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Progression and management of Prediabetes by socioeconomic status and health care consumption. The Tromsø Study 2007-2016.

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TABLE OF CONTENTS

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SUMMARY

Background: Socioeconomic status and healthcare consumption are considered predictors of diabetes development and quality of blood glucose management. However, studies on the association between socioeconomic status and healthcare consumption in people with prediabetes and these outcomes are scarce.

Objective: To examine the relationship between the development of diabetes in people with prediabetes and socioeconomic status as well as healthcare consumption. Furthermore, blood glucose management in people with prediabetes is also examined as diabetic complications usually occur before the diagnosis of diabetes and can be prevented by screening and early management.

Methods: I used a cohort study using data from two waves of the population-based Tromsø Study utilizing socioeconomic variables, anthropometric variables, healthcare consumption, exercise, and smoking information collected from the questionnaire, and HbA1c data collected from laboratory data along with demographic and information on personal and family history of diabetes. These variables are analyzed using binary logistic regression analysis, linear regression analysis, and mediation analysis.

Main results: From the 2690 participants with prediabetes included in wave 6 of the Tromsø Study, 304 representing 11.3% of participants had developed diabetes at follow up 7-8 years later (wave 7 of the Tromsø Study). Those with an upper secondary level of education had 54% higher odds of a diagnosis of diabetes relative to those with four or more years of college/university level of education. While there was a 0.06-unit change in HbA1c levels in participants with the lowest levels of education compared to those with the highest. Furthermore, those with 5 or more GP visits over the 12 months prior to Tromsø 6 had 74% higher odds of getting diagnosed with diabetes than those with 1 visit.

Conclusions: While the association of healthcare consumption on the progression of the disease in the study participants is not established, there is a socioeconomic association with the development of diabetes and glycemic management.

ABBREVIATIONS

ADA - American Diabetes Association

BMI - Body Mass Index

CI - Confidence Interval

DCCT - Diabetes Control and Complications Trial

FBG - Fasting Blood Glucose

GP- General Practitioner

HbA1c – Hemoglobin A1c

NGSP - National Glycohemoglobin Standardization Program

OGTT - Oral Glucose Tolerance Test

OR - Odds Ratio

REK – Research Ethics Committee

SES - Socioeconomic Status

BACKGROUND

Diabetes Mellitus is a chronic metabolic disease that affects millions of people around the world relating to either insulin deficiency or resistance (1). Based on this it is classified into Types 1 and 2, specific types of diabetes due to other causes, and Gestational Diabetes (diabetes associated with pregnancy). Type 1 diabetes is the result of an absolute insulin deficiency secondary to the autoimmune destruction of β-cells and is treated with insulin injections (2). Type 2 diabetes which is the most common type is the result of a combination of impaired insulin secretion and insulin resistance (lack of insulin function) (1). Some of the risk factors for Type 2 Diabetes are obesity, physical inactivity, older age, family history of diabetes, history of gestational diabetes, and genetic predisposition associated with some ethnic groups such as South Asians, Afro-Caribbeans, and Hispanics (3).

Diabetes is one of the most common chronic diseases in Norway with a prevalence of four to seven percent that continues to increase (4–6). In addition, studies from around the world suggest that many people are living with undiagnosed diabetes and prediabetes (7). Diabetes causes several health complications with cardiovascular diseases being the most serious (8). Cardiovascular risk increases with raised glucose values. Furthermore, it is also known to cause organ damage following microvasculature obstruction associated with atherosclerosis (9). This includes diabetic retinopathy, nephropathy, peripheral artery disease, and peripheral neuropathy (9,10). Diabetes is also associated with liver, pancreatic and endometrial cancers, among a variety of other cancers (11,12). Lack of early detection and care for diabetes results in severe complications, including heart attacks, strokes, renal failure, amputations, and blindness (8,13).

Prediabetes reflects the natural history of progression from normoglycemia to diabetes defined by the presence of Impaired glucose tolerance or Impaired fasting glucose (14). It presents with elevated blood glucose above the normal range but below the diabetic diagnostic threshold. It is common for people to shift between different glycemic states thus requiring follow-up. Studies from around the world including Northern Norway have found prediabetes to be prevalent in around a third of their adult participants (15,16).

The diagnosis of diabetes is based on plasma glucose especially the Oral Glucose Tolerance Test (OGTT) and Fasting Blood Glucose (FBG) as well as by Glycated hemoglobin analysis (HbA1c). The gold standard for diagnosis of diabetes is OGTT which requires overnight fasting and 2 hours with the ingestion of a certain amount of glucose to look at fasting and/or 2-hour blood glucose levels. An alternative that is now a recommended part of the standard of care for testing and monitoring for prediabetes and diabetes is HbA1c (17). It demonstrates an individual's average blood glucose levels over the previous 3 months. It does not require fasting or the ingestion of glucose. By the time of diagnosis of Diabetes patients may have established vascular diseases. The rate of undiagnosed diabetes is geographically and socioeconomically variable with some low- and middle-income countries having rates higher than 50% while in Europe the International Federation of Diabetes reports rates of around a third (18).

Health inequalities in Norway are observed in relation to diabetes in a variety of ways. One of the ways this was observed was with age at first diagnosis being earlier for people born in a different country especially women affecting the management of the diseases (19). The education gradient is also connected to the pharmaceutical management of some of the complications of diabetes (20). Another element is how geography has been seen to play a role in the prevalence of diabetes linked with living in a neighborhood characterized by a relative concentration of fast food and an absence of healthy food shops and physical exercise facilities (21).

Studies looking at the relationship between socioeconomic background and the incidence of diabetes in Norway have shown that low levels of education, income, and occupation as well as foreign country of origin and disadvantaged neighborhood of residence are associated with a higher incidence (21–24). However other studies have found an increase in General Practitioner's (GP) service provision to diabetic patients from a low socioeconomic background (25). Studies looking into the incidence among Sami and Non-Sami populations did not find a significant difference (26–28).

In this thesis, we will be looking into how the progression of diabetes from prediabetes and its management is influenced by socioeconomic status and healthcare consumption.

INTRODUCTION

Diagnosis of Diabetes

A diagnosis of diabetes is established by the presence of one of the following factors: biochemical tests (FBG, OGTT, or HbA1c) within the diabetic range or in patients with classic symptoms of hyperglycemia (polyuria, polydipsia, polyphagia) with a random plasma glucose above or equal to 200mg/dl (29). A reported history of diabetes in a participant detected in regular health follow-ups or by other means is a relevant outcome to be taken into consideration.

HbA1c

The HbA1c has increasingly been recommended to test the longer levels (3 months) of blood glucose control as it has several advantages to the FBG and OGTT, including greater convenience (fasting not required), greater preanalytical stability, and less day-to-day variations due to stress and illness (29).

The test should be performed using a method that is certified by the National Glycohemoglobin Standardization Program (NGSP) and standardized or traceable to the Diabetes Control and Complications Trial (DCCT) reference assay. However, the test may be affected by age (most research is based on adults), race/ethnicity, and anemia/hemoglobinopathies (e.g., Pregnant women and those who have received blood transfusion) of the test takers. The goal glycemic target in non-pregnant adults is less than 7% (30,31). Some studies show that socioeconomic status influences glycemic control noted by HbA1c levels (32).

Use of blood sugar lowering and Insulin containing drugs

The treatment of Diabetes includes lifestyle modifications and pharmacologic interventions. These pharmacologic interventions are used to manage the blood sugar levels in an individual. These drugs may or may not contain insulin within them (33). The use of these medications as part of the standard of care for diabetes is aimed at preventing complications (especially the heart and the kidney) related to the disease (34).

Healthcare consumption

Norway has a well-developed universal health care system which nevertheless requires a small patient co-payment. Almost all citizens are registered with a GP who acts as a gatekeeper to specialized care (35). Most patients with diabetes especially with type 2 diabetes are followed up in the primary health care system by GPs. However, patients with type 1 and some type 2 diabetes are followed up by specialists in areas such as internal medicine or endocrinology (36).

