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Educational inequalities in clinical presentation and pharmacological treatment of early type 2 diabetes: A Danish prevalence study

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ABSTRACT

Aims: To examine how educational attainment impacts clinical presentation and pharmacological treatment at type 2 diabetes (T2D) diagnosis.
Methods: Cross-sectional analysis of 10,020 individuals with recently diagnosed T2D enrolled in the Danish prospective DD2 cohort. Sex- and age-adjusted prevalence ratios (aPRs) for detailed clinical characteristics and pharmacotherapy were computed.
Results: In total, 31 % had low, 50 % had moderate, and 19 % had high educational level. Individuals with low rather than high educational level were more often obese (58 % *vs* 49 %, aPR 1.20 [95 % CI 1.14–1.28]); had less healthy lifestyles (current smokers: 22 % *vs* 15 %, aPR 1.53 [1.32–1.76]); sedentary activity level: 21 % *vs* 15 %, aPR 1.36 [1.20–1.55]); and had more often cardiovascular (23 % *vs*. 17 %, PR 1.30 [1.16–1.46]) and microvascular complications (16 % *vs* 13 %, aPR 1.18 [1.02–1.35]). Low education associated with higher triglycerides, more insulin resistance, and poorer kidney function, whereas HbA1c, blood pressure, and LDL cholesterol were identical. The use of medications with cardiovascular benefits and newer organ-protective diabetes medications was similar to, or higher than, that in individuals with high education.
Conclusions: Awareness of the impact of social and educational determinants on T2D presentation at diagnosis is essential to improve treatment and prognosis.

1. Introduction

Socioeconomic position, defined according to education, income, or occupation, is a key determinant of health outcomes [1–3]. Among individuals with type 2 diabetes, low socioeconomic position is associated with an elevated risk of subsequent cardiovascular disease (CVD) [4,5],

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microvascular complications [6], and mortality [7,8]. However, whether social inequality in type 2 diabetes prognosis might be associated with more severe clinical presentation at the time of type 2 diabetes onset, or with inadequate use of preventive pharmacotherapy, is less clear.

Individuals with longstanding type 2 diabetes and lower rather than higher socioeconomic position are associated with less healthy lifestyles in terms of smoking, alcohol consumption, and physical activity; more obesity; and a poorer metabolic profile [9–13]. Other studies have found a similar use of lipid-lowering and antihypertensive drugs across socioeconomic positions, thus suggesting a potential treatment insufficiency if baseline CVD risk is higher in people with lower socioeconomic position [11,12]. Recent studies have also suggested that individuals with type 2 diabetes and lower socioeconomic position might be less likely to receive newer cardiorenal protective glucose-lowering drugs, including sodium-glucose cotransporter-2 inhibitors (SGLT-2i) and glucagon-like peptide-1 receptor agonists (GLP-1RA) [14].

Previous studies examining type 2 diabetes clinical profiles and pharmacotherapy across socioeconomic position groups have been small ($N < 700$) and hospital-based, and have often focused on individuals with a diabetes duration of 10 years or more [9–13]. Limited data are available on individuals with early type 2 diabetes, who might have the greatest potential to benefit from preventive interventions [15]. Prior socioeconomic position studies have often relied on self-reported socioeconomic measures [9,11–13] and have lacked granular data on important health determinants, such as lifestyle behaviors, anthropometric measures, and biomarkers [4,14]. No prior large-scale study based on nationwide data in a setting with free healthcare access and low personal medication costs has examined in detail the clinical and treatment characteristics in individuals with recently diagnosed type 2 diabetes, according to individual-level socioeconomic factors.

Achieved educational level is an important proxy measure of socioeconomic position and is a key risk factor of chronic disease in later life [16]. We performed a detailed investigation of demographic, lifestyle, clinical and metabolic characteristics, and use of medications with cardiovascular benefits, according to educational level, among individuals with recently diagnosed type 2 diabetes in Denmark.

2. Methods

2.1. Design and the DD2 cohort

We designed a cross-sectional study of participants in the Danish Centre for Strategic Research in Type 2 Diabetes (DD2) cohort [17]. The DD2 cohort consists of more than 10,000 individuals with recently diagnosed type 2 diabetes, prospectively enrolled at general practitioners'(GPs) offices or diabetes hospital outpatient clinics since 2010. Eligible participants are individuals aged 18 years or older who have received a recent type 2 diabetes diagnosis in routine clinical care, with the aim to enroll newly diagnosed patients with a short duration of type 2 diabetes (median diabetes duration in the current cohort 1.3 years, quartiles 0.4–2.9 years). Individuals may be included at diagnosis or during any subsequent contact with their treating physician (GPs or specialists). At enrolment, participants complete an online questionnaire on lifestyle behaviors, height, weight history, and family history of diabetes; undergo a clinical examination of weight, waist and hip circumference, and resting heart rate; and provide blood and urine samples for storage in the DD2 biobank [17]. Once enrolled in DD2, participants are followed through registries and receive routine clinical care from their general practitioner and/or specialist, unaffected by participation.

2.2. Setting, data sources, and linkage

In Denmark, free, tax-funded healthcare is provided to all residents including reimbursement of prescribed medication. At birth or immigration, all Danish residents receive a unique civil registration number, which enables the recording of individual-level health care data and virtually complete follow-up [18]. We linked DD2 cohort data to several Danish registries to procure historical data before DD2 enrolment and subsequent follow-up data on each participant (Supplementary Table 1). We retrieved information on sex, citizenship, and cohabitation from the Danish Civil Registration System [18]. Hospital admission and discharge dates, diagnosis codes, and procedure codes were retrieved from the Danish National Patient Registry [19], covering all Danish hospitals (diagnoses made exclusively by GPs are not available in Danish registries). Drug prescription data from community pharmacies in Denmark (covering GPs and specialists) were retrieved from the Danish National Prescription Registry [20]. Educational data were retrieved from the Attainment Register [21], income data were retrieved from Family Income Statistics [22], and employment data were retrieved from the Danish Register for Evaluation of Marginalization database [23]. Additional information on smoking, blood pressure, height, and weight was retrieved from the Danish Adult Diabetes Registry [24]. Routine laboratory clinical care biomarkers (covering blood and urine tests from GPs and specialists) were retrieved from the Danish Adult Diabetes Registry and Nationwide Register of Laboratory Results for Research [25]. Covariate definitions are further described below.

