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# Ecologic Correlation Study on Nutrients/Foods Intake and Mortality for Female Breast Cancer in Korea†

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=Abstract=**In order to investigate the possible role of dietary factors on the recent increase in mortality for female breast cancer in Korea, an ecologic correlation study between per capita intakes of nutrients and foods and the mortality for female breast cancer during the last 10 years was conducted. In spite of the possibility of an ecologic fallacy, the age-adjusted mortality rates for female breast cancer were positively correlated with protein from animal source, total lipid, total animal foods, animal foods to total intake, fresh fish and shellfish, milk and milk products, and meat and meat products. The rates were inversely associated with energy from cereal, total carbohydrate, vegetable foods to total intake, total vegetable foods, daily intake of cereals and grain products, and starch and starch roots. These results suggest that an increased intake of protein- and fat-rich foods rather than carbohydrate-rich foods or vegetables might be associated with the increase in mortality for breast cancer during the last 10 years in Korea.**

Key Words: *Breast neoplasms, Ecologic study, Foods, Nutrients*

## INTRODUCTION

Malignant neoplasms have been known to be the second leading cause of death in Korea, next to cerebrovascular accidents (National Bureau of Statistics 1990). A hospital-admission study based on a large general population revealed a marked increase in cancer morbidity (Yoo *et al.* 1988). The mortality and morbidity for female breast cancer during the 10-year period of 1981-1990 showed an increasing tendency (Yoo and Kim 1992). However, little study has been conducted on the possible factors associated with such an increase in mortality and morbidity.

The role of dietary factors in the etiology of cancer has become increasingly apparent. Strong evidence indicates that dietary factors may be strongly associated directly or indirectly, with the development of other major cancers, particularly those related to endogenous

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mones (e.g., breast, endometrial, and prostate cancers), not to speak of direct-contacting sites, such as the colon, rectum, stomach, and esophagus (Henderson 1990).

Although numerous case-control and cohort studies on dietary factors and breast cancers have been conducted (Hirohata *et al.* 1985; Katsouyanni *et al.* 1986; Hirayama 1986; Willet *et al.* 1987; Yu *et al.* 1990; Yoo *et al.* 1992a), the results were not consistent. Since these studies were conducted within the same population in the same chronological years, the variations of dietary habits between individuals are considered to be relatively small (Kato *et al.* 1987). Futhermore, there are few methods to measure dietary intake in an individual correctly. A population-based ecologic study on long-term trends may be an alternative approach to identify dietary factors associated with the trend of breast cancer mortalities in a country, because the difference in dietary intake over the periods of years are typically large and the average of diets consumed for persons in one period gives a statistically more stable value than the diets of individuals.

This study was conducted to investigate the possible role of dietary factors in the recent increase in mortality for female breast cancer through an ecologic correlation study between per capita nutrients and foods intake and the mortality for female breast cancer in Korea.

## MATERIALS AND METHODS

For the information on mortality statistics, data based on national death certificates was used (National Bureau of Statistics 1981-1990). Since the proportion of deaths diagnosed by physicians has still been less than 50%, only the classifiable deaths were included in the observation of long-term trends in mortality. A crude mortality rate for each year was standardized based on the census population in 1985 (National Bureau of Statistics 1985). For the standardization, the estimated population in each age group was obtained from abridged census data on population and housing collected yearly by the government (National Bureau of Statistics 1981-1990). All the cases classified into ICD-174 by the 9th revision of the ICD code were regarded as female breast cancer (WHO 1979).

Nutritional data on per capita nutrients and food intake was collected from the National Nutritional Survey, 1969-1988 (Ministry of Health and Social Affairs, 1969-1988). Subjects for the survey were selected by proportional probability sampling as households; 1,000 households from 50 districts. Food consumption for 2 days was measured and the quantity of food consumed by a family was weighed. Nutrients per capita per day were used as follows; total energy (kcal), total protein (g), total lipid (g), total carbohydrate (g), protein from animal source (%), and energy from cereals (%). Animal foods were classified into total animal foods (g), proportion of animal foods to total intake (%), meat and products (g), eggs (g), fresh fish and shellfish (g), processed fish and shellfish (g), milk and milk products (g), and animal oils and fats (g), while vegetable foods were itemized as total vegetable foods (g), proportion of vegetable foods to total intake (%), cereals and grain products (g), legumes and their products (g), starch and starch roots (g), fresh vegetables (g), processed vegetables (g), fruits (g), seaweeds (g), seasonings and beverages (g), and vegetable oils and fats (g).

