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« F&V AND TYPE 2 DIABETES »

Editorial

Fruits and vegetables: important to prevent type 2 diabetes?

The evidence from prospective studies that the consumption of fruits and vegetables reduces the risk of cardiovascular events is overwhelmingly supportive. In contrast, prospective studies have overall produced quite heterogeneous results when evaluating the risk to develop type 2 diabetes. The accompanied meta-analysis in this issue indicates here that - overall – a higher consumption of fruits and vegetables will not help to stem the tide of the diabetes epidemic. While this might be seen as disappointing, we need to keep in mind that observational studies may not be able to capture the true effect of diet on disease risk. Error in measuring participants' diet could potentially lead to a strongly underestimated effect, as is suggested by one study presented in this issue. The application of more accurate methods to assess dietary intake in epidemiologic studies, e.g. by the use of biomarkers, is a promising approach here to clarify the role of fruits and vegetables. Also, further research is needed to identify mechanisms by which fruits and vegetables may lower diabetes risk. Fruits and vegetables contribute importantly to fiber intake, besides whole grains. Here, a second study in this issue suggests that higher fiber intake reduces hepatic lipid accumulation and sub-chronic inflammation, central mechanisms in the development of insulin resistance.

Nevertheless, most studies evaluating both risk of cardiovascular disease and type 2 diabetes observed quite contradictory associations. Thus, we may still need to acknowledge that the effect of fruits and vegetables on risk of type 2 diabetes may be considerably weaker compared to the effect on cardiovascular risk. However, intervention studies like the PREDIMED-Reus trial strongly suggest that dietary patterns that favour fruits and vegetables at the cost of red meats and include fat predominantly from plant sources are not only heart-healthy but also dramatically reduce the risk of type 2 diabetes.

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Increasing Green leafy vegetable consumption can decrease the risk of type 2 diabetes

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The prevalence of type 2 diabetes is currently estimated at 6.4% worldwide and is predicted to rise[1]. There is evidence to support lifestyle modification programs to successfully prevent or delay the onset of type 2 diabetes[2]. Several lifestyle interventions have promoted increased intake of fruit and vegetables. In addition, high intakes of fruit and vegetables have been linked to a reduction in risk of cancer and cardiovascular disease. Diabetes is a strong, independent risk factor for cardiovascular disease and often the conditions exist together, sharing common modifiable risk factors. Therefore, we aimed to investigate the independent effects of fruit and vegetable consumption on the incidence of type 2 diabetes.

The electronic databases MEDLINE, EMBASE, CINHAL, BNI and the Cochrane library were searched for both Medical Subject Headings and keywords on diabetes, prediabetes, fruit and vegetables. Prospective cohort studies with an independent measure of fruit and vegetable intake by self-report and data on type 2 diabetes incidence were selected for inclusion in the review. All data on fruit and vegetable intake was standardised into servings per day. Random effects meta-analysis was used to estimate overall hazard ratios and 95% confidence intervals for the association between fruit and vegetable intake and risk of type 2 diabetes.

Increasing green leafy vegetable consumption decreases risk of type 2 diabetes

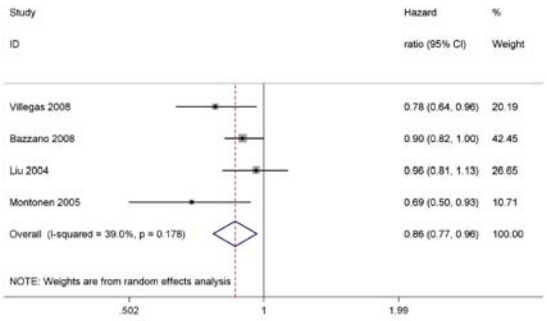
The search identified 3,446 articles. Six studies met all the inclusion criteria[3-8]; four included data on the consumption of green leafy vegetables[3-6]. The combined population resulted in 223,512 participants, aged between 30 to 74 years. We specifically looked at the lowest versus the highest intake values. The meta-analysis did not show any significant reductions in risk of type 2 diabetes for increased consumption of fruit, vegetables or fruit and vegetables combined, however there was a trend towards benefit from their increased consumption. All studies which examined the intake of green leafy vegetables showed a reduction in risk of type 2 diabetes with greater consumption. Summary estimates showed that those with highest intake as compared to the lowest intake had a 14% reduction in risk (p=0.01) of type 2 diabetes (hazard ratio 0.86, 95% confidence interval 0.77 to 0.96). Several differences existed between the studies in our review, therefore we carried out a sensitivity analysis to explore potential sources of bias. We examined sex of participants, location of study, quality of article, length of follow up, and how intake of fruit and vegetables were grouped. No significant interactions existed between these variables and therefore results should be drawn with caution. Measuring true dietary intake is very difficult. Food frequency questionnaires are open to criticism and to both random and systematic errors; such errors could have lead to an underestimation of the true effect of fruit and vegetables.

