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IDENTIFYING DETERMINANTS AFFECTING FOOT ULCER MANAGEMENT OUTCOMES AND COSTS BASED ON INSURANCE REIMBURSEMENT DATA OF DIABETIC PATIENTS IN ESTONIA

Master's thesis

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JALAHAAVANDITE KÄSITLUSE TULEMUSLIKKUST JA KULUSID MÕJUTAVATE TEGURITE LEIDMINE EESTI DIABEEDIPATSIENTIDE RAVIKINDLUSTUSE ANDMETE PÕHJAL

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Juhendaja: Priit Kruus
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Author’s declaration of originality

I hereby certify that I am the sole author of this thesis. All the used materials, references to the literature and the work of others have been referred to. This thesis has not been presented for examination anywhere else.

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Abstract

Background: Costs associated with the management of diabetes are high in the world. Foot ulcer is one of the complications of diabetes. Foot ulcer costs are a significant part of the diabetes costs. Number of patients with diabetes is increasing with each year there is a need to investigate ways to decrease the diabetes costs. *Aim:* The main aim of this thesis is to evaluate foot ulcer management costs and find determinants that are affecting the outcomes of the diabetic foot ulcer in Estonia. *Methods:* A registry-based retrospective study based on 2009-2018 insurance data was conducted. C5.0 Node model was used to find the factors affecting foot ulcer outcomes. *Results:* In 2018 foot ulcer management direct medical costs took 0,4% of total EHIF budget (4436225 euros) on healthcare services, prescriptions, and medical devices. The costs are mainly influenced by the healthcare service costs. Medical device costs have the least impact on the total costs of managing foot ulcers. Main determinants that affected the outcomes were GP, family nurse and specialist care visits. *Conclusions:* By increasing primary care, specialist care and home nursing importance could improve the outcomes of the disease.

This thesis is written in English and is 61 pages long, including 7 chapters, 13 figures and 15 tables.

Annotatsioon

Jalahaavandite käsitluse tulemuslikkust ja kulusid mõjutavate tegurite leidmine Eesti diabeedipatsientide ravikindlustuse andmete põhjal

Taust: Diabeediga seotud ravi kulud on maailmas kõrged. Jalahaavand on üks diabeedi komplikatsioonidest ning moodustab küllaltki suure osa kogu diabeedi kuludest. Suhkrutõvega patsientide arv suureneb iga aastaga ning on oluline uurida kuidas vähendada diabeediga seotud kulutusi. *Eesmärk:* Käesoleva töö põhieesmärk on hinnata jalahaavandite käsitluse kulusid ning leida tegurid, mis mõjutavad jalahaavandi käsitluse tulemuslikkust Eestis. *Meetodid:* Registripõhine tagasivaatav uuring teostati kindlustuse 2009.-2018. andmete põhjal. C5.0 Node mudelit kasutati jalahaavandite tulemuslikkust mõjutavate tegurite leidmiseks. *Tulemused:* Jalahaavandite käsitlemiseks kulus 0,4% (4436225 eurot) kogu Haigekassa tervishoiu teenuste, retsepti ja meditsiiniseadmete eelarvest. Kulusid mõjutavad peamiselt osutatud tervishoiuteenuse kulud. Kõige väiksemad kulud olid seotud meditsiiniseadmetega. Peamised haiguse tulemuslikkust mõjutanud tegurid olid perearsti, pereõe ning eriarstiabi külastused. *Kokkuvõte:* Esmatasandi arstiabi, eriarsti ning koduõenduse rolli suurendamisega võivad haiguse tulemuslikkused paraneda.

Lõputöö on kirjutatud inglise keeles ning sisaldab teksti 61 leheküljel, 7 peatükki, 13 joonist, 15 tabelit.

List of abbreviations and terms

DM	*Diabetes Mellitus*
DFU	Diabetic foot ulcer
ICD-10	International Statistical Classification of Diseases and Related Health Problems (10^{th} revision)
EHIF	Estonian Health Insurance Fund
ED	Emergency department
ATC	The Anatomical Therapeutic Chemical
WHO	World Health Organization

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Introduction

Diabetes according to WHO is a chronic disease, which is characterized by insufficient insulin production by the pancreas or the ineffectiveness of the insulin (blood sugar regulating hormone) produced. DM brings a huge financial burden to diabetic people and their families, to health systems and national economies. [1] According to the International Diabetes Federation estimation, diabetes prevalence was 8.8% (approximately 425 million adults) of the world population of 20-79-year-olds in 2017. Based on the same estimation approximately 12,5% (651 billion EUR) of total world health expenditure was spent on diabetes patients aged 20-79 years. [2] Diabetes costs can be decreased by lowering DM complications' costs. Out of control diabetes can cause many complications, like blindness, kidney failure, lower limb amputation and several other. [1] In 2007 about 33% of diabetes costs were linked to foot ulcers in the United States. [4] About 20% of England National Health service diabetes costs were spent on foot complications. [3] It was estimated that in 2017 6.1% (64681 adults) of Estonian adults had diabetes and possibly approximately 23125 adults have undiagnosed diabetes. It was estimated that in Estonia in 2017, the DM cost per patient was 1563,89 EUR. [2] There is lack of information on how much is spent on diabetes and its complications in Estonia. There is lack of available statistics on how many people with diabetes have foot ulcer in Estonia and how much managing of foot ulcers costs for the Estonian Health Insurance Fund (EHIF). Based on statistics EHIF may spend a 20% of diabetes cost on diabetic patients with foot ulcers and therefore it is important to investigate factors that affect the costs. Based on the analysis it is possible to propose recommendations on how to make foot ulcer treatment economically more efficient.

This thesis concentrates on the economic aspect of DM and its complication foot ulcer. The aim of this thesis is to evaluate the costs of foot ulcer management among diabetic people and factors that are affecting the outcomes in Estonia. Direct medical costs to EHIF are used for the cost analysis. Multivariate regression analysis is used to determine the factors based on the insurance data. Based on the factors, possible recommendations to decrease the costs are proposed.

The objectives of this analysis are:

- To evaluate foot ulcer costs among patients with DM.
- To find factors that are affecting the outcomes of foot ulcer among diabetic patients.
- To develop a model for predicting foot ulcer outcomes among patients with diabetes.

The research questions that help to achieve the thesis aim are:

1. How much does EHIF spend on diabetic peoples' foot ulcer management in a year?
2. What are the main factors affecting the costs of foot ulcer management?
3. How do the costs differ depending on the outcome?
4. What are the factors that affect disease outcomes the most?

The thesis includes 7 chapters, including an introduction. The second chapter gives an overview of DM and foot ulcers to understand what are the disease management challenges associated with foot ulcers. It also concentrates on statistics to help the reader better understand the scope of the disease and its costs. The third chapter is an overview of the literature, outlining possible factors that are affecting foot ulcer costs. Chapter four describes the methodology and methods of analysis. The fifth chapter presents the result of the analysis and chapter six is a discussion based on the study results and literature. The final seventh chapter concludes everything in the thesis.

1 Overview of diabetes and its complication diabetic foot ulcer

This chapter gives an overview of diabetes mellitus as a disease and foot ulcer as a complication of DM. The chapter presents data on the costs of those diseases and the current situation in Estonia.

1.1 Diabetes

Diabetes is a group of different metabolic diseases. The common indicator between different types of diabetes is hyperglycaemia - high blood sugar. [5] According to ICD-10 codes, there are 5 different diabetes diagnoses. The main diabetes types are insulin and non-insulin dependent DM and malnutrition-related DM (MRDM). ICD-10 includes diagnoses for other specified diabetes and unspecified diabetes. [6]

Insulin-dependent DM is also known as type 1 diabetes and is caused by an autoimmune reaction. The body cannot produce the insulin it needs because the immune system attacks insulin-producing beta cells in the pancreas. It usually occurs at an early age and patients must inject insulin every day to keep their glucose levels in order. Usual symptoms of the disease are excessive thirst, frequent urination, little energy, hunger, sudden weight loss, and bad vision. Patients need daily insulin injections or other treatment and regular blood glucose observation and a healthy lifestyle and diet to keep the disease under control. [6]

Non-insulin dependent DM is type 2 diabetes. This type is the most common diabetes and usually occurs in adults. On the contrary of type 1 diabetes, the patient's body can produce insulin, but the body is resistant to it and therefore the insulin is not effective. Usual symptoms for type 2 diabetes are frequent urination, abnormal thirst, weight loss, and blurred vision. Often people with type 2 diabetes do not know about their condition because the symptoms are usually less noticed. The entire time a person does not treat and manage the disease the body is being damaged by excess blood glucose and therefore patients might get complications before the diabetes is even diagnosed. There are several risk factors that cause type 2 diabetes like being overweight, physical inactivity and poor nutrition. Genetics and age are also a contributing factor to the development of type 2 diabetes. Patients with the disease usually do not need daily insulin treatment and different oral medications help them keep blood glucose levels in control. [6] Even though

in many cases type 2 diabetes is preventable it still accounts for the most diabetes cases [2].

A very rare type of diabetes is MRDM and it is known as tropical diabetes or tropical pancreatic DM. MRDM patients are usually skinny, severely hyperglycaemic, they have problems with insulinopenia, insulin resistance and failure of beta-cells in the pancreas. [7]

1.1.1 Prevalence and incidence

Although there are new developments in treatments of DM and higher awareness, the number of diabetic patients increases with each year. [6] The International Diabetes Federation estimated that in 2017 there were 425 million people in the world and 58 million people in Europe with diabetes. In their analysis, it was estimated that in 2017 approximately 6.1% of Estonian adults (64681 adults) had diabetes. It was estimated that 23125 adults have undiagnosed diabetes. [2] In 2014 Estonia had 6060 new diabetes diagnoses. About 9% of the new diagnoses were type 1 diabetes and others were type 2 diabetes. [8]

1.1.2 Economic aspects of diabetes

The total health expenditure related to people (20-79-year-olds) with diabetes is constantly rising. It was estimated that in 2017 the health expenditure was approximately 610 billion euros. In 2015, the estimation was approximately 619 billion euros making the estimation grow 8% in two years. It is estimated that by 2045 the health expenditure of diabetes will rise to approximately 698 billion euros. If the analysis would include 18-99-year-olds then the expenditure by 2045 would rise to approximately 862 billion euros. It was estimated by the International Diabetes Federation that in 2017 DM cost per patient was approximately 1450 EUR in Estonia. [2]

DM costs are related to disease complications. One of the complications of DM is foot ulcers. In 2007, about 33% of diabetes costs in the world were linked with foot ulcers. [2] In England about 20% (approximately 747 million euros per year) of total diabetes care fund is used to pay for diabetic foot ulcer management. This expense does not take into consideration patients' indirect costs like the inability to work, meaning that the actual cost is higher. [3]

There are several types of foot ulcer. Diabetic foot ulcers (DFU) are one of the complications of diabetes. Venous leg ulcer prevalence is higher in people with DM compared to other people. [9] It is important to investigate, why foot ulcer management costs are driving total diabetes costs so high.

1.2 Diabetic foot ulcer

A study which combined different reviews showed that the global prevalence of diabetic foot ulcer is 6.3% and in Europe, the prevalence is 5.1%. Men and patients with type 2 diabetes are more likely to develop a foot ulcer [10]. A study by Zimny et al. (2002) investigated the healing time of a DFU wound based on the origin of the disease. [11] Patients with neuropathic foot ulcerations had an average healing time of 77.7 days, neuroischemic group wounds healed on average in 123.4 days. Three out of eight wounds with the origin of peripheral occlusive vascular disease did not heal. The average ulcer duration for those healed wounds on average was 133 days. [11] A retrospective study based on UK data calculated the mean healing time for patients with diabetes and foot ulcers. The mean healing time for a wound was 4,4 months, which is approximately 134 days, considering that 2 months have 31 and 3 months 30 days. [12] With Wagner classification it is possible to divide foot ulcer by the severity of the disease into grades. Lowest grade zero is characterised with no open lesions and highest grade five is already extensive gangrene of the entire foot. [13] Treating highest grade foot ulcers costs 8 times more than treating low-grade foot ulcers. [4]

2 Overview of literature

A research review was conducted to find papers that analysed factors that affect foot ulcer outcomes including costs in DM patients. Articles were searched from the Pubmed database. Keywords (“diabetic” or “diabetes mellitus”), (“cost” or “expenditure” OR “reimbursement”), (“factors” OR “determinants”) and “analysis” were searched from all fields and keywords (“ulcer” or “leg” or “foot” or “feet” or “limb”) were searched from titles. The Pubmed database also provides different synonyms for the keywords, therefore there were more keywords related to this search. The search included only articles that were 5 or fewer years old. This search resulted in 54 articles.

These articles were evaluated based on their abstracts. If the abstract was missing the author investigated the full article. Based on the abstract evaluation, articles were excluded if it was not clear how the analysis was conducted, the methodology overview was too general, the study focused on a specific aspect, or the data for the analysis was generated in the article.

