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a nationwide study in primary care

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Prevalence of cardiovascular disease and evaluation of standard of care in type 2 diabetes: a nationwide study in primary care

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Objective Cardiovascular disease (CVD) complicates type 2 diabetes. Empagliflozin and liraglutide have demonstrated improved survival in patients with type 2 diabetes and established CVD. We assessed prevalence and standard of care of patients with type 2 diabetes and established CVD managed in primary care.

Patients and methods A total of 129 general practitioners in both rural and urban areas, responsible for 348 373 patients, identified their patients with type 2 diabetes. The identification was based on a search for International Classification of Primary Health Care 2 codes in the general practitioners' electronic patient record systems. Patients with concomitant CVD were identified and characterized.

Results A total of 17 113 (4.9%) patients were diagnosed with type 2 diabetes. Type 2 diabetes with concomitant CVD was found in 3665 (21.4%) patients, with their mean age being 72 years, and 34.6% were women. Mean estimated glomerular filtration rate was 68.2 ml/min, and 22.2% had microalbuminuria or macroalbuminuria. Standard of care was fair: mean glycated hemoglobin was 52.3 mmol/mol (Diabetes Control and Complications Trial = 6.9%), mean blood pressure was 131.4/75.7 mmHg, and mean low-density lipoprotein cholesterol was 2.0 mmol/l.

Conclusion In a nationwide database survey in primary care, the prevalence of CVD in patients with type 2 diabetes was high (21.4%). Standard of care was largely in accordance with national guidelines. Identification of eligible patients is possible with existing electronic patient record systems. Identifying this high-risk subgroup of patients with type 2 diabetes and optimizing their treatment might add further cardiovascular benefits as suggested by recent cardiovascular outcome trials. *Cardiovasc Endocrinol* 6:145–151 Copyright © 2017 The Author(s). Published by Wolters Kluwer Health, Inc.

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Introduction

Patients with diabetes are at increased risk of developing a number of serious microvascular and macrovascular complications [1]. Across all ages, the relative risk of developing cardiovascular disease (CVD) is ~ 2 for patients with diabetes compared with the general population [2,3], and CVD contributes significantly to the increased, albeit decreasing over time, mortality rate [4,5]. Still, CVD accounts for up to 50% of deaths in patients with diabetes [4]. Furthermore, the prevalence of diagnosed type 2 diabetes is constantly rising from 415 million globally in 2015 to an estimated 642 million in 2025 [6]. In Denmark, 290 000 were diagnosed with type 2 diabetes in 2012, and a further 180 000 were estimated to be undiagnosed [7].

Until recently, UK Prospective Diabetes Study (UKPDS) [8] and PROspective pioglitAzone Clinical Trial In macroVascular Events (PROactive) [9] were the only interventional studies on glucose-lowering therapies demonstrating positive effects on cardiovascular (CV) outcomes. However, both studies have limitations. In UKPDS, the demonstrated effect was achieved in a small subgroup of overweight patients treated with metformin compared with conventional, primarily nonpharmacological therapy. In the PROactive study, the secondary 3P major adverse cardiac events endpoint was significantly reduced, but the heterogeneous composite primary endpoint failed to reach significance. In 2015 and 2016, two cardiovascular outcome trials (EMPA-REG OUTCOME [10] and LEADER [11]) evaluating the long-term CV safety according to the Food and Drug Administration recommendations for new antidiabetic drugs were published (*http://www.fda.gov/downloads/ Drugs/GuidanceComplianceRegulatoryInformation/Guidance/*

ucm071627.pdf). In both EMPA-REG OUTCOME, assessing the safety of the sodium–glucose cotransporter 2 (SGLT2) inhibitor empagliflozin, and LEADER, assessing the safety of the glucagon-like peptide 1 receptor agonist liraglutide, the addition of empagliflozin or liraglutide to standard therapy of type 2 diabetes leads to a significant reduction of the primary composite endpoint of CV death, nonfatal myocardial infarction, and nonfatal stroke, compared with placebo. Reduction of the primary endpoint was predominantly driven by a reduction in CV death in both studies. Moreover, empagliflozin also demonstrated a significant reduction in the risk for hospitalization owing to heart failure [12].

