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Examining time trends in medical practices using register-based data

– A study on changing coronary heart disease care among persons with diabetes

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ACADEMIC DISSERTATION

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YMPÄRISTÖMERKKI
MILJÖMÄRKT
441 729
Painotuote

Supervisors
Professor Ilmo Keskimäki
University of Tampere
School of Health Sciences
Tampere, Finland

Docent, Research Director Kristiina Manderbacka
National Institute of Health and Welfare
Helsinki, Finland

Reviewers
Adjunct professor, Research Director Janne Martikainen
University of Eastern Finland
School of Pharmacy
Kuopio, Finland

Docent, Research professor Veikko Salomaa
University of Helsinki
Hjelt institute, Department of Public Health
Helsinki, Finland

Opponent
Professor Mats Brommels.'O F 'Rj F
Karolinska Institutet
Stockholm, Sweden

Abstract

Medical practices are not invariable over time but change concurrently with changes in technology: for many clinical problems, new diagnostic and treatment options are available. In addition to the adoption of new health care technology, other factors associated with changes in medical practice are legislation, resources, policy programmes, and clinical guidelines.

The study examined changes in medical practices in coronary heart disease (CHD) treatment among persons with diabetes. From the mid-1990s, Finnish CHD treatment practice trends in medication and coronary revascularisations were examined at the level of the entire health care system and between different patient groups.

The study used individual-level register-based data and compared yearly cohorts of the Finnish population with diabetes and/or CHD. Data concerning filled prescriptions of anti-hypertensive medication and lipid-lowering medication were gathered from the health insurance register. Coronary revascularisations were identified in the Finnish Hospital Discharge Register. Of the four longitudinal sub-studies, two examined the use of medication to prevent CHD complications, one study examined access to coronary revascularisation, and one study focused on persons with a history of coronary revascularisation and examined their treatment pathways. Risk-adjustment methods were used to control confounding factors and thereby to ensure comparability between patient groups and socioeconomic groups.

Use of medication to prevent CHD and its complications increased in all patient groups. Among patients with newly diagnosed CHD, beta blocker use was found to be generally equitable throughout the study period. Newer renin-angiotensin-aldosterone system inhibitors were more commonly used by patients with diabetes. Among patients with CHD, socioeconomic differences were found in lipid-lowering medication use before 2000, but the differences disappeared after a health insurance reform in which reimbursement of drug costs for lipid-lowering medication among CHD patients increased from the basic reimbursement (50%) to a higher category (75%). In 2000–2006, the use of lipid-lowering medication among newly diagnosed diabetes patients differed in the lowest income quintile from other income groups, remaining about 10 percentage units lower compared to the overall level.

During the study period, the use of PCI (percutaneous coronary intervention) increased substantially and CABG (coronary artery bypass graft) decreased in 1995–2002 in Finland. However, CABG remained the more common of the two procedures among patients with diabetes and CHD. Despite the increase of coronary revascularisations, a socioeconomic gradient was found in access to the operation throughout the study period. During the study period (1998–2007), medical practices in performing coronary revascularisation changed to performing the operation at the first hospital admission. Among patients with diabetes, pathways to coronary revascularisation included more emergency admissions compared to patients with CHD only.

The results of this study on changes in CHD treatment over time among patients with diabetes and/or CHD indicate that, in general, recommended treatment practices have become more common. Knowledge of how trends and factors associated with medical practice change over time adds to our understanding of medical practices and their development. The non-experimental methods used in the study to investigate changes in medical practice over time in different patient groups proved to be suitable for describing the level and distribution of treatment overall and in different patient groups.

Keywords: register-based study; medical practices; longitudinal study; diabetes; coronary heart disease

Tiivistelmä

Lääketieteelliset hoitokäytännöt eivät ole pysyviä, vaan ne muuttuvat osana teknologista kehitystä, jonka ansiosta moniin oireisiin ja tauteihin on tarjolla uusia diagnoosi- ja hoitomenetelmiä. Terveydenhuollon uusien teknologioiden lisäksi myös muut tekijät kuten lainsäädäntö, käytettävissä olevat voimavarat, kansan-terveysohjelmat ja hoitosuositukset vaikuttavat lääketieteellisten hoitokäytäntöjen muutokseen.

Tämän tutkimuksen tarkoituksena on kuvata lääketieteellisten hoitokäytäntöjen muutosta sepelvaltimotaudin hoidossa yleensä ja erityisesti niiden potilaiden keskuudessa, joilla on myös diabetes. Tutkimuksessa kuvataan sepelvaltimotaudin sekä lääkkeellisen että invasiivisen hoidon kehitystä 1990-luvun puolestavälistä alkaen koko terveydenhuollon tasolla ja potilasryhmittäin.

Tutkimuksessa käytetään yksilötasoisia rekisteriaineistoja ja verrataan vuosikohorteittain suomalaisia diabeetikoita, joilla on tai ei ole sepelvaltimotautia. Tiedot ostetuista verenpainelääkkeistä ja veren rasva-arvoja alentavasta lääkityksestä on saatu reseptilääkkeiden korvausrekisteristä ja tiedot sepelvaltimoiden pallolaajennuksista ja ohitusleikkauksista hoitoilmoitusrekisteristä. Osatutkimusten tutkimusasetelmat hyödyntävät rekisteritutkimuksen mahdollisuuksia pitkittäis-tutkimukseen: kaksi osatutkimusta tarkastelee sepelvaltimotautilääkitystä, yhdessä tutkimuksessa tarkastellaan sepelvaltimotaudin invasiiviseen hoitoon pääsyä, ja yhdessä tutkimuksessa tarkastellaan toimenpidettä edeltäviä hoitopolkuja niiltä, joille oli tehty sepelvaltimoiden pallolaajennus tai ohitusleikkaus. Eri ryhmien välisten vertailujen luotettavuuden lisäämiseksi mallinnuksessa käytetään rekisteriaineistoihin sopivia vakiointimenetelmiä.

Sepelvaltimotaudin hoidossa käytettävä lääkitys lisääntyi tarkasteluajanjaksolla kaikissa potilasryhmissä. Sepelvaltimotautipotilailla ei ollut tutkimusajanjaksolla sosioekonomisia eroja beettasalpaajien, eikä angiotensiinikonvertaasientsyymin estäjien (ACE:n estäjien) tai angiotensiinireseptorin salpaajien käytössä. Uudemmat ACE:n estäjät ja angiotensiinireseptorin salpaajat olivat sepelvaltimotautia ja diabetesta sairastavilla yleisemmin käytössä kuin niillä, joilla oli ainoastaan sepelvaltimotauti. Sosioekonomisia eroja veren rasva-arvoja alentavassa lääkityksessä havaittiin sepelvaltimotautipotilailla ennen vuotta 2000, mutta erot

katosivat samana vuonna toteutetun lääkekorvausjärjestelmän muutoksen jälkeen. Tuolloin veren rasva-arvoja alentavan lääkityksen, käytännössä statiinien, erityiskorvausoikeus (75 %) laajennettiin koskemaan myös sepelvaltimo-tautipotilaita. Statiinien käyttö uusien diabetespotilaiden keskuudessa erosi alimman sosioekonomisen ryhmän osalta vuosina 2000–2006: käyttö oli noin 10 prosenttiyksikköä muita matalammalla tasolla.

Sepelvaltimoiden pallolaajennusten määrä lisääntyi Suomessa huomattavasti ja ohitusleikkausten määrä väheni 1995–2002, diabeetikoiden keskuudessa ohitus-leikkaukset kuitenkin säilyivät yleisemmin käytettynä hoitomuotona. Vaikka toimenpiteiden yhteislukumäärä lisääntyi huomattavasti, oli sepelvaltimotaudin invasiivisissa hoitotoimenpiteissä portaittaisia sosioekonomisia eroja: mitä ylempi tuloryhmä sitä suurempi leikkaustodennäköisyys. Sydäntoimenpiteen läpikäyneistä potilaista diabeetikoilla oli muita enemmän r⊛kx{uv{um⊛{pvg⏽® toimenpiteeseen lqj ∨cxcmc'hoitopolulla.

Tutkimusajanjaksolla sepelvaltimotaudin hoitokäytännöt muuttuivat ja suositusten mukaiset hoitokäytännöt lisääntyivät. Tieto hoitokäytäntöjen kehityssuunnista ja hoitokäytäntöjen muutokseen liittyvistä tekijöistä voi auttaa kehittämään käytäntöjä. Tutkimuksessa käytetty epäkokeellinen, todellisia potilasaineistoja hyödyntävä rekisteripohjainen tutkimusmenetelmä osoittautui käyttökelpoiseksi, kun tarkas-teltiin hoitokäytäntöjen muutosta ja hoitotoimenpiteiden jakautumista eri ryhmissä.

Avainsanat: rekisteritutkimus; hoitokäytännöt; pitkittäistutkimus; diabetes; sepel-valtimotauti

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Abbreviations

ACE inhibitors	Angiotensin-converting enzyme inhibitors
ATC	Anatomical Therapeutic Chemical, international classification system used for the classification of pharmaceuticals
AMI	Acute myocardial infarction
CABG	Coronary artery bypass graft
CHD	Coronary heart disease
CI	Confidence interval
DEHKO	Development Programme for the Prevention and Care of Diabetes
DM	Diabetes mellitus
ESC	European Society of Cardiology
EU	European Union
FinDM	Diabetes in Finland project
ICD	International Classification of Diseases
MI	Myocardial infarction
MONICA	Monitoring of trends and determinants in cardiovascular disease
NHI	National Health Insurance
NOMESCO	Nordic Medico-statistical Committee
OECD	Organisation for Economic Co-operation and Development
PCI	Percutaneous coronary intervention
RAAS inhibitors	Renin-angiotensin-aldosterone system inhibitors
SII	Social Insurance Institution in Finland
STAKES	National Research and Development Centre for Welfare and Health
THL	National Institute for Health and Welfare
WHO	World Health Organization

1 Introduction

The present study focused on changes in medical practice over time in medication use and surgical operations to prevent and treat coronary complications among persons with diabetes. The question is important for several reasons. An important issue is the technological change that has taken place in the treatment and prevention of coronary heart disease CHD. Secondly, both diabetes and CHD are common chronic diseases, but earlier studies of medication use and surgical operations have mainly concerned hospitalised MI patients, and results concerning unselected patient populations have been scarce. Thirdly, some studies from other countries have reported that CHD treatment for patients with diabetes has not been as intensive as for those without diabetes, even though the treatment guidelines underline the importance of active prevention and treatment of CHD complications among patients with diabetes. Fourthly, this study was undertaken to detect potential undertreatment of certain patient groups by examining medication use and coronary revascularisations by socioeconomic position. Fifthly, an initiative to focus on prevention of diabetes as well as to prevent CHD and its complications among patients with diabetes (DEHKO) was launched to address the increasing burden on health care system during the study years. For these reasons the medical practices were extracted from administrative registers, and using individual-level information, the sub-studies explore changes in medical practice over time. The changes over time are discussed in the context of concurrent interventions in health insurance and treatment recommendations as well as changes in resources.

2 Background of the study

2.1 Conceptual background

Background of the study

The focus of earlier research	Factors contributing to changes	Empirical studies examining medical practice changes over time	Factors contributing to medical practices in CHD care
• (Small) area variation in medical practices • Changes over time	• Legislation and resources • Health technology • Policy measures (national strategies) • Clinical guidelines	• Literature review of register-based studies • Methodological perspective on medical practices studied and registers used	Finnish context from the mid- 1990s: • Resources increased in revascularisations • Changes in reimbursement policy • National diabetes programme • Current Care guidelines

Conclusions from earlier literature

Figure 1.   The conceptual background of the study

The present study first describes the key concept of the study, medical practices, and the shift of focus in earlier literature from regional variations to changes in medical practice over time. Secondly, factors affecting changes in medical practices are introduced. Thirdly, a landscape of empirical research on changes in medical practice over time using register-based data is presented. Fourthly, factors affecting medical practices in CHD treatment are described from the mid-1990s onwards in Finland with a special interest in patients with diabetes. Finally, using Finnish register-based data, changes in the treatment of CHD are examined in terms of medication and coronary revascularisation. The sub-studies describe changes in medical practice over time in an unselected patient population, focusing on persons with diabetes.

2.1.1 Changing medical practices

Medical practices are considered to include those activities in the care process where the physician and the patient meet: diagnosis, prescriptions, surgical and other treatment, hospital admissions and discharge. Medical practice is often also considered to be based on scientific evidence (Andersen & Mooney, 1990) and to be produced in a continual process of interaction between medical practice and medical science. Nevertheless, there is a lack of evidence on some interventions, and moreover, despite the available evidence, the actual practices may differ from those recommended. (Andersen & Mooney, 1990; Farlex, 2012) The present evidence comes from studies that reported variations in medical practices even after taking into account clinical variables and patient characteristics (McPherson et al., 1982; Andersen & Mooney, 1990). Whereas the main focus in studies concerning medical practice variation has been on geographical variations, i.e. regional differences in health service production, medical practice variations have also been examined across time periods (Westert et al., 2004; Fonarow et al., 2007; Chin et al., 2011).

An early study of regional variation in health services was published by Glover in the UK in the late 1930s. The study reported variations in the rate of tonsillectomy procedures between regions, and it has inspired replications later. (Glover 1938; McPherson 2008) Medical practice variation has been documented in the USA since the 1970s by pioneers such as Wennberg and Gittelsohn. They described differences in common surgical procedures and, for instance, reported large variations in the history of hysterectomy among women under the age of 75. The percentage of women who had undergone a hysterectomy varied from 25% to 70% between towns. (Wennberg & Gittelsohn, 1973) Since these classic pioneer studies, a large body of literature has examined small area variations in medical treatments in the industrialised countries (Keskimäki et al., 1994; Black et al., 1995; Birkmeyer et al., 1998; Dunn et al., 2005; Lysdahl & Borretzen, 2007; Bhatnagar et al., 2010; Maheshwari et al., 2011; Pearce-Smith, 2011; Welch et al., 2011).

Examining medical practice variations between health care providers requires large-scale administrative databases. Collecting information on health care utilisation into electronic databases has provided opportunities to calculate population-based rates in many countries since the 1970s. After taking clinical variables and patient characteristics into account using relevant statistical methods, the studies reported variation in the measured rates of surgical procedures and also pharmacological treatments. For instance, international comparisons of common surgical procedures between the USA, the UK, Canada and the Nordic countries showed remarkable variation between countries. However, variations within countries have been reported to be as large as those between countries. (McPherson et al., 1982;

Andersen & Mooney, 1990; NOMESCO, 2011) The topic has attracted widespread interest. At the international level, the Organization for Economic Cooperation and Development (OECD) and the Nordic Medico-statistical Committee (NOMESCO) in the Nordic countries regularly gather and publish information on variations in health care between member states (OECD, 2011; OECD, 2012). At the national level, many countries such as the USA, Australia, the UK, the Netherlands, Sweden and Norway regularly monitor medical practice variation within the country (Page et al., 2007; NHS,2011a; NOMESCO,2011; Westert et al., 2011; The Dartmouth Atlas Project Group, 2013).

Variation in medical practices can be both warranted and unwarranted. Unwarranted variation is "variation in the utilisation of health care services that cannot be explained by variation in patient illness or patient preferences" (Wennberg, 2002). Two main sources of unwarranted variation have been identified, namely health service resources available (e.g. health care professionals and their skills, techniques, medical devices, availability of operating theatres, waiting lists and regulation of supply) and practice patterns among physicians, i.e. appropriateness of intervention or referral practices (de Jong, 2008; O'Donnell 2000). Both health service resources and practice patterns have been reported to have an effect on clinical decision making (McPherson, 1990). From the perspective of patients, sometimes an opportunity to request a second opinion from a different physician is needed (van Dalen et al., 2001; Moumjid et al., 2007). Warranted variation is preference-sensitive instead of supply-sensitive and echoes informed and shared decision making between the patient and health care professionals (Appleby et al., 2011; Mercuri & Gafni, 2011).

There are areas in the practice of medicine where evidence of best treatment is weak. Uncertainties of patient care and clinical decisions that doctors face sometimes overshadow the inherent uncertainty of the medical profession. (de Jong, 2008; McPherson, 2008) Uncertainty can concern the best option for effective treatment in terms of prognosis or in terms of quality of life. An example of this is in the treatment choices between surgical and radiation therapy for prostate cancer (Fowler et al., 1988; Barry et al., 1995; Kirschner-Hermanns & Jakse, 2002).

At the population level, unwarranted variation in treatment practices could be examined after adjusting for different comorbidities by studying variation between sub-populations (between men and women, between age groups, between income groups). An approach of this type documents potential inequalities in health care utilisation. Earlier mainly cross-sectional research has reported both positive and negative associations between patients' socioeconomic position and rates of surgical procedures (Keskimäki et al., 1994; Skinner et al., 2003; Westert et al., 2003; Blum & Ibrahim, 2012) and medication treatments (Fialova et al., 2005; Gaskin et al.,

2006; Rothberg et al., 2008; Sargen et al., 2012; Rowlingson et al., 2013; Aarnio et al., 2014).

Examining medical practice variations in health service utilisation provides a strategy for non-experimental assessment of health care (Andersen & Mooney, 1990). Practice variation may be studied at different levels, from considering the individual physician or patient as a decision maker to the level of an entire health care system. Data requirements change depending on the focus of the research: studies on variation between physicians (micro level) use qualitative methods or surveys, while studies on variation between health care organisations (hospitals, practices) (meso level) and medical practice variations between countries (macro level) use administrative databases. Repeated study of databases opens opportunities to examine changes in medical practices over time.

The theory of diffusion of innovation can be used as an alternative framework to monitor treatment methods used in health care. In the theory, the focus has been on individuals as adopters on the one hand and as the locus of decision on the other. Moreover, at the organisational level focus has been on communication channels, on management of treatment or on profession and population opinions. While individuals can be seen as change agents for adoption of the innovation in this theory, public health programmes can also be seen as one of the external change agencies. Contextual factors affecting diffusion also include structural factors such as resources available and regulation. A dissemination curve starts with initial introduction and ends at a point of saturation where no further diffusion occurs in the absence of changes in other factors. Typically, many factors are in place at the time of change, and when monitoring diffusion, causation cannot be attributed to any one component conclusively. (McClellan & Kessler, 2002; Berwick, 2003; Dearing, 2008)

2.1.2 Factors affecting changes in medical practices

Many factors contribute to changes in medical practices over time at the level of society at large and at the level of the health care system. These factors are part of changes in the general operational environment of health care, such as technological and societal changes. In this chapter, the key factors associated with changes in medical practices are discussed on three levels: the macro level referring to the policy level, the meso level referring to the health care and community level, and the micro level referring to the individual patient or physician level. (WHO, 2002)

The health care system where medical practices take place comprises complicated systems of networks, but reducing the description to three levels (macro, meso, and micro) makes it easier to present the picture systematically, while understanding that each of the levels interacts with and influences the others. For each level, common challenges have been identified. At the macro level, a lack of coordination in policy-working may increase the likelihood for waste and fragmentation of health services. Lack of standards for health care and intersectoral care of chronic conditions, are examples mentioned. Meso-level challenges include lack of continuity of treatment for chronic conditions, lack of continuing education for health care professionals, practices being not informed (or followed) by evidence, lack of disease prevention, and non-functional information systems. Micro-level concerns are connected with clinical decision making, the patient-doctor relationship, the empowerment of patients and improving health care workers' communication skills. (WHO, 2002) For research purposes, the data needed differ at each of these levels. Register data cannot usually provide information on micro-level factors; therefore, despite their importance, these are beyond the scope of this register-based study.

2.1.2.1 Legislation and resources

Overall, national governance coordinates population health and health care through a variety of mechanisms: enforcing laws and rules, collecting taxes, coordinating action, achieving policy coherence and ensuring democratic decision-making procedures and accountability (Frenk & Moon, 2013). The right to health care services is expressed in legislation and national government responsibilities including the directing of health care systems (Wennberg & Peters, 2004). In the governance of health care, the main tool is legislation supported by financial instruments. There are many players in the field of health care (e.g. professional organisations, patient organisations, unions, insurers, enterprises), and therefore national governments cannot take their influence for granted. (Jakubowski & Saltman, 2013)

Legislation affects the quality of health care by setting standards for health care professionals and health technologies. Firstly, licencing medical doctors, nurses, physiotherapists and pharmacists guarantees quality in health care through legislation (Finlex, 1994; Grol, 2001). Secondly, legislation seeks to ensure the safety of technologies (e.g. drugs, medical devices) used in health care (EMA, 2013).

