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FinDM database on diabetes in Finland

This paper describes the collection of database of the *Diabetes in Finland (FinDM)* project which aims to identify all potential persons with diabetes from national registers in Finland between 1964 and 2017. Further, it lists the definitions used in the research of diabetes and its complications in the project.



Abstract

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Diabetes is a major global health problem. In Finland like elsewhere its prevalence has increased rapidly. While diabetes is a strong risk factor for complications including micro- and macrovascular diseases, it is also associated with several comorbidities. Although the outcomes of diabetes care have improved, the increasing prevalence of diabetes will request additional resources in health care. For planning measures to tackle challenges resulted from diabetes and to evaluate diabetes care efficient tools for monitoring are needed. This publication describes the structure of the diabetes database compiled in the Diabetes in Finland (FinDM) project to monitor diabetes and its care. The publication presents the methods used to construct the database and to define the main indicators used as well as reviews research carried out using the earlier editions on the FinDM data.

The FinDM project aims to explore the incidence, prevalence, and related complications and comorbidities as well as care and cost of care of diabetes in Finland. The purpose is to form a comprehensive description of diabetes and its consequences and to comprise all persons with diabetes in Finland. Further, the aim is to extend the database to cover data related to effectiveness and quality of care and use of resources in primary and specialised health care.

In compiling the FinDM database, several national administrative registers were used to identify potential persons with diabetes diagnosis between 1964 and 2017. Comprehensive follow-up data were collected from various register sources. Inclusion and exclusion criteria were defined for the data and algoritms drawing on register data were developed to identify different types of diabetes, comorbidities and complications.

The current FinDM database comprises data on 1,151,199 distinct individuals, of whom 887,210 were defined as persons with diabetes. The FinDM database has reached a good coverage by 2017 with comprehensive follow-up data. In the future, linkage of the database to the primary health care and diagnostic data is needed. Further, a faster updating of data is a necessity to ensure up-to-date information. Thus far, some 60 research publications have been published on a wide scope concerning diabetes and its complications.

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Background

Diabetes is a major health problem in Finland and globally. In 2002 the number of people in Finland with diagnosed diabetes was under 200 000 (Niemi and Winell 2005). In a Finnish study over 10 000 people in Finland were tested in 2007 with oral glucose tolerance test. It showed that two thirds of persons with type 2 diabetes (T2D) did not know they had the disease (Salopuro et al 2010). It was also estimated that the number of persons with T2D had doubled every seven years until the year 2000 (Niemi and Winell 2005).

Globally, the number of people living with diabetes is estimated to be 463 million corresponding to 9.3% of adults aged 20–79 years (International Diabetes Federation 2019). The International Diabetes Federation has predicted that the global increase of people living with diabetes will be even faster in the future than it has been in the past decades. The prevalence of diabetes is strongly affected by demographic, environmental, societal and genetic factors.

In terms of population health, diabetes is a strong risk factor for cardiovascular diseases, especially macrovascular diseases, such as coronary heart disease and atherosclerotic conditions. Elevated blood glucose causes also microvascular complications like neuro-, nephro- and retinopathy. In addition, several other comorbidities including depression and several cancers have been found to be associated to diabetes.

Due to the high and increasing prevalence of diabetes the resources needed to treat the condition and its complications are substantial. To tackle the related human and financial challenges, it is of utmost importance to succeed in preventing diabetes and its complications.

The aim of the Diabetes in Finland (FinDM) project is to study the incidence, prevalence, care and costs of diabetes as well as complications and comorbidities related to diabetes. For the purpose, a database based on a linkage scheme of a wide range of health care administrative registers has been constructed in the project. Furthermore, the aim is to extend the database to cover data related to effectivity and quality of care and use of resources in primary and specialised health care. The FinDM database has also been compiled in order to boost and strengthen register-based research on diabetes in Finland.

The FinDM project was launched in 2003 as a collaboration of the National Research and Development Centre for Welfare and Health (STAKES), Social Insurance Institution (KELA) and Finnish Diabetes Association. Over the years the project has gradually developed linkage schemes and methodology for monitoring the diabetes situation in Finland (Niemi and Winell 2005, Sund and Koski 2009). Currently, the project works in collaboration with the Diabetes Quality Register of the Finnish Institute for Health and Welfare (THL).

This publication describes the structure of the diabetes database compiled in the FinDM project and presents the methods used to construct the database and to define the main indicators used. The current database is the third major revision of the structure of the original FinDM data compilation. In order to give an introduction to the research potentials of the FinDM data, the publication also shortly reviews research carried out using the earlier versions of the FinDM database.

Classification of diabetes

Diabetes is a group of diseases where the common feature is elevated blood glucose resulting from disturbance in insulin production that can vary from a total lack of insulin to elevated insulin level, often com-

bined with insulin resistance (impairment of insulin action in the target tissues). The changes in insulin production and effect can be of genetic, epigenetic, environmental or life-style origin.

Diabetes is classified into different types according to the type of changes in insulin production or insulin effect. According to the International Classification of Diseases (ICD 10) there are five main groups of diabetes classified as E10-E14. The two most common are type 1 (E10) and type 2 diabetes (E11). Acute or chronic pancreatitis may cause secondary diabetes with insulin deficiency. Corticosteroid use can result to secondary diabetes with insulin resistance. There are also various forms of diabetes due to monogenic origin.

In T1D, the insulin producing cells in pancreas are destroyed in an autoimmune process. This can take place from the infant period to the age of forty years and beyond. In T1D, insulin production in pancreas decreases drastically from the normal level even to non-production. This results in highly elevated blood glucose, and without insulin compensation, to ketoacidosis and death. Autoimmune diabetes starting later in life (Latent autoimmune diabetes in adults; LADA) often manifests as slowly progressing T1D. It is usually first considered and treated as T2D until the shortage of insulin calls for insulin treatment.

In T2D, blood glucose is not lowered by insulin in a normal way due to insulin resistance. This results in elevated insulin levels. If pancreas fails to compensate for insulin resistance, blood glucose increases to diabetes levels. Obesity, especially excess fat in liver, and lifestyle habits such as unhealthy diet, lack of exercise and sedentary behavior predispose to insulin resistance and T2D. T2D is a part of the metabolic syndrome, which is characterized by dyslipidaemia, hypertension and abdominal obesity.

Pregnancy and weight gain increase the need for insulin. If the pancreas is not able to compensate for the increased need of insulin, gestational diabetes, defined as hyperglycemia first time diagnosed during pregnancy, may develop. Gestational diabetes is usually treated with diet but also metformin or insulin treatment is used. Women with gestational diabetes are at increased risk for developing diabetes later in life.

In register research the different types of diabetes are often difficult to distinguish which results in using only three major categories, i.e. type 1, type 2 and gestational diabetes. As a result, the diabetes categories are not distinctly defined but, for instance, autoimmune diabetes LADA may fall in either category of type 1 and type 2 depending on the progress of the disease process.

Incidence and prevalence of diabetes

The incidence and prevalence of diabetes have grown fast worldwide (International Diabetes Federation 2019). The same development has been observed in Finland during the last decades (Niemi and Winell 2005, Abouzeid et al 2015). Obesity and sedentary lifestyle play major roles in developing of T2D (Wu et al 2014). This is already reflected in the high number of T2D among young people (Mayer-Davis et al 2017).

An increase in the incidence of T1D has taken place as well. The increase has been especially steep in childhood T1D in Finland (Harjutsalo et al 2013). The changes in the incidence of adulthood T1D are not well known.

In both T1D and T2D, the prevalence has increased both due to the growing incidence and longer life-expectancy of people with diabetes.

Complications and comorbidities associated with diabetes

Inadequate management of diabetes increases the risk of micro- and macrovascular complications. Retinopathy, nephropathy and neuropathy are associated with elevated blood glucose levels and hypertension. Cardiovascular complications are common in diabetes (Beckman et al 2013). Diabetes is also a strong risk factor for chronic kidney disease and renal failure (Skupien et al 2019, Thomas et al 2016).

Several other comorbidities with a less direct link have been associated with diabetes. These conditions found to be more common among people with diabetes include depression (Roy and Lloyd 2012), dementia (Ninomiya 2019), and mortality due to accidents, suicide and alcohol (Niskanen et al 2018).

Economic burden of diabetes

T1D and T2D are associated to increased health care costs (Seuring et al 2015, Ng et al 2014). Due to the high prevalence, diabetes brings considerable economic burden on societies worldwide, and this burden is expected to grow.

High costs accrued from diabetes and its treatment have also been observed in Finland. An increase of 35% in the total health care costs among persons with diabetes has taken place between 2002 and 2011. In the year 2011, estimated health care costs of persons with diabetes were 8.8% of the total health care expenditure in Finland (Koski et al 2018).

