

## Diet and mortality from common cancers in Brazil: an ecological study <sup>1</sup>

Dieta e mortalidade para os tipos mais frequentes de câncer no Brasil: um estudo ecológico <sup>1</sup>

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**Abstract** A prospective ecological evaluation of mortality from common malignancies with dietary risk factors and alcohol consumption was carried out among 10 state capitals of Brazil. Regression analysis was used to examine the association of dietary intake with mortality rates of the most common cancers among adults age 30 years and older. Age-adjusted cancer mortality rates varied 2.4 to 3.3 fold across the state capitals. A positive relationship was observed between energy intake and colon, lung, and esophageal cancer ( $p \leq 0.02$  for each). Colon cancer mortality was positively associated with consumption of total fat, eggs, alcohol, mate tea, cereals, and vegetables ( $p \leq 0.01$ ). Lung cancer was positively associated with mate and cereal intake ( $p < 0.05$ ). Stomach cancer was associated with consumption of eggs ( $p = 0.04$ ); and negatively associated with consumption of high fiber foods, fruits, and vitamin A and C ( $p \leq 0.05$ ). Esophageal cancer was positively associated with fat intake, mate and cereals ( $p \leq 0.05$ ) and negatively associated with vitamin A ( $p = 0.02$ ); prostate cancer was negatively associated with vitamin C ( $p = 0.007$ ). Breast cancer was not associated with any of the factors studied. The marked variation in cancer mortality rates in Brazil may be partially related to the high variation in dietary components or other diet associated factors.

**Key words** Epidemiology; Cancer; Mortality; Diet; Ecological Study

**Resumo** Realizou-se um estudo ecológico com base em dados de 10 capitais brasileiras e, através de análise de regressão linear, examinou-se a associação entre dieta e as taxas de mortalidade para as principais localizações de câncer, entre adultos com 30 anos ou mais. As taxas de mortalidade ajustadas por idade variavam de 2,4 a 3,3 vezes entre as capitais. Consumo de energia associou-se positivamente com câncer de colon, pulmão e esôfago ( $p \leq 0,02$  em cada associação). Mortalidade por câncer de colon associou-se positivamente com o consumo de gordura, ovos, álcool, mate, cereais e vegetais ( $p \leq 0,01$ ); câncer de pulmão associou-se ao consumo de mate e cereais ( $p < 0,05$ ); câncer de estômago associou-se positivamente com ovos ( $p = 0,04$ ) e, negativamente, com o consumo de fibras, frutas e vitaminas A e C ( $p \leq 0,05$ ). Câncer de esôfago foi positivamente associado com consumo de gordura e mate ( $p \leq 0,05$ ) e, negativamente, com vitamina A ( $p = 0,02$ ); câncer de próstata associou-se negativamente com vitamina C ( $p = 0,007$ ). Câncer de mama não se associou a nenhum dos fatores estudados. A importante variação nas taxas de mortalidade por câncer no Brasil podem ser parcialmente associadas as variações em componentes da dieta ou a fatores a ela associados.

**Palavras-chave** Epidemiologia; Câncer; Mortalidade; Dieta; Estudo Ecológico

## Introduction

Cancer is the second leading cause of mortality in Brazil. In 1987 cancers constituted 9.6% of the 799 thousand deaths. The most common anatomical sites of cancer mortality were stomach, lung, esophagus, prostate and colon (Ministério da Saúde, 1988). Among women, breast cancer was the leading cause of cancer mortality (Ministério da Saúde, 1988).

Diet may play an important role in determining the risk of several cancers, and numerous dietary components with diverse mechanisms of action have been implicated in their pathogenesis. Geographical correlation studies of cancer mortality rates have had an important role in the establishment of nutritional etiological hypotheses. For example, the association between breast and colon cancer with consumption of animal protein and fat was first shown based on mortality data of 32 countries (Armstrong & Doll, 1975). In a more recent international regression analysis between cancer incidence rates and fat consumption, strong associations were shown for cancers of the breast, colon, rectum, ovary and prostate (Prentice & Sheppard, 1990). The authors of that study concluded that ecological studies can provide valuable information and even clarify associations that could not be proved by more rigorous analytic epidemiologic techniques, since conventional epidemiologic techniques, developed to examine etiological relationships in individuals, are generally unable to detect small increases of relative risk.

