

# High prevalence of depressive symptoms among people with pediatric-onset and adolescent-onset type 1 diabetes: A cross-sectional analysis of the Diabetes Study from the Center of Tokyo Women's Medical University

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## Keywords

Depression, Hypoglycemia unawareness, Type 1 diabetes

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*J Diabetes Investig* 2022; 13: 1626–1632

doi: [10.1111/jdi.13835](https://doi.org/10.1111/jdi.13835)

## ABSTRACT

**Aims/Introduction:** To investigate the prevalence of depressive symptoms by the age of onset of type 1 diabetes, and its association with the condition of individuals with pediatric- and adolescent-onset type 1 diabetes.

**Materials and Methods:** This single-center cross-sectional study enrolled Japanese participants with type 1 diabetes. All participants completed a questionnaire about their diabetes-related condition and the Patient Health Questionnaire-9, which was used to evaluate depression. Individuals with a Patient Health Questionnaire-9 score of  $\geq 10$  points were defined as having moderate depressive symptoms.

**Results:** A total of 1,267 participants (mean age 40 years; mean duration of type 1 diabetes 21 years; 68% female; mean glycated hemoglobin 7.8%) were included and classified according to the age of onset of type 1 diabetes to identify the proportion of moderate depressive symptoms in each group: 21% (0–12 years), 18% (13–19 years) and 13% (20–40 years). The prevalence of moderate depressive symptoms was significantly higher among participants with pediatric-onset type 1 diabetes ( $P < 0.05$ ). Moderate depressive symptoms were associated with increased glycated hemoglobin, neuropathy and hypoglycemia unawareness.

**Conclusions:** Regular screening for depressive symptoms and hypoglycemia awareness is important. Healthcare professionals should provide appropriate psychosocial care for people with pediatric-onset and adolescent-onset type 1 diabetes from childhood through to adulthood.

## INTRODUCTION

Type 1 diabetes is a chronic disease that frequently manifests during childhood and requires daily intensive self-management. For a smooth transition from the pediatric to adult medical care departments, patients with type 1 diabetes must be mentally independent and psychosocially mature<sup>1</sup>. However, 15% of children aged 13–19 years report a mental burden associated

with type 1 diabetes<sup>2,3</sup>. Compared with their counterparts without diabetes, adolescent children with type 1 diabetes are more likely to have mental health problems, such as depression, eating disorders and adjustment disorders<sup>4–6</sup>. The SEARCH for Diabetes in Youth Study carried out in the USA showed that 14% of young people with type 1 diabetes had mild depression, whereas 8.6% had moderate-to-severe depression<sup>7</sup>. Therefore, we hypothesized that individuals with pediatric-onset type 1 diabetes are more likely to develop depressive symptoms than those with adult-onset type 1 diabetes.

Received 14 March 2022; revised 19 April 2022; accepted 5 May 2022

The complications of depression negatively affect self-care behaviors, such as compliance with insulin administration and self-measurement of blood glucose levels<sup>4,8</sup>, which result in poor glycemic control, diabetic ketoacidosis<sup>9</sup>, chronic complications in early adulthood and deterioration of the quality of life<sup>10–12</sup>. Therefore, psychiatric problems in childhood and adolescence often hinder smooth medical care transition, and these problems continue even after the transfer to the adult care department. It is, therefore, important to evaluate the long-term perspective of the lives of individuals with type 1 diabetes.

In a recent cross-sectional analysis of the Diabetes Study from the Center of Tokyo Women's Medical University (DIACET), we reported that 24.7% and 14.5% of participants with type 1 diabetes had mild and moderate-to-severe depression, respectively<sup>13</sup>. However, we did not study the prevalence of depressive symptoms with regard to the age of onset of type 1 diabetes. Therefore, in the present study, we aimed to investigate the impact of age of onset of type 1 diabetes on the prevalence of depressive symptoms to highlight the burden of depressive symptoms in pediatric and adolescent-onset type 1 diabetes in adulthood, and clarify the association between depressive symptoms and diabetes-related complications. The insights from this analysis are expected to provide support for necessary care, including the definition of a transition period, to ameliorate depression in individuals with type 1 diabetes.

