



Pharmacoepidemiological study report ER-9451

Realization of the clinical practice guidelines for diabetes
in Finland – A case study of the usability of electronic
patient information systems and national registers to
support evidence based decision making in health care

Authors:	Pia Vattulainen, Jarmo Hahl, Tatu Miettinen
Study number:	ER-9451
Sponsor:	Pharma Industry Finland PIF (Lääketeollisuus ry)
Report version:	V1.0
Report date:	9 August 2017

Study information

Title	Realization of the clinical practice guidelines for diabetes in Finland – A case study of the usability of electronic patient information systems and national registers to support evidence based decision making in health care
Version identifier of the final study report	ER-9451
Date of last version of the final study report	9.8.2017
EU PAS register number	N/A
Active substance	ATC codes A10A* and A10B*
Medicinal product	Any antidiabetic medication
Product reference	N/A
Procedure number	N/A
Marketing authorization holder(s)	Several
Joint PASS	No
Research question and objectives	The overall objective of the study was to evaluate whether the electronic patient information systems and national registers can be used to support evidence based decision making in health care. The specific scientific objectives were to evaluate how the key elements of the Current Care guideline for diabetes (by the Finnish Medical Society Duodecim) are realized in practice and to investigate which factors explain successful implementation of treatment recommendations.
Country(-ies) of study	Finland
Author	Pia Vattulainen (pia.vattulainen@epidresearch.com) Jarmo Hahl (jarmo.hahl@medaffcon.fi) Tatu Miettinen (tatu.miettinen@medaffon.fi)
Sponsor Contact person	Pharma Industry Finland PIF (Lääketeollisuus ry) Nadia Tamminen (nadia.tamminen@laaketeollisuus.fi)

Table of Contents

1	Abstract.....	5
2	List of abbreviations.....	7
3	Approvals	8
4	Investigators and other responsible parties	9
5	Milestones.....	9
6	Rationale and background.....	10
7	Research question and objectives.....	11
8	Amendments and updates	11
9	Research methods	11
9.1	Study design	11
9.2	Setting	11
9.2.1	Data collection in two phases.....	12
9.2.2	Protection of human subjects.....	12
9.3	Subjects	12
9.4	Variables.....	13
9.4.1	Index date and baseline period	13
9.4.2	Outcomes.....	14
9.4.3	Other explanatory variables	15
9.5	Data sources and measurement	16
9.6	Study size	18
9.7	Data transformation.....	18
9.8	Statistical methods.....	18
9.9	Quality control	18
10	Results	19
10.1	Project timelines	19
10.2	Receipt of data from different data sources.....	20
10.3	Participants	20
10.4	Descriptive data	22
10.4.1	Availability of records and laboratory data	23
10.4.2	Baseline characteristics.....	23
10.4.3	Availability and quality of smoking, BMI, dietary habits and physical exercise records	25
10.4.4	Laboratory values at baseline	25
10.4.5	Concomitant medications at baseline	27
10.4.6	Comorbidities at baseline	28
10.5	Realization of the Current Care guideline: Diabetes medications and related measurements	30

10.5.1	Initiation of metformin as first drug after index date	30
10.5.2	Dietary advice and exercise consultation provided within 1 month after index date	30
10.5.3	Follow-up of HbA _{1c}	31
10.5.4	Treatment intensification	32
10.6	Realization of Current Care guideline: Frequency of follow-up measurements – HbA _{1c} and S-LDL.....	33
10.6.1	Frequency of follow-up of HbA _{1c}	33
10.6.2	HbA _{1c} on target	33
10.6.3	S-LDL on target.....	34
10.7	Realization of the Current Care guideline: Follow-up measurements every 12 to 15 months.....	36
10.7.1	At least one P/S-Crea measurement taken after index date.....	36
10.7.2	At least one U-Alb measurement taken after index date.....	38
10.7.3	At least one visit to dentist and to foot therapist after index date.....	40
10.8	Realization of the Current Care guideline: Follow-up measurements every 1-3 years.....	40
10.8.1	At least one P-ALAT measurement taken after index date	40
10.8.2	At least one S-LDL measurement taken after index date.....	42
10.8.3	At least one fundus photography taken within 12 to 15 months after index date	43
10.9	Realization of the Current Care guideline: Treatment decisions (other than diabetes treatment) based on follow-up measurements.....	45
10.9.1	Blood pressure over 140/90 mmHg.....	45
10.9.2	Renal insufficiency	46
10.9.3	Microalbuminuria	46
10.10	Other endpoints.....	47
10.10.1	Mortality during follow-up	47
10.10.2	Amputations of the lower extremities.....	48
10.10.3	Long absences from work.....	48
10.10.4	Severe hypoglycemic events.....	49
11	Summary	49
12	References.....	50
13	Appendices.....	50

1 Abstract

Rationale and background

Local and nationwide patient information systems and health care registers contain routinely saved patient information important for pharmacoepidemiologic research. Combination of both two source types would serve as a valuable resource in studies evaluating risks, benefits and costs. The aim of this study was to identify whether and how the electronic patient information systems and national registers can be used for research purposes in Finland. This aim was piloted in patients with type 2 diabetes, to assess how the Finnish Current Care guideline for diabetes is realized in practice.

Research question and objectives

The overall objective of the study was to evaluate whether and how the electronic patient information systems and national registers can be used to support evidence based decision making in health care.

The specific objectives were

- to identify the research permission processes for accessing patient level data from various data sources,
- to evaluate how the key elements of the Current Care guideline are realized in practice in type 2 diabetes,
- to evaluate the equality of data in local and nationwide medication registers, and
- to evaluate the cost and use of resources and to explore the costs of different outcomes in the implementation of recommendations.

Study design & setting

This was a retrospective database linkage study using patient information system data from selected primary and specialty health care organisations with linkage to nationwide registers.

Population

This study included patients with an incident type 2 diabetes during 2009-2012.

Data sources

- Patient information systems from the study sites
- Prescription register, Register for reimbursed medications and Sickness allowance register (SII)
- Hospital care register and Primary care register (National Institute for Health and Welfare)
- Causes of death registry (Statistics Finland)

Study size

The sites to be selected were to use patient information systems provided either by Tieto Oyj, CGI Oy (former Logica Oy) or Mediconsult Oy. Before the initiation of the study, the study population was estimated to cover a large proportion of type 2 diabetes patients, based on originally planned study sites that were (included but not limited to) primary and specialty health care organizations from Helsinki/Uusimaa, Hämeenlinna, Rauma, Oulu, Keski-Pohjanmaa, Pohjois-Pohjanmaa, Kainuu, Pohjois-Karjala, Sipoo, Hanko, Porvoo.

The final 4 study sites were hospital districts of Kainuu, Kanta-Häme and Pohjois-Karjala and Health services of Oulu city. Final study size was 11022 patients.

Results & Conclusions

Research process was slow, mainly due to long expectation times of data permits and data extraction, and part of the originally planned study sites had to be left out for economical or other reasons.

All the study questions could not be answered based on the data received. The SPAT codes for dietary advice or exercise consultation were available only from 2010, some of the endpoints of interest (e.g. fundus photography or visit to foot therapist) were not equally recorded in the study sites, or were not available at all.

Laboratory measurement were frequently recorded, although there were differences between sites. With diagnoses, drugs and laboratory records, several findings about realization of Current Care Guideline were done:

- According to Current Care Guideline, metformin is the recommended drug of choice in newly diagnosed diabetes patients. Metformin was the most common drug as first diabetes drug. Among all the study patients 9382 (85%) had prescription of an antidiabetic medication (A10A* or A10B*) during follow-up.
- Metformin was used as the first antidiabetic medication by 8375 patients representing 76% from the whole cohort.
- Metformin was started as the first line treatment in 89% from those who started an antidiabetic treatment.
- Other first line treatments were insulin (6.2%), dipeptidyl peptidase-4-inhibitors (2.5%) and sulphonylureas (1.3%).
- Within a year after index date over half of the newly diagnosed diabetes patients had follow-up for HbA_{1c} (71%), P/S-Crea (73%), S-LDL (61%) and P-ALAT (66%) but only 32% had U-Alb measurements.
- Half of the study population had at least one HbA_{1c} measurement within 3 months after the index date. The control rate of HbA_{1c} remained quite stable, over half of the patients had records also during the 2nd and 3rd year after index date.
- Treatment was intensified (i.e., a 2nd treatment was added to treatment regime) in 15.6% of patients during six months after elevated HbA_{1c} (>6.5%) level was observed.
- EGFR below 60 mL/min is contraindication for metformin use. Among the patients with low eGFR, metformin was prescribed for 44.1% during the first six months after such measurement.
- 29.6% of the patients whose blood pressure was higher than 140/90 mmHg were not prescribed ACE/ARB treatment at any time during the study follow-up.
- 80.6% of patients with albuminuria (cU-Alb or nU-Alb \geq 20 microg/min) were prescribed ACE/ARB treatment during the study.

2 List of abbreviations

ACE inhibitor	Angiotensin converting enzyme inhibitor
ARB	Angiotensin receptor blockers
ATC code	Anatomical therapeutic chemical classification system code
BMI	Body mass index
CAD	Coronary-artery disease
CNS	Central nervous system
COPD	Chronic obstructive pulmonary disease
ENCePP	European Network of Centres for Pharmacoepidemiology and Pharmacovigilance
eGFR	Estimated glomerular filtration rate
HD	Hospital district
HbA _{1c}	Glycohemoglobin
ICD-10	International classification of diseases, 10 th revision
ID	National identification number
ICPC-2	International Classification of Primary Care
ISPE	International Society for Pharmacoepidemiology
LDL	Low density lipoprotein
NCSP code	The Nordic Medico-Statistical Committee (NOMESCO) classification of surgical procedures code
P	Plasma
P-ALAT	P-alanine amino transferase
PASS	Post-authorization safety study
PAES	Post-authorization efficacy study
P/S	Plasma or serum
S	Serum
SF	Statistics Finland
SID	Study identification number
SII	Social Insurance Institution
SPAT	Finnish classification for procedures in primary care
TIA	Transient ischemic attack
THL	National Institute for Health and Welfare

3 Approvals

We have reviewed this pharmacoepidemiological study report (dated 9 August 2017) and approve it.

Principal investigator:



4.9.2017

Signature

Date

Pasi Korhonen, Ph.D., Adj. prof. biostatistics
EPID Research
Metsänneidonkuja 12
FI-02130 Espoo
Finland

Sponsor project lead/On behalf of the sponsor:



24.8.2017

Signature

Date

Nadia Tamminen, MSSc
Pharma industry Finland
Porkkalankatu 1
FI-00180 Helsinki
Finland

4 Investigators and other responsible parties

Study funding:	Pharma Industry Finland PIF Lääketeollisuus ry
Study conduct:	EPID Research Oy and AT Medical Affairs Consulting Oy
Principal investigator:	Pasi Korhonen (Ph.D., Adj. prof. biostatistics), EPID Research
Co-investigators:	Miika Linna (D.Sc., Adj. prof. health economics), University of Helsinki, Aalto University Tatu Miettinen (M.D.), Medaffcon Oy Jarmo Hahl (M.Sc. econ), Medaffcon Oy Fabian Hoti (Ph.D.), EPID Research Tuire Prami (née Tirkkonen) (Ph.D.), EPID Research Pia Vattulainen (M.Sc.), EPID Research
Project manager:	Anu Sulamaa (M.Sc.), , Crown CRO Oy Nadia Tamminen (MSc), Pharma Industry Finland PIF, successor to Anu Sulamaa
Steering committee:	Pasi Korhonen, Tatu Miettinen, Jarmo Hahl, Anu Sulamaa, prof. Jaakko Tuomilehto (University of Helsinki), Leo Niskanen (Helsinki University Hospital), Hannes Enlund (Fimea, retired during the project), Pertti Happonen (Fimea, successor to Enlund), Miika Linna (Aalto University, HEMA Institute), Jari Haukka (University of Helsinki), Raija Sipilä (Finnish Medical Society Duodecim), Elli Leppä (Pharmaceutical Information Centre), Nadia Tamminen (Pharma Industry Finland)
Study sites:	Hospital districts of Kainuu, Kanta-Häme and Pohjois-Karjala and Health services of Oulu city

5 Milestones

Milestone	Planned date	Actual date	Comments
Start of study permit process	04/2013	04/2013	
Approval of Ethical Review Board of HUS	None	05/2013	
End of study permit process	09/2013	05/2014	
Start of data collection (Data request sent, start of phase 1)	09/2013	05/2014	
Statistical analysis plan approved	None	07/2014	
End of data collection (Datasets available, end of phase 2)	11/2013	11/2015 02/2016 03/2016 02/2017	Statistics Finland (SF) Social Insurance Institution (SII) National Institute for Health and Welfare Regional data
Start of data analysis	11/2013	08/2016	
End of data analysis	04/2014	03/2017	
Start of study reporting process	02/2014	01/2017	

End of study reporting process	04/2014	08/2017	
Start of scientific reporting process	04/2014	06/2017	

6 Rationale and background

Diabetes is a chronic and progressive disease, that affects already more than 500 000 people in Finland (Diabetes, Current Care Summary, 2011). It is characterized by dysfunctions in insulin secretion and sensitivity, and by hyperglucagonemia resulting increased levels of blood sugar. Type 2 diabetes patients, and particularly those who are have uncontrolled diabetes, are at increased risk of vascular complications. These include both microvascular (diabetic nephropathy, retinopathy and neuropathy) and macrovascular (peripheral vascular disease, coronary heart disease and cerebrovascular) complications. It has been shown that intensive drug treatment policy decreases these complications when compared to less intensive treatment policy (UKPDS 33 and 34, 1998).

Life-style interventions were previously recommended as the first treatment choice in patients with new type 2 diabetes. However, as life-style interventions are difficult to put successfully into effect, the Current Care guideline for diabetes recommends that metformin should be initiated concomitantly with life-style interventions (Diabetes, Current Care Summary, 2011). The Current Care guideline also includes a clear algorithm of treatment choices after initiation of metformin treatment as well as detailed guidance for the holistic treatment of a type 2 diabetes patients.

It is not well established how the Current Care guideline is realized in practice and whether there are national variations in following this guideline. This study aims to investigate the realization of the guideline in practice by using different patient information sources.

Patient information systems and nationwide health care registers contain information on diagnoses, prescriptions, medical treatments and procedures, home care, first aid care, and laboratory measurements. This information is recorded on patient level during normal daily routines when treating patients in hospitals and health care centers or filling in prescriptions from pharmacies. The nation-wide health care registers are currently used in pharmacoepidemiologic research. The use of patient and laboratory information systems has been limited due to difficult and lengthy research permission processes when acquiring data from several different sites using various information systems. Combination of these two sources for research purposes would serve as a valuable resource for evaluation of risks, benefits and costs of various treatments and assessing how clinical practice guidelines are realized in practice in large populations. Such research would in turn support evidence based decision making in health care and potentially guide better use of resources.

There is an increasing need for the evaluation of medicines in real-life setting. Due to limited knowledge of the effects of new medical treatments after clinical trial experimentation the competent authorities may require further post-authorization safety and efficacy studies (PASS and PAES) or drug utilization studies from the marketing authorization holder. This may involve evaluation of the effect the treatment on a rare outcome (e.g. cancer) or in a special population (e.g. elderly or pregnant women) requiring access to reliable patient level information on treatments and outcomes in large populations.

The aim of this study was to identify whether and how the electronic patient information systems and national registers can be used for research purposes in Finland. This aim was piloted in patients with type 2 diabetes, a disease of great public health importance.

7 Research question and objectives

The overall objective of the study was to evaluate whether and how the electronic patient information systems and national registers can be used to support evidence based decision making in health care.

The primary objectives were

- to identify the research permission processes for accessing patient level data
 - from electronic patient information systems from different health care organizations and
 - from the nation-wide health care registers,
- to evaluate how the key elements of the Current Care guideline are realized in practice in type 2 diabetes mellitus patients (study cohort including only incident cases), and
- to evaluate the equality of data in local and nationwide medication registers.

The secondary objectives were

- to evaluate the cost and use of resources and to explore the costs of different outcomes in the implementation of recommendations, (Note: This aspect is to be addressed in a separate report or publication.)
- to compare different areas in Finland in relation to realization of the Current Care guideline for type 2 diabetes (study cohort including only incident cases), and
- to investigate which factors explain successful implementation of treatment recommendations.

8 Amendments and updates

None

9 Research methods

9.1 Study design

This was a retrospective database linkage study using patient information system data from selected primary and specialty health care organisations with linkage to nationwide registers.

9.2 Setting

Primary and specialty health care organisations with sufficient geographical coverage in Finland using different patient information systems were selected. Originally planned study site regions were Helsinki/Uusimaa, Hämeenlinna, Rauma, Oulu, Keski-Pohjanmaa, Pohjois-Pohjanmaa, Kainuu, Pohjois-Karjala, Sipoo, Hanko and Porvoo. Final study sites were Health services of the City of Oulu, and the Hospital districts (HD) of Kanta-Häme, Kainuu and Pohjois-Karjala. Patient information systems were provided either by Tieto Oyj (City of Oulu, Kanta-Häme HD and Kainuu HD) or Mediconsult Oy (Pohjois-Karjala).

9.2.1 Data collection in two phases

The study data was received in two phases. At first phase, study cohort was identified using reimbursed diabetes drugs and reimbursement decisions for diabetes from Social Insurance Institution (SII) and diagnoses, written prescriptions, laboratory measurements and nutrition counseling in electronic patient information systems within the selected study sites during 2007-2012. Patients, who had record referring to diabetes during 2009-2012, were selected to study cohort and the date of first record was set as index date. Patients with diabetes history within two years before index date (i.e. diagnoses and written prescriptions in local registries and reimbursed diabetes drugs and reimbursement decisions for diabetes), and patients who had only type 1 diabetes records (i.e. diagnoses in local registries or reimbursement decisions for only type 1 diabetes) were excluded from study cohort. List of selected cohort National identification numbers (IDs) were sent to Tieto Oyj, Mediconsult Oy, SII, National Institute for Health and Welfare and Statistics Finland (SF) for study data collection.

When all study data were received (i.e., after receiving the phase 2 study data), additional check for index dates was done using new study data with the same data sources than earlier (local registries: diagnoses, written prescriptions, laboratory measurements and nutrition counselling, SII registers: purchased prescriptions, reimbursement for diabetes). If phase 2 data provided events that would have been used as index events at first phase, they were set as index events. Two-year history for diagnoses, drugs and reimbursements were rechecked. SII data for place of domicile was used for excluding patients who were not living in study site area during the follow-up. Because most outcomes required records from local registries (e.g. laboratory measurements), only patients living in a singular study site were included in study. That removed also patients with abroad place of domicile before index.

9.2.2 Protection of human subjects

This was a fully register-based study and patients were not contacted in any phase of the study. Being a member of the study cohort did not affect the treatment of the patient.

National identification numbers

At first phase, all data was delivered with the National identification number (ID). Artificial study IDs (SIDs) were formed by MD5 one-way hashing algorithm. The lists including both IDs and SIDs were kept separately from the rest of the data and the personnel analysing the data was working with the data including SIDs only.

For the second phase data requests both IDs and SIDs were given to register holders but the results were asked to include SIDs only. This way patient level data could be linked while transferring the IDs as little as possible.

9.3 Subjects

Study population:

Inclusion criteria:

- The broad study population comprised all patients who had a diagnosis for diabetes (ICD-10 code E10*, E11*, E13* or E14*, or ICPC-2 code T89 or T90), a written prescription for diabetic medication (ATC code A10A* or A10B*), HbA_{1c} value $\geq 6.5\%$, glucose tolerance test ≥ 11 mmol/L or nutrition counselling related to diabetes in the electronic patient information systems within the selected study sites, or patients who had purchased prescriptions for diabetic medication (ATC code A10A* or A10B*) or who had special reimbursement for diabetes (refund code 103) in the Social Insurance Institution (SII) registers during 2009-2012.

For each patient the first date of such event mentioned above was called **index date**. The following exclusion criteria were used to identify patients with an **incident** (first time) diagnosis for **type 2 diabetes**.

Exclusion criteria:

- Patients with a diagnosis for diabetes (ICD-10 code E10*, E11*, E13* or E14*, or ICPC-2 code T89 or T90) or a written prescription for diabetic medication (ATC code A10A* or A10B*) in the electronic patient information systems **within two years prior to index date**.
- Patients with a purchased prescription for diabetic medication (ATC code A10A* or A10B*) in the prescription register of the SII within two years prior to index date.
- Patients with special reimbursement decisions for diabetes (reimbursement category no 103) in the reimbursement register of the SII within two years prior to index date.
- Patients with abroad place of domicile within two years prior to index date.
- Patients with place of domicile not including in the study site areas at the end of any of the study years.
- Patients carrying **only** diagnosis for type 1 diabetes (ICD-10 code E10* or ICPC-2 code T89) in the electronic patient information systems (without codes E11*, E13*, E14* or T90 = clear type 1 diabetes mellitus patients).
- Patients with special reimbursement decision 103 for diagnosis E10* (type 1 diabetes) **only** in the reimbursement register of the SII (without codes E11*, E13* or E14* = clear type 1 diabetes mellitus patients).

9.4 Variables

9.4.1 Index date and baseline period

Index date: The date of the first record referring to diabetes during 2009-2012 for each study subject. Records included written or purchased A10A* or A10B* drug or reimbursement decision 103, diabetes diagnose, record of elevated level of HbA_{1c} or glucose tolerance test or nutrition counseling related to diabetes. Nutrition counseling for diabetes was used only if patient had other record referring to diabetes on same date. Available records were the same that were used as index events; therefore, nutrition counseling was not used as independent index event.

Baseline period: Records for baseline were collected from year 2007, whenever possible. Because first possible index date was 1.1.2009, each patient had at least two years baseline time. Baseline period ended day before index date. Records for concomitant diseases in baseline were collected from all the data available before index date. Records for concomitant medications were collected from four months before index date. For laboratory values and blood pressure, the closest record during one year before index date was used. If such measurement was not available, the closest record within one month after index date was approved. For Body Mass Index (BMI) and smoking, the closest record before index date was used; if records before index date were not available, the closest record within one month after index date was approved. Figure 1 shows the timelines.

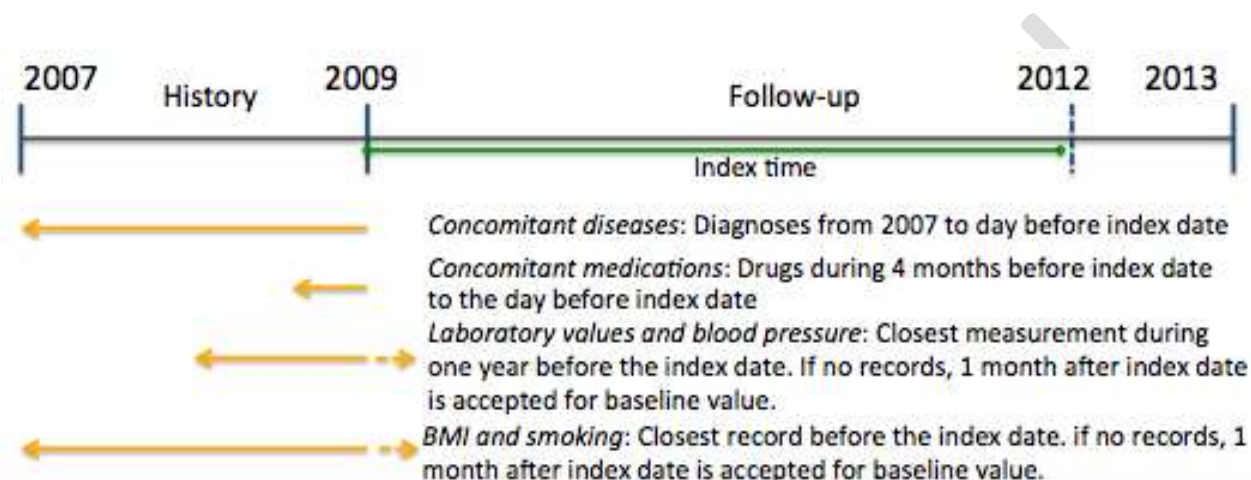


Figure 1 Timelines for baseline and study index time

9.4.2 Outcomes

Realization of the Current Care guideline: Diabetes medications and related measurements

- Initiation of metformin as 1st line treatment
- Dietary advice and exercise consultation provided
- Follow-up of HbA_{1c}
- Treatment intensification during follow-up by adding 2nd or 3rd line treatment

Realization of the Current Care guideline: Frequency of follow-up measurements –HbA_{1c} and S-LDL

- Frequency of follow-up of HbA_{1c}
- HbA_{1c} on target
- Follow-up of serum (S)-LDL
- S-LDL on target

Realization of the Current Care guideline: Follow-up measurements every 12 to 15 months

- At least one plasma/serum creatinine (P/S-Crea) measurement taken within 12 to 15 months after index date
- At least one urine albumine (U-Alb) measurement taken within 12 to 15 months after index date
- At least one visit to foot therapist or similar health care professional within 12/15/>15 month after index date
- At least one visit to dentist within 12 months after index date

Realization of the Current Care guideline: Follow-up measurements every 1-3 years

- At least one P-alanine amino transferase (P-ALAT) measurement taken within 12 to 36 months after index date
- At least one S-LDL measurement taken within 12 to 36 months after index date
- S-LDL on target
- At least one fundus photography taken within 36 months after index date

Realization of the Current Care guideline: Treatment decisions (other than diabetes treatment) based on follow-up measurements

- Blood pressure > 140/90 mmHg: Prescription of ACE inhibitor/ Angiotensin receptor blockers (ARB) filled within 1/3/6 months after
- Renal insufficiency: Prescription of metformin filled within 1/3/6/>6 month
- Microalbuminuria: Prescription of ACE inhibitor/ARB filled within 1/3/6/>6 months
- S-LDL >2.5 mmol/L or >1.8 mmol/L if prior diagnoses of coronary artery disease/stroke/ Transient ischemic attack (TIA)/peripheral arterial disease: prescription of statins filled within 1/3/6/>6 months

Other endpoints (without events for cost estimation)

- Mortality
- Amputations of lower extremities
- Absence from work
- Severe hypoglycemic events

9.4.3 Other explanatory variables

Other explanatory variables were to be fixed at baseline.

