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Published in:
European Journal of Preventive Cardiology

DOI (link to publication from Publisher):
10.1093/eurjpc/zwab065

Publication date:
2022

Document Version
Publisher's PDF, also known as Version of record

ESC European Society of Cardiology

European Journal of Preventive Cardiology (2021) **28**, 1819–1828
doi:10.1093/eurjpc/zwab065

FULL RESEARCH PAPER
Diabetes and Metabolic Syndrome

Socioeconomic position and first-time major cardiovascular event in patients with type 2 diabetes: a Danish nationwide cohort study

Alexander C. Falkentoft [1]*, Bochra Zareini [2], Julie Andersen [3], Charlotte Wichmand[1], Tina B. Hansen[1,4], Christian Selmer [5], Morten Schou [2], Peter Haulund Gæde[6], Peter Bisgaard Staehr[7], Mark A. Hlatky [8], Christian Torp-Pedersen[9,10], Gunnar H. Gislason [2,3], Thomas Alexander Gerds [3,11], Niels E. Bruun [1,12], and Anne-Christine Ruwald [1,2]

[1]Department of Cardiology, Zealand University Hospital, University of Copenhagen, Sygehusvej 10, 4000 Roskilde, Denmark; [2]Department of Cardiology, Herlev-Gentofte Hospital, University of Copenhagen, Gentofte, Denmark; [3]The Danish Heart Foundation, Copenhagen, Denmark; [4]Department of Regional Health Research, University of Southern Denmark, Odense, Denmark; [5]Department of Endocrinology, Bispebjerg and Frederiksberg Hospital, University of Copenhagen, Copenhagen, Denmark; [6]Department of Endocrinology, Regional Hospital, Slagelse, Denmark; [7]Department of Cardiology, North Denmark Regional Hospital, Hjørring, Denmark; [8]Department of Medicine, Stanford University School of Medicine, Stanford, CA, USA; [9]Department of Cardiology, Nordsjaellands Hospital, Hillerød, Denmark; [10]Department of Cardiology, Aalborg University Hospital, Aalborg, Denmark; [11]Section of Biostatistics, Department of Public Health, University of Copenhagen, Copenhagen, Denmark; and [12]Departments of Clinical Medicine, Faculty of Health and Medical Sciences, Copenhagen and Aalborg Universities, Denmark

Received 15 January 2021; revised 22 March 2021; editorial decision 3 April 2021; accepted 8 April 2021; online publish-ahead-of-print 25 May 2021

Aims The association between socioeconomic position and cardiovascular disease has not been well studied in patients with type 2 diabetes. We aimed to examine the association between socioeconomic position and first-time major adverse cardiovascular events (MACE) in patients with type 2 diabetes.

Methods and results Through the Danish nationwide registers, we identified all residents with newly diagnosed type 2 diabetes between 2012 and 2017. Based on sex-stratified multivariable cause-specific Cox regression models, we calculated the standardized absolute 5-year risk of the composite outcome of first-time myocardial infarction, stroke, or cardiovascular mortality (MACE) according to income quartiles. A total of 57 106 patients with type 2 diabetes were included. During 155 989 person years, first-time MACE occurred in 2139 patients. Among both men and women, income was inversely associated with the standardized absolute 5-year risk of MACE. In men, the 5-year risk of MACE increased from 5.7% [95% confidence interval (CI) 4.9–6.5] in the highest income quartile to 9.3% (CI 8.3–10.2) in the lowest income group, with a risk difference of 3.5% (CI 2.4–4.7). In women, the risk of MACE increased from 4.2% (CI 3.4–5.0) to 6.1% (CI 5.2–7.0) according to income level, with a risk difference of 1.9% (CI 0.8–2.9).

Conclusion Despite free access to medical care in Denmark, low-socioeconomic position was associated with a higher 5-year risk of first-time MACE in patients with incident type 2 diabetes. Our results suggest prevention strategies could be developed specifically for patients with low-socioeconomic position.

Keywords Type 2 diabetes • Cardiovascular disease • Socioeconomic position

* Corresponding author. Tel: +45 509 08969, Email: a.falkentoft@gmail.com

Introduction

Patients with type 2 diabetes (T2D) have excess rates of adverse cardiovascular outcomes and all-cause mortality, two-fold higher than the general population.[1,2] Identification of patients with T2D at higher risk of these events could help target primary prevention strategies and improve long-term outcomes.

Socioeconomic factors are known to affect health and, thus, socioeconomic position (i.e. an individual's social position relative to other members of a society) may be a good marker of disadvantaged patients.[3] In high-income countries, low-socioeconomic position has consistently been associated with a higher incidence of T2D,[4] myocardial infarction,[5] and stroke.[6] However, there is a paucity of studies investigating whether socioeconomic disparities in cardiovascular disease also exist in patients with T2D. Most of the available evidence suggest an inverse association with socioeconomic position.[7–11] Yet, the evidence is inconsistent.[12,13] Further, prior studies did not systematically account for confounders like comorbidities,[7] individual-level socioeconomic data,[7,8] type or duration of diabetes,[7,11,12] or did not examine first-time cardiovascular events.[7–10,12,13] In addition, no large cohort study has investigated the association between socioeconomic position and cardiovascular events in a contemporary population of patients with T2D after implementation of glycated haemoglobin (HbA1c) in the diagnostic criteria, emphasizing the need for updated research of this topic.[14]

In Denmark, the healthcare system offers free, equal, and universal access for all residents and, thus, provides a setting without the influence of financial barriers in access to medical care. We aimed to examine the association between socioeconomic position and first-time cardiovascular event in a Danish nationwide cohort of patients with incident T2D.

Methods

Data sources

We conducted a nationwide cohort study using the registers in Denmark where all residents are provided with a unique and personal civil registration number that enables individual-level linkage of nationwide registers. In this study, we combined information from (i) the Danish National Patients Register that holds information on all admissions to hospitals since 1977, and outpatient visits since 1995, coded according to the International Classification of Diseases (ICD)-8 from 1977 to 1993, and the ICD-10 system since 1994[15]; (ii) the Register of Medicinal Product Statistics (the national prescription register) that holds information about all dispensed prescriptions since 1995 according to the anatomical therapeutical chemical (ATC) classification system[16]; (iii) the Danish Civil Registration System register that holds information on sex, date of birth, immigration, emigration, cohabitation status, and vital status[17]; (iv) the Danish Income Statistics Register with information on income[18]; (v) the Danish Student Register with information on highest attained educational level[19]; and (vi) the Danish Register of Causes of Death that holds information on causes of death from death certificates.

