Title:

Gender differences in diabetes self-care in adults with type 1 diabetes: Findings from the T1D Exchange Clinic Registry

Running title: Gender Differences in Diabetes Self-Care in Type 1 Diabetes

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Abstract (Word count 223; Limit is 250 words)

Objective: To evaluate gender differences in diabetes self-care components including glycemic, blood pressure and lipid control, utilization of diabetes technologies and acute diabetes complications in adults with type 1 diabetes.

Methods: Data from the Type 1 Diabetes Exchange registry were utilized to explore gender differences. A total of 9,481 participants over the age of 18 were included in the analysis, 53% were female. Variables of interest included glycemic control measured by hemoglobin A1c (HbA1c), systolic and diastolic blood pressures, presence of dyslipidemia, insulin delivery modality, and rates of acute complications.

Results: Glycemic control was similar in women and men (mean HbA1c in both groups: $8.1\%\pm1.6\%$ (64±16 mmol/mol), (p=0.54). More women used insulin pump therapy (66% vs. 59%, p<0.001) but use of sensor technology was similar (p=0.42). Women had a higher rate of diabetic ketoacidosis (DKA) (5% vs. 3%, p<0.001) and eating disorders (1.7% vs. 0.1%, p<<0.001). Rates of severe hypoglycemia were not different between men and women (p=0.42). Smoking (6% vs 4%, p<0.001), systolic (125±14.2 vs. 121±14.4, p<0.001) and diastolic blood pressure (73.3±9.5 vs. 72.2±9.3, p<0.001) and rate of dyslipidemia (28% vs. 23%, p<0.001) were higher in men.

Conclusion: While glycemic control in type 1 diabetes was similar regardless of gender, rates of DKA and eating disorders were higher in women while rates of smoking, hypertension and dyslipidemia were higher in men.

1 Introduction

The influence of gender on morbidity and mortality is being acknowledged for many diseases including type 1 diabetes. At any age, women with type 1 diabetes have a higher risk of death, both from any cause and, particularly, from cardiovascular diseases as compared to men with type 1 diabetes (1, 2). Yet, the reasons for excess mortality in women with type 1 diabetes are not completely understood.

Optimal control of blood glucose, blood pressure and lipids are known to reduce the cardiovascular risk in patients with type 1 diabetes (3-5). Few studies have reported gender differences in glycemic and lipid control in patients with type 1 diabetes. Data from the Diabetes Follow-up Registry in Germany and Austrian has demonstrated female gender was associated with poor glycemic control, elevated body mass index (BMI), total cholesterol, and LDL-cholesterol (3). Women with type 1 diabetes are also less likely than men to receive antihypertensive agents or lipid lowering drugs despite their observed high cardiovascular risk (5). However, these studies did not provide explanations for the gender inequities in poor glycemic control. Diabetes self-care related to insulin delivery, frequency of glucose monitoring, and lifestyle contribute to glycemic control (6). Similarly, the use of diabetes technologies, such as insulin pumps and continuous glucose monitoring systems, have been shown to improve glycemic control and reduce acute diabetes complications including diabetic ketoacidosis (DKA) and severe hypoglycemia (SH) (7,8). Yet, it is unknown whether gender differences exist in diabetes self-care and the utilization of diabetes technologies.

Therefore, the present study aimed to examine the gender differences in glycemic, blood pressure and lipid control, use of advanced diabetes-management technologies and occurrence of

acute diabetes complications in adults with type 1 diabetes from the T1D Exchange (T1DX) clinic registry

2 Research Design and Method

2.1 Study population:

The T1DX clinic registry includes more than 30,000 individuals with type 1 diabetes followed in a network of over 80 adult and pediatric diabetes clinics across the United States. Each clinic received approval from an institutional review board (IRB). Informed consent was obtained according to IRB requirements from adult participants. Data were collected for the clinic registry central database from participants' medical records and comprehensive questionnaire completed by the participant.

