DR SURESH RAMA CHANDRAN (Orcid ID : 0000-0001-5944-4886)
MS NATALIE ZAREMBA (Orcid ID : 0000-0002-1720-1621)
DR PRATIK CHOUDHARY (Orcid ID : 0000-0001-7635-4735)
DR DAVID HOPKINS (Orcid ID : 0000-0002-0451-0900)
DR MARIETTA STADLER (Orcid ID : 0000-0001-6869-9960)

Article type : Research Article

Full title: Disordered eating in women with type 1 diabetes: Continuous glucose monitoring reveals the complex interactions of glycaemia, self-care behaviour and emotion

Running title: Disordered eating in type 1 diabetes: CGM reveals the complex interactions

Suresh Rama Chandran[1,7], MD, Natalie Zaremba[2], MSc, Amy Harrison[2,3], PhD, Pratik Choudhary[1,2], MD, Yee Cheah[1], PhD, Jacqueline Allan[2], PhD, Fredrik Debong[4], Fiona Reid[5], Janet Treasure, Prof [3], David Hopkins[6], FRCP, Khalida Ismail[3], Prof, Marietta Stadler[2,3], MD

1. Department of Diabetes, King's College Hospital, London, UK
2. Diabetes Research Group, Weston Education Centre, King's College London, London, UK
3. Department of Psychological Medicine, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK
4. Hihealth, Vienna, Austria
5. Faculty of Life Sciences and Medicine, Population Health, King's College London, London, UK
6. Institute of Diabetes Endocrinology and Obesity, King's Health Partners, London, UK
7. Department of Endocrinology, Singapore General Hospital, Singapore

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/dme.14446

Corresponding author:
Dr Marietta Stadler
Diabetes Research Group
Weston Education Centre
10 Cutcombe Road
SE5 9RJ
London, UK

Email: Marietta.stadler@kcl.ac.uk

Word count main document: 3997
Word count abstract: 236
Figures: 2
Tables: 4
Supplementary Material: 6 Tables
No of references: 30

Conflict of Interest Disclosure: FD was a co-founder of and former Head of R&D at mySugr GmbH. He left the position in 2018, with no stock retained after acquisition by Roche Diagnostics in 2017. The rest of the authors have nothing to declare.

Novelty Statement

- Disordered eating in type 1 diabetes has no effective treatment despite a significant impact on self-care behaviour, insulin use and glycaemia.
- People with disordered eating and type 1 diabetes spend longer duration in level 2 hyperglycaemia (>13.9 mmol/L) and have higher variability of glucose levels, and this was associated with inappropriate diabetes self-care actions and negative emotions.
- A complex interaction between glycaemia, emotions and self-care behaviours exist in people with type 1 diabetes and disordered eating.

Acknowledgements

We sincerely thank Dexcom® and mySugr® for allowing us to use their respective systems free of charge. The authors are incredibly grateful to the people with diabetes volunteering as research participants and to the members of the STEADY (Safe management of Type 1 diabetes and Eating Disorders StudY) group and public involvement group advising on the study design.

Funding sources

S.R.C's salary was funded by the Ministry of Health, Singapore as part of the Health Manpower Development Program. N.Z.'s salary was part-funded by King's College London, Diversity & Inclusion, parenting leave funds awarded to M.S. and by NIHR via the NIHR Clinician Scientist award to MS; J.T. and K.I. are part-funded by the NIHR Mental Health Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London. M.S. was funded through a National Institute of Health Research (NIHR) Academic Clinical Lectureship, NIHR Clinician Scientist Fellowship and Academy of Medical Sciences Starter Grant for Clinical Lecturers funded by Diabetes-UK (2017); The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

Author contributions

S.R.C. analysed and interpreted the data and co-wrote the first draft with M.S. and was involved in manuscript revisions. N.Z. collected the data and reviewed the manuscript, A.H., P.C., Y.C., and J.A. were involved in the interpretation of the data and manuscript review. F.D. provided input in use of the mySugr app, interpreted data and reviewed the manuscript. F.R reviewed the study

methodology, statistical methods, data presentation and reviewed the whole manuscript. J.T., D.H. and K.I. were involved in study design, data interpretation and manuscript review. M.S. conceived the study concept, designed the study, analysed, and interpreted the data, co-wrote the first draft with S.R. and revised the manuscript. M.S. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Abstract

Objectives: Glycaemia in people with type 1 diabetes and disordered eating is not well characterised. We explored the glycaemia, self-care behaviour and emotional state of women with type 1 diabetes and disordered eating.

Research design and methods: Thirteen women with and ten without disordered eating and type 1 diabetes participated in this case-control study. We used a mixed-methods approach with a 7-day blinded continuous glucose monitoring and real-time record of non-prompted capillary glucose, emotion, activity, and physical symptoms on a diabetes diary using a smartphone application (mySugr®). We compared groups using Mann-Whitney U test or Fisher's exact test. We conducted thematic analyses of free text diary entries (NVivo®) and quantitative analysis of emotion/ symptom tags.

Results: People with type 1 diabetes and disordered eating spent longer time above range in level 2 hyperglycaemia (>13.9 mmol/L, Median [Interquartile range]: 21% [16,60] vs 5% [2,17], p=0.015). They had lower time in range and similar time below range compared to those without disordered eating. The standard deviation of capillary glucose was significantly higher in the disordered eating group (4.7 mmol/L [4.5, 6.1] vs 3 [2.8, 3.2], p=0.018). The median of the percentage of rising trends was three times higher in the disordered eating group. They also had higher negative emotional and physical symptoms associated with high blood glucose (>15 mmol/L).

Conclusions: Disordered eating has a significant impact on the glycaemia and emotion of a person with type 1 diabetes.