Diabetes complications have a substantial impact on the health care costs (Williams et al 2002, American Diabetes Association 2018, Brommer et al 2018). In Finland in 2011, health care costs of persons with diabetic complications were on average 2.2-fold compared to persons with diabetes but without complications (Koski et al 2018).

The impact of diabetes has been demonstrated on work ability and diabetes may be a cause to sick leave, early disability retirement, and lower productivity at work. When assessing the costs of diabetes to the whole society, these productivity costs may contribute heavily. In 2007 the costs of lost productivity were estimated to equal the health care costs caused by diabetes in Finland (Jarvala et al. 2010).

Purpose and objectives of the research

The aim of the FinDM research project is to study the incidence, prevalence, care and costs of diabetes as well as complications and comorbidities related to diabetes.

In addition, as a challenge of the current phase of the project the aim is to develop the database to improve the coverage of data related to efficiency and safety of care and use of resources in primary and specialised health care. The FinDM project includes research on regional differences of the incidence of diabetes and its complications, as well as regional differences in costs and care. Further, the research aims to find associations of diabetes care with rare conditions in patients with diabetes.

The FinDM project co-operates actively with the Finnish Quality Register (FQR) pilot for diabetes. The FQR pilots are coordinated by the Finnish Institute for Health and Welfare (THL). The project aims to develop permanent quality register for the care of eight diseases and conditions in health care in Finland (Jonsson et al 2019).

The FinDM database may be used for research purposes on certain conditions. The FinDM research project has been granted permission by the competent register authorities to use the FinDM data along the lines defined in the FinDM research project plan. According to the agreed procedure, each new research proposal has to be approved by the FinDM advisory board making decisions on the use of the FinDM data. As far as possible, the contact persons and members of the advisory board of the FinDM project offer their advice and co-operate with external researchers. In the case of a new external research project, the FinDM project has to apply for the extension for the research permission from the register authorities in order to disclose new research topics or new users for the FinDM data.

Data and definitions

The FinDM database has been compiled using register-based data from several national administrative and health care registries. The database comprises register data from the Finnish Institute for Health and Welfare (THL), the Social Insurance Institution of Finland (KELA), Statistics Finland, the Finnish Centre for Pensions (ETK) and the Finnish Kidney and Liver Association.

The permissions to use the register data were obtained through applications to respective register holders:

- THL (THL/1047/6.02.00)
- KELA (74/522/2018)
- Statistics Finland (TK-53-922-18)
- ETK (ETK/SUTI 18012)
- Finnish Kidney and Liver Association (excerpt of proceedings, 1st December 2014 (§4b))
- Statistics Finland for sociodemographic and census data (TK-53-531-16)

Researchers approved to use the FinDM database have to sign confidentiality obligations for the respective register holders. The ethical approval for the study was received from the Research Ethics Committee of THL (excerpt of proceedings 5/2018 (§791)).

Identification of people with diabetes

The FinDM project aims to identify all persons who have been diagnosed for diabetes in Finland by collecting any potential entries concerning diabetes in registers.

Individuals were deemed potentially having diabetes if they met at least one of the following criteria:

- Diabetes diagnosis in the Hospital Discharge Register (ICD-8, 1969-1986)
- Diabetes diagnosis in the Hospital Discharge Register (ICD-9, 1987-1993)
- Diabetes diagnosis in the Care Register for Health Care (ICD-9, 1994-1995)
- Diabetes diagnosis in the Care Register for Health Care (ICD-10, 1996-2017)
- Diabetes diagnosis in the Register of Primary Health Care Visits (ICD-10 and ICPC-2, 2011-2017)
- Diabetes diagnosis or entry (checkbox for diabetes, insulin initiation and pathological result in glucose tolerance test) in the Medical Birth Register (mother and child, ICD-9 and ICD-10, 1987-2017)
- Diabetes diagnosis in the Causes of Death Statistics (ICD-8, ICD-9 and ICD-10, 1971-2017)
- Entitlement to elevated reimbursement for antidiabetic medications (codes 103, 171, 215, 285, 371) in the Special Reimbursement Register (1964-2017)
- Entries of purchase of antidiabetic medications (ATC codes A10*) in the Prescription database (1993-2017)

Diagnosis codes used in the identification of persons with diabetes are presented in Table 1.

The personal identity codes (Digital and Population Data Services Agency 2020) of potential persons with diabetes from registers maintained by THL and Statistics Finland were forwarded to KELA and completed with the personal identity codes of potential persons with diabetes in the KELA registers. In KELA, the cohort was scrutinized to manage individuals with altered personal identity codes. In addition, the cohort was attached with data on municipality of residence on December 31st in each year in 1986-2017. After that the personal identity codes were replaced with research numbers by THL. The register authority within THL, in the capacity of the register holder, maintains the key to personal identity codes and research num-

bers for update and linkage purposes. The FinDM database is accessed by the researchers using the pseudonymised research numbers.

Table 1. Diagnosis codes used in the identification of persons with diabetes.

	ICD-8	ICD-9	ICD-10	ICPC-2
Type 1 diabetes		250?B	E10, O24.0	T89
Type 2 diabetes		250?A	E11, O24.1	T90
Other type of diabetes		250?C	E12, E13, O24.2, P70.2	
Gestational diabetes	7611	6480, 7750	O24.4, O24.9, P70.0, P70.1	W85
Unspecified	250	250?X, 3620	E14, G59.0, G63.2, H28.0, H36.0, I79.2, M14.2, M14.6, N08.3, O24.3	

The final cohort comprises 1,151,199 distinct individuals with potential diabetes.

Follow-up data

Figure 1 describes the collection of follow-up data for the cohort of potential persons with diabetes.

Data including visits to specialised health care were obtained from the Hospital Discharge Register and the Care Register for Health Care (Finnish Institute for Health and Welfare 2020a) between 1969 and 2017, including ambulatory visits to specialised health care in 1998-2017. Data of visits to the public primary care were obtained from the Register of Primary Health Care Visits (Finnish Institute for Health and Welfare 2020c) in 2011-2017. Data on care periods in social care institutions were collected from the Care Register of Social Welfare (Finnish Institute for Health and Welfare 2020d) between 1994 and 2017. The compiled data on care include variables concerning, among others, service provider, specialty, date of arrival and discharge, discharge destination, main and subsidiary diagnoses as well as main and subsidiary procedures.

Data on all deliveries were obtained from the Medical Birth Register (Finnish Institute for Health and Welfare 2020b) in 1987-2017. All cases of cancer were obtained from the Finnish Cancer Registry between 1953 and 2017 (Pukkala et al 2018). Data on visual impairment were provided by the Finnish Register of Visual Impairment (Finnish Federation of the Visually Impaired 2020) for 1983-2017. Data on treatment and diagnoses of patients with nephropathy were obtained from the Finnish Registry for Kidney Diseases (Finnish Kidney and Liver Association 2020) in 1965-2013.

The dates and causes of death were obtained from the Causes of Death Statistics (Statistics Finland 2020b) in 1971-2017. Data include information on causes determined by a doctor, diagnoses pertaining to the primary cause of death, indirect cause of and contributory causes of death.

Sociodemographic and census data were linked to the data in the remote access environment Fiona of Statistics Finland. Several FOLK modules (Statistics Finland 2020b) starting from the population census of 1970 are available for use in Fiona including data on income, education, employment, pensions and households.

The Register of Special Reimbursement of medicines (Social Insurance Institution 2020b) was used to obtain entitlements to special reimbursement between 1964 and 2017. The register contains entitlements to reimbursement of medicine expenses at the special rate, to limited reimbursement, or to reimbursement for clinical nutrients, which are approved when certain criteria are met. The data includes dates, codes and diagnoses for the special reimbursements. Data on reimbursable purchases of medications between 1994 and 2017 were provided by the Prescription database (Social Insurance Institution 2020a) including ATC code, date of purchase, costs, defined daily dose (DDD) and information on package identification numbers. In addition, data on pensions (including national and disability pensions) and imbursements for private services as well as on sickness, care and rehabilitation allowances (Social Insurance Institution 2020c) were obtained from KELA. Data on disability pensions also included diagnoses on which the disability pensions were based.

Data on approved and rejected earnings-related and national pensions were collected from the Pension Register (Finnish Centre for Pensions 2020) of the Finnish Centre for Pensions. Information included the type and duration of pension together with monthly payments and accruals covering years 1998-2017. Together, pension data from KELA and ETK contain information of all pensions in Finland.

Finally, from the Earnings and Accrual Register of the Finnish Centre for Pensions, data on employment and periods of entrepreneurship as well as periods when person did not receive income as paid salary were collected for years 1998-2017. Data include annual income and benefits from these periods.

Further, permissions to use the register data obtained from the respective register holders allow us to link data on visits to primary health care providers and data obtained from the Prescription Centre and Patient Data Repository of the Kanta services (Kanta Services 2020) to the data.



Figure 1. Collection of follow-up data for the diabetes cohort.