2.3. Study cohort

We included 10,139 participants enrolled in the DD2 cohort from 2010 to 2021. We excluded participants who did not reside in Denmark for at least 1 year before enrolment to ensure baseline data availability. Furthermore, participants without any available information on educational level before enrolment were excluded (Fig. 1).

2.4. Educational level

Educational level at enrolment was grouped according to International Standard Classification of Education (ISCED) level into low (1–2), moderate, (3–4), or high (≥5) education for participants born in or before 1960; or low (1–2), moderate (3–5), or high (≥6) education for participants born after 1960 [26]. We used the birth year of 1960 as the cutoff because vast structural changes in the Danish educational system, including increased compulsory schooling, occurred after 1960 [27]. Supplementary Tables 2–3 describe Danish educational levels in relation to international standards.

2.5. Outcomes

We included the following characteristics as outcomes: lifestyle behaviours, anthropometric measures, metabolic risk factors, presence of CVD and microvascular complications, and use of selected medications near the time of diagnosis (Supplementary Table 4). For lifestyle behaviours, we focused on current smoking; excessive alcohol consumption, defined as ≥14 units of alcohol per week for women and ≥21 units of alcohol per week for men; and having a leisure time physical activity level of sedentary, defined primarily as reading, watching television, or other sedentary activities. We defined obesity as BMI ≥30 kg/m^2, and central obesity as waist circumference ≥88 or 102 cm for women or men, respectively. Based on common guideline recommendations for metabolic and vascular risk factor targets, we assessed the presence of LDL cholesterol levels ≥2.6 mmol/L, triglyceride levels ≥1.7 mmol/L, and HbA1c levels ≥7.0 % (53 mmol/mol). We also examined the presence of a previously defined hyperinsulinemic type 2 diabetes subgroup according to the homeostasis model assessment-2 (HOMA2) (i.e., HOMA2 beta cell function ≥115.3 % and HOMA2 insulin sensitivity <63.5 %, Supplementary Table 4) [28]. CVD included hospital and procedure codes for ischaemic heart disease, angina pectoris, heart failure, stroke, and peripheral arterial disease recorded up to 10 years before DD2 enrolment, and hypertension included diagnosis codes or

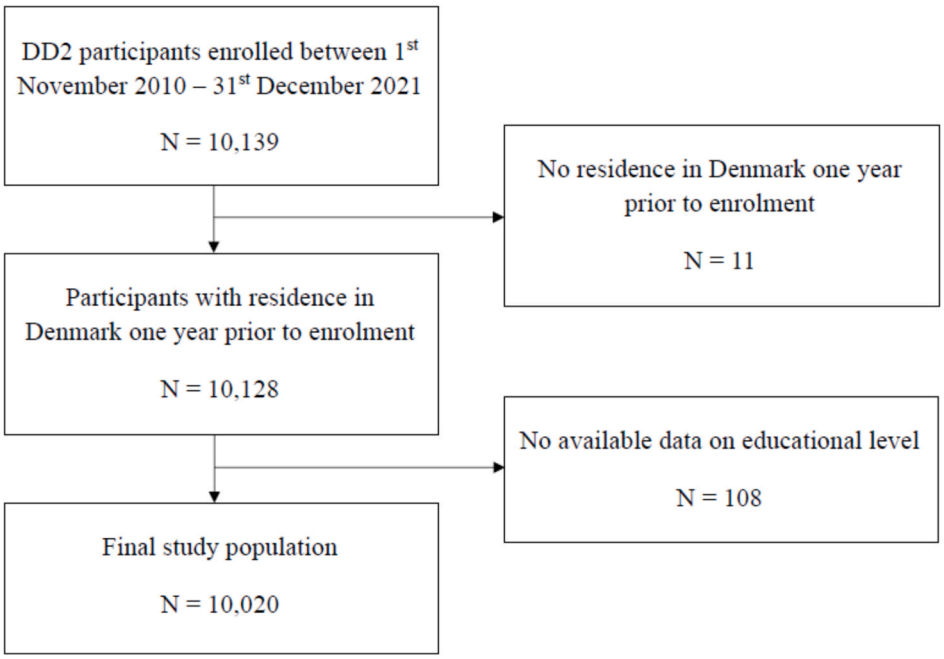

Fig. 1. Flowchart of the study cohort.

use of an antihypertensive medication. Microvascular complications included a composite outcome of neuropathy, eye disease, and nephropathy, defined according to hospital diagnosis and procedure codes, as well as estimated glomerular filtration rate (eGFR) levels (used for nephropathy). Selected medications with cardiovascular benefits included the use of angiotensin-converting-enzyme inhibitors (ACE)/angiotensin II receptor antagonists (ARBs), statins, SGLT-2i, and/or GLP-1RAs during a window of 1 year before to 1 year after DD2 enrolment.

2.6. Covariates

To characterise the type 2 diabetes cohort, we included data from the Danish nationwide registries (Supplementary Table 4). Income was assessed as the 3-year mean household-level liquid assets at DD2 enrolment and was subsequently categorised according to income quartile into low (<P25), moderate (P25–P75), or high (>P75). Employment status was defined according to social benefits registrations in the year preceding DD2 enrolment and was categorised as employed, unemployed, retired, or unknown (Supplementary Table 5). The duration of diabetes was defined as the number of years from the first diabetes record until DD2 enrolment. The first diabetes record was defined as a hospital diagnosis code for diabetes, a redeemed glucose-lowering drug prescription, an HbA1c measurement ≥48 mmol/mol, registration in the Danish Adult Diabetes Registry, or enrolment in the DD2 cohort. The diabetes duration was zero for individuals with no other recorded diabetes event prior to DD2 enrolment. Information on the use of other glucose-lowering drugs, loop diuretics, anticoagulants, and thromboprophylaxis were retrieved within one year preceding DD2 enrolment.

