Weight Loss Comparable Across Diet Schemes

Weight-loss diets emphasising different proportions of fat, protein, and carbohydrate content were found equally successful in a population-based study. However, the author of an editorial commenting on this report argued that the dietary goals were only partly achieved. The study noted that behavioural factors have a large influence on weight loss.

In a direct comparison of four different diets, all study groups showed similar weight losses, decreases in waist circumference (WC), and improvements in CV risk profiles. Satiety, hunger, satisfaction with the diet, and attendance at group support sessions also were similar across all four groups, regardless of the percentages of fat, protein, and carbs the diets allowed.

“These divergent results suggest that any type of diet, when taught for the purpose of weight loss with persistence, can be effective,” said Frank M. Sacks of Harvard School of Public Health. They assessed the diets of 811 subjects aged 30-70 years who had a BMI of 25-40 kg/m² and were highly motivated to lose weight. The subjects were taught their diets, given daily meal plans and lists of carb-rich foods with a low glycaemic index, and supported with individual and group counselling. A total of 645 of them (80%) completed the 2-year study.

About a third lost at least 5% of their initial body weight. Weight reductions differed by <0.5 kg across the four diet groups, and decreases in WC differed by less than 0.5 cm. CV risk factors such as cholesterol and BP improved to the same degree in all groups.

Diets that are successful in causing weight loss can emphasise a range of fat, protein, and carbohydrate compositions. Such diets can be tailored to individual patients on the basis of their personal and cultural preferences and may have the best chance for long-term success (N. Engl. J. Med. 2009;360:859-73).

None of the diets was particularly effective in the long term, Martijn B. Katan, of VU University, Amsterdam, said in an accompanying editorial. Weight loss averaged 6 kg at 6 months, but thereafter subjects tended to regain weight so that final losses averaged only 3-4 kg at 2 years. Even these small losses might not have been sustained if the trial had continued, Katan said (N. Engl. J. Med. 2009;360:923-5).

The participants were highly educated, enthusiastic, and carefully selected. They were offered 59 group and 13 individual training sessions [with professionals] over the course of 2 years. Nonetheless, their BMI averaged 31-32 and was moving up again as the trial ended.

Moreover, the macro-nutrient goals for each of the four diets were not reached. Protein intake was intended to differ among the four groups by 10% of energy, but it differed by only 1%-2%. Similarly, carbohydrate intake was supposed to differ by 30%, but both extremely low and extremely high carb intakes proved difficult to achieve, so the actual difference turned out to be only 6% of energy.

The attendance at group behavioural counselling sessions had a strong association with weight loss and the effect was seen across diet groups. Those who attended two-thirds of their sessions during the 2 yrs lost about 9 kg, and regain after 6-12 months was about 20% of that seen in previous studies. That suggests that behavioural factors rather than micro-nutrient metabolism have a greater influence on weight loss.

There is a general difficulty to quantify behaviour as a factor in weight loss, saying: “Cognition and feeling have a huge impact” on food consumption. “Participants may eat less not because of the protein or carb content of a diet but because of the diet’s reputation or because of the taste of particular foods in the diet.”
The way that diabetes is diagnosed in the USA is about to change. An expert panel organised by the American Diabetes Association (ADA) will issue a report making a person’s blood level of glycosylated haemoglobin (HbA\textsubscript{1c}) an accepted method for diagnosing diabetes. Although the decision is not yet finalised, “the group will likely recommend HbA\textsubscript{1c} as the preferred test,” placing it above the current diagnostic standard (FBG) and also above the historic criterion for diabetes diagnosis (OGTT), said Sue Kirkman, the ADA’s vice president for clinical affairs.

The report from the ADA’s Expert Committee on Diagnosis and Classification of Diabetes will also set the HbA\textsubscript{1c} cut point for diagnosing diabetes, but this value has not yet been finalised. The use of HbA\textsubscript{1c} for diagnosis stands to legitimise the method that is commonly used by many primary care physicians, said Mayer B. Davidson, an endocrinologist professor of medicine at the University of California. He applauded the decision, noting that “HbA\textsubscript{1c} is a more valid way to look at what is going on with glucose,” compared with glycaemia levels.

Adoption of HbA\textsubscript{1c} as the primary diagnostic method also stands to make the diagnosis of diabetes substantially easier, meaning that more people will probably be tested and identified. “Since the HbA\textsubscript{1c} test doesn’t require fasting, it will be more convenient,” Kirkman said. “In the United States, [the percentage] of people with diabetes who are undiagnosed is now about 25%. Making the diagnosis easier will further decrease the number of people who are undiagnosed.

The Expert Committee is an ad hoc group that the ADA convenes when there is a need to revisit some area related to diagnosis or classification. The current deliberations began last year, and the group constituted members from the ADA, and also from the EASD and IDF. It is hoped that all three organisations will adopt the recommendations so that there is a world-wide standard.

