Stomach cancer incidence in Brazil: an ecologic study with selected risk factors [1]

Incidência de câncer de estômago no Brasil: estudo ecológico com fatores de risco selecionados [1]

Sergio Koifman [2]
Rosalina Jorge Koifman [2]

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[2] *Department of Epidemiology and Quantitative Methods, National School of Public Health, Oswaldo Cruz Foundation, Ministry of Health, Av. Leopoldo Bulhões 1480, Rio de Janeiro, RJ 21041-210, Brazil.*

Abstract *Contrary to many industrialized countries in which a sharp decline in stomach cancer incidence has been observed, Brazil still shows intermediate to high incidence rates. An ecologic analysis was performed to explore variables possibly associated with the development of stomach cancer. Cluster analysis, principal component analysis, and factor analysis were carried out with population data, including the following: stomach cancer incidence rates in the early 1990s obtained from population-based cancer registries in Porto Alegre, Campinas, Fortaleza, Belém, and Goiânia; and data from a Brazilian national survey on family expenditures (several diet consumption items and availability of home refrigerators) carried out in 1974-75. The results suggested that past availability of a home refrigerator, i.e. food preservation, may have played an important role in currently observed differences in stomach cancer incidence among the various populations studied in Brazil. Differences in living standards among populations in these cities also appear to have played an important role in the observed incidence differences.*
Key words *Stomach; Cancer; Risk Factors; Cluster; Factor*

Resumo *De forma distinta daquela verificada em muitos países industrializados onde se vem observando um marcado declínio das taxas de incidência de câncer de estômago, o Brasil ainda apresenta taxas consideradas intermediárias ou elevadas desta doença. Visando realizar um estudo exploratório das possíveis razões para estas diferenças, se realizou um estudo ecológico através de análise de agrupamento (cluster), análise de componentes principais e análise fatorial. Foram incluídos nestas análises as taxas de incidência de câncer de estômago no início da década de 90 – determinadas pelos registros de câncer de base populacional no país (Porto Alegre, Campinas, Fortaleza, Belém e Goiânia) –, bem como aqueles obtidos através de inquérito nacional de despesas familiares (ENDEF) realizado em 1974-75. Este levantou dados pormenorizados do consumo de diversos alimentos, bem como da disponibilidade de geladeiras nas diferentes regiões do país. Os resultados obtidos sugerem que a hetereogeneidade quanto à disponibilidade de geladeiras na década de 70, e portanto da conservação de alimentos, pode ter desempenhado um importante papel em relação às diferenças de incidência de câncer de estômago hoje observadas entre aquelas cidades. Diferenças quanto às condições de vida podem ter também desempenhado importante papel explicativo das diferenças hoje observadas na incidência de câncer de estômago entre as populações das cidades analisadas.*
Palavras-chave *Estômago; Câncer; Fatores de Risco; Cluster; Fatorial*

Introduction

Despite the sharp decline in the incidence of stomach cancer observed in various countries (Howson et al., 1986; Tominaga, 1987), this is still one of the most relevant tumors in Brazil, as observed in all population-based cancer registries in the country. Indeed, it is observed among the three most frequent types of cancer in men (and among the five most frequent in women) in all Brazilian population-based cancer registries (INCA, 1995). Compared to the world's highest age-standardized incidence rates for stomach cancer, occurring in Japan (Parkin et al., 1992), ranging from 80 to 90 cases per hundred thousand men in the 1980s, and the lowest, in New South Wales, Australia (11.8 during 1983-87), the Brazilian rates were 53.6 in São Paulo (1978), 51.6 in Belém (1989), 31.6 in Fortaleza (1985), 29.0 in Porto Alegre (1991), 26.2 in Campinas (1992), and 22.4 in Goiânia (1991).

Even considering some evidence of a temporal decline in mortality rates, there are still remarkably high incidence rates for this cancer in Brazil. This fact has thus been a source of concern, and the search is under way for improving our understanding of the disease distribution.

Certain risk factors are suspected to play an important role in the development of stomach cancer, perhaps explaining the distinct epidemiological patterns observed among different populations. These include various agents with damaging effects on the normal gastric epithelium, as mentioned in the literature. *Helicobacter pylori* infection (Taylor & Blaser, 1991; Forman et al., 1994; Nightingale & Grueber, 1994; Munõz, 1994), perhaps mainly during early periods of life (Goodman & Correa, 1995), nitrosamine precursors in industrialized foods (Mirvish, 1994), and facilitating factors associated with either a salt-rich diet, alcohol intake, or deficient consumption of fresh fruits and vegetables have been mentioned as associated with stomach cancer (Antonioli, 1994; Hwang et al., 1994; Kodama et al., 1984; Risch et al., 1985; Stehr et al., 1985).

