Register-based evaluation of primary care

Focus on chronic disease

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"Not everything that can be counted counts. Not everything that counts can be counted."

> *William Bruce Cameron - A Casual Introduction to Sociological Thinking, 1963*

"Without data, you're just another person with an opinion."

> *W. Edwards Deming*

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ABSTRACT

Background: Options for following up primary care at the regional level have increased in Sweden, partly as a result of a national reform in 2009. In Region Västra Götaland (VGR) this was the starting point for a quality initiative with about 100 indicators, using extensive healthcare registers.

Aim: To perform a register-based evaluation of aspects on chronic disease management in primary care after the primary care reform in VGR.

Patients and methods: The four studies were based on individual patient data from national and regional health data and quality registers.

In **Studies I and II,** effects of pay for performance were analysed for patients and medical data in a quality register, as well as the association of inappropriate medications with the tendency to code for medication reviews. **Results:** Paying for data entry led to increased coverage, completeness and reliability. Paying for medication review coding was not associated with a greater reduction of inappropriate medications at highly reimbursed primary care centres than at others.

In **Study III**, visit patterns at primary care centres in relation to blood pressure target achievement for patients with hypertension were studied. **Results:** Current care for hypertension was based mainly on appointments with physicians. Patients at primary care centres with more appointments with nurses than physicians reached blood pressure targets to a greater extent.

In **Study IV**, adherence to guidelines and the potential of improvement for lipid-lowering therapy in patients with established coronary heart disease were studied. **Results:** Fewer than 20% of patients reached the current target for LDL cholesterol, and estimates based on a risk model showed that improved treatment could substantially reduce the number of future cardiovascular events.

Conclusion: Individual-based regional data from healthcare and quality registers offer comprehensive sources of analysis of clinical practice, effects of reimbursement systems and guideline adherence for large groups of primary care patients.

SAMMANFATTNING PÅ SVENSKA

Våra vårdcentraler/hälsocentraler är navet i svensk sjukvård. Det är där de allra flesta patienter tas om hand gällande allt från oro för sjukdom, råd kring enkla självläkande tillstånd, akuta sjukdomar och till patienter med kroniska sjukdomar samt svårt multisjuka. Här sköts allt från hälsokontroller av nyfödda barn till vård i livets slutskede på våra äldreboenden.

För att säkra kvaliteten på vården behöver vi registrera och mäta en del av det vi gör för att med hjälp av resultaten kunna bedriva utvecklingsarbete till nytta för patienterna och därmed också öka jämlikheten i vården. I samband med vårdvalsreformen 2009 i primärvården i Västra Götalandsregionen strukturerades insamlingen av data från vårdcentralernas journalsystem vilket har medfört tillgång till stora mängder information som ligger till grund för den ekonomiska ersättningen till vårdcentralerna. Det är dock inte lätt att bedöma kvaliteten utifrån denna information då det finns många felkällor vid registrering och tolkning av data. Allt som utgör kvalitet kan inte mätas och det som kan mätas är inte alltid till nytta. Det finns dock ett antal kvalitetsregister i Sverige där data från vårdcentraler och annan vård samlats och som visats vara till nytta för ökad kunskap och utveckling av vården om den bearbetas och tolkas på ett strukturerat sätt.

I studierna i denna doktorsavhandling har data från flera av dessa register använts för att analysera hur registrering av olika mått på vården rörande kroniska sjukdomar i primärvården i Västra Götalandsregionen har påverkats av vårdvalsreformen. Olika kvalitetsaspekter belyses också med hjälp av data från registren.

Det kan kännas intuitivt tilltalande att stimulera önskvärda åtgärder eller resultat inom vården med pengar och därmed få mer av det som ökar nyttan för patienterna. Sådana ekonomiska incitament används och har använts i primärvården i syfte att förbättra vården. Detta leder dock inte alltid i den riktning som var tanken och i värsta fall till och med åt helt fel håll. I en av studierna visas att pengar kopplade till medicinska mål såsom blodtryck kan leda till att man börjar registrera annorlunda än man gjorde innan. Även om resultaten pekar mot en faktisk sänkning av blodtrycket så kan sådana effekter på registreringsbeteendet leda till mindre tillförlitliga data. En positiv effekt av att betala för registrering är att registreringen ökar och ju mindre data som fattas desto mer användbara blir registren. Ett annat incitament har varit att ersätta den specifika åtgärden att registrera en kod för att läkemedelsgenomgång har genomförts. Detta i syfte att våra äldre ska ha en

mer adekvat läkemedelsbehandling. Vi har inte kunnat visa att läkemedelsbehandlingen förbättras vid de vårdcentraler som får mest pengar på grund av många koder jämfört med de vårdcentraler som inte kodar i samma omfattning.

Andra sätt att försöka förbättra vården kan vara att strukturera den, speciellt för de kroniska folksjukdomarna. För till exempel diabetesvården krävs att varje vårdcentral i regionen har en diabetes-sjuksköterska. Detta tillsammans med uppföljning av mål-värden för diabetesvård har ökat kvalitén på vården i Sverige jämfört med andra länder. Motsvarande organisation finns inte för till exempel högt blodtryck. I en av studierna visas att vid de vårdcentraler där vården baseras på fler besök till sjuksköterska än till läkare har patienterna större chans att nå målblodtrycket. En förklaring kan vara att en förskjutning av uppgifter från läkare till sjuksköterska ofta sker med tydliga strukturerade rutiner för hur de berörda patienterna ska tas om hand samt att mer tid avsätts för dessa patienter och därmed ökas sannolikheten att riktlinjer följs.

Riktlinjer för kroniska sjukdomstillstånd kan ta lång tid att introducera i den dagliga vården på vårdcentralerna. Vi har visat att det finns stor förbättringspotential i omhändertagandet av patienter som har kranskärlssjukdom. Alltför få har en tillräckligt bra blodfettssänkande behandling och om fler skulle få det skulle färre insjukna i en ny hjärtinfarkt eller i stroke.

Sammanfattningsvis är det viktigt att fortsätta att mäta och utvärdera vården men vi måste vara medvetna om begränsningarna som finns inbyggda i mätandet. Dessa begränsningar skulle kunna illustreras av några engelska begrepp och citat:

- ”The streetligtht effect” eller ”low-hanging fruits” – att vi letar efter saker där det är lättast att hitta dem eller vi väljer att mäta det som lätt går att mäta
- ”Hitting the target but missing the point” – att uppsatta mål nås i form av registrerade koder till exempel men den önskade effekten uteblir

Granskning och kontroll av det arbete som utförs tar allt mer plats på bekostnad av att utföra själva arbetet. Istället för att ständigt försöka hitta fler sätt att mäta och kontrollera verksamheten bör man också ha tilltro till personalens vilja att göra gott och skapa en arbetsmiljö där det finns utrymme att utvärdera sina egna resultat och utifrån dessa skapa strukturer och arbetssätt i syfte att hjälpa patienterna på bästa sätt.

LIST OF PAPERS

This thesis is based on the following studies, referred to by their Roman numerals.

I.   Ödesjö H, Anell A, Gudbjörnsdottir S, Thorn J, Björck S. Short-term effects of a pay-for-performance programme for diabetes in a primary care setting: an observational study, Scand J Prim Health Care. 2015 Dec;33(4):291-7.

II.   Ödesjö H, Anell A, Boman A, Fastbom J, Franzén S, Thorn J, Björck S. Pay for performance associated with increased volume of medication reviews but not with less inappropriate use of medications among the elderly - an observational study. Scand J Prim Health Care. 2017 Sep;35(3):271-278.

III. Ödesjö H, Adamsson Eryd S, Franzén S, Hjerpe P, Manhem K, Rosengren A, Thorn J, Björck S. Visit patterns at primary care centres and individual blood pressure level – a cross-sectional study. Scand J Prim Health Care. 2019 Mar;37(1):53-59.

IV.   Ödesjö H, Björck S, Franzén S, Hjerpe P, Manhem K, Rosengren A, Thorn J, Adamsson Eryd S. Better adherence to lipid-lowering guidelines for secondary prevention may lead to a substantial reduction of cardiovascular events. Submitted.

CONTENT

ABBREVIATIONS

ACG	Adjusted clinical groups
AMI	Acute myocardial infarction
ANCOVA	Analysis of covariance
ANOVA	Analysis of variance
ATC	Anatomical Therapeutic Chemical classification system
BMI	Body mass index
BP	Blood pressure
CI	Confidence interval
CHD	Coronary heart disease
COPD	Chronic obstructive pulmonary disease
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
HbA1c	Glycated haemoglobin
ICD	International Classification of Diseases
KVÅ	Klassifikation av vårdåtgärder (classification of care measures)
LISA	Statistics Sweden Longitudinal Database
LDL-C	Low-density lipoprotein cholesterol
LOCF	Last observation carried forward
NDR	National Diabetes Register
NPR	National Patient Register

OR	Odds ratio
P4P	Pay for performance
PCC	Primary care centre
QregPV	Regional primary care register
RCT	Randomised controlled trial
SBP	Systolic blood pressure
SCB	Statistics Sweden
Vega	Regional administrative healthcare database
VGR	Region Västra Götaland
WHO	World Health Organisation

INTRODUCTION

Quality is, depending on the area of interest, difficult or impossible to define and measure. The WHO definition of quality of care is "the extent to which health care services provided to individuals and patient populations improve desired health outcomes".

This thesis does not attempt to evaluate quality of primary care as a whole, only a few important aspects after a national reform in Sweden 2009. The reform was accompanied by a search for indicators to monitor and analyse the performance of primary care centres. This thesis deals with quantitatively important areas in which relevant results can be directly translated to clinical practice.

PRIMARY CARE AND THE REFORM

SWEDEN

Swedish primary care differs in important ways from specialised care. Specialised care follows patients with specific diseases, typically for a limited period of time. Primary care follows patients with varying conditions and diseases for long periods of time [1]. The definition of primary care and its scope varies between countries and regions, but the Organization for Economic Co-operation and Development (OECD) has identified some common features: first-line care, provided in the proximity of the patient, patient-focused as opposed to specialised care that has a disease or organ focus, broad in its context and a coordinator of the patients total care needs [2]. The importance of primary care for both initial assessment and chronic disease management is well-known [3-5]. More than 60 % of the 68 million medical appointments in Sweden every year are at primary care centres (PCCs) [6].

Swedish primary care is structured in 21 different regions. Their management, regulation and compensation systems are based on national laws including the Health and Medical Services Act (Hälso- och sjukvårdslagen 2017:30), Patient Act (Patientlagen 2014:821) and Patient Data Act (Patientdatalagen 2008:355). All regions offer primary care within a publicly financed system including both public and private providers. Approximately 43% of PCCs are privately run [7]. Healthcare expenditures in Sweden are funded chiefly (80%) by tax revenue [8].

Largely due to long-term accessibility problems, a primary care reform was launched in 2009 [9]. The government introduced a relatively deregulated market model by which compensation is associated with the individual patient. The legislation mandated new primary care systems with free choice of healthcare provider by 1 January 2010 (Lag om valfrihetssystem 2008:962) [10]. The systemic change was based on a model that included freedom of establishment as well [11, 12]. The reform also involved regional follow-up of PCC performance in order to ensure fair allocation among them.

REGION VÄSTRA GÖTALAND (VGR)

The primary care reform was launched in VGR on 1 October 2009. It was the starting point for an extensive regional quality initiative.

VGR is located in south-west Sweden. The region is mixed urban and rural with approximately 1.7 million inhabitants (2011, 17% of the national population). Gothenburg, the second largest city in Sweden with close to 600, 000 inhabitants is there. About three-fourths of the population lives in medium-sized to large urban areas. Approximately 200 PCCs operate there in the wake of the reform, as opposed to 140 earlier. Roughly 47% are privately run.

Following the reform, significant resources were devoted to development of an extensive follow-up system based largely on register data. The aim was to combine various sources to yield both statistical information and quality measures at the local level, as well as analysis and follow-up at the regional level. Starting in 2011, a total of 140 indicators were implemented and published online, including patient selection, specific chronic diseases, drug use, patient satisfaction, drug treatment of the elderly etc. [13]. Among the sources were drug prescription data, quality registers and the regional patient administrative database.