Inclusion and exclusion criteria for people with diabetes

The cohort of potential people with diabetes was processed to create a research database which includes individuals who are, with sufficient accuracy, identified as persons having diabetes.

Individuals are included in the research if they have a diabetes diagnosis in the Hospital Discharge Register, the Care Register for Health Care, the Register of Primary Health Care Visits, or the Cause of Death statistics. Further, an entitlement to special reimbursement for antidiabetic medications in the Special Reimbursement Register or a purchase of antidiabetic medications in the Prescription database count for inclusion in the research data. The date of the first entry of diabetes in the registers was defined as the date of the onset of diabetes.

A major separation criterion in the database concerns gestational diabetes. Diagnosis codes for gestational diabetes were searched for in the Hospital Discharge Register, the Care Register for Health Care, the Register of Primary Health Care Visits, and the Cause of Death statistics. Besides, any entry for gestational diabetes in the Medical Birth Register was deemed as a criterion of gestational diabetes. If no other entries for diabetes except gestational diabetes were found, these persons were defined as persons with gestational diabetes. In addition, the Hospital Discharge Register was searched for diagnoses of pregnancy (ICD-8: 650-662) preceeding the year of 1987. These dates were modified to cover the time for pregnancy (9 months) and postpartum period (2 months) and compared to the individual's other dates of diabetes entries. If all entries of diabetes diagnosis for the individual occurred during the time of pregnancy and postpartum period, they were defined as persons with gestational diabetes. Respectively, deliveries from the Medical Birth Register since 1987 were compared to purchases of antidiabetic medications in the Prescription database. If no other entries of diabetes diagnosis for the individual was found and the purchases of antidiabetic medications only occurred during the time of pregnancy and postpartum period, those individuals were defined as being diagnosed with gestational diabetes. The identification of persons with gestational diabetes in the FinDM database enables research also on gestational diabetes.

Another separation criterion of research data is polycystic ovary syndrome (PCOS). Metformin is also used as medication among women with PCOS. In accordance with the definition of the National Diabetes Register of Denmark (Carstensen et al 2011), women with purchases of metformin (ATC code: A10BA02) in the age between 20 and 39 years as an only indication on diabetes were excluded from the diabetes cohort. In addition, the Hospital Discharge Register, the Care Register for Health Care and the Register of Primary Health Care Visits were searched for diagnoses of PCOS (ICD-9: 2564, and ICD-10: E282), which can be used in later analyses concerning links between PCOS and diabetes.

Finally, the individuals with only one purchase of metformin (ATC code: A10BA02) in the registers were considered to have insufficient evidence on diabetes and they were excluded from the research data.

After the introduction of inclusion and exclusion criteria to the database, 887,210 persons were included in the diabetes cohort.

Classification of people with diabetes

Due to several reasons the definite classification of people with diabetes into the T1D and T2D categories was challenging as in many other register studies. First, the classification and recording practices of diseases, such as ICD-8, ICD-9, ICD-10 and ICPC-2, has changed during the study period of 1964-2017. Second, the time span of the different register sources varies considerably during the study period. Third, the care practices including the use of medication varied during the study period. Fourth, the follow-up time from the onset of diabetes until death or the end of 2017 varied greatly from null to decades.

Due to the complicity of classification in diabetes types, we decided to classify persons with diabetes based on the information of the first year following the onset of diabetes to achieve an equal potential time for consideration. The following hierarchy was created on which the definition was based (using diagnosis codes presented in Table 1).

1. A diagnosis code for the special reimbursement for antidiabetic medication in the Special Reimbursement Register
2. A diagnosis code for diabetes in hospital discharges of the Hospital Discharge Register or the Care Register for Health Care
 - a. Diagnosis made in specialised care
 - b. Main diagnosis being more precise than subsidiary diagnosis
 - c. Latter date of diagnosis being more precise than former date
3. A diagnosis code for diabetes in the ambulatory visits to specialised health care in the Care Register for Health Care
 - a. Diagnosis made in specialised care
 - b. Main diagnosis being more precise than subsidiary diagnosis
 - c. Latter date of diagnosis being more precise than former date
4. A diagnosis code for diabetes in the Register of Primary Health Care Visits
 - a. Main diagnosis being more precise than subsidiary diagnosis
 - b. Latter date of diagnosis being more precise than former date
5. Purchases of antidiabetic medications in the Prescription database
 - a. Only purchases of insulin (ATC code: A10A) => T1D
 - b. Only purchases of insulin (ATC code: A10A) and metformin (ATC code: A10BA02) and age of under 40 years => T1D
 - c. Other => T2D
6. A diagnosis code for diabetes in the Cause of Death Statistics
 - a. Primary causes of death being more important than contributory causes of death
7. Age at the onset of diabetes
 - a. Age of under 40 years => T1D
 - b. Age of 40 years or more => T2D

Definition of the follow-up indicators of diabetes

Indicators used in the follow-up were formed in order to identify complications and outcomes of diabetes. Chosen indicators are based on the earlier research conducted in the project. To coordinate the methodological approaches, the FinDM definitions were compared with the definitions developed in the FQR pilot on diabetes to finalise the list of the indicators.

Diagnosis and procedure codes used to define major complications and outcomes of diabetes in the FinDM project are presented in Table 2.

Some of the other follow-up indicators of interest include gastric bypass, liver disease (NAFLD, liver cirrhosis, liver cancer), mouth infection, severe depression, psychotic disorders, dementia, thyroid disorders, coeliac disease and osteoporosis.

Table 2. Diagnosis and procedure codes used to define major complications and outcomes of diabetes.

	Category	ICD-10	Procedure codes
1.	Cardiovascular complications	<i>includes subcategories 1.1.-1.4.</i>	
1.1.	Ischemic heart disease	I20-I25	FNA-FNE, FN1AT, FN1BT, FN1ST, FN1YT, FN2, FN3CT, TFN40, TFN50 (and relevant supplementary codes for patients with advanced cardiac condition)
1.2.	Acute myocardial infarction (AMI)	I21, I46, R96, R98	
1.3.	Heart failure	I50	
1.4.	Atrial fibrillation and flutter	I48	
2.	Cerebrovascular complications in diabetes	I63.0-I63.5, I63.7-I66.9, I67.2, I69.3, G45	PA
2.1.	Ischemic stroke	I63.0-I63.5, I63.7-I64.9, G45	
3.	Foot complications in diabetes	<i>includes subcategories 3.1.-3.4.</i>	
3.1.	Peripheral artery disease (PAD)	I70.2, I79.2, E10.5, E11.5, E12.5, E13.5, E14.5	PD-PG
3.2.	Non-traumatic amputation	<i>includes subcategories 3.2.1.-3.2.2.</i>	
3.2.1.	Major amputation		NFQ10, NFQ20, NGQ10, NGQ20, NHQ10, NHQ20
3.2.2.	Minor amputation		NHQ30, NHQ40
3.3.	Diabetic foot ulcer	L03.1, L97, S91, T93, M86.1-M86.4, M86.6-M86.9	NHK99, NHS20, NHS99, NHW, QDB05, QDG20, QDG30, QDG99
3.4.	Charcot foot	M146	
4.	Diabetic nephropathy	E10.2, E11.2, E12.2, E13.2, E14.2, N08.3, N18, Z49, Z94	KAS, TK800, TK820
4.1.	Chronic kidney disease	N18	
4.2.	Dialysis	Z49	TK800, TK820
4.3.	Transplantation of kidney		KAS
4.4.	Transplanted kidney status	Z94	

Table 2. (continued).

5.	Eye complications in diabetes	E10.3, E11.3, E12.3, E13.3, E14.3, H28.0, H34, H36.0, H40.5, H42.0, H43.1, H45.0, H54	CKC12/CKD05/CKD60/CKD65 +E10-E14
5.1.	Diabetic retinopathy	H36.0, H43.1+E10.6/E11.6/E12.6/E13.6/E14.6, H45.0+E10.6/E11.6/E12.6/E13.6/E14.6	CKC12/CKD05/CKD60/CKD65 +E10-E14
5.2.	Blindness and impaired vision	H54	
6.	Diabetic neuropathy	E10.4, E11.4, E12.4, E13.4, E14.4, G57.1, G57.3, G57.5, G59.0, G63.2, G73.0, G99.0, H49, I95.1, N48.4	
7.	Death (causes as underlying cause of death)	Any cause	
7.1.	Cardiovascular death	I21, I46+R96/R98, I63, I64, G45	
7.2.	Cancer death	C00-D48	
7.3.	Accidental death	V01-X59	
7.4.	Suicide	X60-X84	

Description of primary data

Numbers of persons with diabetes

The incident number of persons with T1D in the FinDM database has remained relatively stable after the first years of the database of 1964 and 1965. The number of newly diagnosed persons with T1D peaked in 2008 with 2,144 new cases. In 2017, 1,504 new persons with T1D were identified. Likewise, 2008 was the year with the highest number (36,252) of incident T2D. In the last year of follow-up, 2017, the incident number of T2D was 22,961 (Figure 2).

