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## Socioeconomic differences in the development and prevention of type 2 diabetes Focus on education and lifestyle

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#### ACADEMIC DISSERTATION

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## ABSTRACT

During recent decades, changes in society and environment have led to changes in lifestyle. As a result, risk factors for type 2 diabetes, such as obesity and physical inactivity, have increased in the population. Further, socioeconomic factors play a role in the development of type 2 diabetes, with those in the low socioeconomic group being at highest risk. As a consequence, type 2 diabetes and health differences in the population are increasing and affecting both society and individuals.

The aim of the present study was to examine the role of socioeconomic status in determining the risk factors, occurrence, comorbidities, and prevention of type 2 diabetes.

This study included 25- to 64-year-old men and women who participated in either one of the three population-based cross-sectional surveys, or in an intervention study. The population-based surveys were the evaluation study for the implementation project (FIN-D2D, n=3642) of the Finnish national diabetes prevention programme (DEHKO), the Finnish risk factors survey (FINRISK, n=38689 and n=32972), and the Health Behaviour and Health among the Finnish Adult Population (AVTK, n=10831) postal survey from different study years. Also, data from the Finnish Diabetes Prevention Study (DPS, n=522), a randomized clinical intervention trial, were used in this study. The data originated from questionnaires and/or health examinations including laboratory tests, and educational level was used as the indicator for socioeconomic status. When appropriate, the incident diagnoses of type 2 diabetes and other chronic diseases were identified through linkage with the national registers on reimbursement rights, hospitalizations, and mortality.

Hyperglycaemia was more common among those with low education compared with those with medium and high education. Obesity, unhealthy diet and smoking were all inversely related to educational level. Incidence of type 2 diabetes increased from the 1970s to 2000s among men but not among women. Body mass index was the strongest explanatory factor for the association between education and type 2 diabetes. However, among men with low and middle educational attainment, diabetes incidence increased over time even after adjusting for body mass index.

We did not find evidence that educational level would independently predict the development of comorbidity among people with diabetes. Further, in people with increased risk of type 2 diabetes, counselling to improve lifestyle and prevent diabetes was effective in all educational groups. The FIN-D2D project was active for 4 years, and during that time populationlevel awareness of the national diabetes prevention programme increased in both the implementation and control areas, but remained consistently higher in the implementation area. We found no association between educational level and awareness. Self-reported lifestyle changes were more common among women than among men; however, the association between lifestyle changes and awareness of the programme was stronger in men.

In conclusion, the incidence of type 2 diabetes has increased among Finnish men, but not among women, and has occurred predominantly among men with low and middle educational attainment. Obesity explained some but not all of this variation between socioeconomic classes. On the other hand, no evidence was found to suggest that low socioeconomic status increases the development of comorbidities among people with diabetes or decreases the effectiveness of lifestyle intervention aiming to prevent type 2 diabetes among people at risk. Furthermore, the national diabetes prevention programme succeeded in increasing awareness of type 2 diabetes among the population, regardless of socioeconomic status. This study provides knowledge to support future activities to prevent type 2 diabetes and other chronic diseases and suggests that interventions can diminish health disparities.

# TIIVISTELMÄ

Tyypin 2 diabetes on yleistynyt nopeasti suomalaisessa väestössä viime vuosikymmeninä. Lisääntymisen ajatellaan johtuvan pitkälti lihavuuden yleistymisestä, liikunnan vähentymisestä, ja väestön ikääntymisestä. Myös sosioekonomiset tekijät ovat yhteydessä tyypin 2 diabeteksen kehittymiseen; alemmassa sosioekonomisessa asemassa olevilla henkilöillä riski sairastua on suurentunut. Sekä tyypin 2 diabeteksen ehkäisy että terveyserojen kaventaminen ovat kansanterveyden edistämisen painopistealueita.

Tämän tutkimuksen tavoitteena oli selvittää sosioekonomisia eroja tyypin 2 diabeteksen, sen riskitekijöiden ja lisäsairauksien esiintymisessä sekä ehkäisytoimien vaikuttavuudessa.

Tutkimuksessa käytettiin kansallisen diabeteksen ehkäisyohjelman eli DEHKOn toimeenpanohankkeen (FIN-D2D) arviointitutkimuksen (n=3642), kansallisen riskitekijätutkimuksen (FINRISKI, n=38689 ja n=32972) sekä aikuisväestön terveyskäyttäytymistä ja terveyttä kartoittavan postikvselvn n=10831) väestöpohjaisia aineistoja. Lisäksi (AVTK, kävtettiin satunnaistetun Diabeteksen ehkäisytutkimuksen (DPS, n= 522) aineistoa. Tutkimuksessa tarkasteltiin 25-64 -vuotiaiden miesten ja naisten tervevstarkastusten mittaustuloksia ja vastauksia lomakekyselyihin, kuten tietoja vastaajien koulutustasosta. Suhteellista koulutusta käytettiin sosioekonomisen aseman indikaattorina. Tiedot diabeteksen ja sen lisäsairauksien ilmaantuvuudesta seuranta-aikana saatiin yhdistämällä FINRISKI -aineistoihin kansallisen eritvislääkekorvaus-, hoitoilmoitus- ja kuolinsyyrekisterin tietoja.

Tyypin 2 diabetes ja muut sokeriaineenvaihdunnan häiriöt olivat yleisempiä alemmassa koulutusryhmässä ylimpään verrattuna, samoin kuin diabeteksen riskitekijöistä lihavuus, epäterveelliset ruokatottumukset ja tupakointi. Miehillä diabeteksen ilmaantuvuus suureni seuranta-aikana, ja samanaikaisesti myös miesten lihavuus yleistyi kaikissa koulutusryhmissä. Lihavuuden yleistyminen selitti osittain diabeteksen ilmaantuvuuden kasvua, mutta ei poistanut kokonaan koulutusryhmien välillä havaittuja eroja. Naisilla diabeteksen ilmaantuvuus ei lisääntynyt seuranta-aikana.

Useat riskitekijät ennustivat lisäsairauksien ilmaantuvuutta tyypin 2 diabetesta sairastavilla. Koulutusryhmittäisiä eroja lisäsairauksien ilmaantuvuudessa ei kuitenkaan havaittu tyypin 2 diabetesta sairastavilla henkilöillä. Myöskään kohonneen diabetesriskin henkilöille kohdennetun elintapaneuvonnan tehokkuudessa ei havaittu eroja koulutusryhmien välillä, kun tarkasteltiin elintapamuutoksia tai diabeteksen ilmaantuvuutta. Väestön tietoisuus käynnissä olevasta kansallisesta diabeteksen ehkäisyohjelmasta parani ohjelman toimeenpanohankkeeseen osallistuvilla alueilla, mutta myös alueilla, jotka eivät osallistuneet hankkeeseen. Henkilön koulutustausta ei ollut yhteydessä tietoisuuteen hankkeesta. Naiset raportoivat miehiä useammin muuttaneensa elintapojaan kuluneen vuoden aikana, mutta miehillä elintapamuutokset olivat naisia useammin yhteydessä tietoisuuteen diabetesohjelmasta.

Tämä tutkimus osoittaa diabeteksen ilmaantuvuuden suurentuneen miehillä viime vuosikymmeninä. Tyypin 2 diabetes on yleisempää alemmissa koulutusryhmissä kuin ylimmässä koulutusryhmässä, ja havaittua yhteyttä selittävät tunnetut riskitekijät, eritvisesti lihavuus, Monet riskitekijät ennustavat myös diabeteksen lisäsairauksien ilmaantuvuutta, mutta koulutustaustan havaittu olevan vhtevdessä lisäsairauksien ei ilmaantuvuuteen. Tulokset osoittavat tyypin diabeteksen 2 ehkäisytoimenpiteiden toimivan kaikissa koulutusryhmissä, niin korkean diabetesriskin henkilöillä kuin väestössä. Tieto tukee niiden toimenpiteiden kehittämistä ja suuntaamista, joilla pyritään ehkäisemään tyypin 2 diabetesta ja kaventamaan terveyseroja suomalaisessa väestössä.

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## LIST OF ORIGINAL PUBLICATIONS

This thesis is based on the following original publications, which are referred to in the text by the Roman numerals.

- I Wikström K, Lindström J, Tuomilehto J, Saaristo TE, Korpi-Hyövälti E, Oksa H, Vanhala M, Niskanen L, Keinänen-Kiukaanniemi S, Uusitupa M, Peltonen M. Socioeconomic differences in dysglycemia and lifestyle-related risk factors in the Finnish middle-aged population. The FIN-D2D survey. European Journal of Public Health 2010; 21(6):768-774.
- II 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. European Journal of Epidemiology 2015; 30(8):649-659.
- III Wikström K, Lindström J, Harald K, Peltonen M, Laatikainen T. Clinical and lifestyle-related risk factors for incident multimorbidity: 10-year follow-up of Finnish populationbased cohorts 1982-2012. European Journal of Internal Medicine 2015; 26(3):211-216.
- Wikström K, Peltonen M, Eriksson JG, Aunola S, Ilanne-Parikka P, Keinänen-Kiukaanniemi S, Uusitupa M, Tuomilehto J, Lindström J.
   Educational attainment and effectiveness of lifestyle intervention in the Finnish Diabetes Prevention Study. Diabetes Research and Clinical Practice 2009; 86(1):e1-5.
- Wikström K, Lindström J, Tuomilehto J, Saaristo TE, Helakorpi S, Korpi-Hyövälti E, Oksa H, Vanhala M, Keinänen-Kiukaanniemi S, Uusitupa M, Peltonen M. National diabetes prevention program (DEHKO): Awareness and self-reported lifestyle changes in Finnish population. Public Health 2015; 129(3):210-217.

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\*K. Wikström and M. Abouzeid share the primary authorship of the 2<sup>nd</sup> publication. It has been used in the Public Health thesis of M. Abouzeid.

# ABBREVIATIONS

ATC	Anatomical Therapeutic Chemical (classification system code)		
AVTK	Health Behaviour and Health among the Finnish Adult		
	Population survey		
BMI	body mass index		
CI	confidence interval		
DEHKO Development Programme for the Prevention and Care			
	Diabetes (= National diabetes prevention programme)		
DPP	Diabetes Prevention Program		
DPS	Diabetes Prevention Study		
FIN-D2D	D Implementation project of the DEHKO		
FINGER	Finnish Geriatric Intervention Study to Prevent Cognitive		
	Impairment and Disability		
FINRISK	Finnish risk factors survey		
HbA1c	glycated haemoglobin		
HR	hazard ratio		
ICD	International Classification of Diseases		
IFG	impaired fasting glucose		
IGT	impaired glucose tolerance		
OGTT	oral glucose tolerance test		
OR	odds ratio		
RR	relative risk		
SES	socioeconomic status		
ST2D	screen-detected type 2 diabetes		
T2D	type 2 diabetes		
TT2D	total type 2 diabetes		
WHO	World Health Organization		

## **1 INTRODUCTION**

The population is ageing rapidly in Finland; a quarter of the population is predicted to be 65 years old or older by 2030 (Statistics of Finland 2015). In parallel, new health issues have emerged worldwide, such as the increasing prevalence of type 2 diabetes (Shaw, Sicree & Zimmet 2010, International Diabetes Federation 2015). It is well known that the incidence of type 2 diabetes and its comorbidities increases with age. Furthermore, changes in society and the environment have led to changes in lifestyle during recent decades. As a result, lifestyle-related risk factors for type 2 diabetes have increased among the population. In addition to ageing and its effect on morbidity, health disparities between population subgroups are one of the main concerns for health policy in Finland (Palosuo 2009). In general, health has improved in all socioeconomic groups, but the improvement has been more pronounced within the high socioeconomic groups. Therefore, despite the continuous actions aiming to diminish the disparities in health, the differences between socioeconomic groups have actually widened during recent decades (Palosuo & Sihto 2016).

In Western societies, lower socioeconomic status is associated with an increase in the prevalence of type 2 diabetes and its comorbidities (Espelt et al. 2008). This association is partly explained by the higher prevalence of lifestyle-related risk factors, such as obesity, physical inactivity, and smoking among people with lower socioeconomic status (Kumari, Head & Marmot 2004). In addition, type 2 diabetes in connection with low socioeconomic status is often associated with poor quality of life, greater use of health services, higher healthcare costs, hospitalizations and mortality (Espelt et al. 2008, Marengoni et al. 2011). Further, it has been suggested that socioeconomic status may determine the care of diabetes, those with lower socioeconomic status having worse management of clinical risk factors and worse adherence to recommended treatment, and as a consequence, a higher number of serious complications (Grintsova, Maier & Mielck 2014). Consequently, type 2 diabetes and health differences are causing a considerable burden to society and individuals.

Previously, clinical trials and implementation studies have confirmed that type 2 diabetes is preventable by beneficial lifestyle changes among people with a high risk of type 2 diabetes (Tuomilehto et al. 2001, Knowler et al. 2002, Absetz et al. 2009), and the management of risk factors provides possibilities also for the prevention of comorbidities among people with type 2 diabetes (Gaede et al. 2003). However, little is known about the effectiveness of lifestyle intervention among high-risk individuals with different socioeconomic background. Further, the evidence on the effectiveness of type 2 diabetes prevention activities at the population level across different socioeconomic groups is insufficient.

In the current study, the association of socioeconomic status with the occurrence of type 2 diabetes and its risk factors was examined over time among the Finnish population. Further, the risk factors for incident comorbidities among people with type 2 diabetes were examined. Finally, the impact of socioeconomic status on the prevention of type 2 diabetes in high-risk individuals and at the population level was examined to provide support for future prevention approaches as well as to reduce health disparities among the ageing population.

## 2 REVIEW OF THE LITERATURE

## 2.1 TYPE 2 DIABETES

#### 2.1.1 DEFINITION AND PATHOPHYSIOLOGY

Type 2 diabetes is defined as a metabolic disorder with insulin deficiency and/or insulin resistance resulting in increased blood glucose concentration. Insulin resistance means the inability of insulin to sufficiently stimulate glucose uptake in tissues, and insulin deficiency is a decreased ability of the pancreatic beta cells to secrete insulin (World Health Organization 1985, World Health Organization 1999, World Health Organization & International Diabetes Federation 2006).



Figure 1. Pathogenesis of type 2 diabetes (DeFronzo 2009, Zheng, Ley & Hu 2018)

The pathogenesis of type 2 diabetes is complex (Figure 1). Briefly, impaired insulin secretion from the beta cells in the pancreas and insulin resistance in the skeletal muscle and liver represent the core defects in type 2 diabetes. Also, the adipose tissue is resistant to the effect of insulin and as a consequence, the levels of free fatty acids increase in plasma. Increased fatty acids levels impair insulin secretion, induce insulin resistance and stimulate gluconeogenesis in the liver and kidneys (DeFronzo 2009, Zheng, Ley & Hu 2018). Further, the kidneys have an important role in maintaining glucose

homeostasis by glucose reabsorption (Triplitt 2012). The gut is a major endocrine organ and its incretin hormones stimulate insulin secretion in response to meals, inhibit glucagon secretion and delay stomach emptying, but the secretion and the effect of these hormones is decreased in the stages of hyperglycaemia (Sanusi 2009). In the brain and central nervous system, insulin affects feeding behaviour and energy metabolism, but these functions are disturbed as a consequence of decreased insulin sensitivity (Schwartz, Porte 2005).

The manifestation of type 2 diabetes may take several years, and most of the people suffering stages of intermediate hyperglycaemia, including impaired glucose tolerance (IGT) and impaired fasting glucose (IFG), may be unaware of the progressive disease for a long time (Unwin et al. 2002). Type 2 diabetes and other forms of hyperglycaemia can be diagnosed by an oral glucose tolerance test (OGTT), with blood glucose values measured during fasting and after a glucose load. The interpretation of the OGTT results as diagnostic criteria has twice been published and revised by the World Health Organization (WHO) (World Health Organization 1985, World Health Organization 1999). According to the latest criteria, the diagnostic cut-off point for type 2 diabetes is exceeded when the fasting glucose value is  $\geq$ 7.0 mmol/l or the 2-hour post-load glucose value is  $\geq$ 11.1 mmol/l. The WHO classification also includes criteria for the diagnosis of IGT and IFG, and all criteria are presented in Table 1 (World Health Organization 1999).

Glucose tolerance	Plasma glucose (mmol/l)
Normal glucose tolerance	
Fasting glucose	≤6.0 and
2 hours post glucose load	<7.8
Impaired fasting glucose	
Fasting glucose	6.1–6.9 and
2 hours post glucose load	<7.8
Impaired glucose tolerance	
Fasting glucose	<7.0 and
2 hours post glucose load	7.8–11.0
Type 2 diabetes	
Fasting glucose	≥7.0 or
2 hours post glucose load	≥11.1
HbA1c	≥6.5% (48 mmol/mol)

Table 1. Classification of glucose tolerance

HbA1c=glycated haemoglobin.

In 2011, the WHO published a new guideline in which it accepted glycated haemoglobin (HbA1c) as an option for the diagnosis of type 2 diabetes (World Health Organization 2011). However, it refrained from recommending it to be used as a measure of non-diabetic hyperglycaemia, because HbA1c is not effective in detecting IFG or IGT. The detection of stages of intermediate hyperglycaemia is important, because such individuals do not only have a higher risk of developing type 2 diabetes, but also of developing diabetic complications (DECODE Study Group & European Diabetes Epidemiology Group 2003, Levitan et al. 2004, World Health Organization & International Diabetes Federation 2006)

#### 2.1.2 EPIDEMIOLOGY

The prevalence of type 2 diabetes has been increasing during recent decades and is reaching epidemic proportions worldwide (Chan et al. 2009, Yang et al. 2010, Shaw, Sicree & Zimmet 2010, Danaei et al. 2011, Forouhi & Wareham 2014, Ogurtsova et al. 2017). The global prevalence of diabetes was estimated to be 8.8% in 2015, and it has been predicted to increase to 10.4% by the year 2040, with the majority of the incident cases emerging in India and China (International Diabetes Federation 2015, Ogurtsova et al. 2017). In Europe, the age-adjusted diabetes prevalence was 7.3% in 2015, and it is estimated that approximately 90% of all diabetic cases are type 2 (International Diabetes Federation 2015). In addition to the diagnosed diabetes cases, there are a large number of people with IGT, IFG and undiagnosed type 2 diabetes (Unwin et al. 2002, DECODE Study Group 2003, Mayor 2005, Beagley et al. 2014).

In Finland, the age-adjusted prevalence of diabetes in 45- to 64-year-old Finns was 5.7% for men and 4.6% for women in the 1980s (Tuomilehto et al. 1991). In the 1990s, the age-adjusted prevalence of type 2 diabetes among the 45- to 64-year-old population was found to be 10.2% in men and 7.4% in women, and a large number of these diabetes cases were previously undiagnosed (Ylihärsilä et al. 2005). In 2004–2005, a population-based survey was conducted among the 45- to 74-year-old population, and the prevalence of diagnosed type 2 diabetes was found to be 7.1% and 3.9% in men and women, respectively. In the same study, the prevalence of previously undiagnosed type 2 diabetes was 9.3% in men and 7.3% in women. Furthermore, the overall prevalence of hyperglycaemia was 42% and 33.4%, respectively (Saaristo et al. 2008). According to the register-based data, the total number of people with type 2 diabetes in Finland increased by 77% between 1997 and 2007 (Sund & Koski 2009), and the number is still increasing (Koski 2017). The current estimated amount of people with type 2 diabetes is approximately 500 000, of whom about 150 000 are undiagnosed (Finnish Diabetes Association 2016).

The rising prevalence of type 2 diabetes can be explained by several factors, such as changes in diagnostic criteria, increased awareness leading to more testing and detection of new cases, increased life expectancy of people with diabetes, and a real increase in the incidence of type 2 diabetes. The reasons for the real increase are particularly the ageing of the population, the impact of urbanization on the environment and lifestyles, and the worldwide obesity epidemic (Finucane et al. 2011, Chen, Magliano & Zimmet 2011, Gallus et al. 2015, NCD Risk Factor Collaboration Group 2016). Finland has not been immune to the obesity epidemic (Vartiainen et al. 2010, Lahti-Koski et al. 2010). The population-based FINRISK survey from 2012 suggested that the increasing trend in obesity might be levelling off (Borodulin et al. 2015, Männistö et al. 2015), but the most recent study again indicated that the prevalence of obesity in the working-age population has continued to increase (Koponen et al. 2018).

Increasing incidence rates of type 2 diabetes have been documented internationally. However, population-level trends in type 2 diabetes incidence over decades have been reported only in a few studies, because the data covering the longer follow-up periods are sparse (Hardoon et al. 2010, Cheng et al. 2013, Franco et al. 2013, Maruthur 2013). In Finland, the increasing diabetes incidence over time has been documented among middle-aged men (Strandberg & Salomaa 2000), twins (Kaprio et al. 1992), young adults (Lammi et al. 2008) and among Finnish men and women aged 30 years or more (Laakso et al. 1991). Peltonen et al. reported that the incidence of diabetes increased among men and women aged over 35 years until 2012, and thereafter the trend seems to be levelling off (Peltonen et al. 2015). Also, the recent report of the Finnish Diabetes Association indicated that the amount of new diabetes diagnoses per year has diminished during recent years (Koski 2017).

### 2.1.3 RISK FACTORS

Known risk factors for type 2 diabetes can be categorized as modifiable or non-modifiable. The most important non-modifiable risk factors are age, sex and genetic factors. Age increases the risk of type 2 diabetes which has been explained by age-related decline in beta-cell function, by an increase in the level of other risk factors and by accumulating risk exposure during a lifetime (Chang & Halter 2003, Qiao et al. 2005). Some difference in risk exists by sex. Overall prevalence of type 2 diabetes is slightly higher in men than women (Wild et al. 2004). However, men in general have a shorter life expectancy, and thus there are less affected men than women worldwide (Wild et al. 2004, International Diabetes Federation 2015). A family history of diabetes and diabetes during pregnancy increase the risk of diabetes later in life, and these associations are partly explained by genetic factors (Valdez et al. 2007, Kaaja & Rönnemaa 2008). An offspring's risk of getting diabetes is approximately 40% if one parent has type 2 diabetes, and approaches 70% if both parents have type 2 diabetes (Groop et al. 1996). Genome-wide association studies have identified genetic variants that increase the risk of type 2 diabetes by ~20%, and most of these variants regulate insulin secretion, and a minority reduce insulin action in tissues (Fuchsberger et al. 2016). Also, preterm birth and low or high birth weight are associated with an increased risk of type 2 diabetes in adulthood (Wei et al. 2003, Whincup et al. 2008, Kajantie et al. 2010).

Obesity, physical inactivity, unhealthy diet and smoking are the modifiable risk factors of type 2 diabetes (Ford, Williamson & Liu 1997, Hu 2011, Ardisson Korat, Willett & Hu 2014). Increased body mass index (BMI), as an indicator of obesity, has consistently been one of the strongest risk factors for the development of diabetes (Colditz et al. 1995, Field et al. 2001, Wang et al. 2005). Among US female nurses, the relative risk of diabetes was 38.8 in the BMI group over 35 kg/m<sup>2</sup> and 20.1 in the BMI group 30.0-34.9 kg/m<sup>2</sup> compared with the BMI group less than 23.0 kg/m<sup>2</sup> during 16 years of followup (Hu et al. 2001a). This increasing prevalence of type 2 diabetes in parallel with the increase in BMI has also been seen among men during 13 years of follow-up (Wang et al. 2005). In addition to overall obesity, the presence of abdominal adiposity increases a person's risk of diabetes, and waist circumference has been shown to be a valid predictor of abdominal adiposity (Chan et al. 2003, Wang et al. 2005).

Physical inactivity is a well-known risk factor for type 2 diabetes (Jeon et al. 2007, Fogelholm 2010, Sieverdes et al. 2010). A review of prospective cohort studies provides evidence that people who regularly engage in moderate physical activity have about a 30% lower risk of type 2 diabetes than their inactive counterparts (Jeon et al. 2007). In the same review, a similar decrease in diabetes risk was seen for regular walking as compared with no walking. An unhealthy diet also plays an important role in the development of type 2 diabetes, and dietary risk factors are often related to Western diets (Hu et al. 2001b, Montonen et al. 2005). In particular, a high intake of total and saturated fat and low fibre intake are associated with an increased type 2 diabetes risk (Hu et al. 2001b, Hu, van Dam & Liu 2001c, Lindström et al. 2006).