## MATERIALS AND METHODS

### Participants

This single-center cross-sectional study enrolled Japanese participants who had type 1 diabetes with an age of onset of  $\leq 40$  years, were hospitalized at or regularly visited the Diabetes Center of Tokyo Women's Medical University, had participated in the DIACET survey initiated in October 2012 and had complete data for all nine items of the Patient Health Questionnaire-9 (PHQ-9).

### DIACET and PHQ-9

The protocol of the DIACET study has been described previously<sup>14</sup>. The PHQ-9 is a self-administered questionnaire on health status, including glycemic control, medications and diabetes-related complications (e.g., presence of diabetic retinopathy, hemodialysis treatment, diabetic neuropathy and hypoglycemia unawareness). Neuropathy was diagnosed from the presence of numbness or pain in the hands and feet. Furthermore, the use of oral antihypertensive and therapeutic agents for dyslipidemia was investigated. The PHQ-9 questionnaires were distributed to eligible participants during regular outpatient visits or during hospitalizations between October 2012 and February 2013, and the completed PHQ-9 forms were returned by postal mail or collected during the subsequent outpatient visit or hospitalizations. The PHQ-9 assesses the presence, frequency and severity of depressive symptoms<sup>15</sup>. For each item, respondents are instructed to choose one of the following scores according to the frequency of occurrence within

a 2-week period: 0, not at all; 1, several days; 2, more than half of the days; or 3, nearly every day. Based on the total score of the responses to all questions (0–27), participants were categorized into three groups according to the severity of depression as: no (0–4), mild<sup>5–9</sup> or moderate depressive symptoms ( $\geq 10$ ). The Japanese version of the PHQ-9 showed adequate validity and reliability in the evaluation by Muramatsu *et al.*<sup>16</sup> Data on glycated hemoglobin (HbA1c) levels were obtained for the 90 days before and after the distribution of the questionnaire, and were measured using high-performance liquid chromatography. Hypoglycemia unawareness was defined as hypoglycemia requiring another individual's assistance or a lack of symptoms when blood glucose was  $< 70$  mg/dL.

### Statistical analysis

Continuous data are expressed as the arithmetic mean  $\pm$  standard deviation, and categorical data are expressed as the frequency with percentage. Among the three groups classified according to the age of onset, the Jonckheere–Terpstra test was used to compare continuous data, whereas the Cochran–Armitage test was used for binary data. Data from the two groups that were classified by the severity of depression according to the PHQ-9 scores ( $< 10$  and  $\geq 10$ ) underwent one-way ANOVA testing to compare continuous data, and the  $\chi^2$ -test to compare binary data. For multivariate analysis using JMP 15 (SAS Institute, Cary, NC, USA), the following candidate variables were used to identify the risk of moderate depressive symptoms: age, duration of diabetes, sex, HbA1c, hypoglycemia unawareness, retinopathy, neuropathy and hemodialysis.

## RESULTS

In the present study, we included 1,279 people who had been diagnosed with incident type 1 diabetes at  $\leq 40$  years-of-age. In this cohort, the mean age was  $40 \pm 13$  years, 68% of the participants were female and the mean duration of type 1 diabetes was  $21 \pm 11$  years. When classified by the age of onset, 413, 259 and 607 participants had developed type 1 diabetes in childhood (0–12 years, pediatric-onset type 1 diabetes), adolescence (13–19 years, adolescent-onset type 1 diabetes) and adulthood (20–40 years, adult-onset type 1 diabetes), respectively. Table 1 shows the differences in the clinical characteristics among the three groups. Participants in the pediatric-onset type 1 diabetes group were significantly younger ( $P < 0.0001$ ), had a significantly longer duration of type 1 diabetes ( $P < 0.0001$ ), and had a significantly higher prevalence of hypoglycemia unawareness and retinopathy ( $P < 0.0005$  and  $P < 0.0001$ , respectively). The prevalence of oral administration of therapeutic agents for hypertension and dyslipidemia was higher in the adult-onset group ( $P < 0.05$  and  $P < 0.0005$ , respectively). The frequency and severity of depressive symptoms according to the age at onset of type 1 diabetes are shown in Figure 1. Moderate depressive symptoms were noted in 21%, 18% and 13% of participants with pediatric-onset, adolescent-onset and adult-onset type 1 diabetes, respectively. The