Making HbA\textsubscript{1c} an accepted diagnostic test has been on the table for years. Recently William C. Knowler spelled out the case in favour of using glycosylated haemoglobin, as well as the shortcomings of this approach. The strengths of HbA\textsubscript{1c} as a diagnostic tool include the following:

- A more standardised assay and with less inter-laboratory variability, compared with blood glucose measurements.
- A better index of overall glycaemia.
- Consistency in using the same assay for diagnosis that’s also routinely used to monitor patient treatment and to predict the risk for long-term complications.
- No need for fasting before the specimen is drawn.
- No effect from acute changes in blood glucose levels, such as those caused by illness.

Another attraction of HbA\textsubscript{1c} is that when the level goes above 7.0%, it becomes strongly correlated with the development of microvascular complications. There is no absolute way to diagnose diabetes. Basing diagnosis on a test that can reliably predict the risk for microvascular complications is attractive because these complications are fairly specific to diabetes.

But relying on HbA\textsubscript{1c} for diagnosis also has limitations. The test is not universally available around the world. And a person’s HbA\textsubscript{1c} level can be affected by haemoglobinopathies, variations in red cell turnover, and unexplained racial differences.

Perhaps most importantly, switching the diagnostic criterion will create a break from the past that might make it hard to reconcile old epidemiologic observations with new ones. A similar break occurred in 1997, when the ADA switched its diagnostic standard from the blood glucose level 2 hours following an oral glucose challenge to a fasting blood glucose level. That switch resulted in a sudden spike in the number of patients diagnosed with diabetes. At that time, the ADA decided against adopting HbA\textsubscript{1c} as its diagnostic standard because the tests for measuring it were not sufficiently standardised.

The fact that an HbA\textsubscript{1c} cut point for diagnosis has still not been set highlights the controversy this issue generates. A cut point of 6.5% has “some useful properties,” but 5.5% is “a level to raise concern” that a person is at risk for eventually developing diabetes. Choosing a cut point “is a complicated issue that depends on how harmful are missed diagnoses and over-diagnosis”.

In contrast, Davidson, not a member of the current Expert Committee, leans toward a cut point of 7.0% because of its significance for microvascular disease, but adds that he is in the minority in the endocrinology community and that it’s unlikely the diagnostic threshold will be set so high.
Weight gain after initiation of insulin therapy investigated

A reduced level of physical activity explains much of the weight gain that some patients with type 2 diabetes experience after initiating insulin therapy, new data suggest.

Researchers from the Netherlands studied 20 patients with type 2 diabetes who had been started on insulin therapy in the period 2001-2006. The patients were divided into two groups based on the amount of weight gain experienced when beginning insulin therapy: a group of 10 patients who were weight gainers (an increase of 1 kg or more every 2 months within the first 18 months) and a group of 10 patients who did not gain weight (maximum weight gain 2 kg or less within the first 18 months, and a stable body weight after this period).

After a mean of 4 years of insulin therapy, mean body weight had increased from 79.1 kg to 92.7 kg in the weight gain group, and had decreased slightly from 88 kg to 86 kg in the non-weight gain group.

The weight gainers had significantly higher levels of total cholesterol, LDL-cholesterol, adiponectin, and leptin. There were no significant differences between the two groups in mean HbA1c reduction, blood pressure, fasting insulin, C-peptide, and C-reactive protein.

The patients who gained weight had a significantly higher percentage of total body fat than the non-gainers, although trunk fat mass was not significantly different. The gainers, however, were found to have a significantly lower energy expenditure (as determined by patients wearing a body monitoring system for five consecutive days).

The researchers concluded that the cardiovascular risk profile deteriorates in patients with type 2 diabetes who gain weight. They added: “The increase in body weight in gainers seems mainly explained by lower physical activity levels. It may be important to assess lifestyle characteristics before onset of insulin treatment in order to predict and potentially intervene in those at risk for extensive body weight increase”.

Source: EASD 44th annual scientific meeting, Rome, Italy, 7-11 September 2008, presentation number 974.

Perform OGTT Before Coronary Angiography

Impaired glucose tolerance (IGT) significantly increases the risk of future cardiovascular events in patients undergoing elective coronary angiography. The researchers suggest that all patients undergoing the procedure have an oral glucose tolerance test (OGTT) in order to more accurately determine risks.

Specialists from centres in Austria and Liechtenstein enrolled 1,040 patients about to undergo coronary angiography for suspected coronary artery disease, and gave an OGTT to those without known diabetes. The patients were then followed up for 3 years. Overall, 394 of the patients were found to have normal glucose tolerance, 190 had IGT, and 456 had type 2 diabetes (previously known in 244 patients, and newly diagnosed by OGTT in 212 patients).

The incidence of cardiovascular events in the follow-up period was significantly higher in the patients with IGT (14.9%) and patients with type 2 diabetes (13.4%), than in the patients with normal glucose tolerance (8.9%). There was no significant difference in the risk of cardiovascular events between patients with IGT and patients with type 2 diabetes.

In a regression analysis, the hazard ratios for cardiovascular events were 1.89 (95% confidence interval (CI) 1.11-3.24) for patients with IGT, and 1.73 (95% CI 1.10-2.74) for patients with type 2 diabetes.

