Regional Variation and Influencing Factors in the Utilization of Diverse Healthcare Services: a Comprehensive Analysis Approach

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Abstract

The ubiquity and persistence of regional variation in healthcare utilization have been studied and widely documented in the last decades, and raise increasing attention and concerns from health services researchers, healthcare professionals as well as health policymakers. The observed regional variation may to a substantial extent reflect suboptimal healthcare use due to unequal access to care, which could result in detrimental consequences to the quality, equity, and efficiency of healthcare. Regional variation in healthcare utilization could be driven by multiple factors, including individual's socio-demographic and clinical characteristics, physician/facility availability, as well as healthcare system-related factors. Among the potential drivers, the systematic ones (e.g. health insurance-related factors) should be particularly focused on, because they offer the most potential for widespread improvement. Changing the laws, initiation of national programs, or adjusting insurance schemes are big levers to reduce variation on a national level.

Existing studies on regional variation analysis of healthcare utilization mainly focused on detecting the existence and evaluating the degree of regional variation in healthcare utilization, and they had several limitations. First, numerous analyses were focusing on only one region of a country, without nationwide coverage. Second, the selection of studied healthcare services was often arbitrary and opportunity driven. Third, the potential causes and drivers of variation were rarely explored. The majority of studies used conventional small area variation analysis (SAVA), and only a few studies controlled for a limited number of possible influencing factors. Finally, most studies investigated only one healthcare service, or one category of similar services, without comparison across diverse services to explore the potential common patterns. The evidence is stronger if influencing factors show consistent effects across multiple healthcare services.

This thesis addresses the above-mentioned problems as much as possible. The overall aim was to assess regional variation and potential influencing factors, especially health insurance-related factors, of the utilization of diverse healthcare services with Swiss claims data, using a comprehensive analysis approach developed based on the existing methods. The thesis consists of three articles: in the first one preoperative chest radiography was used as a test case to develop the analysis approach based on the existing methods of healthcare regional variation analysis including small area variation analysis, multilevel regression analysis, and spatial autocorrelation analysis. In the second article I applied the approach to four management measures strongly recommended for diabetes patients. Besides, multilevel regression modelling

was extended by taking spatial autocorrelation into consideration, as an additional exploration for evaluating spatial clustering patterns in healthcare utilization. In the third article I applied the comprehensive approach to 24 healthcare services, and summarized and compared findings across all these services. Regional variation after controlling for multiple influencing factors was generally small among all selected services. The most interesting finding was the substantial and consistent effects of health insurance-related factors among most services. A higher annual deductible level was mostly associated with lower utilization. Supplementary insurance, supplementary hospital insurance, and having chosen a managed care model were associated with higher utilization of most services. Managed care models showed a tendency towards more recommended care.

The findings implied that it could be a potential way to improve healthcare utilization through adjustment of insurance scheme design, which may further benefit the quality, equity, and efficiency of the healthcare system, and may also inform health policy formulation. The comprehensive approach aids in the identification of regional variation and influencing factors of healthcare services use in Switzerland as well as comparable settings worldwide. Built on the current study findings, further research could focus on exploring potential spatial clustering patterns in the utilization across multiple healthcare services, and identifying specific regions with generally superior or inferior performance regarding healthcare utilization.

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Chapter I

Introduction

Regional variation in healthcare utilization

Importance and relevance of regional variation analysis

The ubiquity and persistence of variation in healthcare utilization across geographic regions has raised awareness and concerns from healthcare professionals, health services researchers, and policymakers since decades ago, and are receiving more and more attention nowadays. Regional variation in healthcare utilization potentially caused by unequal access to care or various clinical practice styles raises concerns regarding the equity, quality, and efficiency of the healthcare system, and may result in detrimental consequences in both health outcomes and healthcare expenditures [1]. From a health policy perspective and concerning the healthcare system performance, it is fundamental to detect the existence and evaluate the degree of regional variation, and more importantly, to investigate potential drivers of regional variation in healthcare utilization, that is, to find out if regional variation is justified by the underlying medical need, or if it is a sign of misallocation of healthcare resources or inappropriate healthcare use such as over- and underuse [2]. Therefore, research on regional variation in healthcare utilization is of great significance, and it helps identify potential influencing factors and problematic regions, and could further provide insights to health policymaking and targeted intervention programs [3].

Documented large regional variation

Considerable regional variations in the utilization of healthcare services has been studied and widely documented by researchers worldwide. As one of the leading pioneers, John Wennberg and the Dartmouth Institute has done a lot of conceptual and methodological work on research of variation in healthcare utilization [4-7]. The *Dartmouth Atlas of Health Care Project* [8], which was led by John Wennberg and launched more than 20 years ago, has documented glaring variation across the US regions in the utilization of different types of healthcare services, such as surgical procedures, post-acute care, end of life care, etc. [9-11]. Influenced by the *Dartmouth Atlas of Health Care*, researchers and policymakers across the globe have recognized the importance of regional variation in healthcare utilization, and several countries and regions have also created their own atlases of healthcare, including Canada [12], Australia [13], England [14], Norway [15], Spain [16], Switzerland [17], and the European Collaborative [18].

Large and potentially inappropriate regional variation in preventive interventions, screening and diagnostic tests, pharmaceutical prescriptions, and surgical procedures has been described all over the world [3, 19]. Variation in influenza vaccination was as high as 15-fold across regions in Michigan as observed in a study from the US [20]. A study reported a three-fold difference in mammography for breast cancer screening across multiple countries from Europe, Asia, and North America [21]; another study from Canada reported a 50-fold difference in MRI scans for breast cancer pre-diagnosis across Ontario [22]. Research on surgical procedures mainly focused on elective procedures. After adjusting for socio-demographic, hospital, and distance variables, regional variation in elective primary hip and knee replacement was almost three-fold in the UK [23]; another study from Korea showed a four-fold regional variation in knee arthroplasty [24]. Two studies on caesarean section reported considerable regional variation in a few European countries and the US [25, 26]. For Switzerland, a large degree of variation in the use of hysterectomy has been reported as early as 1988 [27]. Marked regional variation in healthcare utilization between the German- and French-speaking parts of Switzerland has been noted, for example, in the prescription of antibiotics [28]. Swiss studies also observed regional variation in avoidable hospitalizations and end-of-life care for cancer patients [29, 30].

Warranted and unwarranted regional variation

Part of the observed variation in healthcare utilization across regions could be justified by patient needs or preferences, and it is defined as warranted variation. However, it has been suggested that regional variation reported in studies was too large to be simply explained by variation in the actual care needs of different populations [31]. Therefore, the ubiquitous and large regional variation may to a substantial extent reflect inappropriate healthcare use, which may be over- or underuse. The term of unwarranted variation was coined by John Wennberg, and was defined as the regional variation in healthcare utilization that is not due to patient needs or preferences [32]. Unwarranted variation reveals three areas: overuse of healthcare such that more harm than good is done; underuse of healthcare such that cost-effective services are not performed sufficiently; inequity of healthcare such that services are not accessible to parts of the population, possibly because of their social background.

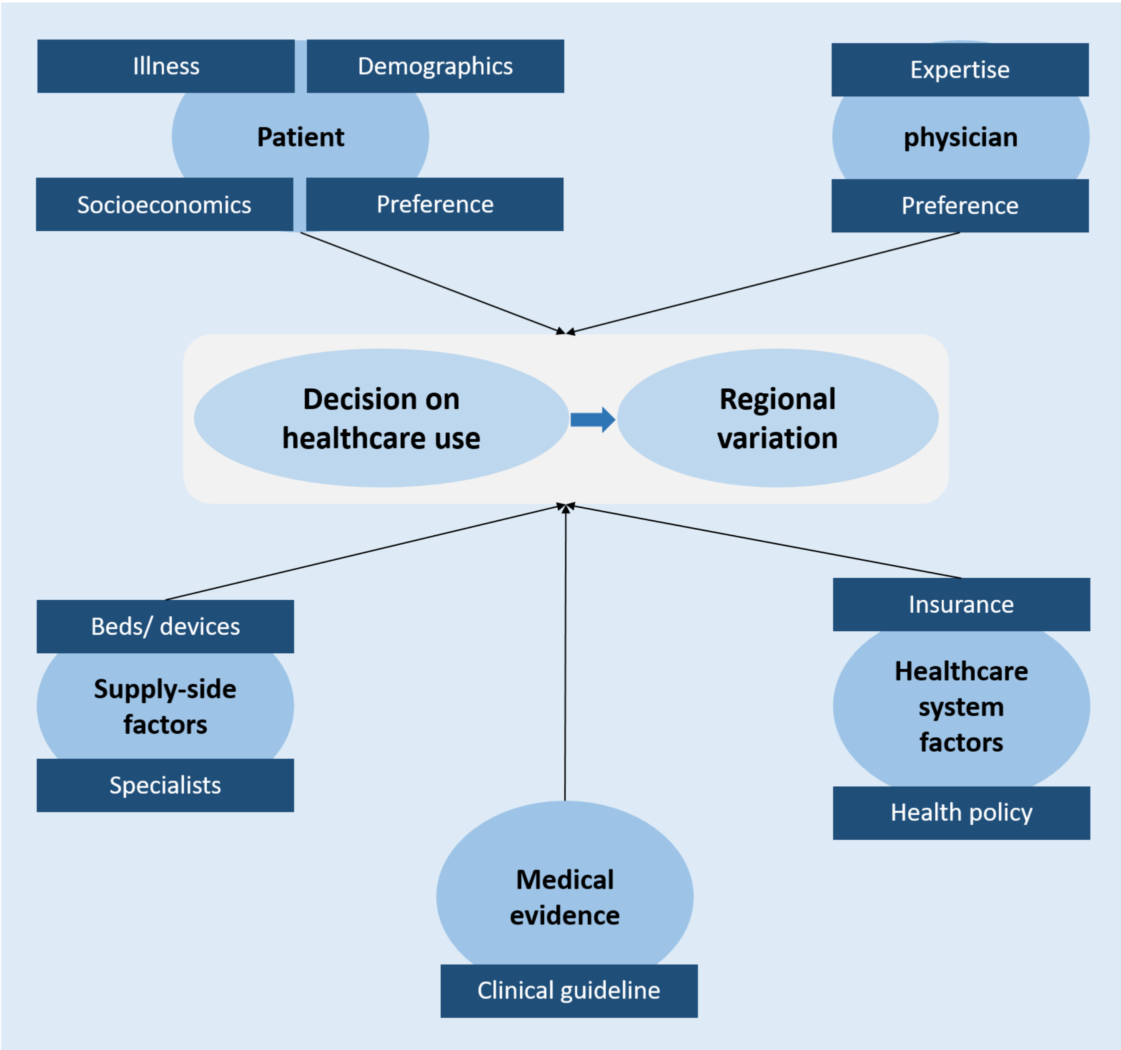
John Wennberg and colleagues have proposed three categories of healthcare services of which the causes and remedies of unwarranted variation may differ [33]. Effective care is the services that are based on sound medical evidence, and their benefits far exceed the harms, therefore they should be received by all eligible patients. Theoretically, utilization rates should be close to 100%, and the common problem is underuse. Effective care is normally recommended in clinical guidelines with high-level evidence and class I recommendation (namely there is evidence and/or general agreement that a given treatment or procedure is beneficial, useful, and effective). For example, two crucial diabetes management measures - biannual glycated haemoglobin testing and annual eye examination are strongly recommended to all patients with diabetes by both Swiss and international guidelines [34-36]. The second type is preference-sensitive care, or elective care, for which there are multiple options of healthcare services to the same condition, and the decision largely depends on patient preferences. However, the decision is practically determined by physician opinion (or physician judgement) rather than patient preferences. John Wennberg called for a change in the physician-patient relationship to enhance the role of patient and support more informed patient choice [32]. For example, whether having caesarean section or vaginal delivery is normally a shared decision between the patient and the physician when there is no absolute indication for caesarean section. The third type is supply-sensitive care, which is not about a certain healthcare service per se, but the frequency of healthcare that is used routinely to treat patients. Examples of such care include physician visits, hospital admissions, intensive care unit admission, imaging exams. Local capacity and availability of specialists or facilities drive the use [32].

Although the categorization of healthcare services provides an analytical framework for understanding and investigating healthcare variation, it is not straightforward to determine the category of a specific healthcare service and on many occasions the three categories are not mutually exclusive. For instance, influenza vaccination is recommended to all elderly (>65) people and patients with certain chronic conditions [37]. However, the decision to get vaccinated depends on the patient’s preferences to a large extent. Another example is imaging services for disease diagnosis with well-proven effectiveness, but the decision on the utilization could be largely influenced by the local resource capacity of imaging equipment.

Influencing factors of regional variation

To minimize unwarranted variation in healthcare utilization across regions, it is vital to explore and understand potential influencing factors. Regional variation in healthcare utilization may be driven by multiple factors, including patient socio-demographics, clinical characteristics, physician- and facility-related factors, as well as healthcare system-related factors. They can function as personal, financial, and organizational modifiers of access to care [38]. Figure 1 presents the mapping of potential influencing factors for regional variation in healthcare utilization, based on a more comprehensive graphical overview of potentially relevant influences in the UK by Appleby et al. [31].

Figure 1. Influencing factor of regional variation in healthcare utilization.



Patient-related factors

Patients' demographic, socioeconomic, and clinical characteristics have been found to be associated with regional variation in healthcare utilization. A German study found that social variables such as gender and mother language of parents had an impact on variation in child vaccination rates across different school districts [39]. Studies also reported that regional variation in healthcare utilization could also be explained by age, comorbidity index, socioeconomic status, education, and urban-rural resident location [40-42]. A review on the utilization of common surgical procedures reported that the involvement of patient preferences into treatment decisions could result in regional variation [43].

Provider-related factors

Not many studies have investigated the influence of physicians' characteristics on regional variation in healthcare utilization, such as their awareness and preferences on clinical practice guidelines. One study found that physician beliefs about the surgery indications could influence the utilization and regional variation in the utilization of surgical procedures [43]. Besides, the local healthcare resources and accessibility [44, 45], and lack of or poor adherence to guidelines [46] are also important drivers of regional variation.

Healthcare system-related factors: the Swiss setting

Healthcare system-related factors including health insurance schemes, health policies, and national legislation or programs are of great importance, because their modification may offer big levers to reduce unwarranted variation at a national level. However, very few studies have investigated their effects on regional variation in healthcare utilization. Most of the available studies which were mainly conducted in the US only concluded that the uninsured patients had lower healthcare utilization compared to the insured patients or patients with private insurance [47, 48].

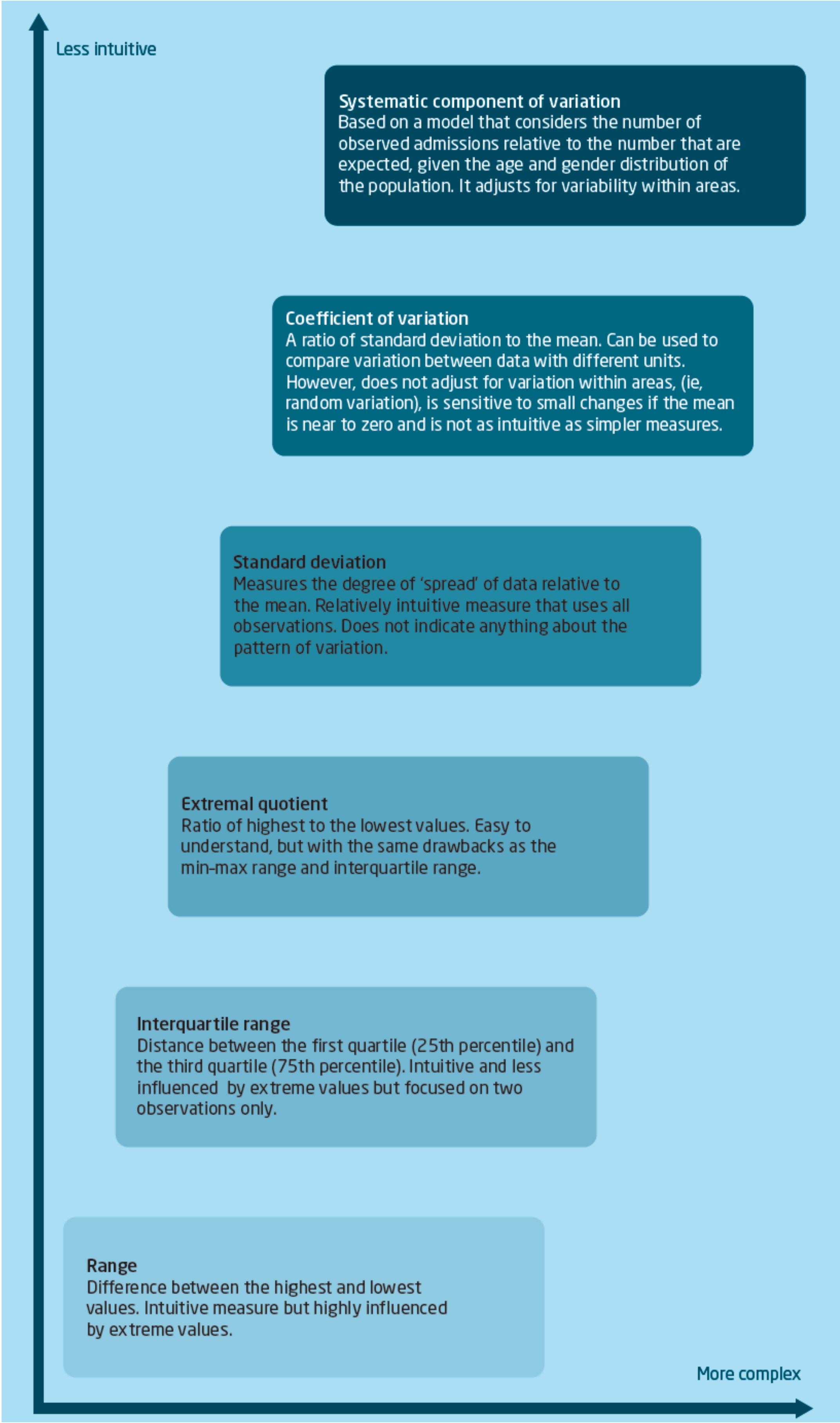
Switzerland has a system with universal care access and high out-of-pocket expenditures. Although no free healthcare services are provided by the state, basic health insurance from one of the private insurers is compulsory for all residents in Switzerland. While non-insurance does practically not occur in Switzerland, foregoing healthcare due to out-of-pocket payments is a well-documented phenomenon [49]. However, part of the cost of the services received is paid by the patient insured, which is done by means of an annual deductible ranging from 300 to 2500 Swiss francs. Insurance companies offer the standard basic insurance model (with free choice of physicians) and alternative insurance models (i.e. managed care models) including 1) the Health Maintenance Organisation (HMO) model, under which the patient has to always first consult a specific HMO centre in the event of illness; 2) family doctor model, under which the patient has to first contact his or her family doctor in the event of illness; 3) Telemedicine model, under which the patient has to call a telephone service and get a referral to a doctor or hospital; and other models [50]. People choosing managed care models benefit from premium reductions of up to 25 percent on basic health insurance compared to the standard model. In addition to the basic health insurance, people are also provided with various options of supplementary insurance such as dental insurance, and supplementary hospital insurance which allows for hospitalization in semiprivate or private wards. The benefit package in the basic mandatory health insurance is the same for everybody, defined by federal law, which makes Switzerland an interesting case for studying other effects.

Methods of regional variation analysis

Small area variation analysis

Analysis of variation in healthcare utilization across regions or healthcare providers has led to the development of small area variation analysis (SAVA) since the 1980s. SAVA is a very popular methodology in health services research to describe how healthcare utilization rates vary across well-defined small geographic regions [51]. In addition to the simple descriptive statistics normally used in SAVA including range, interquartile range (IQR), extremal quotient (EQ), standard deviation (SD), and coefficient of variation (CV), a complicated and much more reliable measure has been developed - systematic component of variation (SCV). Compared to the simple descriptive statistics, one of the key advantages of SCV is that it facilitates comparison of utilization rates between geographic units of different population size and for interventions of different frequency, by removing the random component of variation, [52, 53]. SCV has been demonstrated to perform generally well in the identification and quantification of variation beyond chance, and could be used to compare the variability of different healthcare services [54, 55]. The Empirical Bayes statistic represents a relevant alternative, and non-parametric bootstrapping techniques have been recommended for confidence interval estimation [55]. Age- and gender differences between populations of different geographic units are taken into account in the calculation of SCV, based on standardization techniques [31, 52]. SCV has become one of the most widely used measure when describing regional variation in healthcare utilization, and has been applied in numerous studies [31, 43, 56]. The complexity and reliability of the commonly used SAVA measures are shown in Figure 2 [31].

Figure 2. Measures in small area variation analysis [31]



Multilevel regression analysis and further potentials

In spite of the good performance of SCV, it lacks the multivariable adjustment for other possible influencing factors except for age and sex. Multilevel regression analysis could serve as an alternative that allows for exploring the effects of multiple influencing factors on regional variation at different levels (e.g. patient, healthcare provider, and geographic unit). The potential role of multilevel regression analysis in health services research and specifically in the analysis of regional variation has been mentioned previously [57], and a number of studies have pursued approaches of this type [58-60], including a recent Swiss study applying multilevel approach to regional variation analysis in vertebroplasty and kyphoplasty [61].

The potential of this approach can be further developed, e.g. calculating median odds ratio (MOR) and variance partition coefficients (VPCs) based on the random effect from multilevel models to assess the degree of between-region variation after controlling for multiple influencing factors [62]. They could be compared among diverse healthcare services as the SAVA measures.

Another aspect in the analysis of regional variation in healthcare utilization is the possibility of spatial autocorrelation between geographic units due to spill-over effect or unmeasured confounders [63], which could be detected by calculating Moran’s I statistic [64]. If substantial autocorrelation is detected, it should be taken into account in analysis to avoid incorrect parameter and standard error estimates, which is possible using specific extensions to regression techniques (e.g. spatial lag models, spatial error models) [63], or the Bayesian statistical models such as the Integrated Nested Laplace Approximations (INLA) approach [65-68].

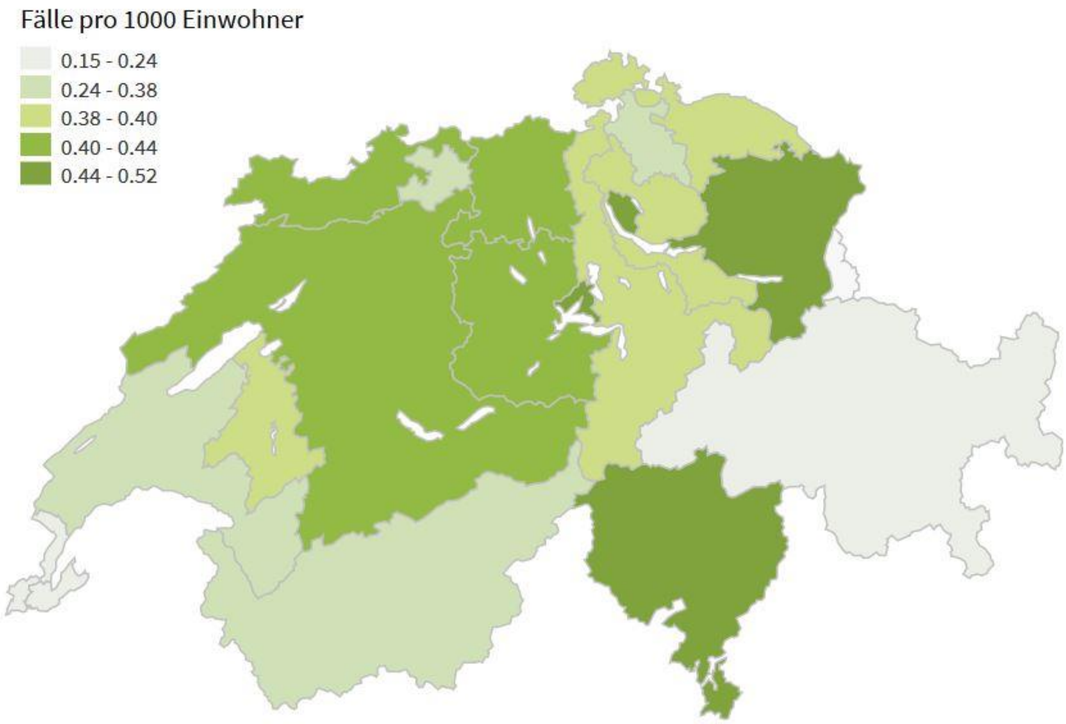
Major concerns of previous studies

Although there were a large number of studies on the topic of regional variation in healthcare utilization, they share a few common problematic issues.

Definition of Region units and coverage

A systematic review of variation in healthcare utilization in OECD countries reported that only about half of studies covered an entire country, and the rest only focused on a part of a country such as provinces, cities, and counties [3]. Without nationwide coverage, the benefit from the study findings could be limited in terms of understanding and reducing unwarranted variation efficiently at a national level. The unit in regional variation analysis ranged from provinces, municipalities, to specific areas such as health services areas, or hospital referral regions. Using relatively large areas as analysis unit, e.g. states in the US, could potentially mask true variation across small regions. This is also the case in Switzerland where 26 cantons or canton-like regions have been used as the unit of regional variation analysis in most studies. The sizes of cantons are extremely uneven, and the potential imbalanced performance within some big cantons have not been explored. For example, the map of coronary bypass surgery rates in Switzerland from the Swiss atlas project is shown in Figure 3 [17]. The sizes of regions vary remarkably, and variation in the utilization of coronary bypass surgery within large regions was not revealed.

Figure 3. Utilization rates of coronary bypass surgery in Switzerland [17]



Selection of healthcare services

The selection of studied services has often been arbitrary and opportunity driven. The majority of existing studies have concentrated on high-impact clinical conditions and common healthcare services, and many other conditions were much less often studied. The most frequently studied clinical conditions were cancer and cardiovascular diseases such as breast and colorectal cancer, acute myocardial infarction (AMI), and stroke. [3]. The corresponding healthcare services ranged from physician visits, screening services, drug prescriptions to surgical procedures, with more than 60% of studies focusing on the use of hospitals such as hospital (re)admissions [3].

Insufficient research on influencing factors

Despite an overwhelming number of studies assessing regional variation in healthcare utilization, the effects of possible influencing factors were rarely studied. Adjustment for multiple factors has not been described for small area variation analysis, which is still the mainstream research tool for regional variation analysis in healthcare utilization. Although multilevel regression analysis provides another possibility for healthcare variation analysis, and especially for the exploration of potential influencing factors, only a limited number of factors have been controlled for in a few studies, mainly focusing on patients' socio-demographic and clinical characteristics [61, 69, 70]. A thorough investigation of other healthcare system factors, especially health insurance-related factors, is still missing.

Lack of cross-services comparison

Most studies have assessed regional variation in the utilization of a single healthcare service, and a few studies covering multiple services only focused on one category of related services, for example, similar surgical procedures [52, 61]. Studies simultaneously exploring and comparing regional variation and influencing factors of a variety of healthcare services are currently missing. Systematic component of variation (SCV) in small area variation analysis has been applied for comparison of regional variation (controlled for only age and sex) between different healthcare services [31, 43, 52]. However, the effects of potential influencing factors and the degree of regional variation after adjusting for multiple factors across diverse healthcare services have not been paid much attention to. Evaluating and comparing the effects of influencing factors, especially health insurance-related factors, on regional variation in the utilization across multiple services is in particular important. If consistent effects among diverse services could be observed, the findings may offer valuable insights to help improve insurance design and the healthcare system performance.

Limitations introduced by data availability

Nearly half of existing studies on healthcare variation analysis used health administrative data routinely collected mainly for billing purposes, other common data sources included registry data and survey data [3]. The use of health insurance claims data or similar administrative data for health services research and variation analysis in healthcare utilization has a longstanding tradition in the US [71-73] and is gaining in importance in other countries. In Switzerland, insurance claims data has been used in related studies, such as cantonal variation in preoperative chest X-ray utilization [74], regional variation of end-of-life care [30], and variation in healthcare expenditure [75]. Use of claims data has certain strengths, for example, it is convenient and timesaving to perform data collection and management; claims data usually has relatively good coverage of entire country and population, making it possible to conduct nationwide variation analysis; It also contains detailed information with regard to individual health insurance characteristics, which allows analysis particularly focusing on the effects of insurance-related factors. One of the key disadvantages of Swiss claims data is the lack of reliable information on diagnosis information for outpatient healthcare services. However, the resulting possibility of misclassification of patient identification and services utilization could be to some extent compensated for by evaluating the information on drug use, outpatient service codes, and hospitalizations.