After exclusion, 9 articles remained for further analysis, which had economic aspect used like it is intended in this study. From the included articles 3 investigated factors for developing a foot ulcer. One study investigated what are the risk factors for necrotising soft-tissue infections. Based on the included articles, a short overview of their study type, analysis method for determining factors and parameters used in the analysis are presented below. Based on the results, the author has a better understanding of what type of analysis is the most popular one and what is the best option to use in the thesis. An overview of those articles is presented in Table 1.

Table 1 Overview of literature

Study	**Study type**	**Analysis method for determining factors**	**Parameters that were considered evaluation factors that affect foot ulcer costs**
[12]	Cross-sectional study	Multivariable analyses (economic and	Clinical outcomes: patient disposition from the ED (major

	(emergency department (ED) patients)	sociodemographic factors), multinomial regression (for patient disposition), Generalized linear model (GLM) framework (economic and clinical outcomes) and for specifications gamma distribution and log-link	and minor amputation, death, treat-and-release, transfer, inpatient admission) Economic outcomes: medical-service charges (adjusted, the perspective of the payer) and length of stay Sociodemographic factors, year, hospital, characteristic, comorbid conditions
[13]	A retrospective study using a national database	Multivariable analysis (assess relative increases)	Hospital charges, demographic and hospital characteristics, income, comorbidities, insurance type, diagnostic imaging, revascularization, amputation and length of stay.
[14]	A cross-sectional study of a cohort (assessing factors for developing foot ulcer)	Univariate analysis (for assessing risk factors), Multivariate logistic regression analysis (to find potential confounders)	Many parameters, for example: Age, DM duration, gender, type of DM etcetera.
[15]	Community-based cross-sectional study (assessing factors for developing foot ulcer)	Multivariate logistic regression analysis	Many parameters, for example: Socio-demographic details, history of DM, dietary habits, tobacco use and alcohol consumption, clinical aspects (blood pressure, the occurrence of peripheral neuropathy and peripheral arterial disease (PAD), feet examination results, foot care related education etcetera.
[16]	Single-centre retrospective study (assesses factors associated with prolonged length of hospital stay)	Univariate analysis using Pearson correlation analysis (to determine factors), multivariate analysis (to determine factors) and	Baseline and clinical characteristics (gender, age etcetera), wound characteristics (location, number etcetera), laboratory measurements

		multiple regression analysis (investigation of factors signification)	
[17]	A retrospective nationwide study (about pressure ulcers)	Multivariate analysis and linear regression (for continuous variable) and logistic regression (for categorical variables) to investigate possible risk factors for outcomes. Coefficients came from multivariate regression (compared regular and ulcer group)	Outcomes: length of stay, total hospital charge, in-hospital mortality, patient disposition. A lot of different variables like malnutrition, peripheral vascular disease, DM etcetera.
[18]	A retrospective study (for different disease: Necrotising soft-tissue infections)	Univariate analysis and multivariate logistic regression analysis	Many variables like age, gender, DM, liver and renal dysfunction etcetera, death, amputation
[19]	A prospective study (concentrated on factors of developing foot ulcer)	Univariate analysis (factors for developing foot ulcer) and multivariate analysis (for the possibility of clustering patients)	Parameters like: age, DM, glycaemic control, obesity, smoking etcetera.
[20]	A retrospective audit of the hospital and interhospital records	General linear mixed model (for variable related to the cost of wound treatment)	Variables like age, ethnicity, gender, smoking etcetera, treatment modality

Factors in previously mentioned articles that had a significant impact on economic or/and clinical outcomes of foot ulcer (not pressure ulcer) were: living location (urban or non-urban), health coverage program type, living in lowest income quartile region, comorbidities, open revascularization (therapy), endovascular revascularization (therapy), minor amputations, severity of the wound, 7-day mean blood glucose levels and albumin levels.

Different statistical analysis methods used in the studies were univariate analysis (4), multivariate logistic regression analysis (4), multivariate analysis (2), multiple regression analysis (1), linear regression (1), logistic regression (1), multivariate regression (1), general linear mixed model (1). Most studies had a combination of those options.

Previously mentioned analysis methods are investigated to find the most suitable method for this thesis.

2.1 Relevant statistical analysis methods in literature

This chapter gives a brief overview of different types of analyses that were used in previously mentioned articles. There were univariate and multivariate analysis and different types of regressions. A general linear mixed model was the only different type of analysis.

2.1.1 Univariate and multivariate analysis

The univariate analysis uses only one variable and is the easiest form of analysing data. In essence, it is a single variable with its value. It does not consider relationships and causes. [21] Multivariate analysis is a set of techniques for studying relationships among multiple variables at the same time. Usually, it is used for studies, which involve more than one dependent variable (for example outcome), multiple independent variables (in other words predictors) or both. Opposite to univariate analysis, it considers relationships and causes. Researchers use this analysis method to see the correlation between the independent and dependent variables. Multiple regression is a statistical technique that can be used to conduct a multivariate analysis. [24]

2.1.2 Regression analysis

Regression analysis helps to determine what kind of variables have the highest impact on outcomes. It also shows how the factors are affecting each other. There are two types of variables in regression analysis: dependent and independent variables. The first variable is the one that analyst tries to understand or predict and second variables are these which predictably affect the dependent variable. [23] There are several types of regression techniques. There are linear, logistic, polynomial, stepwise, ridge, lasso and ElasticNet regression techniques (equations are different). Choosing the best option depends on the data (before choosing a method, data should be explored) and statistic programs help to

choose the best possible option based on the data used to conduct regression analysis. [24]

2.1.3 General linear mixed model

The general linear mixed model is a flexible analysis technique, which has regression-like analysis dependent and independent variables. This analysis method allows the user to choose multiple variables from one source. For example, outcomes can be measured multiple times for the same person. It concentrates on a person's view of the variables. For example, the individual remission probability can be calculated using this analysis. [25]

2.1.4 Costs

In the health care field, there are several types of costs that can be included in the cost analysis. This subchapter gives an overview of the different costs and their meaning.

Costs can be categorised into three groups: direct, indirect and intangible costs. Direct costs are related to patients' illnesses and health care interventions. Direct costs can be divided into two: medical and non-medical costs. Direct medical costs are costs related to health care services like medication and specialist visit costs. Non-medical direct costs include patients' out-of-pocket expenses like traveling to a health care facility and costs for babysitting services, while a parent is in the treatment. Indirect costs are harder to measure, because those costs reflect patients' productivity loss due treatment and disease and time lost from work, but also patients' family members productivity loss because of helping the patient. [28] Intangible costs are the most difficult to measure, because they refer to patient pain, worrying about the health and other effects that affect patients quality of life. [29]

2.1.5 Determinants

According to World Health Organization (WHO) different determinants of health are socio-economic and physical environment and person's behaviours and characteristics. These are factors that are affecting individual's health. For example one of the factors affecting the health is health care services access and usage to prevent and treat diseases that influence the health of the individual. [31] In this thesis the determinants are defined by the datapoints available from EHIF databases.

3 Methodology and methods

3.1 Overview of the study design

A retrospective registry-based cohort study is conducted to achieve the thesis' aims. Data related to foot ulcers of diabetic patients from 2009-2018 is extracted from the EHIF registries. This study is done from an EHIF perspective, meaning that direct costs that EHIF covered for the patient are included in the analysis.

To answer the first research question, EHIF data on ulcer management is used to calculate how big the direct costs are. The data is then visualised by year. To answer the second research question of this thesis, the costs for different outcome groups will be also calculated. Possible outcomes for patients with foot ulcers are described in chapter 3.2.5.

Different analysis methods are used to answer the third research question. Since it is not clear what are the main determinants that affect the overall foot ulcer outcomes, multivariate and regression analysis must be conducted to determine the factors affecting the outcomes. Multivariate regression analysis helps to determine variables, which might be affecting the outcomes and the impact of the variables on the outcomes. Regression types will be chosen based on the outcomes and variables used in the analysis. For data analysis Tableau[1] software is used, which helps easily to visualize the data. Excel regression functionality is used to conduct a regression analysis based on the data.

3.2 Description of data

Data for calculating the costs related to diabetes people foot ulcer management is obtained from EHIF databases. The data consists of anonymized patient demographic information, medical bills, diagnoses, health services, medicine prescriptions, and medical devices.

This study only includes patients with health insurance. Patients without insurance are not covered by the EHIF but if they need inevitable treatment then EHIF might pay for the medical help. [30] Since their foot ulcer treatment can be very different from the insured patients, it would affect the end results. These patients perhaps could not have

[1] https://www.tableau.com/

received any medical help because of financial problems before their disease got to that point that they need inevitable medical help. These patients would need a different analytical approach and are thus excluded from the current analysis.

EHIF database patients' diagnoses are in ICD-10 codes and therefore the diagnosis data is described using ICD-10 codes. Patients suitable for this study had to have one of the DM diagnoses E10, E11, E12, E13 or E14. Patients with ulcer diagnoses were chosen from patients with diabetes. The ulcer diagnosis codes can be divided into two categories: DFU and other foot ulcers. DFU diagnosis codes are E10.5, E11.5, E12.5, E13.5, and E14.5. Other foot ulcers are non-pressure chronic ulcer of the lower limb, not elsewhere classified ulcer L97, varicose veins of lower extremities with ulcer I83.0, varicose veins of lower extremities with both ulcer and inflammation I83.2 and venous insufficiency I87.2. These diagnosis codes were chosen by searching ICD-10 codes related to ulcers.

The previously described inclusion criteria and appending 10-year time (2009-2018) period resulted in 32836 patients who are eligible for this study. Foot ulcer management costs are calculated based on those patients' data about their medical bills, medical devices and medicine prescriptions associated with the disease.

Medical bills included in the dataset can be related to any of the ulcer diagnoses. Only medical devices related to ulcer diagnoses are included in this study. Medical device group codes related to foot ulcers are 9MS0053 (wound dressings for the treatment of venous ulcers), 9MS0054 (wound dressings for the treatment of DFU), and 9MS0074 (compression products) [31]. Medicine prescriptions associated with foot ulcer treatment are included. Prescription information includes diagnosis code, prescriptions with previously mentioned foot ulcer diagnoses are searched. Approximately 175000 foot ulcer related medical bills are included with these patients.

3.2.1 Data variables and units

EHIF data variables and units are:

- Demographic variables:
    - Anonymous patient identification code (random numeric code).
    - Age group (10-year period groups).
    - Year of death.
- Medical bills
    - Anonymous patient identification code (random numeric code).

    - Bill number.
    - Bill starting date.
    - Bill ending date.
    - Main diagnosis code (ICD-10 code).
    - Cost of bill (in Euros).
    - Region (in the time of medical bill).
- Data connected with healthcare services
    - Bill number.
    - Healthcare service code (EHIF specific codes).
    - Service cost.
- Data connected with concurrent diagnoses
    - Bill number.
    - Diagnosis code (ICD-10 code).
    - Diagnosis stage.
- Prescriptions data
    - Anonymous patient identification code (random numeric code).
    - ATC Classification System code.
    - Package code.
    - Date of prescribing.
    - Status of prescription.
    - Bought packages count.
    - Cost to EHIF.
- Medical device data
    - Anonymous patient identification code (random numeric code).
    - Date of prescribing.
    - Medical device group and code.
    - Medical device compensation code and name.
    - Diagnosis code.

One patient gets one identification code and it is the same in every data table. Patient codes are anonymous and assigned by EHIF to protect patients' identities. The start and end date of the medical bills show the duration of different healthcare services provided for the patient.

3.2.2 Healthcare services

Medical bill includes a list of different healthcare services. According to EHIF the healthcare services are all the medical services, procedures and the drugs used in the hospital. And also other items that are included in the health insurance package. These services are provided for the patient with health insurance on a medical indication. [34]

3.2.3 Prescriptions

Prescriptions are used for the management of diseases. Medicines used during the healthcare service providing are already included in the healthcare service cost and therefore the prescriptions include medicines that patient has to take at home et cetera.

EHIF provides reimbursements for the prescriptions, meaning that EHIF pays for some part of the medicinal product. There is a list of products that EHIF partly or fully reimburses. Based on the retail price and reference price a product discount is provided. [26] Estonia has digital prescriptions, which are written using an electronic method. [27] EHIF has data on those digital prescriptions. Based on the prescription data, price costs on medical products are calculated.

3.2.4 Medical device

Medical devices are medical tools (instrument, device, software et cetera), which can be used to treat diseases and injuries or are used to keep the disease under control. Medical devices are for example blood sugar measuring accessories, wound dressing and sleep disorder treatment devices and masks. Medical devices are prescribed by the doctor. EHIF has a list of medical devices with reference prices and the percentage that is reimbursed by the EHIF. The list is updated every year and therefore the device limit price may differ year to year. Medical devices are like medicine prescriptions but handled in a different database. [28] Medical device cards are digital from the end of 2012. Patients' medical device history is digitally available from that time. [29] EHIF data has a gap in the data about the devices bought in 2012 because not all of the data was digitalised. This gap is considered in the analysis of the 2012 medical device costs.

