Cardiovascular Diabetology

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# Sex inequalities in cardiovascular risk factors and their management in primary prevention in adults living with type 1 diabetes in Germany and France: findings from DPV and SFDT1

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## Abstract

**Introduction & objectives** To evaluate whether cardiovascular risk factors and their management differ in primary prevention between adult males and females with type 1 diabetes (T1D) in two European countries in 2020–2022 and sex inequalities in achievement of standards of care in diabetes.

**Methods** We used 2020–2022 data of patients without a cardiovascular history in the Prospective Diabetes Follow-up registry (DPV) centres, in Germany, and the Société Francophone du Diabète– Cohorte Diabète de Type 1 cohort (SFDT1), in France.

**Results** We included 2,657 participants from the DPV registry and 1,172 from the SFDT1 study. Body mass indexes were similar in females and males with similar proportions of HbA1c < 7% (DPV: 36.6 vs 33.0%, p = 0.06, respectively; SFDT1: 23.4 vs 25.7%, p = 0.41). Females were less overweight compared to men in DPV (55.4 vs 61.0%, p < 0.01) but not in SFDT1 (48.0 vs 44.9%, p = 0.33) and were less prone to smoke (DPV: 19.7 vs 25.8%, p < 0.01; SFDT1: 21.0 vs 26.0%, p = 0.07). Systolic blood pressure was lower in females than males with a higher rate of antihypertensive therapy in case of hypertension in females in DPV (70.5 vs 63.7%, p = 0.02) but not in SFDT1 (73.3 vs 68.6%, p = 0.64). In the case of microalbuminuria, ACEi-ARB were less often prescribed in women than men in DPV (21.4 vs 37.6%, p < 0.01) but not SFDT1 (73.3 vs 67.5.0%, p = 0.43). In females compared to males, HDL-cholesterol levels were higher; triglycerides were lower in both countries. In those with LDL-cholesterol > 3.4 mmol/L (DPV: 19.9 (females) vs 23.9% (males), p = 0.01;

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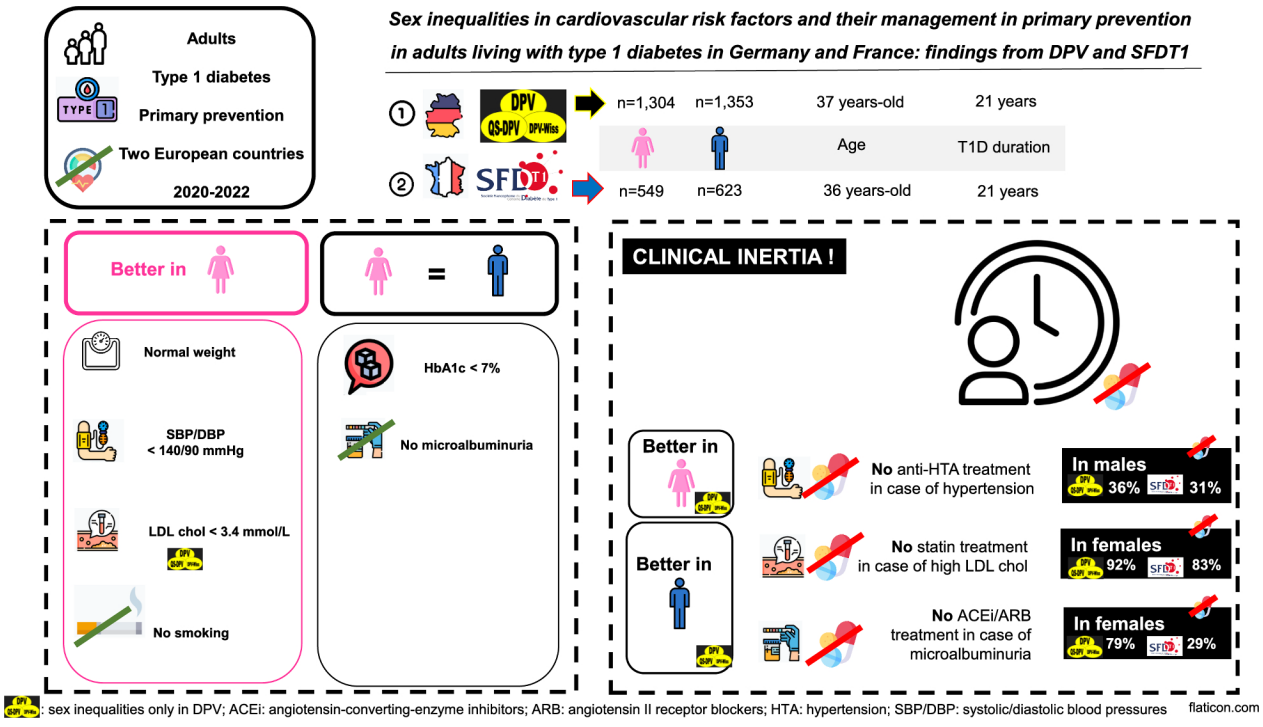
SFDT1 17.0 vs 19.2%, p = 0.43), statin therapy was less often prescribed in females than males in DPV (7.9 vs 17.0%, p < 0.01), SFDT1 (18.2 vs 21.0%, p = 0.42).