The present analysis included 9,481 participants aged 18 years or above with most recent registry data collection from clinical visits between March 1, 2016 and May 31, 2017. Demographic, socioeconomic, and diabetes management characteristics were collected from participant self-reported questionnaires as previously described (9). Participants in the T1DX registry identified themselves as men or women; therefore, we have used the term gender throughout the text consistent with reporting guidelines (10). Transgender individuals were excluded from study. Age, diabetes duration, smoking status, previous diagnosis of eating disorder, statin use, BMI, blood pressure, lipid profiles, and the most recent HbA1c measurement, whether obtained via point-of-care or local laboratory, within three months prior to clinic visit were obtained from the clinic medical record. Frequency of clinic visits was defined using number of reported HbA1c measurements in the 15 months prior to the most recent clinic exam. Method of insulin delivery (multiple daily injections [MDI] or use of insulin pump), use of a continuous glucose monitor (CGM), and frequency of self-monitored blood

glucose (SMBG) levels were collected from medical records. Occurrences of DKA and SH in the 12 months prior to clinic exams were also collected from medical records. DKA was defined as at least one event having hyperglycemia and meeting the following criteria over the prior year: 1) symptoms such as polyuria, polydipsia, nausea or vomiting; 2) serum ketones or large/moderate urine ketones; 3) either arterial blood pH <7.3 or venous pH <7.3 or serum bicarbonate <15; and 4) treatment provided in a health care facility. SH was defined as hypoglycemia resulting in seizure or loss of consciousness. High blood pressure was defined as systolic blood pressure \geq 140 and/or diastolic blood pressure \geq 90. Participant-reported data were analyzed to assess compliance with prescribed medical regimens based on the frequency of missed insulin doses and number of days of physical activity lasting more than 30 minutes.

2.2 Statistical analysis:

Demographic and diabetes-related clinic characteristics were tabulated according to gender overall and within age group (18-24 years, 25-49 years, \geq 50 years) since diabetes management characteristics including glycemic control, lipid profile, blood pressure and hypoglycemia are influenced by age (9, 11-13). Associations between continuous characteristics and gender were tested by t-tests or Wilcoxon rank-sum tests, as appropriate. The relationships between categorical characteristics and gender were examined using chi-square tests. Fisher's exact tests were performed when expected event number was small.

A linear regression model was used to examine the relationship between HbA1c and gender with adjustment for race/ethnicity, duration of diabetes, and insurance status. Gender difference in achieving glycemic control target (less than or equal to 53 mmol/mol [7.0%]) was assessed using multivariate logistic regression adjusting for the above potential confounders. The association between frequency of checking SMBG among non-CGM users and gender was

assessed using a linear regression model adjusted for race/ethnicity, diabetes duration, insurance status, and use of pump. Multivariate logistic regression was performed to examine the association between use of advanced diabetes technology devices (pump and/or CGM) and gender adjusting potential confounders. A multivariate logistic regression model was also used to assess the association between gender and occurrence of at least one SH event. A similar approach was applied to test the gender effect on occurrence of at least one episode of DKA events.

All analyses were completed in overall cohort as well as in each age group (18-24 years old, 25-49 years old, and \geq 50 years old). Data analyses were performed using SAS version 9.4 (2011 SAS Institute Inc., Cary, NC). Adaptive false discovery rate (aFDR) method was performed to adjust for multiple comparisons (14). All p-values are two-sided. Criteria for statistical significance was based on an alpha of 0.01 due to large sample size and multiple comparisons.

3 Result:

3.1 Diabetes Self-care and Management

Of 9,481 adults with type 1 diabetes, 53% were women (n=4,998). The majority of participants (85% women and 86% men) were non-Hispanic White. Forty-eight percent of women and 42% of men reported annual household incomes less than \$75,000 while 53% of women and 51% of men reported having a bachelor's degree or higher. Most participants (79% women and 79% men) had private health insurance (Table 1).

Table 2 provides data regarding the participants' general health and diabetes self-care behaviors based on both gender and age group. Men with type 1 diabetes were more likely to be smokers than women with type 1 diabetes (6% vs. 4%, odds ratio 1.43, 95% CI; 1.19-1.72).

Self-reported frequency of exercise was higher in men compared to women (3.8 vs. 3.3 reported days exercising per week, p<0.001). While the proportion of overweight and obesity was higher among young women (18-24 years; 53% vs. 40%), more middle-aged and older men were identified as overweight or obese (Table 2). Both genders reported at least tri-annual visits.

Of the cohort, 1,321 of MDI users reported frequency of missing basal (long-acting) insulin and 4,170 participants (insulin pump and MDI users) reported their frequency of missing mealtime bolus insulin. 8% of MDI users reported missing basal insulin more than once a week and 20% of adults reported missing at least one mealtime bolus insulin more than once a week. However, there was no difference in the frequency of missing basal insulin or mealtime insulin between men and women with type 1 diabetes (Table 2).