Primary prevention of chronic noncommunicable diseases such as type 2 diabetes is based on the adjustment of the natural history of the disease by modifying known risk factors such as diet and weight. The diagnosis of prediabetes is a gateway for possible lifestyle changes such as dietary and physical activity interventions to decrease the risk of development of diabetes (37). In addition, a more thorough follow-up of patients with prediabetes can lead to a reduction of undiagnosed diabetes as well as the organ damage that occurs before the diagnosis of diabetes (38). However, the impact healthcare consumption has on the diagnosis of diabetes and the level of glycemic control in people who have prediabetes is unclear (38–41).

Socioeconomic status

Health inequality is one of the major concerns of the Norwegian government (42). Despite Norway being one of the most equitable and developed nations on the planet with a population generally enjoying good health systematic inequities linger (43). Life expectancy, quality of life, health care system interactions, and utilization are unevenly distributed among social groups in the population according to income, educational status, geography, and country of birth (21,44,45). The prioritization of health equality becomes even more pertinent with the aging population as these inequities have been seen to worsen with it (46,47).

Covariates

Age

Diabetes is highly prevalent in the aging population with over one-quarter of people over the age of 65 years having diabetes, and half of older adults having prediabetes. Improvements in insulin delivery, technology, and care have led to an increasing prevalence of diabetes in older age (48).

However, the incidence of diabetes increases with age until about age 65 years after which it seems to plateau (49).

Sex

Studies show that men have a higher prevalence of diabetes than women. Furthermore, the age of onset of a new diagnosis is also somewhat earlier among men with rising prevalence as they age peaking at 55–59 years. On the other hand, women are at risk of pregnancy-related diabetes which also influences future incidence of diabetes (50,51).

Body Mass Index

Body Mass Index (BMI) is calculated from height and weight with weight in kilograms divided by the square of height in meters (37). This helps in documenting the weight status of an individual with those with a BMI between 25 and 29.9 being considered overweight and those higher than 30 being considered different classes of obesity. Obesity is chronic and often progressive with multiple complications including an increased risk of diabetes. The management of obesity has been shown to lead to a delay in the progression from prediabetes to type 2 diabetes (37).

Family history of Diabetes

Family history of diabetes which includes a history of diabetes from maternal, paternal, or siblings has been shown to lead to an earlier and higher incidence of diabetes in an individual. This is linked to genetic factors that also predispose to central obesity as well as a higher risk of insulin resistance among other factors (52–55).

Smoking History

Tobacco use in general and smoking, in particular, has been associated with a higher risk among adults with chronic conditions as well as in adolescents and young adults with diabetes. Studies have shown that smoking may have a role in the development of type 2 diabetes (56). However, the years immediately following the cessation of smoking may represent a time of increased risk for diabetes. As such this is a time when individuals should be monitored for diabetes development and receive lifestyle and behavior change interventions for diabetes prevention (34).

Physical Activity

The term physical activity comprises all movement that utilizes energy and is an important part of diabetes prevention and management. While exercise is a structured and designed physical activity to improve physical fitness. These are related to an individual's BMI, blood glucose levels, and cardiovascular health (56). Studies have demonstrated a significant reduction or delay in the incidence of Type 2 diabetes in adults among those on intensive lifestyle interventions. The American Diabetes Association (ADA) recommends 150 minutes per week of moderate-intensity physical activity, such as brisk walking in participants with diabetes along with a low-calorie diet (34).

Pregnancy

Pregnancy is associated with several health conditions including hypertension and diabetes(57). During pregnancy, a woman could develop a type of diabetes called Gestational Diabetes (57). This is usually diagnosed with the same diagnostic measurements used for other types of diabetes (57). The management of gestational diabetes might require the use of glucose-lowering or insulin-containing drugs (57). However, this type of diabetes resolves after the termination of pregnancy. Nevertheless, it is often associated with the development of Gestational Diabetes in a future pregnancy, conversion to type 2 diabetes as well as its effects on the fetus (57).

PURPOSE OF THE THESIS

To my knowledge, no studies have examined the relationship between the diagnosis of diabetes and blood glucose management in people with prediabetes and socioeconomic status as well as healthcare consumption. In this thesis, we examine the eventual progression from prediabetes to diabetes and the role of socioeconomic status and healthcare consumption. The relationship between the management of blood glucose level (glycemic control) and socioeconomic status and healthcare consumption is another aspect that we will explore in this study.

This thesis aims to enhance the understanding of how socioeconomic status and healthcare consumption influence the eventual development and management of diabetes among Norwegians with prediabetes. This is a timely and important topic as Norway faces a growing prevalence of diabetes and with possible undiagnosed cases screening and prevention programs for those at a higher risk are important. Furthermore, the management of blood glucose plays an important part in the prevention of diabetic complications that occur even before the diagnosis of diabetes.

RESEARCH QUESTIONS

1. What is the relationship between socioeconomic status and the development of diabetes in participants with prediabetes?
2. What is the relationship between socioeconomic status and change in HbA1c in participants with prediabetes?
3. What is the relationship between healthcare consumption and the development of diabetes as well as the change in HbA1c in participants with prediabetes?

The socioeconomic variable that is being considered is the level of education. Healthcare consumption is measured as the number of GP consultations in the 12 months before the surveys.

METHODS AND MATERIALS

This is a cohort study using data from two waves of the population-based Tromsø Study conducted every 7-8 years. I used socioeconomic variables, anthropometric variables, healthcare consumption, exercise, and smoking information collected from the questionnaire, and HbA1c data collected from laboratory data along with demographic and information on personal and family history of diabetes.

To define the HbA1c range of normoglycemic, prediabetic, and diabetic participants I am using the WHO guidelines (58) with those being termed as prediabetic having an HbA1c level between 5.7% and 6.4% while those who are termed as diabetic having an HbA1c level of 6.5% and higher.