**Table 1** | Comparison of clinical characteristics and diabetic complications among people with type 1 diabetes classified according to the age of onset

	Overall (n = 1279)	Age of onset (years)			P-value
		0–12 (n = 413)	13–19 (n = 259)	20–40 (n = 607)	
Age (years)	40 ± 13	32 ± 12	36 ± 10	46 ± 12	<0.001 <sup>†</sup>
Women (%)	68	69	74	65	0.103
Duration of diabetes (years)	21 ± 11	25 ± 12	20 ± 10	18 ± 10	<0.001 <sup>†</sup>
HbA1c (%)	7.8 ± 1.2	8.0 ± 1.3	7.7 ± 1.2	7.7 ± 1.1	<0.001 <sup>†</sup>
(mmol/mol)	61 ± 11	63 ± 12	60 ± 11	60 ± 10	
Unawareness of hypoglycemia (%)	54	62	50	49	<0.001 <sup>†</sup>
Retinopathy (%)	31	38	32	26	<0.001 <sup>†</sup>
Neuropathy (%)	20	21	19	20	0.803
Hemodialysis (%)	2	2	4	1	0.184
Hypertension (%)	21	16	21	23	0.013 <sup>†</sup>
Dyslipidemia (%)	14	9	12	17	<0.001 <sup>†</sup>

Data were analyzed using a logistic regression model adjusting for age, duration of diabetes, sex, glycated hemoglobin (HbA1c), presence of unawareness of hypoglycemia, retinopathy, neuropathy and hemodialysis. <sup>†</sup>Adjusted P-values <0.05. OR, odds ratio; PHQ-9, Patient Health Questionnaire-9.

prevalence of moderate depressive symptoms significantly increased with lower age of onset ( $P < 0.05$ , Cochran–Armitage propensity test). In contrast, the prevalence of mild depressive symptoms was nearly similar for all the groups classified by the age of onset.

To examine the clinical characteristics of participants with pediatric-onset and adolescent-onset type 1 diabetes with moderate depressive symptoms, we categorized the participants into two subgroups according to their total PHQ-9 scores: <10 points and  $\geq 10$  points (Table 2). Consequently, we observed significantly higher HbA1c levels ( $P < 0.0001$ ), and higher rates of neuropathy ( $P < 0.0001$ ), retinopathy ( $P < 0.0001$ ) and hemodialysis ( $P < 0.05$ ) in participants with moderate depressive symptoms.

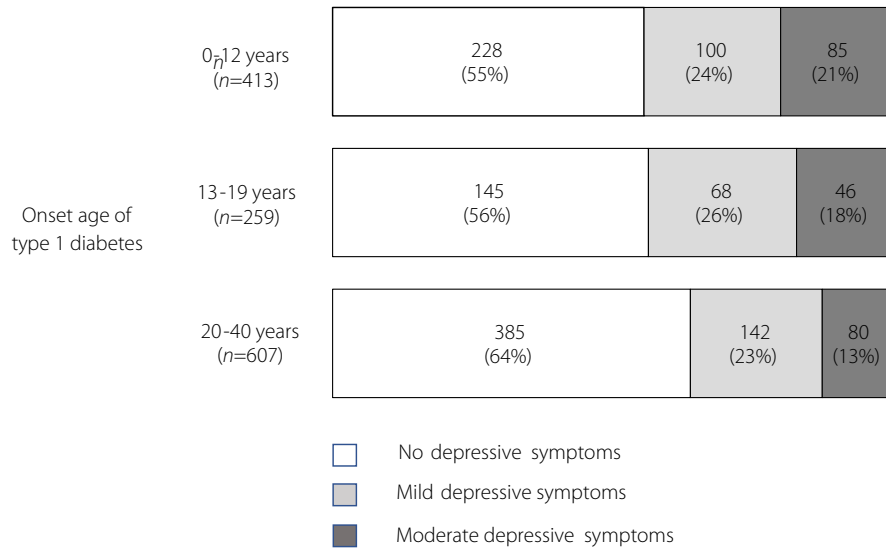
The results of multivariate logistic regression analysis for the likelihood of moderate depressive symptoms are shown in Table 3. A PHQ-9 score  $\geq 10$  points was treated as a categorical outcome variable. Age, duration of diabetes, sex, HbA1c level, hypoglycemia unawareness, retinopathy, neuropathy and hemodialysis were selected as explanatory variables. In pediatric-onset and adolescent-onset type 1 diabetes, the likelihood of moderate depressive symptoms increased by 70% ( $P < 0.05$ ) with the presence of hypoglycemia unawareness, whereas no correlation was observed between depression and hypoglycemia unawareness in participants with adult-onset type 1 diabetes. High HbA1c levels and the presence of neuropathy were related to moderate depressive symptoms at all ages of onset. Among participants with adult-onset type 1 diabetes, women had more depressive symptoms than men.