Across all age groups, men had higher systolic blood pressures compared to women (mean 125 ± 14.2 in men vs. 121 ± 14.4 in women, p<0.001). Although diastolic blood pressure was also higher in men regardless of age, there was no gender difference in diastolic blood pressure in youngest cohort of participants (72.3 \pm 8.5 in women vs. 72.1 \pm 9.5 in men, p=0.46). More men failed to attain goal blood pressures (16% in men vs. 11% in women, p<0.001), defined as systolic blood pressure under 140 and/or diastolic blood pressure under 90 mmHg.

Twenty-eight percent of men had dyslipidemia compared to 23% of women (p<0.001). Frequency of dyslipidemia did not differ by gender in young adults; however, after age 25 years, a higher proportion of men had dyslipidemia (Table 2). Use of statin was higher in men with type 1 diabetes compared to women with type 1 diabetes (38% vs. 31%, p<0.001). The clinic-reported frequency of eating disorders was higher among women across all ages compared to men (1.7% vs 0.1%, p<0.001).

3.2 Glycemic control, use of diabetes technology, and acute diabetes complications

There was no difference in glycemic control (assessed by mean HbA1c) between women and men (8.1% [65 mmol/mol] vs. 8.1% [65 mmol/mol], p=0.54). The difference in glycemic control was non-significant even after adjusting for oral contraceptive use (p=0.68). Similarly, there were no gender differences in frequencies of adults achieving targeted HbA1c of <7.0% (<53 mmol/mol) between young (11% vs. 13%, p=0.56), middle aged (28% vs. 27%, p=0.21) or older adults (26% vs. 29%, p=0.10) with type 1 diabetes (Table 3).

Women were significantly more likely to report insulin pump use compared to men (66% vs. 59%, p<0.001) (Table 3). As demonstrated in table 3, CGM use was similar between genders (29% vs.27%, p=0.42). Frequency of blood glucose self-monitoring was higher among young and middle aged women compared to men, while those over 50 years had similar frequency of testing regardless of gender. There was no gender difference in the frequency of clinic-reported SH events (2% in women vs. 2% in men, p=0.42). However, frequency of at least one episode of DKA was higher in women as compared to men (5% vs. 3%, p<0.001) (Table 2). Importantly, the frequency of DKA was highest in young women who had a 1.7 fold increase in the frequency of DKA as compared to young men.

4 Discussion

While previous studies have reported higher mortality in women with type 1 diabetes compared to men, the data available from the T1DX registry provided us a unique opportunity to analyze over 9,000 adults with type 1 diabetes to understand what clinical, metabolic, and therapeutic differences may exist between the genders that could impact the cardiovascular risk and mortality. Intriguingly, there was no difference in glycemic control; yet, modifiable risk factors for cardiovascular disease including rates of smoking, hypertension, and dyslipidemia

were higher in men than women. Conversely, women were noted to have a higher rate of DKA and clinic-reported eating disorders.

While smoking was higher in men with type 1 diabetes, the rates of smoking were lower in the T1DX registry participants with type 1 diabetes as compared with data from the general US population (15). As smoking in the presence of diabetes is known risk factor for micro- and macro-vascular complications (16,17), clinicians should focus on smoking cessation and prevention strategies for adults with type 1 diabetes.

Additionally, BMI is a known cardiovascular risk factor (18) and although no gender differences were observed in BMI, a large proportion of study participants had higher than recommended BMI levels. Only 39% of women and 34% of men with type 1 diabetes in the T1D Exchange cohort had normal BMIs, which is in line with recent data reporting increasing prevalence of overweight and obesity in patients with type 1 diabetes (19). The prevalence of obesity in patients with type 1 diabetes is higher in the US compared to Germany and Austria based on data from their DPV registry (20) contributing to challenges in achieving optimal glycemic and metabolic control and prevention of cardiovascular diseases. Despite higher rates of obesity (26.1% vs. 25.2%), women with type 1 diabetes reported lower rates of exercise (3.3 days vs 3.7 days) compared to men with type 1 diabetes.

In our study, women with type 1 diabetes had higher rates of DKA compared to men that could be in part explained by a higher frequency of eating disorders described in the women in our cohort. Studies have reported 2-3 fold higher risks for eating disorders in women with type 1 diabetes (21). Eating disorders and omission of insulin have been associated with poor glycemic control, higher rates of diabetes-related complications, and a three-fold increase in the risk of

mortality (22). It is possible that with the rising obesity epidemic, insulin omission is growing and thus clinicians should be screen eating disorder in young women with type 1 diabetes.