Study population

We identified all Danish residents with incident diabetes between 1 January 2012 and 31 December 2017. The date of diagnosis was defined as the time of first redeemed prescription of an antidiabetic drug (ATC A10) or as the time of first registered code of diabetes as primary diagnosis (ICD-10 codes E10–E14, O24, or H36.0), whichever came first. In the Danish registers, these two approaches have a positive predictive value of 95% and 97% and a sensitivity of 72% and 64%, respectively.[20]

We excluded patients younger than 40 years of age at time of diagnosis in order to exclude patients with type 1 diabetes and since income is relatively stable after 40 years of age.[21] Further exclusion criteria are presented in the population flowchart (*Figure 1*). Moreover, we accounted for polycystic ovary syndrome by only including prescriptions of metformin in women after they had turned 40 years, if they were in metformin monotherapy and without a code of diabetes. Lastly, patients with gestational diabetes were not considered initially but were included if they subsequently developed diabetes (definition in Supplementary material online, *Table S1*).

Since initial treatment of T2D (antidiabetic, antihypertensive, and lipid-lowering treatment) is likely to be changed during the first months after diagnosis and in order to exclude patients with pre-existing, non-clinically recognized ischaemic heart disease, study entry date was set to 90 days after date of incident diabetes diagnosis. Thus, all incident T2D patients without existing ischaemic heart disease, prior stroke, and/or peripheral artery disease, who were alive at this time were included in the study.

Socioeconomic position

We used equivalized disposable income as the primary proxy for socioeconomic position. This was measured as the total disposable income of the household and divided by the weighted number of individuals living in the household, using the Organization for Economic Co-operation and Development (OECD) modified scale where first adult counted as 1, further adults as 0.5, and individuals younger than 14 years as 0.3.[18] Income was corrected for inflation to year 2015. In order to minimize the effect of yearly variations, income was measured as the 5-year mean prior to the study entry date (90 days after diagnosis of T2D) and was grouped according sex- and age-group-specific quartiles (40–64, 65–79 years). Thus, patients were assigned to one of four income groups (lowest, second lowest, second highest, and highest).

Patients' highest attained educational level were divided into three groups according to the International Classification of Education (ISCED)[23]; (i) basic education (ISCED level 0–2); (ii) high school or vocational education (ISCED level 3); and (iii) higher education including short-term higher education, bachelor's/master's/doctoral degree or equivalent (ISCED level 5 or higher).

Baseline medication and comorbidities

Medical treatment at baseline was identified through ATC-codes and defined as at least one redeemed prescription 180 days prior to baseline (Supplementary material online, *Table S2*). Comorbidities were defined according to hospital ICD-codes from the Danish National Patient register (10 years before study entry) (Supplementary material online, *Table S1*, definitions and ICD-codes). Moreover, dispensation of relevant pharmacotherapy was also applied for defining hypertension, chronic obstructive pulmonary disease/asthma, depression, and bipolar or psychotic disorders (Supplementary material online, *Table S1*).

Outcomes

The primary outcome was first-time major adverse cardiovascular event (MACE), defined as stroke, myocardial infarction, or cardiovascular death (defined by ICD-10 codes in Supplementary material online, *Table S1*), whichever came first. The first occurrence of stroke, myocardial infarction, cardiovascular mortality, and all-cause mortality was examined as secondary outcomes. The diagnoses of stroke and myocardial infarction