## DISCUSSION

In the present single-center cross-sectional cohort analysis, we clarified the difference in the prevalence of depressive

symptoms by the age of onset of type 1 diabetes in participants with the disease. The prevalence of moderate depressive symptoms was significantly higher in participants with pediatric-onset and adolescent-onset type 1 diabetes than in those with adult-onset type 1 diabetes. Furthermore, moderate depressive symptoms were associated with high HbA1c, presence of neuropathy and hypoglycemia unawareness among participants who were aged <20 years at the onset of type 1 diabetes.

The prevalence of depression in type 1 diabetes was 2.4- to 3.8-fold higher than that of people without type 1 diabetes<sup>17</sup>. In a meta-analysis, 30% of participants with type 1 diabetes diagnosed at age <20 years had depressive symptoms<sup>18</sup>. Recently, it was reported that 9–20% of adult patients with type 1 diabetes showed higher scores on the PHQ-9 ( $\geq 10$  points)<sup>19,20</sup>. The results of the present study are very similar to those of previous studies. However, when 77 children with type 1 diabetes in Japan aged 10–18 years were evaluated using the Children's Depression Inventory, none showed depressive symptoms<sup>21</sup>. Compared with the present result, reasons that could explain the difference in the proportion of depressive symptoms in other studies are the sample size and the advances in the treatment of type 1 diabetes. In the present study, we evaluated depressive symptoms in people living with type 1 diabetes for an average of 21 years. The number of participants who persistently experienced depressive symptoms from childhood to adulthood is unclear. Furthermore, the environment around children with type 1 diabetes has changed remarkably in the past few decades (e.g., diet therapy and the choice of freedom in foods have greatly improved with the dissemination of carbohydrate-counting therapy). Currently, individuals can choose their insulin requirements according to their lifestyle. However, most pediatric-onset and adolescent-onset type 1 diabetes participants in the present study received strict dietary



**Figure 1** | Frequency and severity of depressive symptoms according to the age at onset of type 1 diabetes. Participants were categorized into three groups based on the severity of depressive symptoms on the total Patient Health Questionnaire-9 (PHQ-9) score. The prevalence of moderate depressive symptoms significantly increased with a lower age of onset of type 1 diabetes ( $P < 0.05$ ).

**Table 2** | Comparison of clinical characteristics and diabetic complications among people with pediatric and adolescent onset (aged 0–19 years) type 1 diabetes classified by the presence or absence of moderate depressive symptoms

	PHQ-9 score		P-value
	<10 n = 541	≥10 n = 131	
Age (years)	34 ± 12	35 ± 10	0.587
Age of onset (years)	11 ± 5	11 ± 5	0.897
Women (%)	70	76	0.242
Duration of diabetes (years)	23 ± 12	24 ± 10	0.565
HbA1c (%)	7.6 ± 1.0	8.6 ± 1.8	<0.001 <sup>†</sup>
Unawareness of hypoglycemia (%)	57	61	0.3311
Retinopathy (%)	32	52	<0.001 <sup>†</sup>
Neuropathy (%)	15	41	<0.001 <sup>†</sup>
Hemodialysis (%)	2	6	<0.019 <sup>†</sup>

Data are given as mean ± standard deviation or percentage. Trends in the age, duration and glycated hemoglobin (HbA1c) were determined using one-way ANOVA test, and those in frequency using the Cochran–Armitage trend test. <sup>†</sup>Adjusted P values <0.05. PHQ-9, Patient Health Questionnaire-9.

and exercise therapy guidance at the time of type 1 diabetes onset, and it is possible that the burden of diabetes has continued until now.

