A Prospective Study of the Association Between Quantity and Variety of Fruit and Vegetable Intake and Incident Type 2 Diabetes

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OBJECTIVE—The association between quantity of fruit and vegetable (F&V) intake and risk of type 2 diabetes (T2D) is not clear, and the relationship with variety of intake is unknown. The current study examined the association of both quantity and variety of F&V intake and risk of T2D.

RESEARCH DESIGN AND METHODS—We examined the 11-year incidence of T2D in relation to quantity and variety of fruit, vegetables, and combined F&V intake in a case-cohort study of 3,704 participants (n = 653 diabetes cases) nested within the European Prospective Investigation into Cancer and Nutrition-Norfolk study, who completed 7-day prospective food diaries. Variety of intake was derived from the total number of different items consumed in a 1-week period. Multivariable, Prentice-weighted Cox regression was used to estimate hazard ratios (HRs) and 95% CIs.

RESULTS—A greater quantity of combined F&V intake was associated with 21% lower hazard of T2D (HR 0.79 [95% CI 0.62–1.00]) comparing extreme tertiles, in adjusted analyses including variety. Separately, quantity of vegetable intake (0.76 [0.60–0.97]), but not fruit, was inversely associated with T2D in adjusted analysis. Greater variety in fruit (0.70 [0.53–0.91]), vegetable (0.77 [0.61–0.98]), and combined F&V (0.61 [0.48–0.78]) intake was associated with a lower hazard of T2D, independent of known confounders and quantity of intake comparing extreme tertiles.

CONCLUSIONS—These findings suggest that a diet characterized by a greater quantity of vegetables and a greater variety of both F&V intake is associated with a reduced risk of T2D.

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Type 2 diabetes (T2D) is one of the most common noncommunicable diseases worldwide and is a leading cause of premature mortality (1), morbidity (2), and health care expenditure (3). Lifestyle intervention trials that include dietary changes have been shown to be effective in preventing the development of T2D (4). However, it is still largely unknown which aspects of the diet confer this beneficial effect.

A World Health Organization expert consultation recommended a minimum intake of 400 g or five portions (based on an average portion weighing 80 g) of combined fruits and vegetables (F&V) per day for the prevention of several major noncommunicable diseases, including T2D (5). In addition, the five-a-day program in the U.K. and similar programs in other countries (e.g., the U.S.) (6) recommend consuming a variety of different F&V, thereby ensuring adequate intake of micronutrients, dietary fiber, and a multitude of other important bioactive compounds (7). Yet, the specific role of variety in F&V intake and T2D has not been examined. Additionally, as studies have generally used a food frequency questionnaire (FFQ) to assess F&V intake, which is suitable for ranking individuals according to their relative but not absolute intake (8), there is also an absence of research on the importance of meeting the five-a-day quantity recommendation for F&V intake. The use of a prospective food diary offers a more precise measure of dietary intake and can overcome some of the limitations of the FFQ (9), but so far no studies have used this dietary assessment method in relation to T2D risk.

In order to develop effective dietary public health strategies for T2D prevention, it is essential to clarify the contribution of both quantity and variety of F&V intake to T2D risk. The aim of this study was therefore to evaluate the association between the quantity and variety of fruit, vegetables, and combined F&V consumption, as assessed using a prospective 7-day food diary, and incident T2D.

RESEARCH DESIGN AND METHODS

Study population

The Norfolk component of the European Prospective Investigation into Cancer and Nutrition (EPIC-Norfolk) study recruited 25,639 men and women aged 40–79 years at baseline in 1993–1997. The EPIC-Norfolk study was initiated to investigate the relationship between diet and cancer but has since broadened its scope to include a range of chronic diseases, including T2D. The recruitment procedures, collection of questionnaire data, and anthropometric and dietary measures have been described in detail elsewhere (10,11). In brief, participants residing in Norfolk, England, were recruited from age-sex registers of general practices and attended a baseline health check. Follow-up of participants constituted

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a postal questionnaire at 18 months, a second health check in 1998–2000, and a further postal questionnaire in 2002–2004.

From the 25,639 participants in EPIC-Norfolk at baseline, we ascertained incident cases of T2D (n = 892) and selected a random subcohort of 4,000 participants. This subcohort was representative of the entire EPIC-Norfolk cohort in terms of age, BMI, education level, physical activity level, smoking status, and total energy intake (data not shown). Among the subcohort, there were 143 individuals who developed incident T2D during follow-up. Of the 4,749 participants, we excluded those with unknown diabetes status (n = 1) or prevalent diabetes at baseline (n = 121), those with fewer than 7 days of diary data (n = 435) or who did not return a diary (n = 15), or those with missing information on potential confounding variables (n = 73). Participants with prevalent myocardial infarction, stroke, or cancer were also excluded (n = 400). The final sample for analysis consisted of 653 incident T2D cases and a subcohort of 3,166 individuals (including 115 incident T2D cases). All volunteers gave written informed consent, and the study was approved by the Norwich district ethics committee.