The influence of legislation goes far beyond the activities that are the most visible to health care professionals and citizens, such as health service funding. National governance can steer by allocation of resources as well as by controlling

expenditure. Both central and local government make decisions on policy preferences, where the health care sector competes with other sectors of society for resources. Furthermore, within health care various sectors such as primary care and specialist hospital care compete for resources. (Sintonen & Pekurinen, 2006)

Many opportunities for controlling medical costs have been recognised at the national level and at the EU level. National authorities have used positive lists of reimbursed medicines, which are likely for instance to improve prescriptions among physicians and moreover to place an obligation on pharmacists for generic substitution. (Keskimäki & Vuorenkoski, 2003; Pekurinen & Häkkinen, 2004; Häkkinen, 2008; Carone et al., 2012) The use of positive lists of reimbursed medical costs for certain diseases has been evaluated by Cochrane collaboration, and the review suggests that when incentives are directed to the patient they are more likely to facilitate adequate drug treatment than hinder it (Austvoll-Dahlgren et al., 2008).

2.1.2.2 Health technology

Health technology is defined as "any intervention that may be used to promote health, to prevent, diagnose or treat disease or for rehabilitation or long-term care" and forms a part of innovations used in health care. Health technologies include pharmaceuticals, devices, procedures and organisational systems used in health care. (WHO, 2011; INAHTA, 2013)

Technological change in surgical procedures offers more accessible surgery to a wider population of patients; moreover, these new methods, including mini-invasive techniques, are increasingly used in day surgery whereas older techniques have usually demanded in-patient treatment. PTCA was introduced in Switzerland in 1977, and one of its first applications was in the treatment of CHD in the USA (Pyörälä & Olkinuora, 1986; Head et al. 2013).

Adopting new health technologies in health care increases the range of medical alternatives (de Jong, 2008). A new technology can replace an older technology or substitute it. Treatments for certain conditions involve trade-offs between primary and secondary care and in cases where a pharmaceutical treatment and a surgical procedure are acceptable therapeutic alternatives. While innovations are global, the use of health technology takes place locally at a certain point in time, challenging the means of delivering health care services. (McClellan & Kessler, 2002)

The management of chronic disease treatment is challenging. These challenges become apparent in the case of CHD treatment: on the one hand, there is a need for immediate action at the time of a heart attack, and on the other there is a need for

persistent long-term treatment in the prevention of complications of CHD. The logic and demands of long-term treatment and single episodic provision of treatment differ. (WHO, 2002; Nolte et al., 2006; Nolte & McKee, 2008)

Technological change in health care over time has been empirically described in treatment of myocardial infarction (MI). Differences between industrialised countries in the medical practices of MI treatment were described in the 1990s and 2000s (Yusuf et al., 1998; Hasdai et al., 2002; Mandelzweig et al., 2006). Recently, new drugs such as statins and invasive reperfusion techniques for coronary revascularisation have been adopted in the care of MI. Patterns of technology adoption between industrialised countries in treatment of MI have been studied (McClellan & Kessler, 2002). Comparison of invasive procedures proposes that they were more common in the USA than in the UK and Finland in the 1990s, suggesting that the economic capability of a country measured by GDP (gross domestic product) has a positive impact on the adoption of new and expensive technologies. (McClellan & Kessler, 2002; Bech et al., 2009) Concurrently with technological changes in MI treatment, a clear descending trend in MI mortality has been reported. The reasons behind the MI mortality decline are the subject of ongoing debate, and arguments of relative importance of medical technology versus risk reduction through lifestyle changes have been presented (Laatikainen et al., 2005; Ford et al., 2007; Ford & Capewell, 2011).

2.1.2.3 Public health programmes

Policy measures related to health and health care include national strategies, action plans, frameworks or development programmes focusing on specific diseases. The unifying principle of these policy measures is that they operate on a top-down basis. In industrialised countries, government stakeholders conduct these national actions. (Ministry of Health and Care Services in Norway, 2007; NHS, 2011b; Commonwealth of Australia, 2013; Public Health Agency of Canada, 2013). Besides national authorities, international organisations such as the WHO and the International Diabetes Federation provide frameworks to improve health. These plans vary in their content and scope; some of them have a particular focus on primary prevention and others on tackling secondary complications (WHO, 2002; Jacob & Serrano-Gil, 2010). The justifications of these plans include reasons related to the marked health impact of the disease, such as high prevalence and increasing incidence of the disease, high numbers of undiagnosed cases in the population and high costs of treatment, or large variation in the treatment of the disease and need for reducing area variation or socioeconomic inequities in health. (Ministry of Health and Care Services in Norway, 2007; NHS, 2011b; Commonwealth of Australia, 2013; Public Health Agency of Canada, 2013)

Finland has a long tradition of supporting public health programmes, and policy tends to be based on an approach that combines prevention, community involvement, multi-sectorial collaboration and a high risk strategy in health care. The strategies for attaining the objectives have varied from mass media campaigns to management of treatment practices in health care. There have been national projects focusing on diabetes prevention and care and on asthma, allergy, and mental health care. (Haahtela et al., 2006; Saaristo et al., 2007; Haahtela et al., 2008; Mieli, 2009; Aarne et al., 2011; Aarne et al., 2011; Kauppi et al. 2013)

Diabetes programmes with national policies and practices to address and respond to disease have been implemented in many industrialised countries. The growing number of people at a high risk of developing diabetes challenges health care services in Europe. In the health care strategy, targets have been set to reduce the risk of diabetes, to enhance early diagnosis of diabetes and to facilitate the adoption of evidence-based research findings in health care practices. In the Nordic countries, Sweden, Norway and Denmark have national plans for diabetes and additionally national registers to monitor treatment. (Jacob & Serrano-Gil, 2010; Foundation of European Nurses in Diabetes, 2012; WHO, 2013) In Finland, DEHKO was a national eleven-year Development Programme for the Prevention and Care of Diabetes. Besides preventing type 2 diabetes, the programme focused on improving early diagnosis of type 2 diabetes and preventing diabetes-related complications (Saaristo et al., 2007).

2.1.2.4 Guidance tools in health care

Efforts towards rationalisation and unification of medical practices have included the production of guidelines, protocols and descriptions of appropriate treatment pathways within and between care providers, leading the way towards standardisation of the care process. (Groenewegen & Westert, 2004) In general, codes of good medical practice have a broader scope than treatment guidelines, which promote clinical decision making. The codes of good medical practice are intertwined with ethical, regulatory and educational aspects of medical practice. (American Medical Association, 2008; Australian Medical Council, 2013; General Medical Council, 2013). In Finland, no separate definitions of good medical practice have been issued, but such definitions are included in the national treatment guidelines – the Current Care guidelines produced by the Finnish Medical Society Duodecim – and the Physicians' Code of Ethics produced by the Finnish Medical Association (The Finnish Medical Association, 2005; Käypä hoito -toimitus, 2008). Overall, codes of good medical practice have two functions: they provide guidance

for the physicians and let the public know what they can expect from physicians (Gill & Griffin, 2010).

Clinical guidelines include syntheses of available evidence from randomised controlled studies, meta-analyses and observational studies via expert opinions. Guidelines are intended as a basis for treatment choices and do not have legislative power. Guidelines are expected to be easy-to-read support for the practical work of physicians and, when used, to decrease inconsistencies between treatment practices. (NICE 1990; Käypä hoito -toimitus, 2008; NICE 2013) It has also been argued that guidance tools are a threat to clinical decision making and professional autonomy (Woolf et al., 1999; Nummenmaa, 2007; de Jong, 2008).

Many stakeholders have produced clinical guidelines, e.g. European and American specialist organisations and the international Cochrane collaboration. At the national level, responsibilities for the production of clinical guidelines vary between countries. Actors may include national medical associations, specialist associations, non-governmental organisations and patient organisations, including consumer interest groups. The number of clinical guidelines has increased substantially, yet there is a lack of evidence concerning multimorbidity and specific populations such as the elderly and women (Lewsey et al., 2000; Bartlett et al., 2005; Campbell-Scherer, 2010; Hróbjartsson et al., 2013). The task of updating recommendations is a specific challenge in the production of guidelines, but current guidelines are commonly seen as valuable educational resources for health care (Kingston et al., 2000).

The development of clinical guidelines and progress in their usability began at different times in different countries. In Finland, production of the Current Care guidelines was initiated in 1994 by the Finnish Medical Society Duodecim. (Woolf et al., 1999; Kingston et al., 2000; Grol, 2001; Roine et al., 2003; Käypä hoito -toimitus, 2008) Before that, there were 700 different recommendations or guidelines from various actors (Vuori, 2013; Varonen, 1997). By 2013, there were more than 100 systematically produced Current Care guidelines (Käypä hoito -toimitus, 2008; Current Care editors, 2013). These guidelines are national and take European recommendations into account but adapt them to local circumstances (Voipio-Pulkki, 2007; Komulainen, 2013). In the UK, the NICE guidelines include cost-effectiveness argumentation of care in the production of the guidelines, but the Finnish Current Care guidelines only consider evidence on the effectiveness of the treatment (Grol, 2001; Käypä hoito -toimitus, 2008). Few systematic studies exist in Finland regarding the impact of Current Care guidelines on the quality of clinical practices.

2.1.3 Empirical studies using register-based data and examining changes in medical practice – literature review with methodological perspective

A literature review on register-based studied was conducted to provide context to the empirical part of this study. It was intended not as a comprehensive review but to give a general methodological perspective on medical practices studied and registers used. Focusing only on register-based studies excludes medical practices that are not recorded in registers. Empirical reports were chosen as they were estimated to provide the most reliable information on the study of treatment trends. The search strategy of the progress of the study selection is described in Appendix 1.

2.1.3.1 Medical practices examined

The articles (24) reviewed focused mainly on three types of medical practices: medication use, operative or other specialist medical treatments performed in hospitals and non-specific analysis of hospitalisations. Hospitalisations were especially examined when analysing mental health services. Most of the articles analysing operative treatment focused on invasive treatment of CHD, but there was heterogeneity in the definitions of invasive treatment. Analysis of CHD related medical practices was the focus in nine of the 24 studies, mental health related hospitalisations were the focus in six and other hospital treatments in four; one study concerned avoidable hospitalisations and four studies concerned medication use. Studies examining medication use mainly analysed development in recommended treatment or changes in medication use within specific drug categories. Studies on operative or other in-hospital medical practices examined the use of recommended interventions; studies on hospitalisations concerned the increase or decrease of admissions or the length of stay.

2.1.3.2 Type of registers used

The registers used in the earlier studies were diverse, ranging from administrative registers to research registers, quality registers and benchmark registers. Some of the administrative registers used are obligatory and nationwide, like many Finnish registers, but there were also regional registers. Data collected specifically for research use utilised well-documented definitions of diagnosis, such as the ones used in the MONICA research. The quality registers for a specific disease might be obligatory or voluntary. The coverage of these registers varied. In the USA, benchmarking registers are voluntary and limited to a sample of hospitals.

2.1.3.3 Methods applied

Background variables used in the analyses were related to the data available in the registers. The articles compared men versus women, different age groups, yearly cohorts, different diagnostic groups and/or different treatment groups. The studies were heterogeneous in the criteria of forming the groups, and therefore comparisons between studies are difficult. The studies reported temporal trends in medical practices in the USA (7), Canada (1), Nordic countries (7) and other European countries (8). One study was a multi-centre study including hospitals from several countries. The follow-up time varied from three to 28 years.

Methods used in the studies varied from simple descriptive figures tabulated in different ways to sophisticated comparisons taking into account case-mix correction using regression models. The interpretation of the results of these studies is complicated because of underlying differences in the case mix. The patients' ages, their comorbidity and the years examined influenced the outcomes. Differences in the methods of analysis are partly due to differences in the information available in each of the registers and partly due to statistical procedures available at the time of publishing the results. The most common procedure in case-mix correction was age adjustment. Some articles from the USA used case-mix corrections both at patient level (e.g. comorbidities, medication) and at hospital level (e.g. annual number of operations). Case-mix corrections used in the analyses varied according to case-mix relevant information obtained from the registers used for study data. Most of the studies were descriptive and did not allow causal inferences.

2.1.3.4 Findings of the register-based studies

Findings of the studies were reviewed in particular from the perspective of evidence based or health policy driven treatment and focused on: temporal trends in medication use; operative or other specific treatment in hospitals; and hospitalisations. Registers provide an encouraging source for repeated measurements and enable examining changes in medical practice over time.

When examining temporal trends in changes in medical practice in mental health care, the researchers focused on hospitalisations and length of stay during health policy reform of deinstitutionalisation (Kaltiala-Heino et al., 2003; Pijl & Sytema, 2003; Arvidsson & Ericson, 2005; Lay et al., 2007; Siponen et al., 2007). The results in different countries and for different diseases varied, but in many cases hospitalisation rates decreased or disappeared altogether, as was the case with mild mental disorders (Munk-Jorgensen et al., 1992). In Sweden, inpatient care decreased among persons with a diagnosis of schizophrenia (Arvidsson & Ericson, 2005),

whereas in Finland inpatient treatment of severe mood disorders increased (Kaltiala-Heino et al., 2003).

The second type of hospitalisation studies focused on avoidable hospitalisations or ambulatory care sensitive conditions, i.e. conditions for which hospitalisation is considered to be potentially avoidable through preventive care and early disease management, usually in a primary care setting (Page et al., 2007). One study reported a decrease in childhood asthma admissions (Priftis et al., 2007). Hospitalisations for a specific diagnosis have also been analysed. Pregnancy-related hospitalisations with stroke were found to increase in the USA. However, according to the study this was not due to medical practice variations but, instead, due to risk profile changes. (Kuklina et al., 2011)

Research concerning medication use examined both diffusion of a new treatment and establishment of evidence-based medication. The introduction of antiretroviral therapy diminished hospitalisation dramatically among HIV-positive children in the USA (Kourtis et al., 2007); a sharp decline in hormone therapy prescriptions, which increase the risk of breast cancer, was observed among menopausal women in Germany (Katalinic et al., 2009); psychoactive drug use was reported to be relatively stable although a slight decrease of anxiolytics, which can be highly addictive, was observed in the Netherlands (Ravera et al., 2010); a change in treatment strategy was observed in the use of disease-modifying anti-rheumatic drugs, the use of these drugs for early-stage rheumatoid arthritis increasing (Rantalaiho et al., 2011); and in overall use of evidence-based medication, the treatment of CHD increasingly favours evidence-based treatment (Zahn et al., 2000; Marques-Vidal et al., 2003; Fonarow et al., 2007; Peterson et al., 2008; Fagring et al., 2010; Nguyen et al., 2010).

Finally, some of the studies focused on the diffusion of specific treatments, such as safer methods for hemodialysis in Canada, where guidelines recommended the arteriovenous fistula as the hemodialysis access of choice. The study observed treatment practice change in hemodialysis; but instead of safer methods gaining ground, incident catheter use in hemodialysis increased, fistulas use decreased, and graft use remained stable. Prevalent catheter use increased, and fistulas and grafts decreased. The study reported significant regional variation in the use of incident and prevalent fistulas use. (Moist et al., 2008)

In Sweden, researchers examined the increase in arthroplasty operations of the knee. The researchers concluded that the increase was mainly due to arthritis being increasingly treated by arthroplasty and that the increase was associated with population change. (Robertsson et al., 2000) In the USA, researchers reported an increasing trend in the use of cardiac catheterisation and PCI and a decreasing trend

in the use of coronary bypass surgery, suggesting a change of treatment strategy in a less invasive direction (Peterson et al., 2008). An increasing trend towards cardiac catheterisation was observed in a multicentre study including data from several countries (Nguyen et al., 2010). A decreasing trend in hospitalisations due to cataract operations was found among children in Italy; ophthalmologists used an unusual intraocular lens implantation operation in children in one fourth of the cases (Ricci et al., 2009).

2.1.3.5 Remarks on the register–based studies

Studies focusing on change in medical practices using register-based data yield information about treatment trends. The medical practices in the literature review had three main focuses: medication use, operative or other specific hospital treatments, and hospitalisations. Only the studies on medication use provided information on medical practices outside secondary or specialised medical care in hospitals.

The coverage of the source registers varied from very small area level databases to comprehensive national-level registers, the data being collected in administrative or project-driven work. There were both voluntary and compulsory registers. These context-specific features had an impact on the opportunities to report and the methods available. The case-mix correction used most widely was simple age adjustment, and socioeconomic factors were taken into consideration occasionally. The role of case-mix in the interpretation of the results is essential. Overall, the complexity of the data and the methods used in the analysis of trends in medical practices seemed to increase over time.

Three different research interests could be detected in the studies. Firstly, medical practices and their trends were studied when new health technology (drug or surgical procedure) was adopted. Secondly, studies were conducted when evidence on adverse effects of some medical practice had accumulated. A third interest was to monitor the diffusion of evidence-based medical practice or effects of health policy steering mechanisms. The majority of the studies examining diffusion of health technology focused on the change in medical practices in CHD, where progress of evidence-based drug therapy and use of the less invasive coronary revascularisation technique had become more widespread. An example of the second type of interest is hormone therapy. When increased risk of breast cancer was found to be associated with hormone therapy among menopausal women, real-world monitoring of treatment trends and differences between areas reported a sharp decline in hormone therapy prescriptions. An example of the third type of interest is the policy reform in the treatment of mental disorders. Many countries have enacted a health policy

reform to deinstitutionalise mental health patients by reducing resources for hospital treatment. The studies reported not only diminishing hospitalisations but changes in the length of stay. The result of the diminishing hospitalisations was constant across studies, but results concerning length of stay and services replacing hospital care differed. It is difficult to compare the results of different studies even if they concern the same medical practices, since they use different methodologies and different study settings and come from different points in time.

The landscape provided by this literature review suggests that studies on trends in medical practices using register-based data yield relevant information about health care. Studying trends provides an opportunity to assess how the use of health technology (e.g. drugs, surgical operations) has changed in real-world treatment practices: whether the trends are increasing or decreasing and whether the treatment is well-established or fluctuating. For clinicians, studies on trends in medical practices can provide an overall picture of possible undertreatment or overtreatment of a disease, an overview of whether the medical practice studied replaces earlier medical practice or adds to it, and, if the dataset is large and representative enough, an impression of whether medical practices are targeted according to need. The studies provided information on aggregated trends in medical practices in the context of changes in resources used, in health policy and use of clinical guidelines and diffusion of specific medical practices. In summary, the studies on trends in medical practices are at least partly context-specific but may be used for assessing the functioning of health care, for benchmarking practice and for planning of service delivery.

2.2 Factors contributing to medical practices in coronary heart disease care in Finland from the mid-1990s

2.2.1 Resource increase in coronary revascularisations

In Finland, two policy measures have had the effect of increasing resources in coronary revascularisation operations: an increase in investment in the operation in hospitals, and an increase in the number of cardiologists.

In the late 1980s and early 1990s, assessment for the need for services with new surgical opportunities to treat CHD was considered to be important, because CHD mortality among the Finnish population was one of the highest in international comparison (Rönnemaa et al., 1991; Salomaa et al., 1996; Melkas, 2013). This assessment was made by working groups at the National Board of Health and the subsequent National Board of Welfare and Health (Pyörälä & Olkinuora, 1986;

Alanko & Hokkanen, 1991; Idänpään-Heikkilä et al., 1994). Later, a working group for coronary heart disease nominated by STAKES reassessed the need for coronary revascularisation operations and gave recommendations on quality indicators (Pyörälä & Olkinuora, 1986; Alanko & Hokkanen, 1991; Idänpään-Heikkilä et al., 1994).

In 1993, the annual need for angioplasty (PCI) and bypass surgery procedures (CABG) in the Finnish population was estimated to be 3 000–4 000 higher than the supply for PCIs and 4 500–5 000 higher than the supply for CABGs. At that time, Finnish hospitals performed 1 400 PCIs and 3 700 CABGs annually (Idänpään-Heikkilä et al., 1994). In 2001, the supply of PCI was 4 000, and a government expert group recommended a substantial increase of PCI treatments over to 10 000. (Tierala, 2001) Thereafter, the number of PCI procedures has increased (Figure 1).