2.7. Statistical analysis

We calculated medians and quartiles for continuous variables and counts (n) and proportions (%) for categorical variables. We used a Poisson regression model with robust estimates to calculate crude and age- and sex-adjusted prevalence ratios (aPRs) for the following clinical outcomes: lifestyle behaviours, anthropometric measures, metabolic and vascular risk factors, CVD and microvascular complications, and use of selected medications. Individuals with a high education served as the reference group. Analyses were stratified by pre-existing CVD and obesity at enrolment, because those factors might have influenced the choice of glucose-lowering and other preventive medications. The proportions of missing data are shown in Supplementary Table 6.

All data management and statistical analyses were performed in RStudio 2023.09.1 + 494 for Windows.

2.8. Ethics

All DD2 participants provided written informed consent at enrolment. The Danish Regional Ethics Committee on Health Research for Southern Denmark (record no. S-20100082) and the Danish Data Protection Agency (record nos. 2008-58-0035 and 2016-051-000001/2514) approved the DD2 project.

3. Results

3.1. Demographic and socioeconomic characteristics

A total of 10,139 individuals were enrolled in DD2 between 2010 and 2021 (Fig. 1). After restriction to individuals with residence in Denmark and available educational level data, our study population included 10,020 individuals. In total, 3102 (31 %) had low education, 5002 (50 %) had moderate education, and 1916 (19 %) had high education.

Individuals with low education were slightly older than those with moderate or high education (low education: median 63 years; moderate education: median 60 years; high education: median 61 years) and had a higher percentage of women (low: 47 %; moderate: 37 %; high: 43 %). Low educational level was associated with a slightly longer median diabetes duration than moderate or high educational level (low: 1.3 years; moderate: 1.2 years; high: 1.1 years). Individuals with low education were also more likely to live alone (low: 39 %; moderate: 31 %; high: 33 %), to have low income (low: 36 %; moderate: 22 %; high: 17 %), and to be unemployed (low: 30 %; moderate: 21 %; high: 13 %) or retired from the workforce (low: 47 %; moderate: 38 %; high: 37 %) than individuals with moderate or high education.

3.2. Clinical presentation

3.2.1. Lifestyle and anthropometric characteristics

Individuals with lower education had a higher prevalence of current smoking (low education: 22 %; moderate education: 18 %; high education: 15 %; aPR of 1.53 [95 % CI 1.32–1.76] for low *vs* high; aPR of 1.20 [95 % CI 1.04–1.38] for moderate *vs* high) and tendency to report a sedentary leisure-time activity level (low: 21 %; moderate: 17 %; high: 15 %; aPR of 1.36 [95 % CI 1.20–1.55] for low *vs* high; aPR of 1.12 [95 % CI 0.99–1.26] for moderate *vs* high). The proportion with obesity, i.e. BMI $\geq$ 30 kg/m^2, was generally high, and obesity was more common among individuals with lower education (low: 58 %; moderate: 55 %; high: 49 %; aPR of 1.20 [95 % CI 1.14–1.28] for low *vs* high; aPR of 1.11 [95 % CI 1.05–1.07] for moderate *vs* high). A similar pattern was observed for greater waist circumference in individuals with lower education (Fig. 2).

3.2.2. Metabolic and vascular risk factors

Across all educational level groups, we observed similar median HbA1c levels (~48 mmol/mol [6.5 %] in all three groups), LDL cholesterol levels (~2.2 mmol/L in all three groups), and systolic and diastolic blood pressure (~130/80 mmHg in all three groups) (Table 1). In contrast, lower education was associated with a higher prevalence of triglyceride levels $\geq$1.7 mmol/L (low education: 53 %; moderate education: 51 %; high education: 47 %; aPR of 1.15 [95 % CI 1.08–1.22] for low *vs* high; aPR of 1.08 [95 % CI 1.02–1.15] for moderate *vs* high) and hyperinsulinemic type 2 diabetes (low: 32 %; moderate: 28 %; high: 26 %; aPR of 1.18 [95 % CI 1.04, 1.34] for low *vs* high; aPR of 1.08 [95 % CI 0.96–1.23] for moderate *vs* high) (Fig. 2).

3.2.3. Comorbidities and type 2 diabetes complications

At enrolment, individuals with lower education had a higher prevalence of pre-existing CVD (low education: 23 %; moderate education: 20 %; high education: 17 %; aPR of 1.30 [95 % CI 1.16–1.46] for low *vs* high; aPR of 1.21 [95 % CI 1.08–1.35] for moderate *vs* high) (Fig. 3 and Table 1). Lower education was also associated with a higher prevalence of any microvascular complication (low: 16 %; moderate: 13 %; high: 13 %; aPR of 1.18 [95 % CI 1.02–1.35] for low *vs* high; aPR of 1.06 [95 % CI 0.93–1.21] for moderate *vs* high), among which the most common complication was nephropathy (low: 9.6 %; moderate: 7.2 %; high: 6.7 %; aPR of 1.16 [95 % CI 0.96–1.41] for low *vs* high; aPR of 1.15 [95 % CI 0.95–1.39] for moderate *vs* high). Examination of more sensitive biomarkers of kidney disease available in both primary and secondary care indicated a similar association between lower educational level and higher prevalence of eGFR levels <60 mL/min/1.73 m^2 (e.g., aPR of 1.20 [95 % CI 0.98–1.48] for low *vs* high), but not of urine albumin-creatinine ratio measurements >30 mg/g (~20 % in all three groups) (Fig. 3).

