

ORIGINAL ARTICLE

Dietary vitamin D intake and risk of type 2 diabetes in the European Prospective Investigation into Cancer and Nutrition: the EPIC-InterAct study

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BACKGROUND/OBJECTIVES: Prospective cohort studies have indicated that serum vitamin D levels are inversely related to risk of type 2 diabetes. However, such studies cannot determine the source of vitamin D. Therefore, we examined the association of dietary vitamin D intake with incident type 2 diabetes within the European Prospective Investigation into Cancer and Nutrition (EPIC)-InterAct study in a heterogeneous European population including eight countries with large geographical variation.

SUBJECTS/METHODS: Using a case-cohort design, 11 245 incident cases of type 2 diabetes and a representative subcohort ($N = 15\,798$) were included in the analyses. Hazard ratios (HR) and 95% confidence intervals (CIs) for type 2 diabetes were calculated using a Prentice-weighted Cox regression adjusted for potential confounders. Twenty-four-hour diet-recall data from a subsample ($N = 2347$) were used to calibrate habitual intake data derived from dietary questionnaires.

RESULTS: Median follow-up time was 10.8 years. Dietary vitamin D intake was not significantly associated with the risk of type 2 diabetes. HR and 95% CIs for the highest compared to the lowest quintile of uncalibrated vitamin D intake was 1.09 (0.97–1.22) ($P_{\text{trend}} = 0.17$). No associations were observed in a sex-specific analysis. The overall pooled effect (HR (95% CI)) using the continuous calibrated variable was 1.00 (0.97–1.03) per increase of 1 $\mu\text{g/day}$ dietary vitamin D.

CONCLUSIONS: This observational study does not support an association between higher dietary vitamin D intake and type 2 diabetes incidence. This result has to be interpreted in light of the limited contribution of dietary vitamin D on the overall vitamin D status of a person.

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INTRODUCTION

Besides the 'classical' function of vitamin D in calcium homeostasis, additional biological effects of vitamin D on diabetes-related outcomes have been identified. The results of experimental cell, animal and human studies support a role of vitamin D in the prevention of type 2 diabetes.^{1–4} However, the mechanisms by which vitamin D may affect type 2 diabetes risk are not fully understood. Effects of vitamin D on insulin secretion, insulin sensitivity as well as on inflammatory and autoimmune conditions associated with diabetic conditions are reported.^{4–9}

Evidence from prospective observational studies for an inverse association between vitamin D status, as characterised by serum 25-hydroxyvitamin D (25(OH)D) measurements, and type 2 diabetes is strong.^{10–12} After combining the data from nine prospective studies that measured serum 25(OH)D, participants in the highest (versus lowest) quartile of 25(OH)D showed a 41% (95% confidence interval (CI), 33–48%) lower risk of type 2 diabetes though any causal inference of this association remains unconfirmed.¹³ Moreover, a recent meta-analysis combining results from 14 observational studies reported a significant

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inverse association for circulating 25(OH)D but not for dietary vitamin D.¹⁴ Serum 25(OH)D concentration, the accepted biomarker of vitamin D status, reflects both the endogenous synthesis in the skin (following UVB exposure) and the dietary intake of vitamin D. Though, in general, the contribution of dietary vitamin D to the overall vitamin D status is of minor importance as compared to the endogenous synthesis of vitamin D, intra- and inter-subject variation in UVB exposure can be high, and the importance of vitamin D from diet substantially increases in situations with limited UVB exposure. Thus, analyses on the impact of dietary vitamin D and diabetes risk are meaningful. Mitri and colleagues combined data from three cohort studies and found a borderline, significant inverse association between vitamin D intake > 500 U/d (12.5 µg/d) and type 2 diabetes incidence (versus subjects with a vitamin D intake < 200 U/d (5 µg/d)); the relative risk was 0.87 (95% CI, 0.76–0.99).¹¹ However, only one out of three cohort studies reported a significant inverse association.^{15–17}

Due to its large sample size, the InterAct project within the European Prospective Investigation into Cancer and Nutrition (EPIC) provides the opportunity to investigate the association between the incidence of type 2 diabetes and dietary vitamin D prospectively in both men and women. Furthermore, the study allows a relatively wide range of dietary intake levels since data from different European countries are included.