- Age at index (<50, 50-59, 60-69, 70-79, ≥80)
- Gender
- Smoking

- BMI
- Blood pressure (<130/80, not <130/80)
- HbA_{1c} value (<6.5, 6.5-6.9, 7-7.9, ≥8 %)
- S-LDL value (<1.8, 1.8-2.5, ≥2.5 mmol/L)
- P/S-Crea (<130, 130-150, ≥150 μmol/L)
- Concomitant medications at baseline (5 most common medication during baseline in study cohort by 3-digits ATC code)
 - Beta blocking agents (C07)
 - Agents acting on the renin-angiotensin system (C09)
 - Lipid modifying agents (C10)
 - Psycholeptics (N05)
 - Calcium channel blockers (C08)
- Concomitant diseases at baseline (6 most common diseases during baseline in study cohort among diseases listed in protocol)
 - Chronic hypertension
 - Coronary artery disease
 - Respiratory diseases (Asthma bronchiale, COPD, chronic bronchitis)
 - Atrial fibrillation
 - Dyslipidemia
 - Cancers (excl. in situ cancers)

9.5 Data sources and measurement

Data sources in 1st phase

National databases

SII

- Purchased prescriptions (ATC A10A* and A10B*)
- Decisions for diabetes reimbursements (code 103)

Local registries

- Written prescriptions (ATC A10A* and A10B*)
- Diabetes diagnoses (ICD-10 code E10*, E11*, E13* or E14*, or ICPC-2 code T89 or T90)

- Laboratory measurements (HbA_{1c} value \geq 6.5% and Glucose tolerance test \geq 11 mmol/L)

Data sources in 2nd phase

SII

- Purchased prescriptions
- Places of domicile
- Reimbursements for dental care
- Reimbursement decisions
- Rehabilitation decisions
- Sickness allowance register

National Institute for Health and Welfare

- Hospital care register (Diagnoses, Operations and other NCSP procedures)
- Primary care register (Diagnoses, operations and other procedures, dental care)
- Home care register

Causes of death registry

- Causes and dates of deaths

Local registries

- Written prescriptions
- Diagnoses
- Laboratory measurements
- Procedures
- SPAT codes (Finnish classification for procedures in primary care)
- Contacts
- Records (BMI, blood pressure, smoking)
- Visits
- Billing

9.6 Study size

The potential regions of study sites were (included, but not limited to) Helsinki, Espoo, Hämeenlinna, Rauma, Oulu, Keski-Pohjanmaa, Pohjois-Pohjanmaa, Kainuu, Itä-Savo, Joensuu, Sipoo, Hanko and Porvoo. The sites were to use patient information systems provided either by Tieto Oyj, CGI Oy (former Logica Oy) or Mediconsult Oy who jointly have over 95% of the market share in Finland. Thus, it was anticipated that a large proportion of type 2 diabetes patients from the selected sites were captured in the study population. The final 4 study sites were hospital districts of Kainuu, Kanta-Häme and Pohjois-Karjala and the Health services of the city of Oulu. The final study size was 11022 patients.

9.7 Data transformation

R language (<http://www.r-project.org>) was used in data management for creating the analysis database and in statistical analysis for creating tabulations and graphics as well as in all statistical modeling. R language is described more detailed in report "R: Regulatory Compliance and Validation Issues: A Guidance Document for the Use of R in Regulated Clinical Trial Environments" (<http://www.r-project.org/doc/R-FDA.pdf>).

Full audit trail starting from raw data obtained from register holders, and ending to statistical tables and graphs in reports has been maintained. Source code of data management and data analyses is kept for inspection for five years after publication of results. The study data may be inspected by the sponsor's independent representative(s), steering committee, or by the competent authorities.

9.8 Statistical methods

In all analyses, each patient was followed from index date until date of death or 31.12.2013 whichever happened first. Number of patients for each outcome was tabulated for each study site separately and for total study cohort. Most outcomes had several time periods to be analysed (e.g. from index date to 6 months after index, or 12 to 15 months after index date). For those outcomes number of patients were tabulated and percentages by study cohort were calculated for each time period.

Logistic regression analyses were performed for study outcomes. Because of the heterogeneity of data between sites and missing records they were not assumed to be valid for formal estimation, therefore they are not presented in this report.

Missing values

Missing values in laboratory measurements and other covariates were set as "Unknown".

Amendments to the statistical analysis plan

N/A

9.9 Quality control

The study was conducted as specified in the study protocol and in the statistical analysis plan. The study protocol was written by following the ENCePP Code of Conduct (ENCEPP 2016). The study protocol also followed the key elements of the Guideline for Good Pharmacoepidemiology Practices by International Society for Pharmacoepidemiology (ISPE 2007). EPID Research followed its internal quality requirements during the conduct of the statistical analyses and reporting of the study.

10 Results

10.1 Project timelines

The study protocol was approved in April 2013, after which data permit applications were sent to register holders and request for opinion to Ethics Committee. Data permit from SF and a favourable opinion of Ethics Committee were received within a month, from National Institute of Health and Welfare (THL) in 8 months, whereas SII permit was received after one year.

Right after obtaining the final approvals in May 2014, data requests were sent to register holders (SII, THL and local registries) for phase 1 data extraction. THL delivered the data in June 2014, local registries of the study sites in February 2015, and SII in October 2015. Study cohort was identified using the first phase data.

The second data requests with ID and SID lists of the selected patients of the cohort were sent for phase 2 data extraction in November 2015. Data extraction from SF, SII and THL was finalized by April 2016. From local databases data was received by May 2016, but the laboratory data had to be updated due to lack of records from early study years. Last laboratory update data was received in February 2017. Timelines are shown in Figure 2.

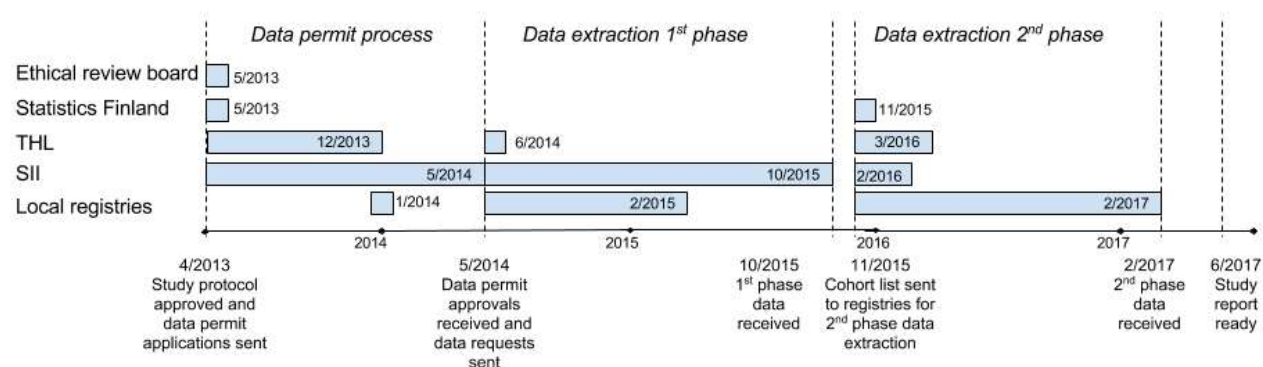


Figure 2 Data permit and process timelines

10.2 Receipt of data from different data sources

Study data was collected starting from the year 2007, when available. From hospital discharge register and SII registers data were available from 2007, whereas primary care register had records from the beginning of the year 2011. From local registries, diagnoses were available from 2007. In general, the availability of data was depending on study site. From Pohjois-Karjala HD all records except diagnoses were available only from the year 2009. See details for timelines in local registers Figure 3.

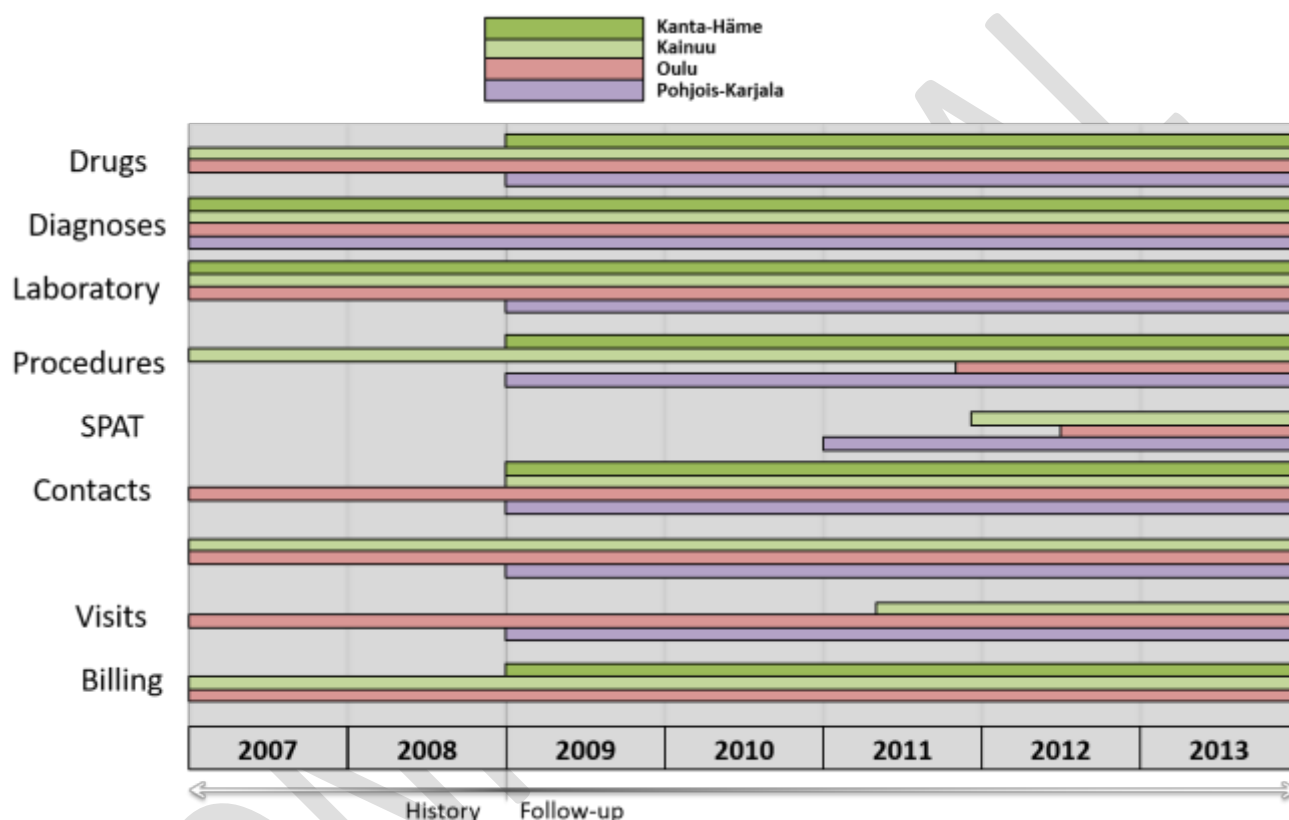


Figure 3 Local registries data timelines

10.3 Participants

Study data was collected in two phases. At first phase, patients with diabetes records during 2007-2012 were requested from local data holders, THL and SII. A total of 66937 patients were retrieved. The IDs were replaced with SIDs that were formed by MD5 one-way hashing algorithm. The algorithm produces always the same value from the inputted identification number, enabling records from different data sources to be combined later. Index dates and exclusion criteria were collected from each data and the date of first diabetes record during 2009-2012 was set as final index date.

After exclusions (not records during 2009-2012, having only type 1 diabetes diagnoses, history of diabetes records within two years before index date) the cohort size was 15771 patients. List of SIDs and IDs of selected study cohort were sent to data holders for study data collection. The data was delivered with SIDs only.

After receiving the second phase study data, the index dates were rechecked using the local registries and SII records. If phase 2 data provided events that would have been used as index events at first phase, they were set as index events. Also, the 2-years history before index concerning diabetes diagnoses, written prescriptions in local registries, reimbursed diabetes drugs and special reimbursement decisions in SII record were rechecked. After this checking 15011 patients remained in the cohort.

Final study sites were HDs of Kainuu, Kanta-Häme and Pohjois-Karjala and Health services of Oulu city. Because most outcomes require records from local registries (e.g. laboratory measurements), only patients with a singular study site were included in study. That removed also patients with abroad place of domicile before index. After the patients not-alive-at-index were excluded, total cohort size was 11022 individuals. Population flowchart and study sites map is presented in Figure 4.

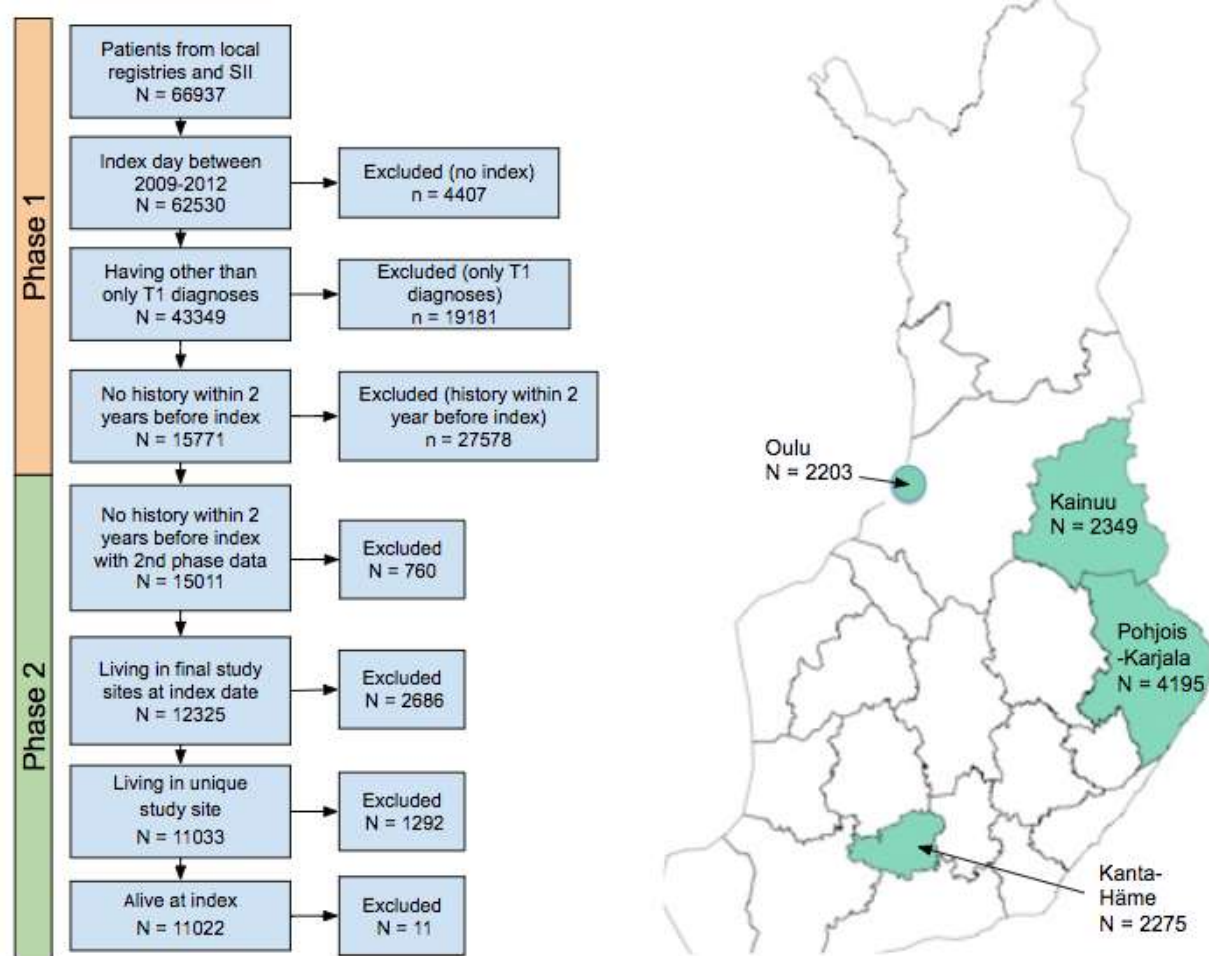


Figure 4 Population flowchart and study sites map

Index events at index dates

All the events at index date were listed (Table 1). Most common index events were associated with drugs (e.g., purchased diabetes drug, “SII drug” 3708 (33.6%) and written prescription “Local drug” 1636 (14.8%). Among study cohort 3123 (28.3%) had diabetes diagnose as index event. For laboratory measurements, elevated level of HbA_{1c} (glycohemoglobin) was much more common index event 3028 (27.5%) than glucose tolerance test 737 (6.7%) which was usually recorded as ‘done’ instead of value, when checking the variable from second phase data.

Nutrition counselling was defined as SPAT1139 (nutrition survey) or SPAT1306 (nutrition and weight control counselling) and to ensure that it is related to diabetes, other record of diabetes was required from the same date. Because it was not used as independent inclusion criteria, and because SPAT records were collected only late study years, the criterion was rare index event: 81 (0.7%) patients.

Table 1 Events at index date

	Kainuu patients N = 2349	Kanta-Häme patients N = 2254	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
SII drug	665 (28.31%)	1274 (56.00%)	559 (25.37%)	1210 (28.84%)	3708 (33.64%)
Diagnose	580 (24.69%)	183 (8.04%)	593 (26.92%)	1767 (42.12%)	3123 (28.33%)
Glyco- hemoglobin	1010 (43.00%)	552 (24.26%)	500 (22.70%)	966 (23.03%)	3028 (27.47%)
Local drug	408 (17.37%)	17 (0.75%)	317 (14.39%)	894 (21.31%)	1636 (14.84%)
Glucose tolerance	10 (0.43%)	237 (10.42%)	39 (1.70%)	100 (2.38%)	737 (6.69%)
Reimb. 103	16 (0.68%)	101 (4.44%)	55 (2.50%)	15 (0.36%)	187 (1.70%)
Counselling	32 (1.36%)	0 (0.00%)	27 (1.23%)	22 (0.52%)	81 (0.73%)
Sum of patients	2721 (115.84%)	2364 (103.91%)	2441 (110.80%)	4974 (118.57%)	12500 (113.41%)

10.4 Descriptive data

All ICD-10 and ICPC2 diagnoses, SPAT codes, laboratory measurements etc. are listed in Appendix 2, except the ATC codes and diagnoses of comorbidities at baseline that are listed in study protocol (ENCePP e-register of studies: <http://www.encepp.eu/encepp/viewResource.htm?id=14809>).

An assessment of the quality of the different data was not formally performed nor an assessment of the equality of data in local and nationwide medication registers. Instead an assessment of the availability of each type of data was assessed.

10.4.1 Availability of records and laboratory data

The availability of the laboratory and other records data is presented in Table 2. Timelines for baseline period data collection are shown in Figure 1. All requested data except information about dietary and exercise habits were received, but records for some of the baseline characteristics (e.g. amount of smoking and foot therapist visits) were very few. Dietary advice and exercise consultation were followed using SPAT codes; those were not recorded before 2011.

Table 2 Availability of study data

	Baseline	Follow-up
BMI	3560 (32,3%)	Not followed
Smoking	1582 (14,4%)	Not followed
Amount of smoking	58 (0,5%)	Not followed
Dietary or exercise habits	No records	Not followed
Blood pressure	3933 (35,7%)	Not followed
HbA1c	6953 (63,1%)	9215 (83.6%)
P/S-Crea	7745 (70,3%)	9758 (88.5%)
S-LDL	6747 (61,2%)	8859 (80.4%)
U-Alb	Not followed	6505 (59.0%)
P-ALAT	Not followed	9069 (82.3%)
Dietary advice	Not followed	494 (4.5%)
Exercise consultation	Not followed	190 (1.7%)
Dental visits	Not followed	6158 (55.9%)
Foot therapist visit	Not followed	113 (1.0%)
Fundus photography	Not followed	2031 (18.4%)
Total	11022 (100%)	11022 (100%)

Source: Appendix 1; Tables 2.1, 2.2 and 9.1

10.4.2 Baseline characteristics

Age at index, gender, information about smoking and BMI was collected for baseline information. Number of patients are shown in Table 3 (Appendix 1; Table 2.1).

Mean age of the patients was 63 ± 12.8 years. 14.3% of patients were younger than 50 years, and 31.7% of patients were older than 70 years. There was a minor gender difference, as 52.3% of the patients were male. Overall, BMI data was available in 32.3% of patients. Majority (55.3%) of these patients were obese (BMI >30) and 8.6% extremely obese (BMI >40). Respectively, only 11.6 % were not overweight (BMI<25).

Table 3. Baseline characteristics

	Kainuu patients N=2349	Kanta-Häme patients N=2275	Oulu patients N=2203	Pohjois-Karjala patients N=4195	Total N=11022
Age* at index (years)					
<50	297 (12.64%)	378 (16.62%)	377 (17.11%)	526 (12.54%)	1578 (14.32%)
50-59	556 (23.67%)	594 (26.11%)	512 (23.24%)	1004 (23.93%)	2666 (24.19%)
60-69	699 (29.76%)	692 (30.42%)	639 (29.01%)	1259 (30.01%)	3289 (29.84%)
70-79	566 (24.10%)	453 (19.91%)	459 (20.84%)	940 (22.41%)	2418 (21.94%)
80 and over	231 (9.83%)	158 (6.95%)	216 (9.80%)	466 (11.11%)	1071 (9.72%)
range (min,max)	(0.93, 98.55)	(4.12, 100.68)	(6.78, 94.67)	(6.18, 98.25)	(0.93, 100.68)
mean (+/-sd)	63.96 (12.48)	61.87 (12.65)	62.67 (13.36)	64.14 (12.59)	63.34 (12.77)
median (Q1,Q3)	64.06 (56.14, 73.24)	62.11 (53.70, 70.67)	62.95 (53.71, 72.32)	64.10 (55.92, 73.31)	63.50 (55.05, 72.59)
Sex					
Male	1262 (53.72%)	1211 (53.23%)	1094 (49.66%)	2195 (52.32%)	5762 (52.28%)
Female	1087 (46.28%)	1064 (46.77%)	1109 (50.34%)	2000 (47.68%)	5260 (47.72%)
Smoking					
Yes	23 (0.98%)	2 (0.09%)	18 (0.82%)	487 (11.61%)	530 (4.81%)
No	25 (1.06%)	0 (0.00%)	0 (0.00%)	1027 (24.48%)	1052 (9.54%)
No records	2301 (97.96%)	2273 (99.91%)	2185 (99.18%)	2681 (63.91%)	9440 (85.65%)
Previous smoking					
Info available	5 (0.21%)	0 (0.00%)	0 (0.00%)	11 (0.26%)	16 (0.15%)
No records	2344 (99.79%)	2275 (100.00%)	2203 (100.00%)	4184 (99.74%)	11006 (99.85%)
Amount of smoking					
10-20/day	7 (0.30%)	0 (0.00%)	0 (0.00%)	8 (0.19%)	15 (0.14%)
Below 10/day	8 (0.34%)	0 (0.00%)	0 (0.00%)	2 (0.05%)	10 (0.09%)
Above 20/day	5 (0.21%)	0 (0.00%)	0 (0.00%)	2 (0.05%)	7 (0.06%)
No smoking	25 (1.06%)	0 (0.00%)	0 (0.00%)	1 (0.02%)	26 (0.24%)
No records	2304 (98.08%)	2275 (100.00%)	2203 (100.00%)	4182 (99.69%)	10964 (99.47%)
BMI					
<25	52 (2.21%)	0 (0.00%)	106 (4.81%)	256 (6.10%)	414 (3.76%)
25-29.9	188 (8.00%)	0 (0.00%)	307 (13.94%)	682 (16.26%)	1177 (10.68%)
30-34.9	189 (8.05%)	0 (0.00%)	294 (13.35%)	674 (16.07%)	1157 (10.50%)
35-39.9	82 (3.49%)	0 (0.00%)	145 (6.58%)	279 (6.65%)	506 (4.59%)
≥ 40	51 (2.17%)	0 (0.00%)	75 (3.40%)	180 (4.29%)	306 (2.78%)
Unknown	1787 (76.07%)	2275 (100.00%)	1276 (57.92%)	2124 (50.63%)	7462 (67.70%)

Source: Appendix 1; Table 2.1

Note: Age was not used as exclusion criterion. Registers may have incorrect records of type 2 diabetes.

10.4.3 Availability and quality of smoking, BMI, dietary habits and physical exercise records

All registers with ICD-10 codes were used to find ICD-10 diagnosis for smoking. Primary care register was searched for ICPC2 code for smoking. In addition to ICD-10 or ICPC2-diagnoses, primary care register, Kainuu HD and Pohjois-Karjala HD had classified records for smoking status. Kainuu HD and Pohjois-Karjala HD had also text fields containing smoking information. Text mining was used to find the information about smoking, amount of smoking and previous smoking. For previous smoking only availability of information was searched.

BMI records were available from Kainuu HD, Health Services of Oulu city and Pohjois-Karjala HD. Pohjois-Karjala and primary care register had records of height and weight and BMI was counted from those. Very high and very low BMI records were checked, and if assumed erroneous, the records were excluded. If a patient had several BMI records and his/her BMI value had increased or decreased more than 10 units in a considerably short time period, the record was checked for errors. Information about dietary habits or physical exercise was not found.

10.4.4 Laboratory values at baseline

Laboratory values at baseline are shown per study site in Table 4 (Appendix 1; Table 2.2).