A detailed dietary survey conducted in Brazil in 1974-1975 allowed examination of cancer mortality associations, approximately fifteen years later in ten metropolitan cities. For these cities we analyzed the association of mortality rates from the more common cancers with a number of dietary factors that have been considered risk factors in other studies. Foods and food groups were analyzed in addition to nutrient composition of the diet, because numerous food components may interact producing effects different from those of nutrients (Steinmetz & Potter, 1993b).

The design of the current study and the characteristics of the Brazilian population overcame some of the problems in international ecological studies of diet and cancer. Limiting the study to a single, large country could potentially be more informative than international comparisons because the ethnic composition of the population and case ascertainment criteria are not likely to vary as widely (Franco et al., 1988). Also, dietary data in this study were

derived from a standardized 7-day food weighing among individual households, an improvement over national food disappearance data used in many international comparisons (Willett & Stampfer, 1990).

## Methods

### Dietary data

Dietary data used in this study were based on the 1974/75 Estudo Nacional da Despesa Familiar (ENDEF) (FIBGE, 1983). The ENDEF was a nutritional survey of a national probability sample of 55,000 Brazilian households using two stage probability sampling. Data were derived from a 7-day food weighing performed by trained interviewers. The interviewers visited each household in the morning and afternoon and weighted all ingredients to be used in all meals and the leftovers of the previous meal. All reported food intakes outside the household were also registered for each member of the family. Intake was calculated for calories and nutrients based on the composition tables of ENDEF (FIBGE, 1985). There were 1650 foods and 235 prepared foods recorded during the survey.

### Mortality data

Mortality rates were calculated dividing the cause specific numbers of deaths for the years 1987-1989 by three and using as denominator the 1988 estimated population. Denominators for the calculation of mortality rates in 1988 were estimated from the growth rate of the population in the period between the censuses of 1980 and 1991. Age-adjustment of mortality was made through direct standardization (30-39, 40-49, 50-59, 60-69, 70 and older) to the 1980 national population census. The underlying cause of death for adults 30 years or older for the years 1987-1989 was coded according to the Ninth Revision of the International Classification of Diseases (ICD), based on data published by the Brazilian Minister of Health (Ministério da Saúde, 1988, 1992, 1993). Mortality was examined for the most common cancers: stomach cancer (ICD 151), esophageal cancer (ICD 150), colon cancer (ICD 153), lung cancer (ICD 162), female breast cancer (ICD 174), and prostate cancer (ICD 185). The 1987-1989 mortality data were used because the effects of differences in intake would be reflected in cancer mortality after periods of at least 10 years. Capitals of the metropolitan areas of Brazil

(Table 1) were chosen as the unit of analysis because the quality of their mortality data was better than the state as a whole.

#### Data analysis

Nutrient analysis included total energy, fat, vitamin C, and vitamin A. We also analyzed the consumption (in grams) of red meat, animal fat (butter plus lard), eggs, alcohol, coffee, mate (a green tea), beans, fruits, cereals, vegetables, potatoes, and high fiber foods (cereals, beans, vegetables, and fruits). The variable called vegetables included: lettuce, collard, cauliflower, cabbage, onions, other green leafed vegetables, tomato, chayote, pumpkin, squash, okra, cucumber and other vegetable-fruits, and roots of carrot and beets.