**Conclusion** In both studies, females in primary prevention have a better cardiovascular risk profile than males. We observed a high rate of therapeutic inertia, which might be higher in females for statin treatment and nephroprotection with ACEi-ARB, especially in Germany. Diabetologists should be aware of sex-specific differences in the management of cardiorenal risk factors to develop more personalized prevention strategies.

**Graphical abstract**




**Keywords** Blood pressure, Body mass index, Cardiovascular, Gender, Lipids, Registry, Real-world-evidence, Sex, Smoking, Type 1 diabetes

## Introduction

Cardiovascular morbidity and mortality are a significant concern in persons living with type 1 diabetes (T1D) [1–4]. The incidence of T1D is rising with an earlier age of onset [5]. It leads to earlier and more prolonged exposure to hyperglycemia, two conditions associated with cardiovascular disease [1, 2, 4, 6–8]. In addition to HbA1c levels and diabetes duration, other cardiovascular risk factors have been documented in T1D, including older age, higher LDL cholesterol and triglycerides levels, hypertension, smoking, nephropathy, sedentary lifestyle, and male sex [4, 6, 7].

As in the general population [9], females have an overall lower risk of cardiovascular disease than males with T1D [6, 7]. However, the magnitude of cardioprotection in females with T1D is reduced [3] compared to females without diabetes [2]. This result may be due to sex differences in the prevalence of cardiovascular risk factors and inequalities in their control and management.

Therefore, we aimed to explore in patients with T1D in primary cardiovascular prevention (i) sex differences in the prevalence of cardiovascular risk factors and their management (ii) and sex inequalities in achievement of American Diabetes Association standards of care in diabetes. We examined data from two European countries where recent data were available: the multicenter Prospective Diabetes Follow-up Registry (DPV) in Germany (www.d-p-v.eu) and the Société Francophone du Diabète– Cohorte Diabète de Type 1 (SFDT1) in France [10].

## Methods

### The DPV and SFDT1 cohorts

In both countries, we included patients aged 18 years or older whose T1D had been diagnosed between 6 months

and < 35 years and whose first insulin treatment had occurred within one year since diagnosis. We included the patients without a history of cardiovascular events, namely acute coronary syndrome, coronary angioplasty, coronary artery bypass graft, stroke, surgery of the supra-aortic trunks, angioplasty of the lower limbs, arterial surgery of the lower limbs, heart failure and lower limb amputation not due to trauma.

DPV was started in 1995 on a national basis, with the inclusion of adult patients beginning in 2000. Standardized anonymous data are collected based on an electronic health record system. Data include routine medical data on presentation, care and outcome [11]. Every 6 months, anonymized data are transferred from the participating centres to the central administrative unit at Ulm University, checked for validity, and included in the cumulative DPV database. Data are used for quality improvement by comparing indicators of treatment and outcome (benchmarking) and for patient-centred research projects. Additional information on the initiative and a complete list of all publications is available at d-p–v.eu. For the present analysis, we used data from all medical visits between January 2020 and December 2022, which were documented by participating centres located in Germany and included more than 100 patients.

The primary objective of the SFDT1 cohort study is to evaluate the risk factors/determinants of incident major adverse cardiovascular events in individuals with T1D. The study has been previously described [10]. The current analysis was performed on data collected by a medical doctor during the baseline visit on eligible participants enrolled between June 2020 and October 2022.

