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ARTICLE

Lifestyle factors and mortality risk in individuals with diabetes mellitus: are the associations different from those in individuals without diabetes?

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Abstract
Aims/hypothesis Thus far, it is unclear whether lifestyle recommendations for people with diabetes should be different from those for the general public. We investigated whether the associations between lifestyle factors and mortality risk differ between individuals with and without diabetes.
Methods Within the European Prospective Investigation into Cancer and Nutrition (EPIC), a cohort was formed of 6,384 persons with diabetes and 258,911 EPIC participants without known diabetes. Joint Cox proportional hazard regression models of people with and without diabetes were built for the following lifestyle factors in relation to overall mortality risk: BMI, waist/height ratio, 26 food groups, alcohol consumption, leisure-time physical activity, smoking. Likelihood ratio tests for heterogeneity assessed statistical differences in regression coefficients.

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Results Multivariable adjusted mortality risk among individuals with diabetes compared with those without was increased, with an HR of 1.62 (95% CI 1.51, 1.75). Intake of fruit, legumes, nuts, seeds, pasta, poultry and vegetable oil was related to a lower mortality risk, and intake of butter and margarine was related to an increased mortality risk. These associations were significantly different in magnitude from those in diabetes-free individuals, but directions were similar. No differences between people with and without diabetes were detected for the other lifestyle factors. *Conclusions/interpretation* Diabetes status did not substantially influence the associations between lifestyle and mortality risk. People with diabetes may benefit more from a healthy diet, but the directions of association were similar. Thus, our study suggests that lifestyle advice with respect to mortality for patients with diabetes should not differ from recommendations for the general population.

Keywords Adiposity · Alcohol · Diabetes · Lifestyle · Mortality · Nutrition · Physical activity · Smoking

Abbreviations

CVD	Cardiovascular disease
EPIC	European Prospective Investigation into Cancer and Nutrition
FFQ	Food frequency questionnaire

Introduction

Individuals with diabetes mellitus have an increased risk of cardiovascular disease (CVD) and premature mortality [1, 2]. It has been estimated that diabetes confers a 1.8-fold increased risk of mortality [3]. A major objective of diabetes management is to prevent or minimise micro- and macrovascular complications, typically through lifestyle modifications and pharmacotherapy [4, 5], the former of which usually emphasises reducing body weight (or maintaining a healthy body weight), regular physical activity, moderate alcohol consumption and a healthy diet [5, 6]. The evidence supporting these recommendations has rarely been derived from studies of people with diabetes [5, 7].

To strengthen the evidence base for public health decision-making, we have previously investigated associations between selected lifestyle factors and mortality in a large European cohort of individuals with prevalent diabetes. Measures of abdominal adiposity, but not general adiposity, were found to be associated with higher mortality risk [8]. Furthermore, our results on alcohol consumption support the current international recommendation that people with diabetes can consume alcohol within the recommended upper limits [9]. Moreover, people with diabetes who undertake moderate amounts of physical activity are at appreciably lower risk of death than inactive persons [10].

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Several other studies have also investigated the relationship between lifestyle and mortality in individuals with diabetes; moreover, many other studies have systematically excluded persons with diabetes to simplify the analysis, making it unclear how to apply these results to such people. Because diabetes increases mortality risk [11], it has been hypothesised that persons with diabetes should benefit to a greater extent from a healthy lifestyle [5], but no indications were found in the existing literature that associations between lifestyle factors and risk of mortality differ between people with and without diabetes.

Whether lifestyle recommendations should differ between persons with and without diabetes is also of particular interest for individuals living with undiagnosed diabetes today [12] or those with impaired glucose tolerance [13]. The rationale of adopting lifestyle habits in line with the recommendation in this stratum of the population is further supported by the large body of evidence showing CVD risk as well [13, 14].

We investigated the associations of BMI, waist/height ratio, 26 food groups, alcohol consumption, physical activity and smoking with overall mortality in individuals with diabetes compared with those without in a large European prospective study. Our aim was to provide empirical evidence relating to whether different healthy lifestyle recommendations for individuals with diabetes and the general public are justified.

