German Institute of Human Nutrition
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Translation of science into action: the potential role of diet reducing disease risk

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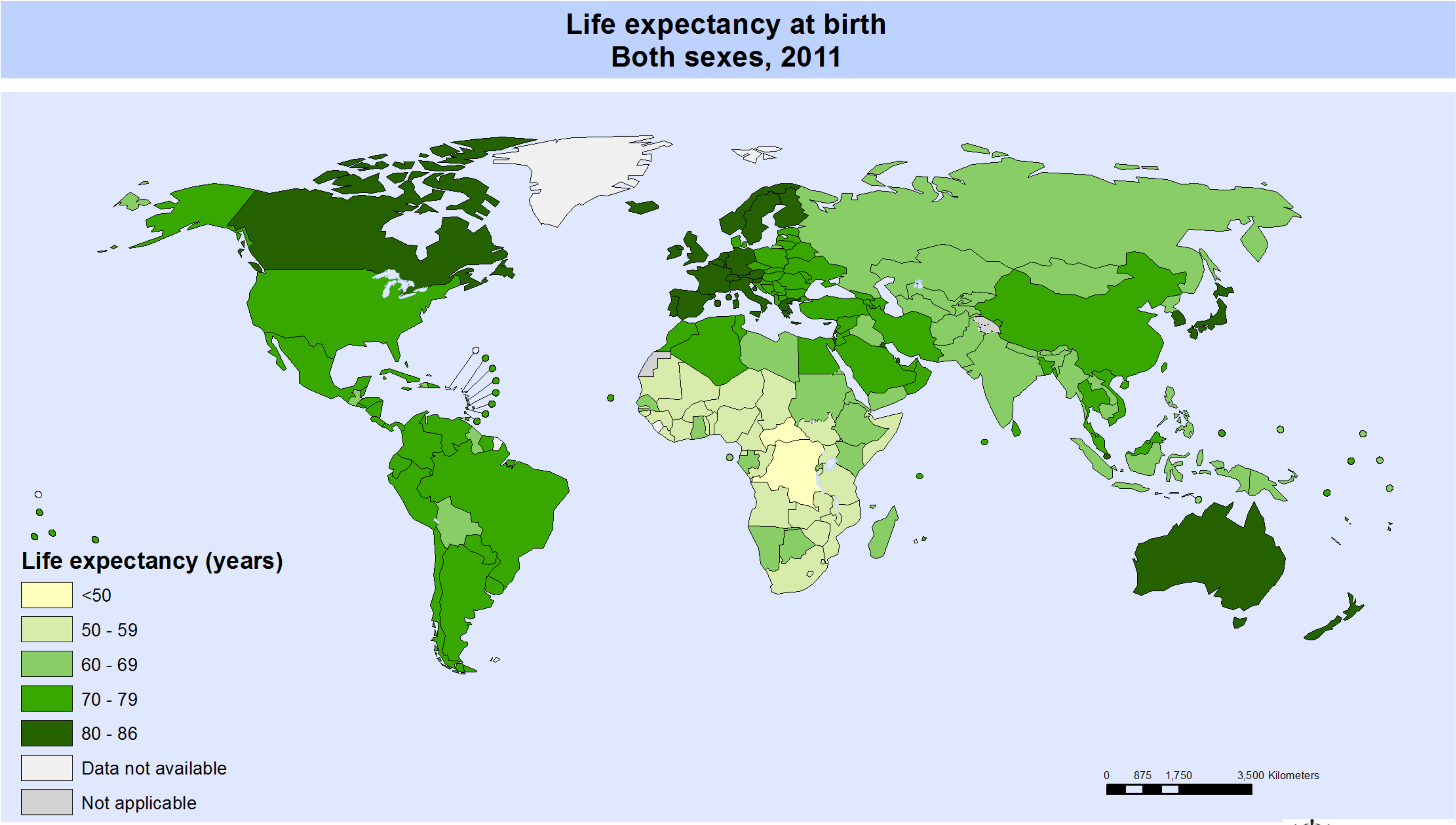
Leibniz-Gemeinschaft

Background

- In the area of diet and chronic diseases, it is important to understand which life style factors including diet are linked to chronic diseases
- It is also important to investigate which of the dietary factors linked to chronic diseases has which potential to reduce the occurrence of chronic diseases
- Dietary factors with a high potential of influencing the occurrence of diseases should be preferred targets of investigations regarding mechanisms and public health measures

Life expectancy in the world



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

World Health Organization

Role of Nutrition Societies

The Nutrition Societies and its members can be the focal point for

- Collecting the evidence (systematic reviews and meta-analyses) including evaluation by expert groups
- Elucidating the biological mechanisms
- Fostering the methodological developments (techniques, statistical methods)
- Translation of the evidence into actions
- Evaluation and promotion of the selected measures

Collecting the evidence how diet is linked to the disease burden

- Prospective studies (observational and interventive) and their meta-analyses should have a preference against cross-sectional or retrospctive study designs when searching the literature for the role of diet for risk of diseases

- It is also important to evaluate the literature how solid is the knowledge regarding mechanisms supporting the epidemiological observations (biological plausability)

A note regarding observational and intervention study designs in research into dietary behaviour

- Dietary recommedations and/or their translation into practice have to address foods. Foods contain usually energy and many other nutritional valuable compounds that are in most instances not the target of the research. Thus, the interpretation of such studies could be biased since the initial research hypothesis is mostly favored.

- Intervention studies with foods are difficult to perform and not easy to interpret. It investigates only one or two interventions and it is unclear whether alternative intervention might have similar or even stronger effects

Epidemiological observational approach

- Observational prospective studies have the advantage that exposure can be invested regarding many endpoints (if the study is large enough) and one can investigate many alternatives when diet is concerned

Experiences and examples

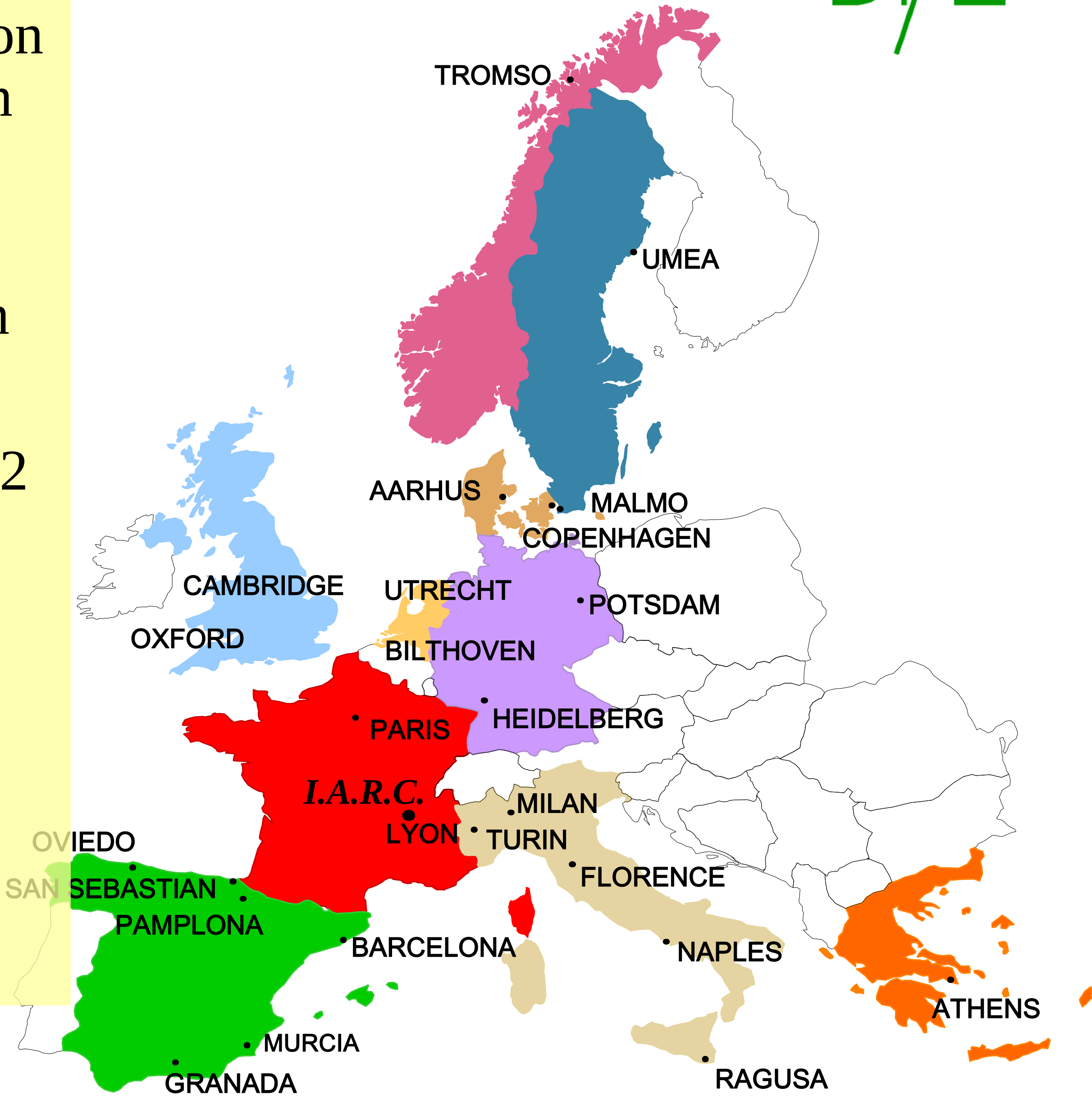
- The basis of all collections of the evidence is the results single studies.

- For Europe, the European Prospective Investigation into Cancer and Nutrition (EPIC) played an important role in contributing observational evidence to the dietary field due to their applied methodology, to their size, and to the regional distribution

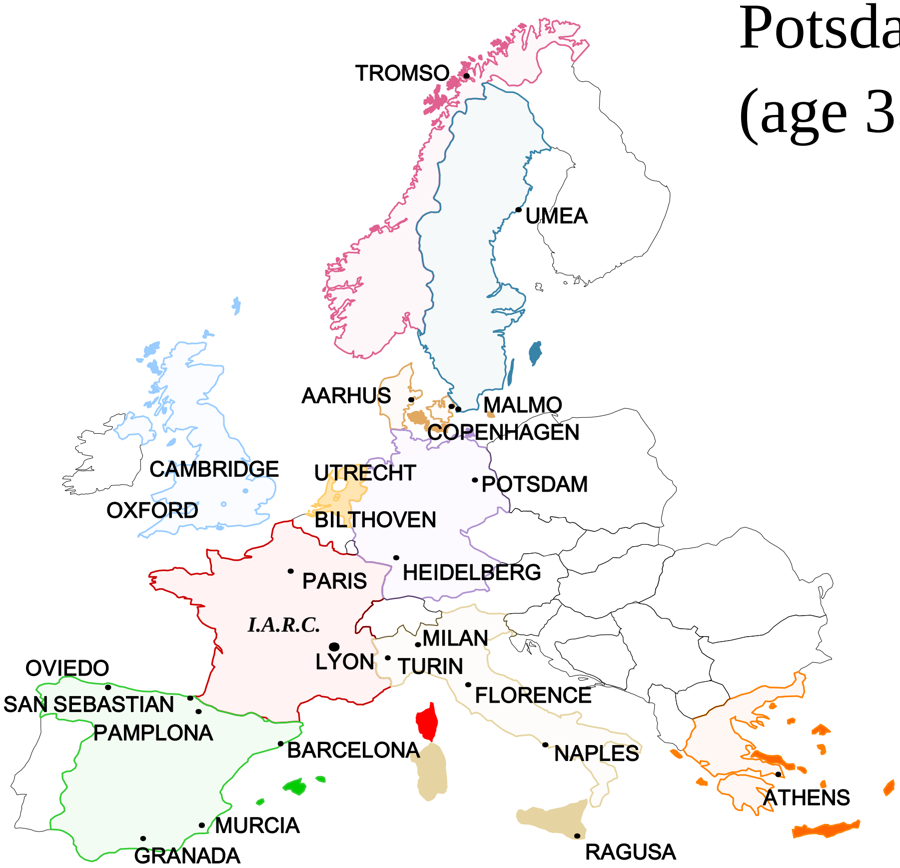
- Newer cohort studies with a better and more detailed assessment including the collection of many biomaterials are now underway in many European countries. However, it will take about 5 to 10 further years before they are becomming productive