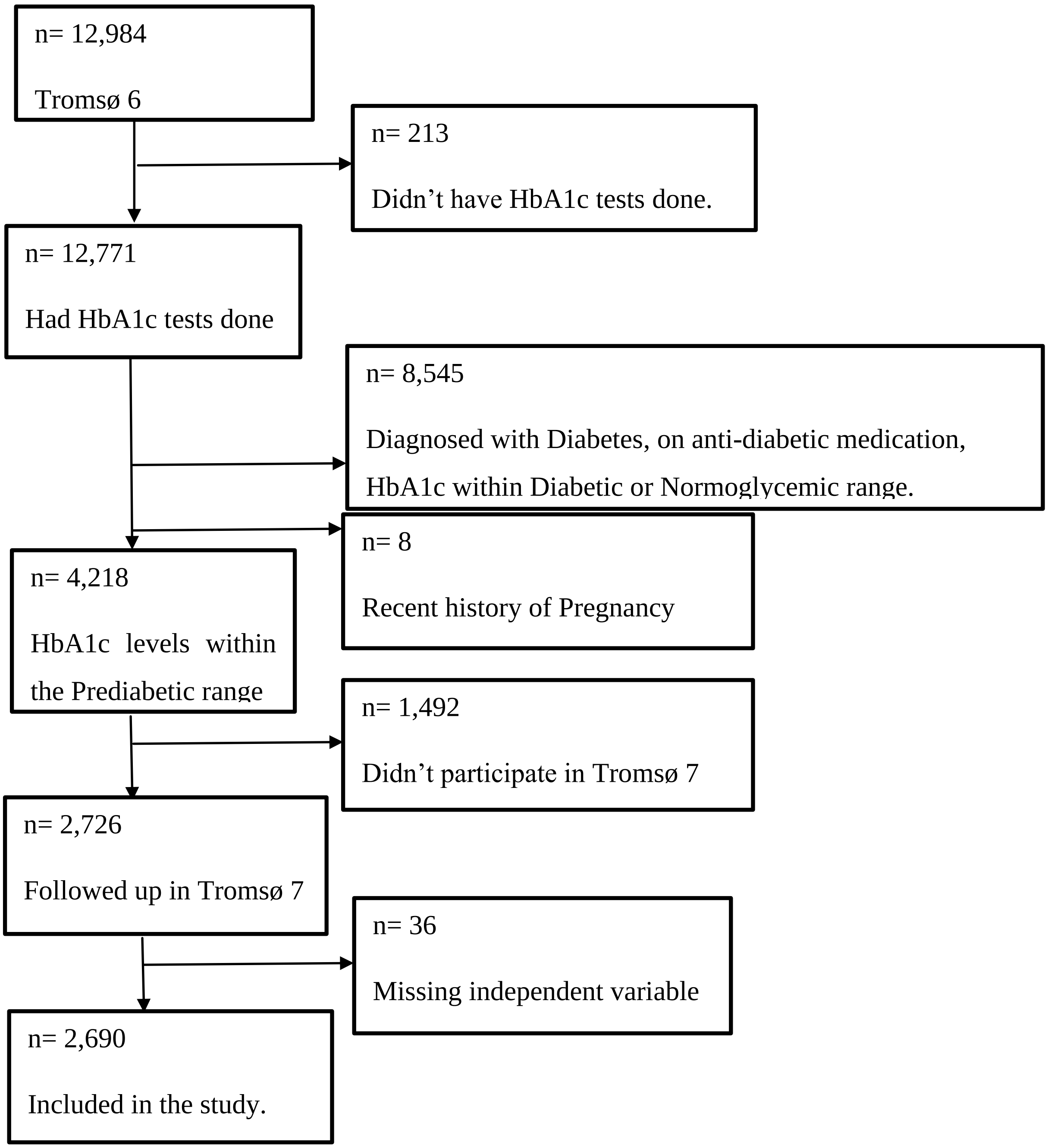
Study Population

The Tromsø Study is a large population-based longitudinal study among inhabitants of the Tromsø municipality, Northern Norway, with a population of around 75,000 (59). The study was initiated in 1974, and seven data collections (Tromsø1–7) have been performed to date involving 45,473 residents attending one or more surveys. The study has collected comprehensive data on health and socio-demographic factors using various techniques such as questionnaires, biological samples, and clinical surveys. The main reason for the initiation of the Tromsø Study in 1974 had been to further the understanding of the causes of the high cardiovascular deaths in Norway and especially in Northern Norway but was later on expanded to study other chronic diseases as well (60).

Study Sample

I used data from people who participated in Tromsø 6 (2007–2008) and Tromsø 7 (2015–2016), who answered the questions on the required variables. I looked at those who were prediabetic in Tromsø 6 with follow-up of HbA1c and diabetes status in Tromsø 7 (Figure 1).

Figure 1. Flow Chart of participants. The Tromsø Study 2007-2016.



Study Design

The variable selections were based on the current literature, looking at the relationship between the outcome, exposure, and covariates. The outcome of a diagnosis of diabetes is based on the combination of self-reported diabetes, the use of antidiabetic medication, and/or HbA1c levels in the diabetic range. Body mass index (BMI) is to be categorized based on WHO guidelines with those below 18.5 being underweight, between 18.5 and 24.9 normal weight, between 25 and 29.9 pre-obesity and those above 30 being obese (39).

Outcome

HBA1C: This continuous variable was based on a blood sample that was collected in the two consecutive Tromsø surveys (Tromsø 6 and 7) and was analyzed within 24 hours at UNN (laboratory ISO certification NS-EN ISO 15189:2012). This variable on top of being used as an outcome measurement also served as an exclusion criterion for the sample from Tromsø 6. For that purpose, those outside the prediabetes range are excluded.

Reported Diabetes diagnosis: This binary variable was based on the answer to the questionnaire question “Do you have, or have you had diabetes?” with responses coded as 0 for No and 1 for Yes. This variable beyond being used as an outcome measurement also served as an exclusion criterion for the sample from Tromsø 6.

Blood glucose lowering drugs: This binary variable was based on the answer to the questionnaire question “Drugs containing blood glucose lowering drugs exl insulin ATC=A10B and/or DIABETES_TABLETS_T6=1” with responses coded as 0 for No and 1 for Yes. This variable beyond being used as an outcome measurement also served as an exclusion criterion for the sample from Tromsø 6.

Insulin-containing drugs: This binary variable was based on the answer to the questionnaire question “Drugs containing insulin ATC=A10A and/or INSULIN_T6=1” with responses coded as 0 for No and 1 for Yes. This variable beyond being used as an outcome measurement also served as an exclusion criterion for the sample from Tromsø 6.

A new variable was computed for those who developed diabetes by Tromsø 7 by using a positive result in any of the variables for HbA1c above 6.5%, history of diabetes, and those on insulin-containing drugs or glucose-lowering drugs coding as 1 while a negative in all coding as 0.

Exposure

Education level: This categorical variable was based on answers to the question "What is the highest levels of education you have completed?" with responses coded as 1 for "Primary/secondary school, modern secondary school", 2 for "Technical school, vocational school, 1-2 years senior high school", 3 for "High school diploma", 4 for "College/university less than 4 years" and 5 for "College/university 4 years or more".

Health care consumption: This continuous variable was based on answers to the question "If you have visited a general practitioner (GP) the last 12 months, how many visits have you made?".

Confounders/Mediators

Age: This categorical variable was categorized from the age of participants collected during Tromsø 6. It has been categorized into groups with 10 years and has been coded as 30 for those between the ages of 30 and 39, 40 for those between the ages of 40 and 49, 50 for those between the ages of 50 and 59, 60 for those between the ages of 60 and 69, 70 for those between the ages of 70 and 79 and 80 for those 80 years old and above.

Sex: This binary variable is coded as 0 for females and 1 for males.

Family history of Diabetes: This binary variable is compiled from the answers to the questionnaire questions "Mother or father has or has had diabetes", "Child has or had diabetes" and "Sibling(s) has or had diabetes" from Tromsø 6 with responses coded as 0 for No and 1 for Yes.

Body mass index: This categorical variable from Tromsø 6 was calculated from weight and height measurements which were measured with light clothing and no shoes with a Jenix DS-102 scale (DongSahn Jenix, Seoul, Korea). These were categorized into groups and coded as 1 for those with an index less than 25, 2 for those with 25, and higher but less than 30, and 3 for those with 30 or higher.

Level of Physical Activity: This categorical variable from Tromsø 6 was based on answers to the question "Describe your exercise and physical exertion in leisure time over the last year. If your activity varies throughout the year, give an average." with response categorized into Sedentary for those reporting "Reading, watching TV, or other sedentary activity?", Mild for those reporting "Walking, cycling, or other forms of exercise at least 4 hours a week? (including walking or cycling to places of work, Sunday-walking, etc.)", Moderate for those reporting "Participation in recreational sports, heavy gardening, etc.? (note: duration of activity at least 4 hours a week.)" and Heavy for those reporting "Participation in hard training or sports competitions, regularly several times a week?". These categories were coded as 1 for Sedentary, 2 for Mild, 3 for Moderate, and 4 for Heavy.

Smoking history: This categorical variable from Tromsø 6 was based on answers to the question "Do you/did you smoke daily?" with responses coded as 1 for "Yes, now", 2 for "Yes, previously" and 3 for "Never".

Exclusion

Recent history of Pregnancy: This categorical variable from Tromsø 6 and 7 was based on answers to the question "Are you pregnant at the moment?" with responses coded as 1 for "Yes", 2 for "No" and 3 for "Uncertain".

