

**Citation:**

Sluijs I, Beulens JW, van der A DL, Spijkerman AM, Grobbee DE, van der Schouw YT. Dietary intake of total, animal and vegetable protein and risk of type 2 diabetes in the European Prospective Investigation into Cancer and Nutrition (EPIC)-NL study. *Diabetes Care*. 2010 Jan; 33 (1): 43-48. Epub 2009 Oct 13.

**PubMed ID:** [19825820](#)

**Study Design:**

Prospective cohort study

**Class:**

B - [Click here](#) for explanation of classification scheme.

**Research Design and Implementation Rating:**

POSITIVE: See Research Design and Implementation Criteria Checklist below.

**Research Purpose:**

Examined the association among dietary total, vegetable and animal protein intake and type 2 diabetes incidence and whether consuming 5% energy from protein at the expense of 5% energy from either carbohydrates (CHO) or fat was associated with diabetes risk.

**Inclusion Criteria:**

- Prospect-EPIC cohort: Women aged 49-70 years living in Utrecht and vicinity
- MORGEN-EPIC cohort: Adults aged 21-64 years from three Dutch towns.

**Exclusion Criteria:**

- Prevalent diabetes (N=615)
- Abnormal energy intake (kcal <600 or >5,000 per day) (N=108)
- Missing nutritional data (N=213)
- Missing follow-up (N=981).

**Description of Study Protocol:****Recruitment**

- MORGEN-EPIC cohort participants selected from random samples of the Dutch population in three Dutch towns
- Recruitment for the Prospect-COHORT not described in this publication but consisted of adults that lived in Utrecht and vicinity.

## **Design**

Participants from the European Prospective Investigation into Cancer and Nutrition (EPIC)-NL study Dutch cohort made up of the Prospect-EPIC and MORGEN-EPIC cohorts.

### **Dietary Intake/Dietary Assessment Methodology**

- Daily dietary intake was obtained from a validated, self-administered FFQ containing questions on the usual frequency of consumption of 79 main food items during the year preceding enrollment
- This questionnaire allows estimation of the average daily consumption of 178 foods
- The FFQ was administered once at baseline and sent to participants by mail
- Participants returned the FFQ during the physical examination screening, where difficulties in filling out the questionnaire were discussed
- A registered dietitian (RD) checked the FFQ for inconsistencies, which were resolved by contacting the participant.

### **Blinding Used**

Not applicable.

### **Intervention**

Not applicable.

### **Statistical Analysis**

- Protein intake, adjusted for total energy intake by the regression residual method, was categorized into quartiles
- Cox proportional hazard models were used to calculate crude and adjusted hazard ratios (HRs) and 95% CI for the associations between quartiles of protein intake and diabetes
- P for trend was estimated by including median protein intakes per quartile as continuous variables in the Cox regression models
- A multivariate model including total energy intake and energy percentages of protein and other macronutrients was used
- Macronutrient intakes were entered into the model per 5% energy. Total energy intake was entered into the model to keep energy intake constant. By leaving out energy percentages from CHO in the regression model, it was possible to examine the difference in diabetes risk associated with consumption of 5% energy from protein at the expense of 5% energy from CHO, while total energy intake is kept constant
- Similarly, the difference in diabetes risk associated with consumption of 5% energy from protein at the expense of 5% energy from fat, while energy intake is held constant, is presented.

## **Data Collection Summary:**

### **Timing of Measurements**

- Baseline measurements (dietary intake and physical examination) with follow-up over 10 years
- Diabetes occurrence assessed in two follow-up questionnaires with three- to five-year intervals
- Weight derived from mailed follow-up questionnaires or physical examination.

## Dependent Variables

Type 2 diabetes (T2D):

- Self-reported in two follow-up questionnaires with three- to five-year intervals
- In the Prospect study, incident cases of diabetes were detected via a urinary glucose strip test
- Incident diabetes was verified against medical records.

## Independent Variables

- Total protein
- Animal protein
- Vegetable protein.

## Control Variables

- Sex
- Age
- Nutritional factors [energy-adjusted intake of saturated fat, monounsaturated fat, and polyunsaturated fat, cholesterol, vitamin E, magnesium, fiber, and glycemic load (continuous)]
- Alcohol consumption
- Physical activity
- Blood pressure
- Education
- Parental history of diabetes
- BMI
- Waist circumference.

## Description of Actual Data Sample:

- *Initial N*: Prospect-EPIC=17,357 women; MORGEN-EPIC=22,654 men and women
- *Attrition (final N)*: 38,094
- *Age*: Varied across quartiles from 48±12 years to 51±11 years
- *Ethnicity*: Dutch participants
- *Other relevant demographics*: Mean protein intake=75.7g per day with animal protein the majority:
  - Main contributors to animal protein intake were:
    - Meat (39%)
    - Milk products (29%)
    - Cheese (18%)
  - Main contributors to vegetable protein intake were:
    - Bread (43%)
    - Fruit and vegetables (14%)
    - Potatoes (9%)
- *Anthropometrics*: BMI varied across quartiles from 24.7±3.7 to 26.7±4.3kg/m<sup>2</sup>
- *Location*: The Netherlands.

## Summary of Results:

- During 10 years of follow-up, 918 incident cases of diabetes were documented. Diabetes risk increased with higher total protein (HR between extreme quartiles=2.15; 95% CI: 1.77, 2.60; P for trend <0.001) and animal protein intake (HR=2.18; 95% CI: 1.80, 2.63; P for trend <0.001). Adjustment for confounders (age, sex, dietary factors and diabetes risk factors) did not materially change these results. Further adjustment for adiposity measures attenuated the associations. Vegetable protein intake was not related to diabetes (HR between extreme quartiles=0.84; 95% CI: 0.70, 1.01; P for trend=0.10)
- Consumption of 5% energy from protein at the expense of 5% energy from fat increased diabetes risk, with an HR of 1.31 (95% CI: 1.06,1.61) for each 5% energy from protein exchanged for 5% energy from fat in the final model. For consuming 5% energy from protein at the expense of 5% energy from carbohydrate, an HR of 1.28 (95% CI: 1.01, 1.61) was observed in the final model. Similar results were observed for animal protein. No associations with consuming 5% energy from vegetable protein were observed.

### Author Conclusion:

- Diets high in animal protein are associated with an increased diabetes risk
- Our findings also suggest a similar association for total protein itself instead of only animal sources
- Consumption of energy from protein at the expense of energy from either carbohydrates or fat may similarly increase diabetes risk. This finding indicates that accounting for protein content in dietary recommendations for diabetes prevention may be useful.

### Reviewer Comments:

### Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

### Validity Questions

1.	Was the research question clearly stated?	Yes
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1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
<b>2.</b>	<b>Was the selection of study subjects/patients free from bias?</b>	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
<b>3.</b>	<b>Were study groups comparable?</b>	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
<b>4.</b>	<b>Was method of handling withdrawals described?</b>	Yes
4.1.	Were follow-up methods described and the same for all groups?	???
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes

4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	???
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
<b>5.</b>	<b>Was blinding used to prevent introduction of bias?</b>	N/A
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
<b>6.</b>	<b>Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were intervening factors described?</b>	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	N/A
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
<b>7.</b>	<b>Were outcomes clearly defined and the measurements valid and reliable?</b>	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes

7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
<b>8.</b>	<b>Was the statistical analysis appropriate for the study design and type of outcome indicators?</b>	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	No
<b>9.</b>	<b>Are conclusions supported by results with biases and limitations taken into consideration?</b>	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
<b>10.</b>	<b>Is bias due to study's funding or sponsorship unlikely?</b>	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes