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Gender differences in cardiovascular risk profiles and diabetes care among adults with type 2 diabetes in Germany

The cardioprotective effects of female *vs.* male gender are lost or even reversed in the presence of diabetes mellitus [1]. Yet, investigating gender differences in cardiovascular risk profiles and indicators of diabetes care among adults with diabetes can help to clarify such differences in diabetes-related complications [2]. A study using data from general-practice clinics across southwest Germany found that women with type 2 diabetes (T2D) were less likely to receive medications for treatment of coronary heart disease (CHD) than men with T2D in the presence of CHD [3]. However, data from large population-based studies are scarce, particularly in Germany [4]. Thus, the present report on gender differences in cardiovascular risk profiles and diabetes care is based on a nationwide representative sample of adults with T2D in Germany, using data from the most recent German National Health Interview and Examination Survey (DEGS1 2008–2011).

Of the 7115 DEGS1 participants aged 18–79 years, a total of 591 (309 men, 282 women) had diabetes as defined by a history of physician-diagnosed diabetes or current use of antidiabetic drugs [5]. After excluding those with type 1 diabetes ($n = 8$) and women with gestational diabetes ($n = 42$) as described previously elsewhere [5], as well as patients with T2D aged < 40 years ($n = 15$), the present study was finally based on data from 526 T2D patients (302 men, 224 women) aged 40–79 years (Table 1). As previously described in detail [6], data collection comprised:

- sociodemographic factors and health-related behaviours using self-administered questionnaires;
- personal history of physician-diagnosed diabetes, cardiovascular disease (CVD), hypertension and hyperlipidaemia, age at diagnosis of diabetes, diabetes-specific complications, diabetes-related self-management and diabetes care indicators based on computer-assisted personal interviews;
- detailed review of all medications used within the past 7 days;
- and highly standardized anthropometric, blood pressure (BP) and laboratory measures, including glycated haemoglobin A_{1c} (HbA_{1c}), serum total cholesterol and high-density lipoprotein (HDL) cholesterol, serum creatinine and semiquantitative measures of albuminuria.

DEGS1 was approved by the Federal and State Commissioners for Data Protection and the Charité-Universitätsmedizin Berlin ethics committee (No. EA2/047/08). Survey participants provided their written informed consent prior to the interviews and examinations.

Gender-specific prevalence estimates and 95% confidence intervals (CIs) were calculated for cardiovascular risk variables and indicators of diabetes care as per the current clinical guideline recommendations for primary and secondary prevention of CVD in patients with diabetes [7]. Absolute differences in prevalence estimates among women compared with men were also calculated and adjusted for current age, diabetes duration (the difference between age at diagnosis and current age) and potential confounders, including region of residence, community size, living alone and educational attainment (classified as primary, middle and high), according to the international Comparative Analysis of Social Mobility in Industrial Nations (CASMIN) [6]. Stata SE 14 software (StataCorp LLC, College Station, TX, USA) was used for all statistical analyses.

Among the eligible adults diagnosed with T2D, men and women did not differ significantly in mean age (65.1 years *vs.* 66.6 years), age at diabetes diagnosis (54.7 years *vs.* 54.3 years), diabetes duration (10.2 years *vs.* 12.1 years), prevalence of physician-diagnosed hypertension (76.8% *vs.* 83.0%) or hyperlipidaemia (58.0% *vs.* 55.2%), or region of residence or community size (data not shown). Compared with men, women with T2D were less likely to be highly educated (4.6% *vs.* 13.2%) and more likely to be living alone (30.0% *vs.* 16.2%, respectively).

As for cardiovascular risk profiles, women with T2D had a higher prevalence of elevated non-HDL cholesterol and central obesity, but a lower CVD prevalence compared with men (Table 1). In both genders, $> 90\%$ of adults with T2D had at least one classic CVD risk factor. Women performed better than men in some indicators related to self-management (glucose self-monitoring, eye examination within the past 12 months). Most notably, among insulin users, nearly all men and women reported self-monitoring of blood glucose (data not shown). Moreover, women with T2D overall were significantly and consistently less likely than men to use guideline-recommended medications for CVD prevention [statins, antithrombotic medications ($> 90\%$ aspirin)], although these differences were less pronounced and not statistically significant among those diagnosed with CVD. Women were also significantly less likely to use first-line antihypertensive medications such as angiotensin-converting enzyme inhibitors (ACEIs)/

Table 1
Cardiovascular risk profiles and indicators of diabetes care in men and women aged 40–79 years with type 2 diabetes who participated in the German National Health Interview and Examination Survey (DEGS1 2008–2011).

	Men (n = 302)				Women (n = 224)				Prevalence differences[b]		
	n	%[a]	95% CI[a]		n	%[a]	95% CI[a]		%[a]	95% CI[a]	
Cardiovascular risk profiles											
Non-HDL ≥ 130 mg/dL (3.4 mmol/L)	182	59.5	52.1	66.4	163	75.3	67.9	81.5	**16.5**	**6.6**	**26.5**
Blood pressure ≥ 140/80 mmHg	125	41.2	33.9	49.0	93	40.5	32.6	48.9	−4.3	−14.0	5.4
Central obesity (waist circumference: men > 102 cm, women > 88 cm)	208	67.8	60.5	74.3	191	82.6	74.1	88.7	**17.8**	**8.2**	**27.4**
Body mass index ≥ 30 kg/m^2	159	50.5	42.8	58.2	129	60.4	52.1	68.1	9.4	−2.0	20.7
Current smoker	50	19.4	13.8	26.5	38	17.7	12.0	25.2	−3.2	−12.6	6.2
No participation in any sports activity	133	46.5	38.7	54.5	101	50.5	41.9	59.0	−3.2	−14.4	8.0
At least one of the above risk factors	286	93.3	87.6	96.5	222	98.9	95.6	99.7	**5.0**	**1.1**	**8.8**
Diabetes-specific complications[c]	60	19.6	14.8	25.4	47	24.3	17.8	32.2	6.9	−2.6	16.4
Chronic kidney disease[d]	140	41.9	35.1	49.0	86	38.4	29.9	47.7	−7.3	−18.1	3.5
Cardiovascular disease (CVD)[e]	120	42.5	34.8	50.6	66	31.3	23.5	40.4	**−13.8**	**−24.2**	**−3.4**
Diabetes care indicators											
Self-monitoring of glucose	176	61.5	54.8	67.8	147	65.6	56.7	73.5	**12.1**	**3.3**	**20.8**
Holder of a diabetes passport	161	51.3	44.0	58.6	131	59.1	50.5	67.2	9.0	−0.7	18.7
Ever participated in a diabetes education programme	173	60.9	53.9	67.4	137	61.9	53.2	69.8	8.3	−2.0	18.6
HbA_{1c} < 7.0% (53 mmol/mol)	195	63.7	56.1	70.7	150	67.1	58.4	74.8	2.4	−8.5	13.3
Individualized HbA_{1c} goal[f] achieved	220	79.9	72.9	85.4	156	80.4	72.7	86.3	1.1	−7.5	9.7
HbA_{1c} test within past 12 months	256	91.8	85.8	95.4	190	95.5	91.5	97.7	3.5	−1.0	8.0
Eye examination within past 12 months	218	72.7	65.4	79.0	176	86.1	80.1	90.6	**12.6**	**4.1**	**21.2**
Foot examination within past 12 months	181	60.5	52.8	67.7	126	63.1	54.1	71.3	4.2	−6.4	14.9
Statin use overall	129	42.2	34.6	50.2	75	31.1	24.0	39.2	**−10.7**	**−20.8**	**−0.6**
Patients with history of CVD	80	66.2	52.0	78.0	35	49.5	35.2	63.8	−16.9	−33.9	0.2
Antithrombotic medication use overall	98	35.1	28.8	42.1	58	25.2	18.5	33.3	**−10.7**	**−20.0**	**−1.5**
Patients with history of CVD	66	60.0	48.2	70.8	37	52.4	37.4	67.1	−10.0	−28.4	8.3
ACEI/ARB use overall	203	65.7	57.9	72.8	134	55.4	46.6	63.8	**−11.9**	**−22.8**	**−0.9**
Patients with history of hypertension	182	77.9	69.7	84.4	129	63.2	52.8	72.5	**−14.0**	**−25.7**	**−2.3**
Antihypertensive drug use overall	234	75.5	67.9	81.8	180	77.7	69.4	84.2	1.1	−7.0	9.1
Patients with history of hypertension	204	87.5	79.5	92.7	168	87.5	78.1	93.3	−0.4	−7.0	6.2
Diabetes treatment pattern											
No treatment at all	34	13.4	8.8	19.7	33	19.5	12.7	28.6	2.2	−6.0	10.4
Diet only	28	8.3	5.4	12.6	29	11.4	7.4	17.0	4.5	−1.2	10.2
Insulin only (with/without diet)	35	11.4	7.5	17.0	22	12.3	7.5	19.4	−0.6	−7.7	6.4
Insulin + oral agents (with/without diet)	36	12.9	8.9	18.3	31	14.2	8.8	22.1	4.1	−2.9	11.0
Oral agents only (with/without diet)	159	54.0	46.3	61.5	106	42.7	34.5	51.3	−10.1	−21.4	1.3

All drugs, including antidiabetics, with documented use within the past 7 days; ACEI/ARB: angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker; HDL: high-density lipoprotein.

[a] Weighted to German population as of 31 December 2010.

[b] Women *vs.* men; 95% confidence intervals (CIs) derived from multivariable logistic-regression models adjusted for age (40–49, 50–59, 60–69, 70–79 years), community size (rural, or small, middle, large cities), region (east, northwest, central, south), educational attainment (primary, middle, high), living alone (yes/no), diabetes duration (< 5, 5–14, ≥ 15 years); statistically significant differences ($P < 0.05$, two-sided tests) in bold.

[c] Self-reported diabetic nephropathy, diabetic retinopathy, diabetic neuropathy, diabetic foot, diabetes-related amputation.

[d] Estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2, presence of moderate-to-severe albuminuria.

[e] Self-reported history of physician-diagnosed heart failure, stroke, myocardial infarction, other coronary heart disease in people aged ≥ 40 years.

[f] < 7.0% (53 mmol/mol) for those aged < 45 years, < 8.0% (64 mmol/mol) for those aged 45–79 years with diabetes-specific complications or comorbid CVD; < 6.5% (48 mmol/mol) for those aged < 45 years, < 7.0% (53 mmol/mol) for those aged 45–64 years, < 7.5% (58 mmol/mol) for those aged 65–79 years with no diabetes-specific complications or comorbid CVD.

angiotensin II receptor blockers (ARBs), whether overall or only in those with a history of physician-diagnosed hypertension. No statistically significant gender differences related to antidiabetic treatment were observed.

Consistent with previous epidemiological studies, both central obesity and atherogenic dyslipidemia were more prevalent in women than in men with T2D [1]. The greater prevalence of elevated non-HDL cholesterol in women than in men may be partly explained by less statin use in women than in men with T2D, as observed here and previously [8]. Women appear to do better than men with regard to selected indicators of diabetes self-management, including eye examinations [9] and glucose monitoring [8], but not HbA1c testing [8,9] or foot examinations [9]. This probably reflects the conflicting results from previous studies indicating better adherence to medical advice and annual visits among women than men with T2D [9], but also the wider variability of diabetes care provided to women compared with men.