Inclusion and Exclusion Criteria

As shown in Figure 1 participants included have HbA1c levels within a prediabetic range in Tromsø 6 in 2007/08 (between 5.7% and 6.4%) and followed up in Tromsø 7 in 2015/16. While excluding those with missing data on socioeconomic status variables, GP visits, and HbA1c in Tromsø 6. Furthermore, prevalent cases defined as those with diabetes at the baseline based on self-reported diabetes, use of antidiabetic medications, and an HbA1c level above 6.5% (≥48 mmol/mol) are excluded. In addition, those who were pregnant during Tromsø 6 and 7 are excluded.

Ethical Considerations

Ethical considerations taken for this study include the anonymization of study participants by categorization and the limitation of identifying variables beyond what is necessary. The data requested was anonymous and could not be traced back to individuals. REK approval was not necessary. The data was stored in a password-protected computer. The data will be deleted after the completion of this research study.

STATISTICAL ANALYSIS

All analyses were conducted using R and Statistical Package for the Social Sciences (SPSS) version 29. For this thesis results with p-values less than 0.05 are taken as statistically significant.

The data was checked for any errors and cleaned. For the analysis, the age groups were combined from 10-year ranges to 20-year ranges to avoid underpowering. Similarly, the group with high school diplomas was merged with those with some high school education, vocational education, and technical school education. The group with heavy levels of physical activity was merged with those with moderate physical activity.

The number of GP consultations over the 12 months prior to Tromsø 6 was categorized into its quartile. A new variable was computed from the change in HbA1c from Tromsø 6 to 7 by subtracting the HbA1c result collected during Tromsø 7 from the result collected during Tromsø 6.

Logistic regression models were employed to evaluate the association between the computed diabetes variable as the dependent variable and education as well as the number of GP consultations as the independent. This was done after making sure that assumptions of non-multicollinearity and linearity were fulfilled, in addition to checking for outliers.

Linear regression models were used when the change in HbA1c levels from Tromsø 6 to Tromsø 7 was included as a continuous outcome.

Furthermore, the relationship between the diagnosis of diabetes, as well as the change in HbA1c levels from Tromsø 6 to Tromsø 7 and healthcare consumption, was assessed in models with the diagnosis of diabetes as a dependent variable and the number of GP visits during Tromsø 6 as an independent variable was assessed using logistic and linear regressions, respectively.

In all regression models, age, sex, and history of diabetes were added as possible confounding factors.

An interaction test was done to assess the interaction between education and sex by including both main effects and cross-product terms between sex and indicator variables for each category of education in separate regression models.

For this thesis based on literature, we have taken BMI, level of physical activity, and smoking history as possible mediators since they are influenced by education and are known to affect the diagnosis and management of diabetes. Therefore, mediation analysis was done using the MEDFLEX package on R.

Models

The result section presents seven different models:

Model 1: The diagnosis of Diabetes was used as the dependent variable in a binary logistic regression analysis with the level of education adjusted for age, sex, and family history of diabetes taken as the independent variable. *(Table 3)*

Model 2: Subgroup analysis for model 1 was conducted for sex. *(Table 3)*

Model 3: The total, direct, and indirect effects of the association between the diagnosis of diabetes and education were examined using mediation analyses, with BMI, level of physical activity, and smoking history as possible mediators adjusted for age, sex, and family history of diabetes. *(Tables 4 and 5)*

Model 4: The change in HbA1c levels between Tromsø 6 and 7 was used as the dependent variable in a multiple linear regression analysis with the level of education adjusted for age, sex, and family history of diabetes as the independent variable. *(Table 6)*

Model 5: Subgroup analysis for model 4 was conducted for sex. *(Table 6)*

Model 6: The total, direct, and indirect effects of the association between the change in HbA1c levels and education were examined using mediation analyses, with BMI, level of physical activity, and smoking history as possible mediators adjusted for age, sex, and family history of diabetes. *(Tables 7 and 8)*

Model 6: The diagnosis of Diabetes was used as the dependent variable in a binary logistic regression analysis with the number of GP consultations over 12 months prior to Tromsø 6 taken as the independent variable. *(Table 9)*

Model 7: The change in HbA1c levels between Tromsø 6 and 7 was used as the dependent variable in a multiple linear regression analysis with the number of GP consultations over 12 months prior to Tromsø 6 as the independent variable. *(Table 10)*

RESULTS

Description of the Participants

The thesis included 2690 participants who fulfilled the inclusion and exclusion criteria mentioned above and as such were prediabetic in Tromsø 6 and followed up in Tromsø 7. The participants were divided into two groups based on the compiled diabetes variable using a positive result for HbA1c above 6.5, history of diabetes, and those on insulin-containing drugs or glucose-lowering drugs in Tromsø 7. Those who developed diabetes numbered 304 representing 11.3% of participants and those who did not develop diabetes numbered 2386 representing 88.7%.

As seen in Table 1 the two groups are compared on various variables such as sex, age, education, GP visits, family history of diabetes, body mass index, physical activity, and smoking history. The two groups had similar proportions of males (50.1%) and females (49.9%) with similar age distributions.

Overall, 31.7% of the participants had a college/university degree. Furthermore, the diabetic group had lower levels of education than the non-diabetic group, with fewer participants having a college/university degree (27.6% vs 32.3%). The diabetic group had more GP visits over the 12 months prior to Tromsø 6 on average (3.88 vs 3.18) than the non-diabetic group with a further increase in the average number of GP visits prior to Tromsø 7 (0.62 vs 0.45).

Table 1 also shows that 22.5% of the participants had a family history of diabetes with the diabetic group having a higher percentage of participants with a family history of diabetes than the non-diabetic group (30.9% vs 21.4%). In addition, the diabetic group had a higher percentage of obese participants than the non-diabetic group (44.6% vs 22.1%), and a lower percentage of participants with a body mass index less than 25 (8.3% vs 30.1%). Nevertheless, overall the most common BMI was within the overweight range (25 - 29.9) (47.8%) with relatively equal distribution among both groups.

Table 1 additionally shows that the diabetic group had a higher percentage of participants who were sedentary compared to those who were moderately or heavily physically active than the non-diabetic group (28.1% vs 14% and 17.3% vs 18.1%, respectively). However, the two groups had similar smoking histories, with similar percentages of current smokers, former smokers, and never-smokers.

Table 1. Descriptive characteristics by Diagnosis of Diabetes[1], The Tromsø Study 2007 - 2016

		Glycemic State		
		Total	**Non-Diabetic**	**Diabetic**
N		2690 (100)	2386 (88.7)	304 (11.3)
Sex				
	Female	1343 (49.9)	1201 (50.3)	142 (46.7)
	Male	1347 (50.1)	1185 (49.7)	162 (53.3)
Age				
	30-49	443 (16.5)	396 (16.6)	47 (15.5)
	50-69	1795 (66.7)	1591 (66.7)	204 (67.1)
	70+	452 (16.8)	399 (16.7)	53 (17.4)
Level of Education				
	Primary	873 (32.5)	771 (32.3)	102 (33.6)
	Upper Secondary	962 (35.8)	844 (35.4)	118 (38.8)
	University College < 4 years	429 (15.9)	380 (15.9)	49 (16.1)
	University College ≥ 4 years	426 (15.8)	391 (16.4)	35 (11.5)
Number of GP visits[2]				
	Mean	3.42	3.18	3.88
	Median	2	2	3
	Standard Deviation	3.39	2.92	3.71
	Range	55	44	29
	Quartiles (25, 50, 75)	1, 2, 4	1,2,4	2,3,5

Table 1. Descriptive characteristics by Diagnosis of Diabetes[1], The Tromsø Study 2007 – 2016 (cont.)