MATERIALS AND METHODS

Study design and population

EPIC is a multi-centre prospective cohort study conducted since 1992 in 10 European countries.¹⁸ In the present EPIC-InterAct study, a nested case-cohort design within 8 of the 10 countries contributing to the EPIC cohort was used.¹⁹ The current analysis is based on data from EPIC participants in Denmark, France, Germany, Italy, the Netherlands, Spain, Sweden and the United Kingdom (UK).

Following the case-cohort design, the study population consisted of a random baseline sample of 16 154 participants (subcohort) and 12 403 incident cases of type 2 diabetes (including 778 from the subcohort), that is, all participants of the entire cohort with a first diagnosis of type 2 diabetes between recruitment and 31 December 2007.¹⁹

The final study sample after excluding participants without dietary information ($N=736$) consisted of 27 043 participants, including 15 798 members of the subcohort and 11 994 incident diabetes cases (including 749 cases from the subcohort).

Dietary assessment

Diet over the previous 12 months was assessed using dietary assessment instruments that were specifically developed for each participating country.¹⁸ The questions were structured by common food groups except for the questionnaires used in Italy and Spain, where questions were structured by country-specific meals.

All participants were asked to report their average consumption of each food by structured categories ranging from never or less than once per month to six or more times per day. In Germany, Italy, The Netherlands and Spain individual average portions were estimated, whereas standard portions were assigned to the participants in Denmark, the United Kingdom and Umeå, Sweden. A combination of methods for estimating portion size was used in Malmö, Sweden. All dietary measurement instruments have been validated previously in a series of studies within the various source populations participating in EPIC.²⁰

Daily intake of vitamin D, calcium and magnesium was calculated by means of a standardized food composition data base across EPIC countries.²¹

Demographic and lifestyle factors

To collect information on education, medical history (surgeries and previous illnesses), tobacco and alcohol consumption, and physical activity and other lifestyle factors, additional questionnaires were used. Height and weight were measured at baseline, except for the France and Oxford-UK study centre, where height and weight was self-reported.¹⁸

Ascertainment of type 2 diabetes

Ascertainment and verification of incident diabetes has been described in detail elsewhere.¹⁹ In brief, incident cases were identified by self-reports (history of diabetes, physician-diagnosed diabetes, antidiabetic drug use), linkage to primary and secondary care registers, linkage to drug registers, hospital admissions and mortality data. Further verification of the diabetic cases came from individual medical record reviews.

Statistical analysis

Cox proportional hazard models adapted for case-cohort design according to the Prentice method were used to calculate HR and 95% CI.²² A Cox model was used with stratification by age (in 1-year categories), centre and sex. Incident type 2 diabetes was the outcome variable and age was used as the underlying timescale.

Hazard ratios for dietary vitamin D intake are presented comparing quintiles taking the lowest quintile as reference. Quintile cutpoints were defined among subcohort members only. Different models were run to disentangle the effects of dietary vitamin D on type 2 diabetes: model 1: adjusted for total energy (kcal/day, cont.); model 2: adjusted for non-fat-energy (kcal/day, cont.), fat (g/day, cont., monounsaturated, polyunsaturated and saturated fat), physical activity (occupational, recreational and household activity; inactive, moderately inactive, moderately active, active, missing),²³ and model 3: as model 2 with further adjustment for *a priori* defined potential confounders and risk factors for diabetes: Body mass index (BMI) (kg/m², cont.), education level (none or primary school, technical/professional school, secondary school, longer education including university degree, unknown), smoking status (never, former, current, unknown), alcohol intake (g/day, cont.). Sensitivity analyses were performed excluding incident cases that occurred within the first two years of follow-up as well as additional adjustment for waist-hip ratio.