### Data collection

For SFDT1, we used for each patient data that were collected at inclusion. For DPV, we used data of all available visits within the period 2020–2022 and aggregated values for each patient as median (continuous variables) or maximum (binary variables). We considered the following descriptive variables (Tables 1 and 2):

- Individual characteristics: age, sex, and diabetes duration,
- Personal history of diabetes-related complications: retinopathy, nephropathy and neuropathy. Retinopathy diagnosis was retrieved from medical reports. Nephropathy was defined as microalbuminuria (albuminuria/creatininuria > 3 mg/mmol) or estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73m$^2$ (CKD-EPI equation). Neuropathy was defined as impaired ankle reflexes, impaired perception or pain in feet or legs or any sign of autonomic neuropathy,

**Table 1** Characteristics of patients in primary prevention in the DPV registry (Germany) and the SFDT1 cohort (France)

| | DPV | | SFDT1 | |
|---|---|---|---|---|
| | Available subjects (n) | Total | Available subjects (n) | Total |
| Characteristics | | n = 2,657 | | n = 1,172 |
| Age (years) | 2,657 | 37 (28–52) | 1,172 | 36 (27–49) |
| Diabetes duration (years) | 2,657 | 21 (12–32) | 1,172 | 21 (12–30) |
| Complications | | | | |
| Retinopathy | 1,400 | 201 (14.4%) | 1,163 | 455 (39.1%) |
| Nephropathy | 1,939 | 392 (20.2%) | 873 | 141 (16.2%) |
| Estimated glomerular filtration rate < 60 ml/min | 2,384 | 119 (5.0%) | 1,060 | 30 (2.8%) |
| Albuminuria | 1,961 | 305 (15.6%) | 882 | 122 (13.8%) |
| Neuropathy | 2,657 | 1,279 (48.1%) | 1,091 | 304 (27.9%) |
| Cardiovascular risk factors and management | | | | |
| HbA1c (%) | 2,616 | 7.4 (6.7–8.3) | 1,139 | 7.5 (7.0–8.3) |
| CSII | 2,657 | 790 (29.7%) | 1,165 | 592 (50.8) |
| Body mass index (kg/m$^2$) | 2,626 | 26.0 (22.9–29.9) | 1,100 | 24.7 (22.3–28.3) |
| Systolic blood pressure (mmHg) | 2,596 | 125 (118–135) | 1,100 | 122 (113–132) |
| Diastolic blood pressure (mmHg) | 2,596 | 79 (70–80) | 1,100 | 73 (66–79) |
| Antihypertensive treatment | 2,657 | 656 (24.7%) | 1,172 | 220 (18.8) |
| Total cholesterol (mmol/L) | 2,178 | 4.8 (4.2–5.4) | 1,029 | 4.5 (3.9–5.2) |
| HDL cholesterol (mmol/L) | 2,174 | 1.5 (1.3–1.9) | 1,037 | 1.5 (1.2–1.8) |
| Triglycerides (mmol/L) | 2,155 | 1.1 (0.8–1.6) | 1,037 | 0.8 (0.6–1.2) |
| LDL cholesterol (mmol/L) | 2,175 | 2.8 (2.3–3.4) | 1,029 | 2.6 (2.0–3.1) |
| Lipid-lowering treatment | 2,657 | 368 (13.9%) | 1,140 | 281 (24.6) |

Data are given as the median (lower–upper quartile) or n (%)

*CSII* continuous subcutaneous insulin infusion

**Table 2** Characteristics and complications of patients in primary prevention by sex in the DPV registry (Germany) and the SFDT1 cohort (France)

| | DPV | | | SFDT1 | | |
|---|---|---|---|---|---|---|
| | **Females** | **Males** | **p** | **Females** | **Males** | **p** |
| | 1,304 (49.1%) | 1,353 (50.9%) | | 549 (46.8%) | 623 (53.2%) | |
| Age (years) | 37 (28–51) | 38 (28–52) | 0.417 | 36 (27–49) | 37 (28–49) | 0.658 |
| Diabetes duration (years) | **22 (13–33)** | **21 (11–31)** | **0.002** | 22 (13–31) | 20 (11–30) | 0.055 |
| Retinopathy | 96 (14.1%) | 105 (14.6%) | 0.787 | 202 (37.0%) | 253 (41.0%) | 0.181 |
| Nephropathy | 190 (19.7%) | 202 (20.7%) | 0.596 | 63 (15.9%) | 78 (16.3%) | 0.956 |
| eGFR < 60 ml/min | 66 (5.6%) | 53 (4.4%) | 0.156 | 16 (3.2%) | 14 (2.5%) | 0.644 |
| Albuminuria | 140 (14.4%) | 165 (16.7%) | 0.164 | 51 (13.0%) | 71 (14.5%) | 0.612 |
| Neuropathy | 615 (47.2%) | 664 (49.1%) | 0.324 | 146 (28.6%) | 158 (27.2%) | 0.646 |