3.2.5 Outcomes

Outcomes as success measures are selected based on literature. The most common outcomes covered in literature were amputation, healed wound, unhealed wound, costs, and death. Foot ulcer patients can be divided into three main categories: 1) patients with healed wound, 2) patients with unhealed wound and 3) patients with an amputated wound. This approach was used in a UK study [12], which analysed costs and outcomes related to diabetic foot ulcers. This division helps to analyse the factors that are affecting the outcomes of the disease and get a better understanding of how the costs are distributed between those groups. The overall health aim is to decrease patients with not healed or amputated wounds. This study does not investigate on how to prevent foot ulcers since the data used in this study does not reflect on what was done before the first diagnosis of foot ulcer which would be relevant to analyse the prevention of disease. That would be another possible research topic.

3.2.6 Determinants

Outcomes are affected by different determinants. In this thesis the determinants are the healthcare services provided, prescriptions and medical devices written out. Also additional determinants are patients characteristics like age, sex and region during the treatment. Clinical factors are not included in this study. A study was conducted, which investigated the foot ulcer documentation process in home nursing in Estonia. It resulted that the document process varies by the provider and some of the providers are using unstructured free-text forms to document the wounds. Some of the providers used wound card templated, but they are not compatible with the Estonian Health Information System and therefore there is lack of information exchange among healthcare professionals. [39] Therefore it is very complicated task to include all the clinical factors of the patients receiving wound care, since it would require to identify all the sources of wound care and free-text analysing and matching the data with EHIF data.

3.2.6.1 Healed and unhealed wound

A retrospective study on UK data calculated median healing time of wounds for patients with diabetes and foot ulcer. Median healing time was 4,4 months, which is approximately 134 days, considering that 2 months have 31 and 3 months 30 days. [12] This average healing time is taken into a reference in this thesis to determine whether a patient has a healed or an unhealed wound during the median time. This helps to determine the cost and other differences between patients with healed or unhealed wounds during the median time. Treatment time is calculated by subtracting the date of the first medical bill, prescription or medical device from the date of the last medical bill, prescription or medical device with a concurrent or main diagnosis of foot ulcer. Comparison of healed and unhealed wound group helps to determine how to reduce healing time, improve outcomes and lower costs. This thesis takes the time point of 141 days, by taking account a 5% error rate. Healed wound group might contain patients who died during the 141-day treatment and therefore their wound might not have healed during the 141 days. Data consist of a patient year of death. Healed patients with death in the same year or if their first treatment was less than 141 days before (after 12 of August) the end of the year and death occurred in the next year are excluded from the dataset since their treatment might have been interrupted and their wound might have not healed. (Meaning that there is a chance that the death occurred during the 141-day treatment

duration). Since there is no data about why the patient died it cannot be determined that foot ulcer was the cause of the death.

3.2.6.2 Amputation

Sometimes the disease cannot be treated and the wound needs an amputation. Healthcare service codes, which are marked on medical bills, are used to determine, whether the wound is amputated or not. There are several healthcare service codes related to amputation. Healthcare service codes related to amputation service are extracted from the EHIF healthcare services list [36]. Old codes that are not used in recent years are also added to the list of amputation codes [37]. Amputations related with other parts of the body other than foot or leg were excluded from the list, for example, cervical amputation. This resulted in a list of 22 different amputation service codes: 7121, 113O, 113, 114O, 114, 213O, 213, 285O, 285, 0N2101, 0N2102, 0P2102, 0N2120, 10102, 90403, 5461, 10102, 10601, 10204, 30111, 30604, 20603. There are some medical bills that did not have an ulcer diagnosis (main and concurrent diagnosis) but amputation was done. These patients were excluded since the amputation reason most probably was not foot ulcer related.

3.2.6.3 Costs

This study will include only direct medical costs related to healthcare services, prescriptions, and medical devices during patients' foot ulcer managing. Other direct non-medical costs, indirect and intangible costs are not included in this study since that information should be retrieved from other databases. This study is done from the EHIF perspective and therefore does not consider patients' direct medical costs.

3.2.6.4 Deaths

The death statistics from EHIF are not very accurate according to EHIF contact. This information is considered for evaluation. Death as the outcome is not investigated, because it is not clear whether the foot ulcer was the reason why the patient died.

3.3 Data preparation for calculating costs

The data is in an Excel file format (.xlsx file format) and before starting the analysis in the Tableau application, the data points were converted to suitable formats using Excel application.

3.3.1 Data on patients

One Excel file contains information of all the patients whose information was given. Data is about patients in 38318 rows, from which 10 are duplicates and 77 people there have no information regarding their medical bills and/or medical devices and/or prescription drugs. Duplicated data was removed and patients without any information regarding their disease management were removed. There are 38231 patients with data on the foot ulcer management from the last 10 years. This file has a sheet with county codes and counties, which are used in the medical bill data. All of the other data is already in a suitable form so that is easy to use in Tableau application.

3.3.2 Data on medical bills

The medical bill file consists of multiple sheets. The first sheet has information about general practitioner (GP) visit bills with the main diagnosis being foot ulcer and the second sheet of specialists bills with the main diagnosis as a foot ulcer. The third sheet has other medical bills with either concurrent diagnosis of a foot ulcer or with some specific healthcare service which was predefined. Some healthcare services were predefined to catch foot ulcer bills that have different and more general diagnosis code. The last sheet has data regarding bills on concurrent diagnoses. Different types of medical bills (GP, specialist, others) are merged into one sheet because they have the same columns and an additional column is added to separate the type of medical bill was added. The dates are formatted using Excel functions, in order for Excel to understand the dates. The medical bill sheet has two date columns with a start and end date, based on which the duration of the medical bill column was added. This file also has a separate sheet of concurrent diagnoses.

Health care services for medical bills are in a separate Excel file, with three different sheets based on the medical bill type. These sheets were merged into one, for easier analysing and a medical bill type column was added. There are 136359 services related to medical bills with zero cost. GP and family nurse visits have zero costs because GPs are paid for the headcount and therefore there is no specified cost on how much the family doctor or nurse visit costs. These costs need to be estimated to get the real picture of the GP costs for managing the foot ulcer among diabetes people. A study [38] calculated the price of the family doctor and nurse visits in 2016 based on EHIF statistics. The result was that a family doctor and nurse visit costs 17,4€. This cost is applied to all of the

family doctor and nurse visits and also a family doctor and nurse home visits for all of the years in this thesis.

3.3.3 Data on prescriptions

A prescription file has only one sheet. During the years 2009-2010 the costs are in Estonian Krona (EEK) and in 2011 there are 403 prescriptions with price but no unit. These prescriptions are written out in 2010 when EEK was the main currency in Estonia. Based on a close look up of these costs, it is very likely that these costs are the sum of different costs in different currencies. For example, two packages were bought in EUR and four in EEK. (Different calculations based on other data proved that this concept is true because the calculations matched with the other prescription prices). Since the drugs values fluctuate between the pharmacies sold, it is a lot of work to match the real price in EURs. Therefore, for overall cost estimation, it is suitable to use data from 2012. Dates are formatted to suitable form. The package count has several different types of units which all mean the same so these are converted into a number format without unit type. In 2017 and 2018 there are 969 prescriptions without an EHIF discount. (18967 sold prescription in 2017 and 2018 in total) therefore the proportion of prescriptions without a discount is really low and does not have a huge impact on the overall costs.

3.3.4 Data on medical devices

The data on medical devices is gathered onto one sheet. Medical device data does not have any costs and therefore the costs need to be calculated. EHIF has published data regarding the medical device group, package number, packages sold and EHIF costs on these packages for each year [31]. Based on that information an average package cost that EHIF reimbursed is calculated. For matching the prices from the overall statistics medical device group, the package number and year are taken into account. The same package can be in both groups. Therefore considering the medical device group information gives more precise results. EHIF statistics on medical devices are from 2014, therefore the costs for 2012 and 2013 need to be calculated based on 2014 average costs. Since the medical device has data when the device was written the patient could have bought the device in the next year. 33 devices did not have any trace of bought devices in the overall statistics, therefore, it can be assumed that the device was bought the next year. By adding 1 year to those medical devices which are written out from 2014 (because 2012 and 2013 prices

were already based on 2014 prices) 15 medical devices got the price. 18 medical devices bought in 2012 or 2013 remained without price. Since the prices are looked taking account medical device group in 2014 this group specification was removed, 9 devices got price. 9 devices remained without price. 2 devices got prices from 2015 considering group, 4 devices got the price from 2016 considering group and 1 device got price from 2016 not considering group. For 2 medical devices, there is no track of price in the years on 2014-2018. 2013 Riigiteataja has a limit price and reimbursement by EHIF for these medical device packages. It is assumed that those 2 medical devices were bought with a limit price and EHIF paid for 50% of the total package cost. [39] Based on the average package cost and packages bought, medical device costs price are calculated. Dates were formatted it Excel for easier analysis in Tableau.

Data is imported to Tableau application after preparation. Data is joined using common fields. Tableau prepares data into one big table. This results in duplication of the data. For example, if the patient has four medical bills and one prescription, this one prescription is presented four times in the table. For excluding duplications each table needs unique id, this unique id was added to each table that did not already have a unique field. After that Tableau calculated field functionality is used with the definition of the unique id. By using those calculated fields Tableau gives correct results regarding statistics and does not duplicate the data. These calculated fields are made one by one if the need for calculating the variable comes. Based on the previous data preparation it is possible to calculate the overall costs for managing foot ulcers.

3.4 Data preparation for determining factors affecting outcomes

A model for identifying determinants that are affecting outcomes requires comparable data as an input for an accurate prediction. Foot ulcer has a high recurrence risk meaning that patients are likely to get a new wound during their lifetime [30]. This thesis investigates the medical data of foot ulcer management starting from the first diagnosis to get the most accurate results. The data does not represent the management of a foot ulcer patient during their whole lifetime but captures treatment data during the period of 2009-2018. Since it is not possible to identify when the patient had their first ulcer diagnosis, it is important to extract some years from the beginning of the observable period. Health care specialists have the opportunity to mark the first instance of the

diagnosis with a "+", but it is not always used and the data does not include any diagnoses with a "+" sign. The literature review concluded that 40% of patients have ulcer recurrence within one year after the wound has healed and almost 60% of patients have a recurrence within 3 years after ulcer healing and 65% of those have a recurrence within 5 years [30]. This study excludes patients who have at least one medical bill, prescription or medical device during the years of 2009-2011. The thesis also excludes patients who got their first treatment during the years 2016-2018, to get the most accurate view on one patient's whole foot ulcer treatment journey. After excluding patients with a medical history in 2009-2012 and first treatment, medical device and/or prescription during 2016-2018, the data set resulted in a total of 13979 patients. Among them are 190 patients with amputated wound, 7443 patients with healed wound during the first 141 days and 6346 patients with an unhealed wound. Removing people, who died during the 141 day time in the healed group resulted in 6017 patients, who have a healed wound and did not die during the 141 days of disease management.

2063 of the healed patients have a treatment duration of 0 days, meaning that their medical bill was opened and closed on the same day. They have only prescription(s) and/or medical devices written on one day and therefore their disease treatment and management duration is 0 days. In the healed wound group there are a lot of patients whose treatment duration was quite short. An article calculated the mean time of healing DFU wound based on grades. Grade I wound is with a good prognosis of healing with a mean of 5.8 weeks of healing time. [30] These wounds are not severe and therefore need less attention to managing. Patients with up to 5.8 weeks (41 days) treatment duration are excluded from the analysis for the best comparison between groups. This resulted in 1016 patients whose healing time was between 41 and 141 days.

There are a lot of variables that shape patients' treatments. Some services, prescriptions, and medical devices are less frequently used. For increasing the effect on the outcome and improving the model accuracy, variables are grouped. Analysis of the most used healthcare services, ATC group drugs and medical devices is conducted to categorize data.

The analysis includes healed patients' whole treatment duration, unhealed patients' first 141 days of medical history and for amputated patients first 141 days before amputation medical history is used.

For the modelling, the data was exported back to the Excel format in order to use the file as an input for IBM SPSS Modeler. This was done due to the fact that Excel is more suitable for structuring and formatting the data without increasing the risk of data-loss. The analysis includes an Excel file, which is put together from Tableau results, where each row represents one patient. Each value needs to be numerical to use it in the analysis. Each column defines patients overall metrics like sex, county and age group, but from there based on the categories conducted each column will include category name and times person received the service or bought prescription package or medical device package. For the unhealed group, each count is divided by the treatment duration to get the count for one day. For the amputated and unhealed group the count is divided by 141 days to get the count for one day because this is the time their wound could have healed. This will ensure that all of the patients have the data on the same scale.