Furthermore, smoking and excessive alcohol use are associated with an increased risk, and moderate alcohol consumption with a decreased risk, of developing type 2 diabetes (Patja et al. 2005, Willi et al. 2007, Baliunas et al. 2009). All of these modifiable lifestyle factors either impair insulin action or cause insulin resistance over time. Therefore, management of the modifiable

risk factors is the key element in preventing the development of type 2 diabetes.

### 2.1.4 COMORBIDITIES

Type 2 diabetes is characterized by the development of comorbidities which themselves can be characterized as microvascular (neuropathy, nephropathy and retinopathy) and macrovascular (cardiovascular disease, stroke, and peripheral vascular disease) complications (American Diabetes Association 2006, Fowler 2008). These complications (Figure 2) account for the majority of severe morbidity and mortality associated with type 2 diabetes (Gerstein 1997, Stratton et al. 2000, Geiss et al. 2006, Fowler 2008). It has been repeatedly shown that diabetes patients have an increased prevalence of complications already at the time of diagnosis of diabetes (Harris et al. 1992, Engelgau, Narayan & Herman 2000, Gedebjerg et al. 2018).



Figure 2. Major complications of type 2 diabetes (International Diabetes Federation 2017, Zheng, Ley & Hu 2018).

In general, the accumulation of unhealthy lifestyle factors is associated with increased likelihood of comorbidity, because many chronic diseases share the same pool of risk factors (Fortin et al. 2014, Ferretti 2015). Type 2 diabetes is associated with clustered risk factors for cardiovascular disease; adults with diabetes have a high prevalence of hypertension, elevated low-density lipoprotein cholesterol, and obesity (Preis et al. 2009, Lorber 2014, Gedebjerg et al. 2018). The risk of cardiovascular morbidity and mortality has been shown to be 2- to 4-fold among diabetic populations compared with non-diabetic populations (Fox 2010). Further, the effect of type 2 diabetes on the risk of cardiovascular diseases seems to be stronger in women compared with men, with women having a higher relative risk of stroke (RR=2.28 vs (1.83) and coronary heart disease (RR=2.82 vs 2.16) compared with men (Juutilainen et al. 2005, Peters et al. 2015). Therefore, efforts to prevent or postpone the onset of type 2 diabetes may be the most essential way to reduce diabetes-related cardiovascular morbidity and mortality (Fox et al. 2007). Secondly, management of risk factors is one of the most important ways to reduce the risk of cardiovascular diseases and other complications among people with diabetes (Gaede et al. 2003, Motala et al. 2006, Fox et al. 2007).

Results of the study by Forssas et al. suggested improvements in the management of diabetes, as the risk of serious complications decreased in a total population with diabetes in Finland during an 18-year period (Forssas et al. 2016). However, other studies have suggested that management of both hypertension and obesity is insufficient in Finland. Only about one-third of patients with hypertension have optimal treatment levels (Laatikainen et al. 2013), and most type 2 diabetes patients do not reach the treatment targets for hypertension (Pajunen et al. 2014, Johansson, Ahola & Jula 2016). Instead, the serum cholesterol levels among patients with diabetes are relatively well controlled in Finland, although there is still room for improvement (Vartiainen et al. 2013). Still, more attention needs to be paid to better recognition and multifactorial management of risk factors in order to avoid serious complications and clustering of multiple complications.

#### 2.1.5 PREVENTION

#### **Evidence from clinical trials**

Landmark clinical trials have demonstrated that type 2 diabetes can be prevented or postponed by changes in lifestyle among high-risk individuals (Pan et al. 1997, Tuomilehto et al. 2001, Knowler et al. 2002), and the benefits of lifestyle changes are sustainable for many years after the active intervention period (Lindström et al. 2006, Li et al. 2008, Diabetes Prevention Program Research Group 2009). The Chinese Da Qing Diabetes Prevention Study included three different types of lifestyle intervention group, and interventions led to a significant decrease in the incidence of type 2 diabetes in all groups over a 6-year period. The risk reductions were 31%, 46% and 42% in the diet, exercise and diet-plus-exercise groups, respectively (Pan et al. 1997). After 20 years of follow-up, there was a 43% reduction in diabetes incidence (Li et al. 2008) in the combined lifestyle intervention group compared with the control group.

In the Finnish DPS, the participants were randomized either to an intervention or a control group. In the intervention group, participants received an intensive and individually-tailored diet and exercise counselling. The control groups received general counselling on healthy lifestyles. Intensive lifestyle intervention induced beneficial changes in weight, diet and physical activity, and reduced the risk of type 2 diabetes by 58% over a 4-year period (Tuomilehto et al. 2001), without a difference in effectiveness between men and women. In addition, lifestyle intervention led to beneficial changes in other clinical and metabolic factors, such as waist circumference, serum triglycerides and total cholesterol to HDL cholesterol ratio (Lindström et al. 2003). After 7 years of follow-up, there was still a 43% relative reduction in the incidence of diabetes between the groups (Lindstrom et al. 2006); this finding is consistent with the results of the Chinese Da Qing Diabetes Prevention Study.

In the US Diabetes Prevention Program (DPP), the type 2 diabetes risk reduction was 58% in the lifestyle group and 31% in the metformin group compared with the placebo group (Knowler et al. 2002). In the lifestyle group and in the metformin group, diabetes incidence was reduced by 34% and by 18% after 10 years of follow-up, respectively (Diabetes Prevention Program Research Group 2009). It is noteworthy that evidence to show that lifestyle intervention to prevent type 2 diabetes also prevents the appearance of comorbidities of diabetes is still scarce. In the DPS, no difference in cardiovascular disease morbidity or mortality was seen between the intervention and control groups after the 10-year follow-up. This might be due to a true lack of effect but could also be explained by a small sample size, short follow-up time, or a selected group of volunteer participants (Uusitupa et al. 2009). In the DPP, no difference in the prevalence of microvascular complications was seen between the treatment groups after 15 years of follow-up (Diabetes Prevention Program, Research Group et al. 2015). However, the Chinese Da Oing Diabetes Prevention Study indicated that lifestyle intervention can reduce the incidence of cardiovascular and all-cause mortality. After 23 years of follow-up, the cumulative incidence of cardiovascular mortality was 11.9% and 19.6% in the intervention and control groups, respectively (Li et al. 2014).

#### From evidence to practice

Based on the accumulating evidence from clinical trials, many efforts have been made to translate the trials into community-based programmes. Largescale implementation of the current evidence about diabetes prevention is essential to prevent the disadvantages of diabetes to individuals and societies. In Finland, the implementation project of the Finnish national diabetes prevention programme (called FIN-D2D) was carried out during 2003–2008. The project area consists of five hospital districts, including 1.5 million residents (Saaristo et al. 2007). The aims of FIN-D2D were to raise the awareness of the risk factors, consequences and prevention of type 2 diabetes among the population, and to identify high-risk individuals and to arrange lifestyle interventions for them in primary and occupational healthcare (Finnish Diabetes Association 2009). In addition, FIN-D2D included a strategy for the early diagnosis and management of type 2 diabetes (Saaristo et al. 2007, Finnish Diabetes Association 2009).

As part of the evaluation of FIN-D2D, two population-based FIN-D2D surveys were conducted. Based on the results, the prevalence of morbid obesity (BMI  $\geq$ 40 kg/m<sup>2</sup>) and the mean waist circumference decreased significantly more in the FIN-D2D area compared with the control area during the project period (Salopuro et al. 2011). Further, a modest average weight reduction of 1.0 kg was seen among the participants in the high-risk cohort of FIN-D2D after the 1-year follow-up (Saaristo et al. 2010). Based on the results, FIN-D2D efficiently identified high-risk individuals and offered them lifestyle counselling. The implementation of the FIN-D2D programme was feasible in the area where the programme was established although the achieved changes in clinical risk factors were more modest than the reported changes in the clinical trials (Saaristo et al. 2010).

Several other implementation projects have been carried out in different parts of the world to implement and scale up the prevention practices, especially among high-risk individuals (Laatikainen et al. 2007, Ackermann et al. 2008, Absetz et al. 2009, Makrilakis et al. 2010, Johnson et al. 2013, Dunkley et al. 2014, Ely et al. 2017). Recent meta-analysis of 22 implementation studies showed the drop-off in intervention effectiveness in real-world settings; for example, achieved mean weight loss was about onethird to one-half of the levels reported in the DPP and DPS (Dunkley et al. 2014). However, the observed change in weight was concluded to be clinically meaningful as regards to the development of type 2 diabetes (Dunkley et al. 2014), because each kilogram of mean weight loss has been shown to be associated with a 16% reduction in future diabetes incidence (Hamman et al. 2006). Similarly, the review of Aziz et al. indicated that diabetes prevention programmes could be effective in diabetes risk reduction even when effectiveness in weight loss is quite low (Aziz et al. 2015). However, many of the previous implementation projects and studies have been carried out in healthcare settings and among high-risk individuals. Further experiences and results from large-scale settings and population strategies are urgently needed.

## 2.2 SOCIOECONOMIC GRADIENT AND TYPE 2 DIABETES

#### 2.2.1 INDICATORS OF SOCIOECONOMIC STATUS AS DEFINER OF HEALTH DIFFERENCES

The most often used indicators of socioeconomic status are education, occupation and income (Galobardes et al. 2006, d'Errico et al. 2017). Although these indicators correlate with each other, the strength of the associations with health outcomes can differ. In addition, indicators can affect health at different stages of life and through different pathways, and they cannot be used interchangeably (Winkleby et al. 1992, Lahelma et al. 2004, Braveman et al. 2005, Geyer et al. 2006).

Education is usually acquired first, indicating skills and knowledge that are likely to promote healthy lifestyles. Occupation indicates status and power, physical activity in work, and work exposures. It is also strongly related to income and levels of consumption. Increasing income indicates increasing possibilities to pay lifestyle costs or healthcare, and to maintain good health (Lahelma et al. 2004, Galobardes et al. 2006). Systematic differences in health between education, occupation and income groups are called socioeconomic health differences. Socioeconomic health differences have been observed in many chronic illnesses, including coronary heart disease, diseases of the nervous system, arthritis and type 2 diabetes (Dalstra et al. 2005).

#### 2.2.2 PATHWAYS FOR SOCIOECONOMIC DIFFERENCES IN TYPE 2 DIABETES

Socioeconomic differences in type 2 diabetes can evolve by different pathways. The common, causal pathways are related to the society, environment, population groups and individuals (Diderichsen, Evans & Whitehead 2001, Blas & Sivasankara Kurup 2010). Figure 3 depicts the model for causal pathways contributing to the development of socioeconomic differences in type 2 diabetes, based on previously published frameworks (Diderichsen, Evans & Whitehead 2001, Brown et al. 2004, Blas & Sivasankara Kurup 2010). Briefly, difference in social context, including aspects of social hierarchy, industrialization, and urbanization, leads to differences in social and physical environments. Different environmental exposures can lead to differences in vulnerability to diabetes between population groups. Social position also independently contributes to the predisposition to diabetes. This predisposition to type 2 diabetes is typically associated with increasing prevalence of known risk factors. Finally, differences in vulnerability lead to differences in the outcomes and consequences of type 2 diabetes, including the quality and the cost of diabetes care, and in comorbidities, between individuals. Further, Figure 3 indicates the possible pathways for interventions that aim to reduce disparities in type 2 diabetes at the society as well as individual level.



Figure 3. Causal pathways for socioeconomic differences in type 2 diabetes.

#### 2.2.3 SOCIOECONOMIC DIFFERENCES IN TYPE 2 DIABETES AND ITS RISK FACTORS

In Western societies, a social gradient in the prevalence of type 2 diabetes is well established, with the socioeconomically disadvantaged ('vulnerable population groups') having a greater burden than those in higher social strata (Espelt et al. 2008, Agardh et al. 2011, Sacerdote et al. 2012). In the first National Health and Nutrition Examination Survey (NHANES I, USA), socioeconomic status, assessed using education, occupation and income, was inversely associated with type 2 diabetes incidence in women. The association was less consistent in men (Robbins et al. 2005). Results from the UK's Whitehall II study evaluating the association of social position with type 2 diabetes indicated increased type 2 diabetes risk with decreasing employment grade among men (Kumari, Head & Marmot 2004). The population-based European Prospective Investigation into Cancer and Nutrition study showed that people with type 2 diabetes were less likely to have high educational attainment compared with control subjects (Heidemann et al. 2005). In the KORA survey, undiagnosed type 2 diabetes was related to low occupation and income level in German women (Rathmann et al. 2005).

The Swedish study of middle-aged men and women found that low educational level was associated with type 2 diabetes in women and IGT in both genders. Among both genders, also a low adult occupational position was associated with type 2 diabetes (Agardh et al. 2007). In the Northern Finland Birth Cohort, a longer unemployment period increased the risk of prediabetes and screen-detected type 2 diabetes (ST2D) after adjustments for risk factors. The associations were attenuated after adjustments among women (Rautio et al. 2017). The results of a large-scale longitudinal study among Finnish male employees, where diabetes diagnoses were based on the national drug reimbursement register, showed that low educational attainment independently increased the risk of incident diabetes during the 18-year follow-up (Kouvonen et al. 2008).

In some of the previously mentioned studies, the excess risk of type 2 diabetes associated with lower socioeconomic status was partly explained by established risk factors such as obesity, physical inactivity and smoking (Agardh et al. 2004, Kumari, Head & Marmot 2004, Rathmann et al. 2005, Rautio et al. 2017). Similar marked differences in health behaviours between socioeconomic groups have been reported in most European countries. In Europe as a whole, education-related differences in smoking are very consistent. Smoking has been shown to be more common among people with lower rather than higher education (Mackenbach et al. 2008, Lahelma et al. 2010). However, there are striking differences among countries in the magnitude, trends, and even the direction of these smoking differences

between genders (Cavelaars et al. 2000, Mackenbach et al. 2008). In Finland, smoking is more common both in men and in women with the lowest educational attainment (Helldan & Helakorpi 2015). In addition, those in higher socioeconomic groups have been shown to be more likely to follow healthier food habits, such as consuming more vegetables or using oil in cooking instead of butter, than those in lower socioeconomic groups in Western societies (Hulshof et al. 2003, Lallukka et al. 2007, Lahelma et al. 2010, Seiluri et al. 2011). Further, people in higher socioeconomic groups have been shown to adhere better to physical activity recommendations (Martinez et al. 1999, Borodulin et al. 2008, Lahelma et al. 2010).

Being overweight is known to be one of the strongest risk factors for the development of diabetes. Socioeconomic differences in being overweight and in obesity have been widely reported, with individuals with a lower socioeconomic position having a higher BMI than individuals with a higher socioeconomic position in Europe (Martinez et al. 1999, Ward et al. 2007, Mackenbach et al. 2008). Results from the study of Roskam and Kunst showed that in European countries, low educational attainment was a stronger predictor of being overweight than low occupational class or household income, especially among women (Roskam & Kunst 2008). In the ATTICA study, Greek men and women with higher socioeconomic level had significantly lower prevalence of obesity compared with their counterparts with lower socioeconomic level. Further, the association between socioeconomic status and obesity was mainly explained by dietary and other lifestyle habits (Manios et al. 2005).

Also in Finland, low socioeconomic position, measured by education, income and occupational social class, has been found to predict obesity among middle-aged men and women (Lahelma et al. 2010, Borodulin et al. 2012). Borodulin et al. examined the mediators between socioeconomic status and BMI. The strongest and most consistent mediators were infrequent use of fruit and fresh vegetables and the proportion of time spent sitting among both genders. Additionally, gender-specific mediators, such as leisure time physical activity in women, were found (Borodulin et al. 2012).

Associations and possible explanatory factors between socioeconomic status and type 2 diabetes have been documented both in national and international literature. However, as longitudinal studies examining secular trends in type 2 diabetes incidence by socioeconomic status are lacking, it is not known whether these patterns have changed over time.

# 2.2.4 SOCIOECONOMIC STATUS, TREATMENT AND COMORBIDITIES OF DIABETES

It has been proposed that socioeconomic status may determine the treatment of diabetes, those with higher socioeconomic status having better access to care, better management of glucose, blood pressure and lipid levels and better adherence to recommended care, and as a consequence, a lower number of serious complications. HbA1c is used as a measure of the longterm control of blood glucose levels. The study by Sundquist et al. showed that less than half of Swedish men and women with diabetes reached the recommended levels of HbA1c, and even a smaller amount of people reached the recommended lipid levels. Furthermore, individuals with the lowest income levels were least likely to reach the recommended level (Sundquist et al. 2011). Reisig et al. reported similar findings from Germany (Reisig et al. 2007), as did Bachmann et al. from the UK (Bachmann et al. 2003). In addition, Bihan et al. found an association with deprivation and glycaemic control as well as with the risk of microvascular complications among French diabetic patients (Bihan et al. 2005). The review of Grintsova et al. showed that a low socioeconomic status is often associated with poorer diabetes care and worse glycaemic control, resulting in a higher risk of complications (Grintsova, Maier & Mielck 2014).

In Denmark, low education and low income were associated with the worse treatment goals for blood pressure among the diabetic population. However, low socioeconomic status was not associated with the goals related to HbA1c level (Heltberg et al. 2017). In Finland, only a few studies have examined the socioeconomic status differences in the process and outcomes of type 2 diabetes (Sikiö et al. 2014, Toivakka et al. 2015). In the region of North Karelia, area-level socioeconomic factors were associated with treatment outcomes of type 2 diabetes. Achieving the recommended HbA1c level was associated with having a better neighbourhood socioeconomic status as defined by the information available from Statistics Finland (Sikiö et al. 2014).

Results from the previous studies have shown that the diabetic population is at higher risk of mortality and incidence of cardiovascular disease compared with the general population (Haffner et al. 1998, Fox 2010, Nwaneri, Cooper & David Bowen-Jones 2013). In addition, diabetes mortality and comorbidity have been shown to be related to disparities in socioeconomic position in Europe, and also in Finland (Chaturvedi et al. 1998, Espelt et al. 2008, Forssas et al. 2010). Walker et al. reported that the association of socioeconomic status with mortality in diabetic groups was only partly explained by different burdens of comorbidities of diabetes (Walker et al. 2015). Further research is needed to clarify how mortality and the development of comorbidities among people with diabetes are linked to socioeconomic status.

# 2.2.5 THE ROLE OF SOCIOECONOMIC STATUS IN THE PREVENTION OF TYPE 2 DIABETES

Based on the available convincing evidence, preventive measures targeted at the known modifiable risk factors of type 2 diabetes can successfully prevent the development of diabetes among high-risk individuals (Pan et al. 1997, Tuomilehto et al. 2001, Knowler et al. 2002). Also, many efforts to translate the existing clinical research evidence into community-based programmes have been made (Johnson et al. 2013, Dunkley et al. 2014). However, only a few earlier studies have considered the role of socioeconomic status as a modifying factor of the effectiveness of lifestyle intervention in diabetes prevention.

At the individual level, socioeconomic status influences health behaviours, as described earlier. Lifestyle change is always a process of behavioural change. Socioeconomic status may have a role in the processes of behavioural change at different phases of an intervention. According to previous studies, the association between socioeconomic status and lifestyle is partly mediated by psychosocial factors, such as sense of control (Taylor & Seeman 1999). In addition, self-efficacy, action and coping planning, and social support are factors which have been shown to predict health behaviours (Taylor & Seeman 1999, Schwarzer et al. 2007), and these psychosocial mechanisms leading to lifestyle changes could also differ between socioeconomic groups. However, the study by Hankonen et al. reported that these mechanisms were similarly evident regardless of educational group in the GOAL Lifestyle Implementation Trial to prevent type 2 diabetes among the Finnish population (Hankonen et al. 2009). Results indicated that all persons were likely to proceed to behavioural change with the same mechanisms regardless of educational background.

Weight reduction and weight loss maintenance have been identified as key elements in the lifestyle interventions aiming at the prevention of type 2 diabetes among high-risk individuals (Penn et al. 2013). The review of Ball and Crawford was based on the hypothesis that individuals with lower socioeconomic status would have a smaller ability to lose weight and a greater risk of gaining weight over time than individuals with higher socioeconomic status (Ball & Crawford 2005). The review supported the hypothesis: adults with lower occupational status had a greater risk of gaining weight. Also, when education was used as the indicator of socioeconomic status, the association still existed but was not so clear (Ball & Crawford 2005). On the other hand, a lifestyle intervention study of obese patients with diabetes showed that patients with lower educational attainment lost more weight than those with higher educational attainment (Gurka et al. 2006).

The study of Magnee et al. analysed the effectiveness of lifestyle interventions aimed at preventing obesity or promoting healthy dietary habits or physical activity between different socioeconomic status groups in the Netherlands (Magnee et al. 2013). According to the results, some interventions were more effective in higher socioeconomic status groups, whereas some others showed better effectiveness in lower socioeconomic status groups. However, most of the interventions showed no differences in intervention effectiveness between the socioeconomic status groups. The differential effects on obesity, diet or physical activity were associated with the setting, age group, intensity and follow-up time of interventions (Magnee et al. 2013). The analyses indicated that 'high-intensity' community interventions, such as the Hartslag Limburg project, an integrative community-based cardiovascular disease prevention programme, may be most likely to contribute to reducing socioeconomic differences in physical activity, diet, or prevention of obesity (Schuit et al. 2006, Magnee et al. 2013)

In the US DPP randomized study, socioeconomic status, defined by employment and income, was unrelated to achieving either the weight or other goals of lifestyle intervention among high-risk individuals (Wing et al. 2004). However, results from the US DPP showed racial/ethnic disparities in the effectiveness of lifestyle intervention (Ely et al. 2017). Further, income status modified the outcomes of intervention between racial/ethnic groups. The achieved weight loss was smaller among non-Hispanic whites with low income than Hispanics (Ritchie et al. 2018). Recently, the results from the DE-PLAN-Krakow study indicated that lower education, along with higher BMI and a history of increased glucose, predicted successful weight loss among high-risk individuals in the type 2 diabetes implementation study (Gilis-Januszewska et al. 2018).

To sum up, even though people with lower socioeconomic status tend to have, on average, higher body weight and a less healthy lifestyle which predispose them to the development of type 2 diabetes, previous research suggests that low socioeconomic status does not necessarily have a negative impact on adherence to lifestyle change. However, more research is needed to evaluate the effect of socioeconomic status on the prevention of type 2 diabetes, especially at the population level, but also among high-risk groups. It has been estimated that interventions that aim to reduce classic, modifiable risk factors of type 2 diabetes and cardiovascular disease could actually eliminate most of the socioeconomic differences in coronary heart disease mortality, if interventions were to be successfully implemented across all socioeconomic strata (Kivimäki et al. 2008). Figure 4 summarizes the existing evidence about the associations between socioeconomic status and type 2 diabetes, and presents the basis for this study.



Figure 4. Framework of the present study.

# 3 AIMS OF THE STUDY

The overall aim of this study was to examine the role of socioeconomic status on the risk factors, occurrence, comorbidities, and prevention of type 2 diabetes in Finland.

The specific aims were:

- 1. To study the association between socioeconomic status and the prevalence and incidence of type 2 diabetes, and to explore the explanatory factors for differences in diabetes risk (Study I & II).
- 2. To study socioeconomic, clinical and lifestyle-related risk factors for the incidence of comorbidities among people who have diabetes (Study III).
- 3. To explore the role of educational background in the effectiveness of lifestyle intervention to prevent type 2 diabetes among high-risk individuals (Study IV).
- 4. To evaluate the effect of the national diabetes prevention programme on population-level awareness and health habits, and to explore which sociodemographic factors are associated with the effectiveness of the programme (Study V).

## **4 STUDY POPULATIONS AND METHODS**

The present study utilized several data sources including three populationbased surveys: the evaluation survey of FIN-D2D, the national Finnish risk factors survey (FINRISK), and the Health Behaviour and Health among the Finnish Adult Population (AVTK) annual survey from different study years. Furthermore, the Finnish DPS clinical study data were used. The use of different data sources is depicted in Figure 5 and summarized in Table 4.



Figure 5. Data used in Studies I–V.

## 4.1 FIN-D2D SURVEYS 2004 AND 2007 (STUDY I)

The Finnish Development Programme for the Prevention and Care of Diabetes (DEHKO), coordinated by the Finnish Diabetes Association, was active in Finland during the years 2000–2010. DEHKO was reinforced by an implementation project for type 2 diabetes prevention (FIN-D2D) that was ongoing from 2003 to 2008 (Saaristo et al. 2007). As part of the evaluation of FIN-D2D, two population-based cross-sectional surveys were carried out in 2004 and 2007 to detect, for example, changes in population-level rates of type 2 diabetes, hyperglycaemia and obesity during the project period. The survey area covered the three hospital districts of South Ostrobothnia, Central Finland, and Pirkanmaa.