A proposed explanatory model involving these agents (Correa, 1992) is based on the premise that epithelium-irritating factors like a salt-rich diet could facilitate bacterial activity, including that of *H. pylori* and others (Megraud et al., 1989), leading to gastric epithelial lesion (chronic gastritis), facilitating the direct action of carcinogens (i.e. nitrosamines). On the other hand, a vitamin-rich diet could impede endogenous nitrosamine production from nitrite – and nitrate-rich foodstuffs (Weisburger, 1985; Bartsch et al., 1988). The exact steps and chronological order in which all these factors intervene remains to be ascertained.

A decline of stomach cancer in Japan was also observed simultaneously to the increase in the availability of household refrigerators in that country (Howson et al., 1986; Tominaga, 1987). This fact was interpreted as evidence of the impact of better food preservation on the development of stomach cancer.

This paper reports on our ecologic analysis of associations between currently observed incidence rates of stomach cancer in different Brazilian populations and exposure of the latter to a series of the above-mentioned risk factors nearly a decade previously.

Methodology

Age-standardized incidence rates for stomach cancer by gender in 1989-91 were obtained from the Brazilian cities of Porto Alegre, Belém, Fortaleza, Campinas, and Goiânia, in which population-based cancer registries are currently being kept. Population sample data from either the cities themselves (Belém, Porto Alegre, and Fortaleza) or non-metropolitan urban areas in which others are located (Goiania and Campinas) were gathered in 1974-75 by ENDEF, a national survey of Brazilian family expenditures (FIBGE, 1978).

The national survey gathered information on all family expenditures from a statistically representative sample of all Brazilian regions. Two to three times a day for an entire week, an interviewer weighed all food that was eaten or residual (cooked but uneaten) at home. This survey provided a large store of data on diet characteristics in the various regions, including estimated per capita consumption of specific foodstuffs like vegetables, fruits, citrus fruits, beans, fresh fish, salted fish, fresh red meat, canned meat, salt, tomato sauce, sausage, and alcoholic beverages, among others.

The same survey produced information on the distribution of family ownership of goods based on total expenditures, including consumption and taxes. Therefore, availability of home refrigerators among lower socioeconomic strata (i.e., the percentage of refrigerator-owning families in the 40th percentile for income distribution) in the mid-1970s in the same regions was also obtained.

Furthermore, we performed and discuss the results of a hierarchical cluster analysis, a principal components analysis, and a factor analysis with varimax rotation based on the aforementioned variables. Hierarchical cluster analysis was performed with SPSS software and principal components and factor analysis were developed with BMDP software.

Results

Recent age-standardized incidence rates of stomach cancer and both specific diet item intake and refrigerator availability in 1974-75 in selected Brazilian cities are presented in Table 1. The highest incidence rates are observed in Belém and Fortaleza for men (with the same plus Goiânia for women), while the lowest rates are seen in Campinas and Porto Alegre.

Past consumption of diet items also shows important variability among the different populations, mainly for vegetables, citrus fruits, sausages, fresh fish, and alcoholic beverages. Indeed, Porto Alegre's population had a sausage and liquor mean intake eight to ten times higher than observed in Belém and Fortaleza. On the other hand, citrus fruit and vegetable mean consumption in Porto Alegre was two to three times that of Belém and Fortaleza. Belém's population showed a very heavy consumption of fresh fish as compared to all the other cities studied. Average salt consumption was similar in all the cities. Vegetable consumption in Porto Alegre and Campinas was also similar.

The correlation matrix of all these variables (Table 2) shows high correlation coefficients between male incidence rates and consumption of salt (r = -0.97), vegetables (r = -0.90), fresh fish (r = 0.89), and fruits (r = -0.79). A moderate correlation was observed between refrigerator availability (r = -0.59) and consumption of salted fish (r = 0.75) and tomato sauce (r = 0.67).