Spearman correlation coefficients among the dietary variables and linear regressions were calculated using the Statistical Analysis System (SAS). The age-adjusted mortality rate from common malignancies was the dependent variable and the mean per capita intake in the ten cities was the independent variable of interest in linear-regression models. Sex and percentage of smokers were included in the models as independent variables. The percentage of smokers in each capital city was deter-

mined from the Pesquisa Nacional sobre Saúde e Nutrição, carried out in 1989 (Instituto Nacional de Alimentação e Nutrição, 1990), because there were no national data of smoking prevalence on the ENDEF survey. Strength of association was estimated with a sex and smoking adjusted regression coefficient, which represented the estimated adjusted change per 10,000 population for a unit increase in the dietary risk factor.

#### Results

There was considerable variation in age-adjusted malignant neoplasm mortality among the capitals studied as shown by the ratio of the highest to the lowest mortality rates (Table 1). Dietary intake also varied across Brazil (Table 2), with generally increased nutrient intake from north to south. In the northern region the mean energy intake was eighteen hundred calories and in the south it was about twenty-two hundred calories.

Total energy consumption was positively correlated with 10 of the 15 dietary variables (Table 3). Likewise, lipid intake was strongly correlated with 9 of the other dietary variables. There were few significant associations with alcohol and coffee.

Table 1

Cancer mortality rates age-adjusted to the 1980 Brazilian population per 100.000 habitants in 10 capitals of Brazil, 1987-89.

	Sex	Stomach	Lung	Colon	Esophageal	Breast	Prostate
Belém	Men	100.9	76.8	10.9	18.0	-	57.0
	Women	35.1	21.9	10.3	2.9	28.8	-
Fortaleza	Men	100.6	83.0	16.0	26.3	-	96.8
	Women	49.2	25.1	13.4	7.7	59.6	-
Recife	Men	30.1	49.2	6.9	14.2	-	42.2
	Women	17.1	15.3	10.2	50.0	41.3	-
Salvador	Men	43.5	54.5	14.6	16.7	-	59.9
	Women	20.4	11.8	15.4	6.2	42.5	-
Belo Horizonte	Men	77.0	71.0	13.8	36.5	-	56.3
	Women	34.4	19.9	16.0	11.6	48.3	-
Rio de Janeiro	Men	46.7	95.9	17.7	16.3	-	48.4
	Women	24.5	20.8	17.6	4.5	55.1	-
São Paulo	Men	45.9	56.9	13.0	17.2	-	33.3
	Women	29.5	19.7	17.7	5.5	52.5	-
Curitiba	Men	84.0	111.3	20.3	46.1	-	54.3
	Women	37.1	31.4	18.8	12.7	59.2	-
Porto Alegre	Men	40.5	136.0	22.3	35.2	-	62.9
	Women	24.7	29.9	28.5	10.2	70.6	-
Distrito Federal	Men	65.2	77.0	15.2	24.9	-	56.3
	Women	27.0	25.9	15.9	4.0	41.3	-
Highest/Lowest ratio	Men	3.3	2.7	3.2	3.2	-	2.9
	Women	2.9	2.7	2.8	3.2	2.4	-

Table 2

Daily per capita means and range across 10 state capitals for dietary risk factors. Estudo Nacional da Despesa Familiar – ENDEF, 1974-1975.

	Mean	Range	
Energy (kcal)	1944.0	1683.0	2239.0
Vitamin C (mg)	58.1	44.0	72.0
Vitamin A (RE)	572.0	390.0	928.0
Lipids (g)	52.5	33.0	70.0
Animal fat (g)	7.6	3.0	17.0
Red meat (g)	65.2	42.0	92.0
Eggs (g)	15.6	9.0	21.0
Alcohol (g)	8.6	2.0	22.0
Coffee (g)	12.4	9.0	16.0
Mate (g)	0.6	0.0	13.0
Beans (g)	47.0	28.0	67.0
Fruits (g)	98.0	70.0	140.0
Cereals *(g)	222.0	166.0	274.0
Vegetables (g)**	82.0	32.0	117.0
High fiber foods*** (g)	449.0	311.0	540.0
Potatoes (g)	86.2	51.0	142.0

\* rice, wheat, oats, corn.

