Clinical *DIGEST 1*

Major journals

Dietary regimens and their effect on CV risk: The low carbohydrate–high protein diet

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Obesity is a well-recognised risk factor for many chronic diseases, including T2D and cardiovascular disease (CVD). Over recent years, the prevalence of obesity has reached a global epidemic. A number of dietary regimens have been proposed to aid weight control; among these, one of the most popular encourages reduction of carbohydrate intake, and thereby high protein intake. The effects of low carbohydrate–high protein diets on weight control may be relatively short-term. Such diets may be nutritionally acceptable, namely if the protein is mainly from plant sources and simple and refined, rather than complex, carbohydrates are reduced. Such nuances are not widely understood and, as a consequence, concerns have arisen over the long-term health outcomes of such diets, with particular respect to cardiovascular (CV) outcomes. With such issues in mind, the objective of this population-based study was to assess the long-term consequences of low carbohydrate diets, generally characterised by concomitant increases in protein intake, on CV health.

The study cohort was made up of 43 396 women from the Uppsala healthcare region in Sweden, aged 30–49 years at baseline. All completed an extensive dietary questionnaire covering lifestyle, health and disease history, and physical and dietary activity – the mean follow-up was 15.7 years.

Measured outcomes included the association of CVD overall and by diagnostic category, with decreasing carbohydrate intake (in tenths), increasing protein intake (in tenths), and an additive combination of the two variables (the low carbohydrate–high protein score – ranging from a score of 2 to 20, and adjusted for energy intake of saturated and unsaturated fat, and a number of non-dietary variables).

After controlling for all assessed CV risk factors that could act as confounding variables, as well as for total energy and saturated and unsaturated fat intake, per 2-unit increase in the 20-unit low carbohydrate–high protein score, women had a significant 5% increase in CV event incidence. In practical terms, a reduction of 20 g in daily carbohydrate intake and a 5 g increase in daily protein intake would correspond to a 5% increase in the overall CVD risk.

> *" Per 2-unit increase in the 20-unit low carbohydrate–high protein score, women had a significant 5% increase in CV event incidence. In practical terms, a reduction of 20 g in daily carbohydrate intake and a 5 g increase in daily protein intake would correspond to a 5% increase in the overall CVD risk."*

With respect to the biomedical plausibility of these findings, vegetables, fruits and cereals, which are core components of healthy dietary patterns (Trichopoulou et al, 2003) and are important sources of carbohydrates. Reduced intake of these food groups is therefore likely to have adverse effects on CV health. Moreover, several studies have reported that meat consumption or high intake of protein from animal sources may increase the risk of CVD (Zyriax et al, 2005). While this study provides no information with respect to the short-term impact of low carbohydrate–high protein diets on CV health, it does draw attention to their potential associated adverse effects on CV health when used on a regular basis and without consideration of the nature of carbohydrates or the source of proteins.

Trichopoulou A, Costacou T, Bamia C et al (2003) Adherence to a Mediterranean diet and survival in a Greek population. *N Engl J Med* **348**: 2599–608

Zyriax BC, Boeing H, Windler E (2005). Nutrition is a powerful independent risk factor for coronary heart disease in women-- The CORA study: a population-based case-control study. *Eur J Clin Nutr* **59**: 1201–7

BRITISH MEDICAL JOURNAL

Low carbohydrate–high protein diets increase risk of CVD

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1. The authors set out to determine long-term consequences of low carbohydrate-high protein diets on CV health in a random sample of 43 396 Swedish women, aged 30–49 years at baseline.

2. Study participants completed a mailed comprehensive dietary questionnaire that recorded information on aspects of lifestyle, medical history, physical activity and dietary intakes from 11 food groups, focusing on the 6-month period before study enrolment. The women were followed up for a mean of 15.7 years.

3. Outcome measures were an association of first diagnosis of CVD (using linkages with nationwide Swedish registers) with carbohydrate and protein intake. Women were assigned a low protein–high carbohydrate score ranging from 2 to 20 – this was adjusted for energy intake, saturated and non-saturated fat consumption, and non-dietary variables.

4. A total of 1270 CV events were recorded over around 680 000 person-years. CVD incidence increased in relation to a one-tenth decrease in carbohydrate intake or increase in protein intake, and a 2-unit increase in low carbohydrate–high protein score. All associations reached a level of significance.

5. The authors concluded that regular use of low carbohydrate–high protein diets whilst not considering the source of protein (plant versus animal) and nature of carbohydrates (complex versus refined) was associated with an increased CVD risk.

Lagiou P, Sandin S, Lof M et al (2012) Low carbohydrate-high protein diet and incidence of cardiovascular diseases in Swedish women. *BMJ* **344**: e4026.

JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

CVD risk prediction: Use of lipid-related markers

Readability	✓✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 The authors investigated the effects of addition and replacement of total cholesterol and high-density lipoprotein cholesterol (HDL-C) with various lipid parameters (apolipoprotein B and A-1, lipoprotein(a) and lipoprotein-associated phospholipade A2) on prognostic CVD models.

2 Secondly, the authors determined whether adding information on additional lipid markers to CVD risk scores improved reclassification of people across three clinical 10-year CVD risk categories (<10%, 10%−<20% and ≥20%).

3 A total of 165 444 people without CVD from 37 cohorts (recruited between 1968 and 2007) were followed up for an average of 10.4 years. The primary outcome was first-onset CVD (any fatal or non-fatal coronary heart disease event or stroke).

4 Replacement of total cholesterol and HDL-C with lipid parameters in risk models did not improve CVD prediction. Addition of lipid markers to models already using total cholesterol, HDL-C and other conventional risk factors slightly improved prediction of CVD but this was not significant. Improvements in reclassification of CVD risk were less than 1% with each lipid marker.

5 Targeted lipid-related marker assessment in 15 436 people at intermediate risk of CVD (10%−<20% predicted 10-year CVD risk) would reclassify 1.1–4.1% of people into a 20% or higher CVD risk category.

6 The authors concluded that CVD prediction is slightly improved after addition of lipid markers to risk models containing total cholesterol and HDL-C.

Emerging Risk Factors Collaboration, Di Angelantonio E, Gao P et al (2012) Lipid-related markers and cardiovascular disease prediction. *JAMA* **307**: 2499–506

JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

Aspirin increases bleeding but not in people with diabetes

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 Low-dose aspirin treatment is often used as a preventive measure for cardiovascular disease; however, it is associated with gastrointestinal and intracranial haemorrhagic complications.

2 The authors sought to determine the incidence of major bleeding in people with and without diabetes taking aspirin.

ARCHIVES OF INTERNAL MEDICINE

Intensive BP control does not reduce mortality or MI risk

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 People with T2D are at increased risk of cardiovascular diseases, such as myocardial infarction (MI) or stroke, which can be linked to high blood pressure (BP).

JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

Normal weight at diagnosis increases mortality risk

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 The authors aimed to determine the association of weight at diabetes diagnosis with mortality. Pooled analysis of five studies identified 2625 people with incident diabetes contributing 27 125 person-years of follow-up; data included BMI at diagnosis.

3 Administrative data from 4.1 million people in Puglia, Italy, identified 186 425 people on low-dose aspirin and 186 425 matched controls without.

4 During a median follow-up of 5.7 years, the overall incidence rate of haemorrhagic events was 5.58 (95% confidence interval [CI], 5.39–5.77) and 3.60 (95% CI, 3.48–3.72) per 1000 person-years for those on aspirin and without, respectively (incidence rate ratio [IRR], 1.55; 95% CI, 1.48–1.63).

5 Aspirin use was linked with a greater risk of major bleeding, but not in people with diabetes (IRR, 1.09; 95% CI, 0.97–1.22); however, diabetes was an independent risk factor for major bleeding.

De Berardis G, Lucisano G, D'Ettorre A et al (2012) Association of aspirin use with major bleeding in patients with and without diabetes. *JAMA* **307**: 2286–94

2 A systematic review and meta-analysis identified five randomised controlled trials enrolling 7312 adults with T2D that compared the effect of intensive (upper limit of 130 mmHg systolic and 80 mmHg diastolic) versus standard (upper limit of 140–160 mmHg systolic and 85–100 mmHg diastolic) BP targets on all-cause mortality, MI and stroke.

3 Intensive BP targets did not reduce mortality or MI risk, but did show a small decrease in the risk for stroke.

McBrien K, Rabi DM, Campbell N et al (2012) Intensive and standard blood pressure targets in patients with type 2 diabetes mellitus: systematic review and meta-analysis. *Arch Intern Med* 6 Aug [Epub ahead of print]

2 Normal weight was classified as BMI of 18.5–24.99 kg/m^2, whereas being overweight or obese was classified with a BMI ≥25 kg/m^2.

3 In total, 293 participants (11.2%) had normal weight at the time of incident diabetes; during follow-up 449 people died (178 from cardiovascular [CV], 253 from non-CV and 18 from unclassified causes).

4 Total, CV and non-CV mortality rates were higher in those with normal weight at the time of incident diabetes than in those who were overweight or obese – this remained after adjustments.

Carnethon MR, De Chavez PJ, Biggs ML et al (2012) Association of weight status with mortality in adults with incident diabetes. *JAMA* **308**: 581–90

> "*Aspirin use was linked with a greater risk of major bleeding, but not in people with diabetes; however, diabetes was an independent risk factor for major bleeding.*"