

Dietary patterns and breast cancer in Colombia: an ecological study

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Background: The role that diet plays in the development of breast cancer is unclear and breast cancer continues to increase in Colombia and worldwide. The objective of this study was to assess the association between patterns of dietary consumption and the incidence of breast cancer.

Methods: An ecological study was conducted in 24 geodemographic units in which 95% of the women of Colombia live. The association between breast cancer rate (dependent variable) and three dietary patterns established with factor analysis (traditional/starch, fiber/dairy and snack) was investigated using simple and multiple linear regression. The use of variables related to socioeconomic context and the duration of breastfeeding allowed for the control of possible confounding. All information was derived from concurrent national surveys or was obtained directly over a period of time close to the period during which the study was conducted.

Results: There is an inverse relationship between breast cancer rate and illiteracy rate (β =-2808.3), duration of breastfeeding (β =-3354.1), adherence to traditional/fiber dietary patterns (β =-30467) and adherence to the snack dietary pattern (β =-43612). The goodness of fit for the model was R²=84%.

Conclusions: Increasing the duration of breastfeeding, ensuring education to promote health and following traditional food consumption patterns, regardless of what foods are consumed, can protect against the development of breast cancer.

Keywords: breast neoplasms, Colombia, diet, feeding behavior, food consumption, literacy

Introduction

Nutritional epidemiology has evolved from the study of nutrients to the study of dietary patterns. In Colombia, it was recently established that there are three food patterns: traditional/starch (TSP), fiber/dairy (FDP) and snack (SP) (see Table S1, in the supplementary material online).¹ However, the relationship of these patterns to the development of cancer is not known. Twenty-six studies that have linked breast cancer to eating patterns found that a diet similar to the 'Mediterranean' dietary pattern was protective, that 'Western' diets increase risk and that traditional dietary patterns were not associated with the development of breast cancer. However, in these studies, the Latino diet was not represented.² Studies on diet and breast cancer in Latin America are limited or nonexistent, and the variability of the diet in Latin America is lower in relation to developed countries, therefore it is not possible to generalize the results of these studies.³ Despite the many studies on diet and breast cancer, according

to the World Cancer Research Fund and the American Institute for Cancer Research, no convincing evidence has been presented that the consumption of any food or nutrient, with the exception of alcohol, is a risk factor for the development of breast cancer.³

Colombia has an intermediate cancer incidence compared with the rest of the world; in the Americas, it ranks 25th among 34 countries in cancer incidence and has half of the incidence found in the country with the highest incidence, the USA.⁴ In Colombia during the period 2007–2011, the incidence of breast cancer adjusted by age (BCI) was 33.8 per 100 000 women. In Colombian women, breast cancer has the highest cancer incidence and prevalence, accounting for 12.9% of all cancers in women and is the primary cause of cancer deaths. In addition, survival is low as a consequence of the inefficiency of the health system. Delays in diagnosis and treatment compromise rehabilitation and increase mortality. Inequality is also an issue, and survival is higher in high socioeconomic strata, as the type of affiliation with the health regime improves. Breast cancer is

© The Author(s) 2019. Published by Oxford University Press on behalf of Royal Society of Tropical Medicine and Hygiene. This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com considered an undesirable effect of development and its effects, which include greater longevity, higher levels of literacy and education in general, higher levels of human development and increased per capita income.⁵ Once breast cancer is diagnosed, survival is higher in women with higher education and income levels.⁶ Breast cancer is multicausal. Sex, age, genetics, personal and family history, exposure to radiation, obesity, menarche before age 12, late menopause, motherhood at > 30 y of age, nulliparity, alcohol consumption and hormone replacement therapy have been declared risk factors.^{7,8}

The objective of this study was to assess the degree of association between food consumption patterns and BCI in Colombia and to determine the possibility of predicting BCI at an ecological level based on biological and socioeconomic variables that express various dimensions of social and economic development (here known as the 'context' in which BCI occurs).

Material and methods

This ecological study was conducted in 2019 in Colombia. Secondary information on BCI and the context in which breast cancer develops is reported periodically by various state agencies and is classified as official.

Population and sample

The study population was the 33 geodemographic units of Colombia. The sample (n=24) corresponds to all the geodemographic units of the country with information on BCI, wherein 95% of the Colombian population lives. The information from these 24 units represents women between 18 and 64 y of age.