In both FIN-D2D surveys, a random sample of 4500 people was drawn from the National Population Register, stratified by sex and 10-year age groups (45–54, 55–64 and 65–74 years) separately for each geographic region. The study protocol included questionnaires, a health examination and laboratory measurements, such as an OGTT. Trained nurses carried out all survey measurements and drew fasting venous blood samples. An OGTT was carried out according to the WHO recommendations (World Health Organization 1999). A detailed description of the study methodology has been published previously (Saaristo et al. 2008). The Ethics Committee of the Hospital District of Helsinki and Uusimaa approved the study protocol. All participants gave their written informed consent prior to participation in the survey.

Study I is based on the data from the FIN-D2D surveys. All men (n=3000) and women (n=3000) aged 45 to 64 years were included in the study population. Of these, 1764 men and 2027 women participated in the health examination (59% and 68%, respectively). Participants who experienced some kind of problem during the OGTT (e.g. vomiting) or whose blood samples could not be reliably measured for some reason (e.g. haemolysis) (n=81) and those with inaccurate or missing data on education (n=68) were excluded. After these exclusions, altogether 1696 (57%) men and 1946 (65%) women were included in the analyses of Study I.

#### 4.1.1 SOCIOECONOMIC AND LIFESTYLE VARIABLES

Participants' socioeconomic status was defined by educational attainment. Also, household income level was used as an indicator of socioeconomic status, but these results are not included in this thesis. The educational level was ascertained via the question 'How many years have you attended school and studied full-time' with the results divided into three categories according to years of completed education: low (0-9 years), medium (10-12 years) and high education (13 years or more).

BMI was calculated from measured body weight (in light indoor clothing) and height as kg/m<sup>2</sup>. Obesity was defined as BMI 30 kg/m<sup>2</sup> or above. Physical inactivity, unhealthy diet, smoking and alcohol use were assessed by the use of a self-administered questionnaire. Physical activity in leisure time was assessed with a four-category question. The information on physical activity habits was dichotomized by dividing people into 'inactive' and 'active'. Those who chose the lowest physical activity option 'I just read, watch TV, and do other activities that do not physically strain me in my leisure time' were defined as physically inactive and all other categories were 'active'.

The questionnaire contained questions about the participant's usual intake of rye bread, cooked vegetables, and fresh vegetables ('How often do you usually eat...'). Type of milk and fat were also enquired about ('If you drink milk, what kind is it usually?', 'What kind of fat do you usually use on your bread... or for cooking?'). Diet was assessed by a food behaviour index where achieving each item, including eating vegetables daily, using soft margarine or low-fat spread on bread, using vegetable oil in cooking, eating rye bread daily and drinking skimmed milk or milk containing 1% fat, earned one score point. The summed score ranged from zero to five and 'unhealthy diet' was defined as a score value of zero or one.

Smoking was defined as being a current smoker. Alcohol consumption was calculated based on self-reported use of alcohol. Men who consumed more than 14 drinks per week and women who consumed more than seven drinks per week were defined as excessive alcohol users.

# 4.1.2 GLUCOSE TOLERANCE EVALUATION AND CLASSIFICATION

An OGTT was used to define the glucose tolerance status of study participants. Glucose tolerance was classified according to the WHO 1999 criteria (World Health Organization 1999). Participants with previously diagnosed type 2 diabetes were classified as having 'known diabetes' (type 2 diabetes, T2D). Participants who had a fasting plasma glucose level  $\geq$ 7.0 mmol/l or 2-hour plasma glucose  $\geq$ 11.1 but no previous diagnosis of diabetes were classified as having ST2D. Combined T2D and ST2D formed the group 'total type 2 diabetes' (TT2D). IGT was defined as 2-hour plasma glucose  $\geq$ 7.8 and <11.1 mmol/l and fasting plasma glucose <7.0 mmol/l. Individuals with fasting plasma glucose  $\geq$ 6.1 but <7.0 mmol/l, and 2-hour plasma glucose <7.8 mmol/l were classified as having IFG. Participants with

TT2D, IGT or IFG were classified as having abnormal glucose tolerance, which is called hyperglycaemia in this thesis (Table 2).

Table 2. C	Classification	of hypergl	ycaemia
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Hyperglycaemia	Defined by
Total type 2 diabetes (TT2D):	
Known type 2 diabetes (T2D)	Self-administered study questionnaire
Screen-detected type 2 diabetes (ST2D)	<ul> <li>Oral glucose tolerance test</li> <li>Fasting glucose ≥7.0 mmol/l or</li> <li>2 hours post glucose load ≥11.1 mmol/l</li> </ul>
Impaired glucose tolerance (IGT)	Oral glucose tolerance test • Fasting glucose <7.0 mmol/l and • 2 hours post glucose load 7.8-11.0 mmol/l
Impaired fasting glucose (IFG)	Oral glucose tolerance test • Fasting glucose 6.1-6.9 mmol/l and • 2 hours post glucose load <7.8 mmol/l

### 4.2 THE NATIONAL RISK FACTORS SURVEY (FINRISK) FROM 1972 TO 2002 (STUDIES II & III)

The national risk factors survey in Finland originates from the North Karelia Project (Puska et al. 1983). The first survey was carried out in 1972 and repeated in 1977, with the purpose of evaluating the North Karelia Project. Later on, the survey was conducted every 5 years, first as part of the WHO MONICA Project (Multinational Monitoring of Trends and Determinants in Cardiovascular Disease) (1982–1992) and then as the national FINRISK Study to evaluate the national trends in risk factors (1997–2012) (World health statistics quarterly 1988, Vartiainen et al. 2010, Borodulin et al. 2015). In each survey round, study questionnaires, a health examination and laboratory measurements were included in the study protocol. The aim was to keep the methodology and questionnaires as similar as possible over time, although some changes were made to retain relevancy. In this study, the needed ethics approvals were issued by the Ethics Committee of the National Public Health Institute and the Coordinating Ethics Committee of the Hospital District of Helsinki and Uusimaa.

Detailed descriptions of the methodology of the risk factors survey have been published previously (Vartiainen et al. 2010). Briefly, a cross-sectional risk factors survey was conducted using nationally representative, independent random samples. Two study areas were sampled in 1972, and the number of
areas was increased to five in 1997 (the North Karelia, the Northern Savo, the regions of Turku, Loimaa and Oulu, and the cities of Helsinki and Vantaa). A random sample of 6.6% of the population born between 1913 and 1947 was drawn in both study areas in 1972 and 1977 (Vartiainen et al. 2010). From 1982 onward, samples were drawn from the National Population Register and were stratified by sex and 10-year age groups (25–34, 35–44, 45–54, and 55–64 years) for each geographic region. The sample size of each 10-year age stratum was 500 in all study areas in 1982. In 1987, each 10-year age stratum included altogether 500 men and women in North Karelia and 250 in other areas. Between 1992 and 2002, the sample size of each stratum was 250 in all areas (Vartiainen et al. 2010).

Studies II and III are based on the data from FINRISK surveys. The analyses of study II were restricted to participants aged 30-59 years at baseline, because this age range was common for all FINRISK cohorts. During 1972-1997 the response rates among participants within the age category 30-59 years ranged from 72% to 91%. Overall, 39476 men and women underwent survey measurements between 1972 and 1997. Participants with pre-existing diabetes (either self-reported or diagnosis received from register) at baseline were excluded (n=787). For those subjects who by chance participated in multiple FINRISK surveys, only data from the earliest was used. After the exclusions, the final study population included 18806 men and 19883 women, and study cohorts were grouped according to the decade of survey for the analysis.

The analyses of study III were restricted to participants aged 25-64 years at baseline as this age range was common in surveys conducted between 1982 and 2002. During 1982–2002 the response rate was 75% among participants aged 25–64 years (n=36684). If subjects participated, by chance, in multiple FINRISK surveys (n=1024), only data from the earliest survey was used. For the analyses, three cohorts were formed: one cohort including men and women who were free from diabetes. cardiovascular diseases, asthma/chronic obstructive pulmonary disease, cancer and rheumatoid and other arthritis at baseline ('initially disease-free'), one cohort with diabetes at baseline, and one cohort with cardiovascular diseases at baseline. Participants with the co-existence of two or more of the selected chronic diseases (diagnosis either self-reported or received from registers) at baseline were excluded from the analyses (n=441). The final study population included altogether 32972 participants, of which 15904 were men and 17068 women.

# Medication Reimbursements, Hospital Discharge, and Causes of Death Registers

The national healthcare registers were used to compile the data set utilized in Studies II and III. The registers of the Finnish Social Insurance Institution contain data on granted reimbursements rights and actual drug purchases, with anatomical therapeutic chemical (ATC) classification system code defining the related diagnoses. The National Hospital Discharge Register includes the dates and causes of hospital admissions and discharge dates from all public hospitals in Finland. The National Register of Causes of Death contains data on the date and causes of fatalities. Both registers use codes of the International Classification of Diseases (ICD), and diagnoses have been recorded using ICD-8 until 1986, ICD-9 during 1987–1995, and ICD-10 since 1996. The coverage, accuracy, and reliability of these registers have been documented previously (Rapola et al. 1997, Lahti & Penttilä 2001, Pajunen et al. 2005, Tolonen et al. 2007, Sund & Koski 2009, Sund 2012).

#### 4.2.1 SOCIOECONOMIC AND LIFESTYLE VARIABLES

In Studies II and III, the definition of socioeconomic status was also based on educational attainment, dividing self-reported years of formal study into thirds. As the length of formal education has increased at the population level during recent decades, the educational level was defined using cohortspecific tertiles as cut-off points for low, medium and high education. In Study II, also employment status was used as an indicator of socioeconomic status, but these results are not included in this thesis.

In Study II, BMI was calculated as measured body weight (kg) divided by the square of measured height (m<sup>2</sup>). BMI was classified as underweight/normal (<24.99 kg/m<sup>2</sup>), overweight ( $\geq$ 25 kg/m<sup>2</sup> and <29.99 kg/m<sup>2</sup>), and obese ( $\geq$ 30 kg/m<sup>2</sup>). Physical activity index was generated based on the answers to three questions in the questionnaire: amount and intensity of leisure time physical activity, duration of active travel to work, and amount of physical activity required at work. For each question, response options were categorized into four groups. The summed score ranged from 0 to 12 and based on the scoring, participants were classified as inactive (1–3), moderately active (4–7) and highly active (8–12). Participants who were not working were classified as physically inactive in the workplace and travel to work domains.

Diet was assessed by a combined index, which was generated using questions about the type of milk and cooking fat typically used. An 'unhealthy' milk consumption pattern included milk with a fat content of 1.5% or more,

whereas consuming milk with less than 1.5% fat (or no milk at all) was considered 'healthy'. Type of cooking fat was classified as 'unhealthy' for those using butter, butter/oil mixtures or margarines high in saturated fat, and 'healthy' if participants reported using vegetable oils, soft margarines or no fat at all. Diet was classified as 'healthy' if participants had at least one healthy habit. Smoking was classified as never/occasional smoker, former smoker and current smoker.

In Study III, physical activity in leisure time was assessed with a fourcategory question. Those who chose the option 'I just read, watch TV, and do other activities that do not physically strain me in my leisure time' were defined as physically inactive. Fruit and vegetable intake was used as a surrogate indicator of diet. People who reported eating fruits and vegetables 3–5 times a week or less were defined as low consumers and classified as having an 'unhealthy diet'. Smokers were defined as being those who currently smoke.

BMI, blood pressure, and total serum cholesterol were used as clinical variables in the analyses. The cut-off points were set for BMI at  $\geq 27$  kg/m<sup>2</sup>, for blood pressure at  $\geq 140/90$  mmHg, and for serum cholesterol at  $\geq 5.0$  mmol/l. These values were used as markers of treatment level among people with type 2 diabetes. We chose to use a higher than normal cut-off point for body weight, as BMI in the normal range (<25 kg/m<sup>2</sup>) is very uncommon among people with type 2 diabetes and is also not recommended as the treatment target in the current care guidelines for diabetes (Type 2 diabetes: Current Care Guidelines, 2018).

#### 4.2.2 INCIDENT DIABETES

In Study II, incident diabetes was established by linking survey data with the registers of the Finnish Social Insurance Institution containing data on reimbursement rights (refund code 103). Therefore, the outcome variables (incident diagnoses) represent eligibility for reimbursement based upon diabetes diagnosis, not the specific medication classes used.

Follow-up time for each cohort was set at 10 years to enable comparability of different cohorts. Thus, follow-up of each individual continued until registration on the drug register, death from any cause, or the end of the 10-year follow-up period. For the analyses, cohorts were grouped according to the decade of survey: participants in the 1972 and 1977 surveys were considered collectively, as were those assessed in 1982 and 1987, and 1992 and 1997.

# 4.2.3 INCIDENT COMORBIDITY AMONG PEOPLE WITH DIABETES

In Study III, multimorbidity was defined as the co-existence of two or more chronic diseases (diabetes, cardiovascular diseases, asthma/chronic obstructive pulmonary disease, cancer or rheumatoid and other arthritis) within a person. These diseases were selected as they were the most common chronic disease within this study population. In this thesis, the term 'comorbidity' is used for additional disease occurring at the same time in the same individual as the previously defined diabetes.

The results of incident multimorbidity are presented for people who were free from all five diseases at baseline ('initially disease-free', n=31207), and incident comorbidity for people with diabetes at baseline (n=1249). Data on baseline and incident diagnoses of the chronic diseases during ten years were received from national registers on reimbursement rights and drug purchases, hospitalizations, and mortality (Table 3). Follow-up of each individual was continued until the diagnosis of the second disease, death from any cause, or the end of the ten-year follow-up period.

Table 3. Criteri	a for the s	election of	chronic	diseases	from	the registers
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Disease	Registers and codes for diagnosis
Diabetes	National Hospital Discharge Register &
	National Register of Causes of Death
	• E10-E14 (ICD-10) and their respective ICD-8/9 codes
	Registers of the Finnish Social Security Institute
	<ul> <li>Codes for prescribed medication; ATC class A10</li> </ul>
	Codes for reimbursed medication; DIAB (code 103)
Cardiovascular	a) National Hospital Discharge Register
diseases	<ul> <li>I20, I21, I22 (ICD-10) and their respective ICD-8/9 codes</li> </ul>
a) major coronary	<ul> <li><u>Also revascularization</u> → CABG or angioplasty</li> </ul>
heart disease event	a) National Register of Causes of Death
b) stroke, excluding	• 120-125 146 R06 R08 (ICD-10) and their respective ICD-8/0 codes
SAH (note: includes	
intracerebral haemorrhage)	b) National Hospital Discharge Register & National Register of Causes of Death
_	• I61, I63; not I63, 6, I64 (ICD-10) and their respective ICD-8/9
	codes
A athena (COPD	National Hamital Diashanna Davistar (
Astnma/COPD	National Register of Causes of Death
	• J43, J44, J45, J46 (ICD-10) and their respective ICD-8/9 codes
	Registers of the Finnish Social Security Institute
	<ul> <li>Codes for prescribed medication; ATC classes Ro3BA, Ro3BC, BoaDC, BoaAK</li> </ul>
	<ul> <li>Codes for reimbursed medication: ASTHMA &amp; COPD (code 202)</li> </ul>
	Also, self-reported chronic bronchitis from the FINRISK
	questionnaire during follow-up
Cancer	National Hospital Discharge Register &
	National Register of Causes of Death
	Coo-C43, C45-C97 (ICD-10) and their respective ICD 8/9 codes
Phoumatoid and	National Hospital Discharge Pegicter &
othon ontheitic	National Register of Causes of Death
other artifitis	• M05-M13, M32, M33, M45 (ICD-10) and their respective ICD-8/0
	codes
	Registers of the Finnish Social Security Institute
	Codes for reimbursed medication; RHEUMA (code 202)

ATC=anatomical therapeutic chemical; CABG=Coronary artery bypass grafting; COPD=chronic obstructive pulmonary disease; FINRISK=Finnish risk factors survey; ICD=International Classification of Diseases; SAH=subarachnoid haemorrhage.

## 4.3 DIABETES PREVENTION STUDY (DPS) (STUDY IV)

The influence of socioeconomic status on the effectiveness of lifestyle intervention was examined using data collected during the DPS. The DPS was a randomized, prospective and controlled lifestyle intervention trial that aimed to explore the possibility of the prevention of type 2 diabetes in high-risk individuals with IGT and BMI>25 kg/m<sup>2</sup> at baseline. The study participants were volunteers, and were recruited between 1993 and 1998. The recruitment was done by various methods, for example by advertising in newspapers and by contacting the participants from earlier epidemiological surveys and clinical studies. The eligible subjects (n=522, mean age 55±7, mean BMI 31±4 kg/m<sup>2</sup>, mean fasting plasma glucose  $6.1\pm0.7$  mmol/l and mean plasma glucose 2 hours after glucose load  $8.9\pm1.5$  mmol/l) were randomly assigned to the intensive intervention group (n=265) or the standard care control group (n=257) (Lindström et al. 2006). The goals of the intervention were to reduce body weight, reduce dietary total and saturated fat intake, and increase dietary fibre intake and physical activity.

The study design, participants and interventions have been described in detail previously (Eriksson et al. 1999, Tuomilehto et al. 2001, Lindström et al. 2003). Briefly, the study protocol included questionnaires and clinical and laboratory measurements at baseline and at each annual visit, including an OGTT to diagnose incident diabetes. The Ethics Committee of the National Public Health Institute in Helsinki, Finland, approved the study protocol and all study participants gave written informed consent.

All the participants of the DPS, and data from baseline to end of the intervention (year 4 follow-up), were utilized in the analyses of Study IV.

#### 4.3.1 SOCIOECONOMIC VARIABLES

Also, in this study, educational attainment was used as a surrogate for socioeconomic status. Education was classified as low (elementary or middle school), medium (vocational school) or high (senior high school, college or academic degree). Total years of education data were not available in the DPS data.

#### 4.3.2 LIFESTYLE AND CLINICAL VARIABLES

The changes in physical activity were assessed using a self-administered 12month leisure time physical activity questionnaire (Lakka & Salonen 1992). The data were collected at baseline and at every annual visit of the DPS. The duration (hours/week) of total leisure time physical activity was calculated.

Changes in diet were assessed based on 3-day food diaries, which were filled in by the participants before each annual study visit. A picture booklet of typical portion sizes (Haapa et al. 1985) was used to facilitate the estimation of portion sizes (Ovaskainen, Valsta & Lauronen 1996) and the diaries were checked by the study nutritionist on return. Nutrient intake was calculated using a dietary analysis programme and the database of the National Public Health Institute (Ovaskainen, Valsta & Lauronen 1996).

Clinical variables included BMI (calculated as weight in kg in light indoor clothing, divided by height in metres, squared), waist circumference (midway between the lowest rib and the iliac crest to the nearest 1 mm), blood pressure (two measurements with standard sphygmomanometer in a sitting position from the right arm after a 10-minute rest), serum lipids (total cholesterol, HDL cholesterol, triglycerides; enzymatic assay method), and plasma glucose (locally according to standard guidelines).

The changes in parameters were calculated by subtracting the baseline value from the follow-up value.

#### 4.3.3 INCIDENT DIABETES

Diabetes diagnoses were based on an OGTT as defined by the World Health Organization 1985 criteria (World Health Organization 1985). Type 2 diabetes was diagnosed if either the fasting plasma glucose concentration was  $\geq$ 7.8 mmol/l or the 2-hour plasma glucose concentration was  $\geq$ 11.1 mmol/l. For a definitive diagnosis, a confirmatory OGTT was needed if the first OGTT indicated diabetes. Diabetes incidence was calculated for the 4-year intervention period.

### 4.4 HEALTH BEHAVIOUR AND HEALTH AMONG THE FINNISH ADULT POPULATION (AVTK) 2004–2008 (STUDY V)

The data from the AVTK annual postal survey from years 2004–2008 were used for Study V. Since 1978 these surveys have been conducted annually by the National Institute for Health and Welfare, and the main purpose has been to obtain continuous information on the health behaviours of the adult population (Helakorpi et al. 2004). In the years 2004–2008, to facilitate the evaluation of DEHKO's implementation project for type 2 diabetes prevention – FIN-D2D, some questions regarding knowledge of the ongoing programme and health habit changes were included in the questionnaire. Changes in public awareness of the national diabetes programme and health behaviours during the FIN-D2D project period were assessed using these questions. The ethical regulations of the National Institute for Health and Welfare were applied each survey year.

A random sample of 5000 Finns aged 15 to 64 years was drawn each year from the National Population Register. Participants aged over 35 years were included in this analysis, reflecting the main target group of FIN-D2D activities, from the years 2004–2008 (response rate varied between 64% and 68%). The data set included altogether 10982 men and women. Participants with missing data on awareness of the diabetes prevention programme (n=151) were excluded, and the final data set of Study V included 4935 men and 5896 women.

#### 4.4.1 SOCIOECONOMIC AND LIFESTYLE VARIABLES

Educational level was divided into three groups according to years of completed education: low (0-9 years), medium (10-12 years) and high education (13 years or more).

Changes in physical activity were assessed with a simple question: In the past year, have you increased your physical activity for health reasons? Changes in diet were assessed with the questions: In the past year, have you reduced your use of fat / made changes to the quality of fat used / increased your use of vegetables for health reasons? Further, changes in smoking and alcohol consumption were assessed with the questions: In the past year, have you reduced the amount you smoke and have you reduced your consumption of alcohol? The options for all questions were 'Yes' or 'No'.

#### 4.4.2 AWARENESS OF THE NATIONAL DIABETES PROGRAMME

The respondents were presented with a question asking whether they had heard about the ongoing DEHKO. Those who responded 'yes' were defined as being aware of the programme, and correspondingly, 'no' was considered to indicate non-awareness. This question about awareness of DEHKO was used as a surrogate for population-level knowledge about diabetes and its prevention.

## 4.5 STATISTICAL METHODS

A summary of the data sets, important variables and the statistical methods used in the five studies are presented in Table 4.

Study I. Analyses were carried out separately for men and women. The prevalence of hyperglycaemia and risk factors was calculated among the socioeconomic status groups using logistic regression. The results were presented as proportions (%) and their 95% confidence intervals (CIs), and were adjusted for age and study year. Odds ratios (ORs) and 95% CI for the prevalence of hyperglycaemia between educational groups were also analysed adjusting for age, study year and potential risk factors, such as physical inactivity, unhealthy diet, smoking and excess use of alcohol.

Study II. The baseline risk factor profile was compared between different cohorts, using t-tests or analysis of variance (ANOVA) for continuous measures and chi-square tests for categorical variables. Type 2 diabetes incidence rates per 1000 person-years at risk were calculated for each cohort overall and by educational group. Formal test of interaction between education and cohort did not reach statistical significance. Adjusted hazard ratios (HRs) with 95% CI for developing diabetes over time and between educational groups were calculated using multivariate Cox regression models. The analyses were adjusted for age, BMI, physical activity and dietary fat. The p-values indicate the test for trend. Tests for trend were performed by including the study cohort in the full model as a continuous measure.

Study III. Baseline clinical and lifestyle characteristics were compared between different cohorts, using ANOVA for continuous measures and chisquare tests for categorical variables. Cox proportional hazards models were used to examine associations between the risk factors and the time to development of comorbidity during the 10-year follow-up, adjusting for age, study year and study area. The data were stratified for sex, and the analyses were completed separately for people without baseline diseases, and people with diabetes mellitus at baseline. Results were presented as HR (95% CI) for univariate and multivariate models for comorbidity.

Study IV. Baseline data were presented for the whole study population and the changes for those who completed at least the first intervention year (n=506, 97%). The interactions between the group assignment and educational attainment on changes in selected lifestyle variables were analysed with linear regression, adjusting for sex, age and respective baseline variable. To test whether the effect of intervention on diabetes incidence was independent of educational level, an interaction term between the group

assignment and educational attainment was included in a Cox regression model. This analysis was adjusted for sex, age, and baseline 2-hour postchallenge plasma glucose concentration to eliminate possible effects of baseline differences.

Study V. The trend in awareness of DEHKO-programme during 2004–2008 was presented separately for men and women and for both study areas. The study areas included implementation areas that were actively participating in FIN-D2D activities and control areas that were only subject to nationwide DEHKO communications. The results were presented as proportions (%). For the other analyses, the data from different survey years (2004–2008) were pooled together. Descriptive analyses were carried out separately for both study areas (implementation vs control). Logistic regression analyses were used to evaluate the differences in self-reported changes in health habits among men and women by awareness in both areas. Results were presented as proportions (%) and their 95% CI, and adjusted for age and education. The *p*-values indicate the difference between the analysed groups. The interaction term between the awareness of DEHKO and the study area was added to the models to explore whether the association between awareness of the programme and actual health habit changes was different in the FIN-D2D and control areas.