Keywords: type 1 diabetes, eating disorders, continuous glucose monitoring, blood glucose variability, hyperglycaemia

INTRODUCTION

Type 1 diabetes has an impact on almost every aspect of day to day life of a person [1]. People living with type 1 diabetes must continuously pay close attention to their blood glucose, food intake, activity, and modify their insulin doses to avoid hypo- and hyperglycaemia. Food intake has the most marked and immediate effect on blood glucose leading to a large focus on food and consequent efforts to regulate its impact on blood glucose, sometimes unsuccessfully. These efforts can quickly become an obsession or cause frustration to a person living with type 1 diabetes [2]. These relentless diabetes self-care burdens are predisposing factors for mental health disorders (e.g. depression, eating disorders) and for diabetes-specific distress [3], known to worsen glycaemic control and affect quality of life [4].

Disordered eating in people with type 1 diabetes is a spectrum of conditions ranging from well-defined mental health disorders like anorexia nervosa, bulimia nervosa and binge eating disorder to inappropriate diabetes self-care behaviours like excessive calorie restriction for weight loss, carbohydrate restriction, intense exercise, laxative or diuretic abuse, self-induced vomiting, skipping basal or bolus insulin and intermittent binge eating [5]. People with type 1 diabetes and disordered eating have described their condition as a vicious cycle of diabetes and disordered eating reinforcing each other [6]. Although people with type 1 diabetes and disordered eating have elevated HbA1c [7], there is no knowledge of the actual dynamic of their blood glucose level over time, time in range (TIR) or glucose variability (GV). Disordered eating is a condition that thrives in secrecy and people tend not to report their symptoms and behaviours in clinics; therefore, diabetes clinicians' knowledge of diabetes self-management behaviour in a person with type 1 diabetes is scarce.

Disordered eating is twice as prevalent in type 1 diabetes [8] compared to those without diabetes and can impact negatively on safe diabetes self-care behaviours [9]. Insulin restriction triples risk of mortality in people with type 1 diabetes by accelerating microvascular and macrovascular complications [7]. It also predisposes to acute complications such as diabetic ketoacidosis (DKA) and severe hypoglycaemia from inappropriate insulin doses [10, 11]. There is currently no effective intervention for people with type 1 diabetes and disordered eating [12].

Psychopathology of disordered eating in type 1 diabetes is complex, with various proposed models[9, 13, 14]. A food addiction based model [9] posits that foods with a high glycaemic load are more addictive and cause greater post-meal hunger and activation of reward circuits [15, 16].

A rapid rise of blood glucose after intake of such foods may play a role in driving this. However, in people with type 1 diabetes, similar glucose-kinetics occur when mealtime insulin is restricted or omitted, even without need for an unusually high glycaemic load food. Previous continuous glucose monitoring (CGM) based studies in type 1 diabetes and disordered eating have shown that insulin omission/restriction is associated with higher post-meal glucose [17–19]. Thus, people with disordered eating may experience greater fluctuations in their glucose, which is not reflected in their HbA1c. This study aimed to characterize glycaemia of people with type 1 diabetes and disordered eating and explore association of these glycaemic changes with emotion and diabetes self-care behaviours.

RESEARCH DESIGN AND METHODS

We conducted a case-control study using a mixed-methods approach of combining blinded CGM with emotion and activity self-reported in real-time in a diabetes diary utilising a smartphone application, mySugr®. East of England - Cambridge Central Research Ethics Committee approved this research protocol (IRAS Project ID: 231596).

Participants and Data Collection

Participants with type 1 diabetes, 13 women with self-declared disordered eating and ten women without disordered eating, were recruited after informed consent, through social media advertisements and clinician referrals from January 2018 to January 2019. Exclusion criteria included >1 hospital admission in past year from DKA, BMI <15 or >40kg/m^2, HbA1c >140 mmol/mol (>15%), severe mental illness or advanced diabetes complications.

Participants wore a blinded CGM (DexcomG4® Platinum with 505 Software transmitter and receiver kits) for a week. CGM traces downloaded at end of study using Dexcom® Studio software was inspected and interpreted. We encouraged participants to record details about each meal (e.g. estimated carbohydrate intake, insulin dose taken or free text description of meal), emotions and behaviours around a meal (e.g. skipped insulin, binge eating, feeling guilty about eating, angry at high blood glucose etc), insulin doses, glucose measurements and exercise on diabetes diary. Participants could choose from many pre-set tags (Supplementary Table S1) on diabetes diary or make free text entries. Participants used their own capillary glucose meters for testing and were encouraged to test pre-meals and at bedtime. There were no reminders for data entry nor any limit to number of entries allowed per day. We downloaded diabetes diary data in excel format and exported free-text entries into NVivo11®. Participants received training on wearing blinded CGM

system and use of diabetes diary, mySugr® application. Participants completed revised Diabetes Eating Problem Survey (DEPS-R) [20], 17 items Diabetes Distress Screening Scale [21], Patient Health Questionnaire (PHQ-9), Yale Food Addiction Scale (YFAS)[22] and an 11-item technology questionnaire (Supplementary Table S2) on satisfaction with CGM device and mySugr® application at start and end of study. A higher score indicated a greater degree of disordered eating, diabetes distress, depression, food addiction or satisfaction with technology on respective scales.

Participants also underwent semi-structured interviews to inform a revised theoretical model of disordered eating in type 1 diabetes as part of a sub-study. An experienced clinical psychologist, with expertise in eating disorders, analysed all interviews and confirmed group allocation of all participants.

Data analysis

CGM Analysis

We reviewed all CGM data for quality by calculating Mean absolute relative difference (MARD) for all calibration points using sensor glucose that was closest in time to calibration capillary glucose. We excluded all CGM data before and after a calibration point with a MARD >25%. MS and SR inspected and excluded sections of all CGM downloads with significant gaps, erratic or missing sensor glucose. For each participants' sensor glucose readings, we calculated mean, standard deviation (SD), coefficient of variation (%CV), time in range (TIR; 3.9 - 10 mmol/L), time above range measured at two thresholds(TAR; >10 and >13.9 mmol/L), and time below range measured at two thresholds (TBR; <3.9 and <3 mmol/L) for the entire period. Further, we used EasyGV. Ver. 9.0.R2 (available from https://www.phc.ox.ac.uk/research/technology-outputs/easygv) software to calculate other glycaemic indices from the longest CGM trace without missing data for each participant. Indices calculated were Continuous overall net glycaemic action (CONGA-1hour), Lability Index (LI), Low Blood glucose Index (LBGI), High Blood Glucose Index (HBGI), Glycaemic risk assessment diabetes equation (GRADE), GRADE%- Hypo, Hyper and Euglycaemia, J-Index, Mean of daily differences (MODD), Mean Amplitude of glycaemic excursions (MAGE), Average daily risk ratio (ADRR), M-Value, and Mean absolute glucose (MAG).

