



## Substitution of water or fresh juice for bottled juice and type 2 diabetes incidence: The SUN cohort study

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**Abstract** *Background and aims:* The relationship between juice consumption and type 2 diabetes (T2D) has not been widely evidenced. Our aims were to prospectively evaluate the associations with T2D incidence of: 1) isovolumetric substitution of a water serving/day for one of fruit juice (different types), and of fresh fruit juice for its bottled version; 2) consumption of total, fresh or bottled juice; 3) energy intake from juices.

*Methods and results:* We followed 17,518 adults without T2D at baseline. Beverage consumption was assessed at baseline through a validated food-frequency questionnaire. The outcome was T2D incidence, according to American Diabetes Association's criteria. During a median follow-up of 10.2 years, 142 incident cases of T2D were identified. In substitution models, the substitution of water for bottled juice was associated with a lower T2D incidence, and also if the replacement was done by fresh juice, or especially fresh orange juice [HR 0.75 (95% CI 0.57–0.99), 0.65 (95% CI 0.43–0.98) and 0.56 (95% CI 0.34–0.92); respectively]. Each additional serving/day of bottled juice was directly associated with T2D incidence [HR 1.33 (95% CI 1.01–1.75)]. No significant association was observed for energy coming from bottled juice [HR 1.74 (95% CI 0.94–3.20)]. *Conclusion:* Our results suggest that isovolumetric substitution of water or fresh juice for bottled juice was inversely associated with T2D incidence in a long-term prospective study. Thus, these substitutions could be useful to tackle the diabetes epidemic.

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**Abbreviations:** 95% CI, 95% confidence interval; BJ, bottled juice; BMI, body mass index; BMR, basal metabolic rate; FFQ, food frequency questionnaire; FJ, fresh juice; FNOJ, fresh non-orange fruit juice; FOJ, fresh orange juice; HR, hazard ratio; MET, metabolic equivalent of tasks; SENC, Spanish Society of Community Nutrition; SUN, Seguimiento Universidad de Navarra (University of Navarra follow-up); T2D, type 2 diabetes.

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### Introduction

Type 2 diabetes (T2D) is one of the most prevalent diseases worldwide and is associated with an increased morbidity and mortality. Global efforts are necessary as diabetic people is predicted to reach 642 million by 2040 [1].

One of the modifiable factors with the highest impact on T2D incidence is diet [2]. Recently, several recommendations about beverage consumption have been issued to promote a healthy dietary pattern [3,4], as they may be a

source of added sugars and, therefore, of extra calories. The direct relationship between caloric beverages intake, as sodas, and T2D incidence has been widely evidenced [5], but not for others like fruit juices, which seem to depend on the type of drink [6,7].

Our study had 3 objectives, to assess the potential association between T2D risk and the following exposures: 1: Substitution of a water serving/day for another of fruit juice (all types of fruit juices, bottled juice (BJ), fresh juice (FJ), fresh orange juice (FOJ), or fresh non-orange fruit juice (FNOJ)). We also assessed the substitution of FJ for BJ; 2: categories of consumption of the analyzed types of juices; 3: energy from fruit juices, or BJ. All analyses were performed according to baseline consumption.

## Methods

### Study population

We used data from the project Seguimiento Universidad de Navarra (University of Navarra Follow-up) (SUN), described in detail previously [8], which is a prospective cohort study. Recruitment started in 1999, and is permanently open. Every two years, participants' information is updated. All participants are university graduates, being most of them health professionals. The University of Navarra Research Ethics Committee approved the study [8].

For this analysis we assessed 21,678 participants recruited before March 2013. We excluded 89 patients not susceptible of developing T2D (they reported T2D but did not answer the additional questionnaire to confirm if he/she was a real case; had other types of diabetes; or were canceled or died in the period of time from the T2D declaration and its confirmation), 383 patients who had prevalent T2D (participants treated with insulin, oral anti-diabetics or a medical diagnosis of the disease), 2018 subjects with a total energy intake beyond the predefined limits (<800 Kcal/day and <500 Kcal/day, or >4000 Kcal/day and >3500 Kcal/day in men and women, respectively), 1609 participants who failed to answer the follow-up questionnaires (retention: 91.61%); 61 participants reporting less than two servings/week of liquids, and those not answering more than 9/18 beverage items in the FFQ and drank less than one serving/day of beverages, leaving a total of 17,518 participants for our final analyses.

### Beverage exposure assessment

The baseline validated questionnaire contained a semi-quantitative food frequency questionnaire (FFQ) [9]. It contained 3 beverage items about fruit juices (fresh orange juice, fresh non-orange fruit juice (both included in the term "fresh juice") and bottled juice) and 2 items related to water (tap and bottled water, considered as one item). These beverages serving size was 200 ml. Frequencies of consumption were measured in nine categories, from never/almost never to >6 servings/day. Missing values were recorded as no consumption. Daily intake was obtained by multiplying the frequency of consumption by the

serving size. Trained Nutritionists derived their nutrient content according to Spanish food composition tables.

### Outcome assessment

Probable cases of incident diabetes were those participants free of diabetes at baseline and reported a diagnosis by a doctor at follow-up. They answered to an additional confirmation questionnaire and their medical records were requested. An endocrinologist blind to the exposure confirmed incident cases, according to American Diabetes Association [10].

### Other variables assessment

The baseline questionnaire also inquired about socio-demographics, lifestyle, anthropometrics and medical history. Self-reported data, such as physical activity (total Metabolic Equivalent of Tasks (MET) per hour per week) or Body Mass Index (BMI) had been previously validated [11,12].

### Statistical analyses

We conducted Cox regression analyses to assess the association between T2D incidence and:

- the substitution of one water serving/day for another serving/day of each analyzed type of juice (juices in general, BJ, FJ, FOJ, or FNOJ) [13]. Furthermore, we related the substitution of FJ, FOJ or FNOJ for BJ with the incidence of T2D. Hazard ratios (HR) and 95% confidence intervals (95% CI) for isovolumetric substitutions were estimated as the difference between  $\beta$  coefficients of exchanged beverages and then exponentiated [13].
- categories of consumption of the different types of the analyzed fruit juices. HR and 95% CI were calculated using no consumption as the reference category; the second category consumed less than 1 serving/day, but more than the reference; the following category reported drinking 1–3 servings/day; and the highest category reported more than 3 servings/day. These categories are based on the Spanish Society of Community Nutrition (SENC) recommendations for juice intake [4]. Linear trends were analyzed introducing juice consumption as a continuous variable in the models. We additionally analyzed the association for one-serving/day increment in juice consumption.
- energy intake from juices in general or BJ specifically. We calculated the residuals of energy intake from juices. We categorized them in quintiles and thereafter we evaluated the association between these quintiles and T2D incidence. HR and 95% CI were calculated using the lowest quintile as the reference category.

We fitted a crude univariate model, an age- and sex-adjusted model, and a multiple-adjusted model additionally adjusted for baseline BMI, familiar diabetes history, smoking, adherence to the Mediterranean dietary pattern, physical activity, time spent in sedentary activities,

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