Hierarchical cluster analysis of all the above-mentioned diet items (vegetables excluded), refrigerator availability, and stomach cancer incidence rates resulted in a specficic clustering pattern: Porto Alegre and Goiânia merged first, forming an initial cluster; Fortaleza and Belém then established a second cluster; subsequently these two clusters merged; and Campinas was the last city to merge in the dendogram (Figure 1). When we dropped the variable "refrigerator availability in the 1970s" from the model, the clustering pattern changed: Campinas merged with Goiânia, establishing the first cluster, in which Porto Alegre was subsequently included (Figure 2).

Furthermore, principal components analysis and factor analysis were developed with these variables, and the percentage of total variance explained by the identified common factors was the following: factor 1 – 56.7%; factor 2 – 26.8%; factor 3 – 9.2 %; and factor 4 – 7.2 %. Thus, over 83% of the total variance can be explained by the first two factors. The respective factor-rotated plot (factors 1 and 2) is displayed in Figure 3.

Table 1

Stomach cancer incidence by gender (1990-91) and diet item intake (1974-75) and refrigerator availability (1974-75) in selected Brazilian cities *

Variable	Porto Alegre	Belém	Fortaleza	Goiânia	Campinas
alch	8.0	1.3	0.6	1.8	2.9
bean	13.4	10.6	24.2	18.6	18.8
citrus	10.6	4.6	5.3	10.9	18.3
ffish	2.0	16.2	6.0	2.3	3.3
fruit	34.2	28.7	34.8	35.1	36.1
meat	32.8	33.0	14.6	24.0	18.8
refrig	25.4	14.6	14.4	17.5	48.8
salt	4.5	2.9	3.6	4.5	4.9
saus	3.3	0.3	0.3	0.1	0.4
veget	38.8	14.0	11.7	29.8	38.4
cmeat	0.5	0.4	0.3	0.1	0.4
sfish	0.1	2.1	1.3	0.3	0.4
toms	0.8	0.1	0.1	0.6	1.0
minc	29.0	42.5	44.6	25.3	22.2
finc	6.8	16.8	16.7	16.2	10.8

* Porto Alegre, Campinas, Goiânia, Fortaleza and Belém
alch: per capita annual alcoholic beverage intake (liters), 1974-75
bean: per capita annual bean consumption (kg), 1974-75
citrus: per capita annual citrus fruit consumption (kg), 1974-75
ffish: per capita annual fresh fish consumption (kg), 1974-75
fruit: per capita annual fruit consumption (kg), 1974-75
meat: per capita annual fresh red meat consumption (kg), 1974-75
refrig: refrigerator availability (%) among the 40% poorest families, 1974-75
salt: per capita annual salt consumption (kg), 1974-75
saus: per capita annual sausage consumption (kg), 1974-75
veget: per capita annual vegetable consumption (kg), 1974-75
cmeat: per capita annual canned meat consumption (kg), 1974-75
sfish: per capita annual salted fish consumption (kg), 1974-75
toms: per capita annual tomato sauce consumption (kg), 1974-75
minc: male incidence of stomach cancer (age-standardized rates per 100,000), 1990-91
finc: female incidence of stomach cancer (age-standardized rates per 100,000), 1990-91
Sources: FIBGE, 1978; INCA, 1995.

Discussion

Ecologic analysis has been performed in many situations as a preliminary procedure aimed at generating hypotheses to be further investigated in observational studies. Despite the frequent risk of introducing an ecologic fallacy (Kleinbaum et al., 1982) in which false associations can be raised, ecologic studies can be a useful tool, so long as they are carefully employed with regard to their validity restraints.

Table 2

Correlation matrix of stomach cancer incidence rates (1990-91) and diet item intake and refrigerator availability (1974-75) in selected Brazilian cities*

