Association between Protein Intake and Diabetes Complications Risk Following Incident Type 2

Diabetes: The EPIC-Potsdam Study

Supplemental Material

Supplementary Table S1. Baseline characteristics of study sample in the protein intake change analysis by protein intake groups at baseline

Characteristics	Total (n=663)	Low Protein Intake (n=332)	High Protein Intake (n=331)
Demographics			
Age at diabetes diagnosis (years) (median (Q1, Q3))	59 (53-64)	60 (53-65)	58 (52-63)
Education (n(%))			
No school degree or primary school	296 (44.8)	152 (46.0)	144 (43.4)
Technical or professional school	165 (24.9)	90 (27.1)	75 (22.6)
University degree	202 (30.4)	90 (26.8)	112 (34.0)
Body mass index (kg/m^2) (median (Q1, Q3))	29.9 (27.6-33.2)	29.7 (27.3-32.6)	30.3 (28.1-33.7)
Pre-diagnosis lifestyle			
Physical activity (h/week) (median (Q1, Q3))	1 (0-3)	0.8 (0-2.8)	1.4 (0-3.5)
Smoking status (n (%))			
Never-smoker	247 (37.2)	130 (39.2)	117 (35.2)
Former smoker	303 (45.7)	150 (45.2)	153 (46.1)
Current smoker	113 (17.1)	52 (15.6)	61 (18.7)
Smoking duration (years) (median (Q1, Q3))	13 (0-28)	10 (0-27)	14 (0-28)
Medical information			
Diabetes duration (years) (median (Q1, Q3))	14.2 (12.4-16.0)	14.2 (13.6-16.0)	14.2 (12.4-16.1)
Family history of myocardial infraction (n(%))	113 (17.0)	60 (18.1)	53 (15.9)
Family history of stroke (n(%))	140 (21.0)	73 (22.0)	66 (20.0)
Hypertension (n(%))	534 (80.5)	268 (80.7)	267 (80.4)
Dyslipidaemia (n(%))	475 (71.7)	239 (72.0)	237 (71.3)
*Dietary intake (median (*Q1, Q3*))*			
Energy intake (kJ)	8,781 (7,232-10,654)	7,298 (6,299-8,181)	10,436 (9,417-12,195)
Protein intake (g/day)	78.1 (63.5-95.1)	63.5 (54.1-70.1)	95.1 (84.8-107.4)
Carbohydrate intake (g/day)	228.1 (187.2-279.0)	199.0 (161.5-230.5)	269.6 (226.1-315.6)
Fat intake (g/day)	78.9 (63.3-102.1)	64.3 (54.4-75.7)	100.2 (83.4-114.7)
Alcohol intake (g/day)	9.1 (3.0-22.4)	7.0 (2.3-16.9)	12.2 (4.8-30.3)
Fibre intake (g/d)	21.4 (17.5-26.4)	18.9 (15.6-22.3)	25.3 (20.8-28.9)
PUFA:SFA ratio	0.5 (0.4-0.6)	0.5 (0.4-0.6)	0.4 (0.4-0.5)
Mg intake (mg/d)	0.3 (0.3-0.4)	0.3 (0.2-0.3)	0.4 (0.3-0.4)
Cholesterol intake (mg/d)	0.3 (0.2-0.4)	0.2 (0.2-0.3)	0.4 (0.3-0.4)
Vitamin E intake (mg/d)	11.1 (8.7-13.8)	9.3 (7.6-11.5)	12.8 (10.9-15.6)

Data are presented as median (interquartile range (Q1, Q3)) or n (percentage) as applicable. Table presents combined rounded values from the 10 imputation datasets. Percentages may not correspond to anticipated values.
Low protein intake < 78.1 g/d; High protein intake ≥ 78.1 g/d

Mg: magnesium; PUFA: polyunsaturated fatty acids; SFA: saturated fatty acids.

Supplementary Table S2. HRs and 95% CIs for microvascular and macrovascular complications of type 2 diabetes for isoenergetic substitution (per 5% E) of protein for carbohydrates by sex

	Men		Women	
	Events (n)	Total Protein	Events (n)	Total Protein
Complications		HR (95% CI)		HR (95% CI)
Total complications	240		148	
Model 1		1.04 (0.75, 1.45)		0.99 (0.64, 1.51)
Model 2		0.91 (0.64, 1.30)		0.82 (0.51, 1.33)
Model 3		0.80 (0.51, 1.25)		0.78 (0.43, 1.42)
Macrovascular complications	57		25	
Model 1		0.98 (0.50, 1.91)		0.44 (0.12, 1.58)
Model 2		1.01 (0.50, 2.06)		0.42 (0.11, 1.64)
Model 3		0.96 (0.39, 2.36)		-
Microvascular complications	205		138	
Model 1		1.10 (0.76, 1.59)		1.09 (0.69, 1.71)
Model 2		0.92 (0.62, 1.36)		0.87 (0.52, 1.48)
Model 3		0.81 (0.49, 1.35)		0.86 (0.47, 1.56)
Nephropathy	122		78	
Model 1		1.01 (0.62, 1.62)		1.26 (0.69, 2.33)
Model 2		0.74 (0.43, 1.27)		0.96 (0.46, 1.99)
Model 3		0.91 (0.47,1.80)		1.06 (0.49, 2.32)
Neuropathy	118		92	
Model 1		1.02 (0.63, 1.65)		1.10 (0.63, 1.91)
Model 2		0.96 (0.59, 1.58)		0.81 (0.45, 1.49)
Model 3		0.74 (0.38, 1.45)		0.74 (0.38, 1.46)

Table presents combined rounded values from the ten imputation datasets
Model 1: age, baseline energy intake, baseline fat intake, baseline alcohol intake
Model 2: Model 1 + education, physical activity, BMI, smoking status and duration, family history of myocardial infarction and stroke, prevalent hypertension and dyslipidaemia, antidiabetic, lipid lowering and antihypertensive medication, duration between diet assessment and T2D diagnosis
Model 3: Model 2 + baseline fibre intake, PUFA/SFA ratio, baseline cholesterol intake, baseline Mg intake, baseline vitamin E intake

Supplementary Table S3. HRs and 95% CIs for T2D complications for isoenergetic substitution of animal protein for plant protein (per 5% E)

	Events (n)	HR (95% CI)
Total complications	385	
Model 1		0.84 (0.39, 1.85)
Model 2		0.87 (0.38, 1.98)
Model 3		0.51 (0.20, 1.30)
Macrovascular complications	80	
Model 1		0.25 (0.48, 1.25)
Model 2		0.24 (0.04, 1.50)
Model 3		0.24 (0.03, 1.72)
Microvascular complications	342	
Model 1		1.21 (0.54, 2.70)
Model 2		0.23 (0.52, 2.89)
Model 3		0.70 (0.26, 1.91)
Nephropathy	199	
Model 1		1.15 (0.46, 2.93)
Model 2		1.01 (0.37, 2.72)
Model 3		0.71 (0.22, 2.26)
Neuropathy	210	
Model 1		1.38 (0.47, 4.06)
Model 2		1.47 (0.48, 4.55)
Model 3		0.66 (0.17, 2.59)
Table presents combined rounded values from the ten imputation datasets Model 1: age, sex, baseline energy intake, baseline carbohydrate intake, baseline fat intake, baseline alcohol intake Model 2: Model 1 + education, physical activity, BMI, smoking status and duration, family history of myocardial infarction and stroke, prevalent hypertension and dyslipidaemia, antidiabetic, lipid lowering and antihypertensive medication, duration between diet assessment and T2D diagnosis Model 3: Model 2 + baseline fibre intake, PUFA/SFA ratio, baseline cholesterol intake, baseline Mg intake, baseline vitamin E intake		