Statistical analyses were performed with the statistics package STATA version 9.0 or 11.0 (Stata Corp LLC, Texas) and SAS 9.3 (SAS Institute, Cary, NC).

Study	Data set	Final data	Outcome	Background and explanatory variables	Design and statistical methods
I	FIN-D2D survey 2004 and 2007	n=3642 Age range: 45–64 years	Prevalence of T2D, ST2D, TT2D, IGT, IFG, and total hyperglycaemia based on clinical examination Prevalence of risk factors ( incl. obesity, physical inactivity, unhealthy diet, smoking and excessive use of alcohol) based on questionnaire and clinical examination	Study year, gender, age, education, income, lifestyle factors: obesity, physical activity, diet, smoking, alcohol consumption	Cross- sectional; logistic regression; data stratified for gender
II	FINRISK survey 1972, 1977, 1982, 1987, 1992 and 1997	n=38689 Age range: 30–59 years	Incident diabetes based on drug registers	Study year, study area, gender, age, education, employment status, lifestyle factors: obesity, physical activity, diet, smoking	Longitudinal follow-up; Cox regression; data stratified for cohorts and gender
III	FINRISK survey 1982, 1987, 1992, 1997 and 2002	n=32972 Age range: 25–64 years	Incident multimorbidity based on drug and hospital registers	Study year, study area, gender, age, education, lifestyle factors: obesity, physical activity, diet, smoking; clinical characteristics: blood pressure, lipid and glucose values	Longitudinal follow-up; Cox regression; data stratified for cohorts and gender
IV	DPS 1993-2002 (from baseline to intervention year 4)	n=522 Age range: 40–64 years	Changes in lifestyle and clinical characteristics, such as diet, physical activity and blood pressure, based on questionnaires and clinical examination Incident diabetes based on clinical examination	Gender, age, treatment group, education	Randomized intervention; linear and Cox regression, data stratified for treatment groups
V	AVTK survey 2004, 2005, 2006, 2007 and 2008	n=10831 Age range: 35–64 years	Changes in awareness of DEHKO and lifestyle (incl. diet, physical activity, smoking and alcohol consumption) based on postal questionnaire	Study year, study area, gender, age, education, marital status, awareness of national diabetes programme	Series of cross- sectional studies; logistic regression; data stratified for study area and gender

Table 4. Data sets, variables and statistical methods used in Studies I–V

AVTK=Health Behaviour and Health among the Finnish Adult Population (annual postal survey); DEHKO=Development Programme for the Prevention and Care of Diabetes; DPS=Diabetes Prevention Study; FIN-D2D=implementation project of the DEHKO; FINRISK=Finnish risk factors survey; IFG=impaired fasting glucose; IGT=impaired glucose tolerance; ST2D=screen-detected type 2 diabetes (previously unknown); T2D=type 2 diabetes (previously known); TT2D=total type 2 diabetes (T2D+ST2D).

## 5 RESULTS

### 5.1 EDUCATIONAL DIFFERENCES IN THE PREVALENCE OF HYPERGLYCAEMIA AND RISK FACTORS (STUDY I)

In the FIN-D2D surveys, altogether 1696 men and 1946 women had a laboratory examination including, for example, glucose tolerance testing. The prevalence of TT2D was 15% in men and 9% in women. ST2D accounted over half of all prevalent cases of TT2D in both genders. Altogether 50% of men and 33% of women had hyperglycaemia. Overall, the prevalence of T2D, ST2D and IFG was statistically significantly higher in men than women (p<0.001). Of the hyperglycaemia indicators, only the prevalence of IGT did not differ between men and women.

The mean BMI was similar in men and women  $(27.5 \text{ and } 27.3 \text{ kg/m}^2, \text{ respectively})$ , but obesity was more common among women (25%) than among men (22%). Other risk factors, such as physical inactivity, unhealthy diet, smoking and excess use of alcohol, were more prevalent in men than in women. Of men and women, respectively, 35% and 29% had a low, 33% and 33% had a medium, and 33% and 37% had a high educational level.

#### Hyperglycaemia and risk factors by education

Table 5 shows the age-adjusted prevalence of different forms of hyperglycaemia in the low, medium and high educational categories. The prevalence of TT2D was higher in women with the lowest educational level compared with women with the highest educational level. In both men and women, the difference in the prevalence of total hyperglycaemia was statistically significant between the lowest and highest educational level. This difference was partly explained by the increasing proportion of ST2D by decreasing education. In both genders, an inverse trend between income levels and hyperglycaemia was observed (data not shown), but the inverse trend between education and hyperglycaemia was more consistent and significant.

Table 5. Age-adjusted prevalence (95% confidence interval) of different forms of hyperglycaemia by education among middle-aged men and women in FIN-D2D surveys

		Education	
	Low	Medium	High
Men			
n	591	552	553
T2D	5 (3–7)	5 (3–7)	5 (3–7)
ST2D	11 (9–14)*	9 (7–12)	7 (5–10)
TT2D	17 (14–20)	14 (11–17)	12 (10–15)
IGT	14 (11–17)	12 (9–15)	12 (10–16)
IFG	23 (20–27)*	21 (18–25)	18 (15–21)
Total	56 (52-61)***	49 (45-53)	44 (40–49)
Women			
n	573	645	728
T2D	4 (3–6)*	2 (1-4)	2 (1-3)
ST2D	8 (6–10)*	5 (4–7)	5 (3–7)
TT2D	12 (9–15)**	8 (6–10)	6 (5-9)
IGT	16 (13–19)	13 (11–16)	13 (11–16)
IFG	8 (6–11)	12 (10–15)	9 (7–11)
Total	37 (33–42)**	33 (30-37)	29 (26–33)

IFG=impaired fasting glucose; IGT=impaired glucose tolerance; ST2D=screen-detected type 2 diabetes (previously unknown); T2D=type 2 diabetes (previously known); TT2D=total type 2 diabetes (T2D+ST2D); Total=summed value of different forms of hyperglycaemia.

Statistically significant difference in the prevalence of hyperglycaemia compared with the highest educational group: \*\*\*p<0.001, \*\*p<0.01, \*p<0.05.

Table 6 shows the levels of modifiable risk factors for hyperglycaemia according to educational level. In both genders, obesity (BMI>30), unhealthy diet, and smoking were more common in those with the lowest education. Among men, those with low education were also more likely to be physically inactive. Women and men with higher education reported more often alcohol intakes that indicated excessive alcohol use than those with lower education.

		Education	
	Low	Medium	High
Men			
n	591	552	553
Obesity	28 (24–32)***	19 (16–22)	18 (15–22)
Physical inactivity	25 (22–29)**	22 (19–26)	18 (15–21)
Unhealthy diet	35 (30–39)***	24 (21–29)**	17 (14–21)
Smoking	28 (24–32)**	30 (26–34)***	20 (17–24)
Alcohol use	15 (12–18)*	18 (15–22)	20 (17–24)
Women			
n	573	645	728
Obesity	33 (29–37)***	25 (21–28)*	20 (17–23)
Physical inactivity	20 (17–24)	19 (16–22)	17 (15–20)
Unhealthy diet	23 (19–27)**	18 (15–21)	15 (13–18)
Smoking	20 (17–24)***	17 (14–20)***	10 (8–13)
Alcohol use	8 (6-11)***	11 (9–14)*	16 (14–19)

Table 6. Age-adjusted prevalence (95% confidence interval) of type 2 diabetes risk factors by education among middle-aged men and women in FIN-D2D surveys

Statistically significant difference in the prevalence of risk factors compared with the highest educational group: \*\*\*p<0.001, \*\*p<0.01, \*p<0.05.

## Explanatory factors for the association between education and hyperglycaemia

Figure 6 shows the ORs for the prevalence of TT2D in the low and medium educational categories compared with the highest educational category. In the lowest educational category, women had a higher risk of TT2D compared with women in the highest educational category (OR 1.91; 95% CI 1.27–2.88). Controlling for obesity decreased the educational differences in TT2D (OR 1.58; 95% CI 1.03–2.42). Further controlling for other lifestyle-related risk factors (physical inactivity, unhealthy diet, smoking and excess use of alcohol) did not change the observed differences between educational categories. Among men, there were no statistically significant differences between educational categories and prevalent type 2 diabetes.



Figure 6. Odds ratios (95% confidence interval) for the prevalence of total type 2 diabetes (total T2D) by education among middle-aged men and women in FIN-D2D surveys with adjustment for various risk factors. BMI=body mass index.

The same analyses were conducted using total hyperglycaemia as the outcome variable. The risk of total hyperglycaemia was higher in both men and women with the lowest education (Figure 7). The association was attenuated after controlling for obesity among women. In men, these educational differences remained after adjustments for obesity, physical inactivity, diet, smoking and excess use of alcohol (OR 1.48; 95% CI 1.11–1.96).



Figure 7. Odds ratios (95% confidence interval) for prevalence of hyperglycaemia by education among middle-aged men and women in FIN-D2D surveys with adjustment for various risk factors. BMI=body mass index.

### 5.2 TRENDS AND EDUCATIONAL DIFFERENCES IN TYPE 2 DIABETES INCIDENCE (STUDY II)

Of the 18806 men, 420 developed type 2 diabetes over the 10-year follow-up within all FINRISK cohorts. Of the 19883 women, 339 developed type 2 diabetes over the same follow-up period.

Among men, diabetes incidence increased over time (Table 7). For men, ageadjusted incidence rates per 1000 person-years at risk were 1.56 (95% CI 1.30–1.85) in the 1970s, 2.66 (95% CI 2.24–3.15) in the 1980s and 3.50 (95% CI 2.97–4.10) in the 1990s. This increasing type 2 diabetes incidence was associated with BMI. Comparing the 1990s cohorts to the 1970s cohorts, the HR of type 2 diabetes incidence was 2.18 in the age-adjusted model and it decreased to 1.68 after adjustment for BMI. Further adjustments for physical activity and dietary fat did not affect the observed increases in type 2 diabetes incidence between cohorts.

Among women, there was no statistically significant increase in the diabetes incidence over time (Table 7). For women, age-adjusted incidence rates per 1000 person-years at risk were 1.75 (95% CI 1.49–2.03) in the 1970s, 1.53 (95% CI 1.22–1.90) in the 1980s and 1.82 (95% CI 1.46–2.24) in the 1990s.

NRISK cohorts	
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e among men ai	
lence over time	
f diabetes incid	
nazard ratios o	1992/97
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Tab	197

	H	VZARD RATIOS (95	% confidence interv	al)	
	Age adjusted	Age + BMI	Age + physical activity	Age + dietary fat	Fully adjusted*
Men					
<b>1972/77</b> (n=8968)	1.00	1.00	1.00	1.00	1.00
<b>1982/87</b> (n=5402)	1.65 (1.30–2.11)	1.42 (1.12–1.81)	1.62 (1.27–2.07)	1.66 (1.30–2.12)	1.44 (1.13–1.84)
<b>1992/97</b> (n=4436)	2.18 (1.73–2.76)	1.68 (1.32–2.12)	2.19 (1.72–2.78)	2.17 (1.67–2.81)	1.72 (1.32–2.24)
Test for trend	<i>p</i> <0.001	<i>p</i> <0.001	p<0.001	p<0.001	p<0.001
Women					
<b>1972/77</b> (n=9492)	1.00	1.00	1.00	1.00	1.00
<b>1982/87</b> (n=5520)	0.86 (0.66–1.12)	0.93 (0.71–1.20)	0.88 (0.67–1.14)	0.83 (0.63–1.08)	0.90 (0.69–1.17)
<b>1992/97</b> (n=4871)	1.02 (0.79–1.33)	1.05 (0.81–1.36)	1.09 (0.84–1.41)	0.93 (0.70–1.24)	0.94 (0.71–1.24)
Test for trend	p=0.935	p=0.823	p=0.712	<i>p</i> =0.484	p=0.580
BMI=body mass i	ndex; FINRISK=Finnish	ı risk factors survey.			

BMI=body mass index; FINRISK=Finnish risk factors survey. Men and women aged 30–59 years at baseline were followed for 10 years. \*Adjusted for age, BMI, physical activity and dietary fat.

#### **Diabetes trends by education**

Table 8 shows hazard ratios of type 2 diabetes within each educational category in the 1970s, 1980s and 1990s cohort. The results indicate that the incidence of diabetes increased over time among men within either the low or medium educational category. Among those with higher education, adjustment for BMI affects the results. The increasing incidence between the 1990s and 1970s cohorts became non-significant after controlling for BMI. Adjustments for physical activity or dietary fat did not consistently affect the results. No educational differences in diabetes incidence were found within the cohorts among men (data not shown).

Incidence of type 2 diabetes did not change over time among women within any educational category (Table 8). Within cohorts, some educational differences in diabetes incidence were observed (data not shown). Briefly, diabetes incidence was higher among women in the lowest than in the highest educational category in the 1970s and 1980s cohorts, and the difference in incidence was fully explained by a higher BMI among the women with low education. In the 1990s cohort, women with low education were more likely to develop diabetes than those with medium education.

Table 8. Adjusted haza 1992/97	urd ratios of diabetes	over time by educatioi HAZARD RATIOS (95%	nal attainment and so confidence interval)	ex in FINKISK cohorts	1972/77, 1982/87,
	Age adjusted	Age + BMI	Age + physical activity	Age + dietary fat	Fully adjusted*
Men: low education 1972/77 (n=2028)	1.00	1.00	1.00	1.00	1.00
<b>1982/87</b> (n=1343)	2.12 (1.32–3.41)	2.01 (1.25–3.24)	2.23 (1.39–3.59)	2.07 (1.28–3.34)	2.07 (1.28–3.35)
<b>1992/97</b> (n=1207)	2.52 (1.59–4.00)	2.09 (1.32–3.31)	2.81 (1.76–4.48)	2.33 (1.42–3.84)	2.12 (1.28–3.53)
Test for trend	<i>p</i> <0.001	p=0.002	p<0.001	p=0.001	<i>p</i> =0.003
Men: medium education 1972/77 (n=3321)	1.00	1.00	1.00	1.00	1.00
<b>1982/87</b> (n=1839)	1.56 (1.03–2.38)	1.34 (0.88–2.05)	1.51 (0.99–2.30)	1.51 (0.99–2.31)	1.30 (0.85–1.99)
<b>1992/97</b> (n=1452)	2.44 (1.63–3.63)	1.74 (1.16–2.63)	2.40 (1.60–3.60)	2.12 (1.36–3.32)	1.65 (1.05–2.60)
Test for trend Men: high education	<i>p</i> <0.001	<i>p</i> =0.008	p<0.001	<i>p</i> =0.001	p=0.030
<b>1972/77</b> (n=3517)	1.00	1.00	1.00	1.00	1.00
<b>1982/87</b> (n=2049)	1.28 (0.86–1.92)	1.08 (0.72–1.61)	1.22(0.81 - 1.82)	1.35 (0.90–2.02)	1.08 (0.72–1.64)
<b>1992/97</b> (n=1753)	1.72 (1.18–2.50)	1.37 (0.93–2.00)	1.61 (1.09–2.36)	1.94 (1.26–2.99)	1.43 (0.92–2.22)
Test for trend	<i>p</i> =0.005	p=0.112	<i>p</i> =0.016	<i>p</i> =0.003	p=0.116

Results

		HAZARD RATIOS (95	% confidence interval)		
	Age adjusted	Age + BMI	Age + physical activity	Age + dietary fat	Fully adjusted*
Women: low education					
<b>1972/77</b> (n=2640)	1.00	1.00	1.00	1.00	1.00
<b>1982/8</b> 7 (n=1576)	0.89 (0.57–1.39)	0.82 (0.52–1.29)	0.96 (0.61–1.50)	0.86 (0.55–1.36)	0.84 (0.53–1.34)
<b>1992/97</b> (n=1490)	1.15 (0.76–1.73)	1.00 (0.66–1.51)	1.26 (0.83–1.91)	1.05 (0.67–1.65)	0.92 (0.59–1.43)
Test for trend	p=0.584	p=0.929	p=0.330	p=0.897	p=0.675
Women: medium education 1972/77 (n=3278)	1.00	1.00	1.00	1.00	1.00
<b>1982/87</b> (n=1715)	0.75 (0.47–1.20)	0.87 (0.54–1.38)	0.75 (0.47–1.20)	0.73 (0.46–1.17)	0.85 (0.53–1.37)
<b>1992/97</b> (n=1651)	0.69 (0.42–1.13)	0.73 (0.44–1.19)	0.72 (0.44–1.19)	0.63 (0.37–1.08)	0.68 (0.40–1.16)
Test for trend	p=0.103	p=0.196	p=0.148	p=0.068	p=0.147
Women: high education 1972/77 (n=3466)	1.00	1.00	1.00	1.00	1.00
<b>1982/8</b> 7 (n=2014)	0.72 (0.43–1.22)	0.86 (0.51–1.46)	0.74 (0.44–1.25)	0.67 (0.39–1.14)	0.79 (0.46–1.36)
<b>1992/97</b> (n=1705)	1.22 (0.76–1.94)	1.47 (0.91–2.35)	1.28 (0.80–2.06)	1.02 (0.60–1.72)	1.20 (0.70–2.05)
Test for trend	p=0.585	p=0.173	p=0.456	p=0.875	p=0.629
BMI=body mass indey *Model adjusted for ag	x; FINRISK=Finnish risk fac ge, BMI, physical activity (	tors survey. Men and wom and dietary fat.	en aged 30–59 years at bas	seline were followed for 10	years.

### 5.3 EDUCATION AND THE DEVELOPMENT OF COMORBIDITIES AMONG PEOPLE WITH DIABETES (STUDY III)

Of the FINRISK cohorts' participants (n=32972), 14923 men and 16284 women were initially disease-free, and 586 men and 663 women had diabetes at baseline.

Men with diabetes were significantly older (53 years vs 44 years, p<0.001), more often physically inactive (31% vs 25%, p<0.001), and had higher systolic blood pressure (146 mmHg vs 139 mmHg, p<0.001) and BMI (29 vs 27 kg/m<sup>2</sup>, p<0.001) at baseline than diabetes-free counterparts. Patterns were similar for women. In addition, cholesterol values were significantly higher in women with diabetes (6.1 mmol/l) compared with disease-free women (5.7 mmol/l). However, smoking was more common among women without baseline diseases (20%) than with diabetes (15%). No differences in educational level were found between initially disease-free people and people with diabetes at baseline.

#### Risk factors for incident comorbidity among people with diabetes

The data from the FINRISK survey showed that of men with diabetes at baseline (n=586), 181 were diagnosed with one or more comorbid diseases, either cardiovascular disease (n=127), asthma/chronic obstructive pulmonary disease (n=34), cancer (n=37) or rheumatoid and other arthritis (7), during the follow-up. Common risk factors, such as high blood pressure (HR=1.75, 95% CI 1.19–2.57), physical inactivity (HR=1.80, 95% CI 1.29–2.53), and smoking (HR=1.57, 95% CI 1.12–2.19) at baseline increased the likelihood of incident comorbidity in multivariate models (Table 9).

Of women with diabetes at baseline (n=663), 150 were diagnosed with one or more comorbid diseases, either cardiovascular disease (n=65), asthma/chronic obstructive pulmonary disease (n=35), cancer (n=40) or rheumatoid and other arthritis (n=19), during the follow-up. The statistically strongest predictors of incident comorbidity in multivariate models were having BMI 27 or higher (HR=1.60, 95% CI 1.06–2.43) and being a daily smoker (HR=2.14, 95% CI 1.38–3.33) (Table 9). In the univariate model, also physical inactivity increased the likelihood of comorbidity among women (HR=1.45, 95% CI 1.03–2.06) (data not shown).

Among the people that were initially free of chronic disease, the same predisposing factors for multimorbidity were found (data not shown). However, low education predicted multimorbidity among the disease-free population but was not associated with the development of comorbidity among people with diabetes at baseline.

Table 9. Prospective association of baseline risk factors with incident comorbidity during the 10-year follow-up among men (n=586) and women (n=663) with diabetes at baseline

	Men	Women
	HR (95% CI)	HR (95% CI)
Blood pressure	1.75 (1.19–2.57)	0.96 (0.66–1.40)
(≥140/90 mmHg vs		
<140/90 mmHg) Cholostorol	0.77(0.59, 1.19)	0.06(0.58, 1.58)
(>5 mmol/l vs	0.// (0.53-1.12)	0.90 (0.50-1.50)
<5 mmol/l)		
Body mass index	1.20 (0.83–1.73)	1.60 (1.06–2.43)
$(\geq 27 \text{ kg/m}^2 \text{ vs})$		
<27 kg/m²)		
Current smoker	1.57 (1.12–2.19)	2.14 (1.38–3.33)
(yes vs no)		
Physical activity	1.80 (1.29–2.53)	1.35 (0.93–1.95)
(low vs high)		
Fruit and vegetable	1.20 (0.86–1.67)	0.87 (0.60–1.27)
consumption		
(low vs high)		
Education	0.71 (0.47–1.05)	1.10 (0.70–1.73)
(low vs high)		

CI=confidence interval; HR=hazard ratio.

Values are adjusted by age, study year and study area. This multivariate model includes all explanatory variables at the same time.

### 5.4 EDUCATIONAL ATTAINMENT AND THE EFFECTIVENESS OF LIFESTYLE INTERVENTION TO PREVENT TYPE 2 DIABETES (STUDY IV)

The volunteer, high diabetes risk participants (n=522) of the DPS study were randomly assigned to receive either intensive lifestyle intervention (n=265) or standard care (n=257), for the median duration of 4 years. The distribution of educational attainment was similar in the intervention and the control group. In both groups, 39% of the participants had low, 28% medium, and 33% high educational attainment.

At baseline, there were no significant differences in lifestyle-related risk factors, such as BMI, dietary intakes or leisure time physical activity between the intervention and the control groups (Table 10). A statistically significant association between baseline waist circumference and education was observed in the intervention group only, waist circumference being larger among those with the highest education than those with lower education. No other associations between different educational groups were evident. Also, the clinical factors, such as blood pressure, glucose, and lipid values, were similar in the intervention and the control groups as well as in the different educational groups, except that 2-hour plasma glucose and total serum cholesterol values were higher among those with the lowest than those with the highest education (data not shown).

#### Lifestyle and clinical changes by education

After the first, most intensive intervention year, the effect of intervention did not differ between the educational groups when the changes in clinical and lifestyle factors were used as measures of intervention effectiveness. The only exceptions were that the changes in waist circumference among the control group (Table 10) and serum triglycerides values among the intervention group were inversely associated with educational attainment (data not shown), indicating that lower education was actually associated with better outcome.

			Education		
		Low	Medium	High	n*
<u> </u>		2011		8	P
Intervention group	Baseline	102	74	89	
0F	Year 1	101	70	85	
Control group	Baseline	101	72	84	
	Year 1	98	71	81	
Body mass index (kg/m <sup>2</sup> )					
Intervention group	Baseline	31.5 (5.0)	31.0 (4.0)	31.5 (5.0)	0.848
	Year 1	-2.0 (2.0)	-1.5 (2.0)	-1.5 (1.5)	0.640
Control group	Baseline	31.5 (4.5)	31.0 (4.0)	31.0 (5.0)	0.328
	Year 1	-0.5 (1.5)	-0.5 (1.5)	-0.5 (1.0)	0.533
Waist circumference (cm)					
Intervention group	Baseline	100.0 (11.5)	102.0 (9.0)	104.0 (11.5)	0.028
	Year 1	-5.0 (5.0)	-4.0 (5.5)	-4.0 (5.0)	0.147
Control group	Baseline	100.0 (12.0)	100.5 (9.5)	101.0 (10.5)	0.498
	Year 1	-2.0 (5.0)	-1.5 (5.0)	-0.5 (4.0)	0.017
$E_{ot}(E\%)$					
Fat (E%)	Deceline			a(-1)	0.600
Intervention group	Voor 1	30.0 (7.0)	30.0 (7.0)	30.5 (0.5)	0.632
Control group	Pageline	-4.5(0.5)	-3.0(6.5)	-2.5(7.5)	0.150
Control group	baseline Voor 1	30.5 (0.0)	38.5 (8.0)	37.0 (7.0)	0.011
	rear 1	-1.0 (7.0)	-4.0 (8.0)	-1.5 (7.5)	0.600
Saturated fat (E%)					
Intervention group	Baseline	16.5 (4.0)	16.0 (4.0)	16.5 (4.0)	0.995
	Year 1	-3.0 (4.5)	-2.5(5.0)	-2.5 (4.5)	0.641
Control group	Baseline	16.5 (4.5)	17.5 (4.0)	17.0 (4.5)	0.335
	Year 1	-0.5 (4.5)	-2.0 (5.5)	-1.5 (5.0)	0.286
Fibre (g/1000 kcal)					
Intervention group	Baseline	115(40)	115(40)	120(40)	0.600
Intervention group	Year 1	30(50)	25(4.0)	25(50)	0.537
Control group	Baseline	120(25)	105(2.5)	125(3.6)	0.337
control group	Vear 1	$0 \in (2 \in 5)$	15.3(3.3)	12.3(4.3)	0.708
	I cal I	0.5 (3.5)	1.5 (4.0)	0.5 (5.0)	0.700
Physical activity					
(nours/week)	Raselino	$7 \in (6 \circ)$	70(55)	6 5 (5 5)	0.227
mer vention group	Voor 1	7.5(0.0)	7.0(5.5)	-0.0(5.5)	0.33/
Control group	Racolino	-5(0.0)	8 = (6 =)	-0.0(5.0)	0.554
control group	Vear 1	-05(/.0)	-0 5 (8 E)	10(25)	0.105
	I Cui I	0.0 (0.0)	0.9 (0.9)	1.0 (3.3)	0.109

Table 10. Baseline values and changes in lifestyle-related factors during the first intervention year by education in the intervention and the control group

E%=proportion of total energy consumed. Data are means (standard deviations). \**p*-values are for test of trend.