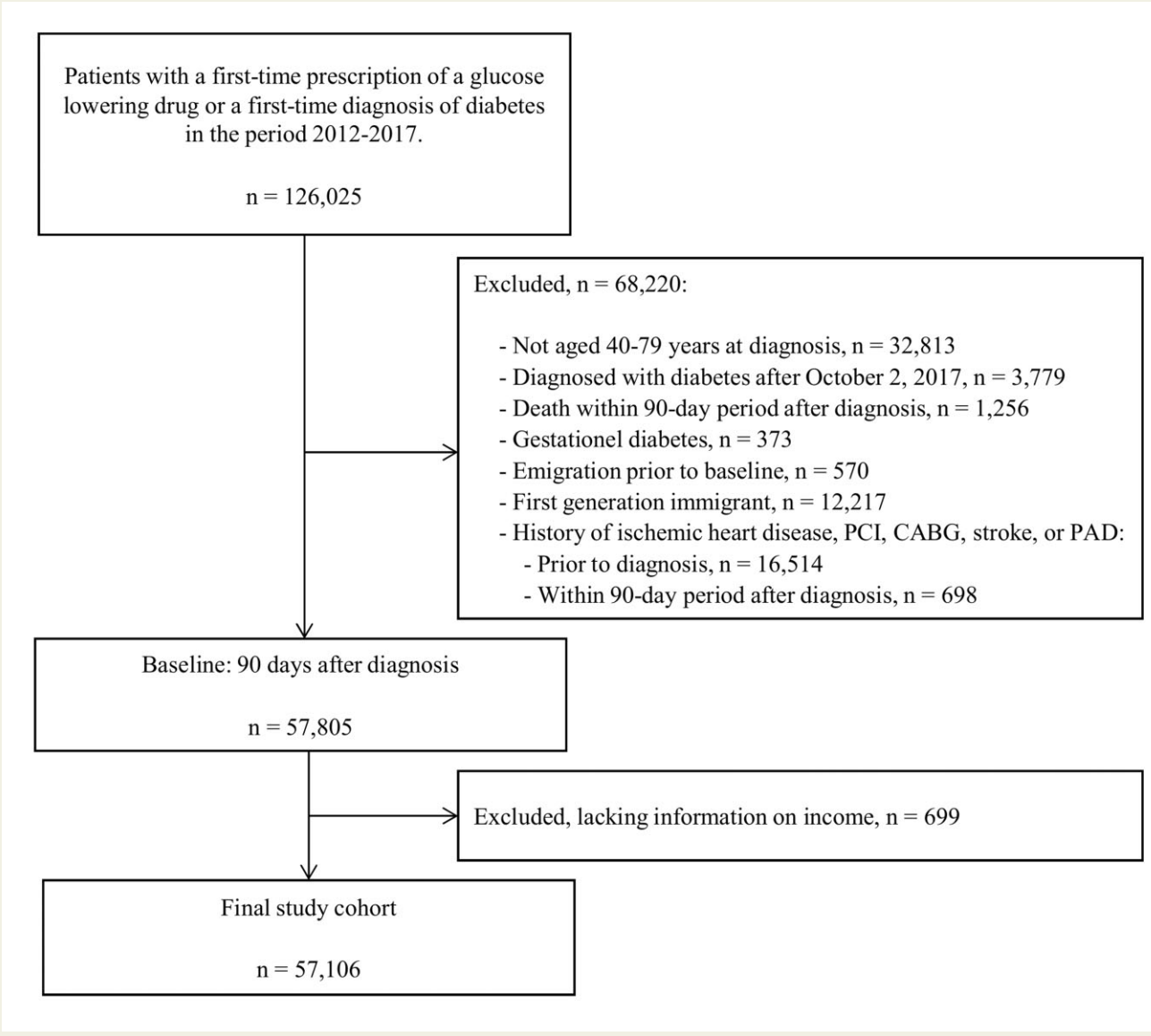

Figure 1 CONSORT study flow diagram. CABG, coronary artery bypass graft surgery; PAD, peripheral artery disease; PCI, percutaneous coronary intervention.

have previously been validated with positive predictive values between 80.5% and 97.0% and 92.4% and 100%, respectively.[15,24]

Statistics

Baseline characteristics were grouped according to income group and presented as frequencies and percentages for categorical variables and as medians with interquartile ranges (IQR) for continuous variables.

All patients were followed from study entry date until event of interest, emigration, death, end of study (MACE, stroke, myocardial infarction, and cardiovascular death: 31 December 2017; all-cause mortality: 31 December 2018), or a maximum of 5 years, whichever came first. All analyses were performed separately for men and women.

The Aalen–Johansen method was used to obtain overall 5-year risks of MACE according to income groups. We used multivariable cause-specific Cox regression to model the hazard rates of the event of interest (MACE, stroke, myocardial infarction, and cardiovascular death) and separately the hazard rate of the competing risk: death without the event of interest.[25] The Cox regression analyses were adjusted for age at baseline (restricted cubic splines with three knots), calendar year, cohabitation status, baseline comorbidities (heart failure, peripheral vascular disease, atrial fibrillation, hypertension, chronic obstructive pulmonary disease, chronic kidney disease, cancer, depression, and bipolar/psychotic disorders), and medication (statins, antithrombotics, anticoagulants, loop diuretics, insulin, metformin, and sulfonylurea). Based on the Cox regression models, we reported the standardized absolute 5-year outcome risks and differences thereof according to income groups.[26] For MACE, we also reported the relative risk ratios.

Analyses of all-cause mortality were performed in the same way based on a Cox regression model for the hazard rate of all-cause death. We repeated all analyses in subgroups according to sex and age-groups (40–64, 65–79 years). Lastly, in sensitivity analyses for MACE, we replaced income groups with educational level.

All analyses were performed in R, version 4.0.3.[27] The level of statistical significance was set at 5%, and the 95% confidence intervals (CIs) were reported for all the outcomes of interest.

Ethics

Retrospective register-based studies do not need ethical approval in Denmark. Permission to use data from the Danish national registries for research has been granted by the Knowledge Center on Data Protection Compliance—The Capital Region of Denmark (approval number: P-2019-348).

Results

Study cohort and baseline characteristics

Diabetes was diagnosed in 126 025 patients in Denmark between 2012 and 2017. After applying the exclusion criteria (*Figure 1*), 57 106 patients were included in the final study cohort. The median age was 60 years (IQR, 52–68 years) among men and 61 years (IQR, 52–69 years) among women. Baseline characteristics varied by income (*Table 1*). In both men and women, patients in the lowest income group were less educated, more likely to live alone, had a higher comorbidity-burden, and were more likely to be treated with cardiovascular medications. Yet, among men, the use of statins and renin-angiotensin system (RAS) inhibitors increased with increasing income level.

Major adverse cardiovascular events

During 155 989 person years, first-time MACE occurred in 2139 patients. Among both men and women, the crude, unadjusted 5-year risk of MACE increased with lower income group: among men, from 5.1% (CI 4.4–5.9) in the highest income group to 10.6% (CI 9.6–11.6) in lowest income group; among women, from 3.9% (CI 3.1–4.6) to 7.6% (CI 6.6–8.6). After standardization, income remained inversely associated with the risk of MACE (*Figure 2*). In men, the standardized 5-year risk of MACE increased from 5.7% (CI 4.9–6.5) in the highest income group to 9.3% (CI 8.3–10.2) in the lowest income group. In women, the standardized 5-year risk of MACE increased from 4.2% (CI 3.4–5.0) to 6.1% (CI 5.2–7.0). When comparing the lowest and highest income groups, we observed an absolute risk difference of 3.5% (CI 2.4–4.7) among men and 1.9% (CI 0.8–2.9) among women (*Figure 3*). When looking at relative measures, we observed 5-year risk ratios of MACE of 1.6 (CI 1.4–1.9; highest vs. lowest income group) among men and of 1.5 (CI 1.1–1.8; highest vs. lowest income group) among women. In age-subgroups, the inverse association between income and MACE was consistent (*Figure 3*). Yet, among the youngest (40–64 years) women, the association was borderline significant. Further, risk differences of MACE increased with male sex and with older age.