Case ascertainment

We ascertained incident T2D cases by self-report of doctor-diagnosed diabetes from three follow-up health and lifestyle questionnaires, i.e., answering "yes" to "Has a doctor ever told you that you have diabetes?" or diabetes medication that was self-reported or brought to the second health check. In addition, external sources of information through record linkage included listing of any EPIC-Norfolk participant in the general practice diabetes register, local hospital diabetes register, hospital admissions data with screening for any diabetes-related admissions among study participants, and Office of National Statistics mortality data with coding for diabetes. Participants who gave a self-report of history of diabetes that could not be confirmed against any other sources of ascertainment were not considered as a confirmed case of T2D. Follow-up was censored at the date of diagnosis of T2D, 31 July 2006, or the date of death, whichever came first.

Assessment of diet and lifestyle variables

At the baseline medical examination, participants were instructed by trained interviewers on how to complete the 7-day food diary (11,12). The food diary consisted of 45 color pages containing food portion photographs and detailed instructions on how to record and describe preparation methods and quantities of foods eaten at main meals, snacks, and between meals. Completed diaries were returned by post to the coordinating center at the University of Cambridge. The food diary has been validated with weighed food records, 24-h urine collections, and blood biomarkers (13).

Intake of F&V (including tinned and dried) was calculated from food diary data to give average daily quantity of intake for each participant. In order to precisely quantify the actual intake of F&V consumed alone or from dishes (in accordance with the U.K. five-a-day public health guidelines) (14), all recorded foods and dishes were disaggregated into their component parts. Composite dishes containing fruits and/or vegetables included homemade and shop-bought desserts, vegetable bakes, stews, pies, and soups, for example. The F&V quantity and type was derived for the composite dishes by using recipes from McCance and Widdowson as previously described (12) and by using ingredients listed on the packages of products and ready-made meals. Potatoes were not included as a vegetable because they differ from vegetables regarding energy and carbohydrate content and are frequently used as a substitute for cereals (15). F&V juices were also not included because they differ from their source of origin in terms of food matrix and fiber content, and as such may be dissimilarly associated with diabetes (16). Variety of fruit, vegetables, and combined F&V intake was derived by calculating the total number of different items consumed at least once in a 1-week period, irrespective of quantity of intake. The groupings of items included 58 different fruit items (range 0–58), 59 different vegetable items (range 0–59), and hence a total of 117 different F&V items consumed over a 1-week period, as recorded in the 7-day food diary.

At recruitment, participants completed a detailed health and lifestyle questionnaire. Participants self-reported their education level (low, O level, A level, or degree), occupational social class (manual or nonmanual), smoking status (current, former, or never), and baseline history of myocardial infarction, stroke, and cancer (yes or no). Area deprivation was assessed from residential postal codes using the Townsend Deprivation Index, which provides a material measure of deprivation and disadvantage based on unemployment, car ownership, home ownership and household overcrowding. A higher Townsend Index score indicates greater deprivation (17). A validated, four-point physical activity index was derived, incorporating occupational and leisure-time components of physical activity (18). Trained nurses measured height, weight, and waist circumference according to standardized protocols (10). BMI was calculated as weight divided by height (kg/m^2). Venous blood samples were taken by trained study nurses. Hemoglobin A_{1c} (HbA_{1c}) was measured halfway through the baseline health check (1995–1997) and was available in approximately half of the EPIC-Norfolk cohort. HbA_{1c} was measured using high-performance liquid chromatography on a Bio-Rad Diamat (Bio-Rad, Richmond, CA), on a sample of EDTA-anticoagulated blood.

Statistical analysis

Baseline characteristics were summarized by tertiles of combined F&V quantity and variety among the subcohort participants, using means with SDs, medians with interquartile ranges (IQRs), or frequencies (where appropriate).

Multivariable, Prentice-weighted Cox regression (19) was used to estimate the associations between quantity and variety of fruit, vegetables, and combined F&V intake and hazard of diabetes, with intake defined as tertiles (with the lowest tertile as the reference category). To check the proportional hazards assumption of the models, interactions between quantity and variety of fruit, vegetables, and combined F&V intake and current age (i.e., the underlying timescale) were tested. The proportional hazards assumption was not violated for quantity and variety of fruit, vegetables, or combined F&V intake (all P values $\geq$0.32). Hazard ratios (HRs) and 95% CIs were estimated using the following modeling strategy. Age was used as the underlying timescale in all models. Model 1 was adjusted for sex. In Model 2, we additionally adjusted for BMI (continuous), waist circumference (continuous), education level (low, O level, A level, or degree), Townsend Deprivation Index (continuous), occupational social class (manual or nonmanual), physical activity level (inactive, moderately inactive, moderately active, or active), smoking status (current, former, or never), family history of diabetes (yes or no), total energy intake (continuous), and season of diary completion (December, January, February = winter; March, April, May = spring; June,

July, August = summer; and September, October, November = autumn). In Model 3, in order to estimate the association between quantity of F&V consumption and hazard of diabetes independent of the effect of variety, we additionally adjusted for variety of F&V intake and vice versa for the analysis of variety in intake. We examined multicolinearity in Model 3 using the variance inflation factor.