3.3. Use of medications

Overall, slightly higher use of any glucose-lowering drug treatment was observed in the low education (87 %) and moderate education (87 %) groups than in the high education (84 %) group (Table 1). In general, GLP-1RA and SGLT-2i use was modest in our cohort. GLP-1RAs were used slightly more frequently in individuals with lower education (low education: 9.5 %; moderate education: 11 %; high education: 8.8 %; aPR of 1.13 [95 % CI 0.95–1.35] for low *vs* high, aPR of 1.17 [95 % CI 0.99–1.38] for moderate *vs* high). In contrast, the use of SGLT-2i was less frequent in individuals with lower education (low: 5.4 %; moderate: 6.6

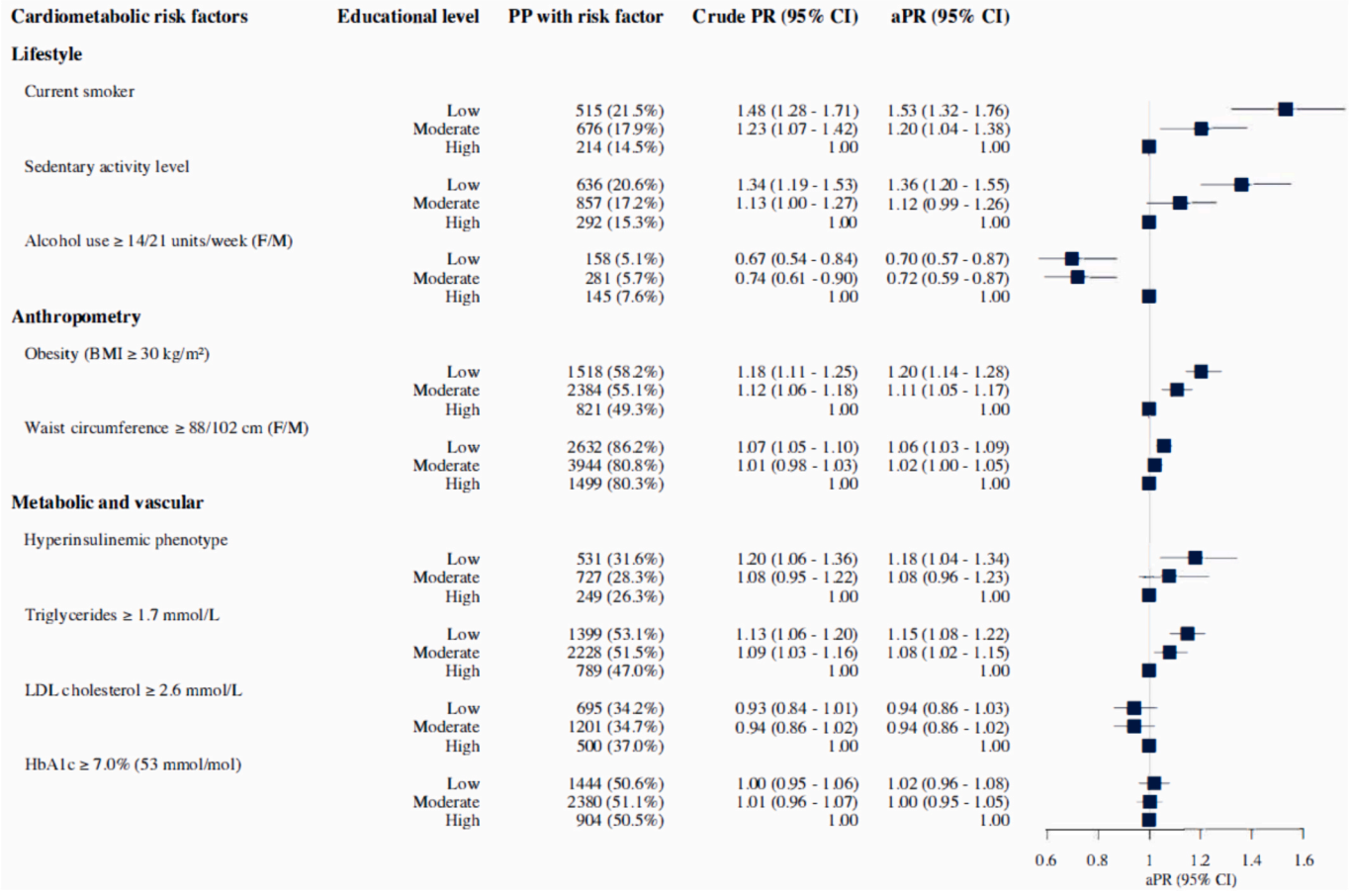

Fig. 2. Crude and adjusted prevalence ratios for cardiometabolic risk factors associated with educational level, with high educational level as the reference.

Table 1
Baseline characteristics of patients with recently diagnosed type 2 diabetes by educational level.