\*\* lettuce, collard, cauliflower, cabbage, onions, other green leaves, tomato, chayote, pumpkin, squash, okra, cucumber and other vegetable-fruits, root of carrot and beets.

\*\*\* cereals, fruits, beans, and vegetables.

Table 3

Spearman correlation coefficients among dietary variables, based on the mean consumption of 10 Brazilian capitals.

Estudo Nacional da Despesa Familiar – ENDEF, 1974-1975.

	Calories	Lipids	Alcohol	Coffee
Lipids (g)	0.92**	1	0.73**	0.81**
Vitamin C (mg)	0.71**	0.67**	0.50	0.58
Vitamin A (RE)	0.29	0.43**	0.62	0.34
Eggs (g)	0.84**	0.87**	0.51	0.68*
Animal fat (g)	0.61**	0.54	0.72**	0.34
Red meat (g)	0.21	0.24	0.21	0.4
Alcohol (g)	0.67*	0.73**	1	0.37
Coffee (g)	0.75**	0.81**	0.37	1
Mate (g)	0.75**	0.80**	0.40	0.74*
Beans (g)	-0.20	-0.14	-0.35	-0.05
Fruits (g)	0.16	0.13	-0.09	0.02
Cereals (g)	0.87**	0.78**	0.51	0.57
Vegetables (g)	0.87**	0.89**	0.60	0.78*
High fiber foods (g)	0.83*	0.85**	0.49	0.68*
Potatoes (g)	-0.18	-0.28	-0.05	-0.03

\* 0.001 &lt; p &lt; 0.05

\*\* P=0.001

Smoking prevalence was positively associated with lung cancer ( $\beta=0.30$ ;  $p=0.0009$ ); esophageal cancer ( $\beta=0.08$ ;  $p=0.02$ ); stomach cancer ( $\beta=0.20$ ;  $p=0.003$ ); and breast cancer ( $\beta=0.18$ ;  $p$ -value=0.03), but was not associated to colon cancer ( $p=0.70$ ), and prostate cancer ( $p=0.85$ ).

The relations between dietary factors and the cause specific mortality due to cancers for the 10 state capitals are shown in Table 4. Because mortality rates for both sexes had the same patterns of association with the dietary variables, the analyses included both sexes where appropriate. Positive relationships were observed between energy consumption and colon ( $p=0.001$ ), lung ( $p=0.002$ ), and esophageal cancer ( $p=0.02$ ). Colon cancer mortality was strongly and positively associated with consumption of total fat, eggs, alcohol, mate, cereals, and vegetables ( $p=0.01$ ). Lung cancer was positively associated with mate and cereal intake ( $p=0.01$ ). Stomach cancer was positively associated with consumption of eggs ( $p=0.04$ ) and negatively associated with consumption of high fiber foods, fruits, and vitamin A and C ( $p=0.05$ ). Esophageal cancer was positively associated with fat intake, mate and cereals ( $p=0.05$ ) and negatively associated with vitamin A ( $p=0.02$ ); prostate cancer was negatively asso-

ciated with vitamin C ( $p=0.007$ ). Breast cancer was not associated with any of the factors studied.

Total energy consumption was strongly correlated with all other dietary variables except vitamin A, red meat, beans, fruits, and potatoes. With further adjustment for energy intake only the negative association of fruits and vitamins with cancer mortality remained significant: stomach cancer with fruits and vitamins A and C, esophageal cancer with vitamin A, and prostate cancer with vitamin C.

## Discussion

The current study was performed to determine the extent that associations of diet and cancer mortality found in developed countries of the northern hemisphere were sustained in Brazil. We also examined potential associations that are more characteristic of the Brazilian diet. Thus, hot maté drinking (chimarrão) was associated with pre cancerous lesions of the esophagus in a endoscopic study in Southern Brazil (Munoz et al., 1987). Our findings showed that chimarrão, a mate consumed in high quantities in the south region of the country, was strongly associated with esophageal cancer. Chimarrão

Table 4

Linear regression coefficients ( $\beta$ ) and p value (p), for the mortality due to stomach, colon, esophageal, breast, lung, and prostate cancer by dietary factors. Models included sex, and percentage of smokers.