Two analyses are conducted between two groups of patients. Investigating the differences between the unhealed and healed wound groups and amputated and healed groups. This analysis provides the differences between the groups and which factors affected the overall outcome the most.

3.5 Method's ethical aspects and limitations

3.5.1 Ethical considerations

This is a retrospective study and anonymized data is used, thus no informed consent was acquired. Nevertheless, the EHIF data is delicate and therefore the presentation of the data is done in an aggregated format so it would not be possible to identify specific patients through some other data sources. The EHIF dataset includes random unique identification codes for specific people and births 10-year groups to ensure confidentiality.

3.5.2 Limitations

This study does not include patients with undiagnosed diabetes or a foot ulcer, which could be caused by undiagnosed diabetes meaning that some patients and some costs are not included in the analysis. This would require a separate study because it would need a very thorough and large analysis to determine the factors that show whether a patient has undiagnosed diabetes or not. Based on the International Diabetes Federation (IDF)

estimation there are approximately 23125 adults with undiagnosed diabetes in Estonia [2].

The cost analysis and determining factors affecting outcomes have its limitations. The quality of the data depends on the data inserted by the health care professionals, meaning that there are most probably human errors in the data. The cost analysis and determining the factors did not include costs for other medical devices used by foot ulcer patients which are not wound dressings. Costs analysis also includes service costs that are not directly related to foot ulcer treatment but were marked in the medical bill, where one of the diagnoses was foot ulcer. There is no information regarding the patients without healthcare insurance and therefore their inevitable treatment costs are not included in the cost analysis. Ambulance data is not included in this data, because EHIF did not finance ambulance services before 2018 [43]. The author of this thesis did not find any medical bills with ambulance services from 2018. Those ambulance services can drive up costs related to foot ulcer management in the next years when EHIF finances those services. One of the aspects of treating a foot ulcer is taking diabetes medication. The determinant analysis did not include DM treatment medications because of a lack of information about the DM treatment.

4 Results

The first subchapter provides insight into the costs associated with managing foot ulcers among patients with DM. The second subchapter shows results about finding the factors affecting the foot ulcer outcomes.

4.1 Total and relative costs and overview of managing foot ulcer

Total costs are calculated based on 7 years of data from 2012 to 2018. All of the costs are in euros. Firstly, there will be an overview of costs separately for medical bills, prescriptions, and medical devices. Secondly, the total costs of foot ulcer management among patients with DM are presented. All of the figures of the costs have additional EHIF budget line to understand whether the costs for managing foot ulcer has risen over the years. Since the prices of healthcare services, medications and medical devices are rising with each year for example because on inflation it would not represent the real growth of the cost of managing the foot ulcer among patients with diabetes.

4.1.1 Total and relative costs and overview of healthcare services

All of the medical bill costs are summed. Medical bills with a main and concurrent diagnosis of foot ulcers are included. These costs also contain services provided to the patient to manage other diseases. For example, a patient went to the doctor with multiple problems caused by different diseases. All of these services and costs are marked to one bill, which is used to calculate the overall foot ulcer management costs. The count of GP visits was observed and multiplied with 17,4 euros in order to estimate the total cost [38]. 26089 patients received at least one healthcare service during the 7-year period. Management costs among foot ulcer patients with DM have grown every year. In 2018, the costs of managing foot ulcer were 3,86 million euros, which takes approximately 0,4% of EHIF healthcare services budget of 2018. The average cost per year was 2,87 million euros and the median cost was 3,0 million euros.

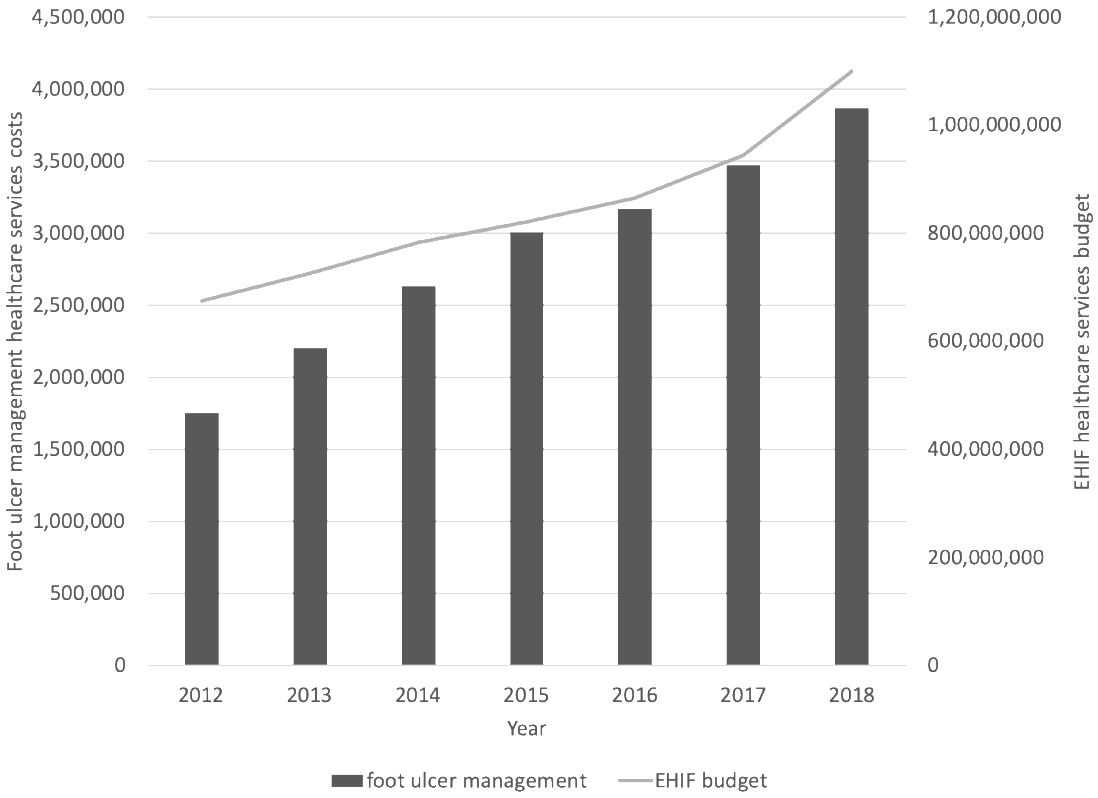

Figure 1 Foot ulcer management healthcare services cost (Source: data inquiry from EHIF 04.04.2019 and [44])

On average, 6375 patients received at least one healthcare service in one year. 2018 has the highest number of patients and 2012 has the lowest (see Table 2).

Table 2 Patients with medical bill (Source: data inquiry from EHIF 04.04.2019)

Year	Patients
2012	5546
2013	6325
2014	6559
2015	6468
2016	6489
2017	6384
2018	6851

With each year the average cost of medical bills increases. The average disease management cost per person is 446,5 euros and the highest cost per person in the year 2018 is 564 euros.

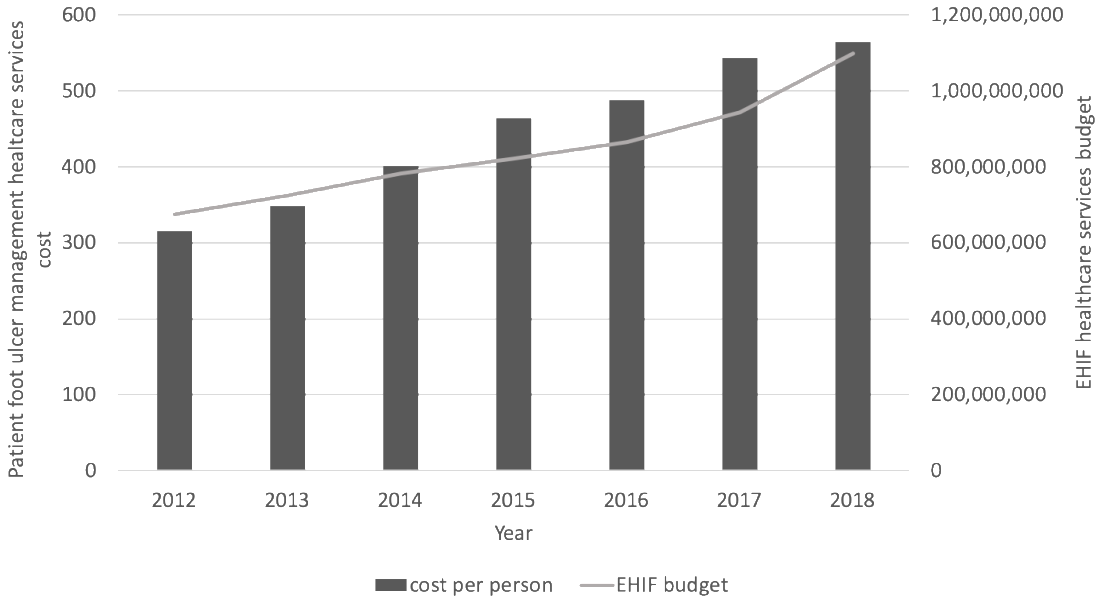

Figure 2 Patient foot ulcer management healthcare services cost (Source: data inquiry from EHIF 04.04.2019 and [44])

Based on how many patients received a service, the top healthcare services are shown below. The total cost of services and the number of services are provided. The percentages in Table 3 and Table 4 are based on the patients who received at least one medical service during the same year. Over half of the patients received a GP and/or family nurse visitation service every year.

Table 3 Percentage of patients in a specific year who received healthcare service (Source: data inquiry from EHIF 04.04.2019)

Healthcare service	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**
GP or family nurse visit	47,71%	59,15%	61,38%	63,51%	64,56%	67,07%	64,87%
specialist first or return visit	45,60%	40,58%	42,93%	41,70%	39,73%	38,53%	39,72%
creatinine, urea, uric acid	22,56%	20,28%	22,12%	23,05%	23,02%	28,37%	28,01%
Glucose (clinical chemistry study)	15,42%	15,11%	15,54%	15,97%	14,73%	25,08%	23,91%
home nursing	12,51%	13,23%	13,98%	14,30%	15,89%	21,41%	20,86%
c-reactive protein	15,38%	15,23%	16,59%	16,43%	15,84%	16,46%	16,84%
independent stationary nursing care	0,00%	0,16%	2,76%	2,78%	2,87%	2,91%	2,45%

carrying patient and/or donor organs with a vehicle of a healthcare provider (except ambulance) - 1 km	0,94%	0,85%	1,02%	1,14%	1,08%	0,72%	0,60%

The most expensive healthcare service is home nursing. In 2018 it accounted for 39,4% of the total foot ulcer management services costs among patients with DM (Table 4).

Table 4 Healthcare service cost from total disease management costs during the same year (Source: data inquiry from EHIF 04.04.2019)

Healthcare service	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**
Home nursing	33,62%	31,05%	32,22%	35,37%	37,93%	37,95%	39,42%
GP or family nurse visit	6,70%	12,45%	11,85%	11,45%	11,77%	10,86%	10,01%
independent stationary nursing care	0,00%	0,42%	9,30%	9,21%	10,24%	8,88%	7,77%
specialist first or return visit	4,38%	3,85%	4,21%	3,82%	3,81%	3,08%	2,97%
Glucose (clinical chemistry study)	0,30%	0,28%	0,22%	0,21%	0,17%	0,29%	0,22%
creatinine, urea, uric acid	0,18%	0,15%	0,16%	0,15%	0,15%	0,19%	0,20%
c-reactive protein	0,05%	0,04%	0,04%	0,04%	0,04%	0,08%	0,07%
carrying patient and/or donor organs with a vehicle of a healthcare provider (except ambulance) - 1 km	0,07%	0,11%	0,08%	0,07%	0,08%	0,06%	0,04%

The most common service provided is home nursing, in 2018 1154 patients received 51016 home nursing services (see Table 5). An average patient received 44,2 home nursing services in 2018.