The present study is the first to identify that depressive symptoms are more frequent in individuals with pediatric-onset and adolescent-onset type 1 diabetes than in those with adult-onset type 1 diabetes. Children with type 1 diabetes go through various life events, such as dreaming of the future, deciding

their life course, entrance exams, romance, employment, marriage and having a child. During these processes, if they feel discriminated against due to type 1 diabetes, their self-affirmation and self-esteem will decrease, and the stigma caused by type 1 diabetes will be internalized, which might result in depressive symptoms<sup>22</sup>. Stigma experienced during adolescence might be more prominently associated with depression due to immaturity. Furthermore, there might be gaps between pediatric and adult diabetes healthcare providers<sup>23</sup>. Diabetes healthcare providers for adults might think that patients with pediatric-onset type 1 diabetes are accustomed to living with type 1 diabetes, and thus might not consider the psychosocial issues of their patients. The present results showed that information about continuous mental support was important to avoid depressive symptoms in individuals, regardless of the duration of type 1 diabetes.

Furthermore, depression is associated with fear and anxiety of hypoglycemia<sup>24</sup>. In addition, depression increases the risk of severe hypoglycemia and diabetic ketoacidosis<sup>20</sup>. Conversely, a history of these conditions increases the risk of depression, and depression and severe hypoglycemia have an interactive relationship<sup>25</sup>. In the present study, moderate depressive symptoms were associated with a history of hypoglycemia unawareness in pediatric-onset and adolescent-onset type 1 diabetes. We could not explain why hypoglycemia unawareness was associated with depressive symptoms in participants with pediatric-onset and adolescent-onset type 1 diabetes but was not associated with depressive symptoms in those with adult-onset type 1 diabetes. Among individuals who experienced severe hypoglycemic events that resulted in an emergency room visit or hospitalization, 75% had an elevated risk of depression compared with individuals who did not experience such events<sup>25</sup>. These events

**Table 3** | Risk of depressive symptoms among people with type 1 diabetes

Age of onset (years)	0–19			20–40		
	PHQ-9 score $\geq 10$			PHQ-9 score $\geq 10$		
	OR	95% CI	P-value	OR	95% CI	P-value
Age	1.02	0.97–1.07	0.401	1.02	0.97–1.07	0.369
Duration of diabetes	0.97	0.93–1.02	0.281	0.96	0.90–1.01	0.268
Women	1.25	0.73–2.13	0.417	1.96	1.01–3.80	0.045 <sup>†</sup>
HbA1c	1.51	1.26–1.81	<0.001 <sup>†</sup>	1.40	1.11–1.76	<0.005 <sup>†</sup>
Unawareness of hypoglycemia	1.70	1.04–2.79	0.036 <sup>†</sup>	1.18	0.66–2.10	0.580
Retinopathy	1.66	0.96–2.85	0.068	1.32	0.66–2.65	0.431
Neuropathy	3.26	1.97–5.40	<0.001 <sup>†</sup>	2.57	1.37–4.81	<0.005 <sup>†</sup>
Hemodialysis	1.80	0.58–5.55	0.306	10.6	1.45–77.6	0.019 <sup>†</sup>

Data were analyzed using a logistic regression model adjusting for age, duration of diabetes, sex, glycosylated hemoglobin (HbA1c), the presence of unawareness of hypoglycemia, retinopathy, neuropathy and hemodialysis. <sup>†</sup>Adjusted *P* values <0.05. OR, odds ratio; PHQ-9, Patient Health Questionnaire-9.

were considered as stressful life events. In the present study, we did not confirm the treatment for hypoglycemia unawareness. People with pediatric-onset and adolescent-onset type 1 diabetes could visit the emergency room more frequently than people with adult-onset type 1 diabetes because of the worry of their parents or caregivers. Additionally, other factors (such as working environment, relationships with family and friends, income, and underlying health conditions besides diabetes) might have a greater influence on depressive symptoms for people with adult-onset type 1 diabetes. Yet, little research has been carried out on the association between depression and hypoglycemia unawareness, and further study, including prospective research, is necessary. Thus, avoiding hypoglycemia unawareness was necessary to decrease depressive symptoms. Currently available technologies, such as continuous glucose monitoring and sensor-augmented insulin therapy, have shown a positive impact on reducing hypoglycemia unawareness<sup>26</sup>.