Table 4 Laboratory and blood pressure measurements at baseline

	Kainuu patients N=2349	Kanta-Häme patients N=2275	Oulu patients N=2203	Pohjois-Karjala patients N=4195	Total N=11022
HbA1c (%)					
<6.5	1123 (47.81%)	658 (28.92%)	767 (34.82%)	1501 (35.78%)	4049 (36.74%)
6.5-6.9	475 (20.22%)	188 (8.26%)	311 (14.12%)	445 (10.61%)	1419 (12.87%)
7.0-7.9	195 (8.30%)	92 (4.04%)	137 (6.22%)	193 (4.60%)	617 (5.60%)
≥ 8	242 (10.30%)	206 (9.05%)	133 (6.04%)	287 (6.84%)	868 (7.88%)
Unknown	314 (13.37%)	1131 (49.71%)	855 (38.81%)	1769 (42.17%)	4069 (36.92%)
P/S Crea (umol/L)					
<130	2006 (85.40%)	1381 (60.70%)	1553 (70.49%)	2627 (62.62%)	7567 (68.65%)
130-150	17 (0.72%)	19 (0.84%)	19 (0.86%)	33 (0.79%)	88 (0.80%)
≥ 150	18 (0.77%)	22 (0.97%)	16 (0.73%)	34 (0.81%)	90 (0.82%)
Unknown	308 (13.11%)	853 (37.49%)	615 (27.92%)	1501 (35.78%)	3277 (29.73%)
GFR (mL/min)					
<60	206 (8.77%)	177 (7.78%)	183 (8.31%)	338 (8.06%)	904 (8.20%)
≥ 60	1835 (78.12%)	1245 (54.73%)	1405 (63.78%)	2356 (56.16%)	6841 (62.07%)
Unknown	308 (13.11%)	853 (37.49%)	615 (27.92%)	1501 (35.78%)	3277 (29.73%)
S-LDL (mmol/L) <2.5					
Yes	348 (17.96%)	308 (15.19%)	252 (13.80%)	434 (12.94%)	1342 (14.67%)
No	1220 (62.95%)	677 (33.38%)	895 (49.01%)	1389 (41.40%)	4181 (45.71%)
Unknown	370 (19.09%)	1043 (51.43%)	679 (37.19%)	1532 (45.66%)	3624 (39.62%)
Total*	1938 (100.00%)	2028 (100.00%)	1826 (100.00%)	3355 (100.00%)	9147 (100.00%)
S-LDL (mmol/L) <1.8					
Yes	45 (10.95%)	27 (10.93%)	34 (9.02%)	57 (6.79%)	163 (8.69%)
No	299 (72.75%)	100 (40.49%)	268 (71.09%)	394 (46.90%)	1061 (56.59%)
Unknown	67 (16.30%)	120 (48.58%)	75 (19.89%)	389 (46.31%)	651 (34.72%)
Total**	411 (100.00%)	247 (100.00%)	377 (100.00%)	840 (100.00%)	1875 (100.00%)
Blood pressure (mmHg)					
<130/80	102 (4.34%)	0 (0.00%)	121 (5.49%)	243 (5.79%)	466 (4.23%)
not <130/80	690 (29.37%)	1 (0.04%)	892 (40.49%)	1884 (44.91%)	3467 (31.46%)
Unknown	1557 (66.28%)	2274 (99.96%)	1190 (54.02%)	2068 (49.30%)	7089 (64.32%)

Source: Appendix 1; Table 2.2

The baseline HbA1c data was recorded in 63.1% of all study patients. The HbA1c data availability was highest in Kainuu HD (86.6%) and lowest in Kanta-Häme HD (50.3%). Overall, 58.2% of the patients whose data were available, had their HbA1c below 6.5% at the index date, 21.4% of patients had their HbA1c over 7% and 12.5%

of patients over 8% at the index date. In regards to patient proportions in different HbA1c-value classes at index date, the data in various HDs was quite similar.

P/S-Crea values were available at baseline in 70.3 % of patients, and of those, the eGFR was lower than 60 mL/min in 11.7% of patients.

The S-LDL values at baseline were studied separately in those patients whose target level was <1.8 mmol/L (with prior diagnosis of coronary artery disease, stroke, TIA or peripheral circulatory complication at baseline in the database, 17.0% of patients), and whose target level was <2.5 mmol/L (without prior diagnosis of coronary artery disease, stroke, TIA or peripheral circulatory complication at baseline in the database, 83.0% of patients). The baseline S-LDL values were available in 65.3% of patients in the target group '<1.8 mmol/L' and only 13.3% of those were in the target. In the target group '<2.5 mmol/L', baseline S-LDL values were available in 60.4% of patients and 24.3% of those had their values below the target.

Blood pressure was recorded electronically in approximately half of the patients in study sites of Oulu and Pohjois-Karjala, in one third of patients in Kainuu HD and not at all in Kanta-Häme HD. At the time the data was collected, the target levels in guidelines were below 130/80 and only 12% of patients (with values recorded) had their values below the target levels.

10.4.5 Concomitant medications at baseline

Most common ATC codes (3 digit level) within 4 months before index date are listed in Table 5 (Appendix 1; Table 2.3).

Table 5 List of the most common concomitant medications at baseline

	Kainuu patients N=2349	Kanta-Häme patients N=2275	Oulu patients N=2203	Pohjois-Karjala patients N=4195	Total N=11022
Concomitant medication					
Beta blocking agents	1020 (43.42%)	879 (38.64%)	905 (41.08%)	1927 (45.94%)	4731 (42.92%)
Agents acting on the renin-angiotensin system	882 (37.55%)	976 (42.90%)	969 (43.99%)	1882 (44.86%)	4709 (42.72%)
Lipid modifying drugs	902 (38.40%)	785 (34.51%)	869 (39.45%)	1634 (38.95%)	4190 (38.01%)
Psycholeptics	474 (20.18%)	363 (15.96%)	619 (28.10%)	879 (20.95%)	2335 (21.18%)
Antiinflammatory and antirheumatic products	473 (20.14%)	382 (16.79%)	513 (23.29%)	859 (20.48%)	2227 (20.21%)
Calcium channel blockers	495 (21.07%)	426 (18.73%)	449 (20.38%)	842 (20.07%)	2212 (20.07%)
Antibacterials for systemic use	395 (16.82%)	416 (18.29%)	515 (23.38%)	824 (19.64%)	2150 (19.51%)
Analgesics	468 (19.92%)	305 (13.41%)	525 (23.83%)	837 (19.95%)	2135 (19.37%)
Diuretics	404 (17.20%)	370 (16.26%)	416 (18.88%)	738 (17.59%)	1928 (17.49%)
Drugs for acid related disorders	451 (19.20%)	361 (15.87%)	402 (18.25%)	621 (14.80%)	1835 (16.65%)
Psychoanaleptics	324 (13.79%)	287 (12.62%)	411 (18.66%)	592 (14.11%)	1614 (14.64%)
Cardiac therapy	386 (16.43%)	241 (10.59%)	319 (14.48%)	592 (14.11%)	1538 (13.95%)
Antithrombotic agents	284 (12.09%)	220 (9.67%)	314 (14.25%)	703 (16.76%)	1521 (13.80%)
Drugs for obstructive airway diseases	308 (13.11%)	236 (10.37%)	328 (14.89%)	542 (12.92%)	1414 (12.83%)

Source: Appendix 1; Table 2.3

Beta blocking agents (42.9%), renin-angiotensin system agents (42.7%), and lipid modifying drugs (38.0%) were the most frequently used medications at baseline. It seems that beta blockers are used often in the treatment of hypertension, because the prevalence of coronary artery disease (CAD) (16.9%) does not explain the substantial overall use of beta blockers.

Interestingly, psycholeptics were used by 21.2% of patients (and psychoanaleptics in 14.6%), although depression, which was the most frequent central nervous system (CNS) diagnosis, was coded in 4.7% of patients only.

10.4.6 Comorbidities at baseline

Concomitant diseases at baseline are presented in Table 6 (Appendix 1; Table 2.4).

For further detail regarding the operational codes of these variables, refer to the study protocol (ENCePP E< register of studies: <http://www.encepp.eu/encepp/viewResource.htm?id=14809>).

Table 6 List of the most common concomitant diseases at baseline

	Kainuu patients N=2349	Kanta-Häme patients N=2275	Oulu patients N=2203	Pohjois-Karjala patients N=4195	Total N=11022
Comorbidities					
Chronic hypertension	673 (28.65%)	576 (25.32%)	762 (34.59%)	1785 (42.55%)	3796 (34.44%)
Coronary artery disease	426 (18.14%)	261 (11.47%)	386 (17.52%)	785 (18.71%)	1858 (16.86%)
COPD, asthma, chronic bronchitis	247 (10.52%)	158 (6.95%)	242 (10.99%)	522 (12.44%)	1169 (10.61%)
Atrial fibrillation	141 (6.00%)	179 (7.87%)	165 (7.49%)	453 (10.80%)	938 (8.51%)
Dyslipidemia	110 (4.68%)	114 (5.01%)	124 (5.63%)	500 (11.92%)	848 (7.69%)
Cancer (excl. In situ cancers)	150 (6.39%)	152 (6.68%)	174 (7.90%)	331 (7.89%)	807 (7.32%)
Stroke and TIA	90 (3.83%)	97 (4.26%)	116 (5.27%)	305 (7.27%)	608 (5.52%)
Chronic cardiac insufficiency	68 (2.89%)	111 (4.88%)	94 (4.27%)	258 (6.15%)	531 (4.82%)
Depression	77 (3.28%)	80 (3.52%)	108 (4.90%)	256 (6.10%)	521 (4.73%)
Obesity	48 (2.04%)	62 (2.73%)	44 (2.00%)	322 (7.68%)	476 (4.32%)
Rheumatoid arthritis	44 (1.87%)	40 (1.76%)	45 (2.04%)	101 (2.41%)	230 (2.09%)
Chronic renal insufficiency	15 (0.64%)	25 (1.10%)	22 (1.00%)	27 (0.64%)	89 (0.81%)
Diabetic retinopathy	3 (0.13%)	3 (0.13%)	0 (0.00%)	0 (0.00%)	6 (0.05%)
Peripheral circulatory complications	0 (0.00%)	1 (0.04%)	1 (0.05%)	2 (0.05%)	4 (0.04%)
Diabetic neuropathy	2 (0.09%)	0 (0.00%)	1 (0.05%)	1 (0.02%)	4 (0.04%)

Source: Appendix 1; Table 2.4

It is difficult to evaluate how reliably various diagnoses are coded or found at baseline.

In general, cardiovascular diseases were the most frequent diagnoses. 34.4% of the patients had chronic hypertension, 16.9% had CAD, and 10.6% respiratory diseases (COPD, asthma bronchiale or chronic brochitis).

Dyslipidemia was recorded as a diagnosis more than twice as frequently in Pohjois-Karjala HD as in other HD areas. Also hypertension, atrial fibrillation, stroke and TIA were more frequently recorded in Pohjois-Karjala HD than elsewhere. Despite 76-87% of the patients had their LDL levels over their respective targets, dyslipidemia was recorded only in 7.7% of the total study population.

The prevalence of atrial fibrillation in this population (mean age 63 years) was 8.5% which may be higher than expected. Diabetic complications, namely retinopathy (0.05%) and neuropathy (0.04%), on the other hand, were rarely recorded.

10.5 Realization of the Current Care guideline: Diabetes medications and related measurements

10.5.1 Initiation of metformin as first drug after index date

Metformin was the most common drug as first diabetes drug. Among all the study patients 9382 (85.1%) had prescription of A10A* or A10B* during follow-up and 8375 (75.98%) had metformin as the first drug. Numbers and percentages of metformin starters are presented in Table 7 (Appendix 1; Table 3.1). Percentages are by total number patients per site and by patients, who start any A10* drug in each site.

The proportion of metformin in first line treatments was 89.3% (Kainuu HD 91.3%, Health services of Oulu city 90.6%, Kanta-Häme HD 90.2% and Pohjois-Karjala HD 86.3%). In those patients, who were being prescribed metformin as first line treatment, 51.3% had received it already at index date, 80.9% had received it in 3 months' time from the index date. In 15.2% of metformin first line patients, the initiation of metformin took more than 6 months from the index date. As metformin is the recommended drug of choice in newly diagnosed diabetes patients, it can be concluded that the diabetes guidelines are realized well in all HDs that were studied.

The next frequent first line treatments were insulin (6.2%), dipeptidyl peptidase-4-inhibitors (2.5%) and sulphonylureas (1.3%).

Table 7 Metformin as first A10* drug

Metformin as first drug		Kainuu HD	Kanta-Häme HD	Oulu city	Pohjois-Karjala HD	Total
A10* during follow-up	Yes	1958 (83.35%)	2185 (96.04%)	1769 (80.30%)	3470 (82.72%)	9382 (85.12%)
	No	391 (16.65%)	90 (3.96%)	434 (19.70%)	725 (17.28%)	1640 (14.88%)
Metformin as first	% by cohort	1788 (76.12%)	1970 (86.59%)	1603 (72.76%)	3014 (71.85%)	8375 (75.98%)
A10* drug	% by drug starters	1788 (91.32%)	1970 (90.16%)	1603 (90.62%)	3014 (86.86%)	8375 (89.27%)

Source: Appendix 1; Table 3.1

Additional information about the first line treatment is given in Appendix 1; Table 3.1: First A10 drug from index date, time from index date to first metformin treatment (patients who start metformin as the first drug), treatments before metformin treatment (patients, who start metformin later).

We did not investigate which factors explain successful implementation of treatment recommendations due to lack of information for many of the variables that could have been important to be considered.

10.5.2 Dietary advice and exercise consultation provided within 1 month after index date

SPAT codes were used for detecting dietary advice (SPAT1139, SPAT1306) and exercise consultation (SPAT1305). SPAT codes are available from primary care register and local registries of the HD of Kainuu and Pohjois-Karjala and the Health services of the city of Oulu since 2011-2012. For Kainuu study site, additional information about dietary advice and exercise consultation was provided. In total, 72 (0.7%) patients had dietary advice and 18 (0.2%) had exercise consultation within one month after the index date. For the patients, who started during

years 2009-2010 (-2011), this information was not available. The numbers of patients with dietary advice and exercise consultation are presented in Appendix 1; Table 3.2.

10.5.3 Follow-up of HbA_{1c}

Half of the study population (5516, 50.1%) had at least one HbA_{1c} measurement within 3 months after the index date, including the index date. Totally 61.3, 71.2% and 79.3% of patients had at least one measurement within 6 months, 12 months and 2 years after index date, respectively. The control rate of HbA_{1c} remained quite stable, as it was controlled in 60.8% of patients at least once during the 2nd year after the index date, and in 58.2% of patients during the 3rd year. Table 8 (Appendix 1; Table 4.1) displays the number of patients with at least one HbA_{1c} measurement over time.

CONFIDENTIAL

Table 8 Number and percentage of patients with at least one HbA1c measurement taken after index date

	Kainuu patients N=2349	Kanta-Häme patients N=2275	Oulu patients N=2203	Pohjois-Karjala patients N=4195	Total N=11022
At least one HbA1c measurement taken after index date					
≤3 months	1587 (67.56%)	909 (39.96%)	1099 (49.89%)	1921 (45.79%)	5516 (50.05%)
≤ 6 months	1903 (81.01%)	1058 (46.51%)	1340 (60.83%)	2455 (58.52%)	6756 (61.30%)
≤ 12 months	2105 (89.61%)	1228 (53.98%)	1543 (70.04%)	2972 (70.85%)	7848 (71.20%)
≤ 18 months	2163 (92.08%)	1308 (57.49%)	1625 (73.76%)	3305 (78.78%)	8401 (76.22%)
≤ 24 months	2191 (93.27%)	1349 (59.30%)	1678 (76.17%)	3526 (84.05%)	8744 (79.33%)
Ever	2220 (94.51%)	1411 (62.02%)	1752 (79.53%)	3832 (91.35%)	9215 (83.61%)
Patients with at least one Hba1c measurement in 1-2 years					
No	605 (26.13%)	1250 (55.73%)	995 (45.96%)	1410 (33.96%)	4260 (39.17%)
Yes	1710 (73.87%)	993 (44.27%)	1170 (54.04%)	2742 (66.04%)	6615 (60.83%)
Total*	2315 (100.00%)	2243 (100.00%)	2165 (100.00%)	4152 (100.00%)	10875 (100.00%)
Patients with at least one Hba1c measurement in 2-3 years					
No	533 (29.74%)	1056 (56.71%)	905 (49.51%)	1176 (35.69%)	3670 (41.81%)
Yes	1259 (70.26%)	806 (43.29%)	923 (50.49%)	2119 (64.31%)	5107 (58.19%)
Total**	1792 (100.00%)	1862 (100%)	1828 (100%)	3295 (100%)	8777 (100%)

*Total: Number of patients having at least 1 year follow-up

**Total: Number of patients having at least 2 years follow-up.

Source: Appendix 1; Table 4.1

10.5.4 Treatment intensification

After starting the first line treatment, 3283 of patients had HbA_{1c} value 6.5% or more. Treatment intensification to 2nd or 3rd line treatment was followed after first such measurement. Table 9 (Appendix 1; Table 3.3) presents the treatment intensifications during 1/3/6/12/24 months after elevated level of HbA_{1c}.

Treatment was intensified (i.e., a 2nd treatment was added to treatment regime) in 15.6% of patients during six months, in 21.0% during the first year after and in 29.2% during the two first years after elevated HbA_{1c} (>6.5%) level was observed.

Table 9 Treatment intensification for patients with elevated HbA_{1c} level after starting first line treatment

	Kainuu patients at risk N = 962	Kanta-Häme patients at risk N = 462	Oulu patients at risk N = 643	Pohjois-Karjala patients at risk N = 1216	Total at risk N=3283
2nd line treatment started if HbA_{1c} ≥6.5%					
≤1 month	53 (5.51%)	42 (9.09%)	51 (7.93%)	84 (6.91%)	230 (7.01%)
≤3 months	94 (9.77%)	59 (12.77%)	84 (13.06%)	128 (10.53%)	365 (11.12%)
≤6 months	135 (14.03%)	86 (18.61%)	114 (17.73%)	178 (14.64%)	513 (15.63%)
≤ 1 year	198 (20.58%)	119 (25.76%)	141 (21.93%)	230 (18.91%)	688 (20.96%)
≤ 2 years	276 (28.69%)	159 (34.42%)	195 (30.33%)	328 (26.97%)	958 (29.18%)
Ever	342 (35.55%)	193 (41.77%)	220 (34.21%)	511 (42.02%)	1266 (38.56%)
range (min,max)	(0.00, 4.72)	(0.00, 4.60)	(0.00, 4.60)	(0.00, 6.59)	(0.00, 6.59)
mean (+/-sd)	1.09 (1.05)	0.99 (1.02)	0.86 (0.99)	1.63 (1.55)	1.25 (1.30)
median (Q1,Q3)	0.84 (0.19, 1.71)	0.63 (0.11, 1.58)	0.46 (0.10, 1.35)	1.18 (0.25, 2.73)	0.85 (0.18,1.96)

Source: Appendix 1; Table 3.3

10.6 Realization of Current Care guideline: Frequency of follow-up measurements – HbA_{1c} and S-LDL

10.6.1 Frequency of follow-up of HbA_{1c}

Frequency for follow-up of HbA_{1c} is presented in Table 10 (Appendix 1; Tables 4.2 - 4.5). The HbA_{1c} values were controlled at least once in 61.3% of patients in 6 months after index date, and in 71.2% and 79.3% of patients in 1 and 2 years after the index date (Appendix 1; Table 4.4). The mean time between any two consecutive HbA_{1c} measurements during the follow-up was 195 days suggesting that HbA_{1c} values were regularly controlled (Appendix 1; Table 4.2).

10.6.2 HbA_{1c} on target

HbA_{1c} on target means, that the minimum of measurements of the patient is fewer than 6.5% within selected time period. Number of patients with HbA_{1c} on target is presented in Tables 4.4 and 4.5 in Appendix 1 as classified results. In those 61% of patients (n=6756) whose HbA_{1c} level was controlled during six months after index date, 59.4% of patients (n=4017) had their HbA_{1c} levels below 6.5% and 84.6% of patients (n=5713) had their HbA_{1c} levels below 7% and, 6% of patients (n=415) had their HbA_{1c} levels over 8% (Appendix 1; Table 4.5).

In those patients, whose HbA_{1c} level was controlled between six and twelve months after the index date, 74.6% of patients (n=3968) had their HbA_{1c} levels below 6.5% and 91.2% of patients (n=4849) had their HbA_{1c} levels below 7%, and only 2.7% (n=143) had their HbA_{1c} levels over 8% (Appendix 1; Table 4.5).

The treatment targets in type II diabetes patients are individualized, and not all patients are necessary aiming below HbA_{1c} level of 6.5%. Therefore, at least in those patients whose HbA_{1c} levels were measured during the first year, the glucose levels were generally well controlled. In this study population, the same trend of good glucose control was maintained also during 2nd and 3rd year.

Table 10 Number and percentage of patients with distribution of HbA1c measurements (minimum HbA1c measurement taken for each patient) by time after index date

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N=11022
Index – 6 months					
Unknown	446 (18.99%)	1217 (53.49%)	863 (39.17%)	1740 (41.48%)	4266 (38.70%)
≤6.5	1013 (43.12%)	576 (25.32%)	833 (37.81%)	1595 (38.02%)	4017 (36.45%)
6.5 - ≤7	571 (24.31%)	261 (11.47%)	304 (13.80%)	560 (13.35%)	1696 (15.39%)
7 - ≤8	194 (8.26%)	125 (5.49%)	124 (5.63%)	185 (4.41%)	628 (5.70%)
8 - ≤9	57 (2.43%)	42 (1.85%)	40 (1.82%)	50 (1.19%)	189 (1.71%)
>9	68 (2.89%)	54 (2.37%)	39 (1.77%)	65 (1.55%)	226 (2.05%)
Total	2349 (100.00%)	2275 (100.00%)	2203 (100.00%)	4195 (100.00%)	11022 (100.00%)
6 – 12 months					
Unknown	854 (36.67%)	1466 (64.92%)	1232 (56.36%)	2075 (49.74%)	5627 (51.41%)
≤6.5	996 (42.77%)	602 (26.66%)	724 (33.12%)	1646 (39.45%)	3968 (36.25%)
6.5 - ≤7	330 (14.17%)	119 (5.27%)	141 (6.45%)	291 (6.98%)	881 (8.05%)
7 - ≤8	100 (4.29%)	53 (2.35%)	57 (2.61%)	116 (2.78%)	326 (2.98%)
8 - ≤9	31 (1.33%)	9 (0.40%)	18 (0.82%)	27 (0.65%)	85 (0.78%)
>9	18 (0.77%)	9 (0.40%)	14 (0.64%)	17 (0.41%)	58 (0.53%)
Total	2329 (100.00%)	2258 (100.00%)	2186 (100.00%)	4172 (100.00%)	10945 (100.00%)
12 – 18 months					
Unknown	1004 (43.37%)	1541 (68.70%)	1333 (61.57%)	2133 (51.37%)	6011 (55.27%)
≤6.5	886 (38.27%)	534 (23.81%)	604 (27.90%)	1610 (38.78%)	3634 (33.42%)
6.5 - ≤7	291 (12.57%)	94 (4.19%)	139 (6.42%)	255 (6.14%)	779 (7.16%)
7 - ≤8	90 (3.89%)	46 (2.05%)	62 (2.86%)	107 (2.58%)	305 (2.80%)
8 - ≤9	24 (1.04%)	19 (0.85%)	12 (0.55%)	30 (0.72%)	85 (0.78%)
>9	20 (0.86%)	9 (0.40%)	15 (0.69%)	17 (0.41%)	61 (0.56%)
Total	2315 (100.00%)	2243 (100.00%)	2165 (100.00%)	4152 (100.00%)	10875 (100.00%)

Source: Appendix 1; Table 4.4

10.6.3 S-LDL on target

Values of S-LDL for patients were followed during follow-up. S-LDL was considered to be elevated, if it was 2.5 mmol/L or over, or 1.8 mmol/L if patient had diagnoses of CAD, stroke, TIA or peripheral circulatory complications at baseline. Number of patients with comorbidities was 2255 (Kainuu HD 489, Kanta-Häme HD 334, City of Oulu 466 and Pohjois-Karjala HD 966) (Appendix 1; Table 4.6: Total).

At index date, 24.3% of patients with target level <2.5 mmol/L, were in target. Respectively, 13.3% of patients with target level <1.8 mmol/L, were in target. After the index date, S-LDL target levels were slightly better achieved, as seen in Table 11 (Appendix 1; Table 4.6).

Of the patients without relevant comorbidities, and whose S-LDL values were measured during the first year, 38.2% had their last measured S-LDL value below their target level of 2.5 mmol/L. The respective percentages for subsequent years were slightly higher, i.e. 40.8% in second year, 43.5% in third year and 47.1% thereafter (Appendix 1; Table 4.8). 36.1% of the patients did not receive statin prescription at any time during the follow-up, even though they had their S-LDL >2.5 mmol/L (Appendix 1; Table 7.9).

Of the patients with comorbidities, and whose S-LDL values were measured during the first year, only 20.0% had their last measured S-LDL value below their target level of 1.8 mmol/L. The respective percentages for subsequent years were slightly higher also in this group, i.e. 21.2% in the second year, 23.4% in the third year and 26.0% thereafter (Appendix 1; Table 4.9). Only 14.3% of the patients did not receive statin prescription at any time during the follow-up, even though they had their S-LDL >1.8 mmol/L (Appendix 1; Table 7.10).

Table 11 Number and percentage of patients with S-LDL measurements. Value is from the last measurement within time period. Patients without prior diagnosis for coronary artery disease, stroke, TIA or peripheral circulatory complication at baseline.