Table 5 Amount of healthcare services provided (Source: data inquiry from EHIF 04.04.2019)

Healthcare service	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**

home nursing	34669	38219	43577	44450	45948	48080	51016
GP or family nurse visit	6734	15764	17923	19746	21415	21678	22220
specialist first or return visit	7334	7140	8249	8027	7714	7232	7327
glucose (clinical chemistry study)	5288	6091	5761	6353	5231	9938	8320
creatinine, urea, uric acid	2793	2757	3221	3269	3242	5647	6029
independent stationary nursing care	0	224	5804	5398	6095	5465	4946
carrying patient and/or donor organs with a vehicle of a healthcare provider (except ambulance) - 1 km	4846	7519	7481	7549	9033	7008	4947
c-reactive protein	819	972	1124	1094	1284	2698	2867

4.1.2 Total and relative costs and overview of prescriptions

Prescription costs are based on how many medicines were bought and how much EHIF paid for the medicine. All of the costs are presented in euros. Prescriptions with a diagnosis of foot ulcers were retrieved. This resulted in 17664 patients with prescriptions and 16389 patients with a realised prescription. 92% of patients bought prescriptions that were written out to them. During a 7-year period, 137224 prescriptions (8,3 prescriptions per patient) were realised and 320656 packages (19,6 packages per patient) of medicine bought. EHIF pays over 500000 euros for the prescriptions for foot ulcer management each year. The highest medicine expenses were in 2016, where a total of 589547 euros was spent by EHIF. The least expenses made by EHIF were in 2017, where the costs were 503291 euros (see Figure 3)

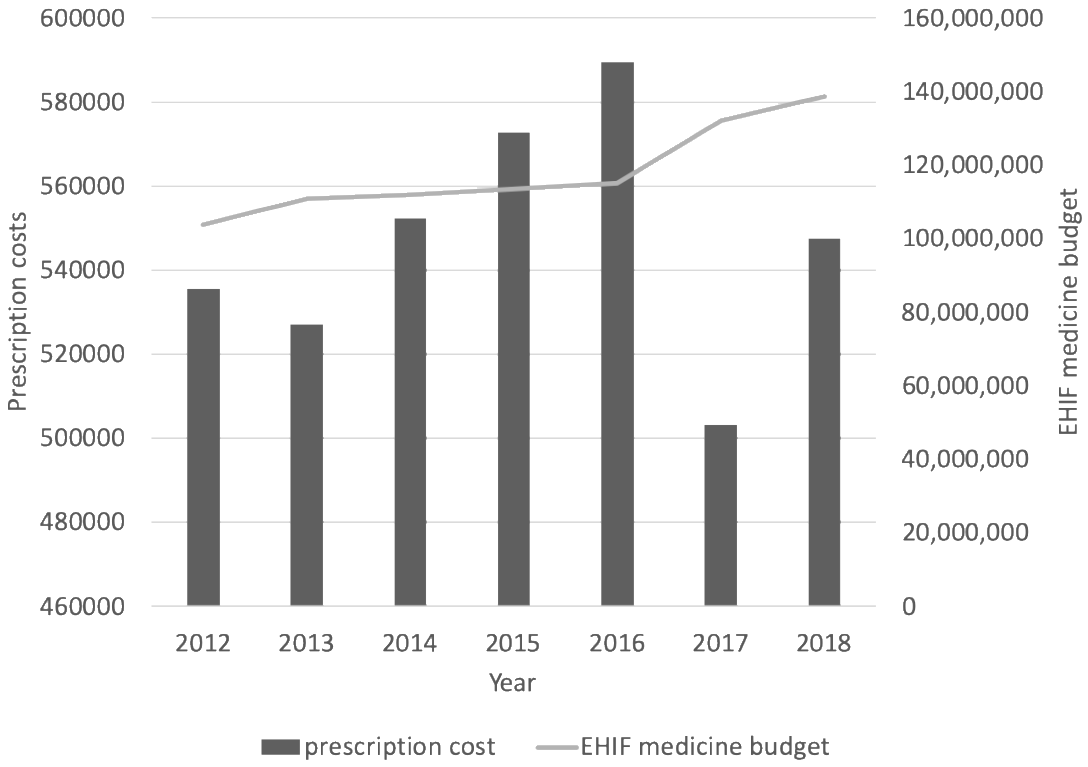

Figure 3 Foot ulcer management medicines cost (Source: data inquiry from EHIF 04.04.2019 and [44])

Each year over 4000 patients realised their prescription. 2016 had the most patients with realised prescriptions, although the medicine costs were the lowest in 2017 the year had quite a lot of patients who realised at least one prescription. (Table 6)

Table 6 Amount of patients with realised prescriptions (Source: data inquiry from EHIF 04.04.2019)

Year	Patients
2012	4239
2013	4543
2014	4795
2015	4864
2016	4886

2017	4654
2018	4876

Figure 4 shows medicines cost per patient during the 7 year period. The most expensive medicine cost per patient was in 2012, with 126,4 euros per patient. The average cost per patient during the 7 year period was 116,6 euros.

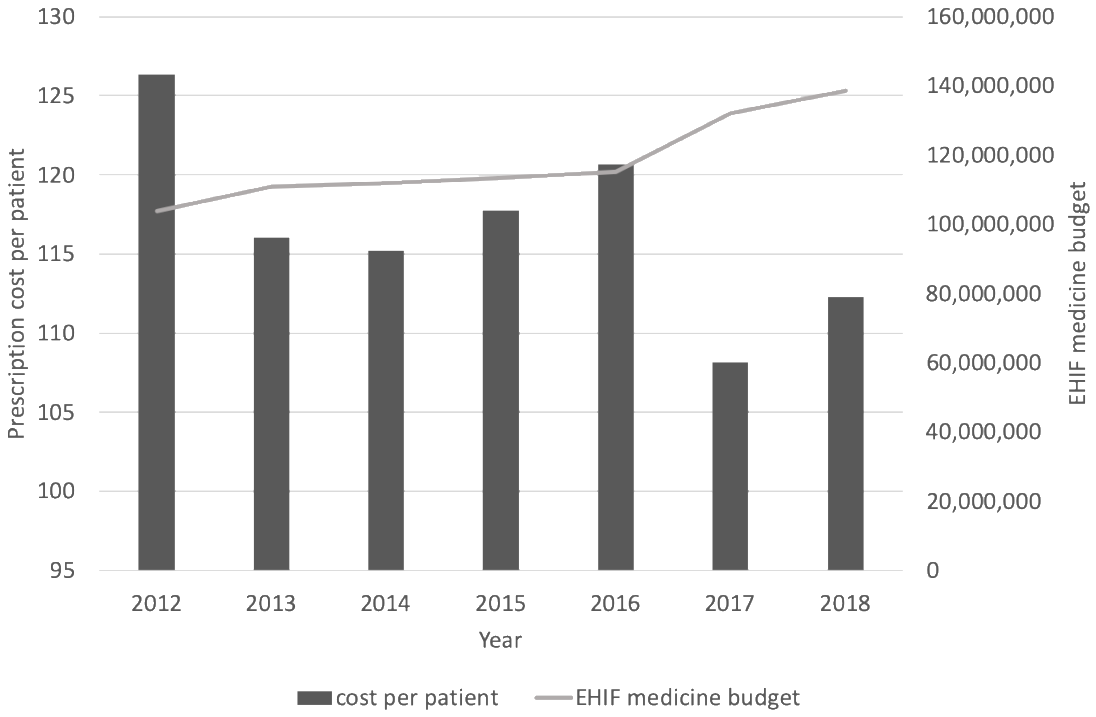

Figure 4 Medicines cost per patient (Source: data inquiry from EHIF 04.04.2019 and [44])

Medicines bought by patients were categorised into The Anatomical Therapeutic Chemical (ATC) Classification System groups. Table 7 shows that the top four ATC groups, which were prescribed to the highest number of patients, were A, D, C and J.

Table 7 Percentage of patients in a specific year who received prescription (Source: data inquiry from EHIF 04.04.2019)

ATC group	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**
Missing	5,97%	7,40%	6,69%	6,70%	5,87%	5,33%	5,33%
A	40,46%	36,08%	35,31%	35,81%	35,30%	34,55%	33,04%
B	1,30%	1,28%	1,36%	1,21%	1,35%	1,16%	1,58%
C	14,46%	14,48%	15,75%	14,56%	13,96%	15,45%	15,05%
D	33,22%	33,90%	34,01%	34,62%	35,76%	35,00%	35,05%

G	0,07%	0,11%	0,10%	0,14%	0,14%	0,21%	0,14%
H	0,12%	0,24%	0,25%	0,31%	0,25%	0,26%	0,27%
J	24,77%	25,78%	26,76%	27,71%	28,65%	29,42%	30,17%
L	0,02%	0,02%	0,04%	0,02%	0,00%	0,02%	0,02%
M	4,74%	4,80%	4,42%	4,81%	4,44%	3,65%	4,16%
N	6,13%	5,57%	6,17%	6,33%	5,91%	7,54%	6,97%
P	0,07%	0,04%	0,17%	0,04%	0,20%	0,19%	0,00%
R	0,54%	0,79%	0,83%	0,74%	0,86%	1,01%	0,90%
S	0,00%	0,00%	0,04%	0,04%	0,08%	0,11%	0,12%
V	0,07%	0,04%	0,04%	0,02%	0,00%	0,00%	0,00%

The most expensive ATC group is A, taking over 90% of the overall prescription costs each year. Followed by C, D and J groups. (Table 8)

Table 8 ATC group cost percentage of overall medicines costs during the same year (Source: data inquiry from EHIF 04.04.2019)

ATC group	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**
Missing	0,03%	0,01%	0,00%	0,00%	0,00%	0,00%	0,00%
A	95,21%	94,94%	94,88%	94,66%	94,46%	93,52%	92,64%
B	0,07%	0,18%	0,29%	0,37%	0,56%	0,76%	1,41%
C	2,38%	2,19%	2,22%	2,20%	2,22%	2,36%	2,43%
D	1,04%	1,20%	1,18%	1,21%	1,22%	1,57%	1,68%
G	0,00%	0,00%	0,00%	0,02%	0,02%	0,02%	0,01%
H	0,00%	0,00%	0,00%	0,00%	0,00%	0,01%	0,00%
J	0,98%	1,06%	1,02%	1,15%	1,07%	1,27%	1,25%
L	0,00%	0,03%	0,02%	0,01%	0,00%	0,00%	0,00%
M	0,14%	0,23%	0,16%	0,16%	0,17%	0,17%	0,25%
N	0,12%	0,14%	0,19%	0,19%	0,25%	0,30%	0,32%
P	0,00%	0,01%	0,01%	0,00%	0,01%	0,01%	0,00%
R	0,01%	0,02%	0,02%	0,02%	0,02%	0,01%	0,02%
S	0,00%	0,00%	0,00%	0,00%	0,00%	0,02%	0,01%
V	0,00%	0,00%	0,00%	0,00%	0,00%	0,00%	0,00%

Most packages were bought with ATC group A. There are some groups that have below 100 packages bought each year. (Table 9)

Table 9 Bought medicine packages (Source: data inquiry from EHIF 04.04.2019)

ATC group	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**
Missing	16874	17758	13495	8829	11719	14238	14154
A	16220	15866	16365	17243	17674	16406	16364
B	143	192	205	204	226	239	338

C	2678	2792	3183	3279	3205	3433	3630
D	4178	4573	4708	5054	5020	5443	5567
G	8	11	6	39	30	27	17
H	9	18	21	18	43	22	18
J	2970	3711	3902	5365	5960	6776	7223
L	1	6	8	1	0	2	1
M	551	661	482	520	448	416	503
N	896	1012	1172	1170	1326	1581	1589
P	5	6	23	3	28	20	0
R	41	65	78	72	79	73	80
S	0	0	3	2	4	23	11
V	0	3	2	1	0	0	0

4.1.3 Total and relative costs and overview of medical devices

Since all of the medical devices are in the medical device group of either DFU or venous ulcer wound dressings, it is assumed that those patients have a foot ulcer. 3129 patients bought at least one medical device during the 7 year period. Medical device group for venous ulcer wound dressings (9MS0053) has higher costs compared to wound dressings for DFU (9MS0054). 2012 has very low costs compared to other years because medical devices were digitalized at the end of 2012. One person bought a medical device from the group 9MS007 (compression products) in 2016 with a total cost on 164 euros for one package. This medical device group is not displayed on the figures, because it is not significant to the total cost. The highest costs for medical devices were in 2017 with 30833 euros. During the same year, prescription costs were lower. (see Figure 5)