On the basis of the positive findings in these outcome studies, we decided to carry out a nationwide survey of patients with type 2 diabetes and established CVD in general practice, where most patients with type 2 diabetes in Denmark are managed. The aims of the survey were to record the prevalence of concomitant CVD in a general practice population of patients with type 2 diabetes and to describe the standard of care in these patients. We searched the patient files for a diagnosis of myocardial infarction, ischemic heart disease with and without angina pectoris, heart failure, transitory cerebral ischemia or stroke, or atherosclerosis/peripheral vascular disease. In addition, atrial fibrillation, hypertension, albuminuria, diabetic retinopathy, demographic data, glycaemic status, kidney function, lipid status, and blood pressure were recorded along with information about current treatment of the patients.

Patients and methods

General practices using one of the five electronic patient record systems were approached. All five systems are certified in accordance with standards for IT systems in Danish Healthcare as governed by the Danish Medicines Agency. The five systems are used by ∼72% of Danish general practitioners (GPs). To obtain a broad sample, 526 general practices of varying size from all regions of Denmark, rural as well as urban areas, were approached, representing ∼1 out of 4 (28.5%) practices in Denmark. The included practices represented different organizational models ranging from solo practices to group settings (Fig. 1).

The practices were invited to participate by Boehringer Ingelheim Danmark A/S (BI, Denmark) sales representatives during the time period 3 May 2016–30th June 2016. GPs accepting the invitation reported their cooperation with BI to the Danish Medicines Agency. The study was approved by the Danish Data Protection Agency (no. H-16023132). In Denmark, registry studies, such as the present one, do not require approval from research ethics committees or from the Danish Medicines Agency.

Identification of patients with type 2 diabetes was made by a search in the GPs' electronic patient record systems using the International Classification of Primary Health Care 2 (ICPC-2) coding system which is anchored in the ICD-10 code system. The ICPC-2 system is fully integrated with ICD-10, and the conversion of ICD-10 codes to ICPC-2 is automatic. An accredited standard has been developed for the use of ICPC-2 in Danish primary healthcare electronic patient record systems. In close to 96% of cases, conversion is unambiguous. In the remaining cases, possible matches are suggested for the GP to choose from. In cases, where a patient is diagnosed by the GP and thus does not have an ICD-10 code, the GP assigns an ICPC-2 code. The primary inclusion criterion was a record of the ICPC-2 – DK diagnosis code T90 (type 2 diabetes), and secondly, a record of at least one of the seven ICPC-2 – DK diagnosis codes for CVD was required:

(1) K74 – Ischemic heart disease with angina pectoris.
(2) K75 – Acute myocardial infarction.
(3) K76 – Ischemic heart disease without angina pectoris.
(4) K77 – Heart failure.
(5) K89/K90 – Transient cerebral ischemia/stroke.
(6) K92 – Atherosclerosis/peripheral vascular disease.

In addition, the following nonrequired diagnoses were recorded: atrial fibrillation (K78) and hypertension (K85/K86/K87).

After primary identification, the following patients were excluded:

(1) Deceased patients.
(2) Patients who were passing through or had moved to another clinic.
(3) Patients whose diabetes was managed in a hospital setting.
(4) Patients who had a kidney transplant or were on dialysis treatment.

Included patients were numbered sequentially for each GP. If more than 20 patients qualified, 20 patients were selected for inclusion by a computerized random draw.