Secondary outcomes

Overall, stroke occurred in 1058 patients, myocardial infarction in 708 patients, cardiovascular death in 1021, and all-cause mortality in 4158 patients. Among men, low income was associated with an increased risk of all secondary outcomes: stroke, myocardial infarction, cardiovascular death, and all-cause mortality (*Figure 4*). In subgroup analyses, this pattern was observed in both age-groups for all secondary outcomes (Supplementary material online, *Figures S1–S4*). Among women, an inverse significant association by income group was observed for the specific secondary outcomes of stroke and cardiovascular death (*Figure 4*). However, we did not observe a significant inverse association by income group with myocardial infarction or all-cause mortality. In subgroup-analyses among the youngest female patients (40–64 years), income reached borderline statistical significance for cardiovascular mortality and all-cause mortality, whereas statistically significance was reached only for stroke among the oldest patients (65–79 years) (Supplementary material online, *Figures S1–S4*).

Educational level

In general, educational level was associated with baseline characteristics in a pattern similar to income levels (Supplementary material online, *Table S3*). Among both men and women, attained educational level was also inversely associated with MACE (Supplementary material online, *Figure S5*). Among men, patients with lowest educational level had a 1.4% (CI 0.4–2.5) higher 5-year risk of MACE than patients in the highest educational level (Supplementary material online, *Figure S5*). The risk difference among women was 1.9% (CI 0.9–2.8). In women, this inverse relation was evident in both age groups (Supplementary material online, *Figure S5*). Among men, the inverse relation between educational level and MACE was significant for youngest patients (40–64 years) but not significant for the oldest patients (65–79 years).

Discussion

This nationwide study is the first large cohort study investigating the association between socioeconomic position and the risk of first-time cardiovascular outcomes in a contemporary population of patients with incidence T2D. Low-socioeconomic position was associated with higher absolute risks of adverse cardiovascular events, independently of comorbidities, among both men and women in patients with T2D. This was observed despite a strong Danish social welfare system, with free access to medical care and education and socioeconomic differences minimized by state, regions, and municipalities. Differences in outcome by socioeconomic position are likely to be more prominent in countries without the strong social safety net found in Scandinavia. Moreover, despite being implemented as a risk modifier in the 2016 European guidelines on cardiovascular disease prevention in clinical practice,[28] socioeconomic position is neither included in systematic cardiovascular risk stratification nor as a risk modifier in the 2019 European guidelines on diabetes, pre-diabetes, and cardiovascular disease.[2] In this context, our findings underscore the importance of considering socioeconomic position in primary preventive strategies for cardiovascular disease among patients with T2D.

Some prior cohort studies have investigated the rates of cardiovascular outcomes according to socioeconomic differences in patients with T2D before the new definition of diabetes.[7–13] Moreover, these studies differed from our study by either using area-based socioeconomic position as a proxy for individual-level socioeconomic position,[7,8] not adjusting for comorbidities or medication,[7,12] using educational levels as primary exposure,[9,13] or by

Table 1 Baseline characteristics of the 57 106 patients with type 2 diabetes according to quartiles of income and sex

Variables	Male				Female			
	Income group				Income group			
	Lowest (n = 7879)	Second lowest (n = 7877)	Second highest (n = 7877)	Highest (n = 7877)	Lowest (n = 6399)	Second lowest (n = 6399)	Second highest (n = 6399)	Highest (n = 6399)
Age	59 (50–70)	59 (50–68)	60 (53–67)	61 (55–67)	60 (50–71)	61 (50–70)	61 (52–68)	61 (54–67)
Income adjusted to 2015 levels in Euros	20 935 (18 674–22 612)	27 755 (25 947–30 280)	35 515 (33 332–38 131)	48 725 (44 114–57 514)	20 457 (18 798–22 445)	26 446 (23 253–29 100)	33 038 (28 859–36 365)	45 207 (40 924–52 442)
Educational level								
Basic education	3829 (50.0)	3033 (39.2)	2152 (27.7)	1215 (15.6)	3713 (59.2)	2912 (46.1)	2023 (31.9)	1234 (19.4)
High school/vocational	3252 (42.5)	3955 (51.1)	4171 (53.6)	3582 (45.9)	2048 (32.6)	2564 (40.6)	2884 (45.4)	2675 (42.1)
Higher education	576 (7.5)	747 (9.7)	1457 (18.7)	3003 (38.5)	515 (8.2)	839 (13.3)	1439 (22.7)	2448 (38.5)
Missing	222	142	97	77	123	84	53	42
Living alone	4839 (61.4)	3002 (38.1)	1863 (23.7)	1405 (17.8)	4099 (64.1)	2995 (46.8)	1878 (29.3)	1166 (18.2)
Comorbidities, (%)								
Heart failure	344 (4.4)	276 (3.5)	221 (2.8)	166 (2.1)	174 (2.7)	148 (2.3)	126 (2.0)	89 (1.4)
Atrial fibrillation	522 (6.6)	525 (6.7)	438 (5.6)	466 (5.9)	293 (4.6)	278 (4.3)	267 (4.2)	213 (3.3)
Hypertension	3301 (41.9)	3444 (43.7)	3360 (42.7)	3348 (42.5)	2885 (45.1)	2964 (46.3)	2917 (45.6)	2769 (43.3)
COPD/asthma	1184 (15.0)	1046 (13.3)	745 (9.5)	621 (7.9)	1205 (18.8)	1130 (17.7)	923 (14.4)	757 (11.8)
Chronic kidney disease	206 (2.6)	218 (2.8)	191 (2.4)	163 (2.1)	154 (2.4)	133 (2.1)	140 (2.2)	97 (1.5)
Cancer	627 (8.0)	711 (9.0)	746 (9.5)	786 (10.0)	571 (8.9)	643 (10.0)	698 (10.9)	789 (12.3)
Depression	1167 (14.8)	866 (11.0)	677 (8.6)	469 (6.0)	1737 (27.1)	1477 (23.1)	1118 (17.5)	826 (12.9)
Bipolar/psychotic disorders	650 (8.2)	465 (5.9)	156 (2.0)	91 (1.2)	667 (10.4)	557 (8.7)	298 (4.7)	163 (2.5)
Pharmacotherapy, (%)								
Statins	3551 (45.1)	3767 (47.8)	3845 (48.8)	3900 (49.5)	3066 (47.9)	3114 (48.7)	3047 (47.6)	3006 (47.0)
RASi	3630 (46.1)	3961 (50.3)	3982 (50.6)	4026 (51.1)	2839 (44.4)	2995 (46.8)	2931 (45.8)	2859 (44.7)
Antithrombotics	1066 (13.5)	1058 (13.4)	993 (12.6)	1013 (12.9)	804 (12.6)	728 (11.4)	695 (10.9)	637 (10.0)
Anticoagulants	570 (7.2)	582 (7.4)	487 (6.2)	472 (6.0)	327 (5.1)	296 (4.6)	296 (4.6)	255 (4.0)
Beta blockers	1363 (17.3)	1374 (17.4)	1199 (15.2)	1139 (14.5)	1197 (18.7)	1206 (18.8)	1146 (17.9)	1013 (15.8)
Loop diuretics	910 (11.5)	749 (9.5)	519 (6.6)	388 (4.9)	868 (13.6)	740 (11.6)	607 (9.5)	440 (6.9)
Thiazide	923 (11.7)	875 (11.1)	772 (9.8)	749 (9.5)	1187 (18.5)	1235 (19.3)	1208 (18.9)	1108 (17.3)
Ca channel blockers	1674 (21.2)	1844 (23.4)	1742 (22.1)	1708 (21.7)	1276 (19.9)	1259 (19.7)	1190 (18.6)	1119 (17.5)
Insulin	665 (8.4)	593 (7.5)	583 (7.4)	526 (6.7)	396 (6.2)	340 (5.3)	348 (5.4)	380 (5.9)
Metformin	7175 (91.1)	7162 (90.9)	7137 (90.6)	7092 (90.0)	5754 (89.9)	5775 (90.2)	5696 (89.0)	5503 (86.0)
Sulfonylurea	254 (3.2)	214 (2.7)	191 (2.4)	162 (2.1)	181 (2.8)	150 (2.3)	161 (2.5)	146 (2.3)
DPP-4 inhibitors	210 (2.7)	196 (2.5)	192 (2.4)	204 (2.6)	170 (2.7)	162 (2.5)	170 (2.7)	136 (2.1)
GLP-1 receptor agonists	100 (1.3)	100 (1.3)	133 (1.7)	179 (2.3)	140 (2.2)	154 (2.4)	218 (3.4)	361 (5.6)
SGLT-2 inhibitors	55 (0.7)	34 (0.4)	52 (0.7)	61 (0.8)	35 (0.5)	31 (0.5)	40 (0.6)	36 (0.6)