Approximately 80 % of a PCC's total revenue is based on capitation derived from age, sex (50%) and disease burden i.e. diagnoses (50%) [12, 14]. As in other regions, pay for performance (P4P) linked to a number of indicators was used enthusiastically. The total P4P payment was 3% of total revenue, the initial intention was to raise it to 10%. The current P4P is approximately 4% maximum. Payment is also based on geography and socioeconomic status according to the Care Need Index (CNI), compensation for interpreters and other separate commitments.

The regional quality follow-up system introduced in VGR is extensive but has not yet been fully studied or evaluated. The system was made possible by large-scale national and regional healthcare registers.

REGISTERS

Sweden has a long tradition of health data registers as well as quality registers, all based on the unique personal identity number [15]. A register may include information about either the total population or a particular cohort. Data can be used for research after approval by an ethical review board. Following is an overview of Swedish registers relevant to this thesis. Details about registers used in the thesis are presented in the methods section.

POPULATION REGISTERS

Population registers reflect demographics. The Population Register (Folkbokföringsregistret) kept by the Swedish Tax Agency (Skatteverket) and the Total Population Register (Registret över totalbefolkningen) kept by Statistics Sweden (Statistiska centralbyrån, SCB) describe the population with data on birth, marital status, family, migration, death and other circumstances [16]. The Tax Agency reports data to the Total Population Register, which is the primary source of demographic data for research purposes.

NATIONAL HEALTH DATA REGISTERS

National health data registers are kept by the Swedish National Board of Health and Welfare (Socialstyrelsen). They are governed by the Health Data Act (Lag om hälsodataregister 1998:543). Among them are the National Patient Register (NPR), Prescribed Drug Register and Cause of Death Register. Healthcare providers must report to these registers.

The NPR can be used for statistics, evaluation, quality assurance and research. Data include hospital and specialised healthcare. Collection of individual patient data from primary care is, however, not permitted by the current legislation (Förordning om patientregister hos Socialstyrelsen 2001:707). The National Board of Health and Welfare has proposed a legislative amendment [17].

REGIONAL HEALTHCARE DATABASES

As opposed to the NPR, regions often collect individual data from primary care in their databases. These registers are similar to the NPR and include primary care details as well.

QUALITY REGISTERS

National (and regional) quality registers are subject to separate regulations. Since the 1970s, the national quality registers have been developed by

healthcare professionals for internal quality assurance and improvement of clinical practice [18]. There are over 100 national quality registers [19, 20]. A quality register is an automated, structured collection of personal data for systematic and continuous quality assurance and improvement. They are governed by the Patient Data Act (Patientdatalagen 2008:355). They serve a selected patient population based on diagnosis or treatment and collect individual patient data from different providers in one common database with the aim of improving care. This structure makes the registers highly suitable for comparative analyses and research. As opposed to national health data registers, patients may opt out. They must be informed prior to entry of their data.

REGISTERS IN PRIMARY CARE

Contrary to the situation for specialised care, entry of primary care data is fragmentised due to legislation and varying regional interpretation [21]. Since individual primary care data cannot be obtained on a national basis, such analysis is performed only at the regional level. National analysis can be conducted only by researchers after a separate applications to each region.

Due to the virtually total absence of national individual primary care data, an initiative on behalf of the National Board of Health and Welfare started in 2000 [22]. The conclusion was that national coordination was possible but would require structured electronic health records. Meanwhile, regional projects were under way. In 2010, the Primary Care Quality (PrimärvårdsKvalitet) initiative was taken by the Swedish Organisation for Primary Care Physicians with the aim of generating national, regional and local data to ensure continuous improvement. Specific quality indicators were developed. Primary Care Quality is chiefly a tool for follow-up and improvement based on local individual patient data. Due to privacy issues, there are still no nationwide individual patient data, only aggregate data on the PCC level are available.

National quality registers are generally constructed and used for specialised care. But the vast majority of patients and most major chronic diseases are handled by primary care. With the exception of the National Diabetes Register (NDR), national quality registers have generally failed to receive widespread acceptance among primary care providers such that national and regional coverage is highly limited. The biggest obstacle is probably that manual data entry is the predominant approach. Given that primary care addresses a broad spectrum of conditions, the method is not feasible.

The regional primary care register in Västra Götaland (QregPV) is the only one that was developed specifically for improvement in the area. Proceeding from data on major chronic diseases, its main purpose is to follow PCC guideline adherence with respect to hypertension or ischaemic heart disease.

PRACTICAL ASPECTS OF REGISTER-BASED RESEARCH

Sweden's 12-digit personal identity number makes it possible to link data from all registers [15]. Approval by a regional ethical review board is a prerequisite to creating datasets that can be combined for use by researchers. A specific register is normally the basis for selecting a patient cohort. Particular data in the register are requested, including the time frame as well as exclusion and inclusion criteria and variables. If data from various registers are to be merged, a request must be sent to all of them. The original dataset is forwarded for construction of files and replacement of personal identity numbers by anonymous identifiers for each patient (pseudonymisation), see Figure 1. Negotiation between the various authorities determines who will perform pseudonymisation and, if requested, keep the code key. The code key is saved in a secure environment, most often at the National Board of Health and Welfare, for possible update during a period specified on the application to the ethical review board. The files from the various data sources are sent to the researchers, who link content based on the pseudonymous identity numbers.

As for the analyses in this thesis, additional protection can be provided at the Centre of Registers in Gothenburg by means of Secure On-line Data Access (SODA) and remote access from local computers. Only researchers working on projects with ethical review board approval may use the remote service. The files of individual patient data cannot normally be downloaded to a local computer.

A major advantage to using population databases and register-based data is that the study period has already passed [23]. Given such real-world data that are not entered for specific use, bias is also minimised. However, retrieval can take some time. Processing periods at the National Board of Health and Welfare may be several months, which must be considered when planning register-based research. Nor can analysis begin until additional refinement has been performed.
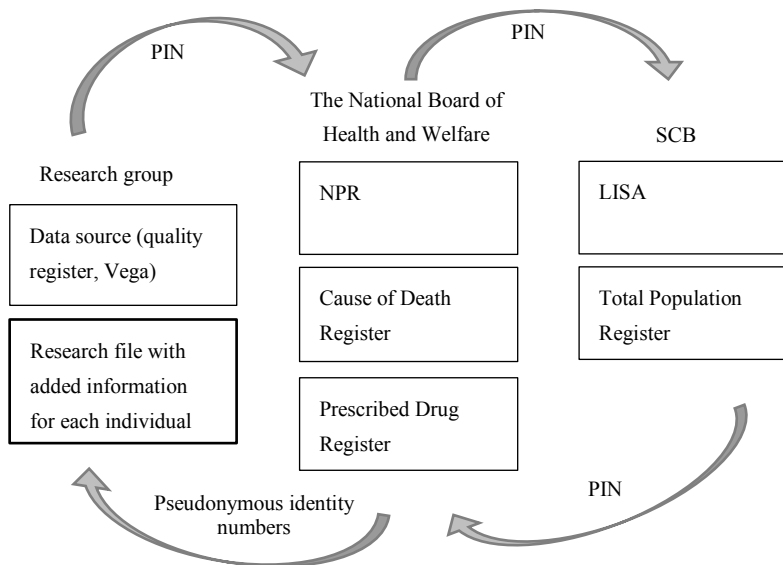
Figure 1. Schematic description of typical data transfer and links to create a patient file for research. Abbreviations: LISA: Statistics Sweden Longitudinal Database; NPR: National Patient Register; PIN: personal identity number; SCB: Statistics Sweden; Vega: regional administrative healthcare database.

POPULATION AND PATIENT INVOLVEMENT

Participation in population and national health data registers is mandatory and patients are not involved in decisions concerning associated research. Before being included in a quality register, they must be informed and given the opportunity to opt out. They are normally told that data may be used for research purposes following approval by an ethical review board. The registers are transparent and typically post information about their purpose and use by researchers to a website. Patient advocacy groups must have representation on the steering committee before national funding can be obtained. Whether or not patients are to be informed and given the opportunity to opt out of register-based research is determined by the ethical review board. When the study population is large, individual patient consent is impractical. However, approval by an ethical review board, including its lay members, is mandatory.

A 2017 report based on surveys and interviews found that the majority of the Swedish population is positive to the use of digital data in healthcare and research [24]. A Finnish study arrived at a similar conclusion [25]. The

respondents were largely satisfied with methods that are broader than individual informed consent. Awareness about register-based research was low among European stroke survivors [26]. Young patients with high educational levels wanted above all to be more involved.

INTERPRETATION OF DATA

The growing availability of Swedish healthcare data has created a demand for transparency and reporting to public servants, media and the general population. The ability to perform comparisons and make decisions is intuitively appealing. This transparency has been provided by *Open Comparisons* (Öppna jämförelser) since 2005 with regional feedback [27]. Since 2015 a website entitled Healthcare in figures (Vården i siffror) has offered similar comparisons [6]. *Open comparisons* can serve as incentives and have been shown to grow in importance over time among British PCCs [28, 29]. Accessible data are key to fruitful discussion and the potential for more targeted quality improvement [30]. While transparency is worthwhile and well-intended, accompanying problems need to be addressed.

A critical analysis has suggested that true transparency is not about publishing available data but an active creative process that proceeds from specific methods [31]. The problems arise from the complicated nature of the healthcare system, which is amenable to independent assessments by experts only. Presenting data without adequate interpretation may give only an illusion of transparency.

A practice can be characterised by means of overall (normative) and technological (concrete) elements [32]. Striving for transparency can measure only a limited number of parameters even while trying to capture a broader context. Unintended consequences for the organisation and its outcomes may arise. New motivational structures emerge as the focus shifts from proper care to compliance with the process, including time-consuming administrative tasks. Performance measurements is not a neutral activity. Other concerns fall by the wayside. It was concluded that "The audit society is a symptom of the times …" and that observation is highly rewarded and considered more important than actual practice [32].

Comparisons between care units should be interpreted with caution as a guidepost and basis for further dialogue [33, 34]. The challenges posed by access to register data by purchasers of healthcare, representatives of the public and media and the risk of misinterpretation was recognised early [18]. Experts understood that quality registers should be used critically and not for

comparison purposes. The importance of medical expertise when interpreting and applying data at both the national and local level was underscored. Noticeable is that many PCCs in the region have no physicians in any leading position.

A central question is whether healthcare quality can be measured by figures, particularly in relation to transparency, open comparisons, follow-up and reimbursement as described in the report *Making Care Even Better* (Ännu bättre vård) by Bo Bergman [33]. Many aspects of healthcare are difficult and tricky to measure. Not all that can be measured, on the other hand, is relevant. Variations between measurements and care units must be taken into consideration. If care units are compared in accordance with a specific variable, the results will inevitably vary. The most interesting possible finding is that the variation is <u>higher</u> than may be expected on a normal or random basis. Thus, trends over time are highly revealing. Ordinary statistical measures suffer from limitations in such comparisons. For instance, the proportion of patients with blood pressure (BP) below a specific target can be misleading since the same value is compatible with both a small dispersion with results just above the target or a large dispersion with many results well above the target. In the first case the PCC might have prioritised patients with the poorest BP, and in the second case those who had almost achieved the target already. Quality care is hard both to define and to measure.

The problems described above call into question all measurements designed to compare quality. But too much scepticism about comparisons could side-track important information and the ability to address key healthcare issues. The studies in this thesis highlight data use that fails to provide increased quality as well as possibilities to improve transparency by interpreting complex data.