Correlation between the intake of each nutrient/food (1969-1988) and the mortality for female breast cancer (1981-1990) was done by the Pearson's simple correlation method using the PC-SAS (SAS Institute, 1988). For the possible lag in time between foods intake and cancer death, a sequential correlation procedure was applied by shifting the year of intake, year by year, until it reached its highest correlation coefficient.

## RESULTS

Table 1 shows a marked increase in mortality for female breast cancer in Korea. With the reference rate in 1981 (1.41 per 100,000 persons),

the rate was almost 1.5 times higher in 1984, reaching an increment ratio of 1.79 in 1990. Total energy remained almost stable or somewhat decreased during the observation period. An increasing trend was most prominent in protein from animal source. A steadily increasing trend was seen in total lipid, while other indices were almost unchanged (Fig. 1). Intakes of most animal foods were steadily increasing between 1969-1988. On the contrary, overall trends in intakes of vegetable foods were decreasing (Figs. 2 and 3).

The age-adjusted mortality rates for female breast cancer were positively correlated with protein from animal source ($r = 0.83$ with lag period of 12 years, $p<0.01$), total lipid ($r = 0.64$ with lag period of 10 years, $p<0.05$), and inversely associated with energy from cereals ($r = -0.77$ with lag period of 12 years, $p<0.01$), and total carbohydrate intake ($r = -0.70$ with lag peri-

Table 1. Increment ratios of age-standardized mortality rates for female breast cancer with a reference of value in 1981 in Korea, 1981-1990

| Years | Age-standardized mortality rate# | Increment ratio | Years | Age-standardized mortality rate# | Increment ratio |
|---|---|---|---|---|---|
| 1981 | 1.41 | 1.0 | 1986 | 2.39 | 1.70 |
| 1982 | 1.87 | 1.33 | 1987 | 2.17 | 1.54 |
| 1983 | 1.95 | 1.38 | 1988 | 2.30 | 1.63 |
| 1984 | 2.14 | 1.52 | 1989 | 2.52 | 1.79 |
| 1985 | 2.04 | 1.45 | 1990 | 2.52 | 1.79 |

