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Are social determinants of health associated with the development of early complications among young adults with type 2 diabetes? A population based study using linked databases

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ABSTRACT

Aims: To quantify the impact of social determinants of health (SDOH) on top of medical determinants on the development of diabetes-related complications in young adults with type 2 diabetes.
Methods: In this observational population-based study, SDOH (income and origin) were linked to routine primary care data. Young adults (18–45 years) with incident type 2 diabetes between 2007 and 2013 were included. The main outcome, the development of the first micro- or macrovascular complication, was analyzed by multivariate Cox regression. Medical determinants included antidiabetic treatment, HbA1c in the year after diagnosis, body mass index, comorbidity and smoking.
Results: Of 761 young adults (median age: 39 years (IQR 33–42), men: 49%, Western origin: 36%, low income: 48%), 154 developed at least one complication (median follow-up 99 months (IQR 73–123)). Young men of non-Western origin were more likely to develop a complication (HR 1.98 (1.19–3.30)), as were young adults with HbA1c > 7% (>53 mmol/mol) (HR: 1.72 95% CI: 1.15–2.57). No associations were found with income. Being women was protective.
Conclusion: In this multi-ethnic population, non-Western origin was associated with the development of complications, but only in men. Low income was not associated with developing complications. The importance of adequate HbA1c regulation was re-emphasized by this study.

1. Introduction

The prevalence of early-onset type 2 diabetes is increasing [1] and well-known microvascular and macrovascular diabetes complications are also appearing at younger ages in this population. Early-onset type 2 diabetes results in higher morbidity and mortality compared to people diagnosed after 45 years of age [2–4]. It has been argued that current high morbidity and mortality rates are the result of underscreening, underdiagnosis and possibly undertreatment of young people with type 2 diabetes. Other explanations are the impact of a longer exposure to obesity [5], poor glycemic control [12–16], dyslipidemia, hypertension and chronic infection in young adults with type 2 diabetes compared to older adults with type 2 diabetes or young adults with type 1 diabetes [6]. Next to these medical factors, diabetes type 2 prevalence in young adults has a suggested association with lower socio-economic status (SES) [7–10]. SES is a multifactorial concept which includes i.a. status of income, occupation and ethnic minority (social determinants of health) (SDOH) [11]. Although the medical determinants of the disease in young adults itself are clear, the relative impact of SDOH on the development of complications in young adults with type 2 diabetes is still not well understood.

Like many Western cities The Hague is a large urban area with large ethnic diversity. In older adults, it has been shown that ethnicity may be a risk factor as well as protective for progression to complications [12].

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Non-Western migrants often have lower SES and type 2 diabetes is more prevalent in people of South-Asian and African origin compared to people of Western origin [2, 5, 8, 11, 13]. In a disease in which both prevalence and risk factors are closely related to a patient's SES, the identification of people at risk for specific outcomes [14] should, next to medical factors, include SDOH at the individual level. However, SDOH are frequently missing from routine care databases and earlier studies were often based on self-reported data, neighborhood deprivation scores [15], or were not corrected for HbA1c-levels [13].

The aim of this study was therefore to quantify the additional impact of ethnic origin and income next to medical determinants on the risk of developing diabetes complications in young adults with type 2 diabetes in a socio-economically diverse region of the Netherlands.

2. Materials and methods

2.1. Design and data sources

In this observational population-based cohort study we used routine care data from primary care practice (PCP)-practices in The Hague from the database ELAN (Extramural Academic Network of the Leiden University Medical Centre) [16]. Data derived from the PCP registries included diagnoses (International Classification of Primary Care, ICPC codes), medication prescriptions (7-digit Anatomic, Therapeutic, Chemical Classification System (ATC) codes) and diagnostic measurements (Dutch registration codes) for approximately 180,000 citizens in The Hague and vicinity. These data were linked to SDOH within the Social Statistical Datasets (SSD) from Statistics Netherlands (SN). SSD covers longitudinal microdata on several domains, including SDOH details [17]) for all governmental registered citizens of the Netherlands.

Currently, 80–85% of type 2 diabetes care in the Netherlands takes place in primary care, and is covered by obliged basic health insurance. Only the most complex cases are referred to secondary care [18,19]. As the adequate registration of diagnosis and diagnostic measurements is encouraged via bundled payments reimbursement schemes, all patients with a diabetes diagnosis can be recognized within the ELAN database [19].