#### **Diabetes incidence by education**

Figure 8 shows that the effect of intervention on diabetes incidence was independent of educational attainment after the 4-year intervention period. In the intervention group, the incidences were 3.7, 5.1 and 3.8 cases per 100 person-years at low, medium and high level of education, respectively (p=0.980). In the control group, the incidences were 7.9, 7.3 and 7.0 cases per 100 person-years across different educational levels (p=0.665). The test of interaction between the educational attainment and treatment group on diabetes incidence was not statistically significant (p=0.611).



Figure 8. Diabetes incidence rates (per 100 person-years) by level of education.

#### 5.5 ASSOCIATION BETWEEN SOCIODEMOGRAPHIC FACTORS, AWARENESS OF THE NATIONAL DIABETES PROGRAMME, AND LIFESTYLE CHANGES (STUDY V)

Using data from AVTK postal surveys, the population-level awareness of DEHKO and changes in health habits were examined during the active phase of the implementation project FIN-D2D. The data were analysed comparing areas (hospital districts of South Ostrobothnia, Central Finland, and Pirkanmaa) that were actively participating in FIN-D2D activities with reference areas that were only subject to nationwide DEHKO communications.

The study population consisted of 10831 men and women. Of them, 3058 were from the FIN-D2D area and 7773 from the control area. In both study areas, the gender distribution was similar (45% men and 54% women). Also, the distribution of other sociodemographic factors such as age, marital status, and education were similar between the areas. In general, awareness of the national diabetes prevention programme was higher in the FIN-D2D project area compared with the control area. In the FIN-D2D and control areas, respectively, 25% vs 20% of men and 48% vs 36% of women were aware of the programme. The awareness increased in both areas and genders from 2004 to 2007 but started to decline in 2008 (Figure 9).



Figure 9. Changes in awareness of the national diabetes programme among 35- to 64-year-old men and women during 2004–2008 in FIN-D2D and control areas.

There were some differences between sociodemographic factors and awareness of the programme in both areas. Women were more often aware of the programme compared with men, and older people compared with younger people. However, we found no evidence suggesting that educational level or marital status was associated with awareness.

In the years 2004–2008, women reported more often than men that they had changed their dietary habits or physical activity during the previous year. However, men reported more often having reduced alcohol consumption and smoking than women. Especially among men, the self-reported changes in health habits were associated with being aware of DEHKO in both study areas (Table 11). Of men, 38% of those who had heard about DEHKO reported that they had reduced the use of fat, while among those who were unaware the proportion was 33%. Further, being aware vs being unaware of DEHKO was associated with self-reported changes in the quality of dietary fat (30% vs 23%), increased consumption of vegetables (38% vs 28%), increased physical activity (28% vs 22%), weight loss (21% vs 16%) and reduced alcohol consumption (17% vs 14%) among men.

Among women, being aware vs being unaware of DEHKO was associated only with changes in the amount (40% vs 36%, respectively) and quality of dietary fat (28% vs 26%), and weight loss during the past year (28% vs 25%). A statistically significant interaction (p=0.040) between area (FIN-D2D vs other) and being aware of DEHKO was found only for weight reduction among women, with self-reported weight loss being more common among those who lived in the FIN-D2D area and were aware of the programme.

Further, being aware vs being unaware of DEHKO was associated with the frequency of self-reported blood glucose measurements during the last year among men and women (data not shown). The proportions were 59% vs 42% in men, and 56% vs 41% in women, respectively.

		Awarene	ess of	
		Yes	No	p
Changes in health habits, % (CI)	:			
Men (n)	FIN-D2D area	347	1037	
	Control area	702	2849	
Reduced use of fat	FIN-D2D area	37 (32-42)	34 (31.0–37)	0.319
	Control area	40 (36–43)	32 (30–34)	<0.001
Changed quality of fat	FIN-D2D area	32 (27–37)	25 (22–27)	0.008
	Control area	27 (24–31)	22 (21–24)	0.007
Increased use of vegetables	FIN-D2D area	38 (33-44)	29 (26–32)	0.001
	Control area	39 (35–42)	28 (26–30)	<0.001
Increased physical activity	FIN-D2D area	29 (24–34)	24 (22–27)	0.093
	Control area	26 (23–30)	21 (19–22)	0.002
Lost weight	FIN-D2D area	20 (16–24)	16 (14–18)	0.118
C C	Control area	22 (19–25)	17 (16–18)	0.003
Reduced alcohol consumption	FIN-D2D area	16 (13–21)	15 (13-17)	0.559
1	Control area	18 (15–21)	14 (13–15)	0.015
Reduced smoking	FIN-D2D area	12 (9–16)	10 (8–12)	0.401
0	Control area	11 (8–13)	10 (9–11)	0.653
Women (n)	FIN-D2D area	797	877	
	Control area	1514	2708	
Reduced use of fat	FIN-D2D area	41 (37–44)	37 (34–41)	0.150
	Control area	40 (38–43)	35 (33–37)	0.001
Changed quality of fat	FIN-D2D area	28 (25–31)	27 (24–30)	0.624
	Control area	29 (26–31)	25 (23–26)	0.008
Increased use of vegetables	FIN-D2D area	37 (34–41)	36 (33–39)	0.647
	Control area	37 (35–40)	35 (34–37)	0.176
Increased physical activity	FIN-D2D area	34 (31–37)	30 (27–33)	0.103
	Control area	31 (29–33)	31 (29–33)	0.901
Lost weight	FIN-D2D area	29 (26–33)	24 (21–27)	0.013
	Control area	26 (24–29)	25 (24–27)	0.591
Reduced alcohol consumption	FIN-D2D area	10 (8–13)	10 (8–12)	0.709
	Control area	10 (9–12)	10 (9–11)	0.605
Reduced smoking	FIN-D2D area	6 (5-8)	8 (6–10)	0.196
	Control area	8 (6-9)	8 (7-9)	0.942

Table 11. Self-reported changes in health habits by awareness of DEHKO among men and women

CI=confidence interval; DEHKO=Development Programme for the Prevention and Care of Diabetes. Results are based on data from years 2004–2008. Values are adjusted for age and education. The *p*-values indicate the difference in self-reported changes in health habits between those who had heard of DEHKO compared with those who had not heard of DEHKO in the area.

## 6 **DISCUSSION**

# 6.1 SUMMARY AND INTERPRETATION OF THE FINDINGS

## 6.1.1 IS EDUCATION ASSOCIATED WITH RISK FACTORS AND PREVALENCE OF HYPERGLYCAEMIA?

Based on the findings from the cross-sectional study reported in this thesis, the prevalence of hyperglycaemia was more common among those with low education compared with the medium and high educational groups. The educational gradient in type 2 diabetes was evident especially among women. In both genders, obesity, unhealthy diet and smoking were all inversely related to education. Adjusting the prediction model with obesity and other diabetes risk factors attenuated the association with hyperglycaemia slightly.

Our findings are in line with previous research: the global number of people with type 2 diabetes is increasing and in developed countries diabetes is more common among people with low socioeconomic status (Robbins et al. 2005, Shaw, Sicree & Zimmet 2010). In Finland, the prevalence of self-reported type 2 diabetes has been shown to be higher in the lower than in the higher educational group among middle-aged men and women since the 1980s (Palosuo 2009), and this study confirms that the difference in the prevalence of known diabetes still exists between educational groups.

The previous studies have focused more on socioeconomic differences in coronary heart disease (Harald et al. 2006, Laaksonen et al. 2008, Lammintausta et al. 2012) than in different forms of hyperglycaemia. The findings of this study showed that previously unidentified (=screen-detected) type 2 diabetes accounted for over half of all prevalent cases of type 2 diabetes, and an increasing proportion of ST2D was found by decreasing education in both genders. Prevalence of screen-detected diabetes has been associated with low socioeconomic status also in earlier studies in other countries. The study of Rathmann et al. found an inverse association between ST2D and occupational status in women but not in men (Rathmann et al. 2005). The finding may indicate that people with higher socioeconomic position have better and more comprehensive healthcare services which include screening tests for undiagnosed diseases. This inequity in healthcare services may be a factor contributing to socioeconomic differences in health and disease in the long run.

As would be expected on the basis of previous literature (Agardh et al. 2004, Kumari, Head & Marmot 2004, Rathmann et al. 2005), the increased diabetes prevalence seen in the low socioeconomic status groups was partly explained by higher risk factor levels. Obesity was the most important contributing factor on the gradient between socioeconomic status and type 2 diabetes. Additional adjustment for other lifestyle-related factors such as physical inactivity, unhealthy eating habits, smoking and excess alcohol use did not change the association between education and diabetes. Previous studies have suggested that traditional risk factors can explain about a third of social disparities in type 2 diabetes (Agardh et al. 2004, Kumari, Head & Marmot 2004, Williams et al. 2010). In the Whitehall cohort, risk factors explained almost half of the association between socioeconomic status and incidence of type 2 diabetes (Stringhini et al. 2012). Still, there is some space for other factors, such as elements of social or psychological environment that could be potential explanatory factors for the socioeconomic differences. Identifying these factors could facilitate more effective prevention interventions, taking into account equity in health.

#### 6.1.2 HAS THE INCIDENCE OF TYPE 2 DIABETES CHANGED OVER TIME AND IF SO, IS THE TREND ASSOCIATED WITH EDUCATIONAL LEVEL?

The incidence of type 2 diabetes has increased over the past 35 years among men, but not among women, based on large, nationally representative cohorts. At the same time, the prevalence of obesity has increased among men throughout educational groups. Adjusting for BMI attenuated the ageadjusted HRs for type 2 diabetes among men in the 1980s and 1990s cohorts compared with the 1970s group. However, among men with low and middle educational attainment, diabetes incidence increased over time and this effect was evident after adjusting for BMI.

Among women, the observed lack of change in diabetes incidence over time can be attributed to developments in obesity prevalence in these cohorts. In women, mean BMI increased between 1972 and 1987; after that no statistically significant changes have been evident (Borodulin et al. 2015). It even seemed that the increasing BMI trend among the middle-aged population might be levelling off (Borodulin et al. 2015), but the most recent study showed again an increase in obesity numbers (Koponen et al. 2018). Further, the recent report of the Finnish Diabetes Association indicated that the amount of new diabetes diagnoses per year has decreased according to the register-based data (Koski 2017). However, more recent analyses do not exist about the changes in type 2 diabetes incidence among the Finnish population, and updated survey-based data are required to monitor the type 2 diabetes incidence trends especially in sub-groups. Our results on temporal changes in diabetes incidence are in line with the findings from the Framingham Offspring Study in the USA. They showed greater 8-year diabetes incidence in middle-aged men in the 1990s compared with the 1970s, after adjusting for age and BMI. In women, there were no statistically significant changes (Fox et al. 2006). Hardoon et al. reported that diabetes incidence increased among British men between 1984 and 2007, with BMI being the main explanator of this variation (Hardoon et al. 2010). In Finland, studies have previously documented trends in diabetes incidence (Laakso et al. 1991, Strandberg & Salomaa 2000, Lammi et al. 2008), but studies examining trends in type 2 diabetes incidence by socioeconomic status over decades have been lacking. One reason for the scarcity of research is the difficulty in identifying incident cases of diabetes via healthcare registers for example as compared with cardiovascular diseases. To our knowledge, this Finnish study is the first to report the incidence of diabetes over successive decades by socioeconomic status, and therefore it is not possible to compare these results to previous ones. Our findings indicate that among men from medium and low socioeconomic groups, a real increase in the incidence of type 2 diabetes has happened. Furthermore, the increase in incidence can only partly be attributed to increasing obesity and there must be some other underlying risk factors that need to be identified and tackled in order to reduce socioeconomic health differences.

#### 6.1.3 IS EDUCATION ASSOCIATED WITH THE DEVELOPMENT OF COMORBIDITIES AMONG PEOPLE WITH DIABETES?

In our study based on the register follow-up of large national cohorts, several modifiable risk factors were found to predict incident comorbidity among people with diabetes. Among men, high blood pressure, physical inactivity, and smoking increased the appearance of comorbidity. Among women, significant predictors of comorbidities were high BMI and smoking. However, we did not find evidence that educational level would independently predict the development of comorbidity among people with diabetes.

Previously, accumulating unhealthy lifestyle factors have been shown to increase the likelihood of multimorbidity, and obesity has been identified as the most important contributing factor (Nagel et al. 2008, Autenrieth et al. 2013, Booth, Prevost & Gulliford 2014, Ruel et al. 2014, Fortin et al. 2014). In Finland, population-level obesity rates and blood pressure levels are relatively high (Borodulin et al. 2015) and therefore contribute to the burden of type 2 diabetes and cardiovascular disease in the population. In this study, the effect of obesity on the risk of comorbidity was clearly observed among women, as was the effect of elevated blood pressure among men. Also, smoking increased markedly the likelihood of comorbidity among both men and women with diabetes. As smoking prevalence has decreased in Finland during recent decades the population risk attributable to smoking has also diminished (Borodulin et al. 2015).

The findings of this study address the potential for risk factor management in diabetes to prevent complications and comorbidity. As previously shown, the risk of type 2 diabetes can be reduced by lifestyle counselling aiming at beneficial changes in weight, diet and physical activity (Tuomilehto et al. 2001, Lindstrom et al. 2013), and the beneficial lifestyle changes can also decrease the future risk of developing a second disease. This was recently demonstrated by the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER). After the 2-year intervention period including nutritional guidance, exercise, cognitive training, and management of clinical risk factors, the mean number of new disease diagnoses was statistically significantly lower among the intervention group participants compared with the control group (Marengoni et al. 2018).

In the present study, low educational level was a significant risk factor for multimorbidity among people without baseline diseases but not for comorbidity among people with diabetes. This finding is inconsistent with previous literature where low socioeconomic status, as an independent risk factor, has been shown to be associated with inferior diabetes treatment, resulting in a higher risk of complications and comorbidities among people with type 2 diabetes (Grintsova, Maier & Mielck 2014). One reason for the inconsistency between our finding and previous ones could be attributed to the relatively low diabetes prevalence and consecutive low number of incident cases among this study subgroup. Secondly, the Finnish healthcare system is based on the egalitarian principle to ensure that all people have equal access to public healthcare. Equal diabetes management among this small patient group could be one possible explanation for the inconsistent results. The benefits of equitable health services might be greatest for those with the lowest socioeconomic status leading to smaller health disparities among the population.

#### 6.1.4 DOES EDUCATION MODIFY THE EFFECTIVENESS OF LIFESTYLE INTERVENTION IN PREVENTING TYPE 2 DIABETES?

Our study showed that prevention activities targeted at people with increased risk of type 2 diabetes were equally effective in all educational groups.

Type 2 diabetes and its risk factors have been shown to be inversely associated with socioeconomic status, for example educational level (Kumari, Head & Marmot 2004, Lahelma et al. 2010). Further, it has been suggested that higher educational level may increase the ability to access information needed to develop healthy lifestyle habits and attitudes (Lahelma et al. 2004, Galobardes et al. 2006). Generally, education has been strongly and consistently associated with health and health behaviours in Finland (Lahelma et al. 2010, Lahelma et al. 2017), but the association between education and the effectiveness of lifestyle counselling has been unclear.

This study has shown that education did not modify the effectiveness of the lifestyle counselling provided to the intervention participants of the DPS. The effect of counselling on lifestyle changes and diabetes incidence was independent of participants' educational background. Previously, socioeconomic status was unrelated to achieving either the weight or other goals of lifestyle intervention in the US DPP study (Wing et al. 2004). Similar to our results, the study of Hankonen et al. showed that low educational background is not a barrier to behavioural change in the GOAL Lifestyle Implementation Trial to prevent type 2 diabetes among the Finnish population (Hankonen et al. 2009). Recently, the results from the FINGER study confirmed that lifestyle intervention to prevent memory disorders was beneficial regardless of participants' socioeconomic status, as measured by income and educational level (Rosenberg et al. 2018). A common factor between the aforementioned DPS and FINGER studies was that the lifestyle counselling was individualized, aiming to support each participant's personal path towards a healthier lifestyle. This approach might also explain the effectiveness of intervention regardless of educational background.

#### 6.1.5 IS THERE AN ASSOCIATION BETWEEN SOCIODEMOGRAPHIC FACTORS, AWARENESS OF THE NATIONAL DIABETES PROGRAMME, AND IMPROVED HEALTH HABITS?

When implementing and scaling up the findings from preventive interventions at a population level, we need to consider several factors, such as coverage and reach of the intervention activities (Aziz et al. 2015). Even a highly effective intervention is likely to have a minimal effect at a population level if it reaches only a fraction of the target group. Previously, awareness of an increased risk of diabetes has been shown to be associated with engagement in preventive, healthy lifestyle activities (Okosun, Davis-Smith & Seale 2012). Therefore, awareness of being at risk may be considered an initiator for changing health behaviour and facilitate prevention, early diagnosis and better management of type 2 diabetes. Thus, the awareness of ongoing preventive activities and diabetes risk factors and the level of adoption of a healthier lifestyle in the population can be used as indicators of the effectiveness of the community-based diabetes prevention programme.

In this study, we interpreted awareness of the ongoing DEHKO to be a surrogate for knowledge about diabetes and its risk factors. As could be expected, the awareness increased among men and women in both the implementation and control areas during the 4 years of the FIN-D2D project period. The level of awareness remained consistently higher in the implementation area. Educational level was not associated with awareness. We also found that among women, awareness was higher throughout the project. However, the awareness of DEHKO started to decline after the activities of the implementation project ceased in the FIN-D2D area. This shows that the awareness was dependent on the intensity of the FIN-D2D activities and it emphasizes the need for sustained, continuing health promotion in communities, instead of short-term projects.

It is well known that sex and age are associated with health beliefs and health behaviours (Ek & Heinström 2011, Ek 2013). In the present study, altogether 25% of the survey population reported that they had made changes in their health habits regardless of their living area or awareness of DEHKO. Women and older people reported more often health habit changes than men and younger people. Interestingly, self-reported changes in lifestyle were associated with awareness of DEHKO more often among men than among women, regardless of whether the person was living in the FIN-D2D implementation area or not. The findings indicate that the activities related to the conduct of the FIN-D2D implementation project, such as risk screening in healthcare services, local media campaigns, events organized by local non-governmental organizations etc., may at least partly explain the reported differences in lifestyle changes among the population. Furthermore, it seems that especially men may benefit from health promotion campaigns.

The results suggest that the national diabetes prevention programme can be considered reasonably effective also at the population level, as measured by raised awareness of DEHKO in the entire population. The population strategy was implemented nationwide in Finland, and the awareness increased also outside the FIN-D2D area. This indicates that large, community-based programmes can have an important impact on health behaviours among the entire population. In addition, the results from the high-risk cohort, encompassing people identified with increased diabetes risk and taking part in the preventive activities offered by primary healthcare according to the FIN-D2D protocol, showed that education and occupation were not associated with effectiveness of lifestyle intervention. The high-risk strategy reached even more people with lower than higher socioeconomic status (Rautio et al. 2011). Previously, the North Karelia Project showed that a large-scale implementation programme can enhance nationwide changes in health behaviours and reduce risk factors of cardiovascular diseases (Puska et al. 1985). In the North Karelia Project, the effect of dietary intervention aiming at reducing the intake of saturated fats was effective in different educational and occupational groups among the whole population (Pietinen et al. 1996).

These all are encouraging findings and offer support for the implementation of prevention activities and the tackling of health differences in the population.

## 6.2 METHODOLOGICAL CONSIDERATIONS

The present study is based on three population-based, cross-sectional surveys (FIN-D2D, FINRISK and AVTK), and one clinical, longitudinal, randomized intervention study (DPS). Also, the possibility of linking the survey data with national registers to create prospective cohorts was unique, compared with studies completed in most other countries. The large sample size and long follow-up period were the main strengths of the cohort analyses in this present thesis. The use of several data sets can be seen as a strength, because in combination they provided diverse and multidimensional information on the role of socioeconomic status in epidemiology, comorbidities, and the effectiveness of interventions for type 2 diabetes. In addition, the use of previously collected and register data can be seen as a sensible use of resources instead of collecting new data.

Population-based health and risk factors surveys offer the possibility of making interpretations about the situations and trends within the population at large. However, when interpreting the results of this study, several methodological aspects should be kept in mind. Declining participation rates is a growing problem in all population health surveys (Reinikainen et al. 2017), and this may introduce bias in the observed results. The selection bias may affect the results if there is a systematic difference in characteristics between participants and non-participants and if participation rates decrease over time (Tolonen et al. 2005). Non-participants generally exhibit a more adverse health profile than participants. This may lead to severe consequences, as seen in the FINRISK survey, with higher total and cause-specific mortality in non-participants (Jousilahti et al. 2005). In the population-based FINRISK survey, lower socioeconomic groups were overrepresented among non-participants (Harald et al. 2007).
According to the previous results of the AVTK, non-participants were often young, low-educated and male (Tolonen et al. 2006). Also, in the FIN-D2D study, non-participation was more common among men and among younger age groups (Wikström et al. 2011). We can hypothesize that the differences between genders and educational groups would be even wider in populationbased surveys if we could include also non-respondents in the analyses. Selection bias may affect also the interpretation of the results from clinical trials. Participants of the DPS were originally volunteers and we can assume that, regardless of their socioeconomic status, they were concerned about their risk of getting diabetes and therefore were more motivated to make lifestyle changes than the population in general.

In this thesis, the socioeconomic measures were based on self-reported questionnaires. Socioeconomic status was defined using one indicator, which does not fully capture the impact of social disparities. Studies should not rely on a single socioeconomic indicator, but if only a single parameter is available, education has been shown to be the most suitable socioeconomic status measure in epidemiological studies (Winkleby et al. 1992, Lahelma et al. 2004). In Finland, education is a useful indicator of socioeconomic status, because it has been shown to be associated strongly with health behaviours (Palosuo 2009). However, its discriminant utility may vary between countries. A challenge of using education as a socioeconomic status indicator in research is that the Finnish school system has changed over time, and vounger age cohorts have in general gained a higher educational attainment than the older age cohorts. Therefore, in this study in the incidence analyses, we assigned the educational status relatively to that of an individual's birth cohort. In this way we could reflect the participant's educational attainment in the distribution of years of formal education that was typical among people born in the same period.

Self-administered questionnaires are a common, cheap and easy way to collect information on health habits of the population in health surveys. However, recall bias and some under- or overestimation of lifestyle habits might have influenced the study information. The FINRISK questionnaire included a non-quantitative food frequency questionnaire and questions with multiple choices. This kind of method can yield information on the overall food habits of the study population, but it did not allow analysis of nutrient intake level. In addition, some items of the FINRISK questionnaires had been modified over time to retain relevancy, partly because of the changes in the dietary and physical activity recommendations and the supply of foodstuffs. Therefore, it was challenging to create indicators for health habits and the formulation of research questions was subject to the availability of the specific information over time. The type of milk and cooking fat and the consumption of fruits and vegetables were the only questions in common and therefore were considered as surrogate indicators of a healthy diet in the FINRISK studies.