In 1995–2001, the population rates of PCI in Finland were average compared with other European countries. In 2002–2003, the rates increased considerably, from 655 to 1 276 per one million people. (Allender et al., 2008) Unfortunately, the inter-country comparability is limited due to lack of information on private hospitals in some countries, which partly explains the differences in statistics. However, the statistics do indicate substantial variation in PCI rates between countries. The European cardiovascular disease statistics did not report the numbers of CABG. Compared to the USA and Canada, the number of coronary revascularisations performed in Finland was lower. (Sydän- ja verisuonitautien ja diabeteksen asiantuntijatyöryhmä, 2005; Alter et al., 2006; Lucas et al., 2006)

In 1997, the number of cardiologists in Finland was 16 per one million residents. The density of cardiologists was among the lowest in the EU countries (the range being from 170 in Greece to 8 in the UK) and lower than in the USA (70). (Block et al., 2000) However, according to the statistics of the Finnish Medical Association, the number of cardiologists in Finland has been consistently increasing. In 2012, there were 225 cardiologists of working age in Finland, or 41 per one million residents (The Finnish Medical Association, 2013) (Figure 2).

To conclude, trends in coronary revascularisation operations since the mid-1990s showed gradual reduction in the numbers of CABG and marked increase and later a levelling off in PCI. Over a twelve-year period (2000–2011), there was a 130% increase in the number of PCI procedures and a 46% decrease in CABG. At the same time, the number of cardiologist of working age increased by 60%. In 2011, there were 2 527 CABG procedures, 8 308 PCI procedures and 215 cardiologists.
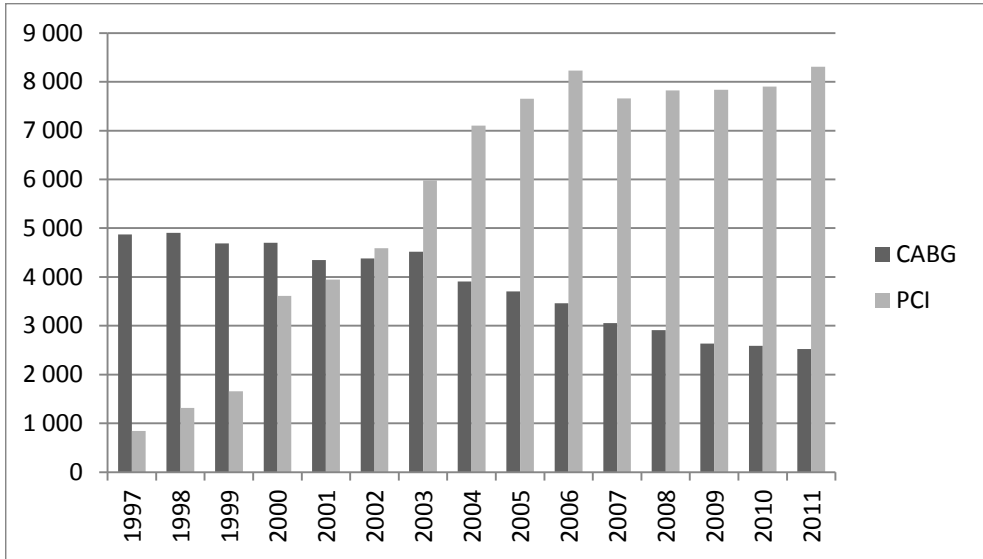
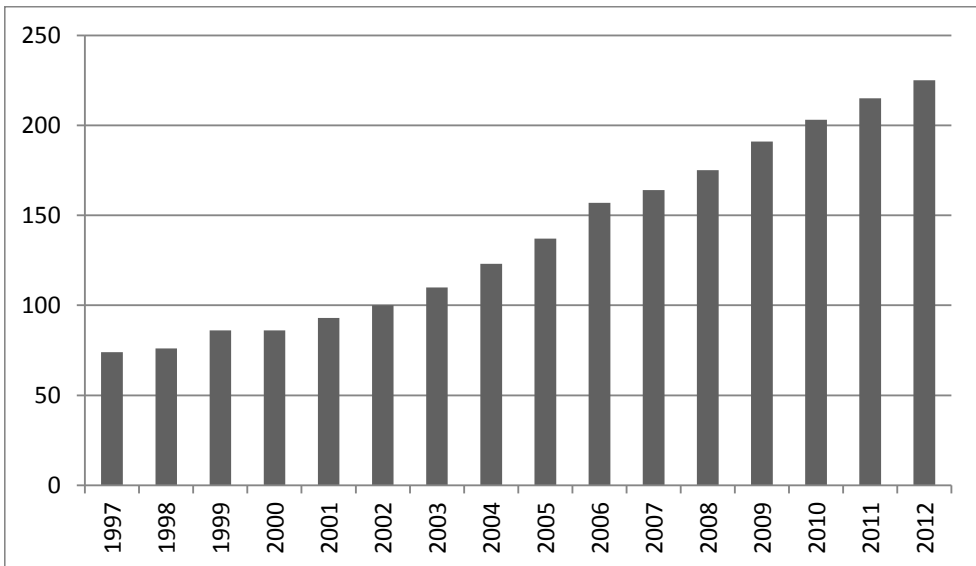**Figure 2.**   The number of coronary revascularisations in Finland (THL, 2013).

Figure 3.   The number of cardiologists of working age in Finland (The Finnish Medical Association).

2.2.2 Changes in reimbursement policy and lipid-lowering medication price

As a response to increasing pharmaceutical expenditure, generic substitution was introduced in 2003 (Finlex, 80/2003; Mossialos & Srivastava, 2008). To facilitate the use of needed medication among patients with CHD, a change in reimbursement policy for lipid-lowering drugs was introduced in 2000. Generic substitution was followed by intense price competition, and the price of lipid-lowering drugs has decreased since then.

In Finland, generic substitution means that the dispensing pharmacy has an obligation to offer a cheaper interchangeable product as a substitute for a prescribed medicine. Efforts to introduce a legislative amendment enacting obligatory generic substitution succeeded in April 2003. This compulsory procedure was introduced to control public expenditure by promoting more competition between pharmaceutical companies. (Keskimäki & Vuorenkoski, 2003; Pekurinen & Häkkinen, 2004; Ahonen & Martikainen, 2005) A voluntary generic substitution was in effect in 1993–1996 and generic prescribing in 1996, but voluntary actions had no considerable effect on expenditure (Keskimäki & Vuorenkoski, 2003; Pelkonen, 2006). Compulsory generic substitution was received well, and at that time only 10% of patients and very few physicians refused the potential prescription substitutions. The procedure includes an option for the prescribing physician to decline generic substitution for medical reasons and for the patient to decline substitution without giving any reason for it and still be reimbursed by the National Health Insurance according to the actual costs of the prescription. (Keskimäki & Vuorenkoski, 2003; Heikkilä & et al 2007; Vuorenkoski, 2008)

More recently, in 2006 a reference price system based on generic pharmaceuticals was introduced. The system establishes a common reimbursement level or reference price for a group of interchangeable medicines. If a pharmaceutical is priced above the reference price, the patient pays the difference between the price of the pharmaceutical and the reference price, in addition to any other co-payments (Dylst et al., 2012). The Pharmaceuticals Pricing Board sets and updates the reasonable wholesale prices four times a year. If a certain medicine is not confirmed as reimbursable, the patients have to pay the full price. The Pharmaceuticals Pricing Board operates under the Ministry of Social Affairs and Health. (STM, 2013)

For patients, reimbursement for medicine expenses is available for prescribed medicines for treatment of an illness. There are three reimbursement categories, the reimbursement covers necessary medicine expenses, and the purchase is for three months at a time. In general, the basic reimbursement covers around half of the cost of prescribed medicine to the patient through national health insurance, but in regard

to certain chronic diseases the reimbursement of selected medicines is increased. In the case of life-saving drugs, such as insulin or thyroxin, the reimbursement to the patient covers the entire cost. The medical criteria required for entitlement to a higher reimbursement rate are set out by the SII. The medical certificate for a higher rate of reimbursement is based on examinations performed by a physician. (National Agency for Medicines & Social Insurance Institution, 2001; Social Insurance Institution in Finland, 2013)

In the mid-1990s, when lipid-lowering drugs were introduced in Finland, they were an expensive medication for the patients (Strandberg et al., 1997). The price of lipid-lowering medication decreased by 78% over a twelve-year period (2000–2011); for patients, the decrease in costs was 77% (Figure 4). In 2011, the number of lipid-lowering medication recipients was 666 590, 200% more than in 2000. (Figure 5).

Table 1 presents policy changes in reimbursement for lipid-lowering medication for three patient groups: patients with familiar hypercholesterolemia, patients with CHD and patients with diabetes. Lipid-lowering medication costs are reimbursed for persons with familiar hypercholesterolemia according to a higher rate of reimbursement, and for persons with diabetes according to basic reimbursement. The greatest change in reimbursement for lipid-lowering medication took place in 2000 when patients with CHD were awarded a higher rate of reimbursement.

Table 1. Policy changes in the reimbursement for lipid-lowering medication.

Year	Policy change	Reimbursements of lipid-lowering medication		
		Patients with familiar hyper-cholesterolemia	Patients with CHD	Patients with diabetes
1998	Voluntary generic prescribing in effect since 1993 Introduction of a two-year delay period for applying higher reimbursements (75% / 100%) for new medicines	75% reimbursement, fixed copayment EUR 5 / prescription	50% reimbursement, fixed copayment EUR 10 / prescription	50% reimbursement, fixed copayment EUR 10 / prescription
2000	NA	no changes	75% reimbursement, fixed copayment EUR 5 / prescription	no changes
2003	Introduction of mandatory generic substitution by pharmacist	no changes	no changes	no changes
2006	Expensive statins (rosuvastatin) reimbursed only when less expensive ones are proved to be ineffective or not tolerated	72% reimbursement fixed copayment (EUR 1.50/item) after the annual ceiling*	72% reimbursement fixed copayment (EUR 1.50/item) after the annual ceiling*	42% reimbursement fixed copayment (EUR 1.50/item) after the annual ceiling*
2012	Restriction of rosuvastatin was removed	no changes	no changes	no changes

*Annual ceiling introduced in 1986, and since 1994 it has remained between EUR 614 and EUR 617.
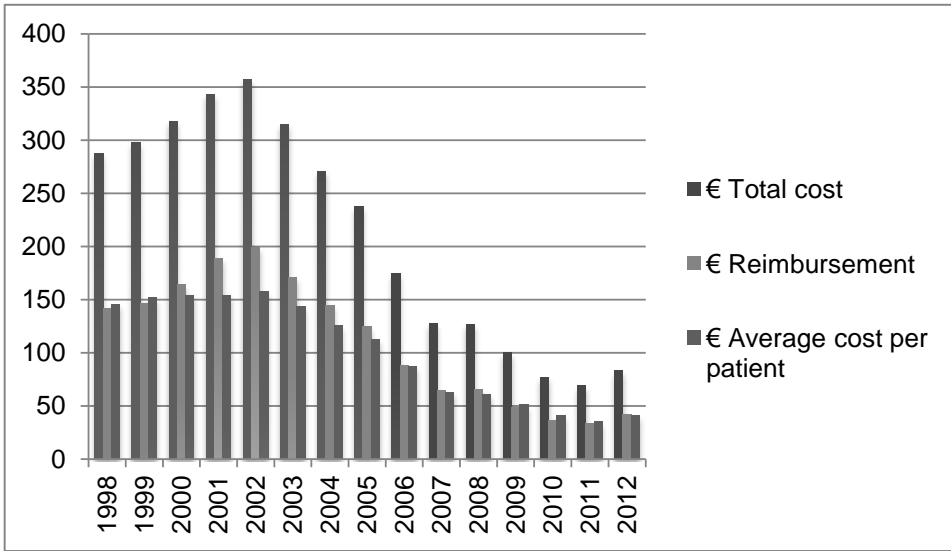
Figure 4.   The average cost (EUR) of lipid-lowering medication (C10) in Finland, divided into the reimbursement by SII and cost to the patient. (SII, 2013)
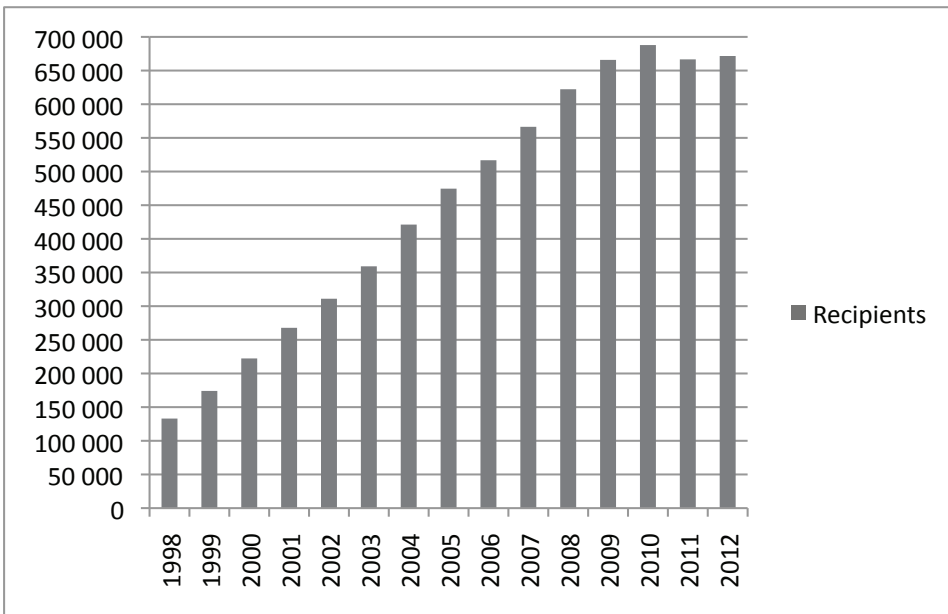

Figure 5.   Number of recipients of lipid-lowering medication (C10) in Finland. (SII, 2013)

2.2.3 National diabetes programme (DEHKO)

Since the 1990s, the challenge presented by diabetes to public health and health care systems has become widely recognised. The number of new diabetes cases has increased, which was associated with an epidemic of overweight (Wild et al., 2004). Diabetes and CHD share many risk factors: overweight, high saturated fat intake, smoking and a sedentary life style. The diseases often occur simultaneously. (Haffner et al. 1998; Juutilainen et al. 2005; Sydän- ja verisuonitautien ja diabeteksen asintuntijaryhmä 2005; Reunanen, 2006a; Reunanen, 2006b; Suomalaisen Lääkäriseura Duodecimin ja Suomen sisätautilääkäreiden yhdistyksen ja Diabetesliiton asettama työryhmä 2007; Suomalaisen Lääkäriseura Duodecimin ja Käypä hoito -johtoryhmän asettama työryhmä 2012) In Finland, research evidence repeatedly suggested that the glycemic control of diabetes as well as prevention of comorbidities had to improve, but in the 1990s the number of diabetes patients was not monitored (Kangas et al., 1996; Valle et al., 1997; Reunanen et al., 2000). It has later been shown that the number of diagnosed diabetes cases increased steadily from the mid-1990s, the number of people diagnosed with diabetes in the population being about 370 000 in 2011 (Figure 6).

The national diabetes programme for Finland was launched in 2000. The programme was called the Development Programme for the Prevention and Care of Diabetes (DEHKO), and its running time was eleven years. The Finnish Diabetes Association was the initiator, organiser and coordinator of the programme. Co-operation was established with clinicians, public authorities, government agencies and NGOs. (Aarne et al., 2011) DEHKO had an implementation project, FIN-D2D (2003–2008), the main objective of which was to develop practices for the prevention and early treatment of diabetes and cardiovascular diseases. (The Finnish Diabetes Association, 2003; Saaristo et al., 2009)

The DEHKO programme focused on the prevention of diabetes and underlined two complementary approaches: the population strategy and high-risk strategy. The population strategy considered the management of diabetes as a community challenge and focused on preventing type 2 diabetes as well as improving early diagnosis of the disease. It included broad targets to improve population health, such as reducing obesity, increasing physical activity and encouraging healthy eating habits. A validated one page questionnaire, 'The Finnish diabetes risk score', for assessing risk for the disease was disseminated. The high-risk strategy was applied to the prevention of diabetes-related complications, i.e. to limiting the progressive nature of type 2 diabetes and its cardiovascular complications. The high-risk strategy was based on experiences from the Finnish Diabetes Prevention Study, which had shown that changes in lifestyles enable prevention of type 2 diabetes (Tuomilehto et

al., 2001; The Finnish Diabetes Association, 2003). These findings were replicated in other randomised clinical studies (Norris et al., 2005). From the patient's perspective, CHD complications decrease quality of life (Wändell, 2005), emphasising the importance of prevention of these complications in the management of type 2 diabetes. The motivation behind DEHKO and later FIN-D2D was that diabetes was increasingly seen as a cardiovascular disease (Haffner et al. 1998). Therefore, treatment of diabetes focused increasingly on preventing coronary complications.

The assessment of DEHKO reported progress in the treatment: diagnosis of diabetes was made earlier, and the recommended metformin treatment increased among type 2 diabetes patients. However, reduction of the risk of arterial disease remained low among patients with diabetes. (Tuomola et al., 2011)
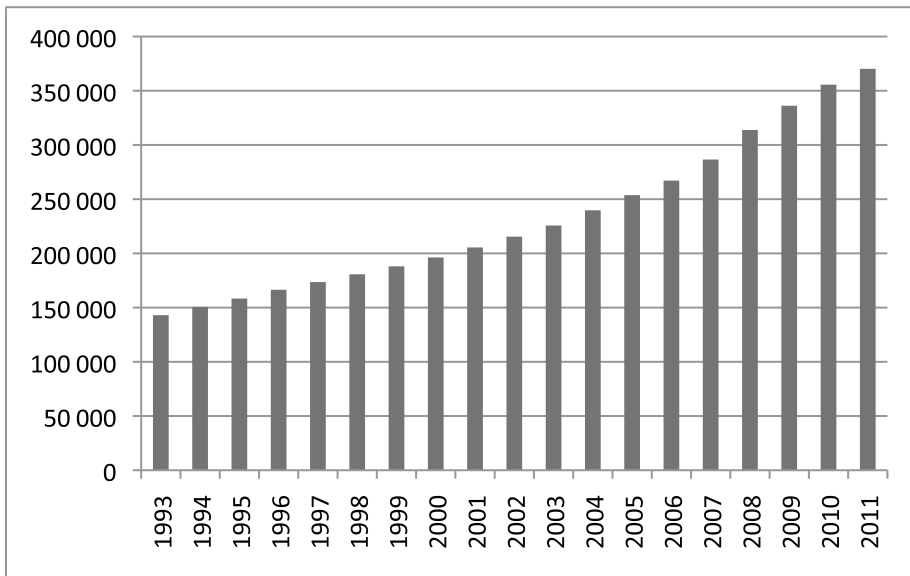
Figure 6.   The prevalence of diabetes measured at the last day of the year according to FinDM II data. (THL, 2013)

2.2.4 Current Care guidelines

Current Care guidelines are produced by the Finnish Medical Society Duodecim in co-operation with various medical specialist societies. These guidelines aim to provide consistent information to support treatment decisions. Public funding for the Current Care guidelines is provided by the Ministry of Social Affairs and Health, SII,

and the Finnish Medical Society Duodecim, and the use of funding is controlled by the National Institute of Health and Welfare. The support from the Ministry of Social Affairs and Health is motivated by concern over variations in quality in clinical practice. (Vainikainen, 2005; Vainikainen, 2009; Komulainen)

Before the production of Current Care guidelines started in 1995, several clinical guidelines or recommendations related to the treatment of coronary heart disease among persons with diabetes had been published in Finland. The first national treatment guideline for type 2 diabetes was published by the Finnish Diabetes Association in 1994 (Uusitupa et al., 1994). In the same year, the European recommendations for prevention and treatment of coronary heart disease were issued; they were disseminated two years later through the Finnish Medical Journal (Suomen Sisätautilääkärien Yhdistyksen, Suomen Kardiologisen Seuran, Suomen Verenpaineyhdistyksen, Kunnallislääkärityhdistyksen, Suomen Teollisuuslääke-tieteen Yhdistyksen ja Suomen Sydäntautiliiton työryhmä, 1996). Later in the early 2000s, the Finnish Medical Association Duodecim published national guidelines on 'Treatment of hypertension', 'Acute coronary syndrome' and 'Dyslipidemias' (Suomen Verenpaineyhdistys ry:n asettama työryhmä, 2002; Suomen Kardiologisen Seuran asettama työryhmä, 2003; Suomen Sisätautilääkärien Yhdistys ry:n asettama työryhmä, 2004; Suomen Sisätautilääkärien Yhdistys ry:n asettama työryhmä, 2004). The European recommendations for prevention and treatment of coronary heart disease were updated and translated into Finnish in 2004 and in 2008 (Suomen Sisätautilääkärien Yhdistyksen, Suomen Kardiologisen Seuran, Suomen Verenpaineyhdistyksen, Kunnallislääkärityhdistyksen, Suomen Teollisuuslääke-tieteen Yhdistyksen ja Suomen Sydäntautiliiton työryhmä, 1996; De Backer et al., 2004; Euroopan kardiologinen seura ja työryhmä, 2008). All the guidelines included general recommendations, and some gave specific recommendations for important subgroups, including patients with diabetes (Lugtenberg et al., 2011).