Methods

Study design and population Within the European Prospective Investigation into Cancer and Nutrition (EPIC), which is an ongoing multicentre prospective study in ten European countries [15], a cohort was defined of participants with a confirmed diagnosis of type 1 or type 2 diabetes at baseline. EPIC is a cohort study including 519,978 participants, aged 35–70 years, from 23 centres in ten European countries who were recruited from 1992 to 2000. Participants were predominantly recruited from the general population residing in a certain geographic area (town, province or country). As described previously [8], 15 EPIC study centres from six European countries provided additional data on diabetes diagnosis and medication. Self-reports of diagnosis obtained at baseline were confirmed by additional information sources. The study was conducted according to the guidelines laid down in the Declaration of Helsinki and was approved by the ethics review boards of the single centres and the International Agency for Research on Cancer in Lyon, France. All participants provided written informed consent. The cohort comprised 6,412 individuals with confirmed diabetes at study entry, and, after exclusion of participants without follow-up information on vital status ($n=28$), the analytical sample included 6,384 individuals with diabetes. Subsequently, 258,911 participants without a verified or a self-reported diabetes diagnosis at baseline from the same EPIC study centres were selected as the group without diabetes. Thus, the analytical sample included 6,384 individuals with and 258,911 individuals without diabetes.

Exposure assessment At baseline, weight and height were measured with participants not wearing shoes. Waist circumference was measured either at the narrowest circumference of the torso or at the midpoint between the lower ribs and iliac crest [8].

Dietary intake during the preceding 12 months was assessed at baseline with country-specific instruments that had been developed. Extensive quantitative dietary questionnaires with up to 300–500 food items, semi-quantitative food frequency questionnaires (FFQs) and combined dietary methods of food records and questionnaires were used [15]. In a series of validation studies in the various source populations, the FFQs had good repeatability, and validity ranged from modest to good [16–19]. In addition, a highly standardised reference dietary measurement was taken from an 8% age-stratified random sample of the cohort ($n=36,994$) using a computerised 24 h dietary recall. Foods were organised into 39 food groups, and intake of 26 meaningful food groups was adjusted for energy with the residual method [20] and analysed as predicted by regression calibration [21].

Alcohol consumption during the preceding 12 months was assessed with the baseline FFQ. Weekly consumption of alcohol retrospectively at the ages of 20, 30, 40 and 50 years was assessed in the lifestyle questionnaire, except in the study centres at Bilthoven, Naples and Sweden. Previous alcohol consumption was defined as none, always moderate, and sometimes heavy consumption. In our previous study, we have shown that 'light alcohol consumers' is a more appropriate reference group than 'non-consumers'; therefore, an alcohol consumption of >0–6 g/day was used as reference [9]. Within EPIC, the amount of alcoholic beverage consumed by comparable age cohorts at certain ages was validated by comparison of self-reported data with the respective per capita measures and showed, in general, good reproducibility [22].

Leisure-time physical activity was assessed with a lifestyle questionnaire at baseline and included information on walking, cycling, gardening, sport, household and do-it-yourself activities; this questionnaire was not validated. Detailed information about smoking was also collected through the lifestyle questionnaire, including smoking status at recruitment and smoking history.

Covariate assessment Educational level and medical history, including prevalent myocardial infarction, stroke and cancer, were also obtained using baseline questionnaires.

For the participants with diabetes, duration since diabetes diagnosis was calculated by subtracting the self-reported year

of diagnosis or, when available, the exact date of diagnosis supplied by the medical practitioner from the year of baseline examination. Information on insulin therapy or use of oral hypoglycaemic agents was either self-reported at the visit to the study centre or obtained during medical verification. The lifestyle questionnaire also included a question on insulin therapy.

Outcome ascertainment Causes and dates of death were ascertained by several methods, depending on the available options in each country, following a standardised protocol. Record links with local, regional or central cancer registries, boards of health or death registries were used in Denmark, Italy, the Netherlands, Spain and Sweden. Germany identified deceased participants by follow-up mailings to participants and their next of kin and subsequent inquiries to municipality registries, regional health departments, physicians or hospitals.