Information sources

The information related to the variables presented below was summarized for each geodemographic unit in the most appropriate way as the proportion (%), mean or, for the duration of breastfeeding, the median.

Dependent variable

The dependent variable was BCI adjusted by age (rate \times 100 000 women). In 2015, the National Institute of Cancerology and the Ministry of Health and Social Care published a report on the incidence, mortality and prevalence of cancer in Colombia that was based on population records related to cancer in the cities of Pasto, Cali, Bucaramanga and Manizales.¹ In this document the BCI was estimated and reported. The details of the methodology used have been described elsewhere.⁴

Context variables

A total of 21 variables were studied in relation to the BCI.

Adherence to dietary consumption patterns. In 2010, Colombia conducted the National Survey on Nutritional Status (Encuesta Nacional de la Situación Nutricional [ENSIN]).⁹ In the ENSIN, a food frequency questionnaire (FFQ) was used to estimate the frequency (times per day) of consumption of foods considered to be of interest to nutrition and public health, given the nutritional and epidemiological profile of Colombia. The FFQ methodology

used in the ENSIN has previously been described in detail.⁹ In 2015, based on the FFQ results obtained in the ENSIN and through factor analysis, it was established that three food consumption patterns—TSP, FDP and SP—coexist within the Colombian population.¹ The adherence of women to each of the three food consumption patterns was established as a z-score. The scores were described as (adhesion score z—minimum value). In this sense, a value of zero indicates lower adherence to a certain pattern in the geodemographic unit.

Excess waist circumference. This measurement was made in the ENSIN using a Rosscraft tape (sensitivity 1 mm) in women between 18 and 64 y of age, excluding pregnant women and those who had given birth within the last 3 mo. This measure establishes abdominal obesity, and excess circumference was designated as \geq 80 cm.⁹

Overweight based on body mass index. At the ENSIN, weight was established using a model 872 electronic balance (Seca, Chino, CA, USA) (sensitivity 100 g) and height was measured using a portable metric from Diseños Flores SRL (San Carlos, Peru) (sensitivity 1 mm) in women between 18 and 64 y of age. The body mass index (BMI, as kg/m²) was established and overweight was designated as BMI $\geq 25.^{9}$

Exclusive breastfeeding (EBF) based on the ENSIN. According to the WHO, EBF is defined in the ENSIN as 'the feeding of only breast milk to a child, and may or may not include oral rehydration or vitamin, mineral or medicine drops'.⁹

Total breastfeeding (TBF) based on the ENSIN. TBF includes EBF. It also includes predominant breastfeeding that is provided in conjunction with family feeding or complementary feeding.⁹

Monetary poverty, 2010. This metric was based on the monetary income of households. As of 2011, the National Administrative Department of Statistics has estimated it using the same methodology and regularly reports this index. Monetary poverty data were obtained from regional bulletins, one per geodemographic unit.¹⁰

Gini coefficient, 2011. This metric represents the level of income inequality in each geodemographic unit and is calculated on a regular basis by the National Administrative Department of Statistics (DANE).¹¹ The Gini coefficient takes values between 0 and 1, where 0 represents perfect equality in the distribution of wealth.

Household food insecurity. The ENSIN estimated household food insecurity (FI) using the Latin American and Caribbean Scale of Food Security (ELCSA). The survey was completed by the head of the household. The ELCSA evaluates a dimension of FI, physical access to food. The official report of ENSIN defines FI as 'the limited or uncertain availability of adequate and safe nutritional foods or the limited and uncertain capacity to obtain adequate food in socially acceptable ways'.⁹

Annual growth rate as gross domestic product (GDP) for the geodemographic units, 2011. This metric represents the growth in the total value of goods and services produced in the geodemographic unit.¹² These results were based on the System of National Accounts (1993 and 2008) of the United Nations (UN) and on the methodology used in the 2005 base of national accounts prepared by DANE.¹² In 2011, Colombia recorded a GDP growth of 6.6%,

mainly due to the performance of mining and quarrying activities (14.5%) and construction (8.2%).