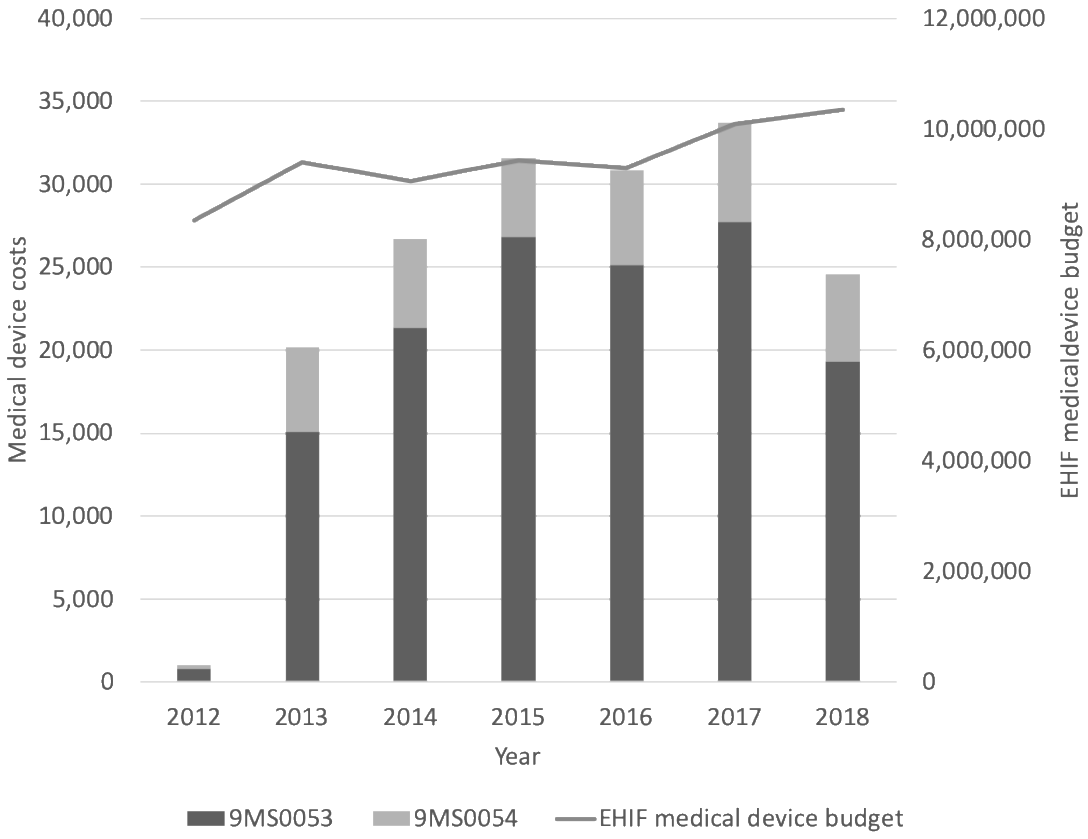

Figure 5 Foot ulcer management medical devices cost (Source: data inquiry from EHIF 04.04.2019)

Table 10 shows that in 2012 there were only 37 patients who bought at least one medical device. This amount is low because of medical devices data digitalization. The average number of patients who bought medical devices during the years 2013-2018 was 696.

Table 10 Patients who bought medical device (Source: data inquiry from EHIF 04.04.2019)

Year	Patients
2012	37
2013	523
2014	730
2015	742
2016	712
2017	722
2018	745

Medical device cost per person was between 27 and 47 euros during the years 2012-2018. The highest cost per person was in 2017. (Figure 6)

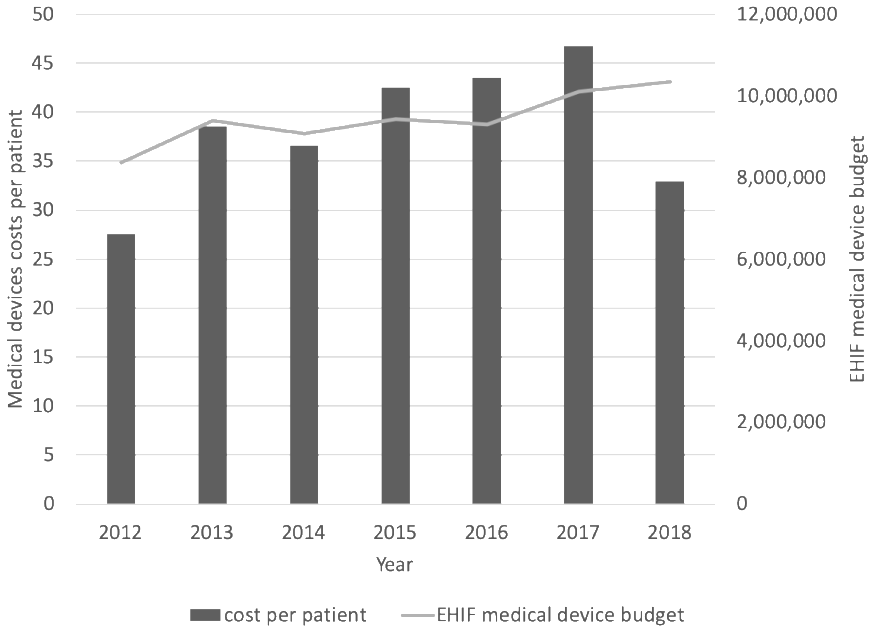

Figure 6 Foot ulcer management medical device cost per patient (Source: data inquiry from EHIF 04.04.2019)

Most of the patients bought wound dressings for a venous foot ulcer. The percentage of patients increased with each year. (Table 11)

Table 11 Percentage of patients in a specific year who bought medical device

Medical device group	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**
9MS0053	67,57%	73,80%	74,38%	75,74%	76,23%	76,45%	75,17%
9MS0054	32,43%	26,20%	25,62%	24,26%	23,77%	23,55%	24,83%

In 2012 quite a few packages were bought, but during the next years over 1500 packages for venous ulcer management and over 550 packages for DFU management were bought (Table 12).

Table 12 Number of packages bought (Source: data inquiry from EHIF 04.04.2019)

Medical device group	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**
9MS0053	115	1706	2060	2546	2424	3018	2071
9MS0054	15	703	746	750	593	586	566

4.1.4 Total and relative costs for managing foot ulcer

The previous subchapters presented results for each direct medical cost separately. This subchapter provides information on costs for the total foot ulcer management. Figure 7 has the EHIF budget of the sum of budgets for healthcare services, prescriptions, and medical devices. The highest costs associated with disease management are healthcare services provided for these patients. Medical devices take a very small proportion of the total costs. Total costs increase year by year but so does the budget. The increase is similar to the budget changes over the years. In 2018 the total costs are 4436225 euros, which makes 0,4% of the same year EHIF budget on healthcare services, prescriptions, and medical devices.

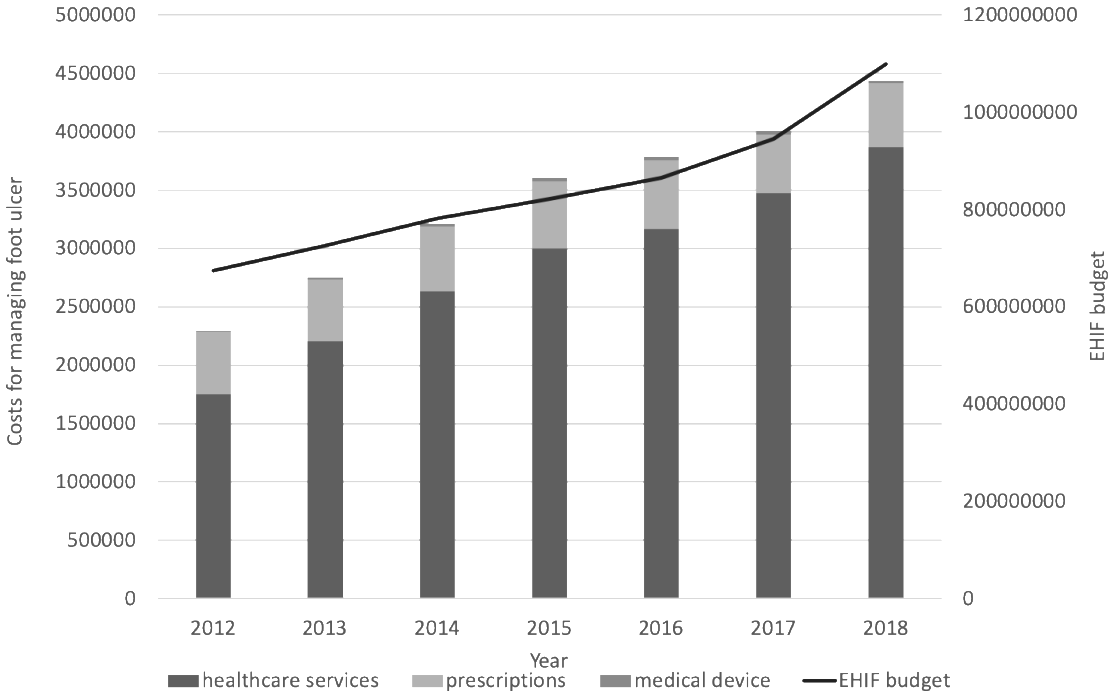

Figure 7 Overall foot ulcer management costs (Source: data inquiry from EHIF 04.04.2019 and [44])

Data shows that in 2018 foot ulcer management took about 0,4% of the EHIF budget on healthcare services, prescriptions, and medical devices [33].

4.2 Determining factors affecting outcomes

For determining factors that affect outcomes there is a need to investigate costs between groups used in the analysis to understand the costs associated with different outcomes. Managing patients with amputated wound costs almost 47 times more than managing healed wound for EHIF. Costs before amputation are almost 8 times smaller per patient. Before amputation cost includes all of the wound management cost before the wound was amputated. (Table 13)

Table 13 Patient whole disease management costs between groups (Source: data inquiry from EHIF 04.04.2019)

Patient group	**Patients**	**Medical bills**	**Prescriptions**	**Medical devices**	**Total**
Healed wound	6017	569402€ **94,6 €/patient**	31001 € **5,2 €/patient**	3033€ **0,5 €/patient**	603436 € **100,3 €/patient**
Unhealed wound	6346	6136887€ **967,0 €/patient**	846247 € **133,4 €/patient**	45400 € **7,2 €/patient**	7028534€ **1107,6 €/patient**
Amputated wound	190	852576€ **4487,2 €/patient**	32643 € **171,8 €/patient**	1234 € **6,5 €/patient**	886453€ **4665,5 €/patient**
Before amputation	190	106169€ **558,8 €/patient**	4095€ **21,6 €/patient**	694€ **3,7 €/patient**	110958€ **584 €/patient**

4.2.1 Grouping healthcare services, medicines and medical devices into groups

Previous results are used to group variables based on the methodology described in section **Error! Reference source not found.**. Wound dressing medical devices are grouped together because there were not many people overall who had bought each group medical device separately. This group is named medical devices.

From prescriptions it turned out that the most used ATC group medicines were in group A, C, D, and J. A is eliminated because it is for alimentary tract and metabolism and a lot of DM medicines are under that group [31]. Since there is no data of patients' overall DM management it would affect the end results so this group of drugs will be excluded from the list. The ATC group C drugs are for the cardiovascular system. For example, a lot of patients used C04 peripheral vasodilators group drugs, which are for widening blood vessels. Without good blood supply healing time of the ulcers may be prolonged, since inadequate blood supply leads to foot ulceration [34]. ATC D group is for dermatological use. In this group patients mainly received for direct foot ulcer using medicines. For example, group D03 is for the treatment of wounds and ulcers. ATC group J is for anti-

infectives for fighting bacteria [31] Since ATC groups C, D and J are more related to foot ulcer care these groups are used in the model separately.

There are 565 different healthcare services, which were provided for all of the patients. Some of the services were provided for only a few people. Based on the number of services provided, EHIF costs and patients receiving the treatment and similarities services were grouped. This resulted in 9 groups.

Healthcare service groups:

1. GP and family nurse visits.
2. Specialist care - specialist and specialist nurse visit.
3. General analysis (clinical chemistry studies like glucose, creatinine, urea, uric acid, cholesterol, triglycerides).
4. Inflammation analysis (C-reactive protein and drug susceptibly testing).
5. Home nursing - home nursing and service called skin ulcer.
6. General investigation (veins and arteries ultrasound, computed tomography angiography and electrocardiography with computer analysis).
7. Nursing care - Independent stationary nursing care and nursing care.
8. Dermatovenereology.
9. Skin transplantation.

4.2.2 Correlations between variables and outcomes

A correlation test performed using all the variables revealed that none of the variables were in a statistically significant correlation with the outcomes independently. The test was performed using Pearson correlation coefficient and Excel [51].

4.2.3 Model results for determining factors affecting outcomes

Since multivariate regressions were the most used analysis type in the reviewed literature, this method is used first with IBM SPSS Modeler. Excels' own regression function is not suitable since it has a maximum number of variables that can be. Logistic regression is chosen from the regressions because its dependent variable (target) is categorical [31]. In this dataset, categorical values are unhealed (0) and healed (1) or amputated (0) and healed (1). By performing logistic regression analysis on both datasets, it did not give accurate results since it predicted for most of the patients to either be unhealed in the first

data set or healed in other datasets. Regression expects that all of the important independent variables are used [52]. This thesis searches suitable model for the dataset from EHIF database and does not look for all of the variables that are affecting the outcomes. This study focuses on analysing the data points provided by EHIF and determining their relative effect on the outcomes, therefore, if there are confounding variables that were not included in the analysis, it's not relevant in terms of the aim of the thesis. Since the logistic regression could not be used, another model had to be considered. The application has an option to perform a suitably and accuracy analysis which suggests the best fitting model for the dataset. The best performing model was accurate predicting all of the groups in both datasets. For unhealed vs healed group, the accuracy was 96,4% and for amputated vs healed the prediction accuracy was 90,4%. The model is called the C5.0 Node. It can build a decision tree or a rule set using an algorithm. It will split the field values to provide maximum information gain. It repeats the splitting process until there are no values to split. It can only predict categorical values. The example provided for using this model predicts which drug should be used in the treatment of disease based on the outcome. This is very similar to what this dataset intends to achieve. [32] The decision tree finds solution by making sequential, hierarchical decisions about the outcome variable based on the predictive variables. The premise for the model is that the independent variables covered in this study have a significant effect on the outcomes. The decision tree model is using a non-parametric method. Therefore, the normal distribution of the dataset is not assumed and the model is built solely on the data sample. The model is classification type. [55] This analysis provides information on predictor importance (for example medication used, GP visit) and its importance percentage. The decision tree model calculates the relative predictor importance by itself. It helps to understand each variable importance in accordance with other variables. Sum of all of the variable's predictor importance gives a whole number 1 or 100%. It does not give the accuracy of the model. [56] Also, it will provide a decision tree diagram that shows how each variable is divided and how patients are divided between these branches. Additionally, it will provide a rule set on how the patients are divided between different variables.

