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(Article begins on next page)

Prepregnancy Consumption of Fruits and Fruit Juices and the Risk of Gestational Diabetes Mellitus

A prospective cohort study

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BRIEF REPOR

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OBJECTIVE—Examine the association of prepregnancy habitual consumption of fruits and fruit juices and gestational diabetes mellitus (GDM) risk.

RESEARCH DESIGN AND METHODS—A prospective study among women with at least one singleton pregnancy in the Nurses' Health Study II from 1991 to 2001.

RESULTS—Among 13,475 women, 860 reported a first diagnosis of GDM. The adjusted relative risks (RRs) for GDM from the lowest to highest quintile of whole fruit consumption were 1.00 (referent), 0.80 (95% CI 0.65-0.98), 0.90 (0.73-1.10), 0.80 (0.64-1.00), and 0.93 (0.76-1.16), respectively. The corresponding RRs for fruit juice were 1.00, 0.82 (0.66-1.01), 0.78 (0.63-0.96), 0.84 (0.68-1.04), and 1.00 (0.81-1.23).

CONCLUSIONS—These data suggest that prepregnancy higher consumption of whole fruits is not associated with an increased GDM risk. The association between fruit juices and GDM risk appears to be nonlinear.

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Ithough dietary factors have long been recognized for their roles in the development of impaired glucose tolerance, the association between intakes of fruit and fruit juice and the risk of gestational diabetes mellitus (GDM) has yet to be investigated. The objective of this study was to assess the association of prepregnancy habitual consumption of fruit and fruit juices and their subgroups with GDM risk in a large prospective cohort of U.S. women.

RESEARCH DESIGN AND METHODS—The Nurses' Health Study II is an ongoing prospective cohort of

female U.S. nurses. The cohort was initiated in 1989 and recruited 116,671 women aged 24 to 44. For this analysis, the final sample consisted of 13,475 women who did not have diabetes and major chronic diseases at baseline and were followed until 2001 (after which most women passed the reproductive age).

GDM cases were self-reported and updated every 2 years. A high validity of self-reported diagnosis of GDM in this cohort has been demonstrated (94% of women who reported to have GDM was confirmed by a physician in a validation study) (1). Dietary intake information was collected by a validated 133-item semiquantitative

food frequency questionnaire (2) designed to assess food intake during the previous year. For this analysis, we summed up the intake of single items to determine the consumption of fruit (nine items) and 100% fruit juices (four items) (for more information, see Supplementary Data).

All statistical analyses were performed using SAS statistical software (version 8.2; SAS Institute, Cary, NC). In primary analyses, we calculated the cumulative average intakes of dietary variables to reduce withinperson variation and to represent long-term dietary intakes. Relative risks (RRs) and 95% CIs of GDM were estimated using Cox proportional hazards models. Tests for nonlinear associations were performed using restricted cubic spline regressions (3).

RESULTS—Among 13,475 eligible women, 860 reported a first diagnosis of GDM. At baseline, the median intake was 1.0 serving/day (Supplementary Table 1). After adjustment for age, parity, race, smoking, alcohol intake, physical activity, family history of diabetes, BMI, and other dietary factors (Table 1; model 3), the RRs across the lowest to highest quintiles of fruit consumption were 1.00 (referent), 0.80 (95% CI 0.65-0.98), 0.90 (0.73-1.10), 0.80 (0.64–1.00), and 0.93 (0.76–1.16). In stratified analyses according to participants' BMI status (<25 or ≥ 25 kg/m²), family history of diabetes (yes or no), parity (1 or \geq 2), or physical activity (low or high), the direction of the association between GDM risk and fruit consumption was consistent in each stratum (data not shown). For subgroups of fruit and the risk of GDM (Table 1), only intake of apple was significantly associated with GDM risk. When apple intake was treated as a continuous variable. each additional serving per day of apple was associated with a 25% lower risk of GDM (95% CI 1-44). The association of 100% fruit juices with GDM risk was nonlinear, with the lowest risk being among women with moderate consumption (Table 1).