	Glycemic State		
	Total	**Non-Diabetic**	**Diabetic**
Change in number of GP visits[3]			
Mean	0.47	0.45	0.62
Median	0	0	0
Standard Deviation	4.03	3.99	4.41
Range	71	71	28
Quartiles (25, 50, 75)	-1, 0, 2	-1, 0, 2	-1, 0, 2
Family History of Diabetes			
Yes	605 (22.5)	511 (21.4)	94 (30.9)
No	2085 (77.5)	1875 (78.6)	210 (69.1)
Body Mass Index			
<25, n (%)	743 (27.6)	718 (30.1)	25 (8.3)
25 – 29.9, n (%)	1284 (47.8)	1141 (47.8)	143 (47.2)
> 30, n (%)	661 (24.6)	526 (22.1)	135 (44.6)
Physical Activity			
Sedentary	452 (18.5)	376 (17.3)	76 (28.1)
Mild	1563 (63.9)	1406 (64.6)	157 (57.9)
Moderate and Heavy	431 (17.6)	393 (18.1)	38 (14)
Smoking History			
Smoking daily	605 (22.8)	537 (22.8)	68 (22.7)
Previously smoked daily	1205 (45.4)	1070 (45.4)	135 (45.0)
Never smoked	847 (31.9)	750 (31.8)	97 (32.3)

[1]Values are number (percent)

[2]Number of GP visits in the 12 months prior to Tromsø 6

[3]Change in number of GP visits in the 12 months prior to Tromsø 6 and Tromsø 7

Table 2 shows the change in HbA1c levels between two surveys (Tromsø 6 and 7) among the participants by various categories such as sex, age, education, body mass index, physical activity, and smoking history. On average participants had a slight increase (0.095) in their HbA1c levels between Tromsø 6 and 7. With a minimum decrease of 0.9 and a maximum increase of 6.6. There is a very slight difference for men and women with the mean change in HbA1c levels for females being 0.087 and for males being 0.104.

The mean change in HbA1c levels for the age groups 30-49, 50-69, and 70+ were 0.108, 0.090, and 0.104, respectively. The mean change in HbA1c levels for the education groups for the increasing levels of education were 0.117, 0.099, 0.075, and 0.064, respectively, which shows that those with a lower level of education had a higher increase in HbA1c levels than those with a higher level of education.

Table 2 also shows that the mean change in HbA1c levels for participants with a BMI less than 25, overweight, and obese showed an increasing pattern (0.047, 0.090, and 0.156, respectively). The mean change in HbA1c levels for participants with sedentary, mild, and moderate/heavy levels of physical activity were 0.127, 0.090, and 0.075, respectively, which shows that those with low levels of physical activity had a slightly higher mean increase in HbA1c levels than those with even mild or moderate/heavy physical activity. However, participants without a history of smoking had a slightly higher increase in HbA1c levels than those that smoked daily or had previously smoked daily (0.105 vs 0.090 vs 0.090).

Additionally, as shown in Table 2 a positive family history of diabetes showed a higher mean increase in HbA1c than those without a family history of diabetes (0.129 vs 0.086). Furthermore, participants with a personal history of diabetes, as well as those using insulin-containing or glucose-lowering drugs, had a higher mean increase in HbA1c levels compared to those that did not (0.585 vs 0.060).

Table 2. Descriptive characteristics by Change in HbA1c levels[1], The Tromsø Study 2007 - 2016

	Minimum, Maximum	Mean	Standard Deviation
Overall	-0.90, 6.60	0.095	0.400
Sex			
Female	-0.90, 6.60	0.087	0.405
Male	-0.80, 3.80	0.104	0.394
Age			
30-49	-0.80, 5.60	0.108	0.515
50-69	-0.90, 6.60	0.090	0.387
70+	-0.90, 1.60	0.104	0.313
Level of Education			
Primary	-0.90, 6.60	0.117	0.461
Upper Secondary	-0.90, 3.80	0.099	0.397
University College < 4 years	-0.80, 2.60	0.075	0.325
University College ≥ 4 years	-0.80, 3.40	0.064	0.332
Body Mass Index			
<25	-0.90, 2.70	0.048	0.263
25 – 29.9	-0.80, 5.60	0.090	0.349
> 30	-0.90, 6.60	0.157	0.565
Physical Activity			
Sedentary	-0.90, 3.10	0.127	0.465
Mild	-0.80, 3.80	0.090	0.344
Moderate and Heavy	-0.50, 5.60	0.075	0.414
Smoking History			
Smoking daily	-0.70, 2.80	0.092	0.388
Previously smoked daily	-0.90, 5.60	0.090	0.387
Never smoked	-0.90, 6.60	0.105	0.429

Table 2. Descriptive characteristics by Change in HbA1c levels[1], The Tromsø Study 2007 – 2016 (cont.)

	Minimum, Maximum	Mean	Standard Deviation
Family History of Diabetes			
Yes	-0.80, 6.60	0.129	0.490
No	-0.90, 5.60	0.086	0.369
Diagnosis of Diabetes			
Yes	-0.90, 6.60	0.656	0.833
No	-0.90, 0.70	0.024	0.217
History of diabetes and use of medication for Diabetes[2]			
Yes	-0.90, 5.60	0.585	0.909
No	-0.90, 6.60	0.060	0.306

[1]Change in HbA1c levels between Tromsø 6 and Tromsø 7

[2]Reproted history of diabetes and use of insulin or glucose-lowering medication during Tromsø 6

Diagnosis of Diabetes

Table 3 presents the association between the diagnosis of diabetes and education adjusted for age, sex, and family history of diabetes in participants with prediabetes. The findings show that there is a statistically significant 54% higher odds of diabetes in those with an upper secondary school education compared to those with 4 or more years of college/university (odds ratio (OR) 1.54; 95% confidence interval (CI) 1.03, 2.29).

Furthermore, sex-specific models showed a borderline significant 95% higher odds of diabetes in women with a college/university education of less than 4 years compared to women with 4 or more years of college/university education (OR 1.95; 95% CI 1.03, 2.29). (Table 3) The association between the diagnosis of diabetes adjusted for age and family history of diabetes and education in men with prediabetes was found not to be statistically significant ($p > 0.05$).

An interaction test looking at the effects of sex on the relationship between education and diagnosis of diabetes was done. However, there was not a statistically significant interaction between them ($p > 0.05$).

Table 3. Odds ratios for diagnosis of diabetes according to Education overall and by sex[1], The Tromsø Study 2007 - 2016

Education	OR (95% CI)	p-value
Overall, n=2690		
University college ≥ 4 years	1 (Reference)	
University college < 4 years	1.37 (0.87, 2.17)	0.177
Upper Secondary	1.54 (1.03, 2.29)	0.034
Primary	1.48 (0.98, 2.22)	0.063
Women, n=1343		
University college ≥ 4 years	1 (Reference)	
University college < 4 years	1.95 (0.99, 3.86)	0.055
Upper Secondary	1.59 (0.88, 2.88)	0.125
Primary	1.64 (0.90, 2.97)	0.105
Men, n=1347		
University college ≥ 4 years	1 (Reference)	
University college < 4 years	1.06 (0.57, 1.97)	0.854
Upper Secondary	1.48 (0.86, 2.52)	0.155
Primary	1.38 (0.78, 2.44)	0.267

OR, odds ratio; CI, confidence interval

[1]Adjusted for age, family history of diabetes, and in the overall sex.

Intermediaries in the Association between Education and Diagnosis of Diabetes

Table 4 presents that there is a statistically significant mediating effect of BMI, level of physical activity, and smoking history in the analysis of the association between the diagnosis of diabetes and education in participants with prediabetes. However, only those with upper secondary education relative to those with 4 or more years of college/university education had a statistically significant association with the diagnosis of diabetes. In this group, the proportion explained by the diabetes risk factors (BMI, level of physical activity, and smoking history) was 43.6%.

Furthermore, as presented in Table 4 in sex-specific models there is a statistically significant mediating effect of BMI, level of physical activity, and smoking history in women with prediabetes on the relationship between the diagnosis of diabetes and education. We observed a significant natural indirect effect in women with primary education relative to those with 4 or more years of college/university education, OR=1.19 (95% CI 1.02, 1.38). Nevertheless, we did not observe a statistically significant total effect in the association between the predictor and the outcome.