Thereafter the guidelines have been updated. The Current Care guideline for diabetes was published in 2007 and updated in 2012 (Suomalaisen Lääkäriseuran Duodecimin ja Suomen Verenpaineyhdistys ry:n asettama työryhmä, 2005; Suomalaisen Lääkäriseuran Duodecimin, Suomen sisätautilääkäreiden yhdistyksen ja Diabetesliiton lääkärineuvoston asettama työryhmä, 2007; Suomalaisen Lääkäriseuran Duodecimin ja Suomen Kardiologinen Seura ry:n asettama työryhmä, 2009; Suomalaisen Lääkäriseuran Duodecimin ja Suomen Sisätautilääkärien Yhdistys ry:n asettama työryhmä, 2009; Suomalaisen Lääkäriseuran Duodecimin ja Suomen Kardiologisen Seuran asettama työryhmä, 2011). In the development of Current Care guidelines, synchronisation and harmonisation with international care guidelines has been the usual course of action (Voipio-Pulkki, 2007).

The treatment recommendations for CHD among patients with diabetes can be generally summarised as follows: Firstly, the guidelines have described with a high level of consistency that there is a need for drug use to prevent CHD and its complications among patients with diabetes; usually, anti-hypertensive drugs and lipid-lowering medication have been recommended. Secondly, while evidence for coronary revascularisation being the best treatment option for diabetes patients has been somewhat weak, the recommendations suggest based on the results and the 10-year follow up of the Bypass Angioplasty Revascularisation Investigation trial that CABG has better long-term treatment outcomes than PCI among patients with diabetes (The BARI Investigators, 2007).

The latest guidelines on diabetes, pre-diabetes and cardiovascular diseases (2013) by the European Society of Cardiology (ESC) underline consistently that patients with diabetes are considered to be at high cardiovascular risk. Moreover, patients with diabetes and cardiovascular disease (MI, angina pectoris) are at a very high risk of recurrent cardiovascular complications. In patients with coronary artery disease and diabetes, medical therapy (ACE inhibitors or angiotensin receptor blockers; beta blockers; statins; aspirin) is recommended. When invasive treatment is needed, the guideline recommends informing the patient about the risks and benefits of CABG vs. PCI and then recommends shared decision-making within the context of the patient's preferences (ESC, 2013). In the Finnish Current Care guideline for Diabetes and in the American Diabetes Association's standards for medical care in diabetes, recommendations for medical therapy among patients with diabetes and CHD are similar to those of the ESC. (ESC, 2013; Suomalaisen Lääkäriseuran Duodecimin, Suomen Sisätautilääkäreiden yhdistyksen ja Diabetesliiton Lääkärineuvoston asettama työryhmä, 2013; American Diabetes Association, 2014) The American Diabetes Association requires beta blockers for patients with a prior MI. (American Diabetes Association, 2014) All in all, the focus of diabetes treatment should change from glycemic control to improving long-term survival related to prevention and treatment of CHD (Wang, 2012).

2.2.5 Remarks on factors associated with coronary heart disease care

In Finland, several factors influencing treatment practices of CHD in the 1990s and 2000s can be identified. Resources for invasive treatments of CHD increased along with the numbers of cardiologists. At the same time, new pharmaceutical treatments emerged, and extension of special reimbursement rights for lipid-lowering medication costs to include patients with CHD was enacted in 2000. Also, obligatory generic substitution was launched in 2003. A programme for prevention and treatment of diabetes as well as for prevention of cardiovascular comorbidities

was conducted in 2000–2010. To improve CHD treatment in Finland, Current Care guidelines have been published and updated.

Overall, these Finnish experiences show progress in the adoption of health technologies in medical practice in the treatment of CHD. Firstly, resources allocated to coronary revascularisations have increased, as has the number of PCI procedures. Secondly, the cost of lipid-lowering medication has decreased overall, and a specific health insurance reform targeted to decrease CHD patients' lipid-lowering medication costs was launched. Concurrently, comprehensive actions in the prevention of diabetes and prevention and treatment of CHD among persons with diabetes took place in the Finnish health care system, resulting in a higher awareness in early diagnosis and treatment of diabetes and its complications.

2.3 Conclusions from earlier literature

Medical practice variation is a useful concept for assessing health care. Variations in medical practice between geographical areas have been demonstrated in a large body of literature (Keskimäki et al., 1994; Black et al., 1995; Birkmeyer et al., 1998; Dunn et al., 2005; Lysdahl & Borretzen, 2007; Bhatnagar et al., 2010; Maheshwari et al., 2011; Pearce-Smith, 2011; Welch et al., 2011). Variations in health care use are partly due to different preferences among patients concerning medical treatment and differences in morbidity, but partly the variation is associated with available health care resources or the practice patterns of physicians (Andersen & Mooney, 1990; McPherson, 1990; Wennberg, 2002). Shifting the focus from regional variation to changes over time yields information on increasing and decreasing trends in specific medical practices and on whether a treatment is well-established or fluctuates.

Many factors in society and the health care system and their development are associated with these trends of medical practice change over time. Identified factors − legislation, resources, adoption of health technology, policy measures and clinical guidelines – operate on several levels from public policy down to the practice of individual actors in health care. These factors can be summarised by their function: regulation, modernisation and standardisation (de Jong, 2008).

The literature review conducted provides a landscape of the ways in which medical practices changes over time have been studied before. Based on register data, earlier studies present information on medication use, operative treatments delivered in hospitals and hospitalisations at times when a new health technology was initialised, or when evidence of adverse effects of a medical practice had accumulated, or when

evidence-based guidelines or health policy steering mechanisms were launched. It can also be assumed that medical practices related to CHD treatment illustrate changes in medical practice in Finland over time more generally.

3 The aims of the study

This study focused on changes in medical practice at the level of the health care system. It is register-based, taking the viewpoint of treatment of CHD among patients with diabetes within health services as a case study of changes in medical practices. The general aim was to examine temporal trends in CHD treatment practices among patients with diabetes. Two medical practices were examined, namely medication to prevent CHD complications and coronary revascularisations.

More specifically, the aims of the sub-studies were:

I   To examine differences in the use of medication to prevent new cardiac events among newly diagnosed CHD patients with diabetes compared to non-diabetic patients and whether the treatment trends in medication vary between socioeconomic groups.

II   To examine differences in the use of lipid-lowering medication among incident diabetes population and whether the annual trends vary by socioeconomic group. The study further examined whether these trends are modified by comorbidities.

III   To analyse whether a diagnosis of diabetes modifies access to revascularisation among newly diagnosed CHD patients at the time of increasing resources for revascularisations. The study further describes changes in trends in revascularisations in this patient group and the possible socioeconomic variation in treatment trends.

IV   To examine differences in pathways to revascularisation among patients with diabetes versus other non-diabetic CHD patients, trends over time in these pathways and the possible modifying effect of comorbidities on the pathways to revascularisation.

4 Data and methods

The present study draws on register-based data and presents four longitudinal sub-studies using yearly cohorts of persons with diabetes and/or CHD. In each sub-study, the study design was tailored to answer the specific research questions and incident or prevalent patient populations were defined for each of the studies.

4.1 Data

The research data sets comprise data obtained from registers maintained by the National Institute for Health and Welfare (THL), the Social Insurance Institution of Finland (SII) and Statistics Finland. The registers used include the Finnish Hospital Discharge Register on hospital care, the register on purchases of medicines reimbursed by the National Health Insurance and employment statistics. The registers are statutory, and the information is regularly collected and updated at the individual level. The compilation of the datasets used in this study is described in detail elsewhere (Niemi & Winell, 2005; Kajantie et al., 2006; Seppälä et al., 2008; Sund & Koski, 2009; Peltola et al., 2011). The datasets for each study are summarised in Appendix 3.

Information on diagnosed diseases utilised data from one or more of the following register sources: Hospital Discharge register, Benchmarking database, Social Insurance Institution register data on persons eligible for special reimbursement of medicine costs due to certain chronic disease, and reimbursed purchases of prescription medicines.

The Finnish Hospital Discharge Register is maintained by the National Institute for Health and Welfare (THL). Data in the register are mainly based on individual-level discharge reports collected annually from all public and private hospitals. The Hospital Discharge Register used the 9th revision of the International Classification of Diseases (ICD) until 1996 and has used the 10th revision since then (Stakes, 1999a; Stakes, 1999b). Surgical operations were classified according to the classification of procedures by the Finnish Hospital League until 1996, and thereafter according to the Nordic Medicostatistical Committee classification (Finnish Hospital League, 1983; NOMESCO, 1996).

The Social Insurance Institution is the registration authority for the special reimbursement register and for the Finnish database on all reimbursed drug

purchases (Martikainen, 2008; Social Insurance Institution in Finland, 2009a). Reimbursed purchases of prescription medicines cover purchases in outpatient care, and the data can be used to represent medicine use even though some patients might not use all medicines they have purchased. (Social Insurance Institution in Finland, 2009b) Medicines were coded according to the Anatomical Therapeutic Chemical (ATC) system in the Social Insurance Institution database on all reimbursed drug purchases (WHO, 2006). The Special Reimbursement Register includes information on individuals who are entitled to reimbursement of medication for certain chronic diseases. The Special Reimbursement Register covers approximately 50 diseases; in the adult population, the most common diseases that are eligible for special reimbursement are chronic hypertension, diabetes and asthma. (National Agency for Medicines & Social Insurance Institution, 2003)

Information of sociodemographic factors was obtained from the annual employment statistics maintained by Statistics Finland. Information on income was derived from national tax register data. (Statistics Finland, 2013)

4.1.1 Definition of the cases

Persons with diabetes

The case definitions of diabetes patients were based on the Social Insurance Institution register data on special reimbursement rights for medicine costs, the prescription register and the Hospital Discharge Register. Persons eligible for special reimbursement for medication costs for diabetes medication (Finnish code 103), those who had bought diabetes medicines (ATC A10) and those with inpatient care due to diabetes (ICD-9 250; ICD10 E10; E11; E13; E14) were defined as having diabetes. Patients with gestational diabetes only were excluded from the analyses. One study (I) concerned an undivided group of diabetes patients, while the others defined diabetes type in three ways: Firstly, the distinction between type 1 and type 2 diabetes was based on information of delivered prescriptions of diabetes medicine and age at the onset of diabetes. Diabetes was defined as type 1 if the onset of the disease was before the age of 30 years; for type 2 diabetes the age limit was 40 years or older. Diabetes type for individuals in the age bracket 30 to 39 was defined as unknown, and they were excluded from the analysis by diabetes type (III). This age-based definition of diabetes type draws from an epidemiological study conducted in Western Finland (Eriksson et al., 1992). Secondly, the definition of diabetes type was based mainly on information of prescriptions of diabetes medicine and identified persons with insulin-dependent diabetes (IDD) and non-insulin-dependent diabetes (NIDD). The insulin-dependent group was defined by

continuous insulin usage and no purchases of other type of diabetes medication (IV). Later, this definition title was found to be misleading among clinicians and changed. For the third definition, non-insulin-treated diabetes mellitus (NITDM) and insulin treated diabetes mellitus (ITDM) were used (II). These definitions tailored for Finnish register-based data were developed by the FinDM II steering board (Sund & Koski, 2009).

Persons with CHD

CHD cases were defined using information from several registers, and information of CHD diagnosis or treatment and special reimbursement rights for CHD medicines was used. Firstly, newly diagnosed CHD patients were identified in hospital inpatient treatments due to CHD using information of MIs (ICD9-codes 410, ICD10-codes I21–I22) and coronary revascularisations. Moreover, information of CHD diagnosis entitling a patient to special reimbursement of medicine costs (206) was used. To ensure that the CHD patients were new cases, the Hospital Discharge Register was searched for previous entries back to 1990 (I, III). The longitudinal data enabled accounting for the time of onset of CHD. The total population of persons diagnosed with diabetes was stratified by CHD status indicated by eligibility for special reimbursement for CHD medicines (206) or hospital inpatient treatment due to CHD. Persons with diabetes were classified into three groups (II): (1) persons with diabetes and no information on CHD before or during the first year after diabetes diagnosis, (2) persons with CHD at least one year before diabetes diagnosis, and (3) persons with coincident diagnosis of CHD and diabetes. Besides these, a total population of persons with the history of first coronary revascularisation procedure was used (IV). This CHD population represented the hospital population which was identified to have a need for and to be eligible for revascularisation.

Other factors

The results were mainly presented separately for men and women. The age bracket of the studies was 40 to 79 years of age. In addition, in the second sub-study of newly diagnosed diabetes patients the age group 30–40 was included, and in the fourth sub-study with total population of coronary revascularisations no upper age limit was imposed. Age was taken into account as a categorical factor. Socioeconomic status was measured using frequently used classifications, including education (basic, secondary, higher) and income quintile. The three categories of education were based on the length of education obtained from the Register of educational achievement. The basic education category corresponds to less than 10 years of education. The intermediate or secondary education category was defined as secondary school and vocational training or upper secondary school matriculation, requiring 10–12 years of education. The category of higher education includes

people with a university degree or qualification requiring 13 or more years of education. Tax register-based income data were adjusted for family size using the OECD equivalence scale, where the first adult is weighted as 1.0, other adults as 0.7 and children under 18 years old as 0.5 (I, III) (OECD, 2005). Income quintiles were derived from the general population, and those with no recorded income were assigned to the lowest income group. To avoid indirect identification, the income variables were edited by Statistic of Finland so that the maximum personal net income was rounded to EUR 50 000 and the maximum family net income to EUR 100 000 per year.

Information on patients' comorbidity was collected from drug reimbursements and hospital data. Information on comorbidities was used to standardise for case-mix between population groups (e.g. CHD patients with and without diabetes). Two studies (I, III) used a modification of Elixhauser's coding algorithms based on ICD codes (Quan et al., 2005). In two studies (II, IV), comorbidity was controlled for using a method developed for Finnish register studies (Lamers & van Vliet, 2004; Quan et al., 2005; Juntunen et al., 2008; Peltola et al., 2011) .

Patient populations in sub-studies

In the first sub-study, a cohort of newly diagnosed CHD patients with and without diabetes in 1997–2002 (5 220 men and 4 046 women with diabetes, 38 280 men and 27 078 women without diabetes) was examined to investigate the use of medication to prevent cardiac complications. Furthermore, medication use was examined by socioeconomic group. In the second sub-study, newly diagnosed diabetes patients in 2000–2006 (67 357 men, 53 696 women) were analysed in annual cohorts to assess the use of lipid-lowering medication after diabetes diagnosis. The study examined whether sex, age or income-related inequalities existed in the use of lipid-lowering medication and whether these differences changed over time. The onset of CHD was also taken into account. Moreover, the study described change in lipid-lowering medication use at the time of diabetes diagnosis by comparing the level of use after the diagnosis to that before it.

In the third sub-study, a cohort of newly diagnosed coronary patients with and without diabetes in 1995–2002 (7 333 men and 6 258 women with diabetes, 57 294 men and 39 945 women without diabetes) was used to investigate access to first coronary revascularisation and whether this changed over time. Access to first coronary revascularisation was examined also by socioeconomic group. In the fourth sub-study, a cohort of patients who underwent their first coronary revascularisation in 1998–2007 was analysed to elaborate differences in coronary care by analysing treatment pathways to first revascularisations among patients with diabetes (11 641

men, 5 904 women) versus other CHD patients (44 498 men, 16 731 women). A summary of datasets and patient populations is presented in Appendix 4.

4.2 Statistical methods

Methods were tailored in each sub-study to answer specific research questions. All sub-studies were longitudinal. Sub-studies I, II, and III measured CHD treatment among newly diagnosed patient populations, while and sub-study IV looked back at CHD events that had already taken place before the first coronary revascularisation.

To investigate the use of medication preventing cardiac complications, filled prescriptions of medication were examined (I). Filled prescriptions, i.e. purchases of prescription drugs, were collected from the registers using ATC codes (C07, C09A, C09B, C09C, C09D and C10). Descriptive analyses, crude and age-adjusted rates of cases in this medication use were calculated first. Secondly, relative differences were examined using regression models and adjusted for age, income, MI (ICD9-codes 410, ICD10-codes I21–I22), year and previous use of medication. Thirdly, the study examined whether the use of medication varied within socioeconomic groups and between time periods.

To examine lipid-lowering medication use among patients with newly diagnosed diabetes in the longitudinal data, careful construction of variables was carried out (II). The first observation window was the medication status defined as filled prescriptions 24–30 months before the diabetes diagnosis, while the second observation window was 6–12 months after diabetes diagnosis. Because CHD is the main indication for lipid-lowering medication, patient groups were defined by the onset of CHD in relation to diabetes onset, separating new cases and cases with CHD before the onset of diabetes. In the descriptive analysis, proportions of persons were calculated in the second observation window for each annual cohort of new diabetes cases divided by patient groups and stratified by income quintile. Furthermore, logistic regression models were used to estimate the association of diabetes diagnosis with the increase in filled prescriptions after the diagnosis as compared to those before the diagnosis. The models were adjusted for age, sex, comorbidities, and the expected overall increase in medication use.

Differences in trends in access to first coronary revascularisation among newly diagnosed CHD patients with and without diabetes were examined in sub-study III. Firstly, trends in access to first revascularisation were estimated by calculating age-adjusted rates for CABG and PCI per 1 000 person-years for the beginning (1995–1996) and the end (2001–2002) of the study period. Secondly, using Cox's

regression models, time trends in operations were analysed adjusting for age, time period and history of MI. Both analyses were performed separately for men and women with and without diabetes and by income quintile. Separate Cox's regression models adjusted for confounders were performed for access to first PCI or to first CAGB separately for diabetes type 1 and 2.

Sub-study IV investigated whether treatment pathways leading to first coronary revascularisation differed between patients with and without diabetes. After defining treatment pathways, descriptive figures were calculated for all CHD patients with a history of first revascularisation. Secondly, change in medical practice was described first as proportions of revascularisations at the first treatment period, and second, as proportions of revascularisations after suboptimal treatment pathways. Suboptimal treatment pathways were defined as pathways containing several cardiac emergency hospitalisations. Finally, differences between patient groups were examined using a logistic regression model adjusting for age, comorbidity and region (Berlin et al., 1999; Juntunen et al., 2008; Sund & Koski, 2009; Peltola et al., 2011).

4.3 Ethical issues

Finland has data protection legislation, which allowed the collection and use of these data for statistical and scientific purposes. The current study was conducted in several large research projects. The data linkages were performed by the competent statistical authorities and approved by the office of the Finnish data protection ombudsman. The research group received anonymised data. The data protection legislation and corresponding regulations and guidelines of STAKES and the National Institute for Health and Welfare were followed. These good practices for register-based research include ensuring the anonymity of the data and guaranteeing safekeeping of the data. (Martikainen, 2008) The study protocol for each of the sub-studies was approved by the Research Ethics Committees of STAKES or the National Institute for Health and Welfare.

5 Results

This study focused on changes in medical practice over time in medication use (I, II) and surgical operations (III, IV) to prevent and treat coronary complications among persons with diabetes.

5.1 Trends in medication

5.1.1 Secondary preventive medication for CHD (sub-study I)

The first study compared secondary preventive medication for coronary heart disease between CHD patients with or without diabetes. Since CHD is a chronic disease, the study focused on those with newly diagnosed coronary heart disease to guarantee similar drug prescribing practices between the two patient groups. Trends in filled prescriptions for CHD medication among persons with newly diagnosed coronary heart disease with and without diabetes were examined in an unselected population; in other words, the population covers hospitalised patients and those who received their diagnosis in primary health care or occupational health care (I). Trends were examined in lipid-lowering medication, beta blockers, ACE inhibitors and Angiotensin II receptor antagonists in 1997–2002. The medications to treat and prevent coronary complications include both older and newer drugs. The lipid-lowering medication mainly comprised statins, which were introduced for the treatment of CHD in the 1990s (Strandberg et al., 1997). To examine potential differences in the use of medication, the results were reported by socioeconomic group.