CONCLUSIONS—In this large prospective study, we found that habitual

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Fruits, fruit juices, and risk of GDM

Table 1—RR (95% CI) of GDM in relation to whole fruits and fruit juice consumption among participants in the Nurses' Health Study II (N=13,475; GDM case subjects n=860)

Whole fruits Servings per day (median) O.35 O.71 O.71 O.74 O.35 O.71 O.75 O.76 Case/PY O.76 O.76 O.77 O.77 O.78 O.77 O.78 O.78 O.79 O.79 O.79 O.79 O.79 O.79 O.79 O.79		Quintiles of cumulative averaged intake					
Servings per day (median)		Q 1	Q 2	Q 3	Q 4	Q 5	P value
Servings per day (median)	Whole fruits						
CasePY 226/108,600 163/120,203 167/101,745 149/103/367 164/110,315 149 Model 1 1,00 0.76 (0.62-0.92) 0.81 (0.67-0.99) 0.88 (0.55-0.84) 0.79 (0.65-0.97) 0.00		0.35	0.71	1.07	1.53	2.36	
Crude incidence per 100,000 PY							
Model 2							
Model 3*	•						0.03
Apples Servings per day (median)							0.44
Apples Servings per day (median) 0.07	Model 3*	1.00					0.76
Servings per day (median)							
Case/PY		0.07	0.11	0.14	0.43	0.79	
Crude incidence per 100,000 PY						113/98,915	
Model 3* 1.00	Crude incidence per 100,000 PY		· ·				
Bananas		1.00		0.82 (0.68-0.98)	0.78 (0.64-0.95)	0.81 (0.65–1.01)	0.045
Servings per day (mediam)			((((((((((((((((((((((,	,	
Case/PY 118/67/968 251/119/713 171/142/903 234/141,743 86/72,302		0	0.07	0.14	0.43	0.72	
Crude incidence per 100,000 PY 174 210 120 165 119 Model 3* 100 0.86 (6.69-1.07) 0.87 (6.68-1.10) 0.89 (0.71-1.12) 0.88 (6.66-1.16) 0.76	9 1 ,						
Model 3*	Crude incidence per 100,000 PY						
Berries (strawberry and blueberry) Servings per day (median) 0 0.07 0.11 0.14 0.43 Case/PY 165/131,181 253/117,085 36/51,764 270/159,316 136/85,283 Crude incidence per 100,000 PY 136 216 70 169 159 Model 3* 1.00 1.17 (0.96-1.43) 1.19 (0.82-1.73) 1.10 (0.90-1.34) 1.04 (0.82-1.31) 0.75 Citrus fruits (orange and grapefruit) Servings per day (median) 0 0.07 0.14 0.21 0.50 Case/PY 162/106,663 250/113,758 173/109,103 119/82,960 156/132,325 Crude incidence per 100,000 PY 152 220 159 143 118 Model 3* 1.00 1.28 (1.05-1.57) 1.08 (0.87-1.35) 1.22 (0.95-1.56) 1.11 (0.88-1.40) 0.99 Raisins Servings per day (median) 0 0.04 0.07 0.14 0.43 Case/PY 226/96,629 163/102,951 167/124,550 140/84,974 164/135,524 Crude incidence per 100,000 PY 108 136 164 135 149 Model 3* 1.00 0.94 (0.72-1.24) 0.92 (0.78-1.09) 0.81 (0.65-1.02) 0.86 (0.68-1.08) 0.19 Other fruits Servings per day (median) 0.07 0.21 0.32 0.50 0.96 Case/PY 213/115,979 135/107,000 185/110,923 166/107,620 161/103,098 Crude incidence per 100,000 PY 184 126 167 154 156 Model 3* 1.00 1.07 (0.86-1.33) 1.04 (0.85-1.28) 0.92 (0.75-1.14) 1.00 (0.80-1.24) 0.70 Fruit juices Servings per day (median) 0.10 0.28 0.57 1.00 1.72 Case/PY 248/119,393 146/114,957 148/98,842 154/103,228 164/108,209 Crude incidence per 100,000 PY 208 1.77 1.50 1.49 1.52 Model 1 1.00 0.82 (0.67-1.01) 0.73 (0.59-0.89) 0.74 (0.60-0.99) 0.83 (0.68-1.01) 0.06 Model 2 1.00 0.85 (0.69-1.05) 0.79 (0.64-0.97) 0.85 (0.69-1.04) 1.00 (0.81-1.22) 0.93 Model 3	•			0.87 (0.68–1.10)		0.88 (0.66–1.16)	0.76