The development in the registers, which make the data source for the FinDM database, are reflected in the incident numbers of both T1D and T2D. T1D was identified from the year 1964, when the Special Reimbursement Register started. From the early 1970s, the emergence of recording of diagnoses in the Hospital Discharge Register produced a surge in incident persons with T2D. This trend was extended with initiation of Prescription database in the early 1990s. Changes in medications and other treatment practices of diabetes, reimbursement practices and programmes to improve diagnosing of T2D patients have also affected the incident numbers of persons with T2D.

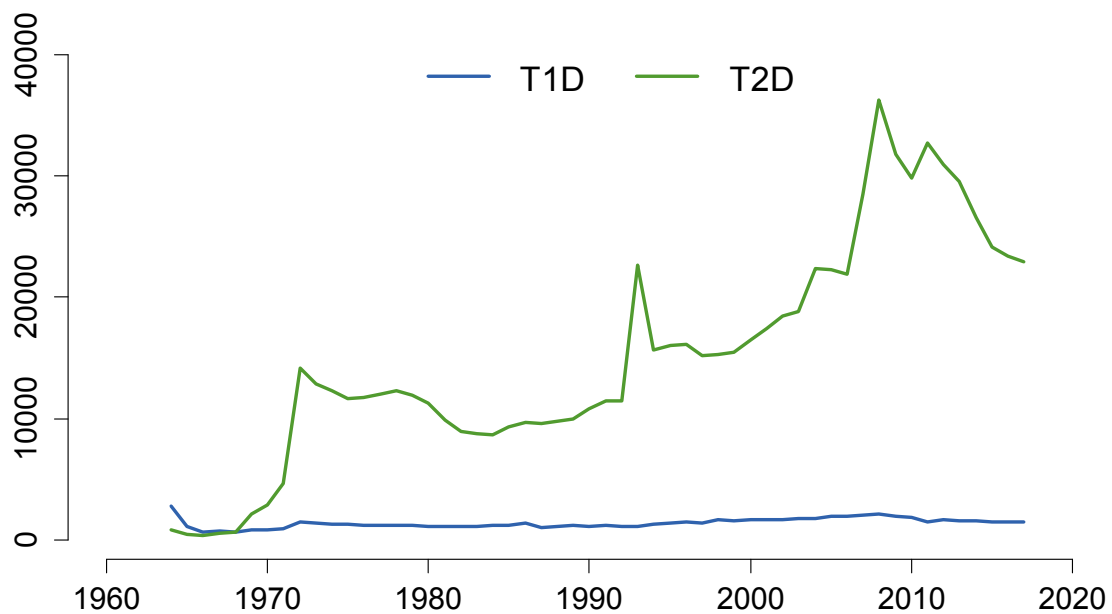


Figure 2. Incident number of persons with type 1 diabetes (T1D) and type 2 diabetes (T2D) in 1964-2017 in Finland.

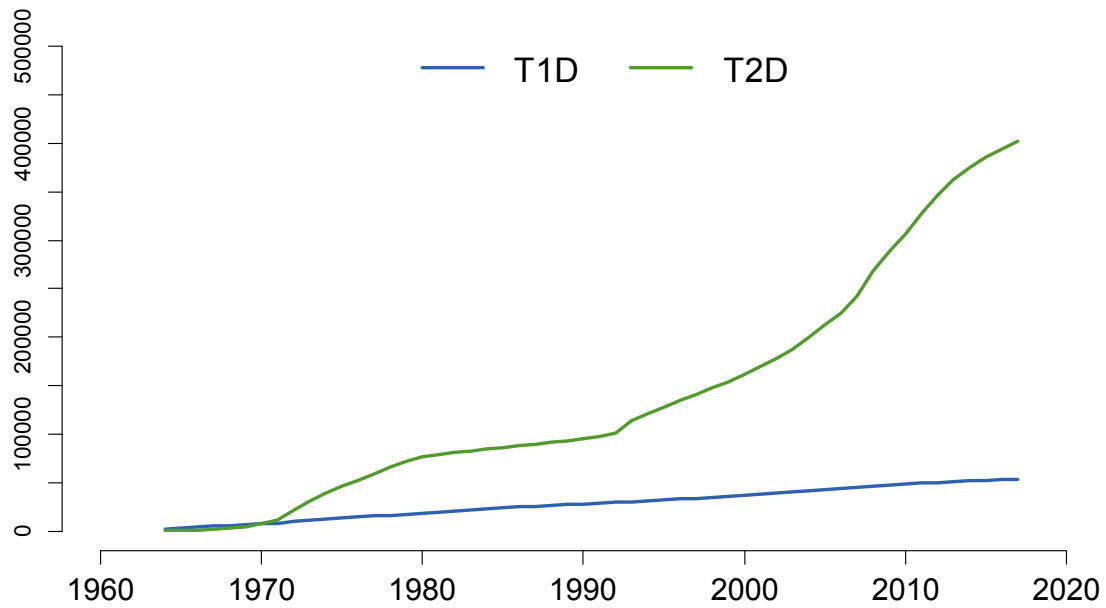


Figure 3. Prevalent number of persons with type 1 diabetes (T1D) and type 2 diabetes (T2D) on the last day of each year in 1964-2017 in Finland.

The number of persons living with T1D has grown steadily throughout the study period being 53,780 in the end of 2017. The prevalence number of T2D has been more dependent on changes in the register sources used, especially during the first decades of the study. Anyhow, the prevalence number of T2D has grown rapidly, especially in 2000s, reaching 401,911 persons by the end of year 2017 (Figure 3).

Incidence and prevalence of persons with diabetes

The age-standardised incidence rate of T1D per 10,000 person years in the general population has varied somewhat in the 2000s. As for T2D, there was an additional increase in the incidence rate around 2008-2011, probably linked to the diabetes prevention and treatment project DEHKO (Diabeteksen ehkäisyn ja hoidon kehittämissuunnitelma 2011, Dehkon 2D -hanke 2009) Since then, however, the increase has levelled off (Figure 4).

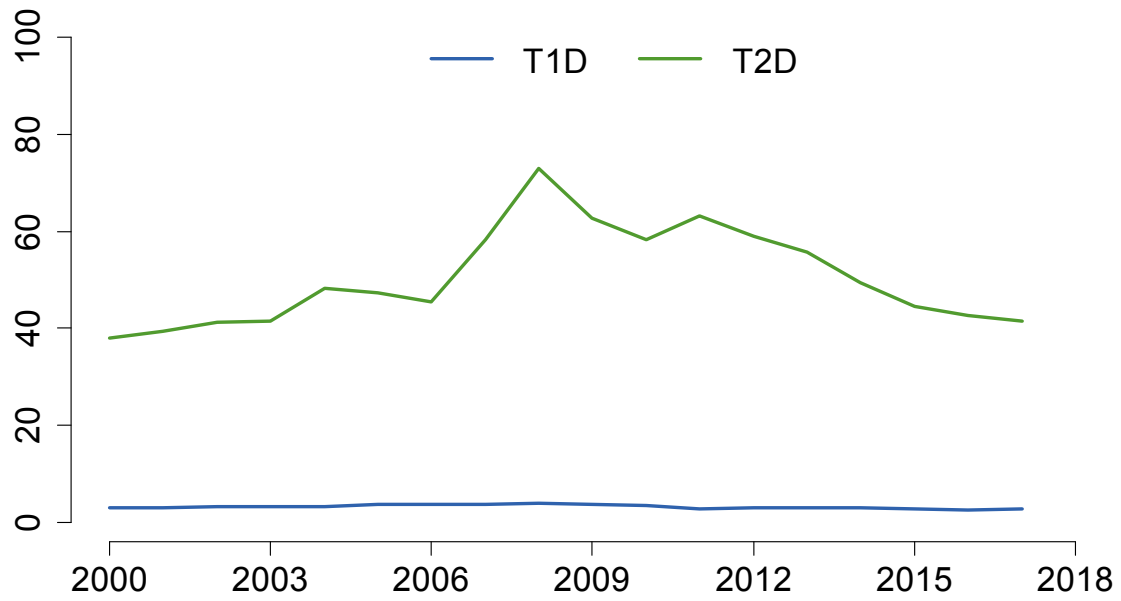


Figure 4. Age-standardised incidence rate per 10,000 person years for type 1 diabetes (T1D) and type 2 diabetes (T2D) in 2000-2017 in Finland.