Our data did not identify gender differences in glycemic control or achieving target HbA1c levels but it highlights that the majority of men and women (~70%) continue to struggle with achieving targeted glycemia as recommended by the American Diabetes Association. While 30 years of follow up in the DCCT and EDIC studies showed associations between HbA1c levels and cardiovascular disease risks (23), other studies have reported excess risk for cardiovascular disease and mortality from cardiac causes regardless of glycemic control in women compared to men with type 1 diabetes (1,2, 24,25). The findings from these studies suggest that glycemic control is an important contributor but not the key risk factor for reducing cardiovascular mortality in women with type 1 diabetes.

Incorporation of technology into the care plan was also assessed and while use of an insulin pump was higher in women with type 1 diabetes there were no gender differences in utilization of CGM therapy. Similarly, frequency of clinical visits per year and SMBG were higher in women with type 1 diabetes. Studies have reported improved glycemic outcomes with the use of insulin pumps in patients with type 1 diabetes (8,26). However, in our study, HbA1c was not different among women and men with type 1 diabetes despite a higher use of insulin pumps among women with type 1 diabetes. Though CGM use has been shown to improve glycemic control and reduce hypoglycemia irrespective of age, gender, education or mode of insulin delivery (7,27), only 30% of adults with type 1 diabetes were using a CGM in our cohort.

The cardio-protection that women in the general population experience compared to men is not seen in those living with diabetes (28). However, there are gender differences in cardiovascular risk factors in the population living with diabetes. We observed higher mean

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systolic and diastolic blood pressures and a higher frequency of dyslipidemia in men with type 1 diabetes. Similarly, use of lipid lowering medications were higher in men with type 1 diabetes. Our findings are in accordance with the Coronary Artery Calcification in Type 1 Diabetes (CACTI) study that reported higher LDL and triglyceride levels in men with type 1 diabetes compared to women (29). The CACTI study, examined insulin resistance and insulin resistancerelated factors in asymptomatic adults with and without type 1 diabetes, as well as coronary artery calcification (CAC) scores over time. In that study, the presence of type 1 diabetes was greatly associated with prevalence of coronary calcification in women compared to men despite similar glycemic control and higher lipids detected in men (29). Studies have reported higher HbA1c, BMI Z-scores, atherogenic lipoprotein subfractions, and insulin resistance in adolescent girls with type 1 diabetes compared to adolescent boys with the condition (30,31). Taken together, gender differences in glycemic control, BMI, or insulin resistance earlier in life (childhood and adolescence) may result in bad metabolic memory and a higher risk for cardiovascular diseases in women with type 1 diabetes as they transition to adulthood. In addition, women with type 1 diabetes are at increased risk for hypertensive disorders in pregnancy (preeclampsia, gestational hypertension, and others), which further increases the risk of cardiovascular disease later in life (32,33).

Although our study provides important examination of potential modifiable risk factors for both glycemic control and clinical care, the data should be interpreted with caution as it is an observational study. Certain outcomes are cross-sectional, such as the use of diabetes technologies and SMBG, and thus do not capture the frequency with which patients utilized diabetes devices (insulin pumps, CGMs, glucose meters) over time. In addition, possibility of unmeasured confounders on the results of the study cannot be ruled out. Data were also

collected from participant self-reported questionnaires, which are subject to recall bias and inaccurate reporting. On the other hand, participants may have felt more comfortable reporting behaviors more truthfully in the anonymized questionnaire as compared to what would be divulged to a clinician in the a routine visit.

While we did not observe differences in glycemic control between men and women with type 1 diabetes, our data identified some differences in modifiable parameters. For men, greater focus on eliciting smoking history and counseling on smoking cessation, identification and treatment of both hypertension and hyperlipidemia may be critical. While for women, insulin dose omission that could potentially be a means to achieve weight maintenance or loss and indicate the presence of an eating disorder may be essential. Furthermore, as insulin omission, eating disorders, and risk of DKA are associated, counseling women about the risk of DKA should be prioritized. Future research to elucidate the gender differences leading to greater risk for cardiovascular disease remains to be done and will require prospective assessment. Yet, our study lays a framework for factors to be considered.

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Dr. Roy Beck is the guarantor of this work, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and accuracy of the data analysis.