Statistical analysis Statistical analyses were performed with SAS 9.2 (SAS Institute, Cary, NC, USA). The LIFETEST procedure was used to create a Kaplan–Meier curve and perform a logrank test. All-cause mortality risk for people with diabetes vs those without was estimated with HRs and 95% CIs using standard Cox proportional hazard regression [23]. Age was used as the underlying time scale, with time of entry defined as the participant's age in years at recruitment, and time of exit defined as the participant's age in years at death or censoring.

To compare associations of lifestyle factors and mortality between persons with and without diabetes, an extension of the Cox proportional hazard model was prepared based on the ideas and methodology of the competing risk model of Lunn and McNeil [24] and a statistical test for the equality of differently adjusted incidence rate ratios devised by Hoffmann et al [25]. In this model, diabetes status was characterised by $\delta=1$, and no known diabetes by $\delta=0$. Product terms of δ and $(\delta-1)$ were added to allow for differences in the effect size of X and the covariates Z by diabetes status. This resulted in exclusion of the covariates for people with diabetes in the risk estimates for those without diabetes and vice versa, although they were included in the joint model. The hazard function $\lambda(t)$ of the Cox model had the following form:

$$\lambda(t) = \lambda_0(t)\ \exp\left\{\beta_1\delta X + \beta_2(1-\delta)X + \delta\theta^{\mathrm{T}}Z + (1-\delta)\theta^{T}Z\right\}$$

where $\lambda_0(t)$ was the unspecified baseline hazard function, β_1 the parameter estimate in diabetic patients, β_2 the parameter estimate in non-diabetic individuals, and Z a vector of covariates.

Robust sandwich estimates for the covariance matrix were not calculated, since the observations were not dependent—in contrast with competing risk analyses. Diabetes status was entered as a stratum variable to allow the baseline hazard functions to have no constant ratio. Moreover, this ensures that the HR for the two groups are identical with those obtained when two separate proportional hazards regression models are used. Subsequently, likelihood ratio tests for heterogeneity were used to quantify differences in β_1 and β_2 for all studied lifestyle factors. The hypothesis for this test states that the two HRs for persons with and without diabetes are equal [25]. In addition, these results from the joint Cox models were compared with a test for interaction. Statistical interaction for diabetes status was tested by adding product terms (exposure × diabetes status) to the standard Cox regression model in the whole sample, also including diabetes status as a covariate.

Putative confounding factors were selected using directed acyclic graphs [26]. HRs were stratified for age and centre and adjusted for sex, self-reported myocardial infarction, stroke or cancer at baseline, educational attainment (none, primary school, secondary school, technical or professional school, or higher), alcohol consumption (grams per day), physical activity (inactive, moderately inactive, moderately active or active), smoking status (never, former [quit ≤10 years ago, 11–20 years ago, >20 years ago] or current), smoking duration (≤10 years, 11–20 years, 21–30 years, 31–40 years, ≥41 years) and smoking intensity (<15, 15–24 or >25 cigarettes smoked daily), and the underlying dietary patterns when there were no exposure variables. To take diet into account, the model was adjusted for the factor loadings for the first three dietary patterns derived from factor analysis on 26 food groups. In participants with diabetes, HRs were additionally adjusted for disease duration (years) and use of diabetes medication (none, insulin, oral hypoglycaemic agents, or both).

Proportions of missing data were by and large similar between persons with and without diabetes and were <1% for BMI, 6–11% for waist/height ratio, 2–3% for diet, <1% for alcohol consumption, 6–12% for physical activity, <1% for smoking status, <1% for education, 1–2% for prevalent myocardial infarction, 6–11% for prevalent stroke and 10–15% for prevalent cancer. Among the participants with diabetes, 29% had missing data on medication and 9% on disease duration. These missing values were imputed with the multiple imputation technique [27] in which 20 duplicate datasets were sampled, with the missing values replaced by imputed values [28, 29].

The robustness of the results was investigated by first excluding those with comorbidities at baseline or a follow-up of <2 years. Second, since people with diabetes may be more likely to under-report their energy intake than those without diabetes, it was checked whether excluding energy misreporters (those who were in the top and bottom 1% of the ratio of energy intake to energy requirement) influenced the results on food groups (177 diabetic and 5,023 non-diabetic participants excluded).

