Enteral nutritional support and use of diabetes-specific formulas for patients with diabetes: a systematic review and meta-analysis

CRD summary
This review assessed the benefits of enteral nutritional support in patients with type 1 or type 2 diabetes. The authors concluded that short- and long-term use of diabetes-specific formulas as oral supplements and tube feeds are associated with improved glycaemic control compared with standard formulas. However, given the methodological limitations of the review and the limited evidence, the authors' conclusions may not be reliable.

Authors' objectives
To determine the benefits of enteral nutritional support in patients with type 1 or type 2 diabetes.

Searching
PubMed, the Cochrane Library, Turning Research into Practice, Clinical Evidence, National Electronic Library for Health Guidelines finder and National Service Frameworks were searched up to August 2004, without any language restrictions; the search terms were reported. Bibliographies of identified trials were also screened, and experts in the field were contacted for additional studies. Only studies with an English translation or abstract were included in the review.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs), non-randomised clinical controlled trials (CCTs) and before-and-after clinical trials (CTs) were eligible for inclusion.

Specific interventions included in the review
Studies of formulas given orally or by tube feeding, which contained at least two macronutrients in addition to micronutrients, were eligible for inclusion. Comparisons of interest included nutritional support versus usual care; diabetes formula versus standard formula; and tube (enteral) versus parenteral nutrition. Formulas providing complete or incomplete nutrition were eligible, as were studies reporting concomitant use of parenteral nutrition or dietary advice. Studies using hypocaloric feeding regimens in obese patients with the intention of weight loss were excluded. The duration of the intervention ranged from a single meal to 3 months.

Participants included in the review
Studies of adults (older than 18 years) of any nutritional status, with type 1 or type 2 diabetes, or stress diabetes caused by acute illness, were eligible for inclusion. Most studies were of patients with type II diabetes. Further details of the participants were available online; where reported, the mean age ranged from 30.4 to 81 years, the mean body mass index from 25 to 30 kg/m2 and the mean fasting glucose from 6.9 to 9.16 mmol/L.

Outcomes assessed in the review
The outcomes of interest included incidence of glycaemia, lipidaemia, nutritional status, medication requirements, quality of life, complications and mortality. The outcomes assessed in the review were: postprandial rise in glucose; peak blood glucose; area under the glucose and insulin response curve (AUC); Akaike's Information Criterion; fasting blood glucose; high-density lipoprotein; triglycerides; and change in total cholesterol.

How were decisions on the relevance of primary studies made?
The authors did not state how the studies were selected at the titles and abstract stage, or how many reviewers performed the selection. At the full paper stage, one reviewer applied the inclusion criteria and a second checked the decisions.
Assessment of study quality
The quality of the RCTs was assessed in relation to randomisation, blinding and withdrawals, using the Jadad scale. One reviewer undertook the quality assessment; assessments were checked by a second reviewer.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. Formulas were categorised as diabetes-specific (containing a high proportion of fat, fructose and fibre) or standard (all other formulations). Where more than two eligible arms of a trial were available, the two interventions closest to a standard and diabetes-specific formula were extracted. Where repeated measurements were reported, the last measurement was extracted. The change from baseline was extracted; mean differences and 95% confidence intervals (CIs) were calculated for each study.

Methods of synthesis
How were the studies combined?
Pooled weighted mean differences (WMDs) and 95% CIs were calculated using fixed-effect Mantel-Haenszel meta-analyses. The correlation between baseline data and post-intervention data was assumed to be zero for the main analysis.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the chi-squared test, and forest plots enabled a visual inspection of the heterogeneity between studies. Subgroup analyses investigating different durations of follow-up, different types of diabetes, and nutritional status of the participants were planned a priori. A sensitivity analysis was conducted to determine the effect of increasing the correlation between baseline data and post-intervention data to 0.5.

Results of the review
Twenty-three studies (n=784) were included in the review: 19 RCTs (n=734), 3 CCTs (n=42) and one before-and-after CT (n=8).

Of the 19 RCTs, three scored 5 for quality, two scored 4, two scored 3, ten scored 2 and two scored 1, out of a possible 5.

Nutritional support versus routine care (2 RCTs).
Oral nutritional supplements produced smaller rises in postprandial glucose, insulin concentrations and AUC than routine care and a standard formula.

Diabetes-specific formula versus standard formula (18 RCTs and 2 CCTs).
Diabetes-specific formula resulted in a reduction in postprandial rise in blood glucose (WMD -0.52, 95% CI: -0.81, -0.24, p=0.012; 6 RCTs), peak blood glucose (WMD -1.28, 95% CI: -1.94, -0.63, p not reported; 2 RCTs), glucose AUC (WMD -1.19, 95% CI: -1.69, -0.7, p not reported; 4 RCTs), insulin AUC (3 RCTs), Akaike's Information Criterion (3 RCTs), fructosamine (1 RCT) and insulin requirements (3 RCTs and 1 CCT). The meta-analyses of postprandial rise in blood glucose and glucose AUC were subject to significant statistical heterogeneity. The effect on fasting blood glucose was variable (3 RCTs). There was no significant difference in total (6 RCTs) or high-density lipoprotein (2 RCTs) cholesterol, blood triglycerides (6 RCTs) or complications (2 RCTs) between diabetes-specific formula and standard formula.

Results from other studies evaluating alternative comparisons (2 RCTs, 1 CCT and 1 CT) did not seem to have been presented.

Authors' conclusions
Short- and long-term use of diabetes-specific formulas as oral supplements and tube feeds are associated with improved glycaemic control compared with standard formulas. Giving nutritional support long-term may have implications for
reducing complications with diabetes-specific compared with standard nutritional formulas.

**CRD commentary**
The research question was clear, with well-defined inclusion criteria. Several relevant sources were searched, however, studies had to have at least an English language abstract to be included, therefore increasing the potential for language bias. Quality was assessed using a scale designed for RCTs; non-RCTs were also included in the review. The validity assessment was conducted in duplicate, but it was unclear whether similar methods were employed to reduce error and bias during the study selection and data extraction processes.

Study details were available online (accessed May 2007; see Web Address at end of abstract), although not at the web address specified in the article. There were some discrepancies between study details presented in the paper and those available online. Fixed-effect meta-analyses were used despite clinical heterogeneity between studies and significant statistical heterogeneity between studies for some outcomes. Results from studies recruiting patients with type I and type II diabetics were included in the same meta-analyses, and few studies considered long-term effects. Considering the limited evidence available and the aforementioned methodological limitations of the review, the authors' conclusions seem overstated, particularly with regards to the impact on complications, and should therefore be treated with caution.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that well-designed, adequately powered trials that aim to determine the role of enteral nutrition and diabetes-specific formulas on the management, clinical outcome and quality of life of malnourished patients with diabetes are required, along with research specifically designed to assess the incidence of complications. The authors went on to say that the establishment of the optimal composition of nutritional feeds designed to assist metabolic control, improve immune function and achieve satisfactory nutritional status would also be useful. The authors also noted that there are few long-term studies examining clinical outcomes.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.