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Systematic review and meta-analysis of the efficacy of interventions for people with Type 1 diabetes mellitus and disordered eating

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What's new?

- This is the first systematic review and meta-analysis to identify interventions available for people with Type 1 diabetes mellitus and co-occurring disordered eating, and to examine intervention content and efficacy.

- Existing interventions do not improve glycaemic control and have little effect on eating psychopathology.
- We suggest that an intensive intervention such as inpatient therapy, with a joint focus on disordered eating and diabetes management, is needed.
- Our data could be used in conjunction with a theoretical model to tailor an intervention for this patient group.

Abstract

Aim To examine the types of interventions currently available for people with Type 1 diabetes mellitus and their effectiveness.

Background The prevalence of disordered eating in people with Type 1 diabetes mellitus is twice that in their counterparts without diabetes, and is associated with worse biomedical outcomes and greater mortality.

Methods Medline, Embase, PsycINFO, the Cochrane Library, PubMed and OpenGrey databases were searched up to August 2016 to identify studies on interventions in people with Type 1 diabetes-associated disordered eating. For the systematic review, intervention components were identified and their effectiveness was examined. For the meta-analysis, the pooled effect sizes of glycaemic control (HbA_{1c}) between pre- and post-treatment in treatment and comparison groups were calculated using a random effects model.

Results Of 91 abstracts reviewed, six studies met the inclusion criteria, of which three had appropriate data for the meta-analysis (n = 118). The pooled effect size was –0.21 95% CI (–0.58 to 0.16; where negative values represent an improvement in HbA_{1c} levels), indicating no statistically significant improvement in the treatment group compared with comparison group. Inpatient therapy appeared to be the most effective treatment, and this had multiple components including cognitive behavioural therapy, psychoeducation and family therapy.

Conclusion Limited or no improvement in glycaemic control and disordered eating symptoms was observed in people with Type 1 diabetes-associated disordered eating who were receiving currently available interventions. The present review suggests that developing an intensive intervention with a joint focus on both disordered eating and diabetes management is needed for this complex patient group.

Introduction

The prevalence of eating problems in people with Type 1 diabetes mellitus is twice that in their counterparts without diabetes [1–5]. Disordered eating behaviour in Type 1 diabetes is most commonly, but not exclusively, associated with bingeing and purging patterns [5,6]. A compensatory behaviour specific to Type 1 diabetes involves reducing or omitting insulin doses, whereby hyperglycaemia is induced to lose glucose calories through the urine [7]. This is the most common weight loss method used by adolescents with Type 1 diabetes [5,8,9], being termed 'diabulimia' [6]. Disordered eating has more severe consequences for people with diabetes [8]. Type 1 diabetes comorbid with eating disorders is clearly associated with higher HbA_{1c} values [10]. In the short term, the consequences of Type 1 diabetes-associated disordered eating include more frequent episodes of diabetic ketoacidosis [11] and hospitalizations [12], whilst long-term complications involve the onset of diabetic microvascular complications at not only a much earlier than expected age [13], but also after a shorter duration of disease. Most seriously, the comorbidity carries more than a threefold risk of mortality [14,15].

The theoretical model proposed by Treasure *et al.* [16] is the latest attempt to address predisposing and maintenance risk factors for disordered eating in Type 1 diabetes. It postulates that the salience given to weight and eating in diabetes management interacts with a perfectionist coping style, leading to an unhelpful focus on food [17–19] and body weight, exacerbating body shape concerns [16]. Further, the goal of perfect glycaemic control can be elusive and frustrating [16]. This may explain the lower self- and body-esteem in this group [20,21]. The link between insulin treatment and changes in weight offers the possibility of a unique way of controlling weight [22]. This leads to wide blood glucose fluctuations (hypo- and hyperglycaemia), which may cause neuroadaptive changes that pre-dispose to an addictive pattern of loss of control over eating to develop [19,23,24]. Lastly, family frictions around the transition to independence can be stressful and can exacerbate psychological problems in adolescents with Type 1 diabetes [25]. Family support may be crucial at this time [26,27], but it remains unclear what the optimum way to transition from family to independent management might be.