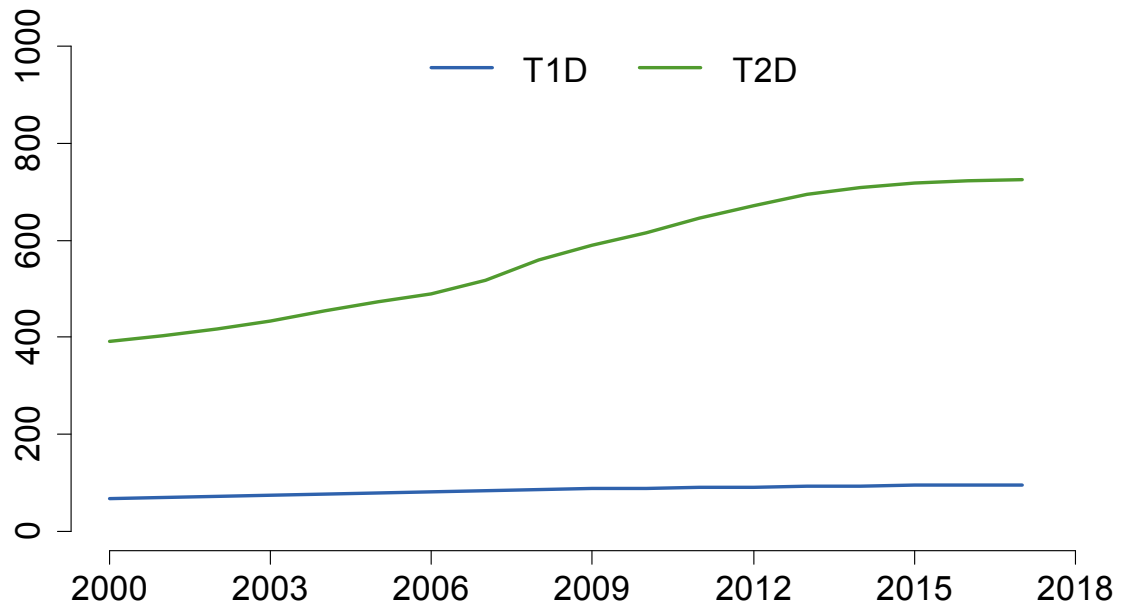


Figure 5. Age-standardised prevalence rate per 10,000 person years for type 1 diabetes (T1D) and type 2 diabetes (T2D) in the last day of each year in 2000-2017 in Finland.

Between 2000 and 2017, the age-standardised prevalence rate of T1D has steadily increased from 68 to 96 per 10,000 in the general population. During the same period for T2D it increased from 391 to 725 per 10,000 person years (Figure 5).

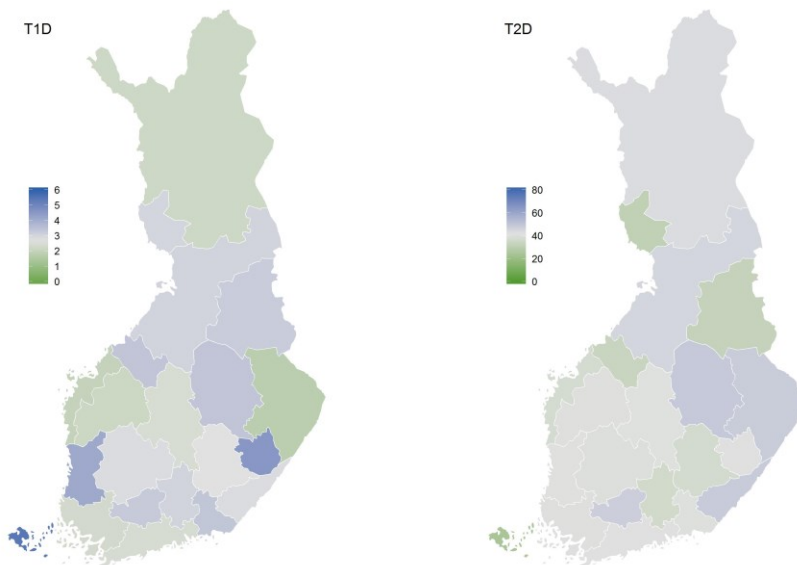


Figure 6. Age-standardised incidence rate per 10,000 person years in 2017 of type 1 diabetes (T1D) and type 2 diabetes (T2D) in the hospital districts and Åland Islands in Finland.

Figure 6 shows the age-standardised incidence rates in the hospital districts and Åland Islands in 2017. The Åland Islands had the highest incidence of T1D and the lowest incidence of T2D but the rates may be unreliable due to the small population. An east-west difference is seen in the incidence of T2D.

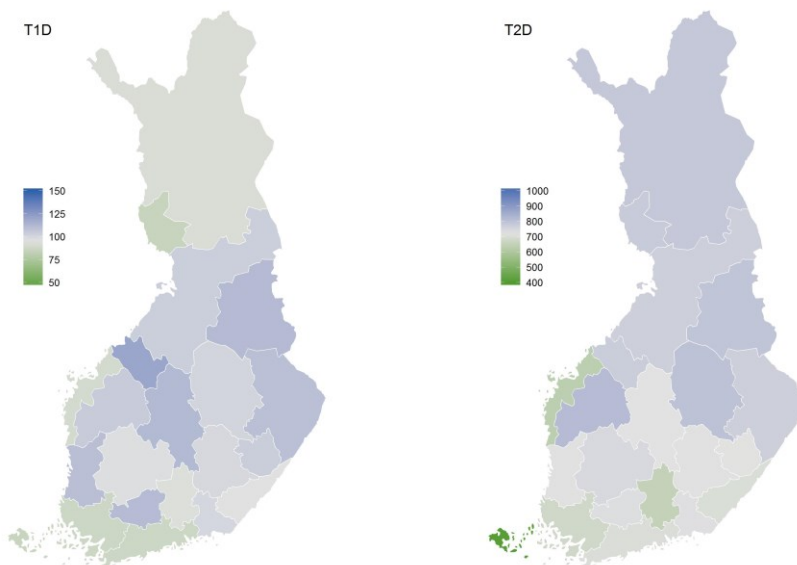


Figure 7. Age-standardised prevalence rate per 10,000 person years in 2017 of type 1 diabetes (T1D) and type 2 diabetes (T2D) in the hospital districts and Åland Islands in Finland.

The age-standardised prevalence rates in the hospital districts in 2017 show lower prevalence of T1D in the coastal and northernmost districts (Figure 7). As for T2D, the coastal and southern districts have lower prevalence rates compared to the northern ones.

The age-standardised incidence and prevalence rates were calculated with direct standardisation method using the total Finnish population in 2017 as the standard population.

Previous use of the FinDM data in research

The FinDM database has been used for wide scope of research on diabetes, and its care, complications and outcomes, as well as costs of diabetes care. In the chapter, the themes of research based on the FinDM data are shortly presented. The numbered references refer to the list of FinDM publications (Appendix 1).

A major objective of launching the FinDM project was to produce comprehensive data on morbidity related to diabetes. Accordingly, the FinDM data have primarily been used for research aiming at epidemiological and public health monitoring of diabetes in Finland, including trends in the incidence and prevalence of diabetes [15, 41, 46-49]. In association to these aims, several publications have been produced on methodological approaches of conducting register-based research on diabetes and of the challenges concerning composing a register on diabetes based on a range of nationwide administrative registers [14, 38, 48, 49, 63, 66].

Complications and comorbidities of diabetes have been a subject of several of studies in the FinDM research project. Several publications have addressed a wider range of complications and attempted to display an overall picture of challenges and occurrence of main complications [24, 25, 41, 45, 53]. Prevention, incidence, and treatment and outcomes of cardiovascular and cerebrovascular diseases have been studied in several articles [2-5, 9-11, 18, 21, 32, 39, 40, 43, 58, 59, 62]. Studies on amputations [1, 7, 13, 17] and renal disease [20, 29, 35, 61, 66] among people with diabetes have also been published. Some studies have concerned the incidence of depression [8, 19] and fractures [44] among people with diabetes.

The FinDM database has been also used for linkages to health care registers which are not included in the original FinDM linkage scheme. Data obtained from the linkage of the FinDM register and the Finnish Cancer Registry have been used for several studies addressing the incidence and prognosis of cancer among people with diabetes [16, 22, 23, 26, 28, 30, 31, 33, 34, 36, 52, 54, 56, 67, 68]. Another major topic based on these data is the associations of pharmaceuticals and cancer incidence among persons with diabetes. This topic has been studied addressing medications used in the care of diabetes [22, 26, 28, 30, 31, 33, 36, 56, 67, 68] and medications used for other purposes [8, 9, 18-22, 39, 59, 62].

The fourth major area of research is mortality among people with diabetes, which has been a frequent topic in the research [6, 12, 16, 28, 31, 33, 37, 61, 67, 68]. Mortality among the diabetes population has also been examined in terms socioeconomic [5, 6, 10, 12, 13, 63] or regional variation [24, 32, 40, 65].

A developing field in the use of the FinDM data is researching the costs accrued to diabetes and its care [42, 45, 50, 55, 57, 60]. Excess costs related medication and service use among people with diabetes have been estimated on a national level. Diabetes and its complications have an effect also on work ability and the participation in the working life [27, 64]. Costs arising from lost productivity due to exit from the labor force (sick leaves, early retirements and premature deaths) have also been estimated.