Human development index (HDI), 2011. This index summarizes the achievements of those who inhabit the geodemographic unit as measured by three dimensions: a long and healthy life, knowl-edge/access to education and a decent standard of living. The HDI is the arithmetic mean of the normalized indices of each of the three dimensions. The health dimension is evaluated based on life expectancy at birth. Education is assessed according to the average years of schooling received by adults ≥ 25 y of age and the gap between the real and theoretical years of schooling that children of school age should have reached. The standard of living is measured through the gross national income per capita.¹³

Gender empowerment index (GEI), 2009. This indicator is reported by the UN Development Program. It measures the level of opportunity of women in three dimensions: participation in politics and decision-making power at government levels; economic participation and decision-making power, which reflects women's participation in the economic and productive apparatus as well as evaluating the relative participation of men in technical and professional positions; and control over economic resources, based on the earnings of women relative to those of men.¹³ The GEI takes values between 0 and 1, where 1 represents the highest possible level of equality of women in relation to men.

Illiteracy rate in women, 2011. The illiteracy rate in women is the ratio of the number of women who declared that they cannot read or write to the total number of women who answered this question in the Great Integrated Household Survey (GEIH), which was conducted by DANE.¹⁴

Maximum schooling in women 15-49 y of age, 2011. This value refers to the maximum average number of years of schooling received by women 15-49 y of age in each of the nine categories in which households in Colombia are classified according to the GEIH.¹⁴

Number of cases of intrafamily abuse in which women are victims, 2012. This is the number of cases of violence between members of the same family in which a woman was the victim; these data are reported by the Colombian Institute of Legal Medicine.¹⁵

Rate of female abuse \times 100 000, 2012. This is the ratio of the number of cases of violence between members of the same family in which a woman was the victim reported by the Colombian Institute of Legal Medicine and the total number of women of childbearing age projected by DANE based on the 2005 census in the same period and geodemographic unit.^{15,16}

Maternal mortality rate \times 100 000, 2010. This is the ratio of the number of pregnancy-related deaths in women (excluding accidental or incidental deaths) to the total number of live newborns according to DANE projections in the same period and geodemographic unit.¹⁷

Health system coverage, 2010. This metric is estimated according to the number of affiliates registered in the Single Affiliate Database in the contributory and subsidized health regimes as of 31 December of each year (data reported by the Ministry of Health and Social Protection) in relation to the population projection published by DANE based on the 2005 census.^{16,18}

Statistical analysis

The statistical analysis was conducted to assess the crude and adjusted association of the three consumption patterns and the context variables in the aeodemoaraphic units with BCI and to determine the possibility of predicting the BCI at the ecological level. The association between the context variables was assessed through simple and multiple linear regression (LR) using the standardized regression coefficient β , the p-value and the 95% CI; in the analysis, the BCI was the dependent variable and the context variables were the independent variables. Three models were used to evaluate the principle of parsimony and to illustrate in the best way possible the effect of dietary patterns and the potential confounding effects of the context variables on breast cancer incidence. The choice of variables used to establish the predictive models (models A-C) was made based on Student's t-statistic and the p-value obtained for each bivariate or multivariate relationship. In addition to the three dietary patterns, which were considered the main explanatory variables, model A includes the variables that are statistically significant in the bivariate analysis. Model B includes the variables that are statistically significant in model A, and model C includes the variables that remain statistically significant in model B as well as the three dietary patterns. The goodness of fit of the linear models in the prediction of BCI at the ecological level was assessed based on the coefficient of determination (R^2) , the Pearson r correlation coefficient and the average difference between the observed BCI and that estimated by the LR models using the Bland and Altman method.¹⁹ All analyses were performed using the statistical package Stata 14.1 (StataCorp, College Station, TX, USA).²⁰ The study was conducted in accordance with the principles set forth in the Declaration of Helsinki.

Results

Characteristics of the population

The average monetary poverty, x±SD, was 41.5±13.8%; the Gini coefficient was 0.52±0.03; the average percentage of GDP growth was 6.0±4.4%; the mean overweight prevalence (BMI \geq 25) was 52.2±5.0%; the mean prevalence of FI was 45.9±11.7%; the average HDI was 0.81±0.05 and the average health system coverage was 88.2±6.6%. Table 1 presents other characteristics of the study population. It is important to highlight the incidence of excess waist circumference and the fact that adherence to the SP of food consumption is less than half that of adherence to the other two food consumption patterns.