Justification and aims of the thesis

This thesis is part of the National Research Programme "Smarter Health Care" (NRP74) project No. 26 titled “How do guidelines and recommendations influence medical treatment?”, funded by the Swiss National Science Foundation (SNSF). The project consisted of three parts: Part 1. selection of healthcare services and assessment of clinical recommendation status; Part 2. study of geographic variation and influencing factors for the utilization of those selected services; Part 3. assessment of clinical and economic outcomes. The main data used in this project is health insurance claims data from one of the biggest health insurance companies in Switzerland. The present thesis mainly focused on part 2 of this NRP74 project, namely to estimate regional variation in healthcare utilization and to explore influencing factors.

Given the potential important implications that could benefit the healthcare system, and the major issues in current studies on regional variation in healthcare utilization described above, additional research is highly needed to remedy these limitations. Therefore, the present thesis tried to address these issues as much as possible from different perspectives.

The overall aim of this thesis was to assess regional variation in and potential influencing factors for the utilization of diverse healthcare services with Swiss claims data, using a comprehensive analysis approach. More specifically, I tried to first, develop a comprehensive analysis approach combining small area variation analysis, and other techniques with great potential in variation analysis including multilevel regression analysis and spatial autocorrelation analysis. Second, study on healthcare services selected through a systematic approach taking many aspects into consideration, including clinical and fiscal importance, policy relevance, public awareness, healthcare types, current medical evidence/ clinical recommendations, etc. The services selection is not directly a main part of the present thesis, and it was done within part 1 of the overall NRP74 project. Third, assess regional variation in healthcare utilization across the whole of Switzerland using smaller regions instead of cantons as region units of analysis. Fourth, investigate in detail the effects of health insurance-related factors on regional variation, which could provide a potential way of optimizing healthcare utilization and reducing unwarranted variation. At last, focus on the summary and comparison of results from diverse healthcare services to try to find out potential common patterns.

Thesis outline

Chapter II describes regional variation in the utilization of preoperative chest radiography, which was used as a test case to develop a comprehensive analysis approach for regional variation analysis on healthcare utilization based on the existing methods. It combines small area variation analysis, spatial autocorrelation analysis, and multilevel regression analysis with the computation of median odds ratio (MOR) and 80% interval odds ratio (IOR-80) (first article).

Chapter III describes the application of the developed approach to the utilization of four strongly recommended diabetes management measures. Multilevel regression analysis in this study has been additionally extended with the Bayesian statistical model which enables correcting for spatial autocorrelation and evaluating spatial clustering patterns in healthcare utilization (second article).

Chapter IV compares and summarizes the degree of regional variation and the effects of potential influencing factors on the utilization of 24 healthcare services of interest, and highlights the consistent effects of health insurance-related factors across diverse services (third article).

Chapter V summarizes the main findings of the three chapters and discusses the contribution to health services research, more specifically to the analysis of regional variation in healthcare utilization, and the significance of the findings in providing important implications to the healthcare system.

First article

Variation of preoperative chest radiography utilization in Switzerland and its influencing factors: a multilevel study with claims data.

Wenjia Wei, Oliver Gruebner, Viktor von Wyl, Beat Brüngger, Holger Dressel, Agne Ulyte, Eva Blozik, Caroline Bähler, Matthias Schwenkglenks

Published in *Scientific reports*

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Second article

Exploring geographic variation of and influencing factors for utilization of four diabetes management measures in Swiss population using claims data.

Wenjia Wei, Oliver Gruebner, Viktor von Wyl, Holger Dressel, Agne Ulyte, Beat Brüngger, Eva Blozik, Caroline Bähler, Julia Braun, Matthias Schwenkglenks

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Third article

Regional variation and effects of health insurance-related factors on the utilization of 24 diverse healthcare services.

Wenjia Wei, Agne Ulyte, Oliver Gruebner, Viktor von Wyl, Holger Dressel, Beat Brüngger, Eva Blozik, Caroline Bähler, Julia Braun, Matthias Schwenkglenks

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Chapter II

Variation of preoperative chest radiography utilization in Switzerland and its influencing factors: a multilevel study with claims data

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Abstract

Clinical recommendations discourage routine use of preoperative chest radiography (POCR). However, there remains much uncertainty about its utilization, especially variation across small areas. We aimed to assess the variation of POCR use across small regions, and to explore its influencing factors.

Patients undergoing inpatient surgery during 2013 to 2015 were identified from insurance claims data. Possible influencing factors of POCR included socio-demographics, health insurance choices, and clinical characteristics. We performed multilevel modelling with region and hospital as random effects. We calculated 80% interval odds ratios (IOR-80) to describe the effect of hospital type, and median odds ratios (MOR) to assess the degree of higher level variation. Utilization rates of POCR varied from 2.5% to 44.4% across regions. Higher age, intrathoracic pathology, and multi-morbidity were positively associated with the use of POCR. Female gender, choice of high franchise and supplementary hospital insurance showed a negative association. MOR was 1.25 and 1.69 for region and hospital levels, respectively. IOR-80s for hospital type were wide and covered the value of one.

We observed substantial variation of POCR utilization across small regions in Switzerland. Even after controlling for multiple factors, variation across small regions and hospitals remained. Underlying mechanisms need to be studied further.

Introduction

Preoperative chest radiography (POCR) is an example of a frequently overused healthcare service, discouraged by international clinical practice guidelines [1]. The Choosing Wisely initiative [2] launched in the US called for more caution in the use of POCR for asymptomatic patients due to its potential uselessness, harm and cost [3]. POCR has been shown to have negligible influence on subsequent patient management as well as clinical outcomes, and to result in significant costs [4-7]. A Swiss version of the Choosing wisely – “Smarter Medicine” initiative was launched by the Society for General Internal Medicine (SGAIM) in May 2014 [8]. Avoidance of POCR for asymptomatic patients is among the top five recommendations published by the SGAIM in May 2016 addressing the overuse of healthcare services [9].

A recent study by Blozik et al. investigated the degree and geographic distribution of POCR utilization in Switzerland across large geographic units. Excessive use of POCR was undetectable in that study, but it demonstrated significant variation in the utilization rates (6% - 28%) at the cantonal level [10]. However, differences between smaller geographic regions were not explored. Summary measures such as national or cantonal POCR utilization rates may mask local trends and true distribution patterns. In Switzerland, there have been no cantonal policy or regulation regarding POCR which might be the driver of utilization variation, and we assume there could be significant within canton variation of POCR use in small regions. Analysis of variation of healthcare utilization in smaller geographic areas has considerable potential to support the planning and delivery of healthcare, through offering valuable insights to health professionals, health policymakers and the general public [11, 12].

Different factors (patient, provider, and region-specific characteristics) may affect POCR utilization, which has not been fully explored to date. One study on preoperative testing before low-risk surgical procedures in Canada showed that POCR utilization was associated with age, preoperative anaesthesia consultation, preoperative medical consultation and healthcare institution [13]. However, the authors did not take the potential impact of health insurance characteristics or patients’ residence into consideration.

The utilization of this potentially avoidable procedure across small areas in Switzerland remains uncertain. Building on the work by Blozik et al. [10], which provided the first overview of POCR utilization in Switzerland, we proceeded to an explicit small area analysis of POCR utilization and variation. The aim of our study was to assess the variation of POCR utilization across 106 Spatial Mobility regions (MS regions), and to investigate the patient, hospital and regional factors potentially influencing POCR utilization and variation in Switzerland.

Material and methods

Study population

We studied patients who received Swiss mandatory health insurance (Obligatorische Krankenpflegeversicherung, OKP) from the Helsana Group. Helsana is one of the largest health insurance companies in Switzerland, and the Helsana database underlying this study included mandatory health insurance claims from approximately 1.2 million people per year, covering about 15% of the whole Swiss population. The study population was patients enrolled with Helsana who were older than 18 years and underwent non-emergency inpatient surgery from 2013 to 2015. We excluded patients with incomplete coverage of mandatory health insurance during 2013 and 2014, asylum seekers, patients living outside Switzerland, Helsana employees, patients with incomplete address information, patients living in nursing homes with lump-sum reimbursement of medication, and emergency inpatient stays. Only the first hospitalization per person during the study period was considered. The data used in the present study was the same as that in the study by Blozik et al. [10].

Basic health insurance bought from a private market of health insurance companies is mandatory for all Swiss residents. The insurance companies are obliged to offer mandatory health insurance at the same price to everyone regardless of their health status. Premiums are lower for children and young adults, and they differ between geographic regions. All appropriate and cost-effective inpatient or outpatient medical treatments are covered by mandatory health insurance. Supplementary hospital insurance is optional and allows for hospitalization in a semiprivate or private ward and treatment in another canton [14]. Enrolees can choose between various annual deductible costs (i.e., a "franchise") ranging from 300 to 2,500 Swiss Francs. The higher the franchise chosen, the lower the premium to pay. There are managed care and standard fee-for-service models of mandatory health insurance. Insured people selecting managed care models have to first consult a specific type of healthcare provider (i.e., a group practice, a defined family doctor, or a telemedicine centre). [14, 15] Thus insured people with managed care models pay fewer premiums compared to standard model users while they use the same fee-for-service tariff.

The study data provided by Helsana were anonymized. According to the national ethical and legal regulations, ethical approval was not needed for this type of analysis. This was confirmed by a waiver of the competent ethics committee (Kantonale Ethikkommission Zürich, waiver dated 11th January 2017).

Outcome and explanatory variables

The outcome variable was the performance of ambulatory chest radiography within two months before any inpatient surgery [16]. Inpatient surgeries were derived from the Swiss Diagnosis Related Groups (DRG) code. Possible influencing factors for POCR performance selected were based on the previous, similar literature [10, 13] or were persumed to be logic, they included:

1) Socio-demographic characteristics, including age, gender, language region (German, French or Italian), purchasing power index per household (describing the per capita income of a postal code region as a proxy for the socioeconomic status of the respective region), and urban or rural residence;

2) Health insurance characteristics, including insurance coverage: only mandatory health insurance or also supplementary health insurance, e.g. the supplementary hospital care insurance, high franchise (more than 500 Swiss Francs), and standard or managed care insurance models;

3) Type of hospital performing surgery. The four hospital types were central hospital (offering the highest level of healthcare services, including university hospitals), primary hospital, surgical hospital and other specialized clinic – as categorized by the Swiss Federal Statistical Office (SFSO);

4) Clinical characteristics, for instance, multi-morbidity, indication of intrathoracic pathology (patients with either cardiovascular disease or respiratory disease based on pharmaceutical cost groups). Since Swiss health insurance claims data do not have a meaningful degree of diagnostic data for outpatient services, pharmaceutical cost groups (PCG) are used to deduce chronic morbidity at the patient level based on drug use [17]. Multi-morbidity was defined as the presence of at least two PCGs.

Geographic unit

Instead of the 26 Swiss cantons, we used 106 MS regions as the geographic units for small area analysis of POCR utilization and variation. MS regions are defined by the SFSO and used in particular as a microregional intermediate level for numerous scientific and regional policy purposes. They are characterized by a certain spatial homogeneity and obey the principle of small-scale labor market areas [18]. Each patient's residence was assigned to the corresponding MS region in the claims data.

Statistical analysis

First, we performed a descriptive analysis of the eligible patients' characteristics, including their socio-demographic, insurance, clinical and hospital characteristics. Second, to have an intuitive, visual impression of the detailed distribution of POCR utilization in Switzerland, we aggregated the patient level outcome and explanatory variables at the MS regional level. Specifically, for each MS region, we calculated the POCR rate, mean age, percentage of women, mean purchasing power index per household, percentage of patients with high franchise and with standard fee-for-service model in the mandatory health insurance, with only mandatory insurance, with supplementary hospital care insurance, with indication of intrathoracic pathology, with multi-morbidity. We also assessed the percentage of patients receiving surgery in each hospital type. We then mapped all relevant variables using the Geographic Information System (GIS) software package QGIS (version 2.14.16) [19] to show their geographic distribution. Third, to explore the spatial autocorrelation present in these variables, we computed the Moran's I statistic and calculated Local Indicators of Spatial Association (LISA) using GeoDa (version 1.10) [20] that were subsequently mapped with GIS. Moran's I measures the correlation of a variable with itself through space, it ranges from -1 to 1. If the value of Moran's I is zero or very close to 0 ($p>0.05$), it suggests there is no spatial autocorrelation (null hypothesis: the variable is totally randomly distributed through space). If Moran's I is positive ($p<0.05$), it indicates there is positive spatial autocorrelation, namely the variable of one region is more similar to the regions close to it compared to regions far from it, and the vice versa if Moran's I is negative. LISA shows exactly where the significant spatial clustering or dispersion happens locally.

To investigate the factors that potentially affected the utilization of POCR, we first conducted logistic regression at the patient level to describe the associations between use of POCR and all potential predictors other than the geographic unit of residence. We applied a manual, step-by-step variable selection process to develop a multivariable logistic regression model with only the relevant variables (with a significant coefficient, $p<0.05$). This multivariable model was then checked for multicollinearity and tested for goodness of fit with the receiver operating characteristic (ROC) curve. We calculated the mean residuals per MS region and checked the spatial correlation with Moran's I statistic.

The nesting of all individuals within MS regions implied a hierarchical data structure. In order to take this into account, we additionally performed multilevel logistic regression (multilevel model 1) with patients as the 1st level and MS regions as the 2nd level. Besides, we also considered the hospitals where surgeries were performed as a random effect in multilevel modeling. However, the 3-level data structure (patient – hospital – MS region of residence) was not entirely hierarchical, namely not all patients residing in one MS region had surgeries in hospitals within the same MS region. To solve this cross-classification issue, we further built a cross-classified multilevel model (multilevel model 2) taking both MS regions and hospitals into consideration as random effects. As the cluster-level covariate in multilevel model 2, the effect of hospital type was quantified using the 80% interval odds ratio (IOR-80) [21-23]. This decision was taken because other than individual-level covariates in multilevel models, cluster-level covariates take only one value in each cluster. The interpretation of standard odds ratios is hence not straightforward for cluster-level covariates. Considering the distribution of odds ratios comparing two patients with different cluster-level covariate values (having surgeries in hospitals of a different type), but identical values for all other covariates, the IOR-80 covers the middle 80% of such odds ratios and has been recommended to describe cluster-level associations. The IOR-80 is narrow if between-cluster variation is small, and vice versa. If IOR-80 contains the value of one, the between-cluster variation is more important than the effect of the cluster-level covariate, if not, the latter is more relevant. To estimate the degree of the random variation, we calculated the median odds ratio (MOR) for both multilevel models. The MOR compares the adjusted odds of POCR utilization in two patients with the same covariates except residing in two randomly selected MS regions (or having surgery by two randomly selected hospitals), and it can be interpreted as the median of these ORs. MOR is always above or equal to one since it is the median odds ratio between the person with a higher propensity and the person with a lower propensity for the outcome of interest [21-23]. MOR could be used directly for comparison with ORs of fixed-effect variables [21-23]. We then drew caterpillar plots of higher-level residuals to identify the MS regions that were significantly different from the average of all MS regions. At last, we checked spatial correlation of the two multilevel models' residuals at MS region level using Moran's I statistic. Due to the multilevel nature of data and the potential effect of MS region and hospitals on POCR utilization, we regarded the cross-classified multilevel regression model as our main model. To justify the random effects, we also calculated the variation partition coefficient (VPC) for both the MS region and hospital levels, in a cross-classified model without covariates.

Results

In total, 47,215 insured patients who experienced hospitalization for non-emergency surgery were analyzed in our study. Among them, 6,121 (13.0%) had ambulatory chest radiography within two months before surgery. Table 1 shows the characteristics of all included patients, patients with POCR, and patients without POCR, respectively. Women accounted for 57.4% of the total study population, and the mean age was 60.3 years. Compared to patients without POCR, patients with POCR were older (mean age: 68.4 vs. 59.1 years old), more frequently male and wealthier. They also preferred mandatory plus additional health insurance, high franchise, standard insurance model and supplementary hospital care insurance; and they were more likely to have an intrathoracic pathology and multi-morbidity; finally, they more often had surgery in a primary hospital or surgical hospital.

POCR raw rates varied from 2.5% to 44.4% across 106 MS regions (the range was 2.3% to 30.7% after age standardization). Geographic distribution of POCR utilization across MS regions is shown in Figure 1. There were considerable geographic variation and clustering of POCR rates. Geographic distribution of all considered influencing factors are shown in Supplementary Figure S1 online. Moran's I value of POCR raw rates across MS regions was 0.26 and was statistically significant ($p<0.001$). It indicates substantial spatial autocorrelation in POCR utilization, namely the POCR use is not randomly distributed among MS regions, and the POCR rate of one region is more similar to its neighbouring regions compared to regions far away. Figure 2 presents a LISA cluster map of POCR raw rates with several significant clusters of POCR utilization across Switzerland. The main high-high spatial cluster (regions with high POCR rates surrounded by neighbours also with high rates) was detected around the canton of Fribourg. The Moran's I statistic and LISA clustering maps of possible influencing factors are shown in Supplementary Figure S2 online.

Table 1. Characteristics of 47215 insured patients undergoing inpatient surgery during the year 2013 to 2015.

Characteristics	Total	Without POCR	With POCR
n	47215	41094 (87.0%)	6121 (13.0%)
Female	27086 (57.4%)	23829 (58.0%)	3257 (53.2%)
Age (mean, SD)	60.3 (17.2)	59.1 (17.4)	68.4 (12.6)
Purchasing power index per household	101.7 (22.7)	101.6 (22.4)	102.8 (24.3)
Urban residence	36457 (77.2%)	31783 (77.3%)	4674 (76.4%)
Language region			
German	37547 (79.5%)	32615 (79.4%)	4932 (80.6%)
French	6157 (13.0%)	5457 (13.3%)	700 (11.4%)
Italian	3511 (7.4%)	3022 (7.4%)	489 (8.0%)
Intrathoracic pathology indication[a]	24566 (52.0%)	20479 (49.8%)	4087 (66.8%)
Multi-morbidity[b]	26267 (55.6%)	22056 (53.7%)	4211 (68.8%)
Insurance coverage			
Mandatory	10875 (23.0%)	9674 (23.5%)	1228 (20.1%)
Mandatory and supplementary	36340 (77.0%)	31447 (76.5%)	4893 (79.9%)
Supplementary hospital care insurance	11858 (25.1%)	10153 (24.7%)	1705 (27.9%)
High franchise (>500 Swiss Francs)	7799 (16.5%)	7163 (17.4%)	636 (10.4%)
Mandatory insurance models			
Standard	24108 (51.1%)	20742 (50.5%)	3366 (55.0%)
Managed care	23107 (48.9%)	20352 (49.5%)	2755 (45.0%)
Type of hospital performing surgery[c]			
Central hospital	19711 (41.7%)	17511 (42.6%)	2200 (35.9%)
Primary hospital	21269 (45.0%)	18298 (44.5%)	2971 (48.5%)
Surgical hospital	5130 (10.9%)	4317 (10.5%)	813 (13.3%)
Other specialized clinic	1105 (2.3%)	968 (2.4%)	137 (2.2%)

POCR: preoperative chest radiography; SD: standard deviation; a. Patients with either cardiovascular disease or respiratory disease based on pharmaceutical cost groups (PCG); b. Patients with two or more than two chronic diseases based on PCG; c. Categorized according to the Swiss Federal Statistical Office (SFSO)

Figure 1. Geographic distribution of POCR utilization across MS regions.

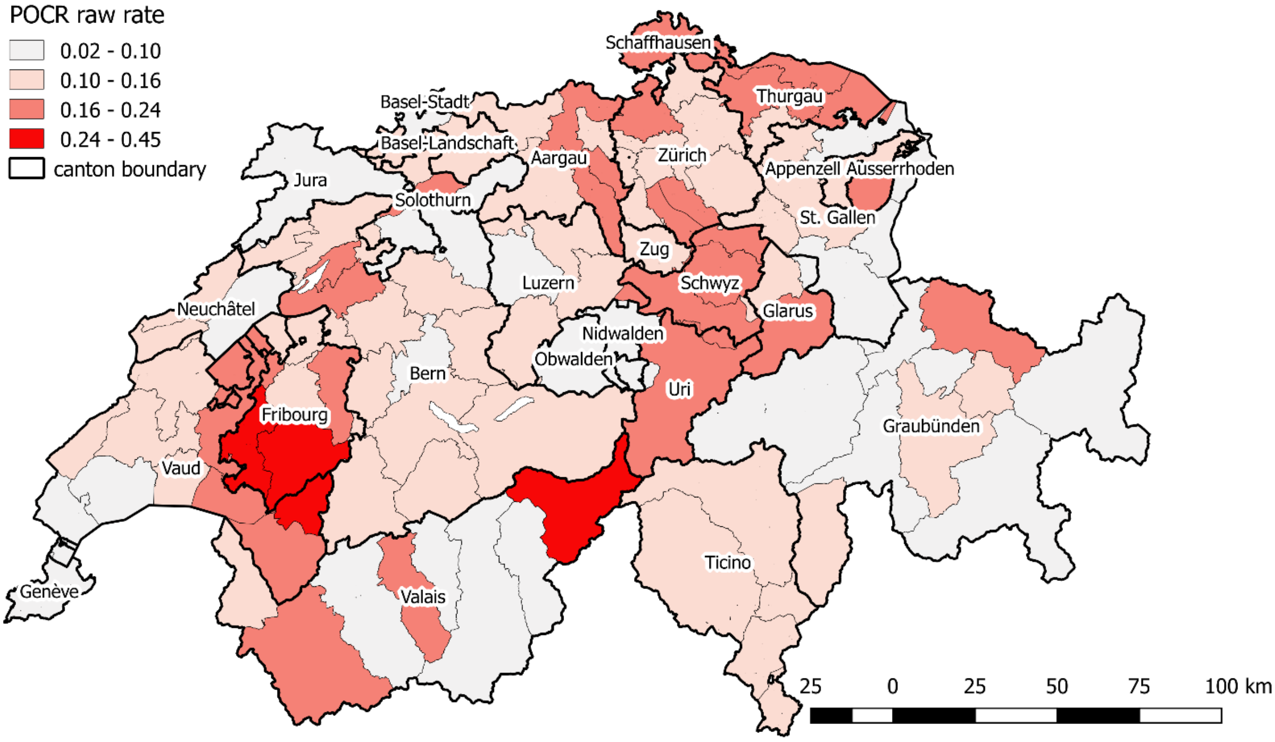
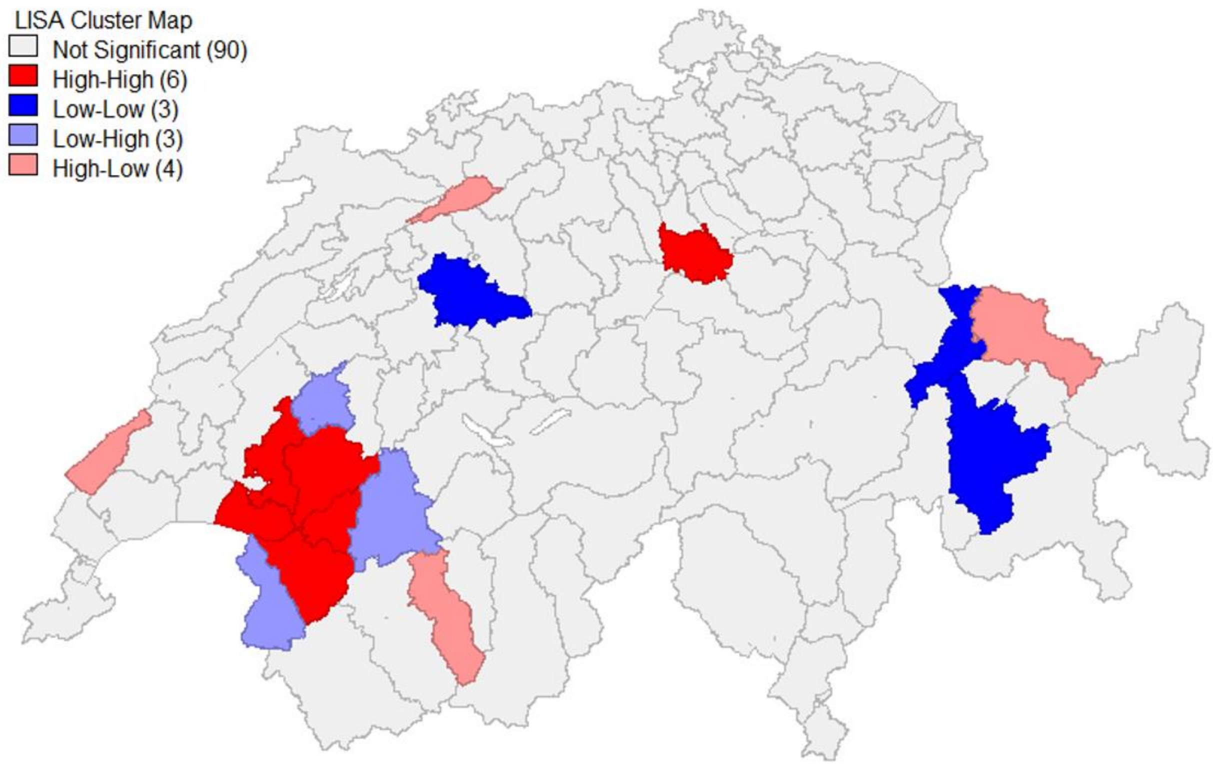


Figure 2. LISA cluster map of POCR raw rates across MS regions.



In the logistic regression model (Table 2), higher age, indication of intrathoracic pathology, multi-morbidity, higher purchasing power index per household, and receiving surgery in hospitals providing lower levels of care (i.e., primary hospitals, surgical hospitals and other specialized clinics) were positively associated with the use of POCR. In contrast, female gender, urban residence, living in the French-speaking compared to German-speaking region, choice of an insurance model with high deductibles and supplementary hospital care insurance showed a negative association. We did not find multi-collinearity and the area under ROC curve (AUC) was 0.67. There was no significant effect modification identified in the model. Moran's I of mean model residuals per MS region was 0.28 ($p<0.01$), indicating the presence of residual spatial correlation remained after the modeling of covariate effects. Therefore, the model assumption of independent residuals was not perfectly met and the model needs to be improved further.

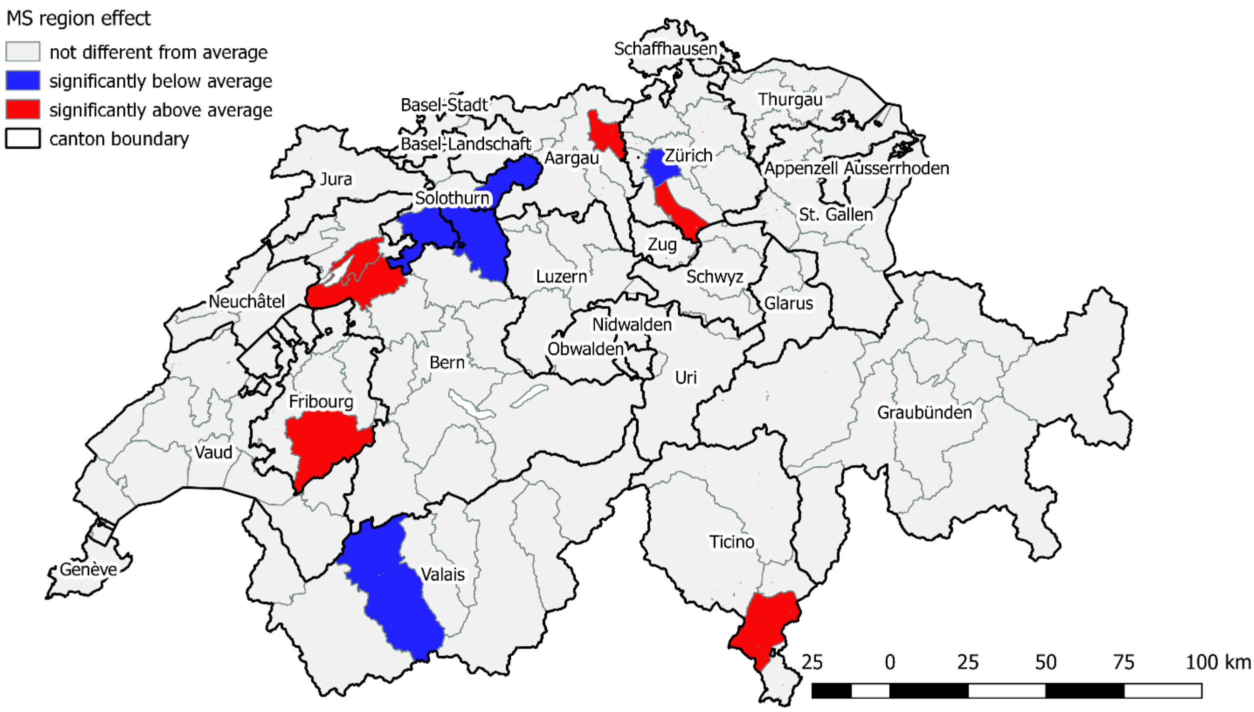
Indicators of purchasing power index per household, urban residence, and language region were not significant and therefore excluded from both multilevel models (Table 2). The effect of hospital type on POCR utilization in multilevel model 1 was remarkable, with odds ratios of 1.37 (95% CI: 1.28-1.46) for primary hospital, 1.62 (95% CI: 1.48-1.78) for surgical hospitals and 1.29 (95% CI: 1.06-1.57) for other specialized clinics compared to central hospitals. In multilevel model 2, only the category of surgical hospitals had a significant OR of 1.44 (95% CI: 1.04-1.99) compared to central hospitals, while the joint p-value for the overall hospital type variable was 0.137. Consistent with that, the IOR-80 for each hospital type compared to central hospitals was relatively wide and contained the value of one, reflecting substantial unexplained variation between hospitals and implying that hospital type did not account for much of this heterogeneity. The median odds ratio (MOR) of MS region in multilevel model 1 was 1.49, suggesting a large amount of variation between MS regions. In multilevel model 2, the MOR of MS region (MOR_{MS}) decreased to 1.25, indicating only moderate heterogeneity between MS regions, while the MOR of hospital was higher (MOR_{HP}=1.69), suggesting a large amount of variation between hospitals, which was also reflected in the wide IOR-80. From the caterpillar plot of multilevel model 2, we identified 11 MS regions significantly differing from the average MS region random effect. Among them, 5 MS regions had a significantly lower probability of performing POCR compared to the average probability (one MS region in canton Zurich, one in canton Bern, one in canton Valais and two in canton Solothurn), and 6 had a significantly higher probability (one in canton Zurich, one in canton Fribourg, one in canton Aargau, one in canton Ticino and two in canton Bern). Figure 3 shows the geographic locations of these 11 MS regions.