At the beginning of study period, 88% of diabetes patients used beta blockers; among patients without diabetes the percentage was 89%. ACE inhibitors were used by 48% of diabetes patients compared to 25% of persons without diabetes, and angiotensin II receptor antagonist use was rare – 2% of patients with diabetes and 6% of those with CHD only. At the end of study period, beta blockers were used by 93% of patients with diabetes and 90% of those without diabetes, the numbers for ACE inhibitors being 61% and 37%, and for angiotensin II receptor antagonists 18% and 11%, respectively.

The patterns of medication use among newly diagnosed CHD patients changed during the study period, the use of RAAS inhibitors increasing especially among patients with diabetes, in line with treatment guidelines. Beta blockers presented a constant pattern of high use (over 85%) throughout the study period (1997–2002); the use of this old drug seemed to have reached a saturation point before the study period, and use remained high in all patient groups during the whole study period.

In lipid-lowering medication use, an increasing trend was found among persons both with and without diabetes. The number of cases of lipid-lowering medication use for men with diabetes varied from 41% to 79%, being 55%–82% for men without diabetes. For women with diabetes, use of lipid-lowering medication was 39% in the beginning and 83% at the end of the study period, being 45%–77% for women without diabetes. Despite the increase, medication use remained at a lower level among men with CHD and diabetes compared to those with CHD only (Risk ratio 0.94; 95% CI 0.90–0.98). When investigating socioeconomic differences among all CHD patients, differences were found in lipid-lowering medication use at the beginning of the study period, suggesting underuse of statins among lower socioeconomic groups among both men and women. However, lipid-lowering medication use increased throughout the study period, and after a health insurance reform in 2000, the socioeconomic differences in medication use disappeared.

5.1.2 Lipid-lowering medication (sub-study II)

The second study described lipid-lowering medication use among patients with newly diagnosed diabetes, taking into account sociodemographic factors and comorbidities. The study (II) also examined the impact of diabetes diagnosis on the use of lipid-lowering medication. This medical practice was described before and after compulsory generic substitution of pharmaceuticals and decreasing prices of lipid-lowering medication.

The study population included annual cohorts of persons with a new diagnosis of diabetes in 2000–2006. In the first study year, 18% of men with diabetes only were on lipid-lowering medication, the percentages being 52% among men with CHD diagnosed before diabetes and 59% among men with coincident diagnosis of CHD and diabetes. In the last study year, the percentages were 38%, 79% and 80%, respectively. In the 2000 cohort, among women 20% of those with diabetes only were on lipid-lowering medication, the percentages being 48% among women with CHD diagnosed before diabetes and 57% among women with coincident diagnosis of CHD and diabetes. In 2006, the percentages were 40%, 73% and 75%, respectively. Hence, a trend of increasing lipid-lowering medication use was

detected among both men and women. The use of lipid-lowering medication before diabetes diagnosis was modest among persons without CHD compared to new diabetes patients with CHD, as expected. At the time of increasing use of lipid-lowering medication, an independent effect of the diagnosis of diabetes on medication use was found. The effect remained throughout the study period, being the largest among patients with coincident diagnosis of diabetes and CHD.

Focusing on changes in lipid-lowering medication use among all new diabetes patients by socioeconomic group, a growing trend was found in all income quintiles. Among the lowest income quintile, the percentage of medication was 20% in 2000 and it was nearly 40% by 2006. There was fluctuation in the ranking of the other income quintiles in different years, but all other quintiles were almost 10% higher than the lowest one throughout the study period.

To summarise, the results indicate that evidence-based drug use for CHD has increased. The use of new drugs to prevent and treat coronary complications (RAAS inhibitors) has increased and is higher among persons with diabetes compared to those with CHD only. From the equity perspective, socioeconomic differences in lipid-lowering medication use among CHD patients have, in general, diminished. However, the use of lipid-lowering medication was lower in the lowest income group compared with the others in the incident diabetes population. Among the diabetes population, the indication for prescription of lipid-lowering medication seems mainly to be CHD; characteristically in the 2006 cohort, the percentage of lipid-lowering medication use was almost 40% among persons with diabetes only but nearly twice as high among persons with CHD.

5.2 Trends in coronary revascularisations

5.2.1 Access to revascularisation (sub-study III)

The third study focused on examining how diabetes modified access to the first coronary revascularisation among a cohort of coronary patients with and without diabetes and socioeconomic differences in access to these operations. The study question was examined in the context of increasing resources being invested in coronary revascularisations during the study years. Specific health technology used in coronary revascularisation was analysed by separately examining CABG and PCI, where CABG represents an invasive technology that has been in use longer and PCI a newer invasive technology. The decision on what the best choice is for specific patients depends on clinical factors.

During the study period (1995–2002), resources for coronary revascularisation increased rapidly (III). Among men with CHD, the likelihood of revascularisation was lower among those with diabetes especially towards the end of the study period. Among men without diabetes, the revascularisation rate increased from 354 (95% CI 341–367) in 1995 to 443 (95% CI 428–458) per 1000 person-years in 2002; among men with diabetes, the rate also increased but less rapidly, from 301 (95% CI 258–344) to 366 (95% CI 363–435). Among women with CHD, the rates were similar level at the beginning of the study period regardless of diabetes status, but the presence of a diabetes diagnosis seemed to increase the likelihood of coronary revascularisation compared to those without diabetes towards the end of the study period. The revascularisation rate among women without diabetes was 224 (95% CI 204–245) in 1995 and 249 (95% CI 227–272) by 2002, simultaneously among women with diabetes, the rate increased from 208 (95% CI 151–265) to 325 (95% CI 255–395).

The majority of first coronary revascularisations was performed using CABG in the mid-1990s in all patient groups. For persons without diabetes, the use of PCI increased in the early 2000s, while among men with diabetes CABG remained the more common of the two procedures. Among women with diabetes, CABG and PCI were used equally often. When examining the diabetes population by diabetes type, the likelihood for using CABG at the first coronary revascularisation was elevated among women with type 1 diabetes and among men and women with type 2 diabetes in the early 2000s. The biggest patient group was men with CHD, and therefore PCI was the most used health technology in first coronary revascularisation in the early 2000s.

The trend in socioeconomic equity in access to these operations by diabetes status was also analysed (III). Among men with CHD both with and without diabetes, a socioeconomic gradient in the use of coronary revascularisation was observed throughout the study period: the lower the income group, the lower the likelihood. The pattern was less consistent among women, in particular among women with both diseases. Despite the increase of resources allocated to coronary revascularisations, a socioeconomic gradient persisted in access to revascularisations regardless of diabetes status.

5.2.2 Pathways to revascularisation (sub-study IV)

During the study period (1998–2007), medical practices changed to favour coronary revascularisation in the first treatment period for CHD, whereas the pathways to the operation have been reported to have been more varied earlier among persons undergoing revascularisation. The fourth study examined hospital treatment pathways leading to the first coronary revascularisation and compared pathways to the treatment among patients with and without diabetes in yearly cohorts in the period 1998–2007 (IV). While the numbers of procedures performed in the first treatment period increased rapidly among men regardless of diabetes status, the numbers remained lower among men with diabetes, especially insulin-dependent diabetes, throughout the study period. Among men without diabetes, the increase was from 28% of operations being performed in the first treatment period in the beginning of the study period to 77% towards the end of the period. Among men with insulin-dependent diabetes, the numbers of coronary revascularisation performed in the first treatment period were 16% and 58%, and among those with non-insulin dependent diabetes 25% and 69%. When modelling the odds for undergoing revascularisation during the first hospital admission at the beginning and the end of the study period (1998–2000; 2005–2007), even after controlling for comorbidities the probability was low (0.73; 95% CI 0.54–0.99) at the beginning and remained low (0.52; 95% CI 0.42–0.64) at the end of the study period among those with insulin-dependent diabetes compared to men without diabetes, and the odds for men with non-insulin dependent diabetes was also low (0.86; 95% CI 0.77–0.96 and 0.79; 95% CI 0.73–0.86) compared to men without diabetes.

For those with CHD only, the figures were 32% at the beginning and 77% at the end of the study period; for women with insulin-dependent diabetes, the figures were 36% and 64%, whereas among women with non-insulin dependent diabetes, the figure increased from 33% to 73%. Among women with diabetes, the odds for undergoing revascularisation in the first hospital admission was similar to that among men. For women with insulin-dependent diabetes, the odds were 0.76 (95% CI 0.52–1.11) at the beginning and 0.59 (95% CI 0.44–0.78) at the end of the study period compared to women without diabetes even after controlling for comorbidities. For women with non-insulin dependent diabetes, the corresponding figures were 0.95 (95% CI 0.83–1.10) and 0.83 (95% CI 0.74–0.93).

The study also examined trends in suboptimal treatment pathways to revascularisation among persons with and without diabetes (IV). Suboptimal treatment pathways were defined as including more than one cardiac emergency hospitalisation during two years preceding first revascularisation. While fewer operations were performed during the first CHD hospitalisation among patients with

diabetes, they also showed a higher probability of suboptimal treatment pathways to revascularisation throughout the study period. Among men with insulin-dependent diabetes, the odds for a suboptimal treatment pathway was elevated [1.67 (95% CI 1.26–2.22) in 1998–2000 and 1.95 (95% CI 1.38–2.76) in 2005–2007] even after controlling for comorbidities. For men with non-insulin dependent diabetes, the odds were similar to those among men without diabetes [1.12 (95% CI 1.00–1.26) and 1.12 (95% CI 0.96–1.30)] in both periods. For women with insulin-dependent diabetes, the figures were 1.52 (95% CI 1.00–2.30) and 1.91 (95% CI 1.22–3.00) after controlling for comorbidities, and for women with non-insulin dependent diabetes, the figures were 1.28 (95% CI 1.10–1.49) and 1.30 (95% CI 1.22–3.00).

Similarly to drug use, an increasing trend in the use of coronary revascularisations was found. A rapid increase of resources increased the number of coronary revascularisations by some 25% in Finland between 1997 and 2002. At that time and consistently afterwards (1998–2007), medical practices have changed so that the use of CABG has decreased while PCI has increased. Despite this, CABG was the more common procedure among patients with diabetes throughout the study period. In pathways leading to coronary revascularisation, patients with diabetes had an elevated risk of delays to their operation, and the pathways might contain several cardiac emergency hospitalisations.

6 Discussion

The overall purpose of this study was to examine changes in medical practices over time using register-based data. More specifically, the study examined changes in medical practices in CHD treatment among persons with diabetes. Two types of medical practices were examined, namely medication use and surgical operations to prevent and treat CHD. The results are based on longitudinal data, and the time window in each sub-study was long enough to observe changes in medical practices. While no empirical data are available concerning the direct influence of external factors influencing the results, the results are discussed in the context of these changes. These Finnish factors include at least increasing resources in coronary revascularisations, decreasing prices of lipid-lowering medication, restricted reimbursement on the use of statins, programme for treatment of diabetes and preventing CHD among persons with diabetes (DEHKO), and production of nationwide clinical guidelines.

The choice of patient group was motivated by the fact that earlier studies in Finland and elsewhere on medical practices in CHD treatment among patients with diabetes have raised concerns about undertreatment (Alter et al., 2003; Gitt et al., 2003; Norhammar et al., 2003; Hetemaa et al., 2006; Salomaa et al., 2007). Earlier studies have also reported socioeconomic differences in access to coronary revascularisations among CHD patients with and without diabetes (Hetemaa et al., 2003; Hetemaa et al., 2004; Hetemaa et al., 2006; Manderbacka et al., 2009). The objectives originated from the lack of studies on health technology change adopted in medical practices and focusing on patient groups with multimorbidity, i.e. patients with two chronic diseases – CHD and diabetes – and in different socioeconomic groups. (McClellan & Kessler, 2002)

The results showed that good treatment practices to prevent vascular complications among persons with diabetes have become more widespread. Methodologically, the used risk-adjustment methods designed specifically for Finnish register-based data ensured justified comparisons between groups and between different time periods. Despite the increase of good treatment practices, the results raise some concerns of undertreatment among patients in a low socioeconomic position and with newly diagnosed diabetes and regarding the managing of treatment pathways to coronary revascularisation among patients with diabetes. This information can be used to develop targeted interventions in CHD treatment aimed at taking special needs of persons with diabetes into consideration.

6.1 Overview of the main results

6.1.1 Use of CHD medication

At the population level, guidelines advise the including of RAAS inhibitors in secondary preventive medication for CHD for hypertensive patients, and lipid-lowering medication is assumed to be a necessity for majority of CHD patients (Ryden et al., 2007; ESC 2013). Trends of increasing medication use for CHD were found among persons with and without diabetes between 1997 and 2002. These findings of growing trends were similar to findings of hospitalised CHD patient samples in Finland and other European countries (Kotseva et al., 2009; Nichols et al., 2012), but these results did not provide subgroup analysis for patients with CHD and diabetes. Comparisons between countries emphasise the fact that prescribing patterns vary: beta blocker use was highest in Finland among hospitalised CHD population, while ACE inhibitor use remained lower compared to the Netherlands and Germany. (Kotseva et al., 2009; Nichols et al., 2012)

The findings of the differences in medication use between CHD patients with and without diabetes showed that the use of RAAS inhibitors was more common among patients with diabetes and CHD, in line with the recommendations of treatment of hypertension among persons with diabetes. The finding that no socioeconomic differences were detected in the use of beta blockers corroborates previous findings among hospitalised MI patients and a sample of prevalent CHD patients in Finland (Salomaa et al., 2001; Salomaa et al., 2007; Manderbacka et al., 2008), whereas some international studies have reported socioeconomic differences in anti-hypertensive medication use in the general population (Corrao et al., 2008; Friedman et al., 2010). In addition, a dissemination study among persons with hypertension reported no systematic differences by socioeconomic status in how rapidly this population adopted new anti-hypertensive medications (ACE inhibitors) (Goldman & Smith, 2005). In terms of subsequent development in Finland, in the last study year (2002) the use of RAAS inhibitors still seemed to have room for growth, while the use of older medication, beta blockers, seemed to have peaked among all newly diagnosed CHD patients.

In Western countries, the use of lipid-lowering medication has increased in the general population since the mid-1990s, as described earlier for Finnish elderly people, hospitalised CHD patients, and hospitalised AMI patients (Walley et al., 2005; Salomaa et al., 2007; Kotseva et al., 2009; Ruokoniemi et al., 2011; Nichols et al., 2012). In light of these studies, the increase in the use of lipid-lowering medication in an unselected CHD population with diabetes was not unexpected. In 2000, the level of lipid-lowering medication use in the Finnish population was

around the European average, and variation of prescribing patterns was reported both in the general population and in the hospitalised CHD population (Walley et al., 2005; Kotseva et al., 2009; Nichols et al., 2012). Similarly to these Finnish results, the use of lipid-lowering medication increased in the whole population and in the hospitalised CHD population (Walley et al., 2005; Kotseva et al., 2009), and the results suggest room for growth in this use among CHD patients both with and without diabetes at the turn of the millennium.

Earlier studies on lipid-lowering medication use reported socioeconomic gradients in the hospitalised AMI population in Canada (Austin et al., 2006; Selmer et al., 2009) and among patients with diabetes in Norway (Selmer et al., 2009) and Denmark (Thomsen et al., 2005). In the patient group comparisons, the lower use of medication found among CHD patients with diabetes raised concerns of undertreatment. (Brown et al., 2004; Mantel-Teeuwisse et al., 2004; Simpson et al., 2005; Ward et al., 2005; Salomaa et al., 2007; Selmer et al., 2009; Neutel et al., 2010; Ohlsson et al., 2010; Eliasson et al., 2011) Findings from this longitudinal study design revealed lower use among lower socioeconomic groups before 2000, but the socioeconomic differences disappeared thereafter. The criteria for the elevated reimbursement for lipid-lowering medication costs were widened to cover patients with CHD in 2000, and it is plausible that this reform, for its part, increased the use of lipid-lowering medication among CHD patients both with and without diabetes and thereby helped to abolish socioeconomic differences.

According to the findings of this study, increasing use of lipid-lowering medication was detected among persons with a new diabetes diagnosis in 2000−2006. However, differences were detected by CHD status: the percentage of users was lowest among persons with diabetes only. Additionally, while a growing trend of lipid-lowering medication was found in all socioeconomic groups, there were consistent differences in the level of use. An increase in lipid-lowering medication use has also been reported in diabetes populations in other Nordic countries (Fhärm et al., 2008; Dominguez et al., 2009; Gudbjornsdottir et al., 2009), the UK, Irland, Germany, Canda, the USA, and Australia (Teeling et al., 2005; Wan et al., 2006; Soljak et al., 2007; Raum et al., 2008; Segars & Lea, 2008; Berthold et al., 2009; Neutel et al., 2010). There are inbuilt differences in the inclusion criteria for diabetes as well as CHD-related comorbidities between the studies, and therefore straightforward comparisons between them are problematic, but comparing the latest studies with the earlier ones it seems that the earlier reported a lower level in lipid-lowering medication use. There are also likely to be differences in prescription patterns for lipid-lowering medication between countries.

Few if any studies have estimated the impact of diabetes diagnosis to the initial use of lipid-lowering medication using longitudinal study design and register-based data.

Because the diagnosis of diabetes implies a contact with health care and because the data allowed looking at lipid-lowering medication before and after diabetes diagnosis, this question was addressed. At the time of increasing use of lipid-lowering medication, an independent effect of diabetes diagnosis on medication was found: the diagnosis increased usage in all patient groups. The effect was largest among those with coincident diagnosis of CHD, suggesting that CHD remains the main indication for lipid-lowering medication. Furthermore, lipid-lowering medication use was lower in the lowest socioeconomic group among patients with diabetes only. This may partly have been due to differences in the reimbursement of medicine costs between persons with diabetes compared to those with CHD. In Finland, prices for lipid-lowering medication decreased continuously from the mid-1990s, and following obligatory generic substitution for pharmacy in 2003 all patients could choose a cheaper generic alternative. In 2006, some statins were relatively cheap, but the cost of medication might still have constituted a threshold for medication use for some patient groups (Doshi et al., 2009; Martikainen et al., 2010). Similar results concerning lesser use of these drugs in the lowest socioeconomic group have been reported in the Danish diabetes population (Dominguez et al., 2009). International guidelines and guidelines in both countries recommended the use of lipid-lowering medication for patients with diabetes (Haffner & American Diabetes Association, 2004; Snow et al., 2004; Suomen Sisätautilääkärien Yhdistys ry:n asettama työryhmä, 2004; Dominguez et al., 2009; Suomalaisen Lääkäriseuran Duodecimin, Suomen Sisätautilääkäreiden yhdistyksen ja Diabetesliiton Lääkärineuvoston asettama työryhmä, 2012). Discussion on prescribing patterns, patients' adherence to medication use and the impact of guidelines to change in medical practices would be helpful for increasing overall understanding of the observed differences. (Roine et al., 2003; Fhärm et al., 2008; Raum et al., 2008; Toth et al., 2009)

These changes in medication took place during years when the number of new diabetes cases increased, which was partly related to an epidemic of overweight and the increasing age of the population, and partly to awareness of the early signs of diabetes. One of the DEHKO programme targets was to advance the timing of the diagnosis. Unfortunately, the empirical study data do not cover the last years of the DEHKO nor the years thereafter, and thus the recent changes in the use of medication among patients with diabetes remain unclear.

6.1.2 Coronary revascularisations

One of the objectives of this nationwide register-based study was to examine whether the diagnosis of diabetes modifies access to coronary revascularisation. At

the time of increasing resources in coronary revascularisations, medical practices in coronary revascularisation to treat already existing CHD have changed. The use of PCI increased substantially, but CABG remained the more common of the two procedures among patients with CHD and diabetes. Among men with diabetes, access to the coronary operation was lower compared to those without diabetes despite the evidence suggesting that patients with a high-risk profile benefit from coronary revascularisation the most, while the gain among low-risk patients is smaller (Yusuf et al., 1994; Lagerqvist et al., 2005). The result is in line with earlier hospital-based studies in Sweden, Germany and Canada (Alter et al., 2003; Norhammar et al., 2003; Otter et al., 2004). The study design was wider than that of earlier studies examining changes in medical practice over time that focused on AMI patients and yields more information concerning a high-risk group (i.e. patients with diabetes) (McClellan & Kessler, 2002). Earlier research reported socioeconomic differences in revascularisation in the CHD population in Finland, Sweden, the UK and Canada in the early 1990s (Keskimäki et al., 1997; Alter et al., 1999; Haglund et al., 2004; Morris et al., 2005; Hetemaa et al., 2006).

