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Plant based eating and health outcome: findings from the EPIC Study – European perspective

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Leibniz-Gemeinschaft

Why to study diet-disease relationships?

Aetiology of diseases

Clear biological meaning of the diet factor

Role within the biological mechnisms of disease formation

Congruent relationships with intermediate disease markers

Public Health implications

Grade of evidence of causal relationships

Strength of the diet-disease relationship

Attributable risk (prevalence of dietary factor)

Chance of change

Public Health importance of well established diet-disease relationships?

Establishment of grade of evidence of a causal diet-disease relationship

Evidence grade I*	
Ia	Meta-Analyses of randomized and controlled intervention studies
Ib	Randomized and controlled intervention study
Ic	Non-randomized/ non-controlled intervention study
Evidence grade II	
IIa	Meta-Analyses of cohort studies
IIb	Cohort study

*according to DGE-Guideline methodology

Public Health importance of well established diet-disease relationships – conversion into practise

Food based dietary guidelines - FBDGs)

Scientific process of developing FBDGs (European Food Safety Authority 2010)

	Step
1	**Identification of diet-health relationships**
2	Identification of country specific diet-related health problems
3	Identification of nutrients of public health importance
4	Identification of foods relevant for food-based dietary guidelines
5	Identification of food consumption patterns
6	Testing and optimising food-based dietary guidelines
7	Graphical representations of food-based dietary guidelines

Grade of evidence of food-disease relationships on the basis of meta-analysis 2016 (13. Nutrition Report)

↓↓ probable inverse relation ↑↑ probable direct relation

Food group	Cancer	Diabetes mellitus Type 2	Coronary heart disease	Stroke
Whole grains	↓↓	↓↓↓	↓↓	↓↓
Vegetables	↓↓	↓	↓↓	↓↓
Fruit	↓↓	↓	↓↓	↓↓
Milk and milk products	↑↓	↓↓	↓	↓
Fermented milk products	o	↓↓	o	↓
Red meat	↑↑	↑	o	↑↑
Processed meat	↑↑	↑↑	↑↑	↑↑
Fish	o	o	↓↓	↓↓
Nuts	↓	↓	↓↓	↓↓
Chocolate/cacao	-	-	↓↓	↓↓

Contribution of prospective observational studies to the diet-disease relationships

Prospective studies always have a time element (disease endpoints occur only with study time)

Only „old“ studies can make a significant contribution

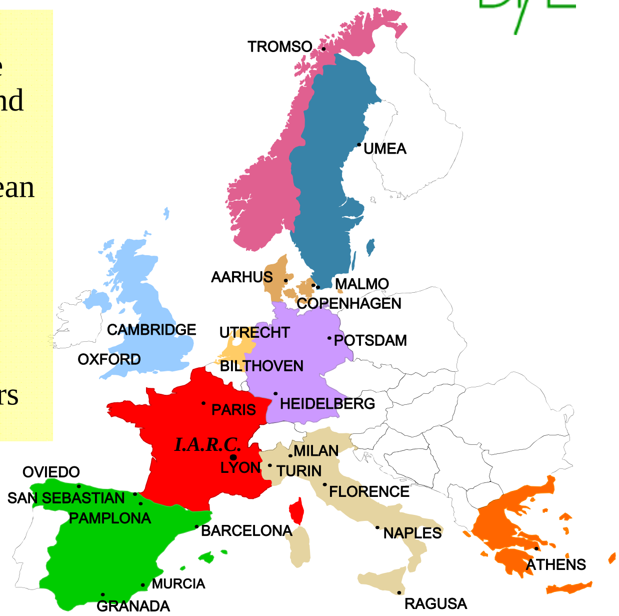
There are numerous endpoints occurring in a study population

Only some of the endpoints are of prime interest for public health such as

- Mortality and cause specific mortality
- Diseases contributing importantly to mortality such as CVD and cancer
- Metabolic diseases increasing risk for diseases contributing to mortality such as type 2 diabetes
- Metabolic disturbances contributing to metabolic diseases and diseases contributing to mortality such as obesity and hypertension

European Prospective Investigation into Cancer and Nutrition (EPIC)

