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Commencement of flash glucose monitoring is associated with a decreased rate of depressive disorders among persons with diabetes (FLARE-NL7)

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ABSTRACT

Introduction Depressive disorders are more common among persons with diabetes, as compared with persons without diabetes. The burden of glucose management is known to associate with depressive symptoms. This study aims to assess the effects of commencement of FreeStyle Libre flash glucose monitoring (FSL-FGM) on the mental health status of persons with diabetes.

Research design and methods Post-hoc analysis of data from a 1-year prospective nationwide FSL-FGM registry. Participants who used FSL-FGM for 12 months and completed the 12-Item Short Form Health Survey version 2 (SF-12^{v2}) questionnaires at baseline, 6 and 12 months were included. An SF-12^{v2} Mental Component Score (MCS) of ≤45 was used as a cut-off to discriminate between persons with and without a depressive disorder.

Results A total of 674 patients were included with a mean age of 48.2 (±15.8) years, 51.2% men, 78.2% type 1 diabetes and baseline HbA1c 62.8 (±13.4) mmol/mol (7.9±1.2%). At baseline, 235 (34.9%) persons had an SF-12 MCS ≤45 while after 6 and 12 months these numbers decreased: 202 (30.0%, p<0.01) and 173 (25.7%, p<0.01). Overall, MCS improved from 48.5 at baseline to 50.7 after 6 months and 51.3 after 12 months. In multivariable regression analysis, age and MCS at baseline were associated with improvement of MCS after 12 months of FSL-FGM use.

Conclusions This analysis suggests that use of FSL-FGM is associated with a decreased rate of depressive disorders among persons with diabetes. Future studies are needed to corroborate these findings.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Depressive disorders are more common among persons with diabetes, as compared with persons without diabetes.
⇒ Use of FreeStyle Libre flash glucose monitoring (FSL-FGM) is associated with improvement of quality of life and reduced diabetes-related distress.

WHAT THIS STUDY ADDS

⇒ This study suggests that commencement of FSL-FGM is associated with a decreased rate of depressive disorders among persons with diabetes.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE AND/OR POLICY

⇒ Persons with diabetes and comorbid depressive disorders could benefit from FSL-FGM initiation and subsequent long-term use, in terms of improvement of their mental health status.
⇒ Future studies are needed to further evaluate the effects of FSL-FGM use on depressive disorder rates in persons with diabetes.

INTRODUCTION

With flash glucose monitoring (FGM) persons with diabetes mellitus (DM) can measure glucose concentrations in the interstitial fluid. The FreeStyle Libre (FSL; Abbott Diabetes Care) FGM is a factory-calibrated FGM that replaces fingerprick testing by intermittent scanning of the sensor. The use of FSL-FGM results in positive effects on glycemic control and quality of life.[1–5]

The prevalence of depression is reported to be 12% in persons with type 1 DM and 28% in persons with type 2 DM.[6 7] As compared with persons without diabetes, this is threefold (for type 1 DM) and twofold (for type 2 DM) higher.[6] Adults with diabetes and comorbid depression have worse glycemic control and more microvascular and macrovascular complications than those not diagnosed with a depressive disorder.[8 9] Intensive self-management, including (painful) fingerpricks, and insufficient insight in causes of variable glucose levels are determinants of depression in DM.[10] As FSL-FGM use alleviates the burden of diabetes self-management and provides insights in glucose excursions,

its use may lead to improved mental well-being and lower rates of depressive disorders.

Longitudinal studies evaluating the effects of FSL-FGM initiation on depression and diabetes-related distress are scarce and show conflicting outcomes. Deshmukh *et al*[11] showed reduced diabetes-related distress during 7 months of FSL-FGM use by persons with diabetes (97% type 1 DM). In another prospective cohort study, a decrease in diabetes-related distress after 12 weeks of use of FSL-FGM was described in youngsters with type 1 DM.[12] Tyndall *et al*[13] demonstrated improvements with regard to total diabetes distress, regimen-related distress and emotional distress among persons with type 1 DM using FSL-FGM, although they paradoxically noticed an increase in depression and anxiety scores on the Hospital Anxiety and Depression Scale (HADS).

Given the negative impact of depression on quality of life, the potential beneficial effects of FSL-FGM on depressive disorders and conflicting (short-term) outcomes of studies evaluating the impact of FGM on mental health, the present study aims to provide more insight into the effects of long-term use of FSL-FGM on mental well-being and depressive disorder rates.