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Table 1: Baseline characteristics of Adults with type 1 diabetes by Gender

	Overall		18-24 years old		25-49 y	ears old	≥50 years old	
	Women	Men	Women	Men	Women	Men	Women	Men
	n=4998	n=4483	n=1661	n=1657	n=1871	n=1482	n=1466	n=1344
Race/Ethnicity – N (%)								
White Non-Hispanic	4216 (85%)	3846 (86%)	1285 (78%)	1318 (80%)	1585(85%)	1281(88%)	1346 (92%)	1247 (93%)
Other Race/Ethnicity	768 (15%)	609 (14%)	373 (22%)	335 (20%)	281 (15%)	181 (12%)	114 (8%)	93 (7%)
Education Level – N (%)								
Less than bachelor's degree	2215 (47%)	2001 (49%)	886 (56%)	882 (57%)	688 (39%)	605 (45%)	641 (47%)	514 (43%)
Bachelor or higher degree	2495 (53%)	2092 (51%)	690 (44%)	668 (43%)	1085(61%)	742 (55%)	720 (53%)	682 (57%)
Household Annual Income –								
N (%)								
≥\$75,000	1875 (52%)	1846 (58%)	579 (53%)	626 (58%)	739 (51%)	617 (55%)	557 (53%)	603 (61%)
<\$75,000	1715 (48%)	1359 (42%)	515 (47%)	452 (42%)	697 (49%)	514 (45%)	503 (47%)	393 (39%)
Insurance Status – N (%)								
Private Insurance	3782 (79%)	3443 (79%)	1249 (79%)	1272 (80%)	1567(87%)	1259(88%)	966 (68%)	912 (70%)
Other/No Insurance	1032 (21%)	891 (21%)	334 (21%)	317 (20%)	237 (13%)	175 (12%)	461 (32%)	399 (30%
T1D Duration (years) - median (IQR)	18.4 (11.3-30.8)	17.1 (10.4-30.1)	11.3 (8.0-15.0)	10.6 (7.2-14.1)	21.5 (14.7-28.7)	19.9 (13.5-27.5)	36 (22.9-46.5)	35 (23.6-45.7)

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	Overall		18-24 years old		25-49 years old		≥50 years old	
	Women n=4998	Men n=4483	Women n=1661	Men n=1657	Women n=1871	Men n=1482	Women n=1466	Men n=1344
Smoker – N (%)	209 (4%)	261 (6%)	50 (4%)	86 (6%)	95 (5%)	103 (7%)	64 (4%)	72 (5%)
Days Exercise Per Week - Mean±SD	3.3±2.1	3.8±2.2	3.5±2.1	4.1±2.2	3.1±2.0	3.4±2.0	3.5±2.3	3.7±2.2
BMI (kg/m2) - Mean±SD	27.5±7.9	27.1±5.9	26.7±8.6	25.3±6.3	28.3±6.5	28.2±5.1	27.5±8.6	28.4±5.6
BMI – N (%)								
Underweight	63 (1%)	52 (1%)	22 (1%)	42 (3%)	19 (1%)	7 (<1%)	22 (2%)	3 (<1%)
Normal	1745 (40%)	1514(38%)	707 (45%)	896 (57%)	555 (35%)	347 (27%)	483 (40%)	271 (24%)
Overweight	1451(33%)	1464(37%)	562 (36%)	411 (26%)	502 (32%)	515 (41%)	387 (32%)	538 (47%)
Obese	1103(26%)	965 (24%)	269 (17%)	228 (14%)	512 (32%)	401 (32%)	322 (27%)	336 (29%)
Number of Visits - Mean±SD	3.3±1.6	3.2±1.6	3.8±1.7	3.6±1.7	3.0±1.6	2.9±1.5	3.2±1.4	3.2±1.5
Frequency of reported missing basal insulin among MDI users – N (%)*								
Never	395 (60%)	375 (57%)	122 (51%)	96 (41%)	117 (58%)	130 (63%)	156 (71%)	149 (69%)
Once a month or less	175 (26%)	198 (30%)	68 (28%)	87 (37%)	57 (28%)	58 (28%)	50 (23%)	53 (25%)
Once a week or less	38 (6%)	48 (7%)	17 (7%)	29 (12%)	13 (6%)	12 (6%)	8 (4%)	7 (3%)
More than once a week	53 (8%)	39 (6%)	34 (14%)	25 (11%)	14 (7%)	8 (4%)	5 (2%)	6 (3%)
Frequency of reported missing bolus insulin – N (%)†								
Never	716 (31%)	591 (32%)	165 (22%)	166 (24%)	272 (31%)	193 (33%)	279 (41%)	232 (40%)
Once a month or less	751 (33%)	572 (31%)	212 (28%)	184 (26%)	304 (35%)	201 (34%)	235 (34%)	187 (32%)
Once a week or less	368 (16%)	368 (19%)	146 (19%)	165 (23%)	137 (16%)	96 (16%)	85 (12%)	98 (17%)
More than once a week	464 (20%)	464 (19%)	229 (30%)	191 (27%)	151 (17%)	99 (17%)	84 (12%)	59 (10%)
Systolic Blood Pressure - Mean±SD	121 ±14.4	125 ±14.2	118 ±11.3	123 ±11.5	119 ±13.8	125 ±14.6	127 ±16.3	129 ±16.1
Diastolic Blood Pressure - Mean±SD	72.2+9.3	73.3±9.5	72.3±8.5	72.1±9.2	73.8±9.5	76.4±9.0	69.9±9.5	71.3±9.5