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N= 11022
Index – 12 months					
S-LDL < 2.5	482 (25.91%)	455 (23.44%)	357 (20.55%)	718 (22.24%)	2012 (22.95%)
S-LDL ≥ 2.5	902 (48.49%)	451 (23.24%)	690 (39.72%)	1206 (37.35%)	3249 (37.06%)
Unknown	476 (25.59%)	1035 (53.32%)	690 (39.72%)	1305 (40.41%)	3506 (39.99%)
Total	1860 (100.00%)	1941 (100.00%)	1737 (100.00%)	3229 (100.00%)	8767 (100.00%)
12 – 24 months					
S-LDL < 2.5	442 (24.10%)	367 (19.15%)	309 (18.04%)	759 (23.69%)	1877 (21.66%)
S-LDL ≥ 2.5	690 (37.62%)	412 (21.50%)	524 (30.59%)	1101 (34.36%)	2727 (31.46%)
Unknown	702 (38.28%)	1137 (59.34%)	880 (51.37%)	1344 (41.95%)	4063 (46.88%)
Total	1834 (100.00%)	1916 (100.00%)	1713 (100.00%)	3204 (100.00%)	8667 (100.00%)
24 – 36 months					
S-LDL < 2.5	339 (23.71%)	326 (20.30%)	256 (17.73%)	639 (25.02%)	1560 (22.18%)
S-LDL ≥ 2.5	487 (34.06%)	313 (19.49%)	398 (27.56%)	825 (32.30%)	2023 (28.76%)
Unknown	604 (42.24%)	967 (60.21%)	790 (54.71%)	1090 (42.68%)	3451 (49.06%)
Total	1430 (100.00%)	1606 (100.00%)	1444 (100.00%)	2554 (100.00%)	7034 (100.00%)
36 – Inf months					
S-LDL < 2.5	284 (27.82%)	271 (23.30%)	222 (21.10%)	476 (27.90%)	1253 (25.35%)
S-LDL ≥ 2.5	331 (32.42%)	222 (19.09%)	289 (27.47%)	568 (33.29%)	1410 (28.53%)
Unknown	406 (39.76%)	670 (57.61%)	541 (51.43%)	662 (38.80%)	2279 (46.11%)
Total	1021 (100%)	1163 (100%)	1052 (100%)	1706 (100%)	4942 (100%)

Source: Appendix 1; Table 4.6

Control measurement was taken from 1100 patients within 3 months after the index date if an elevated level (at least 2.5 or 1.8 mmol/L if comorbidities existed, as listed above) was found at the baseline (Appendix 1; Table 4.10).

10.7 Realization of the Current Care guideline: Follow-up measurements every 12 to 15 months

10.7.1 At least one P/S-Crea measurement taken after index date

The P/S-Crea level was recorded at least once in 72.7% of patients during the first year after index date, in 84.3% during the first 2 years, 87.5% during the first 3 years and 88.5% ever after the index date (Table 12 and Appendix 1; Table 5.1).

CONFIDENTIAL

Table 12 Number and percentage of patients with at least one P/S-Crea measurement taken within 12 to 36 months after index date

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Index – 12 months					
No	316 (13.45%)	875 (38.46%)	692 (31.41%)	1130 (26.94%)	3013 (27.34%)
Yes	2033 (86.55%)	1400 (61.54%)	1511 (68.59%)	3065 (73.06%)	8009 (72.66%)
Index – 24 months					
No	145 (6.17%)	669 (29.41%)	438 (19.88%)	474 (11.30%)	1726 (15.66%)
Yes	2204 (93.83%)	1606 (70.59%)	1765 (80.12%)	3721 (88.70%)	9296 (84.34%)
Index – 36 months					
No	111 (4.73%)	611 (26.86%)	375 (17.02%)	284 (6.77%)	1381 (12.53%)
Yes	2238 (95.27%)	1664 (73.14%)	1828 (82.98%)	3911 (93.23%)	9641 (87.47%)
Ever after index					
No	97 (4.13%)	589 (25.89%)	342 (15.52%)	236 (5.63%)	1264 (11.47%)
Yes	2252 (95.87%)	1686 (74.11%)	1861 (84.48%)	3959 (94.37%)	9758 (88.53%)
Having the first measurement within 0-1 years after index date, if not had before					
No	316 (13.45%)	875 (38.46%)	692 (31.41%)	1130 (26.94%)	3013 (27.34%)
Yes	2033 (86.55%)	1400 (61.54%)	1511 (68.59%)	3065 (73.06%)	8009 (72.66%)
Total	2349 (100.00%)	2275 (100.00%)	2203 (100.00%)	4195 (100.00%)	11022 (100.00%)
Having the first measurement within 2-3 years after index date, if not had before					
No	50 (59.52%)	478 (89.18%)	288 (82.05%)	182 (48.92%)	998 (74.31%)
Yes	34 (40.48%)	58 (10.82%)	63 (17.95%)	190 (51.08%)	345 (25.69%)
Total	84 (100.00%)	536 (100.00%)	351 (100.00%)	372 (100.00%)	1343 (100.00%)
Having the first measurement anytime after 3 years post index date, if not had before					
No	20 (58.82%)	295 (93.06%)	162 (83.08%)	75 (60.98%)	552 (82.51%)
Yes	14 (41.18%)	22 (6.94%)	33 (16.92%)	48 (39.02%)	117 (17.49%)
Total	34 (100.00%)	317 (100.00%)	195 (100.00%)	123 (100.00%)	669 (100.00%)

For cumulative values total are all study patients. For time periods 0-1, 1-2, 2-3, 3-Inf years total are patients who have follow-up at least until starting time of the respective time interval. Also, if patient has his/her first measurement in time interval he/she is not in the risk set for the following time intervals.

Source: Appendix 1; Table 5.1

10.7.2 At least one U-Alb measurement taken after index date

At least one U-Alb measurement taken is presented in Table 13(Appendix 1; Table 5.2). The U-Alb was not recorded as frequently as P/S-Crea; it was recorded at least once in 32.4% of patients during the first year after the index date, in 47.6% during the first 2 years, in 54.9% during the first 3 years and in 59.0% ever after the index date.

CONFIDENTIAL

Table 13 . Number and percentage of patients with at least one U-Alb measurement taken within 12 to 36 months after index date

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Index – 12 months					
No	1254 (53.38%)	1775 (78.02%)	1575 (71.49%)	2848 (67.89%)	7452 (67.61%)
Yes	1095 (46.62%)	500 (21.98%)	628 (28.51%)	1347 (32.11%)	3570 (32.39%)
Index – 24 months					
No	846 (36.02%)	1523 (66.95%)	1311 (59.51%)	2101 (50.08%)	5781 (52.45%)
Yes	1503 (63.98%)	752 (33.05%)	892 (40.49%)	2094 (49.92%)	5241 (47.55%)
Index – 36 months					
No	696 (29.63%)	1373 (60.35%)	1160 (52.66%)	1737 (41.41%)	4966 (45.06%)
Yes	1653 (70.37%)	902 (39.65%)	1043 (47.34%)	2458 (58.59%)	6056 (54.94%)
Ever after index					
No	630 (26.82%)	1290 (56.70%)	1061 (48.16%)	1536 (36.62%)	4517 (40.98%)
Yes	1719 (73.18%)	985 (43.30%)	1142 (51.84%)	2659 (63.38%)	6505 (59.02%)
Having the first measurement within 0-1 years after index date, if not had before					
No	1254 (53.38%)	1775 (78.02%)	1575 (71.49%)	2848 (67.89%)	7452 (67.61%)
Yes	1095 (46.62%)	500 (21.98%)	628 (28.51%)	1347 (32.11%)	3570 (32.39%)
Total	2349 (100.00%)	2275 (100.00%)	2203 (100.00%)	4195 (100.00%)	11022 (100.00%)
Having the first measurement within 1-2 years after index date, if not had before					
No	815 (66.64%)	1496 (85.58%)	1277 (82.87%)	2063 (73.42%)	5651 (77.18%)
Yes	408 (33.36%)	252 (14.42%)	264 (17.13%)	747 (26.58%)	1671 (22.82%)
Total	1223 (100.00%)	1748 (100.00%)	1541 (100.00%)	2810 (100.00%)	7322 (100.00%)
Having the first measurement within 2-3 years after index date, if not had before					
No	392 (72.32%)	1062 (87.62%)	904 (85.69%)	1275 (77.79%)	3633 (81.68%)
Yes	150 (27.68%)	150 (12.38%)	151 (14.31%)	364 (22.21%)	815 (18.32%)
Total	542 (100.00%)	1212 (100.00%)	1055 (100.00%)	1639 (100.00%)	4448 (100.00%)
Having the first measurement anytime after 3 years post index date, if not had before					
No	178 (72.95%)	651 (88.69%)	522 (84.06%)	588 (74.52%)	1939 (81.20%)
Yes	66 (27.05%)	83 (11.31%)	99 (15.94%)	201 (25.48%)	449 (18.80%)
Total	244 (100.00%)	734 (100.00%)	621 (100.00%)	789 (100.00%)	2388 (100.00%)

For cumulative values total are all study patients. For time periods 0-1, 1-2, 2-3, 3-Inf years total are patients who have follow-up at least until starting time of the respective time interval. Also if patient has his first measurement in time interval he is not in the risk set for the following time intervals.

Source: Appendix 1; Table 5.2

10.7.3 At least one visit to dentist and to foot therapist after index date

At least one visit to dentist after the index date is presented in Table 14 (Appendix 1; Table 5.3). Of the total study population, 29.1% of patients had a record of dental visit during the first year. Foot therapist visits were recorded only in random cases (0.13% during the first year), but footrisk score was found more often in Pohjois-Karjala HD than in other HDs (Table 14 and Appendix 1; Table 5.3).

Table 14 Dental and foot therapist visits

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Dental visit under 12 months after index date					
No	1855 (78.97%)	1548 (68.04%)	1365 (61.96%)	3051 (72.73%)	7819 (70.94%)
Yes	494 (21.03%)	727 (31.96%)	838 (38.04%)	1144 (27.27%)	3203 (29.06%)
Foot therapist visit					
Foot therapist visit under 12 months after index date	5 (0.21%)	6 (0.26%)	0 (0.00%)	3 (0.07%)	14 (0.13%)
Foot therapist visit within 12 – 15 months after index date	0 (0.00%)	5 (0.22%)	0 (0.00%)	2 (0.05%)	7 (0.06%)
Foot therapist visit over 15 months after index date	6 (0.26%)	51 (2.24%)	1 (0.05%)	44 (1.05%)	102 (0.93%)
Footrisk score available after index date					
No	2171 (92.42%)	2275 (100.00%)	2203 (100.00%)	2986 (71.18%)	9635 (87.42%)
Yes	178 (7.58%)	0 (0.00%)	0 (0.00%)	1209 (28.82%)	1387 (12.58%)

Source: Appendix 1; Table 5.3

10.8 Realization of the Current Care guideline: Follow-up measurements every 1-3 years

The Current Care guideline for diabetes recommends, that liver enzyme ALAT, lipids and fundus photography are controlled in every 1-3 years. The P-ALAT value was recorded at least once in 62.8%, 76.2%, 80.5%, and 82.3% of patients in 1 year, 2 years, 3 years and ever after the index date, respectively (Table 15 and Appendix 1; Table 6.1).

For the S-LDL value, the respective percentages were 60.7%, 74.5%, 78.9% and 80.4%. (Appendix 1; Table 9.1)

10.8.1 At least one P-ALAT measurement taken after index date

P-ALAT measurements taken after the index date are presented in Table 15 (Appendix 1; Table 6.1).

Table 15 Number and percentage of patients with at least one P-ALAT measurement taken within 12 to 36 months after index date

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Index – 12 months					
No	513 (21.84%)	1222 (53.71%)	812 (36.86%)	1549 (36.92%)	4096 (37.16%)
Yes	1836 (78.16%)	1053 (46.29%)	1391 (63.14%)	2646 (63.08%)	6926 (62.84%)
Index – 24 months					
No	244 (10.39%)	994 (43.69%)	553 (25.10%)	831 (19.81%)	2622 (23.79%)
Yes	2105 (89.61%)	1281 (56.31%)	1650 (74.90%)	3364 (80.19%)	8400 (76.21%)
Index – 36 months					
No	196 (8.34%)	918 (40.35%)	465 (21.11%)	568 (13.54%)	2147 (19.48%)
Yes	2153 (91.66%)	1357 (59.65%)	1738 (78.89%)	3627 (86.46%)	8875 (80.52%)
Ever after index					
No	179 (7.62%)	882 (38.77%)	422 (19.16%)	470 (11.20%)	1953 (17.72%)
Yes	2170 (92.38%)	1393 (61.23%)	1781 (80.84%)	3725 (88.80%)	9069 (82.28%)
Having the first measurement within 0-1 years after index date, if not had before					
No	513 (21.84%)	1222 (53.71%)	812 (36.86%)	1549 (36.92%)	4096 (37.16%)
Yes	1836 (78.16%)	1053 (46.29%)	1391 (63.14%)	2646 (63.08%)	6926 (62.84%)
Total	2349 (100.00%)	2275 (100.00%)	2203 (100.00%)	4195 (100.00%)	11022 (100.00%)
Having the first measurement within 2-3 years after index date, if not had before					
No	102 (68.00%)	713 (90.37%)	347 (79.77%)	389 (59.66%)	1551 (76.55%)
Yes	48 (32.00%)	76 (9.63%)	88 (20.23%)	263 (40.34%)	475 (23.45%)
Total	150 (100.00%)	789 (100.00%)	435 (100.00%)	652 (100.00%)	2026 (100.00%)
Having the first measurement anytime after 3 years post index date, if not had before					
No	42 (71.19%)	454 (92.65%)	191 (81.62%)	157 (61.57%)	844 (81.31%)
Yes	17 (28.81%)	36 (7.35%)	43 (18.38%)	98 (38.43%)	194 (18.69%)
Total	59 (100.00%)	490 (100.00%)	234 (100.00%)	255 (100.00%)	1038 (100.00%)

For cumulative values total are all study patients. For time periods 0-1, 1-2, 2-3, 3-Inf years total are patients who have follow-up at least until starting time of the respective time interval. Also, if patient has his/her first measurement in time interval he/she is not in the risk set for the following time intervals.

Source: Appendix 1; Table 6.1

10.8.2 At least one S-LDL measurement taken after index date

S-LDL measurements taken after the index date are presented in Table 16 (Appendix 1; Table 6.2).

Table 16 Number and percentage of patients with at least one S-LDL measurement taken within 12 to 36 months after index date

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjaa patients N = 4195	Total N=11022
Index – 12 months					
No	590 (25.12%)	1201 (52.79%)	842 (38.22%)	1700 (40.52%)	4333 (39.31%)
Yes	1759 (74.88%)	1074 (47.21%)	1361 (61.78%)	2495 (59.48%)	6689 (60.69%)
Index – 24 months					
No	305 (12.98%)	1010 (44.40%)	606 (27.51%)	895 (21.33%)	2816 (25.55%)
Yes	2044 (87.02%)	1265 (55.60%)	1597 (72.49%)	3300 (78.67%)	8206 (74.45%)
Index – 36 months					
No	256 (10.90%)	953 (41.89%)	528 (23.97%)	587 (13.99%)	2324 (21.09%)
Yes	2093 (89.10%)	1322 (58.11%)	1675 (76.03%)	3608 (86.01%)	8698 (78.91%)
Ever after index					
No	241 (10.26%)	929 (40.84%)	493 (22.38%)	500 (11.92%)	2163 (19.62%)
Yes	2108 (89.74%)	1346 (59.16%)	1710 (77.62%)	3695 (88.08%)	8859 (80.38%)
Having the first measurement within 0-1 years after index date, if not had before					
No	590 (25.12%)	1201 (52.79%)	842 (38.22%)	1700 (40.52%)	4333 (39.31%)
Yes	1759 (74.88%)	1074 (47.21%)	1361 (61.78%)	2495 (59.48%)	6689 (60.69%)
Total	2349 (100.00%)	2275 (100.00%)	2203 (100.00%)	4195 (100.00%)	11022 (100.00%)
Having the first measurement within 2-3 years after index date, if not had before					
No	109 (68.99%)	723 (92.69%)	378 (82.89%)	400 (56.50%)	1610 (76.59%)
Yes	49 (31.01%)	57 (7.31%)	78 (17.11%)	308 (43.50%)	492 (23.41%)
Total	158 (100.00%)	780 (100.00%)	456 (100.00%)	708 (100.00%)	2102 (100.00%)
Having the first measurement anytime after 3 years post index date, if not had before					
No	51 (77.27%)	465 (95.09%)	216 (86.06%)	181 (67.54%)	913 (85.01%)
Yes	15 (22.73%)	24 (4.91%)	35 (13.94%)	87 (32.46%)	161 (14.99%)
Total	66 (100.00%)	489 (100.00%)	251 (100.00%)	268 (100.00%)	1074 (100.00%)

Source: Appendix 1; Table 6.2

10.8.3 At least one fundus photography taken within 12 to 15 months after index date

Number of patients with fundus photography after the index date is presented in Table 17(Appendix 1; Table 6.3).

In order to exclude the patients under follow-up due to existing eye disease, records for patients with fundus photography during baseline were ignored. The fundus photographs were not done or recorded as often as Current Care guidelines suggest, as it was recorded in only 18.3% of patients during the whole study period.

CONFIDENTIAL

Table 17 Number and percentage of patients with at least one fundus photography taken within 12 to 36 months after index date

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Index – 12 months					
No	2263 (96.92%)	2247 (99.21%)	1896 (88.76%)	3773 (91.29%)	10179 (93.65%)
Yes	72 (3.08%)	18 (0.79%)	240 (11.24%)	360 (8.71%)	690 (6.35%)
Total	2335 (100.00%)	2265 (100.00%)	2136 (100.00%)	4133 (100.00%)	10869 (100.00%)
Index – 24 months					
No	2196 (94.05%)	2210 (97.57%)	1851 (86.66%)	3600 (87.10%)	9857 (90.69%)
Yes	139 (5.95%)	55 (2.43%)	285 (13.34%)	533 (12.90%)	1012 (9.31%)
Total	2335 (100.00%)	2265 (100.00%)	2136 (100.00%)	4133 (100.00%)	10869 (100.00%)
Index – 36 months					
No	2056 (88.05%)	2159 (95.32%)	1823 (85.35%)	3401 (82.29%)	9439 (86.84%)
Yes	279 (11.95%)	106 (4.68%)	313 (14.65%)	732 (17.71%)	1430 (13.16%)
Total	2335 (100.00%)	2265 (100.00%)	2136 (100.00%)	4133 (100.00%)	10869 (100.00%)
Ever after index					
No	1868 (80.00%)	2078 (91.74%)	1808 (84.64%)	3124 (75.59%)	8878 (81.68%)
Yes	467 (20.00%)	187 (8.26%)	328 (15.36%)	1009 (24.41%)	1991 (18.32%)
Total	2335 (100.00%)	2265 (100.00%)	2136 (100.00%)	4133 (100.00%)	10869 (100.00%)
Having the first measurement within 0-1 years after index date, if not had before					
No	2263 (96.92%)	2247 (99.21%)	1896 (88.76%)	3773 (91.29%)	10179 (93.65%)
Yes	72 (3.08%)	18 (0.79%)	240 (11.24%)	360 (8.71%)	690 (6.35%)
Total	2335 (100.00%)	2265 (100.00%)	2136 (100.00%)	4133 (100.00%)	10869 (100.00%)
Having the first measurement within 1-2 years after index date, if not had before					
No	2163 (97.00%)	2178 (98.33%)	1817 (97.58%)	3560 (95.37%)	9718 (96.79%)
Yes	67 (3.00%)	37 (1.67%)	45 (2.42%)	173 (4.63%)	322 (3.21%)
Total	2230 (100.00%)	2215 (100.00%)	1862 (100.00%)	3733 (100.00%)	10040 (100.00%)
Having the first measurement within 2-3 years after index date, if not had before					
No	1596 (91.94%)	1764 (97.19%)	1492 (98.16%)	2720 (93.18%)	7572 (94.77%)
Yes	140 (8.06%)	51 (2.81%)	28 (1.84%)	199 (6.82%)	418 (5.23%)
Total	1736 (100.00%)	1815 (100.00%)	1520 (100.00%)	2919 (100.00%)	7990 (100.00%)
Having the first measurement anytime 3 years post index date, if not had before					
No	978 (83.88%)	1202 (93.69%)	1024 (98.56%)	1624 (85.43%)	4828 (89.59%)
Yes	188 (16.12%)	81 (6.31%)	15 (1.44%)	277 (14.57%)	561 (10.41%)
Total	1166 (100.00%)	1283 (100.00%)	1039 (100.00%)	1901 (100.00%)	5389 (100.00%)

For cumulative values total are all study patients. For time periods 0-1, 1-2, 2-3, 3-Inf years total are patients who have follow-up at least until starting time of the respective time interval. Also, if patient has his/her first measurement in time interval he/she is not in the risk set for the following time intervals.

Source: Appendix 1; Table 6.3

10.9 Realization of the Current Care guideline: Treatment decisions (other than diabetes treatment) based on follow-up measurements

10.9.1 Blood pressure over 140/90 mmHg

Number of patients with ACE/ARB prescriptions after the first measurement of high blood pressure (>140/90 mmHg) are presented in Table 18(Appendix 1; Table 7.1). The evaluation of treatment intensification is not possible, as it is not known whether patients had already ACE/ARB treatment at the time the high blood pressure was measured. However, it can be calculated that 29.6% of the patients whose blood pressure was higher than 140/90 mmHg were not prescribed (or did not purchase) ACE/ARB treatment at any time during the study.

Table 18 Number and percentage of patients with ACE/ARB prescriptions after blood pressure measurement >140/90 mmHg

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
0 – 1 month after high blood pressure					
No	612 (71.66%)	0 (NaN%)	457 (63.21%)	1260 (74.78%)	2329 (71.40%)
Yes	242 (28.34%)	0 (NaN%)	266 (36.79%)	425 (25.22%)	933 (28.60%)
Total	854 (100.00%)	0 (NaN%)	723 (100.00%)	1685 (100.00%)	3262 (100.00%)
0 – 3 months after high blood pressure					
No	406 (47.54%)	0 (NaN%)	306 (42.32%)	803 (47.66%)	1515 (46.44%)
Yes	448 (52.46%)	0 (NaN%)	417 (57.68%)	882 (52.34%)	1747 (53.56%)
Total	854 (100.00%)	0 (NaN%)	723 (100.00%)	1685 (100.00%)	3262 (100.00%)
0 – 6 months after high blood pressure					
No	355 (41.57%)	0 (NaN%)	273 (37.76%)	688 (40.83%)	1316 (40.34%)
Yes	499 (58.43%)	0 (NaN%)	450 (62.24%)	997 (59.17%)	1946 (59.66%)
Total	854 (100.00%)	0 (NaN%)	723 (100.00%)	1685 (100.00%)	3262 (100.00%)
Any time after high blood pressure					
No	303 (35.48%)	0 (NaN%)	214 (29.60%)	449 (26.65%)	966 (29.61%)
Yes	551 (64.52%)	0 (NaN%)	509 (70.40%)	1236 (73.35%)	2296 (70.39%)
Total	854 (100.00%)	0 (NaN%)	723 (100.00%)	1685 (100.00%)	3262 (100.00%)

Total are patients who had high blood pressure (>140/90 mmHg) after the index date

Source: Appendix 1; Table 7.1

10.9.2 Renal insufficiency

23.8 of patients had their eGFR below 60 mL/min, which was the limit of contraindication for metformin use (based on metformin Summary of Product Characteristics) at the time of data collection. Among those patients, metformin was prescribed for 44.1% during the first six months after the eGFR measurement. 11.8% of patients had their eGFR below 45 mL/min, and for those patients, metformin was prescribed in 33.6% of patients during the first six months. 5.1% of patients had severe renal failure, and 22.6% of those had metformin prescription within six months after the eGFR measuring day.

The summary data for number and percentage of patients with renal insufficiency (eGFR < 60, < 45 and < 30 ml/min) and rates for metformin prescriptions, are shown in Appendix 1; Tables 7.2 – 7.4.

10.9.3 Microalbuminuria

Prescriptions of ACE/ARB after microalbuminuria (cU-Alb or nU-Alb) is presented in Table 19(Appendix 1; Table 7.6). 80.6% of patients with albuminuria (≥ 20 microg/min) were prescribed ACE/ARB treatment at any time during the study follow-up. Prescriptions of ACE/ARB after dU-Alb, U-AlbCrea or nU-AlbCrea measurements are presented in Appendix 1; Tables 7.7-7.8.

Table 19 Number and percentage of patients with prescriptions of ACE/ARB after albumin measurement

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
cU-Alb or nU-Alb \geq 20 mg/ min					
No	93 (62.00%)	136 (59.91%)	4 (25.00%)	206 (56.44%)	439 (57.92%)
Yes	57 (38.00%)	91 (40.09%)	12 (75.00%)	159 (43.56%)	319 (42.08%)
Total	150 (100.00%)	227 (100.00%)	16 (100.00%)	365 (100.00%)	758 (100.00%)
0 – 1 month after cU-Alb or nU-Alb \geq 20					
No	37 (64.91%)	58 (63.74%)	7 (58.33%)	106 (66.67%)	208 (65.20%)
Yes	20 (35.09%)	33 (36.26%)	5 (41.67%)	53 (33.33%)	111 (34.80%)
Total	57 (100.00%)	91 (100.00%)	12 (100.00%)	159 (100.00%)	319 (100.00%)
0 – 3 months after cU-Alb or nU-Alb \geq 20					
No	18 (31.58%)	31 (34.07%)	4 (33.33%)	59 (37.11%)	112 (35.11%)
Yes	39 (68.42%)	60 (65.93%)	8 (66.67%)	100 (62.89%)	207 (64.89%)
Total	57 (100.00%)	91 (100.00%)	12 (100.00%)	159 (100.00%)	319 (100.00%)
0 – 6 months after cU-Alb or nU-Alb \geq 20					
No	15 (26.32%)	23 (25.27%)	3 (25.00%)	47 (29.56%)	88 (27.59%)
Yes	42 (73.68%)	68 (74.73%)	9 (75.00%)	112 (70.44%)	231 (72.41%)
Total	57 (100.00%)	91 (100.00%)	12 (100.00%)	159 (100.00%)	319 (100.00%)
Any time after cU-Alb or nU-Alb \geq 20					
No	13 (22.81%)	18 (19.78%)	3 (25.00%)	28 (17.61%)	62 (19.44%)
Yes	44 (77.19%)	73 (80.22%)	9 (75.00%)	131 (82.39%)	257 (80.56%)
Total	57 (100.00%)	91 (100.00%)	12 (100.00%)	159 (100.00%)	319 (100.00%)

Source: Appendix 1; Table 7.6

10.10 Other endpoints

10.10.1 Mortality during follow-up

Tables for overall mortality are provided in Table 20 (Appendix 1; Table 8.1).