METHODS

Study design and patient selection

This is a post-hoc analyses of data from the 'FLAsh monitor REgistry in the NetherLands' (FLARE-NL). The FLARE-NL registry had a prospective, observational design (study period June 2016–July 2017) and aimed to assess the effects of FSL-FGM on daily life. Detailed information concerning the 1-year outcomes of the FLARE-NL registry has been published earlier.[2 14] In brief, adults (≥18 years) with DM using insulin were eligible for participation in the FLARE-NL registry; 1365 persons were included. For the present post-hoc analyses, only persons who started FSL-FGM, continued to use it for 12 months and completed the 12-Item Short Form Health Survey version 2 (SF-12^{v2}) questionnaires at baseline, 6 and 12 months (n=674) were included. Based on previous studies, a Mental Component Score (MCS) of ≤45 was used as a cut-off to indicate the presence of a depressive disorder.[15 16]

Outcomes

Primary outcome was the difference in the rate of persons with an SF-12 MCS ≤45 (indicative of a depressive disorder) between baseline and 6 and 12 months after FSL-FGM initiation. Furthermore, changes in MCS over time were investigated for the total population as well as different subgroups. Finally, the association between the difference in MCS over the study period and other variables was assessed.

Study procedures

After informed consent was obtained, the healthcare provider filled out the data necessary for the registry and study participants filled out online questionnaires regarding quality of life and disease burden, including the SF-12^{v2}.[17] The SF-12^{v2} questionnaire measures eight health dimensions: physical functioning, role limitations due to physical problems, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems, and mental health. The Physical Component Summary and the MCS are two subscales derived from the SF-12^{v2}.[18] Glycemic control during follow-up was assessed using self-reported most recent HbA1c values and the number of hypoglycemias (glucose <3 mmol/L in the past 6 months).

Statistical analysis

To determine if variables were normally distributed, histograms and Q–Q plots were used. Categorical data were expressed as n (%), normally distributed data as mean±SD and skewed distributed data as median with IQR. Pairwise t-test was used to compare the MCS after 6 and 12 months with baseline values. P values were adjusted with the Holm method for multiple comparison. A two-sided p<0.05 was considered statistically significant. Univariable linear regression analyses were performed to investigate the association between the difference in MCS over the 12-month study period and other variables. Next, multivariable linear regression analysis was performed to investigate associations between the difference in MCS over the study period as dependent variable and multiple independent covariates (age, sex, baseline HbA1c, number of hypoglycemic episodes and microvascular and macrovascular complications). Data were analyzed with R Statistical Software (V.4.0.3).

RESULTS

A total of 674 persons were included in the study. As presented in table 1, 345 (51.2%) were men and mean age was 48.2 (±15.8) years. Most persons (527 (78.2%)) had type 1 DM. Baseline HbA1c was 62.8 (±13.4) mmol/mol (7.9±1.2%). Microvascular complications were present in 230 (34.1%) and macrovascular complications in 86 (12.8%) persons.

Changes in MCS are presented in table 2. Baseline MCS was 48.5 and improved to 50.7 after 6 months and 51.3 after 12 months. Scores improved over time for both sexes, although baseline MCS was lower among women. At baseline, 235 (34.9%) participants had an SF-12 MCS ≤45, indicative for depressive disorder, which decreased to 202 (30.0%) after 6 months and 173 (25.7%) after 12 months (p<0.01). For men as well as women with a baseline MCS ≤45, scores improved after 6 and 12 months compared with baseline. The MCS after 12 months in these subgroups increased to 45.2±9.2 and 43.6±10.4 for men and women, respectively. Furthermore, improvement of MCS was observed in subgroups with type 1 DM and in all HbA1c subgroups (≤53, >53 and >64 mmol/mol).