In the current study, a socioeconomic gradient in access to the operations was found among men in both patient groups: the higher the socioeconomic group, the higher the probability of coronary revascularisation. Among women with diabetes, the increase in coronary revascularisation rates seems to have improved equity in access to operation. The finding of a socioeconomic gradient among men corresponded with international findings (Haglund et al., 2004; Morris et al., 2005).

During the study period 1998−2007, medical practice concerning the timing of the operation also changed: it became more and more common to perform coronary revascularisation already during the first hospital admission. The results showed that suboptimal pathways including several emergency admissions before access to first coronary revascularisations remain more common among patients with diabetes. It is likely that CABG will more often be planned for a subsequent hospitalisation than PCI and may need more preparatory investigations. However, longer pathways to treatment seem to increase the risk for unscheduled emergency admissions among persons with diabetes, suggesting inability to take into account the needs of these high-risk patients. Nevertheless, the incidence of suboptimal pathways decreased in all patient groups during the study period.

Comparison possibilities to other studies with this study design using individual-level pathways with a retrospective perspective are scarce. A cohort study of MI admissions in hospitals in California reported both ethnic and payer-group differences in the treatment pathways. Minority patients and uninsured patients were less likely to have treatment pathways leading to revascularisation (Blustein et al., 1995).

To conclude, medical practices have changed in two ways during the study period: PCI use increased and CABG use decreased between 1995 and 2007. Among patients with diabetes, CABG was more common throughout the study period, which is also suggested by the evidence that has slowly accumulated. Persons with diabetes have an elevated risk of delays to operation, and the pathways may contain several cardiac emergency hospitalisations. A significant and well-prepared extra investment in coronary artery disease operations and new technology used in PCI enabled spreading good pathways.

During the study period and thereafter, resources to perform coronary revascularisations have increased considerably. Firstly, the number of cardiologists of working age increased year on year from 74 up to 225 between 1997 and 2012 (i.e. the growth percentage was 204%). Secondly, the number of coronary revascularisations increased by 90%, from 5 714 in 1997 to 10 835 in 2011. This increase happened in 1997–2002; after 2003 the numbers stabilised and have stayed at almost the same level since.

There may have been professional uncertainty in the choice of invasive treatment between PCI and CABG for patients with diabetes. The best treatment option of coronary revascularisation for patients with diabetes has been a subject of discussion for a long time (Grundy et al., 1999; Niles et al., 2001; Flaherty & Davidson, 2005; Ryden et al., 2007; Aronson & Edelman, 2010). The bypass Angioplasty Revascularisation Investigation trial suggests that CABG has better long-term treatment outcomes among patients with diabetes at the time of 10-year follow up (The BARI Investigators, 2007).

6.2 Methodological considerations

This national level register-based study used administrative registers with individual linkages and examined changes in medical practices in a time window long enough for observing changes. It also provided information about treatment trends within socioeconomic groups. The present results are significant in at least four respects: firstly, the selection of patient groups was tailored for a longitudinal register-based study; secondly, the analysis took into consideration different case-mixes enabling comparisons between patient groups; thirdly, the data enabled construction of treatment pathways at the individual level; and fourthly, the examination of medical practice change was carried out not only at the level of the health care system as a whole but also from an equality perspective.

The register-based data comprehensively cover all diagnosed and medically treated diabetes cases in Finland. The registers of special reimbursement as well as the prescriptions database are good sources for identifying people with diabetes. Since these registers are administrative and based on actual reimbursement of costs, the coverage is likely to be high. In addition, identification of people with diabetes was done by combining data from several administrative registers (Hospital Discharge Register, Benchmarking database). (Sund & Koski, 2009) However, these data do not include undiagnosed diabetes patients or persons with only dietary treatment for diabetes and without hospital discharges, only cases with a disease identified by physicians. These patient population data facilitated the providing of information about a real-world patient group using health care. Linking individual-level data on socioeconomic factors using unique personal identifiers prevented ecological bias (i.e. assigning individuals socioeconomic status using area-based aggregated level information on deprivation). Combining registers for study use provided already existing follow-up data. Compared with the typical samples of randomised clinical studies, the cases in the longitudinal register-based data gave better coverage of persons from all socioeconomic groups, persons with multimorbidity and women. (Bartlett et al., 2005)

A review of the validity of the Hospital Discharge Register in Finland has been carried out recently (Sund, 2012). At least 32 studies have documented the Register's validity, focusing on certain diseases in certain time periods. Validity research of vascular disease, mental disorders or injuries showed to be the most common among studies comparing the Hospital Discharge Register data to external information. The coverage of the Hospital Discharge Register was found to be good, and more than 95% of discharges could be identified, however, the poor recording of subsidiary diagnoses and secondary operations found in the review limits the Hospital Discharge Register's validity. Sensitivity and positive predictive value are used in validity research besides the coverage, and the results for the Hospital Discharge Register varied depending on the condition and years. Sensitivity can, in other words, be considered as a true-positive rate, and the positive predictive value indicates the proportion of register-detected cases that were confirmed to be true-positives according to some external data (Sund, 2012). For example, a study assessing the validity of Hospital Discharge Register using external information from the FINAMI register in 1988–2002 found the sensitivity for myocardial infarctions to be 82% and the positive predictive value to be 90%. (Pajunen et al. 2005)

Administrative medical databases are massive repositories of data, but they are not primarily collected for research purposes. In Finland, such databases are maintained by the THL and SII, but data collection takes place in various places (hospitals, health care centers, and pharmacies). The legislation (Finlex 556/1989; 774/1989

and 668/2008) assigns a responsibility to health care providers to provide information to the competent authorities keeping these registers (THL, before 2009 Stakes), including information on coronary revascularisation operations. Regarding hospital discharge data, generally identified problems include questions on the usability of the data entry, concerns about the coverage of the data and delays to the completion of the data. (Räsänen 2013) The coverage of Hospital Discharge Register data regarding the additional information page for CHD patients has recently been criticised. Furthermore, a need for the follow-up of treatment outcomes and complications has been voiced. (Laine, 2013; Mustonen, 2012) In the early 1990s, a study documented problems in the reporting of coronary revascularisation procedures (Hetemaa et al. 2003). In the absence of a gold standard, the hospital discharge data concerning numbers of performed coronary revascularisations can be compared to two separate datasets: the Finnish Heart Association collected aggregated data on coronary revascularisation procedures from the mid-1990s up to 2005, and the Finnish Cardiac Society has published annual surveys since 2007 reporting numbers of invasive cardiac procedures at university and central hospitals (Finnish Heart Association, 2006; Mustonen J et al. 2013). Comparing numbers of coronary revascularisations between THL registers and the Finnish Heart Association in 2000, the THL register reported more CAGBs (n=4 703 vs. 4 113, 114%) and fewer PCIs (n=3 648 vs. 3 930, 93%) than the Finnish Heart Association. In 2010, a comparison between THL registers and the Finnish Cardiac Society data found that the THL register had more CAGBs (n=2 587 vs. 2 110, 123%) and fewer PCIs (n=7 970 vs. 8 968, 89%). (Finnish Heart Association, 2006; Mustonen J et al. 2013; THL, 2013)

The coronary revascularisations examined in this study are cases found in the hospital discharge data, the additional information page of CHD patients or the benchmarking register. However, there is no reason to expect that the distribution of the procedures missed in the data used is other than random in the different population groups examined in the present study. It is unlikely that the basic trend would change substantially if some PCIs are missed. The effect of potential regional variation in the reporting of revascularisations to the registers cannot be estimated due to lack of data for comparisons.

Linking the Hospital Discharge Register data with several other registers in order to build comprehensive research databases is suitable for addressing research questions in health services research. However, additional cross-matching of registers or specific validation studies are needed in the future, and therefore efforts for cross-matching registers for validation purposes should be made. Nonetheless, administrative databases can be used as a robust research tool to examine a variety of clinical and demographic themes (Gavrielov-Yusim & Friger, 2014).

Despite the strengths of the data, there are limitations that need to be considered when evaluating the results. Firstly, the register-based data do not cover patients with diabetes treated only with diet. However, recent recommendations tend not to prefer long-term diet try-outs, and instead advise the starting of oral diabetes medication. (Suomalaisen Lääkäriseuran Duodecimin, Suomen Sisätautilääkäreiden yhdistyksen ja Diabetesliiton Lääkärineuvoston asettama työryhmä, 2012; Laakso, 2013) Secondly, with regard to the CHD cases, the definition does not cover those with mild symptoms of CHD, and medicated only with inexpensive nitroglycerin, still the used definitions of diagnosed CHD extended the cases from hospital populations, which have mainly focused on MI. Thirdly, management of diabetes and CHD has strong behavioural components which can increase or decrease the risk of CHD and its complications. Unfortunately, information on behavioural components or clinical data is not provided by registers in Finland, and this should therefore be investigated in separate sample studies. Fourthly, in terms of drug use, the data provide only indirect evidence on the potential effect on the level of drug use of reimbursement schemes or prescription practices or patient choice of whether to purchase the drugs with a higher price. Taking these limitations into account, the results of this study, using administrative registers that collect unselected information on health care use and social status, provide a good information source for investigating changes in medical practice over time.

The methods used in the sub-studies have a number of attractive features: Firstly, a different case-mix between patient groups could be adjusted for in the statistical analysis using common methods for register-based studies (I, III) or tailored adjustment for Finnish register-based data (II, IV). Taking into account differential comorbidity between the patient groups strengthens the conclusions concerning differences between patient groups. Secondly, broad individual-level data and methods were used to examine the effect of sociodemographic determinants through the study period. Thirdly, specific time periods were modelled comparing different time points between patient groups, which enables taking into account changes in patient populations in terms of disease incidence or age at the onset of disease (II, IV). Fourthly, novel study designs were developed to address the study questions from new perspectives: yearly cohorts of new diabetes cases before and after onset of the disease allowed examination of risk-adjusted changes in medication use (II), and a retrospective follow-up enabled focusing on care pathways (IV). Compared to other studies, these qualities make Finnish register-based datasets dependable information sources for studying medical practices. The potential for longitudinal studies provide opportunities to examine changes in these practices.

Finnish register data allow exceptionally comprehensive longitudinal follow-up of individuals, as deterministic record linkages within and between registers using personal identity code can be made. The use of nationwide and individual-level

register-based data and methods with case-mix control provide advantages in comparing subgroups and different time periods; previous studies on medical practices have not always combined these elements concurrently. Besides nationwide administrative registers, certain other types of register have been used to examine medical practices, namely research, quality and benchmark registers. Many of these are regional, or based on one organisation, limited to a sample. Unlike administrative registers, many of them are voluntary. In summary of the methods used in the reviewed register-based studies examining changes in medical practice over time, the comparisons between groups have often used just crude numbers and proportions, and only some studies have used specific case-mix corrections. Nevertheless, the description of medical practice using crude numbers and proportions is an important first step in identifying problems and challenges in health care (Munk-Jorgensen et al., 1992; Robertsson et al., 2000; Pijl & Sytema, 2003; Arvidsson & Ericson, 2005; Fonarow et al., 2007; Priftis et al., 2007; Gibson et al., 2008; Gualano et al., 2010; Ravera et al., 2010). However, if the focus is on comparison of sub-groups, the different case-mix needs to be taken into account, and some international studies have had the ability for this (Zahn et al., 2000; Marques-Vidal et al., 2003; Lay et al., 2007; Moist et al., 2008; Nguyen et al., 2010; Chin et al., 2011; Kuklina et al., 2011). If the relevant individual-based data are available, methods similar to those employed in this dissertation can be used in other health care settings, provided that the numbers of cases in smaller areas (regions, organisations) are not too small. Describing changes in medical practice over time provides a tool for understanding health care.

6.3 Conclusions

Investigated changes in CHD treatment over time among patients with diabetes and/or CHD indicate that, in general, recommended treatment practices have become more common. These changes in treatment practices took place at a time when resources for coronary revascularisations increased, new pharmaceutical treatments were introduced, special reimbursement rights for lipid-lowering medication costs were extended to patients with CHD and generic substitution was launched. Moreover, a programme for prevention and treatment of diabetes and its cardiovascular comorbidities was in operation, and Current Care guidelines were produced. However, the data of this study do not provide direct evidence on whether policy interventions actually led in the direction intended.

This non-experimental method of examining changes in medical practice over time in different patient groups proved to be useful for describing the level and distribution of the treatment overall and in different patient populations. Using

individual-level register-based data and proper risk adjustment methods enables the elimination of individual-level variation and the comparing of different patient groups. Examining variations in medical practice over time using nationwide health care registers can be useful for evaluating changes in society and health policy actions concurrently. Overall, the present study can facilitate the interpretation and understanding the results of empirical studies on changes in medical practice over time.

6.4 Challenges for future research

The findings of this study suggest that good treatment practices to prevent CHD and its complications among persons with diabetes have increased concurrently with increasing resources for coronary revascularisations and a framework focusing on diabetes care, introduction of treatment guidelines and higher reimbursement for lipid-lowering medication costs extended to patients with CHD. After the study period, the Current Care guidelines including diabetes care have been updated and changes for reimbursement levels for CHD medication are planned. There is an apparent need for future studies using a similar non-experimental setting. One area where future studies are needed is changes in medical practice to prevent CHD complications. The results of the current study indicate that evidence-based medication use, i.e. new medication to control adverse events of CHD, has increased, but it is likely that it still remains at a suboptimal level, and further study is needed to find out whether the trend has continued up to the present. Future studies might also assess whether older medication (beta blockers) have been replaced partly by newer ones (RAAS inhibitors) or whether their use remains constantly at a high level as suggested by this study. Lipid-lowering medication use increased concurrently with widened indications for elevated reimbursement and with lower prices, and with obligatory generic substitution. However, the results suggest that socioeconomic differences in the use of lipid-lowering drugs still exist among the persons with a new diabetes diagnosis. Future studies are needed to investigate whether these differences in persons with incident diabetes will disappear. Additionally, further study should assess whether the use of lipid-lowering drugs remains at a high level among high income groups with CHD, or whether the growing concern about the association of lipid-lowering medication use with a small increase in the risk for diabetes or evidence or public preception of muscular pain due to drug use had an effect on the use of lipid-lowering medication (Rajpathak et al., 2009; Parker et al., 2013).

Information about changing medical practices is important when determining the use of resources in health care. Different health technologies used in medical practice

demand different amounts of health care resources. In surgical operations, the overall tendency has been towards less invasive treatment, which requires less treatment days in the hospital. In conclusion, in the past at least there has been professional uncertainty in the invasive treatment of CHD patients with diabetes. The evidence of the best treatment for patients with CHD and diabetes has strengthened somewhat, and on-going adoption of new health technologies has challenged the best treatment choices (Aronson & Edelman, 2010). Register-based data offer possibilities to monitor the impact of drug price and reimbursement decisions in the use of medication, albeit indirectly. Medical practice needs to be studied using real-world data, and register-based studies offer a good opportunity for this.

Concurrently with changes in health technology, factors such as health policy level regulation and resource allocation at a time of diminishing economic capacity associated with changes in medical practice will continue in the future. Special attention needs to be paid to important issues like the implementation of prevention and care of chronic conditions using relevant implementation tools including national strategies. Together with these changes in the macro level of health care, progress in factors at the meso level is likely to continue, e.g. updating of guidelines for evidence-based treatment and organising integrated care for chronic conditions. Future studies in the course of changes in medical practice at the level of the health care system – whether recommended practices will grow and undertreatment and poor practices become less common – are needed.

Appendijes

Appendix 1

The search strategy of article selection and information extraction of the studies

The studies for the literature review were retrieved from Medline, as it is the most comprehensive international bibliographic database within medicine, and also the database likely to contain the highest number of references relevant to the subject. Mesh Terms (Medical Subject Headings terms) used in the search included terms "Health Services" or "Delivery of Health Care", and "Registers" or "Databases", and "Trends". Studies published in English between January 1946 and March 2012 were accepted. (See detailed search strategy and flow diagram of article selection process on the next pages.)

The search strategy yielded 297 titles and abstracts. Of these hits, 243 were excluded after examining the title and the abstract as secondary sources, including review articles, letters and commentaries. The whole text evaluation included 54 published articles, 24 of which were finally chosen to be included in the review (Figure 7). The criteria for including the articles for more detailed analysis were: firstly, that the data were register-based; secondly, that the outcomes of the study were related to medical practices and that the focus was related to health service use. If the article had several focuses such as efficiency or adverse effects of health care interventions, the evaluation took only health service use into account. The third criterion for entry was that the study design had to be longitudinal presenting temporal trends.

The selected earlier studies (24) examining changes in medical practice over time using register-based data are presented in Table 2. Information extracted from the chosen studies included the first author, publication year, title of the study, medical practice(s), country of origin, and time period covered. Information on the study design included patient groups or other groups compared in the study, register(s) and methods used, case-mix correction, and results regarding medical practice in the study. In the earlier empirical studies, the methods used were classified into those focusing on descriptive and analytical approaches; and whether case-mix correction was used, in particular information of sociodemographic factors and comorbidity. Finally, the results were summarised to evaluate whether evidence-based or health policy reform driven medical practice was implemented and what kinds of trends emerged.

Literature search delivered 2.4.2012

Database(s): Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and
Ovid MEDLINE(R) 1946 to Present

Search Strategy:

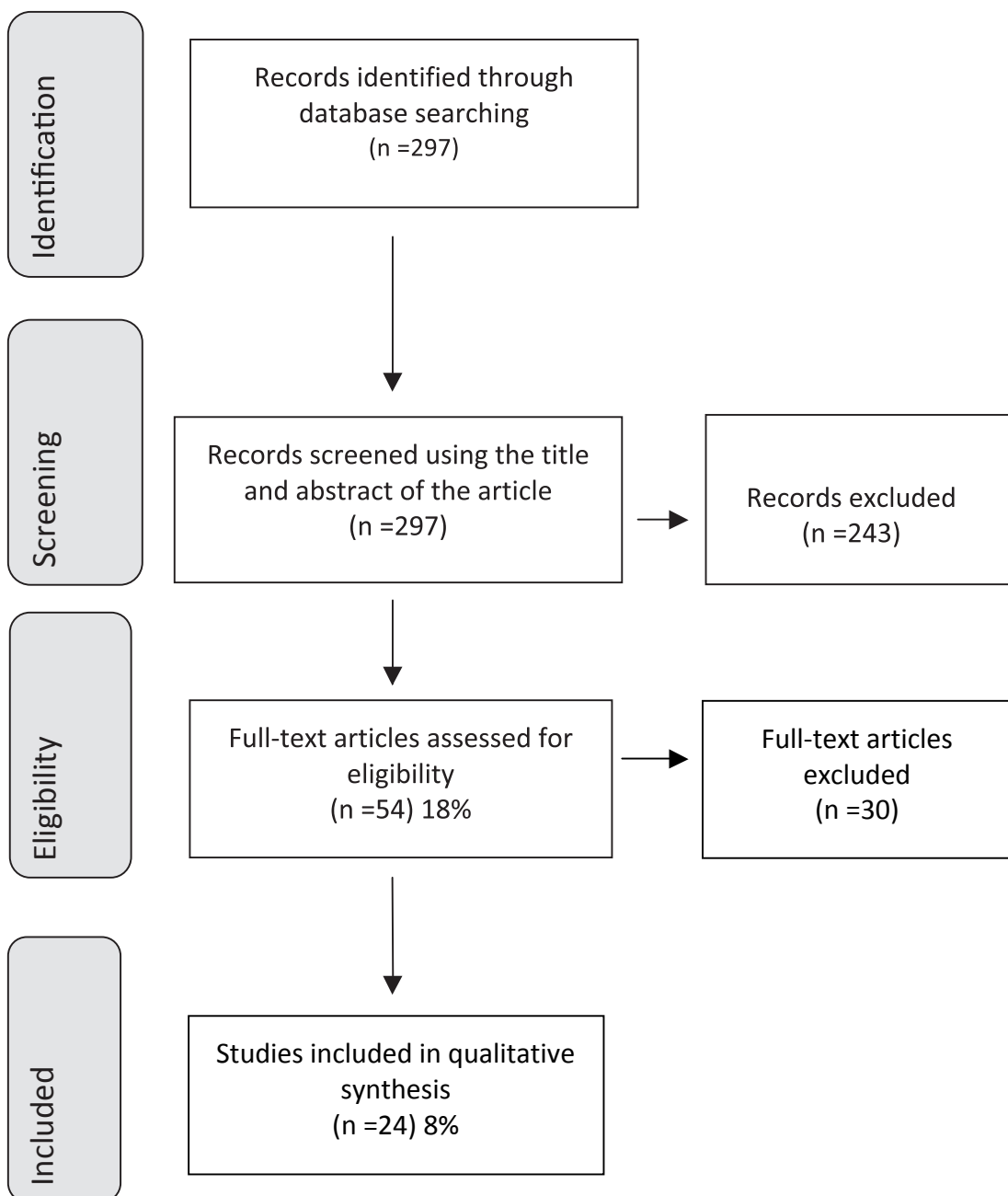| #	Searches	Results
1	exp *Health Services/	781688
2	exp *"Delivery of Health Care"/td [Trends]	15502
3	exp *Public Health/td [Trends]	14047
4	Epidemiology/td [Trends]	514
5	("health care" or "health service*" or "public health" or "health status").ti.	124393
6	or/1-5	892663
7	exp *Registries/	12360
8	exp *Databases, Factual/	19436
9	(register or registers or registry or registries or administrative).ti.	17879
10	or/7-9	42194
11	6 and 10	4048
12	(method* or trend* or develop* or chang* or histor* or theor* or occurence or inciden* or prevalence or increas* or decreas*).ti.	1528746
13	11 and 12	434
14	exp Europe/	997189
15	exp United States/	1012967
16	exp Canada/	107035
17	or/14-16	2057211
18	13 and 17	297

Figure 7. The flow diagram of article selection process

Appendix 2

Table 2. Review of the empirical studies examining changes in medical practice over time using register-based data; description of the study, methods used and main results.