European Prospective Investigation into Cancer and Nutrition (EPIC)

- Aim of study: Investigation of disease risk linked with diet and other life style factors
- 23 centres in 10 European countries
- Recruitment between 1992 and 1998
- Prefered age ranges at recruitment: between 40(35)-64 years
- More than 500,000 study participants (50,000 men and 350,000 women)



EPIC-Potsdam-Study



Potsdam: 27,548 study participants (age 35-65 women, 40-65 men)

Study conduct

- Recruitment and basic examinations
- Follow-up
- Re-examination

Basic examination at recruitment

1994-1998

EPIC = ***E***uropean ***P***rospective ***I***nvestigation into ***C***ancer and Nutrition

EPIC data related to lifestyle and personal history

From questionnaire:

- Tobacco
- Alcohol
- Reproductive history
- Occupation
- Illnesses
- Physical activity
- Socio-economic status

From physical examinations

- Height
- Weight
- Waist circumference
- Hip circumference
- Sitting height

- Blood pressure

EPIC data on diet

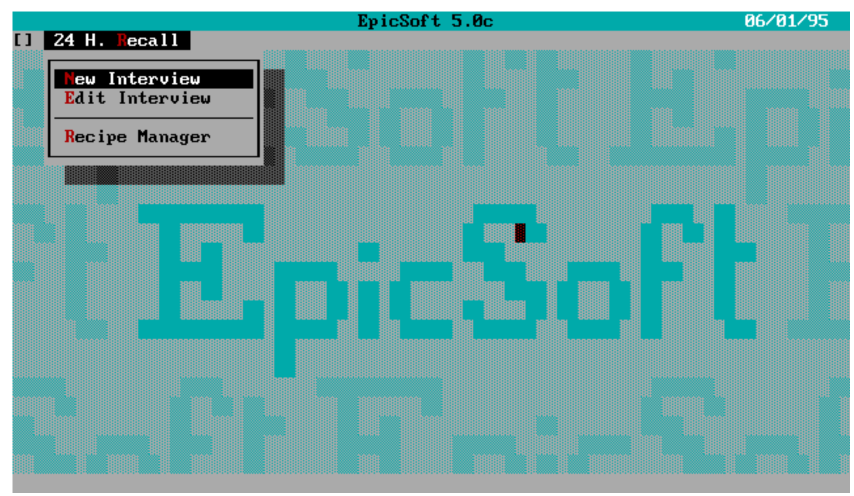
Two dietary measurements:

Dietary questionnaire on usual diet from all 519,978 subjects

- **Very detailed, 150 to 300 foods per questionnaire**
- **To relate diet to disease risk**

One day "actual" diet from a 7% sample of subjects (38,000)

- **Computerized, 3000 foods and 700 recipes per country**
- **To calibrate dietary measurements between countries**



EPIC Biorespository: Plastic straws for storage of plasma, serum, rbc, and buffy coat

Methodology to address diet and chronic diseases

Dietary and other lifestyle factors assessed at baseline

Hard (and soft) endpoints assessed during follow-up

- Weight change (fat accumulation)
- Type 2 Diabetes
- Myocardial infarction
- Stroke
- Total cancer and individudal cancer sites
- Mortality

Study approaches in EPIC

Assessment of risk factors for cancer and mortality
  (Full cohort approach and nested case-control studies with biomarkers)

Assessment of risk factors for type 2 Diabetes
  Interact-Study (Case-cohort approach with 12.403 cases and 16.154 randomly selected controls)

Assessment of risk factors for MI and stroke
  EPIC-Heart and EPIC-CVD (Case-cohort approach with 16.000 cases and 16.154 controls)

Studies on weight gain
  Diogenes and PANACEA (Follow-up data analyses)

The German National Cohort (GNC)

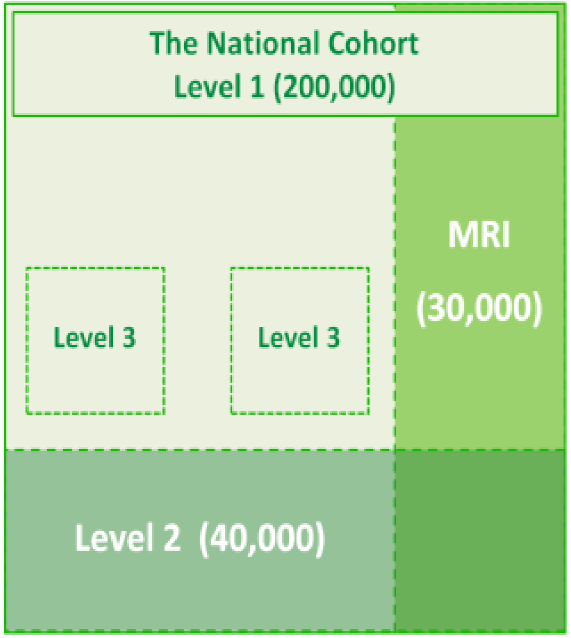
18 Study centers

GESUNDHEITS-
STUDIE

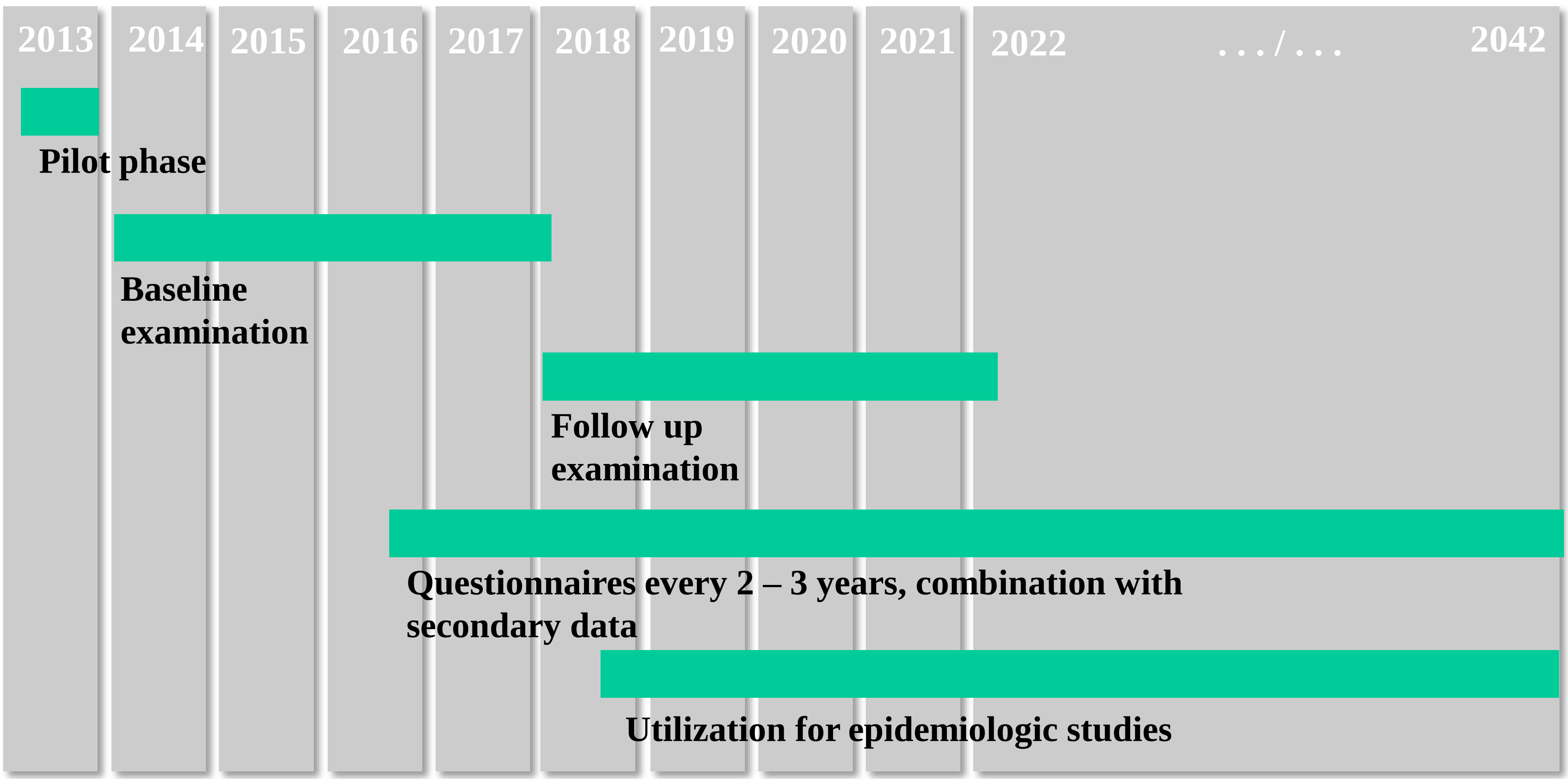
Gefördert vom Bund,
den Ländern und der
Helmholtz-Gemeinschaft

Study design (GNC)

- Prospective population-based cohort study
- 18 study centers
- Participants between 20-69 years old
- Random samples in defined regions
- **Level 1** n=200.000 duration: 2,5 h
- **Level 2** n=40.000 duration 4 h
- **Level 3** n=variable (additional research pro
  external funding)
- **MRI** program, n=30.000, at 5 sites



Time schedule



Examinations and biomaterials

Cardiovascular system
- Blood pressure and heart rate
- ECG, Electrocardiography
- Vascular Explorer (pulse wave)