AREAS OF FOCUS IN THE THESIS

The studies in this thesis have focused on three areas:

- Financial incentives to improve quality of care
- The impact of organisation on quality of care
- The gap between guidelines and clinical practice

After the primary care reform, the majority of quality indicators, several of which are linked to financial incentives, address patients with diabetes, hypertension, coronary heart disease (CHD) and other chronic conditions, as well as multi-pharmacy in the elderly. The incentives have been the subject of public debate; this thesis targets two particular areas. Although incentive

schemes for treatment of chronic disease have attempted to improve quality, adherence to guidelines in regional follow-up systems has been poor. For that reason, other aspects of chronic disease in primary care were also studied. One of them was nurse-based care as a way of better controlling BP in cases of hypertension. Another aspect was adherence to lipid-lowering treatment guidelines and the potential reduction of cardiovascular events among those with established CHD.

FINANCIAL INCENTIVES

The launch of the primary care reform in VGR was accompanied by enthusiasm about financial incentives to improve quality [12]. A brief history of national healthcare systems is useful in this connection.

LOOKING BACK

National healthcare systems have evolved through three phases: 1) equality and accessibility by everyone; 2) cost containment; 3) performance and efficiency enabled by register data [35, 36]. In the wake of economic growth, financing of the healthcare system was only a minor problem during the 1960s and 1970s. Dissatisfaction with rising costs of healthcare in the 1980s led to framework budgets. More decentralised decision-making was also targeted. In the late 1980s and 1990s, low productivity encouraged a greater market orientation such that many regions introduced client and provider organisations. Providers were remunerated on the basis of various productivity indicators. The third phase started in the 2000s with increased focus on quality and results. P4P was inspired by the experiences of both the United States and the National Health Services in the UK. The reform was the opening shot for use of P4P in primary care. The independent regional structure of separate data management and follow up systems resulted in as many reimbursement schemes.

PAYMENT PRINCIPLES

Payment principles are either fixed or variable. Fixed payments may be based on framework budgets for which compensation proceeds from resource consumption. Capitation based on the population may also be viewed as fixed, although payment in a system that includes freedom to choose PCC varies with the number of patients. Capitation may be based on age and sex, or more elaborately on adjusted clinical groups (ACG) that reflect diagnoses in medical charts, as an indicator of disease burden. Someone with diabetes or another chronic disease commands higher payment than a healthy person of the same age and sex.

Variable payments are incentives linked to quality of care and similar parameters. They may be process or outcome measures, such as BP entry or the percentage of patients with BP below a certain target [35, 37]. Classification of care measures (KVÅ) codes are also process-oriented. Outcome measures can be broken down into intermediary (BP target etc.) and final (cardiovascular event, death etc.). Another kind of variable payment is fee-for-service.

PAY FOR PERFORMANCE (P4P)

P4P, which links incentives to desired activities or goal achievement, has become integral to many healthcare systems over the past few decades. P4P can be associated with process, outcome and structural measures, such as employing a diabetes nurse at the PCC [37]. National quality registers, originally developed by healthcare professionals for internal quality assurance purposes, have more recently served as the basis for financial incentives, such as P4P coupled to process and outcome measures.

The various approaches to targeting payment have various advantages and disadvantages. Studies have found improved register entry and results for clinically important indicators such as BP among patients with diabetes [38, 39]. Evidence that P4P has a sustained positive effect is nevertheless weak and inconclusive [40-45]. Clinical practice may change and process measures improve short-term, but the impact on intermediate health outcomes is more doubtful.

Financial incentives may even be counterproductive. The underlying assumption is that targets change behaviour in the desired direction and that abuse of the system is uncommon. Since quality of care is difficult to define, what to measure and reimburse for is a hazy area [46]. The risk arises that healthcare will be channelled in a non-optimal direction due to a focus on quality outcome measures that are low-hanging fruits as targets for payment [47, 48]. The indicators, like coding for various interventions, that can be gauged are often proxies for actual outcomes. You get what you ask for, and you may miss the forest for the trees by attaining the target but not the desired effect.

Defined targets always relate to a subset of total performance [49]. Non-targeted areas may be assigned lesser importance [50, 51]. Patients for whom target attainment is difficult may be ignored [52]. They might just happen to be the people who are in most need of medical attention.

External spurs like P4P may undermine the intrinsic motivation of professionals to do a good job [53]. New data entry requirements may take time away from patient care. If requested information, such as codes for follow-up and monitoring, is not regarded as medically relevant, the negative impact may be even greater.

Moving targets to accommodate results is another potential hazard. The incentive to perform as well as possible disappears [49]. "Ratchet" and "threshold" effects have also been highlighted. The "ratchet effect" refers to resting on one's laurels once a target has been attained [50]. The "threshold effect" refers to the tendency of results to coalesce around the target from both above and below. Superior performance may fall by the wayside.

ORGANISATION – NURSE-BASED CARE

Financial incentives introduced after the primary care reform seek to ensure quality by means of stricter adherence to guidelines for chronic disease. In addition to patient or physician factors, organisational parameters are potential facilitators or obstacles to risk control [54]. For example, nurse-based and team care are proven vehicles of improvement [54, 55]. The PCCs in VGR have been required to employ a diabetes nurse ever since the primary care reform went into effect [56]. Hypertension or CHD are not subject to similar organisational demands. The latest European guidelines for prevention of cardiovascular disease (CVD) recommend teamwork to improve BP control as well as long-term management of hypertension, and stress the role of nurses [57].

A WHO-report identifies task shifting as a means of strengthening staff and improving patient access [58]. The report presents global recommendations and guidelines for HIV while making it clear that other essential health services could benefit from them as well. It conclude that nurses and professionals can safely and effectively perform clinical tasks that have traditionally been the purview of physicians.

Such an approach may be a pragmatic approach to addressing physician shortages [59] on the basis of structured protocols [60]. Maintained quality is vital, and the evidence suggests that the approach, in both primary and secondary prevention, may be superior to standard care [61, 62]. Task shifting may include prescriptions, treatment, referrals etc. Some countries have come further in this respect than Sweden [59].

ADHERENCE TO GUIDELINES

Notwithstanding financial incentives for stricter adherence to guidelines concerning the treatment of risk factors associated with chronic disease, there is still room for improvement. When it comes to secondary prevention of CVD in primary care in VGR, only 20% of patients with a CHD diagnosis attain the low density lipoprotein cholesterol (LDL-C) target of <1.8 mmol/L [63, 64]. The percentage of patients with a CHD diagnosis who attain the recommended target for LDL-C in secondary prevention is increasing but is still low, as in other countries [65, 66].

Recent evidence shows an almost linear relationship between LDL-C level and risk of CVD [67]. Lowering of LDL-C by means of statin treatment effectively reduces risk of CVD recurrence [68]. The same is true of the elderly [69]. Non-adherence to secondary prevention medication including statins, is associated with an increased risk of CVD events and all-cause mortality [70].

Adherence is the responsibility of both the physician and the patient. The physician must be knowledgeable and receptive to current guidelines while the patient must be properly informed and willing to follow recommendations [54, 71]. Attitudes have an impact in both directions. Adherence over time is a particular challenge. Non-adherence may be intentional due to contraindications etc., or unintentional due to ignorance or lack of awareness [72]. Staffing, routines (structured, team-based care, etc.) and other organisational factors also influence adherence to guidelines [73-76]. Clinical inertia plays a part as well [77].

SUMMARY

Primary care is essential to the care and prevention of chronic diseases. Many patients that are at risk for serious complications are taken care of. After the primary care reform, extensive data are available at the regional level. Register-based follow-up of has great potential for quality assessment but careful interpretation is required. Primary care research with high clinical relevance is needed. This thesis has targeted important aspects of quality following the primary care reform in 2009.

AIM

The general aim of this thesis was to perform a register-based evaluation of various aspects of chronic disease management after the launch of an extensive register-based primary care quality initiative in primary care in VGR.

Study I

The aim was to, proceeding from NDR data, assess the effects of a payment programme for primary care, on register entry practices on behalf of individuals with type 2 diabetes. Register data quality and comparability were studied by evaluating characteristics of new patients and data entered after introduction of the P4P payment programme.

Study II

The aim was to determine whether the adoption of a P4P process measure linked to medication review coding had been associated with an increase in the volume of reviews and an improvement in drug treatment among elderly primary care patients based on a series of national indicators.

Study III

The aim was to examine visit patterns as a measure of how care is structured at the PCC level based on real-life data, as well as whether nurse-based approaches were linked to better BP control in primary care patients with hypertension and no complications.

Study IV

The aim was to describe adherence to guidelines concerning secondary prevention lipid-lowering treatment and estimate the potential reduction in CVD events within 5 years if all relevant patients improved in that regard.

PATIENTS AND METHODS

SUMMARY OF METHODS

This thesis is based on four studies, see Table 1. All of them were register-based observational studies based on individual patient data and research questions stemming from regional monitoring system observations.

Table 1. Summary of methods used in the studies

Study	I	II	III	IV
Design	Repeated cross-sectional with a reference group	Repeated cross-sectional	Cross-sectional	Cross-sectional /risk estimation modelling
Level of analysis	Patient	Patient and PCC	Patient and PCC	Patient
Period	2010-2011	2009-2013	2015	2015
Sources of data	NDR	Vega

Prescribed Drug Register

Swedish Population Register | QregPV

Vega

National Patient Register

Prescribed Drug Register

LISA | QregPV

Vega

National Patient Register

Prescribed Drug Register

Cause of Death Register |

Study	I	II	III	IV
Study group	Primary care patients in the NDR (age 18-79)	Patients age 75 or older with at least one PCC appointment during the year	Patients age 40-80 in the QregPV with hypertension and available systolic BP	Patients in the QregPV with a previous diagnosis of CHD (I20-I25)
Total number of patients	84,053	181,210 ~ 95,000 per year	88,945	86,206
Exposure	Region VGR/Skåne (financial incentive programme)	PCC groups 1-3 (based on percentage of patients with a code for medication review)	PCC visit patterns	*Atorvastatin 40/80 mg or LDL-C-target (< 1.8 mmol/L)*
Main outcome variables	Entry, levels and target achievement for HbA1c, BP and LDL-C	Percentage of PCC patients receiving inappropriate drugs according to national indicators	OR for the individual to attain BP ≤ 140/90 mmHg	*Reduction in number of CVD events over 5 years*
Co-variates	Age, sex, diabetes duration	Age, sex, ACG weight	Age, sex BMI, smoking, socioeconomic status, number of drugs,	Age, sex, diabetes, comorbidity, medications

Study	I	II	III	IV
			medications, appointments	
Handling of missing data	Deletion of observations with missing data depending on the analysis	No missing data	Multiple imputation	Use of available variables in the risk model /deletion of observations with missing data in the prediction model
Method	Student's t-test, chi-square, generalised linear model	Generalised linear mixed model for repeated measure-ments	Multi-level generalised linear mixed model	Cox proportional hazard regression

*Study IV did not look at the effect of exposure on an outcome.

Abbreviations: ACG: adjusted clinical groups; BMI: body mass index; BP: blood pressure; CHD: coronary heart disease; CVD: cardiovascular disease; HbA1c: glycated haemoglobin; LDL-C: low density lipoprotein cholesterol; LISA: Statistics Sweden Longitudinal Database; LOCF: last observation carried forward; NDR: National Diabetes Register; OR: odds ratio; PCC: primary care centre; QregPV: regional primary care register; SBP: systolic blood pressure; Vega: regional administrative healthcare database

SOURCES OF DATA

The studies proceeded from national patient data registers and databases, as well as quality registers, depending on the research question to be addressed.

The following registers were used:

NATIONAL DIABETES REGISTER (NDR)

The NDR was launched in 1996 by the Swedish Society for Diabetology as a nationwide, population-based vehicle for improvement of diabetes care quality

[78]. The register contains individual patient data concerning laboratory analyses, clinical characteristics and complications. Separate primary and secondary care units report to the register either online or by means of clinical record databases. The register covered approximately 85% of patients with diabetes in 2011 [79] and an estimated 96.5% today [80]. Although reporting to the NDR is not mandatory in VGR, all PCCs do so given that a diabetes nurse is required and all follow-up data on patients with diabetes must be sent to the region.