Yet, in contrast to our present findings, a US primary care study of patients with diabetes found that women had 19% greater odds of achieving HbA_{1c} levels < 7% than men, and no gender difference in ACEI use was observed [8]. In line with a previous study in Germany of gender differences in diabetes care in a primary care setting [3], our study found no or only slight differences in antidiabetic treatment, albeit with less guideline-adhering treatment for CVD prevention in women than in men. In fact, the current clinical guidelines for CVD prevention in patients with T2D recommend preventative pharmacotherapy with statins and antithrombotic agents for men and women with diagnosed CVD, or high cardiovascular risk as defined by cardiovascular risk scores [1] or the presence of at least one major risk factor [7]. Also, women in our study had a significantly lower CVD prevalence than men, and the observed gender differences in CVD prevention were less pronounced among those diagnosed with CVD. This might be an indication that preventative treatment is largely confined to people with a CVD diagnosis. Nevertheless, it is well possible that CVD is underdiagnosed in women [10], as the proportion of women with T2D in our study with at least one major CVD risk factor was nearly 100% and significantly exceeded the proportion of men.

No gender differences were observed in the achievement of goals for BP or the lifetime prevalence of diagnosed hypertension. In contrast, previous studies have reported a greater prevalence of measured hypertension in women compared with men, especially in older age

groups [1]. However, gender differences regarding BP medication were confined to first-line antihypertensive use, and not overall antihypertensive drug use. This may suggest that women are more susceptible to the well-known adverse effects of ACEIs such as dry coughs, leading to the prescription of alternative antihypertensive agents.

One major strength of the present study is that it used data from a nationally representative sample of patients with T2D, thereby reflecting diabetes care in people with T2D living in communities. There are also limitations implicit in the population-based survey design of the present study. Severely ill persons are likely to be missed. Persons 80 years of age and older were not included in the study, as they are hard to reach and likely to be underrepresented in population surveys. In addition, the absolute number of persons with T2D was rather small compared to studies conducted in the primary care setting or based on diabetes registries.

In conclusion, the results of this nationwide population-based survey of adults aged 40–79 years with T2D in Germany indicate the presence of gender differences in cardiovascular profiles and persistent gender differences in CVD prevention, despite the introduction of disease management programmes for diabetes patients. In addition, gender differences in CVD risk need further elucidation to provide a sound evidence base for future guideline recommendations and diabetes care monitoring.

Contribution statement

Y.D. conceptualized the study, performed the statistical analyses and drafted the manuscript. J.B. supported the statistical analyses, reviewed and edited the manuscript, and contributed to the discussion of results. R.P., H.N. and C.H. reviewed and edited the manuscript, and contributed to the discussion of results. C.S.-N. conceptualized and supervised the study, and substantially contributed to the writing of the manuscript. Y.D. as the guarantor takes full responsibility for the work as a whole, including the study design, access to data, and the decision to submit and publish the manuscript.

All authors read and approved the final version of the manuscript.

Disclosure of interest

The authors declare that they have no competing interest.

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Association of sleep apnoea syndrome and autonomic neuropathy in type 1 diabetes

Introduction

Obstructive sleep apnoea (OSA) is frequently observed in patients with type 2 diabetes (T2D), primarily because of the high prevalence of obesity. OSA is an independent risk factor for cardiovascular morbidity and mortality that also increases the risk of hypertension, stroke, acute coronary syndrome and arrhythmias. Also, OSA contributes to increased insulin resistance and glucose intolerance. A recent meta-analysis documented a high prevalence of sleep-disordered breathing in patients with type 1 diabetes (T1D) [1], while other studies have also examined the association between T1D and OSA [2–4]. Manin et al. [2] found an OSA prevalence [apnoea–hypopnoea index (AHI) $>$ 10/h] of 46% in 67 T1D patients using polysomnography, with severe OSA (AHI $\geq$ 30/h) detected in 19% of these patients, while Borel et al. [3] found sleep apnoea (defined as an AHI $\geq$ 15/h) in 40% of 37 subjects screened by nocturnal oximetry. Schober et al. [4] diagnosed OSA in 10.3% of 58 patients with T1D, who also had a high prevalence of autonomic neuropathy. However, the underlying mechanisms of OSA in T1D are currently poorly understood.

As sweat glands are innervated by autonomic C fibres, quantitative assessment of the sweat response has been proposed