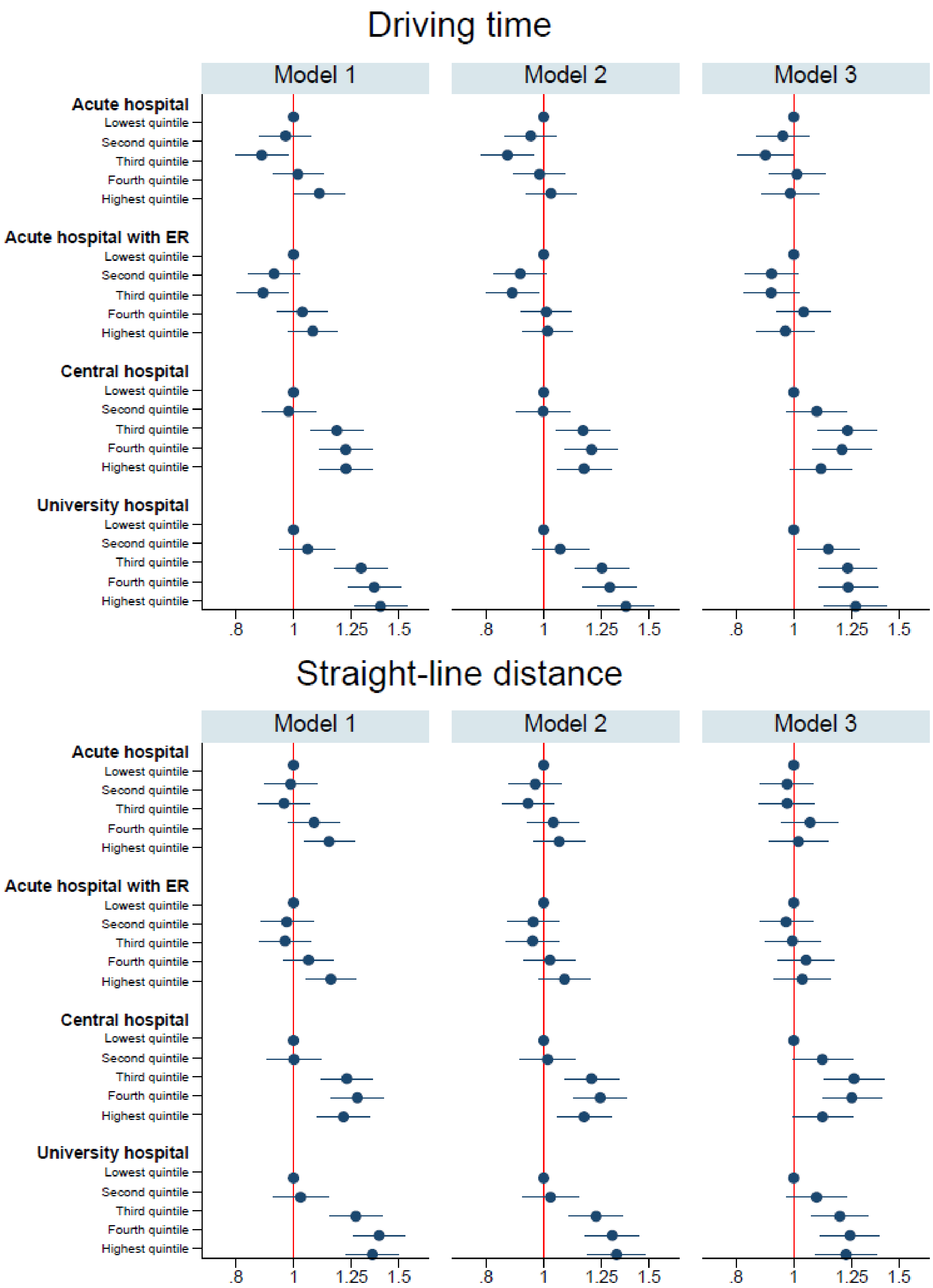

Fig. 2 Cox analyses of AMI mortality - driving time quintiles and straight-line distance quintiles for persons 30-64 years under models 1 to 3 for the four different hospital types

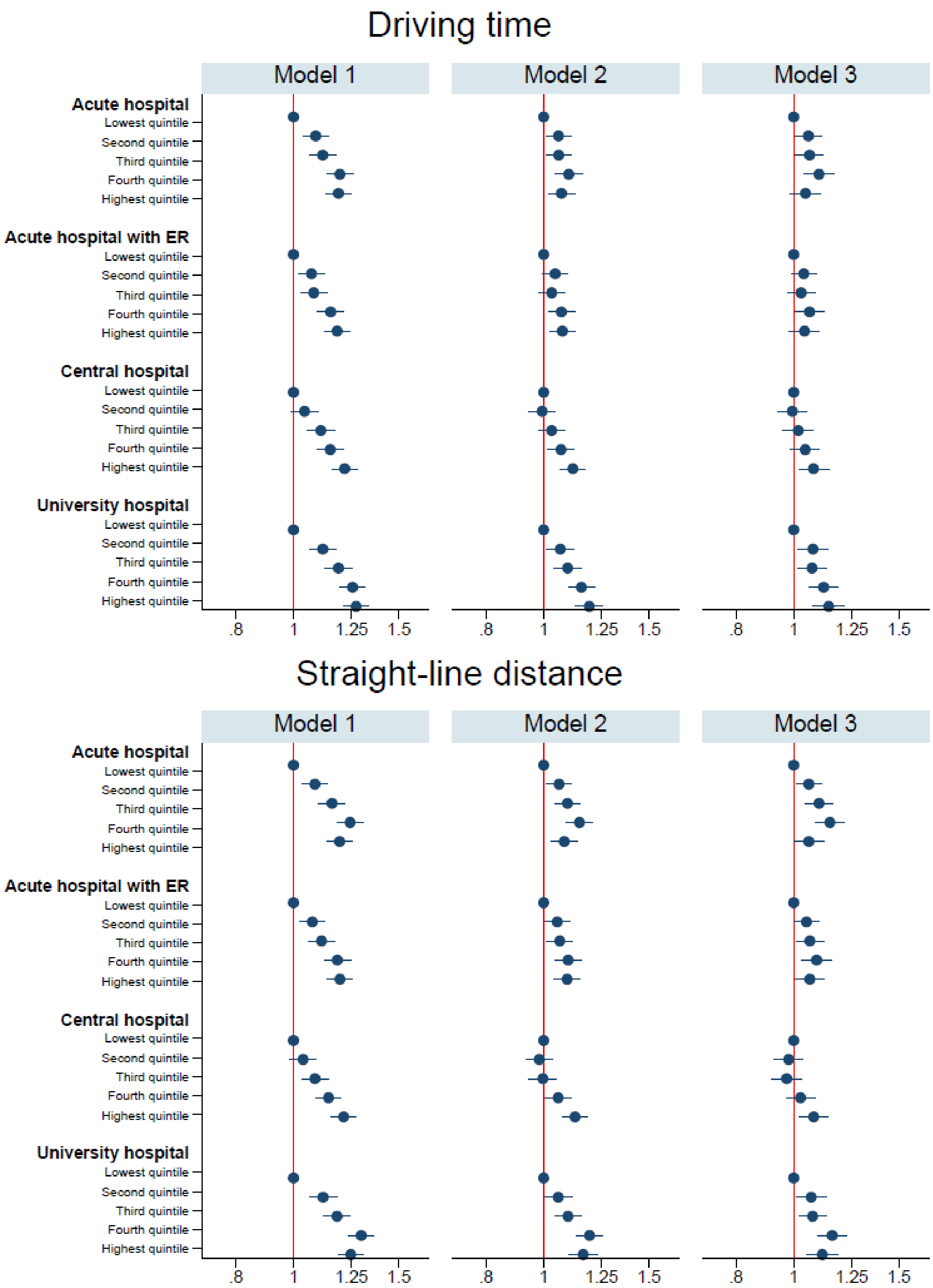

Fig. 3 Cox analyses of AMI mortality - driving time quintiles and straight-line distance quintiles for persons 65 and older under models 1 to 3 for the four different hospital types

