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## The dose-response effect of fruit and vegetable intake on retinal vessel calibre, in healthy individuals at high risk of cardiovascular disease: a randomised controlled trial

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Changes in the retinal vessel caliber (RVC) have been associated with cardiovascular disease (CVD) risk<sup>(1)</sup>. Narrowing of the retinal arterioles and widening of the retinal venules may predict incident hypertension and diabetes<sup>(2)</sup>. To date, there are no trials investigating whether dietary factors can influence RVC. The aim of this study was to examine the dose response effect of fruit and vegetable (FV) intake on RVC in healthy free-living, overweight individuals with a high CVD risk. Ethical approval was received from the Office for Research Ethics Committees Northern Ireland.

Following a 4 week run-in period, during which FV was limited to <2 portions per day, participants were randomized to consume either 2, 4 or 7 portions of FV daily for the next 12 weeks. RVC was measured from digitized fundus images using a semi-automated software program. The central retinal artery equivalent (CRAE) and central retinal vein equivalent (CRVE) were calculated before and after the intervention. Dietary compliance was monitored using completed 4 day food diaries and by measuring a panel of venous blood dietary biomarkers.

Forty one males and 21 females with mean age 56.7 (sd 6.2) years and average FV intake 1.7 portions/day, completed the study. Body composition remained stable throughout the intervention period. During the intervention, participants in the 2, 4 and 7 portions/day groups reported consuming 1.8, 3.7 and 7.6 portions of FV respectively, and serum concentrations of zeaxanthin,  $\gamma$ -cryptoxanthin and lutein increased significantly across the groups in a dose-dependent manner ( $P$  for trend < 0.05). Mean baseline CRAE was 158 (sd 14)  $\mu$ m and CRVE was 235 (sd 22)  $\mu$ m with no significant differences between the groups. Increasing age was a significant determinant of wider retinal venules ( $p = 0.004$ ) whereas baseline systolic blood pressure was a significant determinant of narrower retinal arterioles ( $p = 0.02$ ). Analysis of covariance, using baseline CRAE/CRVE measures as the covariate, indicated no evidence of a dose-response effect of FV intake on CRAE ( $p = 0.98$ ) or CRVE ( $p = 0.93$ ).

To our knowledge, this is the first randomized controlled trial to investigate the effect of increased FV intake on RVC. Despite previous evidence of a beneficial dose-response effect of FV on microvascular function<sup>(3)</sup> (demonstrated by an improvement in forearm blood flow response to intra-arterial acetylcholine), this study found no effect of increasing FV intake on RVC- another indicator of microvascular function. It remains possible that FV may have beneficial effects on RVC in interventions of longer duration or if targeted towards a more vulnerable population.

1. McGeechan K, Liew G, Macaskill P *et al.* (2009) *Ann Intern Med.* **151**, 404–413.

2. Nguyen TT, Wang JJ, Wong TY (2007) *Diabetes Care* **30**, 2708–2714.

3. McCall DO, McGartland CP, McKinley MC *et al.* (2010) *Circulation* **119**, 2153–2160.