Results

After a median follow-up of 9.9 years (interquartile range 8.8–11.0 years), 830 (13%) participants with diabetes and 12,135 (5%) participants without known diabetes had died. Compared with participants without diabetes, those with diabetes were older, more likely to be male and had a higher BMI and waist/height ratio (Table 1). Those with diabetes had lower alcohol consumption and were more likely to be physically inactive and educated to a lower standard than their non-diabetic counterparts. In addition, prevalence of hypertension and heart disease were higher among those with diabetes.

The individuals with diabetes had significantly worse 12-year survival rates than those without (Fig. 1). Moreover, all-cause mortality risk among those with diabetes with respect to those without was HR 1.62 (95% CI 1.51, 1.75) after adjustment for age, sex, prevalent diseases, educational status, BMI, waist/height ratio, diet, alcohol consumption, physical activity and smoking behaviour.

Table 2 shows the HR for overall mortality from a joint model of people with and without diabetes as well as the ratio between the HR and p value for difference. A higher BMI and waist/height ratio were related to increased mortality in diabetes-free individuals. These associations tended to be stronger in those with diabetes, although the difference was not statistically significant.

The comparison of mortality risks by intake of 26 food groups or items showed several statistically significant differences between individuals with and without diabetes. A higher consumption of fruit, legumes, nuts and seeds, pasta, poultry and vegetable oil was associated with a lower mortality risk in individuals with diabetes. Moreover, a higher consumption of butter and margarine was related to a higher mortality risk in individuals with diabetes. Unexpectedly, cakes and cookies and soft drinks were inversely related to mortality in diabetes-free individuals.

Compared with light alcohol consumption (>0–6 g/day), abstinence and high consumption (>60 g/day) of alcohol were associated with increased mortality risk. Moreover, compared with light alcohol consumption, a consumption of 6–60 g/day was associated with a lower mortality risk in persons without diabetes, but not in persons with diabetes. However, these differences were not statistically significant.

Higher amounts of leisure-time physical activity were related to lower mortality rates in persons with and without diabetes, but again these differences were not statistically significant.

Finally, former and current smokers had an increased mortality risk compared with never smokers irrespective of diabetes status.

With the exception of the results for waist/height ratio, the p values from the test for statistical interaction by diabetes status in standard Cox regression models were similar to the

Table 1 General characteristics of 6,384 persons with diabetes and 258,911 persons without diabetes from the EPIC cohort

Characteristic	Diabetic (n =6,384)	Non-diabetic (n =258,911)
Age (years)	57.4 (6.7)	51.8 (9.2)
Male (%)	54	40
BMI (kg/m^2)	28.9 (4.9)	25.8 (4.1)
Waist/height ratio	0.58 (0.08)	0.51 (0.07)
Food group intake (g/day)		
Potatoes	85 (60–116)	76 (50–104)
Vegetables	157 (129–192)	147 (118–180)
Fruit	193 (133–281)	182 (121–277)
Legumes	3 (0–7)	2 (0–6)
Nuts and seeds	1 (0–2)	2 (0–4)
Dairy		
Milk and milk products	137 (64–238)	149 (75–243)
Cheese	31 (24–39)	32 (25–41)
Yogurt	32 (3–71)	39 (11–76)
Grains		
Pasta	16 (8–34)	21 (12–44)
Rice	10 (6–17)	12 (8–19)
Bread	128 (100–164)	121 (94–157)
Breakfast cereals	0 (0–6)	0 (0–12)
Meat		
Red	50 (38–66)	46 (34–60)
Processed	49 (34–70)	41 (28–59)
Poultry	16 (11–23)	15 (11–22)
Offal	1 (0–2)	1 (0–2)
Fish and shellfish	27 (18–41)	27 (17–37)
Eggs	13 (10–18)	13 (11–18)
Fats and oils		
Vegetable oil	2 (1–5)	2 (1–6)
Butter and margarine	22 (7–37)	20 (5–33)
Sugar and confectionery	27 (19–36)	36 (28–46)
Cake and cookies	42 (34–53)	50 (40–62)
Non-alcoholic beverages		
Soft drinks	9 (0–104)	47 (0–194)
Juices	33 (0–96)	43 (13–99)
Tea	26 (0–151)	48 (0–194)
Coffee	487 (211–664)	488 (173–697)
Alcohol consumption	5 (1–20)	8 (2–20)
Leisure-time physical activity (%)		
Low	26	22
Medium	23	21
High	25	23
Very high	26	24
Smoking status (%)		
Never	39	42
Former	28	29
Current	25	28