	alch	bean	citrus	ffish	fruit	meat	refrig	salt	saus	veget	cmeat	sfish	toms	minc	finc
alch	1.00														
bean	-0.42	1.00													
citrus	0.03	0.13	1.00												
ffish	-0.46	-0.49	-0.64	1.00											
fruit	0.19	0.72	0.67	-0.93	1.00										
meat	0.53	-0.96	-0.23	0.36	-0.66	1.00									
refrig	0.30	0.07	0.93	-0.42	0.52	-0.23	1.00								
salt	0.49	0.28	0.90	-0.91	0.86	0.25	0.72	1.00							
saus	0.96	-0.39	0.09	-0.35	0.08	0.54	0.10	0.29	1.00						
veget	0.73	-0.16	0.86	-0.71	0.56	0.17	0.73	0.90	0.53	1.00					
cmeat	-0.24	0.99	-0.11	0.35	0.99	0.89	0.99	-0.51	0.89	0.23	1.00				
sfish	0.94	-0.21	0.90	0.76	-0.18	0.20	-0.10	0.89	0.29	0.84	-0.18	1.00			
toms	0.89	-0.22	0.76	0.86	-0.18	0.16	-0.10	0.91	0.27	0.92	-0.14	0.95	1.00		
minc	-0.48	-0.19	-0.83	0.89	-0.79	0.13	-0.59	-0.97	-0.28	-0.90	-0.46	0.75	0.67	1.00	
finc	-0.86	0.74	-0.21	0.01	0.23	-0.73	-0.32	-0.16	-0.83	-0.54	0.14	0.14	0.14	0.14	1.00

* Porto Alegre, Campinas, Goiânia, Fortaleza, and Belém
alch: per capita annual alcoholic beverage intake (liters), 1974
bean: per capita annual bean consumption (kg), 1974-75
citrus: per capita annual citrus fruit consumption (kg),1974-75
ffish: per capita annual fresh fish consumption (kg), 1974-75
fruit: per capita annual fruit consumption (kg),1974-75
meat: per capita annual fresh red meat consumption (kg), 1974-75
refrig: refrigerator availability (%) among poorest families,1974-75
salt: per capita annual salt consumption (kg), 1974-75
saus: per capita annual sausage consumption (kg), 1974-75
veget: per capita annual vegetable consumption (kg),1974-75
cmeat: per capita annual canned meat consumption (kg), 1974-75
sfish: per capita annual salted fish consumption (kg), 1974-75
toms: per capita annual tomato sauce consumption (kg), 1974-75
minc: male incidence of stomach cancer (age-standardized rates per 100,000), 1990-91
finc: female incidence of stomach cancer (age-standardized rates per 100,000), 1990-91
Sources: FIBGE, 1978; INCA, 1995

In this paper we used an ecologic analysis to improve our understanding of the associations between incidence rates for stomach cancer in Brazil and past exposure to certain possible risk factors often mentioned in the literature. Contrary to other studies on this topic, our analysis includes a large time lag between exposure measurements (1974-75) and outcome (stomach cancer rates in early 1990s). Therefore, we sought to guarantee the appropriate time interval corresponding to the latency period for tumor development, thus allowing for results in hypothetical agreement with current knowledge of carcinogenesis.

A detailed explanation of the statistical foundations of descriptive procedures such as cluster and factor analysis (Kleinbaum et al., 1988; Neter et al., 1990) is beyond the scope of this paper, and the following discussion focuses on the criteria adopted by the authors for interpreting results. Briefly, cluster analysis is a technique in which the observed subjects (Brazilian cities in our case) are grouped according to their similarities for the various study variables (i.e., cancer incidence, diet item intake, home refrigerator availability, or others). In this technique, the concepts of similarity and distance express closeness among the subjects under study. The sum of the squared differences among variables is obtained, providing a distance index called the squared *Euclidean distance,* which is further standardized, and the greater the similarity between two subjects, the lesser the distance between them. A method called single linkage compares distances among subjects and combines them showing the closest distances or greatest similarity. Clusters are organized by comparing the matrix of squared Euclidean distance coefficients after standardization of variables. In one variant of this technique (agglomerative hierarchical clustering), the greater

Figure 1

Dendogram of refrigerator availability (1974-75), diet items intake (vegetables excluded), and current incidence rates of stomach cancer, Brazilian selected cities.

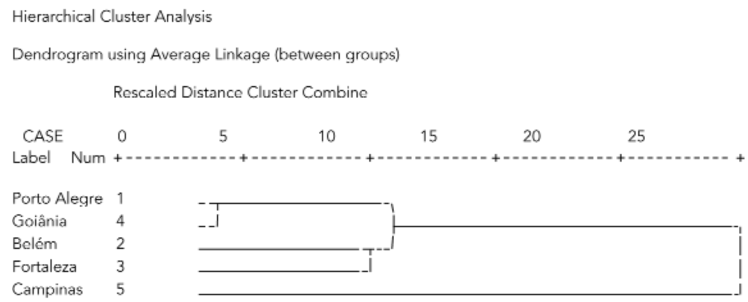
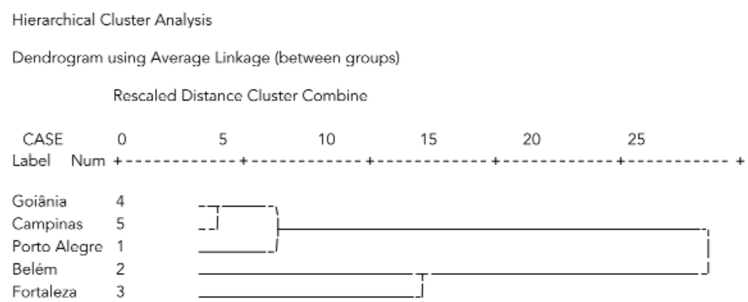