During the period 15 August to 20 October 2016, data were recorded through electronic case record forms specifically designed for the study. Data were entered by a web-client (Angular 2, v 4.0). For data quality assurance, the case record form system had built-in validation checks to capture and question implausible data entries. Data were entered in the case record forms by representatives from BI based on the GPs' 'oral reading' from the electronic patient record system. Thus, only the GP had direct access to the electronic patient record system. Data were processed and presented by means of descriptive statistics. There was no hypothesis testing. Data are presented as mean ± SD (range) or as proportions of patients (%). Handling and analysis of the data were done in Django 1.10 on an Ubuntu 14.04 server.

Fig. 1

526 GPs invited	
146 GPs accepted invitation	
15 GPs withdrew before data-search	
131 GPs recorded data	
2 GPs with invalid data excluded	
129 GPs with valid data	56 GPs from solo practices 21 GPs from collaboration practices 45 GPs from partnership practices with responsibility for own patients 7 GPs from partnership practices with shared responsibility for patients
Overall 348,373 patients managed by 129 GPs	
17,113 (4.9%) patients with a T90 diagnosis (T2DM)	
4,178 (24.4%) patients with at least one prespecified ICPC-2-CV diagnosis code	
	490 (11.7%) patients managed in hospital
	23 (0.6%) patients with a kidney transplant or on dialysis treatment
3,665 (21.4%) patients qualified	
	1,174 randomly excluded for GP clinics with more than 20 qualified patients
2,491 patients chosen for data recording	
	299 patients excluded after recording of data Deceased Passing through Managed elsewhere Wrongly diagnosed Other reasons
2,192 patients recorded in the database	
	189 patients excluded before analysis Lacking required ICPC-2 -CV diagnosis codes Only atrial fibrillation Only hypertension Only atrial fibrillation and hypertension
2,003 patients included in final analysis	

Consort diagram. CV, cardiovascular; GP, general practitioner; ICPC-2, International Classification of Primary Health Care 2; T2DM, type 2 diabetes mellitus.

Results and discussion
Materials
A total of 526 GPs were invited to participate, of whom 131 accepted and 129 provided valid data. Regarding overview of the data flow, refer to Fig. 1 (consort). The included GPs represented 348 373 patients, where 17 113 (4.9%) were diagnosed with type 2 diabetes, and 4198 (24.4%) of these had concomitant CVD. After exclusion of patients managed in a hospital setting or who had a kidney transplant or were on dialysis treatment, 3665 (21.4%) patients were eligible, representing the prevalence of patients with type 2 diabetes and concomitant CVD in general practice. Computerized random selection of 20 patients if more than 20 patients qualified in a clinic excluded 1174 patients, and data cleaning excluded another 488 patients, resulting in 2003 patients being included in the analysis (Fig. 1). The selection of 20 patients was truly random, based only on patient

identification numbers before any data were recorded. Thus, for exclusion of patients, there were no considerations of sex, age, duration of diabetes, or other data.

Demography and clinical status

Patient characteristics are shown in Table 1. Most patients were men (65.4%), age was 72 years, and BMI was 30.1 kg/m^2. Time since diagnosis of type 2 diabetes was less than 5 years in 28.8% and more than 10 years in 33.7% of the patients. Overall, 51 were smokers or exsmokers. Glycated hemoglobin (HbA1c) was 52.3 mmol/mol [Diabetes Control and Complications Trial (DCCT) = 6.9%], 23.5% had HbA1c > 58 mmol/mol (DCCT = 7.5%). Estimated glomerular filtration rate (eGFR) was 68.2 ml/min/1.73 m^2, 36% had eGFR less than 60 ml/min/1.73 m^2. Albuminuria (Albumin creatinine ratio > 30 mg/g) was present in 22.2%. Diabetic retinopathy was diagnosed in 6.2% of the patients. Status regarding albuminuria and retinopathy was unknown for approximately one-third of the patients. Moreover, 90% of the patients had a diabetes control in the past year. Systolic and diastolic blood pressure was 131.4 and 75.7 mmHg, respectively. low-density lipoprotein cholesterol was 2.0 mmol/l and high-density lipoprotein cholesterol was 1.2 mmol/l.