Covariates Total, N (%)	Low N = 3102 (31 %)	Moderate N = 5002 (50 %)	High N = 1916 (19 %)	Overall N = 10,020 (100 %)
Demographics				
Age, years	63.1 (54.2–70.5)	60.3 (51.5–67.5)	61.3 (53.0–68.0)	61.4 (52.5–68.4)
Women	1468 (47 %)	1871 (37 %)	825 (43 %)	4164 (42 %)
Income (quartiles)				
Low	968 (36 %)	949 (22 %)	283 (17 %)	2200 (25 %)
Moderate	1300 (48 %)	2354 (54 %)	744 (44 %)	4398 (50 %)
High	431 (16 %)	1089 (25 %)	679 (40 %)	2199 (25 %)
Employment				
Employed	722 (23 %)	2081 (42 %)	934 (50 %)	3737 (38 %)
Retired	1450 (47 %)	1865 (38 %)	698 (37 %)	4013 (40 %)
Unemployed	922 (30 %)	1020 (21 %)	253 (13 %)	2195 (22 %)
Living alone	1213 (39 %)	1549 (31 %)	632 (33 %)	3394 (34 %)
T2DM duration, years	1.3 (0.4–2.9)	1.2 (0.3–2.7)	1.1 (0.4–2.7)	1.2 (0.4–2.8)
Lifestyle behaviours				
Smoking				
Never	1011 (42 %)	1759 (46 %)	756 (51 %)	3526 (46 %)
Former	873 (36 %)	1349 (36 %)	503 (34 %)	2725 (36 %)
Current	515 (22 %)	676 (18 %)	214 (15 %)	1405 (18 %)
≥14/21 alcohol units/week (F/M)	158 (5.1 %)	281 (5.7 %)	145 (7.6 %)	584 (5.9 %)
Leisure-time physical activity during the past year[a]				
Sedentary	636 (21 %)	857 (17 %)	292 (15 %)	1785 (18 %)
Some physical activity at least 4 h/week	1982 (64 %)	3094 (62 %)	1151 (60 %)	6227 (62 %)
Moderate physical activity at least 4 h/week	454 (15 %)	991 (20 %)	444 (23 %)	1889 (19 %)
Vigorous physical activity several times/week	22 (0.7 %)	36 (0.7 %)	23 (1.2 %)	81 (0.8 %)
Anthropometry				
Weight gain since 20 years of age, kg	30 (20–42)	29.0 (20–40)	28.0 (18–39)	29.0 (19–40)
BMI (kg/m^2)				
<18.5	24 (0.9 %)	26 (0.6 %)	13 (0.8 %)	63 (0.7 %)
18.5–24.9	252 (9.7 %)	491 (11 %)	253 (15 %)	996 (12 %)
25–29.9	815 (31 %)	1428 (33 %)	579 (35 %)	2822 (33 %)
≥30	1518 (58 %)	2384 (55 %)	821 (49 %)	4723 (55 %)
Waist circumference, cm	109 (102–118)	108 (101–116)	107 (100–115)	108 (101–116)
Waist circumference ≥ 88/102 cm (F/M)	2632 (86 %)	3944 (81 %)	1499 (80 %)	8075 (82 %)
Metabolic and vascular risk factors				
Systolic blood pressure, mmHg	130 (124–140)	130 (124–140)	130 (122–140)	130 (124–140)
Diastolic blood pressure, mmHg	80 (74–85)	80 (75–86)	80 (74–86)	80 (74–86)
HDL cholesterol, mmol/L	1.2 (1.0–1.4)	1.2 (1.0–1.4)	1.2 (1.0–1.5)	1.2 (1.0–1.4)
LDL cholesterol, mmol/L	2.1 (1.6–2.8)	2.2 (1.7–2.9)	2.2 (1.7–2.9)	2.2 (1.7–2.9)
LDL cholesterol ≥ 2.6 mmol/L	695 (34 %)	1201 (35 %)	500 (37 %)	2396 (35 %)
Triglycerides, mmol/L	1.7 (1.2–2.5)	1.7 (1.2–2.5)	1.6 (1.1–2.3)	1.7 (1.2–2.4)
Triglycerides ≥ 1.7 mmol/l	1399 (53 %)	2228 (51 %)	789 (47 %)	4416 (51 %)
HbA1c, mmol/mol	48 (43–54)	48 (43–54)	48 (43–54)	48 (43–54)
HbA1c, %	6.5 (6.1–7.1)	6.5 (6.1–7.1)	6.5 (6.1–7.1)	6.5 (6.1–7.1)
HbA1c ≥ 7 % (53 mmol/mol)	808 (28 %)	1336 (29 %)	506 (28 %)	2650 (29 %)
eGFR, mL/min/1.73 m^2	88 (73–98)	92 (78–101)	90 (79–99)	90 (77–100)
eGFR < 60 mL/min/1.73 m^2	266 (10 %)	309 (7.1 %)	108 (6.3 %)	683 (7.8 %)
UACR, mg/g	10 (5–24)	9 (5–24)	9 (5–22)	10 (5–24)
UACR ≥ 30 mg/g	382 (21 %)	644 (20 %)	246 (20 %)	1272 (20 %)
C-peptide, pmol/L	1218 (900–1619)	1151 (853–1558)	1095 (809–1454)	1155 (859–1561)
HOMA2-defined T2DM subgroups				
Classical	1019 (61 %)	1551 (60 %)	575 (61 %)	3145 (61 %)
Hyperinsulinemic	531 (32 %)	727 (28 %)	249 (26 %)	1507 (29 %)
Insulinopenic	125 (7.4 %)	279 (11 %)	116 (12 %)	520 (10 %)
Comorbidities				
Hypertension	2301 (74 %)	3547 (71 %)	1278 (67 %)	7126 (71 %)
Cardiovascular disease	707 (23 %)	1008 (20 %)	324 (17 %)	2039 (20 %)
Myocardial infarction	170 (5.5 %)	231 (4.6 %)	69 (3.6 %)	470 (4.7 %)
Angina pectoris	284 (9.2 %)	410 (8.2 %)	133 (6.9 %)	827 (8.3 %)
Heart failure	128 (4.1 %)	188 (3.8 %)	52 (2.7 %)	368 (3.7 %)
Stroke	194 (6.3 %)	280 (5.6 %)	93 (4.9 %)	567 (5.7 %)
Peripheral arterial disease	135 (4.4 %)	192 (3.8 %)	54 (2.8 %)	381 (3.8 %)
Atrial fibrillation	204 (6.6 %)	292 (5.8 %)	136 (7.1 %)	632 (6.3 %)
Microvascular complications	508 (16 %)	665 (13 %)	248 (13 %)	1421 (14 %)
Nephropathy	298 (9.6 %)	360 (7.2 %)	128 (6.7 %)	786 (7.8 %)
Eye disease	240 (7.7 %)	293 (5.9 %)	132 (6.9 %)	665 (6.6 %)
Neuropathy	230 (7.4 %)	332 (6.6 %)	98 (5.1 %)	660 (6.6 %)
Chronic pulmonary disease	290 (9.3 %)	293 (5.9 %)	115 (6.0 %)	698 (7.0 %)
Hospital-diagnosed obesity	454 (15 %)	620 (12 %)	215 (11 %)	1289 (13 %)
Cancer	226 (7.3 %)	310 (6.2 %)	125 (6.5 %)	661 (6.6 %)
Alcohol-related diseases	86 (2.8 %)	126 (2.5 %)	57 (3.0 %)	269 (2.7 %)
Pharmacological treatment				
GLD treatment	2707 (87 %)	4347 (87 %)	1618 (84 %)	8672 (87 %)
GLD monotherapy	1950 (63 %)	3076 (61 %)	1161 (61 %)	6187 (62 %)
GLD polytherapy	757 (24 %)	1271 (25 %)	457 (24 %)	2485 (25 %)
Metformin	2604 (84 %)	4176 (83 %)	1552 (81 %)	8332 (83 %)