2.2. Study population

All individuals with type 2 diabetes, aged 18–45 years in the year of diagnosis (index year), were included for the period January 1, 2007 to December 31, 2013. A diagnosis of diabetes was based on ICPC code T90.02/T90.00 (type 2 diabetes /diabetes unspecified) and/or the first prescription of medication in ATC group A10B (oral blood glucose-lowering drugs, excluding insulins) in the ELAN dataset [20]. Individuals were excluded when an outcome event occurred before diagnosis, or if a reference to Latent Autoimmune Diabetes in Adults (LADA) or Maturity-Onset Diabetes of the Young (MODY) was mentioned in the description of the ICPC code. People were censored on the date of their first complication, date of death, or if they left the practice, with a follow-up until 31 December 2019.

2.3. Primary outcome

The primary outcome was the development of either a first microvascular or a first macrovascular complication. Microvascular complications included: nephropathy (U99.01), retinopathy (F83), and neuropathy (N94.02). Macrovascular complications included: angina pectoris (K74), myocardial infarction (K75), other ischemic diseases (K76), transient ischemic attack (K89), cerebral infarction (K90), and/or peripheral artery disease (K92.01). In addition, macrovascular complications included cardiovascular- or diabetes-related death as identified in the SSD (national death registries with linked ICD-10 codes).

2.4. Medical determinants

Medical determinants included glucose-lowering treatment, comorbidity and anthropometric measurements (Supplementary material A). Three treatment categories were defined based on Dutch guidelines: 1) lifestyle advice only (no glucose-lowering medication), 2) oral blood glucose-lowering medication (A10B medication prescribed but no A10A medication), and 3) both oral blood glucose-lowering medication and insulin (both A10B and A10A).

Comorbidity (yes/no) was defined as the presence of one or more chronic diseases as defined by Oostrom et al. [21] plus hypertension (ICPC codes K85, K86, K87) and adiposity (A82) prevalent in the index year. Smoking was defined as 'non- smoker', 'previous smoker' or 'current smoker' in all observation years, as lower cardiovascular disease risk is only achieved 10 years after quitting smoking. Mean body mass index (BMI (kg/m^2)) was calculated from all registered or calculated BMIs in a 3-year range around the diabetes diagnosis. Mean HbA1c (%, mmol/mol) was calculated from registered HbA1c 6–18 months after diagnosis, eliminating measurements from the initial phase of the treatment [22] and divided into two categories as a relevant clinical cut-off point: $>$ 7% ($>$53 mmol/mol) or $\leq$ 7% ($\leq$53 mmol/mol) [8].

2.5. SDOH

SDOH included information on sex, age, ethnic origin and income (see Supplementary material A for a detailed description) [23]. Ethnic origin was based on migration background as registered by SN and was clustered into two groups: 'Western' (Dutch and other Western origin) and 'non-Western' (Turkish, Moroccan, South-Asian, and other non-Western). Migration generation was specified as first or second migration generation. Income during the index year was derived from the SN-calculated measure 'standardized disposable household income', which represents the net amount a household can spend on an annual basis, adjusted for any differences in household size and composition, divided into percentiles on a population-wide national level. Income was clustered into 3 categories: 0–33 percentile, 33–66 percentile, and 67–100 percentile.

2.6. Validation sample

To determine the representativeness of the sample of the ELAN-HHTH sample compared to all young adults with type 2 diabetes in The Hague in terms of SDOH, an validation cohort was created based on the medication data files registered in the SSD (Supplementary material A). Incident type 2 diabetes in citizens aged 18–45 years was identified based on reimbursement for diabetes medication (A10B group) during the years of inclusion (2007–2013) and a lack of reimbursement for diabetes medication in the previous year. The SDOH were merged with this sample.

2.7. Statistical analysis

Descriptive statistics were summarized using numbers (%), mean ($\pm$ standard deviation (SD)) and median (+interquartile range (IQR)). The study cohort was compared with the validation sample, taking into account that the validation sample underestimates real incidence as not all newly diagnosed patients are prescribed medication. Groups were compared with chi-square tests, independent sample t-tests or Mann-Whitney U-tests, as appropriate.