Concluding remarks

In general, the FinDM database provides high quality data for monitoring and researching diabetes and its care. The database is comprehensive and covers all persons with diabetes diagnosis in some of the several health care and health insurance registers in Finland. In addition, the FinDM database is a nationwide cohort with a long study period from 1964 to 2017 and wide scope of follow-up data from several register sources. Since 2010, the coverage of persons with diabetes is considered to be good in the FinDM database. However, there are some limitations in the FinDM data. While some persons with type 2 diabetes are treated with lifestyle modification but without any medications, they may have no diagnostic entries on diabetes in any ambulatory care registers and thus they are not included in the FinDM data. An obvious limitation of the FinDM database for research purposes is the lack and poor coverage of indicators describing primary health care and diagnostic data, including visits to occupational health care and private health care producers. Another challenge has been the long intervals in opportunity for updating the cohort to ensure up-to-date data on persons with diabetes.

In the future, the FinDM project aims to continue research on the incidence, prevalence, care and costs of diabetes as well as its complications and comorbidities. The planned new research topics for the future include research on comorbidities and complications not studied earlier as well as participation of persons with diabetes in working life. Among new specific research topics, the project aims to extend the use of the FinDM data to study gestational diabetes and polycystic ovary syndrome and their associations with diabetes. The project is also looking possibilities to link more accurate clinical and diagnostic data from primary and specialised health care to the FinDM database in order to develop the indicators of content and quality of care. The project is supporting to the Finnish Quality Register Pilots in order to facilitate the launch of a national quality register on diabetes. The project is also continuing collaboration with external researchers from other research institutes and universities. As mentioned above the FinDM database is open for research use by external researchers use on the predefined terms as described earlier.

References

- Abouzeid M, Wikström K, Peltonen M, Lindström J, Borodulin K, Rahkonen O, Laatikainen T. Secular trends and educational differences in the incidence of type 2 diabetes in Finland, 1972-2007. *Eur J Epidemiol*. 2015 Aug;30(8):649-59.
- American Diabetes Association. Economic cost of diabetes in the U.S. in 2017. *Diabetes Care* 2018; 41:917-928
- Brommer C, Sagalova V, Heesemann E, Manne-Goehler J, Atun R, Bärninghausen T, Davies J, Vollmer S. Global economic burden of diabetes in adults: Projections from 2015 to 2030. *Diabetes Care* 2018; 41:963-970.
- Beckman J, Paneni F, Cosentino F, Creager M. Diabetes and vascular disease: pathophysiology, clinical consequences, and medical therapy: part I. *Eur Heart J*. 2013; 34:2436–2443.
- Carstensen B, Kristensen JK, Marcussen MM, Borch-Johnsen K. The National Diabetes Register. *Scand J Public Health*. 2011 Jul;39(7 Suppl):58-61.
- Dehkon 2D -hanke (D2D) 2003-2007. Loppuraportti. Suomen Diabetesliitto ry. Kirjapaino Hermes Oy, 2009.
- Diabeteksen ehkäisyn ja hoidon kehittämissuunnitelma DEHKO 2000-2010. Loppuraportti. Kehitys Oy, Pori, 2011.
- Digital and Population Data Services Agency. The personal identity code. 2020. Available from: <https://dvv.fi/en/personal-identity-code>.
- Harjutsalo V, Sund R, Knip M, Groop PH. Incidence of type 1 diabetes in Finland. *JAMA*. 2013 July 24;310(4):427-8.
- International Diabetes Federation. IDF Diabetes Atlas, 9th edn. Brussels, Belgium: 2019. Available at: <https://www.diabetesatlas.org/>.
- Koski S, Ilanne-Parikka P, Kurkela O, Jarvala T, Rissanen P. Diabeteksen kustannukset: Lisäsairauksien ilmaantumisen puolittaminen toisi satojen miljoonien säästöt vuodessa. *Diabetes ja lääkäri*. 2018;47(2):13-17.
- Mayer-Davis EJ, Dabelea D, Lawrence JM. Incidence Trends of Type 1 and Type 2 Diabetes among Youths, 2002-2012. *N Engl J Med*. 2017;377:301.
- Finnish Centre for Pensions. Statistical database. 2020. Available from: <https://www.etk.fi/en/statistics-2/statistics/statistical-database/>.
- Finnish Federation of the Visually Impaired. Finnish register of visual impairment. 2020. Available from: <https://www.nkl.fi/en>.
- Finnish Kidney and Liver Association. Finnish registry for kidney diseases. 2020. Available from: https://www.muma.fi/liitto/suomen_munuaistautirekisteri/finnish_registry_for_kidney_diseases.
- Finnish Institute for Health and Welfare. Care register for health care. 2020a. Available from: <https://thl.fi/en/web/thlfi-en/statistics/information-on-statistics/register-descriptions/care-register-for-health-care>.
- Finnish Institute for Health and Welfare. Medical birth register. 2020b. Available from: <https://thl.fi/en/web/thlfi-en/statistics/information-on-statistics/register-descriptions/newborns>.
- Finnish Institute for Health and Welfare. Register of primary health care visits. 2020c. Available from: <https://thl.fi/en/web/thlfi-en/statistics/information-on-statistics/register-descriptions/register-of-primary-health-care-visits>.
- Finnish Institute for Health and Welfare. Sosiaalihuollon hoitoilmoitusrekisteri. 2020d. Available from: <https://thl.fi/fi/tilastot-ja-data/aineistot-ja-palvelut/rekisterien-tietosuojailmoitukset/sosiaalihuollon-hoitoilmoitusrekisteri>.
- Jonsson PM, Pikkujämsä S, Heiliö PL (eds.) National quality registers in healthcare and social services - operating model, organization and financing.

- Finnish Institute for Health and Welfare (THL). Report 16/2019. Helsinki: 2019.
- Kanta Services. What are the kanta services? 2020. Available from: <https://www.kanta.fi/en/what-are-kanta-services>.
- Ng CS, Lee JY, Toh MP, Ko Y. Cost-of-illness studies of diabetes mellitus: a systematic review. *Diabetes Res Clin Pract.* 2014 Aug;105(2):151-63.
- Niemi M, Winell K. Diabetes in Finland. Prevalence and variation in quality of care. Finnish Diabetes Association & National Research and Development Centre for Welfare and Health; Tampere: 2006.
- Ninomiya T. Epidemiological Evidence of the Relationship Between Diabetes and Dementia. *Adv Exp Med Biol.* 2019;1128:13-25.
- Niskanen L, Partonen T, Auvinen A, Haukka J. Excess mortality in Finnish diabetic subjects due to alcohol, accidents and suicide: a nationwide study. *Eur J Endocrinol.* 2018;179:299-306.
- Pukkala E, Engholm G, Hojsgaard Schmidt LK, Storm H, Khan S, Lambe M, et al. Nordic cancer registries - an overview of their procedures and data comparability. *Acta Oncol* 2018 April 01;57(4):440e55.
- Roy T, Lloyd CE. Epidemiology of depression and diabetes: a systematic review. *J Affect Disord.* 2012;142 Suppl:S8-21
- Salopuro T, Saaristo T, Korpi-Hyövälti E, Oksa H, Keinänen-Kiukaanniemi S, Saltevo J, Vanhala M, Niskanen L, Moltchanova E, Sundvall J, Tuomilehto J, Uusitupa M, Peltonen M. Lihavuuden ja glukoosiainevaihdunnan häiriöiden esiintyvyydessä on selviä alueellisia eroja Suomessa - D2D-hankkeen tuloksia. *Suom Lääkäril* 2010; 65:2381-2388
- Seuring T, Archangelidi O, Suhrcke M. The Economic Costs of Type 2 Diabetes: A Global Systematic Review. *Pharmacoeconomics.* 2015 Aug;33(8):811-31.
- Skupien J, Smiles A, Valo E, Ahluwalia T, Gyorgy B, Sandholm N, Croall S, Lajer M, McDonnell K, Forsblom C, Harjutsalo V, Marre M, Galecki A, Tregouet D, Wu C, Mychaleckyj J, Nickerson H, Pragnell M, Rich S, Pezzolesi M, Hadjadj S, Rossing P, Groop P, Krolewski A, Variations in Risk of End-Stage Renal Disease and Risk of Mortality in an International Study of Patients With Type 1 Diabetes and Advanced Nephropathy. *Diabetes Care.* 2019;42:93-101.
- Social Insurance Institution. Prescription database. 2020a. Available from: <https://www.kela.fi/en/web/en/statistics-by-topic/reimbursements-for-prescription-medicines>.
- Social Insurance Institution. The register of special reimbursement of medicines. 2020b. Available from: <https://www.kela.fi/en/web/en/statistics-by-topic/reimbursement-entitlements-in-respect-of-medicines>.
- Social Insurance Institution. Statistics by topic. 2020c. Available from: <https://www.kela.fi/web/en/statistics-by-topic>.
- Statistics Finland. Official statistics of Finland (OSF): Causes of death [e-publication]. ISSN=1799-5078. Helsinki: Statistics Finland. 2020a. Available from: https://www.stat.fi/til/ksyyt/index_en.html.
- Statistics Finland. Taika - research data catalogue. 2020b. Available from: <https://taika.stat.fi/en/>.
- Sund R, Koski S. FinDM II. On the register-based measurement of the prevalence and incidence of diabetes and its long-term complications. A technical report. Finnish Diabetes Association; Tampere: 2009.
- Thomas MC, Cooper ME, Zimmet P. Changing epidemiology of type 2 diabetes mellitus and associated chronic kidney disease. *Nat Rev Nephrol.* 2016;12:73-81.
- Williams R, Van Gaal L, Lucioni C. Assessing the impact of complications on the costs of Type II diabetes. *Diabetologia.* 2002 Jul;45(Suppl 1):S13-S17.
- Wu Y, Ding Y, Tanaka Y, Zhang W. Risk factors contributing to type 2 diabetes and recent advances in the treatment and prevention. *Int J Med Sci.* 2014; 11:1185-1200.