- Aim of study: Investigation of disease risks linked with diet and other life style factors
- 23 centres in 10 European countries
- Recruitment between 1992 and 1998
- Prefered age ranges between 40(35)-64 years



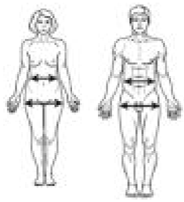
EPIC – study participants

Country	Men	Women	Total
Greece	11,954	16,618	28,572
Spain	15,632	25,808	41,440
Italy	15,171	27,516	42,687
France	0	72,996	72,996
Netherlands	10,280	29,792	40,072
Germany	22,833	30,261	53,094
UK	26,912	61,028	87,940
Danemark	27,179	29,875	57,054
Sweden	23,496	30,334	53,830
Norway	0	37,231	37,231
Total	53,457	366,521	519,978

EPIC data related to lifestyle and personal history

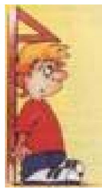
From questionnaires and interviews:

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



From physical examinatio..

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



Blood pressure

Blood concentrations (from aliquoted blood stored in liquid nitrogen)

EPIC data on diet

Two dietary measurements:
Dietary questionnaires 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 results regarding food groups associated with disease risk

Grade of evidence of at least probable (according to nutrition report 2016):

Plant based

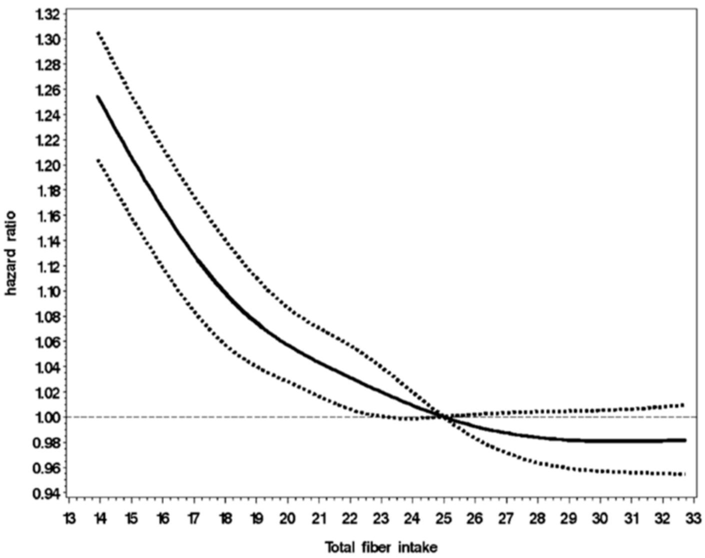
Whole grain foods (dietary fiber)
Vegetable
Fruits
Nuts
Chocolate/Cacoa

Animal based

Milk and milk products/fermented milk products
Fish
Red meat/Processed meat

It is important to see the results for different endpoints based on identical dietary data (and the same blood aliquotes)

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

Fruit and vegetables and mortality - EPIC

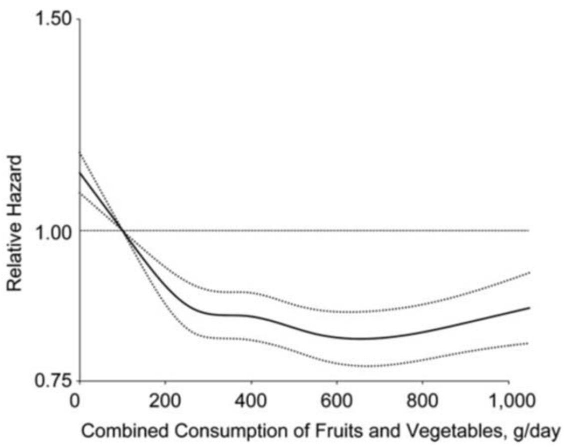


Figure 1. Restricted cubic spline and 95% confidence intervals of the nonlinear relation between fruit and vegetable consumption combined (in grams per day) and all-cause mortality, the European Prospective Investigation Into Cancer and Nutrition, 1992–2010.