We conducted a systematic review to explore the current evidence base with regard to the effectiveness of interventions for this complex patient group with Type 1 diabetes and eating disorders, and to identify the effective components of treatment. In addition, we conducted a meta-analysis to examine the effect of interventions on glycaemic control, namely HbA_{1c} concentration.

Methods

Data sources and search strategies

Medline, Embase, PsycINFO, the Cochrane Library, PubMed and OpenGrey databases were searched for all years up to and including August 2016. The search strategy included three main terms: 'Type 1 diabetes', 'psychotherapeutic' or 'psychoeducational interventions', and 'disordered eating'. Synonyms of these were searched to encompass different disciplines and all ages. The full electronic search strategy is shown in Table S1.

Study selection

Articles retrieved from the search were screened by the first author (P.C.) to identify relevant titles mentioning eating disorders or Type 1 diabetes. Duplicates were removed using a citation manager. Titles and abstracts of potentially eligible articles were independently reviewed by P.C. and a second researcher (C.K.), to determine which fulfilled the eligibility criteria. Any discrepancies were discussed and agreed upon. Articles where a decision could not be made on the basis of reading the title or abstract were read fully. The reference sections of retrieved articles were hand-searched for additional references. A third researcher (J.T.) was consulted at this stage to finalize studies eligible for the systematic review and meta-analysis.

Criteria for inclusion

Studies were included for the systematic review and meta-analysis if they assessed the outcome of treatment interventions for people with comorbid Type 1 diabetes and disordered eating. Studies in which components were psychological or educational, not pharmacological, were eligible for inclusion. Participants of any age and any sex, with a diagnosis of Type 1 diabetes, and either disordered eating, insulin omission or a clinical eating disorder were

considered. All types of studies were eligible for systematic review, but only quasi-experimental or randomized controlled trials (RCTs) with comparison and treatment group pre- and post-intervention HbA_{1c} data available were included in the meta-analysis.

Quality assessment

The quality of reporting of interventions in studies was assessed using the 'template for intervention description and replication' (TIDieR). This is a 12-item checklist that was primarily developed to encourage authors to describe their interventions in sufficient detail to allow replication [28]. The quality of individual studies was examined using the 22 items of the STROBE checklist [29]. A study was considered of high quality if the statistical methods, variables, data and sources of bias were explicit, and the results were comprehensive such that all data were explained and presented.

Data extraction

From each study we extracted: author names; publication year; city and country; study design; sample size; age; sex; treatment components of the intervention; treatment frequency and length; times of outcomes and HbA_{1c}. The authors of three studies [30–32] were contacted to ask for additional raw data. One author responded but could not provide the data required. The TIDieR checklist [28] was used to describe the reporting of the intervention.

Statistical analysis

For the meta-analysis, we compared HbA_{1c} between treatment and comparison groups where mean and SD data were available at the same time point for the two groups. Meta-analyses were conducted for two time points because timings of when HbA_{1c} outcomes were measured varied between studies. To uniformly compare the studies, we used the following time points:

(1) baseline and first follow-up post-intervention and (2) baseline and second follow-up post intervention (Table 1 [31,36,37]).

The effect sizes and standard errors of the studies were pooled using random effects models [33]. A random effects meta-analysis model assumes that, in addition to the presence of a random sampling error, variability of mean effect sizes is also caused by differences in the effect between studies attributable to differences in study populations and procedures (between-study heterogeneity). The effect size estimate in a random effects model describes therefore not one common effect but the average of the effects, and the confidence interval describes the degree of heterogeneity [33]. If heterogeneity is present, random effects models result in estimates with wider confidence intervals than fixed effects models, but were more realistic in the present meta-analysis because of the variety of case mix and settings among studies [34]; the random effects model was chosen because of the variety of comparison groups used.

The Cohen's *d* approach was used to calculate the effect size. We standardized the mean difference in the HbA_{1c} between treatment and comparison groups by calculating the difference between the two mean changes (difference of post- and pre-treatment score) divided by the pooled SD of the difference scores, assuming a correlation of 0.5 between pre- and post-treatment scores. A result of $d = 0.3$, 0.5 and 0.8 represents small, medium and large effect sizes, respectively. Homogeneity of study outcomes was assessed to determine the degree of between-study heterogeneity models using the chi-squared test (Q), and the sample size independent inconsistency measure I^2. The small sample size did not allow assessment of publication bias.