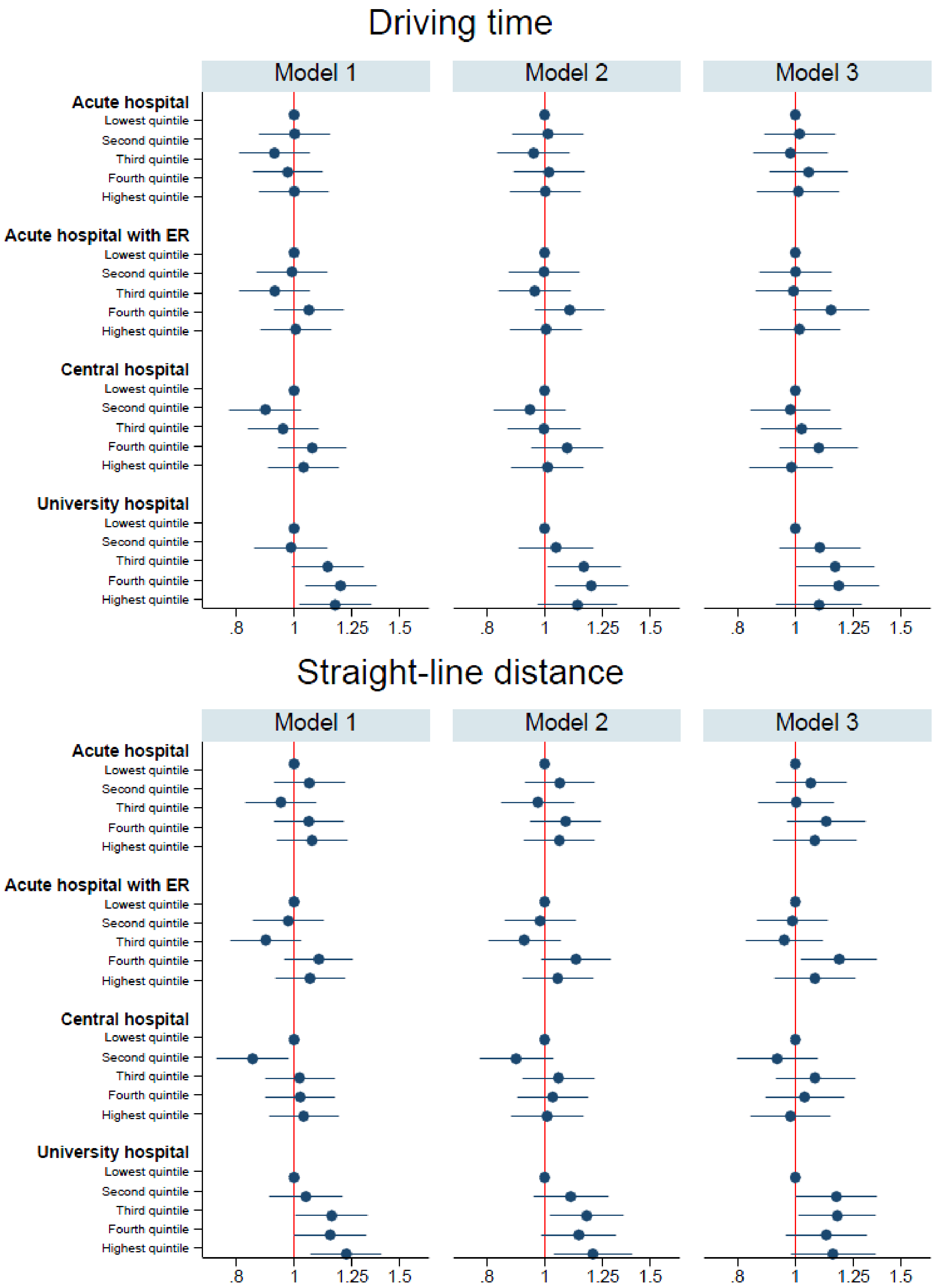

Fig. 4 Cox analyses of stroke mortality - driving time quintiles and straight-line distance quintiles for persons 30-64 under models 1 to 3 for the four different hospital types