Diabetes
- OGTT
- AGE Reader

Cognitive functions test
- Memory, attention/ executive, motor coordination

Pulmonary function
- Spirometry

Musculoskeletal system
- Knee, hip, hand joints

Oral health
- dental chart

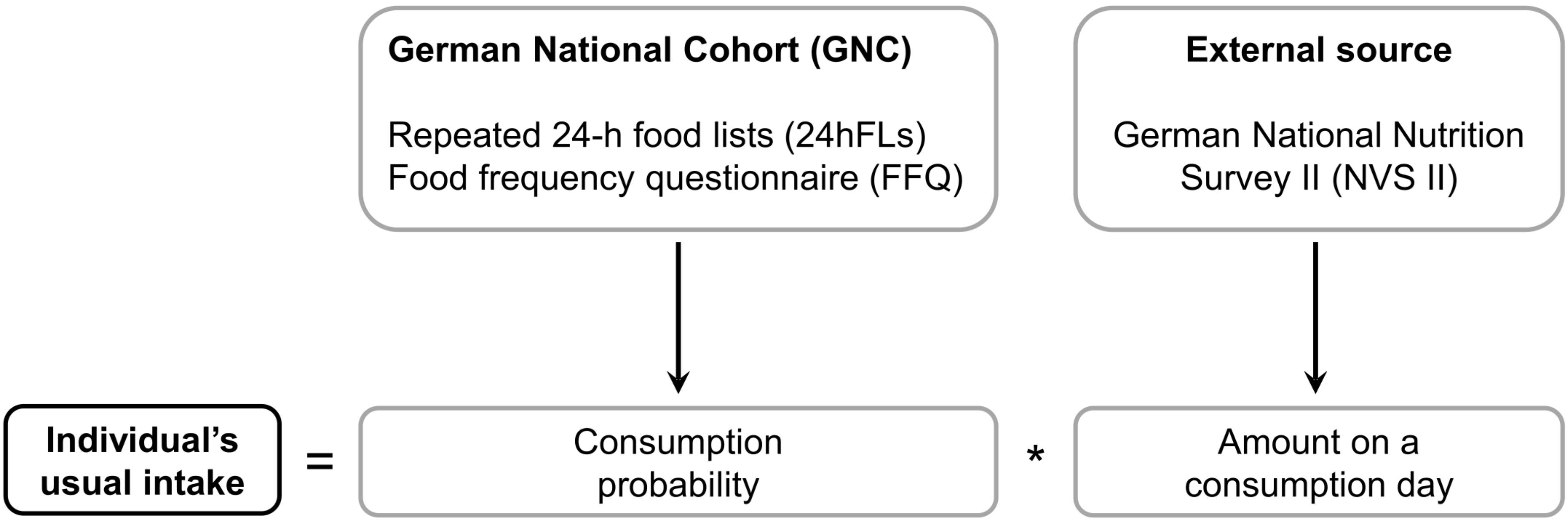
Sensory organs
- Ophthalmological measurements, hearing test, olfactory test

Physical activity and fitness
- 7-day accelerometry
- Ergometric test, hand grip strength

Anthropometry
- weight, body height, BIA, ultrasound, waist and hip circumferences

Collection of biosamples
(blood, urine, nasal swabs, saliva, stool)

Novel dietary assessment strategy: statistical modelling



Dietary components of overall nutritional importance (German FBDG)

Fruit and Vegetables

Grain products

Milk and Milkproducts

Red and processed meat, eggs, fish

Oils

Nutrition Cycle of the German Nutrition Society

Dietary components with a wide investigation in EPIC

Not all of the dietary components of the German FBDG will have the potential to reduce risk and are less studied in EPIC (and also other observational cohorts)

The interest in EPIC regarding foods centered on

- Fruit and Vegetables
- Whole grain products (dietary fiber)
- Red and processed meat

Fruit and vegetables and mortality - EPIC

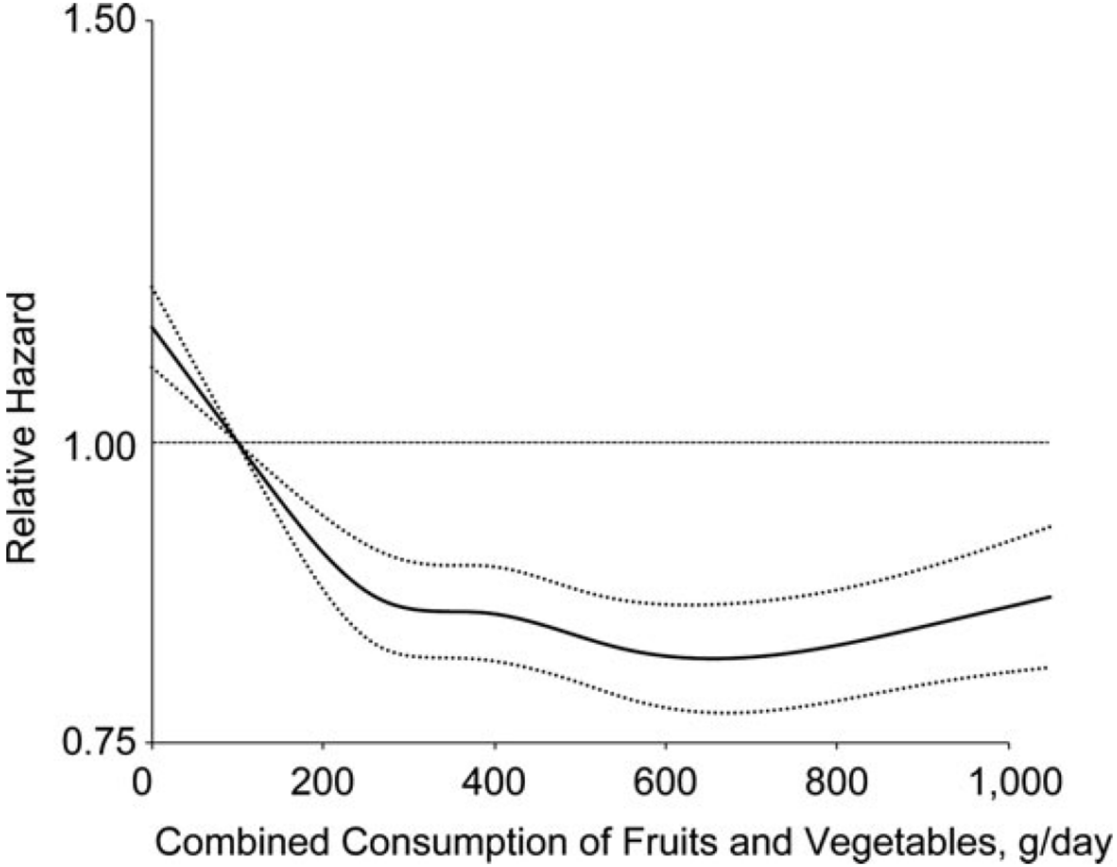


Figure 1. Restricted cubic spline and 95% confidence intervals of the nonlinear relation between fruit and vegetable consumption combined (in grams per day) and all-cause mortality, the European Prospective Investigation Into Cancer and Nutrition, 1992–2010.

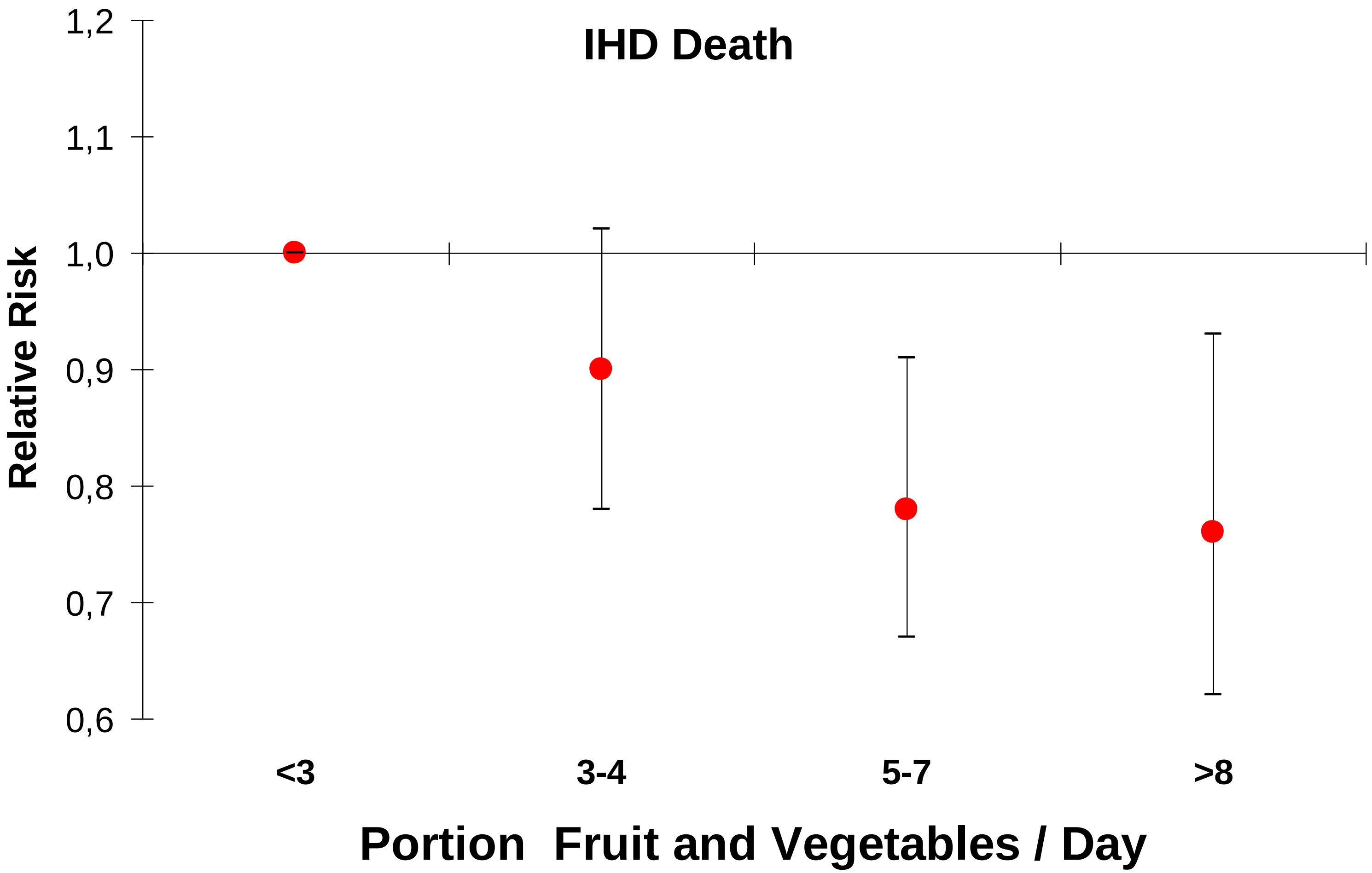
Leenders et al.: Fruit and Vegetable Consumption and Mortality - European Prospective Investigation Into Cancer and Nutrition. Am J Epidemiol. 2013;178:590–602

Fruit and vegetable quintiles and risk of cancer - EPIC

	Quintiles of intake of fruit and vegetables (g/d)				
	Q1	**Q2**	**Q3**	**Q4**	**Q5**
Relative Risk	**1**	**0.95 (0.92-0.99)**	**0.91 (0.88-0.95)**	**0.93 (0.89-0.97)**	**0.89 (0.85-0.93)**