Almost 22% had no pharmacological glucose-lowering treatment, 47.5% were receiving monotherapy, and 30.1% were on dual or triple therapy. Insulin was used by 19.5% either as monotherapy or in combination (Table 2). Incretin-based therapy was used by 12.4% and SGLT2-inhibitor therapy by 4%. Moreover, 82% had cholesterol-lowering treatment, almost exclusively a statin; 94.4% had anticoagulant/antiplatelet treatment (50.1% aspirin); 66.1% were receiving ACE-I or ARB therapy; and 30.3% a loop diuretic (Table 2).

Cardiovascular disease

The mean number of CV diagnoses per patient was 1.5, ranging from 1 to 5 (Table 3). The most frequently registered CV diagnosis was ischemic heart disease with angina pectoris (32.9%) followed by transient cerebral ischemia or stroke (30.6%), myocardial infarction (25.7%), ischemic heart disease without angina pectoris (20.5%), and atherosclerosis/peripheral vascular disease (19.3%) (Table 3). Atrial fibrillation was diagnosed in 18.8% and hypertension in 66.3% of the patients.

Heart failure was diagnosed in 22.3% of the patients, predominantly men (61.9%). The age of patients with heart failure was 73.6 years compared with 71.5 years for patients without (Supplementary Table 2, Supplemental digital content 1, *http://links.lww.com/CAEN/A17*). Patients with heart failure had a slightly higher BMI. The level of lipidemic control (mean cholesterol concentrations) was approximately the same in patients with and without heart failure.

Compared with patients without heart failure, atrial fibrillation was more frequent with heart failure (13.4 vs. 37.4%), whereas the distribution of ischemic heart

Table 1 Demographic/background data

Men	1309 (65.4)
Age (years)	72.0 ± 10.4 (30–100)
Weight (kg) (n = 1563)	88.1 ± 19.7 (43.0–210.0)
BMI (n = 1297)	30.1 ± 5.9 (16.7–67.0)
Smoking (daily/occasionally/stopped/never) (%)	16.9/0.7/33.8/31.8
0–4 years since T2DM diagnosis	576 (28.8)
5–10 years since T2DM diagnosis	720 (35.9)
> 10 years since T2DM diagnosis	676 (33.7)
Time since T2DM diagnosis unknown	31 (1.5)
T2DM control at GP within the past year	1799 (89.8)
HbA1c (mmol/mol) (n = 1988)	52.3 ± 13.4 (25–138)
HbA1c ≥ 58 mmol/mol	470 (23.5)
Systolic blood pressure (mmHg) (n = 1930)	131.4 ± 15.3 (78–202)
Diastolic blood pressure (mmHg) (n = 1930)	75.7 ± 9.9 (45–118)
Systolic blood pressure > 130 mmHg	895 (44.7)
Total cholesterol (mmol/l) (n = 1977)	4.0 ± 1.1 (1.8–10.1)
LDL cholesterol (mmol/l) (n = 1916)	2.0 ± 0.9 (0.2–7.4)
HDL cholesterol (mmol/l) (n = 1978)	1.2 ± 0.4 (0.1–4.7)
LDL cholesterol > 1.8 mmol/l	946 (47.2)
eGFR (ml/min/1.73 m^2) (n = 1936)	68.2 ± 20 (6–91)
eGFR ≥ 60 ml/min/1.73 m^2	1282 (64.0)
Albuminuria status (normo/micro/macro/ unknown) (%)	45.8/18.6/3.6/32.0
Diabetic retinal changes (present/none/ unknown) (%)	6.2/64.5/29.3

Data are presented as number of patients (%) and mean ± SD (range).
eGFR, estimated glomerular filtration rate; GP, general practitioner; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; T2DM, type 2 diabetes mellitus.