Sensor glucose trend analysis

We calculated sensor glucose trend as rate of change in sensor glucose over 15 minutes (e.g. 4th glucose– 1st glucose). A positive difference identified a rising trend, and a negative difference

identified a falling trend in sensor glucose. In keeping with rate of change metrics used for trend arrows on a Dexcom system[23], we considered a change of ± 0.056 mmol/L/min as a stable trend. Rest of sensor glucose trends were divided as a rising (>0.056 to 0.11, >0.11 to 0.17, & >0.17 to 0.22 mmol/L/min) or a falling trend (<-0.056 to -0.11, <-0.11 to -0.17, & <-0.17 to -0.22 mmol/L/min). We added a fourth trend, >0.22 mmol/L/min, not present in Dexcom system, to capture the anticipated large rate of change of glucose in group with disordered eating. We expressed each of these sensor glucose trends as a percentage of total trends identified in each participant, thereby correcting for unequal CGM durations between participants.

Diabetes diary analysis

Participants could make free text entries or choose from pre-set entries in diabetes diary. Supplementary Table S1 shows full list of pre-set tags available in mySugr application. At end of study, all entries were exported to NVivo® and analysed. Following thematic analysis, we categorised entries into diabetes self-care, physical symptoms, disordered eating, activity, and emotion and feelings. Diabetes self-care related entries included self-monitored capillary glucose, insulin bolus, correction bolus, food and mealtime, drinks, alcohol, technical aspects, self-reflection, deliberate insulin omission and cutting corners. Blood glucose awareness related entries included 'feeling high' and 'feeling low'. Physical symptoms recorded included gastrointestinal symptoms, pain, headache, light-headedness, difficulty concentrating, tiredness, fullness, and hunger. Disordered eating related entries included purging, restricting food, binge eating, and body image concerns. Activity related entries included household activities, dining, and travel. Emotion and feeling recorded included positive affect (excited, happy, relaxed, chilled) and negative affect (feeling low, stressed, angry, frustrated, loss of control). We compared median number of entries per category between groups. Further, frequency of emotion and physical symptom entries were stratified based on respective time-matched sensor or capillary glucose and compared between groups. We excluded entries without a time-matched CG or SG from this analysis.

Statistics

We present data as count (n, %), or median and interquartile range (Median [IQR]). Groups were compared using Mann Whitney U test for continuous data or Fisher's exact test for categorical data. Microsoft Excel and SPSS version 25 were used for data extraction, cleaning, and statistical analysis. Correlations between DEPS-R, PHQ-9 and DDS-17 scores and glycaemic indices were assessed using Spearman's rank test.

RESULTS

Thirteen women with type 1 diabetes and disordered eating and ten women with type 1 diabetes participated in this study. Eight participants in disordered eating group had self-referred to the study (of whom seven had received an eating disorder diagnosis at their local service), three were currently under our specialist service for people with type 1 diabetes and disordered eating at King's College Hospital and two under South London and Maudesley eating disorder unit outpatients' service. Of 13 with self-declared disordered eating, 12 had either a historical or an ongoing formal diagnosis of an eating disorder (five had anorexia nervosa, three had bulimia nervosa, two had binge eating disorder, and two had Eating disorder not otherwise specified (EDNOS)) and remaining one woman without any formal diagnosis had a history of insulin restriction for weight loss. Three women (two with EDNOS, one with insulin restriction) had a history of insulin restriction for weight loss or to prevent weight gain.

Baseline characteristics like age, ethnicity, BMI, cigarette smoking, alcohol intake, duration of diabetes, baseline reported total daily insulin dose (TDD), mode of insulin administration, severe hypoglycaemia and DKA episodes in past year were comparable between groups (Table 1). No episodes of severe hypoglycaemia occurred during study period. Recreational drug use was more prevalent in disordered eating group compared to type 1 diabetes (38.5% vs 10%). Interestingly, baseline TDD of insulin was numerically higher in those with disordered eating. However, these insulin dosages reflect prescribed doses of insulin and not actual amount that is taken by the person with disordered eating. The prescribed dose is likely higher in response to higher HbA1c of this group during clinical review and does not necessarily translate to actual amount of insulin administered. Women with type 1 diabetes and disordered eating had significantly higher HbA1c and higher scores on diabetes distress (DDS-17), depression (PHQ-9) and DEPS-R questionnaires compared to those with type 1 diabetes. There were no differences between groups in YFAS or technology questionnaire (Table 2).

Glycaemia

Self-monitored capillary glucose

The disordered eating group recorded fewer capillary glucose (CG) per day and had a significantly higher SD of capillary glucose (Table 3).

Continuous glucose monitoring

The median duration of CGM used for analysis, after excluding areas with suboptimal MARD and significant missing data, was shorter in the disordered eating group. Comparison of the time in range of sensor glucose between groups showed similar TBR, but higher TAR in the disordered eating group and consequently, a lower TIR (Fig. 1, Table 3). TAR, >13.9 mmol/L, had the highest correlation with DEPS-R and DDS-17 scores (Supplementary Table S3). The median of SDs derived from sensor glucose was higher in the disordered eating group with a trend to significance while the median of %CVs was similar between the groups. Among the other glycaemic indices compared GRADE, HBGI, J-Index, and M-value were significantly higher in the disordered eating group (Supplementary Table S4). GRADE, HBGI and M-value are risk scores generated from glucose values, while J-Index is a composite score that incorporates both mean glucose and SD[24].