Higher PHQ-9 scores were associated with increased odds ratios for retinopathy, neuropathy, and end-stage renal disease in both type 1 diabetes and type 2 diabetes<sup>9, 14</sup>. Furthermore, a longitudinal study showed an association between depression and diabetic retinopathy<sup>27</sup> and nephropathy<sup>19, 28</sup>. Therefore, it is important to consider strategies to reduce depressive symptoms to prevent the onset and progression of type 1 diabetes-related complications. Collaborative care interventions with diabetologists and non-physician care coordinators resulted in statistically significant improvements in depressive symptoms and cardiometabolic indices, including HbA1c, blood pressure and low-density lipoprotein cholesterol in individuals with type 2 diabetes<sup>29</sup>. As the duration of type 1 diabetes in pediatric and adolescent-onset cases is longer than the type 1 diabetes duration in adult-onset cases, people with pediatric and adolescent-onset type 1 diabetes are likely to have diabetes-related complications when they are younger. Therefore, the transition period from pediatric to adult diabetes healthcare providers was

appropriate for psychosocial screening<sup>30,31</sup>. Earlier detection of depressive symptoms and collaboration with mental health specialists could prevent the onset and progression of diabetes-related complications.

The present study had several limitations. First, this study was carried out at a single university hospital; therefore, the findings are not generalizable to all individuals with type 1 diabetes. Second, from the perspective of precise intervention for depression, depressive symptoms according to the PHQ-9 should be supplemented by a clinical diagnosis of depression from a psychiatrist. Third, selection bias cannot be ruled out, because participation in the DIACET Study was voluntary, and fewer persons with depression might have participated in the study. Fourth, other conditions, such as family relations, incomes, educations, medical insurance, body mass index, exercise, smoking, alcohol, eating disorders and 25 (OH)D3 levels, could be associated with depressive symptoms. A future prospective study could study these associations in detail. Finally, this was a cross-sectional survey, which limited the identification of a causal relationship between depressive symptoms, the age of onset of type 1 diabetes and complications. Therefore, prospective surveys are necessary to clarify the longitudinal changes in depression symptoms, and the acute and chronic complications in people with type 1 diabetes.

The present study highlighted the association between depressive symptoms and the age of onset of type 1 diabetes among participants with the disease. With the evidence of the elevated prevalence of moderate depressive symptoms in adulthood among individuals with pediatric-onset and adolescent-onset type 1 diabetes, it is important to avoid hypoglycemia unawareness and consider screening for depression regularly, including in the transitional period from childhood to adulthood in individuals with type 1 diabetes. Early detection of depression can facilitate effective treatment and help minimize

the adverse effects on diabetes management and improve clinical outcomes.

## ACKNOWLEDGMENTS

We thank Professor Yasuko Uchigata, former director of the Division of Diabetology and Metabolism, Department of Internal Medicine, Tokyo Women's Medical University, who helped to organize DIACET data in this research, and all the DIACET participants for cooperating with the data collection. We express our sincere gratitude to the physicians in the departments of internal medicine and ophthalmology. We thank Editage for English language editing.

## DISCLOSURE

DIACET is supported through unrestricted research grants from Alcon, Arkrey, Astellas, AstraZeneca, Becton Dickinson, Boehringer Ingelheim, Chugai, Daiichi Sankyo, Eisai, Eli Lilly, Johnson & Johnson, Kaken, KCI, Kissei, Kowa, Kyowa Hakko Kirin, Mitsubishi Tanabe, Mochida, MSD, Nipro, Novartis, Novo Nordisk, Ono, Otsuka, Pfizer, Roche, Sanofi, Santen, Sumitomo Dainippon, Takeda, Teijin, Terumo and Torii.