Table 2 Standard of care

Glucose-lowering treatment	Number of patients [n (%)]
Metformin	1098 (54.8)
Nonpharmacological treatment	436 (21.8)
Insulin	391 (19.5)
Sulfonylurea	158 (7.9)
DPP-4 inhibitor	140 (7.0)
GLP-1 receptor agonist	108 (5.4)
SGLT2 inhibitor	80 (4.0)
Metformin + DPP-4 inhibitor	167 (8.3)
Metformin + SGLT2 inhibitor	10 (0.5)
Others	2 (0.1)
Number of patients on 1 drug treatment	951 (47.5)
Number of patients on 2 drugs treatment	478 (23.9)
Number of patients on 3 drugs treatment	124 (6.2)
Number of patients on 4 drugs treatment	13 (0.6)
Treatment for hypertension and/or heart failure	
β-Blocker	980 (48.9)
ACE inhibitor	762 (38.0)
Calcium antagonist	625 (31.2)
ARBs	563 (28.1)
Others	21 (1.0)
Diuretic treatment	
Loop diuretics	607 (30.3)
Thiazide diuretics	519 (25.9)
Others	215 (10.7)
Cholesterol-lowering treatment	
Statins	1568 (78.3)
Fibrate	7 (0.3)
Others	72 (3.6)
Anticoagulant/antiplatelet treatment	
Aspirin	1003 (50.1)
Others	888 (44.3)

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blockers; DPP-4, dipeptidyl peptidase 4; GLP-1, glucagon-like peptide 1; SGLT2, sodium–glucose cotransporter 2.

disease was almost equal between patients with and without heart failure (Supplementary Table 2, Supplemental digital content 1, *http://links.lww.com/ CAEN/A17*). Patients with heart failure had fewer cerebral events (14.8 vs. 35.1%), lower blood pressure (systolic: 127.2 vs. 132.6 mmHg, diastolic: 74.1 vs. 76.1 mmHg), and lower eGFR (62.3 vs. 69.9 ml/min/1.73 m^2) (Supplementary Table 2, Supplemental digital content 1, *http://links.lww.com/CAEN/A17*). More patients with heart failure than without were receiving insulin (22.9 vs. 18.6%), β-blockers (65.2 vs. 44.3%), and diuretics (77.1 vs. 50.2%), whereas fewer received metformin (55.8 vs. 65.8%) (Supplementary Table 2, Supplemental digital content 1, *http://links.lww.com/CAEN/A17*). The proportion of patients on sulfonylurea treatment was similar with and without heart failure (7.6 vs. 8.0%).

In all, 61% of the included patients had an ECG performed within the past year, of which one-third was abnormal (left ventricular hypertrophy: 16.2%; ST-depression: 16%) (Table 4).

Diabetes duration and complications

CV complications were not only present in patients with a long duration of diabetes. In 28.8% of the patients, type 2 diabetes was diagnosed less than 5 years ago, 35.9% of the

patients were diagnosed between 5 and 10 years earlier, and 33.7% were diagnosed more than 10 years ago (Table 1). In addition to the relatively early onset, the CV complications occurred despite well-controlled lipidemia and blood pressure (Table 1). In 29.8% of patients with heart failure, type 2 diabetes was diagnosed less than 5 years ago, 31.4% were diagnosed with type 2 diabetes between 5 and 10 years earlier, and 37.4% had diabetes for 10 years or more (Supplementary Table 2, Supplemental digital content 1, *http://links.lww.com/CAEN/A17*).

In contrast to the macrovascular complications which were equally prevalent regardless of known duration of diabetes, the prevalence of microvascular complications increased with the known duration of diabetes, particularly after 10 years (diabetic retinopathy: <5 years 2.6%, 5–10 years 4.4%, and ≥10 years 11%; microalbuminuria: <5 years 14.1%, 5–10 years 17.4%, and ≥10 years 24.1%; macroalbuminuria: <5 years 2.8%, 5–10 years 2.9%, and ≥10 years 4.9%) (Supplementary Table 1, Supplemental digital content 1, *http://links.lww.com/CAEN/A17*). Status regarding retinopathy and albuminuria was lacking for a relatively large proportion of the patients (24–37%, respectively depending on diabetes duration).