	Stomach		Colon		Esophageal		Breast*		Lung		Prostate	
	$\beta$	p	$\beta$	p	$\beta$	p	$\beta$	p	$\beta$	p	$\beta$	p
Energy (100 kcal)	-0.39	0.14	0.19	0.001	0.23	0.02	0.19	0.43	0.62	0.002	-0.4	0.23
Lipids (10 g)	-0.48	0.19	0.27	0.0006	0.28	0.05	0.28	0.37	0.69	0.06	-0.63	0.18
Vitamin C (10 mg)	-1.50	0.0006	0.048	0.72	-0.17	0.43	0.017	0.96	0.15	0.78	-1.5	0.007
Vitamin A (10U RE)	-0.79	0.02	0.0097	0.29	-0.03	0.02	0.038	0.13	0.030	0.42	-0.045	0.35
Eggs (10 g)	2.40	0.04	0.77	0.006	0.70	0.15	1.10	0.28	1.9	0.12	-1.8	0.22
Animal fat (10 g)	0.39	0.70	0.40	0.10	0.68	0.09	0.45	0.54	1.4	0.19	-0.51	0.71
Red meat (10 g)	-0.17	0.53	0.081	0.24	-0.088	0.44	-0.05	0.93	0.29	0.31	-0.10	0.69
Alcohol (g)	-0.15	0.06	0.062	0.0001	0.047	0.16	0.092	0.12	0.15	0.07	-0.072	0.56
Coffee (g)	-0.20	0.38	0.099	0.08	0.17	0.27	0.056	0.75	0.25	0.28	-0.51	0.07
Mate (g)	-0.31	0.49	0.35	0.0002	0.45	0.007	0.56	0.13	1.18	0.004	-0.10	0.86
Beans (10 g)	0.17	0.70	-0.011	0.91	-0.063	0.97	0.22	0.50	-0.20	0.66	0.63	0.27
Fruits (10 g)	-0.62	0.008	-0.046	0.48	-0.12	0.24	-0.097	0.58	-0.26	0.33	-0.56	0.10
Cereals (100 g)	-1.50	0.25	0.97	0.001	1.4	0.003	1.70	0.22	3.1	0.01	-1.1	0.52
Vegetables (10 g)	-0.28	0.06	0.086	0.01	0.085	0.17	0.093	0.45	0.17	0.25	-0.33	0.06
High fiber foods (100 g)	-1.20	0.05	0.34	0.02	0.41	0.12	0.51	0.41	0.85	0.20	-0.95	0.22
Potatoes (100 g)	-0.022	0.98	-0.31	0.44	-0.57	0.38	-0.42	0.73	0.26	0.87	-2.3	0.92

\* women only

is drunk using a metal straw at very hot temperatures. A possible effect of beverage temperature on the risk of esophageal cancer in Brazil has been suggested (Munoz et al., 1987), but not substantiated in a case-control study carried out in the same region of the country (Victoria et al., 1987). Composition of the tea may also explain the association, since in our analysis tea was also associated with lung and colon cancer. Yang & Wang (1993) found conflicting results in their review of the associations between cancer and tea (Yang et al., 1993).