In sensitivity analyses, the association between F&V quantity and variety and the hazard of diabetes was also investigated by including other potentially confounding variables in Model 3, including hypertension (yes or no), dairy intake (continuous), total fiber intake (continuous), red and processed meat intake (continuous), and percentage energy from carbohydrate (continuous), protein (continuous), fat (continuous), and alcohol intake (continuous). Analyses were also repeated after additionally excluding participants who *1*) developed diabetes within the first 2 years of follow-up (n = 26), *2*) had a baseline HbA_{1c} level ≥6.5% (n = 15) in the subsample with HbA_{1c} data available (n = 1,333), and *3*) were in the top and bottom 1% of the ratio of energy intake to energy expenditure. Multiplicative interaction terms were added to Model 3 for quantity and variety of combined F&V intake to examine effect modification by sex, age (<60 or ≥60 years), BMI (normal weight <25 kg/m^2, overweight/obese ≥25 kg/m^2), and smoking status (never smoker or ever smoker) by using the Wald test. Additionally, spline regression was used to demonstrate the continuous association between quantity and variety of combined F&V intake and the HR (95% CI) of diabetes with knots placed at quartiles of the distribution (20).

All statistical analyses were performed using Stata/SE 11.1 (Stata-Corp, College Station, TX). Statistical significance was set at $P < 0.05$.

RESULTS—The median (IQR) duration of follow-up was 10.9 (9.8–11.8) years. The median quantity of combined F&V intake was 3.7 (2.5–5.0) portions per day and the mean (SD) variety of combined F&V intake was 11.7 (3.9) items/week. Fewer than 26% of study participants reported consuming at least five portions of F&V per day. There was nearly a threefold difference in quantity and in excess of a twofold difference in variety of combined F&V consumption between the highest versus lowest tertiles of F&V intake (Table 1). Participants who consumed higher quantities and a greater variety of combined F&V had more favorable lifestyle, anthropometric, and dietary profiles. Baseline characteristics by tertiles of quantity and variety of fruit and vegetable intake separately showed similar results (data not shown). The Pearson correlation coefficient between quantity of fruit and quantity of vegetable intake was 0.29, and between variety of fruit and variety of vegetable intake was 0.30. Quantity of combined F&V intake was strongly positively correlated with variety of combined F&V intake (0.60).

As shown in Table 2, quantity of fruit, vegetables, and combined F&V intake were all inversely associated with incident T2D (Model 1). Further adjustment did not appreciably alter the HRs (Model 2). After additionally adjusting for the effects of variety of intake, an inverse association with quantity of vegetable intake remained, but the associations for quantity of fruit and quantity of combined F&V intake with T2D were attenuated, such that fruit was no longer associated and F&V intake was borderline inversely associated with T2D. Further adjustment for hypertension, dairy intake, total fiber intake, percentage energy from carbohydrate, protein, fat, and alcohol intake, and red and processed meat intake did not change our results (data not shown). Those meeting the recommendation to consume at least five portions of F&V per day did not differ from those not meeting this recommendation in hazard of T2D, excluding and including variety of intake (HR 0.85 [95% CI 0.70–1.02] and 0.98 [0.80–1.21], respectively). As shown in Table 3, greater variety in fruit, vegetables, and combined F&V intake was inversely associated with incident T2D in adjusted analyses and also when accounting for quantity of intake. The relative reduction in the hazard of T2D with every additional two-item increase in F&V variety per week was 8% (0.92 [0.87–0.97]). The mean estimated variance inflation factor was <1.9 (<1.6 for both F&V quantity and F&V variety), indicating that colinearity of the variables included in Model 3 was low.

Figure 1 shows the continuous association between quantity and variety of combined F&V intake and T2D. As shown, the HR for T2D decreased between an intake of ~3.5–7.0 portions per day (Fig. 1*A*), and this association was largely unchanged after accounting for the effects of variety of F&V (Fig. 1*B*). For variety, consuming ≥12 different F&V items per week was associated with a decreased HR of T2D (Fig. 1*C*), and this association was largely unaffected after accounting for the effects of quantity of F&V intake (Fig. 1*D*). The percentage of participants achieving a quantity of >3.5 portions per day was 53.2%, and the percentage achieving a variety of >12 different F&V items per week was 40.3%.

Results were unaffected in sensitivity analyses after excluding participants who *1*) developed T2D within the first 2 years of follow-up, *2*) had a baseline HbA_{1c} level of ≥6.5% in the subsample with HbA_{1c} data, and *3*) were in the top and bottom 1% of energy intake to energy expenditure (data not shown). We found no evidence of interaction between either quantity or variety in F&V intake with sex, age, BMI, or smoking status and incident diabetes ($P > 0.10$).

CONCLUSIONS—In this prospective study of nearly 4,000 men and women with dietary information from prospective 7-day food diaries, we observed that a greater quantity of vegetable intake and a greater variety of fruit, vegetables, and combined F&V intake may independently be beneficial for reducing the risk of T2D. After accounting for potential confounding factors and the effects of quantity of intake, each different additional two item per week increase in variety of F&V intake was associated with an 8% reduction in the incidence of T2D.