Data are given as the median (lower–upper quartile) or n (%)

*eGFR* estimated glomerular filtration rate

p-value: comparison between females and males in the DPV registry and then the SFDT1 cohort (p<0.05 in bold)

**Table 3** Cardiovascular risk factors and their management by sex in the DPV registry (Germany) and the SFDT1 cohort (France)

| | DPV | | | SFDT1 | | |
|---|---|---|---|---|---|---|
| | **Females** | **Males** | **p** | **Females** | **Males** | **p** |
| Glucose control | | | | | | |
| HbA1c (%) | 7.4 (6.7–8.3) | 7.4 (6.8–8.3) | 0.050 | 7.5 (7.0–8.2) | 7.5 (6.9–8.4) | 0.519 |
| CSII | **482 (37.0%)** | **308 (22.8%)** | **< 0.001** | **337 (61.7%)** | **255 (41.2)** | **< 0.001** |
| Weight status | | | | | | |
| Body mass index (kg/m$^2$) | 25.8 (22.7–30.1) | 26.3 (23.2–29.7) | 0.180 | 24.8(22.1–28.7) | 24.7 (22.5–27.5) | 0.665 |
| Obesity | 330 (25.5%) | 310 (23.2%) | 0.169 | 92 (18.1%) | 86 (14.5%) | 0.127 |
| Blood pressures | | | | | | |
| Systolic blood pressure (mmHg) | **120 (113–130)** | **130 (120–139)** | **< 0.001** | 119 (110–129) | 125 (117–134) | **< 0.001** |
| Diastolic blood pressure (mmHg) | **76 (70–80)** | **80 (72–82)** | **< 0.001** | **70 (64–77)** | **75 (68–80)** | **< 0.001** |
| Antihypertensive treatment | 304 (23.3%) | 352 (26.0%) | 0.106 | **86 (15.7)** | **134 (21.5)** | **0.013** |
| Lipid parameters | | | | | | |
| Total cholesterol (mmol/L) | **4.8 (4.3–5.5)** | **4.7 (4.1–5.4)** | **< 0.001** | 4.5 (4.0–5.2) | 4.5 (3.9–5.1) | 0.107 |
| HDL cholesterol (mmol/L) | **1.7 (1.4–2.1)** | **1.4 (1.2–1.6)** | **< 0.001** | **1.6 (1.3–1.9)** | **1.4 (1.2–1.6)** | **< 0.001** |
| Triglycerides (mmol/L) | **1.0 (0.7–1.4)** | **1.2 (0.9–1.7)** | **< 0.001** | **0.8 (0.6–1.1)** | **0.9 (0.7–1.2)** | **< 0.001** |
| LDL cholesterol (mmol/L) | **2.8 (2.3–3.3)** | **2.9 (2.3–3.5)** | **0.013** | **2.5 (2.0–3.1)** | **2.6 (2.1–3.2)** | **0.029** |
| Lipid-lowering treatment | **150 (11.5%)** | **218 (16.1%)** | **< 0.001** | 120 (22.6) | 161 (26.4) | 0.152 |

Data are given as the median (lower–upper quartile) or n (%)

*CSII* continuous subcutaneous insulin infusion

P-value: comparison between females and males in the DPV registry and then the SFDT1 cohort, (p<0.05 in bold)

(i) To explore sex differences in the prevalence of cardiovascular risk factors and their management (Tables 1 and 3), we considered the following variables:

- Glycemic control evaluated with routine HbA1c measurement,
- Insulin therapy with a pen or continuous subcutaneous insulin infusion (CSII), including low glucose suspend-predictive low glucose suspend systems or hybrid closed loop,
- Routine measurement of weight and height with the calculation of body mass index (BMI): overweight defined as BMI between 25.0 and 29.9 kg/m$^2$; obesity as BMI ≥ 30 kg/m$^2$),
- Systolic and diastolic blood pressures (SBP and DBP, respectively) measured resting period following current guideline; any antihypertensive treatment (including specifically angiotensin-converting-enzyme inhibitors (ACEi) and angiotensin II receptor blockers (ARB),
- Lipids routinely measured as fasting or non-fasting in DPV and after 12 h fasting in SFDT1; any lipid-lowering treatment (including statin, fibrates, ezetimibe or PCSK9 inhibitor).