REGIONAL ADMINISTRATIVE HEALTHCARE DATABASE (VEGA)

Vega, which was set up in 2000, covers all healthcare contacts in the VGR [21, 81]. The database also includes information about residence, age, sex, PCC and diagnostic codes according to the International Classification of Diseases (ICD). The diagnoses are entered in the electronic patient chart along with a healthcare contact. All care units, including PCCs, must report to Vega. Reimbursement to PCCs for capitation and disease burden is based on data from the database. VGR forwards information from Vega about hospital and other specialised care contacts to the NPR.

REGIONAL PRIMARY CARE REGISTER (QREGPV)

The QregPV started in 2006 as a professional initiative (Allmänmedicinska Sektorsrådets Arbetsgrupp för Kvalitet, ASAK) [64]. QregPV contains data about five major chronic conditions; diabetes, CHD, hypertension, asthma and chronic obstructive pulmonary disease (COPD). Its primary focus nowadays is PCC adherence to guidelines for hypertension and CHD [63]. For patients with diabetes, the NDR serves mostly as a source of data. QregPV initially obtained information from publically owned PCCs only. After the healthcare reform in VGR 2009, privately owned PCCs were also included and it was converted to a quality register. Since 2010, QregPV has been managed by the Centre of Registers in VGR. The variables are BP, glycated haemoglobin (HbA1c), lipids, smoking, height, weight, girth and body mass index (BMI). PCCs report to QregPV on a monthly basis.

PRESCRIBED DRUG REGISTER

The Prescribed Drug Register contains information about all filled prescriptions since 1 July 2005. The Swedish eHealth Agency performs monthly quality checks before data is forwarded to the National Board of Health and Welfare [82, 83]. The register includes data about patient characteristics (age, sex, residence etc.), prescriber characteristics (profession,

specialty, type of care etc.) and medication (date dispensed, formula, container size, dosage etc.). All medications are categorised according to the Anatomical Therapeutic Chemical (ATC) classification system [84].

NATIONAL PATIENT REGISTER (NPR)

The NPR contains information about diagnoses and interventions at hospital since 1964. It became nationwide in 1987 and has included information from both public and private specialised care units outside hospital since [85]. Pursuant to current legislation, the register does not include any primary care information [17]. Diagnoses are categorised according to the ICD [86]. Healthcare providers have supplied data on a monthly basis since 2015 in view of a new code of statutes (SOSFS 2013:35). The Swedish National Inpatient Register which is part of the NPR, has almost complete coverage and was found to offer high validity for many diagnoses [87].

CAUSE OF DEATH REGISTER

The Cause of Death Register contains official national statistics on all fatalities since 1961 [88]. The register is updated once a year. Since 2012, all deaths are included regardless of whether or not the individual was a Swedish citizen. The variables include date, age and cause of death according to the ICD [86].

POPULATION REGISTER

The Population Register is kept by the Swedish Tax Agency with the aim of reflecting personal details, family relationships and composition of the Swedish population [16]. When first entered in the register, an individual is assigned a 10-digit personal identity number that has been in effect ever since 1947 [15]. In 1991, the Tax Agency took over census responsibilities from the Church of Sweden. Life events such as births, marriages and deaths and also place of residence are continuously recorded.

STATISTICS SWEDEN LONGITUDINAL DATABASE (LISA)

Since 1990, LISA has contained data for individuals 16 or older who were entered in the population register as of 31 December for each year. LISA obtains information from several demographic registers concerning the labour market, educational and social sectors, including date of birth, marital status, schooling and income [89].

ETHICAL APPROVAL AND CONSIDERATION

The Regional Ethical Review Board in Gothenburg has approved all studies in this thesis with the following reference numbers: 564-12 (**Study I**), 362-14, T080-15 (**Study II**), 1062-15 (**Study III and IV**).

Ethical approval of register-based research is a balancing act between the benefits for public health and personal privacy. A patient can opt out of a quality register but not a demographic or health data register. Before being included in a quality register, the person is to be informed of that which can be done with written or oral information. Informed consent is not mandatory, and generally not feasible, in register-based research. Study populations may number in the tens of thousands and many of them will be dead once the study is conducted. Informed consent may result in selection bias. Since the studies include so many patients, the risk of violating personal privacy is very small.

STATISTICS

STUDY DESIGN

Register-based studies are a mix of prospective and retrospective design [90]. Data are collected before subsequent studies have been planned, not chiefly for specific research. A register consists rather of a standardised information for a group of individuals. Patient selection, hypothesis generation etc. are the mostly retrospective. Data about exposure and outcome are often prospective. The studies in this thesis are observational and cross-sectional in the sense that the population and the exposure is defined at a point or interval of time. Patients were chosen on a particular date but additional information about them could be obtained before that.

Both **Studies I and II** collected and compared data at different points in time but did not follow a cohort. The design was not longitudinal since patients were not the same at the different points in time.

Studies I, II, III were modelled largely for explanatory rather than predictive purposes. The aim was to test for causal (rather association) hypotheses. **Study IV** designed a model for predictive purposes, primarily to compare number of events, not to anticipate their number as accurate as possible.

MISSING DATA

Missing data are common in register-based studies. If missing data are random, it may be safe to delete these particular cases, but that is not typically the situation. For example, LDL-C values may be missing mostly among older patients with multi-morbidity.

These problems were dealt with in the included studies in the following ways:

- Deletion
    - Observations (**Study I**) – using a subset of observations with complete data or using all possible patients in various analyses depending on the available data. Complete case analysis includes only patients for whom all variables are available.
    - Variables (**Study IV**) – choosing models that do not include variables with large quantities of missing data.
- Imputation
    - Multiple imputation (**Study III**) is a way of replacing missing data with estimated values based on information available in the data set and taken from a distribution. The substitution is performed multiple times, generating a number of data sets whose results are pooled. This compensates for the uncertainty of the imputation.

Before applying the techniques above, the data sets were completed as much as possible by means of last observation carried forward (LOCF). Most registers include information from every contact, several of which may ensure complete data. For instance BP can be entered at one point in time and body weight later on.

CONFOUNDING

A confounder affects both the predictor (independent) and outcome (dependent) variable. Confounding can cause bias which is important to be aware of even if the magnitude of the effect cannot be assessed. Age is a typical confounder that effects almost all predictors and outcomes.

Register-based studies limit the confounders that can be accounted for to those that are accessible in the particular databases. For both ethical and practical reasons, it is rarely possible to collect other information concerning each

patient. Confounders were chosen, for the studies included, on the basis of clinical knowledge and available data.

STATISTICAL METHODS

DESCRIPTIVE STATISTICS
Descriptive statistics were presented using the arithmetic mean and standard deviation for continuous variables, as well as frequencies and percentages for categorical variables.

GROUP COMPARISONS
Comparisons between groups of patients used Student's t-test for continuous variables and $\chi2$-test for categorical variables. Hypothesis tests had a two-sided alternative; a p-value < 0.05 was considered statistically significant. Odds ratios (OR) and estimates were presented with 95 % confidence intervals (CI).

GENERALISED LINEAR MODELS
Regression models examine the association between a dependent variable and one or more continuous independent variables. Analysis of variance (ANOVA) is used for categorical independent variables. ANOVA and regression models are mathematically similar. Analysis of covariance (ANCOVA) is a general linear model (combination of regression and ANOVA) that includes both continuous and categorical independent variables. The dependent variable is continuous in linear regression (and ANOVA).

For binary dependent variables, logistic regression is used instead. In Poisson regression, the dependent variable is a count variable. Generalised linear models are flexible tools that allow for dependent variables with non-normal distribution through the use of link functions. These models can handle variables with binary, Poisson and other distributions.

MIXED MODELS
Mixed generalised linear models are used to capture correlations between observations, for example patients at the same PCC or repeated observations on the same patient, see Figure 2. A distribution of the dependent variable and a suitable link function, for example a binomial distribution with a logistic link function or a Poisson distribution with a log link function, must be chosen.
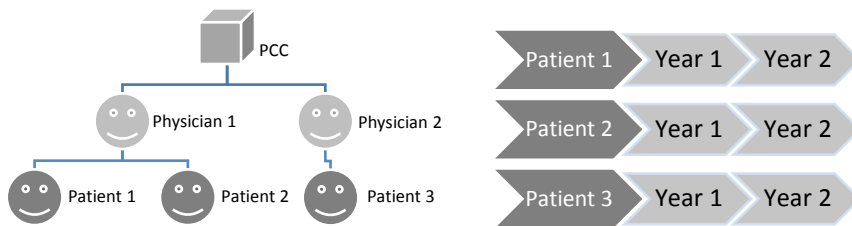
Figure 2. Examples of multilevel mixed models. Abbreviations: PCC: Primary care center

Mixed models include random and fixed factors. Random factors are measures of variance and fixed factors measures of association. The random factor is the variable for which we are not interested in the outcome related to it but want to take the influence of it into consideration and is defined as a distribution. PCC enrolment may be such a random factor when the aim is not to compare PCCs with each other. The fixed factors are the covariates adjusted for in the model and can be defined in levels/numbers, for example age and sex.

SURVIVAL ANALYSIS

Survival analysis examines the risk that an event will occur over time. Individuals are followed until an event (disease, death) is noted. Someone who does not experience an event during the period is referred to as censored, a form of missing data. In this thesis (**Study IV**), data is (right) censored due to end of follow-up or death.

Cox proportional hazard is a regression model that analyses the association between survival time and selected independent variables (risk factors). The hazard function, i.e. the risk that an event will occur at a specified time, is conditional on being event-free until then. The cumulative hazard over time is subsequently modelled. The survival function is the likelihood of not having experienced an event within a specified time. Summing up the individual risks of an event yields the total number of individuals who are predicted to experience it. Estimates from the regression model are hazard ratios (HR) with a 95% confidence interval.

The statistical analyses were performed using SPSS version 20.0 (SPSS Inc., Chicago), SAS version 9.4 (SAS Institute, Cary, NC) and R 3.4.0.

STUDY I – P4P AND DATA ENTRY

STUDY RATIONALE

A new payment programme that was introduced in VGR on 1 January 2011 included incentives linked to entry of patients and medical variables in NDR, as well as medical target attainment. Region Skåne was chosen as the reference because no such targets had been included in its payment scheme. The reference region is similar to VGR in terms of primary care organisation, including population choice, enrolment at PCCs, responsibility for expenditures and structure of the payment programme [12]. Both regions use a fixed payment approach for enrolment (capitation) at PCCs based on age, sex, diagnostic classification and socio-economic indicators. NDR patient entry was rewarded in both counties.

After introduction of the P4P programme in VGR, up to 4% of the total income for a PCC, approximately one-quarter of which was accounted for by diabetes, was based on quality indicators [13]. PCC participation in the incentive programme was mandatory, and there was no system for excluding patients. The P4P programme in VGR rewarded NDR entry, as well as the percentage of patients with:

- a value for HbA1c, BP, LDL-C, albuminuria and smoking
- HbA1c < 52 mmol/mol
- BP < 130/80 mmHg
- LDL-C < 2.5 mmol/L

STUDY POPULATION AND PERIOD

Primary care patients age 18-79 in the NDR from 2008 to 2011 were included for both VGR and the reference region. Data for 2008-2009 were used to determine the patients or patient data that were new to the register in 2010-2011 (not having been entered for the previous two years). Patients were included whether or not they were classified with type 1 or type 2 diabetes given that 97 % have type 2.

STATISTICAL METHODS

Comparisons were performed between both regions and years. The variables assessed were HbA1c, BP, LDL-C and the percentages of patients who reached the targets, as defined above. The percentages of patients with values for the above variables, as well as albuminuria and smoking, were also compared.

The statistical significance tests were Student's t-test for continuous variables and the χ2-test for categorical variables. For regression analyses, a generalised linear model and ANCOVA were used.

STUDY II – P4P AND PROCESS MEASURES

STUDY RATIONALE

VGR has used coding for medication reviews as a P4P quality indicator since 2009 for patients age 75 and older. Payment has varied over the years. At the end of the study period (2013), financial compensation was granted and increased linearly if the percentage of these patients at the PCC, for whom a medication review had been entered within the past 12 months, was between 30-60%.