4.2.3.1 Model results for healed versus unhealed wound group patients

The most important predictors that affected whether the patient wound was healed or not within 141 days are specialist care services and GP or family nurse visits with 44,2% and 22,6% of importance respectively. (Figure 8)

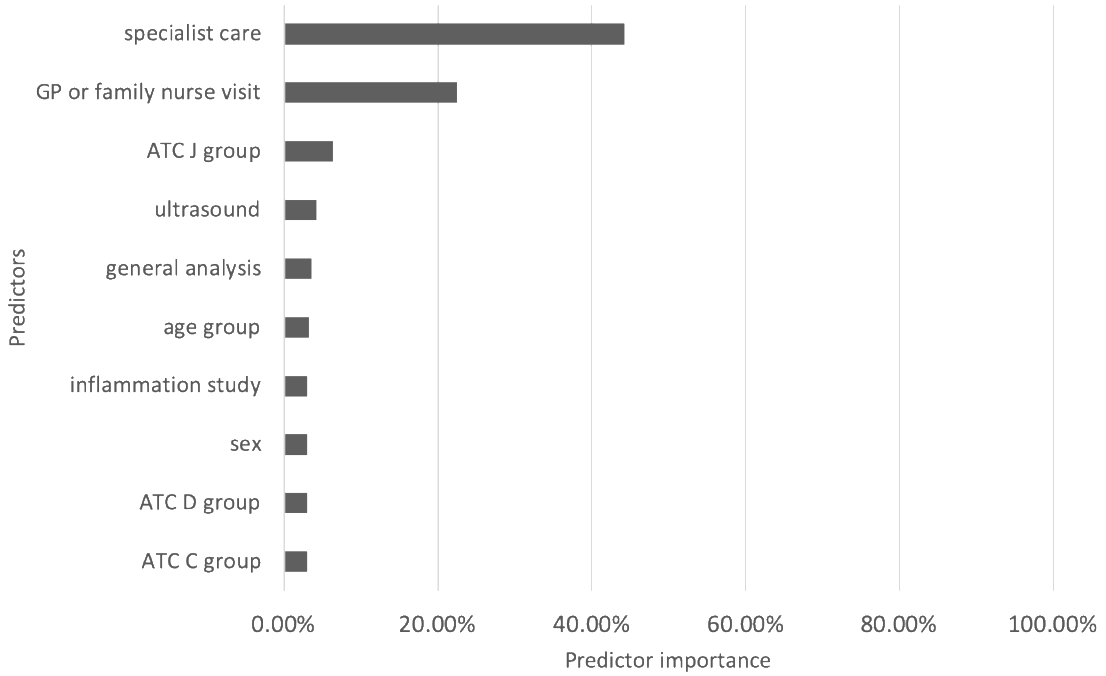

Figure 8 Predictor importance for determining whether a patient ‘s wound was healed or not (Source: data inquiry from EHIF 04.04.2019)

The model predicts whether the patient was healed or unhealed based on predetermined variables. 98,9% of patients from the unhealed group were predicted correctly. The percentage of predicting healed patients correctly was 87,8%. (Table 14)

Table 14 Model predictions (Source: data inquiry from EHIF 04.04.2019)

Healed		**Unhealed**	**Healed**	**Total**
Unhealed	Count of patients	6274	72	6346
	Row %	98.865	1.135	100
Healed	Count of patients	192	824	1016
	Row %	18.898	81.102	100
Total	Count of patients	6466	896	7362
	Row %	87.829	12.171	100

The models' tree depth is 22 and there are 135 nodes. This tree diagram does not fit onto an A4 paper so it will not be shared in the thesis. For example, the first rule in the tree is that GP and family nurse visit per day is less or equal to 0,036 and for the other side it is opposite, higher than 0,036. 92,5% of unhealed patients have GP or family nurse visits less or equal to 0,036 per day (7,5% have more visits). In the healed group 70% have GP or family nurse visits less than 0,036 per day meaning 30% of healed patients have more than 0,036 GP or family nurse visits per day. This grouping will go into depth until every patient has gotten a prediction. 1 in the tree represents a healed patient and 0 represents an unhealed patient. (Figure 9)

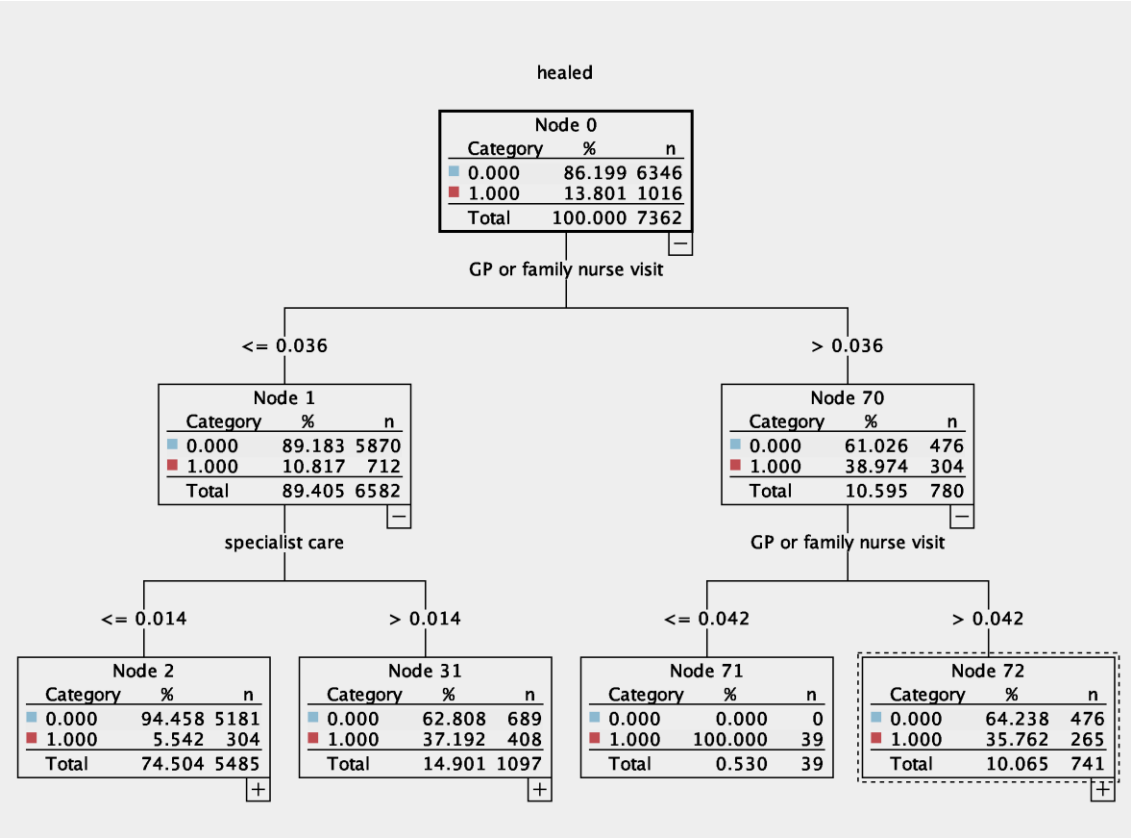

Figure 9 Tree diagram top nodes (Source: data inquiry from EHIF 04.04.2019)

The healed group averages per day were higher compared to the unhealed group in each variable group expect for medical devices. Since it resulted that the specialist care and GP and family nurse visits are the most important predictors it can be seen that the healed group receives more of those visits during the first period of the disease management. (Figure 10)

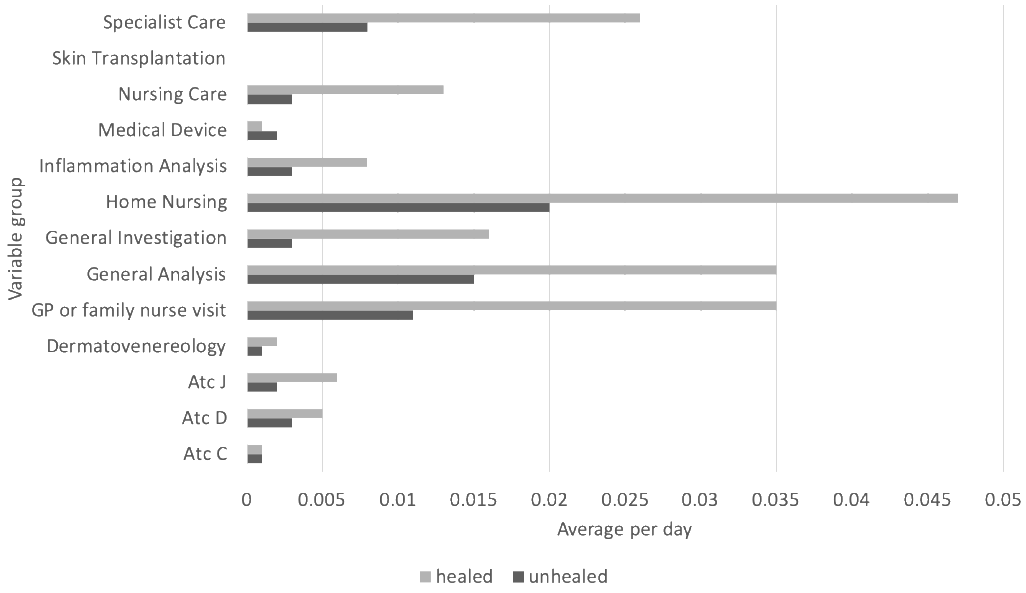

Figure 10 Average services, prescription and medical devices per day (Source: data inquiry from EHIF 04.04.2019)

4.2.3.2 Model results for healed versus amputated wound group patients

The most important predictors were the GP or family nurse visit, specialist care, and home nursing. This model included only 5 categories since others did not have a significant effect on the outcomes. (Figure 11)

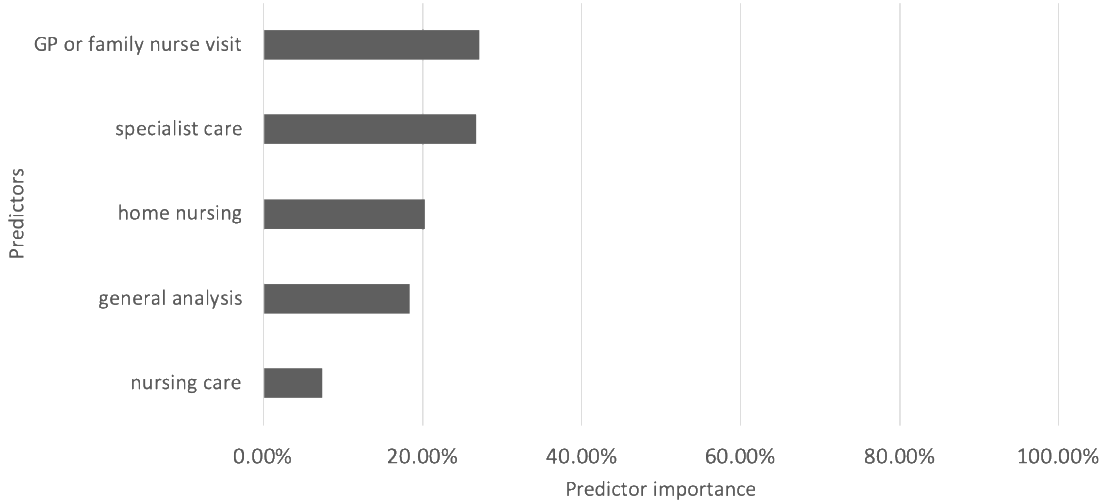

Figure 11 Predictor importance on predicting amputated and healed patients (Source: data inquiry from EHIF 04.04.2019)

The model predicted 70% of patients from the amputated group correctly. The accuracy for predicting healed patients was 98.3%. (Table 15)