Conder difference in diabetes self-care and management

High Blood Pressure – N (%)**	516 (11%)	688 (16%)	63 (4%)	147 (9%)	167 (9%)	233 (16%)	286 (20%)	308 (23%)
Dyslipidemia – N (%)	1145(23%)	1249(28%)	96 (6%)	84 (5%)	388 (21%)	410 (28%)	662 (45%)	755 (56%)
Use of Statin – N (%)	1557(31%)	1722(38%)	75 (5%)	60 (4%)	473 (25%)	605 (41%)	1009(69%)	1057(79%)
Eating Disorder – N (%)	86 (1.7%)	5 (0.1%)	31 (1.8%)	3 (0.1%)	41 (2%)	0 (0%)	14 (1%)	2 (0.1%)

*1,321 of MDI users reported frequency of missing basal insulin

†4,170 participants reported their frequency of missing mealtime bolus insulin.

*High blood pressure is defined as systolic blood pressure ≥ 140 or diastolic blood pressure ≥ 90 . Bold represents statistically significant (p<0.01)

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	Overall		18-24 years old		25-49 years old		≥50 years old	
	Women n=4610	Men n=4064	Women n=1273	Men n=1238	Women n=1871	Men n=1482	Women n=1466	Men n=1344
HbA1c (mmol/mol) - Mean Mean±SD*	65 ±18	65 ±18	74 ± 20	73 ± 20	62 ± 16	62 ± 16	60 ± 12	59 ± 13
HbA1c(%) - Mean±SD*	8.1±1.6	8.1±1.6	8.9±1.9	8.8±1.9	7.8±1.4	7.8±1.4	7.7±1.1	7.6±1.2
HbA1c – N (%) <7.0% ≥7.0%	992 (21%) 3632(79%)	923 (22%) 3218(78%)	171 (11%) 1423(89%)	· · ·	475 (28%) 1222(72%)	371 (27%) 980 (73%)	346 (26%) 987 (74%)	350 (29%) 863 (71%)
Use of Pump – N (%)†	3255(66%)	2609(59%)	1002 (62%)	946 (58%)	1299(71%)	873 (60%)	954 (66%)	790 (59%
Use of CGM – N (%)‡	1427(29%)	1167(27%)	331 (20%)	285 (18%)	657 (36%)	470 (33%)	439 (31%)	412 (31%)
Frequency of Self-Monitored Blood Glucose among non-CGM users - Mean±SD§	4.1±2.4	3.8±2.4	3.6±2.3	3.2±2.2	4.2±2.4	3.8±2.3	4.7±2.3	4.6±2.4
Frequency of Self-Monitored Blood Glucose among non-CGM users – N (%)§								
<4 times per day	1168(41%)	1228(48%)	548 (54%)	634 (61%)	392 (40%)	367 (49%)	228 (27%)	227 (31%
\geq 4 times per day	1659(59%)	1312(52%)	476 (46%)	408 (39%)	579 (60%)	387 (51%)	604 (73%)	517 (69%
Severe Hypoglycemia – N (%)	84 (2%)	86 (2%)	13(<1%)	26 (2%)	44(2%)	26(2%)	27 (2%)	34(3%)
DKA - N (%)	221(5%)	116(3%)	116(7%)	67(4%)	73(4%)	29(2%)	32(2%)	20(2%)