BCI and context variables in the geodemographic units

The statistical normality of the BCI was guaranteed by raising its value to the third power. The bivariate analysis showed a direct relationship between BCI and HDI, maximum level of schooling in women 15–49 y of age and adherence to the FDP. There was an inverse relationship between BCI, monetary poverty, the rate of illiteracy in women, maternal mortality and the TBF. Table 2 shows the coefficients of determination, R^2 and p-values for these comparisons. In addition, the multivariate analysis presented in Table 2 shows the standardized β coefficients of a model in which BCI is a variable that depends on the context variables; this made it possible to guarantee the relevance of

Variable	Mean	SD	
Breast cancer incidence adjusted by age (rate×100 000)ª	31.3	29.0	
Average age of subjects 18–64 y of age, 2010	37.5	2.03	
Excess waist circumference, 2010 (%) ^b	63.0	6.00	
Adherence to the TSP, 2010 ^c	0.82	0.31	
Adherence to the SP, 2010 ^c	0.34	0.22	
Adherence to the FDP, 2010 ^c	0.79	0.30	

^aBased on the variable raised to the third power.

^bPrevalence of excess waist circumference (\geq 80 cm for women).

^cBased on factor analysis with z-scores centered.

each variable in the context since the model did not show multicollinearity between the variables. Table 3 describes the three models (models A-C) that were established through multiple LR to study the association between the BCI and the context variables in the geodemographic units. When bivariate relationships were fitted in the multivariate model (model C), the illiteracy rate (β=−2808.3 [95% CI −3805.2 to −1811.4], p<0.001), TBF $(\beta = -3354.1 [95\% CI - 4953.9 to -1754.2], p < 0.001), adherence$ to TSP (β =-30467 [95% CI -58 282 to -2651], p<0.001) and adherence to SP ($\beta = -43$ 612 [95% CI -78 220 to -9004], p=0.016) remained associated. For model C, the coefficient of determination, R², was 84%. In model C, the correlation between the estimated BCI and the observed BCI was r=0.92 (95% CI 0.82 to 0.97). The Bland and Altman statistic for estimation of the mean difference between the observed BCI in the geodemographic units and the BCI estimated using model C was -0.49(95% CI - 5.60 to 5.70). This allows us to affirm that it is possible to predict the BCI with precision using the equation that supports model C:

 $[BCI = 160237-30467*TSP-43612*SP-10149*FDP -3354*TBF - 2808*Illiteracy rate]^{\frac{1}{3}}.$

Figure 1 shows the relationship between the observed BCI and the estimated BCI obtained using model C. Figure 2 shows the relationship between BCI and the three patterns of food consumption. The evolution of the estimated β for the patterns studied can be seen in alternate models, A' and C (Table S2, Supplementary material online).

Discussion

At an ecological level, five variables explain 84% of the BCI; of these, four are inversely associated: traditional/starch and snack dietary patterns, illiteracy and TBF. In addition, it was established that it is possible to accurately predict the BCI for a particular geodemographic unit using a linear model based on contextual information that state agencies routinely collect. Given that there is no solid evidence on the role of diet at the level of nutrients or food in the development of breast cancer (BCI) and that population registries of cancer in Colombia are deficient and unreliable, these findings have importance.

The study of food patterns rather than food alone in relation to the generation or prevention of breast cancer helps increase our understanding of this disease at the nutritional epidemiologic level; food patterns represent the diet in a greater biological and social sense.² Although diet has been reported to comprise up to 30% of the causal explanation of BCI, the contribution of diet to BCI remains unclear.²³ Studies of dietary patterns and BCI have presented contradictory evidence.² In Italy and Australia, dietary patterns denoted as 'traditional' were not associated with BCI.^{24,25} However, in a region of the southern USA, the traditional dietary pattern as well as a pattern known as the 'Mexican pattern' were shown to be protective.²⁶ Inverse associations between TSP and BCI similar to the association reported here have also been found in Uruguay and Brazil.^{27,28} However, in Japan, the traditional dietary pattern was not associated with the development of breast cancer.²⁹

One limitation of these comparisons is that although they are all based on factor analysis, the foods that make up the dietary patterns are not the same. In Colombia, TSP is a protective factor against overweight, while SP, due to the 'dose' consumed, is not yet a risk factor for the development of overweight, as has been reported in many other studies, but acts more as a confounding variable.¹ A recent meta-analysis based on 32 observational studies found that the risk of BCI is reduced in individuals who follow 'prudent' or 'traditional' patterns of food consumption, in contrast to the so-called Western pattern.³⁰ However, the meta-analysis also discusses the possible confounding factors associated with women. The considerations discussed above illustrate the particularities of food culture, the stages of food and epidemiological transitions and the multiple factors that may contribute to the development of breast cancer.