The review demonstrated that increasing the amount of green leafy vegetables in an individual's diet may help to reduce the risk of type 2 diabetes.

Potential mechanisms by which green leafy vegetables may confer health benefits

Fruit and vegetables could potentially prevent chronic disease due to their antioxidant content; our results support this as green leafy vegetables have high levels of vitamin C and beta carotene, both potent antioxidants. There are a number of other potential mechanisms by which green leafy vegetables may confer health benefits. They have high magnesium content; a recent meta-analysis found magnesium intake to be inversely associated with incidence type 2 diabetes[10]. Green leafy vegetables are good sources of α linolenic acids[11]. Intake may influence the composition of the fatty acid composition of the phospholipid bilayer which is related to insulin sensitivity. Further investigation into the potential beneficial mechanisms of green leafy vegetables is required.

FOREST PLOT COMPARING HIGHEST VERSUS LOWEST INTAKE OF GREEN LEAFY VEGETABLES



THESE FINDINGS SUPPORT RECOMMENDATIONS TO PROMOTE THE CONSUMPTION OF FRUIT AND VEGETABLES IN THE DIET TO PREVENT DIABETES. THE POTENTIAL FOR TAILORED ADVICE ON INCREASING INTAKES OF GREEN LEAFY VEGETABLES AMONG THOSE AT RISK OF TYPE 2 DIABETES SHOULD BE INVESTIGATED FURTHER

META-ANALYSIS OF HIGHEST VERSUS LOWEST INTAKE

Comparison	Studies	Cases / Non-cases	Pooled HR (95% CI)	P value	Heterogeneity I^2	P value
Vegetables only	5[3-6,8]	8563/204,654	0.91 (0.76 to 1.09)	0.32	78.1	0.001
Fruit only	5[3-6,8]	8563/204,654	0.93 (0.83 to 1.01)	0.27	52.6	0.07
Fruit and vegetables	4[4,6-8]	8302/146,715	1.00 (0.92 to 1.09)	0.97	0	0.40
Green leafy vegetables	4[3-6]	7422/169,807	0.86 (0.77 to 0.97)	0.01	39.6	0.18

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Fruits and vegetables and the risk of type 2 diabetes is there an association?

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The global burden of diabetes is increasing, with the latest data from the International Diabetes Federation estimating a prevalence of 285 million in 2010, increasing to a staggering 439 million by 2030[1]. The increased premature ill health, reduced life expectancy, and increased death rate related to the presence of diabetes, provide reason for concern, and make its prevention a major public health priority. That the primary prevention of diabetes is possible through lifestyle behaviours, including a healthy diet, has now been well established by intervention trials among people at high risk of diabetes[2]. However, what the specific contribution might be of the intake of fruits and vegetables to diabetes prevention, is unresolved.

We hypothesised that the inconsistent findings[3-5] for an association between intake of fruit/vegetables and the risk of type 2 diabetes might be explained by the known imprecision and measurement error in assessing fruit/vegetable intake from self-report methods such as the food frequency questionnaire. We thus aimed to examine the association of plasma vitamin C, an objective biomarker of fruit/vegetable intake, and the risk of future diabetes. We also examined the association of diabetes with self-reported fruit and vegetable intake.

The EPIC-Norfolk Study

The European Prospective Investigation of Cancer-Norfolk (EPIC-Norfolk) study is a population-based cohort study. Men and women aged 40-75 years, resident in Norfolk, U.K. were identified from family-doctor age-sex registers, and of 77,754 invited, 25,639 attended for a health check visit in 1993-97. Dietary intake was assessed by a semi-quantitative food frequency questionnaire and vitamin C was measured in blood (plasma) samples. After exclusions, 21,831 individuals (9,815 men; 12,016 women) were eligible for analysis. Participants were without known diabetes at baseline, and we ascertained new-onset diabetes (n=735) over 12 years of follow up[6].

An association might be obscured by measurement error

There was a striking inverse association between plasma vitamin C concentration and the risk of new-onset diabetes, while the association with total fruit/vegetable intake was modest, and lacked the 'dose-response' effect seen with plasma vitamin C (Figure)6. The risk of diabetes in the top fifth (compared to bottom fifth) of the plasma vitamin C distribution was 62% lower (95% confidence limits 48% to 72% lower), while for a similar comparison for fruit/vegetable intake there was a modest 22% reduction in risk of diabetes (95% confidence limits 0% to 40% lower risk). These analyses accounted for other factors, such as potential healthier lifestyles among those who eat greater quantities of fruit/vegetable or have higher vitamin C levels [adjusting for age, sex, family history of diabetes, lifestyle factors (alcohol intake, smoking, physical activity), socio-economic status (education, social class), obesity (body mass index and waist circumference), and intake of vitamin supplements].

