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## « FRUIT & VEGETABLES AND DIABETES »

# <u>Editorial</u>

With regard to fruit and vegetables, prospective studies have so far produced quite inconsistent results when evaluating the risk to develop type 2 diabetes. This might in part be due to measurement error involved in the assessment of dietary intake.

One study in this issue used a quite unique approach to, at least in part, overcome this limitation. Dietary intake was assessed using a prospective 7-day food diary and thus allowed to estimate absolute intake of fruit and vegetables. However, even more interesting than the observed protective effect of higher total intake of fruit and vegetables is the observation that – independent of the quantity – a higher variety of fruit and vegetables consumed seems to reduce diabetes risk.

The second study in this issue deals with gestational diabetes, a common complication of pregnancy affecting increasing proportions of childbearing women. Women with gestational diabetes have an increased risk of type 2 diabetes in later years, however, gestational diabetes has severe effects on the offspring as well. Despite its potential importance there has been little research to the question whether diet before pregnancy is related to risk of gestational diabetes. The study adds valuable information indicating that consumption of fruit juices in moderate amounts might be beneficial, despite the relatively high sugar contents of juices.

The third study in this issue compares macro-level data on food availability and other societal measures with the prevalence of diabetes across countries. Higher availability of fruits and vegetables was related to lower prevalence rates after accounting for other risk factors. However, such data need to be treated quite cautiously given that prevalence rates of diabetes, and of many societal measures, are not collected in comparable time periods nor quality across the globe. Furthermore, macro-level studies are prone to ecological fallacy and results need to be seen to be indicative rather than confirmatory. Still, while there has been considerable effort to explain risk of diabetes within populations, more research is needed to answer what explains the large differences in diabetes prevalence between populations.

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## Fruit and Vegetable Quantity and Variety Both Matter for the Prevention of Type 2 Diabetes

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The recommendation by the World Health Organisation to consume a minimum of 400g or five portions (based on an average portion weighing 80g) of fruits and vegetables (F&V) each day for the prevention of several major chronic diseases, including diabetes, is now widely adopted by health agencies. Furthermore, programmes such as the "five-a-day" programme in the United Kingdom and similar programmes in other countries (e.g. United States) recommend consuming a variety of different F&V.

## Clarify the Respective Contributions of the Quantities and Varieties of F&V Consumption

There is compelling evidence for the effectiveness of lifestyle interventions for the primary prevention of diabetes, with promotion of increased F&V intake forming an important part of lifestyle modification<sup>1-3</sup>. However, the specific role of variety in F&V intake for the prevention of diabetes has not previously been investigated. Given the increasing burden of type 2 diabetes, with a projected rise in numbers with diabetes from 366 million globally in 2011 to 522 million by 2030<sup>4</sup>, it is important to clarify the contribution of both quantity and variety of F&V intake if we are to develop effective dietary public health strategies to prevent the disease.

We designed a study aimed at answering the following questions:

- Is the quantity of F&V intake related to the risk of developing diabetes after accounting for variety of intake?
- Conversely, is the variety of intake related to diabetes risk after accounting for quantity of intake?

## Assessing Quantity and Variety of F&V Intake Using a Food Diary in EPIC-Norfolk

The European Prospective Investigation of Cancer-Norfolk (EPIC-Norfolk) study is a population-based cohort study that recruited 25,639 men and women aged 40-75 years, resident in Norfolk, U.K<sup>5</sup>. All participants attended a health check in 1993-97. Dietary intake was assessed using a prospective 7-day food diary. We ascertained incident cases of diabetes (n=892) over 11 years of follow-up, and a representative comparison group (random subcohort) of 4,000 participants. After exclusions, the final sample consisted of 653 incident cases of diabetes and 3,166 subcohort participants. Average daily quantity of intake of fruits, vegetables, and F&V combined were computed. Variety of fruit, vegetables, and

combined F&V were derived by calculating the total number of different items consumed at least once in a one week period<sup>6</sup>.

## Increasing Variety of F&V, and Increasing Quantity of Vegetable Intake Decrease Risk of Type 2 Diabetes

In adjusted analyses, and after accounting for variety of intake, participants in the top third for quantity of vegetable intake (compared to bottom third) had a 24% lower incidence of diabetes (95% confidence interval (CI) 3% to 40% lower), while there was no relationship with quantity of fruit intake (9% lower; 95% CI ranging from 29% lower risk to 16% increased risk), and for combined F&V intake there was a borderline lower risk (21% lower incident diabetes, 95% CI 0% to 38% lower).

For variety of intake, fruit, vegetables and combined  $F\delta V$  intake were each strongly inversely related to a lower incidence of diabetes with a reduction of:

- 30% [95% CI: 9% to 47%] for fruit variety,
- 23% [95% CI: 2% to 39%] for vegetable variety,
- 39% [95% CI: 22% to 52%] for combined F&V variety.

These reductions were dependent of the effects of quantity of intake. These analyses accounted for important factors that may be related to diabetes risk or to potential healthier lifestyles among those with greater F&V intake, including age, sex, body mass index, waist circumference, education level, deprivation index, occupational social class, smoking status, physical activity level, family history of diabetes, energy intake and season.