In order to account for different levels of sunlight exposure, the EPIC centres were divided into seven latitude groups: below 42°N (Granada, Murcia, Ragusa and Naples); 42°N–44°N (Asturias, Navarra, San Sebastian, Florence and South coast of France—centred in Marseille); 45°N–46°N (Varese, Turin and South of France—centred in Lyon); 47°N–49°N (north-east and west of France—centred in Nantes and Paris, respectively—and Heidelberg); 50°N–51°N (Potsdam, Utrecht, Bilthoven, Cambridge and Oxford); 52°N–56°N (Malmö, Aarhus and Copenhagen); and above 57°N (Norway and Umeå). A further sensitivity analysis was thus performed with additional adjustment for latitude.

Statistical interaction (heterogeneity) was evaluated with the Wald test by including cross-product terms of potential interaction variables (that is, sex, physical activity, BMI) in the respective models. Tests for trend over quintiles of intake (coded 1–5) were performed using the Wald statistics.

To correct for measurement error, dietary intake data calculated from questionnaire data were calibrated against 24-h diet-recall data for a subsample ($N=2347$). A fixed-effects linear model was used in which

Table 1. Dietary vitamin D intake by sex and country in the subcohort^a: the EPIC-InterAct study

Country	Men		Women	
	Median	IQR	Median	IQR
All	3.6	1.6–7.7	2.4	1.1–4.6
France	—	—	1.3	0.7–2.5
Italy	1.3	0.8–2.7	1.0	0.5–2.1
Spain	2.7	1.3–8.7	1.7	0.9–4.4
UK	3.5	1.7–5.2	2.4	1.7–3.8
Netherlands	3.4	2.3–7.4	2.5	1.8–3.9
Germany	2.0	1.1–3.6	1.5	0.8–3.3
Sweden	7.1	4.5–9.6	4.7	3.3–6.7
Denmark	2.9	1.4–7.7	1.7	1.0–3.9

Abbreviations: EPIC, European Prospective Investigation into Cancer and Nutrition; IQR, inter-quartile range. ^aVitamin D intake in µg/day from 24-h recall data ($N=2347$).

Table 2. Baseline characteristics in the subcohort by sex and quintiles of dietary vitamin D intake: the EPIC-InterAct study