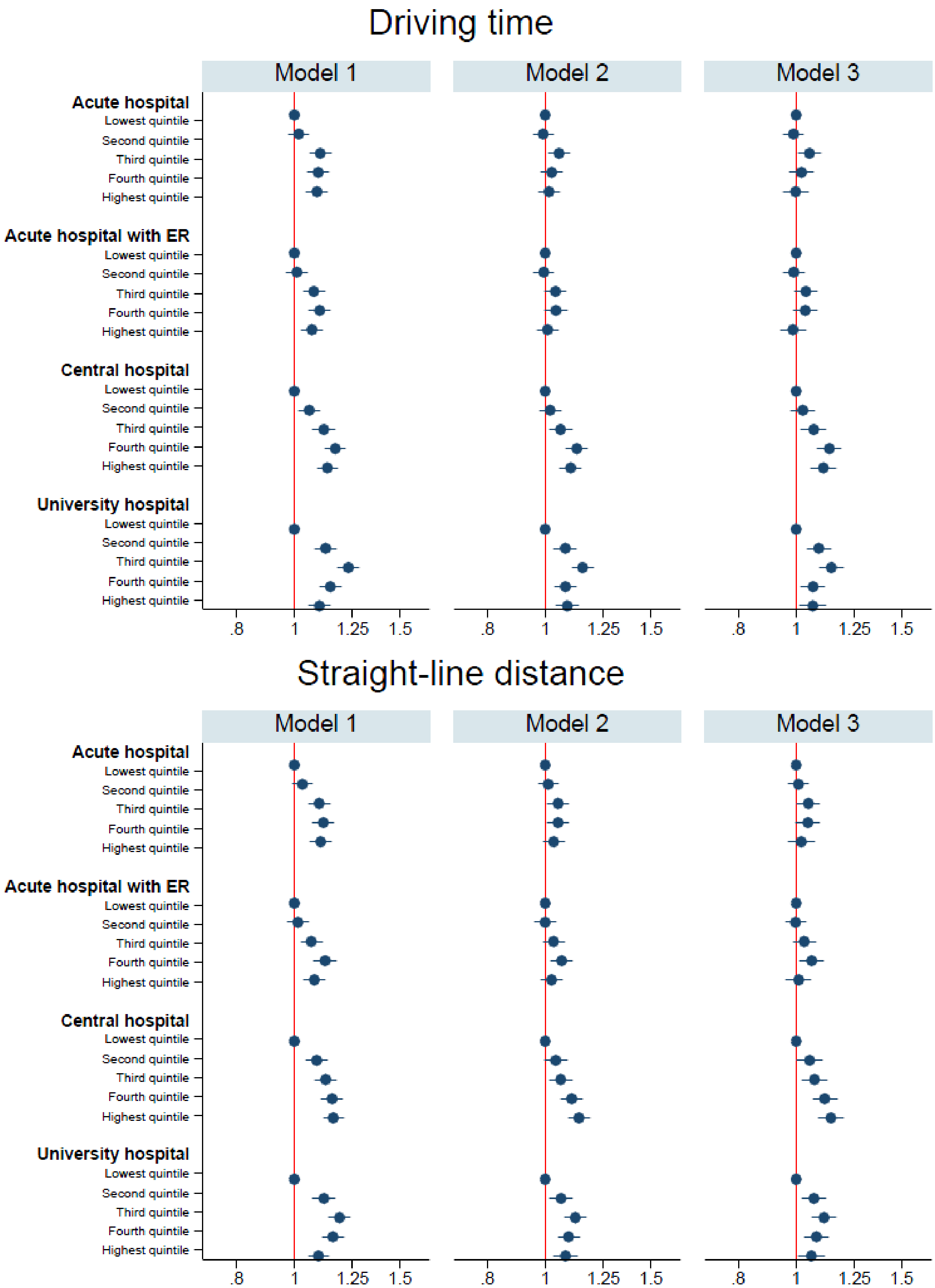

Fig. 5 Cox analyses of stroke mortality - driving time quintiles and straight-line distance quintiles for persons 65 and older under models 1 to 3 for the four different hospital types

Appendix 1 Number of SNC persons by straight-line distance groups to the 4 different hospital types and average driving time

Straight-line distance	Average straight-line distance in km (max)	SNC persons Number	in %
Acute hospital	**4.1 (35.8)**		
<5km		3,066,120	68.3
5 < 10km		1,146,168	25.5
10 < 15km		231,432	5.2
15 < 20km		33,091	0.7
20km+		13,628	0.3
Acute hospital with ER	**4.5 (35.8)**		
<5km		2,909,789	64.8
5 < 10km		1,222,016	27.2
10 < 15km		290,970	6.5
15 < 20km		52,108	1.2
20km+		15,556	0.3
Central hospital	**16.1 (84.4)**		
<5km		1,122,167	25.0
5 < 10km		623,079	13.9
10 < 15km		556,787	12.4
15 < 20km		630,307	14.0
20km+		1,558,099	34.7
University hospital	**33.4 (176.3)**		
<5km		794,125	17.7
5 < 10km		411,948	9.2
10 < 15km		283,952	6.3
15 < 20km		349,764	7.8
20km+		2,650,650	59.0

Appendix 2 Cox analyses of AMI mortality and driving time quintiles for persons 30-64 under models 1 to 3 for the four different hospital types

	Model 1		Model 2		Model 3	
Driving time	**Hazard ratio**	**95% CI**	**Hazard ratio**	**95% CI**	**Hazard ratio**	**95% CI**
Acute hospital		**p<0.001**		**p=0.011**		**p=0.134**
Lowest quintile	1		1		1	
Second quintile	0.970	0.878 - 1.071	0.952	0.862 - 1.052	0.959	0.867 - 1.060
Third quintile	0.885	0.800 - 0.978	0.870	0.786 - 0.963	0.897	0.806 - 0.997
Fourth quintile	1.017	0.923 - 1.120	0.984	0.892 - 1.086	1.012	0.909 - 1.127
Highest quintile	1.104	1.004 - 1.216	1.029	0.933 - 1.134	0.987	0.882 - 1.104
Acute hospital with ER		**p<0.001**		**p=0.011**		**p=0.052**
Lowest quintile	1		1		1	
Second quintile	0.928	0.839 - 1.025	0.914	0.826 - 1.010	0.918	0.830 - 1.015
Third quintile	0.889	0.805 - 0.983	0.885	0.801 - 0.979	0.917	0.825 - 1.018
Fourth quintile	1.035	0.940 - 1.139	1.010	0.917 - 1.114	1.039	0.935 - 1.154
Highest quintile	1.077	0.979 - 1.186	1.015	0.921 - 1.119	0.968	0.868 - 1.081
Central hospital		**p<0.001**		**p<0.001**		**p=0.001**
Lowest quintile	1		1		1	
Second quintile	0.981	0.884 - 1.089	0.998	0.898 - 1.109	1.093	0.973 - 1.227
Third quintile	1.182	1.069 - 1.306	1.164	1.051 - 1.290	1.231	1.097 - 1.380
Fourth quintile	1.223	1.107 - 1.352	1.203	1.086 - 1.333	1.204	1.076 - 1.348
Highest quintile	1.224	1.107 - 1.353	1.169	1.055 - 1.296	1.111	0.987 - 1.251
University hospital		**p<0.001**		**p<0.001**		**p<0.001**
Lowest quintile	1		1		1	
Second quintile	1.056	0.950 - 1.174	1.066	0.957 - 1.188	1.143	1.018 - 1.284
Third quintile	1.298	1.172 - 1.438	1.252	1.127 - 1.391	1.231	1.102 - 1.375
Fourth quintile	1.366	1.233 - 1.512	1.291	1.162 - 1.433	1.233	1.100 - 1.382
Highest quintile	1.398	1.264 - 1.547	1.373	1.231 - 1.532	1.269	1.126 - 1.431

Appendix 3 Cox analyses of AMI mortality and driving time quintiles for persons 65 and older under models 1 to 3 for the four different hospital types