Conclusions

Evidence for the benefits of greater intake of fruits/vegetables for diabetes prevention is elicited strongly and convincingly when plasma vitamin C (a valid biomarker) is used as a proxy for fruit and vegetable intake. In contrast, the same association is attenuated and more modest when self-reported fruit/vegetable intake is used. Because fruit and vegetables are the main source of vitamin C, these findings suggest that eating even a small quantity of fruit/vegetables may be beneficial and that the protection against diabetes increases progressively with the quantity of fruit and vegetables consumed.

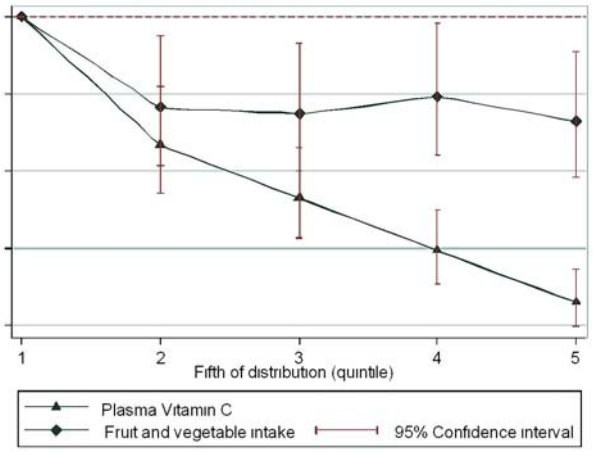

Figure: The association between intake of fruit/vegetables and plasma vitamin C on the risk of new-onset diabetes: EPIC-Norfolk study[6]

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Associations between dietary fiber and inflammation, hepatic function and risk of type 2 diabetes in older men: potential mechanisms for benefits of fiber on diabetes risk

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Dietary fiber is important in regulating blood sugar and several prospective studies have shown dietary fiber to have a protective effect on risk of type 2 diabetes[1, 2]. How much fiber is required and whether some kinds of fiber are better than others, remains uncertain. Moreover why fiber may be protective for diabetes is not clear. Several studies have shown inverse associations between dietary fiber and markers of inflammation, insulin sensitivity and hepatic function[3], factors which have been linked to the development of type 2 diabetes[4]. It has thus been proposed that the mechanisms by which fibre may reduce risk of diabetes may relate to it effect on hepatic function, improving insulin sensitivity or reducing inflammation. We examined prospectively the relationship between dietary fiber and the risk of type 2 diabetes in older men and evaluated the role of insulin and inflammatory and hepatic markers[5].

British Regional Heart Study

The subjects included 3,428 men aged 60 to 79 years without a diagnosis of diabetes who were originally enrolled in the British Regional Heart Study (BRHS) when aged 40-59 years[6]. The men were re-examined in 1998-2000 when aged 60-79 years. The population studied consisted almost entirely of white Europeans (>99%). The men completed a questionnaire which included questions on medical history, lifestyle behaviour and socioeconomic status. Information on fiber intake was obtained from a seven day recall food frequency questionnaire that was developed for use in the World Health Organisation MONICA survey. Anthropometric measurements including body weight, height and waist circumferences were carried out. Blood measurements were taken in the fasting state. Inflammatory markers including c-reactive protein (CRP), interleukin 6 (IL-6) and tissue plasminogen activator (t-PA) were measured. Gamma-glutamyl tranferase (GGT) was used as a marker of hepatic function. The men were followed up for all cause mortality, cardiovascular morbidity and development of type 2 diabetes. During the mean seven years follow up from rescreening in 1998-2000 to July 2006 there were 162 incident diabetes cases.

Dietary fiber and risk of type 2 diabetes

The average intake of total fiber was 25.85g/day. There was a trend towards lower levels of inflammation and hepatic function with increasing intake of total fiber. Those with high fibre intake showed significantly lower levels of inflammation (CRP, IL-6, t-PA) and hepatic function GGT than those with low intake even after taking into account age, lifestyle and demographic characteristics. We observed no significant association between dietary fiber and insulin levels. After adjustment for total energy intake and lifestyle and demographic factors, the lowest quartile of total dietary fiber (≤ 20 g/day) was associated with significantly increased risk for diabetes (relative risk [RR], 1.47; 95% confidence interval [CI], 1.03 - 2.11). Low cereal and low vegetable/fruit fiber intake were both associated with increased risk of diabetes. Dietary fiber was inversely associated with the inflammatory markers CRP and IL-6, as well as with t-PA and GGT. After adjusting for these markers, the increased risk for diabetes seen with low dietary fiber was attenuated (RR, 1.28; 95% CI, 0.89 - 1.86).

Conclusions

The data suggest a diet high in fiber (including both high cereal and high vegetable/fruit fiber intake) may reduce the risk of diabetes via favorable effects on reducing inflammation and attenuating or preventing hepatic fat accumulation. The mechanism for these associations between fiber intake and hepatic function and the inflammatory process however, requires further study. The available evidence suggests that high fiber intake (at least 20 grams/day) should be promoted to help offset diabetes risk.

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