The main finding of the survey was that 21.4% of patients with type 2 diabetes in a nationwide survey in general practice in Denmark have concomitant CV conditions and are thus to be considered high-risk patients (contrasting a frequency of 8% in the Danish population as a whole, data from the Danish heart Association at *www.proxy.danskernessundhed.dk*). Generally, patients with type 2 diabetes were well managed in general practice settings. The most common complication was ischemic heart disease followed by cerebrovascular disease. Furthermore, heart failure was common, as was hypertension and atrial fibrillation. Thus, even in this relatively well-controlled population of patients with type 2 diabetes, therapeutic considerations regarding CV comorbidities should be made, as a significant number of life-years is still lost to CVD in these patients [2,13]. Importantly, the primary driver for the reductions in the primary outcomes of the CV outcome studies with empagliflozin and liraglutide was reduced CV mortality. The present results suggest that 21.4% of patients with type 2 diabetes in general practice may benefit from knowledge gained from these recent CV outcome trials [14]. In general, all CV outcome trials have confirmed overall safety for the tested drugs (saxagliptin, alogliptin, sitagliptin, lixisenatide, empagliflozin, and liraglutide). For empagliflozin and liraglutide, even a benefit extending to reduction in CV and all-cause mortality when compared with placebo and added to standard of care has been shown. Whether benefits demonstrated in these studies extend beyond patients with already established CVD remains unsettled. For heart failure, only empagliflozin has demonstrated a decrease in the need for hospitalization. Other drugs, except saxagliptin

Table 3 International Classification of Primary Health Care 2 cardiovascular diagnosis codes

ICPC-2 diagnosis codes	Number of patients [*n* (%)]
Mean number of ICPC-2 CV diagnoses	1.5 ± 0.8 (1–5)
Required for inclusion	
K74 Ischemic heart disease with angina pectoris	659 (32.9)
K75 Acute myocardial infarction	515 (25.7)
K76 Ischemic heart disease without angina pectoris	411 (20.5)
K77 Heart failure	446 (22.3)
K89/K90 Transitory cerebral ischemia/stroke	613 (30.6)
K92 Atherosclerosis/peripheral vascular disease	387 (19.3)
Additional	
K85, K86, K87 Hypertension	1327 (66.3)
K78 Atrial fibrillation	376 (18.8)

Data are presented as number of patients (%) and mean ± SD (range).
CV, cardiovascular; ICPC-2, International Classification of Primary Health Care 2.

Table 4 Electrocardiography status

	Number of patients [*n* (%)]
ECG within the past year (yes/no/unknown status) (%)	61.4/34/4.2
ECG (normal/abnormal/unknown) (%)	62.9/33.6/3.5
Left ventricular hypertrophy (yes/no/unknown) (%)	16.2/83.3/0.5
ST-depression	66 (16)
No ST-depression	345 (83.5)
ST-depression unknown	2 (0.5)
Not categorized	216 (52.3)

Data are presented as number of patients (%).

leading to an increase in hospitalization, have proved neutral in this respect. Even though the outcome trials may be difficult to interpret owing to their specific and varying patient groups, their short duration and the lack of head-to-head comparisons, we suggest that they are taken into account when deciding on the antihyperglycemic strategy in patients with CV comorbidities.

Here, in a large group of patients with type 2 diabetes and CVD, we report an acceptable concordance with treatment goals of national guidelines. Blood pressure (131/76 mmHg), lipid profile (low-density lipoprotein cholesterol = 2.0 mmol/l), and HbA1c (52.3 mmol/mol; DCCT = 6.9%) as well as the frequency of clinical assessments were within reasonable standards of good care. Overall, 16% of the patients with both type 2 diabetes and CV complications were still active smokers and 20% did not receive statins, definitely areas for improvement.