Table 20 Mortality

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Mortality					
No	2214 (94.25%)	2137 (93.93%)	2057 (93.37%)	3938 (93.87%)	10346 (93.87%)
Yes	135 (5.75%)	138 (6.07%)	146 (6.63%)	257 (6.13%)	676 (6.13%)
Time until death (years)					
Index date - <1	34 (25.19%)	32 (23.19%)	38 (26.032%)	43 (16.73%)	147 (21.75%)
1 - <2	37 (27.41%)	39 (28.26%)	37 (25.34%)	71 (27.63%)	184 (27.22%)
2- <3	27 (20.00%)	31 (22.46%)	40 (27.40%)	74 (28.79%)	172 (25.44%)
3+	37 (27.41%)	36 (26.09%)	31 (21.23%)	69 (26.85%)	173 (25.59%)
range (min,max)	(0.01, 4.90)	(0.00, 4.85)	(0.05, 4.68)	(0.01, 4.91)	(0.00, 4.91)
mean (+/-sd)	2.06 (1.26)	2.04 (1.24)	1.94 (1.19)	2.22 (1.19)	2.09 (1.22)
median (Q1,Q3)	1.83 (1.04, 3.15)	1.93 (1.10, 3.07)	1.88 (0.96, 2.82)	2.28 (1.29, 3.05)	2.05 (1.15,3.02)

Source: Appendix 1; Table 8.1

10.10.2 Amputations of the lower extremities

Only 43 (0.4%) patients from the total of 11022 patients had amputations of the lower extremities during the follow-up (Appendix 1; Table 8.2).

10.10.3 Long absences from work

Number of patients with over 10 days absences from work is presented in Table 21 (Appendix 1; Table 8.3).

Table 21 Number and percentage of patients with absences from work over 10 days during follow-up

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Absence from work (Long absences over 10 days)					
No	2043 (86.97%)	1977 (86.90%)	1932 (87.70%)	3805 (90.70%)	9757 (88.52%)
Yes	306 (13.03%)	298 (13.10%)	271 (12.30%)	390 (9.30%)	1265 (11.48%)

Source: Appendix 1; Table 8.3

10.10.4 Severe hypoglycemic events

Number of patients with severe hypoglycemic events is presented in Table 22. The frequency of severe hypoglycemic events were highest in Kainuu HD (6.8%) and lowest in Pohjois-Karjala HD (1.6%).

Table 22 Number and percentage of patients with severe hypoglycemic events (ICD-10: E11.00 or ICPC-2: T87) during follow-up

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Severe hypoglycemic events					
No	2190 (93.23%)	2195 (96.48%)	2156 (97.87%)	4126 (98.36%)	10667 (96.78%)
Yes	159 (6.77%)	80 (3.52%)	47 (2.13%)	69 (1.64%)	355 (3.22%)

Source: Appendix 1; Table 8.4

11 Summary

The aim of this study was to identify whether and how the electronic patient information systems and national registers can be used for research purposes in Finland. Research process was slow, mainly due to long expectation times of data permits and data extraction, and part of the originally planned study sites had to be left out for economical or other reasons, but it produced interesting, detailed data.

Despite the extent of the data, all the study questions could not be answered. For example the SPAT codes for dietary advice or exercise consultation were available only from 2010, some of the endpoints of interest (e.g. fundus photography or visit to foot therapist) were not equally recorded in the study sites, or were not available at all.

Laboratory measurement were frequently recorded, although there were differences between sites. With diagnoses, drugs and laboratory records, several findings about realization of Current Care Guideline were done:

- Within a year after index date over half of the newly diagnosed diabetes patients had follow-up for HbA_{1c} (71%), P/S-Crea (73%), S-LDL (61%) and P-ALAT (66%) but only 32% had U-Alb measurements.
- Half of the study population had at least one HbA_{1c} measurement within 3 months after the index date. The control rate of HbA_{1c} remained quite stable, over half of the patients had records also during the 2nd and 3rd year after index date.
- According to Current Care Guideline, metformin is the recommended drug of choice in newly diagnosed diabetes patients. Guidelines were realized well, 8375 (75.98%) patients had metformin as the first drug.
- Treatment was intensified (i.e., a 2nd treatment was added to treatment regime) in 15.6% of patients during six months after elevated HbA_{1c} (>6.5%) level was observed.
- EGFR below 60 mL/min is contraindication for metformin use. Among the patients with low eGFR, metformin was prescribed for 44.1% during the first six months after such measurement.
- 29.6% of the patients whose blood pressure was higher than 140/90 mmHg were not prescribed ACE/ARB treatment at any time during the study follow-up.

- 80.6% of patients with albuminuria (cU-Alb or nU-Alb \geq 20 microg/min) were prescribed ACE/ARB treatment during the study.

12 References

Diabetes, Current Care Guideline. Working group set up by the Finnish Medical Society Duodecim, Suomen Sisätautilääkärin yhdistys and Lääkärineuvosto of Finnish Diabetes Association, 2011 (referred 05 April 2013). www.kaypahoito.fi

R Development Core Team. R: A Language and Environment for Statistical Computing. Vienna, 2008.

R: Regulatory Compliance and Validation Issues: A Guidance Document for the Use of R in Regulated Clinical Trial Environments
<http://www.r-project.org/doc/R-FDA.pdf>

UKPDS Group (1998) UK Prospective Diabetes Study 33. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes. Lancet; 352:837B53.

UKPDS Group (1998) UK Prospective Diabetes Study 34. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type II diabetes. Lancet; 352:854B65.

ENCePP Code of Conduct – Implementation Guidance for Sharing of ENCePP Study Data, EMA/409316/2010 Revision 2, dated 14 July 2016

Guideline for Good Pharmacoepidemiology Practices by International Society for Pharmacoepidemiology (ISPE 2007)
https://www.pharmacoepi.org/resources/guidelines_08027.cfm

Pharmacoepidemiological study protocol: ER12-9451 Realization of the clinical practice guidelines for diabetes in Finland – A case study of the usability of electronic patient information systems and national registers to support evidence based decision making in health care
<http://www.encepp.eu/encepp/viewResource.htm?id=14809>.

13 Appendices

Annex 1. List of stand-alone documents

Appendix 1-9451-LTRY-descriptive-tables-2017-08-09.pdf (Tables)

Appendix 2-9451 List of variables and analyses.xlsx (Variable list)



**Realization of the clinical practice guidelines for diabetes in
Finland**

**A case study of the usability of electronic patient
information systems and national registers to support
evidence based decision making in health care**

Study #9451
August 9th 2017

Prepared for
Pharma Industry Finland

By EPID Research Oy

Contents

1	Events at index date	2
2	Baseline summaries	4
3	Realization of the Current Care guideline: Diabetes medications and related measurements	11
4	Realization of the Current Care guideline: Frequency of follow-up of measurements (HbA1c and S-LDL)	15
5	Realization of the Current Care guideline: Follow-up measurements every 12 to 15 months	28
6	Realization of the Current Care guideline: Follow-up measurements every 1-3 years	34
7	Realization of the Current Care guideline: Treatment decisions (other than diabetes treatment) based on follow-up measurements	41
8	Other endpoints	52
9	Measurements during follow-up	57

Chapter 1

Events at index date

Table 1.1: Events at index date. A patient can have several events at index date.

Event	Kainuu		KHSHP		Oulu		PKSHP		Total	
	N	Perc.	N	Perc.	N	Perc.	N	Perc.	N	Perc.
SII drug	665	28.31	1274	56.00	559	25.37	1210	28.84	3708	33.64
Diagnose	580	24.69	183	8.04	593	26.92	1767	42.12	3123	28.33
Glycohemoglobin	1010	43.00	552	24.26	500	22.70	966	23.03	3028	27.47
Local drug	408	17.37	17	0.75	317	14.39	894	21.31	1636	14.84
Glucose tolerance	10	0.43	237	10.42	390	17.70	100	2.38	737	6.69
Reimb. 103	16	0.68	101	4.44	55	2.50	15	0.36	187	1.70
Councelling	32	1.36	0	0.00	27	1.23	22	0.52	81	0.73
Sum of patients	2721	115.84	2364	103.91	2441	110.80	4974	118.57	12500	113.41
Total in study site	2349	100.00	2275	100.00	2203	100.00	4195	100.00	11022	100.00

Chapter 2

Baseline summaries

Table 2.1: Baseline characteristics

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Age at index (years)					
<50	297(12.64%)	378(16.62%)	377(17.11%)	526(12.54%)	1578(14.32%)
50-59	556(23.67%)	594(26.11%)	512(23.24%)	1004(23.93%)	2666(24.19%)
60-69	699(29.76%)	692(30.42%)	639(29.01%)	1259(30.01%)	3289(29.84%)
70-79	566(24.10%)	453(19.91%)	459(20.84%)	940(22.41%)	2418(21.94%)
80 and over	231(9.83%)	158(6.95%)	216(9.80%)	466(11.11%)	1071(9.72%)
range (min,max)	(0.93, 98.55)	(4.12, 100.68)	(6.78, 94.67)	(6.18, 98.25)	(0.93, 100.68)
mean (+/-sd)	63.96 (12.48)	61.87 (12.65)	62.67 (13.36)	64.14 (12.59)	63.34(12.77)
median (Q1,Q3)	64.06 (56.14, 73.24)	62.11 (53.70, 70.67)	62.95 (53.71, 72.32)	64.10 (55.92, 73.31)	63.50(55.05, 72.59)
Sex					
Male	1262(53.72%)	1211(53.23%)	1094(49.66%)	2195(52.32%)	5762(52.28%)
Female	1087(46.28%)	1064(46.77%)	1109(50.34%)	2000(47.68%)	5260(47.72%)
Smoking					
Yes	23(0.98%)	2(0.09%)	18(0.82%)	487(11.61%)	530(4.81%)
No	25(1.06%)	0(0.00%)	0(0.00%)	1027(24.48%)	1052(9.54%)
No records	2301(97.96%)	2273(99.91%)	2185(99.18%)	2681(63.91%)	9440(85.65%)
Previous smoking					
Info available	5(0.21%)	0(0.00%)	0(0.00%)	11(0.26%)	16(0.15%)
No records	2344(99.79%)	2275(100.00%)	2203(100.00%)	4184(99.74%)	11006(99.85%)
Amount of smoking					
10-20/day	7(0.30%)	0(0.00%)	0(0.00%)	8(0.19%)	15(0.14%)
below 10/day	8(0.34%)	0(0.00%)	0(0.00%)	2(0.05%)	10(0.09%)
above 20/day	5(0.21%)	0(0.00%)	0(0.00%)	2(0.05%)	7(0.06%)
no smoking	25(1.06%)	0(0.00%)	0(0.00%)	1(0.02%)	26(0.24%)
No records	2304(98.08%)	2275(100.00%)	2203(100.00%)	4182(99.69%)	10964(99.47%)

Table 2.1: *(continued)*

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
BMI					
<25	52(2.21%)	0(0.00%)	106(4.81%)	256(6.10%)	414(3.76%)
25-29.9	188(8.00%)	0(0.00%)	307(13.94%)	682(16.26%)	1177(10.68%)
30-34.9	189(8.05%)	0(0.00%)	294(13.35%)	674(16.07%)	1157(10.50%)
35-39.9	82(3.49%)	0(0.00%)	145(6.58%)	279(6.65%)	506(4.59%)
≥ 40	51(2.17%)	0(0.00%)	75(3.40%)	180(4.29%)	306(2.78%)
Unknown	1787(76.07%)	2275(100.00%)	1276(57.92%)	2124(50.63%)	7462(67.70%)

Table 2.2: Laboratory and blood pressure measurements at baseline

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
HbA1c(%)					
<6.5	1123(47.81%)	658(28.92%)	767(34.82%)	1501(35.78%)	4049(36.74%)
6.5-6.9	475(20.22%)	188(8.26%)	311(14.12%)	445(10.61%)	1419(12.87%)
7.0-7.9	195(8.30%)	92(4.04%)	137(6.22%)	193(4.60%)	617(5.60%)
≥ 8	242(10.30%)	206(9.05%)	133(6.04%)	287(6.84%)	868(7.88%)
Unknown	314(13.37%)	1131(49.71%)	855(38.81%)	1769(42.17%)	4069(36.92%)
Crea(umol/L)					
<130	2006(85.40%)	1381(60.70%)	1553(70.49%)	2627(62.62%)	7567(68.65%)
130-150	17(0.72%)	19(0.84%)	19(0.86%)	33(0.79%)	88(0.80%)
≥ 150	18(0.77%)	22(0.97%)	16(0.73%)	34(0.81%)	90(0.82%)
Unknown	308(13.11%)	853(37.49%)	615(27.92%)	1501(35.78%)	3277(29.73%)
GFR(ml/min)					
<60	206(8.77%)	177(7.78%)	183(8.31%)	338(8.06%)	904(8.20%)
≥ 60	1835(78.12%)	1245(54.73%)	1405(63.78%)	2356(56.16%)	6841(62.07%)
Unknown	308(13.11%)	853(37.49%)	615(27.92%)	1501(35.78%)	3277(29.73%)
S-LDL(mmol/L) <2.5					
Yes	348(17.96%)	308(15.19%)	252(13.80%)	434(12.94%)	1342(14.67%)
No	1220(62.95%)	677(33.38%)	895(49.01%)	1389(41.40%)	4181(45.71%)
Unknown	370(19.09%)	1043(51.43%)	679(37.19%)	1532(45.66%)	3624(39.62%)
Total*	1938(100.00%)	2028(100.00%)	1826(100.00%)	3355(100.00%)	9147(100.00%)
S-LDL(mmol/L) <1.8					
Yes	45(10.95%)	27(10.93%)	34(9.02%)	57(6.79%)	163(8.69%)
No	299(72.75%)	100(40.49%)	268(71.09%)	394(46.90%)	1061(56.59%)
Unknown	67(16.30%)	120(48.58%)	75(19.89%)	389(46.31%)	651(34.72%)
Total**	411(100.00%)	247(100.00%)	377(100.00%)	840(100.00%)	1875(100.00%)

For laboratory and blood pressure measurement the result of the closest date before index date is used as baseline value. Only dates within one year before the index date are taken account. If history data do not contain any information about these, a value within one month after index date will be accepted.

*Patients without prior diagnosis for coronary artery disease, stroke, TIA, or periferal circulatory complication before baseline measurements.

**Patients with prior diagnosis for coronary artery disease, stroke, TIA, or periferal circulatory complication before baseline measurements.

Table 2.2: (continued)

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Blood pressure					
<130/80	102(4.34%)	0(0.00%)	121(5.49%)	243(5.79%)	466(4.23%)
not <130/80	690(29.37%)	1(0.04%)	892(40.49%)	1884(44.91%)	3467(31.46%)
Unknown	1557(66.28%)	2274(99.96%)	1190(54.02%)	2068(49.30%)	7089(64.32%)

For laboratory and blood pressure measurement the result of the closest date before index date is used as baseline value. Only dates within one year before the index date are taken account. If history data do not contain any information about these, a value within one month after index date will be accepted.

**Patients without prior diagnosis for coronary artery disease, stroke, TIA, or peripheral circulatory complication before baseline measurements.*

***Patients with prior diagnosis for coronary artery disease, stroke, TIA, or peripheral circulatory complication before baseline measurements.*

Table 2.3: List of the most common concomitant medications at baseline

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Concomitant medication*					
Beta blocking agents	1020(43.42%)	879(38.64%)	905(41.08%)	1927(45.94%)	4731(42.92%)
Agents acting on the renin-angiotensin system	882(37.55%)	976(42.90%)	969(43.99%)	1882(44.86%)	4709(42.72%)
Lipid modifying drugs	902(38.40%)	785(34.51%)	869(39.45%)	1634(38.95%)	4190(38.01%)
Psycholeptics	474(20.18%)	363(15.96%)	619(28.10%)	879(20.95%)	2335(21.18%)
Antiinflammatory and antirheumatic products	473(20.14%)	382(16.79%)	513(23.29%)	859(20.48%)	2227(20.21%)
Calcium channel blockers	495(21.07%)	426(18.73%)	449(20.38%)	842(20.07%)	2212(20.07%)
Antibacterials for systemic use	395(16.82%)	416(18.29%)	515(23.38%)	824(19.64%)	2150(19.51%)
Analgesics	468(19.92%)	305(13.41%)	525(23.83%)	837(19.95%)	2135(19.37%)
Diuretics	404(17.20%)	370(16.26%)	416(18.88%)	738(17.59%)	1928(17.49%)
Drugs for acid related disorders	451(19.20%)	361(15.87%)	402(18.25%)	621(14.80%)	1835(16.65%)
Psychoanaleptics	324(13.79%)	287(12.62%)	411(18.66%)	592(14.11%)	1614(14.64%)
Cardiac therapy	386(16.43%)	241(10.59%)	319(14.48%)	592(14.11%)	1538(13.95%)
Antithrombotic agents	284(12.09%)	220(9.67%)	314(14.25%)	703(16.76%)	1521(13.80%)
Drugs for obstructive airway diseases	308(13.11%)	236(10.37%)	328(14.89%)	542(12.92%)	1414(12.83%)
Sex hormones and modulators of the genital system	197(8.39%)	198(8.70%)	183(8.31%)	374(8.92%)	952(8.64%)
Thyroid therapy	182(7.75%)	168(7.38%)	223(10.12%)	297(7.08%)	870(7.89%)
Ophthalmologicals	160(6.81%)	132(5.80%)	194(8.81%)	345(8.22%)	831(7.54%)
Urologicals	190(8.09%)	143(6.29%)	194(8.81%)	299(7.13%)	826(7.49%)
Mineral supplements	128(5.45%)	128(5.63%)	170(7.72%)	215(5.13%)	641(5.82%)
Corticosteroids for systemic use	135(5.75%)	104(4.57%)	115(5.22%)	228(5.44%)	582(5.28%)
Nasal preparations	110(4.68%)	91(4.00%)	171(7.76%)	170(4.05%)	542(4.92%)
Corticosteroids, dermatological preparations	101(4.30%)	92(4.04%)	154(6.99%)	191(4.55%)	538(4.88%)
Antiepileptics	100(4.26%)	91(4.00%)	109(4.95%)	220(5.24%)	520(4.72%)
Antihistamines for systemic use	88(3.75%)	79(3.47%)	134(6.08%)	132(3.15%)	433(3.93%)
Muscle relaxants	81(3.45%)	63(2.77%)	74(3.36%)	113(2.69%)	331(3.00%)
Antigout preparations	58(2.47%)	78(3.43%)	41(1.86%)	140(3.34%)	317(2.88%)
Drugs for constipation	60(2.55%)	33(1.45%)	89(4.04%)	106(2.53%)	288(2.61%)
Drugs for treatment of bone diseases	40(1.70%)	36(1.58%)	48(2.18%)	74(1.76%)	198(1.80%)
Antidiarrheals, intestinal antiinflammatory/antiinfective agents	55(2.34%)	26(1.14%)	48(2.18%)	69(1.64%)	198(1.80%)
Anti-Parkinson drugs	28(1.19%)	23(1.01%)	31(1.41%)	68(1.62%)	150(1.36%)

Table 2.4: List of the most common concomitant diseases at baseline

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Comorbidities*					
Chronic hypertension	673(28.65%)	576(25.32%)	762(34.59%)	1785(42.55%)	3796(34.44%)
Coronary artery disease	426(18.14%)	261(11.47%)	386(17.52%)	785(18.71%)	1858(16.86%)
COPD	247(10.52%)	158(6.95%)	242(10.99%)	522(12.44%)	1169(10.61%)
Atrial fibrillation	141(6.00%)	179(7.87%)	165(7.49%)	453(10.80%)	938(8.51%)
Dyslipidemia	110(4.68%)	114(5.01%)	124(5.63%)	500(11.92%)	848(7.69%)
Cancer(excl. In situ cancers)	150(6.39%)	152(6.68%)	174(7.90%)	331(7.89%)	807(7.32%)
Stroke and TIA	90(3.83%)	97(4.26%)	116(5.27%)	305(7.27%)	608(5.52%)
Chronic cardiac insufficiency	68(2.89%)	111(4.88%)	94(4.27%)	258(6.15%)	531(4.82%)
Depression	77(3.28%)	80(3.52%)	108(4.90%)	256(6.10%)	521(4.73%)
Obesity	48(2.04%)	62(2.73%)	44(2.00%)	322(7.68%)	476(4.32%)
Rheumatoid arthritis	44(1.87%)	40(1.76%)	45(2.04%)	101(2.41%)	230(2.09%)
Chronic renal insufficiency	15(0.64%)	25(1.10%)	22(1.00%)	27(0.64%)	89(0.81%)
Diabetic retinopathy	3(0.13%)	3(0.13%)	0(0.00%)	0(0.00%)	6(0.05%)
Peripheral circulatory complications	0(0.00%)	1(0.04%)	1(0.05%)	2(0.05%)	4(0.04%)
Diabetic neuropathy	2(0.09%)	0(0.00%)	1(0.05%)	1(0.02%)	4(0.04%)

Chapter 3

Realization of the Current Care guideline: Diabetes medications and related measurements

Table 3.1: Initiation of metformin as the first line treatment

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
First A10 drug after index day					
combinations	3(0.15%)	7(0.32%)	4(0.23%)	4(0.12%)	18(0.19%)
DDP4 inhibitors	39(1.99%)	63(2.88%)	37(2.09%)	93(2.68%)	232(2.47%)
insulin	79(4.03%)	107(4.90%)	98(5.54%)	293(8.44%)	577(6.15%)
metformin	1788(91.32%)	1970(90.16%)	1603(90.62%)	3014(86.86%)	8375(89.27%)
other	22(1.12%)	5(0.23%)	4(0.23%)	9(0.26%)	40(0.43%)
sulfonylureas	23(1.17%)	30(1.37%)	21(1.19%)	49(1.41%)	123(1.31%)
thiazolidinediones	4(0.20%)	3(0.14%)	2(0.11%)	8(0.23%)	17(0.18%)
Time from index date to start of metformin as first treatment					
At index date	779(43.57%)	1215(61.68%)	687(42.86%)	1617(53.65%)	4298(51.32%)
Under 1 month	475(26.57%)	416(21.12%)	410(25.58%)	556(18.45%)	1857(22.17%)
1-3 months	188(10.51%)	101(5.13%)	136(8.48%)	191(6.34%)	616(7.36%)
3-6 months	82(4.59%)	46(2.34%)	76(4.74%)	130(4.31%)	334(3.99%)
Over 6 months	264(14.77%)	192(9.75%)	294(18.34%)	520(17.25%)	1270(15.16%)
First treatment before start of metformin					
combinations	0(0.00%)	3(5.26%)	0(0.00%)	1(0.60%)	4(1.22%)
DDP4 inhibitors	7(14.29%)	9(15.79%)	10(18.52%)	16(9.52%)	42(12.80%)
insulin	19(38.78%)	31(54.39%)	33(61.11%)	124(73.81%)	207(63.11%)
other	11(22.45%)	4(7.02%)	2(3.70%)	5(2.98%)	22(6.71%)
sulfonylureas	11(22.45%)	9(15.79%)	8(14.81%)	18(10.71%)	46(14.02%)
thiazolidinediones	1(2.04%)	1(1.75%)	1(1.85%)	4(2.38%)	7(2.13%)

Table 'First A10 drug after index day' has the patients with A10 drugs. Table 'Time from index date to start of metformin as first treatment' has the patients with metformin as first A10 drug. Table 'First treatment before start of metformin' has the patients with metformin as second drug.