Vitamin D ($\mu\text{g/day}$)	Quintile 1 <2.19 (median: 1.6)			Quintile 2 2.19 to <3.13 (median: 2.6)			Quintile 3 3.13 to <4.27 (median: 3.7)			Quintile 4 4.27 to <6.07 (median: 5.0)			Quintile 5 ≥ 6.07 (median: 7.9)		
	N	%		N	%		N	%		N	%		N	%	
Men	N = 744			N = 903			N = 1109			N = 1418			N = 1794		
Smoking status															
Never	201	27		275	30		353	32		461	33		591	33	
Former	278	37		349	39		402	36		515	36		627	35	
Current	259	35		269	30		333	30		430	30		567	32	
Unknown	6	1		10	1		21	2		12	1		9	1	
Education															
Primary school or less	348	47		335	37		413	37		502	35		731	42	
Technical/professional school	140	19		200	22		260	23		351	25		388	22	
Other secondary education	92	12		133	15		132	12		160	11		260	14	
University	154	21		220	24		281	25		385	27		398	22	
Unknown	10	1		15	2		23	2		20	1		17	1	
Physical activity															
Inactive	201	27		258	29		284	26		374	26		348	19	
Moderately inactive	243	33		274	30		339	31		397	28		603	34	
Moderately active	224	30		261	29		314	28		359	25		474	26	
Active	60	8		79	9		91	8		114	8		108	6	
Unknown	16	2		31	3		81	7		174	12		261	15	
	Median	IQR		Median	IQR		Median	IQR		Median	IQR		Median	IQR	
Age at recruitment	52.7	46.3–58.4		52.8	45.9–58.5		52.9	46.5–58.6		53.0	47.3–59.6		53.8	48.6–60.3	
BMI (kg/m^2)	26.7	24.5–28.9		26.4	24.1–28.8		26.2	24.2–28.6		26.3	24.5–28.7		26.2	24.0–28.7	
Total energy (kcal/d)	2048	1685–2457		2256	1860–2713		2330	1963–2736		2443	2052–2869		2678	2273–3150	
Saturated fat (g/d)	24.5	18.6–31.0		30.1	23.4–37.4		32.2	24.9–40.8		34.8	27.0–43.5		41.2	31.8–52.4	
Monounsaturated fat (g/d)	28.3	21.0–38.9		31.5	23.0–41.9		31.5	24.3–42.0		33.6	26.5–42.7		39.2	31.6–48.7	
Polyunsaturated fat (g/d)	9.9	7.6–13.6		11.6	9.2–15.3		13.2	10.4–16.8		14.0	10.9–18.4		16.7	13.2–21.7	
Alcohol (g/d)	13.5	3.1–34.0		16.3	5.4–38.4		16.4	5.2–37.3		14.8	4.9–37.8		13.2	4.1–31.0	
Calcium (mg/d)	804	595–1047		885	669–1173		931	720–1233		968	735–1261		1109	836–1400	
Magnesium (g/d)	335	267–410		351	295–421		369	312–438		391	323–458		412	347–483	
Coffee (g/d)	120	56–413		175	65–500		287	90–600		385	131–665		400	145–675	
Soft drinks (g/d)	0.0	0.0–39.4		6.7	0.0–66.7		8.1	0.0–85.7		16.4	0.0–97.5		21.3	0.0–114	
Total meat (g/d)	101	66–146		119	86–159		130	91–170		134	98–178		142	102–193	
Total fish (g/d)	10.0	3.1–22.4		16.4	8.2–28.4		22.7	12.7–36.3		29.4	15.3–47.6		37.7	15.4–67.7	

Vitamin D ($\mu\text{g/day}$)	Quintile 1 <2.19 (median: 1.6)			Quintile 2 2.19 to <3.13 (median: 2.6)			Quintile 3 3.13 to <4.27 (median: 3.7)			Quintile 4 4.27 to <6.07 (median: 5.0)			Quintile 5 ≥ 6.07 (median: 7.9)		
	N		%	N		%	N		%	N		%	N		%
	N = 2415			N = 2257			N = 2050			N = 1742			N = 1366		
Smoking status															
Never	1416		59	1244		55	1143		56	963		55	694		51
Former	482		20	523		23	440		21	350		20	296		22
Current	494		20	476		21	447		22	408		23	367		27
Unknown	23		1	14		1	20		1	21		1	9		1
Education															
Primary school or less	1077		45	916		41	780		38	672		39	571		42
Technical/professional school	443		18	499		22	508		25	447		26	366		27
Other secondary education	438		18	393		17	363		18	249		14	157		11
University	420		17	408		18	356		17	339		19	255		19
Unknown	37		2	41		2	43		2	35		2	17		1
Physical activity															
Inactive	274		11	263		12	248		12	197		11	151		11
Moderately inactive	611		25	551		24	466		23	435		25	418		31
Moderately active	1237		51	1111		49	951		46	769		44	588		43
Active	244		10	238		11	214		10	156		9	102		7
Unknown	49		2	94		4	171		8	185		11	107		8
	Median		IQR	Median		IQR	Median		IQR	Median		IQR	Median		IQR
Age at recruitment	52.3		45.3–58.8	52.4		46.3–58.7	51.9		46.0–58.5	52.1		46.1–59.3	53.3		47.1–61.0
BMI (kg/m^2)	24.9		22.4–28.3	24.9		22.5–27.9	25.0		22.6–28.1	24.7		22.5–28.0	25.0		22.6–28.2
Total energy (kcal/d)	1625		1353–1926	1836		1529–2185	1916		1604–2282	2001		1695–2404	2185		1861–2563
Saturated fat (g/d)	22.1		16.5–27.8	27.0		21.1–34.0	28.5		21.8–36.3	30.7		24.1–39.0	35.2		26.7–44.0
Monounsaturated fat (g/d)	22.3		16.3–30.5	25.4		19.1–33.8	26.4		20.5–35.0	27.8		22.4–35.8	32.3		26.3–40.2
Polysaturated fat (g/d)	8.8		6.8–11.4	10.7		8.4–14.0	11.5		8.9–14.7	12.3		9.4–16.4	14.2		11.3–18.2
Alcohol (g/d)	1.9		0.0–10.1	3.0		0.3–11.6	3.7		0.4–11.6	4.0		0.6–12.1	5.0		0.7–12.8
Calcium (mg/d)	806		614–1033	904		711–1147	957		727–1212	995		770–1244	1062		861–1326
Magnesium (g/d)	283		233–343	309		257–369	327		275–386	337		283–404	348		300–408
Coffee (g/d)	150		58–437	250		84–500	290		100–523	330		129–582	375		150–600
Soft drinks (g/d)	0.0		0.0–36.2	0.0		0.0–46.2	3.3		0.0–55.7	6.5		0.0–85.7	6.0		0.0–85.7
Total meat (g/d)	75		47–106	91		62–120	94		65–129	95		68–126	99		71–131
Total fish (g/d)	9.5		3.2–21.5	16.1		7.0–29.7	22.7		9.8–36.0	27.2		11.2–46.3	37.8		17.4–66.2