Previous epidemiological studies have reported inconsistent findings for an association between quantity of F&V intake and risk of T2D. Two separate meta-analyses have reported no overall association between fruit, vegetables, and combined F&V intake and diabetes risk, although there was significant heterogeneity of association between the included studies (21,22). The meta-analysis by Carter et al. (21) did however find a significant inverse association between green leafy vegetable intake and risk of T2D (HR for highest vs. lowest intake group 0.86 [95% CI 0.77–0.97]). Although low heterogeneity in F&V consumption may be one explanation for the null findings in some study populations, our current results suggest that it may also be due to differences in the assessment methods used for measuring F&V intake. Most epidemiological studies have used an FFQ to assess quantity of F&V intake. Although FFQs can be used to rank individuals according to their relative intake (8), they are less suitable for the assessment of absolute intake (11,23), which they tend to overestimate. For example,

Table 1—*Descriptive characteristics at baseline by combined F&V quantity and variety tertiles in 3,166 subcohort participants in the EPIC-Norfolk study*

Median (IQR) quantity of intake (portions/day) or mean (SD) variety of intake (no. items/week)	Tertiles of combined F&V quantity				Tertiles of combined F&V variety			
	Low	Medium	High		Low	Medium	High	
	2.1 (1.6–2.5)	3.7 (3.3–4.0)	5.7 (5.0–6.8)	*P* value	8.0 ± 1.8	12.0 ± 0.8	16.3 ± 2.3	*P* value
N	1,055	1,056	1,055		1,265	927	974	
Age at recruitment (years)	58.5 (9.8)	59.1 (9.2)	59.8 (9.0)	0.002	58.8 (9.7)	59.3 (9.4)	59.3 (8.9)	0.24
Men, no. (%)	523 (49.6)	437 (41.4)	408 (38.7)	<0.001	637 (50.4)	393 (42.4)	338 (34.7)	<0.001
Education level, no. (%)				<0.001				<0.001
Low	450 (42.7)	351 (33.2)	345 (32.7)		525 (41.5)	325 (35.1)	296 (30.4)	
O level	97 (9.2)	118 (11.2)	103 (9.8)		123 (9.7)	98 (10.6)	97 (10.0)	
A level	411 (39.0)	443 (42.0)	426 (40.4)		498 (39.4)	369 (39.8)	413 (42.4)	
Degree	97 (9.2)	144 (13.6)	181 (17.2)		119 (9.4)	135 (14.6)	168 (17.3)	
Occupational social class, no. (%)				<0.001				<0.001
Manual	476 (46.2)	432 (41.6)	355 (33.9)		584 (47.2)	352 (38.6)	327 (33.9)	
Nonmanual	555 (53.8)	606 (58.4)	692 (66.1)		653 (52.8)	561 (61.5)	639 (66.2)	
Townsend Deprivation Index	−2.0 (2.2)	−2.2 (2.1)	−2.2 (2.1)	0.30	−1.9 (2.3)	−2.2 (2.1)	−2.3 (2.0)	0.003
BMI (kg/m^2)	26.2 (3.7)	26.1 (3.7)	26.2 (3.9)	0.52	26.4 (3.8)	26.1 (3.8)	26.0 (3.7)	0.002
Waist circumference (cm)	88.4 (11.9)	87.3 (12.2)	86.8 (12.3)	<0.001	88.9 (12.2)	87.2 (11.8)	85.9 (12.3)	<0.001
Physical activity level, no. (%)				<0.001				0.001
Inactive	358 (33.9)	279 (26.4)	270 (25.6)		409 (32.3)	264 (28.5)	234 (24.0)	
Moderately inactive	278 (26.4)	319 (30.2)	329 (31.2)		335 (26.5)	288 (31.1)	303 (31.1)	
Moderately active	207 (19.6)	255 (24.2)	254 (24.1)		273 (21.6)	199 (21.5)	244 (25.1)	
Active	212 (20.1)	203 (19.2)	202 (19.2)		248 (19.6)	176 (19.0)	193 (19.8)	
Smoking status, no. (%)				<0.001				<0.001
Current smoker	191 (18.1)	89 (8.4)	71 (6.7)		201 (15.9)	84 (9.1)	66 (6.8)	
Former smoker	425 (40.3)	446 (42.2)	436 (41.3)		539 (42.6)	374 (40.4)	394 (40.5)	
Never smoker	439 (41.6)	521 (49.3)	548 (51.9)		525 (41.5)	469 (50.6)	514 (52.8)	
Total energy intake (kcal/day)	1,867 (1,559–2,271)	1,918 (1,628–2,279)	1,932 (1,641–2,274)	0.006	1,882 (1,562–2,285)	1,904 (1,621–2,294)	1,929 (1,657–2,242)	0.04
Alcohol intake (% total energy)	1.7 (0.0–6.4)	2.1 (0.0–5.6)	2.1 (0.0–6.0)	0.48	1.6 (0.0–5.6)	1.9 (0.0–5.8)	2.5 (0.5–6.4)	<0.001
Variety in combined F&V intake (no. items/week)	8.8 (2.9)	11.9 (3.0)	14.3 (3.6)	<0.001	—	—	—	—
Variety in fruit intake (no. items/week)	2.3 (1.5)	3.9 (1.5)	5.3 (2.0)	<0.001	—	—	—	—
Variety in vegetable intake (no. items/week)	6.5 (2.4)	8.0 (2.6)	9.1 (2.7)	<0.001	—		—	—
Quantity of combined F&V intake (portions/day)	—	—	—	—	2.5 (1.8–3.5)	3.7 (2.9–4.8)	5.0 (4.0–6.3)	<0.001
Quantity of fruit intake (portions/day)	—	—	—	—	1.1 (0.5–1.9)	1.9 (1.1–2.8)	2.7 (1.8–3.7)	<0.001
Quantity of vegetable intake (portions/day)	—	—	—	—	1.3 (0.9–1.7)	1.8 (1.4–2.3)	2.3 (1.8–2.9)	<0.001

Data are means (SD), medians (IQR), and % for categorical variables. *P* values are from the test for trend for continuous variables and the χ^2 test for categorical variables.