The medication review is an assessment of the patient's medication list and should be performed at least once a year during a doctor's appointment. Pharmacological treatment was assessed in accordance with the National Board of Health and Welfare indicators for appropriate drug treatment among the elderly [91, 92].

STUDY POPULATION AND PERIOD

Annual data for 2009-2013 concerning patients age 75 and older with at least one PCC appointment and who were alive at the end of the year were extracted from Vega, see Figure 3. Only patients enrolled at the same PCC for the entire study period were included. The data included date of birth, sex, PCC, appointments, medication reviews and diagnoses. ACG weight was calculated from diagnoses as of 31 December as a proxy for morbidity. Data for medications and date of death were added from the Prescribed Drug Register and the Population Register.
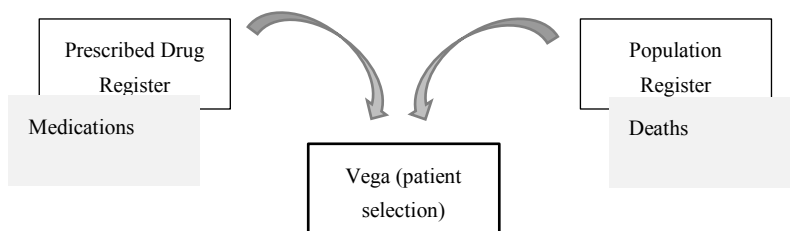

Figure 3. Register data for study II. Vega: regional administrative healthcare database

STATISTICAL METHODS

The PCCs were broken down into three groups of equal size based on the lowest (1), middle (2) and highest (3) percentage of patients for whom a medication review was coded in 2013.

The dependent variables (medication indicators and number of drugs) were modelled by means of a mixed generalised linear model with a compound symmetry matrix that captured correlations between observations of the same patient for the various years. A logistic link function and binomial distribution were used for binary outcomes (medication indicators) and a log link function with Poisson distribution for the number of drugs.

STUDY III – ORGANISATION – NURSE-BASED CARE

STUDY RATIONALE

More than 150,000 primary care patients with hypertension in VGR have individual data reported to the QregPV. Specialised nurses for diabetes and asthma/COPD are mandatory, but PCCs are free to structure their own hypertension care [13]. As presented in regional feedback systems, the proportion of patients reaching BP target is approximately 50% [64]. Structure and team changes with nurse-based care have proven efficient [93].

STUDY POPULATION AND PERIOD

Patients age 40 – 79 with hypertension and no concomitant disease as reported in QregPV on 31 December 2015 were included, see Figure 4. Individuals without PCC enrolment or at PCCs with less than 150 eligible patients were excluded since visit patterns might be too random and less stable over time. Additional information at the individual level was added from Vega, the Prescribed Drug Register, NPR and LISA.
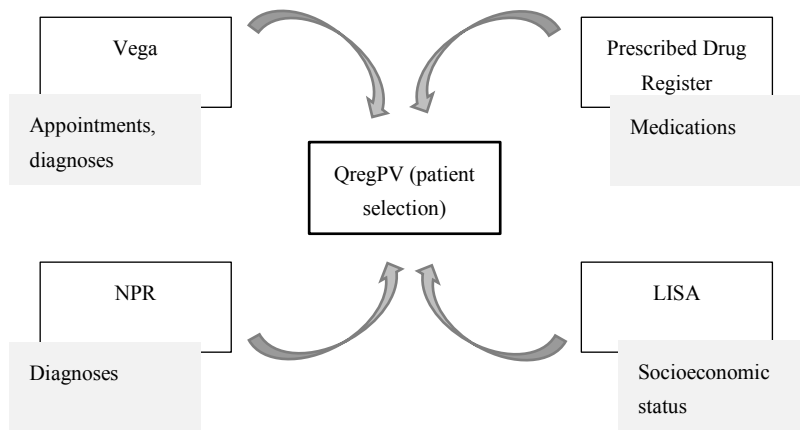

Figure 4. Register data for study III. Abbreviations: LISA: Statistics Sweden Longitudinal Database; NPR: National Patient Register; QregPV: regional primary care register; Vega: regional administrative healthcare database

STATISTICAL METHODS

The PCC visit pattern was characterised by PCC mean number of appointments with nurses and physicians respectively and breakdown of facilities into two

groups depending on the ratio between appointments to the two professions. Nurse-based care was defined as more appointments with nurses than physicians. The likelihood that an individual would have BP ≤ 140/90 mmHg was assessed depending on visit patterns.

A multi-level mixed model was used with a dichotomous dependent variable at the individual level of whether BP ≤ 140/90 mmHg. PCC was modelled as a random factor. The fixed factors were the variables that had been adjusted for. Three different adjustment models were used: 1) adjustment for age and sex only; 2) model 1 plus BMI, smoking, country of birth, marital status, education and number of anti-hypertensive drugs; 3) model 2 plus number of individual appointments with a physician or nurse and which professional had taken BP.

STUDY IV – ADHERENCE TO GUIDELINES

STUDY RATIONALE

Financial incentives have been used in VGR since the healthcare reform of 2009, which included entry of important variables for the care of diagnosed CHD. The proportion of patients in this group who attain the LDL-C target is approximately 20% [64] despite the recommendations of national and international guidelines [57].

STUDY POPULATION AND PERIOD

Patients with diagnosed CHD in QregPV on 31 December 2015 were included in the study. Additional information at the individual level was added from Vega, Prescribed Drug Register, NPR and Cause of Death Register, see Figure 5. A risk estimation cohort from 2011 with follow-up data for five years was used to create a model for the risk of a new CVD event or all-cause mortality.
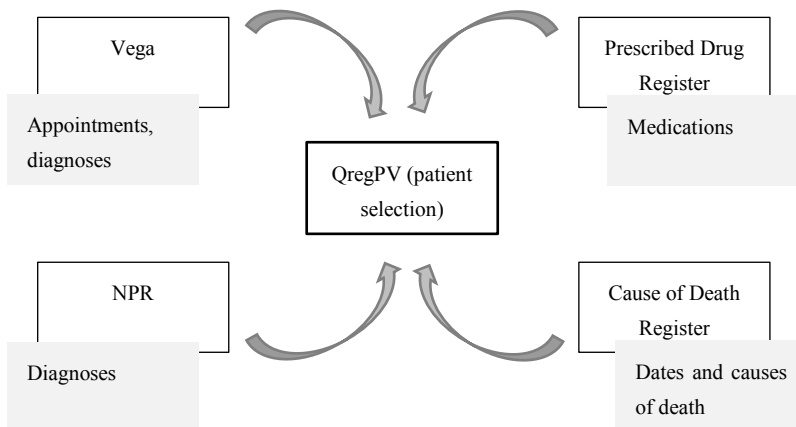

Figure 5. Register data for study IV. Abbreviations: NPR: National Patient Register; QregPV: regional primary care register; Vega: regional administrative healthcare database

STATISTICAL METHODS

A risk prediction model based on Cox proportional hazards regression was used. Follow-up data with endpoints - mortality, acute myocardial infarction (AMI), stroke - were available until 31 December 2015. The variables included in the model were age, sex, diabetes, a history of heart failure and/or atrial fibrillations, stroke or AMI over the past year and treatment with acetylsalicylic acid.

Based on the risk prediction model, the individual risk for a new CVD event or death from all causes over five years was estimated for the study cohort. Summing up individual risks yielded the total number of individuals who were estimated to have experienced an event over 5 years. We performed two adjusted predictions and evaluated the effects of:

- lowering LDL-C to 1.8 mmol/L among patients with higher LDL-C
- administering atorvastatin 40/80 mg to patients with no statin treatment or less potent statin therapy and LDL-C > 1.8

The adjusted predictions were based on published data concerning lowering of risk of CVD or death per 1 mmol/L decrease of LDL-C [68, 94]. Risk reduction with intensified statin treatment was based on expected LDL-C decrease related to the type of statin and dosage from a study designed for that purpose [95].

RESULTS

STUDY I – P4P AND DATA ENTRY

After the introduction of a P4P programme in VGR on 1 January 2011, inclusion of patients in the register continued its long-term rise. The increase occurred in the reference region as well.

Patterns associated with data entry also changed. The percentage of patients with medical variables grew in VGR but not in the reference region, see Table 2. Entry of LDL-C increased most (17.8%).

Table 2, Percentage of patients with entry of separate variable for the study and reference region in 2010 and 2011.

	VGR			**Reference region**		
	2010	**2011**	**Change (%)**	**2010**	**2011**	**Change (%)**
N	39268	44785	14.0	26812	32804	22.3
BP	92.2%	94.5%	2.5	86.8%	85.7%	-1.3
HbA1c	94.4%	95.3%	1.0	93.7%	94.5%	0.9
LDL -C	70.2%	82.7%	17.8	71.1%	69.7%	-1.4
Albuminuria	84.7%	84.5%	-0.2	69.7%	67.1%	-2.0
Smoking	83.4%	91.8%	10.1	86.9%	85.9%	-1.2
Entry of all 5 variables¤	56.7%	71.6%	26.3	46.2%	45.5%	-1.5

¤Information about HbA1c, BP, LDL-C, albuminuria (yes/no) and smoking (yes/no). Abbreviations: BP: blood pressure; HbA1c: glycated haemoglobin; LDL-C: low density lipoprotein cholesterol

Patients and data entered after P4P was introduced differed from those in the register already before 2011. New patients had medical variables that were less well controlled compared to the patients already in the register. Patients with a diabetes diagnosis since at least two years, but first entered in the register in 2011, had lower treatment intensity and higher mean values of HbA1c, BP and LDL-C than those entered also in 2009 or 2010. Patients for whom LDL-C had not been entered in 2009-2010 had significantly higher values than those with entries for all three years: 2.68 (2.65-2.71) mmol/L vs. 2.56 (2.55-2.58) mmol/L. Calculations were adjusted for age, sex and diabetes duration.

BP entry patterns had changed in VGR, i.e., greater preference for sub-target BP and less for round-of values, compared to the reference region see Figure 6.
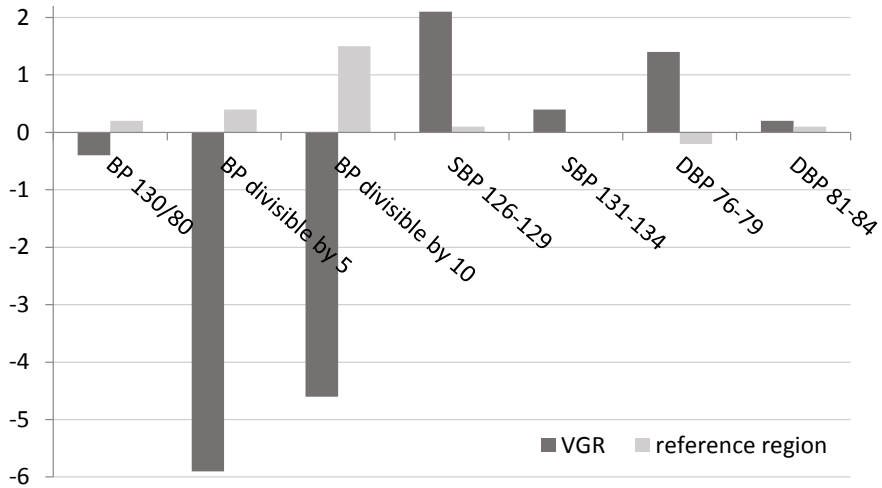

Figure 6. Percentage point change for various subgroups of BP readings in mmHg. Abbreviations: DBP: diastolic blood pressure; BP: blood pressure; SBP: systolic blood pressure; VGR: Region Västra Götaland

The proportion of patients who attained the BP target rose from 23.7% to 28.0% (p < 0.001) while BP decreased from 134.8/76.7 to 133.8/76.4 mmHg (p < 0.001) in VGR: no difference was noted in the reference region, see Table 3. HbA1c and LDL-C levels were down but there was no significant difference between the regions.

Table 3. HbA1c, BP and LDL-C for patients in the NDR for VGR and the reference region in 2010 and 2011.