Results

Study selection

The literature search produced 891 articles, of which 134 mentioned disordered eating or Type 1 diabetes in their title. Duplicates were removed, leaving 91 potentially eligible article titles and abstracts to be screened using the inclusion and exclusion criteria. This yielded 17 for full-text assessment. One additional article was found after manual searching of the reference lists. Six articles fulfilled the criteria for the systematic review and three for the meta-analysis (Fig. 1). Two of the six articles for systematic review [30,32] were excluded from the meta-analysis because they had insufficient comparison group data. The 2002 study by Takii *et al.* [35] was excluded because it was unclear whether it reported data that were later included in their 2003 study [31].

Characteristics of studies included

Six studies were included in the systematic review [30–32,35–37] comprising 205 participants, all of whom were female. Extracted data are summarized in Table 2 [30–32,35–37]. One of the studies included was an RCT [36], four were quasi-experimental studies [30,31,35,37] and one was a cohort study that did not have a comparison group [32]. All studies included in the meta-analysis were either an RCT [36] or had a quasi-experimental design [31,37]. Types of comparison groups were 'treatment as usual' [36], waiting list [37] or an outpatient group (compared with the inpatient group as the treatment group) [31]. Takii *et al*. [31] selected patients for the outpatient (comparison) or inpatient (treatment) group according to previously attended therapy, meaning the participants were not of similar severity in treatment vs comparison group. Intervention components identified from the studies were inpatient therapy [30–32,35], psychoeducation [36,37], 'multidisciplinary'

approaches [32], cognitive behavioural therapy [30–32,35], and family involvement [31,32,35,36].

Quality of studies

Using TIDieR guidelines, all studies did relatively well at describing the rationale of the intervention, but not all described the intervention in detail (Table S2). Approaches such as 'non-dieting', 'non-deprivational' or 'feminist' are not specific and lack examples [32]. Only one study reported detailed descriptions of the therapist's tasks [31]. The interventions differed as to whether they had a collaborative approach between the two disciplines in terms of the skills of those delivering the intervention and the processes used. There appeared to be an emphasis on eating without rules, which is somewhat of a divergent approach to diabetes care and this may be because most of them were set within eating disorder settings. Both studies by Takii *et al.* [31,35] had differing follow-up periods for the treatment and comparison groups (36 and 24 months, respectively), and did not provide immediate post-intervention data for the comparison group. Taking all STROBE criteria into consideration, two studies were of poor to fair quality [30,35], whilst four were of fair quality [31,32,36,37]. The overall risk of bias was medium to high.

Effect of treatment on glycaemic control

The six studies included in the systematic review report a wide range of HbA_{1c} values at both baseline and post-intervention follow-ups. Data vary substantially across studies, with baseline mean ± SD values ranging from 65 ± 9 mmol/mol (8.1 ± 0.8%) to 116 ± 32 mmol/mol (12.8 ± 2.9%) [31,37]. Post-intervention values range from 64 ± 20 mmol/mol (8.0 ± 1.8%), to 119 ± 27 mmol/mol (13 ± 2.5%) [31,35]. Three of the six studies were included in the meta-analysis, and the effect sizes calculated show an improvement in glycaemic

control in the treatment group in comparison to the control group in all three studies. Studies included in the meta-analysis comprised 118 participants [31,36,37]. The effect sizes of between groups HbA_{1c} outcomes, comparing treatment to comparison groups, range from –0.1 (95% CI –1.18 to 0.98) [37] to –1.14 (95% CI –2.13 to –0.15; Table 1) [31], where negative values represent an improvement in HbA_{1c} concentration.

Using a random effects model, the meta-analysis (n=118), revealed a small, insignificant pooled estimate of the mean standardized effect sizes at both first [d=–0.21 (–0.58 to 0.16); P=0.266 (Fig. 2a)] and second time point [d=–0.40 (–0.99 to 0.20); P=0.194 (Fig. 2b)]. Little (Q=0.99, I^2=0%) and moderate (Q=0.1, I^2=43%) between-group heterogeneity was observed for the meta-analyses respectively.