Table 2—*HRs (95% CIs) of incident diabetes for quantity of fruit, vegetables, and combined F&V intake in the EPIC-Norfolk study*

	Low	Medium	High	*P* for trend
Tertiles of quantity of fruit intake				
Case subjects/total (*n*)	261/1,269	193/1,214	199/1,221	
Median (IQR) intake (portions/day)	0.6 (0.3–0.9)	1.8 (1.5–2.1)	3.4 (2.9–4.4)	
Model 1	1 (Reference)	0.72 (0.59–0.86)	0.77 (0.64–0.93)	0.004
Model 2	1 (Reference)	0.72 (0.59–0.87)	0.75 (0.61–0.91)	0.003
Model 3	1 (Reference)	0.81 (0.65–1.00)	0.91 (0.71–1.16)	0.46
Tertiles of quantity of vegetable intake				
Case subjects/total (*n*)	245/1,260	229/1,236	179/1,208	
Median (IQR) intake (portions/day)	1.1 (0.8–1.3)	1.7 (1.6–1.9)	2.6 (2.3–3.1)	
Model 1	1 (Reference)	0.91 (0.76–1.06)	0.72 (0.59–0.87)	0.001
Model 2	1 (Reference)	0.88 (0.73–1.06)	0.72 (0.58–0.87)	0.001
Model 3	1 (Reference)	0.91 (0.74–1.11)	0.76 (0.60–0.97)	0.03
Tertiles of quantity of combined F&V intake				
Case subjects/total (*n*)	268/1,277	188/1,206	197/1,221	
Median (IQR) intake (portions/day)	2.1 (1.6–2.5)	3.7 (3.3–4.0)	5.7 (5.0–6.8)	
Model 1	1 (Reference)	0.70 (0.58–0.84)	0.72 (0.60–0.87)	<0.001
Model 2	1 (Reference)	0.68 (0.56–0.82)	0.68 (0.56–0.83)	<0.001
Model 3	1 (Reference)	0.73 (0.60–0.90)	0.79 (0.62–1.00)	0.04

Data are HRs (and 95% CIs) estimated using Prentice-weighted Cox regression, with age as the underlying timescale variable. Adjustment for covariates was performed using multivariable, Prentice-weighted Cox proportional analyses. Model 1 was adjusted for sex. Model 2 was adjusted for the same covariates as Model 1 plus BMI, waist circumference, education level, Townsend Deprivation Index, occupational social class, smoking status, physical activity, family history of diabetes, energy intake, and season. Model 3 was adjusted for the same covariates as Model 2 plus fruit variety for fruit quantity, vegetable variety for vegetable quantity, or combined F&V variety for combined F&V quantity.

in the EPIC-Norfolk study, mean consumption of F&V was much higher when assessed by FFQ (6.5 portions per day) than by a food diary (3.8 portions per day) (11). For this reason, FFQs are not ideal for examining adherence to, or for informing, public health guidelines. Furthermore, FFQs are based on perceptions of habitual intake, whereas food diaries are based on self-report of foods and amounts actually consumed in real time (8). Additionally, because FFQs contain only a limited list of precoded food items, which tend to be grouped together, unlike the food diary, which is open ended, they may not be as suitable as food diaries for assessing variety of food intake. Despite the fact that variety in F&V intake has

Table 3—*HRs (95% CIs) of incident diabetes for variety of fruit, vegetables, and combined F&V intake in the EPIC-Norfolk study*

	Low	Medium	High	*P* for trend
Tertiles of variety of fruit intake				
Case subjects/total (*n*)	355/1,744	197/1,247	101/713	
Mean intake (no. items/week)	2.0 ± 1.0	4.4 ± 0.5	6.9 ± 1.2	
Model 1	1 (Reference)	0.74 (0.62–0.88)	0.67 (0.54–0.84)	<0.001
Model 2	1 (Reference)	0.72 (0.60–0.86)	0.71 (0.56–0.89)	<0.001
Model 3	1 (Reference)	0.72 (0.59–0.87)	0.70 (0.53–0.91)	0.002
Tertiles of variety of vegetable intake				
Case subjects/total (*n*)	348/1,759	172/1,004	133/941	
Mean intake (no. items/week)	5.5 ± 1.4	8.5 ± 0.5	11.4 ± 1.5	
Model 1	1 (Reference)	0.85 (0.71–1.02)	0.68 (0.56–0.84)	<0.001
Model 2	1 (Reference)	0.85 (0.70–1.03)	0.73 (0.59–0.89)	0.002
Model 3	1 (Reference)	0.87 (0.72–1.07)	0.77 (0.61–0.98)	0.03
Tertiles of variety of combined F&V intake				
Case subjects/total (*n*)	321/1,530	193/1,084	139/1,090	
Mean intake (no. items/week)	8.0 ± 1.8	12.0 ± 0.8	16.3 ± 2.3	
Model 1	1 (Reference)	0.83 (0.69–0.99)	0.57 (0.47–0.70)	<0.001
Model 2	1 (Reference)	0.88 (0.73–1.06)	0.60 (0.49–0.74)	<0.001
Model 3	1 (Reference)	0.88 (0.73–1.07)	0.61 (0.48–0.78)	<0.001