## Maximum Benefit in the Prevention of Diabetes

These findings place particular emphasis on recognising the important and independent role of both quantity and variety, and suggest that a diet characterised by a greater quantity of vegetables and a greater variety of both F&V has the potential to reduce the risk of diabetes. Biologically plausible mechanisms include the low energy and high fibre content of F&V, combined with micronutrients and bioactive phytochemicals.

Overall, as well as consuming at least five portions of F&V each day, we should also select these portions from different fruit and vegetable categories in order to gain the maximum potential benefit for diabetes prevention.

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## Pre-pregnancy Consumption of Fruits and Fruit Juices and Gestational Diabetes

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## Gestational Diabetes, a Common Pregnancy Complication

Gestational Diabetes Mellitus (GDM) is usually defined as glucose intolerance with onset or first recognition in pregnancy. It is a common pregnancy complication that affects between 1-14% of all pregnancies<sup>1</sup>. The incidence of GDM is increasing worldwide, with the increasing burden of obesity among women of reproductive age. GDM has been related to substantial adverse health outcomes for both mothers and offspring and the impact of GDM goes beyond pregnancy. Women with GDM have an increased risk of perinatal morbidity and a considerably increased risk of impaired glucose tolerance and type 2 diabetes in the years after pregnancy. Children of women with GDM are more likely to be obese and have impaired glucose tolerance and diabetes in childhood and early adulthood. Collectively, this information highlights the importance of identifying modifiable factors for this common pregnancy complication, and of preventing GDM among high-risk populations<sup>1,2</sup>.

## Fruits: Rich in Antioxidant but also Rich in Sugar!

Fruits are major sources of certain nutrients such as vitamin C, flavonoids, magnesium, and fibre. Fruits have high antioxidant and fibre content as well as relatively low energy density and low glycemic load. In addition, fruits contain numerous bioactive components, such as vitamins, minerals, carotenoids, folates, flavonoids, and polyphenol, which have been suggested to be beneficial in insulin sensitivity and/or pancreatic  $\beta$ -cell function by relieving oxidative stress<sup>3</sup>.

On the other hand, fruits have relatively high sugar (i.e. fructose) content and thus there is some concern that high consumption of fruits may increase the risk of diabetes. Epidemiological data on habitual fruit intake and diabetes risk among pregnant women are scant. Fruit juices (100% juice) are conventionally considered as healthy and nutritious beverages. However, the relatively high sugar content and low fibre in fruit juices have raised concerns about high consumption during pregnancy. Studies on the association of fruit juices with GDM risk are lacking. In addition, nutrient components and antioxidant profiles of fruit varies by type. Therefore, different fruits and fruit juices may have different health effects. Thus studies on the associations of specific types of fruit with health outcomes are also needed.

#### **Apple Consumption Reduces Risk of GDM**

In a recent study based on a large prospective cohort of U.S. women<sup>2</sup>, the Nurses' Health Study II, we assessed the association of pre-pregnancy habitual consumption of fruit, fruit juices and their subgroups with GDM risk. In general, we observed that habitual high consumption of fruits in total before pregnancy was not associated with increased GDM risk. Among specific fruits, higher apple consumption (>1/day) was associated with a modestly reduced risk of GDM. The finding of an inverse association between apple intake and GDM risk is consistent with two studies on apples and type 2 diabetes risk<sup>4,5</sup>. Apples provide a low glycemic index source of carbohydrate, and are a major source of flavonoids. However, in the current study, the association of apple intake with GDM remained significant after the adjustment of flavonoid intakes. We speculate that other polyphenolic compounds (i.e., catechins), antioxidants (i.e., vitamin C and  $\beta$ -carotene), or unidentified dietary factors in apples, individually or in combination, may contribute to the potentially protective effects of apples on GDM risk<sup>2</sup>.

## For Fruit Juices, We Cannot Conclude

The association of total fruit juices with GDM risk was nonlinear, with the lowest risk being among women in the 3rd quintile of consumption (~half serving/day). The interpretation of this nonlinear association needs to be cautious. On one hand, vitamins, minerals, and phytochemicals in fruit juices may have beneficial effects for diabetes. On the other hand, fruit juices have lower fibre contents and higher glycemic load than whole fruit. At a moderate level of consumption, the beneficial effects from some components (i.e., vitamins and minerals) may counterbalance the potential adverse effects of the rapidly absorbed sugars. In this study, however, we were unable to completely rule out residual confounding from some unmeasured health behaviors associated with moderate fruit juice consumption<sup>2</sup>.

Our data suggest that pre-pregnancy higher consumption of whole fruits in total is not associated with increased GDM risk. There is some evidence that suggested a lower risk of GDM associated with higher apple consumption (>1/day). The association of fruit juices with GDM risk appears to be nonlinear, with the lowest risk being among women with modest consumption. Further studies are warranted to confirm our observation.