Table 1 (continued)

Characteristic	Diabetic (n = 6,384)	Non-diabetic (n = 258,911)
Educational attainment (%)		
None	4	2
Primary school	42	28
Secondary school	27	28
Technical/professional school	11	20
Higher (including university)	16	21
Comorbidities (%)		
Hypertension	55	27
Heart disease	7	1
Stroke	4	1
Cancer	4	3

Continuous variables are shown as mean (SD) when normally distributed and median (interquartile range) when not normally distributed. Categorical variables are shown as percentages

results from the joint regression models and the test for heterogeneity.

Excluding participants with comorbidities at baseline from sensitivity analyses did not substantially influence risk estimates of persons with and without diabetes. Excluding energy misreporters did not affect the results substantially (data not shown).

Discussion

The results from this prospective study confirm that people with diabetes have a higher premature mortality risk than those without diabetes [11]. Diabetes status did not substantially affect the associations between mortality risk and adiposity, physical activity, smoking and alcohol consumption. Importantly, intake of several food groups was more strongly related to mortality risk in individuals with diabetes than in those without diabetes, but the directions of association were generally the same.

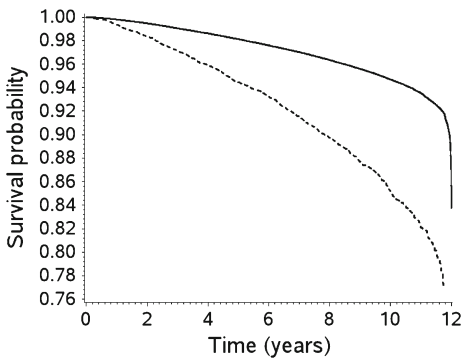

Fig. 1 Twelve-year survival curves for 258,911 participants without diabetes (solid line) vs 6,384 with diabetes (dashed line). p value of logrank test <0.0001

We found three other studies that have tested whether associations between lifestyle and mortality risk are statistically different in people with and without diabetes. Batty et al [30] explored whether diabetes status modified the effect of physical activity on mortality in 352 men with diabetes and 6,056 normoglycaemic men. The association between walking pace and leisure-time physical activity and CVD outcomes was stronger in men with diabetes (p value for interaction was statistically significant). In our study, leisure-time physical activity was associated with a lower mortality risk, but the associations were not different from those in persons without diabetes. Conversely, the National Health and Nutrition Examination Survey I reported no statistically significant interaction by diabetes status for the associations between the lifestyle factors, smoking, BMI, physical activity and mortality [31]. Moreover, in our 2011 study of adiposity and mortality, we tested for statistical interaction between measures of adiposity and diabetes status in relation to mortality in the general EPIC population [8]. No statistically significant interaction was detected. In the present study, we found no statistically significant difference between persons with and without diabetes when comparing the associations between adiposity measures and mortality.

To our knowledge, this study is the first to use the methodology of the competing risk model to quantify and test for differences in epidemiological associations between populations. We believe this was the most appropriate approach to answer our study questions. Our results are comparable with those from a 'standard' test of statistical interaction by diabetes status. However, a p value from a test of interaction only gives an indication of whether the relationship is different between two groups. The competing risk approach enabled us to compare and quantify the differences in strength and the direction of associations between persons with and without diabetes.

We have observed several significant associations between lifestyle factors and mortality risk. Higher adiposity measures, smoking and higher levels of alcohol consumption as well as abstinence were related to increased mortality risk. Furthermore, physical activity was inversely associated with mortality. These associations are well established in the scientific literature in individuals both with and without diabetes. This study further adds to this body of evidence that these associations are not affected by diabetes status.