The main analysis was a multivariate Cox model with a composite score of first complication as outcome (model A). The model was adjusted for age-of-onset, sex, BMI, treatment category, HbA1c groups [24], co-morbidity [8], and smoking status [8,9] as medical determinants, and non-Western origin (yes/no) and standardized household income as SDOH. To assess effect-modification with 1) sex and 2) HbA1c group with 1) ethnicity and 2) income, interaction terms were

added to the fully adjusted model. The assumptions of the proportional hazards model were checked for each variable using a time-dependent covariate and Kaplan-Meier curves and were met.

Two sub-analyses were performed. First, we repeated the analysis with solely microvascular complications (model B) and with solely macrovascular events (model C). The most significant medical determinants were selected using backward elimination, and SDOH were subsequently added [9,13,25,26]. To investigate the role of country of origin and migration generation within persons with a non-Western origin, a sub-analysis identical to the main analysis was performed within this subgroup (Supplementary material C).

Missing data were handled using multiple imputation (MI) (Supplementary material D). The MI procedure of SPSS version 25.0 was used, with the fully conditional specification setting using predictive mean modeling for continuous data, and binary logistic and poly-logistic modeling for categorical data, with 50 iterations and the creation of 10 imputed datasets. Results of the imputed datasets were pooled using Rubin's Rules.

The performance of models A, B and C were assessed in the imputed datasets using discrimination and calibration, with the bootstrapping technique for internal validation [27,28]. The discriminative ability – the ability to distinguish between patients with and without complications – of the model was evaluated on the basis of the Concordance-index (c-index). A c-index of more than 0.7 indicates good model discrimination, 0.5–0.7 moderate discrimination. Model calibration was assessed in each imputed dataset based on the intercept and slope of the calibration curves, plotting predicted probability of complications against the observed complications [29,30]. An ideal slope would be close to one and intercept would be zero.

Analyses were performed using SPSS version 25 and R studio software version 3.6.2, with the MICE, Hmisc and rms packages.

3. Results

3.1. Baseline characteristics

In total, 761 young adults with incident type 2 diabetes aged between 18 and 45 years were identified (Fig. 1). Overall, 154 (20.2%) persons developed a complication during follow-up. Median follow-up was 99 months (IQR 73–123), while median time to complication was 59 months (IQR 29–86).

Median age was 39 years (IQR 33–42), 49.3% were men, a third of the population was of Western origin (35.8%), and half (47.8%) of the population had a low income (percentiles 0–33) (Table 1). Most (58.7%) used only oral blood glucose-lowering drugs and more than one third (39%) had a chronic comorbidity in the index year. In the first year after diagnosis, 36.0% of patients had uncontrolled (HbA1c >7% (>53 mmol/mol)). Analysis of SDOH in the regulated and unregulated HbA1c groups showed similar HbA1c means in the index year for the three income groups and for the Western versus non-Western origin groups (supplementary material B).

Except for smoking (25.8%), BMI (41.9%) and HbA1c (41.9%), proportion of missing data was less than 5%.

3.2. Validation sample

The validation sample was comparable to our study population and characteristics were similar for all included years (data for 2010 are shown in Table 2; for 2007–2013 see Supplementary material E).

3.3. Predictors of complications

Men, but not women, with a non-Western origin were more likely to develop a complication in the follow-up period of 6–12 years (HR (CI95%) 1.98 (1.19–3.30)) (Table 4) Overall, income in the year of diagnosis was not associated with the development of complications (Tables 3 and 4). Young adults, in particular men, with a mean HbA1c > 7% (>53 mmol/mol) in the first year after diagnosis were more likely