Figure 2

Dendogram of diet items intake (1974-75) and current incidence rates of stomach cancer (refrigerator availability excluded), Brazilian selected cities.



the similarity between two compared subjects (cities in our study), the faster their merging, thus yielding a cluster. Subsequently, either the two next closest subjects merge to form a second cluster or an individual subject may merge with the previous one (as shown in Figure 2 with Porto Alegre). Once a cluster is formed, it is not dismissed, and these steps proceed until all subjects have merged into one of the preexisting clusters, thus yielding a dendogram (Figures 1 and 2). Dendograms either display the steps in which the subjects agglomerate (the clustering order shown by cities merging in our study) or the speed by which these steps were carried out.

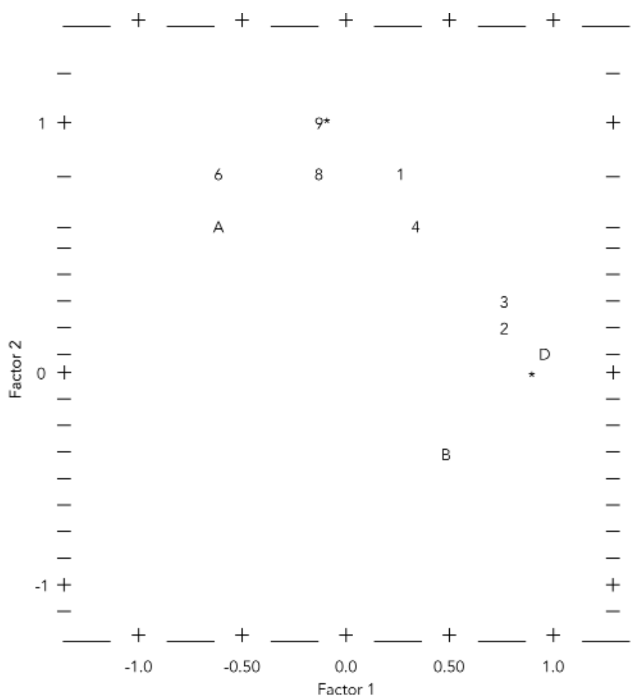
In our study, cluster analysis with all variables – vegetable consumption was further excluded taking into account the similar average proportions observed in both Porto Alegre and Campinas (Table 1) – produced an unexpected result: Campinas was the last city to merge with the previously existing clusters (Figure1). In other words, this meant that Belém, Fortaleza, and Goiânia were indeed closer (or more similar) to Porto Alegre than Campinas, according to all variables selected by the authors. The surprise resulted from our assumption of more similarities between Porto Alegre and Campinas than, for instance, between Belém and the former. Besides displaying low stomach cancer incidence rates, Campinas and Porto Alegre are located in Brazil's industrialized South and have historically had higher living standards than the other geographic populations analyzed in our study. Therefore, considering that this result could be an artifact, we proceeded to investigate variable(s) that might explain this surprising result.

Searching for similarities and differences among the study variables in both cities, we observed that Campinas (indeed, the non-metropolitan urban population from the State of São Paulo as a whole, where Campinas is the largest city) had experienced a higher proportion of refrigerator availability among the poorest strata as compared to other cities included in this study. In fact, refrigerator availability was highest in Campinas (48%) in 1974-75, twice that observed in Porto Alegre and three times that of Fortaleza, Belém, and Goiânia (Table 1). To test this hypothesis – that refrigerator availability could modify a previously expected clustering pattern (immediate merging of Campinas and Porto Alegre) – we attempted to exclude the aforementioned variable from the analysis. When we excluded the variable "refrigerator availability" from the model, Campinas promptly merged with Goiânia, and Porto Alegre further joined this cluster (Figure 2). These different model behaviors based on the presence or absence of prior availability of refrigerators suggest that this covariate, i.e., food preservation, may have played an important role in the current magnitude of stomach cancer incidence observed in the study populations. Moreover, given this observation – even considering the paucity of cities studied in which incidence data on stomach cancer were available – we could predict a major future decline in the incidence of stomach cancer in Brazil following the increased availability of refrigerators in the country.