Abbreviation: IQR, inter-quartile range. *N* = 15 798.

centre and sex-specific recall data were regressed on the dietary intakes.^{24–26} The calibrated dietary data were used to model dietary intake of vitamin D continuously in the whole sample and in the country-specific analysis. We used a meta-analytic approach to investigate heterogeneity across centres (metan procedure in STATA) by pooling the adjusted HR's per centre using the random effects model.

All tests were two-sided and considered to be statistically significant with a *P*-value of ≤ 0.05 . All analyses were conducted using SAS version 9.1 (SAS Institute, Cary, NC, USA) and STATA version 10 for meta-analysis (College Station, TX, USA).

RESULTS

Median vitamin D intake in the subcohorts of the respective countries by sex is shown in Table 1. Dietary vitamin D intake was highest in Sweden and lowest in Italy. Vitamin D intake was higher in men across all countries.

Median age at baseline was 52.7 years (interquartile range 46.5–59.2). The median follow-up time for the study population was 10.8 years. Descriptive characteristics of the subcohort by quintiles of vitamin D intake are shown in Table 2. The percentage of current smokers was lower in men but higher in women with higher vitamin D intake. The increasing numbers of participants with unknown physical activity with increasing vitamin D intake are due to physical activity data not being collected in Umeå, Sweden, where vitamin D intake is high. No differences in BMI were observed by quintiles of vitamin D intake. Total fish, meat, calcium and energy intake was higher in both men and women with increasing vitamin D intake (Table 2).

No significant association was observed between vitamin D intake and type 2 diabetes risk (Table 3). HR and 95% CI in the most adjusted model for the higher quintiles compared with the lowest were 1.04 (0.95–1.14), 1.02 (0.93–1.12), 1.06 (0.96–1.17) and 1.09 (0.97–1.22) (*P*-trend = 0.17) (Table 3). We further performed a separate analysis by sex and did not find any significant association between diabetes incidence and vitamin D intake in either men or women (*P*_{interaction} = 0.40). No statistical interaction was observed between BMI or physical activity groups and dietary vitamin D (*P*_{interaction} > 0.05).

Moreover, there was no statistical interaction between vitamin D and calcium intake (*P* = 0.93).