Table 3: Gender differences in glycemic control, adoption of diabetes technologies and acute diabetes complications

* Multivariate analysis adjusting with following potential covariates: race/ethnicity, diabetes duration, and insurance status. †Multivariate analysis adjusting with following potential covariates: race/ethnicity, diabetes duration, insurance, CGM use and annual household income status. ‡Multivariate analysis adjusting with following potential covariates: race/ethnicity, diabetes duration, insurance, pump use and annual household income status. \$Multivariate analysis adjusting with following potential covariates: race/ethnicity, diabetes duration, insurance, and pump use. Multivariate analysis adjusting with following potential covariates: race/ethnicity, diabetes duration, insurance, and pump use. Multivariate analysis adjusting with following potential covariates: race/ethnicity, diabetes duration, insurance, pump use, CGM use, frequency of SMBG and annual household income status. Bold represents statistically significant (p<0.01)

References

- 1. Huxley RR, Peters SA, Mishra GD, Woodward M (2015). Risk of all-cause mortality and vascular events in women versus men with type 1 diabetes: a systematic review and meta-analysis. Lancet Diabetes Endocrinol;3:198-206
- 2. Lind M, Svensson AM, Kosiborod M et al.(2014) Glycemic control and excess mortality in type 1 diabetes. N Engl J Med 371:1972-1982
- 3. Gerstl EM, Rabl W, Rosenbauer J, Grobe H, Hofer SE, Krause U, Holl RW (2008). Metabolic control as reflected by HbA1c in children, adolescents and young adults with type-1 diabetes mellitus: combined longitudinal analysis including 27,035 patients from 207 centers in Germany and Austria during the last decade. Eur J Pediatr 167:447-453
- Kautzky-Willer A, Stich K, Hintersteiner J, Kautzky A, Kamyar MR, Saukel J, Johnson J, Lemmens-Gruber R (2013). Sex-specific-differences in cardiometabolic risk in type 1 diabetes: a cross-sectional study. Cardiovasc Diabetol 12:78 doi: 10.1186/1475-2840-12-78.
- Schwab KO, Doerfer J, Hecker W et al (2006). Spectrum and prevalence of atherogenic risk factors in 27,358 children, adolescents, and young adults with type 1 diabetes: crosssectional data from the German diabetes documentation and quality management system (DPV). Diabetes Care 29:218-225
- 6. Simmons JH, Chen V, Miller KM et al (2013). Differences in the management of type 1 diabetes among adults under excellent control compared with those under poor control in the T1D Exchange Clinic Registry. Diabetes Care 36:3573-7.
- Beck RW, Riddlesworth T, Ruedy K et al (2017). Effect of Continuous Glucose Monitoring on Glycemic Control in Adults With Type 1 Diabetes Using Insulin Injections: The DIAMOND Randomized Clinical Trial. JAMA 2017;317:371-378
- Karges B, Schwandt A, Heidtmann B, et al (2017). Association of Insulin Pump Therapy vs Insulin Injection Therapy With Severe Hypoglycemia, Ketoacidosis, and Glycemic Control Among Children, Adolescents, and Young Adults With Type 1 Diabetes. JAMA. 318:1358–1366
- Miller KM, Foster NC, Beck RW et al (2015). Current state of type 1 diabetes treatment in the U.S.: updated data from the T1D Exchange clinic registry. Diabetes Care 38:971-978
- 10. Clayton JA, Tannenbaum C (2016). Reporting Sex, Gender, or Both in Clinical Research? JAMA 316:1863-1864
- 11. DuBose SN, Weinstock RS, Beck RW et al (2016). Hypoglycemia in Older Adults with Type 1 Diabetes. Diabetes Technol Ther 18:765-771
- 12. Cengiz E, Xing D, Wong JC et al (2013). Severe hypoglycemia and diabetic ketoacidosis among youth with type 1 diabetes in the T1D Exchange clinic registry. Pediatr Diabetes 14:447-454
- 13. Pinto E (2007). Blood pressure and ageing. Postgrad Med J 83:109-114
- Benjamini Y, Hochberg Y (1995). Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing. Journal of the Royal Statistical Society Series B (Methodological) 57:289-300
- 15. Center for Disease Control and Prevention (2016). Current Cigarette Smoking among Adults in the United States. Available from

https://www.cdc.gov/tobacco/data_statistics/fact_sheets/adult_data/cig_smoking/index.ht m. Accessed 16 April 2018