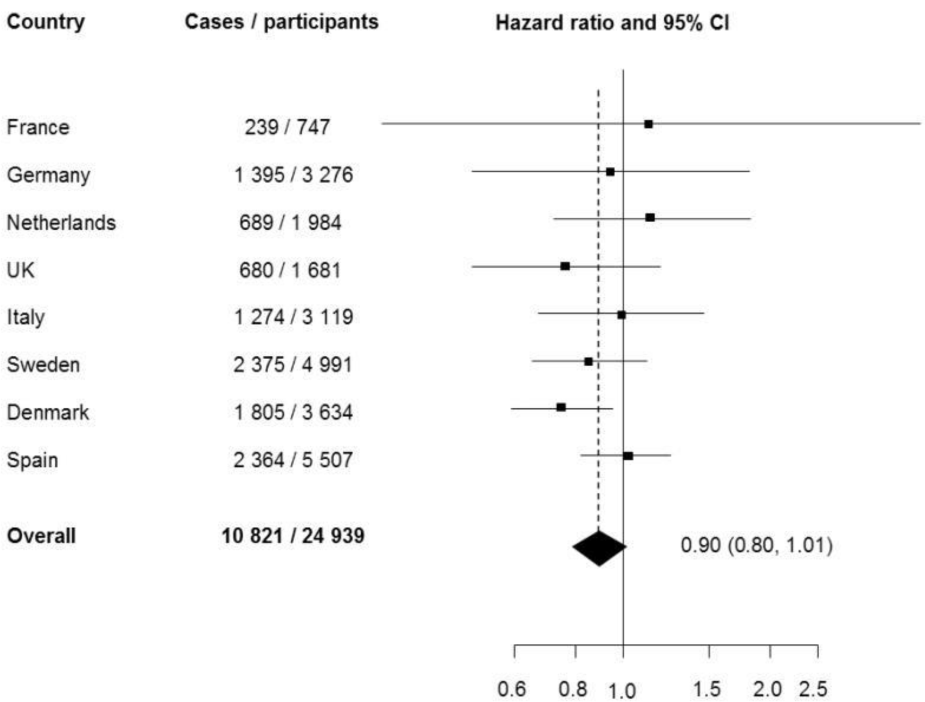
Boffetta et al., JNCI 102, 529-537: 2010

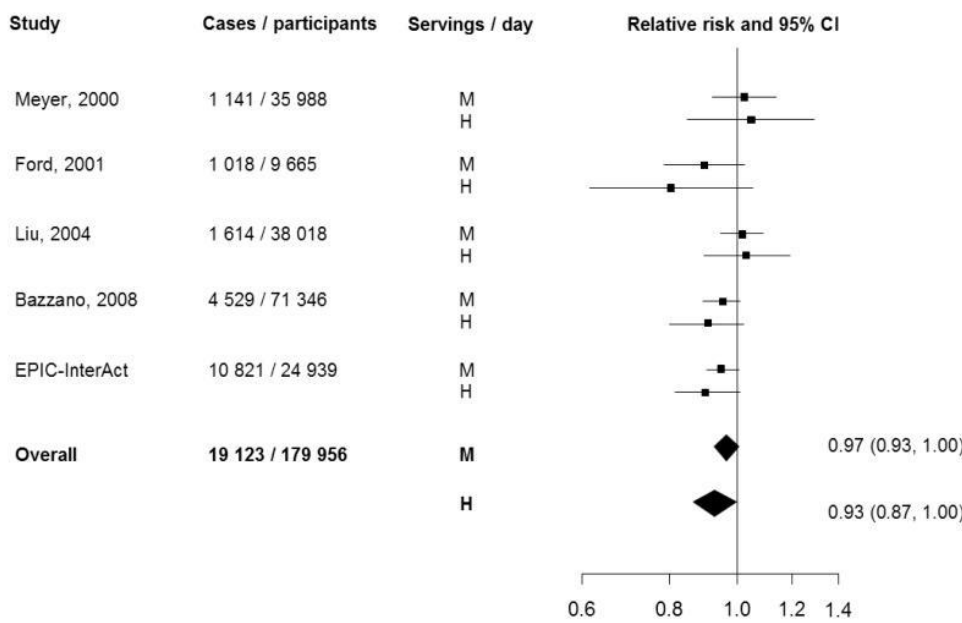
EPIC-Heart study on mortality



Crowe et al., European Heart Journal Advance Access published January 18, 2011

Fruit and vegetables and type 2 diabetes - EPIC





Cooper et al.: Fruit and vegetable intake and type 2 diabetes: EPIC-InterAct prospective study and meta-analysis. Eur J Clin Nutr. 2012; 66: 1082–1092.

Biomarker-score

Table 3

Odds ratios (95% CI) for incident diabetes by quartiles of a combined biomarker score of fruit and vegetable intake and by quartiles of plasma vitamin C, beta-carotene and lutein separately: the EPIC-Norfolk Study.

	Quartiles of the CB-score and plasma vitamin C, beta-carotene and lutein separately					
	Q1 (reference)	**Q2**	**Q3**	**Q4**	**p-trend**	**Per SD increase**
CB-score (mean, SD)	**−0.86 (0.27)**	**−0.27 (0.13)**	**0.19 (0.14)**	**0.93 (0.50)**		
Cases/ total (n)	138/ 311	102/ 311	51/ 311	27/ 311		
Model 1 (95% CI) *	1.00	0.66 (0.47-0.92)	0.28 (0.19-0.41)	0.13 (0.08-0.21)	<0.001	0.42 (0.35-0.50)
Model 2 (95% CI) †	1.00	0.70 (0.49-1.00)	0.34 (0.23-0.52)	0.19 (0.12-0.32)	<0.001	0.49 (0.40-0.58)
Model 3 (95% CI) ‡	1.00	0.83 (0.56-1.22)	0.46 (0.30-0.72)	0.35 (0.20-0.59)	<0.001	0.60 (0.49-0.74)
Vitamin C (mean, SD) §	**25.6 (9.1)**	**44.6 (3.4)**	**56.6 (3.3)**	**74.3 (11.1)**		
Cases/ total (n)	132/ 302	81/ 300	62/ 317	43/ 325		
Model 1 (95% CI) *	1.00	0.54 (0.38-0.76)	0.37 (0.25-0.53)	0.25 (0.17-0.38)	<0.001	0.58 (0.50-0.67)
Model 2 (95% CI) †	1.00	0.59 (0.41-0.85)	0.44 (0.30-0.65)	0.32 (0.21-0.49)	<0.001	0.63 (0.54-0.74)
Model 3 (95% CI) ‡	1.00	0.63 (0.42-0.95)	0.57 (0.37-0.88)	0.47 (0.29-0.75)	0.001	0.73 (0.62-0.87)
Beta-carotene (mean, SD)	**8.9 (2.6)**	**15.5 (1.9)**	**23.3 (2.7)**	**40.8 (16.2)**		
Cases/ total (n)	139/ 311	88/ 311	56/ 311	35/ 311		
Model 1 (95% CI) *	1.00	0.51 (0.36-0.72)	0.28 (0.19-0.41)	0.16 (0.11-0.25)	<0.001	0.44 (0.35-0.54)
Model 2 (95% CI) †	1.00	0.55 (0.38-0.80)	0.34 (0.23-0.52)	0.20 (0.13-0.33)	<0.001	0.51 (0.40-0.63)
Model 3 (95% CI) ‡	1.00	0.62 (0.41-0.92)	0.47 (0.30-0.73)	0.35 (0.21-0.58)	0.001	0.67 (0.53-0.84)
Lutein (mean, SD)	**8.7 (2.0)**	**13.0 (1.1)**	**17.2 (1.3)**	**25.6 (6.4)**		
Cases/ total (n)	120/ 311	85/ 311	66/ 311	47/ 311		
Model 1 (95% CI) *	1.00	0.55 (0.39-0.78)	0.41 (0.28-0.59)	0.28 (0.19-0.41)	<0.001	0.54 (0.45-0.64)
Model 2 (95% CI) †	1.00	0.68 (0.47-0.99)	0.53 (0.36-0.79)	0.41 (0.26-0.63)	<0.001	0.63 (0.53-0.76)
Model 3 (95% CI) ‡	1.00	0.81 (0.54-1.21)	0.73 (0.47-1.11)	0.53 (0.33-0.85)	0.008	0.72 (0.59-0.87)

Data are ORs (95% CI) estimated using logistic regression.

Total n= 1 244 (318 incident diabetes cases and 926 controls).

* Model 1: adjusted for age and sex.

† Model 2: model 1 plus education level, occupational social class, smoking status, physical activity level, family history of diabetes, total energy intake, vitamin supplement use, HDL-cholesterol, and LDL-cholesterol.

‡ Model 3: model 2 plus BMI and waist circumference.

§ The association between plasma vitamin C and T2D was not adjusted for HDL-cholesterol and LDL-cholesterol in model 2 or model 3

Cooper et al.: The association between a biomarker score for fruit and vegetable intake and incident type 2 diabetes: the EPIC-Norfolk study. Eur J Clin Nutr 2015;69:449-454.

Intake of fruit and vegetables and weight gain

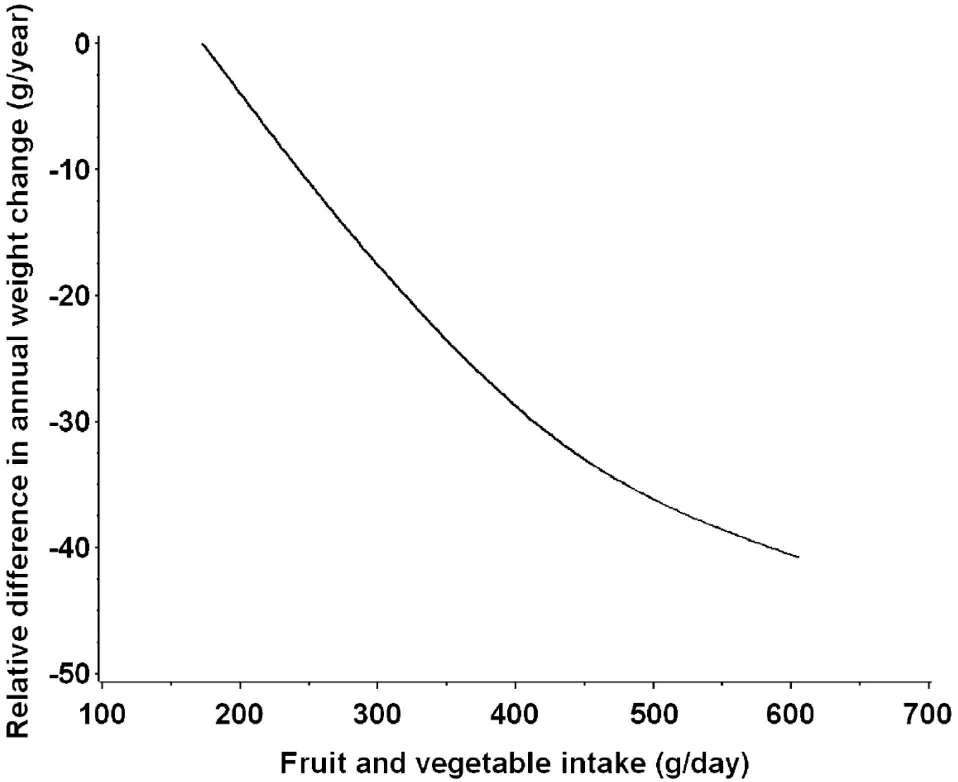


FIGURE 1. Spline model for describing the shape of the association of the intake of fruit and vegetables with weight change. The fifth percentile of fruit and vegetable intake was set as the reference. *P* for nonlinearity = 0.72. Adjusted for age (continuous), sex, cohort (dummy variables), years of follow-up (continuous), baseline weight (continuous), baseline height (continuous), change in smoking status (dummy variables), baseline total physical activity (dummy variables), education (dummy variables), alcohol intake (dummy variables), and, in women, postmenopausal status (yes or no) and postmenopausal hormone use (yes or no).