The study of nutrients or foods has been less useful than the study of food patterns in explaining breast cancer incidence.^{2,3,23-30} The traditional dietary patterns that have been established in various regions and countries are not comparable with respect to the types of foods they include. The important thing here is that the dietary patterns and not

Variable	Biv	variate	Multivariate		
	R ² (%)	p-Value	Standardized β	p-Value	
Total population of women 18–64 y of age, 2011	16	0.02	2.78	0.14	
Average age of women 18–64 y of age, 2010	32	0.00	-0.26	0.74	
Monetary poverty (%), 2011	36	0.00	-0.79	0.54	
GINI coefficient (%), 2011	11	0.11	0.30	0.65	
Excess waist circumference (%), 2010 ^a	3	0.32	0.54	0.52	
Overweight (BMI ≥25) (%), 2010	4	0.24	-0.44	0.74	
Household food insecurity (%), 2010	9	0.10	-0.04	0.97	
GDP change (%), 2011 ^b	0	0.98	0.02	0.97	
HDI, 2010	45	< 0.0001	-0.10	0.92	
Health system coverage (%), 2010	0	0.85	-0.32	0.37	
GEI, 2009	1	0.72	0.17	0.47	
Illiteracy rate in women, 2011	63	< 0.0001	-0.48	0.77	
Maximum schooling, women 15-49 y of age, 2011	44	< 0.0001	0.68	0.27	
Number of cases of abuse against women, 2012	12	0.10	-3.49	0.13	
Rate of female abuse×100 000, 2012 ^c	6	0.25	0.08	0.86	
Maternal mortality rate×100 000, 2010	34	0.00	-0.59	0.44	
Exclusive breastfeeding duration (m), 2010	1	0.74	-0.55	0.36	
Total breastfeeding duration (m), 2010	25	0.01	0.26	0.18	
Adherence to a TSP, 2010 ^d	2	0.42	-0.46	0.38	
Adherence to a SP, 2010 ^d	0	0.71	-0.48	0.35	
Adherence to a FDP, 2010 ^d	27	0.00	-0.58	0.57	

 Table 2.
 BCI adjusted by age (rate × 100 000) and contextual variables in the studied geodemographic units: Colombia, 2007–2011

Dependent variable: breast cancer incidence adjusted by age (rate×100 000).

R²: coefficient of determination (%) achieved in the bivariate relationship.

 β (standardized): partial coefficient of regression achieved in the multivariate relationship and 95% CI. In the linear model, BCI adjusted by age (rate \times 100 000) raised to the third power is the dependent variable and all of the context variables are explanatory.

^aPrevalence of excess waist circumference (\geq 80 cm for women).

^bAnnual growth rate for the geodemographic units. This value represents the growth in the total value of the goods and services produced in the geodemographic unit.

^cDefined as the number of cases of intrafamily abuse in which women are victims/total number of women of childbearing age.

^dBased on factor analysis with z-scores centered.

the foods themselves are the factors that protect against breast cancer. The Mediterranean diet is modeled on the traditional Mediterranean dietary pattern, the Inuit diet of the Eskimos is the traditional diet of the Eskimos, the Mexican diet is the traditional diet of Mexicans, and so on. This indicates that the sensible thing is to defend the local traditional food culture and dietary pattern, and that it is not necessary to adopt diets or alimentary cultures of others to protect women from breast cancer. The SP is a potential confounder because some preparations that are considered 'snacks' can be part of a traditional diet. 'Snack' does not always indicate a food that is ultraprocessed or harmful.³¹ In addition, the unadjusted bivariate relationship of the SP with the BCI could be confusing because it is the least linear relation of the three patterns studied (Figure 2).

TBF has previously been reported to be a protective factor against breast cancer; the risk is reported to be reduced by 4.3%

for every 12 m of breastfeeding and by 14% for mothers who breastfeed compared with those who do not breastfeed.^{7,21} In Colombia, the prevalence of breastfeeding infants for up to 6 m is 63.3% and the median duration of breastfeeding is 14.9 m.⁹ Colombia has deep social and economic inequalities, and is similar to any other middle-income country; that is, the poorest women, who tend to be those who are less educated or illiterate, breastfeed for a longer period.^{7,22} Although the prevalence of breastfeeding by poor women and their wealthy counterparts is far below the optimal level, the differences in TBF between poor and wealthy women in Colombia made it possible to identify an inverse relationship at the ecological level between BCI and the protective effect of TBF on the development of breast cancer.⁹ There is solid evidence at the individual level in this regard.⁷