# : Age-standardized mortality rate to the 1985 Korean population, per 100,000

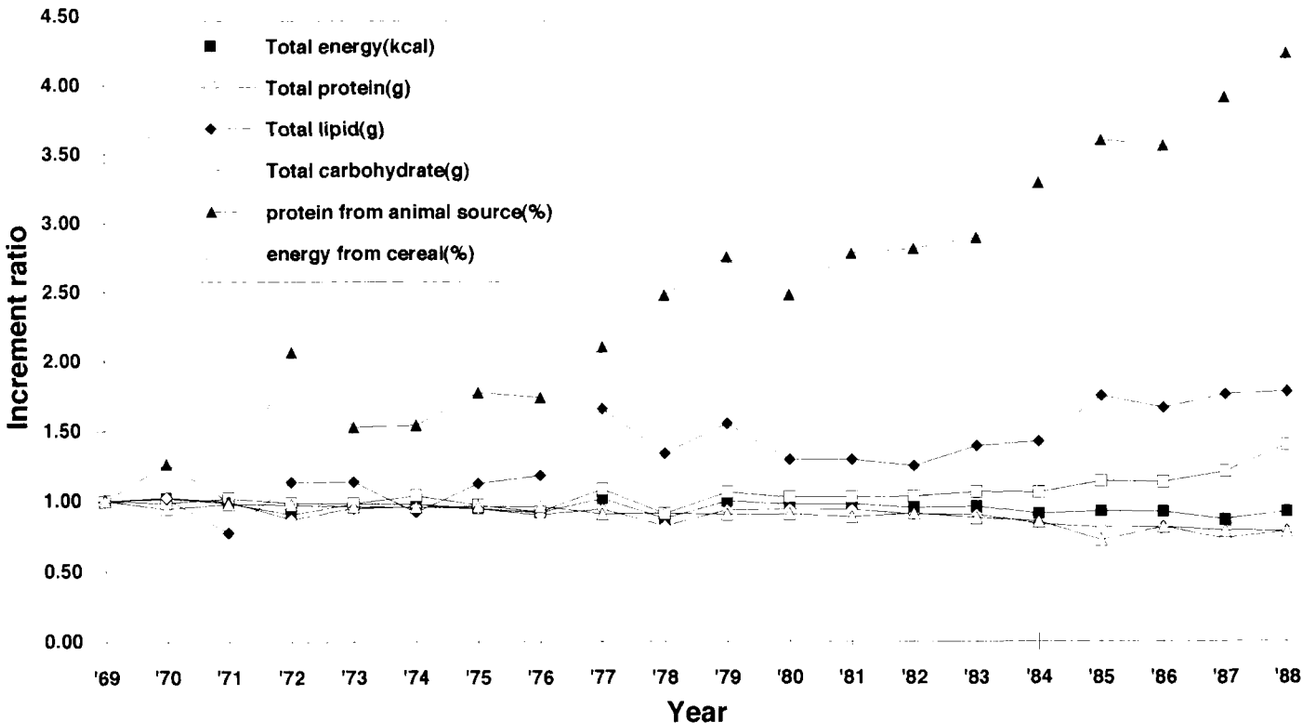


Fig 1. Trends in intake of nutrients per capita per day in Korea, 1969-1988.

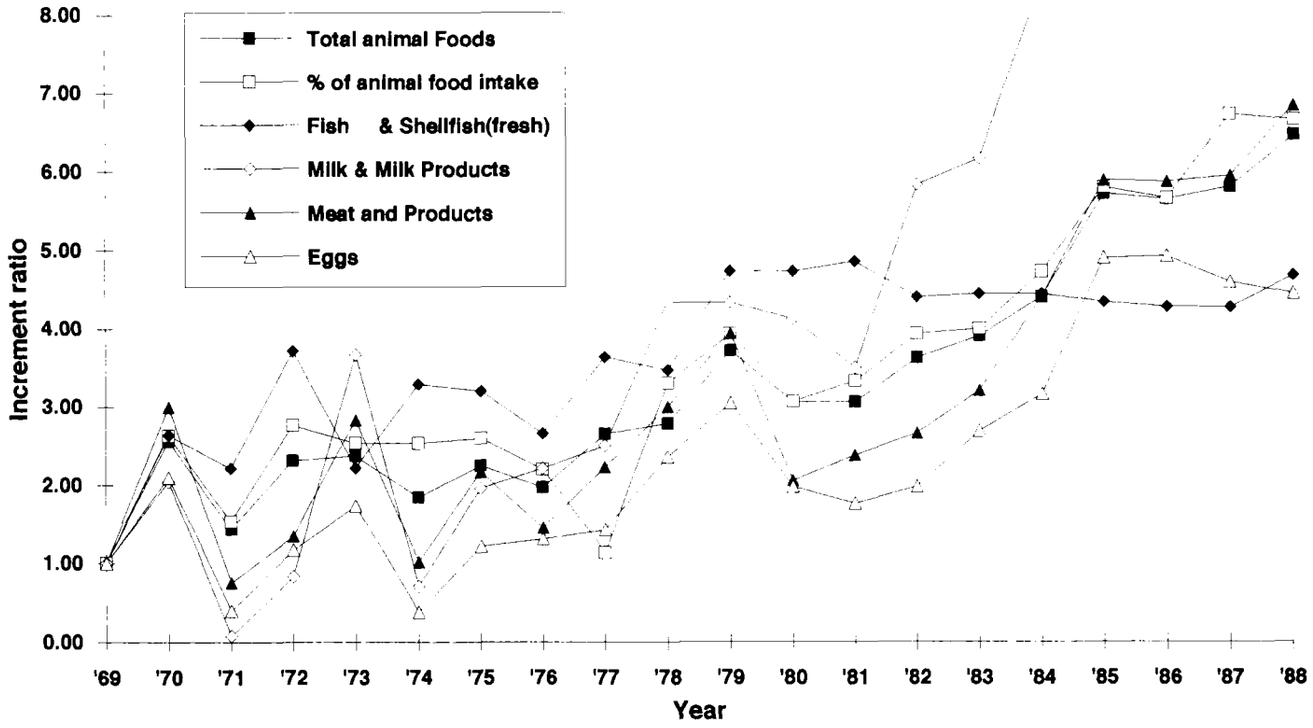


Fig 2. Trends in intake of animal foods per capita per day in Korea, 1969-1988.