To account for potential measurement error when calculating dietary intake from questionnaire data, we further performed an analysis using the continuous intake data calibrated with 24-h-diet recall data from a subsample of the subcohort. The overall estimate showed no association for vitamin D and diabetes risk (HR (95% CI) = 1.00 (0.97–1.03), per 1 µg/day increment) (Figure 1). The corresponding effect estimate using the observed (continuous) data was HR (95% CI) = 1.03 (0.98–1.08). Country-specific hazard ratios for the calibrated vitamin D intake (per 1 µg/day increment) in comparison with the overall effect estimate are shown in the forest plot (Figure 1). There was statistically significant heterogeneity across countries ($I^2 = 60.9\%$, *P* = 0.012). Heterogeneity could in part be explained by the significant positive association in the UK data as exclusion of the UK data resulted in a non-significant and substantially decreased heterogeneity ($I^2 = 18.6\%$, *P* = 0.228). In a sensitivity analysis, we excluded incident cases that occurred within the first two years of follow-up. No considerable changes in the hazard ratios were observed. We furthermore additionally adjusted for waist-hip ratio and did not observe any changes in the effect estimates (waist-hip ratio data are missing for the Umeå centre, *n* = 1796). As a proxy for sun exposure, and thus endogenous vitamin D production, we divided the centres into seven categories according to their latitude. Adjustment for latitude did not notably change the observed risk estimates for vitamin D and type 2 diabetes risk. Furthermore, additional adjustment for calcium intake did not notably change the risk estimates.

Table 3. Dietary vitamin D intake and risk of type 2 diabetes: the EPIC-InterAct study

Quintiles of vitamin D intake (µg/day)	Model 1 ^a		Model 2 ^a		Model 3 ^a	
	HR	95% CI	HR	95% CI	HR	95% CI
<2.19	Ref.		Ref.		Ref.	
2.19–<3.13	1.04	0.96–1.13	1.02	0.94–1.11	1.04	0.95–1.14
3.13–<4.27	1.02	0.94–1.11	1.00	0.91–1.08	1.02	0.93–1.12
4.27–<6.07	1.09	1.00–1.19	1.05	0.96–1.15	1.06	0.96–1.17
≥6.07	1.18	1.06–1.30	1.10	0.99–1.22	1.09	0.97–1.22
<i>P</i> -trend	0.002		0.078		0.170	

Abbreviations: CI, confidence interval; HR, hazard ratio. ^aAll models stratified by sex, age and study centre; model 1: adjustment for total energy; model 2: adjustment for non-fat energy, polyunsaturated fatty acids, monounsaturated fatty acids, saturated fatty acids, physical activity; model 3: as model 2 with further adjustment for education, BMI, smoking, alcohol intake.

DISCUSSION

In this large prospective case-cohort analysis within the European Prospective Investigation into Cancer and Nutrition, dietary vitamin D was not significantly associated with the incidence of type 2 diabetes. This was true for men and women. So far, only few cohort studies prospectively assessed the association between dietary vitamin D with the incidence of type 2 diabetes or diabetes-related outcomes.^{15–17} In line with our results, the Nurses' Health Study did not find a significant association between dietary or total intake of vitamin D and type 2 diabetes.¹⁶ Furthermore, our results corroborate the findings from a large Japanese cohort that reported no association in men or in women.¹⁷ However, the Women's Health Study reported an inverse association between dietary vitamin D intake and the prevalence of metabolic syndrome,¹⁵ and also a meta-analysis of these three studies found a borderline inverse association between vitamin D intake > 500 U/d (> 12.5 µg/d) and type 2 diabetes incidence.¹¹

Systematic reviews focusing on eight randomized trials also did not provide clear evidence for an inverse association of vitamin D supplementation with hyperglycemia or incident type 2 diabetes.¹¹ The so-far largest trial, the Women's Health Initiative (WHI) study, did not observe any risk reduction of type 2 diabetes over 7 years of follow-up in the intervention arm with supplementation of vitamin D (400 IU/d) and calcium (1000 mg/d).²⁷ However, the authors noted that higher doses of vitamin D may have been necessary to affect diabetes risk.

Several explanations are possible as to why we did not observe any association between dietary vitamin D and type 2 diabetes risk in our study: (1) there is indeed no relationship; (2) the amount and variation of dietary vitamin D intake is too low in the population to detect potential effects; especially, dietary vitamin D intake is distinctly lower in most European countries as compared to the US where staple food is frequently fortified with vitamin D, and thus dietary vitamin D intake more effectively impacts on the overall vitamin D status of a person.

