

## Cardiovascular and major journals



### *A mixed bag of ideas for CVD risk reduction and finding diabetes in the vascular clinic*

**Vinod Patel**

Principal Teaching Fellow, Warwick Medical School, University of Warwick and Honorary Consultant in Diabetes and Endocrinology, George Eliot Hospital NHS Trust, Nuneaton

*Consider the bean burger, which looks like a regular burger from the outside but is a healthier option once you look inside: if the individual is obese check whether they are "healthy obese".*

I am afraid no large trial has come across my way to deeply influence practice. Professors Khunti, Barnett and Sattar must all be on holiday! Some intriguing ideas emerge from several less salubrious studies and may influence practice in years to come.

Weight loss strategies often fail for a large variety of reasons. One reason we understand is that the standard message of less fat is translated into more carbohydrates or vice versa. Several previous studies had observed weight loss when carbohydrates are substituted for protein, while other studies have observed weight gain and increased saturated fat intake. The study by Campmans-Kuijpers et al (summarised alongside) set out to explore whether substituting carbohydrate intake with a protein substitution of either plant or animal origin affected weight loss in people with type 2 diabetes trying to lose weight. The outcome measures were weight loss, mortality and cardiovascular disease (CVD) event rates. Disappointingly, weight loss was not observed in either the animal or the plant protein substitution diet groups. However, the plant protein substitution diet was associated with a 21% reduction in all-cause mortality over the mean follow-up period of 9.2 years compared to the animal protein substitution diet.

In the Hinnouho et al study (summarised on the next page), "metabolically healthy (MH)" was defined as individuals who had fewer than two of the following: high triglycerides levels ( $\geq 1.7$  mmol/L) or took lipid-lowering drugs; elevated systolic ( $\geq 130$  mmHg) or diastolic blood pressure ( $\geq 85$  mmHg) or took anti-hypertensive drugs; high fasting glucose ( $\geq 5.6$  mmol/L) or took any medications for diabetes; and low HDL-cholesterol (1.04 mmol/L for men and 1.29 mmol/L for women). The MH-obese phenotype was found to

carry less risk for type 2 diabetes when compared with participants with more than one of the above risk factors (i.e. metabolically unhealthy obese people). However, the CVD risk remained high in the MH-obese group.

In the Silbernagel study (summarised on the next page), the prevalence of diabetes and pre-diabetes was determined in 364 patients with peripheral artery disease, 529 patients with coronary artery disease and 383 without a cardiac diagnosis (control group). The prevalence of type 2 diabetes in people with peripheral artery disease was 49.7%; this was significantly higher than in people with coronary artery disease patients (34.4%;  $P < 0.001$ ) and the control group (21.4%;  $P < 0.001$ ). Adjusted for sex, age and BMI, odds ratios for type 2 diabetes were 2.0 (95% confidence interval [CI], 1.5–2.6) comparing the peripheral artery disease group with the coronary artery disease group ( $P < 0.001$ ) and 4.0 (95% CI, 2.8–5.8) comparing the peripheral artery disease group with controls ( $P < 0.001$ ). The prevalence of pre-diabetes among people without diabetes was high in all three study groups (64.5% in peripheral artery disease group, 63.4% in coronary artery disease groups and 61.8% in the control group), without significant between-group differences. In conclusion, the prevalence of type 2 diabetes is even higher in people with peripheral artery disease than with coronary artery disease. This observation underlines the need to consider impaired glucose regulation in the management of peripheral artery disease.

From these studies maybe more bean burgers should be on the barbecue if the weather improves! We should also be checking the vascular clinic for people with diabetes and pre-diabetes to improve future risk of diabetes and managing CVD risk aggressively. Finally, we could "persuade" our obese patients to become metabolically healthier at the very least with strategies to reduce triglycerides and increase HDL-cholesterol by diet and optimising physical activity. ■

### Cardiovasc Diabetol

#### Swapping carbohydrate intake with protein

Readability ////  
 Applicability to practice ////  
 WOW! Factor ////

**1** The authors aimed to investigate whether dietary carbohydrate substituted with animal and plant protein affected 5-year weight change and all-cause and cardiovascular (CVD) mortality in people with T2D.

**2** In a large multinational study with 15 European cohorts, the total participant group comprised 6107 people.

**3** At recruitment to the study group, validated country-specific food-frequency questionnaires were used to estimate dietary intake. Multivariable adjusted linear regression was used to examine the associations between dietary carbohydrate substitution with protein and 5-year weight change, and Cox regression to estimate hazard ratios for CVD mortality.

**4** After a mean follow-up of 9.2 years, 787 (13%) participants had died, of which 266 (4%) deaths were due to CVD.

**5** Substituting 10 g of dietary carbohydrate with total and animal protein was associated with mean 5-year weight gain.

**6** There was no significant association between plant protein substitution and weight change, but substitution was associated with lower all-cause mortality risk, whereas substitution with total or animal protein was not associated with a change in CVD mortality risk.

**7** Substituting carbohydrate calorie intake with plant-based protein among people with T2D could be beneficial for weight change and all-cause mortality compared to substitution with animal proteins.