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Table 1 (*continued*)

Covariates Total, N (%)	Low N = 3102 (31 %)	Moderate N = 5002 (50 %)	High N = 1916 (19 %)	Overall N = 10,020 (100 %)
Sulfonylurea	195 (6.3 %)	248 (5.0 %)	90 (4.7 %)	533 (5.3 %)
DPP-IV inhibitors	279 (9.0 %)	448 (9.0 %)	172 (9.0 %)	899 (9.0 %)
Insulin	210 (6.8 %)	322 (6.4 %)	115 (6.0 %)	647 (6.5 %)
GLP-1RAs	294 (9.5 %)	533 (11 %)	168 (8.8 %)	995 (9.9 %)
SGLT-2is	169 (5.4 %)	328 (6.6 %)	131 (6.8 %)	628 (6.3 %)
Statins	2462 (79 %)	3841 (77 %)	1410 (74 %)	7713 (77 %)
ACE/ARBs	2037 (66 %)	3224 (64 %)	1174 (61 %)	6435 (64 %)
Beta blockers	800 (26 %)	1166 (23 %)	387 (20 %)	2353 (23 %)
Calcium channel inhibitors	888 (29 %)	1357 (27 %)	477 (25 %)	2722 (27 %)
Thiazides	611 (20 %)	808 (16 %)	304 (16 %)	1723 (17 %)
Loop diuretics	402 (13 %)	433 (8.7 %)	143 (7.5 %)	978 (9.8 %)
Potassium-sparing agents	184 (5.9 %)	251 (5.0 %)	81 (4.2 %)	516 (5.1 %)
Anticoagulants	956 (31 %)	1286 (26 %)	447 (23 %)	2689 (27 %)
Thromboprophylaxis	237 (7.6 %)	337 (6.7 %)	139 (7.3 %)	713 (7.1 %)

Abbreviations: ACE/ARB = angiotensin-converting-enzyme inhibitor/angiotensin II receptor antagonist, BMI = body mass index, CVD = cardiovascular disease, DPP-IV inhibitor = dipeptidyl peptidase 4 inhibitor, eGFR = estimated glomerular filtration rate, GLP-1RA = glucagon-like peptide-1 receptor agonist, HOMA2 = homeostasis model assessment 2, SGLT-2i = sodium-glucose cotransporter II inhibitor, T2DM = type 2 diabetes mellitus, UACR = urine albumin-creatinine ratio, F/M = females/males.
Count data = medians and quartiles; categorical data = numbers and percentages. Values < 10 are shown with one decimal.
[a] Saltin–Grimby Physical Activity Level Scale.

%; high: 6.8 %; aPR of 0.83 [95 % CI 0.66–1.03] for low *vs* high, aPR of 0.92 [95 % CI 0.75–1.11] for moderate *vs* high). Lower education was also associated with more frequent use of statins; ACE/ARBs; and other antihypertensives, such as thiazides, beta-blockers, and calcium channel inhibitors (Fig. 3 and Table 1).

In stratified analyses, individuals with CVD and lower education still used more GLP-1RAs. A similar association with higher GLP-1RA use was found among those with a BMI above 30 kg/m^2 (Supplementary Table 7–8). The association of lower education with less SGLT-2i use was most pronounced in individuals without CVD. The use of statins and ACE/ARBs was generally high (exceeding 90 % for statins and 75 % for ACE/ARBs) in individuals with CVD, with no clear differences across educational levels. Among individuals without CVD, statins and ACE/ARBs were used slightly more in individuals with lower education (Supplementary Table 7).

4. Discussion

In this nationwide study of more than 10,000 individuals with recently diagnosed type 2 diabetes, lower educational level was associated with a larger prevalence of current smoking, leisure-time physical inactivity, obesity, insulin resistance, and diabetes complications (including both CVD and microvascular complications) at the time of type 2 diabetes diagnosis. Notably, lower education was associated with slightly more use of glucose-lowering drugs, statins, ACE/ARBs, and other antihypertensive drugs around the time of type 2 diabetes diagnosis compared to those with higher educational levels. Accordingly, CVD risk factors such as HbA1c, LDL cholesterol, and blood pressure levels were remarkably similar across educational groups. The use of GLP-1RA tended to be higher, and the use of SGLT-2i tended to be lower, among individuals with low rather than high education.

Our data provide a broad picture of the health profile and clinical characteristics of individuals with recently diagnosed type 2 diabetes according to educational achievement. Although the findings from most previous studies on socioeconomic position and CVD are consistent with our results [4–6], few prior studies have investigated social disparities in the occurrence of microvascular complications in early diabetes [6]. We found that low educational level is particularly associated with nephropathy and neuropathy, and, to a lesser extent, eye disease. Hyperglycaemia is a key driver of retinopathy [29,30], whereas risks of neuropathy and nephropathy in type 2 diabetes appear to be closely associated with other metabolic risk factors, including central obesity, insulin resistance, inflammation, dyslipidaemia, and hypertension [31–33]. These findings align with the observed distribution of underlying metabolic risk factors in our cohort.