Table 3.2: Dietary advice and exercise consultation

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Dietary advice and exercise consultation*					
Dietary advice provided within 1 month of index date	14(0.60%)	3(0.13%)	9(0.41%)	46(1.10%)	72(0.65%)
Exercise consultation provided within 1 month of index date	5(0.21%)	1(0.04%)	3(0.14%)	9(0.21%)	18(0.16%)

Table 3.3: Treatment intensification for patients with elevated HbA1c level after starting first line treatment

	Kainuu patients at risk N = 962	Kanta-Häme patients at risk N = 462	Oulu patients at risk N = 643	Pohjois-Karjala patients at risk N = 1216	Total at risk N = 3283
2nd line treatment started if HbA1c \geq 6.5 after 1st line*					
≤ 1 month	53(5.51%)	42(9.09%)	51(7.93%)	84(6.91%)	230(7.01%)
≤ 3 months	94(9.77%)	59(12.77%)	84(13.06%)	128(10.53%)	365(11.12%)
≤ 6 months	135(14.03%)	86(18.61%)	114(17.73%)	178(14.64%)	513(15.63%)
≤ 1 year	198(20.58%)	119(25.76%)	141(21.93%)	230(18.91%)	688(20.96%)
≤ 2 years	276(28.69%)	159(34.42%)	195(30.33%)	328(26.97%)	958(29.18%)
Ever	342(35.55%)	193(41.77%)	220(34.21%)	511(42.02%)	1266(38.56%)
range (min,max)	(0.00, 4.72)	(0.00, 4.60)	(0.00, 4.60)	(0.00, 6.59)	(0.00, 6.59)
mean (+/-sd)	1.09 (1.05)	0.99 (1.02)	0.86 (0.99)	1.63 (1.55)	1.25(1.30)
median (Q1,Q3)	0.84 (0.19, 1.71)	0.63 (0.11, 1.58)	0.46 (0.10, 1.35)	1.18 (0.25, 2.73)	0.85(0.18, 1.96)
3rd line treatment started if HbA1c \geq 6.5 after 1st line*					
≤ 1 month	2(0.21%)	4(0.87%)	3(0.47%)	2(0.16%)	11(0.34%)
≤ 3 months	4(0.42%)	9(1.95%)	6(0.93%)	11(0.90%)	30(0.91%)
≤ 6 months	12(1.25%)	15(3.25%)	10(1.56%)	16(1.32%)	53(1.61%)
≤ 1 year	22(2.29%)	26(5.63%)	23(3.58%)	27(2.22%)	98(2.99%)
≤ 2 years	46(4.78%)	46(9.96%)	40(6.22%)	50(4.11%)	182(5.54%)
Ever	73(7.59%)	63(13.64%)	52(8.09%)	125(10.28%)	313(9.53%)
range (min,max)	(0.04, 4.45)	(0.02, 4.34)	(0.00, 3.29)	(0.01, 6.38)	(0.00, 6.38)
mean (+/-sd)	1.71 (1.09)	1.41 (1.06)	1.36 (0.92)	2.59 (1.65)	1.94(1.42)
median (Q1,Q3)	1.49 (0.94, 2.52)	1.15 (0.58, 2.14)	1.23 (0.66, 1.88)	2.49 (1.33, 3.78)	1.68(0.88, 2.86)

Chapter 4

Realization of the Current Care guideline: Frequency of follow-up of measurements (HbA1c and S-LDL)

Table 4.1: Number and percentage of patients with at least one HbA1c measurement taken after index date

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
At least one HbA1c measurement taken after index date*					
≤3 months	1587(67.56%)	909(39.96%)	1099(49.89%)	1921(45.79%)	5516(50.05%)
≤ 6 months	1903(81.01%)	1058(46.51%)	1340(60.83%)	2455(58.52%)	6756(61.30%)
≤ 12 months	2105(89.61%)	1228(53.98%)	1543(70.04%)	2972(70.85%)	7848(71.20%)
≤ 18 months	2163(92.08%)	1308(57.49%)	1625(73.76%)	3305(78.78%)	8401(76.22%)
≤ 24 months	2191(93.27%)	1349(59.30%)	1678(76.17%)	3526(84.05%)	8744(79.33%)
Ever	2220(94.51%)	1411(62.02%)	1752(79.53%)	3832(91.35%)	9215(83.61%)
Patients with at least one Hba1c measurement in 1-2 years					
No	605(26.13%)	1250(55.73%)	995(45.96%)	1410(33.96%)	4260(39.17%)
Yes	1710(73.87%)	993(44.27%)	1170(54.04%)	2742(66.04%)	6615(60.83%)
Total*	2315(100.00%)	2243(100.00%)	2165(100.00%)	4152(100.00%)	10875(100.00%)
Patients with at least one Hba1c measurement in 2-3 years					
No	533(29.74%)	1056(56.71%)	905(49.51%)	1176(35.69%)	3670(41.81%)
Yes	1259(70.26%)	806(43.29%)	923(50.49%)	2119(64.31%)	5107(58.19%)
Total**	1792(100.00%)	1862(100.00%)	1828(100.00%)	3295(100.00%)	8777(100.00%)

*Total: Number of patients having at least 1 year follow-up

**Total: Number of patients having at least 2 years follow-up.

Table 4.2: Distribution of time between any two consecutive HbA1c measurements during follow-up

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Distribution between any two consecutive HbA1c measurements after index date					
0-1 year	8375(91.38%)	4104(85.91%)	4553(83.65%)	11918(89.56%)	28950(88.55%)
1-2 years	709(7.74%)	616(12.90%)	752(13.82%)	1302(9.78%)	3379(10.34%)
2-3 years	72(0.79%)	46(0.96%)	113(2.08%)	81(0.61%)	312(0.95%)
3-Inf years	9(0.10%)	11(0.23%)	25(0.46%)	7(0.05%)	52(0.16%)
range (min,max)	(1.00, 1331.00)	(1.00, 1463.00)	(1.00, 1620.00)	(1.00, 1378.00)	(1.00, 1620.00)
mean (+/-sd)	183.91 (131.76)	211.22 (157.64)	225.77 (181.11)	185.05 (133.82)	195.33(146.69)
median (Q1,Q3)	156.00 (98.00, 222.00)	178.00 (99.00, 294.00)	176.00 (106.00, 292.00)	149.00 (97.00, 224.00)	161.00(98.00, 241.00)

Table 4.3: Number of measurements with HbA1c <6.5

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
HbA1c <6.5% (all measurements)					
No	4869(42.86%)	1855(30.16%)	2478(34.52%)	4655(27.23%)	13857(33.16%)
Yes	6490(57.14%)	4296(69.84%)	4700(65.48%)	12440(72.77%)	27926(66.84%)

Table 4.4: Number and percentage of patients with distribution of HbA1c measurements (minimum HbA1c measurement taken for each patient) by time after index date

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Index – 6 months					
Unknown	446(18.99%)	1217(53.49%)	863(39.17%)	1740(41.48%)	4266(38.70%)
[0, 6.5)	1013(43.12%)	576(25.32%)	833(37.81%)	1595(38.02%)	4017(36.45%)
[6.5, 7)	571(24.31%)	261(11.47%)	304(13.80%)	560(13.35%)	1696(15.39%)
[7, 8)	194(8.26%)	125(5.49%)	124(5.63%)	185(4.41%)	628(5.70%)
[8, 9)	57(2.43%)	42(1.85%)	40(1.82%)	50(1.19%)	189(1.71%)
[9, Inf)	68(2.89%)	54(2.37%)	39(1.77%)	65(1.55%)	226(2.05%)
Total	2349(100.00%)	2275(100.00%)	2203(100.00%)	4195(100.00%)	11022(100.00%)
6 – 12 months					
Unknown	854(36.67%)	1466(64.92%)	1232(56.36%)	2075(49.74%)	5627(51.41%)
[0, 6.5)	996(42.77%)	602(26.66%)	724(33.12%)	1646(39.45%)	3968(36.25%)
[6.5, 7)	330(14.17%)	119(5.27%)	141(6.45%)	291(6.98%)	881(8.05%)
[7, 8)	100(4.29%)	53(2.35%)	57(2.61%)	116(2.78%)	326(2.98%)
[8, 9)	31(1.33%)	9(0.40%)	18(0.82%)	27(0.65%)	85(0.78%)
[9, Inf)	18(0.77%)	9(0.40%)	14(0.64%)	17(0.41%)	58(0.53%)
Total	2329(100.00%)	2258(100.00%)	2186(100.00%)	4172(100.00%)	10945(100.00%)
12 – 18 months					
Unknown	1004(43.37%)	1541(68.70%)	1333(61.57%)	2133(51.37%)	6011(55.27%)
[0, 6.5)	886(38.27%)	534(23.81%)	604(27.90%)	1610(38.78%)	3634(33.42%)
[6.5, 7)	291(12.57%)	94(4.19%)	139(6.42%)	255(6.14%)	779(7.16%)
[7, 8)	90(3.89%)	46(2.05%)	62(2.86%)	107(2.58%)	305(2.80%)
[8, 9)	24(1.04%)	19(0.85%)	12(0.55%)	30(0.72%)	85(0.78%)
[9, Inf)	20(0.86%)	9(0.40%)	15(0.69%)	17(0.41%)	61(0.56%)
Total	2315(100.00%)	2243(100.00%)	2165(100.00%)	4152(100.00%)	10875(100.00%)

Table 4.4: (continued)

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
18 – 24 months					
Unknown	958(44.98%)	1454(69.97%)	1285(63.11%)	1974(52.14%)	5671(56.54%)
[0, 6.5)	754(35.40%)	487(23.44%)	550(27.01%)	1417(37.43%)	3208(31.98%)
[6.5, 7)	274(12.86%)	70(3.37%)	107(5.26%)	234(6.18%)	685(6.83%)
[7, 8)	95(4.46%)	36(1.73%)	65(3.19%)	92(2.43%)	288(2.87%)
[8, 9)	25(1.17%)	26(1.25%)	11(0.54%)	49(1.29%)	111(1.11%)
[9, Inf)	24(1.13%)	5(0.24%)	18(0.88%)	20(0.53%)	67(0.67%)
Total	2130(100.00%)	2078(100.00%)	2036(100.00%)	3786(100.00%)	10030(100.00%)
24 – 36 months					
Unknown	533(29.74%)	1056(56.71%)	905(49.51%)	1176(35.69%)	3670(41.81%)
[0, 6.5)	790(44.08%)	650(34.91%)	702(38.40%)	1766(53.60%)	3908(44.53%)
[6.5, 7)	316(17.63%)	83(4.46%)	132(7.22%)	185(5.61%)	716(8.16%)
[7, 8)	96(5.36%)	49(2.63%)	51(2.79%)	96(2.91%)	292(3.33%)
[8, 9)	35(1.95%)	13(0.70%)	18(0.98%)	41(1.24%)	107(1.22%)
[9, Inf)	22(1.23%)	11(0.59%)	20(1.09%)	31(0.94%)	84(0.96%)
Total	1792(100.00%)	1862(100.00%)	1828(100.00%)	3295(100.00%)	8777(100.00%)

Table 4.5: Number and percentage of patients with distribution of HbA1c measurements (minimum HbA1c measurement taken for each patient) by time after index date. Patients with HbA1c measurements

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Index – 6 months					
[0, 6.5)	1013(53.23%)	576(54.44%)	833(62.16%)	1595(64.97%)	4017(59.46%)
[6.5, 7)	571(30.01%)	261(24.67%)	304(22.69%)	560(22.81%)	1696(25.10%)
[7, 8)	194(10.19%)	125(11.81%)	124(9.25%)	185(7.54%)	628(9.30%)
[8, 9)	57(3.00%)	42(3.97%)	40(2.99%)	50(2.04%)	189(2.80%)
[9, Inf)	68(3.57%)	54(5.10%)	39(2.91%)	65(2.65%)	226(3.35%)
Total	1903(100.00%)	1058(100.00%)	1340(100.00%)	2455(100.00%)	6756(100.00%)
6 – 12 months					
[0, 6.5)	996(67.53%)	602(76.01%)	724(75.89%)	1646(78.49%)	3968(74.61%)
[6.5, 7)	330(22.37%)	119(15.03%)	141(14.78%)	291(13.88%)	881(16.57%)
[7, 8)	100(6.78%)	53(6.69%)	57(5.97%)	116(5.53%)	326(6.13%)
[8, 9)	31(2.10%)	9(1.14%)	18(1.89%)	27(1.29%)	85(1.60%)
[9, Inf)	18(1.22%)	9(1.14%)	14(1.47%)	17(0.81%)	58(1.09%)
Total	1475(100.00%)	792(100.00%)	954(100.00%)	2097(100.00%)	5318(100.00%)
12 – 18 months					
[0, 6.5)	886(67.58%)	534(76.07%)	604(72.60%)	1610(79.74%)	3634(74.71%)
[6.5, 7)	291(22.20%)	94(13.39%)	139(16.71%)	255(12.63%)	779(16.02%)
[7, 8)	90(6.86%)	46(6.55%)	62(7.45%)	107(5.30%)	305(6.27%)
[8, 9)	24(1.83%)	19(2.71%)	12(1.44%)	30(1.49%)	85(1.75%)
[9, Inf)	20(1.53%)	9(1.28%)	15(1.80%)	17(0.84%)	61(1.25%)
Total	1311(100.00%)	702(100.00%)	832(100.00%)	2019(100.00%)	4864(100.00%)

Table 4.5: (continued)

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
18 – 24 months					
[0, 6.5)	754(64.33%)	487(78.04%)	550(73.24%)	1417(78.20%)	3208(73.59%)
[6.5, 7)	274(23.38%)	70(11.22%)	107(14.25%)	234(12.91%)	685(15.71%)
[7, 8)	95(8.11%)	36(5.77%)	65(8.66%)	92(5.08%)	288(6.61%)
[8, 9)	25(2.13%)	26(4.17%)	11(1.46%)	49(2.70%)	111(2.55%)
[9, Inf)	24(2.05%)	5(0.80%)	18(2.40%)	20(1.10%)	67(1.54%)
Total	1172(100.00%)	624(100.00%)	751(100.00%)	1812(100.00%)	4359(100.00%)
24 – 36 months					
[0, 6.5)	790(62.75%)	650(80.65%)	702(76.06%)	1766(83.34%)	3908(76.52%)
[6.5, 7)	316(25.10%)	83(10.30%)	132(14.30%)	185(8.73%)	716(14.02%)
[7, 8)	96(7.63%)	49(6.08%)	51(5.53%)	96(4.53%)	292(5.72%)
[8, 9)	35(2.78%)	13(1.61%)	18(1.95%)	41(1.93%)	107(2.10%)
[9, Inf)	22(1.75%)	11(1.36%)	20(2.17%)	31(1.46%)	84(1.64%)
Total	1259(100.00%)	806(100.00%)	923(100.00%)	2119(100.00%)	5107(100.00%)

Table 4.6: Number and percentage of patients with S-LDL measurements. Value is from the last measurement within time period. Patients without prior diagnosis for coronary artery disease, stroke, TIA or peripheral circulatory complication at baseline.

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Index – 12 months					
S-LDL <2.5	482(25.91%)	455(23.44%)	357(20.55%)	718(22.24%)	2012(22.95%)
S-LDL ≥ 2.5	902(48.49%)	451(23.24%)	690(39.72%)	1206(37.35%)	3249(37.06%)
Unknown	476(25.59%)	1035(53.32%)	690(39.72%)	1305(40.41%)	3506(39.99%)
Total	1860(100.00%)	1941(100.00%)	1737(100.00%)	3229(100.00%)	8767(100.00%)
12 – 24 months					
S-LDL <2.5	442(24.10%)	367(19.15%)	309(18.04%)	759(23.69%)	1877(21.66%)
S-LDL ≥ 2.5	690(37.62%)	412(21.50%)	524(30.59%)	1101(34.36%)	2727(31.46%)
Unknown	702(38.28%)	1137(59.34%)	880(51.37%)	1344(41.95%)	4063(46.88%)
Total	1834(100.00%)	1916(100.00%)	1713(100.00%)	3204(100.00%)	8667(100.00%)
24 – 36 months					
S-LDL <2.5	339(23.71%)	326(20.30%)	256(17.73%)	639(25.02%)	1560(22.18%)
S-LDL ≥ 2.5	487(34.06%)	313(19.49%)	398(27.56%)	825(32.30%)	2023(28.76%)
Unknown	604(42.24%)	967(60.21%)	790(54.71%)	1090(42.68%)	3451(49.06%)
Total	1430(100.00%)	1606(100.00%)	1444(100.00%)	2554(100.00%)	7034(100.00%)
36 – Inf months					
S-LDL <2.5	284(27.82%)	271(23.30%)	222(21.10%)	476(27.90%)	1253(25.35%)
S-LDL ≥ 2.5	331(32.42%)	222(19.09%)	289(27.47%)	568(33.29%)	1410(28.53%)
Unknown	406(39.76%)	670(57.61%)	541(51.43%)	662(38.80%)	2279(46.11%)
Total	1021(100.00%)	1163(100.00%)	1052(100.00%)	1706(100.00%)	4942(100.00%)

Table 4.7: Number and percentage of patients with S-LDL measurements. Value is from the last measurement within time period. Patients with prior diagnosis for coronary artery disease, stroke, TIA or periferal circulatory complication at baseline.

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Index – 12 months					
S-LDL <1.8	68(13.91%)	48(14.37%)	53(11.37%)	116(12.01%)	285(12.64%)
S-LDL ≥ 1.8	307(62.78%)	120(35.93%)	261(56.01%)	455(47.10%)	1143(50.69%)
Unknown	114(23.31%)	166(49.70%)	152(32.62%)	395(40.89%)	827(36.67%)
Total	489(100.00%)	334(100.00%)	466(100.00%)	966(100.00%)	2255(100.00%)
12 – 24 months					
S-LDL <1.8	67(13.93%)	40(12.23%)	45(9.96%)	116(12.24%)	268(12.14%)
S-LDL ≥ 1.8	244(50.73%)	80(24.46%)	227(50.22%)	448(47.26%)	999(45.24%)
Unknown	170(35.34%)	207(63.30%)	180(39.82%)	384(40.51%)	941(42.62%)
Total	481(100.00%)	327(100.00%)	452(100.00%)	948(100.00%)	2208(100.00%)
24 – 36 months					
S-LDL <1.8	47(12.98%)	33(12.89%)	38(9.90%)	112(15.11%)	230(13.20%)
S-LDL ≥ 1.8	179(49.45%)	73(28.52%)	172(44.79%)	330(44.53%)	754(43.26%)
Unknown	136(37.57%)	150(58.59%)	174(45.31%)	299(40.35%)	759(43.55%)
Total	362(100.00%)	256(100.00%)	384(100.00%)	741(100.00%)	1743(100.00%)
36 – Inf months					
S-LDL <1.8	36(13.64%)	22(12.15%)	38(14.50%)	79(15.37%)	175(14.33%)
S-LDL ≥ 1.8	127(48.11%)	44(24.31%)	113(43.13%)	215(41.83%)	499(40.87%)
Unknown	101(38.26%)	115(63.54%)	111(42.37%)	220(42.80%)	547(44.80%)
Total	264(100.00%)	181(100.00%)	262(100.00%)	514(100.00%)	1221(100.00%)

Table 4.8: Number and percentage of patients with S-LDL measurements. Value is from the last measurement within time period. Patients without prior diagnosis for coronary artery disease, stroke, TIA or peripheral circulatory complication at baseline. Patients with S-LDL measurements.

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Index – 12 months					
S-LDL < 2.5	482(34.83%)	455(50.22%)	357(34.10%)	718(37.32%)	2012(38.24%)
S-LDL ≥ 2.5	902(65.17%)	451(49.78%)	690(65.90%)	1206(62.68%)	3249(61.76%)
Total	1384(100.00%)	906(100.00%)	1047(100.00%)	1924(100.00%)	5261(100.00%)
12 – 24 months					
S-LDL < 2.5	442(39.05%)	367(47.11%)	309(37.09%)	759(40.81%)	1877(40.77%)
S-LDL ≥ 2.5	690(60.95%)	412(52.89%)	524(62.91%)	1101(59.19%)	2727(59.23%)
Total	1132(100.00%)	779(100.00%)	833(100.00%)	1860(100.00%)	4604(100.00%)
24 – 36 months					
S-LDL < 2.5	339(41.04%)	326(51.02%)	256(39.14%)	639(43.65%)	1560(43.54%)
S-LDL ≥ 2.5	487(58.96%)	313(48.98%)	398(60.86%)	825(56.35%)	2023(56.46%)
Total	826(100.00%)	639(100.00%)	654(100.00%)	1464(100.00%)	3583(100.00%)
36 – Inf months					
S-LDL < 2.5	284(46.18%)	271(54.97%)	222(43.44%)	476(45.59%)	1253(47.05%)
S-LDL ≥ 2.5	331(53.82%)	222(45.03%)	289(56.56%)	568(54.41%)	1410(52.95%)
Total	615(100.00%)	493(100.00%)	511(100.00%)	1044(100.00%)	2663(100.00%)

Table 4.9: Number and percentage of patients with S-LDL measurements. Value is from the last measurement within time period. Patients with prior diagnosis for coronary artery disease, stroke, TIA or periferal circulatory complication at baseline. Patients with S-LDL measurements.

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Index – 12 months					
S-LDL <1.8	68(18.13%)	48(28.57%)	53(16.88%)	116(20.32%)	285(19.96%)
S-LDL ≥ 1.8	307(81.87%)	120(71.43%)	261(83.12%)	455(79.68%)	1143(80.04%)
Total	375(100.00%)	168(100.00%)	314(100.00%)	571(100.00%)	1428(100.00%)
12 – 24 months					
S-LDL <1.8	67(21.54%)	40(33.33%)	45(16.54%)	116(20.57%)	268(21.15%)
S-LDL ≥ 1.8	244(78.46%)	80(66.67%)	227(83.46%)	448(79.43%)	999(78.85%)
Total	311(100.00%)	120(100.00%)	272(100.00%)	564(100.00%)	1267(100.00%)
24 – 36 months					
S-LDL <1.8	47(20.80%)	33(31.13%)	38(18.10%)	112(25.34%)	230(23.37%)
S-LDL ≥ 1.8	179(79.20%)	73(68.87%)	172(81.90%)	330(74.66%)	754(76.63%)
Total	226(100.00%)	106(100.00%)	210(100.00%)	442(100.00%)	984(100.00%)
36 – Inf months					
S-LDL <1.8	36(22.09%)	22(33.33%)	38(25.17%)	79(26.87%)	175(25.96%)
S-LDL ≥ 1.8	127(77.91%)	44(66.67%)	113(74.83%)	215(73.13%)	499(74.04%)
Total	163(100.00%)	66(100.00%)	151(100.00%)	294(100.00%)	674(100.00%)

Table 4.10: Number and percentage of patients with at least one S-LDL measurement taken within 3 to 6 months after index date

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
At least one S-LDL measuremnt after index date					
≤3 months	995(42.36%)	660(29.01%)	795(36.09%)	1145(27.29%)	3595(32.62%)
≤6 months	1311(55.81%)	832(36.57%)	1029(46.71%)	1673(39.88%)	4845(43.96%)
Ever	2108(89.74%)	1346(59.16%)	1710(77.62%)	3695(88.08%)	8859(80.38%)
If S-LDL elevated, control measurement taken within 3 months					
No	1566(66.67%)	867(38.11%)	1254(56.92%)	2547(60.72%)	6234(56.56%)
Yes	249(10.60%)	164(7.21%)	226(10.26%)	461(10.99%)	1100(9.98%)
No elevated S-LDL	534(22.73%)	1244(54.68%)	723(32.82%)	1187(28.30%)	3688(33.46%)

Chapter 5

**Realization of the Current Care
guideline: Follow-up measurements every
12 to 15 months**

Table 5.1: Number and percentage of patients with at least one S-Crea measurement taken within 12 to 36 months after index date

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Index – 12 months					
No	316(13.45%)	875(38.46%)	692(31.41%)	1130(26.94%)	3013(27.34%)
Yes	2033(86.55%)	1400(61.54%)	1511(68.59%)	3065(73.06%)	8009(72.66%)
Index – 24 months					
No	145(6.17%)	669(29.41%)	438(19.88%)	474(11.30%)	1726(15.66%)
Yes	2204(93.83%)	1606(70.59%)	1765(80.12%)	3721(88.70%)	9296(84.34%)
Index – 36 months					
No	111(4.73%)	611(26.86%)	375(17.02%)	284(6.77%)	1381(12.53%)
Yes	2238(95.27%)	1664(73.14%)	1828(82.98%)	3911(93.23%)	9641(87.47%)
Ever after index					
No	97(4.13%)	589(25.89%)	342(15.52%)	236(5.63%)	1264(11.47%)
Yes	2252(95.87%)	1686(74.11%)	1861(84.48%)	3959(94.37%)	9758(88.53%)
Having the first measurement within 0-1 years after index date, if not had before					
No	316(13.45%)	875(38.46%)	692(31.41%)	1130(26.94%)	3013(27.34%)
Yes	2033(86.55%)	1400(61.54%)	1511(68.59%)	3065(73.06%)	8009(72.66%)
Total	2349(100.00%)	2275(100.00%)	2203(100.00%)	4195(100.00%)	11022(100.00%)
Having the first measurement within 1-2 years after index date, if not had before					
No	143(45.54%)	667(76.40%)	435(63.13%)	474(41.95%)	1719(57.19%)
Yes	171(54.46%)	206(23.60%)	254(36.87%)	656(58.05%)	1287(42.81%)
Total	314(100.00%)	873(100.00%)	689(100.00%)	1130(100.00%)	3006(100.00%)

For cumulative values total are all study patients. For time periods 0-1, 1-2, 2-3, 3-Inf years total are patients who have follow-up at least until starting time of the respective time interval. Also if patient has his first measurement in time interval he is not in the risk set for the following time intervals.

Table 5.1: (continued)

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Having the first measurement within 2-3 years after index date, if not had before					
No	50(59.52%)	478(89.18%)	288(82.05%)	182(48.92%)	998(74.31%)
Yes	34(40.48%)	58(10.82%)	63(17.95%)	190(51.08%)	345(25.69%)
Total	84(100.00%)	536(100.00%)	351(100.00%)	372(100.00%)	1343(100.00%)
Having the first measurement within 3-Inf years after index date, if not had before					
No	20(58.82%)	295(93.06%)	162(83.08%)	75(60.98%)	552(82.51%)
Yes	14(41.18%)	22(6.94%)	33(16.92%)	48(39.02%)	117(17.49%)
Total	34(100.00%)	317(100.00%)	195(100.00%)	123(100.00%)	669(100.00%)

For cumulative values total are all study patients. For time periods 0-1, 1-2, 2-3, 3-Inf years total are patients who have follow-up at least until starting time of the respective time interval. Also if patient has his first measurement in time interval he is not in the risk set for the following time intervals.

Table 5.2: Number and percentage of patients with at least one U-Alb measurement taken within 12 to 36 months after index date

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Index – 12 months					
No	1254(53.38%)	1775(78.02%)	1575(71.49%)	2848(67.89%)	7452(67.61%)
Yes	1095(46.62%)	500(21.98%)	628(28.51%)	1347(32.11%)	3570(32.39%)
Index – 24 months					
No	846(36.02%)	1523(66.95%)	1311(59.51%)	2101(50.08%)	5781(52.45%)
Yes	1503(63.98%)	752(33.05%)	892(40.49%)	2094(49.92%)	5241(47.55%)
Index – 36 months					
No	696(29.63%)	1373(60.35%)	1160(52.66%)	1737(41.41%)	4966(45.06%)
Yes	1653(70.37%)	902(39.65%)	1043(47.34%)	2458(58.59%)	6056(54.94%)
Ever after index					
No	630(26.82%)	1290(56.70%)	1061(48.16%)	1536(36.62%)	4517(40.98%)
Yes	1719(73.18%)	985(43.30%)	1142(51.84%)	2659(63.38%)	6505(59.02%)
Having the first measurement within 0-1 years after index date, if not had before					
No	1254(53.38%)	1775(78.02%)	1575(71.49%)	2848(67.89%)	7452(67.61%)
Yes	1095(46.62%)	500(21.98%)	628(28.51%)	1347(32.11%)	3570(32.39%)
Total	2349(100.00%)	2275(100.00%)	2203(100.00%)	4195(100.00%)	11022(100.00%)
Having the first measurement within 1-2 years after index date, if not had before					
No	815(66.64%)	1496(85.58%)	1277(82.87%)	2063(73.42%)	5651(77.18%)
Yes	408(33.36%)	252(14.42%)	264(17.13%)	747(26.58%)	1671(22.82%)
Total	1223(100.00%)	1748(100.00%)	1541(100.00%)	2810(100.00%)	7322(100.00%)

For cumulative values total are all study patients. For time periods 0-1, 1-2, 2-3, 3-Inf years total are patients who have follow-up at least until starting time of the respective time interval. Also if patient has his first measurement in time interval he is not in the risk set for the following time intervals.