Effect of treatment on eating disorder symptom outcomes

Significant improvement in eating disorder symptoms in the treatment group compared with the control group post-intervention, as measured by the Eating Disorder Inventory (EDI) [38], were found across four studies. A reduction in EDI symptom score signifies improvement. One study used multivariate analyses to look at the effect of time on eating disorder attitudes [36]. They reported a statistically significant time effect for the treatment group, but not for the comparison group in two of the three subscales of EDI [36], indicating an improvement in attitudes that occurred only in the treatment group over time. Another study analysed the time effect, as well as interaction effect between the treatment and comparison groups, but found no statistically significant time effect or interaction effect between groups, which meant there was no improvement in eating disorder attitudes over time, irrespective of group [37]. Another study reported a statistically significant reduction in global EDI scores in the treatment group compared with the control group [31]. A fourth

study reported statistically significant reductions on each of the five EDI scales [32]. The final study reported a statistically significant reduction in EDI scores at 36 months' follow-up compared with baseline [35].

Insulin omission

Some studies used insulin omission as an outcome measure. One study reported a statistically significant change in the percentage of participants in the inpatient treatment group, compared with the comparison group, who omitted insulin at first visit compared with follow-up [31]. Another study reported a reduction in the number of days insulin was omitted over 28 days in the intervention group compared with the 'treatment as usual' group, but the reduction was not statistically significant [36]. The third study found no statistically significant change in insulin omission between the treatment and waiting list control groups at the post-intervention time point compared with baseline [37].

With no common eating disorder symptom measurement instrument across all studies, a meta-analysis could not be performed on this outcome.

Discussion

The aim of the present review was to identify the components of interventions for those with comorbid Type 1 diabetes and disordered eating, and to examine their effectiveness, in terms of improved glycaemic management and eating disorder symptoms. Six studies were included in this review and our results suggest that there were insignificant improvements in glycaemic control post-intervention in the treatment groups compared with controls, while some improvement in eating disorder symptoms and reduction in insulin omission was

reported in the treatment groups in a few studies [31,32,36]. One study [30] showed no improvements across any of the variables.

The present findings should, however, be interpreted in the context of the quality of studies involved. Some studies carried a higher risk of bias than others, which could influence the interpretation of the results of the present review. Most of the six studies were of fair quality, and some were medium level or had unknown risks of bias, using the STROBE criteria. The RCT [36] had the lowest level risk of bias.

The intensity and complexity of treatment is considered to have an impact on efficacy; inpatient therapy appears to be more effective than outpatient therapy. The average length of stay for inpatient therapy reflects the potential intensity of this treatment. Compared with outpatient therapy, where an intervention took place weekly for 6 weeks, components of inpatient therapy occurred daily for 3–4 months. Inpatient therapy was associated with a moderate change in HbA_{1c} outcomes [31,32], whereas only small effects were found with outpatient psychoeducational interventions. The psychoeducation studies [36,37] also showed a lesser difference in eating disorder symptom reduction compared with the inpatient therapy studies [31,32]. The duration of treatment could therefore have an influence on the intensity and hence effectiveness of treatment. Other reviews have also noted that 'more intensive treatment approaches' than those for uncomplicated eating disorders may be needed to treat eating disorder-associated Type 1 diabetes [39,40].

Inpatient treatment is a complex intervention with multiple components such as psychoeducation, cognitive behavioural therapy, and family work. It also involves frequent nurse supervision, which could potentially overcome barriers of patient disengagement, patients' reporting of incorrect HbA_{1c} values, or dishonesty about insulin administration, that have been observed in outpatient eating disorder treatment [41].

Interventions with family support/involvement components may have a role in reducing eating disorder symptoms as well. Olmsted *et al*. [36] added a 'family component' to their 6-week psychoeducation programme, whilst Alloway *et al*. [37] gave psychoeducation without additional family involvement components. The former programme resulted in a larger change in symptoms [36] than the latter [37]. This has the potential to validate the role of family functioning in the maintenance model described by Treasure *et al*. [16].