The present study is thus far the largest study prospectively assessing the association between dietary vitamin D intake and the risk of type 2 diabetes. Thus, power was high to detect even weak associations. Further strengths of the study were the high quality of physician-verified diagnoses of type 2 diabetes; the calibration of nutrient intake data from questionnaires with that from 24-h recall data; and the inclusion of detailed information on potential confounders in the analysis. However, due to the observational study design, residual confounding cannot completely be ruled out. A further strength of the study is the wide range of intake from different European countries with different

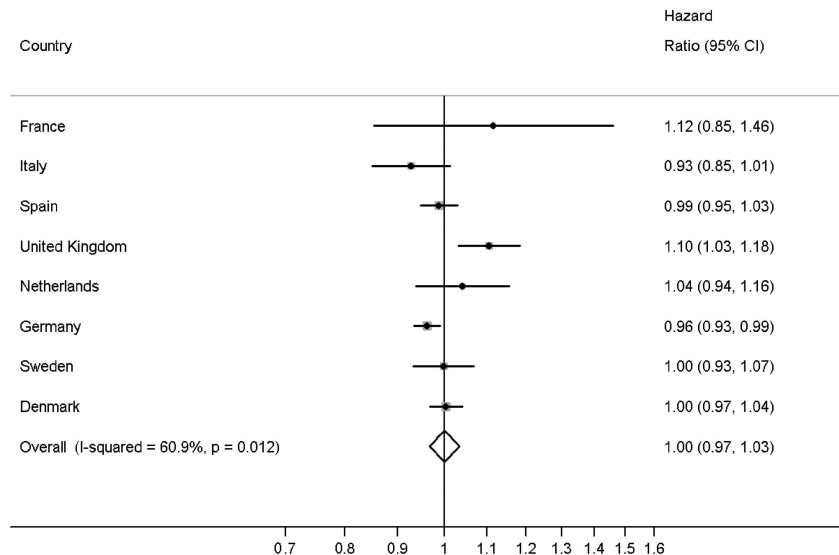


Figure 1. Dietary vitamin D intake (per 1 µg/day increment) and risk of type 2 diabetes, by country and overall: the EPIC-InterAct study. (Models were stratified by sex and age; adjusted for non-fat energy, polyunsaturated fatty acids, monounsaturated fatty acids, saturated fatty acids, physical activity, education, BMI, smoking, alcohol intake.)

eating habits. The intake data in our study was comparable with that in representative studies in Europe.^{28–30} Particularly, the here-presented higher intake in the northern European countries, for example, Sweden, where intake of vitamin D-rich foods and the contribution from fortified foods is high, is in line with previous reports.^{28,31} There are, however, several limitations that should be noted when interpreting the results. Firstly, we did not account for vitamin D from supplements. Additional adjustment on unspecified supplement intake in the study population did not change the risk estimates, but calculated amounts of vitamin D from supplements were not available. Secondly, the contribution of endogenous production of vitamin D (following UVB exposure) could not be addressed here. In a sensitivity analysis, we adjusted for centers' latitude as a proxy for sun exposure, which did not affect the risk estimates. However, since the contribution of diet to the overall vitamin D status of a person is low, studies with information on the entire vitamin D status may lead to a different conclusion. Indeed, prospective observational studies with serum 25(OH)D measurements showed a strong inverse association between vitamin D status and type 2 diabetes.^{10–13} However, these studies can also be subject to substantial residual confounding, for example, by imprecise assessment of outdoor physical activities which are correlated with both UVB exposure and, eventually, with vitamin D status as well as with diabetes risk.

In summary, in the present study we did not observe an association between dietary vitamin D intake and the risk of type 2 diabetes in a large European study population. However, it has to be acknowledged that endogenous production of vitamin D in the skin following UVB exposure is the dominant predictor of vitamin D status in humans.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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