In analysing glucose trends percentages, median of percentage of rising trends in glucose (>0.17 and >0.22mmol/L/min, both $p < 0.05$) was three times higher, and median of falling trends in glucose (>-0.22mmol/L/min, $p = 0.06$) trended higher in disordered eating group (Table 3).

Diabetes Diary usage

Despite the same duration of diabetes diary usage (median of 6 days), the median entries per day (5.5 vs 8.3, $p = 0.030$), were significantly lower in the disordered eating group (Table 4). There were no significant differences in the entries related to disordered eating, blood glucose awareness, physical symptoms, or emotions and feelings across the two groups. The disordered eating group recorded fewer activity-related entries.

Emotional and physical symptoms stratified by corresponding glucose

The disordered eating group had a significantly higher frequency of negative emotions/week (2.0 [1.0, 6.0] vs 0 [0, 1.0], $p=0.030$) at glucose > 15mmol/L and higher frequency of physical symptoms/week when the blood glucose was > 10 mmol/L and > 15 mmol/L (7.0 [3.0, 13] vs 2.5 [1.0, 7.0], $p=0.049$; 4.0 [1.0, 6.0] vs 0 [0, 2.0], $p=0.021$, respectively) (Supplementary Table S5). On sub- analysis, the negative emotional symptoms were only significantly different for capillary glucose but not with blinded sensor glucose (Supplementary Table S6).

DISCUSSION

This study aimed to characterise the glycaemia in people with type 1 diabetes and disordered

eating and its impact on diabetes self-care behaviours and emotion. People with type 1 diabetes and disordered eating spend four times longer in level 2 hyperglycaemia (>13.9 mmol/L) with an associated higher frequency of negative emotions and physical symptoms and had higher glucose variability.

Disordered eating thrives in secrecy and behaviours are often hidden and unknown to the health care providers. Characterization of glycaemic changes could serve as a surrogate marker for early identification of this condition. While a comparison of the typical parameters of TIR, TBR and TAR may not appear hugely different, it is the TAR beyond level 2 hyperglycaemia (>13.9 mmol/L) that is strikingly different. People with disordered eating spend >5.1 hours (21.3% of 24 hours) at glucose more than 13.9 mmol/L compared to 1.2 hours (5% of 24 hours) in people without disordered eating. Recreational drug use is another secret behaviour that is known to be prevalent in those with eating disorders and co-occurs in people with type 1 diabetes and insulin misuse.[25]

Glucose variability (GV) has received much attention recently and presents another dimension of glycaemia not captured by HbA1c. GV is linked to hypoglycaemia and the risk of diabetes complications[26]. Reducing GV is now a recognised therapeutic target in the treatment of diabetes. Glucose variability (GV) as measured by SD was higher in the group with disordered eating. However, it is interesting that %CV, considered the primary metric of GV [26], was not different between the groups. %CV is not different since people with disordered eating have an increase in both mean glucose and SD (CV = SD/Mean glucose).
Interestingly, most commercial CGM download software such as Carelink®, Diasend® report SD, Dexcom® reports both SD and %CV, while Freestyle Libre® reports %CV. Glucose variability has multiple aspects, amplitude, duration, and the rate of change. Neither SD nor %CV captures the rate of change of glucose. The disordered eating group had a higher percentage of rising and falling sensor glucose trends. Glucose variability captured by SD and the rate of change of glucose captured by the percentage of rising and falling trends are characteristic glycaemic changes in disordered eating.

Our study further unravels the complex psychopathology of disordered eating and its relation to glycaemic changes. People with disordered eating experience higher variability of glucose

together with more negative emotions and physical symptoms at high glucose. It was interesting that negative emotions were high only when the glucose value was visible (capillary glucose) and not when it was high on blinded CGM (sensor glucose). The negative emotions linked to high blood glucose could be the result of various thought processes; a feeling of guilt for omitting/restricting insulin, anxiety about the risk of diabetes-specific complications or a sense of failure despite attempts at maintaining glucose within the target range. Such negative emotions could lead to multiple actions. Firstly, a large correction bolus, often resulting in a rapid drop in blood glucose and subsequent hypoglycaemia. This study explains through data this commonly seen clinical phenomenon of food taken without insulin, followed by a negative emotional response to high blood glucose that eventually leads to a correction dose (sometimes termed a "rage bolus") that then leads to a rapid fall of glucose (Fig. 2). There was indeed a trend for a higher percentage of falling trends of glucose in the group with disordered eating, which would support this behaviour. Secondly, studies also suggest that overdosing of insulin at high blood glucose, with subsequent hypoglycaemia may be used as a justification for bingeing on 'restricted food' without insulin, resulting in rapid glucose rises, which further perpetuates this cycle [25, 27]. Thirdly, the negative emotion at high blood glucose and the perceived failure at preventing these may result in reduced blood glucose measurements to avoid the negative emotions associated with it. These negative emotions could be a reason for the lower frequency of blood glucose measurements in the disordered eating group. However, these are self-defeating strategies and often leads to the very situation the person was trying to avoid and further perpetuation of this vicious cycle. For example, a person skipping insulin for meals to restrict insulin often feels guilty or develops negative emotions to subsequent high glucose leading to a large correction bolus. Thus, the strategy did not avoid insulin, but only delayed it at the cost of high blood glucose, negative emotions, and subsequent risk of hypoglycaemia from a large correction dose (Fig. 2).

Two previous studies have used a 3-day blinded CGM in type 1 diabetes with disordered eating and support our findings. Higher DEPS-R scores were associated with higher mean glucose and TAR > 10 mmol/L, while no association was found with TBR and SD [28]. However, the mean DEPS-R score in that study was 12.4 ± 10.1, much lower than that of our study (28.7 ± 15.6). Merwin et al. [17] studied people with a DEPS-R score > 20 and found a correlation between insulin restriction at meals and their mean glucose and TAR >10 mmol/L. Negative affect, 'guilt for eating' and 'break a rule' feelings before eating predicted insulin restriction. The same group

also showed that a higher pre-meal negative affect led to insulin restriction and an objective binge eating episode, which in turn led to higher post-meal glucose and more negative affect [18].