On the other hand, there is a statistically significant mediating effect of BMI, level of physical activity, and smoking history in men with prediabetes on the relationship between education and diagnosis of diabetes. Nevertheless, we did not observe a statistically significant total effect in the association between the predictor and the outcome.

Table 4. Odds ratios for the causal mediation of Diabetes risk factors[1] on the association between education[2] and diagnosis of diabetes, natural direct effect (NDE), natural indirect effect (NIE), and total effect (TE) and their corresponding 95% confidence intervals by sex. The Tromsø Study 2007 - 2016

Education	NDE	NIE	TE
Overall, n=2310			
University college ≥ 4 years	1 (Reference)	1 (Reference)	1 (Reference)
University college < 4 years	1.17 (0.73, 1.91)	1.19 (1.06, 1.31)	1.39 (0.87, 2.27)
Upper Secondary	1.35 (0.90, 2.05)	1.20 (1.07, 1.32)	1.62 (1.08, 2.48)
Primary	1.19 (0.73, 1.92)	1.25 (1.10, 1.40)	1.43 (0.94, 2.25)
Female, n=1098			
University college ≥ 4 years	1 (Reference)	1 (Reference)	1 (Reference)
University college < 4 years	1.95 (0.98, 3.90)	0.97 (0.85, 1.12)	1.92 (0.95, 3.94)
Upper Secondary	1.42 (0.77, 2.64)	1.11 (0.96, 1.26)	1.57 (0.86, 3.00)
Primary	1.26 (0.66, 2.39)	1.19 (1.02, 1.38)	1.49 (0.81, 2.89)
Male, n=1212			
University college ≥ 4 years	1 (Reference)	1 (Reference)	1 (Reference)
University college < 4 years	0.80 (0.41, 1.52)	1.41 (1.16, 1.70)	1.12 (0.59, 2.18)
Upper Secondary	1.23 (0.70, 2.18)	1.34 (1.13, 1.57)	1.65 (0.96, 2.97)
Primary	1.06 (0.57, 1.99)	1.34 (1.09, 1.65)	1.42 (0.80, 2.67)

[1]Body mass index, smoking history, and level of physical activity.

[2]Adjusted for age, family history of diabetes, and in the overall sex.

Table 5 presents a breakdown of the mediating effects of each of the risk factors collectively presented in Table 4. This shows that a significant fraction of the intermediate effect is due to BMI with the proportion explained by BMI in participants with upper secondary education relative to those with 4 or more years of college/university education was 38%.

Table 5. Odds ratios for the causal mediation of Diabetes risk factors[1] on the association between education[2] and diagnosis of diabetes, natural direct effect (NDE), natural indirect effect (NIE), and total effect (TE) and their corresponding 95% confidence intervals by each considered risk factor. The Tromsø Study 2007 - 2016

Education	NDE	NIE	TE
BMI, n=2310			
University college ≥ 4 years	1 (Reference)	1 (Reference)	1 (Reference)
University college < 4 years	1.20 (0.75, 1.93)	1.16 (1.06, 1.27)	1.42 (0.89, 2.27)
Upper Secondary	1.39 (0.91, 2.10)	1.17 (1.07, 1.27)	1.62 (1.08, 2.46)
Primary	1.22 (0.80, 1.90)	1.17 (1.07, 1.28)	1.42 (0.93, 2.23)
Physical Activity, n=2310			
University college ≥ 4 years	1 (Reference)	1 (Reference)	1 (Reference)
University college < 4 years	1.39 (0.86, 2.25)	1.01 (0.97, 1.04)	1.39 (0.86, 2.27)
Upper Secondary	1.58 (1.05, 2.41)	1.02 (0.99, 1.05)	1.62 (1.08, 2.48)
Primary	1.35 (0.86, 2.09)	1.07 (1.02, 1.13)	1.43 (0.94, 2.25)
Smoking, n=2310			
University college ≥ 4 years	1 (Reference)	1 (Reference)	1 (Reference)
University college < 4 years	1.41 (0.86, 2.27)	1.00 (0.95, 1.04)	1.39 (0.87, 2.27)
Upper Secondary	1.63 (1.06, 2.48)	0.99 (0.94, 1.05)	1.62 (1.08, 2.48)
Primary	1.45 (0.92, 2.29)	0.99 (0.92, 1.07)	1.43 (0.94, 2.25)

[1]Body mass index, smoking history, and level of physical activity.

[2]Adjusted for age, family history of diabetes, and sex.

Change in HbA1c

Table 6 presents that there is a statistically significant ($p = 0.02$) relationship between the change in HbA1c levels between Tromsø 6 and 7 and education in participants with prediabetes at baseline in Tromsø 6. The change in HbA1c for those with primary education is 0.06 units higher than those with 4 or more years of college/university education.

Furthermore, as presented in Table 6 in sex-specific models the association between the change in HbA1c and education adjusted in women with prediabetes was found not to be statistically significant ($p > 0.05$). However, there was a statistically significant ($p = 0.01$ and 0.03) relationship between the change in HbA1c and education in men with prediabetes at baseline in Tromsø 6. The mean change in HbA1c for those with upper secondary and primary education was 0.08 units higher than those with 4 or more years of college/university education.

An interaction test was done to examine the effects of sex on the relationship between the diagnosis of diabetes and education. There is a statistically significant interaction among those with upper secondary education ($p = 0.03$).

Table 6. Linear Regression coefficients for the association between the change in HbA1c levels and education overall and by sex[1], The Tromsø Study 2007 - 2016

Education	β (95% CI)	p-value
Overall, n=2690		
University college ≥ 4 years	0 (Reference)	
University college < 4 years	0.01 (-0.05, 0.06)	0.81
Upper Secondary	0.03 (-0.01, 0.08)	0.15
Primary	0.06 (0.01, 0.10)	0.02
Women, n=1343		
University college ≥ 4 years	0 (Reference)	
University college < 4 years	0.00 (-0.08, 0.08)	0.96
Upper Secondary	-0.02 (-0.08, 0.05)	0.64
Primary	0.04 (-0.02, 0.11)	0.22
Men, n=1347		
University college ≥ 4 years	0 (Reference)	
University college < 4 years	0.02 (-0.05, 0.09)	0.58
Upper Secondary	0.08 (0.02, 0.15)	0.01
Primary	0.08 (0.01, 0.14)	0.03

β, coefficient, CI, Confidence Interval

[1]Adjusted for age, family history of diabetes, and in the overall sex.

As presented in Table 7 there was a statistically significant mediating effect of BMI, level of physical activity, and smoking history in participants with prediabetes at baseline on the association between the change in HbA1c and education in participants with upper secondary as well as primary education relative to those with 4 or more years of college/university education. The proportion explained by the diabetes risk factors (BMI, level of physical activity, and smoking history) was 20%.

However, as presented in Table 7 in sex-specific models there was not a statistically significant mediating effect of BMI, level of physical activity, and smoking history in women with prediabetes at baseline in Tromsø 6 on the relationship between the change in HbA1c and education. On the other hand, there is a statistically significant mediating effect of BMI, level of physical activity, and smoking history in men with prediabetes at baseline on the relationship between the change in HbA1c and education in those with upper secondary as well as primary education relative to those with 4 or more years of college/university education. The proportions explained by the mediating factors were 30% and 25%, respectively.