Servings per day (median)				0.01 (0.00 2.120)	(0.00)	0.00 (0.00 =.=0)	
Case/PY		0	0.07	0.11	0.14	0.43	
Crude incidence per 100,000 PY 136 216 70 169 159 Model 3** 1.00 1.17 (0.96-1.43) 1.19 (0.82-1.73) 1.10 (0.90-1.34) 1.04 (0.82-1.31) 0.75 Citrus fruits (orange and grapefruit) Servings per day (median) 0 0.07 0.14 0.21 0.50 Case/PY 162/106,663 250/113,578 173/109,103 11982,960 156/132,325 Crude incidence per 100,000 PY 152 220 159 143 18 Model 3* 1.00 1.28 (1.05-1.57) 1.08 (0.87-1.35) 1.22 (0.95-1.56) 1.11 (0.88-1.40) 0.99 Raisins 1.00 0.04 0.07 0.14 0.43 0.43 Case/PY 226/96,629 163/102,951 167/124,550 140/84,974 164/135,524 Crude incidence per 100,000 PY 108 136 164 135 149 Model 3* 1.00 0.94 (0.72-1.24) 0.92 (0.78-1.09) 0.81 (0.65-1.02) 0.86 (0.68-1.08) 0.19 Case/PY 213/115,979 135/1							
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Servings per day (median) 0 0.07 0.14 0.21 0.50 Case/PY 162/106,663 250/113,788 173/109,103 119/82,960 156/132,325 Crude incidence per 100,000 PY 152 220 159 143 118 Model 3* 1.00 1.28 (1.05–1.57) 1.08 (0.87–1.35) 1.22 (0.95–1.56) 1.11 (0.88–1.40) 0.99 Raisins Servings per day (median) 0 0.04 0.07 0.14 0.43 Case/PY 226/96,629 163/102,951 167/124,550 140/84,974 164/135,524 Crude incidence per 100,000 PY 108 136 164 135 149 Model 3* 1.00 0.94 (0.72–1.24) 0.92 (0.78–1.09) 0.81 (0.65–1.02) 0.86 (0.68–1.08) 0.19 Case/PY 213/115,979 135/107,000 185/110,923 166/107,620 161/103,098 166/107,620 161/103,098 17 1.00 1.02 0.70 1.00 1.02 0.70 0.70 0.70 0.70 0.70 0.70		1.00	1.17 (0.50 1.15)	1.17 (0.02 1.13)	1.10 (0.50 1.51)	1.0 ((0.02 1.31)	0.13
Case/PY 162/106,663 250/113,578 173/109,103 119/82,960 156/132,325 Crude incidence per 100,000 PY 152 220 159 143 118 Model 3* 1.00 1.28 (1.05-1.57) 1.08 (0.87-1.35) 1.22 (0.95-1.56) 1.11 (0.88-1.40) 0.99 Raisins Servings per day (median) 0 0.04 0.07 0.14 0.43 0.43 Case/PY 226/96,629 163/102,951 167/124,550 140/84,974 164/135,524 164 135 149 140 140 164 135 149 140 140 164 135 149 149 140 140 156 164 135 149 149 140 140 140 149 152 140 140 140 140 149 152 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140		0	0.07	0.14	0.21	0.50	
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Case/PY 358/187,290 6/37,012 257/120,486 114/73,367 125/126,474 Crude incidence per 100,000 PY 191 16 213 155 99 Model 3# 1.00 0.75 (0.32–1.73) 1.08 (0.92–1.27) 1.06 (0.85–1.31) 0.97 (0.79–1.20) 0.72 Orange juice Servings per day (median) 0 0.07 0.14 0.43 1.00		0	0.02	0.07	0.14	0.43	
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Servings per day (median) 0 0.07 0.14 0.43 1.00		1.00	0.15 (0.52-1.15)	1.00 (0.92-1.21)	1.00 (0.05-1.51)	0.91 (0.19-1.20)	0.12
		0	0.07	0.14	0.43	1.00	
	9 1 ,						
Crude incidence per 100,000 PY 143 222 171 126 144			,			·	