Campmans-Kuijpers MJ, Stuijs I, Nöthlings U et al (2015) Isocaloric substitution of carbohydrates with protein. *Cardiovasc Diabetol* **14**: 39

## Eur Heart J

### CVD and T2D risk: Metabolically healthy versus metabolically unhealthy obese

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! Factor	✓✓✓

**1** The metabolically healthy obesity (MHO) phenotype is a phenomenon that is not fully understood. As part of the Whitehall II cohort study, the authors investigated the association of the MHO phenotype with cardiovascular disease (CVD) and T2D risk.

**2** A total of 7122 adults (69.7% men) were included in the retrospective analysis of data from 1991–1993; 657 individuals, comprising nearly 10% of the cohort, were obese and nearly half of them were classified as MHO in 1991–1993.

**3** Over the median 17.4 years that followed, there were 828 incident cases of CVD and 798 incident cases of T2D.

**4** Compared with metabolically healthy normal weight individuals, MHO individuals were at increased risk for CVD (hazard ratio [HR], 1.97 [95% confidence interval (CI), 1.38–2.80]) and T2D (HR, 3.25 [95% CI, 2.32–4.54]).

**5** There was also an excess risk in metabolically unhealthy obese people compared with MHO for T2D (HR, 1.98 [95% CI, 1.39–2.83]) but not for CVD (HR, 1.23 [95% CI, 0.81–1.87]).

**6** The MHO phenotype appears to be associated with a lower risk of T2D than the metabolically unhealthy obese, but CVD risk is elevated in both MHO people and metabolically unhealthy obese people.

Hinnouho GM, Czernichow S, Dugravot A et al (2015) Metabolically healthy obesity and the risk of cardiovascular disease and type 2 diabetes: the Whitehall II cohort study. *Eur Heart J* **36**: 551–9

## Diab Vasc Dis Res

### T2D prevalence in peripheral artery disease

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓✓

**1** T2D and pre-diabetes are known to be highly prevalent in people with coronary artery disease (CAD); however, the prevalence of impaired glucose metabolism, encompassing T2D and pre-diabetes, in people with peripheral artery disease (PAD) is not well understood.

**2** Plaque buildup is responsible for causing both CAD and PAD, but the main difference is that CAD is a condition of the heart's arteries while PAD usually refers to a disease of the arteries of the legs, and sometimes neck and kidneys.

**2** The authors compared the prevalence of T2D and pre-diabetes among 364 people with PAD, 529 people with CAD and 383 controls.

**3** The prevalence of T2D in PAD was 49.7%; this was significantly higher than in people with CAD (34.4%;  $P < 0.001$ ) and controls (21.4%;  $P < 0.001$ ).

**4** After adjustment for baseline characteristics, the odds ratio for T2D was two times higher in the PAD group compared to the CAD group ( $P < 0.001$ ), and four times higher in the PAD group compared to the control group ( $P < 0.001$ ).

**5** There were no significant between-group differences for the prevalence of pre-diabetes among those without T2D in all three study groups (CAD, PAD and control groups).

**6** The authors summarised that the prevalence of T2D is much higher in people with PAD than in people with CAD.

Silbernagel G, Rein P, Saely CH et al (2015) Prevalence of type 2 diabetes is higher in peripheral artery disease than in coronary artery disease patients. *Diab Vasc Dis Res* **12**: 146–9

## Int J Cardiol

### Effect of simvastatin–ezetimibe therapy among people with T2D

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓

**1** Simvastatin–ezetimibe combination therapy is a drug combination used for the treatment of dyslipidaemia and has been shown to reduce the risk of major adverse cardiac events (MACEs) among people with acute coronary syndrome.

**2** The beneficial effect of ezetimibe–simvastatin is not known among people with a lower risk of MACEs, so the authors aimed to investigate the differences of MACE risk between people with T2D using either simvastatin–ezetimibe or other high-potency statins.

**3** The total cohort comprised 20 485 Taiwanese adults aged between 40 and 75 years. Roughly half of the cohort were male, and there were 4099 in the simvastatin–ezetimibe group and 16 396 in the high-potency statin-alone group.

**4** In a total of 37 388 person-years, 1100 individuals developed new-onset MACEs.

**5** The annual incidence rate of new-onset MACEs was lower in the simvastatin–ezetimibe group (2.61%) than in the statin group (3.02%) ( $P = 0.0476$ ).

**6** Compared to high-potency statins alone, simvastatin–ezetimibe therapy was associated with a lower incidence of MACEs among individuals with T2D (HR, 0.77; 95% confidence interval, 0.66–0.90).

**7** It has been suggested in the past that high-potency statins are related to an increased risk of new T2D cases and this study supports this theory.

Chang SH, Wu LS, Lee CH et al (2015) Simvastatin–ezetimibe combination therapy is associated with a lower rate of major adverse cardiac events in type 2 diabetics than high potency statins alone. *Int J Cardiol* **190**: 20–5

“Substituting carbohydrate calorie intake with plant-based protein among people with T2D could be beneficial for weight change and all-cause mortality.”