Buijsse et al., Am J Clin Nutr,90, 2009,

Review

Eur J Nutr (2012) 51:637–663
DOI 10.1007/s00394-012-0380-y

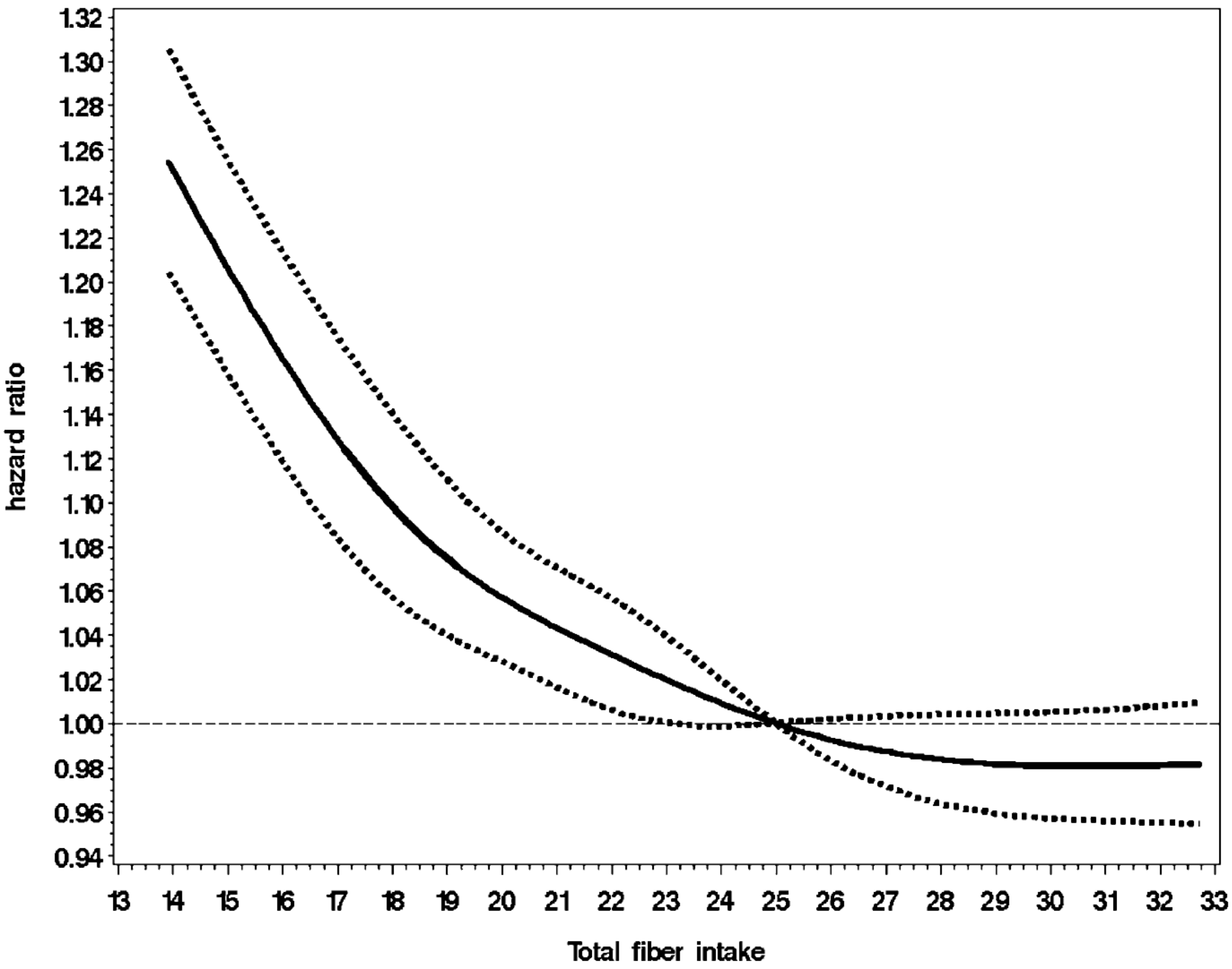
REVIEW

Critical review: vegetables and fruit in the prevention of chronic diseases

Heiner Boeing · Angela Bechthold · Achim Bub · Sabine Ellinger · Dirk Haller · Anja Kroke · Eva Leschik-Bonnet · Manfred J. Müller · Helmut Oberritter · Matthias Schulze · Peter Stehle · Bernhard Watzl

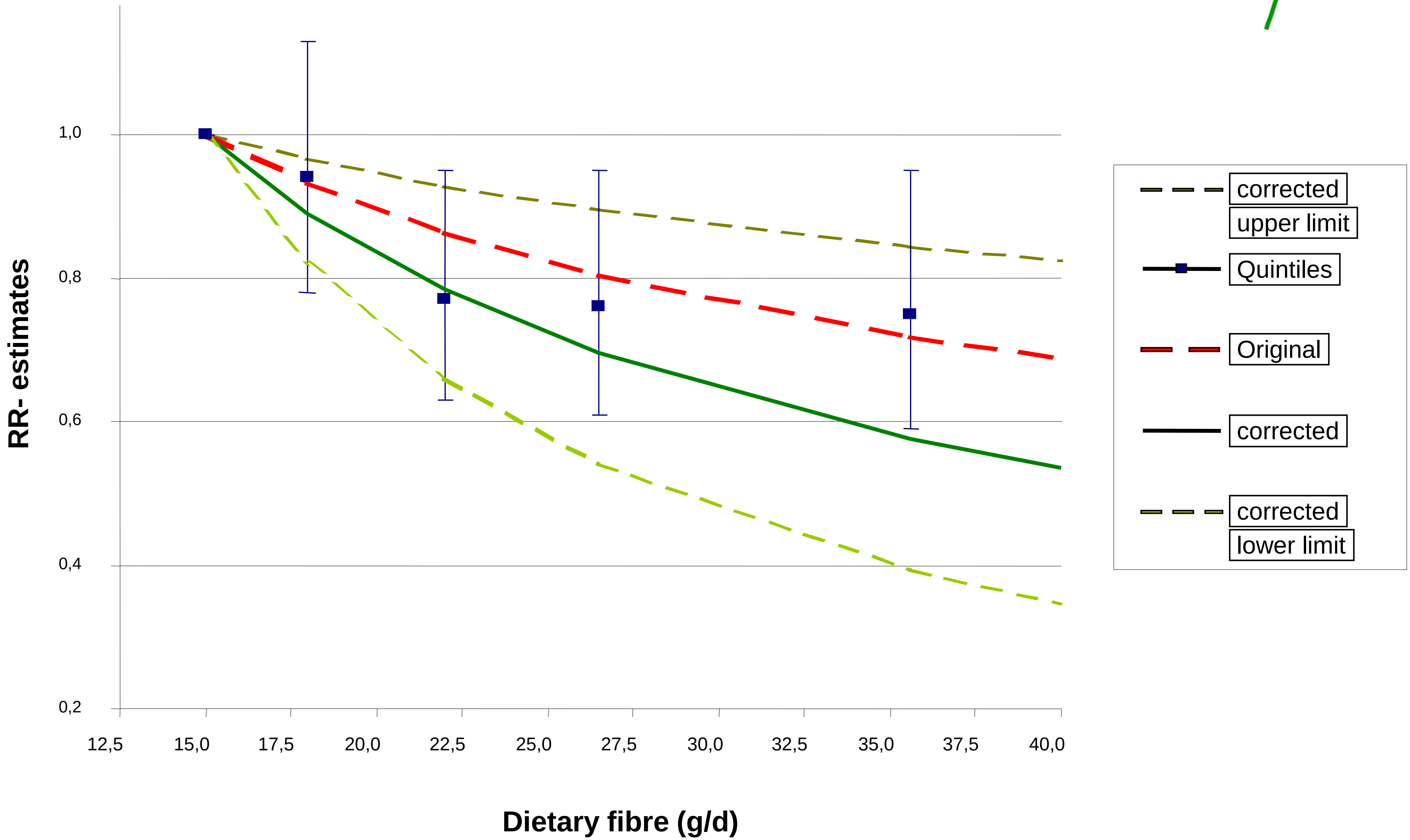
Received: 13 February 2012 / Accepted: 9 May 2012 / Published online: 9 June 2012

Dietary fiber and mortality in EPIC



Chuang et al.,: Fiber intake and total and cause-specific mortality in the European Prospective Investigation into Cancer and Nutrition cohort. Am J Clin Nutr 96:164–74, 2012

Intake of dietary fibre and risk of colon cancer



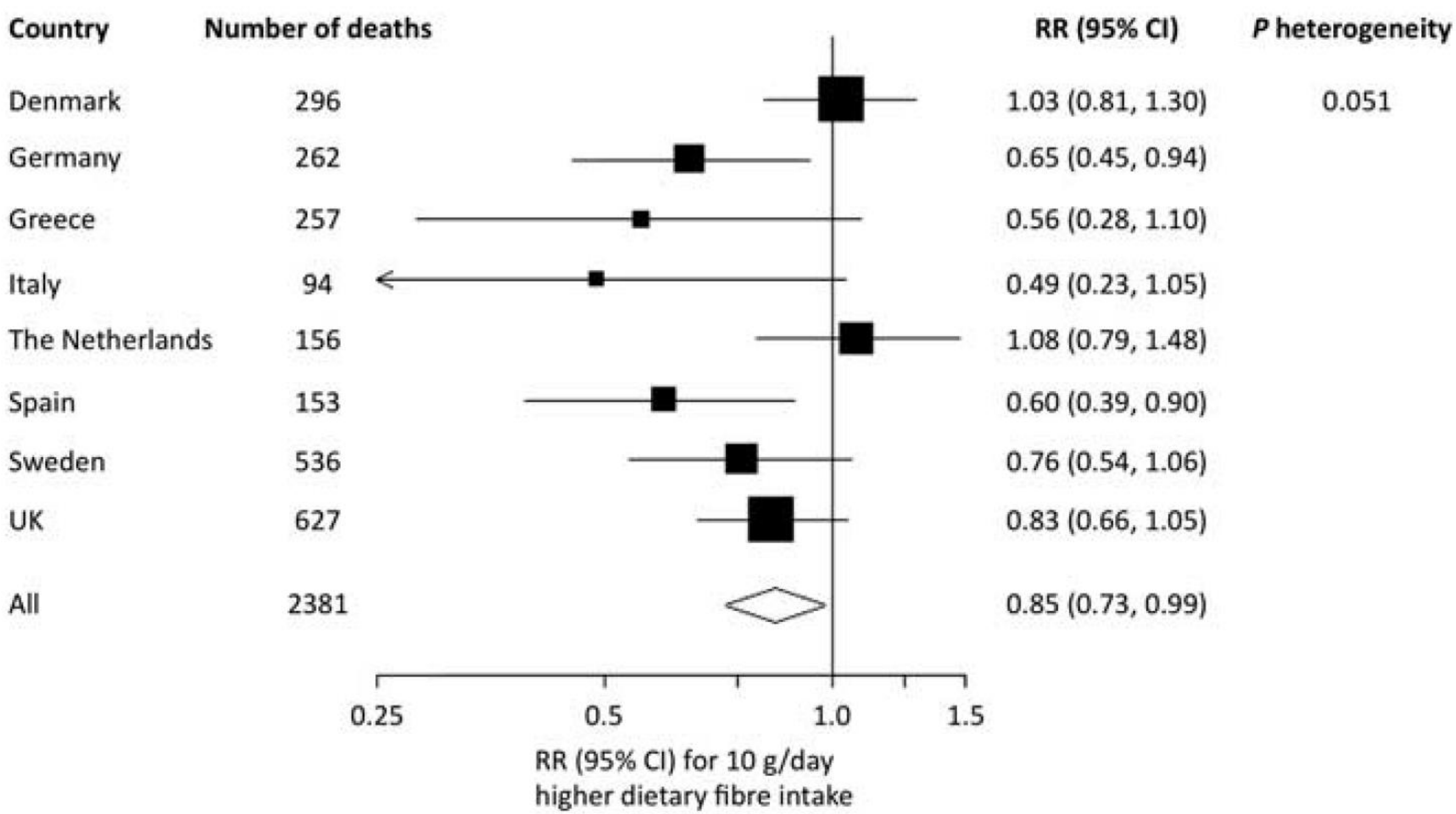
Bingham et al., Lancet, 2003

Relative risk for colon cancer for quintiles of intake of dietary fiber in EPIC

	Quintile of intake of dietary fibre (g/d in 24-HDR)				
	Q1 **Männer** **18.2** **Frauen** **15.9**	**Q2** **21.0** **17.8**	**Q3** **23.2** **19.4**	**Q4** **25.6** **21.3**	**Q5** **30.1** **24.4**
Relative Risk (n=706)	**1**	**0.95 (0.75-1.19)**	**0.75 (0.58-0.96)**	**0.71 (0.55-0.94)**	**0.72 (0.54-0.97)**
Relative Risk (n=1118)	**1**	**0.88 (0.74 -1.05)**	**0.71 (0.58-0.86)**	**0.68 (0.55-0.84)**	**0.74 (0.58-0.93)**
Relative Risk n=4517	**1**	**0.98 (0.89–1.08)**	**0.96 (0.86–1.06)**	**0.94 (0.84–1.05)**	**0.83 (0.72–0.96)**