- 16. Chase HP, Garg SK, Marshall G, Berg CL, Harris S, Jackson WE, Hamman RE (1991). Cigarette smoking increases the risk of albuminuria among subjects with type I diabetes. JAMA 265:614-617
- 17. Ahlen E, Pivodic A, Wedel H, Dahlqvist S, Kosiborod M, Lind M (2016) Glycemic Control, Renal Complications, and Current Smoking in Relation to Excess Risk of Mortality in Persons With Type 1 Diabetes. J Diabetes Sci Technol 10:1006-1014
- 18. Kee CC, Sumarni MG, Lim KH et al (2017). Association of BMI with risk of CVD mortality and all-cause mortality. Public health nutrition 20:1226-1234
- 19. Polsky S, Ellis SL (2015). Obesity, insulin resistance, and type 1 diabetes mellitus. Curr Opin Endocrinol Diabetes Obes 22:277-282
- 20. DuBose SN, Hermann JM, Tamborlane WV et al (2015). Obesity in Youth with Type 1 Diabetes in Germany, Austria, and the United States. J Pediatr 167:627-632 e624
- 21. Nielsen S (2002). Eating disorders in females with type 1 diabetes: an update of a metaanalysis. European Eating Disorders Review 10:241-254
- 22. Goebel-Fabbri AE, Fikkan J, Franko DL, Pearson K, Anderson BJ, Weinger K (2008). Insulin restriction and associated morbidity and mortality in women with type 1 diabetes. Diabetes Care 31:415-419
- 23. Diabetes Control and Complications Trial (DCCT) /Epidemiology of Diabetes Interventions and Complications Study (EDIC) study research team (2016). Intensive Diabetes Treatment and Cardiovascular Outcomes in Type 1 Diabetes: The DCCT/EDIC Study 30-Year Follow-up. Diabetes Care 39:686-693
- 24. Dahlqvist S, Rosengren A, Gudbjornsdottir S et al (2017). Risk of atrial fibrillation in people with type 1 diabetes compared with matched controls from the general population: a prospective case-control study. Lancet Diabetes Endocrinol 5:799-807
- 25. Matuleviciene-Anangen V, Rosengren A, Svensson AM et al (2017). Glycaemic control and excess risk of major coronary events in persons with type 1 diabetes. Heart 103:1687-1695
- 26. Jendle JH, Rawshani A, Svensson AM, Avdic T, Gudbjornsdottir S (2016). Indications for Insulin Pump Therapy in Type 1 Diabetes and Associations With Glycemic Control. J Diabetes Sci Technol 10:1027-1033
- 27. Danne T, Nimri R, Battelino T et al (2017). International Consensus on Use of Continuous Glucose Monitoring. Diabetes Care 40:1631-1640
- Lloyd CE, Kuller LH, Ellis D, Becker DJ, Wing RR, Orchard TJ (1996). Coronary artery disease in IDDM. Gender differences in risk factors but not risk. Arterioscler Thromb Vasc Biol 16:720-726
- 29. Colhoun HM, Rubens MB, Underwood SR, Fuller JH (2000) The effect of type 1 diabetes mellitus on the gender difference in coronary artery calcification. J Am Coll Cardiol 36:2160-2167
- 30. Brown TL, Maahs DM, Bishop FK, Snell-Bergeon JK, Wadwa RP (2016). Influences of gender on cardiovascular disease risk factors in adolescents with and without type 1 diabetes. Int J Pediatr Endocrinol 2016:8
- 31. Cree-Green M, Maahs DM, Ferland A et al (2016). Lipoprotein subfraction cholesterol distribution is more atherogenic in insulin resistant adolescents with type 1 diabetes. Pediatr Diabetes 17:257-265

- 32. Behrens I, Basit S, Melbye M et al (2017). Risk of post-pregnancy hypertension in women with a history of hypertensive disorders of pregnancy: nationwide cohort study. BMJ 358:j3078
- 33. Ray JG, Vermeulen MJ, Schull MJ, Redelmeier DA (2005). Cardiovascular health after maternal placental syndromes (CHAMPS): population-based retrospective cohort study. Lancet 366:1797-1803

Highlights

- Highlights the gender differences in diabetes self-care and acute complications among US adults with type 1 diabetes
- Future research is necessary to close the gender gap in diabetes care

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