In the FIN-D2D study exploring the prevalence of hyperglycaemia in the population, diagnosis of screen-detected diabetes was based on a single OGTT, which is the standard practice in prevalence studies. However, it should be noted that in clinical practice the diagnosis, in the absence of clear symptoms, always has to be confirmed with a second test on a separate day, as there is clear intraperson day-to-day variability in glucose values (Mooy et al. 1996). The true prevalence of clinically diagnosed diabetes thus is lower than that seen in the surveys.

While analysing the incident diabetes, data on incident diagnoses of diabetes were received from national register on reimbursement rights, and the follow-up time was restricted to 10 years for each cohort. The validity of the diabetes diagnosis in the reimbursement register is high as diagnosis is based on explicit, predefined criteria. Diabetes screening patterns, changes in treatment guidelines and regimes and thresholds for initiating treatment have changed over time, which may have a large impact on the incidence trends. Importantly, the application of those may be different in different socioeconomic groups. For example, increased incidence is likely to reflect improved case detection over time, possibly particularly among less educated men. Changes in diagnostic criteria for diabetes over time (World Health Organization 1985, World Health Organization 1999) may have influenced case assessment, but our findings cannot simply be ascribed to such changes as these would be expected to uniformly influence all educational levels and both genders. In addition, there was not a way to include type 2 diabetes treated only with lifestyle modification into the outcome data as these cases do not appear in the register based on drug reimbursements. Finally, this study only captures diagnosed diabetes. The true incidence of type 2 diabetes is likely to be higher than the results suggest.

In the analyses investigating incident comorbidity among people with diabetes, data on diagnoses of the chronic diseases during the 10 years were received from national registers on reimbursement rights and drug purchases, hospitalizations, and mortality. Even though the validity of diagnosis in Finnish registers of hospital diagnoses and deaths has been found to be good (Sund & Koski 2009, Sund 2012), some misclassification is always present in register data. From an epidemiological perspective, an important limitation is that only diagnoses of inpatients could be included in the National Hospital Discharge Register. To limit the effect of this barrier, the data from registers of the Social Insurance Institution were obtained in order to create a more comprehensive database of chronic diseases, covering also drug purchases and reimbursement rights for outpatients. Further, the number of affected people for many disease combinations was low, which is

in accordance with the age distribution within our study cohort. Therefore we restricted the analyses to the most common diseases. The relatively low incidence of many chronic diseases within the population may lead to low statistical power and random associations. Therefore, the findings should be interpreted with caution.

## 7 CONCLUSIONS AND FUTURE DIRECTIONS

In this thesis, the association between socioeconomic status and type 2 diabetes has been approached from different viewpoints, using several data sources and study designs, with educational attainment as a surrogate for socioeconomic status.

- 1. In agreement with previous research, we found that type 2 diabetes and its modifiable risk factors are associated with socioeconomic status. Over the past 35 years, the incidence of type 2 diabetes increased among Finnish men but not among women. Increases occurred predominantly among men with low and middle educational attainment, and obesity explained some but not all of this variation between socioeconomic classes.
- 2. Regarding people who already have diabetes, there were several clinical- and lifestyle-related risk factors that predisposed to the development of comorbidity. However, no evidence was found to suggest that socioeconomic status was a factor in the development of comorbidity.
- 3. Lifestyle intervention to prevent type 2 diabetes was feasible and equally effective across socioeconomic groups in the clinical trial setting.
- 4. The national diabetes prevention programme succeeded in increasing awareness of type 2 diabetes among the whole population, regardless of socioeconomic status. Men who reported being aware of the programme also reported more lifestyle changes.

The existing evidence on health promotion and chronic disease prevention indicates that population-wide behavioural changes are possible. The present results, suggesting the non-existence of a social gradient in the effectiveness of diabetes prevention in both the clinical trial setting and population-based health promotion programmes, are encouraging for prevention activities in general. However, they also indicate that community level activities need to be sustainable and long term to have a long-standing effect.

An important question for future research is how to increase the coverage and reach of prevention activities especially among vulnerable population groups, for example those with low socioeconomic status. It is well established that low socioeconomic status people are under-represented in health surveys and clinical trials, and the same probably is true also for health promotion activities. It is important to realize that prevention activities could actually increase health disparities if only people with higher socioeconomic status participate. Attention should be paid to actions promoting health and preventing diseases targeted at people with lower socioeconomic status. Successful actions among those with the highest prevalence of risk factors and chronic diseases would benefit the health of the whole population.

At the moment, the Finnish healthcare system is under reform. The ambitious aims of the Finnish social welfare and healthcare reform are to improve the well-being of citizens and decrease socioeconomic differences in health and welfare, and to guarantee equity in access to services. However, it is not clear how the implementation of the reform will affect health promotion activities in the population. Therefore, it is important, during and after the reform, to collect information on health promotion and disease prevention practices, experiences and outcomes and to continue monitoring changes in public health and health differences between socioeconomic groups.

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## REFERENCES

- Absetz, P., Oldenburg, B., Hankonen, N., Valve, R., Heinonen, H., Nissinen, A., Fogelholm, M., Talja, M. & Uutela, A. "Type 2 diabetes prevention in the real world: three-year results of the GOAL lifestyle implementation trial". Diabetes Care 2009;32(8):1418-1420.
- Ackermann, R.T., Finch, E.A., Brizendine, E., Zhou, H. & Marrero, D.G.
   "Translating the Diabetes Prevention Program into the community. The DEPLOY Pilot Study". Am J Prev Med 2008;35(4):357-363.
- Agardh, E.E., Ahlbom, A., Andersson, T., Efendic, S., Grill, V., Hallqvist, J. & Ostenson, C.G. "Explanations of socioeconomic differences in excess risk of type 2 diabetes in Swedish men and women". Diabetes Care 2004;27(3):716-21.
- Agardh, E.E., Ahlbom, A., Andersson, T., Efendic, S., Grill, V., Hallqvist, J. & Ostenson, C.G. "Socio-economic position at three points in life in association with type 2 diabetes and impaired glucose tolerance in middle-aged Swedish men and women". Int J Epidemiol 2007;36(1):84-92.
- Agardh, E., Allebeck, P., Hallqvist, J., Moradi, T. & Sidorchuk, A. "Type 2 diabetes incidence and socio-economic position: a systematic review and meta-analysis". Int J Epidemiol 2011;40(3):804-818.
- American Diabetes Association. "Diagnosis and Classification of Diabetes Mellitus". Diabetes Care 2006;29(suppl 1):s48.
- Ardisson Korat, A., V., Willett, W.C. & Hu, F.B. "Diet, lifestyle, and genetic risk factors for type 2 diabetes: a review from the Nurses' Health Study, Nurses' Health Study 2, and Health Professionals' Follow-up Study". Current nutrition reports 2014;3(4):345-354.
- Autenrieth, C.S., Kirchberger, I., Heier, M., Zimmermann, A.K., Peters, A., Doring, A. & Thorand, B. "Physical activity is inversely associated with multimorbidity in elderly men: results from the KORA-Age Augsburg Study". Prev Med 2013;57(1):17-19.
- Aziz, Z., Absetz, P., Oldroyd, J., Pronk, N.P. & Oldenburg, B. "A systematic review of real-world diabetes prevention programs: learnings from the last 15 years". Implement Sci 2015;10:172.
- Bachmann, M.O., Eachus, J., Hopper, C.D., Davey Smith, G., Propper, C., Pearson, N.J., Williams, S., Tallon, D. & Frankel, S. "Socio-economic inequalities in diabetes complications, control, attitudes and health service use: a crosssectional study". Diabet Med 2003;20(11):921-929.
- Baliunas, D.O., Taylor, B.J., Irving, H., Roerecke, M., Patra, J., Mohapatra, S. & Rehm, J. "Alcohol as a risk factor for type 2 diabetes: A systematic review and meta-analysis". Diabetes Care 2009;32(11):2123-2132.
- Ball, K. & Crawford, D. "Socioeconomic status and weight change in adults: a review". Soc Sci Med 2005;60(9):1987-2010.
- Beagley, J., Guariguata, L., Weil, C. & Motala, A.A. "Global estimates of undiagnosed diabetes in adults". Diabetes Res Clin Pract 2014;103(2):150-160.
- Bihan, H., Laurent, S., Sass, C., Nguyen, G., Huot, C., Moulin, J.J., Guegen, R., Le Toumelin, P., Le Clesiau, H., La Rosa, E., Reach, G. & Cohen, R. "Association among individual deprivation, glycemic control, and diabetes complications: the EPICES score". Diabetes Care 2005;28(11):2680-2685.

- Blas, E. & Sivasankara Kurup, A. Equity, social determinants and public health programmes. World Health Organization, Geneva, 2010.
- Booth, H.P., Prevost, A.T. & Gulliford, M.C. "Impact of body mass index on prevalence of multimorbidity in primary care: cohort study". Fam Pract 2014;31(1):38-43.
- Borodulin, K., Laatikainen, T., Lahti-Koski, M., Jousilahti, P. & Lakka, T.A.
  "Association of age and education with different types of leisure-time physical activity among 4437 Finnish adults". J Phys Act Health 2008;5(2):242-251.
- Borodulin, K., Vartiainen, E., Peltonen, M., Jousilahti, P., Juolevi, A., Laatikainen, T., Männistö, S., Salomaa, V., Sundvall, J. & Puska, P. "Forty-year trends in cardiovascular risk factors in Finland". Eur J Public Health 2015;25(3):539-546.
- Borodulin, K., Zimmer, C., Sippola, R., Mäkinen, T.E., Laatikainen, T. & Prättälä, R. "Health behaviours as mediating pathways between socioeconomic position and body mass index". Int J Behav Med 2012;19(1):14-22.
- Braveman, P.A., Cubbin, C., Egerter, S., Chideya, S., Marchi, K.S., Metzler, M. & Posner, S. "Socioeconomic status in health research: one size does not fit all". JAMA 2005;294(22):2879-2888.
- Brown, A.F., Ettner, S.L., Piette, J., Weinberger, M., Gregg, E., Shapiro, M.F., Karter, A.J., Safford, M., Waitzfelder, B., Prata, P.A. & Beckles, G.L.
  "Socioeconomic position and health among persons with diabetes mellitus: a conceptual framework and review of the literature". Epidemiol Rev 2004;26:63-77.
- Cavelaars, A.E., Kunst, A.E., Geurts, J.J., Crialesi, R., Grotvedt, L., Helmert, U., Lahelma, E., Lundberg, O., Matheson, J., Mielck, A., Rasmussen, N.K., Regidor, E., do Rosario-Giraldes, M., Spuhler, T. & Mackenbach, J.P.
  "Educational differences in smoking: international comparison". BMJ 2000;320(7242):1102-1107.
- Chan, D.C., Watts, G.F., Barrett, P.H. & Burke, V. "Waist circumference, waist-tohip ratio and body mass index as predictors of adipose tissue compartments in men". QJM 2003;96(6):441-447.
- Chan, J.C., Malik, V., Jia, W., Kadowaki, T., Yajnik, C.S., Yoon, K.H. & Hu, F.B. "Diabetes in Asia: epidemiology, risk factors, and pathophysiology". JAMA 2009;301(20):2129-2140.
- Chang, A.M. & Halter, J.B. "Aging and insulin secretion". Am J Physiol Endocrinol Metab 2003;284(1):e7-12.
- Chaturvedi, N., Jarrett, J., Shipley, M.J. & Fuller, J.H. "Socioeconomic gradient in morbidity and mortality in people with diabetes: cohort study findings from the Whitehall Study and the WHO Multinational Study of Vascular Disease in Diabetes". BMJ 1998;316(7125):100-105.
- Chen, L., Magliano, D.J. & Zimmet, P.Z. "The worldwide epidemiology of type 2 diabetes mellitus--present and future perspectives". Nat Rev Endocrinol 2011;8(4):228-236.
- Cheng, Y.J., Imperatore, G., Geiss, L.S., Wang, J., Saydah, S.H., Cowie, C.C. & Gregg, E.W. "Secular Changes in the Age-Specific Prevalence of Diabetes Among U.S. Adults: 1988–2010". Diabetes Care 2013;36(9):2690-2696.
- Colditz, G.A., Willett, W.C., Rotnitzky, A. & Manson, J.E. "Weight gain as a risk factor for clinical diabetes mellitus in women". Ann Intern Med 1995;122(7):481-486.

- Dalstra, J.A.A., Kunst, A.E., Borrell, C., Breeze, E., Cambois, E., Costa, G., Geurts, J.J.M., Lahelma, E., Van Oyen, H., Rasmussen, N.K., Regidor, E., Spadea, T. & Mackenbach, J.P. "Socioeconomic differences in the prevalence of common chronic diseases: an overview of eight European countries". Int J Epidemiol 2005;34(2):316-326.
- Danaei, G., Finucane, M.M., Lu, Y., Singh, G.M., Cowan, M.J., Paciorek, C.J., Lin, J.K., Farzadfar, F., Khang, Y.H., Stevens, G.A., Rao, M., Ali, M.K., Riley, L.M., Robinson, C.A., Ezzati, M. & Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group (Blood Glucose) "National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2.7 million participants". Lancet 2011;378(9785):31-40.
- DECODE Study Group "Age- and sex-specific prevalences of diabetes and impaired glucose regulation in 13 European cohorts". Diabetes Care 2003;26(1):61-69.
- DECODE Study Group & European Diabetes Epidemiology Group "Is the current definition for diabetes relevant to mortality risk from all causes and cardiovascular and noncardiovascular diseases?". Diabetes Care 2003;26(3):688-696.
- DeFronzo, R.A. "From the Triumvirate to the Ominous Octet: A New Paradigm for the Treatment of Type 2 Diabetes Mellitus". Diabetes 2009;58(4):773-795.
- d'Errico, A., Ricceri, F., Stringhini, S., Carmeli, C., Kivimäki, M., Bartley, M., McCrory, C., Bochud, M., Vollenweider, P., Tumino, R., Goldberg, M., Zins, M., Barros, H., Giles, G., Severi, G., Costa, G., Vineis, P. & LIFEPATH Consortium "Socioeconomic indicators in epidemiologic research: A practical example from the LIFEPATH study". PLoS One 2017;12(5):e0178071.
- Diabetes Prevention Program Research Group "10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study". The Lancet 2009;374(9702):1677-1686.
- Diabetes Prevention Program, Research Group, Nathan, D.M., Barrett-Connor, E., Crandall, J.P., Edelstein, S.L., Goldberg, R.B., Horton, E.S., Knowler, W.C., Mather, K.J., Orchard, T.J., Pi-Sunyer, X., Schade, D. & Temprosa, M. "Longterm Effects of Lifestyle Intervention or Metformin on Diabetes Development and Microvascular Complications: the DPP Outcomes Study". The Lancet Diabetes & Endocrinology 2015;3(11):866-875.
- Diderichsen, F., Evans, T. & Whitehead, M. "The social basis of disparities in health," in T. Evans, M. Whitehead, F. Diderichsen, et al. (eds). Challenging inequalities in health: From ethics to action. New York: Oxford University Press, 2001.
- Dunkley, A.J., Bodicoat, D.H., Greaves, C.J., Russell, C., Yates, T., Davies, M.J. & Khunti, K. "Diabetes prevention in the real world: effectiveness of pragmatic lifestyle interventions for the prevention of type 2 diabetes and of the impact of adherence to guideline recommendations: a systematic review and metaanalysis". Diabetes Care 2014;37(4):922-933.
- Ek, S. & Heinström, J. "Monitoring or avoiding health information-the relation to inner inclination and health status". Health Info Libr J 2011;28(3):200-209.
- Ek, S. "Gender differences in health information behaviour: a Finnish populationbased survey". Health.Promotion International 2013;30(3):736-745.

- Ely, E.K., Gruss, S.M., Luman, E.T., Gregg, E.W., Ali, M.K., Nhim, K., Rolka, D.B. & Albright, A.L. "A National Effort to Prevent Type 2 Diabetes: Participant-Level Evaluation of CDC's National Diabetes Prevention Program". Diabetes Care 2017;40(10):1331-1341.
- Engelgau, M.M., Narayan, K.M. & Herman, W.H. "Screening for type 2 diabetes.". Diabetes Care 2000;23(10):1563-1580.
- Eriksson, J., Lindström, J., Valle, T., Aunola, S., Hämäläinen, H., Ilanne-Parikka, P., Keinänen-Kiukaanniemi, S., Laakso, M., Lauhkonen, M., Lehto, P., Lehtonen, A., Louheranta, A., Mannelin, M., Martikkala, V., Rastas, M., Sundvall, J., Turpeinen, A., Viljanen, T., Uusitupa, M. & Tuomilehto, J. "Prevention of type II diabetes in subjects with impaired glucose tolerance: the Diabetes Prevention Study (DPS) in Finland. Study design and 1-year interim report on the feasibility of the lifestyle intervention programme". Diabetologia 1999;42(7): 793-801.
- Espelt, A., Borrell, C., Roskam, A.J., Rodriguez-Sanz, M., Stirbu, I., Dalmau-Bueno,
  A., Regidor, E., Bopp, M., Martikainen, P., Leinsalu, M., Artnik, B.,
  Rychtarikova, J., Kalediene, R., Dzurova, D., Mackenbach, J. & Kunst, A.E.
  "Socioeconomic inequalities in diabetes mellitus across Europe at the beginning of the 21st century". Diabetologia 2008;51(11):1971-1979.
- Ferretti, F. "Unhealthy Behaviours: An International Comparison". PLoS One 2015;10(10):e0141834.
- Field, A.E., Coakley, E.H., Must, A., Spadano, J.L., Laird, N., Dietz, W.H., Rimm, E. & Colditz, G.A. "Impact of overweight on the risk of developing common chronic diseases during a 10-year period". Arch Intern Med 2001;161(13):1581-1586.
- Finnish Diabetes Association. Dehkon 2D hanke (D2D) 2003-2007. Loppuraportti. Finnish Diabetes Association, Tampere, 2009.
- Finnish Diabetes Association, Diabetes in Finland 2016. Available: www.diabetes.fi [2017, Nov 4].
- Finucane, M.M., Stevens, G.A., Cowan, M.J., Danaei, G., Lin, J.K., Paciorek, C.J., Singh, G.M., Gutierrez, H.R., Lu, Y., Bahalim, A.N., Farzadfar, F., Riley, L.M., Ezzati, M. & Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group (Body Mass Index) "National, regional, and global trends in body-mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9.1 million participants". Lancet 2011;377(9765):557-567.
- Fogelholm, M. "Physical activity, fitness and fatness: relations to mortality, morbidity and disease risk factors. A systematic review". Obes Rev 2010;11(3):202-221.
- Ford, E.S., Williamson, D.F. & Liu, S. "Weight change and diabetes incidence: findings from a national cohort of US adults". Am J Epidemiol 1997;146(3):214-222.
- Forouhi, N.G. & Wareham, N.J. Epidemiology of diabetes, 2014.
- Forssas, E., Arffman, M., Koskinen, S., Reunanen, A. & Keskimäki, I. "Socioeconomic differences in mortality among diabetic people in Finland". Scand J Public Health 2010;38(7):691-698.
- Forssas, E., Arffman, M., Manderbacka, K., Keskimäki, I., Ruuth, I. & Sund, R. "Multiple complications among people with diabetes from Finland: an 18-year follow-up in 1994–2011". BMJ Open Diab Res Care 2016;4:e000254.

- Fortin, M., Haggerty, J., Almirall, J., Bouhali, T., Sasseville, M. & Lemieux, M. "Lifestyle factors and multimorbidity: a cross sectional study". BMC public health 2014;14(1):686.
- Fowler, M.J. "Microvascular and Macrovascular Complications of Diabetes". Clinical Diabetes 2008;26(2):77.
- Fox, C.S., Coady, S., Sorlie, P.D., D'Agostino RB, S., Pencina, M.J., Vasan, R.S., Meigs, J.B., Levy, D. & Savage, P.J. "Increasing cardiovascular disease burden due to diabetes mellitus: the Framingham Heart Study". Circulation 2007;115(12):1544-1550.
- Fox, C.S., Pencina, M.J., Meigs, J.B., Vasan, R.S., Levitzky, Y.S. & D'Agostino RB,
  S. "Trends in the incidence of type 2 diabetes mellitus from the 1970s to the 1990s: the Framingham Heart Study". Circulation 2006;113(25):2914-2918.
- Fox, C.S. "Cardiovascular Disease Risk Factors, Type 2 Diabetes Mellitus, and the Framingham Heart Study". Trends Cardiovasc Med 2010;20(3):90-95.
- Franco, M., Bilal, U., Orduñez, P., Benet, M., Morejón, A., Caballero, B., Kennelly, J.F. & Cooper, R.S. "Population-wide weight loss and regain in relation to diabetes burden and cardiovascular mortality in Cuba 1980-2010: repeated cross sectional surveys and ecological comparison of secular trends". BMJ 2013;346:f1515.
- Fuchsberger, C., Flannick, J., Teslovich, T.M., Mahajan, A., Agarwala, V., Gaulton, K.J., Ma, C., Fontanillas, P., Moutsianas, L., McCarthy, D.J., Rivas, M.A., Perry, J.R.B., Sim, X., Blackwell, T.W., Robertson, N.R., Rayner, N.W., Cingolani, P., Locke, A.E., Tajes, J.F., Highland, H.M., Dupuis, J., Chines, P.S., Lindgren, C.M., Hartl, C., Jackson, A.U., Chen, H., Huyghe, J.R., van de Bunt, M., Pearson, R.D., Kumar, A., Muller-Nurasyid, M., Grarup, N., Stringham, H.M., Gamazon, E.R., Lee, J., Chen, Y., Scott, R.A., Below, J.E., Chen, P., Huang, J., Go, M.J., Stitzel, M.L., Pasko, D., Parker, S.C.J., Varga, T.V., Green, T., Beer, N.L., Day-Williams, A.G., Ferreira, T., Fingerlin, T., Horikoshi, M., Hu, C., Huh, I., Ikram, M.K., Kim, B.J., Kim, Y., Kim, Y.J., Kwon, M.S., Lee, J., Lee, S., Lin, K.H., Maxwell, T.J., Nagai, Y., Wang, X., Welch, R.P., Yoon, J., Zhang, W., Barzilai, N., Voight, B.F., Han, B.G., Jenkinson, C.P., Kuulasmaa, T., Kuusisto, J., Manning, A., Ng, M.C.Y., Palmer, N.D., Balkau, B., Stancakova, A., Abboud, H.E., Boeing, H., Giedraitis, V., Prabhakaran, D., Gottesman, O., Scott, J., Carey, J., Kwan, P., Grant, G., Smith, J.D., Neale, B.M., Purcell, S., Butterworth, A.S., Howson, J.M.M., Lee, H.M., Lu, Y., Kwak, S.H., Zhao, W., Danesh, J., Lam, V.K.L., Park, K.S., Saleheen, D., So, W.Y., Tam, C.H.T., Afzal, U., Aguilar, D., Arya, R., Aung, T., Chan, E., Navarro, C., Cheng, C.Y., Palli, D., Correa, A., Curran, J.E., Rybin, D., Farook, V.S., Fowler, S.P., Freedman, B.I., Griswold, M., Hale, D.E., Hicks, P.J., Khor, C.C., Kumar, S., Lehne, B., Thuillier, D., Lim, W.Y., Liu, J., van der Schouw, Y T, Loh, M., Musani, S.K., Puppala, S., Scott, W.R., Yengo, L., Tan, S.T., Taylor, H.A., Jr, Thameem, F., Wilson, G.S., Wong, T.Y., Njolstad, P.R., Levy, J.C., Mangino, M., Bonnycastle, L.L., Schwarzmayr, T., Fadista, J., Surdulescu, G.L., Herder, C., Groves, C.J., Wieland, T., Bork-Jensen, J., Brandslund, I., Christensen, C., Koistinen, H.A., Doney, A.S.F., Kinnunen, L., Esko, T., Farmer, A.J., Hakaste, L., Hodgkiss, D., Kravic, J., Lyssenko, V., Hollensted, M., Jorgensen, M.E., Jorgensen, T., Ladenvall, C., Justesen, J.M., Karajamaki, A., Kriebel, J., Rathmann, W., Lannfelt, L., Lauritzen, T., Narisu, N., Linneberg, A., Melander, O., Milani, L., Neville, M., Orho-Melander, M., Qi,

L., Qi, Q., Roden, M., Rolandsson, O., Swift, A., Rosengren, A.H., Stirrups, K., Wood, A.R., Mihailov, E., Blancher, C., Carneiro, M.O., Maguire, J., Poplin, R., Shakir, K., Fennell, T., DePristo, M., de Angelis, M.H., Deloukas, P., Gjesing, A.P., Jun, G., Nilsson, P., Murphy, J., Onofrio, R., Thorand, B., Hansen, T., Meisinger, C., Hu, F.B., Isomaa, B., Karpe, F., Liang, L., Peters, A., Huth, C., O'Rahilly, S.P., Palmer, C.N.A., Pedersen, O., Rauramaa, R., Tuomilehto, J., Salomaa, V., Watanabe, R.M., Syvanen, A.C., Bergman, R.N., Bharadwaj, D., Bottinger, E.P., Cho, Y.S., Chandak, G.R., Chan, J.C.N., Chia, K.S., Daly, M.J., Ebrahim, S.B., Langenberg, C., Elliott, P., Jablonski, K.A., Lehman, D.M., Jia, W., Ma, R.C.W., Pollin, T.I., Sandhu, M., Tandon, N., Froguel, P., Barroso, I., Teo, Y.Y., Zeggini, E., Loos, R.J.F., Small, K.S., Ried, J.S., DeFronzo, R.A., Grallert, H., Glaser, B., Metspalu, A., Wareham, N.J., Walker, M., Banks, E., Gieger, C., Ingelsson, E., Im, H.K., Illig, T., Franks, P.W., Buck, G., Trakalo, J., Buck, D., Prokopenko, I., Magi, R., Lind, L., Farjoun, Y., Owen, K.R., Gloyn, A.L., Strauch, K., Tuomi, T., Kooner, J.S., Lee, J.Y., Park, T., Donnelly, P., Morris, A.D., Hattersley, A.T., Bowden, D.W., Collins, F.S., Atzmon, G., Chambers, J.C., Spector, T.D., Laakso, M., Strom, T.M., Bell, G.I., Blangero, J., Duggirala, R., Tai, E.S., McVean, G., Hanis, C.L., Wilson, J.G., Seielstad, M., Frayling, T.M., Meigs, J.B., Cox, N.J., Sladek, R., Lander, E.S., Gabriel, S., Burtt, N.P., Mohlke, K.L., Meitinger, T., Groop, L., Abecasis, G., Florez, J.C., Scott, L.J., Morris, A.P., Kang, H.M., Boehnke, M., Altshuler, D. & McCarthy, M.I. "The genetic architecture of type 2 diabetes". Nature 2016;536(7614):41-47.