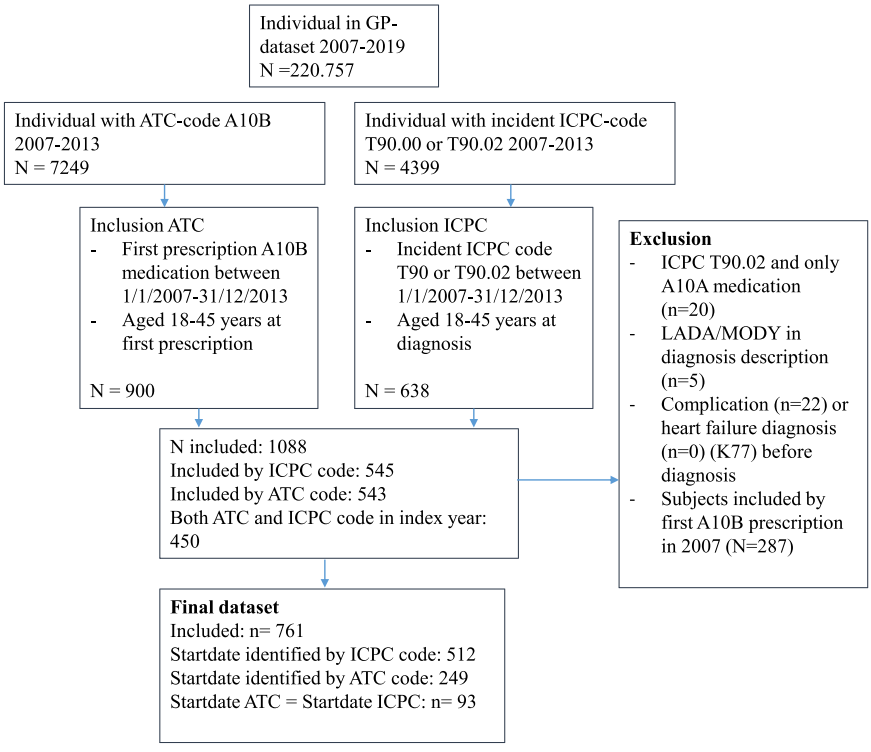

Fig. 1. Flow-chart of patient inclusion.

Table 1
Pooled baseline characteristics of 10 imputed datasets index year.

		First micro- or macrovascular complication	
	Total (N = 761)	With complication (n = 154)	Without complication (n = 607)
Social determinants of health			
Age in years	39 (33–42)	40 (35–43)	39 (33–42)
Men,	375 (49.3)	97.8 (63.5)	277.2 (45.7)
Standardized household income	363.4 (47.8)	74.9 (48.6)	288.5 (47.5)
Percentile	230.5 (30.3)	55.2 (35.8)	175.3 (28.9)
0–33	167.1 (22.0)	24 (15.6)	143.1 (23.6)
33–66			
66–100			
Ethnicity group	272.6 (37.4)	45.4 (29.5)	227.2 (37.4)
Dutch or Western origin	488.4 (64.2)	108.6 (70.5)	379,8 (62,6)
Non-Western origin	272.6 (35.8)	45.4 (29.5)	227.2 (37.4)
Origin	76 (10.0)	21 (13.6)	55 (9.1)
Dutch or other Western	92.2 (12.1)	15 (9.7)	77.2 (12.7)
Turkey	165.6 (21.8)	38.8 (25.2)	126.8 (20.9)
Morocco	154.8(20.3)	33.9 (22.0)	120.9 (19.9)
South-Asian			
Other non-Western			
Medical determinants			
Diabetes treatment class	200 (26.3)	33 (21.4)	167 (27.5)
Lifestyle	447 (58.7)	97.5 (63.3)	349.5 (57.6)
Oral blood glucose-lowering drugs	114 (15.0)	23.6 (15.3)	90.4 (14.9)
Insulin **and** oral blood glucose-lowering drugs			
Chronic comorbidity at diagnosis	296.5 (39.0)	60.9 (39.5)	235.6 (38.8)
Of which:	104 (13.7)	25(16.2)	78.9(13.0)
Hypertension	71.7 (9.4)	14.1 (9.1)	57.6(9.5)
Adiposity	79.1 (10.4)	10.1 (6.6)	69 (11.4)
Mental illness	45.6 (6.0)	< 10 (< 6.5)	< 10 (<1.6)
Chronic neck and back pain	11 (1.5)	< 10 (< 6.5)	< 10 (<1.6)
Arthrosis	12 (1.6)	< 10 (< 6.5)	< 10 (<1.6)
Alcohol abuse			
Complications diagnosis-specified	70 (9.2)	70 (45.4)	n/a
Retinopathy	18 (2.4)	18 (11.7)	
Nephropathy	15 (2.0)	15 (9.7)	
Polyneuropathy	24 (3.2)	24 (15.6)	
Cerebrovascular incident/TIA	41 (5.4)	41 (26.5)	
Ischemic heart disease	< 10 (<1.5)	< 10 (<6.5)	
Peripheral artery disease	< 10 (<1.5)	< 10 (<6.5)	
Cardiovascular or diabetes-related death			
HbA1c	48.62	52.12	47.55
mmol/mol	(43.20 −57.02)	(45.24–64.38)	(43.03–55.65)
%	6.6 (6.1–7.4)	6.9 (6.3–8.0)	6.5 (6.1–7.2)
Poorly controlled HbA1c	274 (36.0)	74.7 (48.5)	199.3 (32.8)
BMI kg/m^2	31.93 (6.18)	31.32 (5.13)	32.10 (6.43)
Smoking	286.2 (37.6)	42.8 (27.8)	243.4 (40.1)
Never	95.7 (12.6)	18.7 (12.1)	77 (12.7)
Former	379.1 (49.8)	92.6 (60.1)	286.5 (47.2)
Current			