Currently, available treatments do not yield any significant improvement to people with type 1 diabetes and disordered eating [12]. Diagnosis of type 1 diabetes is a significant disruption to the life of a person demanding large behavioural changes. The early adaptive strategies that a person employs has a substantial impact on their future diabetes self-care and psychological well-being[29]. It appears that inappropriate diabetes self-care behaviours are a key factor [2] in the development of disordered eating in type 1 diabetes. This calls for early psychological support to foster realistic expectations in people with newly diagnosed type 1 diabetes paired with the early introduction of essential skills and knowledge for flexible insulin dosing for normal eating, to avoid large glucose fluxes. Another important theme was the higher negative affect associated with high blood glucose, which drives inappropriate diabetes self-care behaviours. We believe that early clinical conversations have a major impact on how people view each blood glucose value. The use of 'time in range', identified by people with diabetes as a key metric [30], as opposed to strict target ranges is a move in the right direction as this gives people with diabetes the 'permission' to be 'out-of-range' for a certain period. Thus, a glucose value outside the range may not be immediately seen as a failure, resulting in inappropriate insulin doses. We believe that utilising TIR as a glycaemic target in early conversations with a newly diagnosed person with type 1 would provide a more realistic picture of the expected glycaemia in a person with type 1 diabetes.

Results suggest that insulin restriction might be decreased by helping people with type 1 diabetes respond effectively to the heightened negative affect (e.g., anxiety, guilt) and encouraging them to take a less rigid, punitive approach to diabetes management [17]. We believe that introduction of adaptive emotional regulation strategies to people with type 1 diabetes early, potentially together with structured, flexible insulin therapy education may reduce the development of inappropriate behaviours like avoidance of diabetes self-care.

Strengths and Limitations

Our study presents real-life data comparing type 1 diabetes women with and without disordered eating. A significant strength of our research is in successfully recruiting 13 people with type 1

diabetes and disordered eating, despite this group being usually secretive and not willing to participate in clinical trials. We used a non-intrusive approach without any alerts for data entry. Participants were free to decide the frequency of their interaction with the blood glucose diary application. Although a prompt-based system would have captured more data, we believe that this would have resulted in observer bias, alert fatigue and incorrect data capture. Ours is the first study using a CGM system for seven days together with real-time diabetes diary in people with type 1 diabetes and disordered eating.

There are several limitations identified. Our study had a relatively small sample size, and therefore non-significant differences do not rule out the possibility of real effects. Although we attempted to match the groups as best possible, they were not perfectly matched (for example, for age and ethnicity), and the possibility of unmeasured confounder bias cannot be excluded. We also acknowledge the issue of multiple testing; however, each analysis had a prior study hypothesis. Only white women with type 1 diabetes and disordered eating volunteered for this study in a tertiary care setting. Hence, extrapolation of our findings to men, other ethnicities and care settings must be done with caution. Although the women in the control group had no self-declared disordered eating nor any known records of a past eating disorder, some scored higher on DEPS-R. A higher DEPS-R score in the control group may identify behaviours related to problems of accepting living with diabetes and not necessarily disordered eating behaviour. We believe that we have underestimated some of the differences between the groups due to the limitations of the maximum sensor value on commercial CGM system used, 22.2 mmol/L. Further, more data loss in the disordered eating group due to missed calibrations and missing data was also not ideal. It is possible that some periods of wide fluctuations in sensor glucose due to disordered eating behaviours were excluded or not captured. The use of a diabetes diary to document events related to diabetes and disordered eating is a major cognitive and behavioural change. Indeed, people with disordered eating had a 50% lower frequency of entries on the diabetes diary. In keeping with our minimally intrusive approach, we did not insist on meal marking and hence the analysis of factors that may trigger a meal-based behaviour could not be done. Findings from this study must be re-affirmed in a larger sample with attempts to overcome the limitations identified. Nevertheless, we believe that this study reveals a complex interaction of glycaemia, emotions, and self-care in people with disordered eating and type 1 diabetes.

CONCLUSION

People with type 1 diabetes and disordered eating spend a significantly higher percentage of time in level 2 hyperglycaemia, associated with negative affect and higher glucose variability, and contributed by inappropriate diabetes self-care behaviour.

References

[1] Vanstone M, Rewegan A, Brundisini F, et al. Patient Perspectives on Quality of Life With Uncontrolled Type 1 Diabetes Mellitus: A Systematic Review and Qualitative Meta-synthesis. *Ont Health Technol Assess Ser* 2015; 15: 1–29.

[2] Broadley MM, Bishop T, White MJ, et al. The relationship between attentional bias to food and disordered eating in females with type 1 diabetes. *Appetite* 2019; 140: 269–276.

[3] de Groot M, Golden SH, Wagner J. Psychological conditions in adults with diabetes. *Am Psychol* 2016; 71: 552–562.

[4] Bernstein CM, Stockwell MS, Gallagher MP, et al. Mental health issues in adolescents and young adults with type 1 diabetes: prevalence and impact on glycemic control. *Clin Pediatr (Phila)* 2013; 52: 10–15.

[5] Toni G, Berioli MG, Cerquiglini L, et al. Eating Disorders and Disordered Eating Symptoms in Adolescents with Type 1 Diabetes. *Nutrients*; 9. Epub ahead of print 19 August 2017. DOI: 10.3390/nu9080906.

[6] Staite E, Zaremba N, Macdonald P, et al. 'Diabulima' through the lens of social media: a qualitative review and analysis of online blogs by people with Type 1 diabetes mellitus and eating disorders. *Diabet Med* 2018; 35: 1329–1336.