Next, a higher consumption of fruit, legumes, nuts and seeds, pasta, poultry and vegetable oil was associated with a lower mortality risk. Furthermore, a higher consumption of butter and margarine was related to a higher mortality risk. These associations were significantly stronger in persons with diabetes than in their non-diabetic counterparts. We cannot

Table 2 HR (95% CI) for selected lifestyle factors and mortality in 6,384 persons with and 258,911 persons without diabetes and the ratio between these HRs

Lifestyle factor	Diabetic	Non-diabetic	Ratio	*p* value difference	*p* value interaction
Adiposity[a]					
BMI					
Q1	1	1	1		
Q2	0.80 (0.61, 1.05)	0.84 (0.80, 0.89)	0.95 (0.72, 1.25)	0.71	0.30
Q3	0.78 (0.61, 1.00)	0.84 (0.80, 0.89)	0.93 (0.72, 1.20)	0.56	0.16
Q4	0.90 (0.72, 1.13)	1.03 (0.97, 1.08)	0.88 (0.70, 1.11)	0.27	0.03
Continuous (per kg/m^2)	1.02 (1.00, 1.03)	1.01 (1.01, 1.02)	1.01 (0.99, 1.02)	0.37	0.56
Waist/height ratio					
Q1	1	1	1		
Q2	0.73 (0.52, 1.04)	0.94 (0.89, 1.00)	0.78 (0.55, 1.11)	0.16	0.03
Q3	0.74 (0.54, 1.01)	0.95 (0.89, 1.01)	0.78 (0.56, 1.07)	0.12	0.01
Q4	0.97 (0.73, 1.30)	1.22 (1.15, 1.29)	0.80 (0.60, 1.08)	0.14	0.003
Continuous (per unit)	9.28 (4.78, 18.01)	6.83 (5.15, 9.06)	1.36 (0.70, 2.64)	0.37	0.47
Food groups[a]					
Potatoes (per 100 g)	1.10 (0.91, 1.32)	0.96 (0.90, 1.01)	1.15 (0.95, 1.38)	0.16	0.09
Vegetables (per 100 g)	0.74 (0.64, 0.86)	0.85 (0.81, 0.90)	0.87 (0.75, 1.02)	0.08	0.05
Fruit (per 100 g)	0.85 (0.79, 0.92)	0.97 (0.95, 1.00)	0.88 (0.81, 0.94)	0.001	0.001
Legumes (per 10 g)	0.88 (0.81, 0.96)	1.03 (1.00, 1.05)	0.86 (0.79, 0.94)	0.001	<0.0001
Nuts and seeds (per g)	0.94 (0.90, 0.97)	0.99 (0.98, 1.00)	0.95 (0.91, 0.98)	0.01	0.02
Dairy					
Milk (products) (per 50 g)	1.01 (0.99, 1.04)	1.01 (1.01, 1.02)	1.00 (0.98, 1.02)	0.83	0.97
Yogurt (per 10 g)	1.01 (1.00, 1.02)	1.00 (1.00, 1.00)	1.01 (1.00, 1.02)	0.21	0.06
Cheese (per 10 g)	0.99 (0.94, 1.05)	0.96 (0.95, 0.98)	1.03 (0.98, 1.09)	0.23	0.06
Grains					
Pasta (per 10 g)	0.93 (0.90, 0.96)	0.99 (0.98, 1.00)	0.94 (0.92, 0.98)	0.001	0.001
Rice (per 10 g)	0.93 (0.86, 1.00)	0.96 (0.94, 0.98)	0.97 (0.90, 1.05)	0.46	0.40
Bread (per 10 g)	0.87 (0.71, 1.07)	0.81 (0.76, 0.82)	1.08 (0.88, 1.33)	0.47	0.38
Breakfast cereals (per 10 g)	1.00 (0.97, 1.02)	0.97 (0.97, 0.98)	1.02 (1.00, 1.05)	0.09	0.02
Meat					
Red (per 10 g)	1.00 (0.96, 1.04)	1.01 (1.00, 1.02)	0.99 (0.96, 1.03)	0.73	0.29
Processed (per 10 g)	1.03 (1.00, 1.07)	1.03 (1.02, 1.04)	1.00 (0.97, 1.04)	0.86	0.80
Poultry (per 10 g)	0.89 (0.83, 0.96)	0.97 (0.95, 1.00)	0.91 (0.85, 0.99)	0.02	0.01
Offal (per g)	1.00 (0.97, 1.03)	1.01 (1.01, 1.02)	0.99 (0.96, 1.01)	0.30	0.16
Fish and shellfish (per 10 g)	0.99 (0.96, 1.02)	1.00 (0.96, 1.02)	0.99 (0.96, 1.02)	0.52	0.18
Eggs (per 10 g)	1.04 (0.96, 1.12)	1.09 (1.06, 1.12)	0.95 (0.88, 1.03)	0.21	0.09
Fats					
Vegetable oil (per g)	0.97 (0.96, 0.98)	0.99 (0.98, 1.00)	0.98 (0.97, 0.99)	<0.0001	<0.0001
Butter and margarine (per g)	1.05 (1.02, 1.09)	1.00 (0.99, 1.02)	1.05 (1.01, 1.09)	0.01	0.004
Sugar and confectionery (per 10 g)	1.06 (0.99, 1.12)	1.05 (1.03, 1.07)	1.00 (0.94, 1.07)	0.89	0.81
Cakes and cookies (per 10 g)	1.03 (0.99, 1.08)	0.97 (0.96, 0.99)	1.06 (1.02, 1.10)	0.01	0.002
Non-alcoholic beverages					
Soft drinks (per 10 g)	1.04 (0.99, 1.09)	0.98 (0.96, 0.99)	1.06 (1.01, 1.12)	0.02	0.01
Juices (per 10 g)	0.98 (0.94, 1.01)	0.97 (0.96, 0.98)	1.01 (0.98, 1.04)	0.61	0.30
Tea (per 100 g)	0.99 (0.97, 1.02)	1.00 (0.96, 1.03)	1.00 (0.96, 1.03)	0.75	0.84
Coffee (per 100 g)	0.99 (0.97, 1.01)	0.98 (0.97, 0.98)	1.01 (0.99, 1.03)	0.28	0.34
Alcohol consumption (g/day)[b]					
0	1.55 (1.26, 1.89)	1.32 (1.24, 1.41)	1.17 (0.95, 1.44)	0.15	0.41
>0–6	1	1	1		