Continued on p. 1081

	Quintiles of cumulative averaged intake					
	Q 1	Q 2	Q 3	Q 4	Q 5	P value†
Model 3#	1.00	1.02 (0.83–1.24)	0.90 (0.73–1.12)	0.94 (0.75–1.17)	0.97 (0.77–1.20)	0.70
Other fruit juice						
Servings per day (median)	0	0.04	0.07	0.22	0.61	
Case/PY	279/130,957	64/92,336	171/95,936	144/124,723	202/100,649	
Crude incidence per 100,000 PY	213	69	178	115	201	
Model 3#	1.00	1.22 (0.91–1.64)	0.92 (0.76–1.11)	1.03 (0.84–1.27)	1.04 (0.86–1.26)	0.64

Model 1: adjusted for age (5-year category) and parity (0, 1, 2, or \geq 3). Model 2: adjusted variables in model 1 plus race/ethnicity, cigarette smoking status (never, past, or current), family history of diabetes in a first-degree relative (yes or no), alcohol intake (five categories: 0, 0.1–5.0, 5.1–15.0, or \geq 15 g/day), physical activity (quintile), BMI (nine categories: $<21.0, 21.0–22.9, 23.0–24.9, 25.0–26.9, 27.0–28.9, 29.0–30.9, 31.0–32.9, 33.0–34.9, or <math>\geq$ 35.0 kg/m²). Model 3: adjusted variables in model 2 plus intake of cereal fiber (quintile), processed meat (quintile), red meat (quintile), sugar-sweetened beverages (quintile), and fruit juice* (quintile) or apple# (quintile). PY, person-years. †P value for the test of linear trend. *Model 3 fruit juice quintile. #Model 3 apple quintile.

high consumption of fruits before pregnancy was not associated with increased GDM risk. For whole fruit, a slightly lower risk was observed in the 2nd and 4th quintiles as compared with the lowest quintile after controlling for known risk factors of GDM. Among specific fruits, higher apple consumption was associated with a modestly reduced risk of GDM. The association of total fruit juices with GDM risk was nonlinear, with the lowest risk being among women in the 3rd quintile of consumption.

We are unaware of published studies that prospectively examine the association of prepregnancy consumptions of fruit and fruit juices with the risk of GDM. Previous prospective studies on fruit intake and type 2 diabetes risk have yielded mixed results (4-8). Fruits have high antioxidant and fiber 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 **β**-cell function by relieving oxidative stress (9). However, fruits also contain a relatively high amount of sugar (i.e., fructose), which has been directly linked to impaired pancreatic β -cell function in humans (10). It is highly likely that the overall health effect of whole fruit is a mix of many bioavailable compounds present in whole fruit and is dependent on the individuals' baseline consumption level.

Our finding of an inverse association between apple intake and GDM risk is consistent with two studies on apples and type 2 diabetes risk (11,12). Apples provide a low glycemic index source of carbohydrate, and are a major source of flavonoids. However, in the current study, flavonoids were not significantly associated with GDM risk, and the association of apple

intake with GDM remained significant after the adjustment of flavonoid intakes (data not shown). We speculate that other polyphenolic compounds (i.e., catechins), antioxidants (i.e., vitamin C and β -carotene), or unidentified dietary factors in apples, individually or in combination, may contribute to the potentially protective effects of apples on GDM risk.

The association of total fruit juices with GDM risk was nonlinear. 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 fiber 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.

In conclusion, our data suggest that prepregnancy higher consumption of whole fruits is not associated with increased GDM risk. 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 observations.

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No potential conflicts of interest relevant to this article were reported.

L.C. contributed to the design and analysis of the study and wrote the manuscript. F.B.H. interpreted the results and reviewed and edited the manuscript. E.Y. conducted the technique review and reviewed and edited the manuscript. D.K.T. reviewed and edited the manuscript. W.C.W. reviewed, edited, and commented on the manuscript. C.Z. contributed to the design and analysis of the study and reviewed and edited the manuscript. L.C. and C.Z. are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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