	Model 1		Model 2		Model 3	
Driving time	**Hazard ratio**	**95% CI**	**Hazard ratio**	**95% CI**	**Hazard ratio**	**95% CI**
Acute hospital		**p<0.001**		**p=0.004**		**p=0.012**
Lowest quintile	1		1		1	
Second quintile	1.089	1.038 - 1.144	1.059	1.009 - 1.112	1.058	1.008 - 1.111
Third quintile	1.119	1.065 - 1.177	1.060	1.008 - 1.115	1.063	1.008 - 1.121
Fourth quintile	1.195	1.136 - 1.257	1.102	1.047 - 1.160	1.102	1.042 - 1.166
Highest quintile	1.189	1.132 - 1.249	1.071	1.019 - 1.126	1.046	0.987 - 1.109
Acute hospital with ER		**p<0.001**		**p=0.031**		**p=0.272**
Lowest quintile	1		1		1	
Second quintile	1.072	1.021 - 1.125	1.045	0.996 - 1.097	1.039	0.990 - 1.091
Third quintile	1.081	1.028 - 1.137	1.032	0.981 - 1.085	1.029	0.976 - 1.085
Fourth quintile	1.154	1.097 - 1.214	1.071	1.017 - 1.127	1.063	1.006 - 1.123
Highest quintile	1.183	1.127 - 1.243	1.075	1.023 - 1.130	1.042	0.985 - 1.103
Central hospital		**p<0.001**		**p<0.001**		**p=0.036**
Lowest quintile	1		1		1	
Second quintile	1.044	0.992 - 1.098	0.994	0.944 - 1.046	0.995	0.940 - 1.053
Third quintile	1.111	1.056 - 1.170	1.031	0.979 - 1.087	1.017	0.960 - 1.078
Fourth quintile	1.152	1.097 - 1.210	1.070	1.017 - 1.125	1.045	0.989 - 1.105
Highest quintile	1.218	1.162 - 1.277	1.119	1.066 - 1.175	1.079	1.019 - 1.143
University hospital		**p<0.001**		**p<0.001**		**p<0.001**
Lowest quintile	1		1		1	
Second quintile	1.120	1.062 - 1.180	1.067	1.011 - 1.125	1.077	1.017 - 1.141
Third quintile	1.189	1.130 - 1.252	1.097	1.042 - 1.156	1.073	1.016 - 1.134
Fourth quintile	1.256	1.196 - 1.319	1.157	1.100 - 1.216	1.122	1.062 - 1.186
Highest quintile	1.273	1.213 - 1.335	1.193	1.131 - 1.257	1.145	1.079 - 1.214

Appendix 4 Cox analyses of stroke mortality and driving time quintiles for persons 30-64 under models 1 to 3 for the four different hospital types

	Model 1		Model 2		Model 3	
Driving time	**Hazard ratio**	**95% CI**	**Hazard ratio**	**95% CI**	**Hazard ratio**	**95% CI**
Acute hospital		**p=0.767**		**p=0.923**		**p=0.897**
Lowest quintile	1		1		1	
Second quintile	1.002	0.875 - 1.149	1.013	0.883 - 1.161	1.017	0.886 - 1.167
Third quintile	0.927	0.808 - 1.064	0.958	0.834 - 1.101	0.982	0.848 - 1.136
Fourth quintile	0.976	0.852 - 1.117	1.016	0.885 - 1.167	1.053	0.906 - 1.224
Highest quintile	1.001	0.874 - 1.146	1.003	0.873 - 1.152	1.012	0.864 - 1.186
Acute hospital with ER		**p=0.439**		**p=0.353**		**p=0.187**
Lowest quintile	1		1		1	
Second quintile	0.992	0.865 - 1.139	0.998	0.869 - 1.145	1.001	0.872 - 1.150
Third quintile	0.928	0.808 - 1.066	0.962	0.837 - 1.106	0.993	0.859 - 1.150
Fourth quintile	1.059	0.926 - 1.211	1.101	0.962 - 1.262	1.148	0.991 - 1.330
Highest quintile	1.006	0.878 - 1.153	1.006	0.875 - 1.156	1.016	0.869 - 1.189
Central hospital		**p=0.081**		**p=0.353**		**p=0.495**
Lowest quintile	1		1		1	
Second quintile	0.896	0.779 - 1.029	0.945	0.821 - 1.088	0.982	0.840 - 1.147
Third quintile	0.958	0.835 - 1.100	0.997	0.866 - 1.148	1.025	0.876 - 1.199
Fourth quintile	1.072	0.937 - 1.227	1.091	0.950 - 1.253	1.095	0.941 - 1.274
Highest quintile	1.037	0.905 - 1.188	1.012	0.879 - 1.164	0.986	0.839 - 1.159
University hospital		**p=0.010**		**p=0.074**		**p=0.224**
Lowest quintile	1		1		1	
Second quintile	0.989	0.858 - 1.140	1.045	0.904 - 1.208	1.099	0.940 - 1.285
Third quintile	1.138	0.990 - 1.308	1.163	1.008 - 1.342	1.166	1.004 - 1.355
Fourth quintile	1.196	1.042 - 1.373	1.197	1.038 - 1.380	1.183	1.013 - 1.380
Highest quintile	1.171	1.020 - 1.345	1.135	0.973 - 1.323	1.096	0.927 - 1.296

Appendix 5 Cox analyses of stroke mortality and driving time quintiles for persons 65 and older under models 1 to 3 for the four different hospital types

	Model 1		Model 2		Model 3	
Driving time	**Hazard ratio**	**95% CI**	**Hazard ratio**	**95% CI**	**Hazard ratio**	**95% CI**
Acute hospital		**p<0.001**		**p=0.059**		**p=0.063**
Lowest quintile	1		1		1	
Second quintile	1.017	0.975 - 1.061	0.992	0.951 - 1.034	0.990	0.949 - 1.033
Third quintile	1.104	1.058 - 1.153	1.055	1.010 - 1.101	1.053	1.006 - 1.102
Fourth quintile	1.096	1.049 - 1.146	1.025	0.980 - 1.072	1.021	0.972 - 1.073
Highest quintile	1.091	1.045 - 1.139	1.015	0.971 - 1.060	0.998	0.948 - 1.051
Acute hospital with ER		**p<0.001**		**p=0.110**		**p=0.090**
Lowest quintile	1		1		1	
Second quintile	1.009	0.968 - 1.053	0.995	0.954 - 1.037	0.991	0.950 - 1.034
Third quintile	1.077	1.032 - 1.125	1.041	0.996 - 1.087	1.039	0.992 - 1.087
Fourth quintile	1.102	1.055 - 1.152	1.042	0.997 - 1.090	1.036	0.987 - 1.087
Highest quintile	1.070	1.025 - 1.117	1.009	0.966 - 1.054	0.988	0.940 - 1.039
Central hospital		**p<0.001**		**p<0.001**		**p<0.001**
Lowest quintile	1		1		1	
Second quintile	1.059	1.014 - 1.107	1.019	0.974 - 1.065	1.026	0.977 - 1.078
Third quintile	1.120	1.071 - 1.171	1.061	1.014 - 1.110	1.070	1.018 - 1.126
Fourth quintile	1.170	1.121 - 1.221	1.129	1.081 - 1.180	1.137	1.084 - 1.193
Highest quintile	1.135	1.089 - 1.183	1.103	1.057 - 1.152	1.111	1.056 - 1.169
University hospital		**p<0.001**		**p<0.001**		**p<0.001**
Lowest quintile	1		1		1	
Second quintile	1.128	1.078 - 1.180	1.081	1.032 - 1.131	1.091	1.039 - 1.146
Third quintile	1.231	1.179 - 1.286	1.154	1.105 - 1.206	1.145	1.093 - 1.200
Fourth quintile	1.149	1.100 - 1.199	1.081	1.035 - 1.129	1.068	1.017 - 1.120
Highest quintile	1.101	1.055 - 1.149	1.088	1.039 - 1.140	1.066	1.012 - 1.124

Appendix 6 Cox analyses of AMI mortality and straight-line distance quintiles for persons 30-64 under models 1 to 3 for the four different hospital types