Table 2. Results of logistic regression model and multilevel models for the association between POCR utilization and influencing factors.

	Logistic regression	Multilevel model 1[d]	Multilevel model 2[e]
Fixed effects (OR and 95% CI)			
Age	1.033 (1.031, 1.036)	1.034 (1.031, 1.036)	1.034 (1.032, 1.036)
Female gender	0.841 (0.796, 0.890)	0.838 (0.793, 0.887)	0.840 (0.794, 0.890)
High franchise (>500 Swiss Francs)	0.756 (0.690, 0.829)	0.755 (0.688, 0.828)	0.746 (0.679, 0.818)
Supplementary hospital care insurance	0.934 (0.876, 0.995)	0.928 (0.870, 0.989)	0.901 (0.842, 0.965)
Intrathoracic pathology indication[a]	1.137 (1.055, 1.225)	1.145 (1.062, 1.235)	1.149 (1.064, 1.240)
Multi-morbidity[b]	1.107 (1.026, 1.193)	1.113 (1.031, 1.120)	1.122 (1.039, 1.211)
Purchasing power index per household	1.002 (1.001, 1.004)		
Urban residence	0.911 (0.852, 0.973)		
Language region			
German	1		
French	0.852 (0.782, 0.929)		
Italian	1.059 (0.954, 1.177)		
Type of hospital performing surgery[c]			
Central hospital	1	1	1
Primary hospital	1.356 (1.276, 1.441)	1.367 (1.281, 1.458)	1.210 (0.932, 1.571)
IOR-80			0.45 – 3.26
Surgical hospital	1.571 (1.436, 1.718)	1.621 (1.478, 1.778)	1.436 (1.036, 1.991)
IOR-80			0.53 - 3.88
Other specialized clinic	1.212 (1.002, 1.465)	1.291 (1.064, 1.566)	1.434 (0.917, 2.240)
IOR-80			0.53 – 3.87
Random effects			
MOR_{MS}		1.49	1.25
MOR_{HP}			1.69
Moran's I of residuals	0.29 (p<0.01)	0.34 (p<0.01)	0.066 (p=0.115)

OR: odds ratio; CI: confidence interval; MOR_{MS}: median odds ratio of MS region effect; MOR_{HP}: median odds ratio of hospital effect; IOR-80: 80% interval odds ratio; a. Patients with either cardiovascular disease or respiratory disease based on pharmaceutical cost groups (PCG); b. Patients with two or more chronic diseases based on PCG; c. Categorized according to the Swiss Federal Statistical Office (SFSO); d. Estimating random effects for MS regions only; e. Cross-classified model estimating random effects for both MS regions and hospitals.

Figure 3. MS regions significantly different from the average MS region effect identified from caterpillar plot of the cross-classified multilevel model.



The Moran's I of multilevel model 1 residuals at MS region level was 0.34 (p<0.01). However, after taking hospital into consideration as random effect, multilevel model 2 residuals at MS region level showed little spatial correlation (Moran's I = 0.066, p=0.115), implying that the model assumption was met and cross-classified multilevel model solved spatial correlation issue well. The VPCs for the MS region and hospital levels were 1.6% and 8%, respectively.

Discussion

We found substantial variation in POCR utilization rates across 106 MS regions in Switzerland. Different factors including patient socio-demographic and clinical characteristics, health insurance features, and hospital-related factors appeared to affect POCR utilization. Moderate variation of POCR utilization across MS regions and especially hospitals persisted after the adjustment for these factors, hinting at the existence of additional influences not covered by our dataset.

Due to very limited clinical and economic benefit of POCR in asymptomatic patients, both the US Choosing Wisely initiative and Smarter Medicine in Switzerland have put POCR on their lists of procedures that should be avoided except for special situations [3, 9]. A study from the

US showed a prevalence of 91.5% for POCR among patients with unremarkable history and physical examination results in 2013 [24]. Another US study using 2009 Medicare claims data showed a 5.5% POCR utilization rate [25]. Two studies in Canada examined hospital databases from 2005 to 2007 and 2008 to 2013, and reported 23.3% and 10.8% POCR utilization rates in Alberta and Ontario, respectively [13, 26]. Overall POCR rate in our study was 13.0%, which did not differ much from the previous findings except the one for the US with a 91.5% POCR rate (for which we have not found an obvious explanation). However, these results may not be entirely comparable because of different sample selection and outcome definition. For example, there were differences regarding the databases used (health insurance claims data, further healthcare administrative data or hospital discharge data), the age ranges of the study populations (patients above 18 years or only the elderly patients), the surgery types included (inpatient vs. outpatient surgeries, low risk surgeries, elective surgeries, or non-cardiothoracic surgeries), and the time period before surgery ("preoperative" was defined inconsistently as 14, 30 or 60 days before surgery in different studies). In our study, we considered POCR performed within two months before any inpatient surgeries in all patients, without excluding cardiothoracic surgeries or patients with cardiopulmonary diseases. Therefore, a certain degree of POCR utilization was expected and would be justified in the present study.

The first study investigating the geographic variation of POCR utilization in Switzerland so far, by Blozik et al., demonstrated a substantial variation of POCR rates at the cantonal level. Across the 26 Swiss cantons, the observed minimum was 6% in the canton of Obwalden and the maximum 28% in the canton of Schwyz [10]. When using smaller geographic units – MS regions in our study, we observed considerable small area variation (raw rate of POCR utilization rate across MS regions: 2.5% to 44.4%), also within cantons. The three MS regions with the highest POCR rates were in cantons of Valais and Fribourg, and the three with the lowest POCR rates were in cantons of St. Gallen, Valais and Graubünden.

Our cross-classified multilevel results suggested that the most relevant factors of POCR utilization available in our claims data were older age, male gender, indication of intrathoracic pathology, choice of an insurance model with low deductibles, having supplementary hospital insurance, and multi-morbidity. Older patients generally have worse health status and more comorbidities, thus they tend to be treated with more caution; the same applies to patients with multi-morbidity. Lower use of POCR in women may be partly related to different types of surgery performed on men and women; this possibility could be further explored with detailed surgery information. Patients with cardiovascular or respiratory disease were more likely to receive POCR, not unexpected for patients with an intrathoracic pathology. The health insurance related factors indicated that patients choosing a higher franchise had a lower probability of POCR. One reason may be that patients choosing a higher franchise are normally healthier, besides, higher out-of-pocket costs could make them more reluctant to undergo POCR. Patients with supplementary hospital care insurance had a slightly lower probability of POCR. This finding might be due to patients' selection of "better" or "more expensive" care such as ultrasound or MRI, compared to POCR. However, we expect inpatient POCR to be generally rare (see below). There have been few other studies investigating possible influencing factors of POCR utilization. One US study [13] found that older age, certain comorbidities and preoperative consultations played an important role. Our finding of an impact of health insurance-related factors as an example of non-clinical patient-sided factors on POCR is relatively novel.

The MOR_{MS} in multilevel model 2 implies that moderate unexplained variation of POCR utilization across MS regions persisted after controlling for the available influencing factors. Based on both the wide IOR-80 of hospital type and the relatively high MOR_{HP} value in multilevel model 2, the between hospital variation of POCR utilization was substantial and cannot be explained by hospital type. Hospitals made a more relevant contribution than MS regions to the variation of POCR utilization. Similarly, Blozik et al. also observed large variance between hospitals within a canton, and concluded that individual hospitals proceed very differently with the placement of the POCR [10]. The residual between-MS region and between-hospital variation after modeling might be due to certain regional or hospital-level determinants that we could not control for in our study, for instance, provider density, attitude of physicians or patients, acceptance of guidelines. Although there was very few literature studying impact factors of POCR variation, some studies exploring factors influencing utilization of other health services might give us some insight into possible neglected predictors. For example, Chen I et al. concluded that neighbourhood education could affect hysterectomy utilization rate[27]. Another study found that primary care use was influenced by the density of primary care practices[28]. They might be included in further studies. In addition, the underlying mechanisms that account for the 11 MS regions being significantly different from the average effect should also be further investigated closely and locally for better health service provision and resource allocation. Most previous studies [29-31] only conducted descriptive assessments of regional variations of healthcare utilization, reporting, for example, interquartile range, extremal quotient (EQ), coefficient of variance (CV) and systematic component of variation (SCV). They usually did not control for potential influencing factors. Our study highlighted a more advanced and comprehensive method of regional variation estimation through multilevel modelling, which we will transfer and apply to studies planned for other healthcare services of interest.

The present study was based on claims data before the “Smarter Medicine” initiative was introduced in Switzerland in 2016. A possible follow-up study might provide additional insights into the influence of negative recommendation on POCR utilization. The study had a few limitations. First, due to the limitation of health insurance claims data some potentially important variables such as whether or not there was an indication for POCR, the physicians’ and patients’ preferences, etc. were lacking. Also, our data on POCR utilization were based on claims data from the outpatient sector. We had no details of services, treatments or procedures during inpatient episodes. POCR use during inpatient stays would not have been captured. However, due to financial incentives encouraging the transfer of diagnostic measures to before inpatient stays, we assume that inpatient POCR occurred relatively rarely [10]. We did not have information on where the outpatient POCR were performed, but we do not consider this as very relevant for the decision for or against POCR use. Furthermore, the results came from a single health insurance company in Switzerland. Enrolees of other Swiss health insurers might theoretically show different patterns of use. However, the results presented here were based on an insured population of 1.2 million people from all regions of Switzerland. Helsana internal data show no evidence of deviation in basic characteristics of its own customers compared to the whole population. The benefit package of the obligatory health insurance is defined at the federal level and the same for all health insurance companies, and all physicians collaborate with all insurance providers. Thus we assume no huge difference between our study population from Helsana and whole Swiss population. Even if the Helsana population is not perfectly representative of whole population, we believe it has no big impact on the association results in our study. The results should be generalizable to a large extent for the whole Switzerland. In addition, theoretically, there might have been a surgery because of the chest radiography which we were not able to identify, although we believe the proportion of such situation would be quite small.

In conclusion, our study observed substantial variation of POCR utilization across MS regions in Switzerland. Patients’ socio-demographics and clinical characteristics, choice of health insurance, and hospital-related factors influenced POCR utilization. Despite controlling for these influencing factors, variation across MS regions and especially across hospitals persisted, implying a hospital specific effect. Underlying mechanisms need to be further clarified.

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Competing interests

The author(s) declare no competing interests.

Author contributions

M.S, V.vW and H.D generated the idea of the present study. B.B, E.B and C.B did data preparation and data management. W.W, O.G and A.U performed statistical analysis and wrote the main manuscript text. All authors together decided on the analysis methodology and reviewed the manuscript.

Data availability

The dataset that supports the findings of the current study are from the Helsana Group, but are not publicly available as they are individual-level, health-related claims data on human subjects, albeit anonymised. However, the data are available from the Helsana Group, upon reasonable request.

Figure S1. Geographic distribution of possible influencing factors of preoperative chest radiography (POCR) use in Switzerland.

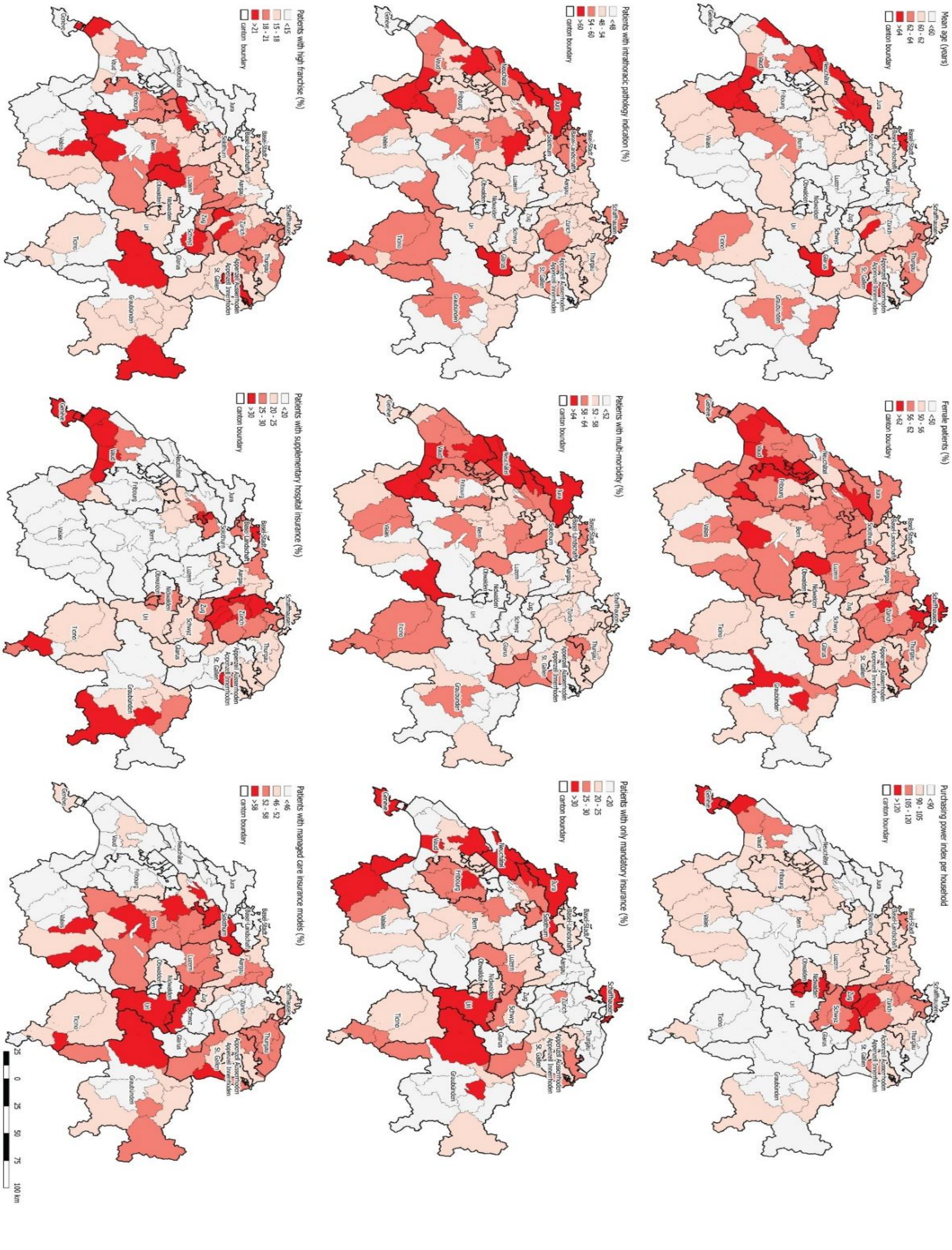
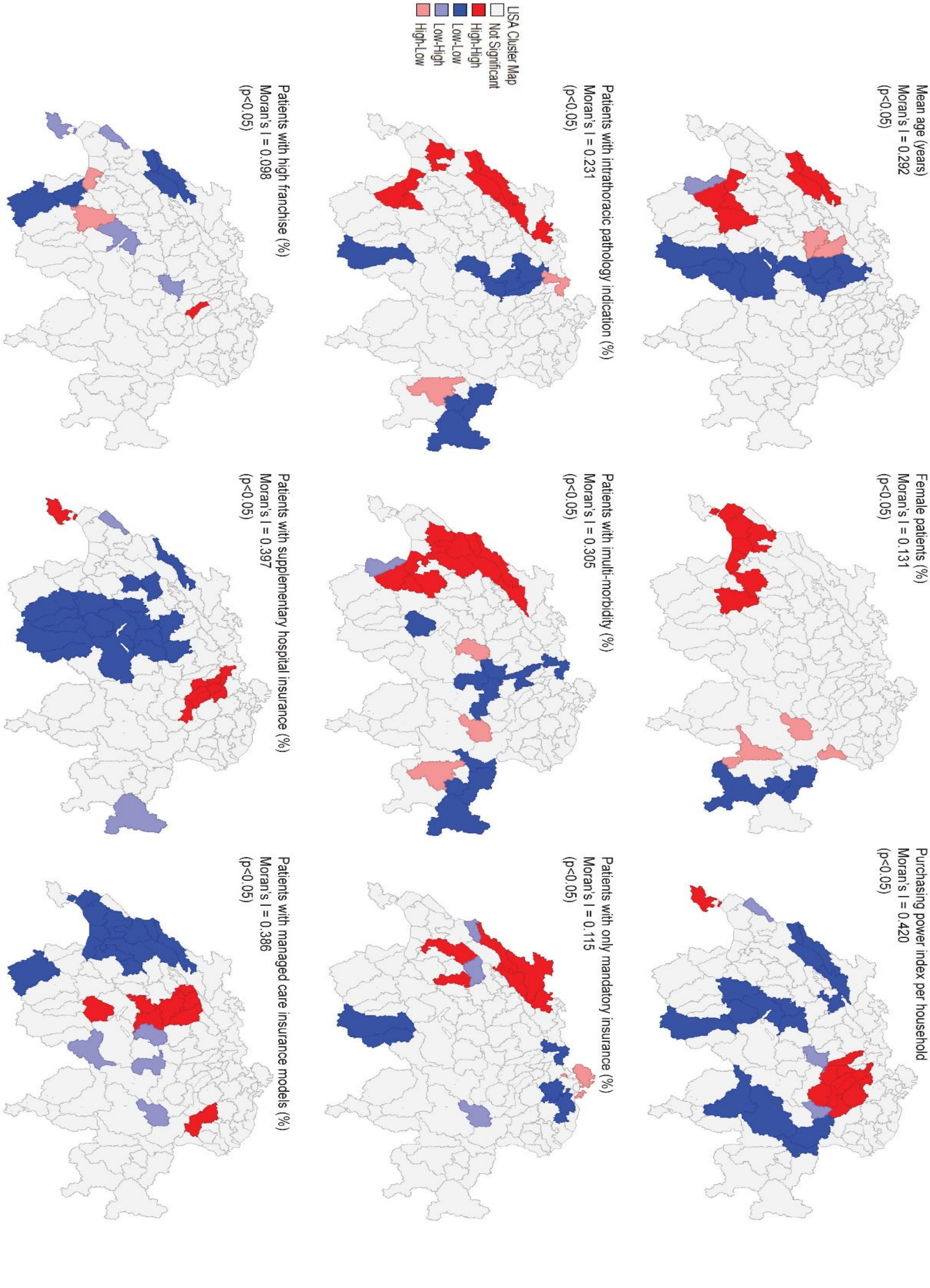


Figure S2. Local Indicators of Spatial Association (LISA) clustering maps of possible influencing factors of preoperative chest radiography (POCR) use in Switzerland.



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Chapter III

Exploring geographic variation of and influencing factors for utilization of four diabetes management measures in Swiss population using claims data

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Abstract

Introduction

Four strongly recommended diabetes management measures are biannual glycated haemoglobin (HbA1c) testing, annual eye examination, kidney function examination, and low-density lipoprotein (LDL) testing in patients below 75 years. We aimed to describe regional variation in the utilization of the four measures across small regions in Switzerland and to explore potential influencing factors.

Research Design and Methods

We conducted a cross-sectional study of adult patients with drug-treated diabetes in 2014 using claims data. Four binary outcomes represented adherence to the recommendations. Possible influencing factors included socio-demographics, health insurance preferences and clinical characteristics. We performed multilevel modelling with Medstat regions as the higher level. We calculated the median odds ratio (MOR), and checked spatial autocorrelation in region level residuals using Moran's I statistic. When significant, we further conducted spatial multilevel modelling.

Results

Of 49,198 diabetes patients (33,957 below 75 years), 69.6% had biannual HbA1c testing, 44.3% each had annual eye examination and kidney function examination, and 55.5% of the patients below 75 years had annual LDL testing. The effects of health insurance preferences were substantial and consistent. Having any supplementary insurance (odds ratios (OR) across measures were between 1.08 and 1.28), having supplementary hospital care insurance (1.08-1.30), having chosen a lower deductible level (e.g. CHF 2500 compared to CHF 300: 0.57-0.69), and having chosen a managed care model (1.04-1.17), were positively associated with recommendations adherence. The MORs (1.27-1.33) showed only moderate unexplained variation, and we observed inconsistent spatial patterns of unexplained variation across the four measures.

Conclusion

Our findings indicate that the uptake of strongly recommended measures in diabetes management could possibly be optimized by providing further incentives to patients and care providers through insurance scheme design. The absence of marked regional variation implies limited potential for improvement by targeted regional intervention, while provider-specific promotion may be more impactful.

Significance of the study

What is already known about this subject?

- Better adherence to clinical guidelines and recommendations could increase clinical outcomes of diabetes patients.
- Little is known about the utilization and its regional variation of recommended measures in diabetes management.

What are new findings?

- In a healthcare system with mandatory health insurance, choosing a lower deductible level, choosing a managed care model and having supplementary insurance were associated with better adherence.
- Unexplained variation after adjusting for possible influencing factors was not pronounced, and inconsistent spatial patterns were observed across different measures.

How might these results change the focus of research or clinical practice?

- The findings imply a potential to optimize the utilization of recommended healthcare services by providing further incentives through insurance scheme design.

INTRODUCTION

Diabetes is one of the most common chronic diseases. The global prevalence in adults over 18 years was 8.5% (around 422 million) in 2014, and deaths directly caused by diabetes were estimated at 1.6 million in 2016[1]. In Switzerland, an estimated 500,000 persons suffer from the condition, which is responsible for around 2% of all deaths [2]. Diabetes can be treated and its complications delayed through various measures, including constant medical care, restricted diet, physical activity and regular screening [3].

A variety of clinical guidelines on diabetes management have been developed nationally and internationally to improve outcomes. The Swiss Society of Endocrinology and Diabetology (SGED) has developed “The criteria for good disease management of Diabetes in primary care” in 2013 and revised it in 2017[4]. The American Diabetes Associations, the European Society of Cardiology, and the European Association for the Study of Diabetes report and annually adapt clinical guidelines on diabetes as well [5, 6]. Some recommendations on diabetes management are crucial and consistently present in almost all clinical guidelines, for instance, biannual glycated haemoglobin (HbA1c) testing, annual eye examination and low-density lipoprotein (LDL) testing. Studies have shown strong evidence that the complications of diabetes could be reduced through managing risk factors such as increased HbA1c, low-density lipoproteins (LDL), and blood pressure [7-9]. It has also been reported that adherence to clinical guidelines had a positive influence on clinical outcomes including mortality and hospitalizations [10-12].

In the present study, we used four strong standard recommendations included in most diabetes clinical guidelines, that is, diabetes patients should undergo 1) at least two HbA1c tests per year, 2) at least one eye examination per year, 3) at least one kidney function examination per year, and 4) at least one LDL test per year (only in patients below 75 years). One study in Switzerland using health insurance claims data for the years 2011-2013 reported overall adherence to these recommendations but did not perform an in-depth assessment of drivers of utilization or geographic variation [13]. Generally, few studies have investigated the adherence to clinical recommendations on diabetes management.

Various factors may affect the utilization of healthcare services for diabetes, including characteristics of patients, healthcare providers, health insurance, and regions. This could result in geographic variation in utilization. Such variation in utilization may be unwarranted, which would to some extent reflect unequal access [14]. The four diabetes recommendations are clear and based on high-quality evidence, and the corresponding management measures are not preference-sensitive [15]. Moreover, access to healthcare in general and the four measures in particular is very good in Switzerland. Therefore, we expected little unexplained variation after adjusting for possible influencing factors in the present case [16].

The aims of this study were to a) investigate the utilization levels of the above-defined strongly recommended measure in diabetes management, b) explore potential factors influencing utilization, and c) assess the regional variation in utilization of the four measures across small regions in Switzerland.

MATERIALS AND METHODS

Study population

We used health insurance claims data provided by the Helsana Group, one of the largest health insurance companies in Switzerland. The Helsana database underlying this study included mandatory health insurance claims from around 1.2 million people, covering 15% of the Swiss population. Adults (older than 18 years) enrolled with Helsana who were prescribed any diabetes medication (the Anatomical Therapeutic Chemical (ATC) code was used to identify diabetes medications) between 1st January 2014 and 27th December 2014 were analysed. We excluded enrolees with incomplete insurance coverage in 2014 or not surviving until the end of 2014, patients living outside Switzerland, asylum seekers, Helsana employees, patients with incomplete address information, and patients living in nursing homes with lump-sum reimbursement. Since diagnosis information was not available for outpatient services, we could not distinguish between type 1 and type 2 diabetes.

Basic health insurance (covering a federally defined benefit package) is mandatory in Switzerland and private insurance companies are obliged to offer it to anyone irrespective of their health status. Mandatory health insurance includes appropriate and cost-effective in- and outpatient health services. A variety of annual deductibles (300 - 2,500 Swiss Francs(CHF)) can be chosen, and selecting a higher deductible leads to a lower premium. Enrolees can also choose between standard and managed care models, where the latter require a specific general practitioner or telemedicine provider as the first contact when a new health problem arises, hence are cheaper [17, 18]. In addition to mandatory health insurance, a variety of supplementary health insurance products can be bought, for instance, supplementary hospital care insurance which allows for hospitalization in semiprivate/private wards [17].

Outcome and explanatory variables

We differentiated the participants according to whether they received diabetes medication between 5th January 2013 and 31th December 2013 (prevalent cases if they received it, incident cases if they did not). The date of the first prescription of any diabetes medication in 2014 (incident cases) or 1st January 2014 (prevalent cases) was considered as the index date for each participant. The following 360 days were regarded as the assessment period, which was used to define if the recommendations were being adhered to.

We defined binary outcome variables for the four measures under study: in the assessment period, a) at least two HbA1c tests, b) at least one eye examination (ophthalmologist visit was used as a proxy of eye examination), c) at least one kidney function examination (i.e. serum creatinine and/or albuminuria test), and d) at least one LDL test (or total cholesterol + high-density lipoprotein (HDL) + triglycerides test) for patients below 75 years [19].

The explanatory variables included a) socio-demographics, including age, gender, language region, purchasing power index per household, and urban/rural residence, b) health insurance preferences, including having both mandatory and supplementary insurance, having supplementary hospital care insurance, standard or managed care model, choice of annual deductible, and c) clinical characteristics, including number of comorbidities (pharmaceutical cost groups (PCG) were used to deduce chronic morbidity based on drug use[20]) and incident or prevalent diabetes treated with oral medication or insulin. In addition, a region level variable - ophthalmologist density per 10,000 inhabitants - was used specifically for the study of eye examinations.

Geographic unit

We used Medstat regions as the geographic units for regional variation analysis. Medstat regions (N=705) are defined by the Swiss Federal Statistical Office to reflect hospital catchment areas in a way that they are large enough to provide anonymity for each person hospitalized in Switzerland [21]. Each patient’s residence was assigned to the corresponding Medstat region in the claims data.

Statistical analysis

First, we performed a descriptive analysis of study population's characteristics. We distinguished between all eligible patients and the subpopulation below 75 years, relevant for the assessment of LDL testing.

Second, we mapped out the raw utilization rates of the four measures across Medstat regions to show their geographic distribution. We checked spatial autocorrelation of regional utilization rates by computing the global Moran's I statistic [22]. Moran's I measures the correlation of a variable with itself through space, with a value range from -1 to 1. Moran's I values very close to 0 suggest the studied variable is randomly distributed through space. If Moran's I is positive with $p<0.05$, it indicates that neighbouring regions are more similar than distant regions, and the vice versa if Moran's I is negative with $p<0.05$.