Results are displayed n (%),mean ±SD or median (IQR)

to develop a complication (HR (CI95%) 1.72 (1.15–2.57)) (Model A, Table 3). Women were less likely to develop a complication (HR (CI95%) 0.59 (0.41–0.84)). Crude estimates (only adjusted for medical determinants) were comparable to the fully adjusted HRs (Supplementary material F).

No other effect modification than origin by sex was found (Supplementary material F).

3.4. Sub-analyses

The sub-analysis with first microvascular complication as outcome (model B) showed that young adults of non-Western origin (HR (CI95%) 2.23 (1.34–3.71)) were more likely to develop a complication, as were persons with a mean HbA1c > 7% (>53 mmol/mol) (HR: 1.76 95% CI: 1.04–2.99). Women (HR (CI95%): 0.50 (0.31–0.79)), and those treated with medication (HR (CI95%) A10B: HR: 1.95 (1.08–3.52) and: A10B+A10A: 2.38 (1.12–5.06)), were less likely to develop a complication.

The sub-analysis with first macrovascular complications as outcome (model C) showed that older age (HR (CI95%) 1.09 (1.03–1.15)) and current smokers in the index year (HR (CI95%) 2.19 (1.11–4.32)) were more likely to develop a macrovascular complication, while non-Western origin (HR (CI95%) 0.61 (0.37–1.00)) appeared to be protective.

Sub-analysis of young adults with non-Western origin showed no association between complications and country of origin or migration generation (Supplementary material C).

Our model discriminated with a C-index of 0.64 and an optimism-corrected C-index of 0.62, indicating moderate to good discriminative ability. Pooled intercept and slope of the calibration curves of the model were 0.054 and 0.95, and 0.24 and 0.70 when optimism-corrected, respectively, indicating reasonably good calibration (Table 3).

Table 2
Baseline characteristics validation sample.

	Study cohort 2010 (N = 127)	Validation sample 2010 (N = 622)
Age (median ± IQR)	38(33–42)	39(33–42)
men n (%)	60(47.2)	299(48.1)
Diabetes treatment class n (%)	36 (28.4)	N/A
Lifestyle	76 (59.8)*	550(88.4)*
Oral blood glucose-lowering drugs	15(11.8)	72(11.6)
Insulin **and** oral blood glucose-lowering drugs		
Standardized household income n (%)	58 (45.7)	283 (45.5)
0–33 percentile	34 (26.8)	195 (31.4)
33–66 percentile	28 (22.0)	133 (21.4)
66–100 percentile	7 (5.5)	12 (1.9)
Missing		
Ethnicity group n (%)	79 (62.2)	434 (69.7)
Non-Western origin	48 (37.8)	188 (30.3)
Origin	10 (7.9)	83 (13.3)
Dutch or other Western	14 (11.0)	55 (8.8)
Turkey	26 (20.5)	146 (23.5)
Morocco	29 (22.8)	150 (24.1)
South-Asian		
Other non-Western		

* indicates significantly different from validation sample 2010 $p < 0.05$. If no missing values are reported, number of missing values = 0

4. Discussion

4.1. Summary of the main findings

The results of this study suggest that in young adults with type 2 diabetes in an urban region, men with non-Western origin were more likely to develop diabetes complications. Being women was relatively protective. For microvascular complications only, a non-Western origin also emerged as a possible risk factor in both sexes. Income was not associated with developing diabetes complications in addition to the medical determinants. Overall, poor regulated HbA1c in the first year after diagnosis appeared to be the most important risk factor.

Prevalence of diabetes is undeniably associated with socio-economic context [10,26]. Independent from HbA1c-regulation, being of non-Western origin appeared to be a risk factor for the development of complications in young men, but not women. Country of origin or migration generation was not explanatory. The higher risk might be explained by higher diabetes prevalence in men [10,31] or

Table 3
Risk estimates of developing micro- or macrovascular complications in young adults with type 2 diabetes 6–12 years after diagnosis†.