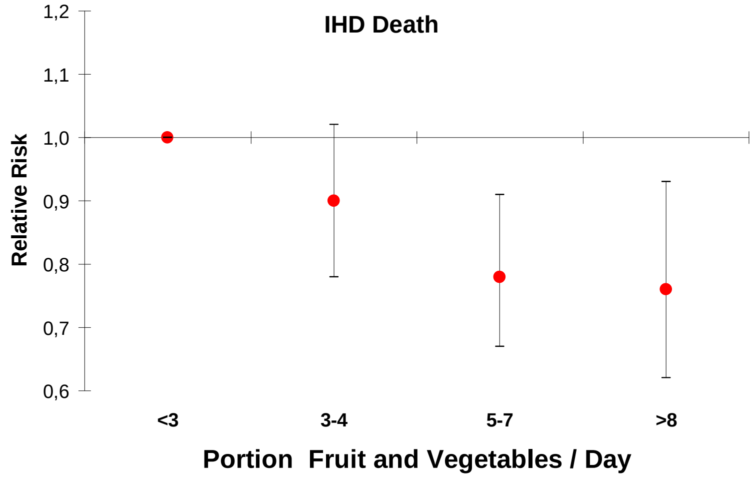
Leenders et al.: Fruit and Vegetable Consumption and Mortality - European Prospective Investigation Into Cancer and Nutrition. Am J Epidemiol. 2013;178:590–602

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)**

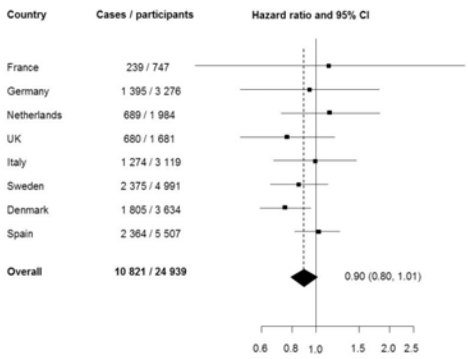
Boffetta et al., JNCI 102, 529-537: 2010

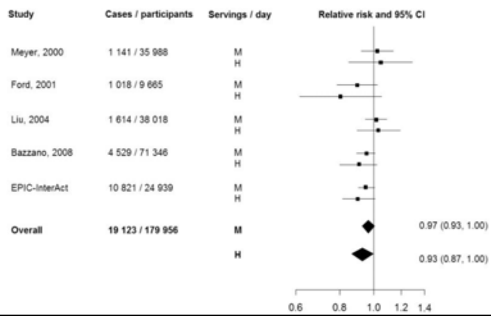
EPIC-Heart study on mortality



Crowe et al., European Heart Journal 2011, 32:1235-1243

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.

Polyphenols as marker of food intake

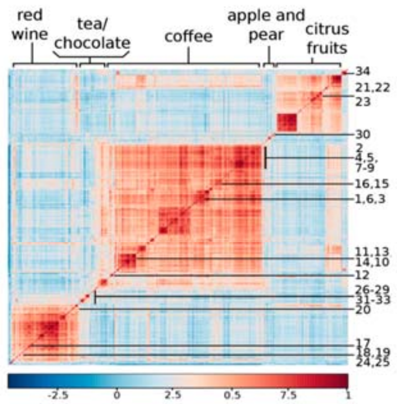


FIGURE 3 Metabolite-metabolite correlation analysis of the 2272 mass spectral features correlated to dietary intakes of 6 polyphenol-rich foods (24-h dietary recalls). The heat map shows clusters for each food made of mass spectral features derived from metabolites co-occurring in a same food and excreted in the same urine samples. Numbers refer to the annotated polyphenol metabolites (Table 1).

William MB Edmands,Pietro Ferrari, Joseph A Rothwell, Sabina Rinaldi, Nadia Slimani, Dinesh K Barupal,Carine Biessy, Mazda Jenab, Franc¸oise Clavel-Chapelon, Guy Fagherazzi, Marie-Christine Boutron-Ruault,Verena A Katzke, Tilman Ku¨hn, Heiner Boeing, Antonia Trichopoulou,Pagona Lagiou,Dimitrios Trichopoulos, Domenico Palli, Sara Grioni, Rosario Tumino, Paolo Vineis, Amalia Mattiello, Isabelle Romieu, and Augustin Scalbert: Polyphenol metabolome in human urine and its association with intake of polyphenol-rich foods across European countries. Am J Clin Nutr 2015;102:905–13