	Model 1		Model 2		Model 3	
Straight-line distance	**Hazard ratio**	**95% CI**	**Hazard ratio**	**95% CI**	**Hazard ratio**	**95% CI**
Acute hospital		**p=0.001**		**p=0.094**		**p=0.413**
Lowest quintile	1		1		1	
Second quintile	0.989	0.894 - 1.094	0.968	0.875 - 1.071	0.975	0.881 - 1.079
Third quintile	0.964	0.873 - 1.066	0.941	0.851 - 1.041	0.975	0.877 - 1.084
Fourth quintile	1.083	0.983 - 1.194	1.038	0.941 - 1.146	1.065	0.955 - 1.187
Highest quintile	1.147	1.041 - 1.264	1.062	0.962 - 1.172	1.018	0.909 - 1.140
Acute hospital with ER		**p<0.001**		**p=0.071**		**p=0.651**
Lowest quintile	1		1		1	
Second quintile	0.974	0.881 - 1.077	0.960	0.868 - 1.062	0.971	0.877 - 1.074
Third quintile	0.968	0.876 - 1.069	0.958	0.867 - 1.059	0.995	0.896 - 1.106
Fourth quintile	1.060	0.961 - 1.168	1.024	0.928 - 1.131	1.049	0.942 - 1.168
Highest quintile	1.155	1.049 - 1.272	1.084	0.983 - 1.195	1.034	0.925 - 1.154
Central hospital		**p<0.001**		**p<0.001**		**p<0.001**
Lowest quintile	1		1		1	
Second quintile	1.002	0.903 - 1.112	1.016	0.914 - 1.129	1.117	0.995 - 1.254
Third quintile	1.228	1.111 - 1.358	1.203	1.086 - 1.333	1.262	1.125 - 1.415
Fourth quintile	1.279	1.158 - 1.413	1.244	1.123 - 1.378	1.251	1.118 - 1.400
Highest quintile	1.213	1.096 - 1.342	1.169	1.054 - 1.297	1.118	0.996 - 1.255
University hospital		**p<0.001**		**p<0.001**		**p=0.001**
Lowest quintile	1		1		1	
Second quintile	1.028	0.924 - 1.142	1.027	0.921 - 1.144	1.092	0.971 - 1.228
Third quintile	1.271	1.148 - 1.408	1.224	1.103 - 1.359	1.195	1.070 - 1.333
Fourth quintile	1.391	1.258 - 1.539	1.304	1.175 - 1.446	1.243	1.110 - 1.391
Highest quintile	1.356	1.225 - 1.500	1.325	1.187 - 1.479	1.224	1.087 - 1.378

Appendix 7 Cox analyses of AMI mortality and straight-line distance quintiles for persons 65 and older under models 1 to 3 for the four different hospital types

	Model 1		Model 2		Model 3	
Straight-line distance	**Hazard ratio**	**95% CI**	**Hazard ratio**	**95% CI**	**Hazard ratio**	**95% CI**
Acute hospital		**p<0.001**		**p<0.001**		**p<0.001**
Lowest quintile	1		1		1	
Second quintile	1.086	1.034 - 1.141	1.061	1.011 - 1.115	1.060	1.009 - 1.113
Third quintile	1.160	1.103 - 1.220	1.097	1.043 - 1.153	1.102	1.045 - 1.162
Fourth quintile	1.244	1.183 - 1.308	1.148	1.091 - 1.208	1.150	1.087 - 1.217
Highest quintile	1.194	1.136 - 1.255	1.082	1.029 - 1.139	1.060	0.999 - 1.125
Acute hospital with ER		**p<0.001**		**p=0.001**		**p=0.036**
Lowest quintile	1		1		1	
Second quintile	1.075	1.024 - 1.129	1.054	1.003 - 1.106	1.051	1.000 - 1.103
Third quintile	1.114	1.060 - 1.172	1.065	1.012 - 1.120	1.064	1.009 - 1.122
Fourth quintile	1.184	1.125 - 1.246	1.100	1.044 - 1.158	1.092	1.032 - 1.156
Highest quintile	1.196	1.138 - 1.256	1.095	1.042 - 1.151	1.064	1.005 - 1.127
Central hospital		**p<0.001**		**p<0.001**		**p=0.001**
Lowest quintile	1		1		1	
Second quintile	1.037	0.986 - 1.091	0.983	0.934 - 1.035	0.980	0.927 - 1.037
Third quintile	1.086	1.032 - 1.144	0.997	0.946 - 1.051	0.973	0.918 - 1.032
Fourth quintile	1.145	1.090 - 1.203	1.057	1.005 - 1.112	1.027	0.971 - 1.085
Highest quintile	1.213	1.157 - 1.272	1.129	1.076 - 1.185	1.080	1.022 - 1.142
University hospital		**p<0.001**		**p<0.001**		**p<0.001**
Lowest quintile	1		1		1	
Second quintile	1.121	1.063 - 1.182	1.058	1.002 - 1.116	1.069	1.009 - 1.134
Third quintile	1.183	1.125 - 1.244	1.099	1.044 - 1.157	1.075	1.019 - 1.135
Fourth quintile	1.298	1.237 - 1.363	1.194	1.136 - 1.255	1.160	1.098 - 1.225
Highest quintile	1.247	1.188 - 1.309	1.165	1.104 - 1.230	1.116	1.053 - 1.184

Appendix 8 Cox analyses of stroke mortality and straight-line distance quintiles for persons 30-64 under models 1 to 3 for the four different hospital types

	Model 1		Model 2		Model 3	
Straight-line distance	**Hazard ratio**	**95% CI**	**Hazard ratio**	**95% CI**	**Hazard ratio**	**95% CI**
Acute hospital		**p=0.366**		**p=0.510**		**p=0.449**
Lowest quintile	1		1		1	
Second quintile	1.061	0.925 - 1.217	1.060	0.924 - 1.216	1.062	0.925 - 1.219
Third quintile	0.950	0.827 - 1.092	0.974	0.847 - 1.121	1.004	0.866 - 1.163
Fourth quintile	1.059	0.924 - 1.213	1.084	0.945 - 1.244	1.127	0.968 - 1.311
Highest quintile	1.072	0.935 - 1.228	1.058	0.921 - 1.216	1.079	0.920 - 1.265
Acute hospital with ER		**p=0.032**		**p=0.049**		**p=0.027**
Lowest quintile	1		1		1	
Second quintile	0.978	0.851 - 1.123	0.983	0.856 - 1.129	0.989	0.861 - 1.137
Third quintile	0.897	0.780 - 1.031	0.924	0.803 - 1.064	0.959	0.827 - 1.111
Fourth quintile	1.100	0.963 - 1.257	1.129	0.986 - 1.291	1.185	1.022 - 1.373
Highest quintile	1.063	0.929 - 1.217	1.051	0.916 - 1.206	1.079	0.924 - 1.261
Central hospital		**p=0.034**		**p=0.185**		**p=0.311**
Lowest quintile	1		1		1	
Second quintile	0.853	0.741 - 0.981	0.896	0.777 - 1.033	0.933	0.798 - 1.090
Third quintile	1.022	0.893 - 1.169	1.055	0.918 - 1.212	1.079	0.925 - 1.260
Fourth quintile	1.024	0.895 - 1.173	1.032	0.897 - 1.186	1.037	0.890 - 1.208
Highest quintile	1.037	0.906 - 1.188	1.010	0.878 - 1.160	0.982	0.841 - 1.147
University hospital		**p=0.028**		**p=0.132**		**p=0.238**
Lowest quintile	1		1		1	
Second quintile	1.047	0.909 - 1.205	1.106	0.957 - 1.278	1.172	1.002 - 1.371
Third quintile	1.156	1.006 - 1.329	1.176	1.019 - 1.357	1.176	1.012 - 1.366
Fourth quintile	1.150	0.999 - 1.323	1.141	0.988 - 1.318	1.127	0.963 - 1.319
Highest quintile	1.223	1.065 - 1.404	1.204	1.034 - 1.404	1.156	0.981 - 1.362