During the past decade, new organ-protective glucose-lowering therapies, including GLP-1RAs and SGLT-2is have become central to treating type 2 diabetes [34,35]. As expected, the overall use of these drug classes remained low in our cohort of individuals with very early type 2 diabetes. Interestingly, individuals with low education more often used GLP-1RAs, but not SGLT-2is, than those with high education. The higher prevalence of GLP-1RA use among those with lower education might be attributed to a higher prevalence of severe obesity in this group. In contrast, in a prior study of American veterans with type 2 diabetes, all non-white racial groups had lower odds of being prescribed either an SGLT-2i or GLP-1RA, compared with white individuals (ORs between 0,72–0,95) [36]. Danish citizens receive generous public reimbursement for most prescription medications, including SGLT-2i and GLP-1RA. Thus, Danish citizens are reimbursed for 85 % of medicine expenses above approximately 525 Euro/year, and 100 % of expenses above 2855 Euro/year, equivalent to a maximum individual expense of approximately 615 Euro/year (2024). Additionally, individuals receiving social benefits or pensions may qualify for further support, including full or partial coverage of medication costs through municipal assistance programs. This reimbursement might have influenced the treatment differences observed in Danish versus US studies. Notwithstanding, a Danish cohort study of metformin users who initiated second-line glucose-lowering drugs between 2012 and 2020 has found an association between lower income and a modestly lower probability of GLP-1RA or SGLT-2i initiation at a median of 4 years after type 2 diabetes diagnosis [14]. Directly comparing those findings with our results is difficult, given that glucose-lowering drug use was assessed at different time points. Of note, the DD2 project is nationwide, and all general practitioners are invited to participate; however, some refrain from participation. Physicians participating in the DD2 project might potentially have greater familiarity with current treatment guidelines, thus possibly leading to a higher use rate of the cardiorenal protective GLP-1RAs and SGLT-2is independently of patients' socioeconomic position, as compared with other physicians.

The reasons for the slightly lower use of SGLT-2is in our patients with low education may be complex. They might include medication costs and financial constraints despite high reimbursement; personal scepticisms against starting a new medication, which may be more prevalent among patients with lower education; physicians' concerns about potential side effects such as the risk of infections, dehydration, or ketoacidosis that may all be increased in people with lower education; and physicians' knowledge of current evidence [37]. Also, the slightly lower use of SGLT2i in those with lower education might simply mirror a more frequent choice of GLP-1RA in the same, possibly more obese group, as double therapy with both medications remains infrequent in early type 2 diabetes.

Our study has limitations. First, because the DD2 project is a prospective cohort actively recruiting participants with type 2 diabetes after informed consent, the generalizability of the findings to all individuals diagnosed with type 2 diabetes might be affected. However, the DD2 project includes participants from rural and urban clinics throughout Denmark, and both the demographic and clinical characteristics of the cohort are consistent with those of population-based cohorts of all individuals with first-treated type 2 diabetes in Denmark [38].