Appendix 1. List of FinDM publications

Peer-reviewed scientific articles in international journals

- [1] Winell K, Niemi M, Lepantalo M. The national hospital discharge register data on lower limb amputations. *Eur J Vasc Endovasc Surg.* 2006 July 01;32(1):66-70.
- [2] Winell KM, Paakkonen R, Pietila A, Niemi MK, Reunanen AR, Salomaa VV. Case fatality rates after first acute coronary syndrome in persons treated for type 2 diabetes show an improving trend. *Diabetologia.* 2010 March 01;53(3):472-80.
- [3] Winell K, Paakkonen R, Pietila A, Reunanen A, Niemi M, Salomaa V. Prognosis of ischaemic stroke is improving similarly in patients with type 2 diabetes as in nondiabetic patients in Finland. *Int J Stroke.* 2011 August 01;6(4):295-301.
- [4] Winell K, Pietila A, Niemi M, Reunanen A, Salomaa V. Trends in population attributable fraction of acute coronary syndrome and ischaemic stroke due to diabetes in Finland. *Diabetologia.* 2011 November 01;54(11):2789-94.
- [5] Forssas EH, Keskimaki IT, Reunanen AR, Koskinen SV. Coronary heart disease among diabetic and nondiabetic people - socioeconomic differences in incidence, prognosis and mortality. *J Diabetes Complications.* 2008 February 01;22(1):10-7.
- [6] Forssas E, Arffman M, Koskinen S, Reunanen A, Keskimaki I. Socioeconomic differences in mortality among diabetic people in Finland. *Scand J Public Health.* 2010 Nov;38(7):691-8.
- [7] Ikonen TS, Sund R, Venermo M, Winell K. Fewer major amputations among individuals with diabetes in Finland in 1997-2007: A population-based study. *Diabetes Care.* 2010 December 01;33(12):2598-603.
- [8] Manderbacka K, Sund R, Koski S, Keskimaki I, Elovainio M. Diabetes and depression? secular trends in the use of antidepressants among persons with diabetes in Finland in 1997-2007. *Pharmacoepidemiol Drug Saf.* 2011 April 01;20(4):338-43.
- [9] Vehko T, Manderbacka K, Arffman M, Sund R, Reunanen A, Keskimaki I. Changing patterns of secondary preventive medication among newly diagnosed coronary heart disease patients with diabetes in Finland: A register-based study. *Scand J Public Health.* 2010 May;38(3):317-24.
- [10] Vehko T, Manderbacka K, Arffman M, Reunanen A, Keskimaki I. Increasing resources effected equity in access to revascularizations for patients with diabetes. *Scand Cardiovasc J.* 2010 Aug;44(4):237-44.
- [11] Vehko T, Sund R, Manderbacka K, Hakkinen U, Keskimaki I. Pathways leading to coronary revascularisation among patients with diabetes in Finland: A longitudinal register-based study. *BMC Health Serv Res.* 2011 August 03;11:180.
- [12] Forssas E, Manderbacka K, Arffman M, Keskimaki I. Socio-economic predictors of mortality among diabetic people. *Eur J Public Health.* 2012 Jun;22(3):305-10.
- [13] Venermo M, Manderbacka K, Ikonen T, Keskimaki I, Winell K, Sund R. Amputations and socioeconomic position among persons with diabetes mellitus, a population-based register study. *BMJ Open.* 2013 April 08;3(4):10.1136/bmjopen.2012.002395. Print 2013.
- [14] Kiiwet R, Sund R, Linna M, Silverman B, Pisarev H, Friedman N. Methodological challenges in international performance measurement using patient-level administrative data. *Health Policy.* 2013 September 01;112(1-2):110-21.
- [15] Harjutsalo V, Sund R, Knip M, Groop PH. Incidence of type 1 diabetes in Finland. *JAMA.* 2013 July 24;310(4):427-8.
- [16] Forssas E, Sund R, Manderbacka K, Arffman M, Ilanne-Parikka P, Keskimaki I. Increased cancer mortality in diabetic people treated with insulin: A

- register-based follow-up study. *BMC Health Serv Res.* 2013 July 09;13:267.
- [17] Winell K, Venermo M, Ikonen T, Sund R. Indicators for comparing the incidence of diabetic amputations: A nationwide population-based register study. *Eur J Vasc Endovasc Surg.* 2013 November 01;46(5):569-74.
- [18] Vehko T, Sund R, Arffman M, Manderbacka K, Ilanne-Parikka P, Keskimaki I. Monitoring the use of lipid-lowering medication among persons with newly diagnosed diabetes: A nationwide register-based study. *BMJ Open.* 2013 November 04;3(11):e003414.
- [19] Manderbacka K, Jokela M, Sund R, Elovainio M. Treatment of depression in diagnosed diabetes: Common cause or detection bias? *Psychol Med.* 2014 April 01;44(6):1205-12.
- [20] Helve J, Sund R, Haapio M, Groop PH, Gronhagen-Riska C, Finne P. Medication among patients with type 1 diabetes and predialytic renal disease. *Diabetes Res Clin Pract.* 2014 March 01;103(3):510-5.
- [21] Ruokoniemi P, Sund R, Arffman M, Helin-Salmivaara A, Huupponen R, Keskimaki I, et al. Are statin trials in diabetes representative of real-world diabetes care: A population-based study on statin initiators in Finland. *BMJ Open.* 2014 Jun 19;4(6):e005402.
- [22] Levin D, Bell S, Sund R, Hartikainen SA, Tuomilehto J, Pukkala E, et al. Pioglitazone and bladder cancer risk: A multipopulation pooled, cumulative exposure analysis. *Diabetologia.* 2015 March 01;58(3):493-504.
- [23] Carstensen B, Read SH, Friis S, Sund R, Keskimaki I, Svensson AM, et al. Cancer incidence in persons with type 1 diabetes: A five-country study of 9,000 cancers in type 1 diabetic individuals. *Diabetologia.* 2016 May 01;59(5):980-8.
- [24] Manderbacka K, Arffman M, Lumme S, Lehto M, Winell K, Keskimaki I. Regional trends in avoidable hospitalisations due to complications among population with diabetes in Finland in 1996-2011: A register-based cohort study. *BMJ Open.* 2016 August 22;6(8):e011620.
- [25] Forssas E, Arffman M, Manderbacka K, Keskimaki I, Ruuth I, Sund R. Multiple complications among people with diabetes from Finland: An 18-year follow-up in 1994-2011. *BMJ Open Diabetes Res Care.* 2016 October 04;4(1):e000254.
- [26] Arima R, Marttila M, Hautakoski A, Arffman M, Sund R, Ilanne-Parikka P, et al. Antidiabetic medication, statins and the risk of endometrioid endometrial cancer in patients with type 2 diabetes. *Gynecol Oncol.* 2017 September 01;146(3):636-41.
- [27] Hakkarainen P, Sund R, Arffman M, Koski S, Hanninen V, Moilanen L, et al. Working people with type 1 diabetes in the Finnish population. *BMC Public Health.* 2017 October 12;17(1):805-8.
- [28] Arima R, Hautakoski A, Marttila M, Arffman M, Sund R, Ilanne-Parikka P, et al. Cause-specific mortality in endometrioid endometrial cancer patients with type 2 diabetes using metformin or other types of antidiabetic medication. *Gynecol Oncol.* 2017 December 01;147(3):678-83.
- [29] Helve J, Sund R, Arffman M, Harjutsalo V, Groop PH, Gronhagen-Riska C, et al. Incidence of end-stage renal disease in patients with type 1 diabetes. *Diabetes Care.* 2018 March 01;41(3):434-9.
- [30] Urpilainen E, Marttila M, Hautakoski A, Arffman M, Sund R, Ilanne-Parikka P, et al. The role of metformin and statins in the incidence of epithelial ovarian cancer in type 2 diabetes: A cohort and nested case-control study. *BJOG.* 2018 July 01;125(8):1001-8.
- [31] Arima R, Marttila M, Hautakoski A, Arffman M, Sund R, Ilanne-Parikka P, et al. Antidiabetic medication, statins and the risk and prognosis of non-endometrioid endometrial cancer in women with type 2 diabetes. *Anticancer Res.* 2018 July 01;38(7):4169-78.
- [32] Winell K, Arffman M, Pietila A, Salomaa V. Regional differences in the incidence of diabetic cardiovascular events reflect the quality of care. *Scand Cardiovasc J.* 2018 October 01;52(5):232-7.