Third, we performed multilevel multivariable logistic regression for each measure, with patients as the lower-level units and Medstat regions as the higher-level units. Decisions on inclusion of explanatory variables were based on the deviance information criterion (DIC) [23]. We included age as a quadratic term to allow for non-linear relationships. The Medstat region-level variable of ophthalmologist density per 10,000 inhabitants was included in the model for eye examination. To estimate the degree of random variation in the multilevel models, we calculated the median odds ratio (MOR) at the Medstat region level. The MOR compares the adjusted odds of being adherent to the recommendation in two patients with identical characteristics, but living in two randomly selected Medstat regions. It is defined as the median of all possible, resulting odds ratios (ORs). The MOR is never below one as the comparison is always between the higher-propensity region and the lower-propensity region, for the outcome of interest [24-26]. A higher MOR indicates a higher level of unexplained variation in utilization after multivariable adjustment, and it can be compared directly with the ORs of the fixed effects [24-26]. We then checked for the presence of spatial autocorrelation in the model residuals at the Medstat region level, for each measure [22].

Finally, in cases with significant spatial autocorrelation present in the multilevel model residuals, we further developed Bayesian hierarchical logistic regression models capturing spatial variation at the Medstat region level through the Integrated Nested Laplace Approximations (INLA) approach [27-30]. This was performed with the R-INLA package [31]. The covariates included in the spatial multilevel models were the same as in the multilevel multivariable models above. The marginal effects of age divided into 50 groups were inspected graphically, which was more intuitive than reporting regression coefficients. The finally remaining geographic variation across Medstat regions was mapped out for each measure.

Statistical analyses were performed using R 3.4.4 [32], STATA 13, and MLwiN 3.04 [33] integrated in STATA using the runmlwin package. Mapping was conducted with QGIS 1.14.16 [34], and spatial clustering analysis was done with GeoDa 1.10 [35].

RESULTS

A total of 49,198 diabetes patients were analysed in this study. The mean age was 66.6 years, and women accounted for 45.0% of the whole study sample. Overall, 34,254 (69.6%) patients had at least two HbA1c tests in their assessment period, 21,808 (44.3%) patients had at least one kidney function examination, and 21,804 (44.3%) patients had at least one eye examination. Among the 49,198 diabetes patients, 33,957 were below 75 years and were analysed for LDL testing. In this subpopulation, 18,851 (55.5%) patients had at least one LDL test in the assessment period. The mean age was 60.1 years, and 41.2% were women. Table 1 shows the socio-demographics, health insurance preferences and clinical characteristics of the total population and of the below 75 years, respectively.

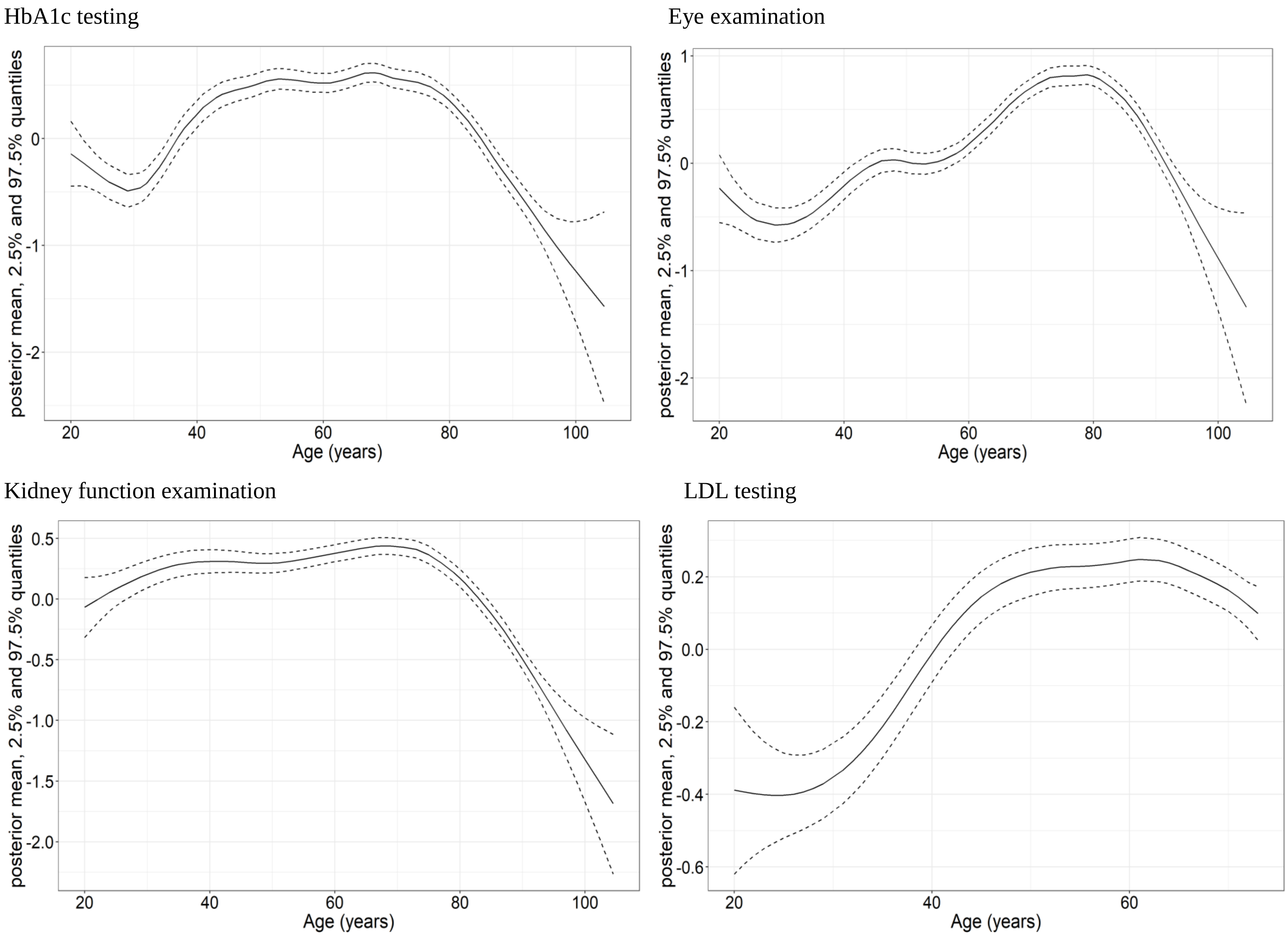
The ORs and 95% confidence/credible intervals (95%CIs) of all explanatory variables (except age, shown in Figure 1) in both the multilevel multivariable models and the spatial multilevel models are shown in Figure 2 (full numerical details are available from supplementary table S1 and S2). For each pair of models representing one outcome, covariate effects were similar, except for language region. Regarding socio-demographics, women were more likely to follow the recommendations of eye examination and kidney function examination, while the opposite was true for LDL testing. Purchasing power index was positively associated with eye examination and kidney function examination, while it was negatively associated with HbA1c testing. Living in an urban area had a positive association with kidney function examination and LDL testing. Compared to the German speaking area, living in the French or Italian speaking area of Switzerland demonstrated a negative association with HbA1c testing and eye examination, as well as positive associations with LDL testing and kidney function examination. As expected, these associations were strongly attenuated in the spatial multilevel models. The effects of health insurance preferences and clinical characteristics were mostly consistent across the four measures. Having any supplementary insurance (odds ratios across measures were between 1.08 and 1.28), having supplementary hospital care insurance (1.08-1.30), having chosen a managed care insurance model (1.04-1.17), and having more comorbidities (e.g. having more than two morbidities compared to none: 1.25-1.57), were all positively associated with being adherent to the recommendations. Having chosen a higher deductible level had a negative association with being adherent to the recommendations (e.g. CHF 2500 compared to CHF 300: 0.57-0.69). Prevalent cases receiving insulin compared to incident cases had a positive association with HbA1c testing, eye examination and kidney function examination, while having a negative association with LDL testing. A positive association between ophthalmologist density and eye examination was found in both models of eye examinations, with an odds ratio of 1.13 in the spatial multilevel model.

Table 1. Characteristics of N = 49,198 diabetes patients.

Characteristics	Total	With biannual HbA1c testing	With annual eye examination	With annual kidney function examination	Age below 75 years	With annual LDL testing
n	49198	34254 (69.6%)	21804 (44.3%)	21808 (44.3%)	33975	18851 (55.5%)
Female gender	22138 (45.0%)	15136 (68.4%)	10314 (46.6%)	9982 (45.1%)	13977 (41.2%)	7572 (54.2%)
Age (mean, sd)	66.6 (13.7)	66.6 (13.0)	69.1 (12.2)	66.4 (13.0)	60.1 (11.2)	60.7 (10.5)
Purchasing power index (mean, sd)	99.8 (20.6)	99.6 (20.4)	100.45 (21.3)	100.0 (20.8)	99.5 (20.0)	99.7 (20.4)
Urban residence	38478 (78.2%)	26596 (69.1%)	17039 (44.3%)	17437 (45.3%)	26562 (78.2%)	14914 (56.1%)
Language						
German	35882 (72.9%)	26587 (74.1%)	16493 (46.0%)	15369 (42.8%)	24911 (73.4%)	12833 (51.5%)
French	9226 (18.8%)	5333 (57.8%)	3636 (39.4%)	4259 (46.2%)	6472 (19.1%)	4442 (68.6%)
Italian	4090 (8.3%)	2334 (57.1%)	1675 (41.0%)	2180 (53.3%)	2572 (7.6%)	1576 (61.2%)
Insurance coverage						
Only mandatory	13120 (26.7%)	8673 (66.1%)	4787 (36.5%)	5669 (43.2%)	10380 (30.6%)	5662 (54.5%)
Mandatory and supplementary	36078 (73.3%)	25581 (70.9%)	17017 (47.2%)	16139 (44.7%)	23577 (69.4%)	13189 (55.9%)
High deductible (>500 CHF)	2770 (5.6%)	1692 (61.1%)	888 (32.1%)	978 (44.9%)	2262 (6.7%)	1058 (46.8%)
Mandatory insurance models						
Standard	29097 (59.1%)	19973 (68.6%)	12870 (44.2%)	12900 (44.3%)	19207 (56.6%)	10639 (55.4%)
Managed care	20101 (40.9%)	14281 (71.0%)	8934 (44.4%)	8908 (44.3%)	14750 (43.4%)	8212 (55.7%)
Supplementary hospital care insurance	8582 (17.4%)	6085 (70.9%)	4544 (52.9%)	3965 (46.2%)	5336 (15.7%)	3038 (56.9%)
Multimorbidity (mean, sd)	2.6 (1.7)	2.6 (1.7)	2.8 (1.7)	2.7 (1.7)	2.4 (1.7)	2.5 (1.7)
Diabetes category						
Incident	6198 (12.6%)	4003 (64.6%)	2109 (34.0%)	2646 (42.7%)	4971 (14.6%)	2661 (53.5%)
Oral drug only	30329 (61.6%)	20294 (66.9%)	12976 (42.8%)	13318 (43.9%)	20084 (59.1%)	11331 (56.4%)
Insulin	12671 (25.8%)	9957 (78.6%)	6719 (53.0%)	5844 (46.1%)	8902 (26.2%)	4859 (54.6%)
Ophthalmologist density /10000 inhabitants	0.09 (0.17)	-	0.09 (0.18)	-	-	-

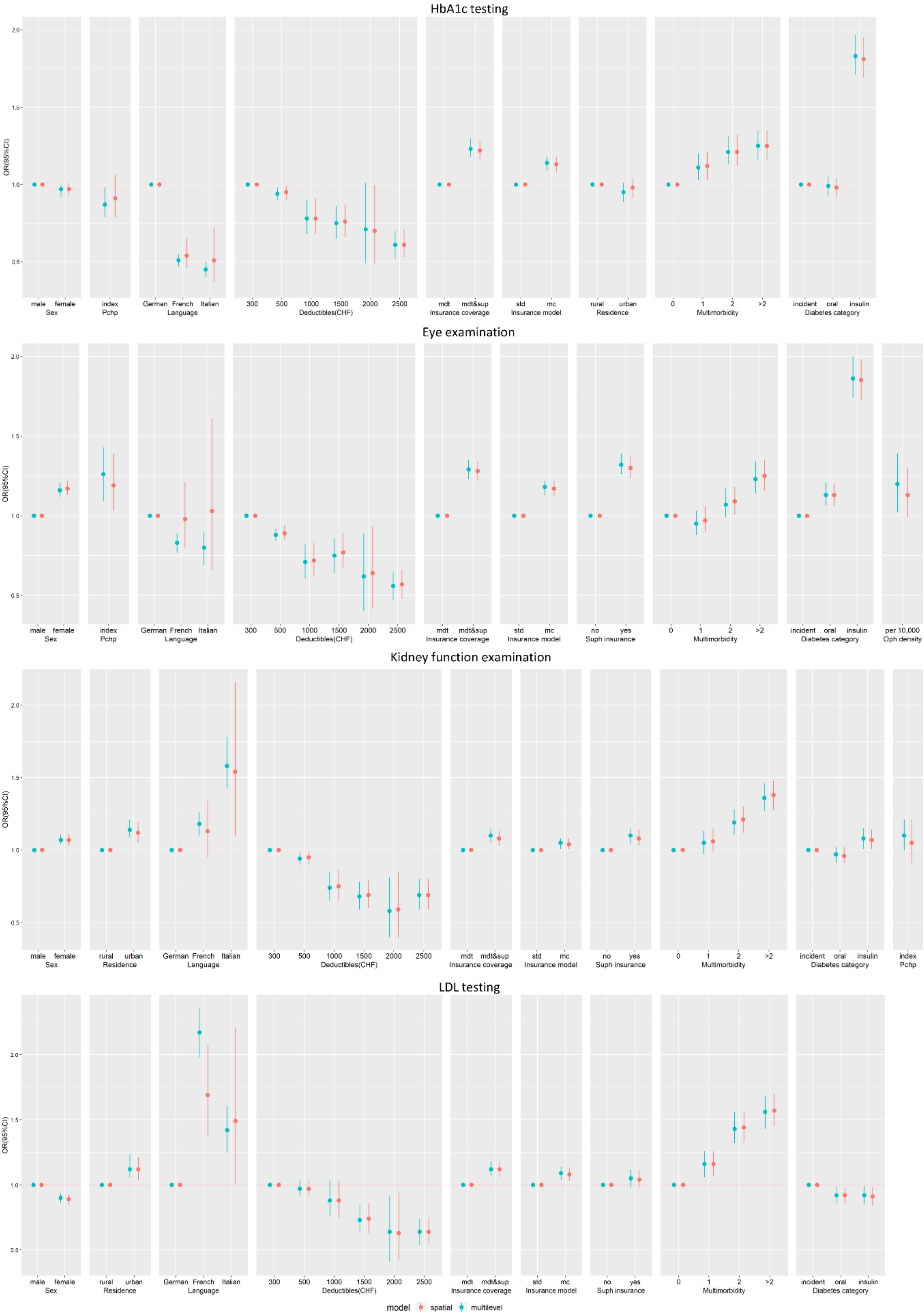
sd: standard deviation; HbA1c: glycated haemoglobin; LDL: low-density lipoprotein; CHF: Swiss franc; Multimorbidity: pharmaceutical cost groups (PCG) were used to deduce chronic morbidity based on drug use.

Figure 1. Age effect in spatial multilevel models.



HbA1c: glycated haemoglobin; LDL: low-density lipoprotein.

Figure 2. Fixed effects in multilevel multivariable models and spatial multilevel models.



OR: odds ratio; CI: confidence/credible interval; HbA1c: glycated hemoglobin; LDL: low-density lipoprotein; CHF: Swiss franc; Pchp: purchasing power; mdt: mandatory insurance; sup: supplementary insurance; std: standard; mc: managed care; Suph insurance: supplementary hospital insurance; Oph: ophthalmologist; Multimorbidity: pharmaceutical cost groups (PCG) were used to deduce chronic morbidity based on drug use.

The geographic distribution of the utilization of the four measures across Medstat regions is shown in Figure 3. By visually inspecting the maps, we noted considerable geographic variation for each measure, with quite different spatial patterns. For HbA1c testing, utilization rates were generally higher in the German-speaking north and middle part of Switzerland, while there was no such pattern visible for the other three measures. Positive and statistically significant ($p<0.05$) Moran's I values of the raw rates indicating the presence of spatial autocorrelation were 0.46 for HbA1c testing, 0.27 for eye examination, 0.21 for kidney function examination, and 0.35 for LDL testing. After multilevel multivariable model adjustment, Moran's I values of the residuals at the Medstat region level decreased to 0.12 ($p<0.0001$) for HbA1c testing, 0.13 ($p=0.0001$) for kidney function examination, and 0.07 ($p=0.004$) for LDL testing. Only for eye examination, we found a slight increase of spatial autocorrelation to 0.30 ($p<0.001$) after model adjustments. In consequence, we regarded the spatial multilevel models as most appropriate, because they accounted for the spatial structure in the data. The MORs in the multilevel multivariable models, describing variation between Medstat regions, were 1.28 for HbA1c testing, 1.31 for eye examination, 1.27 for kidney function examination, and 1.33 for LDL testing.

The unexplained spatial variation remaining after multivariable adjustment through spatial multilevel models for each measure is shown in Figure 4. The OR values in the Figure 4 represent the odds of being adherent to the recommendation in one specific Medstat region compared to the average odds in the whole of Switzerland. We observed spatial clusters of better adherence in the northeast and middle parts of the country for HbA1c testing, in the north and east parts for eye examination, in the southwest and southeast parts for kidney function examination, and in the southwest part for LDL testing.

Figure 3. Raw utilization rates of four diabetes management measures across 705 Medstat regions. HbA1c: glycated hemoglobin; LDL: low-density lipoprotein.

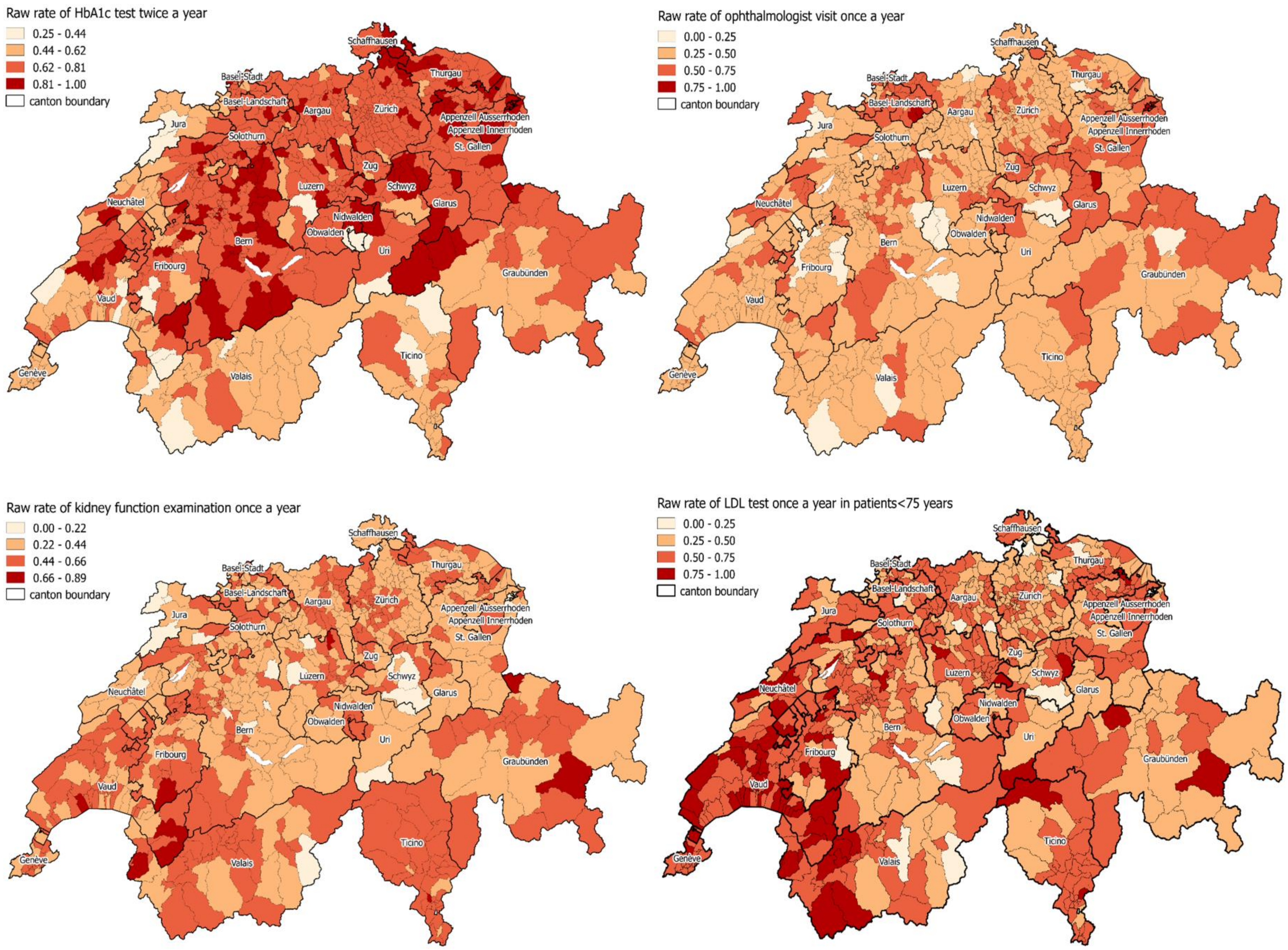
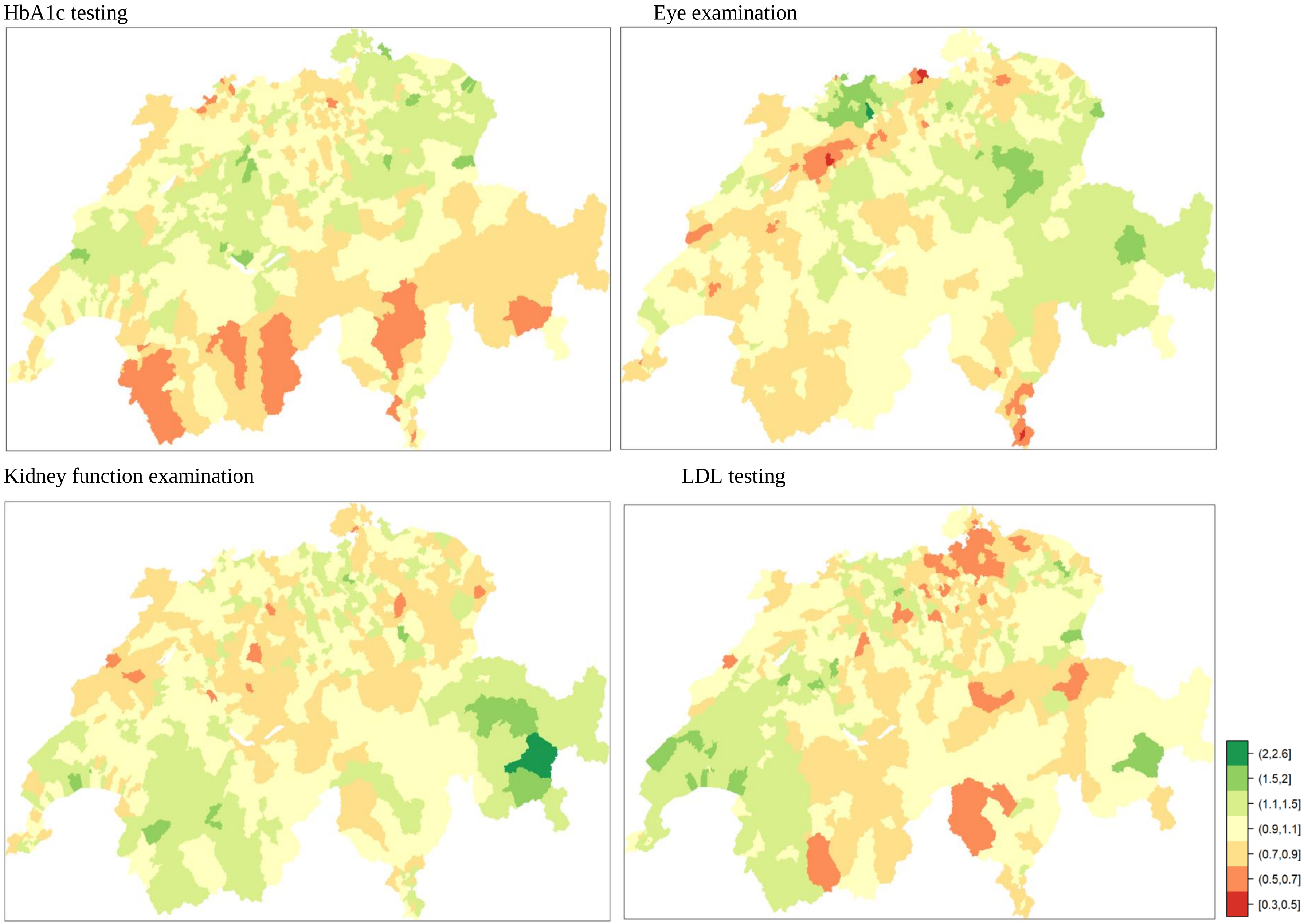


Figure 4. Unexplained variation in the utilization of four diabetes management measures in spatial multilevel models (Odds ratio values represent the odds of being adherent to the recommendation in one specific region compared to the average odds in the whole of Switzerland).



HbA1c: glycated hemoglobin; LDL: low-density lipoprotein.

DISCUSSION

Observed utilization rates in 2014 in Switzerland of four strongly recommended measures in diabetes management were 69.6% for biannual HbA1c testing, 44.3% for annual eye examination, 44.3% for annual kidney function examination, and 55.5% for annual LDL testing (in patients below 75 years). Associations between health insurance preferences and utilization were consistent across the four measures. Having supplementary insurance, choosing a lower deductible level, and choosing a managed care insurance model, were positively associated with being adherent to the recommendations. After adjusting for all available influencing factors and spatial autocorrelation, the unexplained regional variation was only moderate. There was no common pattern of spatial clustering visible across the four studied measures.

The observed utilization rates suggest that the underlying recommendations were not being followed perfectly. In a previous study using year 2011 to 2013 data from the same data source, similar utilization rates were reported: 70.0% of patients had biannual HbA1c testing, 44.2% an annual eye examination, 12% both serum creatinine and albuminuria testing annually, and 59.0% an annual lipid profile (total cholesterol, HDL and LDL, and triglycerides) [13]. The much higher rate of annual kidney function examination found in our study was mainly due to the use of a different definition of kidney function examination – a serum creatinine and/or albuminuria test.

Overall, few studies assessing the utilization of management measures recommended for diabetes patients exist, and some with discrepant findings. Some studies from the US, Japan and Italy are directly comparable with ours as they reported on the utilization of at least one of our four measures of interest. For HbA1c testing, one study conducted in Texas, USA, reported a 54.8% biannual utilization rate [36], while the utilization rate in an Italian study was relatively low (33.9%) [37]. By contrast, a study from Japan using claims data found an annual utilization rate of 95.8% [38]. For eye examination, studies in the US reported utilization rates of 15.3% (using claims data) [39], 70% (using telephone survey data) [40], and 75% (data from rural Latinos) [41]. A Japanese study reported a utilization rate of 35.6% [38], and the rate in the Italian study was even lower (15.6%) [37]. The Italian study also reported a utilization rate of LDL testing of 52.1%, which was similar to the finding in our study [37]. However, these different reports may not be entirely comparable to our study since the data sources and definitions of adherence to recommendations were different.

Patients' socio-demographics were associated with healthcare utilization. The probability of undergoing the four recommended measures was generally high between age 50 to 80 years, and decreased strongly thereafter. This was expected, because the elderly may have more barriers to accessing healthcare services due to poor health status. Moreover, the measures may become less important in the elderly as comorbidities and life expectancy affect priority setting and the benefit of preventing long-term complications. Women were more likely to undergo eye examination and kidney function examination in our study, which was consistent with previous findings [38, 42, 43]. However, women were less likely to undergo annual LDL testing, which might be due to more attention to the risk of cardiovascular disease in men. Myocardial infarction and related conditions have traditionally been perceived as predominantly male diseases. Living in an urban area was positively associated with more utilization of annual kidney function examination and LDL testing, which may be partly explained by easier access to healthcare facilities than in rural areas. The language region effects on the utilization of the four measures found in the present study indicated that the language region plays an important role in influencing healthcare utilization, which might be due to different culture and norms in each language region [44, 45].