- Gaede, P., Vedel, P., Larsen, N., Jensen, G.V., Parving, H.H. & Pedersen, O.
  "Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes". N Engl J Med 2003;348(5):383-393.
- Gallus, S., Lugo, A., Murisic, B., Bosetti, C., Boffetta, P. & La Vecchia, C.
  "Overweight and obesity in 16 European countries". Eur J Nutr 2015;54(5):679-689.
- Galobardes, B., Shaw, M., Lawlor, D.A., Lynch, J.W. & Davey Smith, G. "Indicators of socioeconomic position (part 1)". J Epidemiol Community Health 2006;60(1):7-12.
- Gedebjerg, A., Almdal, T.P., Berencsi, K., Rungby, J., Nielsen, J.S., Witte, D.R., Friborg, S., Brandslund, I., Vaag, A., Beck-Nielsen, H., Sorensen, H.T. & Thomsen, R.W. "Prevalence of micro- and macrovascular diabetes complications at time of type 2 diabetes diagnosis and associated clinical characteristics: A cross-sectional baseline study of 6958 patients in the Danish DD2 cohort". J Diabetes Complications 2018;32(1):34-40.
- Geiss, L.S., Pan, L., Cadwell, B., Gregg, E.W., Benjamin, S.M. & Engelgau, M.M. "Changes in incidence of diabetes in U.S. adults, 1997-2003". Am J Prev Med 2006;30(5):371-377.
- Gerstein, H.C. "Dysglycemia, not just diabetes, is a continuous risk factor for cardiovascular disease". Evid Based Cardiovasc Med. 1997;1(4):87-88.
- Geyer, S., Hemström, O., Peter, R. & Vagero, D. "Education, income, and occupational class cannot be used interchangeably in social epidemiology. Empirical evidence against a common practice". J Epidemiol Community Health 2006;60(9):804-810.
- Gilis-Januszewska, A., Piwonska-Solska, B., Lindström, J., Wojtowicz, E., Tuomilehto, J., Schwarz, P.E.H., Kissimova-Skarbek, K., Szybinski, Z.,

Windak, A. & Hubalewska-Dydejczyk, A. "Determinants of weight outcomes in type 2 diabetes prevention intervention in primary health care setting (the DE-PLAN project)". BMC Public Health 2018;18(1):1.

- Grintsova, O., Maier, W. & Mielck, A. "Inequalities in health care among patients with type 2 diabetes by individual socio-economic status (SES) and regional deprivation: a systematic literature review". Int J Equity Health 2014;13:43.
- Groop, L., Forsblom, C., Lehtovirta, M., Tuomi, T., Karanko, S., Nissén, M., Ehrnström, B., Forsén, B., Isomaa, B., Snickars, B. & Taskinen, M. "Metabolic Consequences of a Family History of NIDDM (The Botnia Study): Evidence for Sex-Specific Parental Effects". Diabetes 1996;45(11):1585-1593.
- Gurka, M.J., Wolf, A.M., Conaway, M.R., Crowther, J.Q., Nadler, J.L. & Bovbjerg, V.E. "Lifestyle intervention in obese patients with type 2 diabetes: impact of the patient's educational background". Obesity 2006;14(6):1085-1092.
- Haapa, E., Toponen, T., Pietinen, P. & Räsänen, L. Annoskuvakirja. Painokaari Oy, Helsinki, 1985.
- Haffner, S.M., Lehto, S., Ronnemaa, T., Pyörälä, K. & Laakso, M. "Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction". N Engl J Med 1998;339(4):229-234.
- Hamman, R.F., Wing, R.R., Edelstein, S.L., Lachin, J.M., Bray, G.A., Delahanty, L., Hoskin, M., Kriska, A.M., Mayer-Davis, E.J., Pi-Sunyer, X., Regensteiner, J., Venditti, B. & Wylie-Rosett, J. "Effect of weight loss with lifestyle intervention on risk of diabetes". Diabetes Care 2006;29(9):2102-2107.
- Hankonen, N., Absetz, P., Haukkala, A. & Uutela, A. "Socioeconomic status and psychosocial mechanisms of lifestyle change in a type 2 diabetes prevention trial". Ann Behav Med 2009;38(2):160-5.
- Harald, K., Pajunen, P., Jousilahti, P., Koskinen, S., Vartiainen, E. & Salomaa, V. "Modifiable risk factors have an impact on socio-economic differences in coronary heart disease events". Scand Cardiovasc J 2006;40(2):87-95.
- Harald, K., Salomaa, V., Jousilahti, P., Koskinen, S. & Vartiainen, E. "Nonparticipation and mortality in different socioeconomic groups: the FINRISK population surveys in 1972-92". J Epidemiol Community Health 2007;61(5):449-54.
- Hardoon, S.L., Morris, R.W., Thomas, M.C., Wannamethee, S.G., Lennon, L.T. & Whincup, P.H. "Is the Recent Rise in Type 2 Diabetes Incidence From 1984 to 2007 Explained by the Trend in Increasing BMI?". Diabetes Care 2010;33(7):1494-1496.
- Harris, M.I., Klein, R., Welborn, T.A. & Knuiman, M.W. "Onset of NIDDM occurs at least 4-7 yr before clinical diagnosis". Diabetes Care 1992;15(7):815-819.
- Heidemann, C., Hoffmann, K., Spranger, J., Klipstein-Grobusch, K., Mohlig, M., Pfeiffer, A.F. & Boeing, H. "A dietary pattern protective against type 2 diabetes in the European Prospective Investigation into Cancer and Nutrition (EPIC)--Potsdam Study cohort". Diabetologia 2005;48(6):1126-34.
- Helakorpi, S., Patja, K., Prättälä, R., Aro, A. & Uutela, A. "Health behaviour and health among Finnish adult population, spring 2004. Kansanterveyslaitoksen julkaisuja B:13/2004.
- Helldan, A. & Helakorpi, S. Health behaviour and health among Finnish adult population, spring 2014. Terveyden ja hyvinvoinnin laitos, raportti 6/2015.

- Heltberg, A., Andersen, J.S., Kragstrup, J., Siersma, V., Sandholdt, H. & Ellervik, C. "Social disparities in diabetes care: a general population study in Denmark". Scand J Prim Health Care 2017;35(1):54-63.
- Hu, F.B., Leitzmann, M.F., Stampfer, M.J., Colditz, G.A., Willett, W.C. & Rimm,
   E.B. "Physical activity and television watching in relation to risk for type 2 diabetes mellitus in men". Arch Intern Med 2001a;161(12): 1542-1548.
- Hu, F.B., Manson, J.E., Stampfer, M.J., Colditz, G., Liu, S., Solomon, C.G. & Willett, W.C. "Diet, lifestyle, and the risk of type 2 diabetes mellitus in women". N Engl J Med 2001b;345(11):790-797.
- Hu, F.B., van Dam, R.M. & Liu, S. "Diet and risk of Type II diabetes: the role of types of fat and carbohydrate". Diabetologia 2001c;44(7):805-817.
- Hu, F.B. "Globalization of Diabetes". Diabetes Care 2011;34(6):1249-1257.
- Hulshof, K.F., Brussaard, J.H., Kruizinga, A.G., Telman, J. & Lowik, M.R. "Socioeconomic status, dietary intake and 10 y trends: the Dutch National Food Consumption Survey". Eur J Clin Nutr 2003;57(1):128-137.
- International Diabetes Federation, IDF Diabetes atlas. International Diabetes Federation, Brussels, Belgium 2015.
- International Diabetes Federation, IDF Diabetes Atlas, International Diabetes Federation, Brussels, Belgium 2017.
- Jeon, C.Y., Lokken, R.P., Hu, F.B. & van Dam, R.M. "Physical activity of moderate intensity and risk of type 2 diabetes: a systematic review". Diabetes Care 2007;30(3):744-752.
- Johansson, J., Ahola, T. & Jula, A. "Sepelvaltimotautia sairastavien hypertension hoito vastaa melko hyvin hoitosuosituksia – diabetespotilaiden ei". Suomen Lääkärilehti 2016;20:1445-1451.
- Johnson, M., Jones, R., Freeman, C., Woods, H.B., Gillett, M., Goyder, E. & Payne, N. "Can diabetes prevention programmes be translated effectively into realworld settings and still deliver improved outcomes? A synthesis of evidence". Diabet Med 2013;30(1):3-15.
- Jousilahti, P., Salomaa, V., Kuulasmaa, K., Niemelä, M. & Vartiainen, E. "Total and cause specific mortality among participants and non-participants of population based health surveys: a comprehensive follow up of 54 372 Finnish men and women". J Epidemiol Community Health 2005;59(4):310-315.
- Juutilainen, A., Lehto, S., Rönnemaa, T., Pyorälä, K. & Laakso, M. "Type 2 diabetes as a "coronary heart disease equivalent": an 18-year prospective populationbased study in Finnish subjects". Diabetes Care 2005;28(12):2901-2907.
- Kaaja, R. & Rönnemaa, T. "Gestational diabetes: pathogenesis and consequences to mother and offspring". The review of diabetic studies: RDS 2008;5(4):194-202.
- Kajantie, E., Osmond, C., Barker, D.J.P. & Eriksson, J.G. "Preterm Birth—A Risk Factor for Type 2 Diabetes?: The Helsinki Birth Cohort Study". Diabetes Care 2010;33(12):2623-2625.
- Kaprio, J., Tuomilehto, J., Koskenvuo, M., Romanov, K., Reunanen, A., Eriksson, J., Stengard, J. & Kesäniemi, Y.A. "Concordance for type 1 (insulin-dependent) and type 2 (non-insulin- dependent) diabetes mellitus in a population-based cohort of twins in Finland". Diabetologia 1992;35(11):1060-1067.
- Kivimäki, M., Shipley, M.J., Ferrie, J.E., Singh-Manoux, A., Batty, G.D., Chandola, T., Marmot, M.G. & Smith, G.D. "Best-practice interventions to reduce socioeconomic inequalities of coronary heart disease mortality in UK: a prospective occupational cohort study". Lancet 2008;372(9650):1648-1654.

- Knowler, W.C., Barrett-Connor, E., Fowler, S.E., Hamman, R.F., Lachin, J.M., Walker, E.A., Nathan, D.M. & Diabetes Prevention Program Research Group "Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin". N Engl J Med 2002;346(6):393-403.
- Koponen, P., Borodulin, K., Lunqvist, A., Sääksjärvi, K. & Koskinen, S. "Terveys, toimintakyky ja hyvinvointi Suomessa: FinTerveys 2017 –tutkimus". Terveyden ja hyvinvoinnin laitos, raportti 4/2018.
- Koski, S. Diabetesbarometri 2017. Suomen Diabetesliitto ry, 2017.
- Kouvonen, A.M., Väänänen, A., Woods, S.A., Heponiemi, T., Koskinen, A. & Toppinen-Tanner, S. "Sense of coherence and diabetes: a prospective occupational cohort study". BMC Public Health 2008;8:46.
- Kumari, M., Head, J. & Marmot, M. "Prospective study of social and other risk factors for incidence of type 2 diabetes in the Whitehall II study". Arch Intern Med 2004;164(17):1873-80.
- Laakso, M., Reunanen, A., Klaukka, T., Aromaa, A., Maatela, J. & Pyorala, K. "Changes in the prevalence and incidence of diabetes mellitus in Finnish adults, 1970-1987". Am J Epidemiol 1991;133(9):850-857.
- Laaksonen, M., Talala, K., Martelin, T., Rahkonen, O., Roos, E., Helakorpi, S., Laatikainen, T. & Prättälä, R. "Health behaviours as explanations for educational level differences in cardiovascular and all-cause mortality: a followup of 60 000 men and women over 23 years". Eur J Public Health 2008;18(1):38-43.
- Laatikainen, T., Dunbar, J.A., Chapman, A., Kilkkinen, A., Vartiainen, E., Heistaro, S., Philpot, B., Absetz, P., Bunker, S., O'Neil, A., Reddy, P., Best, J.D. & Janus, E.D. "Prevention of type 2 diabetes by lifestyle intervention in an Australian primary health care setting: Greater Green Triangle (GGT) Diabetes Prevention Project". BMC Public Health 2007;7:249.
- Laatikainen, T., Jula, A., Kastarinen, M., Salomaa, V., Borodulin, K., Harald, K., Peltonen, M., Jousilahti, P. & Vartiainen, E. "Verenpainetasot ja hoitotasapainopaino FINRISKI-tutkimusalueilla 1982-2012". Suomen Lääkärilehti 2013;24:1809a.
- Lahelma, E., Lallukka, T., Laaksonen, M., Martikainen, P., Rahkonen, O., Chandola, T., Head, J., Marmot, M., Kagamimori, S., Tatsuse, T. & Sekine, M. "Social class differences in health behaviours among employees from Britain, Finland and Japan: the influence of psychosocial factors". Health Place 2010;16(1):61-70.
- Lahelma, E., Martikainen, P., Laaksonen, M. & Aittomäki, A. "Pathways between socioeconomic determinants of health". J Epidemiol Community Health 2004;58(4):327-332.
- Lahelma, E., Pentala, O., Helldán, A., Helakorpi, S. & Rahkonen, O. "36-year trends in socioeconomic differences in self-rated health among Finnish adults". Eur J Publ Health 2017;27(suppl\_3):ckx187.289.
- Lahti, R.A. & Penttilä, A. "The validity of death certificates: routine validation of death certification and its effects on mortality statistics". Forensic Sci Int 2001;115(1-2):15-32.
- Lahti-Koski, M., Seppänen-Nuijten, E., Männistö, S., Härkänen, T., Rissanen, H., Knekt, P., Rissanen, A. & Heliövaara, M. "Twenty-year changes in the prevalence of obesity among Finnish adults". Obesity reviews: an official

journal of the International Association for the Study of Obesity 2010;11(3):171-176.

- Lakka, T.A. & Salonen, J.T. "Intra-person variability of various physical activity assessments in the Kuopio Ischaemic Heart Disease Risk Factor Study". Int J Epidemiol 1992;21(3):467-472.
- Lallukka, T., Laaksonen, M., Rahkonen, O., Roos, E. & Lahelma, E. "Multiple socio-economic circumstances and healthy food habits". Eur J Clin Nutr 2007;61(6):701-710.
- Lammi, N., Blomstedt, P.A., Moltchanova, E., Eriksson, J.G., Tuomilehto, J. & Karvonen, M. "Marked temporal increase in the incidence of type 1 and type 2 diabetes among young adults in Finland". Diabetologia 2008;51(5):897-899.
- Lammintausta, A., Immonen-Raiha, P., Airaksinen, J.K., Torppa, J., Harald, K., Ketonen, M., Lehto, S., Koukkunen, H., Kesäniemi, A.Y., Karja-Koskenkari, P., Salomaa, V. & FINAMI Study Group "Socioeconomic inequalities in the morbidity and mortality of acute coronary events in Finland: 1988 to 2002". Ann Epidemiol 2012;22(2):87-93.
- Levitan, E.B., Song, Y., Ford, E.S. & Liu, S. "Is nondiabetic hyperglycemia a risk factor for cardiovascular disease? A meta-analysis of prospective studies". Arch Intern Med 2004;164(19):2147-2155.
- Li, G., Zhang, P., Wang, J., An, Y., Gong, Q., Gregg, E.W., Yang, W., Zhang, B., Shuai, Y., Hong, J., Engelgau, M.M., Li, H., Roglic, G., Hu, Y. & Bennett, P.H. "Cardiovascular mortality, all-cause mortality, and diabetes incidence after lifestyle intervention for people with impaired glucose tolerance in the Da Qing Diabetes Prevention Study: a 23-year follow-up study". Lancet Diabetes Endocrinol. 2014;2(6):474-480.
- Li, G., Zhang, P., Wang, J., Gregg, E.W., Yang, W., Gong, Q., Li, H., Li, H., Jiang, Y., An, Y., Shuai, Y., Zhang, B., Zhang, J., Thompson, T.J., Gerzoff, R.B., Roglic, G., Hu, Y. & Bennett, P.H. "The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study". Lancet 2008;371(9626):1783-1789.
- Lindström, J., Ilanne-Parikka, P., Peltonen, M., Aunola, S., Eriksson, J.G., Hemio, K., Hämäläinen, H., Härkönen, P., Keinänen-Kiukaanniemi, S., Laakso, M., Louheranta, A., Mannelin, M., Paturi, M., Sundvall, J., Valle, T.T., Uusitupa, M., Tuomilehto, J. & Finnish Diabetes Prevention Study Group "Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study". Lancet 2006;368(9548):1673-1679.
- Lindström, J., Louheranta, A., Mannelin, M., Rastas, M., Salminen, V., Eriksson, J., Uusitupa, M. & Tuomilehto, J. "The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity". Diabetes Care 2003;26(12):3230-3236.
- Lindström, J., Peltonen, M., Eriksson, J.G., Ilanne-Parikka, P., Aunola, S., Keinanen-Kiukaanniemi, S., Uusitupa, M., Tuomilehto, J. & Finnish Diabetes Prevention Study, (DPS) "Improved lifestyle and decreased diabetes risk over 13 years: long-term follow-up of the randomised Finnish Diabetes Prevention Study (DPS)". Diabetologia 2013;56(2):284-293.
- Lindström, J., Peltonen, M., Eriksson, J., Louheranta, A., Fogelholm, M., Uusitupa, M. & Tuomilehto, J. "High-fibre, low-fat diet predicts long-term weight loss and decreased type 2 diabetes risk: the Finnish Diabetes Prevention Study". Diabetologia 2006;49(5):912-920.

- Lorber, D. "Importance of cardiovascular disease risk management in patients with type 2 diabetes mellitus". Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy 2014;7:169-183.
- Mackenbach, J.P., Stirbu, I., Roskam, A.J., Schaap, M.M., Menvielle, G., Leinsalu, M., Kunst, A.E. & European Union Working Group on Socioeconomic Inequalities in Health "Socioeconomic inequalities in health in 22 European countries". N Engl J Med 2008;358(23):2468-2481.
- Magnee, T., Burdorf, A., Brug, J., Kremers, S.P., Oenema, A., van Assema, P., Ezendam, N.P., van Genugten, L., Hendriksen, I.J., Hopman-Rock, M., Jansen, W., de Jong, J., Kocken, P.L., Kroeze, W., Kwak, L., Lechner, L., de Nooijer, J., van Poppel, M.N., Robroek, S.J., Schreurs, H., van Sluijs, E.M., Steenhuis, I.J., van Stralen, M.M., Tak, N.I., te Velde, S.J., Vermeer, W.M., Wammes, B., van Wier, M.F. & van Lenthe, F.J. "Equity-specific effects of 26 Dutch obesity-related lifestyle interventions". Am J Prev Med 2013;44(6):57.
- Makrilakis, K., Liatis, S., Grammatikou, S., Perrea, D. & Katsilambros, N.
  "Implementation and effectiveness of the first community lifestyle intervention programme to prevent Type 2 diabetes in Greece. The DE-PLAN study". Diabet Med 2010;27(4):459-465.
- Manios, Y., Panagiotakos, D.B., Pitsavos, C., Polychronopoulos, E. & Stefanadis, C. "Implication of socio-economic status on the prevalence of overweight and obesity in Greek adults: the ATTICA study". Health Policy 2005;74(2):224-232.
- Marengoni, A., Rizzuto, D., Fratiglioni, L., Antikainen, R., Laatikainen, T., Lehtisalo, J., Peltonen, M., Soininen, H., Strandberg, T., Tuomilehto, J., Kivipelto, M. & Ngandu, T. "The Effect of a 2-Year Intervention Consisting of Diet, Physical Exercise, Cognitive Training, and Monitoring of Vascular Risk on Chronic Morbidity-the FINGER Randomized Controlled Trial". J Am Med Dir Assoc 2018;19(4):355-360:e1
- Marengoni, A., Angleman, S., Melis, R., Mangialasche, F., Karp, A., Garmen, A., Meinow, B. & Fratiglioni, L. "Aging with multimorbidity: A systematic review of the literature". Ageing Research Reviews 2011;10(4):430-439.
- Martinez, J.A., Kearney, J.M., Kafatos, A., Paquet, S. & Martinez-Gonzalez, M.A. "Variables independently associated with self-reported obesity in the European Union". Public Health Nutr 1999;2(1A):125-133.
- Maruthur, N.M. "The growing prevalence of type 2 diabetes: increased incidence or improved survival?". Curr Diab Rep 2013;13(6):786-794.
- Mayor, S. "Quarter of people with diabetes in England are undiagnosed". BMJ 2005;331(7518):656.
- Montonen, J., Knekt, P., Härkänen, T., Järvinen, R., Heliövaara, M., Aromaa, A. & Reunanen, A. "Dietary patterns and the incidence of type 2 diabetes". Am J Epidemiol 2005;161(3):219-27.
- Mooy, J.M., Grootenhuis, P.A., de Vries, H., Kostense, P.J., Popp-Snijders, C., Bouter, L.M. & Heine, R.J. "Intra-individual variation of glucose, specific insulin and proinsulin concentrations measured by two oral glucose tolerance tests in a general Caucasian population: the Hoorn Study". Diabetologia 1996;39(3):298-305.
- Motala, A.A., Pirie, F.J., Rauff, S. & Bacus, H.B. "Cost-effective management of diabetes mellitus". Ethn Dis 2006;16(2):79-84.