Table 1 Baseline characteristics of all participants (n=674)

Male sex, n (%)	345 (51.2)
Age, years	48.2 (15.8)
HbA1c, mmol/mol	62.8 (13.4)
HbA1c, %	7.9 (1.2)
Type of diabetes	
Type 1 DM, n (%)	527 (78.2)
Type 2 DM, n (%)	98 (14.5)
LADA, n (%)	37 (5.5)
MODY, n (%)	3 (0.4)
Other forms, n (%)	9 (1.3)
Complications	
Microvascular complications, n (%)	230 (34.1)
Neuropathy, n (%)	88 (13.1)
Albuminuria, n (%)	110 (16.3)
Retinopathy, n (%)	100 (14.8)
Macrovascular complications, n (%)	86 (12.8)
Angina pectoris, n (%)	15 (2.2)
Myocardial infarction, n (%)	22 (3.3)
PCI, n (%)	30 (4.5)
CABG, n (%)	23 (3.4)
TIA, n (%)	17 (2.5)
CVA, n (%)	14 (2.1)
Peripheral arterial disease, n (%)	32 (4.7)
Diabetes-related hospital admissions past 12 months, yes, n (%)	74 (11.0)
Diabetes-related work absenteeism past 6 months, yes, n (%)	25 (3.7)
Estimated strips use per day	2.0 (0–5.5)
Presence of any hypoglycemic events in past 6 months, n (%)	622 (92.3)
Estimated or measured number of hypoglycemic events in past 6 months	40.0 (15–80)
Therapy	
Insulin monotherapy, n (%)	575 (85.6)
OBGLD, n (%)	1 (0.1)
Insulin and OBGLD, n (%)	96 (14.3)

Data are presented as number (%), mean (SD) or median (25th, 75th percentile).
CABG, coronary artery bypass grafting; CVA, cerebral vascular event; DM, diabetes mellitus; LADA, latent autoimmune diabetes in adults; MODY, maturity-onset diabetes of the young; OBGLD, oral blood glucose lowering drug; PCI, percutaneous coronary intervention; TIA, transient ischemic attack.

In multivariable regression model (R^2=0.14, p=0.001) with age, sex, baseline HbA1c, baseline number of hypoglycemic episodes, the presence of microvascular and macrovascular complications, delta HbA1c and baseline MCS, only age (standardized beta −0.17, 95% CI −0.29 to −0.07) and baseline MCS (standardized beta −0.50, 95% CI −0.60 to −0.39) were significantly associated with improvements in MCS over 12 months (table 3).

DISCUSSION

This study describes the effect of FSL-FGM initiation on the prevalence rate of depressive disorders in persons with diabetes, estimated by the number of SF-12^{v2} MCS ≤45. After 6 and 12 months of FSL-FGM use, fewer persons had an MCS indicative of a depressive disorder as compared with baseline. The overall MCS also improved during follow-up, demonstrating improved mental well-being among FSL-FGM users.

Factors associated with depression and depressive disorders in persons with diabetes are female sex, higher HbA1c, non-white ethnicity, lower income, lower education level, a more sedentary lifestyle and presence of microvascular and macrovascular complications.[8 9 19] In the present study, the depressive disorder rate was higher among women. Importantly, for men as well as women, the proportion of persons with a depressive disorder improved after FSL-FGM initiation. In contrast to our findings, Tyndall *et al*[13] observed that initiation of FSL-FGM in persons with type 1 DM was associated with worsening of depression scores, measured by the HADS, although total diabetes distress levels were reduced. Of notice, newly elevated HADS depression scores after FSL-FGM commencement were related to greater social deprivation and lower income categories, a risk factor for depression and depressive disorders by itself.[13] Our study population may be wealthier, since participants had to finance half of the costs of the FSL-FGM themselves, and—although hypothetical—this might account for the differences in study outcomes.

The observed improvement in mental health was associated with baseline MCS. Although the change in mental health was not significantly associated with the baseline number of hypoglycemic events, the link between both has been described in previous studies. Diabetes distress is associated with fear of hypoglycemia in persons with type 1 diabetes.[11] Overend *et al*[20] attributed a lower hypoglycemia frequency, a decrease in hypoglycemia severity and less fear of hypoglycemia among persons who initiated FSL-FGM as a key positive impact on well-being.[20] Improvement of diabetes distress after FSL-FGM initiation correlated with improvement of glycemic control and hypoglycemia unawareness.[11] These observations suggest that the negative impact of (fear of) hypoglycemias on mental health could be modified by FSL-FGM initiation, although this definitely is possible to hypothesize another explanation.

This study has limitations. First and foremost, a considerable number of persons included in the original FLARE-NL registry dropped out after 6 and 12 months, without reporting a reason for discontinuation. We hypothesize that the voluntary nature of participation in this registry and the longer duration of follow-up (as compared with other studies) might be of influence here.