In all, 22% of the patients were not in treatment with glucose-lowering drugs, which is in contrast to Danish guidelines suggesting that metformin should be given to all. This is, however, in accordance with other studies also showing a clinical inertia toward this general recommendation [15]. Even though many patients had a significant duration of type 2 diabetes (~70% of patients had diabetes for >5 years), almost half (47.5%) were managed with one drug only, with metformin being the most frequent oral drug. Approximately 20% of the patients had insulin, which is a somewhat larger proportion than generally expected in the Danish type 2 diabetes population (~14%) [16], most likely reflecting the fact that more than 33% of the patients had a diabetes duration longer than 10 years. The use of sulfonylureas was relatively low (7.9%), possibly reflecting the debate on the cardiac safety profile of this drug class [17,18]. Relatively few patients were treated with the more recently introduced drug classes, SGLT2 inhibitors, glucagon-like peptide 1 receptor agonists, and dipeptidyl peptidase 4 inhibitors.

Heart failure was frequent in patients with CVD (22%) in primary care. Only 65–70% of the patients received an ACE inhibitor or a β-blocker which may be explained by a high frequency of patients with preserved ejection fraction, which is supported by the high proportion of women in this subgroup (38%). The patients with heart failure were older and as expected a higher frequency had atrial fibrillation. Based on recent published trials, it may be speculated how patients with diabetes and heart failure are best treated with respect to second-line therapy for glycemic control. In the recent European guidelines for heart failure, empagliflozin has an IIA recommendation for prevention of heart failure [19], and trials evaluating SGLT2 inhibitors in patients with echocardiographic phenotyped heart failure with and

without concomitant diabetes are ongoing. Two small trials evaluating liraglutide in patients with documented reduced left ventricular ejection fraction suggest that patients with heart failure may not benefit from liraglutide and that there might be a safety concern [20,21], whereas in contrast, the larger well-powered LEADER trial in a subgroup of patients with a 'history of heart failure' showed no signal of harm. At present, it may therefore be suggested that empagliflozin can prevent admission with congestion/heart failure in patients with diabetes and CVD. However, we have to await results from ongoing trials evaluating SGLT2 inhibitors in patients with echocardiographic phenotyped heart failure before it can be concluded that treatment with an SGLT2 inhibitor improves long-term outcome in patients with long-term heart failure with preserved and reduced ejection fraction.

The study included data from practices covering a broad geographical and organizational range. The study population was large and identified based on the clearly defined diagnosis codes in validated certified electronic patient record systems, and data were systematically collected. Furthermore, the retrospective nature of the study secured data representing real-life management of patients, preventing bias in selection of patients and avoiding a strict protocol-defined treatment as seen in a prospective setup.

Limitations include some degree of physicians' subjectivity in the coding. There may be some selection bias related to practices choosing to participate having a particular interest in diabetes and CV comorbidity. The overall quality of the data is subject to the extent of follow-up and the quality of the GPs' recording of patient data. There is a lack of status regarding retinopathy and albuminuria for approximately one-third of the patients and some degree of lacking of data for BMI and smoking status. Finally, the validity of the results does not extend beyond the basis of patients correctly diagnosed and recorded at the participating GP clinics.

Conclusion
In this nationwide database survey in primary care in Denmark, the prevalence of CVD in patients with type 2 diabetes was high (21.4%). Standard of care was largely in accordance with national guidelines. Identification of eligible patients is possible with existing electronic patient record systems. Identifying this high-risk subgroup of patients with type 2 diabetes and optimizing their treatment might add further CV benefits as suggested by recent CV outcome trials.

Acknowledgements

Conflicts of interest

Jorgen Rungby is in the advisory panel of Boehringer Ingelheim Pharmaceuticals Inc., Novo Nordisk A/S, Merck & Co. Inc. Morten Schou, Per Warrer, and Lars Ytte is in the advisory panel of Boehringer Ingelheim Pharmaceuticals Inc. Gert S. Andersen is an employee of Boehringer Ingelheim Pharmaceuticals Inc.

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