(ii) To explore sex inequalities in achievement of standards of care in diabetes (Fig. 1), we considered the following specific targets in primary cardiovascular prevention according to the American Diabetes Association standards of care in diabetes 2018 [12]:

- HbA1c level < 7%,

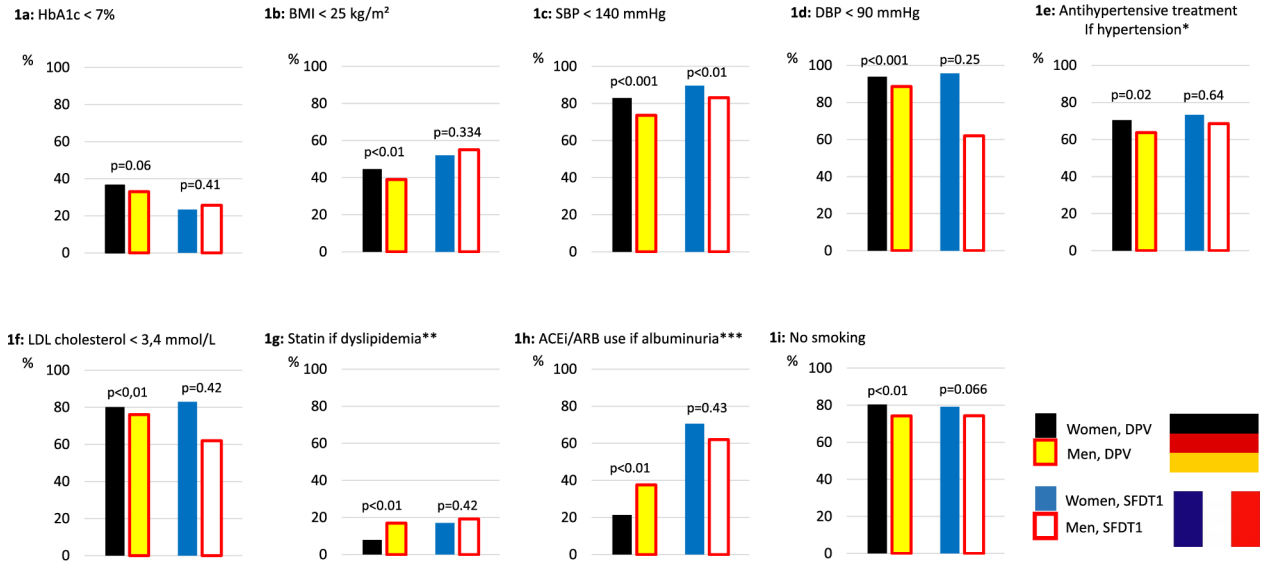



**Fig. 1** Achievement of standards of care in diabetes in primary cardiovascular prevention stratified by sex in the DPV (Germany) and the SFDT1 (France) studies. *ACEi* angiotensin-converting-enzyme inhibitors, *ARB* angiotensin II receptor blockers, *BMI* body mass index, *DPB* diastolic blood pressure, *SBP* systolic blood pressure; *defined as SBP ≥ 140 mmHg or ≥ 90 mmHg or antihypertensive treatment; **defined as LDL cholesterol ≥ 3.4 mmol/L; ***defined as albuminuria/creatininuria > 3 mg/mmol

- BMI < 25 kg/m$^2$,
- SBP < 140 mmHg and DBP < 90 mmHg; and antihypertensive treatment in case of hypertension (defined as SBP ≥ 140 mmHg or DPB ≥ 90 mmHg or antihypertensive treatment),
- LDL cholesterol < 3.4 mmol/L; and use of statin if LDL cholesterol is ≥ 3.4 mmol/L,
- Use of ACEi-ARB in case of microalbuminuria and
- No current self-reported smoking.