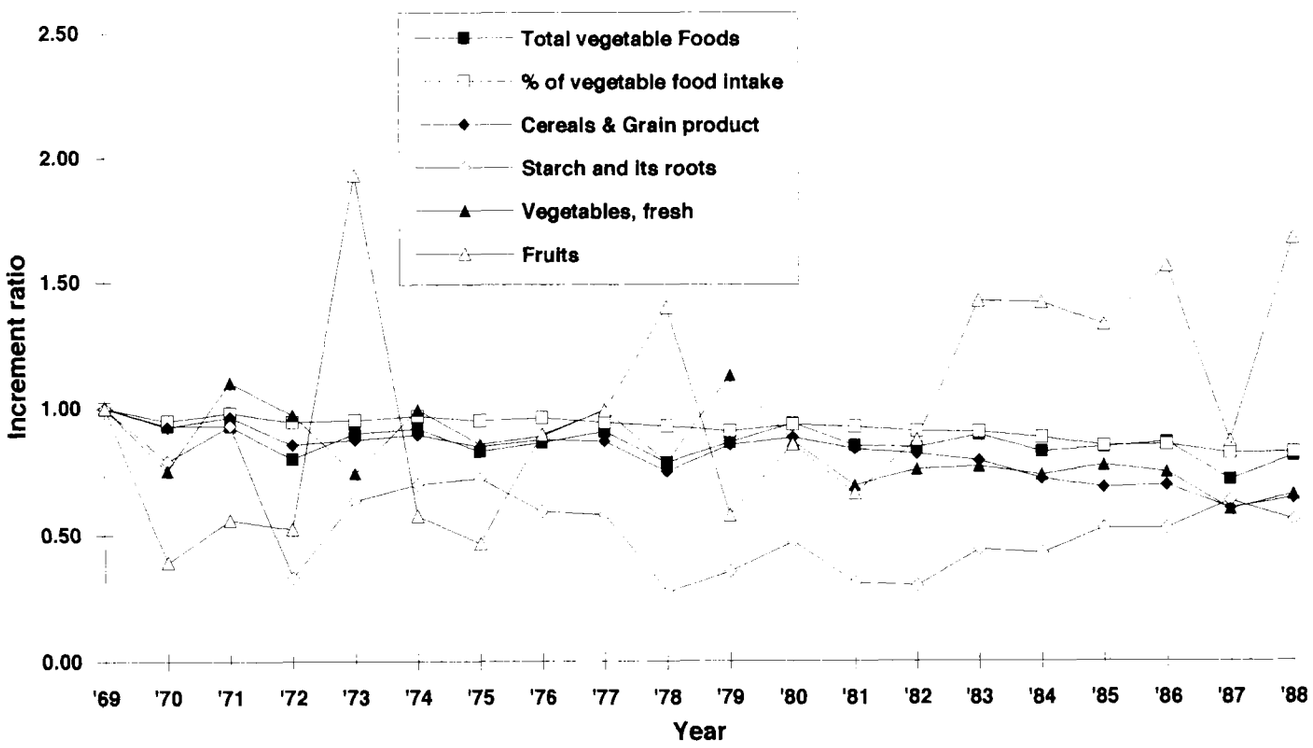


Fig 3. Trends in intake of vegetable foods per capita per day in Korea, 1969-1988.

od of 12 years, $p<0.05$). Total energy and total protein intake were negatively correlated, but were not statistically significant (Table 2).

Among some selected animal foods, the age-adjusted mortality rates for female breast cancer were positively correlated with total animal foods ($r = 0.70$ with lag period of 10 years, $p<0.05$), and animal foods to total intake ($r = 0.56$ with lag period of 10 years, $0.05<p<0.1$). Fresh fish and shellfish ($r = 0.89$ with lag period of 12 years, $p<0.01$), milk and milk products ($r = 0.70$ with lag period of 10 years, $p<0.05$), and meat and meat products ($r = 0.53$ with lag period of 10 years, ns) were also positively correlated with the age-adjusted mortality rates for female breast cancer (Table 3).