Year	VGR		Reference county		p diff 2011-2010
	2010	**2011**	**2010**	**2011**	
N	39 268	44 785	26 812	32 804	
HbA1c					
mmol/mol	53.5 (13.2)	52.9 (13.4)	54.1 (13.1)	53.8 (13.5)	0.139
<52 (%)	53.5	56.6	51.9	53.4	<0.001
BP					
systolic, mmHg	134.8 (15.9)	133.8 (15.7)	135.7 (15.9)	135.6 (15.7)	<0.001
diastolic, mmHg	76.7 (9.6)	76.4 (9.7)	76.5 (9.5)	76.6 (9.6)	<0.001
< 130/80 (%)	23.7	28.0	22.3	22.2	<0.001
LDL-C					
mmol/L	2.71 (0.89)	2.68 (0.91)	2.68 (0.93)	2.65 (0.94)	0.139
< 2.5 (%)	45.4	47.3	47.0	48.3	<0.001

Abbreviations: BP: blood pressure; HbA1c: glycated haemoglobin; LDL-C: low density lipoprotein cholesterol

Although the greatest impact of entry was found around the target, patients with higher BP were also affected. Patients with poorly controlled systolic BP (SBP ≥140) in VGR saw larger decreases than in the reference region (-9.3 vs -6.3 mmHg, p < 0.001).

STUDY II – P4P AND PROCESS MEASURES

After the introduction of payment linked to entry of a code for medication reviews, the percentage of codes increased rapidly at all PCCs: those that coded for many reviews (Group 3), for a few (Group 1) and in between (Group 2), see Figure 7. In 2009-2013, the proportion of patients with a code increased from 3.2% to 44.1 %. Meanwhile, ACG weight, a measure of disease burden, also increased.
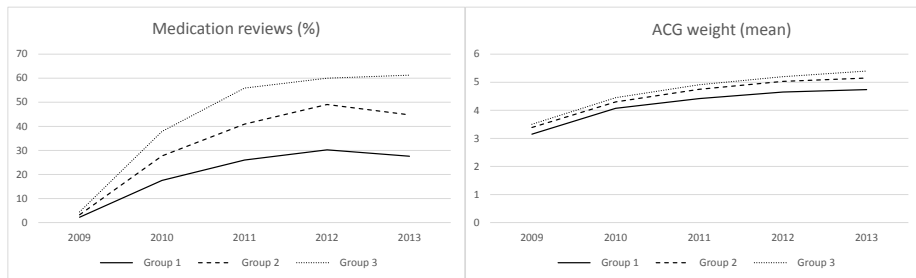

Figure 7. Percentage of patients with a medication review code and mean ACG weight in the three PCC groups; Group 1 (few), Group 3(many).

The percentage of patients with inappropriate drugs and polypharmacy was generally lower in Group 3 than in Group 1. The percentage who were receiving inappropriate drugs or 10 or more drugs decreased in Group 1 as well as in Group 3, see Figure 8. The percentage who had filled prescriptions of three or more psychotropic, antipsychotic or non-steroidal anti-inflammatory drugs (NSAID) also decreased. Prescriptions for statins, which are not considered inappropriate, were included for comparison purposes.
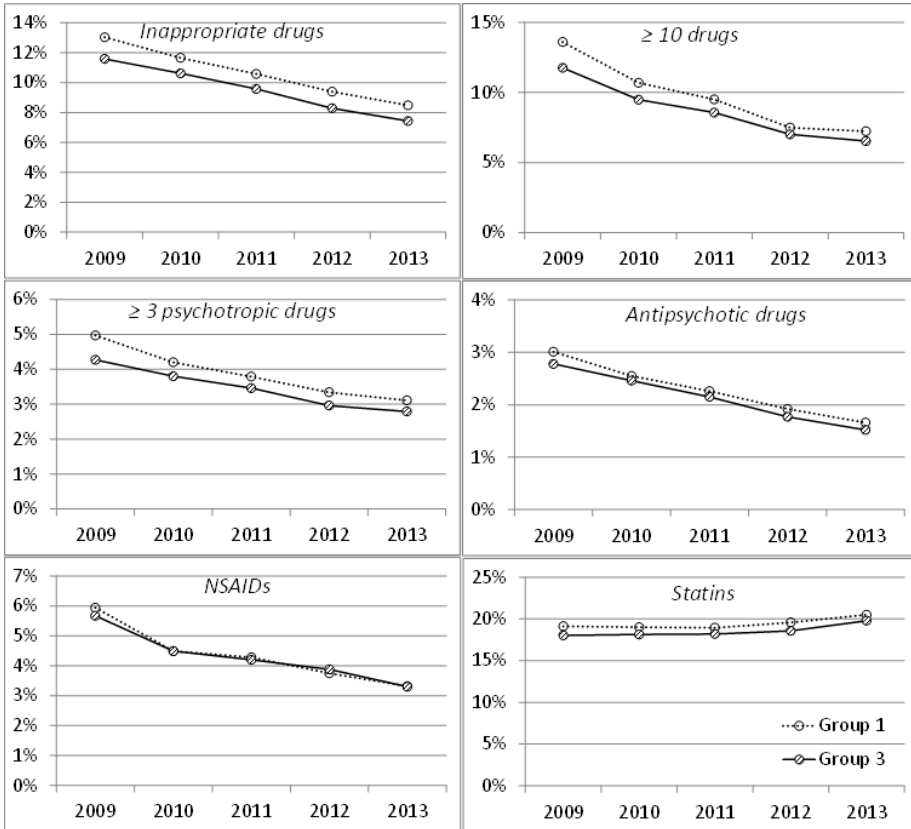
Figure 8. Group 1 and 3 over time, percentage of patients taking inappropriate, ten or more, three or more psychotropic, antipsychotic, non-steroidal anti-inflammatory (NSAID) drugs or statins. The estimates are based on mixed generalised linear models. Group 1 (few), Group 3(many).

There were no significant differences in improvement between the groups from 2009 to 2013 for any of the indicators, see Table 4.

Table 4. Estimated ratios for all drug indicators comparing 2013 to 2009 including odds ratios for all variables except the number of drugs, for which a simple ratio is used.

	Group 1	Group 2	Group 3
Number of drugs	0.80 [0.79, 0.81]	0.82 [0.81, 0.83]	0.81 [0.80, 0.82]
Inappropriate drugs	0.62 [0.59, 0.65]	0.64 [0.61, 0.67]	0.61 [0.58, 0.64]
Long acting benzodiazepines	0.57 [0.53, 0.62]	0.60 [0.56, 0.66]	0.56 [0.51, 0.62]
Drugs with anticholinergic effect	0.71 [0.67, 0.76]	0.74 [0.69, 0.78]	0.73 [0.68, 0.78]
Propiomazine	0.62 [0.56, 0.68]	0.60 [0.54, 0.66]	0.54 [0.48, 0.60]
Tramadol	0.55 [0.50, 0.61]	0.56 [0.51, 0.62]	0.55 [0.50, 0.62]
Ten or more drugs	0.50 [0.47, 0.52]	0.54 [0.51, 0.56]	0.53 [0.50, 0.55]
Three or more psychotropic drugs	0.61 [0.57, 0.66]	0.65 [0.61, 0.70]	0.64 [0.60, 0.69]
Antipsychotics	0.55 [0.50, 0.60]	0.62 [0.57, 0.67]	0.54 [0.49, 0.60]
NSAIDs	0.54 [0.51, 0.58]	0.56 [0.52, 0.60]	0.57 [0.53, 0.61]
Statins	1.09 [1.05, 1.13]	1.13 [1.10, 1.17]	1.12 [1.08, 1.16]

Abbreviations: NSAID: Non-steroidal anti-inflammatory drugs

STUDY III – ORGANISATION – NURSE-BASED CARE

A total of 52 of 188 PCCs in VGR had nurse-based care according to the definition of this study, i.e. more appointments with nurses than physicians for hypertension. Mean number of appointments at the PCCs varied substantially: 0 to 2.3 for nurses and 0.4 to 2.8 for physicians.

Patient characteristics (age, sex, BMI, smoking) did not differ between PCCs with nurse-based approaches and others. Patients at nurse-based PCCs had somewhat lower mean BP (136.9 vs 137.8 mmHg) and the percentage who were being treated properly was higher: BP $\leq$ 140/90 (64.6% vs. 62.3%) and BP $\geq$ 150 (17.6% vs. 20.1%). More patients had antihypertensive treatment (87.8% vs. 85.1%) and the total mean number of appointments was higher (2.7 vs. 2.4) at nurse-based PCCs. With a fully adjusted model, the chance of having a BP $\leq$ 140/90 was 10% higher at PCCs with nurse-based care than at PCCs that had more appointments with physicians, see Figure 9.
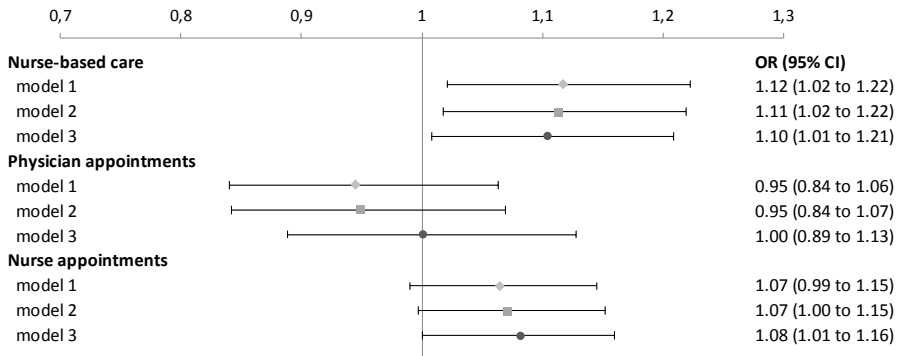

Figure 9. OR that the patient would attain BP ≤140/90 mmHg: at nurse-based PCCs and with an increased mean number of appointments with physicians and nurses respectively at the PCC (the OR represents the increased odds with an increase of one in the mean number of appointments). Three different adjustment models were used: 1) adjustment for age and sex only, 2) model 1 plus BMI, smoking, country of birth, marital status, education and number of anti-hypertensive drugs, 3) model 2 plus number of individual appointments with a physician or nurse and whether BP had been taken by a physician or nurse.

There was a tendency towards higher chance of attaining the BP target with a larger ratio at the PCC between appointments with nurses and physicians, see Figure 10.
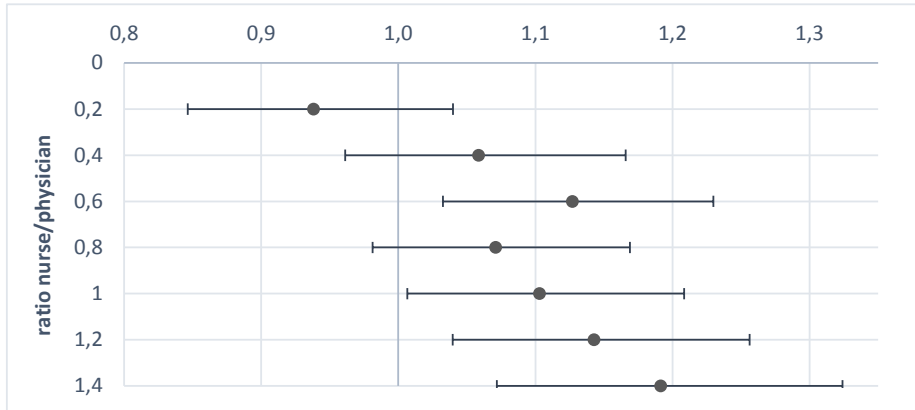

Figure 10. OR that a patient would attain BP ≤140/90 mmHg with a greater nurse/physician appointment ratio at the PCC (nurse-based care is defined as a ratio > 1). Calculations were based on model 3: adjustment for age, sex, BMI, smoking, country of birth, marital status, education, number of anti-hypertensive drugs, number of individual appointments with a physician or nurse and whether BP had been taken by a physician or nurse.