### Statistical analyses

Continuous variables were expressed as median (lower–upper quartile). Categorical variables were described as the number and percentages. The associations between sex and patient characteristics were analyzed using the Chi-2 test for qualitative variables. For quantitative variables, we used the non-parametric Mann–Whitney test because we assume that the data on cardiovascular risk factors and their management in our two populations might have a similar shape but do not have a normal or symmetric distribution. All tests were two-sided at a 0.05 significance level.

Statistical analyses were conducted using SAS version 9.4 (build TS1M7, SAS Institute Inc, Cary, NC) in DPV, and using R studio R version 4.2.2 with Rpackages "dplyr", "tibble"lubridate","upstartr" in SFDT1 study.

## Results

### Inclusion

A total of 3,082 adult patients had available data in the dedicated DPV centres. Of them, we excluded the 425 subjects (overall 13.8%) with a history of cardiovascular disease—whose prevalence was 11.8% in females and 15.6% in males (p < 0.01). We therefore included 2,657 patients from the DPV, with 1,304 females (49.1%). Of all patients included, 631 (23.7% of DPV inclusions), 702 (26.4%) and 1,324 (49.8%) had their last visit in 2020, 2021 and 2022, respectively.

A total of 1,264 adult patients had available data in the SFDT1 centres. Of them, we excluded 80 participants with a history of cardiovascular disease—whose prevalence was 3.5% in females and 8.7% in males (p < 0.01). We also excluded 12 participants with missing data in cardiovascular history. We therefore included 1,172 participants (549 females, 46.8%) in primary cardiovascular prevention. Of these, 242 (20.6%), 335 (28.6%) and 595 (50.8%) had been included in 2020, 2021 and 2022, respectively.

Their baseline characteristics are shown in Table 1. Diabetes duration was slightly longer in females than men in DPV (p < 0.01) and SFDT1 (p = 0.06). The rates of diabetes-related complications were similar in females and males (Table 2).

### Cardiovascular risk factors: control and related treatments according to sex (Table 3)

In both cohorts, HbA1c levels were similar in females and males, and females were more prone to use CSII than

multiple daily insulin injections. BMI was also similar in both sexs.

In both countries, blood pressures were higher in males than in females, with a higher rate of antihypertensive therapy in males than in females in SFDT1. Overall, lipid values were more favourable in females than in males, despite more lipid-lowering treatment in males than females in DPV (not statistically significant in SFDT1).

#### Achievement of standards of care in diabetes according to sex (Fig. 1)

HbA1c < 7% was obtained at a similar rate in females as in males in both cohorts. Normal weight was more frequent in females than males in DPV (44.6 vs 39.0%, p < 0.01) but not in SFDT1 (52.0 vs 55.1% respectively, p = 0.33).

Females achieved blood pressure goals more frequently than males in both cohorts. SBP or DBP above the targets (140/90 mmHg) was reported in 431/1,281 females and 553/1,320 males in DPV (33.6 vs 41.9% respectively, p < 0.01). In these patients, antihypertensive therapy was more frequently prescribed in females than males in DPV (70.5 vs 63.7, p = 0.02) but not SFDT1 (73.3 vs 68.6%, p = 0.64).

Females achieved LDL cholesterol goal more frequently than males in DPV registry. LDL cholesterol > 3.4 mmol/l was observed in 260/1,304 females and 323/1,353 males in DPV (19.9 vs 23.9%, p = 0.01); and 81/476 females and 106/553 males in SFDT1 (17.0 vs 19.2%, p = 0.42). In these patients, statin therapy was less frequently used in females than males in DPV (7.9 vs 17.0%, p < 0.01) but not SFDT1 (18.2 vs 21.0%, p = 0.78).

Micro or macroalbuminuria was observed in 14.4% of females and 16.7% of males in DPV (p = 0.16); and 13.0% of females and 14.5% of males in SFDT1 (p = 0.61) (Table 2). In these patients, ACEi-ARB therapy was less frequently prescribed in females than males in DPV (21.4 vs 37.6%, p < 0.01) but not SFDT1 (70.6 vs 62.0%, p = 0.43).

Females were more frequently non-smokers than males (DPV 80.3 vs 74.2, p < 0.01; SFDT1 79.1 vs 74.3%, p = 0.07).