Bingham et al., Lancet 2003, Bingham et al., Cancer Epidemiol Biomarker, 2005, Murphy et al., PLOS One, 2012

Intake of dietary fibre and risk of death of IHD



Crowe et al.. Dietary fibre intake and ischaemic heart disease mortality: the European Prospective Investigation into Cancer and Nutrition - Heart study. European Journal of Clinical Nutrition (2012) 66, 950–956

Grains and Type 2 Diabetes

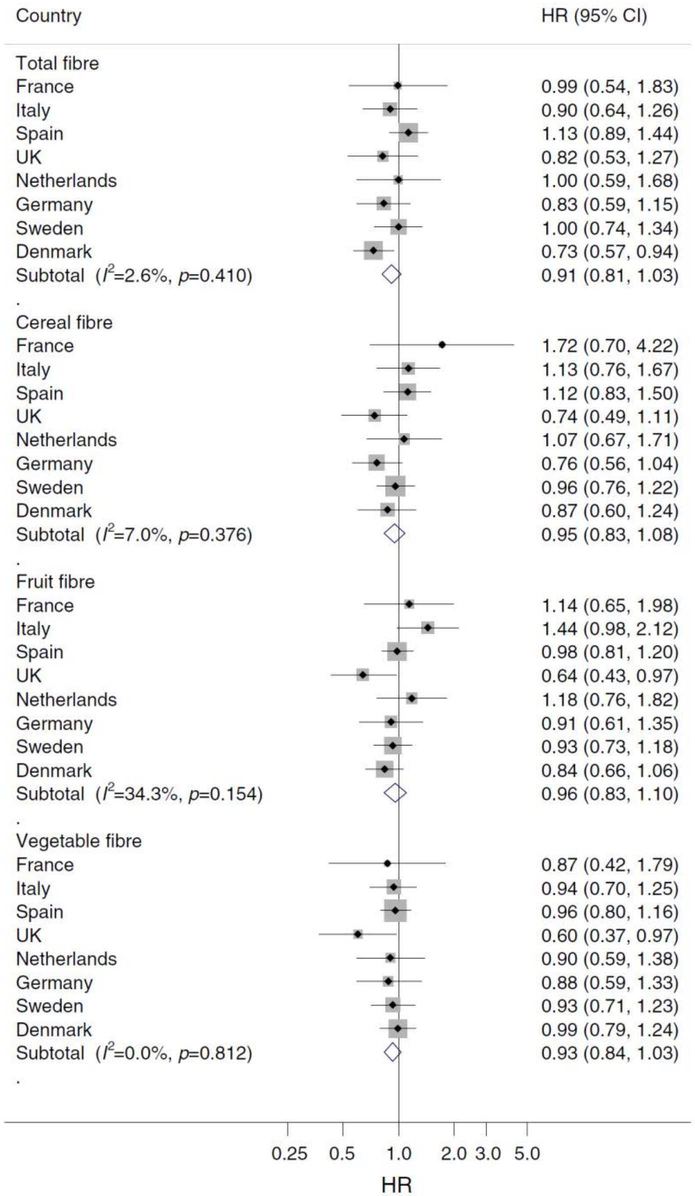


Fig. 1 Association between cereal fibre, fruit fibre and vegetable fibre consumption and risk of type 2 diabetes in the EPIC-InterAct study (n= 26,088). Country-specific $HR_{Q4 \text{ vs } Q1}$ (95% CIs) were pooled using random effects meta-analysis. HRs were adjusted for sex, smoking status, physical activity, education level, sex-specific alcohol categories, energy, energy-adjusted carbohydrate, magnesium intake, vitamin B_1 intake, saturated fatty acids and BMI. The x-axis is on a log scale

InterAct Consortium. Dietary fibre and incidence of type 2 diabetes in eight European countries: the EPIC-InterAct Study and a meta-analysis of prospective studies. Diabetologia. 2015;58:1394-1408

Grains and Type 2 Diabetes (Meta-Analysis)

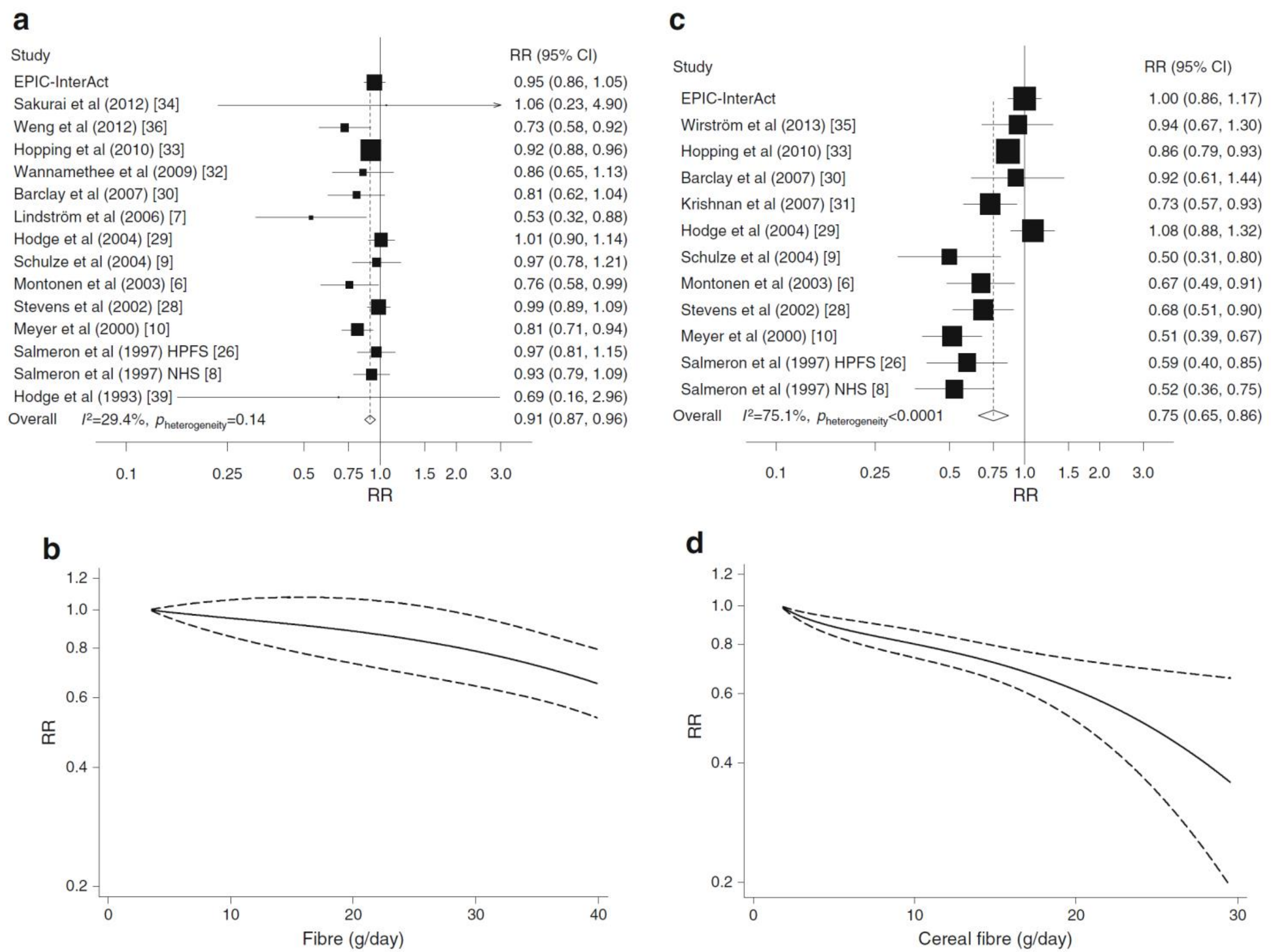


Fig. 2 Dietary total fibre (**a**, **b**) and cereal fibre (**c**, **d**) and type 2 diabetes, linear dose–response meta-analyses per 10 g/day (**a**, **c**) and non-linear dose–response meta-analyses (**b**, **d**). In (**a**) and (**c**), the RR of each study is represented by a square, and the size of the square represents the weight of each study to the overall estimate. The 95% CIs are represented by horizontal lines, and the diamond represents the overall estimate and its 95% CI. The *x*-axis is on a log scale. In (**b**) and (**d**), the solid lines represent the best-fitting fractional polynomial, and the dashed lines represent 95% CIs

InterAct Consortium. Dietary fibre and incidence of type 2 diabetes in eight European countries: the EPIC-InterAct Study and a meta-analysis of prospective studies. Diabetologia. 2015;58:1394-1408

Meat consumption and mortality

	Observed HR[a] (95% CI)	Calibrated HR[a] (95% CI)
Red meat (per 100 g)	1.02 (0.98 to 1.06)	1.02 (0.98 to 1.06)
Processed meat (per 50 g)	1.09 (1.06 to 1.12)	1.18 (1.11 to 1.25)
Poultry (per 50 g)	0.96 (0.92 to 0.99)	0.95 (0.87 to 1.04)