Supplementary Table S4. HRs and 95% CIs for microvascular and macrovascular complications of type 2 diabetes for isoenergetic increase of protein intake from baseline to follow-up (per 5% E) at the expense of carbohydrates with dietary assessment date being the entry time (baseline)

	Total		Low Protein Intake		High Protein Intake	
Complications	Events (n)	HR (95% CI)	Events (n)	HR (95% CI)	Events (n)	HR (95% CI)
Total complications	257		122		135	
Model 1		0.99 (0.93, 1.06)		0.97 (0.88, 1.07)		1.03 (0.94, 1.12)
Model 2		1.01 (0.93, 1.09)		0.93 (0.83, 1.05)		1.02 (0.88, 1.17)
Model 3		0.98 (0.89, 1.08)		1.02 (0.83, 1.25)		0.92 (0.76, 1.11)
Microvascular complications	238		114		124	
Model 1		1.02 (0.96, 1.09)		1.01 (0.92, 1.12)		1.04 (0.95, 1.14)
Model 2		1.06 (0.97, 1.16)		0.99 (0.87, 1.12)		1.09 (0.93, 1.28)
Model 3		1.02 (0.92, 1.14)		1.01 (0.81, 1.26)		1.01 (0.84, 1.22)
Nephropathy	147		69		78	
Model 1		1.01 (0.94, 1.09)		0.97 (0.86, 1.09)		1.08 (0.96, 1.22)
Model 2		1.02 (0.91, 1.15)		0.80 (0.61, 1.05)		1.10 (0.87, 1.38)
Model 3		0.92 (0.80, 1.05)		0.73 (0.03, 2.06)		0.84 (0.61, 1.15)
Neuropathy	147		71		76	
Model 1		1.04 (0.95, 1.14)		1.08 (0.92, 1.27)		1.02 (0.90, 1.15)
Model 2		1.01 (0.90, 1.14)		0.97 (0.74, 1.29)		1.04 (0.82, 1.33)
Model 3		0.98 (0.83, 1.12)		1.03 (0.66, 1.59)		0.91 (0.54, 1.52)
Table presents combined rounded values from the ten imputation datasets Model 1: age, sex, energy intake, baseline protein intake, fat intake (baseline and follow-up), alcohol intake (baseline and follow-up), duration between baseline and diet assessment, duration between T2D diagnosis and diet assessment Model 2: Model 1 + education, physical activity (baseline and follow-up), BMI (baseline and follow-up), smoking status and duration (baseline and follow-up), family history of myocardial infarction and stroke, prevalent hypertension and dyslipidaemia, antidiabetic, lipid lowering and antihypertensive medication Model 3: Model 2 + fibre intake (baseline and follow-up), PUFA/SFA ratio (baseline and follow-up), cholesterol intake (baseline and follow-up), Mg intake (baseline and follow-up), vitamin E intake (baseline and follow-up)						

Supplementary Table S5. HRs and 95% CIs for macrovascular complications for isoenergetic substitution of total protein for carbohydrates (per 5% E) among participants with prevalent type 2 diabetes

Complications	Events (n)	HR (95% CI)
Myocardial Infarction	44	
Model 1		1.09 (0.59, 2.01)
Model 2		1.07 (0.63, 1.80)
Model 3		0.98 (0.46, 2.10)
Stroke	52	
Model 1		0.73 (0.39, 1.38)
Model 2		0.83 (0.42, 1.63)
Model 3		0.41 (0.16, 1.01)
Total Cardiovascular Diseases	93	
Model 1		0.83 (0.55, 1.25)
Model 2		0.97 (0.64, 1.47)
Model 3		0.64 (0.39, 1.06)
Model 1 = sex, age, energy intake, alcohol intake, fat intake Model 2 = Model 1 + education, physical activity, BMI, smoking status and duration, family history of myocardial infarction and stroke, antidiabetic, lipid lowering and antihypertensive medication Model 3 = Model 2 + fibre intake, PUFA/SFA ratio, cholesterol intake, Mg intake, vit E intake Covariates are based on baseline questionnaire.		