The European Prospective Investigation into Cancer and Nutrition (EPIC)

Carlos A Gonzalez*

Department of Epidemiology, Institut Català d'Oncologia (ICO), Av. Gran Via s/n, km 2.7, 08907 L'Hospitalet, Barcelona, Spain

Abstract

Objective: To describe the main finding produced so far by the EPIC project, which aims to improve the scientific knowledge of nutritional factors involved in cancer. Design and setting: Prospective cohort study in 23 centres from 10 European countries. Dietary assessment method varied by countries: in some cases a diet history by personal interview was carried out, while in most countries a self-administered semi-quantitative food-frequency questionnaire was used; in one case the questionnaire was combined with a food record. Information on a wide range of lifestyle factors and anthropometric measurements were also collected for most participants.

Subjects: The cohort includes 521 468 men and women mostly aged between 39 and 69 years, whereas blood samples are available for 387 889 subjects.

Results: To date 24185 cancer cases have been identified in the follow-up of the cohort. The publications produced by each centre can be consulted on the EPIC website (http://www.iarc.fr/epic/). Among initial findings concerning the associations between cancer and dietary factors, one of the most important results is a protective effect of high fibre intake and fish consumption against colorectal cancer, while high red and processed meat intake increase the risk. Regarding lung cancer the first analyses found a protective effect of fruit intake but no association with vegetable consumption. No association was observed between vegetables and fruit intake and the risk of prostate cancer or breast cancer. Finally, data from Cambridge point to an interesting result regarding breast cancer: no association was observed with saturated fat intake measured by food-frequency questionnaire, but according to the food diary a daily intake of 35 g doubles the risk of breast cancer compared to women with daily intake of 10 g or less.

Keywords
Nutrition
Prospective studies
Cancer research
Dietary assessment methods
Colorectal cancer
Lung cancer
Breast cancer

Main characteristics

In spite of decades of epidemiological investigation, scientific evidence on the relationship between cancer at several sites and some foods is still insufficient or inconsistent and prevents the establishment of solid conclusions¹. There are various reasons that may explain this situation: biologically relevant foods associated with cancer are ingested many years before tumour appearance, food habits are very difficult to measure with exactitude, and food-frequency questionnaires usually used contain important measuring errors². The presence of recall bias, the lack of statistical power and/or the homogeneity of food habits among study participants are also important limitations. The European Prospective Investigation into cancer and Nutrition (EPIC) is realised with the goal of improving scientific knowledge on nutritional factors involved with cancer³, and to contribute scientific bases for public health interventions directed in promoting a healthy diet and lifestyles. One of its greatest advantages is the wide range of variability in food intake, the product of large differences still observed today between Mediterranean countries (Greece, Italy and Spain) and the dietary patterns of Northern Europe, and its great statistical power, being one of the largest prospective cohort study realised in the world.

EPIC⁴ started in 1993 with data and blood sample collection in 23 centres in 10 European countries (Fig. 1): Germany, Denmark, Spain, France, Greece, Holland, Italy, Norway, United Kingdom and Sweden, coordinated by the WHO's International Agency for Research on Cancer (IARC). In Spain, it is realised in five geographic areas (Asturias, Granada, Guipuzcoa, Murcia and Navarra) coordinated by the Catalan Institute of Oncology's Epidemiological Department. The European cohort is formed by 521 468 individuals (of which 366 521 are women) mostly between the ages of 34 and 69 years. For

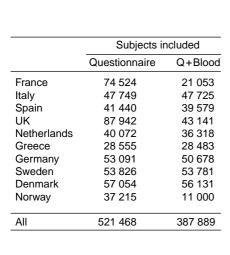




Fig. 1 EPIC collaborating centres and cohort subjects

biochemical, hormone and genetic analyses, 387 889 blood samples are available.

Based on validation study results, various diet measurement methods were adopted, to suit the needs of each country, that include: self-administered semi-quantitative food-frequency questionnaires (with approximately 260 food items), diet history questionnaires (with more than 600 food items) administered by means of interviews and semi-quantitative foodfrequency questionnaires combined with a food record. Also a 24-hour recall was applied by means of a computerised program (EPIC-SOFT) in a sub-sample of 8%, to calibrate the dietary measuring instruments, with the objective of correcting systematic errors produced by the over- or underestimation of intakes⁵. A wide range of information was gathered on habits, lifestyles and medical history. Height, weight and waist and hip circumference were measured, and blood samples were obtained, the majority conserved in liquid nitrogen. To date, 24195 cases of cancer (7272 in men and 16923 in women) have been identified by means of the computerised link with population-based cancer registries, except in Greece, France and Germany, where active follow-up is being realised. After various years of work, a standardised food composition table (EPIC Nutrient Database-ENDB) for the 10 participating countries is almost complete.