Data are HRs (and 95% CIs) estimated using Prentice-weighted Cox regression, with age as the underlying timescale variable. Adjustment for covariates was performed using multivariable, Prentice-weighted Cox proportional analyses. Model 1 was adjusted for sex. Model 2 was adjusted for the same covariates as Model 1 plus BMI, waist circumference, education level, Townsend Deprivation Index, occupational social class, smoking status, physical activity, family history of diabetes, energy intake, and season. Model 3 was adjusted for the same covariates as Model 2 plus fruit quantity for fruit variety, vegetable quantity for vegetable variety, or combined F&V quantity for combined F&V variety.

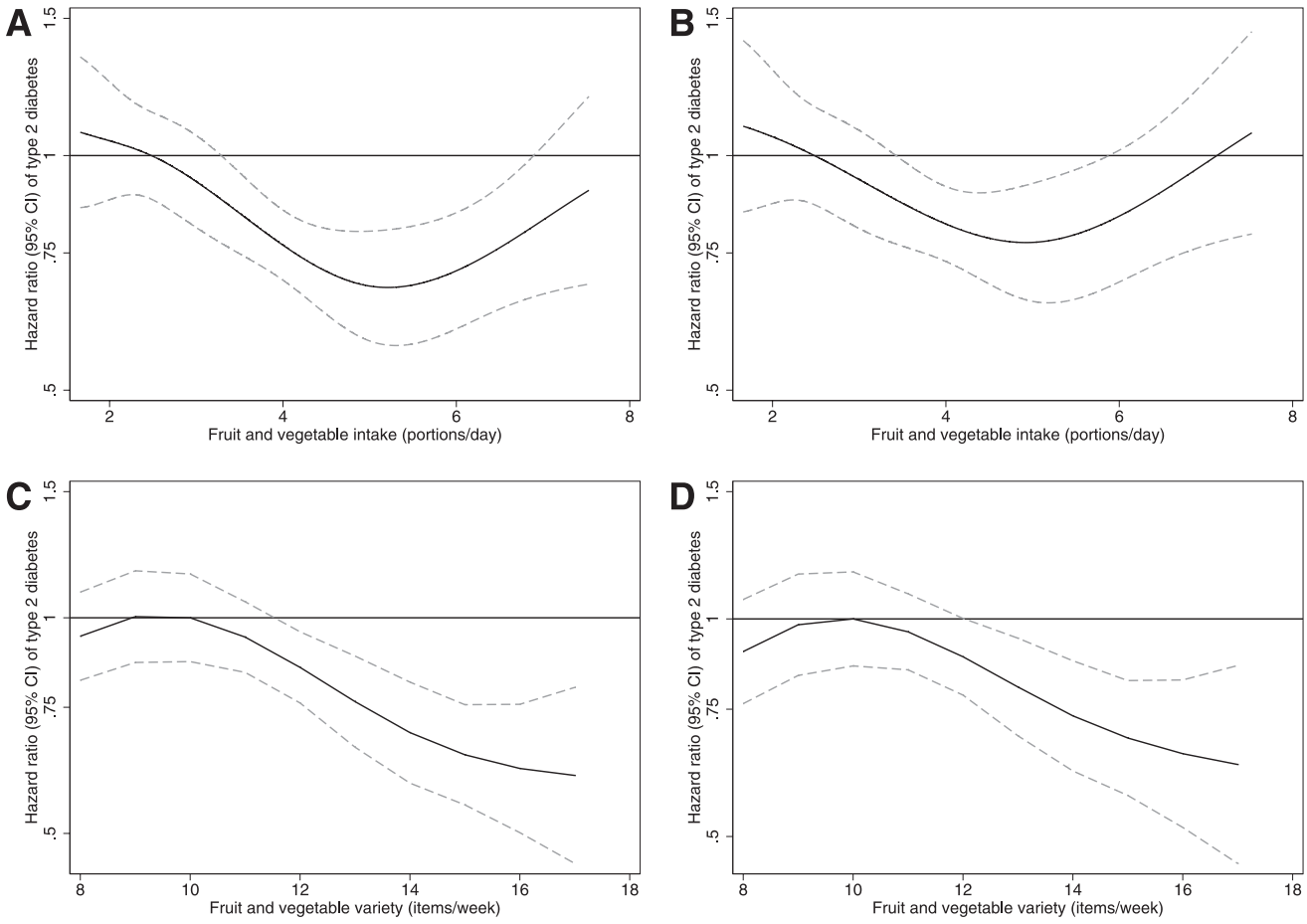

Figure 1—*The upper percentile of the first tertile for quantity and variety of F&V intake was used as the reference category.* A*: The association between quantity of F&V intake and HR (95% CI) of diabetes adjusted for sex, BMI, waist circumference, education level, Townsend Deprivation Index, occupational social class, physical activity level, smoking status, family history of diabetes, total energy intake, and season.* B*: Same as* A *but additionally adjusted for variety of F&V intake.* C*: The association between variety of F&V intake and HR (95% CI) of diabetes adjusted for sex, BMI, waist circumference, education level, Townsend Deprivation Index, occupational social class, physical activity level, smoking status, family history of diabetes, total energy intake, and season.* D*: Same as* C *but additionally adjusted for quantity of F&V intake.*