Data are presented as median values [interquartile ranges (IQR)] for continuous variables and as numbers (percentages) for categorical variables.
COPD, chronic obstructive pulmonary disease; DPP-4, dipeptidyl peptidase 4; GLP-1, glucagon-like peptide 1; RAS, renin-angiotensin system; SGLT-2, sodium glucose co-transporter 2.

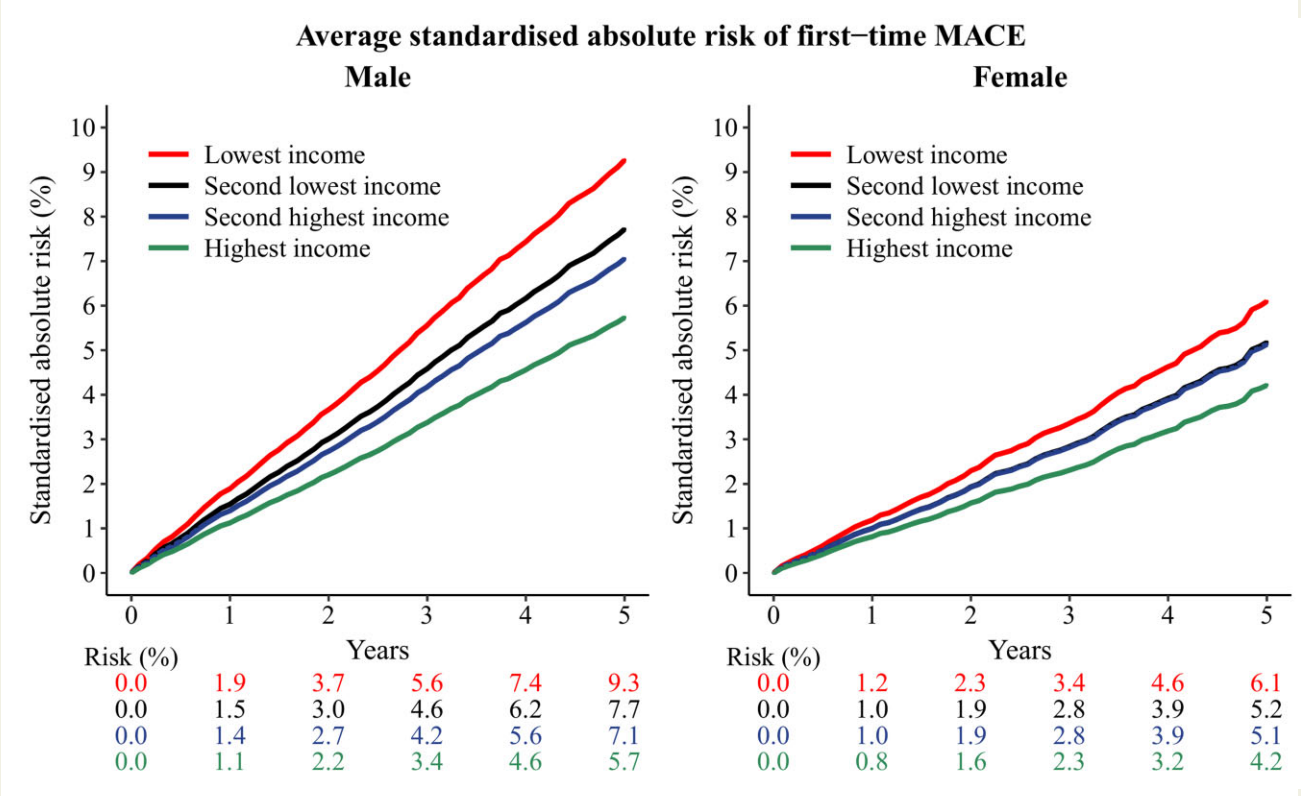

Figure 2 Average standardized absolute risk of first-time MACE according to income group and sex, among patients with incident type 2 diabetes. Time zero indicates 90 days after diagnosis of type 2 diabetes. Standardized to the distribution of residual age, calendar year, cohabitation status, baseline comorbidities, and medication according to income group. MACE, major adverse cardiovascular event.