STUDY IV – ADHERENCE TO GUIDELINES

A total of 18% of a secondary preventive population of 37,120 patients with previous CHD attained the high-risk LDL-C target (≤1.8 mmol/L). The mean LDL-C was 2.7 mmol/L and 32% were not receiving any statin treatment. Among the non-controlled patients, whose LDL-C was > 1.8 mmol/L, an average reduction of 1.2 mmol/L (40%) was required to reach the target. Statin treatment was most common (70%) for age 50-75. Prescriptions filled declined rapidly after the age of 80.

If all patients received atorvastatin 80 mg, the mean LDL-C would presumably decrease from 2.7 to 1.9 mmol/L overall and from 3.0 to 2.0 mmol/L for all non-controls (LDL-C >1.8 mmol/L).

Based on individual risks, the estimated number of CVD events over 5 years was 9,209/37,120 (24.8%). If all patients who were receiving no or less intensive statin treatment were given atorvastatin 80 mg, a reduction of CVD events by 14.2% (7,901 vs 9,209) was predicted. If all patients attained LDL-C ≤1.8 mmol/L the predicted number of events would be reduced by 17.7% (7,577 vs 9,209). If all patients were prescribed 80 mg atorvastatin, the predicted proportion who experienced a CVD event would be reduced by 32.9% (967) among non-statin users and 5.4% (339) among users.

Assuming the same risk throughout the study population, including those without an LDL-C entry (n = 57,341), the potential reduction in number of CVD events among patients with CHD over 5 years with atorvastatin 80 mg would be over 2,000.

DISCUSSION

The primary care reform in VGR accelerated the change in attitude about evaluation and follow-up of healthcare performance. The transition that had begun in specialised care with *Open Comparisons* (Öppna jämförelser) now culminated for primary care. Inclusion of both privately and publicly owned PCCs demanded new methods of data collection; a register-based quality initiative was launched.

The focus of this thesis was financing and follow-up as well as potential areas for improvement among major groups of patients. Financial incentives, the effect of organisation on quality of care and the gap between clinical practice and guidelines were studied.

RESULTS DISCUSSION

P4P AND DATA ENTRY

The entry of patients in the NDR has been one of the most common indicators for regional primary care P4P programmes. The performance target was initially used by 9 out of 21 regions [35]. The design of the P4P programme in VGR, however, was unique in that the entry of separate variables and medical targets were also reimbursed.

Study I found significant and clinically relevant changes in entry behaviour after the adoption of a detailed P4P programme. Coverage and completeness of data both increased.

In both VGR and the reference region, entry of patients was reimbursed, and inclusion increased, in the NDR. Entry of separate variables was reimbursed in VGR only where it increased compared to the reference region. The impact on entries in VGR after the introduction of payment linked to diagnoses also boosted entry of chronic conditions, which qualify for higher reimbursement than minor health problems [96]. Increased register entry linked to financial incentives confirms the results of previous studies [38, 39, 50, 52, 97-99].

Patients entered after the start of the P4P programme were not as well-controlled with regard to HbA1c, BP or LDL-C as those who were already registered before. Individual variables that had been missing before were not as well-controlled as already included data either. Similar results have been described for other Nordic registers [34, 100]. These results show that data

were not missing at random and that low coverage and missing data pose a risk of overestimating performance. This can also lead to misinterpretations in both research and public comparisons [18, 33].

In other words, reimbursement boosts data entry but incentives linked to medical targets may also change entry behaviour. An increased preference for entry of BP values just below the target of <130/80 mmHg was accompanied by an 18% increase in patients who attained it. A greater preference for BP values just below target has been described earlier [101, 102]. In addition to the effect around target, there was also a decrease in systolic BP in patients with BPs in the higher range (systolic BP >140) in VGR not seen in the reference region. The greater percentage of patients who attained the specific target was probably a round-off effect that does not explain the decline in mean systolic BP. One possible explanation is that reimbursement sharpened the focus on BP and antihypertensive treatment. We did not investigate whether PCCs that benefited from the incentive programme showed reduced BP or simply fewer round-off values.

When payment for entry of patients in a register is combined with that for separate medical variables, data become more complete and useful. But paying merely for inclusion of a patient is hardly meaningful since it results in missing data that can cause performance to be overestimated. Reimbursement linked to variables, such as BP, that are prone to bias, may alter data entry behaviour and compromise comparability of data.

P4P AND PROCESS MEASURES

The search for relevant measures that can track follow-up of care among the elderly and other primary care patients has led to an innovative but questionable design of indicators. The KVÅ codes for these measures are used for control and reward rather than clinical purposes, see Figure 11 for examples. This contrasts with diagnostic coding, since such conditions are familiar to the physician and form the basis for decisions concerning treatment and follow-up. The KVÅ codes used in primary care are often accompanied by long descriptions of details about their criteria as opposed to easily identifiable follow-up measures like electrocardiogram (ECG) and surgical procedures.

ICD10 (diagnose code)		KVÅ code	
F41.9	Anxiety disorder	DV098	Implemented action package according to rehabilitation plan
I10.9	Hypertension	DV133	Qualified advisory talk on physical activity
J20.9	Acute bronchitis	DV112	Advisory talk on tobacco use

Figure 11. Examples of ICD and KVÅ codes used in VGR

Study II looked at financial incentives linked to a KVÅ code for medication reviews, a process measure. The number of patients for whom a code was entered increased rapidly after the introduction of financial compensation, albeit with a large variation between PCCs. Prescriptions improved among the PCCs with the lowest payment for coding of medication reviews as much as among those with the highest payment. No significant differences in improvement over five years was detected between the two groups of PCCs. The results of the study do not show a clear relationship between indicator and outcome, i.e., between a high proportion of patients with a KVÅ code and better pharmacological treatment of the elderly.

Process measures have been described as more sensitive to financial incentives than outcome measures [51, 103, 104]. For an improvement in a process measure to be of clinical importance, a direct association between the indicator and desired outcome is needed. This is rarely the case for healthcare process measures [47, 105]. There is a risk that the coding target will be reached but not the effect (better medical treatment) [48, 106]. Evidence for medication reviews as a means of reducing hospitalisation and death is also lacking [107-110]. Coding for process measures with a weak association between the indicator and outcome is of doubtful value, "hitting the target but missing the point" is a known problem with process indicators [47].

Our results show that not even a clearly defined KVÅ code is likely to be meaningful for follow-up of primary care quality. The financial incentive was followed by adjusted behaviour and an increase in the number of medication reviews entered but not better medical treatment. For several other KVÅ codes used in primary care there is no apparent association between the indicator and

outcome. This type of incentive carries the risk of measuring and reimbursing adaptation to an incentive programme instead of health-related results. The focus is on quantity rather than quality and the incentive becomes similar to fee-for-service.

ORGANISATION – NURSE-BASED CARE

Due to the extent of regional administrative and medical data, organisational measures can also be evaluated. PCC level characteristics can be related to outcomes for individual patients after controlling for personal characteristics. The focus of **study III** is on hypertension, the largest diagnostic group in primary care, all of whom are at risk of serious complications unless treated properly.

Study III examined real-world visit data. Nurse-based care, as a part of PCC enrolment, was associated with better BP control in cases of uncomplicated hypertension. Although earlier published data and European guidelines point out the benefits of nurse-based care, major variations were found among the PCCs in terms of both mean numbers of appointments and the ratio between those with nurses and physicians. The higher the percentage of appointments with nurses at the PCC, the greater the likelihood that the BP target would be attained for individual patients. These findings are consistent with previous studies which have concluded that team-based care and other quality improvement strategies that transfer part of the responsibility to non-physicians, are effective [54, 93]. Team-based care that transfers tasks from physicians to nurses as used in many countries has proven to be at least as effective as standard approaches [54, 59-61, 111].

Target variation in BP control is certainly more patient than PCC-related but PCC factors including nurse-based care is also part of the equation. The large patient population is growing and even a small contribution to better control should have a clinically important impact on the ability to mitigate the consequences of hypertension. Modest reduction of BP at the population level has been shown to be efficient in limiting CVD events [112, 113].

Many of the financial incentives are directed at care and risk factor management of hypertension, CHD and other long-term conditions. The growing number of patients with chronic disease places greater demands on healthcare services. Nevertheless, adherence to guidelines is still unsatisfactory. PCCs in VGR are required to have specially trained nurses for diabetes and COPD but not for cardiovascular conditions. Nurse-based care

and other organisational variables have an untapped potential and should be considered when structuring approaches to chronic disease.

ADHERENCE TO GUIDELINES

Adherence to guidelines for care of chronic disease has been addressed in a number of ways. But a significant percentage of patients are still not attaining targets for diabetes, hypertension, CHD and other long-term conditions. Financial incentives linked to medical targets were not used for CHD cases during the study period. Payment was nevertheless linked to entry of LDL-C. P4P linked to LDL-C and BP targets for patients with CHD was introduced in 2016 but eliminated in 2017 [114]. European guidelines concerning the target for LDL-C among very high-risk patients have been the same (< 1.8 mmol/L) since 2011 in [115].

The results of **study IV** show that two-thirds of a primary care population with established CHD were receiving statin treatment and only a minority were attaining treatment goals for LDL-C. An improvement in that regard could spare many patients a new CVD event in 5 years. The greatest potential was seen among patients who are not currently receiving statin treatment. A recent Swedish study explored short-term adherence to statins and the possible impact on CVD events among 5,904 post-AMI patients [116]. The study projected a 15% (132-343 patients) reduction in the number of events over 10 years if LDL-C is lowered to 1.8 mmol/L. The patients were younger and the treatment gap narrower than in our study.

Short-term adherence to lipid-lowering treatment after AMI has gradually improved in Sweden to approximately 90% [117]. Adherence to statin treatment among the primary care study population was 68% and only a small percentage had an event over the past year. One reason for the discrepancy may be that adherence declines with time [118]. A delay in the adoption of new primary care guidelines for patients whose last event occurred many years earlier is also likely. Scepticism about treating the elderly with statins due to fear of adverse effects and expectations of only minor benefits may also come into play. In recent years, statin treatment has been proven to be safe and effective for the aged as well [69]. We found that the percentage receiving statin treatment diminishes substantially after 75 corroborating another Swedish study of patients with previous CVD [119].

The potential for avoiding new CVD events if guidelines concerning lipid-lowering treatment were followed more closely appears to be substantial. Greater awareness among both physicians and patients is needed if adherence

is to improve. Besides knowledge, physicians need appropriate organisational conditions. Structures that facilitate follow-up of these patients such as team-based care, would presumably boost patient and physician adherence.

METHODOLOGICAL CONSIDERATIONS – STRENGTHS AND LIMITATIONS

Depending on the research issue, the study design, setting, group breakdown and choice of analysis should always be questioned. Designs and methods were chosen on basis of relevance and feasibility.

All studies were observational and register-based as opposed to RCTs, limiting the ability to make causal interpretations. Nevertheless, the large number of patients is a major advantage and the data reflect clinical settings unaffected by research protocols. The patient population for RCTs is often strictly selected. STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) is an international initiative that generates checklists to improve quality [120]. We tried to follow those criteria.

The inclusion of so many patients requires register data, which restricts the number of available variables. The studies could have been supplemented by information about PCC level based on regional or survey data from their staffs. Such data may though be incomplete and incorrect due to low response frequency and recall problems.

The overall aim of this thesis was to perform a register-based evaluation regarding certain aspects of primary care chronic disease management following the reform. The questions arose from problems and experiences associated with everyday practice as well as observations derived from aggregate data. Thus, no designs other than register-based observational studies were considered.

Most research questions are amenable to alternative approaches. There is no inherent conflict between register-based and other studies. The various approaches complement each other. Register-based studies proceed from a large number of patients and comparatively few variables. Related issues can be addressed by studies based on electronic health record reviews, questionnaires, interviews with patients, staff and administrators or qualitative study designs. Such results proceed from comparatively few patients and much more extensive data for each one. An RCT is also an option when looking at organisational factors such as nurse-based care [61].