been advocated by many national and international bodies (5–7), no studies that we are aware of have explored associations between variety in intake and risk of T2D. Our current findings suggest that quantity (at least 3.5 portions of F&V per day) and variety (at least 12 different F&V items per week) in F&V intake are both inversely and independently associated with T2D. However, only ~50% and 40% of the participants reported meeting these thresholds for quantity and variety of intake, respectively.

There are several unique strengths of our study, including the large sample size, prospective study design, use of a 7-day prospective food diary with disaggregated F&V data, thorough assessment of new cases of T2D with self-report information supplemented by external sources, and comprehensive information on covariates, thus minimizing sources of bias and confounding. Another strength of our study was that we had HbA_{1c} data available on a subsample of participants and were thus able to demonstrate that our findings were unlikely to have been influenced by the presence of previously undiagnosed cases of T2D at baseline. However, several potential limitations of our study merit discussion. First, because of the observational nature of the study, we cannot exclude the possibility of residual confounding or confounding by unmeasured factors. Second, we used baseline dietary consumption data to characterize individuals and did not take into account possible misclassification with respect to changes in consumption patterns over time. However, as this type of misclassification is likely to be nondifferential, the effect would be to attenuate the observed HRs toward the null, suggesting that the true associations between quantity and variety in F&V intake may be stronger than reported in the current study. We were also not able to adjust for lifestyle factors (e.g., smoking and physical activity) that may have changed during follow-up. Finally, our population is predominantly of European-Caucasian origin (99.1%) and middle aged. Thus, the generalizability of our findings to other populations may be limited. Nevertheless, in comparison with the general population of England, EPIC-Norfolk participants are comparable with respect to characteristics including anthropometry, blood pressure, and lipids (10).

The biological mechanisms for the inverse associations of F&V intake and diabetes risk are not clear. Our findings suggest that F&V may be inversely associated with diabetes through two distinct

but complementary pathways. A plausible biological mechanism to explain the beneficial effect of quantity of F&V intake on T2D is via the low energy and high fiber content of F&V, and as such their ability to reduce the overall energy content of the diet. It has previously been demonstrated that those who consume the highest quantity of F&V, in comparison with low consumers, have a lower risk of weight gain (24,25), a major risk factor for diabetes (26). A decreased risk of T2D with increasing quantities of vegetable intake in particular may be explained by the fact that vegetables are generally consumed with other foods as part of a meal and therefore may displace or buffer the harmful effects of deleterious foods from the diet, such as energy-dense foods or foods that increase the risk of T2D. Alternatively, higher consumption of specific vegetables, particularly green leafy vegetables, might reduce the risk of T2D due to the presence of relatively high concentrations of potentially beneficial bioactive compounds (21). The biological mechanisms for the inverse associations of variety of F&V intake with T2D are not clear but may be attributable to individual or combined effects of the many different bioactive phytochemicals contained in F&V (e.g., vitamin C and carotenoids) (27,28). Thus, consumption of a wide variety of F&V will increase the likelihood of consuming these phytochemicals. As the current study was not designed to examine mechanisms of association, future studies will be required to investigate this further.

In conclusion, using the prospective 7-day food diary to assess F&V intake, we found that a greater variety of fruit, vegetables, and combined F&V intake is associated with a reduced risk of T2D, whereas for quantity, only greater vegetable, but not fruit intake, was associated with a reduced risk. These findings support current public health recommendations encouraging consumption of F&V as part of a balanced diet and place particular emphasis on the important and independent role that both quantity and variety in F&V intake may play in helping to prevent the development of T2D.

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A.J.C. conceived and designed the study, analyzed and interpreted the data, drafted the manuscript, and had full access to all the data in the study and takes responsibility for the accuracy of the data analysis. S.J.S. analyzed and interpreted the data. M.A.H.L. analyzed data and contributed to the discussion. R.N.L. acquired the data. K.-T.K. obtained funding and acquired the data. N.J.W. obtained funding, acquired the data, and conceived and designed the study. N.G.F. conceived and designed the study and analyzed and interpreted the data. All authors critically revised the manuscript for important intellectual content and approved the final version. N.G.F., N.J.W., and K.-T.K. 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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References