## Discussion

### Main results

We investigated risk factors and care in two primary prevention cohorts in European people living with T1D. First, we found similar results in Germany and France, considering risk factors, with better control in females than males for blood pressure, HDL-cholesterol, triglyceride levels, and fewer smoking habits. Second, we observed clinical inertia in both countries concerning the prescription of statin in case of LDL-cholesterol above the target and ACEi-ARB in case of microalbuminuria. Third, this inertia was more evident in females than males in Germany.

#### Glucose, weight and blood pressure control, smoking: a better cardiovascular profile in females than males

Around one-quarter of the participants of DPV and SFDT1 had an HbA1c < 7.0%, in agreement with recent data from the United States [13, 14]. As others [13, 15–18], we have found that females had similar HbA1c levels and at target as males. Females were reported to be less likely to achieve an HbA1c < 7.0% than males in some studies [14, 19, 20]. On the contrary, a publication from the entire DPV registry had shown that, in adult patients, women constantly showed lower HbA1c values than men from 2004 to 2018 [21]. The different DPV results found in the current study may be explained by the restricted selection criteria (2020–2022 data, participants in primary prevention, participating specialized centres located in Germany defined by including more than 100 patients) and a lower statistical power than in the previous study [21]. Note that the use of CSII was higher in women than in men in our two cohorts, as previously shown [17, 20, 21].

We report overweight or obesity in more than one-half of the participants of DPV and SFDT1, as recently reported in the United States [13, 14]. We found in Germany that females were more likely than males to have a normal weight, as in recent data from the United States [14]. The inverse had been shown in earlier studies in Scotland [22] and Italy [23].

Blood pressures were at target in around 80% of participants of DPV and SFDT1. The latter percentage was around 33% in the Diabetes Control and Complications Trial (DCCT) [14]. As previously reported [13–15, 17–20], we have observed lower DBP and SBP levels in females than in males. In the SFDT1 cohort, fewer antihypertensive treatments were reported in females than males, as shown in many former studies [13–15, 17–20]. Finally, as previously reported [22, 23], females were less likely to be active smokers.

#### Lipid control is better in females than in males

In people living with T1D, higher HDL-cholesterol and lower triglyceride levels are usually described in females than males [14–16, 20, 22, 23]. We found the same results in the present study in Germany and France. We also found lower levels of LDL-cholesterol in females than males, and this was only found in one Finnish study [19], while levels were similar in both sex in others [14–16, 20, 22, 23].

LDL-cholesterol was at target in around 80% of DPV participants and in 70% of SFDT1 participants, respectively. This percentage has not been previously described in the literature in primary prevention individuals with T1D. To note, the longitudinal rate of achieving LDL cholesterol level < 70 mg/dl was recently reported to be 31.5% in women and 32.2% in men in the DCCT/Epidemiology

of Diabetes Interventions and Complications (EDIC) study [14]; and 30.6% and 32.0%, respectively, in a Dutch registry [18].

### Clinical inertia when LDL-cholesterol is above the target and in case of microalbuminuria

We report a very low rate of statin treatment (13% in DPV and 15% in SFDT1) in patients with LDL-cholesterol ≥ 3.4 mmol/L. This may be due to the absence of randomized controlled trials in patients with T1D and the uncertainty of the benefit/risk balance in the long term in often young patients [4, 24]. However, a study of more than 24,000 patients in primary prevention and with T1D showed that, over 6 years, those treated with lipid-lowering treatment as compared to those who were untreated had a hazard ratio of 0.56 (95% confidence interval 0.48–0.64) for death from any cause and 0.85 (0.74–0.97) for coronary heart disease [25].

Clinical inertia was also observed, to a lesser extent, for ACEi-ARB use in the case of albuminuria (around 70% in DPV and 35% in SFDT1). This is an issue as it is associated with a 50% reduction in the risk of a composite of death, dialysis, and renal transplantation [26]. The results show that cardiovascular prevention is still insufficient in the DPV and SFDT1 centres. To note, clinical inertia for statin and ACEi-ARB therapy, when recommended, was more prominent in females than males in DPV but not in SFDT1. Statin prescription was previously shown to be better applied in males than females with T1D in the United States [17] and Italy [20].