not excluding patients with prevalent cardiovascular disease.[7–10,12,13] Moreover, they all differed from our study by reporting rates and not absolute risks, and not investigating patients with T2D after the implementation of the new diagnostic criteria.[7–13] Our findings were consistent with most of the studies,[7–11] yet, inconsistent with a few.[12,13]

One Scottish cohort study examined socioeconomic position, based on an area score, and found a strong inverse association with age-adjusted rates of ischaemic heart mortality and cerebrovascular mortality.[7] These results were observed, despite using area-based socioeconomic position, which is likely to underestimate the true individual-level effect due to non-differential misclassification.[29] Furthermore, they did not adjust for comorbidities nor medication and did not investigated first-time cardiovascular events.

Socioeconomic position may determine health. However, health may also determine patients' current socioeconomic position, generating social selection.[30] Therefore, to take this limitation into account, we aimed to reduce the risk of reverse causation between income, T2D, and MACE by excluding patients with prevalent cardiovascular disease and by investigating patients with incident T2D. Moreover, we accounted for baseline comorbidities by standardization and also examined attained educational level in which reverse causation is less like as it is usually determined in the young adulthood before the onset of T2D and cardiovascular disease.

One Swedish cohort study,[9] one Italian cohort study,[12] and one large sub-study of a multinational, randomized controlled study,[13] investigated differences in educational attainment among patients with T2D without excluding patients with prior cardiovascular events. The Swedish study found only minor socioeconomic differences on major cardiovascular events.[9] Inconsistent with our findings, the large clinical sub-study reported no significant socioeconomic differences in the rates of major cardiovascular events in subgroup analysis of patients from countries with established market economies.[13] Likewise, the Italian cohort study did not find any socioeconomic differences in incidence rates of cardiovascular mortality, stroke, and myocardial infarction in overall analysis of a mixed population of patients with type 1 diabetes and T2D.[12] Yet, in sub-group analysis, they found significant differences in patients aged 20–64 years.

Despite being more robust against reverse causality, educational level may not be optimal in an elderly population and may result in non-differential misclassification towards no effect.[3] Thus, for patients in the active professional life and during the first years of retirement, income and wealth are suggested as the most proper indicators of socioeconomic position.[3] Further, crude dichotomized categorizations of educational level and not accounting for differences in educational systems across countries, may also have explained the lack of significant findings in the large multinational sub-study.[13] Lastly, due to cultural and regional differences in markers of socioeconomic

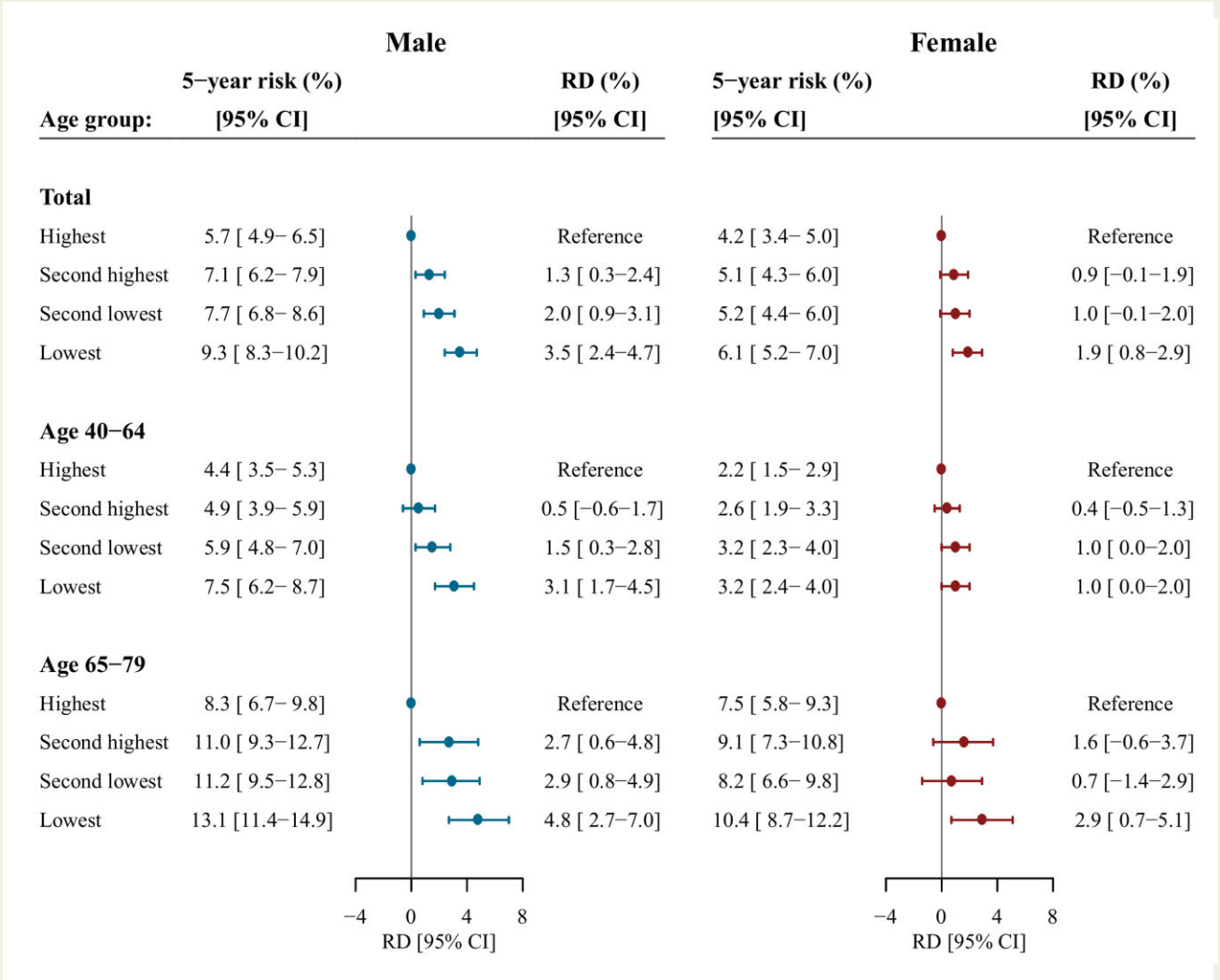

Figure 3 Forest plot depicting standardized absolute 5-year risk differences of MACE according to income group stratified by sex and age group, among patients with incident type 2 diabetes. Standardized to the distribution of residual age, calendar year, cohabitation status, baseline comorbidities, and medication according to income group. CI, confidence interval; MACE, major adverse cardiovascular event; RD, risk difference.