BT received speakers honoraria from Ono, Mitsubishi Tanabe, Sumitomo Dainippon, MSD, Boehringer Ingelheim, Novo Nordisk, Takeda, Taisho, Chugai and Daiichi Sankyo; research grants from Novartis and Eli Lilly; and scholarship grants from MSD, Nipro, Novo Nordisk, Terumo, Baxter, Sanwakagaku, Taisho, Boehringer Ingelheim, Santen, Ono, Sumitomo Dainippon, Chugai, Teijin, Daiichi Sankyo, Mitsubishi Tanabe, Abbott, Alcon, Astellas and Bayer. The other authors declare no conflict of interest.

Approval of the research protocol: This study was approved by the Tokyo Women's Medical University Ethics Committee (approval no. 2481-R, 5 March 2021) in accordance with the tenets underlying the Declaration of Helsinki (as revised in Fortaleza, Brazil, October 2013).

Informed consent: All participants provided informed consent for participation in the study.

Registry and the registration no. of the study/trial: N/A.

Animal studies: N/A.

## REFERENCES

1. Urakami T, Uchigata Y, Narazaki A, *et al.* A questionnaire survey on the actual condition of transitional medical care in type 1 diabetes - Report from the Committee of Health Care Transition in Type 1 Diabetes. *J Japan Diab Soc* 2020; 63: 776–783 [Japanese].
2. Naar-King S, Idalski A, Ellis D, *et al.* Gender differences in adherence and metabolic control in urban youth with poorly controlled type 1 diabetes: the mediating role of mental health symptoms. *J Pediatr Psychol* 2006; 31: 793–802.
3. Holmes CS, Chen R, Streisand R, *et al.* Predictors of youth diabetes care behaviors and metabolic control: a structural equation modeling approach. *J Pediatr Psychol* 2006; 31: 770–784.
4. Delamater AM, de Wit M, McDarby V, *et al.* ISPAD Clinical Practice Consensus Guidelines 2018: Psychological care of children and adolescents with type 1 diabetes. *Pediatr Diabetes* 2018; 19(Suppl. 27): 237–249.
5. Blanz BJ, Rensch-Riemann BS, Fritz-Sigmund DI, *et al.* IDDM is a risk factor for adolescent psychiatric disorders. *Diabetes Care* 1993; 16: 1579–1587.
6. Young V, Eiser C, Johnson B, *et al.* Eating problems in adolescents with Type 1 diabetes: a systematic review with meta-analysis. *Diabet Med* 2013; 30: 189–198.
7. Lawrence JM, Standiford DA, Loots B, *et al.* Prevalence and correlates of depressed mood among youth with diabetes: the SEARCH for Diabetes in Youth study. *Pediatrics* 2006; 117: 1348–1358.
8. McGrady ME, Laffel L, Drotar D, *et al.* Depressive symptoms and glycemic control in adolescents with type 1 diabetes: mediational role of blood glucose monitoring. *Diabetes Care* 2009; 32: 804–806.
9. Rewers A, Chase HP, Mackenzie T, *et al.* Predictors of acute complications in children with type 1 diabetes. *JAMA* 2002; 287: 2511–2518.
10. Butwicka A, Fendler W, Zalepa A, *et al.* Psychiatric disorders and health-related quality of life in children with type 1 diabetes mellitus. *Psychosomatics* 2016; 57: 185–193.
11. Kongkaew C, Jampachaisri K, Chaturongkul CA, *et al.* Depression and adherence to treatment in diabetic children and adolescents: a systematic review and meta-analysis of observational studies. *Eur J Pediatr* 2014; 173: 203–212.
12. Hood KK, Huestis S, Maher A, *et al.* Depressive symptoms in children and adolescents with type 1 diabetes: association with diabetes-specific characteristics. *Diabetes Care* 2006; 29: 1389–1391.
13. Ishizawa K, Babazono T, Horiba Y, *et al.* The relationship between diabetes mellitus and depression: analysis using the Diabetes Study from the Center of Tokyo Women's Medical University (DIACET). *Tokyo Women's Med Univ J* 2017; 87: E198–E206 [Japanese].
14. Ishizawa K, Babazono T, Horiba Y, *et al.* The relationship between depressive symptoms and diabetic complications in elderly patients with diabetes: analysis using the Diabetes Study from the Center of Tokyo Women's Medical University (DIACET). *J Diabetes Complications* 2016; 30: 597–602.
15. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001; 16: 606–613.
16. Muramatsu K, Miyaoka H, Kamijima K, *et al.* The patient health questionnaire, Japanese version: validity according to the mini-international neuropsychiatric interview-plus. *Psychol Rep* 2007; 101: 952–960 [Japanese].