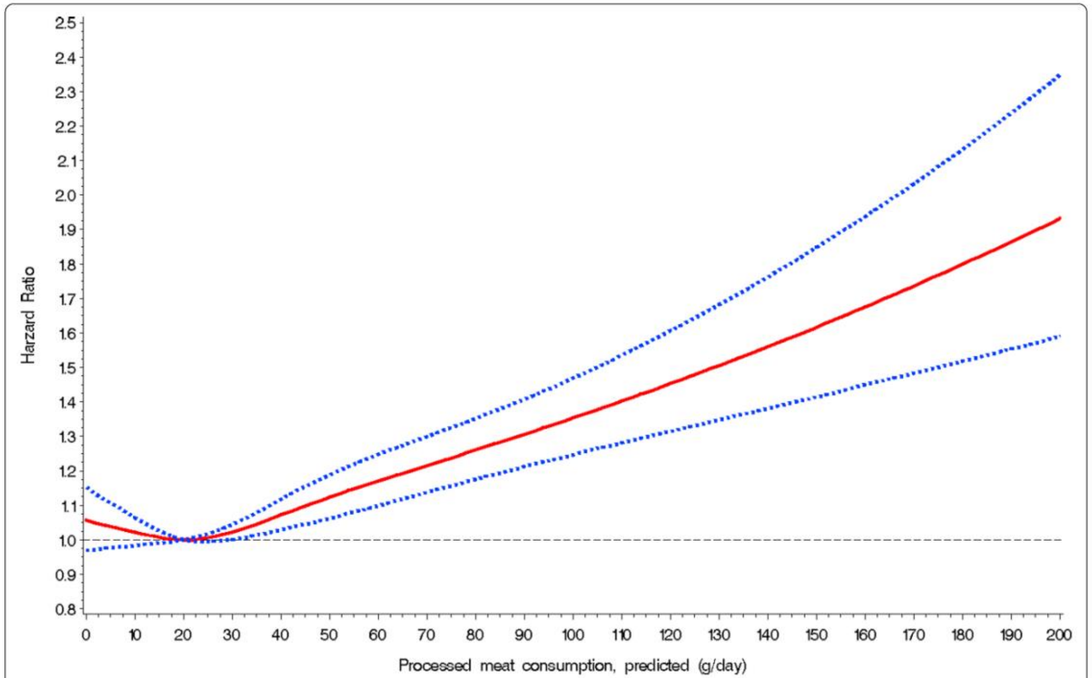
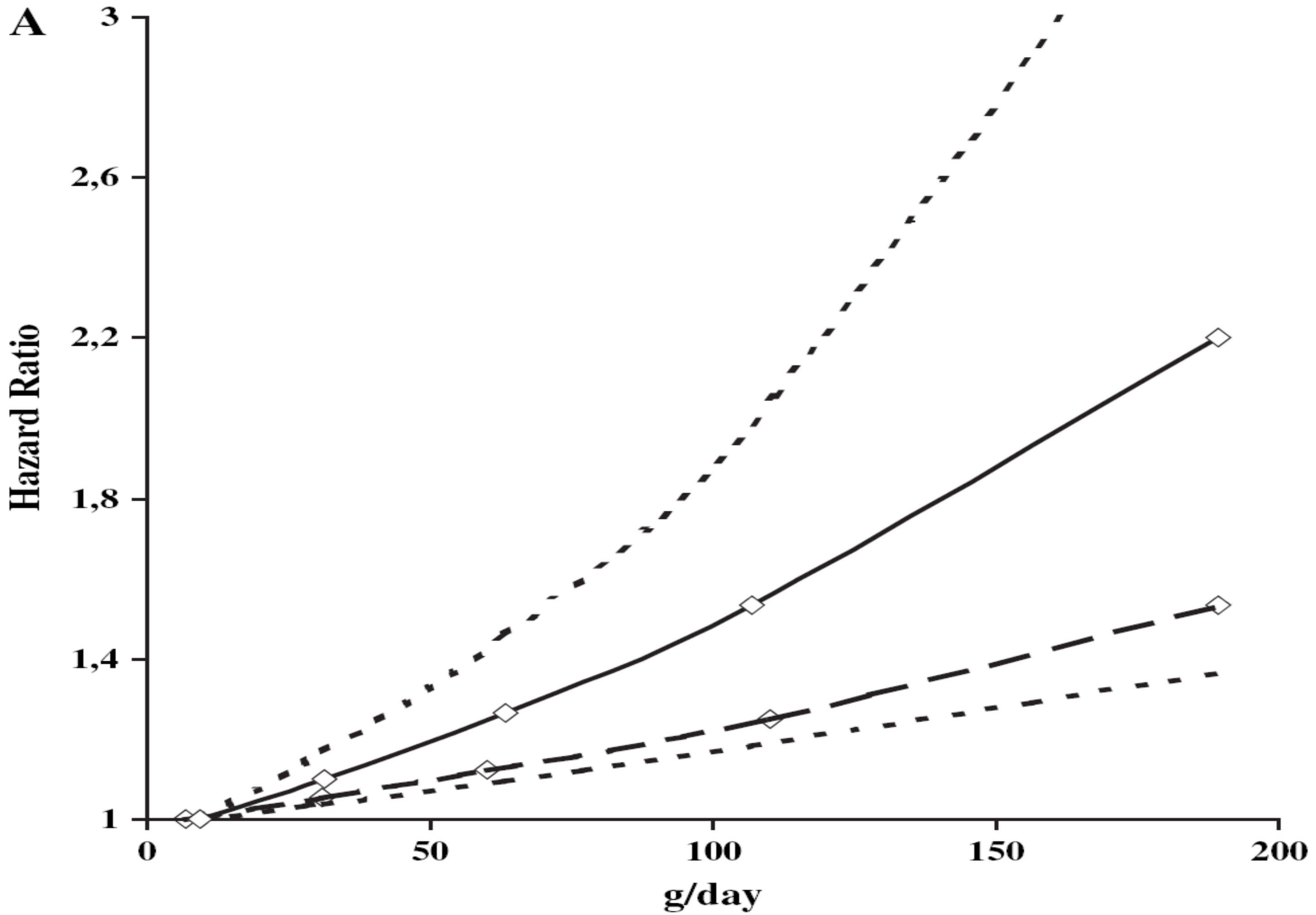


Figure 1 Nonparametric regression curve for the relation of processed meat intake at recruitment with all-cause mortality, European Prospective Investigation into Cancer and Nutrition (EPIC), 1992-2009. Solid line, effect estimate; dotted lines, 95 percent confidence interval.

Rohrmann et al.: Meat consumption and mortality - results from the European Prospective Investigation into Cancer and Nutrition. BMC Medicine 2013 11:63

Meat consumption and risk for colon cancer - EPIC



Norat et al., JNCI, 2006

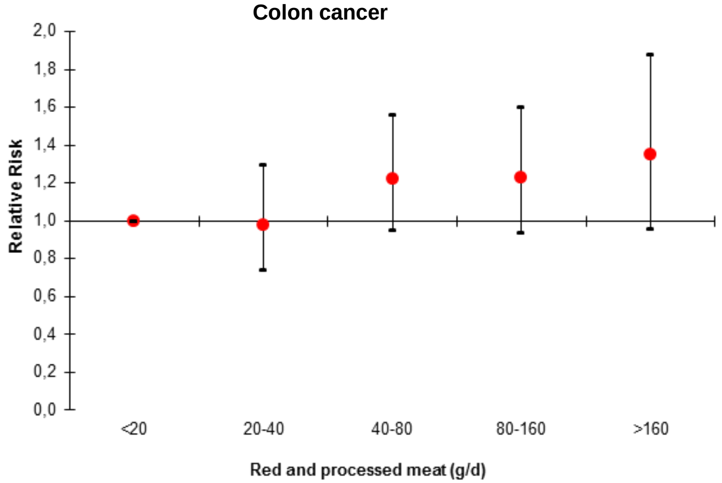
Cross over design: Effect of red meat and haem on total N-nitroso compounds excretion

n=12	Low red meat	High red meat	vegetarian
ATNC (µg/d) Mean ±SE	42.1 ±5.3	190.1 ±21.6	63.3 ± 5.3

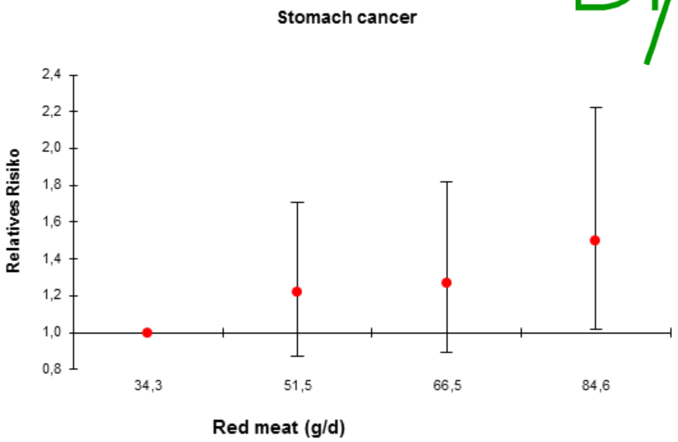
n=9	Low red meat	Haem supplementation	Inorganic iron supplementation
ATNC (µg/d) Mean ±SE	77.5 ±9.0	156.8 ±22.7	60.7 ± 9.5

Cross et al., Cancer Res, 2003

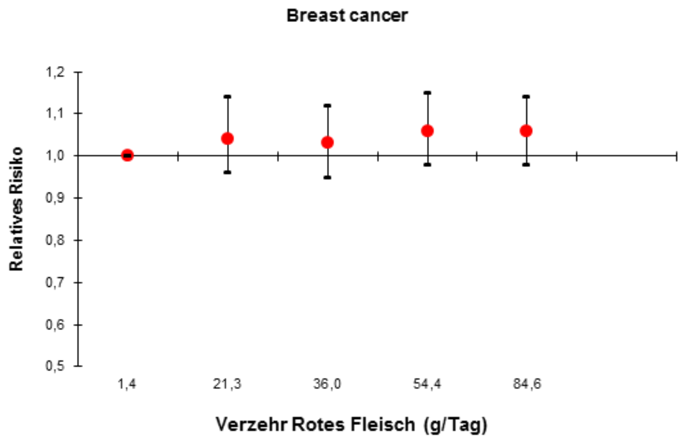
Investigations across cancer endpoints: Relative risks by intake of processed and/or red meat in EPIC



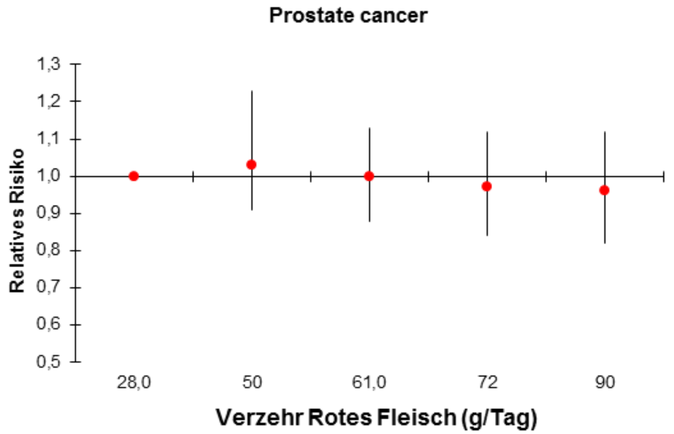
Norat et al., JNCI, 2006



Gonzales et al.,JNCI 2006



Pala et al, Am J Clin Nutr 2009



Allen et al., Br J Nutr, 2008

Meat intake and risk of type 2 Diabetes

Relative Risk by 50 g/d increment

Total meat	1.08 (1.05, 1.12)
Red meat	1.10 (1.04, 1.15)
Processed meat	1.13 (1.04, 1.22)
Poultry	1.04 (0.91, 1.18)
Offals	0.99 (0.92, 1.07)
Meat iron intake (per 1 mg)	1.03 (0.99, 1.07)

Bendinelli et al., Interact consortium: Association between dietary meat consumption and incident type 2 diabetes: the EPIC-InterAct study. Diabetologia (2013) 56:47–59