Table 2 (continued)

Lifestyle factor	Diabetic	Non-diabetic	Ratio	*p* value difference	*p* value interaction
>6–12	0.85 (0.67, 1.09)	0.80 (0.75, 0.85)	1.07 (0.83, 1.37)	0.60	0.81
>12–24	1.00 (0.80, 1.26)	0.79 (0.75, 0.84)	1.27 (1.00, 1.60)	0.05	0.14
>24–60	1.05 (0.83, 1.32)	0.87 (0.82, 0.93)	1.20 (0.94, 1.53)	0.15	0.49
>60	1.37 (1.02, 1.84)	1.13 (1.04, 1.23)	1.21 (0.89, 1.65)	0.21	0.94
Continuous (per 12 g)	0.95 (0.92, 0.99)	0.94 (0.93, 0.95)	1.02 (0.98, 1.06)	0.36	0.86
Leisure-time physical activity[a]					
Low	1	1	1		
Medium	0.92 (0.77, 1.09)	0.86 (0.81, 0.90)	1.07 (0.89, 1.29)	0.46	0.80
High	0.86 (0.71, 1.03)	0.88 (0.83, 0.93)	0.98 (0.81, 1.18)	0.80	0.25
Very high	0.74 (0.60, 0.91)	0.81 (0.77, 0.86)	0.91 (0.74, 1.13)	0.40	0.07
Continuous (per category)	0.93 (0.88, 0.98)	0.94 (0.92, 0.96)	0.99 (0.93, 1.05)	0.65	0.03
Smoking status[a]					
Never	1	1	1		
Former	1.36 (1.13, 1.64)	1.29 (1.23, 1.36)	0.85 (0.66, 1.08)	0.60	0.73
Current	2.29 (1.91, 3.01)	2.27 (2.17, 2.38)	1.01 (0.84, 1.22)	0.92	0.26

[a] Model 1: age- and centre-stratified and adjusted for sex, prevalence of heart disease, cancer or stroke, educational attainment, diabetes medication use (in diabetic individuals), and the following when there were no exposure variables: alcohol consumption, smoking behaviour, physical activity and underlying dietary patterns

[b] Model 1 additionally adjusted for alcohol consumption in the past

completely rule out the possibility that these differences are due to chance, since many differences were tested for. Assuming that the observed differences in associations are true differences, we hypothesise that they can be explained by the same underlying mechanisms as are involved in the prevention of diabetes. Fruits, legumes, nuts, seeds, pasta, poultry and vegetable oil are rich in vitamins, antioxidants, unsaturated fatty acids, polyphenols and fibre and low in saturated fat and sugars. These compounds may be responsible for improving endothelial function, blood pressure and blood lipids, as well as lowering oxidative stress, inflammation, insulin resistance and impaired glucose tolerance, and thus diabetes, CVD and overall mortality [32–36].

In conclusion, it appears that the intake of some food groups is more beneficial (fruits, legumes, nuts, seeds, pasta, poultry, vegetable oil) or more detrimental (soft drinks, butter, margarine, cake, cookies) with respect to mortality risk in people with diabetes. This may indicate that individuals with diabetes may benefit more from a healthy diet than people without diabetes. However, since the directions of association were generally the same, recommendations for a healthy diet should be similar.

Our study could be interpreted in the context of impaired glucose tolerance or undiagnosed diabetes. The clinical diagnosis of diabetes is defined by the level of hyperglycaemia, giving rise to risk of macro- and microvascular complications [13]. Diabetes can be considered a continuing process of declining glycaemic control, where individuals shift from health to impaired glucose tolerance, undiagnosed diabetes and finally diagnosed diabetes. It has been shown that glycaemic control is related to increasing risk of macrovascular complications throughout the whole range of concentrations, even below the diabetic threshold [14]. Impaired glucose tolerance has already been shown to be associated with increased CVD risk [37]. Even more complicated in this context, about 50% of all people with type 2 diabetes are believed to be undiagnosed [13]. Our findings highlight that these difficulties in recognising and diagnosing diabetes and its different stages are of minor importance with respect to healthy diet and lifestyle recommendations, because no difference in recommendations depending on the stage of the disease seems necessary.

Under-reporting of energy intake has been widely acknowledged in obese people, and it has also been reported that obese individuals with diabetes under-report their energy intake more than obese individuals without diabetes [38]. Indeed, a larger proportion of people with diabetes were classified as energy misreporters than those without diabetes. However, associations were not affected when those classified as energy misreporters were excluded. Energy adjustment seems to minimise the problems related to selective misreporting [20, 39]. Moreover, although people with diabetes are supposed to undergo nutrition and health counselling, this was not reflected in their lifestyle behaviours in the present or other studies [40, 41].

This study benefitted from a large sample size, multicentric design, verification of diabetes diagnoses, wide range of variables and a long follow-up period. Moreover, multiple

imputation of missing values and appropriate confounder selection and adjustment were used to reduce potential bias. Self-reports of diabetes at baseline were confirmed with a second information source, but when no additional information source was available, we were unable to discriminate true- from false-positive case classifications. Because no systematic screening was conducted, selection bias might have been introduced in different ways. For example, we cannot rule out the possibility that only the most advanced cases were classified as diabetes, or that people with a family history of diabetes or other concomitant comorbidities who have more contact with healthcare services were identified as having diabetes. Furthermore, we do not know whether the participants without diabetes at baseline have since developed the disease during follow-up. This could have reduced the external validity of our study. However, selective participation should not impair aetiological associations between a lifestyle factor and an outcome. Because aetiological associations were the main objective of the study, we do not think that the representativeness has biased the results.

In conclusion, we observed that diabetes status did not appear to influence the relations between most lifestyle factors and mortality risk. This study suggests that, with respect to mortality, lifestyle advice for people with diabetes should not differ from the existing recommendations for the general population. It may be that those with diabetes benefit more from a healthy diet than diabetes-free individuals. However, this has to be confirmed in further studies.

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