Appendix 9 Cox analyses of stroke mortality and straight-line distance quintiles for persons 65 and older under models 1 to 3 for the four different hospital types

	Model 1		Model 2		Model 3	
Straight-line distance	**Hazard ratio**	**95% CI**	**Hazard ratio**	**95% CI**	**Hazard ratio**	**95% CI**
Acute hospital		**p<0.001**		**p=0.103**		**p=0.206**
Lowest quintile	1		1		1	
Second quintile	1.032	0.989 - 1.076	1.012	0.970 - 1.055	1.009	0.967 - 1.053
Third quintile	1.100	1.054 - 1.149	1.050	1.006 - 1.097	1.049	1.001 - 1.098
Fourth quintile	1.118	1.070 - 1.169	1.050	1.004 - 1.099	1.047	0.996 - 1.100
Highest quintile	1.106	1.060 - 1.155	1.033	0.989 - 1.080	1.020	0.969 - 1.074
Acute hospital with ER		**p<0.001**		**p=0.035**		**p=0.071**
Lowest quintile	1		1		1	
Second quintile	1.013	0.972 - 1.057	1.000	0.959 - 1.043	0.998	0.957 - 1.041
Third quintile	1.067	1.021 - 1.114	1.033	0.988 - 1.079	1.032	0.985 - 1.080
Fourth quintile	1.126	1.077 - 1.177	1.066	1.019 - 1.114	1.062	1.011 - 1.115
Highest quintile	1.080	1.035 - 1.127	1.025	0.981 - 1.070	1.010	0.961 - 1.062
Central hospital		**p<0.001**		**p<0.001**		**p<0.001**
Lowest quintile	1		1		1	
Second quintile	1.090	1.043 - 1.139	1.042	0.996 - 1.089	1.054	1.004 - 1.106
Third quintile	1.128	1.078 - 1.179	1.062	1.014 - 1.111	1.074	1.020 - 1.130
Fourth quintile	1.156	1.108 - 1.207	1.107	1.060 - 1.157	1.117	1.064 - 1.172
Highest quintile	1.162	1.114 - 1.211	1.139	1.091 - 1.188	1.144	1.089 - 1.201
University hospital		**p<0.001**		**p<0.001**		**p<0.001**
Lowest quintile	1		1		1	
Second quintile	1.121	1.071 - 1.173	1.063	1.015 - 1.113	1.071	1.019 - 1.127
Third quintile	1.190	1.140 - 1.242	1.123	1.075 - 1.173	1.114	1.063 - 1.167
Fourth quintile	1.160	1.111 - 1.210	1.094	1.048 - 1.143	1.082	1.031 - 1.135
Highest quintile	1.097	1.051 - 1.145	1.081	1.032 - 1.133	1.060	1.007 - 1.116

3 Discussion

3.1 Main findings

Regional variation of avoidable hospitalizations in Switzerland (Article 1)

In 2010, 3.1% of all hospital stays were AH. Patient's characteristics differed between low and high volume hospitals. The study results showed 3.6-fold variation between the 59 HSAs from 2008 to 2010 and up to 12-fold variation within one year. Lower rates of all AH were found in areas with very high supply of primary care physicians, increased AH rates in areas with more specialists (irrespective of the disease group) and in areas with higher proportion of rural residents. No association was found with reimbursement system and hospital capacity.

Adequate treatment of emergency STEMI patients? (Article 2)

Using the hospital discharge and hospital statistics of 2010 and 2011 we identified 9,696 STEMI cases, 71.6% of them received a PCI or CABG. Older and female patients were less likely to receive revascularization which suggests that the treatment guidelines may not be uniformly applied in Switzerland. Other variables as the insurance status, the infrastructure of the hospital, or the language region of the hospital didn't affect the receipt of revascularization. A sensitivity analysis showed that being admitted to a small hospital first, limits the chance of receiving a revascularization.

The geography of cost of end of life care in Switzerland (Article 3)

The data of six large Swiss health insurances were utilized to examine the cost at the end of life of all deceased customers who died between 2008 and 2010. Cardiovascular disease and cancer were the main causes of death. Cancer deaths accumulated the largest costs, followed by diseases of the nervous system, respiratory diseases and CVD. Cause of death and age were the major drivers of high cost of end of life care. The language region also played a role: In the French speaking part of Switzerland the EOLC costs were 28% to 35% higher. No effect was found for health care supply measures. Still, large geographical variation in cost were observed, which couldn't be explained with the variables included in the analyses.

Distance to hospital and AMI and stroke mortality (Article 4)

The Swiss National Cohort was used to examine the relationship between distance from the place of residence to different hospital types and the risk of dying from acute myocardial infarction or stroke. The AMI mortality risk for the young (below 65 years) and old (65+ years) Swiss population increases with the distance to a central or university hospital. An elevated risk of stroke mortality was also found for the older Swiss population. For both, AMI and stroke mortality, the observed associations were rather small.

3.2 Strengths and limitations

Study-specific strengths and limitations are discussed in detail in each of the articles comprising this thesis. In general, all studies aimed to cover the whole country and followed a population-based approach which was sometimes limited by data quality and accessibility. To my knowledge, the consideration of the referral pattern in the hospital discharge statistics is unique. In contrast, previous studies incorporated the variables “whereabouts before entry” and “stay after exit” to distinguish whether the patient was referred from or to a hospital, another health care provider, home or elsewhere. None considered the exact referral pathway between different hospitals of each patient.

This thesis provides an overview of a great part of the data available for health services research in Switzerland. The data can be used to monitor trends of identified deficits although I discovered several limitations that need to be addressed in the future.

Given the extent of the data and the numerous different institutions involved in the data collection, missing records or values are an issue. For example, 300 hospitals are deriving data for the hospital discharge statistics from their hospital information system. Delayed software updates can lead to incorrect data values as seen with the assignment of patients’ MedStat in some hospitals (Berlin et al., 2014). Furthermore, the coding quality between hospitals can differ in terms of the completeness and accuracy of diagnoses and treatments and this can affect the results of studies using data from multiple hospitals. Since cantons utilize the hospital discharge data statistics for their health care planning, correct data about places of residence and the number of treatments performed are essential.