Table 7. Linear regression coefficients for the causal mediation of Diabetes risk factors[1] on the association between education[2] and the change in HbA1c levels, natural direct effect (NDE), natural indirect effect (NIE), and total effect (TE) and their corresponding 95% confidence intervals by sex. The Tromsø Study 2007 - 2016

Education	NDE	NIE	TE
Overall, n=2310			
University college ≥ 4 years	0 (Reference)	0 (Reference)	0 (Reference)
University college < 4 years	0.00 (-0.04, 0.05)	0.01 (0.00, 0.01)	0.01 (-0.04, 0.06)
Upper Secondary	0.04 (0.00, 0.08)	0.01 (0.00, 0.02)	0.05 (0.00, 0.09)
Primary	0.04 (-0.01, 0.09)	0.01 (0.00, 0.02)	0.05 (0.00, 0.10)
Female, n=1098			
University college ≥ 4 years	0 (Reference)	0 (Reference)	0 (Reference)
University college < 4 years	0.00 (-0.07, 0.07)	0.00 (0.00, 0.00)	0.00 (-0.08, 0.08)
Upper Secondary	-0.01 (-0.06, 0.05)	0.00 (-0.01, 0.01)	-0.01 (-0.07, 0.05)
Primary	0.04 (-0.04, 0.11)	0.00 (-0.02, 0.01)	0.03 (-0.03, 0.10)
Male, n=1212			
University college ≥ 4 years	0 (Reference)	0 (Reference)	0 (Reference)
University college < 4 years	0.00 (-0.06, 0.06)	0.03 (0.01, 0.05)	0.03 (-0.05, 0.10)
Upper Secondary	0.07 (0.01, 0.13)	0.03 (0.00, 0.04)	0.10 (0.03, 0.16)
Primary	0.06 (-0.01, 0.12)	0.02 (0.00, 0.05)	0.08 (0.00, 0.15)

[1]Body mass index, smoking history, and level of physical activity.

[2]Adjusted for age, family history of diabetes, and in the overall sex.

Table 8 presents a breakdown of the mediating effects of each of the risk factors collectively presented in Table 7. This shows that once again a significant fraction of the intermediate effect is due to BMI with the proportion explained by BMI in participants with upper secondary as well as primary education relative to those with 4 or more years of college/university education being 20%.

Table 8. Linear regression coefficients for the causal mediation of Diabetes risk factors[1] on the association between education[2] and diagnosis of diabetes, natural direct effect (NDE), natural indirect effect (NIE), and total effect (TE) and their corresponding 95% confidence intervals by each considered risk factor. The Tromsø Study 2007 - 2016

Education	**NDE**	**NIE**	**TE**
BMI, n=2310			
University college ≥ 4 years	0 (Reference)	0 (Reference)	0 (Reference)
University college < 4 years	0.00 (-0.04, 0.05)	0.01 (0.00, 0.01)	0.01 (-0.04, 0.06)
Upper Secondary	0.04 (0.00, 0.08)	0.01 (0.00, 0.01)	0.05 (0.00, 0.09)
Primary	0.04 (0.00, 0.09)	0.01 (0.00, 0.01)	0.05 (0.00, 0.10)
Physical Activity, n=2310			
University college ≥ 4 years	0 (Reference)	0 (Reference)	0 (Reference)
University college < 4 years	0.01 (-0.04, 0.06)	0.00 (0.00, 0.00)	0.01 (-0.04, 0.06)
Upper Secondary	0.04 (0.00, 0.09)	0.00 (0.00, 0.00)	0.05 (0.00, 0.09)
Primary	0.05 (0.00, 0.10)	0.00 (0.00, 0.01)	0.05 (0.00, 0.10)
Smoking, n=2310			
University college ≥ 4 years	0 (Reference)	0 (Reference)	0 (Reference)
University college < 4 years	0.01 (-0.03, 0.06)	0.00 (-0.01, 0.00)	0.01 (-0.04, 0.06)
Upper Secondary	0.05 (0.00, 0.09)	0.00 (-0.01, 0.00)	0.05 (0.00, 0.09)
Primary	0.06 (0.01, 0.11)	0.00 (-0.01, 0.01)	0.05 (0.00, 0.10)

[1]Body mass index, smoking history, and level of physical activity.

[2]Adjusted for age, family history of diabetes, and sex.

Table 9 shows that there is a statistically significant association between the diagnosis of diabetes and the number of GP consultations in the 12 months prior to Tromsø 6 in participants with prediabetes adjusted for age, sex, family history of diabetes, smoking history, BMI, and level of physical history. Those with 5 or more visits had 74% higher odds of getting diagnosed with diabetes than those with 1 visit, OR = 1.74 (95% CI 1.12, 2.71).

However, as presented in Table 9 in sex-specific models there is not a statistically significant association between the diagnosis of diabetes and the number of GP consultations in the 12 months prior to Tromsø 6 in participants with prediabetes adjusted for age, sex, family history of diabetes, smoking history, BMI, and level of physical history in either women or men.

Table 9. Odds ratios for diagnosis of diabetes according to the number of GP consultations over the 12 months prior to Tromsø 6 overall and by sex[1], The Tromsø Study 2007 - 2016

Number of GP consultations	**OR (95% CI)**	**p-value**
Overall, n=1835		
1 visit	1 (Reference)	
2 visits	1.18 (0.75, 1.86)	0.474
3 or 4 visits	1.43 (0.93, 2.19)	0.100
5 or more visits	1.74 (1.12, 2.71)	0.014
Women, n=885		
1 visit	1 (Reference)	
2 visits	1.20 (0.58, 2.49)	0.627
3 or 4 visits	1.70 (0.87, 3.33)	0.120
5 or more visits	1.89 (0.93, 3.81)	0.077
Men, n=950		
1 visit	1 (Reference)	
2 visits	1.17 (0.65, 2.09)	0.606
3 or 4 visits	1.23 (0.70, 2.16)	0.483
5 or more visits	1.66 (0.92, 2.95)	0.087

OR, odds ratio; CI, confidence interval

[1]Adjusted for age, family history of diabetes, smoking history, BMI, level of physical activity, and in the overall sex.

As shown in Table 10 there is not a statistically significant association between change in HbA1c and the number of GP consultations over the 12 months prior to Tromsø 6 in participants with prediabetes adjusted for age, sex, family history of diabetes, smoking history, BMI, and level of physical history. This lack of a statistically significant association persisted in sex-specific models.

Table 10. Linear Regression coefficients for the association between the change in HbA1c levels and the number of GP consultations over the 12 months prior to Tromsø 6 overall and by sex[1], The Tromsø Study 2007 - 2016

Number of GP consultations	β (95% CI)	p-value
Overall, n=1835		
1 visit	0 (Reference)	
2 visits	0.03 (-0.02, 0.07)	0.30
3 or 4 visits	0.03 (-0.01, 0.08)	0.15
5 or more visits	0.02 (-0.03, 0.07)	0.44
Women, n=885		
1 visit	0 (Reference)	
2 visits	0.02 (-0.04, 0.09)	0.52
3 or 4 visits	0.04 (-0.03, 0.10)	0.28
5 or more visits	0.02 (-0.05, 0.10)	0.51
Men, n=950		
1 visit	0 (Reference)	
2 visits	0.03 (-0.04, 0.09)	0.44
3 or 4 visits	0.02 (-0.04, 0.09)	0.48
5 or more visits	0.02 (-0.05, 0.09)	0.64

β, coefficient, CI, Confidence Interval

[1]Adjusted for age, family history of diabetes, smoking history, BMI, level of physical activity, and in the overall sex.

DISCUSSION

Diagnosis of Diabetes

Summary

The results show that there was a significant association between the diagnosis of diabetes at follow up (Tromsø 7) and education in participants that had prediabetes at baseline in Tromsø 6. This was statistically significant in those with an upper secondary level of education having 54% higher odds of diagnosis of diabetes relative to those with four or more years of college/university level of education. However, the associations were not significant in sex-specific models. This association was seen to be partly explained by factors other than education mainly BMI which explained 38% of the effect.

Our results compared to previous studies.