	Main outcome		Sub-analysis	
	Model A: first micro OR macrovascular complication		Model B: first microvascular complication	Model C: first macrovascular complication
	Pooled data after MI (n = 761, complications = 154) Hazard ratio (95% CI)	Complete case analysis (n = 574, complications 154) Hazard ratio (95% CI)	Pooled data after MI (n = 761, complications = 98) Hazard ratio (95% CI)	Pooled data after MI (n = 761, complications = 72) Hazard ratio (95% CI)
SDOH				
Sex (women)	0.59 (0.41–0.84)*	0.51 (0.30 – 0.88) *	0.50 (0.31 – 0.79)*	0.83 (0.50 – 1.38)
Age (years)	1.03 (1.00–1.06)	1.02 (0.97 – 1.07)	0.99 (0.96 –1.03)	1.09 (1.03 – 1.15)*
Standardized household	1.24 (0.86 – 1.79)	1.18 (0.68 – 2.02)	1.29 (0.80.–2.06)	1.18 (0.70 – 1.97)
income (Reference: 0–33 percentile)	0.78 (0.47 – 1.28)	0.94 (0.49 – 1.80)	1.12 (0.62 – 2.03)	0.50 (0.23 –1.10)
33–66 percentile				
66–100 percentile				
Ethnicity group	1.29 (0.87 – 1.90)	1.79 (0.96 –3.35)	2.23 (1.34 – 3.71)*	0.61 (0.37 – 1.00)*
Non-Western (reference: Western)				
Medical determinants index year				
Diabetes treatment class	1.40 (0.93–2.11)	1.43 (0.74 – 2.76)	1.95 (1.08 – 3.52)*	N/A
(reference: no medication)	1.25 (0.70 – 2.22)	0.72 (0.24 – 2.16)	2.38 (1.12 – 5.06)*	N/A
A10B medication				
Combination of A10B and A10A				
HbA1c> 7% (>53 mmol/ mol)	1.72 (1.15 – 2.57)*	2.67 (1.63 – 4.37)*	1.76 (1.04 – 2.99)*	N/A
(reference HbA1c ≤7% (≤53 mmol/mol)				
Mean BMI	1.00 (0.97 – 1.03)	0.99 (0.95 – 1.04)	N/A	N/A
Co-morbidity (yes)	1.10 (0.78 – 1.54)	0.81 (0.50 – 1.34)	N/A	N/A
Smoking (reference: never)	1.17 (0.59 – 2.35)	1.53 (0.66 – 3.55)	1.45 (0.61 – 3.47)	1.04 (0.19 – 5.81)
Former	1.51 (0.98 – 2.31)	1.75 (0.99 – 3.12)	1.38 (0.79 – 2.39)	19. (1.11 – 4.32)*
Current				
*indicates statistically significant compared to reference category $p < 0.05$				
† all displayed HR are adjusted for the effects of all other determinants in the model				
Internal validation				
C-index optimism-corrected	0.62 (0.64)		0.66 (0.67)	0.67 (0.68)
(non-corrected)	0.24 (0.054)		0.26 (0.39)	0.12 (−0.02)
Calibration curve	0.70 (0.95)		0.73 (0.99)	0.86 (1.02)
optimism-corrected (non-corrected)				
Intercept				
Slope				

non-measured factors as genetic predisposition [5], adaptation to a Western (sedentary) lifestyle or other cultural factors [10]. Correspondingly, the sub-analyses suggested that people of non-Western origin of both sexes were more likely to develop microvascular complications, while in contrast, for macrovascular complications non-Western origin appeared to be protective. We hypothesize that longer follow-up time and larger sample size may reveal more conclusive results to distinguish the risk for macrovascular- and microvascular complications separately.

Sex differences may be explained by behavioral or biological factors [32], which were not quantified in this study. Another explanation is that in our study the number of events in women was too little to reveal the same risk factors in both sexes, in which poor recognition of cardiovascular disease in women may also play a role [32].

Income was, in this population with a relatively large percentage of low income, not associated with the development of complications. Our results suggest that when HbA1c is regulated, biological or cultural factors are of greater importance than income for the development of complications within both native-Dutch as people with non-Western ethnicity.