1. Alwan A. *Global Status Report on Noncommunicable Diseases 2010: Description of the Global Burden of NCDs, Their Risk Factors and Determinants*. Geneva, World Health Organization, 2011
2. Nathan DM. Long-term complications of diabetes mellitus. N Engl J Med 1993;328:1676–1685
3. Jönsson B; CODE-2 Advisory Board. Revealing the cost of type II diabetes in Europe. Diabetologia 2002;45:S5–S12
4. Gillies CL, Abrams KR, Lambert PC, et al. Pharmacological and lifestyle interventions to prevent or delay type 2 diabetes in people with impaired glucose tolerance: systematic review and meta-analysis. BMJ 2007;334:299
5. World Health Organization/UN Food and Agriculture Organization. *Diet, Nutrition and the Prevention of Chronic Diseases: Report of a Joint FAO/WHO Expert Consultation*. Geneva, World Health Org., 2003 (Tech. Rep. Ser., no. 916)
6. U.S. Department of Agriculture and U.S. Department of Health and Human Services. *Dietary Guidelines for Americans, 2010, 7th ed.* Washington, DC, U.S. Govt. Printing Office, December 2010
7. National Health Service. 5 A Day [Internet]. Available from http://www.nhs.uk/livewell/5aday/pages/5adayhome.aspx/. Accessed 1 July 2011
8. Willett WC. *Nutritional Epidemiology*. 2nd ed. New York, Oxford University Press, 1998
9. Bingham SA, Luben R, Welch A, Wareham N, Khaw KT, Day N. Are imprecise methods obscuring a relation between fat and breast cancer? Lancet 2003;362:212–214
10. Day N, Oakes S, Luben R, et al. EPIC-Norfolk: study design and characteristics of the cohort. European Prospective Investigation of Cancer. Br J Cancer 1999;80 (Suppl. 1):95–103
11. Bingham SA, Welch AA, McTaggart A, et al. Nutritional methods in the European Prospective Investigation of Cancer in Norfolk. Public Health Nutr 2001;4:847–858
12. Welch AA, McTaggart A, Mulligan AA, et al. DINER (Data Into Nutrients for Epidemiological Research)—a new data-entry program for nutritional analysis in the EPIC-Norfolk cohort and the 7-day diary method. Public Health Nutr 2001;4:1253–1265
13. Bingham SA, Gill C, Welch A, et al. Validation of dietary assessment methods in the UK arm of EPIC using weighed records, and 24-hour urinary nitrogen and potassium and serum vitamin C and carotenoids as biomarkers. Int J Epidemiol 1997;26 (Suppl. 1):S137–S151
14. National Health Service. 5 A Day: What Counts? [Internet]. Available from http://www.nhs.uk/Livewell/5ADAY/Pages/Whatcounts.aspx. Accessed 20 October 2011
15. Agudo A, Slimani N, Ocké MC, et al. Consumption of vegetables, fruit and other plant foods in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohorts from 10 European countries. Public Health Nutr 2002;5(6B):1179–1196
16. Bazzano LA, Li TY, Joshipura KJ, Hu FB. Intake of fruit, vegetables, and fruit juices and risk of diabetes in women. Diabetes Care 2008;31:1311–1317
17. Townsend P, Phillimore P, Beattie A. *Health and Deprivation: Inequality and the North*. London, Croom Helm, 1988
18. Wareham NJ, Jakes RW, Rennie KL, et al. Validity and repeatability of a simple index derived from the short physical activity questionnaire used in the European Prospective Investigation into Cancer and Nutrition (EPIC) study. Public Health Nutr 2003;6:407–413
19. Barlow WE, Ichikawa L, Rosner D, Izumi S. Analysis of case-cohort designs. J Clin Epidemiol 1999;52:1165–1172
20. Greenland S. Dose-response and trend analysis in epidemiology: alternatives to categorical analysis. Epidemiology 1995;6:356–365
21. Carter P, Gray LJ, Troughton J, Khunti K, Davies MJ. Fruit and vegetable intake and incidence of type 2 diabetes mellitus: systematic review and meta-analysis. BMJ 2010;341:c4229
22. Hamer M, Chida Y. Intake of fruit, vegetables, and antioxidants and risk of type 2 diabetes: systematic review and meta-analysis. J Hypertens 2007;25:2361–2369
23. Feskanich D, Rimm EB, Giovannucci EL, et al. Reproducibility and validity of food

intake measurements from a semiquantitative food frequency questionnaire. J Am Diet Assoc 1993;93:790–796
24. Buijsse B, Feskens EJ, Schulze MB, et al. Fruit and vegetable intakes and subsequent changes in body weight in European populations: results from the project on Diet, Obesity, and Genes (DiOGenes). Am J Clin Nutr 2009;90:202–209
25. Mozaffarian D, Hao T, Rimm EB, Willett WC, Hu FB. Changes in diet and lifestyle and long-term weight gain in women and men. N Engl J Med 2011;364:2392–2404
26. Hu FB, Manson JE, Stampfer MJ, et al. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. N Engl J Med 2001;345:790–797
27. Harding AH, Wareham NJ, Bingham SA, et al. Plasma vitamin C level, fruit and vegetable consumption, and the risk of new-onset type 2 diabetes mellitus: the European prospective investigation of cancer—Norfolk prospective study. Arch Intern Med 2008;168:1493–1499
28. Hozawa A, Jacobs DR Jr, Steffes MW, Gross MD, Steffen LM, Lee DH. Associations of serum carotenoid concentrations with the development of diabetes and with insulin concentration: interaction with smoking: the Coronary Artery Risk Development in Young Adults (CARDIA) study. Am J Epidemiol 2006;163:929–937