Furthermore, principal components and factor analyses were developed. Both statistical techniques were used to identify hidden relationships among the study variables. This was performed by determining the proportion of variance explained by common factors, or "communalities", and then splitting the variables according to their relationships with these factors. In reality, a factor is a construct produced by a researcher, and the best results are obtained in a principal components

Figure 3

Rotated factor loadings.



Variables are denoted by 1,...,9, a,...,Z overlaps are denoted by an asterisk.
Symbol variable.
1: vegetable consumption; 2: fresh red meat consumption; 3: sausage consumption; 4: fresh fish consumption; 5: salted fish consumption; 6: salt consumption; 7: tomato sauce consumption; 8: citrus fruit consumption; 9: alcoholic beverage consumption; A: male incidence of stomach cancer; B: female incidence of stomach cancer; C: bean consumption; D: refrigerator availability; E: fruit consumption; F: canned meat consumption

analysis when a higher proportion of the explained variance yielded by the study variables is achieved with the least number of factors. Nevertheless, visualization of these relationships in space is often not a simple matter. Factor analysis uses techniques in which the coordinates of each variable are maintained after different kinds of spatial rotation. Rotation is useful for improving identification of different groups of variables spatially situated in a spectrum of varying distances to the different identified factors. This is obtained through identification of factor loadings corresponding to each of the study variables. This study adopted a varimax-rotated solution, because it limits the number of variables with high loadings in one factor, thus enhancing factor interpretation. A fine resolution is achieved when the study variables only show high factor loadings for one factor. Thus, factor analysis may allow one to explore hidden connections between the analyzed variables which otherwise would be not easily identified or even suspected.

In this study, a principal component analysis identified common factors among the study variables displaying some hidden relationships. Indeed, the first two factors explained 83% of the total variance, a quite reasonable result. After rotation, factor 1 displays high positive correlation with the variables refrigerator availability, female incidence of stomach cancer, and consumption of canned meat, fruits, beans, fresh red meat, and sausage. On the other hand, factor 2 shows close associations between the variables male incidence of stomach cancer and consumption of salted fish, tomato sauce, alcoholic beverages, salt, citrus fruits, vegetables, and fresh fish.

As previously mentioned, interpretation of results yielded by factor analysis usually is not straightforward, but some observations can be made. The first is that male and female incidence of stomach cancer are associated with both factors at different levels. Secondly, it was not possible to clearly aggregate known risk or protective variables. Despite the fact that a simple structure appears to have been achieved by rotation – all variables fail to display large loadings in both factors – it is difficult to identify the hidden common relationships between the study variables in this particular case. If we only consider variables with high loadings for one factor, factor 1 appears to be associated with cheaper diet components in Brazil (i.e., beans, canned meat, and sausage), quite differently than observed with factor 2. In this sense, factor 1 appears to involve "homeliness" (homemade meals, cheaper diet items, refrigerator availability), while factor 2 may indicate "affluence" (e.g., consumption of alcoholic beverages and salted and unsalted fish, which used to be, and generally still are more expensive than red meat in Brazil).

As a whole, both approaches (cluster and factor analysis) appear to improve our understanding and interpretation of the possible factors involved in the persistently high rates of stomach cancer incidence observed in Brazil. On the one hand, refrigerator availability in the country – still low in the 1970s, ranging from 15 to 25% among the poorest families in the study cities, except for those located in the State of São Paulo –, appears to have played a major role in the further differentiation between incidence rates for stomach cancer in the early 1990s. On the other hand, differences in living standards and other conditions associated with diet patterns may also help explain the prevailing incidence of stomach cancer in Brazil.

Conclusions

Past availability of refrigerators (1970s) appears to be the major contributing variable in the observed differences of stomach cancer incidence in the early 1990s among selected Brazilian cities (Belém, Porto Alegre, Goiânia, Fortaleza, and Campinas). Differences in living standards among these cities also appears to have played an important role in current cancer incidence.

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