One of the key findings in the present study was the association between health insurance preferences and utilization of diabetes management measures, in a setting with mandatory insurance and universal access to care. Very few studies have explored the effect of health insurance-related factors on services utilization in diabetes patients. Most of the available studies only concluded that uninsured patients were less likely to use healthcare services than insured patients or patients with private insurance [36, 40]. While non-insurance does practically not occur in Switzerland, foregoing healthcare due to out-of-pocket payments is a well-documented phenomenon [46]. This is one of the first studies to look into potential influences of health insurance characteristics on utilization of measures on diabetes management in detail. Overall, we found consistent effects of health insurance characteristics on utilization across the four measures of interest, and they persisted after controlling for other important influences such as age, health status, and to some extent income (defined by regional purchasing power index). Patients with higher deductibles tend to be healthier and willing to take more risks, and some invoices may be missed in these patients, which may partially explain our observation of lower utilization of the measures of interest. However, higher out-of-pocket costs may also make patients more reluctant to use these measures, which would make high deductibles a financial barrier to recommended healthcare [47]. Similarly, patients having supplementary insurance may be wealthier, and on average more health conscious. Thus they may tend to seek care more frequently and regularly, as observed in our study. Patients choosing a managed care model had more utilization of the measures studied than patients choosing an insurance model offering completely free physician choice. This finding is of great interest because it may indicate that strengthening a coordinative role of primary care physicians in managed care and providing financial incentives to the insured for choosing such models may also positively impact certain healthcare utilization indicators or outcomes. More health insurance incentives for participation in managed care models could be considered to achieve optimized healthcare utilization.

Presence of comorbidities was associated with more utilization, which may be due to more health awareness, and regular contact with healthcare providers. The finding of the lower uptake of LDL testing among prevalent cases was unexpected, as we would have expected prevalent patients to be more adherent to disease management and treatment compared to new patients [48]. The ophthalmologist density covariate reflected the access to eye examination services, and thus partly explained the higher utilization of eye examinations in patients living in regions with more ophthalmologists.

The unexplained geographic variation of utilization across small regions after adjusting for all available factors was only moderate for all four measures. One possible reason could be that we were unable to control for locally specific factors in our models. For example, physician-level factors such as age, years in practice, the awareness of and attitude towards clinical guidelines and recommendations varies across physicians and could affect the communication with patients and finally the patients' behaviours [49]. In addition, some patient level characteristics were not captured in our data source, e.g. educational level or marital status, as well as patients' preferences, which were demonstrated to be potentially related to the utilization of healthcare services [40]. By mapping out the unexplained spatial variation, we noted that the spatial patterns of regional variation were inconsistent across the four measures studied. These patterns indicated that the utilization of the four measures strongly recommended to diabetes patients differ substantially within Switzerland. The spatial variation of utilization might be even less prominent after controlling for more potentially influential factors unmeasured in the present study, such as physician characteristics which could not be captured from the claims data. Combination of different data sources may serve as a promising approach in future studies.

In addition to the limitations mentioned above, further potential weaknesses should be noted about this study. First, the health insurance claims data have limited clinical information; e.g.

outpatient diagnoses are lacking. The study population was selected according to the prescription of any diabetes medication, which may have led to some misclassification of prevalent and incident cases, this might partially account for the unexpected finding of more utilization of LDL testing in incident patients. It was impossible to distinguish between type 1 and type 2 diabetes. Patients with type 1 diabetes are a small fraction (approximately 8% in Switzerland in 2014[50]); they normally get the illness when they are young, tend to be well treated by specialists and are generally better at self-management. Due to the high costs of insulin injections and the associated medical supplies and devices, choosing a low deductible level is expected in type 1 diabetes patients. Such different behaviours may have had an impact on utilization of the four measures, and influenced our results to a certain degree. Besides, the laboratory tests results were not available from claims data and it was impossible to estimate the proportion of targets achieved for the diabetes management measures. Second, we used claims data from a single health insurer. Enrolees of other health insurers might theoretically have different characteristics and show different healthcare use patterns. However, the results presented were based on a population of 1.2 million covering all regions in Switzerland. The benefit package of the mandatory health insurance is defined at the federal level and is the same for all health insurers. Thus we expect little deviation of enrolees' features compared to the total Swiss population, and the results should be generalizable to the whole of Switzerland.

In conclusion, we observed that the utilization of four diabetes management measures was not optimal in Switzerland although these measures have been recommended broadly and are based on strong evidence. Socio-demographics, health insurance preferences and clinical characteristics were associated with their utilization. The presence of supplementary insurance, a lower deductible level and participation in a managed care plan were associated with higher utilization, consistently across the four measures. After controlling for available factors and spatial autocorrelation, maps of remaining variation indicated inconsistent patterns of utilization in the four measures. Our findings indicate that the uptake of strongly recommended measures for diabetes management could possibly be optimized by providing further incentives to insured and care providers through insurance scheme design. By contrast, due to the absence of marked regional variation patterns we conclude that there may be only limited potential for improvement by targeted regional intervention (e.g. awareness and promotion campaigns). Moreover, our novel approach aids in the identification of geographic variation and influencing factors of healthcare services use in Switzerland and comparable settings worldwide.

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Competing Interests Statement

The authors declare no competing interests.

Contributorship Statement

M.S, V.vW and H.D developed the underlying study program and generated the idea of the present study. B.B, E.B, C.B and A.U did data preparation and data management. W.W, O.G and J.B performed statistical analysis and wrote the main manuscript text. All authors together defined the analysis methodology, interpreted the statistical results and critically reviewed the manuscript.

Data Sharing Statement

The data underlying this study cannot be shared publicly because they are the property of Helsana (https://www.helsana.ch/en/helsana-group), and have restricted public access on grounds of patient privacy. The data are managed by Helsana and subsets of the database are available for researchers after request and under specific conditions. Data are available from Helsana (gesundheitskompetenz@helsana.ch) for researchers who meet the criteria for access to confidential data. Helsana will consider the possibilities of the research proposal and decide to grant access if the research questions can be answered with use of the Helsana data. When requests are granted, data are accessible only in a secure environment.

Table S1. ORs and 95%CIs of fixed effects in multilevel multivariable models and spatial multilevel models for HbA1c testing, eye examination and kidney function examination.

Characteristics	Biannual HbA1c testing		Annual eye examination		Annual kidney function examination	
	multilevel model	spatial multilevel model	multilevel model	spatial multilevel model	multilevel model	spatial multilevel model
Female gender	0.97 (0.92, 1.00)	0.97 (0.93, 1.01)	1.16 (1.12, 1.21)	1.17 (1.13, 1.22)	1.07 (1.04, 1.11)	1.07 (1.03, 1.11)
Urban residence	0.95 (0.89, 1.01)	0.98 (0.91, 1.04)	-	-	1.14 (1.09, 1.21)	1.12 (1.05, 1.19)
Purchasing power index	0.87 (0.79, 0.98)	0.91 (0.79, 1.06)	1.26 (1.09, 1.43)	1.19 (1.03, 1.39)	1.10 (1.00, 1.21)	1.05 (0.91, 1.21)
Language						
German	1	1	1	1	1	1
French	0.51 (0.47, 0.55)	0.54 (0.46, 0.65)	0.83 (0.77, 0.89)	0.98 (0.80, 1.21)	1.18 (1.10, 1.26)	1.13 (0.95, 1.34)
Italian	0.45 (0.40, 0.50)	0.51 (0.37, 0.72)	0.80 (0.69, 0.90)	1.03 (0.66, 1.61)	1.58 (1.43, 1.78)	1.54 (1.10, 2.16)
Deductible (CHF)						
300	1	1	1	1	1	1
500	0.94 (0.90, 0.98)	0.95 (0.90, 0.99)	0.88 (0.84, 0.92)	0.89 (0.85, 0.94)	0.94 (0.90, 0.98)	0.95 (0.90, 0.99)
1000	0.78 (0.68, 0.90)	0.78 (0.68, 0.91)	0.71 (0.61, 0.82)	0.72 (0.62, 0.83)	0.74 (0.65, 0.85)	0.75 (0.65, 0.86)
1500	0.75 (0.65, 0.86)	0.76 (0.66, 0.87)	0.75 (0.64, 0.86)	0.77 (0.67, 0.89)	0.68 (0.59, 0.78)	0.69 (0.60, 0.79)
2000	0.71 (0.49, 1.01)	0.70 (0.49, 1.00)	0.62 (0.40, 0.89)	0.64 (0.42, 0.93)	0.58 (0.40, 0.81)	0.59 (0.40, 0.85)
2500	0.61 (0.52, 0.70)	0.61 (0.53, 0.71)	0.56 (0.47, 0.65)	0.57 (0.48, 0.66)	0.69 (0.59, 0.80)	0.69 (0.59, 0.80)
Insurance coverage						
Only mandatory	1	1	1	1	1	1
Mandatory and supplementary	1.23 (1.18, 1.30)	1.22 (1.16, 1.28)	1.29 (1.23, 1.35)	1.28 (1.22, 1.34)	1.10 (1.05, 1.15)	1.08 (1.03, 1.13)
Mandatory insurance model						
Standard	1	1	1	1	1	1
Managed care	1.14 (1.09, 1.18)	1.13 (1.08, 1.18)	1.18 (1.13, 1.22)	1.17 (1.12, 1.22)	1.05 (1.01, 1.08)	1.04 (1.00, 1.08)
Supplementary hospital insurance	-	-	1.32 (1.26, 1.39)	1.30 (1.24, 1.37)	1.10 (1.04, 1.15)	1.08 (1.03, 1.14)
Multimorbidity						
none	1	1	1	1	1	1
1	1.11 (1.03, 1.20)	1.12 (1.03, 1.21)	0.95 (0.88, 1.03)	0.97 (0.90, 1.06)	1.05 (0.97, 1.13)	1.06 (0.99, 1.15)
2	1.21 (1.13, 1.31)	1.21 (1.12, 1.32)	1.07 (0.99, 1.17)	1.09 (1.01, 1.18)	1.19 (1.11, 1.28)	1.21 (1.12, 1.30)
>2	1.25 (1.16, 1.35)	1.25 (1.16, 1.35)	1.23 (1.14, 1.34)	1.25 (1.16, 1.35)	1.36 (1.27, 1.46)	1.38 (1.28, 1.48)
Diabetes category						
Incident	1	1	1	1	1	1
Oral drug only	0.99 (0.93, 1.05)	0.98 (0.92, 1.04)	1.13 (1.07,1.21)	1.13 (1.06, 1.20)	0.97 (0.91, 1.02)	0.96 (0.91, 1.02)
Insulin	1.83 (1.71, 1.97)	1.81 (1.69, 1.95)	1.86 (1.74, 2.00)	1.85 (1.73, 1.98)	1.08 (1.01, 1.15)	1.07 (1.00, 1.14)
Ophthalmologist density/10000 inhabitants	-	-	1.20 (1.02, 1.39)	1.13 (0.99, 1.30)	-	-

OR: odds ratio; CI: confidence/credible interval; HbA1c: glycated haemoglobin; CHF: Swiss franc; Multimorbidity: pharmaceutical cost groups (PCG) were used to deduce chronic morbidity based on drug use.

Table S2. ORs and 95%CIs of fixed effects in multilevel multivariable models and spatial multilevel models for LDL testing.

Characteristics	Annual LDL testing	
	multilevel model	spatial multilevel model
Female gender	0.90 (0.86, 0.94)	0.89 (0.85, 0.93)
Urban residence	1.12 (1.06, 1.24)	1.12 (1.04, 1.21)
Language		
German	1	1
French	2.17 (1.98, 2.36)	1.69 (1.38, 2.07)
Italian	1.42 (1.25, 1.61)	1.49 (1.01, 2.21)
Deductible (CHF)		
300	1	1
500	0.97 (0.92, 1.03)	0.97 (0.92, 1.03)
1000	0.88 (0.76, 1.03)	0.88 (0.75, 1.03)
1500	0.73 (0.63, 0.85)	0.74 (0.63, 0.86)
2000	0.64 (0.41, 0.92)	0.63 (0.42, 0.94)
2500	0.64 (0.54, 0.74)	0.64 (0.55, 0.75)
Insurance coverage		
Only mandatory	1	1
Mandatory and supplementary	1.12 (1.07, 1.18)	1.12 (1.06, 1.18)
Mandatory insurance model		
Standard	1	1
Managed care	1.09 (1.04, 1.14)	1.08 (1.03, 1.13)
Supplementary hospital insurance	1.05 (0.98, 1.12)	1.04 (0.98, 1.11)
Multimorbidity		
none	1	1
1	1.16 (1.06, 1.26)	1.16 (1.07, 1.26)
2	1.43 (1.32, 1.56)	1.44 (1.33, 1.57)
>2	1.56 (1.43, 1.68)	1.57 (1.45, 1.70)
Diabetes category		
Incident	1	1
Oral drug only	0.92 (0.86, 0.99)	0.91 (0.84, 0.98)
Insulin	0.92 (0.85, 0.99)	0.92 (0.86, 0.98)

OR: odds ratio; CI: confidence/credible interval; LDL: low-density lipoprotein; CHF: Swiss franc; Multimorbidity: pharmaceutical cost groups (PCG) were used to deduce chronic morbidity based on drug use

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Chapter IV

Regional variation and effects of health insurance-related factors on the utilization of 24 diverse healthcare services

This chapter is based on the third article
Submitted to *Implementation Science*

ABSTRACT

Objectives: We aimed to a) describe regional variation in the utilization of 24 diverse healthcare services in eligible populations in Switzerland, and b) identify potential influencing factors, especially health insurance-related characteristics, and explore the consistency of their effects across the selected services.

Design and Setting: Cross-sectional population-based study in Switzerland using health insurance claims data for the year 2014. The studied healthcare services were predominantly outpatient, ranging from screening to secondary prevention. We performed a comprehensive methodological approach including small area variation analysis, spatial autocorrelation assessment, and multilevel modelling using 106 small regions as the higher level.

Participants: For each selected service, the target population was identified based on applicable clinical recommendations. Individual-level information included socio-demographics, clinical characteristics, health insurance-related characteristics, and resident region.

Main outcome measure: For each service, the outcome variable was the use of the service by eligible individuals. The degree of adjusted variation in healthcare utilization was evaluated by median odds ratios (MORs).

Results: Unadjusted utilization rates varied considerably across the 24 healthcare services, ranging from 3.5% (osteoporosis screening) to 76.1% (recommended thyroid disease screening sequence). The effects of health insurance-related characteristics were mostly consistent. A higher annual deductible level was mostly associated with lower utilization. Supplementary insurance, supplementary hospital insurance and having chosen a managed care model were associated with higher utilization of most services. Managed care models showed a tendency towards more recommended care. After adjusting for multiple influencing factors, the unexplained regional variation was generally small across the 24 services, with all MORs below 1.5.

Conclusions: The observed utilization rates seemed suboptimal for many of the selected services. For all of them, the unexplained regional variation was relatively small. Our findings confirmed the importance and consistency of effects of health insurance-related factors, indicating that healthcare utilization might be further optimized through adjustment of insurance scheme designs.

SUMMARY BOX

Section 1: What is already known on this topic

- Large regional variation in the utilization of healthcare services exists
- Healthcare utilization and regional variation may be driven by multiple factors

Section 2: What this study adds

- Across various healthcare services, utilization was substantially and consistently associated with health insurance-related characteristics, such as managed care versus standard fee-for-service care model, supplementary in addition to mandatory insurance, and annual deductibles
- Residual regional variation in utilization after multivariable adjustment was small

Introduction

A recent systematic review found a substantial evidence base for large variation in the utilization of healthcare services across regions, hospitals, and healthcare providers [1]. The ubiquity and persistence of such variation cannot simply be explained by variation in the actual care needs of different populations [2]. A substantial portion may reflect inappropriate variability due to unequal access to care, potentially detrimental for quality of care and costs [3]. This unwarranted component, although difficult to quantify, should be minimized in order to improve the quality, equity, and efficiency of healthcare [4]. Regional variation may be driven by multiple factors, including patient socio-demographics, clinical characteristics, availability of physicians and healthcare facilities, and healthcare system-related factors [2]. They can function as personal, financial, and organizational modifiers of access to care [5]. System-related factors (e.g. relating to health insurance systems, national legislation or programs) are of strong interest, because their modification may offer big levers to reduce unwarranted variation at a national level. The credibility of related findings is stronger if effects are consistently observed across diverse healthcare services.

Existing studies of regional variation in utilization mostly applied methods of small area variation analysis (SAVA) [1]. Several problems were identified. First, numerous analyses focused on only part of a country, without nationwide coverage. Second, the selection of studied healthcare services was often arbitrary and opportunity-driven, suggesting that future studies should focus on services of high clinical importance, policy relevance, and public awareness. Third, the causes and drivers of variation were rarely explored. Only few studies controlled for a limited number of possible influencing factors such as individual socio-demographics or clinical characteristics [6, 7]. Finally, most studies assessed the variation in utilization of a single service, or one category of services (e.g. related surgical procedures) [8, 9]. More comprehensive studies simultaneously comparing a wider range of services are currently missing. Around 40% of studies of variation in healthcare utilization used administrative data routinely collected for billing purposes. Although subject to certain limitations (e.g. restricted clinical information), health insurance claims data play an important role in health services research [10, 11].

In the present study, we aimed to select a variety of healthcare services and their target populations based on applicable clinical recommendations, and to describe regional variation in their utilization in Switzerland, a system with universal care access and high out-of-pocket expenditures, using claims data. Specific goals were to a) evaluate unadjusted and adjusted regional variation in utilization in eligible populations, b) identify potential influencing factors, especially health insurance-related characteristics, and c) explore the consistency of these factors' effects across the selected services.

Methods

Selection of healthcare services and eligible populations

Our selection of healthcare services focused on primary healthcare for major non-communicable diseases and was based on a systematic approach described earlier [12]. Recommendation statements from clinical practice guidelines of Swiss, European and relevant international medical societies, used in Switzerland, were considered pragmatically according to clinical relevance, expected frequency of service use, size of the eligible population, and feasibility to identify the population and service from Swiss health insurance claims data. Some services outside primary healthcare were included to extend the spectrum of populations investigated and reflect services currently debated in Switzerland.

The final selection consisted of 24 services reflecting different categories of care, including screening (N=4), diagnosis (N=6), primary prevention (N=1), treatment (N=4) and secondary prevention (N=9). Table 1 lists their descriptions, eligible populations, and recommendation status.

Study design and populations

Our cross-sectional study used mandatory health insurance claims data provided by Helsana, one of the largest health insurers in Switzerland. The underlying database covered around 1.2 million people, 15% of the Swiss population. The eligible population for each healthcare service was identified from persons enrolled with Helsana during 2014 (Table 1). Asylum seekers, Helsana employees, enrolees living outside Switzerland, with incomplete address information, or living in nursing homes with lump-sum reimbursement of some healthcare services were excluded.

Table 1. Definition and description of selected 24 healthcare services.

Category	Healthcare service	Service description and frequency	Study population	Recommendation
Screening	Colon cancer screening	Colonoscopy/ year	Anyone 50-69 years old	Colonoscopy should be done every 10 years for people 50-69 years old.
	Breast cancer screening	Mammography/ year	50-74 years old women	Mammography should be done every 2 years for 50-74 years old women.
	Prostate cancer screening	Prostate-specific antigen (PSA) testing/ year	50-70 years old men	Routine prostate cancer screening with PSA testing is not recommended.
	Osteoporosis screening	Dual-energy x-ray absorptiometry (DXA)/ year	People over 60 and with risk factors[a] of spontaneous fractures	DXA densitometry is recommended for patients with spontaneous fractures or increased risk of them.
Diagnosis	DM: HbA1c test	Glycated hemoglobin (HbA1c) test twice/ year	Adult drug-treated diabetes patients	HbA1c test should be done for diabetes patients at least twice a year.
	DM: kidney exam	Albuminuria and serum creatinine tests/ year	Adult drug-treated diabetes patients	Albuminuria and serum creatinine tests should be done for diabetes patients at least once a year.
	DM: LDL test	Low-density lipoprotein (LDL) test/ year	Adult drug-treated diabetes patients under 75 years old	LDL test should be done for diabetes patients at least once a year.
	DM: eye check	Ophthalmologist visit/ year	Adult drug-treated diabetes patients	Eye exam should be performed for diabetes patients at least once a year.
	TSH	Thyroid stimulating hormone (TSH) test without T3 and T4 tests on the same day	Adults without thyroid disease and receiving TSH test	TSH should be measured as an initial screening test for hypo/hyperthyroidism, while T3 and T4 test should follow if TSH is abnormal.
	POCR	Outpatient preoperative chest radiography (POCR) up to 2 months before surgery	Adult patients with inpatient surgical procedures	Routine chest radiography is not recommended before surgery.
Primary prevention	Influenza vaccination	Influenza outpatient vaccination/ year	People over 65 years old or with a specified chronic condition[b]	People over 65 years old and patients with chronic conditions, specified by Federal Office of Public Health, should be vaccinated against influenza every year.
Treatment	BZD	Cumulative prescription of benzodiazepines (BZD) for >8 weeks/ year	Anyone over 65 years old	Long-term use of benzodiazepines and other hypnotics is discouraged for old patients.
	PPI	Cumulative prescription of proton pump inhibitors (PPI) or H2 histamine receptor antagonists (H2) for >8 weeks/ year	Adults receiving PPI or H2 drugs	PPI should not be used at maximal dose for prolonged periods of time.
	Outpatient procedures	Specified surgical procedures[c] done in the outpatient setting	Adult patients with specified surgical procedures (either as in- or outpatient)	If none of the special conditions apply, certain surgical procedures should be done in the outpatient setting.
	C-section	Cesarean section (C-section)	Women giving birth without absolute indications[d] for C-section	C-section should not be performed unless absolute or relative indications are present.

Table 1. continued

Secondary prevention	AMI: aspirin	Aspirin prescription within 2 weeks after acute myocardial infarction (AMI)	Adult patients with AMI	All myocardial infarction patients should take aspirin long-term.
	AMI: statin	High-dose statin prescription within 2 weeks after AMI	Adult patients with AMI	All myocardial infarction patients should get statins long-term.
	AMI: beta-blocker	Beta-blocker prescription within 2 weeks after AMI	Adult patients with AMI	All myocardial infarction patients with heart failure or impaired function should get beta-blockers long-term.
	AMI: ACE/ARB	Angiotensin converting enzyme (ACE) or angiotensin receptor blocker (ARB) antihypertensive medication prescription within 2 weeks after AMI	Adult patients with AMI	All myocardial infarction patients with heart failure or impaired function should get ACE or ARB antihypertensive medication long-term.
	AMI: P2Y	P2Y antiplatelet drug[e] prescription within 2 weeks after AMI	Adult patients with AMI	All myocardial infarction patients should get P2Y antiplatelet drugs for at least 1-12 months according to the bleeding risk profile and AMI treatment.
	PPI with NSAID	PPI prescription within 1 month or up to 3 months before initial long-term nonsteroidal anti-inflammatory drug (NSAID) prescription	Adult patients with a cumulative NSAID prescription of >8 weeks at maximal dose	Patients taking long-term NSAID and with risk factors for gastric ulcer[f] should also take PPI.
	PAD: statin	Prescription of statins within 3 months after peripheral artery disease (PAD) identification	Adult patients undergoing diagnostic or treatment procedures for PAD	Statins are recommended for all patients with PAD.
	Afib: anticoagulation	Oral anticoagulation prescription within 2 weeks after atrial fibrillation (Afib) identification	Adult patients with atrial fibrillation diagnosis and additional risk factors[g]	All patients with atrial fibrillation should be prescribed oral anticoagulation for embolic events prevention according to the CHA_2DS_2-VASc score.
	GKK	Glucocorticoid (GKK) prescription within 1 month or up to 3 months before disease-modifying antirheumatic drug (DMARD) prescription	Adult patients with a new prescription of DMARD by a rheumatologist	Short-term glucocorticoids should be taken with newly prescribed DMARD.

a. Recent distal radius, proximal humerus, vertebral or femoral fracture, use of drugs increasing the risk of osteoporosis, use of oral glucocorticoids, diabetes, ankylosing spondylitis, osteogenesis imperfecta, rheumatoid arthritis, inflammatory bowel disease, Cushing's disease, alcohol or nicotine abuse, chronic liver disease, gastrectomy, malnutrition, hypogonadism, hyper- or hypothyroidism, and hyperparathyroidism. Patients currently treated or diagnosed with osteoporosis were excluded. b. Cardiovascular disease, chronic pulmonary disease, diabetes, chronic liver disease, renal failure, immune deficiency, systemic neurologic disorders. c. Varicose veins ligation and stripping, surgical procedures of haemorrhoids, inguinal hernia and cervix, knee arthroscopy and meniscectomy, tonsillectomy. d. Placental, umbilical cord or fetal pathology, HIV or genital HSV infection, or multiple pregnancy. e. Clopidogrel, prasugrel or ticagrelor. f. Concurrent use of antiplatelet, anticoagulant drugs, oral glucocorticoids or recent hospitalization with any major bleeding. g. Risk factors (congestive heart failure, hypertension, age 65-74 or ≥75 years old, diabetes, previous stroke, transient ischemic attack, or thromboembolism, cardiovascular disease, female sex) were extracted from available claims data and summed according to CHA2DS2-VASc score. Patients with CHA2DS2-VASc score of ≥2 for males and ≥3 for females were included. DM: diabetes mellitus

Swiss mandatory health insurance covers a federally defined, uniform benefit package for anyone living in Switzerland regardless of health status. A higher annual deductible (of Swiss Francs 500, 1000, 1500, or 2500) can be chosen instead of the legal minimum of 300, implying lower premiums. People can also choose between standard fee-for-service and managed care models [13, 14], the latter requiring a specific general practitioner or telemedicine provider as the first contact for a new health problem, and resulting in lower premiums. In addition to mandatory insurance, a variety of supplementary insurance products can be bought, for instance, supplementary hospital insurance allowing for hospitalization in semiprivate or private wards.

The data provided by Helsana were anonymized. According to the national ethical and legal regulations, ethical approval was not needed for this type of analysis. This was confirmed by a waiver of the competent ethics committee (Kantonale Ethikkommission Zürich, dated 11th January 2017, BASEC-Nr. Req-2017-00011).

Outcome and explanatory variables

For each of the selected services, the outcome variable was whether the service was used by each member of the eligible population (Table 1). Candidate explanatory variables available for all 24 healthcare services included a) socio-demographics, i.e. age, gender, language region, purchasing power index, and urban/rural residence, b) health insurance-related characteristics, including having any supplementary insurance, having supplementary hospital insurance, choice of a standard or managed care model, choice of annual deductible, c) number of chronic comorbidities as indicated by pharmaceutical cost groups [15]. In people with supplementary hospital insurance, we could not distinguish the additional presence of other supplementary insurances but only evaluate a mixed effect. To verify the effect of supplementary hospital insurance, we performed sensitivity analyses using different combinations of available explanatory variables. We further included service-specific clinical conditions of relevance and a few service-specific non-individual level variables. For preoperative chest radiography (POCR), the type of hospital performing the surgery (central, primary, surgical, or other specialized hospital) was considered. For breast cancer screening, we determined if a cantonal-level breast cancer screening program existed. Analysis of eye examinations in diabetes patients considered ophthalmologist density per 10,000 inhabitants in each region. For surgical procedures recommended to be performed in outpatient settings, hospital bed density per 1,000 inhabitants in each region was considered.

Geographic units

We used spatial mobility regions (mobilité spatiale - MS) as the geographic level of analysis (N=106). MS regions are defined by the Swiss Federal Statistical Office and used as intermediate-size units of analysis for scientific and regional policy purposes [16]. Each study participant's residence was assigned to the corresponding MS region.

Statistical analysis

A four-step analytical approach was applied to all selected healthcare services. In the first step, we descriptively analysed each study population's characteristics.

Second, we calculated raw utilization rates per MS region and described the degree of regional variation using small area variation analysis (SAVA). We computed extremal quotient (EQ), interquartile range (IQR), coefficient of variation (CV) and systematic component of variation (SCV). SCV estimates the systematic component of variation between small regions by subtracting random from total variation, considering age and sex [8, 17]. SCV above 3, between 5.4 and 10, and above 10 suggest relevant, considerable, and very high variation in utilization, respectively [18]. We further checked spatial autocorrelation of regional utilization rates with global Moran's I statistic [19]. Moran's I measures the correlation of a variable with itself across space, ranging from -1 to 1. Moran's I close to 0 suggests random distribution across space. Significantly positive (negative) Moran's I values indicate that neighbouring regions are more similar (dissimilar) than distant regions.

Third, we performed two-level logistic regression modelling with individuals as the lower-level and MS regions as the higher-level of analysis. For POCR, a cross-classified model was developed, with hospitals where surgeries were performed as an additional level cross-classified with MS regions, as we assumed an impact of hospitals on POCR utilization [20]. A sensitivity analysis used our standard, two-level approach. Inclusion of explanatory variables was based on the deviance information criterion [21]. We calculated multivariable-adjusted odds ratios (ORs) and 95% confidence intervals (95%CIs) to estimate the effect of explanatory variables on utilization.