Table 2 Changes in Mental Component Score (MCS) after 6 and 12 months of FSL-FGM use in different subgroups

	Baseline (A)	6 months (B)	12 months (C)	P value A vs B	P value A vs C
MCS	48.5±10.2	50.7±9.9	51.3±9.9	<0.001	<0.001
n	674	674	674		
MCS in women	47.1±10.4	48.9±9.8	49.6±10.2	0.03	0.003
n	329	329	329		
MCS in men	49.9±9.9	52.4±9.7	52.9±9.2	0.001	<0.001
n	345	345	345		
MCS in persons with a baseline MCS ≤45	36.9±6.0	43.4±9.4	44.2±9.9	<0.001	<0.001
n	235	235	235		
MCS in women with a baseline MCS ≤45	36.9±6.0	42.9±9.3	43.6±10.4	<0.001	<0.001
n	137	137	137		
MCS in men with a baseline MCS ≤45	37.0±6.0	44.0±9.6	45.2±9.2	<0.001	<0.001
n	98	98	98		
MCS in persons with a baseline MCS >45	54.8±5.5	54.6±7.6	55.1±7.4	0.87	0.87
n	439	439	439		
MCS in persons with type 1 DM	48.3±10.3	50.6±10.0	51.5±9.9	<0.001	<0.001
n	527	527	527		
MCS in persons with type 2 DM	48.5±10.2	50.4±9.7	50.5±9.4	0.49	0.46
n	98	98	98		
MCS in persons with an HbA1c ≤53 mmol/mol	48.4±10.5	51.7±10.0	51.9±9.9	0.005	0.004
n	176	176	176		
MCS in persons with an HbA1c >53 mmol/mol	48.6±10.1	50.4±9.8	51.2±9.8	0.01	0.001
n	497	497	497		
MCS in persons with HbA1c >64 mmol/mol	48.9±10.2	50.1±9.9	51.1±10.3	0.36	0.04
n	251	251	251		

Data are presented as mean±SD.
DM, diabetes mellitus; FSL-FGM, FreeStyle Libre flash glucose monitoring.

Table 3 Multivariable analysis for change in MCS

	Standardized beta	P value
Age	−0.17 (−0.29 to −0.07)	0.001
Male sex	−0.02 (−0.31 to 0.29)	0.51
Baseline HbA1c, mmol/mol	0.02 (−0.11 to 0.14)	0.80
Number of hypoglycemic events past 6 months	−0.11 (−0.23 to 0.01)	0.08
Macrovascular complications	−0.08 (−0.42 to 0.27)	0.66
Microvascular complications	−0.10 (−0.43 to 0.13)	0.38
Delta of HbA1c, mmol/mol	−0.01 (−0.15 to 0.12)	0.86
Baseline MCS	−0.50 (−0.60 to −0.39)	<0.001

Standardized beta regression coefficients are presented with 95% CIs.
MCS, Mental Component Score.

Post-hoc analysis of baseline characteristics between persons with and without available data during follow-up demonstrated that persons without available data were more often male (57.4% vs 50.2%, p=0.017) significantly younger (44.2 (±16.1) vs 48.2 (±15.8), p<0.001) and had a higher HbA1c (66.1 (±15.1) vs 62.1 (±13.0), p<0.001). Given the number of participants who did not fill in the questionnaires and the fact that data were patient reported, recall bias may be present. Since participants had to finance half of the costs of the FSL-FGM themselves, this will contribute to selection bias, as the selected participants probably will be more affluent than the average population with DM. We did not have access to FSL-FGM data (as data were gathered from 2016 to 2017) and therefore information such as time in range and other glycemic metrics is not available. Although the SF-12^{v2} MCS is not a regular screening tool for depression and depressive disorders in persons with diabetes, the SF-12^{v2} is considered as a valid generic instrument for measuring quality of life in this population.[17] As data on depression and depressive disorders in adults using

FSL-FGM are lacking to date, this study provides some information to fill this gap. Nevertheless, our findings should be interpreted with caution and its clinical relevance has to be proven in future studies.

CONCLUSIONS

The observed outcomes suggest that the depressive disorder rate among persons with diabetes is reduced after longer term FSL-FGM use, as compared with the period preceding FSL-FGM commencement.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval This study involves human participants and was approved by the Medical Ethical Committee of Isala (Zwolle, The Netherlands) (METC 16.0346). Participants gave informed consent to participate in the study before taking part.

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