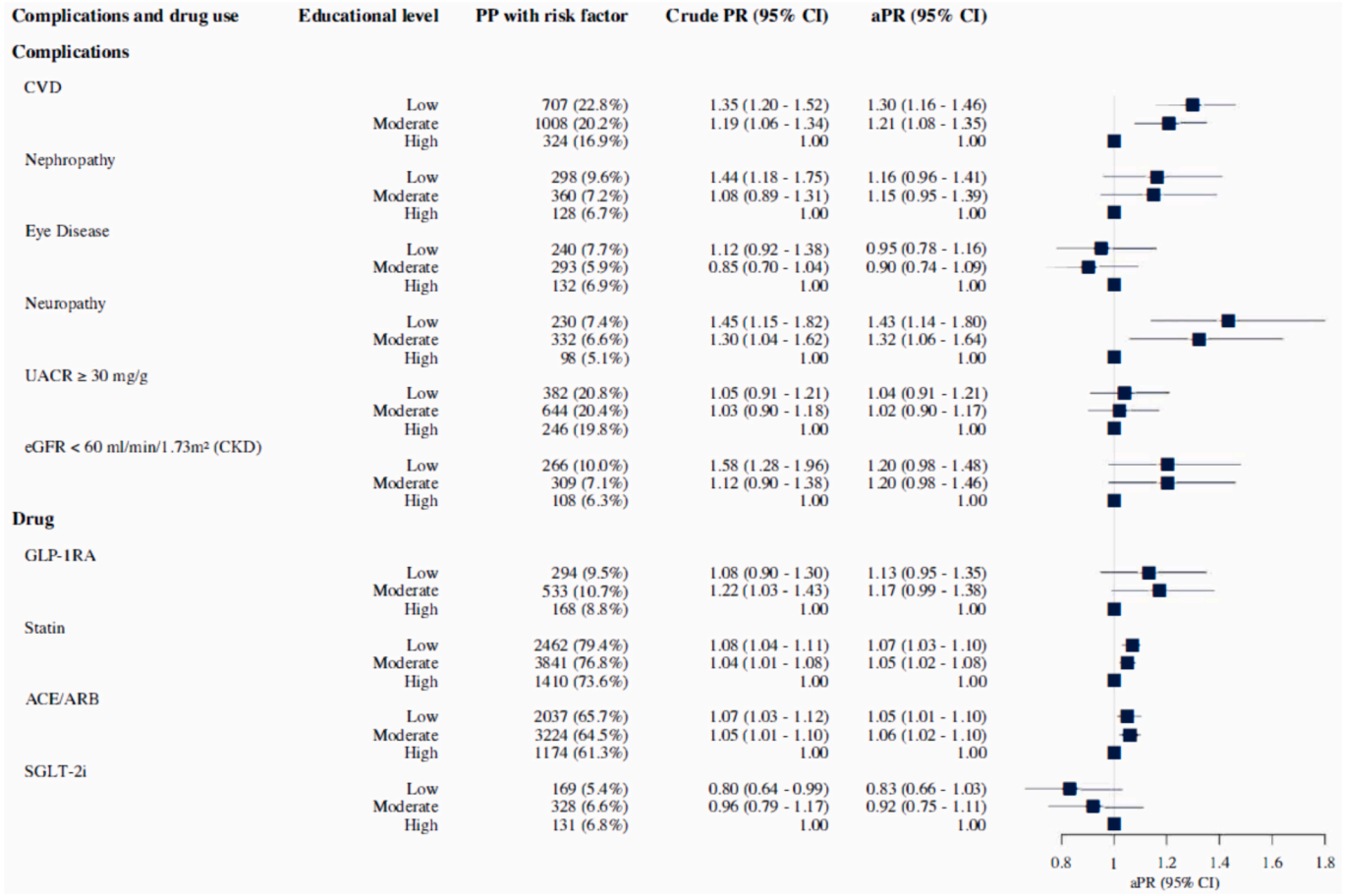

Fig. 3. Crude and adjusted PRs for comorbidities and drug use associated with educational level, with high educational level as the reference.

Specifically, our study showed an educational level distribution comparable to that in a recent nationwide type 2 diabetes study, despite slight differences in inclusion criteria [4]. Second, a reverse pathway might exist between socioeconomic position and other characteristics assessed at baseline. For example, pre-existing comorbidities might have negatively affected the current socioeconomic position at type 2 diabetes diagnosis. We selected education as a key upstream socioeconomic marker since it is typically completed in early adulthood, preceding the onset of chronic diseases that usually develop later in life [16]. Third, we lacked granular data on psychosocial factors (e.g., loneliness, self-assessed health status, or quality of life). Fourth, misclassification of self-reported lifestyle behaviours might have occurred.

Scientific Statements from the American Heart Association, the American Diabetes Association, and the European Association for the Study of Diabetes recognize that social determinants of health are independent risk factors of comorbidities and complications, both in the general population and among individuals with type 2 diabetes [1,2,34]. The effects of these upstream social determinants might be mediated through several classical risk factors (e.g., smoking, physical inactivity, poor diet, or obesity), through adverse psychological mechanisms (e.g., stress, depression, or loneliness), and through comorbidities present before type 2 diabetes diagnosis (e.g., chronic kidney disease and CVD), which are prevalent in more vulnerable patient subgroups [1,2,34,39]. Our study confirmed that low educational level is associated with many of these risk factors, even early during the type 2 diabetes course. Thus, individuals with low rather than moderate or high education had less healthy lifestyle behaviours, were more often obese, and had more pre-existing CVD and microvascular complications at the time of type 2 diabetes diagnosis. In the universal and tax-funded Danish healthcare system where the vast majority of medication costs are reimbursed, individuals with low education also received a high level of glucose-lowering and cardiovascular preventive pharmacotherapy, in accordance with their high CVD risk profiles. Correspondingly, they had similar levels of traditional CVD risk factors such as HbA1c, cholesterol, and blood pressure to those in individuals with higher education. Nonetheless, individuals with low rather than moderate or high educational level had more pronounced central obesity, higher triglycerides, more insulin resistance, and poorer kidney function at the time of type 2 diabetes diagnosis; these metabolic factors have traditionally been more challenging to treat than classical CVD risk factors [40,41]. Individuals with low education may therefore constitute a vulnerable subgroup of patients with type 2 diabetes who may particularly benefit from a targeted multifactorial preventive approach. Therapies may include both patient-centered interventions, to support health literacy, self-management education and support, and interventions for primary care physicians who provide healthcare for many patients with low educational status [14,37]. Emerging therapies targeting weight loss, triglyceride-rich lipoproteins and lipoprotein a, low-grade inflammation, and cardiorenal protection have emerged [31,41,42], and individuals with low socioeconomic position may constitute a key target group for additional preventive pharmacotherapy.

5. Conclusion

Among individuals with early type 2 diabetes, those with low education may be a particularly vulnerable group with a high accumulation of obesity, cardiovascular-kidney-metabolic risk factors, and comorbidities even in the early years of diabetes. It can be anticipated that the educational gradient of complications will only worsen as the duration

of diabetes increases. These people may particularly benefit from a multifactorial and targeted approach. Because of the high costs of emerging therapies, future socioeconomic inequalities in treatment initiation should be monitored and prevented.

CRediT authorship contribution statement

Marie T. Sørensen: Writing – review & editing, Writing – original draft, Visualization, Methodology, Formal analysis, Conceptualization. **Frederik P.B. Kristensen:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Conceptualization. **Jens S. Nielsen:** Writing – review & editing, Resources, Project administration, Investigation, Data curation, Conceptualization. **Diana H. Christensen:** Writing – review & editing, Supervision, Conceptualization. **Sia K. Nicolaisen:** Writing – review & editing, Software, Methodology, Data curation, Conceptualization. **Henning Beck-Nielsen:** Writing – review & editing, Investigation, Funding acquisition, Conceptualization. **Peter Vestergaard:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Conceptualization. **Niels Jessen:** Writing – review & editing, Funding acquisition, Conceptualization. **Michael H. Olsen:** Writing – review & editing, Resources, Conceptualization. **Torben Hansen:** Writing – review & editing, Resources, Conceptualization. **Allan Vaag:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization. **Henrik T. Sørensen:** Writing – review & editing, Supervision, Methodology, Investigation, Funding acquisition, Conceptualization. **Reimar W. Thomsen:** Writing – review & editing, Supervision, Methodology, Investigation, Funding acquisition, Conceptualization.

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Department of Clinical Epidemiology, Aarhus University Hospital, receives funding for other studies from companies in the form of research grants to (and administered by) Aarhus University. None of those studies have any relation to the present study. The other authors report no potential conflicts of interest relevant to this article.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2025.112231.

Data availability

The data are available for research upon request to the Danish Health Data Authority and within the framework of the Danish data protection legislation and any required permissions from authorities.

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