17. Barnard KD, Skinner TC, Peveler R. The prevalence of comorbid depression in adults with Type 1 diabetes: systematic literature review. *Diabet Med* 2006; 23: 445–448.
18. Buchberger B, Huppertz H, Krabbe L, *et al.* Symptoms of depression and anxiety in youth with type 1 diabetes: a systematic review and meta-analysis. *Psychoneuroendocrinology* 2016; 70: 70–84.
19. Schmitt A, McSharry J, Speight J, *et al.* Symptoms of depression and anxiety in adults with type 1 diabetes: associations with self-care behaviour, glycaemia and incident complications over four years - Results from diabetes MILES-Australia. *J Affect Disord* 2021; 282: 803–811.
20. Trief PM, Foster NC, Chaytor N, *et al.* Longitudinal changes in depression symptoms and glycemia in adults with type 1 diabetes. *Diabetes Care* 2019; 42: 1194–1201.
21. Sekiguchi M, Sakano Y, Takagaki K, *et al.* The influence of psychological factors on glycemic control with type 1 diabetes in adolescents. *Jpn Psychosom Med* 2017; 57: 1046–1055 [Japanese].
22. Kato A, Fujimaki Y, Fujimori S, *et al.* How self-stigma affects patient activation in persons with type 2 diabetes: a cross-sectional study. *BMJ Open* 2020; 10: e034757.
23. Garvey KC, Telo GH, Needleman JS, *et al.* Health Care transition in young adults with type 1 diabetes: perspectives of adult endocrinologists in the U.S. *Diabetes Care* 2016; 39: 190–197.
24. Liu J, Bispham J, Fan L, *et al.* Factors associated with fear of hypoglycaemia among the T1D Exchange Glu population in a cross-sectional online survey. *BMJ Open* 2020; 10: e038462.
25. Gilsanz P, Karter AJ, Beerl MS, *et al.* The bidirectional association between depression and severe hypoglycemic and hyperglycemic events in type 1 diabetes. *Diabetes Care* 2018; 41: 446–452.
26. Little SA, Leelarathna L, Walkinshaw E, *et al.* Recovery of hypoglycemia awareness in long-standing type 1 diabetes: a multicenter 2 × 2 factorial randomized controlled trial comparing insulin pump with multiple daily injections and continuous with conventional glucose self-monitoring (HypoCOMPASS). *Diabetes Care* 2014; 37: 2114–2122.
27. Pouwer F, Geelhoed-Duijvestijn PH, Tack CJ, *et al.* Prevalence of comorbid depression is high in out-patients with Type 1 or Type 2 diabetes mellitus. results from three out-patient clinics in The Netherlands. *Diabet Med* 2010; 27: 217–224.
28. Horiba Y, Ishizawa K, Takasaki K, *et al.* Effect of depression on progression to end-stage renal disease or pre-end-stage renal disease death in advanced diabetic nephropathy: a prospective cohort study of the Diabetes Study from the Center of Tokyo Women's Medical University. *J Diabetes Investig* 2022; 13: 94–101.
29. Ali MK, Chwastiak L, Poongothai S, *et al.* Effect of a collaborative care model on depressive symptoms and glycosylated hemoglobin, blood pressure, and serum cholesterol among patients with depression and diabetes in India: the INDEPENDENT Randomized Clinical Trial. *JAMA* 2020; 324: 651–662.
30. Baucom KJW, Turner SL, Tracy EL, *et al.* Depressive symptoms and diabetes management from late adolescence to emerging adulthood. *Health Psychol* 2018; 37: 716–724.
31. d'Emden H, McDermott B, D'Silva N, *et al.* Psychosocial screening and management of young people aged 18–25 years with diabetes. *Intern Med J* 2017; 47: 415–423.