position and differences in the composition of society and healthcare, results from other countries may not translate into a Danish setting.

Thus, one of the strengths of our study is that we used equivalized disposable income as indicator of socioeconomic position in our population. Further, we accounted for yearly variations and minimized the risk of a potential bias due to acute illness by examining the 5-year mean income prior to inclusion.[29] Thus, examining income in our study yielded clear and apparent results among both men and women. Although not directly comparable, disparities in educational attainment for men were not as evident. Among women, the disparities in educational attainment were almost similar as income, and may indicate that the beneficial effects of having high educational attainment, including enhanced health literacy, could be more pronounced for women than men.

In a large Swedish cohort study, low 1-year gross income and low educational level conferred higher rates of cardiovascular mortality as compared with the less deprived patients with T2D.[10] These disparities were most pronounced for income and was observed independently of HbA1c, smoking, body mass index, and estimated glomerular filtration rate. Yet, they did not account for yearly variations of income, did not investigate the household income, had higher risk of reverse causation as patients with prior cardiovascular events were not excluded, did not investigate myocardial infarction or stroke, did not investigate absolute risks, and did not investigate patients after the implementation of the new diagnostic criteria.[10]

We chose to report the socioeconomic differences in cardiovascular outcomes separately for men and women, as it is commonly accepted that men in general have significantly higher absolute risks of cardiovascular outcomes than comparable women.[28] As expected, this approach yielded higher absolute risk differences between income groups among men, than among women. Yet, when looking at

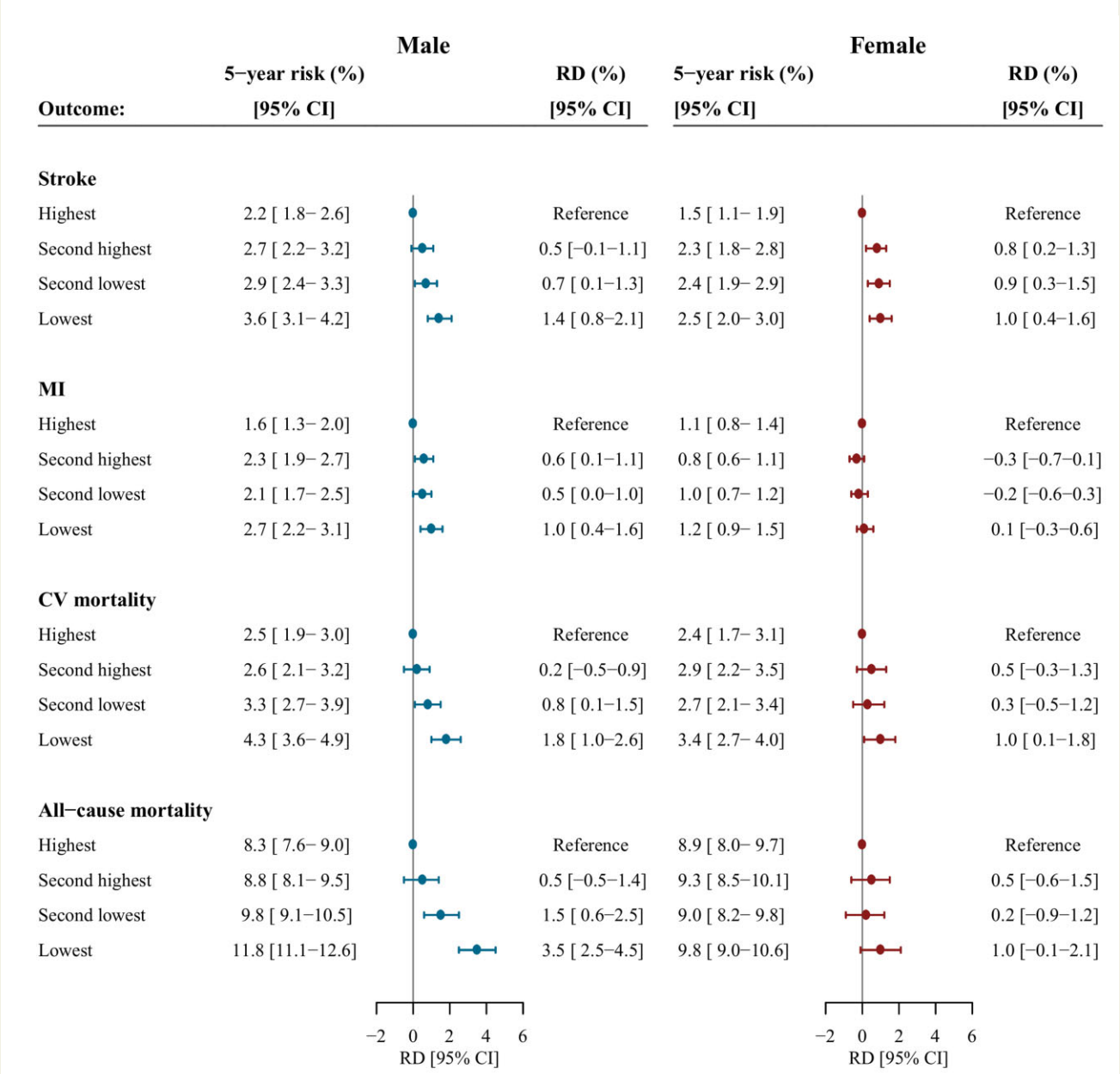

Figure 4 Forest plot depicting standardized absolute 5-year risk differences of all secondary outcomes according to income groups and sex, among patients with incident type 2 diabetes. Standardized to the distribution of residual age, calendar year, cohabitation status, baseline comorbidities, and medication according to income group. CI, confidence interval; MACE, major adverse cardiovascular event; RD, risk difference.

the relative risk differences in MACE by income group, the risk ratios were similar among men and women. Despite observing crude, unadjusted income inequalities (data not shown) of all-cause mortality in the oldest female patients (65–79 years), we did not observe inequalities after standardization. This indicate that a differential baseline comorbidity-burden across income group seem to be an influential driver for socioeconomic disparities in 5-year survival for older female patients. However, we might have observed significant inequalities with longer follow-up time with less influence of baseline comorbidities.