In the last step, we assessed the degree of unexplained regional variation after multilevel modelling by calculating median odds ratios (MORs) and variance partition coefficients (VPCs). MOR is extrapolated from the variance of random effects in multilevel models. It compares the adjusted odds of using the analysed service in two individuals with identical characteristics, but living in two randomly selected regions. The median of all possible resulting ORs is defined as MOR. MOR is always above one, as the higher-propensity region is always compared with the lower-propensity region for the outcome of interest. VPC represents the proportion of total variation accounted for systematic differences between MS regions. The interpretation of the magnitude of MOR should be related to VPC [22]. A relatively big MOR in combination with a considerable VPC indicates substantial regional variation [22]. In addition, we checked for spatial autocorrelation in model residuals across MS regions, again using global Moran’s I statistic [23, 24].

Statistical analyses were performed using R 3.4.4 [25], STATA 13, and MLwiN 3.04 [26] integrated in STATA using the runmlwin package [27]. Spatial autocorrelation analysis was done with GeoDa 1.10 [28]. The results from all selected healthcare services were finally compared graphically.

Results

Study populations

Across the 24 selected healthcare services, eligible population size ranged from 409,960 for influenza vaccination to 1,992 for new prescription of a disease-modifying anti-rheumatic drug (DMARD) that should be prescribed concomitantly with a glucocorticoid (Table 2). The mean age of populations ranged from 31.9 years (women giving birth without absolute indications for C-section), to 80.8 years (patients with atrial fibrillation and indication for oral anticoagulation). Overall utilization varied from 3.5% of older people with risk factors for fractures receiving osteoporosis screening, to 76.1% of eligible people receiving a thyroid-stimulating hormone (TSH) test as recommended.

Table 2. Basic characteristics of study populations for selected 24 healthcare services.

Service category	Healthcare service	Total Number	Age (mean, sd)	Female gender	Utilization rate
Screening	Colon cancer screening	276387	58.6 (5.8)	142675 (51.6%)	5.9%
	Breast cancer screening	178145	61.0 (7.2)	-	20.9%
	Prostate cancer screening	145874	59.1 (6.2)	-	28.4%
	Osteoporosis screening	97237	72.5 (8.5)	60812 (62.5%)	3.5%
Diagnosis	DM: HbA1c test	49198	66.6 (13.0)	22138 (45.0%)	69.6%
	DM: kidney exam	49198	66.6 (13.0)	22138 (45.0%)	44.3%
	DM: LDL test	33975	60.1 (11.2)	13977 (41.2%)	44.3%
	DM: eye check	49198	66.6 (13.0)	22138 (45.0%)	55.5%
	TSH	169232	56.8 (18.5)	111847 (66.1%)	76.1%
	POCR	47215	60.3 (17.2)	27086 (57.4%)	13.0%
Primary prevention	Influenza vaccination	409960	64.1 (16.3)	230202 (56.2%)	20.9%
Treatment	BZD	243951	75.0 (7.6)	141986 (58.2%)	18.6%
	PPI	153523	55.7 (17.8)	93543 (60.9%)	55.5%
	Outpatient procedures	10656	50.5 (13.7)	7719 (72.4%)	61.4%
	C-section	9449	31.9 (5.1)	-	28.5%
Secondary prevention	AMI: aspirin	2232	72.4 (13.7)	801 (35.9%)	47.0%
	AMI: statin	2232	72.4 (13.7)	801 (35.9%)	34.2%
	AMI: beta-blocker	2232	72.4 (13.7)	801 (35.9%)	42.1%
	AMI: ACE/ARB	2232	72.4 (13.7)	801 (35.9%)	43.8%
	AMI: P2Y	2232	72.4 (13.7)	801 (35.9%)	46.8%
	PPI with NSAID	95072	61.0 (16.2)	60804 (64.0%)	43.5%
	PAD: statin	23868	63.6 (16.5)	12113 (50.7%)	28.5%
	Afib: anticoagulation	8291	80.8 (7.9)	4037 (48.7%)	27.5%
	GKK	1992	59.2 (15.3)	1369 (68.7%)	58.7%

sd: standard deviation; DM: diabetes mellitus; HbA1c: glycated haemoglobin; LDL: low-density lipoprotein; TSH: thyroid stimulating hormone; POCR: outpatient preoperative chest radiography; BZD: benzodiazepines; PPI: proton pump inhibitor; C-section: Caesarean section; AMI: acute myocardial infarction; ACE: angiotensin converting enzyme; ARB: angiotensin receptor blocker; P2Y: clopidogrel, prasugrel or ticagrelor; NSAID: nonsteroidal anti-inflammatory drug; PAD: peripheral artery disease; Afib: atrial fibrillation; GKK: Glucocorticoid.

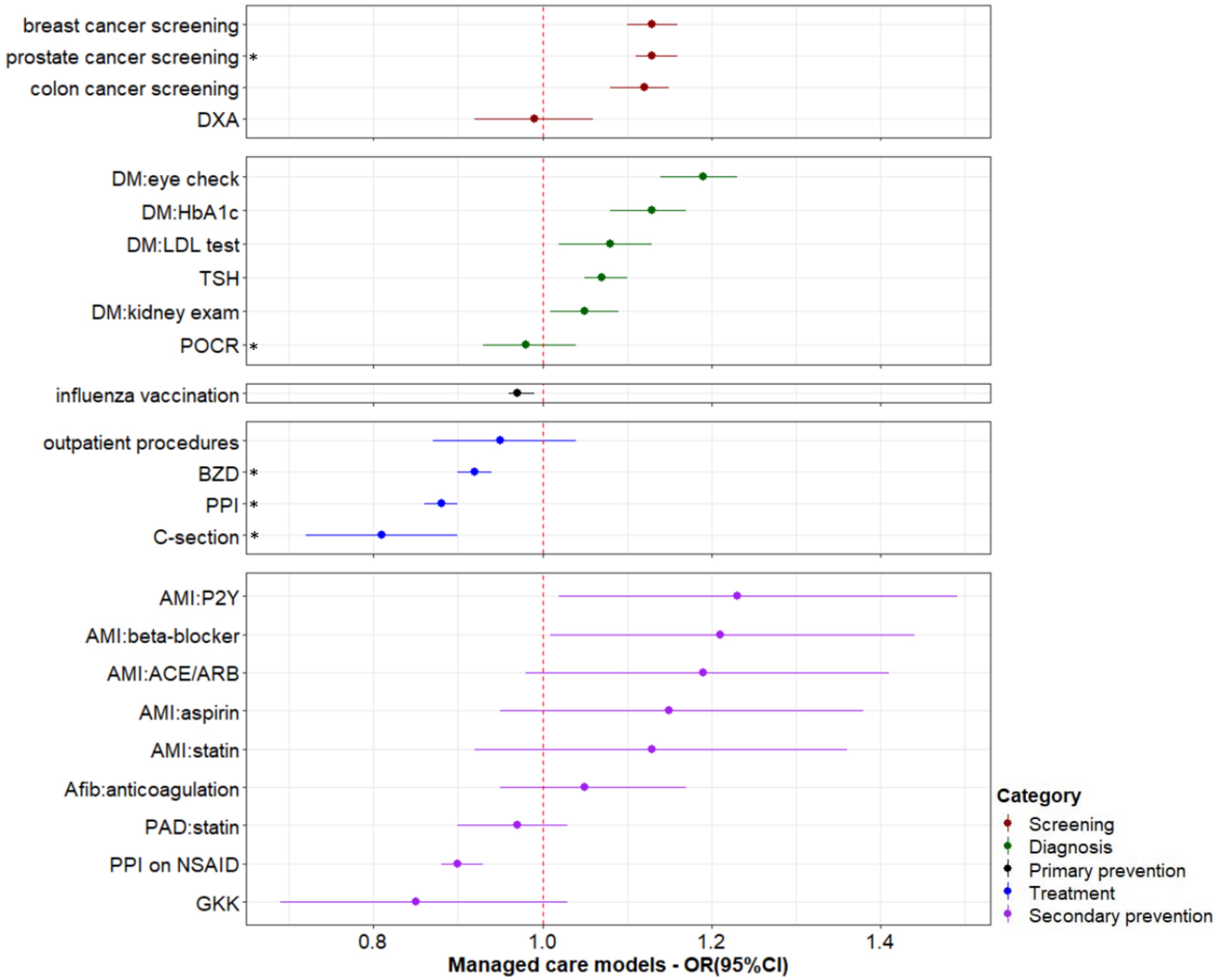
Effects of explanatory variables

After multivariable adjustment, we observed inconsistent associations between socio-demographic variables and healthcare utilization (Table S1). Age showed a nonlinear effect in most cases; utilization typically reached a peak between 50-70 years and then decreased (Figure S1). Gender effects were mostly not prominent. However, there was an OR of 3.66 (95%CI: 3.10, 3.99) for osteoporosis screening use in women, while the OR for statin prescription in women with peripheral artery disease was 0.52 (95%CI: 0.49, 0.55). Having more comorbidities was significantly associated with increased use of most services, but not secondary prevention medication after acute myocardial infarction (AMI) or oral anticoagulation in patients with atrial fibrillation.

The effects of health insurance-related characteristics were mostly consistent across the 24 healthcare services. Having chosen a managed care model was significantly associated with increased use of most services in the categories of screening, diagnosis and secondary prevention, but decreased use of the four services in the treatment category (three of which were not recommended; the fourth were surgical procedures in the outpatient setting). The strongest effect was noted for C-section, with an OR of 0.81 (95%CI: 0.73, 0.91) (Figure 1). Having any supplementary insurance was associated with increased use of most services (Figure 2). A negative effect was again seen for C-section, with an OR of 0.86 (95%CI: 0.77, 0.96). Having supplementary hospital insurance was also associated with increased use of most services, including C-section with an OR of 1.58 (95%CI: 1.37, 1.83). People with supplementary hospital insurance were also more likely to undergo surgical procedures with potential for being performed in the outpatient setting, as inpatients (Figure 3). Related sensitivity analyses showed consistent results. Having a higher deductible was associated with lower utilization of most healthcare services (Figure 4). All ORs and 95%CIs are shown in Table S1.

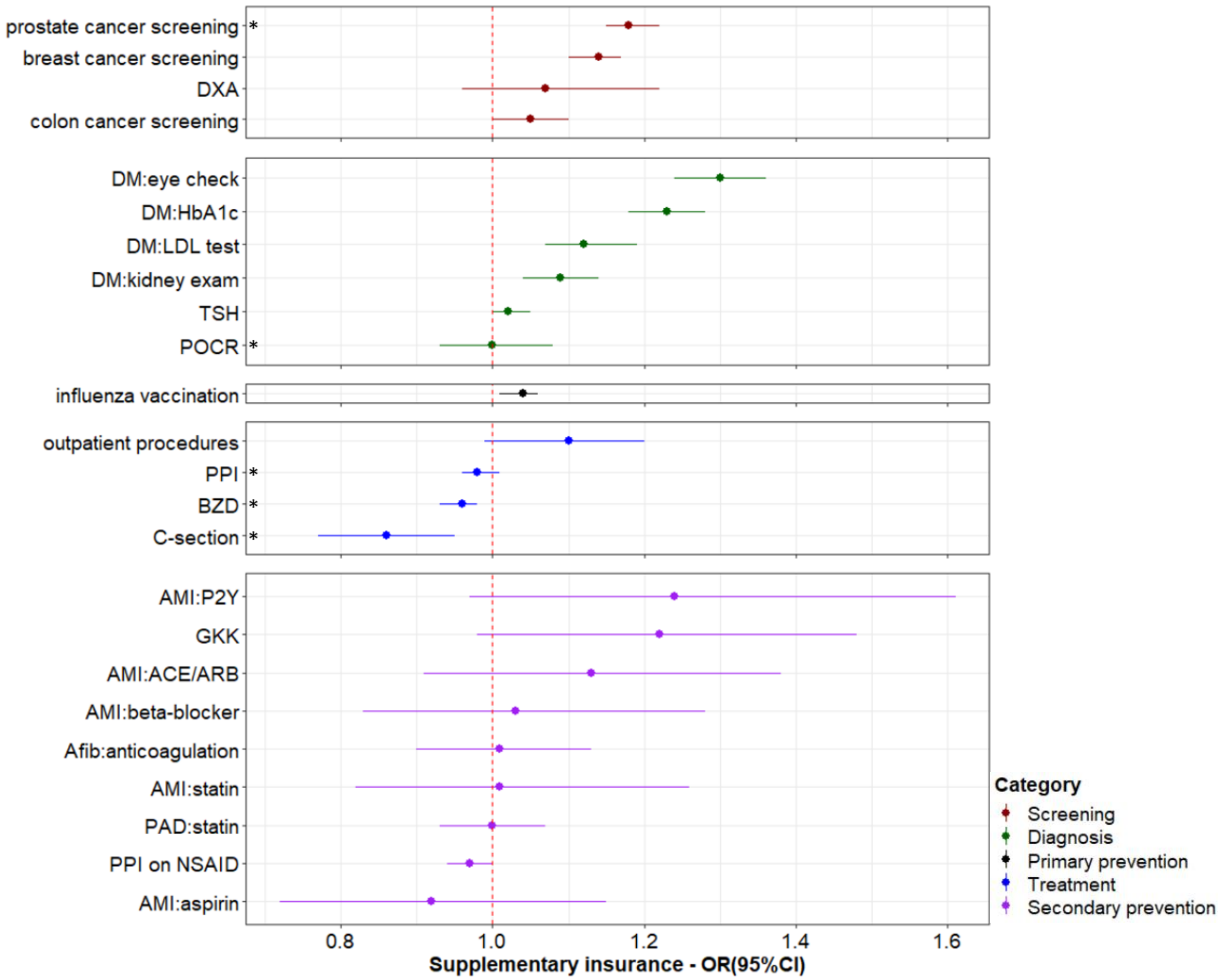
Service-specific factors were associated with healthcare utilization. Patients having surgery in primary, surgical and other specialized hospitals were more likely to receive POCR than patients in central hospitals. Residing in a canton with a coordinated breast cancer screening program was associated with increased mammography utilization with an OR of 1.80 (95%CI: 1.66, 1.97). Associations of ophthalmologist density with eye examinations in diabetes patients with an OR of 1.09 (95%CI: 0.93, 1.23) and of hospital bed density with having surgical procedures in the outpatient setting with an OR of 0.97 (95%CI: 0.94, 1.01)) were non-significant.

Figure 1. Effects of managed care models on healthcare services utilization.



*Indicates services that are discouraged and therefore an odds ratio <1 indicates better conformity with recommendations, for all other services, an odds ratio >1 indicates greater use and better guideline conformity. OR: odds ratio; CI: confidence interval; DM: diabetes mellitus; DXA: Dual-energy x-ray absorptiometry; HbA1c: glycated haemoglobin; LDL: low-density lipoprotein; TSH: thyroid stimulating hormone; POCR: outpatient preoperative chest radiography; BZD: benzodiazepines; PPI: proton pump inhibitor; C-section: Caesarean section; AMI: acute myocardial infarction; ACE: angiotensin converting enzyme; ARB: angiotensin receptor blocker; P2Y: clopidogrel, prasugrel or ticagrelor; NSAID: nonsteroidal anti-inflammatory drug; PAD: peripheral artery disease; Afib: atrial fibrillation; GKK: Glucocorticoid.

Figure 2. Effects of supplementary insurance on healthcare services utilization.



*Indicates services that are discouraged and therefore an odds ratio <1 indicates better conformity with recommendations, for all other services, an odds ratio >1 indicates greater use and better guideline conformity. OR: odds ratio; CI: confidence interval; DM: diabetes mellitus; DXA: Dual-energy x-ray absorptiometry; HbA1c: glycated haemoglobin; LDL: low-density lipoprotein; TSH: thyroid stimulating hormone; POCR: outpatient preoperative chest radiography; BZD: benzodiazepines; PPI: proton pump inhibitor; C-section: Caesarean section; AMI: acute myocardial infarction; ACE: angiotensin converting enzyme; ARB: angiotensin receptor blocker; P2Y: clopidogrel, prasugrel or ticagrelor; NSAID: nonsteroidal anti-inflammatory drug; PAD: peripheral artery disease; Afib: atrial fibrillation; GKK: Glucocorticoid.

Figure 3. Effects of supplementary hospital insurance on healthcare services utilization.

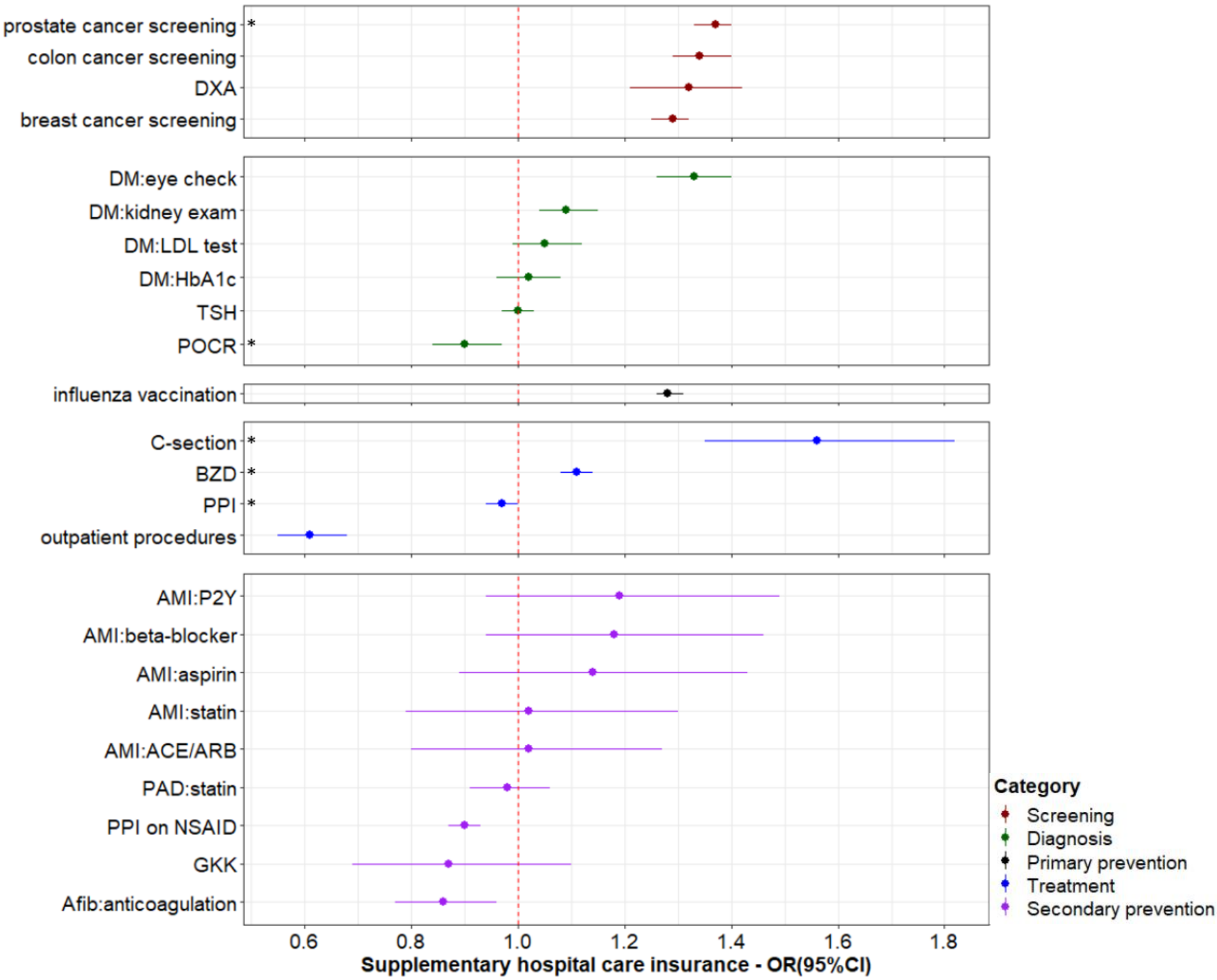


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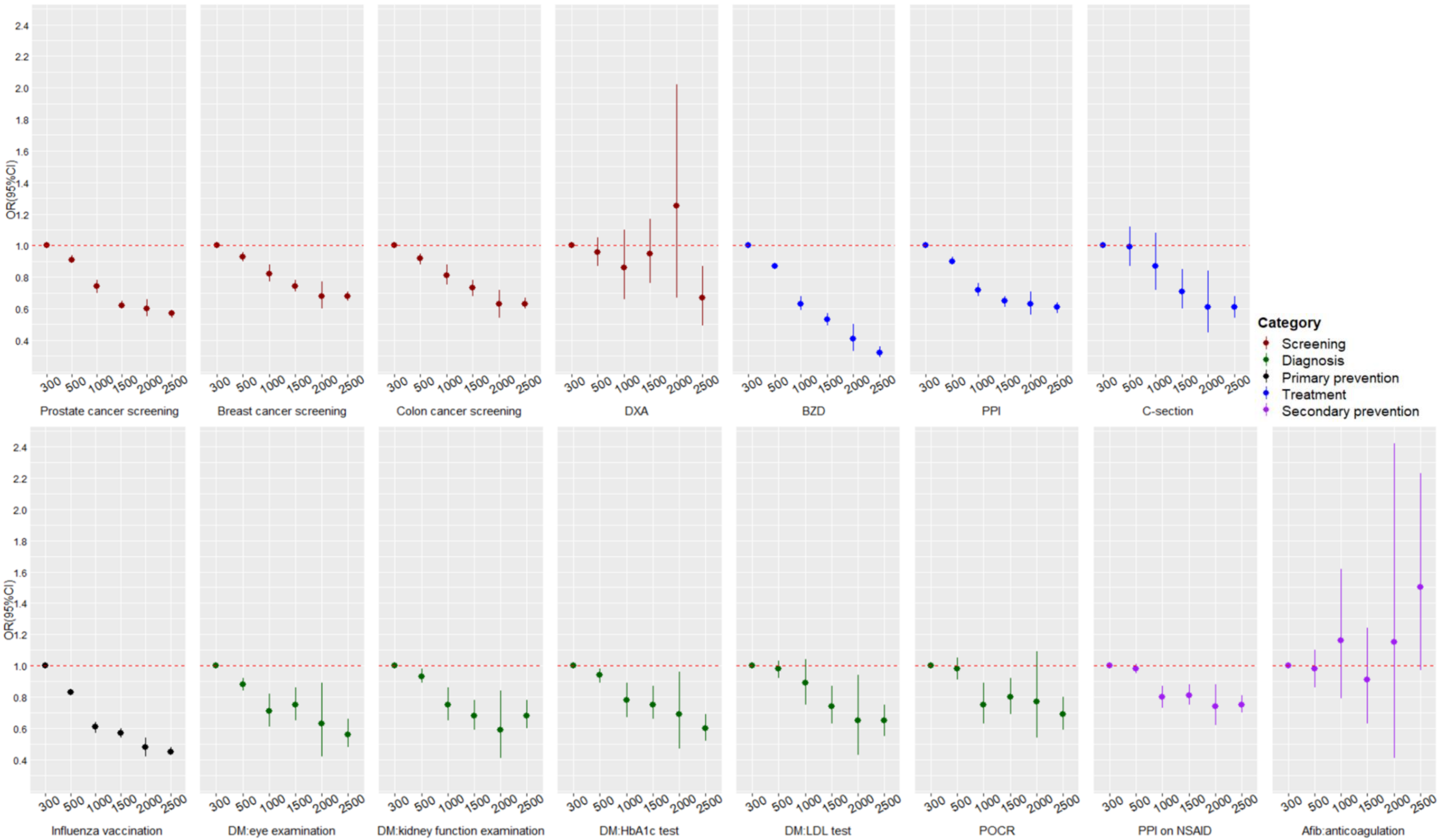
Figure 4. Effects of annual deductible level (Swiss Francs) on healthcare services utilization.



OR: odds ratio; CI: confidence interval; DM: diabetes mellitus; DXA: Dual-energy x-ray absorptiometry; HbA1c: glycated haemoglobin; LDL: low-density lipoprotein; TSH: thyroid stimulating hormone; POCR: outpatient preoperative chest radiography; BZD: benzodiazepines; PPI: proton pump inhibitor; C-section: Caesarean section; AMI: acute myocardial infarction; ACE: angiotensin converting enzyme; ARB: angiotensin receptor blocker; P2Y: clopidogrel, prasugrel or ticagrelor; NSAID: nonsteroidal anti-inflammatory drug; PAD: peripheral artery disease; Afib: atrial fibrillation; GKK: Glucocorticoid.

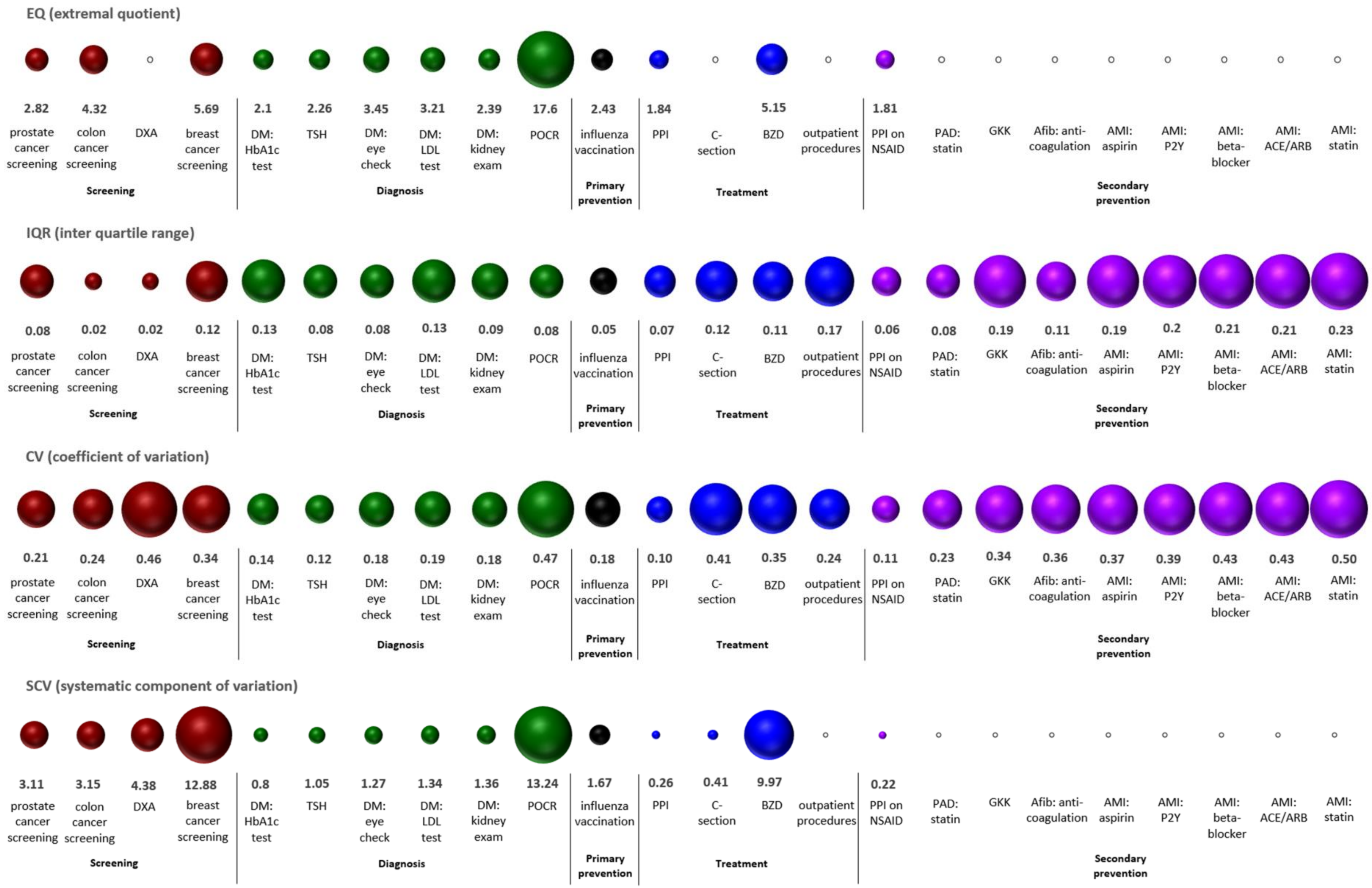
Unadjusted and adjusted regional variation

Figure 5 illustrates the degree of unadjusted regional variation across 24 healthcare services; full numerical results are presented in Table S2. SCV indicated relevant variation for POCR (13.24), breast cancer screening (12.88), and long-term benzodiazepine use in older people (9.97).