Table 15 Model predictions (Source: data inquiry from EHIF 04.04.2019)

healed		**Amputated**	**Healed**	**Total**
Amputated	Count of patients	133	57	190
	Row %	70.000	30.000	100
Healed	Count of patients	17	999	1016
	Row %	1.673	98.327	100
Total	Count of patients	150	1056	1206
	Row %	12.438	87.562	100

The model results are displayed as a decision tree with a depth of 7 and 22 nodes. From the tree, it shows that amputated patients had a more general analysis done per day compared to the healed group. (Figure 12)

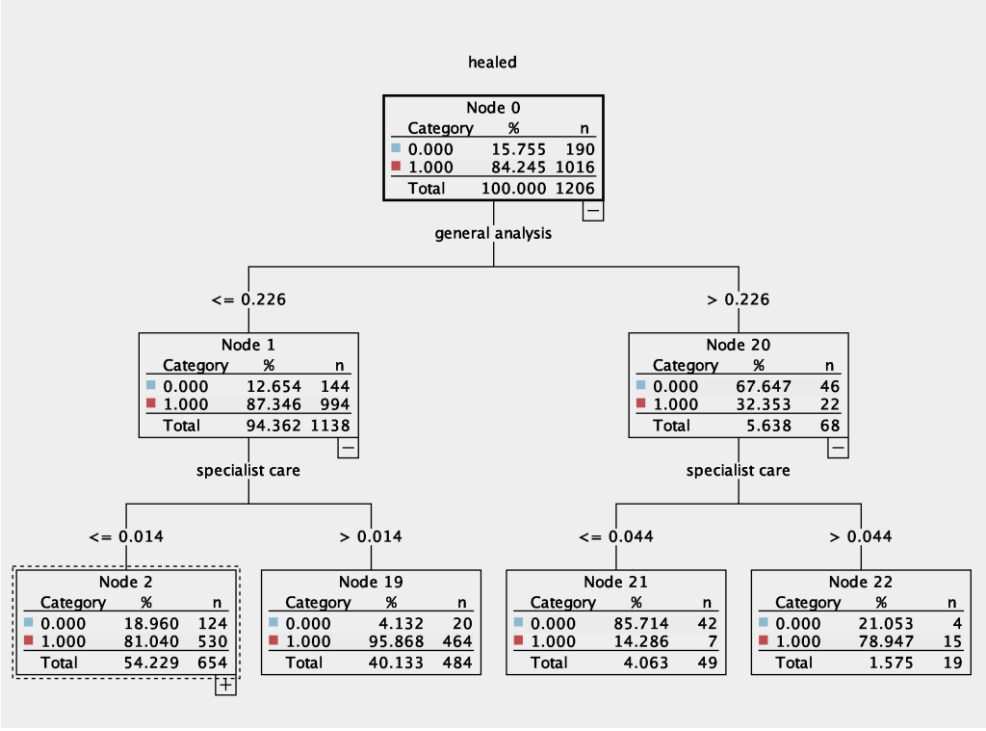

Figure 12 Tree diagram top nodes (Source: data inquiry from EHIF 04.04.2019)

Amputated patients had a more general analysis and investigation done, medical devices nursing care services. Other variable averages were higher in the healed group. (Figure 13)

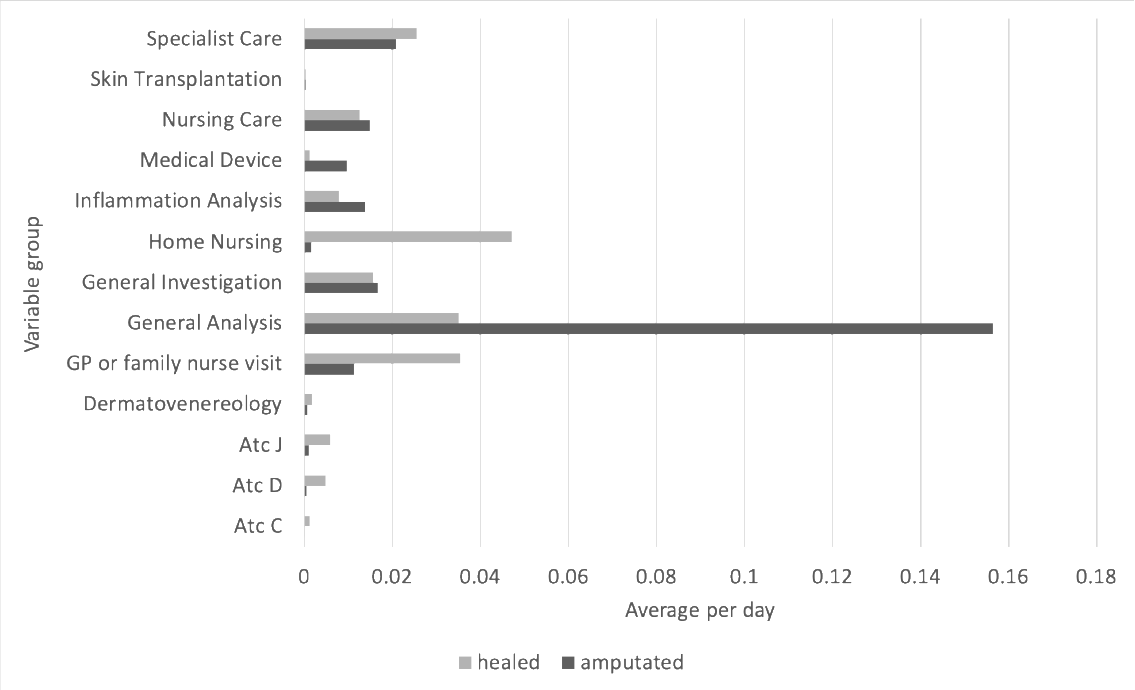

Figure 13 Average services, prescription and medical devices per day (Source: data inquiry from EHIF 04.04.2019)

4.2.4 Model's performance

One of the most important evaluation metrics is Area Under The Curve (AUC) Receiver Operating Characteristics (ROC) curve for checking classification model's performance. AUC shows the degree of separability meaning the ability to distinguish differences between classes. Higher AUC value shows the model ability to predict correctly 0s as 0s and 1s as 1s. An excellent model has AUC value near to 1. AUC value near to 0 shows worst measure of separability and value 0,5 means that there is no class separation. [57] The AUC value is calculated using IBM SPSS Modeler functionality on the models. The AUC value for healed versus unhealed group comparison is 0,953 and for the healed versus amputated group it is 0,877.

5 Discussion

In 2018 foot ulcer management among DM patients took 0,4% of total EHIF budget on healthcare services, prescriptions, and medical devices. This percentage is quite high considering the costs in this thesis are for a single disease group and for a single complication. Foot ulcer patients do not use many medical devices compared to medicines. Only about half of the patients bought at least one medical device. The total management cost is primarily driven by providing healthcare services to patients. Most patients received at least one healthcare service during their disease management.

For calculating all of the costs related to foot ulcer management the analysis should include direct medical costs for the patient and indirect and intangible costs as well.

The costs between different groups of patients differ quite a lot. It costs 47 times more to treat a patient with amputated wounds and 11 times more to treat a patient whose wound did not heal within 141 days compared to those patients whose wound healed within 141 days for EHIF. In the UK study during 12-month period DFU wound management mean National Health Service cost for the unhealed group was 4,1 times more and for the amputated wound it was 7,9 times more compared to the healed wound group. The cost per wound was approximately 3000€, 12335€ and 23690€ for healed, unhealed and amputated wound respectively. These cost reflects 1 year duration and therefore the total patient wound care cost is higher and the differences between the groups as well. [13] Managing the proportions of patients within groups, so that there would be more patients with healed wounds and fewer patients with unhealed and amputated wounds, could decrease the overall disease management costs significantly.

Model made in this study had great separability, mainly in the healed versus unhealed group comparison. The model predicted that in the unhealed versus healed group comparison, the main predictors affecting outcomes were specialist care and GP or family nurse visit. It turned out that in the healed group the average number of specialist and GP

or family nurse visits per day was higher. Increasing the visits among the unhealed group patients presumably would decrease the treatment duration. In the amputated and healed wound group comparison the main predictors affecting the overall outcomes were GP or family nurse visits, specialist care, and home nursing. From data it was seen that the healed group received more of those services compared to the amputated group. Therefore, more main predictor services are provided for the patient to get the disease under control.

To understand the delay between getting a foot ulcer and going to the doctor needs to be calculated in a separate study because based on the dataset used in this study it is not possible to investigate what happened to the patient before first foot ulcer treatment.

Increasing the GP or family nurse visits and specialist care visits in the unhealed and amputated groups could offer better outcomes for those patients. Increasing the main predictor home nursing service in the amputated group could result in less amputations. There were 6346 patients in the unhealed and 190 patients in the amputated group, compared to 6017 in the healed group (1016 whose treatment duration was at least 41 days). There are a lot of patients whose wound healing time could be shorter and outcomes better.

Increasing the visit times would affect the overall health system in Estonia. Doctors and nurses would have more work and the waiting times could increase. Therefore, other disease management outcomes could get worse because other patients are not getting to the doctor fast enough. Therefore, it would be important to find alternatives for offering better care for all of the patients in Estonia.

The model showed the most important predictors that affect the foot ulcer outcomes among patients with diabetes. It was also seen how many times per day during first 141 days patient received the most important services. Therefore based on the EHIF data it possible to predict future patients' amputation and long healing time. This information could be provided to the family doctors, who can either increase the primary care role importance in the disease management or refer the patient to the specialist care or home nursing. By adding more variables to the model, the model could be made more precise. This would require a separate study to investigate what are the all variables that are affecting the foot ulcer management outcomes. This thesis did not include any clinical

factors, because it would need a separate study to get all the clinical factors into suitable form by analysing free-text format data and finding all the databases. Also it did not include any non-medical factors that the EHIF database could not provide like work place and income, which are in the separate databases. Since it would be a lot of work to connect all the different databases, it would not be an easy task to give the family doctors the risk percentage of the patient. But based on the EHIF data, that is in rather good format it is much easier to do so.

The data needs to be organised and prepared into a suitable format that the model can read and predict based on the variables and the outcomes. The model can only read numerical values and therefore some values need to be converted to numerical values. In this study, each row represented one patient and the patient's characteristics. Getting the data into a suitable format needs a lot of data preparation and analysis to understand what variables can be used for the model and how should the variables be grouped. Data needs to be unified between groups of people for the analysis to be as accurate as possible. The model gives incorrect results if incomparable values are included in the data. For example, if the number of services provided for the one patient group is based on data from one year and for the other group from three years of data, it would be obvious that the other group got more services because they had more time to go to the doctor. By advanced grouping and variables used, the model can give very good results on what are the predictors that affect the disease outcome. If there would be a unified system on how to prepare data for the model analysis it would save time on data preparation. Consulting with experts of the area under investigation would decrease the time for categorisation the values. There are a wide variety of applications that could be used to run the model. Big corporations like EHIF have their own team of analysts who use certain applications that are best suited for the company's needs. Using a similar method described in this thesis but in a more effective manner could help EHIF to analyse different determinants that affect disease outcomes and based on the results changes in the Estonian healthcare system could be made.

This study included only costs for which EHIF paid for. The results chapter gave an overview of the costs of foot ulcer management among patients with DM in Estonia. This data can be used by EHIF to investigate more in depth on how to decrease foot ulcer and DM management costs.

6 Summary

The aim of this thesis was to evaluate foot ulcer management costs among patients with diabetes and investigate determinants that are affecting the foot ulcer outcomes in Estonia.

In 2018 foot ulcer management direct medical costs took 0,4% of total EHIF budget (4436225 euros) on healthcare services, prescriptions, and medical devices. The costs are mainly influenced by the healthcare service costs. Medical device costs have the least impact on the total costs of managing foot ulcers.

Foot ulcer management costs for patients with healed wounds are 11 times less than for patients with unhealed wounds and 47 times less than patients with amputated wounds. For improving the outcomes of the patients an analysis was conducted to understand the key factors affecting the outcomes. From comparison between groups of healed and unhealed patients it was concluded that GP and family nurse and specialist care visits are the main determinants. By increasing GP, family nurse and special care visits it could have positive impact on the outcome and treatment duration. Predictors affecting the outcomes of the amputated versus healed wound patients' the most were GP and family nurse and specialist care visits and home nursing. Patients with healed wound received more of those services compared to the patients with amputated wound and therefore the increase in those visit times could result in improved outcomes. Improving foot ulcer care should be a part of a prevention strategy. If the patient receives professional treatment with a delay, it can be difficult to heal the wound or do it in adequate time.

Increasing number of GP, family nurse, specialist care and home nursing visits could improve the outcomes based on the analysis. Increasing the visits by patient burdens the healthcare system and therefore there is a need to find alternative solutions.

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