Our findings show that socioeconomic disparities persist in patients with T2D who, *per se*, have an elevated risk of cardiovascular outcomes, as compared with the general population. This was evident after just 5 years of follow-up. Thus, since duration of T2D is a significant risk factor, longer follow-up may have resulted in more prominent disparities.[2] Moreover, these results add evidence to prior studies investigating socioeconomic position as a negatively marker for a range of chronic lifestyle diseases.[31] As previously noted, we observed socioeconomic disparities in spite of free access to medical care. Therefore, other mechanisms than unequal access to medical

care may explain the link between socioeconomic disparities and adverse cardiovascular outcomes in Denmark in patients with T2D. Such mechanisms may include differences in individual health behaviour (smoking, exercise, adherence to diets, medications, and annual diabetes check-ups), factors that influence health behaviour (health literacy, stress, mental health, and social network) and in part have direct effects (stress), quality of care, and biological cardiovascular risk factors (lipids, HbA1C, or blood pressure).[5,32,33] As we aimed to investigate patients' current socioeconomic position in newly diagnosed patients with T2D, we tried to capture some of these effects prior to diagnosis of T2D by adjusting for baseline comorbidities and medication. Therefore, these mechanisms may be particularly evident after diagnosis of T2D in our study and might reflect areas for intervention.

Clinical implications

From a clinical perspective, multiple interventions may be required in order to reduce the disparities observed in this study. First, incorporation of socioeconomic position in cardiovascular risk assessment might be beneficial. Second, patient-centred interventions, including education, empowerment, and self-management strategies may be particularly important for these patients in order to modify undesirable health behaviour. Third, these patients may benefit from early risk screening for cardiovascular disease, more frequent follow-up, and aggressively targeting biological cardiovascular risk factors (lipids, glucose-levels, blood pressure, and albuminuria) that have associations with low-socioeconomic position.[34,35] However, since socioeconomic disparities may be a result of accumulative exposure throughout life, it is unknown whether these strategies can level out the social gradient for cardiovascular events after diagnosis with T2D.[21] Randomized clinical trials focusing on this subject are needed in order to gain further insight.

Strengths and limitations

The major strengths of our study is the large sample size with minimal loss to follow-up, minimal risk of selection bias, and detailed individual-level data ensured by the Danish nationwide registers. Moreover, due to the prospective data collection in the registers, we had no recall bias and minimal differential drop-out bias.

However, our study has some limitations that we have to address. First, our cohort relies on redeemed prescriptions for antidiabetic drugs and discharge diagnoses of diabetes with high positive predictive values but a sensitivity of 72% and 64%, respectively.[20] Therefore, although the combined sensitivity is most likely higher, we may have excluded some patients with untreated T2D.

Second, outcomes relied on discharge codes. Yet, discharge diagnoses of myocardial infarction, and stroke have been validated with high positive predictive values.[15,24]

Third, we cannot completely rule out that some of the observed socioeconomic disparities in MACE were attributable to social selection. Thus, despite introducing a blanking period of 90 days after diagnosis of T2D, some patients might have had undetected cardiovascular disease at study entry which may have led to a reduction in working capacity and, hence, income. Moreover, some of the observed disparities may have been attributable to residual confounding, as we did not have access to information on behavioural (alcohol consumption, smoking status, diet, exercise, body mass index), biological (lipids, HbA1C, or blood pressure), or psychological (such as stress or health literacy) cardiovascular risk factors at study entry. However, we did account for those risk factors that had caused comorbidities or initiation of medication prior to 90 days after diagnosis of T2D.

Fourth, we had a potential detection bias underestimating the observed socioeconomic disparities, since the lowest socioeconomic group may be underdiagnosed with myocardial infarction and stroke. However, we also investigated fatal events from death certificates.

Lastly, as our study is observational, it represents associations, and no causal conclusions can be drawn.

Conclusions

In patients with incident T2D, low-socioeconomic position was associated with a significantly higher 5-year risk of first-time MACE among both men and women. This excess risk was independent of comorbidities and occurred despite of a universal health care system with free access to medical care. Our results indicate the importance of primary preventive strategies targeting patients with low-socioeconomic position. Future research investigating mediating pathways and intervention studies targeting patients with low-socioeconomic position are needed to improve outcomes in disadvantaged patients.

Supplementary material

Supplementary material is available at *European Journal of Preventive Cardiology* online.

Funding

This work was supported by grants from 'Region Sjaelland Den Sundhedsvidenskabelige Forskningsfond'; and from 'Murermester Lauritz Peter Christensen og hustru Kirsten Sigrid Christensens Fond'.

Conflict of interest: A.C.F. reports grants from 'Region Sjaelland Den Sundhedsvidenskabelige Forskningsfond' and from 'Murermester Lauritz Peter Christensen og hustru Kirsten Sigrid Christensens Fond' for the conduct of this study. T.B.H. reports personal fees from Novo Nordisk, outside the submitted work. M.S. reports lecture fees from Novo Nordisk, AstraZeneca, and Boehringer Ingelheim, outside the submitted work. C.T.P. reports grants from Bayer and Novo Nordisk, outside the submitted work. N.E.B. reports grant from Novo Nordisk, outside the submitted work A.C.R. reports speaker honorarium from Novartis, outside the submitted work. All other authors have no conflicts of interest.

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