While to my knowledge there has not been an exactly similar study done looking at the diagnosis of diabetes in those who had been identified as having prediabetes, we can draw upon the existing literature to contextualize our study. For example, previous studies have examined the relationship between the diagnosis of diabetes and several factors including education such as a study utilizing the Tromsø study between 1994 and 2005 showing an association between education and diagnosis of diabetes with 54% to 74% higher odds of diabetes in women and men respectively with primary education relative to those with 4 or more years of college/university education (22). This shows a slightly stronger association between education and diagnosis of diabetes than my results but similarly shows that those with lower levels of education had higher odds of being diagnosed with diabetes. Furthermore, another population-based study based in Oslo between 2000 and 2002 had a similar outcome with participants with lower levels of education having a 68% to 78% higher odds of being diagnosed with diabetes (21). Similarly, this study shows a stronger association between education and diagnosis of diabetes than my results. These stronger associations might mean that over the last few years, there has been a decrease in this relationship in Norway, especially in Northern Norway. However, contrary to this study the aforementioned studies do not specifically include people with prediabetes as such the effects of education are not limited to those with prediabetes.

Change in HbA1c levels between Tromsø 6 and Tromsø 7.

Summary

At baseline, the participants in this study had an HbA1c level in the prediabetic range. When we look at the change in the level between Tromsø 6 and Tromsø 7 we are examining the management of the participant's blood glucose and its impacts on the prevention of diabetic complications. This change was mostly an increase in HbA1c levels with a mean increase of 0.095 which is a slight increase in HbA1c levels over the period between the two surveys.

The results present that there is a statistically significant relationship between education and change in HbA1c levels between Tromsø 6 and 7 in participants with prediabetes during Tromsø 6 with a 0.06-unit change in HbA1c levels in participants with the lowest levels of education compared to those with the highest. Moreover, it was found to only be statistically significant in men with lower levels of education having an increase of 0.08 units in HbA1c levels between Tromsø 6 and 7. The overall change in HbA1c levels between Tromsø 6 and 7 was seen to be partly explained by factors other than education mainly by BMI which explained 20% of the effect.

Our results compared to previous studies.

We can use the existing literature to provide context for our study. For example, a previous study has examined the relationship between the change in HbA1c levels and a few factors including education. A study based in the United States done among participants with prediabetes and risk factors for change in HbA1c levels over 1 year found that a higher level of education was associated with the change in HbA1c levels by a factor of -0.25 units (32). However, contrary to the results of our study the study showed a decrease in HbA1c levels in the association between education in participants with prediabetes. This could be due to the short follow-up period, or the sample used for the study being from a healthcare setting which might have led this sample to have had an intervention that is not taken into consideration. Furthermore, the 7-year duration between our two surveys could be associated with numerous changes in lifestyle and medical conditions and compounded by the fact that HbA1c levels show us the level of glycemic control over the 3 months prior to the test.

Healthcare Consumption

Summary

The results show that the association between the number of GP consultations in the 12 months prior to Tromsø 6 and the diagnosis of diabetes in participants was only statistically significant in participants with five or more visits relative to those with only 1 visit. This could be due to participants being screened as having an elevated risk for diabetes or being diagnosed with diabetes consumption as is attested by the increase in the number of GP visits in those participants who developed diabetes and having more follow-ups or due to other illnesses leading to increased healthcare consumption. However, the glycemic control of participants represented by the change in HbA1c levels between Tromsø 6 and 7 was not found to be significantly associated with the number of GP consultations in the 12 months prior to Tromsø 6. We would expect a decrease or stability in the HbA1c levels between Tromsø 6 and 7 if the participants had been identified and were being managed for prediabetes to prevent the development of diabetes and diabetic complications.

Our results compared to previous studies.

A previous study based in Ireland shows that there is a positive association between diabetes and the frequency of GP visits (40). While another study also based in Ireland shows that there is not a statistically significant association between the number of GP visits and the diagnosis of diabetes (38). Furthermore, a study based in the Netherlands looking at patient characteristics including the number of GP visits for diabetes in the 12 months prior to the study did not have a statistically significant association with HbA1c levels (39). In addition, a Finnish study looking at primary healthcare interventions and their association with improvement in glucose tolerance found that there was not a statistically significant association (41).

Even though these studies are not population-based, and some included targeted interventions the association of healthcare consumption was only associated with the diagnosis of diabetes in participants with many visits. While there does not seem to be a significant association between healthcare consumption and glycemic control in the studies in congruence with this thesis's results.

Limitations

Selection Bias: The Tromsø study has been noted to have participants that tend to be more likely female, rural residents, living with someone/married, employed, healthier with a lower prevalence of several chronic diseases, have a healthier lifestyle, and have a somewhat higher education level compared to the total Tromsø population (61).

The Results of this thesis are based on a large sample of the prediabetic population in the Tromsø municipality. However, ethnic minorities are under-represented as such there might be issues with generalizability. The living standards and healthcare systems in Tromsø are similar to those in the rest of Norway. Conversely, as the sample population was 30 years and older with the majority being between the ages of 50 and 79 these results are representative of the prediabetic population over the age of thirty and are generalizable to this demographic in Norway and other places with similar living standards and healthcare systems.

Recall Bias: As some of the predictors are based on self-reported responses requiring accurate recall of potentially confusing questions there is a possibility of misremembering. This is especially relevant to the number of GP consultations in the 12 months prior and physical activity. As well as on the history of diabetes as participants may classify several types of diseases as Type 2 Diabetes Mellitus including Diabetes insipidus as well as other diseases with temporary insulin insufficiency or resistance.

Another potential risk is the risk of misclassification in the diagnosis of participants was the use of a compiled variable with a history of diabetes classified as those that currently have diabetes, those that do not, and those with a history of diabetes. A description of those that had a history of diabetes is not clear and can include other types of diabetes or diseases which cause transient symptoms of insulin insufficiency or resistance could be included.

Furthermore, as we used the number of GP consultations in the 12 months prior to Tromsø 6 as one of the exposures for this study in the 7-year gap between Tromsø 6 and 7 there could be a varying number of GP consultations therefore this could impact the interpretation of the results. In addition, in this study for the assessment of healthcare consumption the use of the number of GP consultations might miss those that could be consulting with other types of healthcare workers such as specialists. The 7-year gap between the HbA1c measures could be misleading as HbA1c measures the glycemic control over the 3 months prior to it and the lengthy period between the two surveys there could have been huge variability in HbA1c levels due to a myriad of lifestyle changes including diet and exercise as well as pharmacological management.

Statistical analysis: A number of variables were grouped to increase the power of the analysis such as the number of GP consultations which were grouped into quartiles but initially didn't have a normal distribution. Grouping of continuous variables assumes that there is homogeneity within groups which may not be the case as those grouped with 5 or more visits to the GP includes those with a much higher number of visits (55 being the maximum). Furthermore, there is also difficulty comparing it with other studies as other studies use different parameters for grouping cases.

Residual confounding: There is a possibility that there are variables unaccounted for that affect the relationship between the predictors and the outcomes.

On the other hand, the variable used as a proxy for socioeconomic factors was education which has been shown to influence the outcomes but other socioeconomic factors such as income could have an effect that was not observed in this thesis.

Strengths

This thesis is based on a cohort of the Tromsø study from two consecutive surveys giving it a large population-based sample and a high number of HbA1c measurements that were standardized. Furthermore, the compiled diagnosis of diabetes was based on a combination of factors including self-reported diabetes, use of insulin and glucose-lowering medications as well as an HbA1c level within the diabetic range which strengthen the sensitivity of the outcome measurement including diagnosed and undiagnosed participants with diabetes.

The 7-year gap between the exposure and the outcome is useful in that diabetes is a chronic disease and the longer follow-up period allows us to see the impact over a longer time.

CONCLUSION

The results show that there is a socioeconomic impact on the diagnosis of diabetes and the glycemic management of people with prediabetes while the effect of healthcare consumption on the progression of the disease in people with prediabetes is not recognized. This alludes to the need to look deeper at the potential causes of healthcare consumption’s relationship with blood glucose management. This might entail the need for more targeted interventions among those with prediabetes. Further studies are necessary with more regular follow-ups to assess how the predictors affect the progression of diabetes and blood glucose management especially in people with prediabetes as it is an important screening tool to prevent diabetic complications.

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