On the other hand, the rates were inversely correlated with vegetable foods to total intake ($r = -0.73$ with lag period of 12 years, $p<0.05$) and total vegetable foods ($r = -0.69$ with lag period of 12 years, $0.05<p<0.1$). Daily intake of cereals and grain products ($r = -0.81$ with lag period of 12 years, $p<0.01$), and starch and starch roots ($r = -0.77$ with lag period of 12 years, $p<0.01$) were the negatively correlated variables. Correlation with vegetables and fruits were not so prominent

Table 2. Chronological correlation coefficients between nutrients and age-standardized mortality rates for female breast cancer in Korea

| Nutrients | lag period (years) | r | lag period (years) | r | lag period (years) | r |
|---|---|---|---|---|---|---|
| Protein from animal source (%) | 12 | 0.83** | 11 | 0.74* | 10 | 0.77** |
| Total lipid (g) | 12 | 0.58*** | 11 | 0.63* | 10 | 0.64* |
| Total protein (g) | 12 | -0.05 | 11 | -0.04 | 10 | -0.01 |
| Total energy (kcal) | 12 | -0.49 | 11 | -0.37 | 10 | -0.05 |
| Total carbohydrate (g) | 12 | -0.70* | 11 | -0.63* | 10 | -0.37 |
| Energy from cereal (%) | 12 | -0.77** | 11 | -0.53 | 10 | -0.74* |

* : $p < 0.05$
** : $p < 0.01$
*** : $0.05 < p < 0.1$

Table 3. Chronological correlation coefficients between intake of some selected animal foods and age-standardized mortality for female breast cancer in Korea

| Dietary factors | lag period (years) | r | lag period (years) | r | lag period (years) | r |
|---|---|---|---|---|---|---|
| Total animal foods | 12 | 0.69* | 11 | 0.45 | 10 | 0.70* |
| % of animal foods to total intake | 12 | 0.44 | 11 | 0.31 | 10 | 0.56*** |
| Fish and shellfish, fresh | 12 | 0.89** | 11 | 0.51 | 10 | 0.68* |
| Milk and products | 12 | 0.39 | 11 | 0.63* | 10 | 0.70* |
| Meat and products | 12 | 0.26 | 11 | 0.35 | 10 | 0.53 |
| Fish and shellfish, processed | 12 | 0.23 | 11 | -0.18 | 10 | -0.02 |
| Eggs | 12 | 0.17 | 11 | 0.35 | 10 | 0.64 |
| Oils and fats, animal | 12 | -0.02 | 11 | -0.37 | 10 | -0.02 |

* : $p < 0.05$
** : $p < 0.01$
*** : $0.05 < p < 0.1$

(Table 4).

## DISCUSSION

This study suggests that dietary factors may be associated with the recent increase in mortality for breast cancer in Korea. In spite of the possibility of an ecologic fallacy, it can be drawn from the study results that an increase in the intake of animal food, rich in protein and fat, may play a role in the development of breast cancer in this country. Moreover, a concomittent decrease in intakes of cereals, starch, and some vegetables, may be another factor for such a change in mortality. Particularly noteworthy was that total energy intake did not correlate with the mortality rate of breast cancer.

Research in the area of diet and cancer is progressing somewhat slowly because current methods used for assessing dietary intake are relatively crude, which may result in measurement errors, and because the interrelationships between various dietary components are believed to be complex and are not well understood (Henderson 1990). Nevertheless, much of the evidence on diet and cancer risk derives from epidemiologic studies. Ecologic correlation studies permit analysis of various items of diet simultaneously, especially in international comparisons or in chronological comparisons in a country, that might not be observable in case-control or cohort studies. Considering that this type of study is most useful for generating hypotheses about dietary factors related to cancer risk, ecologic correlation study permits relatively inexpensive and rapid generation of hypotheses regarding the causes of breast cancer ( U.S. Department of Health and Human Services 1988). Such comparisons usually rely on average values of food intake in a population rather than on individual measures, and they tend to focus on cancer mortality rather than on incidence. It can be emphasized that we used the data on 'per capita food intake' as an index of dietary factors, rather than 'food consumption' which includes foods wasted.

Interest in dietary fat as a possible explanation for differences in breast cancer rates during the last 10 years has been stimulated by several ecologic studies, in which a very strong correlation between national per capita consumption of fat and age-adjusted rates of breast cancer was

Table 4. Chronological correlation coefficients between intake of some selected vegetable foods and age-standardized mortality rates for female breast cancer in Korea