Meat consumption and weight gain

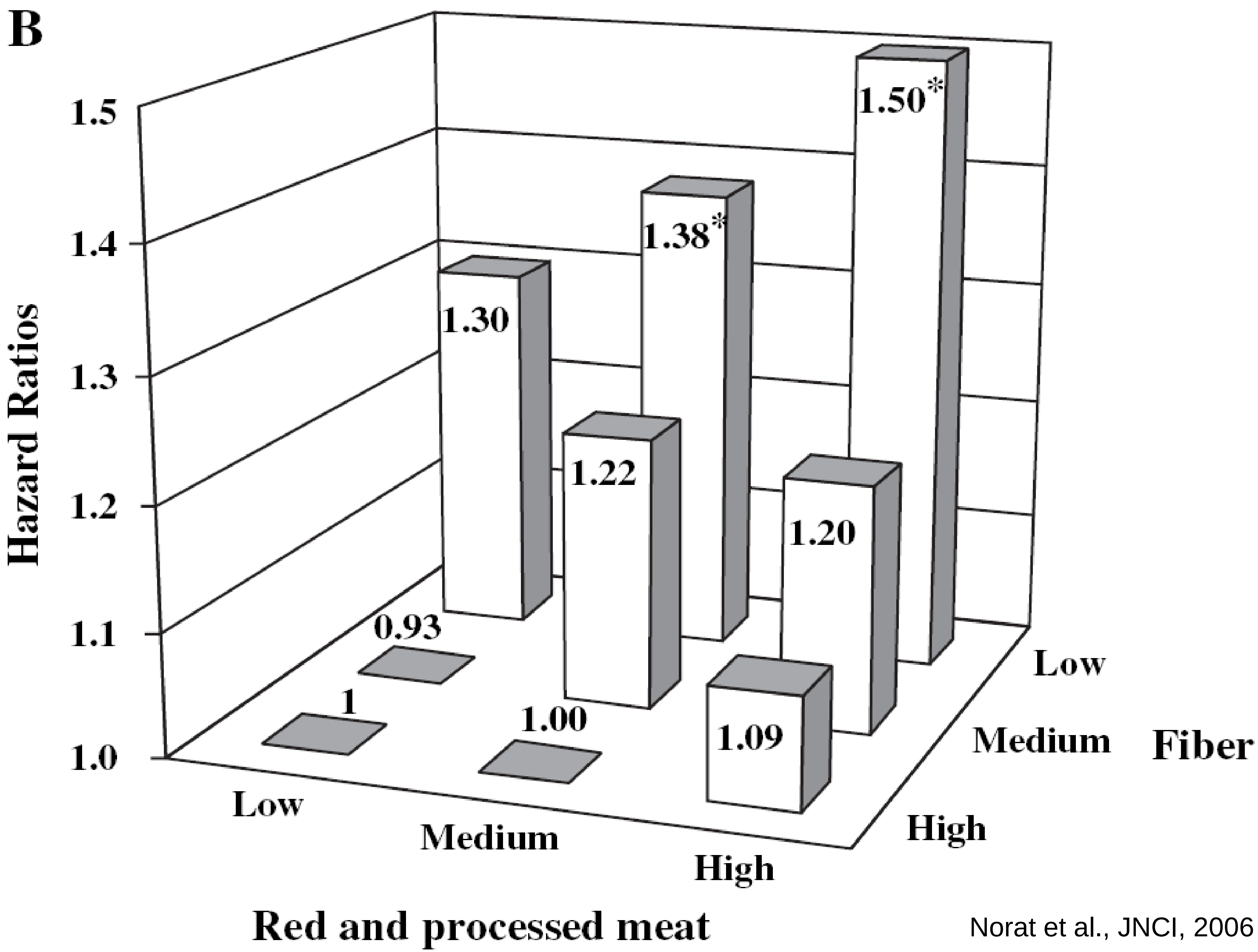
Adjusted increase in annual weight change (in g/y) for a 100-kcal increase in meat consumption before and after calibration in the European Prospective Investigation into Cancer and Nutrition (n = 373,803)[1]

	β	95% CI	P value
Total meat			
Calibrated data			
M1	13	(−5, 31)	0.15
M2	71	(47, 95)	<0.00001
M3	65	(39, 90)	<0.00001

[1] M1, model 1 (adjusted for sex, age, and an indicator of meat consumption); M2, model 2 (adjusted as in M1 + educational level, physical activity level, smoking status, initial BMI, follow-up time, total energy intake, energy from alcohol, and plausible total energy intake reporting); M3, model 3 (adjusted as in M2 + dietary factors 1 and 2 derived from maximum likelihood factor analysis).

Vergnaud et al.; Am J Clin Nutr 92; 398-407, 2010

Relative risk for colon cancer at levels of dietary fibre and red meat/processed meat



Norat et al., JNCI, 2006

Intervention study with meat and whole grains - design

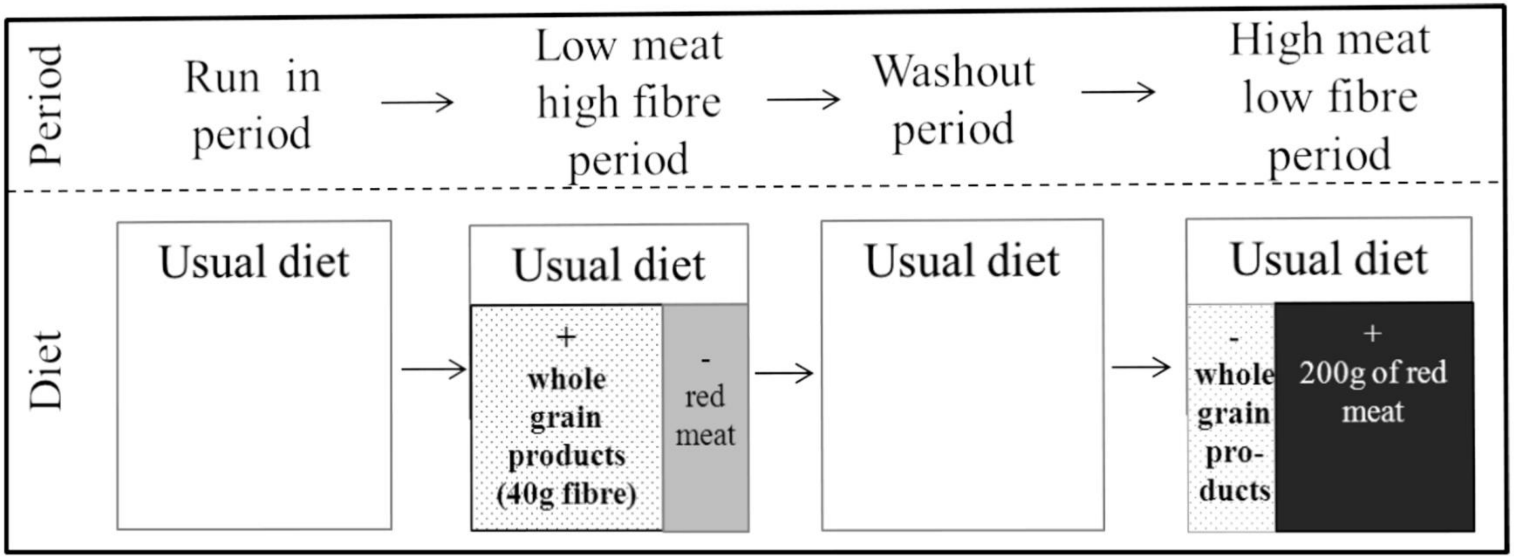


Figure 2. Diet plan for participants with diet succession: whole grain diet, washout period and red meat diet.
doi:10.1371/journal.pone.0109606.g002

Foerster et al.: The influence of whole grain products and red meat on intestinal microbiota composition in normal weight adults: a randomized crossover intervention trial. PLoS One. 2014; 9:e109606

Intervention study with meat and whole grains - results

Table 4. Intervention effects on factors retained after factor analysis (FA) with bands changed due to an intervention and correlations of corresponding factors with measures of obesity (BMI-body mass index, Waist circ.- waist circumference) and sex.

FA included changed bands (n = 16)			Correlations of factors with			
Factor (Eigenvalue/explained variance)	Intervention effect		Measures of obesity			Sex
	RM	WG	BMI	Weight	Waist circ.	
	p-Values		Correlation coefficients			
1 (4.3/31.3%)	0.001	0.29	−0.28*	−0.27*	−0.30*	0.23*
2 (2.9/30.9%)	0.22	<0.0001	−0.22*	−0.13	−0.12	0.06
3 (1.8/19.8%)	0.76	0.22	−0.06	−0.07	−0.07	0.05
4 (1.3/12.4%)	0.50	0.009	0.21*	0.18	0.19	−0.20*
5 (1.1/12.2%)	0.25	0.70	−0.05	−0.03	−0.02	−0.08

* Correlation significant on level $p<0.05$.
doi:10.1371/journal.pone.0109606.t004

Foerster et al.: The influence of whole grain products and red meat on intestinal microbiota composition in normal weight adults: a randomized crossover intervention trial. PLoS One 2014; 9:e109606

Biomarkers, meat intake, and type 2 diabetes

TABLE 3
Association with type 2 diabetes risk for biomarkers that fulfilled mediation criteria 2 and 3[1]

Selected biomarker	HR (95% CI)[2]	p_{raw}	p_{FDR}
Glycine	0.66 (0.57, 0.77)	<0.001	<0.001
Diacyl PC 36:4	1.20 (1.07, 1.35)	0.002	0.003
Diacyl PC 38:4	1.24 (1.12, 1.38)	<0.001	<0.001
Lyso-PC 17:0	0.78 (0.68, 0.89)	<0.001	<0.001
Hydroxy-SM 14:1	0.83 (0.73, 0.94)	0.004	0.007
Ferritin	1.28 (1.15, 1.42)	<0.001	<0.001

[1]Biomarkers were selected based on the mediation criteria 2 and 3—that is, a significant ($P_{FDR} < 0.05$) association with total red meat consumption in either men or women and at least a similar trend ($P_{FDR} < 0.1$) in the other (criterion 2) and equally directed associations with type 2 diabetes risk (criterion 3). Raw *P* values and FDR-controlled *P* values (corrected for the 21 tests conducted among all metabolites that fulfilled mediation criterion 2) from a 2-sided Wald-test (H_0: $\beta = 0$). FDR, false discovery rate; PC, phosphatidylcholine; SM, sphingomyelin.

[2]Diabetes-HR per SD in serum concentration; the associations of 21 preselected metabolites with type 2 diabetes risk were evaluated in Cox models in the case cohort ($n = 2681$) adjusted for total red meat intake, total energy intake (MJ/d), age (years), sex, BMI (in kg/m^2), sports (h/wk), biking (h/wk), smoking (4 stages: never smoker, former smoker, current smoker <20 units/d, or current heavy smoker >20 units/d), education (4 stages: no vocational training or in training, vocational training, technical school, or technical college or university degree), antihypertensive medication (yes/no), antidyslipidemic medication (yes/no), intake of beverages (alcohol, coffee, sugar-sweetened beverages) (g/d), and intake of whole-grain bread, refined-grain bread, butter, margarine, cabbage, cooked vegetables, mushrooms, potatoes, sauce, and poultry (g/MJ).

Wittenbecher et al.: Amino acids, lipid metabolites, and ferritin as potential mediators linking red meat consumption to type 2 diabetes. Am J Clin Nutr 2015;101:1241–50.

Conclusion

- It appears that a cohort study such as EPIC can substantially contribute to identify dietary potentials for prevention
- According to the results of the EPIC - (and other) Studies, some nutritional factors appear to be prime candidates of a healthy diet due to their wide range of endpoints associated with reduced risk
- The search for causal biological mechanisms linked to key aspects of a healthy diet seems to be important
- It remains to see whether other areas of dietary intake have similar impact on disease risk than the prime candidates fruit and vegetables, whole grain products, and meat