Table 5.2: (continued)

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Having the first measurement within 2-3 years after index date, if not had before					
No	392(72.32%)	1062(87.62%)	904(85.69%)	1275(77.79%)	3633(81.68%)
Yes	150(27.68%)	150(12.38%)	151(14.31%)	364(22.21%)	815(18.32%)
Total	542(100.00%)	1212(100.00%)	1055(100.00%)	1639(100.00%)	4448(100.00%)
Having the first measurement within 3-Inf years after index date, if not had before					
No	178(72.95%)	651(88.69%)	522(84.06%)	588(74.52%)	1939(81.20%)
Yes	66(27.05%)	83(11.31%)	99(15.94%)	201(25.48%)	449(18.80%)
Total	244(100.00%)	734(100.00%)	621(100.00%)	789(100.00%)	2388(100.00%)

For cumulative values total are all study patients. For time periods 0-1, 1-2, 2-3, 3-Inf years total are patients who have follow-up at least until starting time of the respective time interval. Also if patient has his first measurement in time interval he is not in the risk set for the following time intervals.

Table 5.3: Dental and foot therapist visits

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Dental visit under 12 months after index date					
No	1855(78.97%)	1548(68.04%)	1365(61.96%)	3051(72.73%)	7819(70.94%)
Yes	494(21.03%)	727(31.96%)	838(38.04%)	1144(27.27%)	3203(29.06%)
Foot therapist visit*					
Foot therapist visit under 12 months after index date	5(0.21%)	6(0.26%)	0(0.00%)	3(0.07%)	14(0.13%)
Foot therapist visit within 12 – 15 months after index date	0(0.00%)	5(0.22%)	0(0.00%)	2(0.05%)	7(0.06%)
Foot therapist visit over 15 months after index date	6(0.26%)	51(2.24%)	1(0.05%)	44(1.05%)	102(0.93%)
Footrisk score available after index date					
No	2171(92.42%)	2275(100.00%)	2203(100.00%)	2986(71.18%)	9635(87.42%)
Yes	178(7.58%)	0(0.00%)	0(0.00%)	1209(28.82%)	1387(12.58%)

Chapter 6

**Realization of the Current Care
guideline: Follow-up measurements every
1-3 years**

Table 6.1: Number and percentage of patients with at least one P-ALAT measurement taken within 12 to 36 months after index date

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Index – 12 months					
No	513(21.84%)	1222(53.71%)	812(36.86%)	1549(36.92%)	4096(37.16%)
Yes	1836(78.16%)	1053(46.29%)	1391(63.14%)	2646(63.08%)	6926(62.84%)
Index – 24 months					
No	244(10.39%)	994(43.69%)	553(25.10%)	831(19.81%)	2622(23.79%)
Yes	2105(89.61%)	1281(56.31%)	1650(74.90%)	3364(80.19%)	8400(76.21%)
Index – 36 months					
No	196(8.34%)	918(40.35%)	465(21.11%)	568(13.54%)	2147(19.48%)
Yes	2153(91.66%)	1357(59.65%)	1738(78.89%)	3627(86.46%)	8875(80.52%)
Ever after index					
No	179(7.62%)	882(38.77%)	422(19.16%)	470(11.20%)	1953(17.72%)
Yes	2170(92.38%)	1393(61.23%)	1781(80.84%)	3725(88.80%)	9069(82.28%)
Having the first measurement within 0-1 years after index date, if not had before					
No	513(21.84%)	1222(53.71%)	812(36.86%)	1549(36.92%)	4096(37.16%)
Yes	1836(78.16%)	1053(46.29%)	1391(63.14%)	2646(63.08%)	6926(62.84%)
Total	2349(100.00%)	2275(100.00%)	2203(100.00%)	4195(100.00%)	11022(100.00%)
Having the first measurement within 1-2 years after index date, if not had before					
No	241(47.25%)	986(81.22%)	544(67.75%)	818(53.26%)	2589(63.72%)
Yes	269(52.75%)	228(18.78%)	259(32.25%)	718(46.74%)	1474(36.28%)
Total	510(100.00%)	1214(100.00%)	803(100.00%)	1536(100.00%)	4063(100.00%)

For cumulative values total are all study patients. For time periods 0-1, 1-2, 2-3, 3-Inf years total are patients who have follow-up at least until starting time of the respective time interval. Also if patient has his first measurement in time interval he is not in the risk set for the following time intervals.

Table 6.1: (continued)

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Having the first measurement within 2-3 years after index date, if not had before					
No	102(68.00%)	713(90.37%)	347(79.77%)	389(59.66%)	1551(76.55%)
Yes	48(32.00%)	76(9.63%)	88(20.23%)	263(40.34%)	475(23.45%)
Total	150(100.00%)	789(100.00%)	435(100.00%)	652(100.00%)	2026(100.00%)
Having the first measurement within 3-Inf years after index date, if not had before					
No	42(71.19%)	454(92.65%)	191(81.62%)	157(61.57%)	844(81.31%)
Yes	17(28.81%)	36(7.35%)	43(18.38%)	98(38.43%)	194(18.69%)
Total	59(100.00%)	490(100.00%)	234(100.00%)	255(100.00%)	1038(100.00%)

For cumulative values total are all study patients. For time periods 0-1, 1-2, 2-3, 3-Inf years total are patients who have follow-up at least until starting time of the respective time interval. Also if patient has his first measurement in time interval he is not in the risk set for the following time intervals.

Table 6.2: Number and percentage of patients with at least one S-LDL measurement taken within 12 to 36 months after index date

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Index – 12 months					
No	590(25.12%)	1201(52.79%)	842(38.22%)	1700(40.52%)	4333(39.31%)
Yes	1759(74.88%)	1074(47.21%)	1361(61.78%)	2495(59.48%)	6689(60.69%)
Index – 24 months					
No	305(12.98%)	1010(44.40%)	606(27.51%)	895(21.33%)	2816(25.55%)
Yes	2044(87.02%)	1265(55.60%)	1597(72.49%)	3300(78.67%)	8206(74.45%)
Index – 36 months					
No	256(10.90%)	953(41.89%)	528(23.97%)	587(13.99%)	2324(21.09%)
Yes	2093(89.10%)	1322(58.11%)	1675(76.03%)	3608(86.01%)	8698(78.91%)
Ever after index					
No	241(10.26%)	929(40.84%)	493(22.38%)	500(11.92%)	2163(19.62%)
Yes	2108(89.74%)	1346(59.16%)	1710(77.62%)	3695(88.08%)	8859(80.38%)
Having the first measurement within 0-1 years after index date, if not had before					
No	590(25.12%)	1201(52.79%)	842(38.22%)	1700(40.52%)	4333(39.31%)
Yes	1759(74.88%)	1074(47.21%)	1361(61.78%)	2495(59.48%)	6689(60.69%)
Total	2349(100.00%)	2275(100.00%)	2203(100.00%)	4195(100.00%)	11022(100.00%)
Having the first measurement within 1-2 years after index date, if not had before					
No	279(49.47%)	992(83.85%)	582(71.15%)	869(51.91%)	2722(64.21%)
Yes	285(50.53%)	191(16.15%)	236(28.85%)	805(48.09%)	1517(35.79%)
Total	564(100.00%)	1183(100.00%)	818(100.00%)	1674(100.00%)	4239(100.00%)

For cumulative values total are all study patients. For time periods 0-1, 1-2, 2-3, 3-Inf years total are patients who have follow-up at least until starting time of the respective time interval. Also if patient has his first measurement in time interval he is not in the risk set for the following time intervals.

Table 6.2: (continued)

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Having the first measurement within 2-3 years after index date, if not had before					
No	109(68.99%)	723(92.69%)	378(82.89%)	400(56.50%)	1610(76.59%)
Yes	49(31.01%)	57(7.31%)	78(17.11%)	308(43.50%)	492(23.41%)
Total	158(100.00%)	780(100.00%)	456(100.00%)	708(100.00%)	2102(100.00%)
Having the first measurement within 3-Inf years after index date, if not had before					
No	51(77.27%)	465(95.09%)	216(86.06%)	181(67.54%)	913(85.01%)
Yes	15(22.73%)	24(4.91%)	35(13.94%)	87(32.46%)	161(14.99%)
Total	66(100.00%)	489(100.00%)	251(100.00%)	268(100.00%)	1074(100.00%)

For cumulative values total are all study patients. For time periods 0-1, 1-2, 2-3, 3-Inf years total are patients who have follow-up at least until starting time of the respective time interval. Also if patient has his first measurement in time interval he is not in the risk set for the following time intervals.

Table 6.3: Number and percentage of patients with at least one fundus photography taken within 12 to 36 months after index date

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Index – 12 months					
No	2263(96.92%)	2247(99.21%)	1896(88.76%)	3773(91.29%)	10179(93.65%)
Yes	72(3.08%)	18(0.79%)	240(11.24%)	360(8.71%)	690(6.35%)
Total	2335(100.00%)	2265(100.00%)	2136(100.00%)	4133(100.00%)	10869(100.00%)
Index – 24 months					
No	2196(94.05%)	2210(97.57%)	1851(86.66%)	3600(87.10%)	9857(90.69%)
Yes	139(5.95%)	55(2.43%)	285(13.34%)	533(12.90%)	1012(9.31%)
Total	2335(100.00%)	2265(100.00%)	2136(100.00%)	4133(100.00%)	10869(100.00%)
Index – 36 months					
No	2056(88.05%)	2159(95.32%)	1823(85.35%)	3401(82.29%)	9439(86.84%)
Yes	279(11.95%)	106(4.68%)	313(14.65%)	732(17.71%)	1430(13.16%)
Total	2335(100.00%)	2265(100.00%)	2136(100.00%)	4133(100.00%)	10869(100.00%)
Ever after index					
No	1868(80.00%)	2078(91.74%)	1808(84.64%)	3124(75.59%)	8878(81.68%)
Yes	467(20.00%)	187(8.26%)	328(15.36%)	1009(24.41%)	1991(18.32%)
Total	2335(100.00%)	2265(100.00%)	2136(100.00%)	4133(100.00%)	10869(100.00%)
Having the first measurement within 0-1 years after index date, if not had before					
No	2263(96.92%)	2247(99.21%)	1896(88.76%)	3773(91.29%)	10179(93.65%)
Yes	72(3.08%)	18(0.79%)	240(11.24%)	360(8.71%)	690(6.35%)
Total	2335(100.00%)	2265(100.00%)	2136(100.00%)	4133(100.00%)	10869(100.00%)
Having the first measurement within 1-2 years after index date, if not had before					
No	2163(97.00%)	2178(98.33%)	1817(97.58%)	3560(95.37%)	9718(96.79%)
Yes	67(3.00%)	37(1.67%)	45(2.42%)	173(4.63%)	322(3.21%)
Total	2230(100.00%)	2215(100.00%)	1862(100.00%)	3733(100.00%)	10040(100.00%)

For cumulative values total are all study patients. For time periods 0-1, 1-2, 2-3, 3-Inf years total are patients who have follow-up at least until starting time of the respective time interval. Also if patient has his first measurement in time interval he is not in the risk set for the following time intervals.

Table 6.3: (continued)

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Having the first measurement within 2-3 years after index date, if not had before					
No	1596(91.94%)	1764(97.19%)	1492(98.16%)	2720(93.18%)	7572(94.77%)
Yes	140(8.06%)	51(2.81%)	28(1.84%)	199(6.82%)	418(5.23%)
Total	1736(100.00%)	1815(100.00%)	1520(100.00%)	2919(100.00%)	7990(100.00%)
Having the first measurement within 3-Inf years after index date, if not had before					
No	978(83.88%)	1202(93.69%)	1024(98.56%)	1624(85.43%)	4828(89.59%)
Yes	188(16.12%)	81(6.31%)	15(1.44%)	277(14.57%)	561(10.41%)
Total	1166(100.00%)	1283(100.00%)	1039(100.00%)	1901(100.00%)	5389(100.00%)

For cumulative values total are all study patients. For time periods 0-1, 1-2, 2-3, 3-Inf years total are patients who have follow-up at least until starting time of the respective time interval. Also if patient has his first measurement in time interval he is not in the risk set for the following time intervals.

Chapter 7

Realization of the Current Care guideline: Treatment decisions (other than diabetes treatment) based on follow-up measurements

Table 7.1: Number and percentage of patients with ACE/ARB prescriptions after blood pressure measurement >140/90

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
0 – 1 month after high blood pressure					
No	612(71.66%)	0(<i>NaN</i> %)	457(63.21%)	1260(74.78%)	2329(71.40%)
Yes	242(28.34%)	0(<i>NaN</i> %)	266(36.79%)	425(25.22%)	933(28.60%)
Total	854(100.00%)	0(<i>NaN</i> %)	723(100.00%)	1685(100.00%)	3262(100.00%)
0 – 3 months after high blood pressure					
No	406(47.54%)	0(<i>NaN</i> %)	306(42.32%)	803(47.66%)	1515(46.44%)
Yes	448(52.46%)	0(<i>NaN</i> %)	417(57.68%)	882(52.34%)	1747(53.56%)
Total	854(100.00%)	0(<i>NaN</i> %)	723(100.00%)	1685(100.00%)	3262(100.00%)
0 – 6 months after high blood pressure					
No	355(41.57%)	0(<i>NaN</i> %)	273(37.76%)	688(40.83%)	1316(40.34%)
Yes	499(58.43%)	0(<i>NaN</i> %)	450(62.24%)	997(59.17%)	1946(59.66%)
Total	854(100.00%)	0(<i>NaN</i> %)	723(100.00%)	1685(100.00%)	3262(100.00%)
Any time after high blood pressure					
No	303(35.48%)	0(<i>NaN</i> %)	214(29.60%)	449(26.65%)	966(29.61%)
Yes	551(64.52%)	0(<i>NaN</i> %)	509(70.40%)	1236(73.35%)	2296(70.39%)
Total	854(100.00%)	0(<i>NaN</i> %)	723(100.00%)	1685(100.00%)	3262(100.00%)

Total are patients who have high blood pressure (higher than 140/90) after index.

Table 7.2: Number and percentage of patients with prescriptions of metformin after GFR measurements <60

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
GFR <60 mL/min					
No	1672(74.25%)	1259(74.67%)	1470(78.99%)	3039(76.76%)	7440(76.25%)
Yes	580(25.75%)	427(25.33%)	391(21.01%)	920(23.24%)	2318(23.75%)
Total	2252(100.00%)	1686(100.00%)	1861(100.00%)	3959(100.00%)	9758(100.00%)
0 – 1 month after GFR <60					
No	419(72.24%)	327(76.58%)	315(80.56%)	762(82.83%)	1823(78.65%)
Yes	161(27.76%)	100(23.42%)	76(19.44%)	158(17.17%)	495(21.35%)
Total	580(100.00%)	427(100.00%)	391(100.00%)	920(100.00%)	2318(100.00%)
0 – 3 months after GFR <60					
No	318(54.83%)	228(53.40%)	268(68.54%)	629(68.37%)	1443(62.25%)
Yes	262(45.17%)	199(46.60%)	123(31.46%)	291(31.63%)	875(37.75%)
Total	580(100.00%)	427(100.00%)	391(100.00%)	920(100.00%)	2318(100.00%)
0 – 6 months after GFR <60					
No	272(46.90%)	204(47.78%)	243(62.15%)	576(62.61%)	1295(55.87%)
Yes	308(53.10%)	223(52.22%)	148(37.85%)	344(37.39%)	1023(44.13%)
Total	580(100.00%)	427(100.00%)	391(100.00%)	920(100.00%)	2318(100.00%)
Any time after GFR <60					
No	218(37.59%)	167(39.11%)	188(48.08%)	461(50.11%)	1034(44.61%)
Yes	362(62.41%)	260(60.89%)	203(51.92%)	459(49.89%)	1284(55.39%)
Total	580(100.00%)	427(100.00%)	391(100.00%)	920(100.00%)	2318(100.00%)

Total are patients who have GFR measurement <60 mL/min after index.

Table 7.3: Number and percentage of patients with prescriptions of metformin after GFR measurements <45

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
GFR <45 mL/min					
No	1994(88.54%)	1469(87.13%)	1650(88.66%)	3492(88.20%)	8605(88.18%)
Yes	258(11.46%)	217(12.87%)	211(11.34%)	467(11.80%)	1153(11.82%)
Total	2252(100.00%)	1686(100.00%)	1861(100.00%)	3959(100.00%)	9758(100.00%)
0 – 1 month after GFR <45					
No	199(77.13%)	177(81.57%)	177(83.89%)	420(89.94%)	973(84.39%)
Yes	59(22.87%)	40(18.43%)	34(16.11%)	47(10.06%)	180(15.61%)
Total	258(100.00%)	217(100.00%)	211(100.00%)	467(100.00%)	1153(100.00%)
0 – 3 months after GFR <45					
No	165(63.95%)	141(64.98%)	154(72.99%)	364(77.94%)	824(71.47%)
Yes	93(36.05%)	76(35.02%)	57(27.01%)	103(22.06%)	329(28.53%)
Total	258(100.00%)	217(100.00%)	211(100.00%)	467(100.00%)	1153(100.00%)
0 – 6 months after GFR <45					
No	147(56.98%)	134(61.75%)	144(68.25%)	341(73.02%)	766(66.44%)
Yes	111(43.02%)	83(38.25%)	67(31.75%)	126(26.98%)	387(33.56%)
Total	258(100.00%)	217(100.00%)	211(100.00%)	467(100.00%)	1153(100.00%)
Any time after GFR <45					
No	128(49.61%)	123(56.68%)	124(58.77%)	307(65.74%)	682(59.15%)
Yes	130(50.39%)	94(43.32%)	87(41.23%)	160(34.26%)	471(40.85%)
Total	258(100.00%)	217(100.00%)	211(100.00%)	467(100.00%)	1153(100.00%)

Total are patients who have GFR measurement <45 mL/min after index.

Table 7.4: Number and percentage of patients with prescriptions of metformin after GFR measurements <30

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
GFR <30 mL/min					
No	2141(95.07%)	1589(94.25%)	1767(94.95%)	3760(94.97%)	9257(94.87%)
Yes	111(4.93%)	97(5.75%)	94(5.05%)	199(5.03%)	501(5.13%)
Total	2252(100.00%)	1686(100.00%)	1861(100.00%)	3959(100.00%)	9758(100.00%)
0 – 1 month after GFR <30					
No	92(82.88%)	85(87.63%)	79(84.04%)	190(95.48%)	446(89.02%)
Yes	19(17.12%)	12(12.37%)	15(15.96%)	9(4.52%)	55(10.98%)
Total	111(100.00%)	97(100.00%)	94(100.00%)	199(100.00%)	501(100.00%)
0 – 3 months after GFR <30					
No	80(72.07%)	77(79.38%)	73(77.66%)	175(87.94%)	405(80.84%)
Yes	31(27.93%)	20(20.62%)	21(22.34%)	24(12.06%)	96(19.16%)
Total	111(100.00%)	97(100.00%)	94(100.00%)	199(100.00%)	501(100.00%)
0 – 6 months after GFR <30					
No	73(65.77%)	75(77.32%)	70(74.47%)	170(85.43%)	388(77.45%)
Yes	38(34.23%)	22(22.68%)	24(25.53%)	29(14.57%)	113(22.55%)
Total	111(100.00%)	97(100.00%)	94(100.00%)	199(100.00%)	501(100.00%)
Any time after GFR <30					
No	66(59.46%)	71(73.20%)	64(68.09%)	162(81.41%)	363(72.46%)
Yes	45(40.54%)	26(26.80%)	30(31.91%)	37(18.59%)	138(27.54%)
Total	111(100.00%)	97(100.00%)	94(100.00%)	199(100.00%)	501(100.00%)

Total are patients who have GFR measurement <30 mL/min after index.

Table 7.5: Number and percentage of patients with prescriptions of metformin after S-CREA >150 mmol/L

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
S-CREA >150 mmol/L					
No	2111(93.74%)	1558(92.41%)	1751(94.09%)	3716(93.86%)	9136(93.63%)
Yes	141(6.26%)	128(7.59%)	110(5.91%)	243(6.14%)	622(6.37%)
Total	2252(100.00%)	1686(100.00%)	1861(100.00%)	3959(100.00%)	9758(100.00%)
0 – 1 month after CREA >150					
No	109(77.30%)	110(85.94%)	93(84.55%)	228(93.83%)	540(86.82%)
Yes	32(22.70%)	18(14.06%)	17(15.45%)	15(6.17%)	82(13.18%)
Total	141(100.00%)	128(100.00%)	110(100.00%)	243(100.00%)	622(100.00%)
0 – 3 months after CREA >150					
No	96(68.09%)	99(77.34%)	86(78.18%)	211(86.83%)	492(79.10%)
Yes	45(31.91%)	29(22.66%)	24(21.82%)	32(13.17%)	130(20.90%)
Total	141(100.00%)	128(100.00%)	110(100.00%)	243(100.00%)	622(100.00%)
0 – 6 months after CREA >150					
No	90(63.83%)	94(73.44%)	80(72.73%)	201(82.72%)	465(74.76%)
Yes	51(36.17%)	34(26.56%)	30(27.27%)	42(17.28%)	157(25.24%)
Total	141(100.00%)	128(100.00%)	110(100.00%)	243(100.00%)	622(100.00%)
Any time after CREA >150					
No	80(56.74%)	88(68.75%)	73(66.36%)	187(76.95%)	428(68.81%)
Yes	61(43.26%)	40(31.25%)	37(33.64%)	56(23.05%)	194(31.19%)
Total	141(100.00%)	128(100.00%)	110(100.00%)	243(100.00%)	622(100.00%)

Total are patients who have S-CREA measurement >150 mmol/L after index.

Table 7.6: Number and percentage of patients with prescriptions of ACE/ARB after albumin measurement

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
cU-Alb or nU-Alb \geq 20 mg/min					
No	93(62.00%)	136(59.91%)	4(25.00%)	206(56.44%)	439(57.92%)
Yes	57(38.00%)	91(40.09%)	12(75.00%)	159(43.56%)	319(42.08%)
Total	150(100.00%)	227(100.00%)	16(100.00%)	365(100.00%)	758(100.00%)
0 – 1 month after cU-Alb or nU-Alb \geq 20					
No	37(64.91%)	58(63.74%)	7(58.33%)	106(66.67%)	208(65.20%)
Yes	20(35.09%)	33(36.26%)	5(41.67%)	53(33.33%)	111(34.80%)
Total	57(100.00%)	91(100.00%)	12(100.00%)	159(100.00%)	319(100.00%)
0 – 3 months after cU-Alb or nU-Alb \geq 20					
No	18(31.58%)	31(34.07%)	4(33.33%)	59(37.11%)	112(35.11%)
Yes	39(68.42%)	60(65.93%)	8(66.67%)	100(62.89%)	207(64.89%)
Total	57(100.00%)	91(100.00%)	12(100.00%)	159(100.00%)	319(100.00%)
0 – 6 months after cU-Alb or nU-Alb \geq 20					
No	15(26.32%)	23(25.27%)	3(25.00%)	47(29.56%)	88(27.59%)
Yes	42(73.68%)	68(74.73%)	9(75.00%)	112(70.44%)	231(72.41%)
Total	57(100.00%)	91(100.00%)	12(100.00%)	159(100.00%)	319(100.00%)
Any time after cU-Alb or nU-Alb \geq 20					
No	13(22.81%)	18(19.78%)	3(25.00%)	28(17.61%)	62(19.44%)
Yes	44(77.19%)	73(80.22%)	9(75.00%)	131(82.39%)	257(80.56%)
Total	57(100.00%)	91(100.00%)	12(100.00%)	159(100.00%)	319(100.00%)

Total are patients who have cU-Alb or nU-Alb \geq 20 mg/min after index.

Table 7.7: Number and percentage of patients with prescriptions of ACE/ARB after albumin measurement

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
dU-Alb \geq 30 mg/d					
No	0(<i>NaN</i> %)	0(<i>NaN</i> %)	0(<i>NaN</i> %)	1(20.00%)	1(20.00%)
Yes	0(<i>NaN</i> %)	0(<i>NaN</i> %)	0(<i>NaN</i> %)	4(80.00%)	4(80.00%)
Total	0(<i>NaN</i> %)	0(<i>NaN</i> %)	0(<i>NaN</i> %)	5(100.00%)	5(100.00%)
0 – 1 month after dU-Alb \geq 30					
No	0(<i>NaN</i> %)	0(<i>NaN</i> %)	0(<i>NaN</i> %)	3(75.00%)	3(75.00%)
Yes	0(<i>NaN</i> %)	0(<i>NaN</i> %)	0(<i>NaN</i> %)	1(25.00%)	1(25.00%)
Total	0(<i>NaN</i> %)	0(<i>NaN</i> %)	0(<i>NaN</i> %)	4(100.00%)	4(100.00%)
0 – 3 months after dU-Alb \geq 30					
No	0(<i>NaN</i> %)	0(<i>NaN</i> %)	0(<i>NaN</i> %)	1(25.00%)	1(25.00%)
Yes	0(<i>NaN</i> %)	0(<i>NaN</i> %)	0(<i>NaN</i> %)	3(75.00%)	3(75.00%)
Total	0(<i>NaN</i> %)	0(<i>NaN</i> %)	0(<i>NaN</i> %)	4(100.00%)	4(100.00%)
0 – 6 months after dU-Alb \geq 30					
No	0(<i>NaN</i> %)	0(<i>NaN</i> %)	0(<i>NaN</i> %)	1(25.00%)	1(25.00%)
Yes	0(<i>NaN</i> %)	0(<i>NaN</i> %)	0(<i>NaN</i> %)	3(75.00%)	3(75.00%)
Total	0(<i>NaN</i> %)	0(<i>NaN</i> %)	0(<i>NaN</i> %)	4(100.00%)	4(100.00%)
Any time after dU-Alb \geq 30					
No	0(<i>NaN</i> %)	0(<i>NaN</i> %)	0(<i>NaN</i> %)	1(25.00%)	1(25.00%)
Yes	0(<i>NaN</i> %)	0(<i>NaN</i> %)	0(<i>NaN</i> %)	3(75.00%)	3(75.00%)
Total	0(<i>NaN</i> %)	0(<i>NaN</i> %)	0(<i>NaN</i> %)	4(100.00%)	4(100.00%)

Total are patients who have dU-Alb \geq 30 mg/d after index.

Table 7.8: Number and percentage of patients with prescriptions of ACE/ARB after albumin measurement

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
U-AlbCrea or nU-AlbCrea \geq 2.5, 3.5 mg/mmol					
No	1348(79.57%)	248(70.25%)	278(58.16%)	1620(80.44%)	3494(76.98%)
Yes	346(20.43%)	105(29.75%)	200(41.84%)	394(19.56%)	1045(23.02%)
Total	1694(100.00%)	353(100.00%)	478(100.00%)	2014(100.00%)	4539(100.00%)
0 – 1 month after U-AlbCrea or nU-AlbCrea \geq 2.5, 3.5					
No	229(66.18%)	76(72.38%)	125(62.50%)	275(69.80%)	705(67.46%)
Yes	117(33.82%)	29(27.62%)	75(37.50%)	119(30.20%)	340(32.54%)
Total	346(100.00%)	105(100.00%)	200(100.00%)	394(100.00%)	1045(100.00%)
0 – 3 months after U-AlbCrea or nU-AlbCrea \geq 2.5, 3.5					
No	134(38.73%)	47(44.76%)	68(34.00%)	170(43.15%)	419(40.10%)
Yes	212(61.27%)	58(55.24%)	132(66.00%)	224(56.85%)	626(59.90%)
Total	346(100.00%)	105(100.00%)	200(100.00%)	394(100.00%)	1045(100.00%)
0 – 6 months after U-AlbCrea or nU-AlbCrea \geq 2.5, 3.5					
No	109(31.50%)	33(31.43%)	56(28.00%)	134(34.01%)	332(31.77%)
Yes	237(68.50%)	72(68.57%)	144(72.00%)	260(65.99%)	713(68.23%)
Total	346(100.00%)	105(100.00%)	200(100.00%)	394(100.00%)	1045(100.00%)
Any time after U-AlbCrea or nU-AlbCrea \geq 2.5, 3.5					
No	80(23.12%)	27(25.71%)	42(21.00%)	94(23.86%)	243(23.25%)
Yes	266(76.88%)	78(74.29%)	158(79.00%)	300(76.14%)	802(76.75%)
Total	346(100.00%)	105(100.00%)	200(100.00%)	394(100.00%)	1045(100.00%)

Total are patients who have U-AlbCrea or nU-AlbCrea \geq 2.5 mg/mmol for men and \geq 3.5 mg/mmol for women after index.

Table 7.9: Number and percentage of patients with prescriptions of statins after measurement of S-LDL >2.5 mmol/L

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
0 – 1 month after S-LDL >2.5					
No	1090(77.75%)	609(70.98%)	728(67.35%)	1615(74.66%)	4042(73.44%)
Yes	312(22.25%)	249(29.02%)	353(32.65%)	548(25.34%)	1462(26.56%)
Total	1402(100.00%)	858(100.00%)	1081(100.00%)	2163(100.00%)	5504(100.00%)
0 – 3 months after S-LDL >2.5					
No	842(60.06%)	470(54.78%)	583(53.93%)	1268(58.62%)	3163(57.47%)
Yes	560(39.94%)	388(45.22%)	498(46.07%)	895(41.38%)	2341(42.53%)
Total	1402(100.00%)	858(100.00%)	1081(100.00%)	2163(100.00%)	5504(100.00%)
0 – 6 months after S-LDL >2.5					
No	756(53.92%)	410(47.79%)	523(48.38%)	1157(53.49%)	2846(51.71%)
Yes	646(46.08%)	448(52.21%)	558(51.62%)	1006(46.51%)	2658(48.29%)
Total	1402(100.00%)	858(100.00%)	1081(100.00%)	2163(100.00%)	5504(100.00%)
Any time after S-LDL >2.5					
No	576(41.08%)	297(34.62%)	362(33.49%)	754(34.86%)	1989(36.14%)
Yes	826(58.92%)	561(65.38%)	719(66.51%)	1409(65.14%)	3515(63.86%)
Total	1402(100.00%)	858(100.00%)	1081(100.00%)	2163(100.00%)	5504(100.00%)

Total are patients who have S-LDL measurement >2.5 mmol/L after index and who did not have prior diagnosis of coronary artery disease or stroke/TIA or peripheral circulatory complications at baseline.

Table 7.10: Number and percentage of patients with prescriptions of statins after measurement of S-LDL >1.8 mmol/L

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
0 – 1 month after S-LDL >1.8					
No	253(61.41%)	111(66.87%)	197(55.65%)	513(70.95%)	1074(64.89%)
Yes	159(38.59%)	55(33.13%)	157(44.35%)	210(29.05%)	581(35.11%)
Total	412(100.00%)	166(100.00%)	354(100.00%)	723(100.00%)	1655(100.00%)
0 – 3 months after S-LDL >1.8					
No	123(29.85%)	52(31.33%)	89(25.14%)	272(37.62%)	536(32.39%)
Yes	289(70.15%)	114(68.67%)	265(74.86%)	451(62.38%)	1119(67.61%)
Total	412(100.00%)	166(100.00%)	354(100.00%)	723(100.00%)	1655(100.00%)
0 – 6 months after S-LDL >1.8					
No	84(20.39%)	37(22.29%)	53(14.97%)	194(26.83%)	368(22.24%)
Yes	328(79.61%)	129(77.71%)	301(85.03%)	529(73.17%)	1287(77.76%)
Total	412(100.00%)	166(100.00%)	354(100.00%)	723(100.00%)	1655(100.00%)
Any time after S-LDL >1.8					
No	59(14.32%)	23(13.86%)	32(9.04%)	122(16.87%)	236(14.26%)
Yes	353(85.68%)	143(86.14%)	322(90.96%)	601(83.13%)	1419(85.74%)
Total	412(100.00%)	166(100.00%)	354(100.00%)	723(100.00%)	1655(100.00%)

Total are patients who have S-LDL measurement >1.8 mmol/L after index and prior diagnosis of coronary artery disease or stroke/TIA or peripheral circulatory complications at baseline.

Chapter 8

Other endpoints

Table 8.1: Mortality

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Mortality					
No	2214(94.25%)	2137(93.93%)	2057(93.37%)	3938(93.87%)	10346(93.87%)
Yes	135(5.75%)	138(6.07%)	146(6.63%)	257(6.13%)	676(6.13%)
Time until death					
[0,1)	34(25.19%)	32(23.19%)	38(26.03%)	43(16.73%)	147(21.75%)
[1,2)	37(27.41%)	39(28.26%)	37(25.34%)	71(27.63%)	184(27.22%)
[2,3)	27(20.00%)	31(22.46%)	40(27.40%)	74(28.79%)	172(25.44%)
[3,Inf)	37(27.41%)	36(26.09%)	31(21.23%)	69(26.85%)	173(25.59%)
Total	135(100.00%)	138(100.00%)	146(100.00%)	257(100.00%)	676(100.00%)
range (min,max)	(0.01, 4.90)	(0.00, 4.85)	(0.05, 4.68)	(0.01, 4.91)	(0.00, 4.91)
mean (+/-sd)	2.06 (1.26)	2.04 (1.24)	1.94 (1.19)	2.22 (1.19)	2.09(1.22)
median (Q1,Q3)	1.83 (1.04, 3.15)	1.93 (1.10, 3.07)	1.88 (0.96, 2.82)	2.28 (1.29, 3.05)	2.05(1.15, 3.02)

Table 8.2: Number and percentage of patients with amputations of the lower extremities (NSCP: NFQ20, NGQ10, NGQ20, NHQ10, NHQ20, NHQ30, NHQ40) during follow-up

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Amputations					
No	2341(99.66%)	2263(99.47%)	2198(99.77%)	4177(99.57%)	10979(99.61%)
Yes	8(0.34%)	12(0.53%)	5(0.23%)	18(0.43%)	43(0.39%)

Table 8.3: Number and percentage of patients with absences from work over 10 days during follow-up

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Absence from work (Long absences over 10 days)					
No	2043(86.97%)	1977(86.90%)	1932(87.70%)	3805(90.70%)	9757(88.52%)
Yes	306(13.03%)	298(13.10%)	271(12.30%)	390(9.30%)	1265(11.48%)

Table 8.4: Number and percentage of patients with severe hypoglycemic events (ICD-10: E11.00 or ICPC-2: T87) during follow-up

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
severe hypoglycemic events					
No	2190(93.23%)	2195(96.48%)	2156(97.87%)	4126(98.36%)	10667(96.78%)
Yes	159(6.77%)	80(3.52%)	47(2.13%)	69(1.64%)	355(3.22%)

Chapter 9

Measurements during follow-up

Table 9.1: Measurements done

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Measurement done for HbA1c*					
[0 – 6) months	1903(81.01%)	1058(46.51%)	1340(60.83%)	2455(58.52%)	6756(61.30%)
[0 – 1) year	2105(89.61%)	1228(53.98%)	1543(70.04%)	2972(70.85%)	7848(71.20%)
[0 – 2) years	2191(93.27%)	1349(59.30%)	1678(76.17%)	3526(84.05%)	8744(79.33%)
[0 – 3) years	2212(94.17%)	1389(61.05%)	1731(78.57%)	3742(89.20%)	9074(82.33%)
Ever after index	2220(94.51%)	1411(62.02%)	1752(79.53%)	3832(91.35%)	9215(83.61%)
Total	2349(100.00%)	2275(100.00%)	2203(100.00%)	4195(100.00%)	11022(100.00%)
Measurement done for S-CREA*					
[0 – 6) months	1665(70.88%)	1097(48.22%)	1190(54.02%)	2328(55.49%)	6280(56.98%)
[0 – 1) year	2033(86.55%)	1400(61.54%)	1511(68.59%)	3065(73.06%)	8009(72.66%)
[0 – 2) years	2204(93.83%)	1606(70.59%)	1765(80.12%)	3721(88.70%)	9296(84.34%)
[0 – 3) years	2238(95.27%)	1664(73.14%)	1828(82.98%)	3911(93.23%)	9641(87.47%)
Ever after index	2252(95.87%)	1686(74.11%)	1861(84.48%)	3959(94.37%)	9758(88.53%)
Total	2349(100.00%)	2275(100.00%)	2203(100.00%)	4195(100.00%)	11022(100.00%)
Measurement done for S-LDL*					
[0 – 6) months	1311(55.81%)	832(36.57%)	1029(46.71%)	1673(39.88%)	4845(43.96%)
[0 – 1) year	1759(74.88%)	1074(47.21%)	1361(61.78%)	2495(59.48%)	6689(60.69%)
[0 – 2) years	2044(87.02%)	1265(55.60%)	1597(72.49%)	3300(78.67%)	8206(74.45%)
[0 – 3) years	2093(89.10%)	1322(58.11%)	1675(76.03%)	3608(86.01%)	8698(78.91%)
Ever after index	2108(89.74%)	1346(59.16%)	1710(77.62%)	3695(88.08%)	8859(80.38%)
Total	2349(100.00%)	2275(100.00%)	2203(100.00%)	4195(100.00%)	11022(100.00%)
Measurement done for U-Alb*					
[0 – 6) months	733(31.20%)	304(13.36%)	425(19.29%)	738(17.59%)	2200(19.96%)
[0 – 1) year	1095(46.62%)	500(21.98%)	628(28.51%)	1347(32.11%)	3570(32.39%)
[0 – 2) years	1503(63.98%)	752(33.05%)	892(40.49%)	2094(49.92%)	5241(47.55%)
[0 – 3) years	1653(70.37%)	902(39.65%)	1043(47.34%)	2458(58.59%)	6056(54.94%)
Ever after index	1719(73.18%)	985(43.30%)	1142(51.84%)	2659(63.38%)	6505(59.02%)
Total	2349(100.00%)	2275(100.00%)	2203(100.00%)	4195(100.00%)	11022(100.00%)

Table 9.1: (continued)

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Measurement done for P-ALAT*					
[0 – 6) months	1424(60.62%)	817(35.91%)	1039(47.16%)	1898(45.24%)	5178(46.98%)
[0 – 1) year	1836(78.16%)	1053(46.29%)	1391(63.14%)	2646(63.08%)	6926(62.84%)
[0 – 2) years	2105(89.61%)	1281(56.31%)	1650(74.90%)	3364(80.19%)	8400(76.21%)
[0 – 3) years	2153(91.66%)	1357(59.65%)	1738(78.89%)	3627(86.46%)	8875(80.52%)
Ever after index	2170(92.38%)	1393(61.23%)	1781(80.84%)	3725(88.80%)	9069(82.28%)
Total	2349(100.00%)	2275(100.00%)	2203(100.00%)	4195(100.00%)	11022(100.00%)
Dietary advice*					
[0 – 6) months	29(1.23%)	8(0.35%)	25(1.13%)	70(1.67%)	132(1.20%)
[0 – 1) year	45(1.92%)	11(0.48%)	37(1.68%)	89(2.12%)	182(1.65%)
[0 – 2) years	74(3.15%)	22(0.97%)	61(2.77%)	117(2.79%)	274(2.49%)
[0 – 3) years	104(4.43%)	33(1.45%)	83(3.77%)	145(3.46%)	365(3.31%)
Ever after index	132(5.62%)	60(2.64%)	132(5.99%)	170(4.05%)	494(4.48%)
Total	2349(100.00%)	2275(100.00%)	2203(100.00%)	4195(100.00%)	11022(100.00%)
Exercise consultation*					
[0 – 6) months	11(0.47%)	1(0.04%)	5(0.23%)	17(0.41%)	34(0.31%)
[0 – 1) year	14(0.60%)	2(0.09%)	13(0.59%)	21(0.50%)	50(0.45%)
[0 – 2) years	27(1.15%)	8(0.35%)	27(1.23%)	33(0.79%)	95(0.86%)
[0 – 3) years	41(1.75%)	12(0.53%)	41(1.86%)	44(1.05%)	138(1.25%)
Ever after index	51(2.17%)	27(1.19%)	62(2.81%)	50(1.19%)	190(1.72%)
Total	2349(100.00%)	2275(100.00%)	2203(100.00%)	4195(100.00%)	11022(100.00%)
Dental visits*					
[0 – 6) months	307(13.07%)	512(22.51%)	575(26.10%)	693(16.52%)	2087(18.93%)
[0 – 1) year	494(21.03%)	727(31.96%)	838(38.04%)	1144(27.27%)	3203(29.06%)
[0 – 2) years	757(32.23%)	991(43.56%)	1161(52.70%)	1790(42.67%)	4699(42.63%)
[0 – 3) years	983(41.85%)	1164(51.16%)	1333(60.51%)	2144(51.11%)	5624(51.03%)
Ever after index	1146(48.79%)	1253(55.08%)	1412(64.09%)	2347(55.95%)	6158(55.87%)
Total	2349(100.00%)	2275(100.00%)	2203(100.00%)	4195(100.00%)	11022(100.00%)

Table 9.1: (continued)

	Kainuu patients N = 2349	Kanta-Häme patients N = 2275	Oulu patients N = 2203	Pohjois-Karjala patients N = 4195	Total N = 11022
Foot therapist visits*					
[0 – 6) months	3(0.13%)	4(0.18%)	0(0.00%)	1(0.02%)	8(0.07%)
[0 – 1) year	5(0.21%)	6(0.26%)	0(0.00%)	3(0.07%)	14(0.13%)
[0 – 2) years	8(0.34%)	17(0.75%)	0(0.00%)	16(0.38%)	41(0.37%)
[0 – 3) years	10(0.43%)	34(1.49%)	1(0.05%)	26(0.62%)	71(0.64%)
Ever after index	11(0.47%)	55(2.42%)	1(0.05%)	46(1.10%)	113(1.03%)
Total	2349(100.00%)	2275(100.00%)	2203(100.00%)	4195(100.00%)	11022(100.00%)
Fundus photography*					
[0 – 6) months	39(1.66%)	9(0.40%)	118(5.36%)	245(5.84%)	411(3.73%)
[0 – 1) year	75(3.19%)	20(0.88%)	256(11.62%)	363(8.65%)	714(6.48%)
[0 – 2) years	143(6.09%)	57(2.51%)	304(13.80%)	539(12.85%)	1043(9.46%)
[0 – 3) years	284(12.09%)	108(4.75%)	333(15.12%)	740(17.64%)	1465(13.29%)
Ever after index	472(20.09%)	189(8.31%)	348(15.80%)	1022(24.36%)	2031(18.43%)
Total	2349(100.00%)	2275(100.00%)	2203(100.00%)	4195(100.00%)	11022(100.00%)

Index events

Inclusion criteria	Codes	Registeries				
		National	Kainuu HD	Kanta-Häme HD	Oulu city	Pohjois-Karjala HD
Diagnoses of diabetes	ICD-10: E10*, E11*, E13*, E14* ICPC-2: T89, T90	-	ICD-10 codes ICPC-2 codes	ICD-10 codes	ICD-10 codes ICPC-2 codes	ICD-10 codes ICPC-2 codes
Written prescription	A10A*, A10B*	-	Written prescriptions	Written prescriptions	Written prescriptions	Written prescriptions
HbA1c ≥ 6.5%	-	-	B -GHb-A1C (1560) B -HbA1c (6128)	B -GHb-A1C (1560) B -Hb-A1C (1560) B -Hb-A1C% (1560) B -HbA1c (6128) B -Hb-A1c (6128)	B -Hb-A1C (1560) B -HbA1c (6128)	B -HbA1C B -Hb-A1c
Glucose tolerance ≥ 11 mmol/L	LPt-Gluk-R (20271)	-	P-Gluk	P-Gluk 0 P- Gluk 1H P-Gluk 2H	P-Gluk	Pt-Gluk-R1-0 Pt-Gluk-R1-1 Pt-Gluk-R1-2
Nutrition counselling related to diabetes	SPAT1139 (Nutrition survey) SPAT1306 (nutrition and weight control counselling)	-	SPAT codes	SPAT codes	SPAT codes	SPAT codes
Purchased prescriptions	A10A*, A10B*	SII: reimbursed drugs	-	-	-	-
Special reimbursement for diabetes	103	SII: reimbursement decisions	-	-	-	-

THL1: Hospital discharge register, THL2: Primary care register, SII: Social insurance institution, SF: Statistics Finland

Baseline characteristics

Baseline characteristics	Codes/classification	Registeries				
		National	Kainuu HD	Kanta-Häme HD	Oulu city	Pohjois-Karjala HD
Index site	Kainuu , KHSHP , Oulu, PKSHP	SII: Municipalities	-	-	-	-
Age (extacted from original ID)	<50, 50-59, 60-69, 70-79, 80 and over	-	-	-	-	-
Gender (extacted from original ID)	Male, Female	-	-	-	-	-
Smoking	ICD-10: Z720 ICPC-2: P17	THL1: ICD-10 codes THL2: ICPC-2 codes ICD-10 codes, smoking records	ICD-10 codes, Smokng records	ICD-10 codes	ICD-10 codes, smoking records	ICD-10 codes, smoking records
BMI	<25 25-29.9 30-34.9 35-39.9 ≥ 40	THL2: Records of heigth and weigth	BMI records	No records	BMI records	Records of BMI, heigth and weigth
Dietary habits	Any records	-	-	-	-	-
Physical exercide	Any records	-	-	-	-	-
Concomitant diseases at baseline	Diagnoses and reimbursement codes listed in protocoll, Annex 3	THL1: ICD-10 codes THL2: ICPC-2 codes, ICD-10 codes SII: Reimbursement decisions, reimbursed drugs	ICD-10 codes	ICD-10 codes	ICD-10 codes	ICD-10 codes
Concomitant medications at baseline	ATC-codes (3 digit level)	SII: reimbursed drugs	Written prescriptions	Written prescriptions	Written prescriptions	Written prescriptions

THL1: Hospital discharge register, THL2: Primary care register, SII: Social insurance institution, SF: Statistics Finland

Laboratory and blood pressure measurements

Baseline characteristics	Codes/classification	Registeries				
		National	Kainuu HD	Kanta-Häme HD	Oulu city	Pohjois-Karjala HD
HbA1c	<6.5, 6.5-6.9, 7.0-7.9 >=8	-	B -GHb-A1C (1560) B -HbA1c (6128) B -HbA1cVT (11246)	B -Hb-A1C% (1560) B -HbA1c (6128)	B -Hb-A1C (1560) B -HbA1c (6128)	B -HbA1c B -Hb-A1C B -Hb-A1C*
P/S-CREA	<130, 130-150, >= 150	-	fS-Krea (2143) P -Krea (4600)	fS-Krea (2143) P -Krea (4600, 2142)	fS-Krea (10302) P -Krea (4600)	P -Krea, P -Krea*
Calculated GFR	<60, >= 60	-	Calculated using CKD-EPI formula from fS-Krea (2143) P -Krea (4600)	Calculated using CKD-EPI formula from fS-Krea (2143) P -Krea (4600, 2142)	Calculated using CKD-EPI formula from fS-Krea (10302) P -Krea (4600)	Calculated using CKD-EPI formula from P -Krea, P -Krea*
S-LDL	<1.8, 1.8-2.5, >=2.5	-	fP-Kol-LDL (4599, 9999)	fP-Kol-LDL (4599)	fP-Kol-LDL (4599)	fP-Kol-LDL
	-	-				
P-ALAT	-	-	P -ALAT (1024)	P -ALAT (1024)	P -ALAT (1024)	P -ALAT (1024)
cU-Alb (3557)	-	-	No records	cU-Alb (3557, 35570)	No records	cU-Alb
nU-Alb (4836)	-	-	nU-Alb-Mi (4836)	cU-Alb-Mi (4084)	cU-Alb-Mi (4084)	cU-Alb-Mi
dU-Alb (3134)	-	-	-	-	dU-Alb (3134)	dU-Alb
U-AlbCrea (4511)	-	-	U -AlbKre (4511)	U -AlbKre (4511)	U -AlbKre (4511)	U -AlbKre
nU-AlbCrea (23572)	-	-	No records	No records	No records	No records
U-Alb	-	-	U-Alb (1029, 9012)	U -Alb (316, 1029)	U -Alb (1029)	U -Alb
Blood pressure	<130/80, not <130/80	-	Local blood pressure data	-	Local blood pressure data	Local blood pressure data

Drugs

Baseline characteristics	ATC codes	Registeries				
		National	Kainuu HD	Kanta-Häme HD	Oulu city	Pohjois-Karjala HD
Metformin	A10BA02	SII: reimbursed drugs	Written prescriptions	Written prescriptions	Written prescriptions	Written prescriptions
Metformin combinations	A10BD03 A10BD05 A10BD07 A10BD08 A10BD11 A10BD13	SII: reimbursed drugs	Written prescriptions	Written prescriptions	Written prescriptions	Written prescriptions
Insulin	ATC: A10A	SII: reimbursed drugs	Written prescriptions	Written prescriptions	Written prescriptions	Written prescriptions
DDP4 inhibitors	ATC: A10BH	SII: reimbursed drugs	Written prescriptions	Written prescriptions	Written prescriptions	Written prescriptions
Sulfonylureas	ATC: A10BB	SII: reimbursed drugs	Written prescriptions	Written prescriptions	Written prescriptions	Written prescriptions
Thiazolidinediones	A10BD03 A10BD05 A10BD09 A10BG02 A10BG03	SII: reimbursed drugs	Written prescriptions	Written prescriptions	Written prescriptions	Written prescriptions
GLP-1 analogues	A10BX04 A10BX07	SII: reimbursed drugs	Written prescriptions	Written prescriptions	Written prescriptions	Written prescriptions
SGLT-2 inhibitors	A10BX09	SII: reimbursed drugs	Written prescriptions	Written prescriptions	Written prescriptions	Written prescriptions
ACE/ARB drugs	Listed in study protocol Annex 6	SII: reimbursed drugs	Written prescriptions	Written prescriptions	Written prescriptions	Written prescriptions

Other records

Baseline characteristics	Codes/classification	Registeries				
		National	Kainuu HD	Kanta-Häme HD	Oulu city	Pohjois-Karjala HD
Dietary advise	SPAT1139 (Nutrition survey) SPAT1306 (nutrition and weight control counselling) Other relevant information	THL2: SPAT codes	SPAT codes Records of dietary advice	No SPAT codes or other records available	SPAT codes	SPAT codes
Exercise consultation	SPAT1305 (Exercise counselling) Other relevant information	THL2: SPAT codes	SPAT codes, Records of excercise consultation	No SPAT codes or other records available	SPAT codes	SPAT codes
Visit to foot therapist	SPAT1225 (Foot therapy) SPAT1299 (Other procedure related to foot therapy) Service type: T55 (Foot therapy)	THL2: SPAT codes, service type	SPAT codes (dates from 1.12.2011) 'Ravintotailiikuntaohj aus' [Diabeetikon jalkojenhoito])	No SPAT codes or other records available	SPAT codes	SPAT codes
Foot risk score available		No records	Records of foot risk score	No records	No records	Records of foot risk score
Visit to dentist	Service type: T60 Professional: 2222, 3225 or 51325 Procedure of mouths Reimbursements of dental visits	THL2: Service type, professional, procedures of mouths SII: reimbursements of dental visits	No records	No records	No records	No records
Death	Any code	SF: Causes of death	No records	No records	No records	No records
Amputations	NCSP codes NFQ20, NGQ10, NGQ20, NHQ10, NHQ20, NHQ30, NHQ40	THL1: NCSP-codes for procedures	NCSP-codes for procedures	NCSP-codes for procedures	NCSP-codes for procedures	NCSP-codes for procedures

Long absences from work		SII: sickness allowance register	No records	No records	No records	No records
Severe hypoglycemic events	ICD-10: E11.00 ICPC-2: T87	THL1: ICD-10 codes THL2: ICD-10 codes, ICPC2 codes	ICD-10 codes	ICD-10 codes	ICD-10 codes	ICD-10 codes

THL1: Hospital discharge register, THL2: Primary care register, SII: Social insurance institution, SF: Statistics Finland