The researchers concluded that IGT and type 2 diabetes are both associated with an approximately doubled risk of future cardiovascular events. An OGTT therefore seems to be essential for reliable cardiovascular risk estimation, they said.

Source: EASD 44th annual scientific meeting, Rome, Italy, 7-11 September 2008, presentation number 1360.
Coffee Components May Improve Glucose Tolerance

Chlorogenic acid and trigonelline, which are present in coffee, may improve glucose tolerance, according to the results of a randomised cross-over trial. "In prospective cohort studies, higher coffee consumption has been associated with a lower risk of type 2 diabetes," writes Aimée E van Dijk, Institute for Health Sciences, VU University Amsterdam. "Associations have been similar for caffeinated and decaffeinated coffee suggesting that coffee components other than caffeine have beneficial effects on glucose homeostasis. Coffee is a major source of the phenolic compound chlorogenic acid and the vitamin B3 precursor trigonelline that have been shown to reduce blood glucose concentrations in animal studies."

The goal of this study was to determine the acute effects of decaffeinated coffee, chlorogenic acid, and trigonelline on glucose tolerance in 15 overweight men. During a 2-hour OGTT, the investigators studied the effects on glucose and insulin concentrations of 12 g decaffeinated coffee, 1 g chlorogenic acid, 500 mg trigonelline, and placebo (1 g mannitol).

Compared with placebo, chlorogenic acid and trigonelline ingestion were associated with significant reductions in glucose (−0.7 µmol/L [P = .007] and −0.5 µmol/L [P = .024], respectively) and insulin (−73 pmol/L [P = .038] and −117 pmol/L [P = .007], respectively) concentrations 15 min after an OGTT. However, insulin and glucose area under the curve values during the OGTT were similar for each of the treatments vs. placebo.

Limitations of this study include that multiple tests were conducted for different time points, increasing the likelihood of chance findings, and difficulty comparing the treatment effects because the decaffeinated coffee supplement contained substantially less chlorogenic acid and trigonelline than the doses given in isolation.

Chlorogenic acid and trigonelline reduced early glucose and insulin responses during an OGTT. This finding is consistent with the hypothesis that these compounds may contribute to the putative beneficial effect of coffee on development of type 2 diabetes*.

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Review: Premixed Insulin Analogies With Other Antidiabetic Agent

Premixed insulin analogues and premixed human insulin provide similar glycaemic control in adults with type 2 DM. Also, premixed analogues provide tighter glycaemic control but cause more hypoglycaemia, compared with long-acting insulin analogues and non-insulin antidiabetic agents.

Those are conclusions of a meta-analysis that compared the efficacy of premixed insulin analogues with other antidiabetic agents in type 2 DM. 45 studies used in the analysis. The researchers also evaluated unpublished data from the U.S. FDA, the European Medicines Agency, and the pharmaceutical industry. But the researchers point out that the findings were based on clinical outcomes such as HbA1c, because most studies in the analysis excluded clinical outcomes such as mortality (Ann. Intern. Med. 2008;149). Thus, the findings cannot be generalised to all diabetic patients. Moreover, because follow-up was short in most studies, conclusions could not be drawn about the long-term comparative effectiveness of premixed insulin analogues.

14,603 patients were enrolled in the 45 studies and the mean age was 59 years. The median duration of follow-up in the trials was 16 weeks. The researchers found that premixed insulin analogues were similar to premixed human insulin in decreasing fasting glucose and HbA1c levels, but were more effective in decreasing postprandial glucose levels (by a mean pooled difference of −1.1 mmol/L). The incidence of hypoglycaemia was similar between the two groups.

Compared with long-acting insulin analogues, premixed insulin analogues were superior in decreasing postprandial glucose levels (by a mean difference of −1.5 mmol/L) and HbA1c levels (by a mean difference of −0.39%) but were inferior in decreasing fasting glucose levels (by a mean difference of 0.7 mmol/L). In addition, premixed insulin analogues were associated with a higher incidence of hypoglycaemia, compared with long-acting insulin analogues by an odds ratio of 2.02.

Qayyum and his associates reported that, compared with non-insulin antidiabetic agents, premixed insulin analogues were more effective in decreasing fasting glucose levels (by a mean difference of −1.1 mmol/L), postprandial glucose levels (by a mean difference of −2.1 mmol/L), and HbA1c levels (by a mean difference of −0.49%). However, use of premixed insulin analogues was associated with a higher incidence of hypoglycaemia, compared with non-insulin antidiabetic agents by an odds ratio of 2.15.

The researchers acknowledged limitations of the study, including the fact that data on clinical outcomes were limited and that the literature search was limited to studies published in English. "Studies with longer follow-up are needed to determine whether the effects observed early in treatment are sustainable long term," they concluded. "Moreover, given that improvement in intermediate clinical outcomes may not always result in improvement in clinical outcomes, studies specifically designed to evaluate clinical outcomes are needed."