Together, this suggests the need for a joint or tailored 'diabetes-associated eating disorder' intervention, whereby the specific needs of each illness are addressed, as well as a focus being given to unique features of the two illnesses being concurrent, such as insulin administration linked to carbohydrate balance. This may mean that the goals and processes of the diabetes and eating disorder teams may need to be fused. For example the diabetes team may need to join up with a slow stepwise programme of increasing insulin administration during which the individual is taught skills for managing the negative emotions elicited by the meaning of diabetes and insulin for them. Meanwhile, the eating disorder team may need to join up with the form of rule-bound eating and adjustments to exercise which are needed as part of good diabetes care.

Whilst these data support what has been argued in the literature for years, evidence previously has been anecdotal, or based only on clinical experience or small sample sizes [41]. This review has strengths in its systematic reporting and analysis of collated data allowing a larger sample size, and its presentation of findings in the larger context of the disordered eating and comorbid Type 1 diabetes complication.

The major limitation of the present review was the small number of studies available. For the most part, the components of the interventions are also poorly described, and only one RCT was performed. In addition, the quality of individual studies was poor to fair, introducing a medium to high risk of bias. Two studies did not have comparison group data [30,32]. A further two studies did not have raw data available and used differing time points for post-intervention follow-up across their treatment and comparison groups [31,35]. One study followed up individuals for 1 month after a 6-week intervention, limiting the value of HbA_{1c} (a 3-month average glycaemic level) as an outcome measure [37]. Another limitation is that the included studies did not always specify the type of eating disorder. This is important as the goals for treatment differ between anorexia nervosa and bulimia nervosa. With more data, a future point of research could be to examine interaction effects of eating disorder type or severity. Additionally, the individuals' attendance to therapy throughout the study was not addressed; however, whilst attrition rate can be reported, measuring active engagement in therapy is difficult. This introduces a limitation that could have influenced the effectiveness reported in the studies.

The included studies also used differing comparison groups; one used a waiting list control [37], others used 'treatment as usual' [30,31,35,36]. This also raises concerns with regard to the degree to which 'treatment as usual' is standardized across studies [42]. Finally, the use

of different instruments to measure eating disorder symptoms meant a meta-analysis could not be performed on this outcome.

Lastly, it should be noted that TIDieR criteria revealed intervention reporting quality to be thorough in only one study [31]. Good reporting increases the validity of findings and the conviction with which the efficacy of interventions can be reported. Not only does this imply that this study [31] may be of more use for future intervention development than others, but it also emphasizes wherein the weaknesses lie in the existing studies in this area of research. We therefore suggest that targeting intervention reporting and describing in the future could provide more insight into the specifics of a successful intervention.

In conclusion, people with Type 1 diabetes-associated eating disorders have a poorer response of their eating disorder symptoms to conventional eating disorder management, and little improvement in their diabetic control. It appears that people with Type 1 diabetes-associated eating disorders require a different form and intensity of intervention. The development of interventions for this group might follow the principles of the Medical Research Council guidelines for developing complex interventions [43]. The first step in this type of approach has been undertaken by the development of a theoretical model [16]. This could be used to tailor conventional eating disorders and diabetes interventions, especially to include concurrent diabetes and eating disorder components.

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Competing interests

None declared.

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Supporting information

Additional Supporting Information may be found in the online version of this article:

Table S1 Search Terms from a full OVID electronic search.

Table S2 Assessing reporting quality of interventions: the TIDieR checklist for each study eligible for systematic review.

FIGURE 1 PRISMA flow chart of information collection for systematic review and meta-analysis.

FIGURE 2 (a) Forest plot presenting the treatment effect results of meta-analysis: treatment effect sizes for HbA_{1c} of first follow-up post-intervention. (b) Forest plot presenting the treatment effect results of meta-analysis: treatment effect sizes for HbA_{1c} of second follow-up post-intervention. ES, effect size.