[33] Urpilainen E, Marttila M, Hautakoski A, Arffman M, Sund R, Ilanne-Parikka P, et al. Prognosis of ovarian cancer in women with type 2 diabetes using metformin and other forms of antidiabetic medication or statins: A retrospective cohort study. *BMC Cancer*. 2018 July 28;18(1):767.

[34] Saarela K, Tuomilehto J, Sund R, Keskimäki I, Hartikainen S, Pukkala E. Cancer incidence among Finnish people with type 2 diabetes during 1989-2014. *Eur J Epidemiol*. 2019 March 01;34(3):259-65.

[35] Finne P, Groop PH, Arffman M, Kervinen M, Helve J, Gronhagen-Riska C, et al. Cumulative risk of end-stage renal disease among patients with type 2 diabetes: A nationwide inception cohort study. *Diabetes Care*. 2019 April 01;42(4):539-44.

[36] Hosio M, Urpilainen E, Marttila M, Hautakoski A, Arffman M, Sund R, et al. Association of antidiabetic medication and statins with breast cancer incidence in women with type 2 diabetes. *Breast Cancer Res Treat*. 2019 June 01;175(3):741-8.

Peer-reviewed scientific articles in domestic journals

[37] Forssas E, Sund R, Manderbacka K, Arffman M, Ilanne-Parikka P, Keskimäki I. Diabeetikoilla yhä suuri ylikuolleisuus muuhun väestöön verrattuna. *Suomen lääkärilehti - Finlands läkartidning*. 2010;65(26-31):2359-67.

[38] Sund R, Harno K, Ranta S, Tolppala E. Comparing the case inclusion in two population-based diabetes registers. *Finnish Journal of eHealth and eWelfare*. 2010;2(3):136-46.

[39] Forssas E, Sund R, Manderbacka K, Vehko T, Arffman M, Ilanne-Parikka P, et al. Sepelvaltimotaudin riskitekijöiden lääkehoito on tehostunut diabeetikoilla. *Suomen lääkärilehti - Finlands läkartidning*. 2011;66(47):3569-75.

[40] Winell K, Arffman M, Salomaa V. Diabeetikoiden akuuttien sydäntapahtumien ja aivoinfarktien ilmaantumisesissa suuria alueellisia eroja. *Duodecim*. 2020;136(5):561-8.

Non-refereed scientific articles in domestic journals

[41] Koski S, Sund R. Diabeetikoiden määrä lisääntyy, mutta lisäsairaudet vähenevät. *Diabetes ja lääkäri*. 2010;39(1):7-11.

[42] Rissanen P, Jarvala T, Codif-tutkimustyöryhmä. Diabeteksen kustannukset Suomessa 1998-2007. *Diabetes ja lääkäri*. 2010;39(1):12-4.

[43] Winell K. Suurten verisuonten sairaudet: Diabeetikoiden ennuste paranee vähitellen, mutta ero muihin säilyy. *Diabetes ja lääkäri*. 2014;43(2):13-5.

[44] Istolainen T, Sund R, Rikkinen T, Kröger H. Lonkkamurtumariski diabetesta sairastavilla. *Suomen Ortopedia ja Traumatologia*. 2017;40:164-8.

[45] Koski S, Ilanne-Parikka P, Kurkela O, Jarvala T, Rissanen P. Diabeteksen kustannukset: Lisäsairauksien ilmaantumisen puolittaminen toisi satojen miljoonien säästöt vuodessa. *Diabetes ja lääkäri*. 2018;47(2):13-7.

Other research-related publications

[46] Niemi M, Winell K. Diabetes Suomessa. Esiintyvyys ja hoidon laadun vaihtelu. *Stakes raportteja*; 8/2005.

[47] Niemi M, Winell K. Diabetes in Finland. Prevalence and variation in quality of care. Finnish Diabetes Association & National Research and Development Centre for Welfare and Health; Tampere: 2006.

[48] Sund R, Koski S. FinDM II. Diabeteksen ja sen lisäsairauksien esiintyvyyden ja ilmaantuvuuden rekisteriperusteinen mittaaminen - Tekninen raportti. Suomen Diabetesliitto; Tampere: 2009.

[49] Sund R, Koski S. FinDM II. On the register-based measurement of the prevalence and incidence of diabetes and its long-term complications. A technical report. Finnish Diabetes Association; Tampere: 2009.

[50] Jarvala T, Raitanen J, Rissanen P. Diabeteksen kustannukset Suomessa 1998-2007 (Costs of diabe-

tes in Finland 1998-2007). Finnish Diabetes Association & University of Tampere; Tampere: 2010.

[51] Hofmacher MM, Smith P (ed.). The health data navigator. Your toolkit for comparative performance analysis. A EuroREACH product. European Centre for Social Welfare Policy and Research ;Vienna: 2013.

[52] Forssas E, Sund R, Manderbacka K, Arffman M, Ilanne-Parikka P, Keskimäki I. Insuliinihoitoisten diabeetikoiden syöpäkuolleisuus on lisääntynyt Suomessa. BestPractice Diabetes ja Sydänsairaudet. 2013;4:7-11.

[53] Winell K, Summanen P. Diabeteksen komplikaatioiden estäminen on onnistunut vain osittain. Pääkirjoitus. Duodecim. 2014;130:1207-09.

[54] Saarela K. Tyypin 1 diabetes ja syöpäriski: Viiden maan tutkimus. BestPractice Onkologia ja Hematologia. 2016.

[55] Haula T, Kuronen M, Saukkonen T, Häkkinen U, Seppälä TT. Diabetes pääkaupunkiseudulla – potilasmäärät, kustannukset ja lisäkustannukset. Työpäpaperi 34/2017. Terveystieteiden tutkimuskeskus (THL); Helsinki.

[56] Arima R, Hinkula M. Metformiini ja kohdun runko-osan syövän ennuste tyypin 2 diabetesta sairastavilla naisilla. BestPractice Onkologia ja Hematologia. 2018.

[57] Koski S, Kurkela O, Rissanen P, Ilanne-Parikka P. Mikä diabeteksessä maksaa? Erikoislääkäri. 2018;4:165-6.

Theses

[58] Winell K. The epidemiology of macrovascular complications of diabetes in Finland 1992-2002 [dissertation]. Helsingin yliopisto; 2013.

[59] Vehko T. Examining time trends in treatment practices using register-based data – A study of changing coronary heart disease care among persons with diabetes [dissertation]. Tampereen yliopisto; 2014.

[60] Puranen A. Sairaanhoidon kustannuksiin alueellisesti vaikuttavat tekijät tyypin 2 diabeetikoilla Suomessa vuonna 2007 [master's thesis]. Tampereen yliopisto; 2014.

[61] Helve J. Survival of patients with type 1 diabetes on renal replacement therapy [dissertation]. Helsingin yliopisto; 2014.

[62] Ruokonieniemi P. From statin efficacy to everyday effectiveness: Studying the gap in between [dissertation]. Turun yliopisto; 2015.

[63] Steele C. Developing statistical models to assess the effects of socioeconomic position on the incidence of and outcome from type 2 diabetes in older adults: Evidence from the CHANCES cohorts [dissertation]. Queen's University Belfast; 2016.

[64] Hakkarainen P. Type 1 diabetes and work [dissertation]. Itä-Suomen yliopisto; 2017.

[65] Van der Velde L. Missing links in the genesis of type 1 diabetes. A geographical approach to the case enteroviruses in the Nordic region.[master's thesis]. Stockholm University; 2018.

[66] But A. Mitigating bias and dealing with multiple time scales in cohort studies: Studying medications and complications of diabetes [dissertation]. Helsingin yliopisto; 2018.

[67] Arima R. Metformin, statins and the risk and prognosis of endometrial cancer in women with type 2 diabetes [dissertation]. Oulun yliopisto; 2019.

[68] Urpilainen E. The role of metformin and statins in ovarian and breast cancer in women with type 2 diabetes [dissertation]. Oulun yliopisto; 2019.