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## Societal Correlates of Diabetes Prevalence: An Analysis Across 94 Countries

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In this study, we quantified relationships between societal-level factors and diabetes prevalence. Researchers have previously explored singular relationships between societal factors – such as availability of certain foods, urbanization, passenger cars, motorways, and governance indicators – and Non-Communicable Diseases (NCDs). We sought to advance the field by quantifying relationships between diabetes and multiple socio-economic variables, isolating effects relative to and independent of interactions with other societal-level influences.

## A Wide Variety of Sources

We used data from the International Diabetes Federation, World Health Organization, World Bank, and Food and Agricultural Organization. We extracted 2010 estimates for country-level diabetes prevalence and identified country-level estimates for variables known to be associated with diabetes at the individual level: total caloric availability; sugar, animal fat, fruit and vegetable (F&V) availability (determined by food production, imports, and exports); proxies for physical inactivity (vehicles per capita and value-added from service sector); Gross Domestic Product per capita (GDP); imports; and age-adjusted mortality rate. We then used statistical models to investigate cross-sectional relationships between these factors and diabetes prevalence in 94 countries\*.

## Higher Availability of Fruits and Vegetables Is Associated with Lower Diabetes Prevalence

Our results indicate significant associations between multiple upstream societal-level indicators and diabetes prevalence, controlling for key factors like GDP per capita (purchasing power parity), mortality rate, and foreign direct investment (a marker of a country's integration into the global economy and exposure to packaged and processed foods). We estimated that a 10% higher availability of calories from F&V is associated with 30.6% lower diabetes prevalence. On the other hand, 10% lower availability of calories from sugar is associated with 61.5% lower diabetes prevalence and 10% lower availability of calories from animal fat is associated with 29.0% lower diabetes prevalence. Five hundred fewer available calories per person per day is associated with 5.2% lower diabetes prevalence.

## What Guidelines to Follow, Concretely?

Without assuming causality, the findings were then put into the

context of individuals in a population. For a 2,000 calories daily diet for the average adult individual, our results suggest that increasing F&V consumption by 5% could be accomplished by increasing the availability of F&V by one or two servings per person per day. This increased consumption would be associated with a 17% lower diabetes prevalence. Conversely, shifting daily energy from sugar by 5% would equate to consuming 100 fewer calories of sugar a day - drinking one less can of regular soda per day or eating half a chocolate bar less - and may be associated with 27% lower diabetes prevalence. Shifting daily energy from animal fat by 5% would equate to consuming 100 fewer calories of animal fat per day, and may be associated with 15% lower population diabetes prevalence. In light of the increasing diabetes burden in developing country regions, policies to increase availability of F&V and limit the unfettered availability of sugar, animal fat, and total calories may be worthy of further careful investigation, within a holistic nutrition strategy.

## **Offer More Fruits and Vegetables to Residents**

At the societal level, behavioral changes could be achieved by a wide variety of policy responses. For example, policy action to increase F&V consumption, including distribution (F&V are highly prone to spoiling before they reach their market destination, particularly in warm climates like India or Africa), cost, subsidies, and encouraging consumption at the individual level. Policy action to decrease sugar or animal fat availability and subsequent consumption, or to increase F&V consumption, could also examine trade policies to ensure that economic policies also consider availability and pricing of healthy versus unhealthy foods. In each case, policy responses should be tailored to the country-specific context, considering needs as well as available resources.

The United Nations High-Level Meeting on NCDs and the recently announced specific goal of a 25% reduction in the deaths due to NCDs by 2025 signifies an opportunity to act, encouraging policymakers to tailor country-level socioeconomic development through policies and resource allocation that continue to promote economic development while minimizing the negative health consequences of such development. We hope that our study may provide value through offering a quantitative understanding of the influence of upstream precipitants of diabetes, and guide conversations and future investigations to consider appropriate economic and social policy responses.



\*Countries included in the analysis were: **East Asia and Pacific**: Australia, China, Indonesia, Republic of Korea, Lao PDR, Mongolia, Philippines, Vietnam. **Europe and Central Asia**: Albania, Armenia, Austria, Belarus, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Georgia, Germany, Greece, Hungary, Italy, Kazakhstan, Kyrgyzstan, Latvia, Luxembourg, Macedonia (FYR), Moldova, Netherlands, Norway, Poland, Russian Federation, Slovakia, Spain, Sweden, Turkey, Ukraine, United Kingdom. South Asia: Bangladesh, Nepal, Pakistan, Sri Lanka. **Latin American and Caribbean**: Argentina, Belize, Bolivia, Brazil, Chile, Colombia, Costa Rica, Dominican Republic, Ecuador, El Salvador, Guatemala, Guyana, Honduras, Mexico, Panama, Peru, St. Vincent and Grenadines, Trinidad and Tobago. **Middle East and North Africa**: Jordan, Morocco, Syrian Arab Republic, Tunisia. Sub-**Saharan Africa**: Angola, Botswana, Cape Verde, Central African Republic, Comoros, Democratic Republic of the Congo, Republic of the Congo, Ethiopia, Gambia, Ghana, Kenya, Liberia, Malawi, Mauritius, Mozambique, Namibia, Rwanda, Senegal, Seychelles, Sierra Leone, South Africa, Sudan, Swaziland, Uganda, Zambia.