		Mean ± SD HbA1c concentration, mmol/mol (%)				
		Pre-treatment,	**Post-intervention**	**1-month follow-up**	**6-month follow-up**	**12-month follow-up**
Alloway *et al.*, 2001 [37]	Comparison group	65 ± 9 (8.1 ± 0.8)	67 ± 10 (8.3 ± 0.9)	67 ± 7 (8.3 ± 0.6)	N/A	N/A
	Treatment group	66 ± 13 (8.2 ± 1.2)	67 ± 12 (8.3 ± 1.1)	66 ± 13 (8.2 ± 1.2)	N/A	N/A
	Effect size (SE)		–0.10 (0.540)	–0.19 (0.541)	N/A	N/A
Olmsted *et al*., 2002 [36]	Comparison group	75 ± 13 (9.0 ± 1.2)	76 ± 17 (9.1 ± 1.6)	N/A	78 ± 16 (9.3 ± 1.5)	N/A
	Treatment group	77 ± 17 (9.2 ± 1.6)	76 ± 17 (9.1 ± 1.6)	N/A	78 ± 19 (9.3 ± 1.7)	N/A
	Effect size (SE)		–0.13 (0.221)	N/A	–0.13 (0.221)	N/A
Takii *et al*., 2003 [31]	Comparison group	116 ± 32 (12.8 ± 2.9)	N/A	N/A	112 ± 24 (12.4 ± 2.2†)	119 ± 27 (13.0 ± 2.5†)
	Treatment group	110 ± 19 (12.2 ± 1.7)	N/A	N/A	89 ± 23 (10.3* ± 2.1†)	81 ± 26 (9.6* ± 2.4†)
	Effect size (SE)		N/A	N/A	–0.65 (0.471)	–1.14 (0.495)

Table 1 HbA_{1c} outcome data and effect sizes (calculated between pre-treatment and follow-ups) for each study included in the meta-analysis

N/A, data not supplied in study.

Effect size is calculated for each follow-up time point, using the pre-treatment baseline data.

*Significant (P<0.05). †SD was calculated using SE value given in paper.

Table 2 Characteristics of studies included in the systematic review

		Alloway *et al.* 2001 [37]	**Olmsted *et al.*, 2002 [36]**	**Takii *et al.*, 2003 [31]**	**Takii *et al.*, 2002 [35]**	**Dickens *et al.*, 2014 [32]**	**Custal *et al.*, 2014 [30]**
Study design		**Quasi-experimental**	**RCT**	**Quasi-experimental**	**Quasi-experimental**	**Cohort study**	**Quasi-experimental**
Sample size	Comparison	6	35	10	9	N/A	20
	Treatment	8	50	9	9	29	20
	Total	14	85	19	18	29	40
Women (%)		100	100	100	100	100	100
Age ± SD	Comparison	31.0 ± 10.3	16 ± 2.0	21.3 ± 4.0	N/S	25.6 ± 9.0	28.0 ± 8.4
	Treatment	32.5 ± 9.3		23.8 ± 5.0			25.3 ± 8.0
City, Country		Edmonton, Canada	Toronto, Canada	Kyushu, Japan	Kyushu, Japan	Western USA	Barcelona, Spain
Treatment setting		OUT	OUT	IN	IN	OUT	OUT-CBT

						and IN	and IN
Intervention components reported in each study	IN			☐	☐	☐	☐
	Psychoeducation	☐	☐				
	MULTI					☐	
	CBT			☐	☐	☐	☐
	FAM		☐	☐	☐	☐	
Treatment frequency		Weekly	Weekly	Daily	Daily	Daily	CBT: N/S IN: Daily
Mean length of treatment		6 weeks	6 weeks	112.3 days	112.3 days	52.9 days	CBT: 16 sessions IN: 3 months
Follow-up period		1 month	6 months	3 years	3 years	Post-intervention	Post-intervention
Outcome measures		HbA_{1c}; self-care inventory; EAT; EDI-3; insulin omission frequency	HbA_{1c}; objective binge-eating episodes; EDI; EDE; insulin omission frequency	HbA_{1c}; EDI; insulin omission frequency	HbA_{1c}; EDI; insulin omission frequency	HbA_{1c}; EDI-3;	Frequency of binges/ vomiting/laxatives/diuretics; EDI-2

CBT, cognitive/behavioural therapy; EAT, Eating Attitudes Test [44]; EDE, Eating Disorder Examinations [45]; EDI, Eating Disorder Inventory [38]; FAM, family involvement; IN, inpatient therapy; MULTI, multidisciplinary approach; N/S, not specified; N/A, not applicable (data not collected); OUT, outpatient therapy.