Another reason for the register-based approach we used is that the results emerge from and are useful in clinical every-day practice. The findings can be conveyed directly to those who perform and govern care by showing that quality improvement matters.

STUDY DESIGN AND SETTING

The regional perspective, including public funding from the same source regardless of who owns the PCC and almost complete register coverage, is a major strength of this thesis. Because the majority of patients with chronic disease are in primary care, it is important that research be performed in that setting. Real life circumstances also pose problems. When examining the introduction of reforms and the like, it is difficult to know whether the effect is due to the intervention or surrounding factors [12]. **Study I** partly overcame this obstacle by means of comparisons with a reference region. Due to the large variation in coding behaviour among the PCCs in the region and the fact that they were all subject to the same reimbursement, **Study II** could compare groups of them. Because of regional differences in terms of entry and reimbursement, a reference region was not feasible.

Studies I and II were repeated cross-sectional instead of longitudinal so as to include as many patients as possible at each point in time. With a longitudinal design, changes over time could have been analysed at an individual rather than aggregate level. But such a design would have missed patients who were first entered in the register between two points in time. **Study I** shows that missing patients are a potential problem if new ones differ from old ones.

The various registers - NDR in **Study I**, Vega in **Study II** and QregPV in **Studies III and IV** - were the basis for selection. Patient coverage is very high in these registers. QregPV uses automated monthly data extraction from electronic health records at PCCs for all patients with the specified diagnoses [63]. Data extraction for Vega is also automated and is used for financial reimbursement in the region. NDR coverage increased in 2008 – 2011 from approximately 60% to 90% and is now almost complete [121]. Coverage in the reference region was approximately 85% in 2011 as opposed to 96% in VGR [79]; more of the reporting was manual (38% vs 31 % according to NDR sources). **Study I** may have missed patients given that reporting to the NDR is mandatory for neither them nor the provider. Since reporting of data about diabetes cases for regional follow-up is mandatory, the NDR is used by all PCCs in VGR and coverage is high.

The prediction model in **Study IV** was based on the literature concerning expected LDL-C reductions in relation to statin type and dosage [95]. This reference is cited in the *Swedish Book of Medicines* (Läkemedelsboken) and British NICE guidelines [122]. A combined risk reduction for CVD (AMI and stroke) per 1 mmol/L decrease in LDL-C was used, because the figures for the outcome of stroke differed substantially among subgroups of studies and there was no combined measure for all of them [68]. Nor was there a combined measure for the outcome of AMI and the risk reduction was greater than for CVD such that our calculations were conservative in that regard.

MISSING DATA

The thesis was based on data from registers with greatly differing rates of missing data. Apart from in **Study I,** data from several registers and health databases were linked by means of personal identity number. Population-based health data registers are complete and do not suffer from any selection bias [123]. The NPR has virtually full coverage [85]. The data concerning prescriptions filled in the Prescribed Drug Register has very high coverage given that retrieval is automated and generated by administrative systems [124]. Coverage in the Cause of Death Register is also complete [125]. The time of death is recorded regardless of whether a cause has been reported. LISA and the Population Register have full coverage. Missing data are common in the NDR and QregPV for certain variables and have been handled variously in **Studies I, III and IV**. Missing data always pose a risk of bias but the magnitude is difficult to assess.

Missing data were not replaced in **Study I** since the associated variables were outcomes (HbA1c, BP, LDL-C). To include as many patients as possible, complete case analysis was not used and everyone for whom data about crucial variables were available appeared. As an example, patients for whom BP was entered but LDL-C missing were included in the calculations for the former variable but not the latter. Use of a complete case strategy would have substantially reduced the number of patients included and compromised the ability to draw meaningful conclusions.

Study II collected data from registers with total coverage, including age and sex. Patients for whom no entries had been made concerning diagnosis or prescriptions filled were presumed not to have the diagnosis or medications.

Study III had missing data regarding smoking and BMI; because these variables were used as covariates (not exposures or outcomes) they were imputed so that the analyses could include all patients. Sensitivity analyses

(testing for robustness) showed no differences between imputed data and complete case analyses.

Study IV had a great deal of missing data in both 2011 and 2015. The variables for which the most data were missing was smoking (79% in 2011, 26% in 2015), BMI (65% in 2011, 25% in 2015) and LDL-C (68% in 2011, 35% in 2015). Given the large quantity of missing data, it was inappropriate to use imputation. Risk estimations without BMI and smoking were performed even though they are known to be linked to CVD. Sensitivity analyses of complete cases with and without these variables did not change the percentage decrease for the number of predicted events. The extent of the missing for LDL-C in 2015 reduced the number of patients with the prediction of a new event and there was no reason to believe that those excluded faced a smaller risk. On the contrary, they were older and less likely to be receiving statin treatment. While assessing LDL-C on an annual basis may not always be necessary, data were obtained up to 900 days before the index date. The results of **Study I**, although for patients with diabetes, suggested that those for whom no values have been entered tend to have higher LDL-C levels.

CONFOUNDING

False results may be an effect of confounding, a problem that is particularly common in observational studies. Uncontrolled confounding may lead to false conclusions. Age and sex are easy to control for by using them as covariates, as was done in all the studies.

Study I also included diabetes duration since it is an important component of risk factor evaluation. Comorbidity is also a major source of confounding. Statistical efforts to control for comorbidity are dependent on the extent to which conditions are known and properly described in the registers. We could have included information on comorbidity and medication in **Study I** but had no reason to suspect that patients in two of the largest Swedish regions would differ. Nor were the entry effects likely to be affected, given that the incentives should be insensitive to them.

Consideration of disease burden is vital in **Study II** because it is associated with medication. ACG weight, a composite measure of disease burden was used instead of ICD-codes. However, the weight might not accurately reflect individual disease burden given that ACG reporting was also financially rewarded during the study period. If PCCs with a high level of medication review coding were more prone to report diagnoses, that form the basis of ACG calculations, the percentage of patients with inappropriate drug use would

appear to be lower for high coding PCCs due to statistical adjustment. As a result, differences between the groups would be overstated. Changes in drug treatment over time, rather than absolute levels, represented the main source of comparison in Study II. Prescriptions filled, independent of diagnostic coding, were also highly informative. Statin prescriptions were similar in all three groups despite variations in ACG weight, suggesting that CVD burden did not differ significantly between high and low coding PCCs.

Study III minimised the impact of comorbidity by excluding patients with a significant problem in that respect. PCCs rather than individuals were studied where uncontrolled confounding would have had a larger impact due to the association between concomitant disease (coded or not) and visit patterns. Appointments, socioeconomic and other individual factors were added to the various adjustment models. Socioeconomic factors as well as BMI and smoking, no doubt differed among the PCCs. However, the results did not vary significantly, regardless of the model chosen.

Study IV did not examine the effect of exposure on an outcome. Estimates for the effect of lipid-lowering treatment or LDL-C reduction were taken from meta-analyses such that unknown confounding should not be a significant problem.

STATISTICAL CONSIDERATIONS

The choice of statistical methods is a balancing act between absolute correctness and robustness, comprehensibility and communicability. Statistical methods most pertinent to the specific aims were used, while analysis was simple but statistically sound.

Study I assessed the difference between regions with respect to improvement from 2010 to 2011 including only patients who had been entered for both years. This was in order to perform the tests for significance for the change over time based on individual data. The obvious disadvantage was the exclusion of new individuals. Given that data were reported for all patients, this limitation was not considered a problem.

Studies II and III grouped PCCs as primary explanatory variables. PCC characteristics - the percentage of patients with a code for medication review (**Study II**) and the percentage of appointments with nurses for hypertension care (**study III**) were used for grouping variables. An underlying continuous variable was categorised such that information was lost but interpretability enhanced. Without categories, higher or lower odds of should be assessed in the light of a one-step increase in the continuous variable. Thus,

comprehensible groups facilitate determination of the clinical relevance of findings. The number of groups and the associated cut-off values were arbitrarily chosen. The use of only two groups would make it more difficult to demonstrate a difference. The more groups, the fewer patients in each one and the less stable the results. **Study II** broke the PCCs down into three groups of equal size. **Study III** relied on two groups depending on whether physician or nurse appointments were predominant.

A mixed model is one way of handling observations that are not independent by means of various levels of abstraction. Other statistically less complex approaches are the analysis of subgroups, aggregation, change scores and dummy variables, though at the expense of less information and problems with missing data. **Study II** analysed repeated data concerning individual medications and **Study III** looked at patients across PCCs. Patients and PCC were treated as random factors while the induced variation but not the specific impact on outcome was taken into account. A compound symmetry covariance (exchangeable) matrix captured the correlation between observations of the same patient (**Study II**) and PCC (**Study III**). All variances are the same in such a matrix, assuming a constant difference between measurements. **Study II** could have used an autoregressive structure for which observations that happen around the same time are more highly correlated. Medications were, however, presumed to be fairly stable over time and it is not certain that measurements far away in time have a small correlation. Correlations between patients at a particular PCC were not hypothesised as differing in any specific way. If a fixed effects model were used rather than a mixed one, the level of the effect would be similar but the confidence intervals narrower. A mixed model compromises precision when the degrees of freedom decreases. **Study II** could also have used PCC as a random factor since exposure was at that level.

Studies II, III and IV obtained data about prescriptions filled from the Prescribed Drug Register. **Study II** took a more elaborate approach to analysing medication data. To more accurately estimate drug exposure on a particular date, consideration was paid to both quantity and dosage [91]. **Studies III and IV** considered a prescription filled within 120 days to be a treatment regardless of amount and dosage. Drugs are prescribed in Sweden for up to 90 days but refills often occur earlier. This approach may overstate the case since having filled one prescription does not necessarily mean that treatment is ongoing. Both approaches reveal whether the patient has filled a prescription but not subsequent adherence.

Study IV used survival analysis with Cox proportional hazards regression. The main event of interest was CVD with death as a potentially competing event. We proceeded from effects on cardiovascular complications by reduction of LDL-C or more intensive lipid-lowering treatment as reported in the literature [68, 94]. Virtually all articles cite hazard or risk ratios that are unsuitable for a model of competing risks, which instead rely on sub-distribution hazard ratios. Cox proportional hazards regression without competing risks can be used when it is reasonable to study the cumulative incidence of an event on the presumption of survival. But the cumulative incidence of events is affected by death, which was not taken into consideration. The total number of events is certainly somewhat smaller than the results indicate but the relative decrease was not necessarily affected.

LDL-C, especially among the oldest patients was missing to some extent in **Study IV**. The likely explanations are general frailty or the continued impact of earlier guidelines that recommended against treating hyperlipidaemia in this age group. As a result, the potential of statin treatment to reduce morbidity was probably understated.

CONCLUSIONS

Regional register data used after the primary care reform to follow up on the care of chronic disease is an important source of information for in-depth analyses. Available data can be used to evaluate findings for groups of patients as well as issues related to PCC organisation and clinical practice.

The findings of the studies covered by this thesis showed that:

- Payment linked to entry of patients and data can lead to more complete, useful and reliable information.

- Payment linked to coding for specific and complex interventions for monitoring and follow-up purposes may improve record keeping but not necessarily the intended effect.

- Recommendations and guidelines for the structure of care and for secondary prevention are not always followed, representing potential for better medical results.

Analyses of regional register data can raise awareness about the impact of regulating care and clinical practice. The findings should be considered by healthcare authorities and in local quality improvement efforts.

IMPLICATIONS AND FUTURE PERSPECTIVES

Due to current legislation, the regional level will form the basis of primary care analysis for the foreseeable future. In other words, it is vital to examine regional initiatives.

The availability of data has strengthened the demand for transparency among both policymakers and the general public. Since open comparisons hold such intuitive appeal, the potential problems must be emphasised more. Otherwise healthcare may be propelled in the wrong direction by illusions of transparency.

If financial incentives are used to improve quality, the consequences of selected strategies and indicators must be examined to avoid burdensome administrative tasks and false starts. Auditing cannot become more important than care itself.

Rising demand for comparisons and strategies for improved primary care quality must be met by resources to analyse the prerequisites of meaningful action.

ACKNOWLEDGEMENT

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