- Männistö, S., Laatikainen, T., Harald, K., Borodulin, K., Jousilahti, P., Kanerva, N., Peltonen, M. & Vartiainen, E. "Työikäisten ylipainon ja lihavuuden kasvu näyttää hidastuneen: kansallisen FINRISKI-terveystutkimuksen tuloksia". Suomen Lääkärilehti 2015;70:969-975.
- Nagel, G., Peter, R., Braig, S., Hermann, S., Rohrmann, S. & Linseisen, J. "The impact of education on risk factors and the occurrence of multimorbidity in the EPIC-Heidelberg cohort". BMC Public Health 2008;8:384.
- NCD Risk Factor Collaboration Group. Worldwide trends in diabetes since 1980: a pooled analysis of 751 population-based studies with 4.4 million participants. Lancet; 2016;387:1513–1530.
- Nwaneri, C., Cooper, H. & David Bowen-Jones "Mortality in type 2 diabetes mellitus: magnitude of the evidence from a systematic review and metaanalysis". Diabetes & Vascular Disease 2013;13(4):192-207.
- Ogurtsova, K., da Rocha Fernandes, J D, Huang, Y., Linnenkamp, U., Guariguata, L., Cho, N.H., Cavan, D., Shaw, J.E. & Makaroff, L.E. "IDF Diabetes Atlas: Global estimates for the prevalence of diabetes for 2015 and 2040". Diabetes Res Clin Pract 2017;128:40-50.
- Okosun, I.S., Davis-Smith, M. & Seale, J.P. "Awareness of diabetes risks is associated with healthy lifestyle behavior in diabetes free American adults: evidence from a nationally representative sample". Prim Care Diabetes 2012;6(2):87-94.
- Ovaskainen, M., Valsta, L. & Lauronen, J. "The compilation of food analysis values as a database for dietary studies – the Finnish experience". Food Chemistry 1996;57:133-136.
- Pajunen, P., Koukkunen, H., Ketonen, M., Jerkkola, T., Immonen-Räihä, P., Karja-Koskenkari, P., Mahonen, M., Niemela, M., Kuulasmaa, K., Palomäki, P., Mustonen, J., Lehtonen, A., Arstila, M., Vuorenmaa, T., Lehto, S., Miettinen, H., Torppa, J., Tuomilehto, J., Kesäniemi, Y.A., Pyörälä, K. & Salomaa, V.
  "The validity of the Finnish Hospital Discharge Register and Causes of Death Register data on coronary heart disease". Eur J Cardiovasc Prev Rehabil 2005;12(2):132-137.
- Pajunen, P., Laatikainen, T., Sundvall, J., Vartiainen, E. & Peltonen, M.
  "Diabetespotilaiden hoitotasapaino FINRISKI 2012 -väestötutkimuksessa". Suomen Lääkärilehti 2014;23:1705-1709.
- Palosuo, H. Health Inequalities in Finland: Trends in Socioeconomic Health Differences 1980-2005. Ministry of Social Affairs and Health, Helsinki, 2009.
- Palosuo, H. & Sihto, M. "Reducing health inequalities in Finland: progressing or regressing?". Nordisk välfärdsforskning 2016;1:55-64.
- Pan, X.R., Li, G.W., Hu, Y.H., Wang, J.X., Yang, W.Y., An, Z.X., Hu, Z.X., Lin, J., Xiao, J.Z., Cao, H.B., Liu, P.A., Jiang, X.G., Jiang, Y.Y., Wang, J.P., Zheng, H., Zhang, H., Bennett, P.H. & Howard, B.V. "Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study". Diabetes Care 1997;20:537-544.
- Patja, K., Jousilahti, P., Hu, G., Valle, T., Qiao, Q. & Tuomilehto, J. "Effects of smoking, obesity and physical activity on the risk of type 2 diabetes in middleaged Finnish men and women". J Intern Med 2005;258(4):356-362.
- Peltonen, M., Laatikainen, T., Lindström, J. & Jousilahti, P. "WHO:n tavoitteena on pysäyttää lihavuuden ja tyypin 2 diabeteksen lisääntyminen Suomessa

tarvitaan tekoja". Tutkimuksesta tiivisti 13, 2015. Terveyden ja hyvinvoinnin laitos, Helsinki.

- Penn, L., White, M., Lindström, J., den Boer, A.T., Blaak, E., Eriksson, J.G., Feskens, E., Ilanne-Parikka, P., Keinänen-Kiukaanniemi, S.M., Walker, M., Mathers, J.C., Uusitupa, M. & Tuomilehto, J. "Importance of weight loss maintenance and risk prediction in the prevention of type 2 diabetes: analysis of European Diabetes Prevention Study RCT". PLoS One 2013;8(2):e57143.
- Peters, S.A.E., Huxley, R.R., Sattar, N. & Woodward, M. "Sex Differences in the Excess Risk of Cardiovascular Diseases Associated with Type 2 Diabetes: Potential Explanations and Clinical Implications". Current Cardiovascular Risk Reports 2015;9(7):36.
- Pietinen, P., Vartiainen, E., Seppänen, R., Aro, A. & Puska, P. "Changes in Diet in Finland from 1972 to 1992: Impact on Coronary Heart Disease Risk". Preventive Medicine 1996;25(3):243-250.
- Preis, S.R., Pencina, M.J., Hwang, S.J., D'Agostino RB, S., Savage, P.J., Levy, D. & Fox, C.S. "Trends in cardiovascular disease risk factors in individuals with and without diabetes mellitus in the Framingham Heart Study". Circulation 2009;120(3):212-220.
- Puska, P., Nissinen, A., Tuomilehto, J., Salonen, J.T., Koskela, K., McAlister, A., Kottke, T.E., Maccoby, N. & Farquhar, J.W. "The community-based strategy to prevent coronary heart disease: conclusions from the ten years of the North Karelia project". Annu rev public health 1985;6(1):147-193.
- Puska, P., Salonen, J.T., Nissinen, A., Tuomilehto, J., Vartiainen, E., Korhonen, H., Tanskanen, A., Ronnqvist, P., Koskela, K. & Huttunen, J. "Change in risk factors for coronary heart disease during 10 years of a community intervention programme (North Karelia project)". Br Med J 1983;287(6408):1840-1844.
- Qiao, Q., Tuomilehto, J., Balkau, B., Borch-Johnsen, K., Heine, R., Wareham, N.J. & DECODE Study Group "Are insulin resistance, impaired fasting glucose and impaired glucose tolerance all equally strongly related to age?". Diabet Med 2005;22(11):1476-1481.
- Rapola, J.M., Virtamo, J., Korhonen, P., Haapakoski, J., Hartman, A.M., Edwards, B.K. & Heinonen, O.P. "Validity of diagnoses of major coronary events in national registers of hospital diagnoses and deaths in Finland". Eur J Epidemiol 1997;13(2):133-138.
- Rathmann, W., Haastert, B., Icks, A., Giani, G., Holle, R., Meisinger, C. & Mielck, A. "Sex differences in the associations of socioeconomic status with undiagnosed diabetes mellitus and impaired glucose tolerance in the elderly population: the KORA Survey 2000". Eur J Public Health 2005;15:627-33.
- Rautio, N., Varanka-Ruuska, T., Vaaramo, E., Palaniswamy, S., Nedelec, R., Miettunen, J., Karppinen, J., Auvinen, J., Järvelin, M.R., Keinänen-Kiukaanniemi, S., Sebert, S. & Ala-Mursula, L. "Accumulated exposure to unemployment is related to impaired glucose metabolism in middle-aged men: A follow-up of the Northern Finland Birth Cohort 1966". Prim Care Diabetes 2017;11(4):365-372.
- Rautio, N., Jokelainen, J., Oksa, H., Saaristo, T., Peltonen, M., Niskanen, L., Puolijoki, H., Vanhala, M., Uusitupa, M., Keinänen-Kiukaanniemi S & FIN-D2D, S.G. "Socioeconomic position and effectiveness of lifestyle intervention in prevention of type 2 diabetes: One-year follow-up of the FIN-D2D project". Scand J Public Health 2011;39(6):561-570.

- Reinikainen, J., Tolonen, H., Borodulin, K., Härkänen, T., Jousilahti, P., Karvanen, J., Koskinen, S., Kuulasmaa, K., Männistö, S., Rissanen, H. & Vartiainen, E.
  "Participation rates by educational levels have diverged during 25 years in Finnish health examination surveys". Eur J Public Health 2017:ckx151.
- Reisig, V., Reitmeir, P., Doring, A., Rathmann, W., Mielck, A. & KORA Study Group "Social inequalities and outcomes in type 2 diabetes in the German region of Augsburg. A cross-sectional survey". Int J Public Health 2007;52(3):158-165.
- Ritchie, N.D., Sauder, K.A., Phimphasone-Brady, P. & Amura, C.R. "Rethinking the National Diabetes Prevention Program for Low-Income Whites". Diabetes Care 2018;41(4):e56-e57.
- Robbins, J.M., Vaccarino, V., Zhang, H. & Kasl, S.V. "Socioeconomic status and diagnosed diabetes incidence". Diabetes Res Clin Pract 2005;68(3):230-236.
- Rosenberg, A., Ngandu, T., Rusanen, M., Antikainen, R., Backman, L., Havulinna, S., Hänninen, T., Laatikainen, T., Lehtisalo, J., Levälahti, E., Lindström, J., Paajanen, T., Peltonen, M., Soininen, H., Stigsdotter-Neely, A., Strandberg, T., Tuomilehto, J., Solomon, A. & Kivipelto, M. "Multidomain lifestyle intervention benefits a large elderly population at risk for cognitive decline and dementia regardless of baseline characteristics: The FINGER trial". Alzheimers Dement 2018;14(3):263-270
- Roskam, A.J. & Kunst, A.E. "The predictive value of different socio-economic indicators for overweight in nine European countries". Public Health Nutr 2008;11(12):1256-66.
- Ruel, G., Shi, Z., Zhen, S., Zuo, H., Kroger, E., Sirois, C., Levesque, J.F. & Taylor, A.W. "Association between nutrition and the evolution of multimorbidity: the importance of fruits and vegetables and whole grain products". Clin Nutr 2014;33(3):513-520.
- Saaristo, T.E., Barengo, N.C., Korpi-Hyövälti, E., Oksa, H., Puolijoki, H., Saltevo, J.T., Vanhala, M., Sundvall, J., Saarikoski, L., Peltonen, M. & Tuomilehto, J.
  "High prevalence of obesity, central obesity and abnormal glucose tolerance in the middle-aged Finnish population". BMC Public Health 2008;8:423-30.
- Saaristo, T., Moilanen, L., Korpi-Hyövälti, E., Vanhala, M., Saltevo, J., Niskanen, L., Jokelainen, J., Peltonen, M., Oksa, H., Tuomilehto, J., Uusitupa, M. & Keinänen-Kiukaanniemi, S. "Lifestyle intervention for prevention of type 2 diabetes in primary health care: one-year follow-up of the Finnish National Diabetes Prevention Program (FIN-D2D)". Diabetes Care 2010;33(10):2146-2151.
- Saaristo, T., Peltonen, M., Keinänen-Kiukaanniemi, S., Vanhala, M., Saltevo, J., Niskanen, L., Oksa, H., Korpi-Hyövälti, E., Tuomilehto, J. & FIN-D2D Study Group "National type 2 diabetes prevention programme in Finland: FIN-D2D". Int J Circumpolar Health 2007;66(2):101-112.
- Sacerdote, C., Ricceri, F., Rolandsson, O., Baldi, I., Chirlaque, M.D., Feskens, E., Bendinelli, B., Ardanaz, E., Arriola, L., Balkau, B., Bergmann, M., Beulens, J.W., Boeing, H., Clavel-Chapelon, F., Crowe, F., de Lauzon-Guillain, B., Forouhi, N., Franks, P.W., Gallo, V., Gonzalez, C., Halkjaer, J., Illner, A.K., Kaaks, R., Key, T., Khaw, K.T., Navarro, C., Nilsson, P.M., Dal Ton, S.O., Overvad, K., Pala, V., Palli, D., Panico, S., Polidoro, S., Quiros, J.R., Romieu, I., Sanchez, M.J., Slimani, N., Sluijs, I., Spijkerman, A., Teucher, B., Tjonneland, A., Tumino, R., van der, A.D., Vergnaud, A.C., Wennberg, P.,

Sharp, S., Langenberg, C., Riboli, E., Vineis, P. & Wareham, N. "Lower educational level is a predictor of incident type 2 diabetes in European countries: the EPIC-InterAct study". Int J Epidemiol 2012;41(4):1162-1173.

- Salopuro, T.M., Saaristo, T., Oksa, H., Puolijoki, H., Vanhala, M., Ebeling, T., Niskanen, L., Tuomilehto, J., Uusitupa, M. & Peltonen, M. "Population-level effects of the national diabetes prevention programme (FIN-D2D) on the body weight, the waist circumference, and the prevalence of obesity". BMC Public Health 2011;11:350.
- Sanusi, H. "The role of incretin on diabetes mellitus". Acta Med Indones 2009;41(4):205-212.
- Schuit, A.J., Wendel-Vos, G.C., Verschuren, W.M., Ronckers, E.T., Ament, A., Van Assema, P., Van Ree, J. & Ruland, E.C. "Effect of 5-year community intervention Hartslag Limburg on cardiovascular risk factors". Am J Prev Med 2006;30(3):237-242.

Schwartz, M.W. & Porte, D.,Jr "Diabetes, obesity, and the brain". Science 2005;307(5708):375-379.

- Schwarzer, R., Schuz, B., Ziegelmann, J.P., Lippke, S., Luszczynska, A. & Scholz, U. "Adoption and maintenance of four health behaviors: theory-guided longitudinal studies on dental flossing, seat belt use, dietary behavior, and physical activity". Ann Behav Med 2007;33(2):156-166.
- Seiluri, T., Lahelma, E., Rahkonen, O. & Lallukka, T. "Changes in socio-economic differences in food habits over time". Public Health Nutr 2011;14(11):1919-1926.
- Shaw, J.E., Sicree, R.A. & Zimmet, P.Z. "Global estimates of the prevalence of diabetes for 2010 and 2030". Diabetes Res Clin Pract 2010;87(1):4-14.
- Sieverdes, J.C., Sui, X., Lee, D.C., Church, T.S., McClain, A., Hand, G.A. & Blair, S.N. "Physical activity, cardiorespiratory fitness and the incidence of type 2 diabetes in a prospective study of men". Br J Sports Med 2010;44(4):238-244.
- Sikiö, M., Tykkyläinen, M., Tirkkonen, H., Kekäläinen, P., Dunbar, J. & Laatikainen, T. "Type 2 diabetes care in North Karelia Finland: do area-level socio-economic factors affect processes and outcomes?". Diabetes Res Clin Pract 2014;106(3):496-503.
- Statistics of Finland. Population projection 2015. Available: http://www.stat.fi/til/vaenn/2015/vaenn\_2015\_2015-10-30\_tau\_001\_en.html [2017, Nov 3].
- Strandberg, T.E. & Salomaa, V. "Factors related to the development of diabetes during a 20-year follow-up. A prospective study in a homogeneous group of middle-aged men". Nutr Metab Cardiovasc Dis 2000;10(5):239-246.
- Stratton, I.M., Adler, A.I., Neil, H.A., Matthews, D.R., Manley, S.E., Cull, C.A., Hadden, D., Turner, R.C. & Holman, R.R. "Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study". BMJ 2000;321(7258):405-412.
- Stringhini, S., Tabak, A.G., Akbaraly, T.N., Sabia, S., Shipley, M.J., Marmot, M.G., Brunner, E.J., Batty, G.D., Bovet, P. & Kivimäki, M. "Contribution of modifiable risk factors to social inequalities in type 2 diabetes: prospective Whitehall II cohort study". BMJ 2012;345:e5452.
- Sund, R. "Quality of the Finnish Hospital Discharge Register: a systematic review". Scand J Public Health 2012;40(6):505-515.

- 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.
- Sundquist, K., Chaikiat, A., Leon, V.R., Johansson, S.E. & Sundquist, J. "Country of birth, socioeconomic factors, and risk factor control in patients with type 2 diabetes: a Swedish study from 25 primary health-care centres". Diabetes Metab Res Rev 2011;27(3):244-254.
- Taylor, S.E. & Seeman, T.E. "Psychosocial resources and the SES-health relationship". Ann NY Acad Sci 1999;896:210-225.
- Toivakka, M., Laatikainen, T., Kumpula, T. & Tykkyläinen, M. "Do the classification of areas and distance matter to the assessment results of achieving the treatment targets among type 2 diabetes patients?". Int J Health Geogr 2015;14:27.
- Tolonen, H., Dobson, A., Kulathinal, S. & WHO MONICA Project "Effect on trend estimates of the difference between survey respondents and non-respondents: results from 27 populations in the WHO MONICA Project". Eur J Epidemiol 2005;20(11):887-898.
- Tolonen, H., Helakorpi, S., Talala, K., Helasoja, V., Martelin, T. & Prättälä, R. "25year trends and socio-demographic differences in response rates: Finnish adult health behaviour survey". Eur J Epidemiol 2006;21(6):409-415.
- Tolonen, H., Salomaa, V., Torppa, J., Sivenius, J., Immonen-Räihä, P., Lehtonen, A.
   & FINSTROKE register "The validation of the Finnish Hospital Discharge Register and Causes of Death Register data on stroke diagnoses". Eur J Cardiovasc Prev Rehabil 2007;14(3):380-385.
- Triplitt, C.L. "Understanding the kidneys' role in blood glucose regulation". Am J Manag Care 2012;18(1 Suppl):11.
- Tuomilehto, J., Korhonen, H.J., Kartovaara, L., Salomaa, V., Stengård, J.H., Pitkänen, M., Aro, A., Javela, K., Uusitupa, M. & Pitkäniemi, J. "Prevalence of diabetes mellitus and impaired glucose tolerance in the middle-aged population of three areas in Finland". Int J Epid 1991;20(4):1010-1017.
- Tuomilehto, J., Lindström, J., Eriksson, J.G., Valle, T.T., Hämäläinen, H., Ilanne-Parikka, P., Keinänen-Kiukaanniemi, S., Laakso, M., Louheranta, A., Rastas, M., Salminen, V. & Uusitupa, M. "Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance". N Engl J Med 2001;344(18):1343-1350.
- Type 2 diabetes. Current Care Guidelines. Working group set up by the Finnish Medical Society Duodecim, the Finnish Society of Internal Medicine and the Finnish Diabetes Association. Helsinki: The Finnish Medical Society Duodecim, 2018. Available: <u>www.kaypahoito.fi</u> [2018, April 10].
- Unwin, N., Shaw, J., Zimmet, P. & Alberti, K G M M "Impaired glucose tolerance and impaired fasting glycaemia: the current status on definition and intervention". Diabetic Medicine 2002;19(9):708-723.
- Uusitupa, M., Peltonen, M., Lindstrom, J., Aunola, S., Ilanne-Parikka, P., Keinänen-Kiukaanniemi, S., Valle, T.T., Eriksson, J.G., Tuomilehto, J. & Finnish Diabetes Prevention Study Group "Ten-year mortality and cardiovascular morbidity in the Finnish Diabetes Prevention Study--secondary analysis of the randomized trial". PLoS One 2009;4(5):e5656.
- Valdez, R., Yoon, P.W., Liu, T. & Khoury, M.J. "Family history and prevalence of diabetes in the U.S. population: the 6-year results from the National Health and

Nutrition Examination Survey (1999-2004)". Diabetes Care 2007;30(10):2517-2522.

- Vartiainen, E., Laatikainen, T., Peltonen, M., Juolevi, A., Männistö, S., Sundvall, J., Jousilahti, P., Salomaa, V., Valsta, L. & Puska, P. "Thirty-five-year trends in cardiovascular risk factors in Finland". Int J Epidemiol 2010;39(2):504-518.
- Vartiainen, E., Laatikainen, T., Strandberg, T., Salomaa, V., Jousilahti, P. & Jula, A. "FINRISKI-tutkimus 2007 ja 2012: Riskiryhmien kolesterolilääkitys vaatii tehostamista". Suomen Lääkärilehti 2013;41:2599a.
- Walker, J., Halbesma, N., Lone, N., McAllister, D., Weir, C.J. & Wild, S.H. "Socioeconomic status, comorbidity and mortality in patients with type 2 diabetes mellitus in Scotland 2004–2011: a cohort study". J Epidemiol Community Health 2015;70(6):596-601.
- Wang, Y., Rimm, E.B., Stampfer, M.J., Willett, W.C. & Hu, F.B. "Comparison of abdominal adiposity and overall obesity in predicting risk of type 2 diabetes among men". Am J Clin Nutr 2005;81(3):555-563.
- Ward, H., Tarasuk, V., Mendelson, R. & McKeown-Eyssen, G. "An exploration of socioeconomic variation in lifestyle factors and adiposity in the Ontario Food Survey through structural equation modeling". Int J Behav Nutr Phys Act 2007;4:8.
- Wei, J.N., Sung, F.C., Li, C.Y., Chang, C.H., Lin, R.S., Lin, C.C., Chiang, C.C. & Chuang, L.M. "Low birth weight and high birth weight infants are both at an increased risk to have type 2 diabetes among schoolchildren in Taiwan". Diabetes Care 2003;26(2):343-348.
- Whincup, P.H., Kaye, S.J., Owen, C.G., Huxley, R., Cook, D.G., Anazawa, S., Barrett-Connor, E., Bhargava, S.K., Birgisdottir, B.E., Carlsson, S., de Rooij, S.R., Dyck, R.F., Eriksson, J.G., Falkner, B., Fall, C., Forsen, T., Grill, V., Gudnason, V., Hulman, S., Hypponen, E., Jeffreys, M., Lawlor, D.A., Leon, D.A., Minami, J., Mishra, G., Osmond, C., Power, C., Rich-Edwards, J.W., Roseboom, T.J., Sachdev, H.S., Syddall, H., Thorsdottir, I., Vanhala, M., Wadsworth, M. & Yarbrough, D.E. "Birth weight and risk of type 2 diabetes: a systematic review". JAMA 2008;300(24):2886-2897.
- Wikström, K., Lindström, J., Tuomilehto, J., Saaristo, T.E., Korpi-Hyövälti, E., Oksa, H., Vanhala, M., Niskanen, L., Keinänen-Kiukaanniemi, S., Uusitupa, M. & Peltonen, M. "Socio-economic differences in dysglycemia and lifestylerelated risk factors in the Finnish middle-aged population". Eur J Public Health 2011;21(6):768-774.
- Wild, S., Roglic, G., Green, A., Sicree, R. & King, H. "Global prevalence of diabetes: estimates for the year 2000 and projections for 2030". Diabetes Care 2004;27(5):1047-1053.
- Willi, C., Bodenmann, P., Ghali, W.A., Faris, P.D. & Cornuz, J. "Active Smoking and the Risk of Type 2 Diabetes: A Systematic Review and Meta-analysis". JAMA 2007;298(22):2654-2664.
- Williams, E.D., Tapp, R.J., Magliano, D.J., Shaw, J.E., Zimmet, P.Z. & Oldenburg, B.F. "Health behaviours, socioeconomic status and diabetes incidence: the Australian Diabetes Obesity and Lifestyle Study (AusDiab)". Diabetologia 2010;53(12):2538-2545.
- Wing, R.R., Hamman, R.F., Bray, G.A., Delahanty, L., Edelstein, S.L., Hill, J.O., Horton, E.S., Hoskin, M.A., Kriska, A., Lachin, J., Mayer-Davis, E.J., Pi-Sunyer, X., Regensteiner, J.G., Venditti, B., Wylie-Rosett, J. & Diabetes

Prevention Program Research Group "Achieving weight and activity goals among diabetes prevention program lifestyle participants". Obes Res 2004;12(9):1426-1434.

- Winkleby, M.A., Jatulis, D.E., Frank, E. & Fortmann, S.P. "Socioeconomic status and health: how education, income, and occupation contribute to risk factors for cardiovascular disease". Am J Public Health 1992;82(6):816-820.
- World Health Organization "Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus". World Health Organization, Department of Non-communicable Disease Surveillance, Geneva, 1999.
- World Health Organization "Diabetes Mellitus: Report of a WHO Study Group". World Health Organization, Geneva, 1985.
- World Health Organization Use of glycated haemoglobin (HbA1c) in diagnosis of diabetes mellitus: abbreviated report of a WHO consultation. World Health Organization, Geneva, 2011.
- World Health Organization & International Diabetes Federation Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia: report of a WHO/IDF consultation. World Health Organization, Geneva, 2006.
- World health statistics quarterly. "Geographical variation in the major risk factors of coronary heart disease in men and women aged 35-64 years. The WHO MONICA Project". World Health Stat Q 1988;41(3-4):115-140.
- Yang, W., Lu, J., Weng, J., Jia, W., Ji, L., Xiao, J., Shan, Z., Liu, J., Tian, H., Ji, Q., Zhu, D., Ge, J., Lin, L., Chen, L., Guo, X., Zhao, Z., Li, Q., Zhou, Z., Shan, G., He, J. & China National Diabetes and Metabolic Disorders Study Group "Prevalence of diabetes among men and women in China". N Engl J Med 2010;362(12):1090-1101.
- Ylihärsilä, H., Lindström, J., Eriksson, J.G., Jousilahti, P., Valle, T.T., Sundvall, J. & Tuomilehto, J. "Prevalence of diabetes and impaired glucose regulation in 45- to 64-year-old individuals in three areas of Finland". Diabet Med 2005;22(1):88-91.
- Zheng, Y., Ley, S.H. & Hu, F.B. "Global aetiology and epidemiology of type 2 diabetes mellitus and its complications". Nat Rev Endocrinol 2018;14(2):88-98.