Principal results obtained to date

The publications realised by each centre based on information gathered with the EPIC cohort of each country can be consulted on the EPIC website (http:// www.iarc.fr/epic/) and the specific EPIC Spain on our website (http://www.epic-spain.com/). The first important results on the comparison of food intake in each centre have been published in a supplement of Public Health Nutrition⁶. In relation to fruit and vegetable intake a wide variation was observed, with greater intake in the south of Spain (Murcia and Granada) and lower intake in Sweden and Norway. The main initial findings on the association between food intake and the most frequent tumours are the following (Table 1). Regarding prostate cancer in 1104 incident cases, no association with fruit and vegetable intake was observed⁷. EPIC results confirmed previous scientific evidence that indicate that this association was not very probable. Regarding colorectal cancer the protective effect of an elevated fibre intake⁸ was confirmed. The results are of great scientific importance, since results of other cohorts, especially those from the USA, questioned the protective effect of fibre. On the other hand, a significant negative association between nut and seed intake was observed for colon cancer in women⁹. Also, the preliminary analysis of an elevated fruit and vegetable intake shows their protective effect on the risk

126 CA Gonzalez

Table 1 Food intake and cancer. Main initial findings of EPIC for most frequent tumours

| Cancer site | Number of cases | Results | Reference |
|------------------|------------------|---|-----------|
| Prostate | 1104 | Fruits: no association | 7 |
| Lung | 860 | Vegetables: no association Fruits: negative association | 11 |
| | | Vegetables: no association | |
| Colon and rectum | 1065 | Dietary fibre: negative association | 8 |
| | 528* | Nuts and seeds: negative association in women | 9 |
| | 1329 | Fish: negative association | 10 |
| | | Red and processed meat: positive association | |
| Breast | 168 [†] | Fat intake: positive association (using a dietary record) | 12 |
| | 3659 | Vegetables: no association Fruits: no association | 13 |

^{*} Colon cancer cases in women.

of suffering colorectal cancer. Elevated fish intake has a protective effect while red meat and specially processed meats increase risk¹⁰. Regarding lung cancer, a first analysis of 860 incident cases observed¹¹ a protective effect by fruit intake and no association with vegetable intake, which also confirms previous scientific evidence available. Lastly, regarding breast cancer, although definite EPIC results are not yet available on the controversial possible association with saturated fat intake, EPIC data from Cambridge¹² show extremely interesting results. It has been observed at this centre that when the association is measured with the food-frequency questionnaire, no association with saturated fat intake was observed, but according to the dietary diary, a daily intake around 35 g doubles the risk of suffering breast cancer in comparison to women with a daily intake of 10 g or less. Finally, we found that the total or specific vegetables and fruit intake is not associated with the risk for breast cancer¹³.

References

- 1 Key TJ, Allen NE, Spencer EA, Travis RC. The effect of diet on risk of cancer. *Lancet* 2002; **360**: 861–8.
- 2 Prentice RL. Dietary assessment and the reliability of nutritional epidemiology reports. *Lancet* 2003; 362: 182–3.
- 3 Bingham S, Riboli E. Diet and cancer–The European Prospective Investigation into Cancer and Nutrition. *Nature Reviews. Cancer* 2004; 4: 206–15.
- 4 Riboli E, Hunt KJ, Slimani N, Ferrari P, Norat T, Fahey M, *et al.* European Prospective Investigation into Cancer and Nutrition (EPIC): study populations and data collection. *Public Health Nutr* 2002; **5**: 1113–24.
- 5 Slimani N, Kaaks R, Ferrari P, Casagrande C, Clavel-Chapelon F, Lotze G, *et al.* European Prospective Investigation into Cancer and Nutrition (EPIC) calibration

- study: rationale, design and population characteristics. *Public Health Nutrition* 2002; **5**: 1125–45.
- 6 Southgate DAT, van Staveren W, Riboli E. Special issue 'Food consumption, anthropometrics and physical activity in the EPIC cohorts from 10 European countries'. *Public Health Nutrition* 2002; 5(6B): 1111–345.
- 7 Key TJ, Allen N, Appleby P, Overvad K, Tjonneland A, Miller A, et al. Fruits and vegetables and prostate cancer: no association among 1104 cases in a prospective study of 130 544 men in the European Prospective Investigation into Cancer and Nutrition (EPIC). International Journal of Cancer 2004; 109: 119–24.
- 8 Bingham SA, Day NE, Luben R, Ferrari P, Slimani N, Norat T, et al. Dietary fibre in food and protection against colorectal cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC): an observational study. *Lancet* 2003; **361**: 1496–501.
- 9 Jenab M, Ferrari P, Slimani N, Norat T, Casagrande C, Overad K, et al. Association of nut and seed intake with colorectal cancer risk in the European Prospective Investigation into Cancer and Nutrition. Cancer Epidemiology, Biomarkers & Prevention 2004; 13: 1595–603.
- 10 Norat T, Bingham S, Ferrari P, Slimani N, Jenab M, Mazuir M, et al. Meat, fish, and colorectal cancer risk: the European Prospective Investigation into Cancer and Nutrition. J Natl Cancer Inst 2005; 97: 906–16.
- 11 Miller AB, Altenburg HP, Bueno-de-Mesquita B, Boshuizen HC, Agudo A, Berrino F, *et al.* Fruits and vegetables and lung cancer: findings from the European Prospective Investigation into Cancer and Nutrition. *International Journal of Cancer* 2004; **108**: 269–76.
- 12 Bingham SA, Luben R, Welch A, Wareham N, Khaw KT, Day N. Fat and breast cancer: are imprecise methods obscuring a relation between fat and breast cancer? *Lancet* 2003; **362**: 212–4.
- 13 van Gils CH, Peeters PHM, Bueno-de-Mesquita B, Boshuizen HC, Lahmann PH, Clavel-Chapelon F, et al. Consumption of vegetables and fruits and risk of breast cancer. *Journal of the American Medical Association* 2005; 293: 183–93.

[†]Only in EPIC Norfolk.