Fruits and vegetables (Steinmetz et al., 1993a; Negri et al., 1991; Block, 1993), and vitamins (Willett, 1990; Block, 1993; Smith & Walter, 1991) have shown a protective effect for many cancer sites. In this study vitamin C, fruits and vegetables were negatively associated only with stomach and prostate cancer. A relatively low intake of fruits and vegetables in Brazil may be a reason for the lack of inverse association for other sites of cancer. Comparing our data on mean consumption of fruits and vegetables with US disappearance data for 1974-1979 (Yu et al., 1991), consumption in Brazil was, respectively one third and half of the estimated consumption for the United States. Nevertheless, it has been suggested that even a very low consumption of fruit may protect against stomach cancer (Block, 1991). Reduced mutagenesis through an antinitrosation mechanism by ascorbic acid may be specific to stomach cancer (Block, 1991), whereas an antioxidant effect may be protective of cancer of other sites (Block, 1993). Therefore, the necessary consumption for protection may vary as a function of the mechanism involved in anticarcinogenesis. Alcohol consumption has been consistently associated with esophageal (Victoria et al., 1987) and colon cancer (Hirayama, 1989). Likewise, our analysis showed a strong positive association of alcohol and colon cancer. In contrast to some other studies that have shown association between fat intake and breast cancer (Armstrong & Doll, 1975; Prentice & Sheppard, 1990) we did not find any factor associated with breast cancer. However, the role of dietary fat in modulating cancer risk has been particularly controversial (Willett & Stampfer, 1990). A large prospective study carried-out in United States did not find that fat consumption was a risk factor for breast cancer (Willett et al., 1987). A criticism of studies in the United States has been that consumption falls in too narrow range in daily fat consumption and it is above the threshold for increased breast cancer risk. The current study had a two fold range in fat consumption across state cap-

itals (33 to 70 grams) and a considerable range as a percent of total calories (17.6 to 28.1 percent). Nevertheless, the consumption of fat in Brazil may fall below the necessary amount to find an association between dietary fat and breast cancer. For example, a much higher daily consumption of fat, ranging from 72 to 155 grams was found in one international comparison (Prentice & Sheppard, 1990).

It would be expected that several of the 96 possible diet-mortality associations in this study would be due to chance. However, a p-value of 0.05 or less was found for 23 of these associations, many of which were consistent with findings of other studies. A possible powerful confounder in this study is the economical diversity among the cities studied. However, in a previous paper we showed that the high variation in cancer among 19 state capitals in Brazil could only be partially related to socioeconomic factors (Sichieri et al., 1992).

Many of the associations of nutrient intake and subsequent cancer mortality disappeared upon controlling for energy intake. Energy consumption was highly correlated with nearly all of the nutrients examined. In this study with only 10 data points per analysis, controlling for energy intake severely reduced the likelihood of finding significant associations. Because of this high correlation, we can not determine whether the numerous nutrient associations we found were independent of energy consumption. It is also possible that energy intake, which is determined by body size, metabolic efficiency and physical activity (Willett, 1990) may be the more important factor associated with cancer mortality.

Ecological studies of diet and cancer have been faulted for several reasons: weakness of much of the international dietary data; strong ecological association between dietary data and socioeconomic factors; ethnic variations among populations studied, and limitation of ecological analysis to study associations between possible risk factors and disease (Morgenstern, 1982). The design of the current study and the unique characteristics of the Brazilian population overcame some of these problems. First, the dietary data were collected among individual households, an improvement over national food disappearance data (per capita difference between production or importation and exportation of foods) used in many international comparisons. Food disappearance data may be quite different from actual consumption. In the United States, for example, food disappearance may be at least 50% greater than actual intake (Willett et al.,

1990). Second, although the population of Brazil is ethnically diverse, its distribution does not vary as widely as international comparisons. Third, data collection was standardized to a degree that is nearly impossible to obtain in international studies. Data were collected in the same language, in the same country, in the same survey, and with the same 7-day food weighing method. Death certification was also performed using a national system. Of the 10 capitals, only Fortaleza reported more than 8 percent of deaths being due to ill-defined causes. Excluding Fortaleza from the analysis made little difference in the results.

Although the design of the current study overcomes several potential biases of international ecological studies there remains the potential for ecological bias. Thus, associations found in this study between dietary factors and cancer mortality may represent true risk factors or differences in exposures for which the diet was a marker, for example genetic background of the population or other factors related to life style. Nevertheless, the results of this ecological analysis should be considered in further studies that focus on the relationships between diet and cancer.

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