Author(s), publication year, and title	Medical practice	Groups compared	Country and time period	Type of register	Method of analysis	Case mix correction	Results
Arvidsson, and Ericson (2005): The development of psychiatric care after the mental health care reform in Sweden. A case register study.	Psychiatric care, inpatient care and visits of outpatient facilities	Diagnostic groups (with and without schizophrenia)	Sweden 1994–2003	Case register of a county hospital, (Administrative register)	Descriptive statistics (numbers)	No	One of the targets in the mental health care reform has been deinstitutionalization. Inpatient care diminished among persons with a diagnosis of schizophrenia, simultaneously the use of group homes increased.
Chin et al. (2011): Trends and predictors of length of stay after primary percutaneous coronary intervention: a report from the CathPCI registry.	Percutaneous coronary intervention (PCI)	Time trends in length of stay in hospital care after first PCI	USA 2005–2009	CathPCI Registry voluntary participating sites (980) submit information from cases (115113 patients, 60% of initial population)	Descriptive statistics (proportions); temporal trends were tested, multivariable modelling	Adjusted by patient level variables (age, sex, race, BMI, insurance status, day of presentation, medication before, prior medical history, other clinical factors, and by hospital level variables (number of beds, location rural-urban, average annual PCI volume, etc.)	Length of stay determinates overall health care costs. Clinical characteristics were relatively similar, but length of stay in hospital after PPCI decreased, however, hospitals varied in discharging low-risk patients early. Mortality risk remained unchanged.
Fagring et al. (2010): Twenty-year trends in incidence and 1-year mortality in Swedish patients hospitalised with non-AMI chest pain.	Discharges for AMI, angina and unexplained chest pain and 1-year mortality	Men and women; time periods; age groups; diagnostic groups (angina, acute myocardial infarction, unexplained chest pain)	Sweden 1987–2006	National Hospital Discharge Register, Death register (Administrative registers)	Descriptive statistics (numbers); incidence and standardised mortality rates; temporal changes were tested by regression	Adjusted by age	The prognosis of patients with AMI improved and the length of stay in hospital decreased. These improvements took place simultaneously with the increase of hospitalisations for chest pain, use of troponin measurements to diagnose MI, and use of evidence-based medications and other procedures for the angina group.

Author(s), publication year, and title	Medical practice	Groups compared	Country and time period	Type of register	Method of analysis	Case mix correction	Results
Fonarow et al. (2007): Temporal trends in clinical characteristics, treatments, and outcomes for heart failure hospitalizations, 2002 to 2004: findings from Acute Decompensated Heart Failure National Registry (ADHERE).	Medication during heart failure hospitalizations	Yearly cohorts	USA 2002–2004	Benchmark registry, Acute Decompensated Heart Failure National Registry (ADHERE) covers 285 hospitals	Descriptive statistics (numbers, proportions); temporal changes were tested	No	Clinical characteristics among patients with hospitalisation due to heart failure were relatively similar, but inhospital morbidity and mortality improved simultaneously with changes in intravenous therapy, increase in evidence-based medications and enhancements in quality-of-care measures.
Gibson et al. (2008): Trends in reperfusion strategies, door-to-needle and door-to-balloon times, and in-hospital mortality among patients with ST-segment elevation myocardial infarction enrolled in the National Registry of Myocardial Infarction from 1990 to 2006.	Reperfusion therapy in myocardial infarction	Men and women; age groups; transfer and nontransfer patients	USA 1990–2006	National Registry of Myocardial Infarction (industry-sponsored)	Descriptive statistics (percentages); temporal changes were tested	No	MI patients' time to treatment shortened and in-hospital mortality diminished simultaneously.
Gualano et al. (2010): Temporal trends in the use of drug-eluting stents for approved and off-label indications: a longitudinal analysis of a large multicenter percutaneous coronary intervention registry.	Invasive treatment of coronary heart disease, especially by bare-metal stent (BMS) and drug-eluting stent (DES)	Patient groups (STEMI, PCI, vein graft intervention); type of stent or operation; subgroup analysis among patients with diabetes	USA 2006–2008	Regional register, the Blue Cross Blue Shield of Michigan Cardiovascular Consortium	Descriptive statistics (frequencies, means, medians); tabulated by sex, age, disease history, type of admission, region	No	This observational real-world study strengthened the evidence that patients treated with drug-eluting stent had increased risk of very late stent thrombosis (compared with patients treated with bare-metal stents). Temporal trend in drug-eluting stent decreasing.
Kaltiala-Heino et al. (2003): Inpatient treatment of mood disorders in the era of de-institutionalisation, depression awareness campaigns and development of new antidepressants.	Inpatient treatment for mood disorders	Yearly cohorts	Finland 1987–1995 (followed until 1997)	National Hospital Discharge Register (Administrative register)	Descriptive statistics (numbers; proportions); standardised numbers; comparison between groups were tested	No	Inpatient treatment of severe mood disorders increased in all kinds of health care institutions, in spite of de-institutionalisation policy.
Katalinic et al. (2009): Trends in hormone therapy and breast cancer incidence - results from the German Network of Cancer Registries.	Menopausal hormone therapy	Hormone therapy groups; time trends; age groups; regions	Germany 1997–2005	Population based survey based on cancer register (breast cancer) and health insurance register (hormone prescription)	Rates, tested by regression analyses	Age standardised	Menopausal hormone therapy increases the risk of female breast cancer. Results show a drop of hormone therapy prescription. There were geographical differences in the prescription of hormone therapy.

Author(s), publication year, and title	Medical practice	Groups compared	Country and time period	Type of register	Method of analysis	Case mix correction	Results
Katalinic et al. (2009): Trends in hormone therapy and breast cancer incidence - results from the German Network of Cancer Registries.	Menopausal hormone therapy	Hormone therapy groups; time trends; age groups; regions	Germany 1997–2005	Population based survey based on cancer register (breast cancer) and health insurance register (hormone prescription)	Rates, tested by regression analyses	Age standardised	Menopausal hormone therapy increases the risk of female breast cancer. Results show a drop of hormone therapy prescription. There were geographical differences in the prescription of hormone therapy.
Kourtis et al. (2007): Trends in hospitalizations of HIV-infected children and adolescents in the United States: analysis of data from the 1994-2003 Nationwide Inpatient Sample.	HIV-related hospitalizations and the average length of hospital stay	Boys and girls; age; diagnostic groups (with and without HIV-infection)	USA 1994–2003	The Nationwide Inpatient Sample database is an all-payer inpatient care database and covers ca 20% of all US community hospitals (nonfederal, short-term general and specialty hospitals whose facilities are open to the public)	Descriptive statistics (numbers), differences tested by regression	Adjusted by age and sex	After introducing antiretroviral therapy in 1997 hospitalizations among HIV-infected children decreased. Compared to children without HIV children with HIV had longer mean hospital stays.
Kuklina et al. (2011): Trends in pregnancy hospitalizations that included a stroke in the United States from 1994 to 2007: reasons for concern?	Hospitalizations due to stroke for women in the antenatal, delivery, and postpartum periods	Timing (antenatal, delivery, and postpartum); by type of stroke	USA 1994–2007	The Nationwide Inpatient Sample is a stratified sample of 20% of all US community hospitals of the HealthcareCost and Utilization Project	Weighted percent, on the basis of the sample estimated numbers, prevalence, rates, tested by regression	Adjusted by age; hospital region; insurance status; comorbidity (heart disease, hypertensive disorders, postpartum hemorrhange, postpartum infections)	Pregnancy-related hospitalizations with stroke increased, especially during the postpartum period. Concurrent hypertensive disorders and heart diseases explained almost all of the increase in postpartum hospitalizations with stroke.
Lay et al. (2007): Trends in psychiatric hospitalisation of people with schizophrenia: a register-based investigation over the last three decades.	Utilisation of inpatient psychiatric services	Men and women; age; time trends; diagnostic groups	Switzerland 1977–2004	A regional psychiatric register data of the Swiss canton Zurich a catchment area comprising about 1.2 million inhabitants	Number of inpatient admissions per year; the median length of individual inpatient episodes; patient-years in treatment; the treatment prevalence by year estimated by regression	Adjusted by age, sex, year, diagnosis	At the time of downsizing of psychiatric hospitals mental health service use among schizophrenia patients decreased, and length of stay shortened simultaneously. For other mental disorders the trend of inpatient treatment increased.

| Author(s), publication year, and title	Medical practice	Groups compared	Country and time period	Type of register	Method of analysis	Case mix correction	Results
Marques-Vidal et al. (2003): Trends in myocardial infarction treatment in subjects aged 35–64 in Southwestern France, 1986–93.	MI treatments during hospitalization	Men and women, different years	France 1986–1993	MONICA / part of WHO-MONICA Project (Monitoring of trends and determinants in Cardiovascular disease)	Descriptive statistics (numbers, percentages); ratios using regression	Adjusted by age, year, blood pressure, smoking status, and history of coronary heart disease	The prescription of the evidence based medication for MI increased: beta-blockers and antiplatelet drugs increased and calcium channel blockers decreased. However, a lower prescription of beta-blockers and angioplasty in women were observed. In men, angioplasty increased steadily.
Moist et al. (2008): Increased hemodialysis catheter use in Canada and associated mortality risk: data from the Canadian Organ Replacement Registry 2001–2004.	Hemodialysis (inhospital)	Type of hemodialysis	Canada 2001–2004	Canadian Organ Replacement Registry on hemodialysis	Descriptive statistics (numbers, percentages); ratios using regression	Access trends were adjusted by age, sex, race, BMI, smoking status, referral type, provinces of residence, cause of end-stage renal disease, and comorbidities	Patients initiating hemodialysis with a catheter have an increased risk for death compared with those using fistula or graft. Incident catheter use in hemodialysis increased, fistula use decreased, and graft use remained stable. Prevalence of catheter use increased, and fistulas and grafts decreased. Different geographical areas vary in incidence and prevalence in the use of catheters.
Peterson et al. (2008): Trends in quality of care for patients with acute myocardial infarction in the National Registry of Myocardial Infarction from 1990 to 2006.	Evidence based medicine and invasive treatment for acute myocardial infarction	Women and men; black and white; age groups; different years	USA 1990–2006	National Registry of Myocardial Infarction (NRMI) a voluntary program for hospitals	Descriptive statistics (numbers); weighted percentages; ratios using regression; time trend were tested	Adjusted for age, sex, race, payer, hospital characteristics, medical history (angina, coronary artery bypass graft surgery, family history of coronary artery disease, heart failure, diabetes, hyperlipidemia, hypertension, previous AMI, PCI, smoker, stroke), clinical presentation, and transfer-in status	The use of recommended therapies (medication, invasive procedures) increased in the treatment of AMI. Cardiac catheterization and percutaneous coronary intervention use increased, whereas coronary bypass surgery use diminished. Women, blacks, and patients ≥75 years old were less likely to receive revascularisation or being discharged with lipid-lowering therapy throughout the study period.

Author(s), publication year, and title	Medical practice	Groups compared	Country and time period	Type of register	Method of analysis	Case mix correction	Results
Pijl and Sytema (2003): The identification of trends in the utilisation of mental health services by elderly: a Dutch case register study.	Use of community- and hospital-based services (24-hour care) due to mental health problems	Type of service (community- vs. hospital-based services); age groups; different years	The Netherlands 1990–1999	A local psychiatric case register	Descriptive statistics (numbers, incidence and prevalence per 1000 population); decade changes (%); unit costs of mental health services	No/ tabulated by age groups	At the time of deinstitutionalisation dominant in mental health policy, mental health service use decreased, but the length of stay increased.
Priftis et al. (2007): Decrease in childhood asthma admissions in Athens, Greece from 2001 to 2005.	Asthma admissions	Different years; age groups	Greece 1978–2006	Hospital registers of the three main Children's hospitals of Athens, covering around 85% of paediatric beds in the region	Estimated admissions per 100000; readmissions/ admissions rates (%); time trends were assessed by regression and tested for trend	No/ divided by age group	Childhood asthma admissions decreased.
Rantalaiho et al. (2011): Trends in treatment strategies and the usage of different disease-modifying anti-rheumatic drugs in early rheumatoid arthritis in Finland. Results from a nationwide register in 2000–2007.	Treatment of early rheumatoid arthritis using disease-modifying anti-rheumatic drugs	Annual cohorts; various anti-rheumatic drug	Finland 2000–2007	National register of medicine re-imbursements (administrative, obligatory registers)	Descriptive statistics (numbers, percentages); comparisons between groups were analysed by analysis of variance	No	There was a change in treatment strategy in the use of disease-modifying anti-rheumatic drugs, and medicine use increased overall.
Ravera et al. (2010): Prevalence, cumulative incidence, monotherapy and combination therapy, and treatment duration of frequently prescribed psychoactive medications in the Netherlands: retrospective database analysis for the years 2000 to 2005.	Psychoactive drug prescriptions	men and women; different years; age groups;	The Netherlands 2000–2005	A regional database including information with pharmacy dispensing data from a population of ⊠500,000 people in the northern region of the Netherlands	Prevalence per 1000; cumulative incidence with CI 95%; survival curves for duration of prescriptions	No/ divided by age group	Psychoactive drug use was relatively stable, although there were some changes in specific drug categories (e.g., slight increase in the prevalence of antipsychotics and antidepressants and slight decrease of anxiolytics). The median treatment duration was longest with antipsychotics and shortest with anxiolytics.

Author(s), publication year, and title	Medical practice	Groups compared	Country and time period	Type of register	Method of analysis	Case mix correction	Results
Siponen et al. (2007): Increase in involuntary psychiatric treatment and child welfare placements in Finland 1996–2003. A nationwide register study.	Involuntary psychiatric inpatient treatment	Boys and girls; age groups; region	Finland 1996–2003	National Hospital discharge register and National child welfare register (administrative, obligatory registers)	Descriptive statistics (numbers, proportions); population standardised rates; comparison between groups tested; correlations tested using regression	No/ divided by hospital district	Both coercive institutionalisation of adolescents in psychiatric hospital and placement trough welfare services increased vastly. Trend not reported by age, sex or region.
Munk-Jorgensen et al. (1992): Trends in psychiatric hospitalization in Denmark: a 10-year register-based investigation.	Admissions to psychiatric hospitals and departments	Men and women; year; main diagnosis groups (schizophrenia, manic depressive psychoses, organic disorders, reactive conditions, other diagnoses); age; number of population of the area	Denmark 1977–1987	National Central psychiatric register includes information on admissions to psychiatric hospitals	direct age standardised rates; trend was analysed by regression	Adjusted by age	At the time of decreasing psychiatric beds in hospitals, admission rates for most psychiatric diagnosis groups decreased, and the decrease was most pronounced in the elderly. However in schizophrenia a trend of increasing admission rates was found.
Nguyen et al. (2010): Age and sex differences, and changing trends, in the use of evidence-based therapies in acute coronary syndromes: perspectives from a multinational registry.	Cardiac medication and procedure use	Men and women; age groups	North and South America, Europe, Australia and New Zealand 1999–2007	The Global Registry of Acute Coronary Events (GRACE) study	Descriptive statistics (numbers, percentages, medians); rates; differences between groups tested; regression models	Adjusted for age, sex, study period, additionally some models used hospital type, co-morbidities, and clinical characteristics	Increasing trend in evidence based medicine and cardiac procedures was reported over time. Utilisation was persistently lower among elderly patients and younger women.
Robertsson et al. (2000): Past incidence and future demand for knee arthroplasty in Sweden: a report from the Swedish Knee Arthroplasty Register regarding the effect of past and future population changes on the number of arthroplasties performed.	Primary knee arthroplasties	Men and women; time; age; diseases (osteoarthritis, rheumatoid arthritis; posttraumatic, osteonecrosis)	Sweden 1976–1997	National register of knee arthroplasty (the Swedish Knee Arthroplasty Register) and census	Descriptive statistics (numbers; percentages) mean of yearly incidence in the time period/ 100000 inhabitants; projected numbers of need of knee arthroplasties in the future	No/ tabulated by age, sex	During the study period osteoarthritis accounted for the largest increase in knee arthroplasties, operations for rheumatoid arthritis remained stable. Oldest age groups had the largest increase in operations.

| Author(s), publication year, and title	Medical practice	Groups compared	Country and time period	Type of register	Method of analysis	Case mix correction	Results
Ricci et al. (2009): Nationwide trends in hospitalization and surgical treatment of congenital and infantile cataract among Italian children 4 years and younger.	Hospitalization and operation of congenital or infantile cataracts	Boys and girls; age groups	Italy 1999–2004	Ministry of Health database on hospital admissions	Descriptive statistics (numbers, percentages); the mean number of admissions or operation per 10000 live births	Adjusted by age, sex	The trend of hospitalizations due to cataract operations remained fairly stable.
Zahn et al. (2000): Decreasing hospital mortality between 1994 and 1998 in patients with acute myocardial infarction treated with primary angioplasty but not in patients treated with intravenous thrombolysis. Results from the pooled data of the Maximal Individual Therapy in Acute Myocardial Infarction (MITRA) Registry and the Myocardial Infarction Registry	Primary angioplasty and thrombolysis for the treatment of acute myocardial infarction	Year; type of AMI treatment (primary angioplasty, intravenous thrombolysis)	Germany 1994–1998	AMI registries: the Maximal Individual Therapy in AMI (MITRA) study and the Myocardial Infarction Registry (MIR)	Descriptive statistics (numbers, percentages, medians) comparisons between groups and trends tested; Multiple logistic regression analysis used to examine adverse events after treatment.	Adjusted by age, sex, characteristics of infarction, previous MI, resuscitation, heart failure at admission, and the type of re-vascularization	The use of evidence based medication increased in both thrombolysis and angioplasty groups, however patients treated with angioplasty were more likely to receive ACE inhibitors. The trend of inhospital delay in AMI treatment decreased among patients treated with primary angioplasty. Hospital mortality and reinfarction rate decreased significantly for primary angioplasty, but were stable for thrombolysis. Results not reported by subgroups.