Census, mortality registry, and health insurance data are routinely collected, as are hospital discharge and hospital statistics. Such data are not designed specifically for research purposes which can present challenges for those trying to do so. Performing observational studies with such data can introduce bias by mechanisms such as missing information. Having no exact place of death limits the interpretation of the relationship of distance to hospital and AMI and stroke mortality (Article 4). No information was available in the hospital discharge statistics about medication given to patients during their hospital stay. Again, this restricts the analysis of the adequate treatment of STEMI patients as information about fibrinolysis is not available in the data set (Article 2).

Another issue in the presented studies is the absence of data about disease prevalence in geographical units in Switzerland. Differences in the disease prevalence can have an impact on the observed regional variation in health care. Measuring such disease prevalence data would require a very cost- and time-intensive data collection process. The hospital discharge statistics provides an important part in the estimation of disease prevalence in Switzerland. Conducting diagnostic and treatment information also in the ambulatory setting could have been a major contribution to the estimation of disease prevalence.

Another challenge in conducting observational studies with these data is that information about health care utilization behaviour is not available. For example, it is difficult to distinguish whether it is lower access to care or the influence of the lower propensity of rural residents to seek care (Longman et al., 2011), or indeed both, that determines the higher rate of avoidable hospitalisations in rural areas.

Due to the lack of a unique identifier for every person living in Switzerland, deterministic and probabilistic linkage techniques were used to connect data sets of different sources (Articles 3 and 4). These techniques do not provide 100% congruency as unlinked or incorrect linked records will occur and the linkage proportions can vary among subgroups, which may affect the results of studies including those here.

In the hospital discharge statistics a so-called anonymous unique person identifier is used. Unfortunately, this person identifier does not identify persons uniquely. The patients first and last name, date of birth and gender is used to generate a unique Hash-code. However, an individual may be assigned more than one Hash-code if, for example, their family name changes. Additionally, I found disparities in age and gender for patients with the same person identifier indicating that the person identifier has been assigned to two or more different persons. The SFSO is aware of these weaknesses since the introduction of the hospital discharge statistics, but they rate it as a negligible problem.

3.3 Implications for policy and future research

3.3.1 Application of treatment guidelines

Similar to studies in other countries, I found differences in revascularization by age and gender. For health care professionals these results indicate that the treatment for older persons and women isn’t optimal and treatment guidelines, providing the best evidence-based knowledge so far, might not be applied properly in Switzerland. Unfortunately, due to major limitations of the data (Article 2) it is not possible to distinguish the reasons for these discovered differences in the treatment of STEMI patients.

It is known that female ACS patients present more frequently with atypical symptoms and with more pre-hospital delay than men (de-Miguel-Balsa et al., 2015; Steg et al., 2012). Also, elderly patients often present with atypical or mild symptoms, which can result in delayed or missed diagnosis of AMI. Both female and elderly patients have a higher risk of bleeding. Although they require special attention in acute diagnostic and in their treatment, the recommended treatment doesn't differ for men and women, and younger and older patients (Steg et al., 2012).

A high degree of awareness for AMI in women and elderly patients is of great importance and medical personnel in Switzerland need to be appropriately trained, with skills reinforced in refresher courses. Although the study presented in this thesis has limitations it still provides an opportunity to monitor the development of the application of treatment guidelines. Additional variables e.g. medical information would be desirable but might blow up and hamper the data collection process.

3.3.2 Missing factors influencing the costs at the end of life

Health care supply measures seem to not play a role in the variation of EOLC costs, whereas the linguistic region does seem to influence the costs of EOLC. The different linguistic regions in Switzerland offer a great opportunity to examine the influences of diverse cultures in one country. However, such huge variations in the cost of health care across Switzerland indicates large inequalities in provision and consumption of health care.

Although a large proportion of the factors influencing the regional variation of EOLC costs throughout Switzerland couldn't be explained in the study (Article 3), it was possible to map the variation and pinpoint the regions of low or high costs and hence potential under- or overuse of services in EOLC. Therefore, future research needs to address the quality of care and patient satisfaction because low costs do not necessarily indicate under-use and vice versa. If higher spending leads to better quality of care and patient satisfaction then this should be the benchmark for the other regions, and conversely.

3.3.3 Distance to hospital matters

The results of the analyses in article 4 show increasing risk of dying from AMI or stroke with distance from a central or university hospital. Unfortunately, major information on the circumstances of the death are missing in the study (e.g. admission to hospital, died on the way to hospital, died at place of onset), which limits the explanatory power of the study. This induces questions for further research e.g. to evaluate effectiveness and quality of the Swiss EMS by illustrating the emergency pathways of AMI or stroke patients, where the patient will be brought to (the nearest hospital or immediately to a stroke unit or catheter laboratory) to perform specialized treatment and how this affects patient outcomes (e.g. mortality).

Between 2002 and 2012, 65 acute hospitals have been closed down or merged, mainly due to economic reasons (O'Dea, 2014). Therefore, another interesting topic to examine would be the influence of hospital closures on medical emergencies such as life-threatening diseases or childbirth.

3.3.4 Supporting ambulatory care to reduce potentially avoidable hospitalisations

In the past decade, it has frequently been reported that Switzerland will face a lack of primary care physicians, mainly in rural and peripheral areas, in the near future (Forster, 2012; Kunz, 2015; Meier, 2014; Sbr, 2014). This thesis showed that a very high density of primary care physicians keeps the AH rates at a low level, whereas a low density of primary care physicians leads to increasing AH rates (Article 1). This would indicate that health policy should promote primary care physicians in deprived areas.

Interestingly, since 2002, Switzerland has established and enforced regulations that prevent physicians from opening an office based practice stating that there are currently too many physicians in Switzerland. Right now, just specialists are not allowed to open a practice, indicating that primary care physicians are needed. Although the government can limit the blockage regulation to certain regions they cannot force physicians to open or take over a practice in a specific deprived region (Brotschi, 2015).

In a report from the Swiss Federal Council regarding strategies to address the lack of physicians and to support primary care in Switzerland, the key recommendation was to train more physicians by increasing the number of university places for medicine, and to improve efficiency by introducing managed care models (Bundesrat, 2011). The core of managed care models is a consortium of primary care and specialized physicians that collaborates to take care of patients. The goals are: being a gatekeeper of the health care system, better coordination, and improvement of quality. The initiative to implement the managed care model was rejected by Swiss voters in the 2012 referendum. A survey showed that most people feared that this would result in the loss of their free choice of physicians (Ses/sda, 2012).

3.4 The data issue – opportunities and challenges in the future

3.4.1 New Research Program "Smarter Health Care"

With regard to the future challenges of the Swiss health care system, the Swiss National Science Foundation (SNSF) recently launched the National Research Program "Smarter Health Care", which aims to support innovative health services research that addresses concrete challenges of chronic disease care in Switzerland. Additionally, the program aims to outline the current weaknesses of Swiss health care data and to recommend targets to improve these data (SNSF, 2015). This thesis provides substantial information about a major component of the Swiss health care data (e.g.

hospital discharge statistics, hospital statistics, mortality registry, SNC, insurance data), its weaknesses and limitations as well as the future challenges and possible improvements for these data.