[7] Goebel-Fabbri AE, Fikkan J, Franko DL, et al. Insulin restriction and associated morbidity and mortality in women with type 1 diabetes. *Diabetes Care* 2008; 31: 415–419.

[8] Jones JM, Lawson ML, Daneman D, et al. Eating disorders in adolescent females with and without type 1 diabetes: cross sectional study. *BMJ* 2000; 320: 1563–1566.

[9] Treasure J, Kan C, Stephenson L, et al. Developing a theoretical maintenance model for disordered eating in Type 1 diabetes. *Diabet Med* 2015; 32: 1541–1545.

[10] Feltbower RG, Bodansky HJ, Patterson CC, et al. Acute complications and drug misuse are important causes of death for children and young adults with type 1 diabetes: results from

the Yorkshire Register of diabetes in children and young adults. *Diabetes Care* 2008; 31: 922–926.

[11] Reinehr T, Dieris B, Galler A, et al. Worse Metabolic Control and Dynamics of Weight Status in Adolescent Girls Point to Eating Disorders in the First Years after Manifestation of Type 1 Diabetes Mellitus: Findings from the Diabetes Patienten Verlaufsdokumentation Registry. *J Pediatr* 2019; 207: 205-212.e5.

[12] Clery P, Stahl D, Ismail K, et al. Systematic review and meta-analysis of the efficacy of interventions for people with Type 1 diabetes mellitus and disordered eating. *Diabet Med* 2017; 34: 1667–1675.

[13] Goebel-Fabbri AE, Fikkan J, Connell A, et al. Identification and treatment of eating disorders in women with type 1 diabetes mellitus. *Treat Endocrinol* 2002; 1: 155–162.

[14] De Paoli T, Rogers PJ. Disordered eating and insulin restriction in type 1 diabetes: A systematic review and testable model. *Eat Disord* 2018; 26: 343–360.

[15] Schulte EM, Avena NM, Gearhardt AN. Which Foods May Be Addictive? The Roles of Processing, Fat Content, and Glycemic Load. *PLOS ONE* 2015; 10: e0117959.

[16] Lennerz BS, Alsop DC, Holsen LM, et al. Effects of dietary glycemic index on brain regions related to reward and craving in men. *Am J Clin Nutr* 2013; 98: 641–647.

[17] Merwin RM, Dmitrieva NO, Honeycutt LK, et al. Momentary Predictors of Insulin Restriction Among Adults With Type 1 Diabetes and Eating Disorder Symptomatology. *Diabetes Care* 2015; 38: 2025–2032.

[18] Moskovich AA, Dmitrieva NO, Babyak MA, et al. Real-time predictors and consequences of binge eating among adults with type 1 diabetes. *J Eat Disord* 2019; 7: 7.

[19] Merwin RM, Moskovich AA, Honeycutt LK, et al. Time of Day When Type 1 Diabetes Patients With Eating Disorder Symptoms Most Commonly Restrict Insulin. *Psychosom Med* 2018; 80: 222–229.

[20] Markowitz JT, Alleyn CA, Phillips R, et al. Disordered eating behaviors in youth with type 1 diabetes: prospective pilot assessment following initiation of insulin pump therapy. *Diabetes Technol Ther* 2013; 15: 428–433.

[21] Polonsky WH, Fisher L, Earles J, et al. Assessing psychosocial distress in diabetes: development of the diabetes distress scale. *Diabetes Care* 2005; 28: 626–631.

[22] Gearhardt AN, Corbin WR, Brownell KD. Preliminary validation of the Yale Food Addiction Scale. *Appetite* 2009; 52: 430–436.

[23] Pleus S, Schoemaker M, Morgenstern K, et al. Rate-of-Change Dependence of the Performance of Two CGM Systems During Induced Glucose Swings. *J Diabetes Sci Technol* 2015; 9: 801–807.

[24] Hill NR, Oliver NS, Choudhary P, et al. Normal reference range for mean tissue glucose and glycemic variability derived from continuous glucose monitoring for subjects without diabetes in different ethnic groups. *Diabetes Technol Ther* 2011; 13: 921–928.

[25] Snyder LL, Truong YK-N, Law JR. Evaluating Substance Use and Insulin Misuse in Adolescents With Type 1 Diabetes. *Diabetes Educ* 2016; 42: 529–537.

[26] Danne T, Nimri R, Battelino T, et al. International Consensus on Use of Continuous Glucose Monitoring. *Diabetes Care* 2017; 40: 1631–1640.

[27] Merwin RM, Moskovich AA, Dmitrieva NO, et al. Disinhibited eating and weight-related insulin mismanagement among individuals with type 1 diabetes. *Appetite* 2014; 81: 123–130.

[28] Eisenberg Colman MH, Quick VM, Lipsky LM, et al. Disordered Eating Behaviors Are Not Increased by an Intervention to Improve Diet Quality but Are Associated With Poorer Glycemic Control Among Youth With Type 1 Diabetes. *Diabetes Care* 2018; 41: 869–875.

[29] Due-Christensen M, Zoffmann V, Willaing I, et al. The Process of Adaptation Following a New Diagnosis of Type 1 Diabetes in Adulthood: A Meta-Synthesis. *Qual Health Res* 2018; 28: 245–258.

[30] Runge AS, Kennedy L, Brown AS, et al. Does Time-in-Range Matter? Perspectives From People With Diabetes on the Success of Current Therapies and the Drivers of Improved Outcomes. *Clin Diabetes* 2018; 36: 112–119.