Figure 6 shows the degree of unexplained regional variation after controlling for the available influencing factors through multilevel modelling. MORs were below 1.5 for all services, and mostly below 1.3. VPCs for all 24 services were within 5.0%, and mostly below 2.0% (Table S2). MOR for POCR in the cross-classified model was 1.25 versus 1.46 in sensitivity analysis, suggesting that some variation among MS regions was accounted for by considering the hospital level. The combination of relatively small MORs and VPCs implied small unexplained variation for all 24 services.

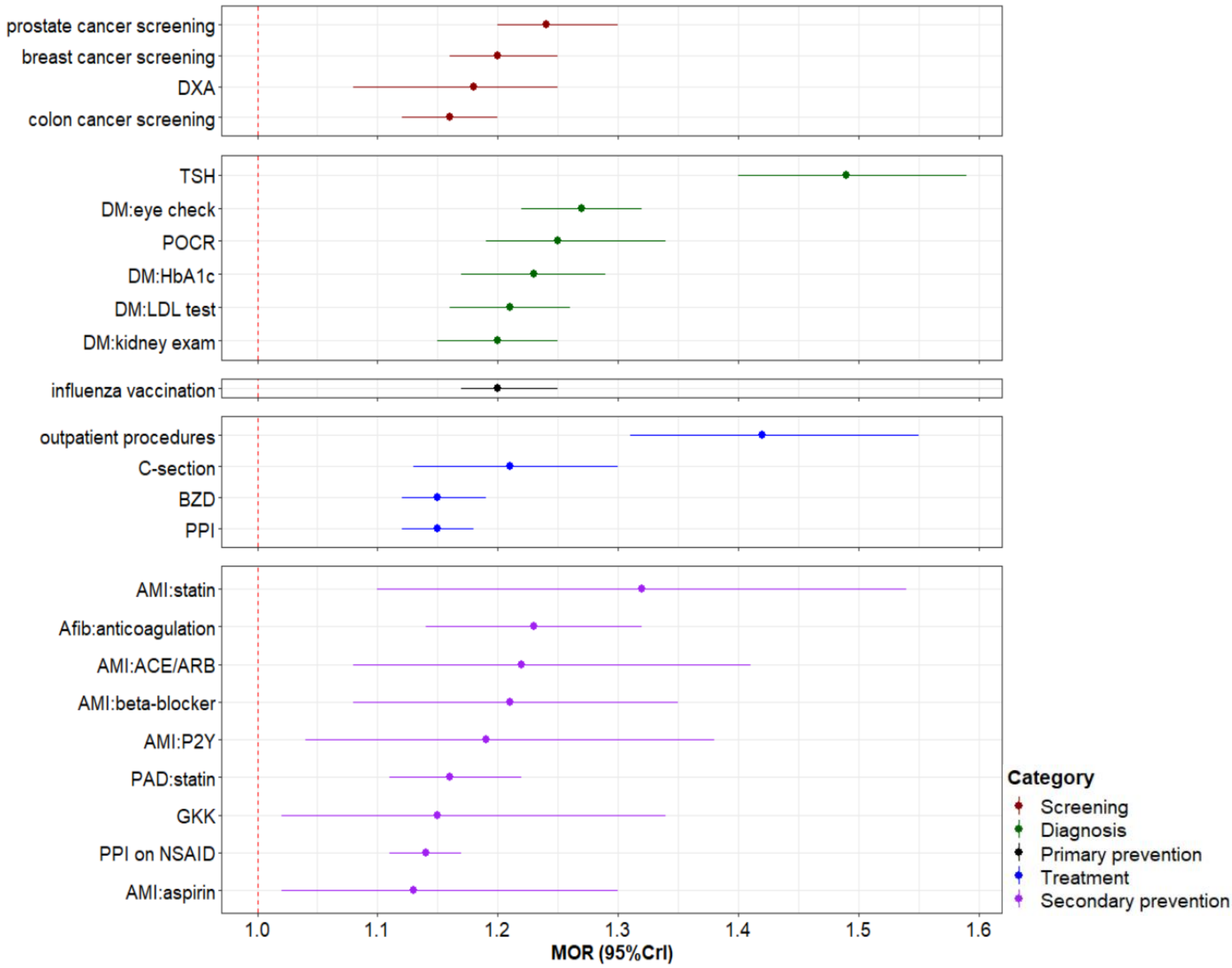
Multilevel model residuals for 10 healthcare services did not show spatial dependence across MS regions, as indicated by insignificant global Moran’s I values. (Table S2).

Figure 5. Degree of unadjusted regional variation across 24 selected healthcare services.



° For some services, EQ and SCV are not applicable due to insufficient study population. DM: diabetes mellitus; DXA: Dual-energy x-ray absorptiometry; HbA1c: glycated haemoglobin; LDL: low-density lipoprotein; TSH: thyroid stimulating hormone; POCR: outpatient preoperative chest radiography; BZD: benzodiazepines; PPI: proton pump inhibitor; C-section: Caesarean section; AMI: acute myocardial infarction; ACE: angiotensin converting enzyme; ARB: angiotensin receptor blocker; P2Y: clopidogrel, prasugrel or ticagrelor; NSAID: nonsteroidal anti-inflammatory drug; PAD: peripheral artery disease; Afib: atrial fibrillation; GKK: Glucocorticoid.

Figure 6. Degree of adjusted regional variation across 24 selected healthcare services.



MOR: median odds ratio; CrI: credible interval; DXA: Dual-energy x-ray absorptiometry; TSH: thyroid stimulating hormone; DM: diabetes mellitus; POCR: outpatient preoperative chest radiography; HbA1c: glycated haemoglobin; LDL: low-density lipoprotein; C-section: Caesarean section; BZD: benzodiazepines; PPI: proton pump inhibitor; AMI: acute myocardial infarction; Afib: atrial fibrillation; ACE: angiotensin converting enzyme; ARB: angiotensin receptor blocker; P2Y: clopidogrel, prasugrel or ticagrelor; PAD: peripheral artery disease; GKK: Glucocorticoid; NSAID: nonsteroidal anti-inflammatory drug.

Discussion

We studied 24 diverse healthcare services recommended or discouraged for target populations in clinical guidelines, mainly for major chronic diseases. Overall utilization rates varied substantially, and suggested suboptimal utilization for many services. After controlling for multiple influencing factors, the unexplained regional variation was generally small. Associations between health insurance-related characteristics and utilization were mostly consistent; associations with other influences were rather service-specific.

Although there are no “appropriate” or “optimal” utilization rates known for many healthcare services, strongly recommended services supported by sound evidence may be considered as effective care, and expected to be highly utilized in eligible populations. For example, the studied tests for diabetes complications and secondary prevention medications for AMI patients would fall into this category. Utilization rates for these services between 34% and 70% indicated suboptimal utilization. The utilization rates of healthcare services discouraged in clinical guidelines were generally low as expected. However, 55.5% of patients used proton pump inhibitors (PPI) for a prolonged time. Avoidance of prolonged PPI use is a top five recommendations for outpatient general internal medicine developed by Smarter Medicine - a Swiss version of the Choosing Wisely [29].

The effects of explanatory variables reflected, to some extent, barriers to and facilitators of access to care. In particular, we found coherent associations with health insurance-related characteristics, in a setting with mandatory insurance and quasi-universal access. The data indicated a negative dose-response effect of deductible level on utilization. People with higher deductibles tend to be healthier and willing to take more risks, and some of their invoices may be missed, which may partially explain this observation. However, higher out-of-pocket costs may also make people more reluctant to use services, constituting a financial barrier [30]. While non-insurance practically does not occur in Switzerland, foregoing healthcare utilization due to out-of-pocket costs has been previously documented [31-33]. People having supplementary insurance in addition to mandatory insurance may be wealthier, and more health-conscious and educated on average. Thus, they may seek, or be willing to accept more care, as we observed for most services. Having supplementary hospital insurance was in general associated with increased utilization of healthcare services. This effect was especially prominent in the case of C-section, which is, to a large extent, a preference-sensitive service [34]. Expectedly, having supplementary hospital insurance also made it more likely for patients to receive specific surgical procedures, recommended to be performed on an outpatient basis, as inpatients Enrolees in managed care models were more likely to use healthcare in two thirds of the studied services, which were mostly recommended ones. This may be partially explained by more health awareness. It may also imply that managed care models provide better coordinated and more guideline-concordant care.

Associations between socio-demographics and healthcare utilization were largely service specific. Effects of language region were not consistent, which may be due to different culture and norms, regional health intervention programs, and different practice styles of healthcare providers [35, 36].

People with more comorbidities were generally more likely to use healthcare services. Worse health may trigger more awareness of health-related issues and more contact with healthcare providers, leading to further care. Exceptions were secondary prevention medications in AMI patients and oral anticoagulation in atrial fibrillation patients. Previous studies also reported that more comorbidities were associated with poor adherence to related recommendations [37, 38].

SAVA detected six healthcare services with SCV values over three, among which breast cancer screening, POCR, and long-term use of benzodiazepines in older people had SCVs around ten, suggesting large regional variation. However, after adjusting for available influencing factors, all MORs were relatively small (1.14 - 1.49). Together with VPCs below 5%, this indicated that the unexplained regional variation in utilization of all considered services was small [22]. The largest unexplained variation was found for TSH testing and surgical procedures performed in the outpatient setting. Both represent preference-sensitive care and decision-making may strongly depend on physicians' preferences and clinical opinions. Only few previous studies have comprehensively assessed and compared variation in utilization across multiple healthcare services, with mixed results. One study reported moderate variation with MORs between 1.27 to 1.74 for some diabetes-related primary care services [7]. Another study reported large variation with MORs between 2.3 to 21.5 for intensive care unit (ICU) use after 13 major surgical procedures across hospitals [6].

In addition to relatively small regional variation across 24 healthcare services, we found moderate spatial autocorrelation, that is, spatial dependence in the unexplained regional variation in utilization for several healthcare services. Further research could assess the spatial clustering of such regional variation, to explore potential overarching patterns across services, and possibly identify regions with generally superior or inferior performance in terms of appropriate healthcare utilization. This might provide valuable insights for local healthcare intervention and promotion programs.

Strengths and limitations

Our study has a number of strengths. First, we used a large dataset representing all regions of Switzerland, resulting in large sample sizes for most of the studied healthcare services. Second, we assessed multiple, diverse services, enabling comparison and a broader perspective. The health insurance claims data used provided detailed information on individual insurance-related characteristics, allowing in-depth analyses. Finally, we performed multilevel multivariable modelling for efficient control of confounding.

Several limitations should be considered. First, our selection of healthcare services and eligible populations was not entirely based on burden of disease criteria, mainly because of limitations dictated by the characteristics of Swiss claims data. Second, clinical information is limited in the claims data; outpatient diagnoses are lacking. This may have led to a certain extent of misclassification of eligibility for and utilization of services. Third, we used claims data from a single insurer. Enrolees of other health insurers may theoretically have different characteristics and patterns of healthcare utilization. However, the claims data were based on 1.2 million people from all regions in Switzerland. The benefit package of the mandatory insurance is federally defined and identical for all health insurers. Thus, we expect little deviation of enrollees' characteristics compared to the whole Swiss population, and the results should essentially be generalizable to the entire country. Fourth, we cannot exclude high variation across different types of units, e.g. healthcare providers for whom we had no detailed information.

Conclusion

Our study is the first to collectively evaluate regional variation in the utilization of diverse healthcare services and related influencing factors, with a particular focus on insurance-related characteristics. The observed utilization rates indicated suboptimal utilization for many services. Regional variation in utilization that remained unexplained after multivariable adjustment was relatively small, implying only limited local variation. With respect to health insurance-related characteristics, higher deductible levels were consistently associated with lower utilization. Increased utilization was generally seen in people having any supplementary insurance, and having supplementary hospital insurance. People having chosen a managed care model were generally more likely to use the recommended but not discouraged care, suggesting a better coordinated, more guideline-adherent care model. These observations indicate that healthcare utilization might be further optimized through adjustment of insurance scheme designs.

CONTRIBUTORSHIP STATEMENT

M.S is identified as the guarantor of the article who accepts full responsibility for the work and the conduct of the study, had access to the data, and controlled the decision to publish. M.S, V.vW and H.D developed the underlying study program and generated the idea of the present study. B.B, E.B, C.B did data preparation and data management. W.W, A.U, O.G and J.B performed statistical analysis and drafted the main manuscript text. All authors together defined the analysis methodology, interpreted the statistical results and critically revised the manuscript. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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COMPETING INTERESTS

W.W, A.U, O.G, V.vW, and J.B has nothing to disclose. H.D Reports grants from Swiss National Science Foundation, during the conduct of the study. M.S reports grants from Swiss National Science Foundation, during the conduct of the study; grants from Helsana Insurance Group, outside the submitted work. E.B reports personal fees from Helsana Group (employment), during the conduct of the study; grants from Novartis Switzerland, grants from Amgen Switzerland, grants from MSD Switzerland, grants from Swiss Cancer Research Foundation, outside the submitted work. B.B and C.B reports personal fees from Helsana Group (employment), grants from Swiss National Science Foundation (SNSF) National Research Program "Smarter Health Care" (NRP 74), project number 26, grant number 407440_167349, during the conduct of the study.

DATA SHARING STATEMENT

The data underlying this study cannot be shared publicly because they are the property of Helsana (https://www.helsana.ch/en/helsana-group), and have restricted public access on grounds of patient privacy. The data are managed by Helsana and subsets of the database are available for researchers after request and under specific conditions. Data are available from Helsana (gesundheitskompetenz@helsana.ch) for researchers who meet the criteria for access to confidential data. Helsana will consider the possibilities of the research proposal and decide to grant access if the research questions can be answered with use of the Helsana data. When requests are granted, data are accessible only in a secure environment.

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TRANSPARENCY STATEMENT

The lead author Matthias Schwenkglenks (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as originally planned have been explained.

Table S1. Effects (OR and 95% CI) of explanatory variables on 24 selected healthcare services utilization in multilevel models.

Healthcare service	Age	Female gender	Urban	Purchasing power index	Language region*		Number of comorbidities		
					French	Italian	1	2	>2
Colon cancer screening	-	0.93(0.90,0.96)	1.07(1.02,1.12)	1.25(1.16,1.38)	0.86(0.79,0.94)	1.11(0.98,1.27)	1.30(1.24,1.36)	1.31(1.25,1.38)	1.45(1.38,1.52)
Breast cancer screening	-	-	1.06(1.03,1.11)	1.09(1.01,1.18)	1.65(1.50,1.81)	1.69(1.43-2.01)	1.26(1.22-1.30)	1.30(1.25-1.35)	1.30(1.25,1.34)
Prostate cancer screening	-	-	1.10(1.07,1.14)	1.20(1.12-1.28)	1.38(1.25,1.53)	1.50(1.28-1.74)	1.66(1.61-1.71)	1.90(1.84-1.95)	1.83(1.79,1.89)
Osteoporosis screening	-	3.66(3.10,3.99)	1.15(1.04,1.27)	1.23(1.01,1.44)	-	-	-	-	-
DM: HbA1c test	-	0.96(0.93,1.00)	0.96(0.90,1.02)	0.88(0.78,0.98)	0.51(0.46,0.58)	0.48(0.39,0.56)	1.10(1.01,1.20)	1.20(1.10,1.30)	1.24(1.14,1.35)
DM: eye check	-	1.16(1.12,1.20)	-	1.16(0.99,1.33)	0.83(0.74,0.95)	0.78(0.64,0.94)	0.95(0.88,1.03)	1.08(1.00,1.17)	1.24(1.15,1.33)
DM: kidney exam	-	1.07(1.04,1.22)	1.14(1.09,1.20)	1.06(0.94,1.21)	1.18(1.07,1.31)	1.53(1.27,1.85)	1.06(0.98,1.14)	1.21(1.13,1.29)	1.38(1.29,1.47)
DM: LDL test	-	0.89(0.85,0.93)	1.12(1.05,1.19)	-	2.12(1.90,2.40)	1.40(1.16,1.71)	1.17(1.08,1.27)	1.45(1.33,1.56)	1.57(1.45,1.70)
TSH	-	0.79(0.77,0.81)	0.97(0.93,1.02)	-	0.91(0.78,1.08)	1.12(0.80,1.39)	-	-	-
POCR	1.03(1.02,1.05)	0.84(0.80,0.89)	-	-	-	-	1.04(0.93,1.15)	1.10(0.99,1.23)	1.16(1.04,1.30)
Influenza vaccination	-	0.86(0.84,0.87)	1.04(1.02,1.07)	1.14(0.99,1.34)	1.03(0.92,1.15)	1.03(0.87,1.20)	1.75(1.70,1.81)	2.53(2.46,2.60)	4.21(4.09,4.32)
BZD	-	1.96(1.89,2.00)	-	-	2.00(1.85,2.13)	2.17(1.92,2.38)	1.92(1.85,2.04)	2.63(2.50,2.78)	4.00(3.85,4.17)
PPI	-	0.80(0.78,0.82)	1.00(0.96,1.03)	0.88(0.83,0.94)	1.10(1.02,1.19)	0.95(0.85,1.09)	1.35(1.31,1.41)	1.72(1.67,1.79)	3.23(3.13,3.33)
Outpatient procedures	-	1.98(1.82,2.16)	0.97(0.85,1.10)	0.71(0.53,0.89)	2.69(2.08,3.59)	0.93(0.62,1.29)	-	-	-
C-section	1.05(1.04,1.06)	-	-	-	0.73(0.61,0.87)	0.79(0.59,1.02)	1.27(1.15,1.41)	1.40(1.20,1.63)	2.14(1.66,2.71)
AMI: aspirin	0.97(0.96,0.98)	1.08(0.88,1.31)	-	-	-	-	0.61(0.41,0.88)	0.33(0.23,0.45)	0.25(0.18,0.34)
AMI: statin	-	0.88(0.70,1.10)	-	-	0.61(0.43,0.85)	0.74(0.48,1.10)	0.57(0.38,0.82)	0.41(0.29,0.56)	0.31(0.23,0.42)
AMI: beta-blocker	0.98(0.97,0.99)	0.99(0.79,1.20)	-	0.50(0.30,0.79)	-	-	0.86(0.58,1.24)	0.63(0.44,0.87)	0.59(0.43,0.79)
AMI: ACE/ARB	0.98(0.97,0.98)	1.00(0.82,1.23)	-	-	-	-	0.73(0.50,1.00)	0.62(0.44,0.83)	0.55(0.41,0.73)
AMI: P2Y	-	0.85(0.69,1.04)	-	-	0.97(0.71,1.25)	1.48(1.02,2.02)	0.65(0.43,0.95)	0.55(0.38,0.78)	0.53(0.37,0.72)
PPI with NSAID	-	1.05(1.02,1.07)	-	-	0.90(0.83,0.97)	1.03(0.91,1.18)	0.97(0.92,1.01)	1.07(1.02,1.12)	1.60(1.54,1.66)
PAD: statin	-	0.52(0.49,0.55)	0.95(0.87,1.05)	-	0.74(0.66,0.83)	1.14(0.93,1.38)	1.42(1.12,1.79)	4.20(3.45,5.14)	6.72(5.58,8.11)
Afib: anticoagulation	-	1.16(1.04,1.29)	-	-	0.99(0.81,1.19)	1.28(0.97,1.64)	1.01(0.70,1.45)	0.85(0.60,1.20)	0.70(0.51,0.98)
GKK	1.01(1.01,1.02)	0.82(0.67,1.02)	-	-	0.54(0.40,0.72)	1.41(0.92,2.05)	1.28(0.94,1.70)	1.46(1.06,1.96)	1.40(1.07,1.81)

Table S1. Continued

Healthcare service	Supplementary insurance	Managed care models	Supplementary hospital insurance	Annual deductible level (Swiss Francs)				
				500	1000	1500	2000	2500
Colon cancer screening	1.05(1.00,1.10)	1.12(1.08,1.15)	1.34(1.29,1.40)	0.92(0.88,0.95)	0.81(0.75,0.88)	0.73(0.68,0.78)	0.63(0.54,0.72)	0.63(0.60,0.67)
Breast cancer screening	1.14(1.10,1.17)	1.13(1.10,1.16)	1.29(1.25,1.32)	0.93(0.90,0.96)	0.82(0.77,0.88)	0.74(0.71,0.78)	0.68(0.60,0.77)	0.68(0.65,0.71)
Prostate cancer screening	1.18(1.14,1.22)	1.13(1.11,1.15)	1.36(1.33,1.40)	0.91(0.89,0.94)	0.74(0.70,0.78)	0.62(0.60,0.65)	0.60(0.55,0.66)	0.56(0.54,0.59)
Osteoporosis screening	1.07(0.96,1.22)	0.99(0.92,1.06)	1.32(1.21,1.42)	0.96(0.87,1.05)	0.86(0.66,1.10)	0.95(0.76,1.17)	1.25(0.67,2.02)	0.67(0.49,0.87)
DM: HbA1c test	1.23(1.18,1.28)	1.13(1.08,1.17)	1.02(0.96,1.08)	0.94(0.89,0.98)	0.78(0.67,0.89)	0.75(0.66,0.87)	0.69(0.47,0.96)	0.60(0.52,0.69)
DM: eye check	1.30(1.24,1.36)	1.19(1.14,1.23)	1.33(1.26,1.40)	0.88(0.84,0.92)	0.71(0.61,0.82)	0.75(0.65,0.86)	0.63(0.42,0.89)	0.56(0.48,0.66)
DM: kidney exam	1.09(1.04,1.14)	1.05(1.01,1.09)	1.09(1.04,1.15)	0.93(0.89,0.98)	0.75(0.65,0.86)	0.68(0.59,0.78)	0.59(0.41,0.84)	0.68(0.60,0.78)
DM: LDL test	1.12(1.07,1.19)	1.08(1.02,1.13)	1.05(0.99,1.12)	0.98(0.92,1.03)	0.89(0.75,1.04)	0.74(0.63,0.87)	0.65(0.43,0.94)	0.65(0.55,0.75)
TSH	1.02(1.00,1.05)	1.07(1.05,1.10)	1.00(0.97,1.03)	-	-	-	-	-
POCR	1.00(0.93,1.08)	0.98(0.93,1.04)	0.90(0.84,0.97)	0.98(0.91,1.05)	0.75(0.63,0.89)	0.80(0.69,0.92)	0.77(0.54,1.09)	0.69(0.59,0.80)
Influenza vaccination	1.04(1.01,1.06)	0.97(0.96,0.99)	1.28(1.26,1.31)	0.83(0.81,0.85)	0.61(0.57,0.64)	0.57(0.54,0.60)	0.48(0.42,0.54)	0.45(0.43,0.48)
BZD	0.96(0.93,0.98)	0.92(0.90,0.94)	1.11(1.08,1.14)	0.87(0.85,0.89)	0.63(0.59,0.68)	0.53(0.49,0.57)	0.41(0.33,0.50)	0.32(0.29,0.36)
PPI	0.98(0.96,1.01)	0.88(0.86,0.90)	0.97(0.94,1.00)	0.90(0.88,0.93)	0.72(0.68,0.76)	0.65(0.61,0.68)	0.63(0.56,0.71)	0.61(0.57,0.64)
Outpatient procedures	1.10(0.99,1.20)	0.95(0.87,1.04)	0.61(0.55,0.68)	-	-	-	-	-
C-section	0.86(0.77,0.96)	0.81(0.73,0.91)	1.58(1.37,1.83)	0.99(0.87,1.12)	0.89(0.71,1.08)	0.72(0.60,0.84)	0.62(0.45,0.83)	0.61(0.53,0.70)
AMI: aspirin	0.92(0.72,1.15)	1.15(0.95,1.38)	1.14(0.89,1.43)	-	-	-	-	-
AMI: statin	1.01(0.82,1.26)	1.13(0.92,1.36)	1.02(0.79,1.30)	-	-	-	-	-
AMI: beta-blocker	1.03(0.83,1.28)	1.21(1.01,1.44)	1.18(0.94,1.46)	-	-	-	-	-
AMI: ACE/ARB	1.13(0.91,1.38)	1.19(0.98,1.41)	1.02(0.80,1.27)	-	-	-	-	-
AMI: P2Y	1.24(0.97,1.61)	1.23(1.02,1.49)	1.19(0.94,1.49)	-	-	-	-	-
PPI with NSAID	0.97(0.94,1.00)	0.90(0.88,0.93)	0.90(0.87,0.93)	0.98(0.95,1.01)	0.80(0.73,0.87)	0.81(0.75,0.88)	0.74(0.62,0.88)	0.75(0.70,0.81)
PAD: statin	1.00(0.93,1.07)	0.97(0.90,1.03)	0.98(0.91,1.06)	-	-	-	-	-
Afib: anticoagulation	1.01(0.90,1.13)	1.05(0.95,1.17)	0.86(0.77,0.96)	0.98(0.86,1.10)	1.16(0.79,1.62)	0.91(0.63,1.24)	1.15(0.41,2.42)	1.50(0.97,2.23)
GKK	1.22(0.98,1.48)	0.85(0.69,1.03)	0.87(0.69,1.10)	-	-	-	-	-

* With reference to German language region. OR: odds ratio; CI: confidence interval; DM: diabetes mellitus; HbA1c: glycated hemoglobin; LDL: low-density lipoprotein; TSH: thyroid stimulating hormone; POCR: outpatient preoperative chest radiography; BZD: benzodiazepines; PPI: proton pump inhibitor; C-section: Cesarean section; AMI: acute myocardial infarction; ACE: angiotensin converting enzyme; ARB: angiotensin receptor blocker; P2Y: clopidogrel, prasugrel or ticagrelor; NSAID: nonsteroidal anti-inflammatory drug; PAD: peripheral artery disease; Afib: atrial fibrillation; GKK: Glucocorticoid.

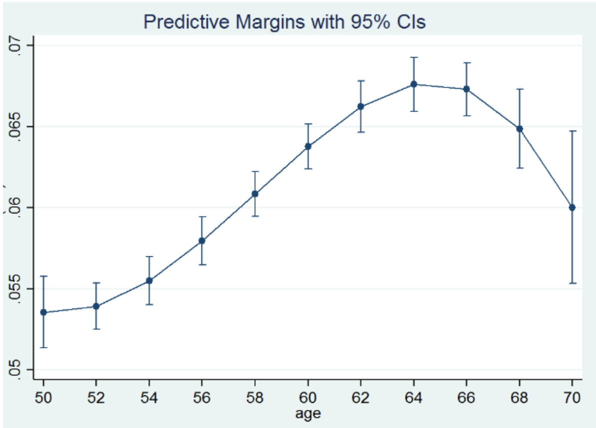
Table S2. Regional variation in utilization across 24 selected healthcare services.