3.4.2 Available and missing data

The data presented in this thesis mainly contains information about hospital location or infrastructure, the density of primary care and specialized practices, and information on individual level from census, mortality registry and hospital discharge statistics. Nonetheless, inferring policy recommendations is limited because a major drawback of all analyses is the lack of a comprehensive ambulatory care data set that includes diagnoses and treatments on an individual level for all ambulant practices for the whole country. In the end of life care study, the attempt to include information on the patient's ambulatory utilization using insurance data was mostly limited to information about the generated costs before death (Article 3).

The lack of comprehensive ambulatory data is known (OECD/WHO, 2011) and also referred to it by the Swiss legislation (Huguenin, 2015). To fulfil the requirements of this legislation the SFSO is preparing the implementation of the statistics of ambulatory health care in Switzerland. Besides the characteristics of the ambulatory practices (e.g. number and profession of staff, infrastructure, range of services), information about the diagnoses or treatments on an individual level for patients being treated with ambulatory care in hospitals will be collected. An expansion of the data collection of individual patient records to all ambulatory primary and specialized care practices is planned for 2017 (SFSO, 2016).

The SFSO states that the private, economical characteristic of the ambulatory sector and the large number of institutions involved will influence the response rate of the ambulatory care data collection. Of note, the Swiss Medical Association, representing physicians, is concerned that the data collection will affect the confidentiality of patients' information and does not apply the data protection regulations properly (Mw/sda, 2012). Thus, similar to the hospital discharge statistics, it might take several years until all ambulatory health care providers will contribute their data.

The SFSO is about to set the variables for collection for the ambulatory health care database using variables from the hospital discharge dataset, such as the person identifier and MedStat, which indicate the place of residence of the patient and the location of the practice. The use of the same method to create the personal identifier across the two databases will enable the linkage of the ambulatory and inpatient data. In this thesis it was shown that these two variables (personal identifier and MedStat) are prone to mistakes. Before the implementation of the new statistics, the

SFSO should consider ways to improve the construction of the personal identifier and the assignment of MedStat regions.

The introduction of the ambulatory care statistics will be the key element to connect ambulatory and inpatient data. For the first time it will be possible to map the pathways of each patient between the ambulatory and inpatient sectors and the pathways between Swiss health care providers.

These linked data sets will enable researchers to study whether avoidable hospitalisations received appropriate care by primary care or specialized care physicians prior to their hospitalisation. This then can be used to validate the application of the OECD avoidable hospitalisation criteria in Switzerland.

3.4.3 Implementation of SwissDRG

Three of the four articles in this thesis utilized routinely collected data on hospital discharges, which were derived from hospital information systems before the implementation of Swiss Diagnosis Related Groups (SwissDRG) in Switzerland at 1st January, 2012. SwissDRG is a tariff system which is used for the reimbursement of inpatient hospital services on the basis of case-based lump sum payments. Prior to 2012, only a few of the 26 cantons were using APDRG, a precursor to the SwissDRG. From 2012 onwards, all hospitals have been obligated to use Swiss-DRG for reimbursement. Several factors contribute to the assignment of a SwissDRG. Namely, the main diagnosis, secondary diagnoses, CHOP codes, severity of the condition, age, gender, length of stay, etc. The aim of the implementation of the SwissDRG is to support transparency and comparability between the hospitals in order to increase efficiency (SwissDRG AG, 2016).

It is expected that hospitals now apply the coding guidelines more carefully than before the implementation of the SwissDRG, since the completeness of the records determine the SwissDRG and consequently the reimbursement. This process should also improve the data quality of the hospital discharge statistics. However, critics are concerned that the introduction of the SwissDRG will cause conflicts between commitment to the patient’s well-being and the economic interests of the hospital (Fässler et al., 2015). Furthermore, the new reimbursement system might lead to misuse by the hospitals by modifying the patients’ condition and treatment codes in order to declare a SwissDRG that results in a higher reimbursement. On the other hand, there is criticism that certain procedures are not appropriately reimbursed by the SwissDRG system (Mehra et al., 2015).

There are some studies investigating possible differences in the length of stay, patient care, outcome and satisfaction both before and after the introduction of SwissDRG (Fässler et al., 2015; Stauber et al., 2014; Thommen et al., 2014). This is an interesting field that needs further investigation. The Swiss Public Health Department has initiated the evaluation of the introduction of the SwissDRG. This involves the examination of changes in quality of inpatient services and the definition of indicators to evaluate the quality. But first of all it has to be proven that the hospital discharge statistics can be used to examine the quality of inpatient services as this data set is the basis of these planned examinations (Swiss Public Health Department, 2016).

This thesis shows that a major limitation of the pre-SwissDRG hospital discharge data is the poor quality of the comorbidities and treatment codes. A comparison of hospital discharge data before and after the introduction should be performed with caution.

Insurance claims for inpatient care didn't include detailed diagnostic or treatment information before the introduction of the SwissDRG. Now, the invoices include the SwissDRG, which can be used to derive the main ICD-10 codes and CHOP codes that lead to this specific SwissDRG. In contrast to the hospital discharge data, the invoice includes the effective costs.

3.4.4 Future research with the available data

The linkage of the hospital discharge and the hospital statistics data sets will be more difficult in the future. While I received two separate data sets and then merged these using the hospital-ID, this won't be possible in the future. Furthermore, not all variables will be available with the same level of detail in the future, since the SFSO is tightening up their data protection. This will hinder the performance of small area analysis and the continuation or replication of the 3 studies from this thesis that based their analysis on these data sets. Several projects of the new National Research Program "Smarter Health Care" will be faced with these difficulties, which will hopefully have an impact on health policy stakeholders to improve data availability.

3.5 Conclusion

The aim of this thesis was to provide a contribution to CVD epidemiology and HSR in Switzerland. The four articles presented addressed different research questions and utilized a wide range of methods and data, reflecting the multidisciplinary field of health services research.

I showed that lower rates of all AH were found in areas with a very high supply of primary care physicians, and increased AH rates in areas with more specialists and in areas with a higher proportion of rural residents.

The study looking into the adequacy of STEMI treatment found that females and older patients were less likely to receive revascularization. This suggests treatment guidelines may not be uniformly applied across Switzerland.

Cause of death and age are strongly associated with cost of end of life care. Place of residence and, in particular, the linguistic region had a significant influence on costs. No effect was found for health care supply measures.

Risk of dying from AMI increased with distance from a central or university hospital for both younger persons and older persons over the age of 65 years in the Swiss National Cohort. For stroke mortality, though, a significant association with distance to the same hospitals was observed only in those 65 years of age and older.

The major data sources of all studies were administrative data, which was not collected for these research purposes. This thesis described the challenges and limitations of the data sources used.

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DECLARATION OF ORIGINALITY

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I hereby declare that this thesis represents my original work and that I have used no other sources except as noted by citations.

All data, tables, figures and text citations which have been reproduced from any other source, including the internet, have been explicitly acknowledged as such.

I am aware that in case of non-compliance, the Senate is entitled to withdraw the doctorate degree awarded to me on the basis of the presented thesis, in accordance with the „Statut der Universität Bern (Universitätsstatut; UniSt)“, Art. 69, of 17 December 2011.

Place, date

Bern, 29.02.2016

Signature