Table 1: Baseline characteristics

Characteristic	Type 1 diabetes with disordered eating N = 13 Median [Interquartile range] or n (%)	Type 1 diabetes N = 10 Median [Interquartile range] or n (%)
Age, years	25 [23, 33]	29.5 [26, 36]
Women, n (%)	13 (100%)	10 (100%)
Ethnicity, n (%)		
White	13 (100%)	8 (80%)
Black	--	--
Asian	--	2 (20%)
Others	--	--
Body Mass Index (kg/m^2)	25.2 [22.7, 27]	27.35 [24.6, 30.6]
Cigarette Smoking (Current or Past)	8 (61.5%)	5 (50%)
Alcohol Consumption	12 (92.3%)	9 (90%)
Recreational Drug Use	5 (38.5%)	1 (10%)
Duration of diabetes (years)	13 (10,19)	10 (5, 20)
Type of therapy, n (%)		
Multiple daily injections	8 (62%)	5 (50%)
Continuous subcutaneous insulin infusion	5 (38%)	5 (50%)
Total daily dose of Insulin (units/day)	41.3 [16.5, 54.8]	30.4 [29.6, 38.3]
Severe hypoglycaemia in the past 12 months, n (%)		
0	11 (84.6%)	10 (100%)
1	1 (7.7%)	--
2	1 (7.7%)	--
Diabetic ketoacidosis in the past 12 months, n (%)		
0	9 (69.2%)	9 (90%)
1	1 (7.7%)	1 (10%)
2	2 (15.4%)	--
5	1 (7.7%)	--
Diabetes eating Problem Survey – Revised, total score	36 (31, 44)	21 (8, 22)

Table 2: Comparison of HbA1c and questionnaire scores between groups.

Characteristic	Type 1 diabetes with disordered eating **N = 13** **Median [Interquartile range]**	Type 1 diabetes **N = 10** **Median [Interquartile range]**	P-value
HbA1c (mmol/mol)	72 (68, 94)	57 (50, 65)	**0.004**
HbA1c (%)	8.7 (8.4, 10.8)	7.35 (6.7, 8.1)	
Diabetes distress score17, total score	3.5 (2.9, 3.9)	2.6 (2.3, 2.9)	**0.012**
Patient Health Questionnaire-9, total score	15 (8, 18)	7.5 (3, 9)	**0.042**
Yale Food Addiction Scale, Total score	3 (1, 10)	0.5 (0, 3)	0.077
Technology Questionnaire			
Start of Study	42 (38, 44)	44 (39, 47)	0.131
End of Study	43 (41, 45)	43 (41, 46)	0.693

Table 3: Comparison of self-monitored capillary glucose (CG) and continuous glucose monitoring (CGM) derived sensor glucose (SG) parameters across type 1 diabetes with and without disordered eating.

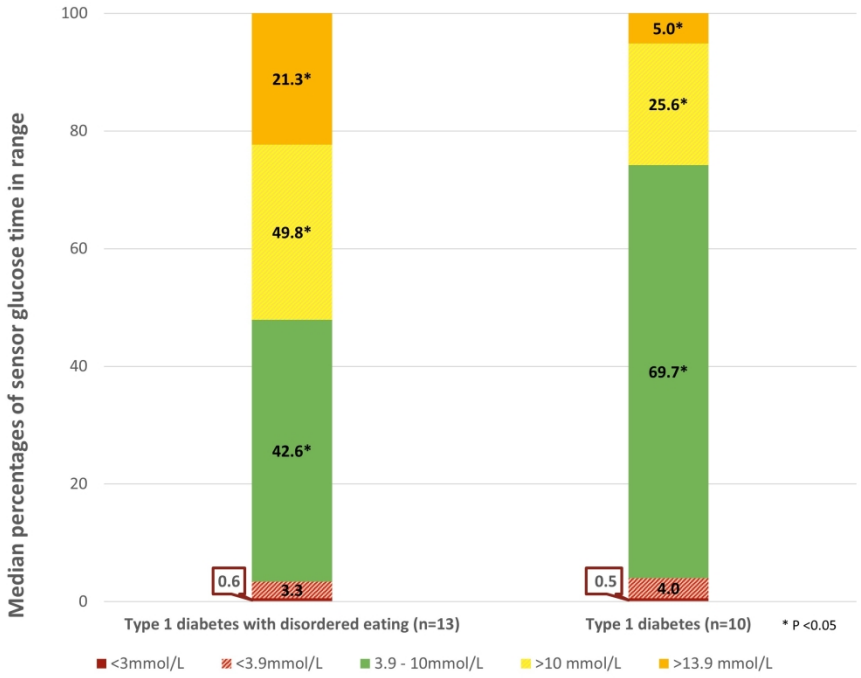
Parameter	Type 1 diabetes with disordered eating (n=13) Median [Interquartile range]	Type 1 diabetes (n=10) Median [Interquartile	P value
Self-monitored capillary glucose (CG)			
Days of CG recording, n	6 (5.7, 6.8)	5.95 (5.2, 7.1)	0.648
Mean CG readings/day, n	4.5 [2.1, 5.3]	6.3 [4.2, 8.4]	**0.030**
Mean CG, mmol/L	9.7 [9.3, 14.9]	8.8 [7.5, 10.1]	0.136
Standard deviation of CG, mmol/L	4.7 [4.5, 6.1]	3 [2.8, 3.2]	**0.018**
Coefficient of variation of CG, %	42.2 [34, 56]	37.8 [33, 44]	1.000
Continuous glucose monitoring (CGM)			
Number of CGM readings used (n)	1589 [1318, 1774]	1883[1579, 1935]	**0.049**
Days of CGM tracing	5.5 [4.6, 6.2]	6.5 [5.5, 6.7]	**0.049**
Mean sensor glucose, mmol/L	10.3 [9.6, 14.9]	8.4 [7.4, 10.6]	**0.036**
Standard deviation, mmol/L	4 [3.4, 4.7]	2.9 [2.7, 3.6]	0.077
Coefficient of Variation (%)	35 [29, 44]	37.3 [31, 40]	1.000
Time in Range (3.9-10 mmol/L)	42.6 [16.1, 56.2]	69.7 [44.6, 76.7]	**0.017**
Time Below Range (< 3.9	3.3 [0, 7.1]	4.0 [1.8, 6.0]	0.522
Time Below Range (<3 mmol/L)	0.6 [0.0, 2.9]	0.5 [0.1, 1.0]	0.927
Time Above Range (>10 mmol/L)	49.8 [38.4, 83.9]	25.6 [19.5, 54.8]	**0.036**
Time Above Range (>13.9	21.3 [17.4, 45.4]	5 [2.2, 11.9]	**0.015**
CGM trends expressed as a percentage of all trends			
Total trends (n)	1580 [1226, 1679]	1767 [1511, 1867]	**0.026**
Rising Trends (%)			
(>0.05 to 0.11 mmol/L/min)	8.4 [7.3, 9.4]	7.9 [6.9, 9.6]	0.852
(>0.11 to 0.17 mmol/L/min)	2.5 [1.9, 3.3]	2.1 [1.5, 2.8]	0.352
(>0.17 to 0.22 mmol/L/min)	1.0 [0.4, 1.3]	0.3 [0, 0.7]	**0.022**
(>0.22 mmol/L/min)	0.3 [0.1, 0.8]	0 [0, 0.3]	**0.024**
Stable Trends (%)			
≥-0.056 to ≤0.056 mmol/L/min	75.8 [70.2, 82.5]	82.2 [74.8, 83.7]	0.208
Falling Trends (%)			
(<-0.05 to -0.11 mmol/L/min)	7.8 [6.3, 11]	7.3 [5.4, 9.4]	0.457
(<-0.11 to -0.17 mmol/L/min)	2 [1.1, 3]	1.2 [0.8, 1.9]	0.239
(<-0.17 to -0.22 mmol/L/min)	0.4 [0.2, 0.7]	0.3 [0, 0.4]	0.384
(<-0.22 mmol/L/min)	0.2 [0, 0.6]	0 [0, 0.1]	0.061