Irrespective of SDOH and sex, HbA1c regulation appeared to be an important predictor of the early development of diabetes-complications in young adults and proactive disease management should therefore primarily focus on HbA1c regulation in all at-risk populations. In agreement with our results, previous studies have highlighted the importance of the first year after diagnosis on the subsequent course of HbA1c-control [3, 8, 9, 24, 33, 34]. HbA1c-regulation is more proximate in the causal pathway to diabetes complications than are SDOH, which may lead to a stronger association in the main analysis, especially with a small number of events. Macrovascular complications were only associated with older age and smoking, suggesting that diabetes regulation plays a less important role in the development of macrovascular complications. However, again considering the young adult population, a longer follow-up may reveal different results.

4.2. *Strengths and limitations*

When using routinely collected data, missing data and data accuracy are common problems [15,35]. The use of MI for the handling of missing data could cause underestimation of the effects, as missing data could indicate either a no-show of the (non-adherent) patient or no clinical indication to measure or register [35]. This implies that the effects of ethnicity and income on the outcomes might have been underestimated in our study. However, our analysis showed a high accuracy and only low levels of missing data for the SDOH.

To improve data accuracy a combination of diagnosis and medication registers was used to identify type 2 diabetes [15]. This enlarged our cohort, although also introduced possible bias. As the prescription of medication is often initially delayed, year of incidence might be less precise in our study population. Furthermore, in some individual cases, metformin may occasionally be prescribed in other disease such as type 1 diabetes or polycystic ovary syndrome, although in such cases the metabolic syndrome is often present.

The internal validation of our model can be considered a strength of

Table 4
Risk estimates of developing micro-or macrovascular complications in young adults with type 2 diabetes 6–12 years after diagnosis, stratified by sex [†].

	Hazard ratio (95%) (confidence interval)			
	Men N = 375 n complications= 99	p-value	Women N = 386 n complications= 58	p-value
Age (years)	**1.04 (1.00–1.08)**	**0.029**	1.00 (0.96–1.05)	0.945
HbA1c > 7% (>53 mmol/mol) (reference HbA1c ≤7% (≤53 mmol/mol)	**2.02 (1.291–3.156)**	**0.002**	1.59 (0.83–3.04)	0.163
Ethnicity group Non-Western (reference: Western)	**1.98 (1.194–3.295)**	**0.008**	0.67 (0.38–1.18)	0.164
Standardized household income (reference: 0–33 percentile)	1.08 (0.68–1.736)	0.737	1.54 (0.85–2.78)	0.153
33–66 percentile	0.74 (0.40–1.36)	0.331	0.80 (0.35–1.83)	0.601
66–100 percentile				

[†] adjusted for: age, HbA1c regulation, ethnicity, income Baseline characteristics and crude estimates are presented in supplementary file F

our study [5,27], as it indicates representativeness and accuracy [27]. However, bootstrapping technique was used: drawing random samples from an imputed dataset might result in bootstrapping potentially non-realistic imputation data, resulting in overfitting [29]. Therefore, the validation outcomes should be interpreted with care. Further steps to improve validation might be, 1) to enlarge the study sample and follow-up period, and 2) carry out an external validation to determine reproducibility.

Lastly, in terms of generalizability, it should be noted that our study was purposely conducted in a socio-economically diverse urban area, and our results are only relevant to comparable healthcare systems and socio-economic compositions.

In conclusion, the results of this study suggested that in young adults with type 2 diabetes in a urbanized population, men with Non-Western origin and those with poorly regulated HbA1c in the first year after diagnosis had the highest risk on developing diabetes-related complications. Being women was protective. This study re-emphasizes the importance of adequate HbA1c-regulation from the moment of diagnosis. Regarding sex and ethnicity differences, our results may guide to more sex- or cultural-specific (preventive) interventions in communities.

Ethics approval

This study involves human participants but an Ethics Committee exempted this study. Ethics Committee Leiden-The Hague -Delft ID 19-035 approval November 2020.

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Contributorship statement

RV, TH, EN designed the study. JS conducted database management quality assurance. TH & EN carried out data management and data analysis; EN, TH, RV, JS interpreted the data. EN wrote the first draft of and revised the manuscript, incorporating contributions from co-authors. RV, JS, TH and MN critically revised the manuscript. All authors agreed on submission and are joint guarantors of this work.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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Data sharing statement

As data contain personal health information and individual socio-economic information, data were strictly used under license for the current study and are therefore not publicly available.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.pcd.2023.01.002.

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