| Dietary factors | lag period (years) | r | lag period (years) | r | lag period (years) | r |
|---|---|---|---|---|---|---|
| Total vegetable foods | 12 | -0.69*** | 11 | -0.54 | 10 | -0.07 |
| % of vegetable foods to total intake | 12 | -0.73* | 11 | -0.53 | 10 | -0.66* |
| Cereal and grain products | 12 | -0.81** | 11 | -0.71* | 10 | -0.49 |
| Starch and starch roots | 12 | -0.77** | 11 | -0.57*** | 10 | -0.60*** |
| Seaaonings, beverages | 12 | -0.31 | 11 | 0.19 | 10 | 0.35 |
| Vegetables, fresh | 12 | -0.10 | 11 | 0.14 | 10 | -0.17 |
| Vegetables, processed | 12 | -0.03 | 11 | -0.36 | 10 | 0.05 |
| Legumes and their products | 12 | 0.00 | 11 | -0.60*** | 10 | 0.23 |
| Fruits | 12 | 0.08 | 11 | 0.42 | 10 | 0.08 |
| Oils and fats, vege | 12 | 0.69 | 11 | 0.47 | 10 | 0.03 |
| Seaweeds | 12 | 0.76** | 11 | 0.16 | 10 | 0.37 |

* : $p < 0.05$

** : $p < 0.01$

*** : $0.05 < p < 0.1$

observed. The risk of breast cancer is correlated with total fat consumption in several international correlation studies (Gray *et al.* 1979; Rose *et al.* 1986). The correlation coefficient between the age-adjusted mortality rate and fat intake per capita per day was 0.984 in Japan (Tominaga and Kato 1990). However, other studies provide inconsistent results. In England, fat intake from non-dairy fat was inversely correlated with breast cancer mortality rates (Stocks 1970). In the United States, regional consumption of eggs, a major cholesterol determinant, was inversely related to breast cancer mortalities, although comsumption of milk, an important fat source, was positively associated (Gaskill *et al.* 1979).

Case-control and cohort epidemiologic studies tend to generate more scientifically favorable results than ecologic correlation studies, because they collect data based on individuals, rather than the population in general. However, they sometimes are limited by narrow ranges of variation in exposure to food groups or nutrients, which reduce the opportunity to see a potentially true biologic association (U.S. Department of Health and Human Services 1988). Although the hypothesis that dietary fat causes breast cancer seems to be very attractive (Henderson *et al.* 1991), it is far from willingly accepted due to many inconsistent results. In a Canadian case-control study, total fat consumption was slightly higher among women in breast cancer cases, but this association was not statistically significant (Miller *et al.* 1978). Other case-control and cohort studies relate the risk for breast cancer to total fat consumption in some studies (Howe 1985) but not all (Graham *et al.* 1982; Hirohata *et al.* 1985; Lubin *et al.* 1986; Katsouyanni *et al.* 1986; Hirayama 1986; Willet *et al.* 1987; Yu *et al.* 1990). A recent case-control study in Japan reported that there was no evidence of an association between a high fat diet and the risk of breast cancer, but green vegetables, as well as the Oriental staples, such as rice and bean curd (tofu), showed an apparent protective effect against breast cancer (Yoo *et al.* 1992a).

Recent studies on the risks for breast cancer in Japan suggests that international difference in the relation between known risk factors and the disease risk may be helpful for further understanding of the etiology of breast cancer (Yoo *et al.* 1992b; Yoo *et al.* 1993). Although further epidemiologic studies are needed to verify the association between diet and breast cancer, some supporting results from animal studies suggest that the association between high fat diet and breast cancer may be causal. Several mechanisms by which dietary fat may increase the risk of breast cancer have been proposed. Estrogens are synthesized by gut flora and this synthesis may be further activated by adding dietary fat. Alternatively, changes in colonic flora mediated by dietary fat may increase the deconjugation and reabsorption of estrogens excreted from the biliary system (Hill *et al.* 1971). In addition to that, the intake of polyunsaturated fatty acids can induce in vivo peroxidation. Adipose tissue can convert androstededione to estrone, and it makes an important contribution to increasing circulating levels of estrogen in postmenopausal women. It is thus possible that dietary fat increases the risk of breast cancer by inducing excessive fat accumulation. Indeed, obesity seems to increase the risk of breast cancer only in older women (de Waard *et al.* 1964).

This study has a limit on completeness, as well as accuracy of the data, because we used data on mortality statistics. Especially dose it so in this country where the proportion of deaths certified by physicians is less than 50% of all deaths notified. Current statistics, however, reported that disease notification has much been improved upto more than 95%. And the proportion of classiciable cause of death among all deaths notified has remained stable (Kim 1989), which is more important to ensure consistency of the statistics for long-term trend analysis. Moreover, there was no significant change in the criteria of classification of the disease during the study period. To draw a firm conclusion about the association of dietary fat and the breast cancer risk in Korea, further case-control and/or

cohort study is needed.

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