Table 4: Comparison of the entries on diabetes diary across type 1 diabetes with and without disordered eating

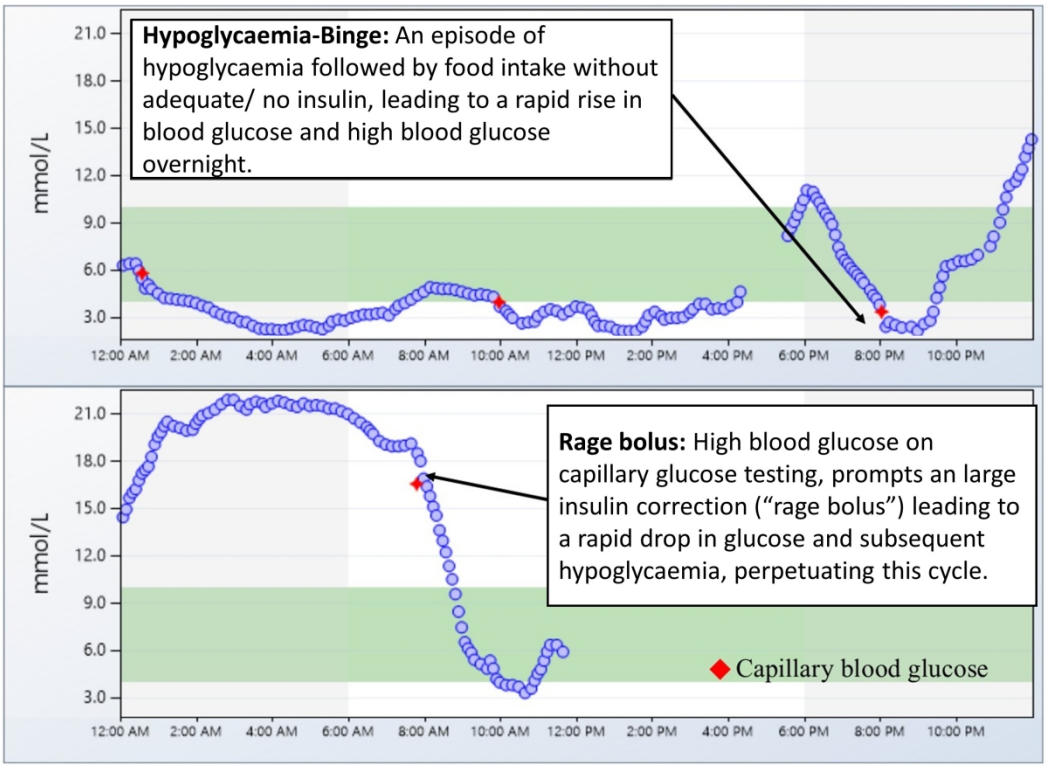
Parameter	Type 1 diabetes with disordered eating (n=13) Median	Type 1 diabetes (n=10) Median	P-value
Diabetes diary use (days)	6 (5.7, 6.8)	5.95 (5.2, 7.1)	0.648
Diabetes diary entries per day (n/day)	5.5 (1.8, 7.4)	8.3 (5.2, 13.6)	**0.030**
Diabetes self-care related entries, total (n)	96 (67, 107)	101.5 (73, 149)	0.483
Blood glucose awareness related enries, total (n)	4 (3, 7)	2.5 (2, 5)	0.343
Physical symptoms related entries, total (n)	13 (10, 22)	8.5 (2, 17)	0.131
Disordered eating behaviour related entries, total (n)	4 (0, 8)	2 (0, 5)	0.284
Activity related entries, total (n)	6 (2, 10)	18 (6, 21)	**0.036**
Emotions and feelings related entries			
Positive affect, (n)	4 (0, 6)	2 (1, 13)	0.605
Negative affect, (n)	9 (6, 13)	5.5 (3, 11)	0.186

Figure 1: Comparison of the median percentages (will not add up to 100%) of time in range of sensor glucose between people with and without disordered eating and type 1 diabetes (bar graph adjusted proportionately to represent 100%)

Figure 2: An example of food intake without adequate insulin leading to a rapid rise in blood glucose with overnight hyperglycaemia. A large bolus taken at high blood glucose ("rage bolus") results in rapid fall of blood glucose and subsequent hypoglycaemia, perpetuating this cycle.



dme_14446_f1.jpg



dme_14446_f2.jpg