Appendix 3

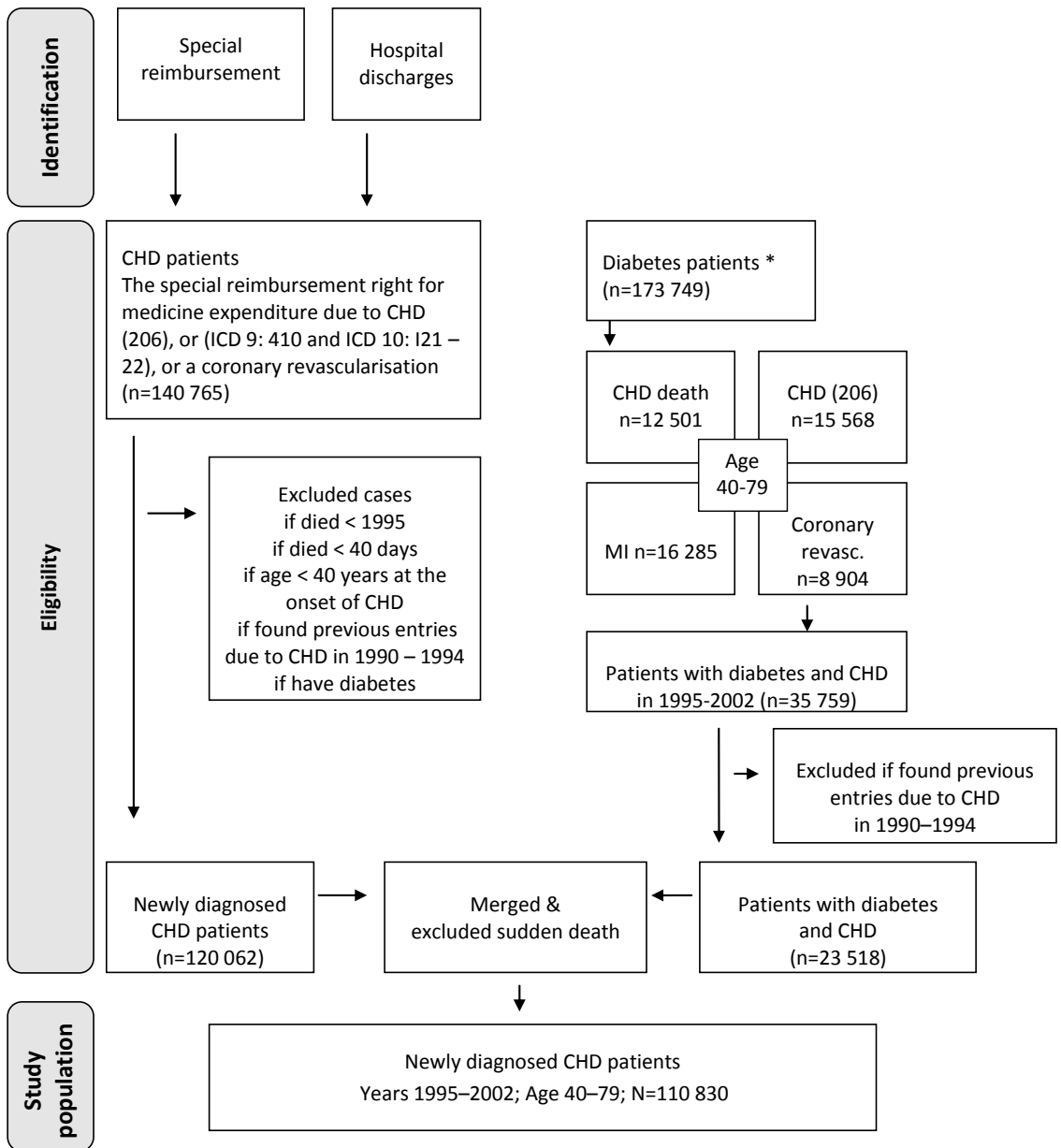**Figure 8.**   Flow diagram of formulation of data in sub-study (I)
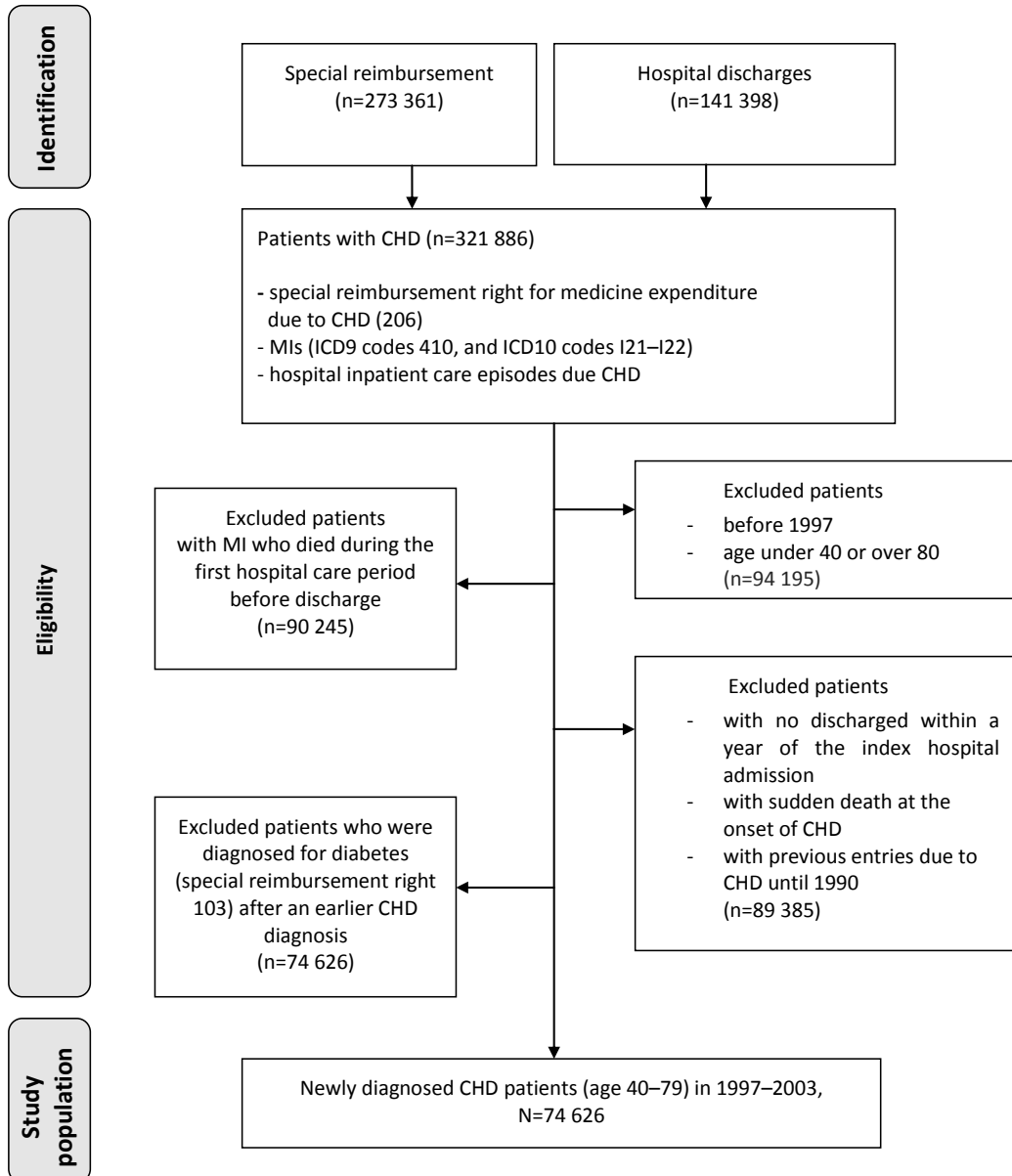
Figure 9. Flow diagram of formulation of data in sub-study (II)
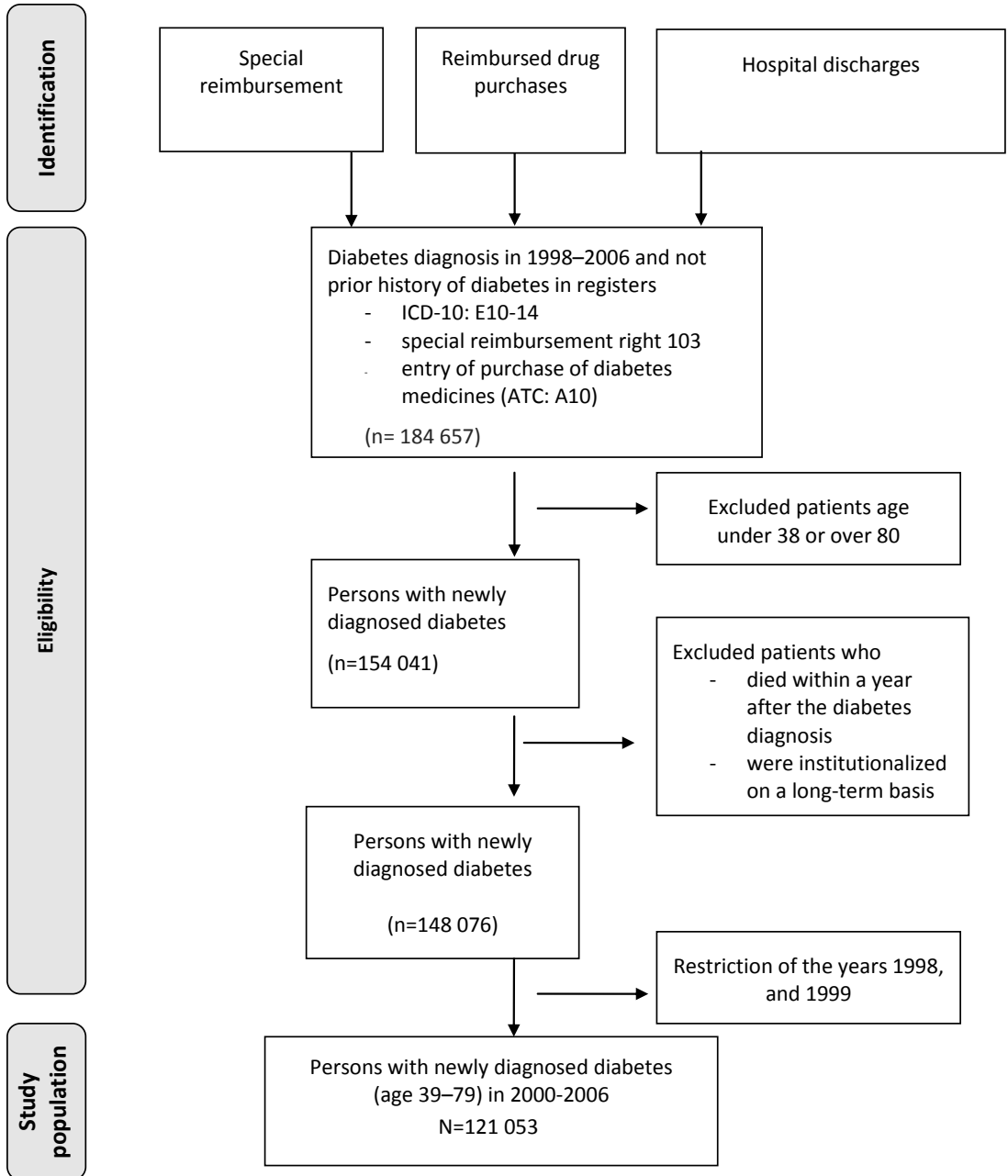
Monitoring the use of lipid-lowering medication among persons with newly diagnosed diabetes: a nationwide register-based study. doi:10.1136/bmjopen-2013-003414

**Figure 10.** Flow diagram of formulation of data in sub-study (III)


```
Identification

    ┌──────────────┐   ┌──────────────┐
    │   Special    │   │   Hospital   │
    │ reimbursement│   │  discharges  │
    └──────────────┘   └──────────────┘
```

CHD patients
The special reimbursement right for medicine expenditure due to CHD (206), or (ICD 9: 410 and ICD 10: I21 – 22), or a coronary revascularisation (n=140 765)

Diabetes patients *
(n=173 749)

CHD death
n=12 501

CHD (206)
n=15 568

Age 40-79

Excluded cases
if died < 1995
if died < 40 days
if age < 40 years at the onset of CHD
if found previous entries due to CHD in 1990 – 1994
if have diabetes

MI n=16 285

Coronary revasc.
n=8 904

Patients with diabetes and CHD in 1995-2002 (n=35 759)

Excluded if found previous entries due to CHD in 1990–1994

Newly diagnosed CHD patients
(n=120 062)

Merged & excluded sudden death

Patients with diabetes and CHD
(n=23 518)

Newly diagnosed CHD patients
Years 1995–2002; Age 40–79; N=110 830

Eligibility

Study population

Increasing resources effected equity in access to revascularizations for patients with diabetes.
doi : 10.3109/14017431.2010.494309
* Diabetes Suomessa Stakes/Raportteja 8/2005

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                                                                                        practices using register-based data

Figure 11.   Flow diagram of formulation of data in sub-study (IV)
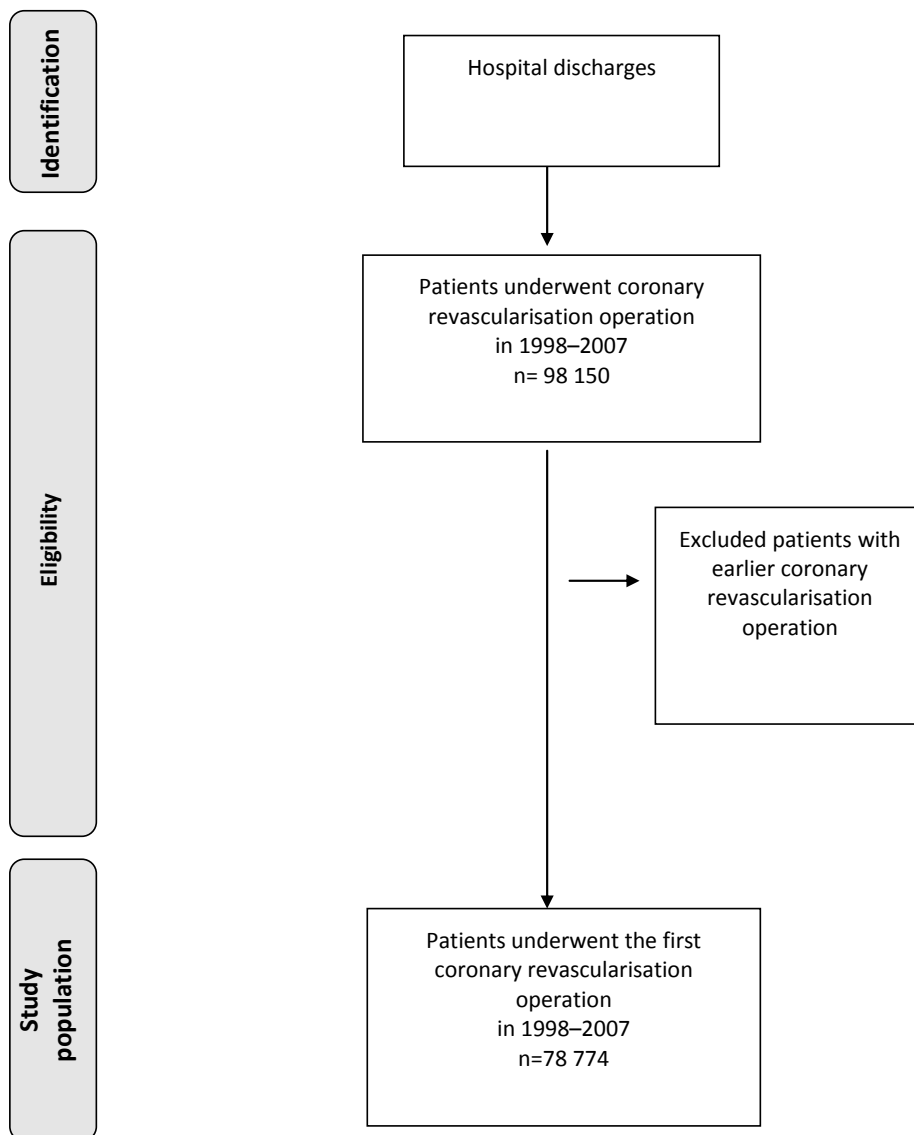
Pathways leading to coronary revascularisation among patients with diabetes in Finland: a longitudinal register-based study. doi:10.1186/1472-6963-11-180.

Appendix 4

Table 3.   Summary of datasets and patient populations

	Title	Setting	Population	Years	Outcomes	Analyses
I	Changing patterns of secondary preventive medication among newly diagnosed coronary heart disease patients with diabetes in Finland: a register-based study	Longitudinal observational study combining individual-level nationwide registers	Newly diagnosed CHD patients aged 40–79 years at the time of their diagnosis (N=74626, 42% women). Of these 43 501 men and 31 125 women, 12% and 13% were diagnosed with diabetes.	1997 - 2003	Medication to prevent adverse cardiovascular events using lipid-lowering medication, ß-blockers, ACE inhibitors, or angiotensin II antagonists.	1) Trends of cases per person-years on medication to prevent adverse cardiovascular events using lipid-lowering medication, ß-blockers, ACE inhibitors, or angiotensin II antagonists. 2) Risk ratios of medicine use in patients with diabetes versus those without diabetes in 1997–1998, 1999–2000 and 2001–2002. 3) Socioeconomic differences during the study period in medicine use.
II	Monitoring the use of lipid-lowering medication among persons with newly diagnosed diabetes: a nationwide register-based study	Longitudinal observational study combining individual-level nationwide registers	Newly diagnosed diabetes patients aged 30–79 years at the time of their diagnosis (N=121 053, 44% women), of which 4% were continuously insulin-treated and the majority were on oral antidiabetic medication. The time of onset of CHD was taken into account when dividing the diabetes population into groups.	2000 - 2006	Lipid-lowering medication after diabetes diagnosis Modelled lipid-lowering medication before diabetes diagnosis	1) The time trend in the use of lipid-lowering medication among persons with newly diagnosed diabetes between 2000–2006. 2) Socioeconomic differences during the study period in lipid-lowering medication. 3) Proportions of lipid-lowering medication use by history of CHD. 4) Describe the change in lipid-lowering medication at the time of diabetes diagnosis comparing medication after diabetes diagnosis to medication before the diagnosis.

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	Title	Setting	Population	Years	Outcomes	Analyses
III	Increasing resources effected equity in access to revascularizations for patients with diabetes	Longitudinal observational study combining individual-level nationwide registers	Newly diagnosed CHD patients aged 40–79 years at the time of their diagnosis: patients with diabetes prior to coronary heart disease were (n=13 591, 46% women), and patients with coronary heart disease without a prior diabetes diagnosis (n=97 239, 41% women) (N=110 830, 42% women)	1995 - 2002	The first coronary revascularisation by operation type CABG (Coronary Artery Bypass Graft Surgery) or PCI (Percutaneous Coronary Intervention)	1) Age-standardised rates per person-years of the first coronary revascularisation by operation type CABG or PCI and by income quintiles for CHD patients with or without diabetes in 1995–1996 and 2001–2002. 2) Hazard ratios comparing trends for first coronary revascularisation between CHD patients with or without diabetes. 3) Risk ratios for access to the first coronary revascularisation by operation type CABG or PCI, Cox's regression models adjusted for age, time–period, comorbidity and myocardial infarction in 1995–1996 and 2001–2002. 4) Hazard ratios for the first CABG or PCI comparing CHD patients with type 1 diabetes or type 2 diabetes to those CHD patients without diabetes, Cox's regression models adjusted for age, time–period, comorbidity and myocardial infarction in 1995–1996 and 2001–2002.
IV	Pathways leading to coronary revascularisation among patients with diabetes in Finland: a longitudinal register-based study	Observational study focusing on population who underwent their first coronary revascularisation - Longitudinal setting	All hospital admissions having CHD as the main diagnosis during two years preceding the first revascularisations among patients with diabetes (n=17 545, 34% for women), and among patients without diabetes (n=61 229, 27% for women) (N=78 774, 29% for women)	1998 - 2007	Pathways during the two years preceding the coronary revascularisation counting all hospital admissions having CHD as the main diagnosis. Pathways were categorised to either revascularisations performed at first treatment period or suboptimal treatment pathways to revascularisations, i.e. pathways containing several cardiac emergency hospitalisations.	1) Trends in the proportions of coronary revascularisation performed during first treatment period in CHD patients with insulin-dependent diabetes, non-insulin-dependent diabetes and without diabetes 2) Trends in the proportions of suboptimal treatment period in these patient groups 3) Odds ratios in coronary revascularisation performed during first treatment period, logistic regression models adjusted for age and comorbidity 4) Odds ratios in suboptimal treatment pathways, logistic regression models adjusted for age and comorbidity

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