Service category	Healthcare service	Unadjusted regional variation				Adjusted regional variation		Moran's I (raw rates)	Moran's I (model residuals)
		EQ (extremal quotient)	IQR (inter quartile range)	CV (coefficient of variation)	SCV (systematic component of variation)	MOR (95% CrI) in multilevel models	VPC (variance partition coefficient)		
Screening	Colon cancer screening	4.32	0.02	0.24	3.15	1.16(1.12,1.20)	0.71%	0.222**	0.084
	Breast cancer screening	5.69	0.12	0.34	12.88	1.20(1.16,1.25)	1.13%	0.622**	0.070
	Prostate cancer screening	2.82	0.08	0.21	3.11	1.24(1.20,1.30)	1.57%	0.551**	0.490**
	Osteoporosis screening	na	0.02	0.46	4.38	1.18(1.08,1.25)	0.87%	0.221**	0.102
Diagnosis	DM: HbA1c test	2.10	0.13	0.14	0.8	1.23(1.17,1.29)	1.40%	0.500**	0.245**
	DM: kidney exam	2.39	0.09	0.18	1.36	1.20(1.15,1.25)	1.12%	0.284**	0.193**
	DM: LDL test	3.21	0.13	0.19	1.34	1.21(1.16,1.26)	1.20%	0.547**	0.239**
	DM: eye check	3.45	0.08	0.18	1.27	1.27(1.22,1.32)	1.82%	0.179**	0.120*
	TSH	2.26	0.08	0.12	1.05	1.49(1.40,1.59)	5.01%	0.301**	0.298**
	POCR	17.6	0.08	0.47	13.24	1.25(1.19,1.34)	1.64%	0.263**	0.066
Primary prevention	influenza vaccination	2.43	0.05	0.18	1.67	1.20(1.17,1.25)	1.14%	0.012	0.014
Treatment	BZD	5.15	0.11	0.35	9.97	1.15(1.12,1.19)	0.66%	0.656**	0.260**
	PPI	1.84	0.07	0.10	0.26	1.15(1.12,1.18)	0.63%	0.199**	0.073
	Outpatient procedures	na	0.17	0.24	negative	1.42(1.31,1.55)	3.92%	0.318**	0.131*
	C-section	na	0.12	0.41	0.41	1.21(1.13,1.30)	1.20%	0.0227	0.070
Secondary prevention	AMI: aspirin	na	0.19	0.37	negative	1.13(1.02,1.30)	0.49%	-0.052	0.057
	AMI: statin	na	0.23	0.50	negative	1.32(1.10,1.54)	2.50%	0.036	0.157*
	AMI: beta-blocker	na	0.21	0.43	negative	1.21(1.08,1.35)	1.16%	0.134*	0.097
	AMI: ACE/ARB	na	0.21	0.43	negative	1.22(1.08,1.41)	1.30%	-0.104	0.007
	AMI: P2Y	na	0.20	0.39	negative	1.19(1.04,1.38)	0.96%	-0.009	0.006
	PPI with NSAID	1.81	0.06	0.11	0.22	1.14(1.11,1.17)	0.57%	0.189**	0.170*
	PAD: statin	na	0.08	0.23	negative	1.16(1.11,1.22)	0.75%	0.247**	0.043
	Afib: anticoagulation	na	0.11	0.36	negative	1.23(1.14,1.32)	1.41%	-0.102	0.100
	GKK	na	0.19	0.34	negative	1.15(1.02,1.34)	0.68%	0.105	-0.001

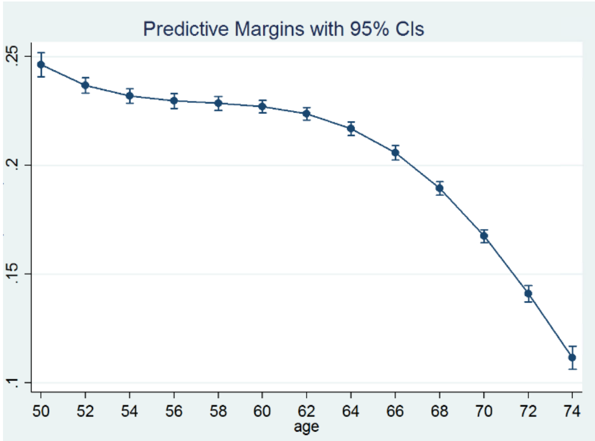
*p<0.05; **p<0.01. MOR: median odds ratio; CrI: credible interval; DM: diabetes mellitus; HbA1c: glycated haemoglobin; LDL: low-density lipoprotein; TSH: thyroid stimulating hormone; POCR: outpatient preoperative chest radiography; BZD: benzodiazepines; PPI: proton pump inhibitor; C-section: Caesarean section; AMI: acute myocardial infarction; ACE: angiotensin converting enzyme; ARB: angiotensin receptor blocker; P2Y: clopidogrel, prasugrel or ticagrelor; NSAID: nonsteroidal anti-inflammatory drug; PAD: peripheral artery disease; Afib: atrial fibrillation; GKK: Glucocorticoid; na: not applicable.

Figure S1. Relationship between age and healthcare services utilization.

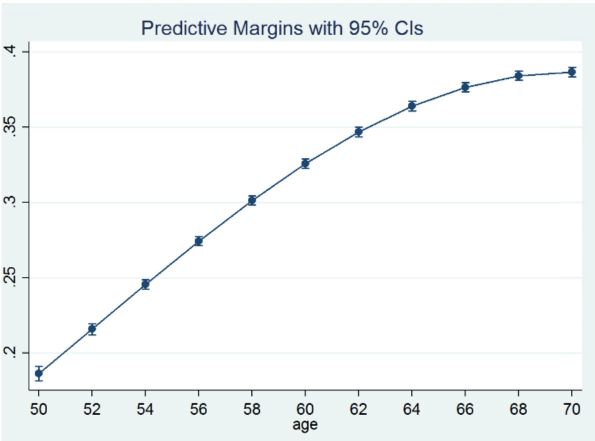
a. Colon cancer screening



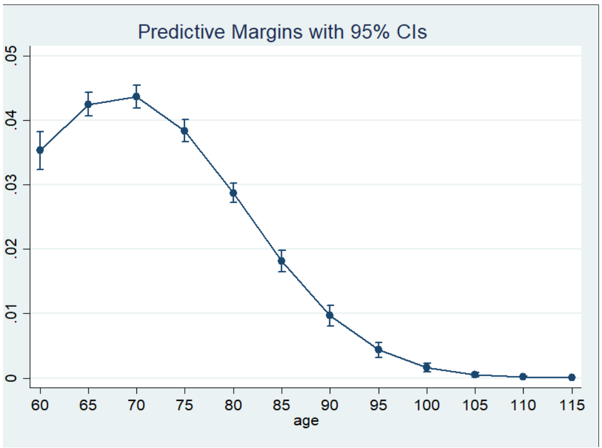
b. Breast cancer screening



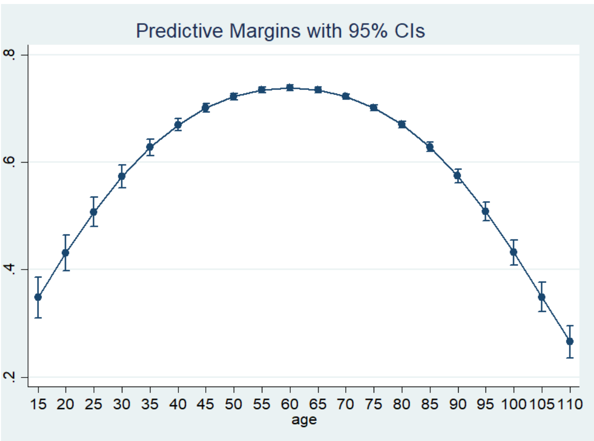
c. Prostate cancer screening



d. Osteoporosis screening



e. DM: HbA1c test



f. DM: kidney exam

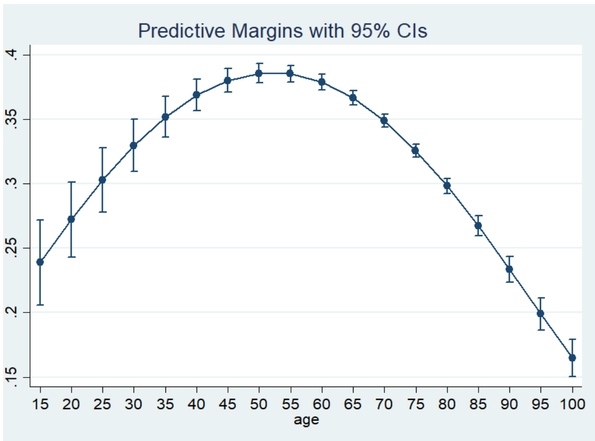
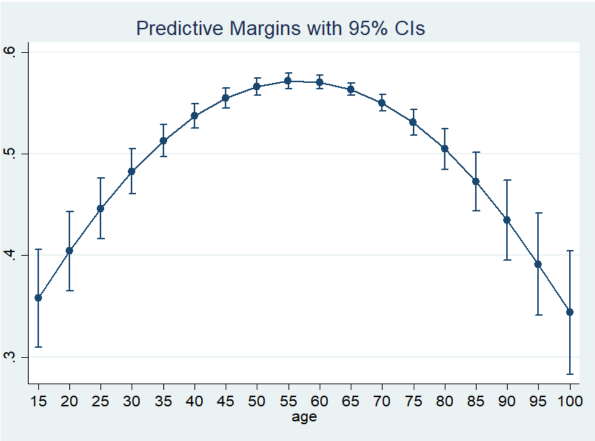
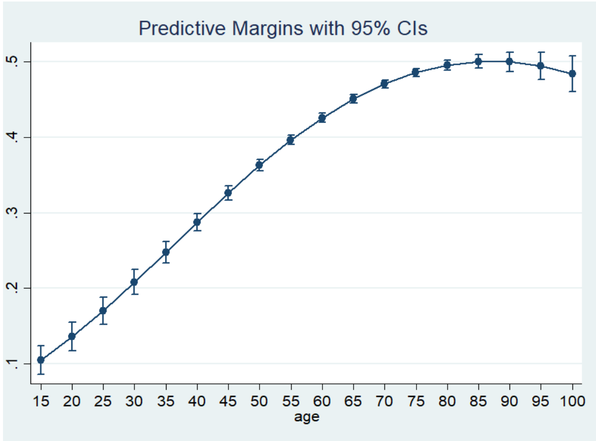


Figure S1. continued

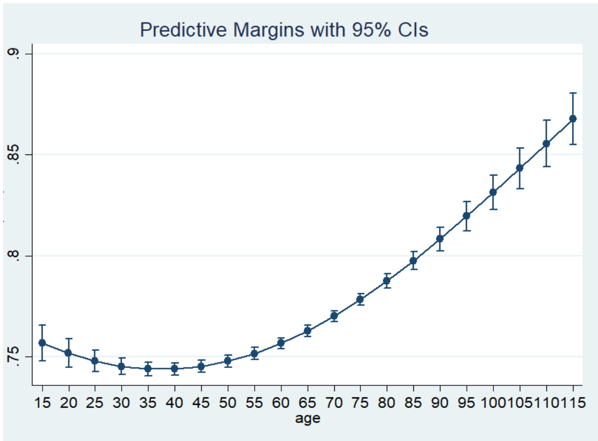
g. DM: LDL test



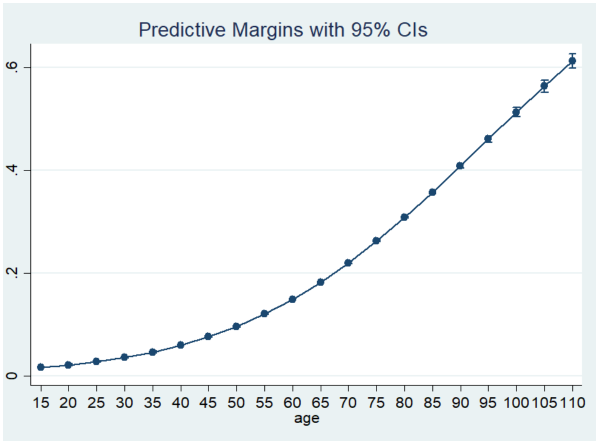
h. DM: eye check



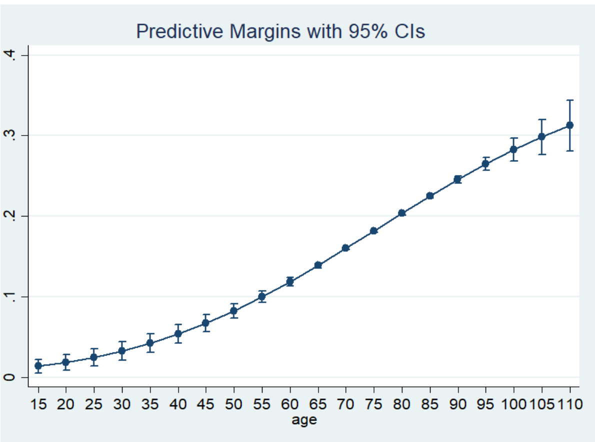
i. TSH test



j. Influenza vaccination



k. BZD



l. PPI

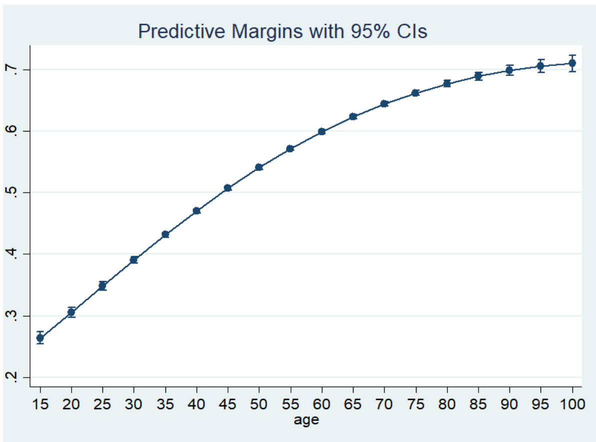
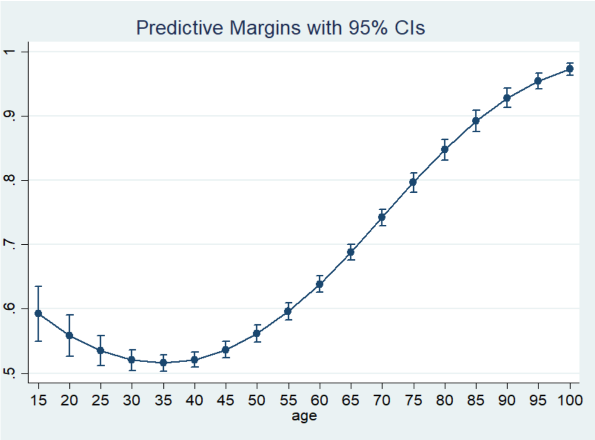
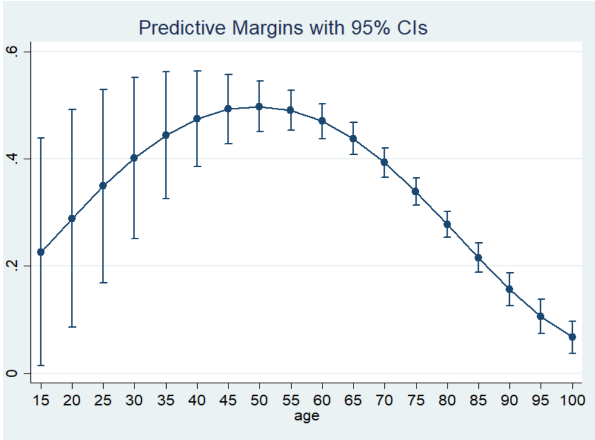


Figure S1. continued

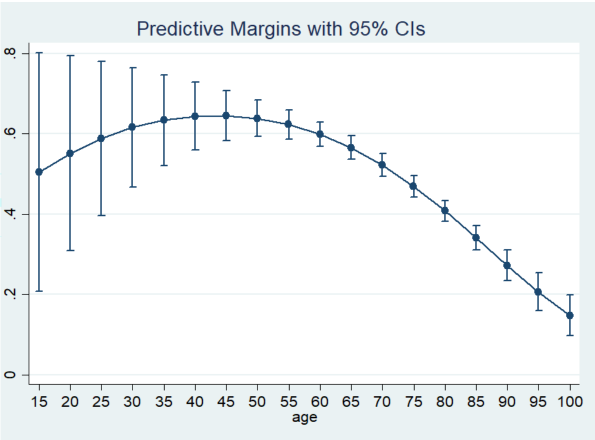
m. Outpatient procedures



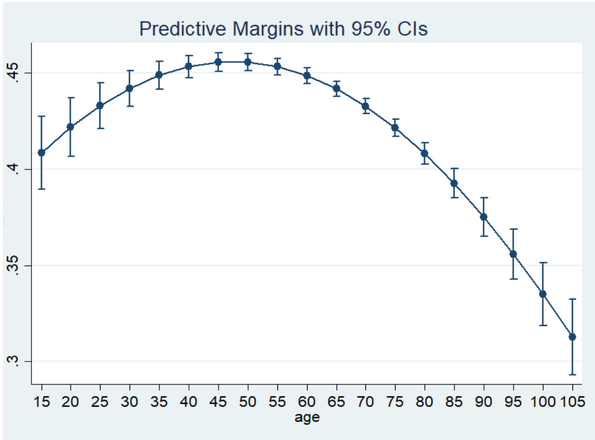
n. AMI: statin



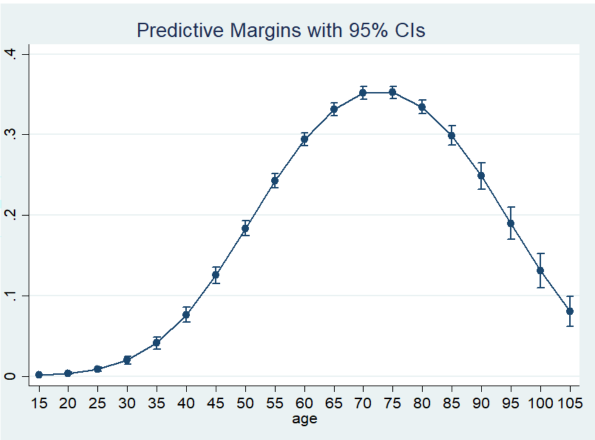
o. AMI: P2Y



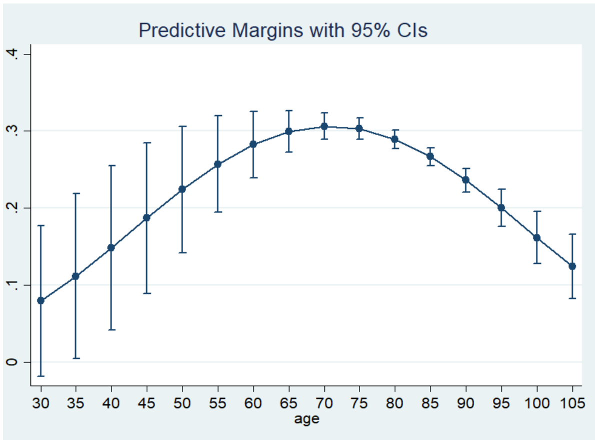
p. PPI with NSAID



q. PAD: statin



r. Afib: anticoagulation



DM: diabetes mellitus; HbA1c: glycated haemoglobin; LDL: low-density lipoprotein; TSH: thyroid stimulating hormone; BZD: benzodiazepines; PPI: proton pump inhibitor; AMI: acute myocardial infarction; P2Y: clopidogrel, prasugrel or ticagrelor; NSAID: nonsteroidal anti-inflammatory drug; PAD: peripheral artery disease; Afib: atrial fibrillation.

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Chapter V

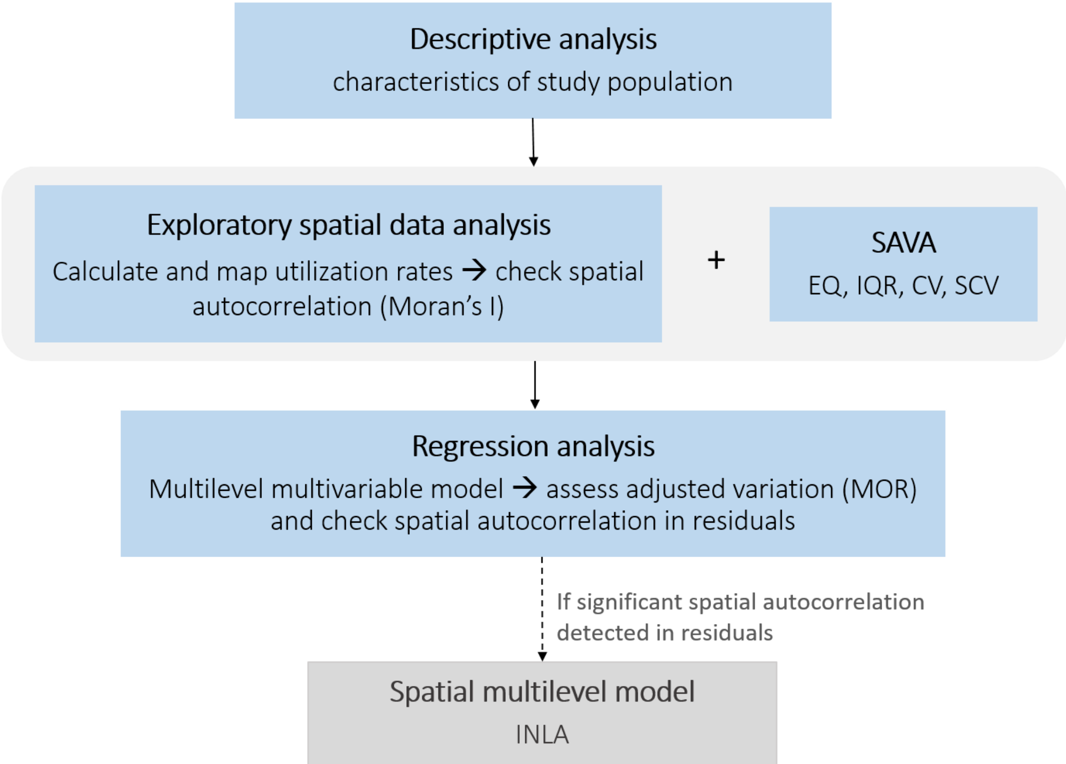
General discussion

The following discussion summarizes the main findings of the thesis and discusses the contribution to health services research especially regional variation analysis in healthcare utilization, and the significance of the findings in providing important implications to the healthcare system.

The thesis proposed a comprehensive analysis approach for study on regional variation in healthcare utilization based on existing methods. It was developed using preoperative chest radiography (POCR) as a test case, the routine use of which is discouraged in international clinical guidelines [1], and also the Choosing Wisely initiatives [2, 3]. The analysis approach consisted of small area variation analysis for describing unadjusted regional variation, multilevel regression modelling for investigating influencing factors, calculation of median odds ratio for assessing adjusted regional variation, spatial autocorrelation analysis using Moran's I statistic, and visualization of regional variation through mapping with geographic information system (GIS) applications.

By applying the comprehensive analysis approach to regional variation analysis in the utilization of four management measures strongly recommended to diabetes patients [4-6], I further extended multilevel regression modelling by taking spatial autocorrelation into account. This was achieved by applying the Bayesian statistical model through the Integrated Nested Laplace Approximations (INLA) approach [7-9]. However, this additional step has not been performed in analysis for other selected healthcare services. There are several reasons. First, performing the INLA model needs a large number of small regions, requiring a relatively big size of the study population that would cover all these regions across the whole of Switzerland. Only Medstat regions (N=705) [10] could be used for such analysis, however, the study populations for around one-third of selected healthcare services were under 10,000, leading to no eligible persons present in many Medstat regions. Besides, analysis results showed insignificant or little spatial autocorrelation in multilevel model residuals for most healthcare services, suggesting healthcare utilization was mostly independent across regions therefore a further correction would not be necessary. To make the analysis approach consistent and results comparable across all selected services, spatial multilevel modelling analysis was conducted as an extra step only for healthcare services for diabetes patients. Figure 1 shows the comprehensive analysis approach including the INLA model for assessing regional variation in healthcare utilization proposed in the thesis.

Figure 1. A comprehensive approach for analysis of regional variation in healthcare utilization



SAVA: small area variation analysis; EQ: extremal quotient; IQR: interquartile range; CV: coefficient of variation; SCV: systematic component of variation; MOR: median odds ratio; INLA: Integrated Nested Laplace Approximations.

Compared to the conventionally used analytical method in regional variation analysis of healthcare utilization, the comprehensive approach proposed in this thesis has many advantages. First, it supplements small area variation analysis (SAVA) which assesses the degree of only unadjusted or partially adjusted regional variation. Calculation of median odds ratio and variance partition coefficient enables the assessment of regional variation after adjustment for multiple influencing factors. Second, multilevel regression analysis taking the random effect at region level into consideration allows for a thorough investigation into the effects of different influencing factors with less bias. In addition, it is convenient to perform a cross-services comparison. Not only unadjusted and adjusted regional variation, but the effects of influencing factors can be easily summarized and compared graphically across diverse healthcare services, making it possible to identify potential common patterns. Finally, although spatial multilevel regression analysis with the INLA approach has not been generally applied in the present thesis, it presents great potential in helping identify spatial clustering patterns in healthcare utilization, which could play an important role in future similar research when considerable spatial autocorrelation appears in healthcare utilization across regions [11].

The 24 diverse healthcare services in this thesis were selected based on a systematic approach considering many aspects especially the related clinical practice guidelines [12]. This systematic selection approach was developed within the first part of our NRP74 project, in which the present thesis is nested. Recommendation statements from clinical practice guidelines used in Switzerland were considered pragmatically according to clinical relevance, expected frequency of service use, size of the eligible population, and feasibility to identify the population and service from Swiss health insurance claims data. The selected services mainly focused on common chronic diseases. They also had a good coverage of different kinds of healthcare services, ranging from screening, diagnosis, primary prevention, treatment, to secondary prevention; from lab tests, imaging, drug prescriptions, to surgical procedures. Therefore, the findings are expected to have relatively good generalizability due to the great diversity of studied services. To the best of our knowledge, the present thesis is the first to analyse regional variation in the utilization of diverse healthcare services that were elaborately selected through a self-developed systematic approach.

It has been observed that the overall utilization rates varied remarkably across services, showing suboptimal utilization in many services, especially the effective ones which are strongly recommended in clinical practice guidelines. After multivariate adjustment, regional variation was generally small in the utilization of all selected services. Multiple factors were significantly associated with healthcare utilization, however, the most interesting finding was the consistent effects of health insurance-related factors among most selected services. A higher annual deductible level was mostly associated with lower utilization. Supplementary insurance, supplementary hospital insurance, and choosing a managed care model were associated with higher utilization of most services. Managed care models showed a tendency towards more recommended care.

The healthcare system in Switzerland has relatively universal care access and high out-of-pocket expenditures. Universal access to care is reflected to a certain extent by generally small regional variation in the utilization of all selected healthcare services observed in our study. However, high out-of-pocket payment from the patient, which has been shown to be a financial barrier to the utilization of healthcare services [13], might be one of the reasons for the reported suboptimal utilization of many healthcare services. People choosing a higher annual deductible tended to have a lower utilization of diverse healthcare services in the present thesis. This phenomenon needs to be regarded from two perspectives - healthcare services with positive or negative recommendations. On the one hand, for effective cares strongly recommended in guidelines such as colorectal cancer screening and diabetes management measures, high deductible could result in potential underuse; on the other hand, low deductible may lead to overuse of healthcare services that are not cost-effective and discouraged in guidelines, for example, the routine use of preoperative chest radiography. Our findings indicate that more appropriate healthcare utilization and a better-performed healthcare system in terms of equity, quality, and efficiency might be achieved through adjustment of insurance scheme design. More specifically, further financial incentives could be considered to encourage some better coordinated and more guideline-adherent care models, like managed care models; and the annual deductible policy might also be slightly adjusted to be more flexible taking healthcare types (effective care, care with debatable evidences, and non-recommended care) into consideration.

Further research

The present thesis has addressed to a large extent the common issues of previous studies on regional variation in healthcare utilization described in the introduction section, however, there are still certain limitations mainly due to the claims data. Although a systematic approach was adopted to select healthcare services, the final selection was largely limited by the characteristics of Swiss claims data. Some information is not available from claims data, for example, the outpatient diagnoses are lacking; there is very little information on healthcare providers' characteristics which is also partially because of data protection rules; and the patient and physician preferences cannot be captured.

To overcome these limitations, future studies could consider using combined data from different sources, for example, information of patients and physicians' preferences could be integrated from survey data which requires a different type of research such as qualitative or mixed methods. Besides, data protection policy for healthcare administrative data might be slightly adjusted to reach a better balance between privacy protection and scientific research. Other directions for further research include: first, time trend analysis to explore the change of regional variation in healthcare utilization over time. Currently, data from the year 2014 was used in the present thesis, and data from two additional time points (year 2016 and 2018) is planned to be analysed in a subsequent project. Second, the following research could focus on potential overarching spatial clustering patterns in the utilization of multiple healthcare services, and identifying specific regions with generally superior or inferior performance. Research findings on potential problematic regions may provide insights into better healthcare resource allocation and the planning and implication of local health promotion and intervention programs.

Concluding remarks

To summarize, the presented thesis is the first to simultaneously assess regional variation in the utilization of multiple healthcare services with great diversity. The consistent effects of health insurance-related factors on healthcare utilization and variation worth special notice, suggesting more appropriate healthcare utilization with less unwarranted variation and a better-performed healthcare system may be potentially achieved through adjustment of health insurance design. Moreover, our comprehensive analysis approach allows for assessing unadjusted and adjusted regional variation in healthcare utilization, investigating thoroughly the effects of influencing factors, and more importantly, comparing results across various healthcare services for exploration of potential consistency. It aids in the identification of regional variation and influencing factors of healthcare services utilization in Switzerland and comparable settings worldwide.

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Contribution to publication

The thesis is part of the NRP74 project mainly designed by Matthias Schwenkglenks (the project PI and my thesis supervisor), Holger Dressel, and Viktor von Wyl from the Epidemiology, Biostatistics and Prevention Institute of the University of Zurich. My contributions to the content and methodology in this thesis include the design of the three reported studies, the development of a statistical analysis plan, the conduct of data management and statistical analysis, the results interpretation, and the writing and critical revision of the manuscripts. I was the lead contributor in the development of the comprehensive analysis approach proposed in the thesis, mainly under the supervision of Matthias Schwenkglenks and greatly supported by Oliver Gruebner from the Epidemiology, Biostatistics and Prevention Institute. I was also partly involved in the data collection and extraction, which were mainly performed by the Helsana colleagues, the partner of our NRP74 project providing insurance claims data. I also contributed to the study population selection criteria and data cleaning. Supervision for the all papers was provided by Matthias Schwenkglenks, Viktor von Wyl, Holger Dressel and Oliver Gruebner. All co-authors reviewed the manuscripts prior to submission.

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