### Strengths and limitations

This analysis presents real-world data from two large multicenter independent cohorts over the three recent years, covering a large cardiovascular parameter set. One of the main limitations of this study is the comparison of two different cohorts with distinct clinical data sources. We report the results and treatment for the patients at the entry in the recruiting centres for SFDT1. Data in the SFDT1 study are mainly from University Hospitals at the current time, and as such, data may not be transferable for all French patients living with T1D. To obtain a comparable population, we included in DPV only adults treated in large diabetes centres (>100 patients) participating in the DPV initiative. This population may also not represent all adults with T1D in Germany. In addition, the following data were not assessed in the current work: completion of screening for risk factors [18, 20], physical activity [13] and cardiac autonomic neuropathy [27]. Finally, we did not separate females before and after 50 years of age, although menopause may interfere with cardiovascular risk also in T1D [1–3]. In DPV, lipids may not have been measured at the fasting state.

### Perspectives

Before they were excluded from our study samples, the percentage of DPV and SFDT1 participants with a cardiovascular history was 13.8% in DPV (females 11.8% and males 15.6%) and 6.3% in SFDT1 (females 3.5% and males 8.7%). Although the patients who were included had the same age and sex ratio in DPV and SFDT1 studies, the higher rate of cardiovascular history in DPV may reflect the moderate cardiovascular risk in Germany and the low one in France [28]. This percentage is lower than older reports [7, 29] but is in line with recent data [30]. This is likely due to improved cardiovascular management in the T1D population [31–33]. We also have confirmed that males had a higher prevalence of cardiovascular disease than females in our two cohorts [6, 7], although they had very similar age and diabetes duration.

We observed that cardiovascular prevention could be improved in people living with T1D, and we think such a benchmark if repeated annually, could help caregivers improve their performances.

As reported in primary care [34], we observed, especially in DPV, disparities in care by sex. From a medical perspective, this may be due to a lower perception of cardiovascular risk and a lower cardiovascular benefit of statin in females than males [35]. From a patient's perspective, females may have the perception of a lower cardiovascular risk. They also have been described to be more prone to medication non-adherence [36]. This also might be due to therapies stopped during pregnancy and not prescribed thereafter, but this does not explain the difference in Germany and France, as mean age was similar for women in both countries here.

## Conclusion

Overall, our findings reveal sex differences in clinical inertia in cardiovascular and nephroprotection in adults in primary prevention living with T1D. Our results indicate that even if females living with T1D have an overall lower risk of cardiovascular disease than their male counterparts, they should be more frequently considered for cardiovascular and nephroprotection. We therefore suggest that sex and sex-specific risk factors should be systematically integrated into diabetes care to develop personalized prevention strategies further.

#### Abbreviations

| | |
|---|---|
| ACEi | Angiotensin-converting-enzyme inhibitors |
| ARB | Angiotensin II receptor blockers |
| BMI | Body mass index |
| CSII | Continuous subcutaneous insulin infusion |
| DBP | Diastolic blood pressure |
| DCCT | Diabetes Control and Complications trial |
| DPV | The multicenter Prospective Diabetes Follow-up Registry |
| EDIC | Epidemiology of Diabetes Interventions and Complications |
| eGFR | Estimated glomerular filtration rate |
| SBP | Systolic blood pressure |
| SD | Standard deviation |

SFDT1 Société Francophone du Diabète– Cohorte Diabète de Type 1
T1D Type 1 diabetes

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**Author contributions**
E.C., M.A., JP.R., G.F. and RW.H. conceived and designed this study. M.A. (DPV) and G.F. (SFDT1) had full access to all the study data and were responsible for the integrity of the data and the accuracy of the data analyses. M.A. analyzed the DPV data and G.A. the SFDT1 data. All authors participated in the collection of the data. E.C. drafted the paper. All authors critically revised the manuscript for important intellectual content and gave final approval for publication.

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**Availability of data and materials**
Data for the present analysis can be provided from the first authors on reasonable request. For reasons of data protection, data on individual level cannot be provided. However, remote data analysis is possible.

## Declarations

**Ethics approval and consent to participate**
Analysis of anonymized data from the DPV registry has been approved by the ethics committee of the Medical Faculty of Ulm University (ethics approval 314/21). SFDT1 was approved by an ethical committee on 5 November 2019 and is declared in clinical trial NCT04657783.

**Consent for publication**
Not applicable.

**Competing interests**
The authors declare no competing interests.

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