Polyphenols as marker of food intake

Raul Zamora-Ros, David Achaintre, Joseph A. Rothwell, Sabina Rinaldi1, Nada Assi1, Pietro Ferrari1, Michael Leitzmann, Marie-Christine Boutron-Ruault, Guy Fagherazzi, Aurélie Auffret, Tilman Kühn, Verena Katzke, Heiner Boeing, Antonia Trichopoulou, Androniki Naska, Effie Vasilopoulou, Domenico Palli, Sara Grioni, Amalia Mattiello, Rosario Tumino, Fulvio Ricceri, Nadia Slimani, Isabelle Romieu & Augustin Scalbert: Urinary excretions of 34 dietary polyphenols and their associations with lifestyle factors in the EPIC cohort study. Scientific Reports | 6:26905 , 2016

Food	Consumers (n)	Polyphenol (Spearman correlation coefficient)
Red wine	121	Gallic acid ethyl ester (0.69), resveratrol (0.59), gallic acid (0.48), hydroxytyrosol (0.43), tyrosol (0.36), (+)-catechin (0.34), *p*-coumaric acid (0.27), 4-hydroxyphenylacetic acid (0.19), 3,4-dihydroxyphenylacetic acid (0.15)
Coffee	410	Caffeic acid (0.65), protocatechuic acid (0.60), ferulic acid (0.58), *m*-coumaric acid (0.53), 3,4-dihydroxyphenylpropionic acid (0.51), 3-hydroxybenzoic acid (0.39), vanillic acid (0.31)
Tea	117	Gallic acid (0.38), (−)-epicatechin (0.30), (+)-catechin (0.22), quercetin (0.19)
Chocolate	111	(−)-Epicatechin (0.22), vanillic acid (0.15)
Citrus fruits	185	Hesperetin (0.60), naringenin (0.56), kaempferol (0.33)
Citrus juices	131	Hesperetin (0.15), naringenin (0.15), kaempferol (0.10)
Apple and pear	226	Phloretin (0.40), (−)-epicatechin (0.20), 3,4-dihydroxyphenylacetic acid (0.19), homovanillic acid (0.16)
Berries	42	*p*-Coumaric acid (0.20), (+)-catechin (0.19)
Onion, garlic	220	Quercetin (0.17), apigenin (0.11), isorhamnetin (0.10)
Olive oil	238	Hydroxytyrosol (0.36), tyrosol (0.31), 3,4-dihydroxyphenylacetic acid (0.17), apigenin (0.17)
Olives	44	Hydroxytyrosol (0.34), 3,4-dihydroxyphenylacetic acid (0.29), homovanillic acid (0.22), tyrosol (0.11)
Bread, non-white	260	3,5-Dihydroxybenzoic acid (0.45), 3,5-dihydroxyphenylpropionic acid (0.43), enterolactone (0.25), daidzein (0.20), enterodiol (0.20), genistein (0.19), m-coumaric acid (0.16), ferulic acid (0.13)
Breakfast cereals	32	3,5-Dihydroxybenzoic acid (0.17), 3,5-dihydroxyphenylpropionic acid (0.16), daidzein (0.15), equol (0.08), enterolactone (0.08)
Soya products	9	Genistein (0.17), daidzein (0.10)

Table 3. Urinary polyphenols most highly correlated to recent food intake in the EPIC cohort. The top two to nine polyphenols (out of 34 measured polyphenols) most highly correlated with the intake of each food group are listed. The number of reported correlations for each food group was based on current knowledge on polyphenol food composition and polyphenol metabolism. Some additional polyphenols may also be correlated to intake of each food, but they were excluded if not known as a component of the food considered or as a possible metabolite derived from a component of this food.

Summary and conclusion

- The interest in food-disease relationships is high due to their potential important public health implications
- A prospective cohort is accruing person time of follow up regarding disease endpoints with advancement of time and is contributing study results to grade the evidence of a causal relation between a dietary factor and a disease endpoint
- EPIC is one of the few prospective cohort studies that could look back to a follow up of more than 20 years and a wide range of endpoints.
- The EPIC published about food groups of high public health interest and will have the perspective to exploid in addition to the interview data also the blood samples