In developing countries, an association of education with BCI has already been established. Illiteracy puts women at a disadvantage in practicing self-care, limits effective access to health

Table 3. Linear regression models that explain BCI adjusted by age (rate×100 000) in the studied geodemographic units: Colombia, 2007–2011

Variable	Model					
	Aa	p-Value	Ba	p-Value	Ca	p-Value
Monetary poverty (%), 2011	250.7	0.48	NA	NA	NA	NA
HDI, 2010	-171 378	0.32	NA	NA	NA	NA
Illiteracy rate in women (%), 2011	-3141.7	0.01	-2867.7	< 0.0001	-2808.3	< 0.0001
Maximum schooling in women 15-49 y of age, 2011	8070.6	0.23	NA	NA	NA	NA
Maternal mortality rate×100 000, 2010	-149.1	0.12	NA	NA	NA	NA
Total breastfeeding duration (m), 2010	-2344.3	0.01	-2563	< 0.0001	-3354.1	< 0.0001
Adherence to a FDP, 2010 ^b	2505.4	0.91	NA	NA	-10 149	0.51
Adherence to a TSP, 2010 ^b	NA	NA	NA	NA	-30 466.5	0.03
Adherence to a SP, 2010 ^b	NA	NA	NA	NA	-43 612.3	0.02
R ²	0.81		0.76		0.84	
R ² (adjusted)	0.73		0.73		0.79	
Intercept	166 610		101 325		160 237	
n	24	ł	2	4		24

Dependent variable: breast cancer incidence adjusted by age (rate × 100 000).

NA: does not apply.

 R^2 : coefficient of determination (%).

^aCoefficient β .

^bBased on factor analysis with z-scores centered.

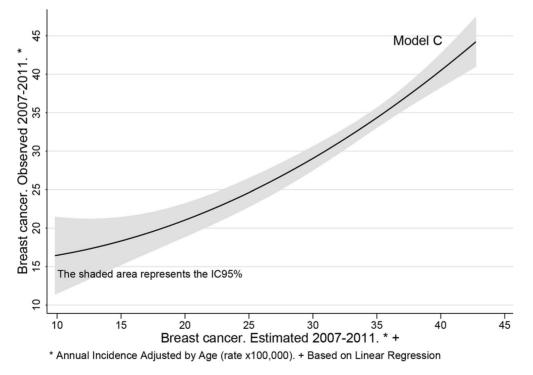


Figure 1. Observed BCI adjusted by age v estimated BCI: Colombia, 2007–2011.

services and interacts with poverty. As a result, illiterate women have poor attitudes toward and limited knowledge of and control over their own health. $^{\rm 32}$

The main limitation of this study is its inability to establish causality. However, ecological studies incorporate aspects of the environment into the analysis through the use of proximal

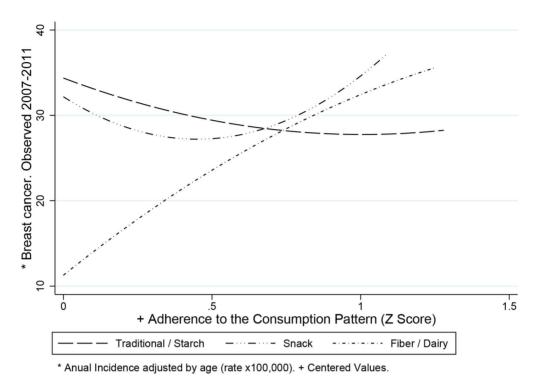


Figure 2. BCI adjusted by age and adherence to dietary patterns: Colombia, 2007–2011.

variables, allowing the incorporation of interactions that are difficult to observe at the individual level. The variables referred to as 'context' represent complex information that is difficult to obtain and can only be accessed through national surveys or routine data collections whose statistical quality is guaranteed and financed by the state. The results presented here contribute to the scant evidence on diet and breast cancer in Latin America. Furthermore, accurate prediction of BCI provides a basis for the development and evaluation of public health actions in Colombia.

Conclusions

It was concluded that, at the ecological level, the illiteracy rate, TBF, TSP and SP explain the BCI in Colombian women. In addition, it was possible to predict the BCI based on the context variables that illustrate the level of development in Colombia. Regardless of the type of food involved, the consumption of traditional diets seems to protect against the development of breast cancer. The SP behaves as a confounding variable. This happens because the frequency of consumption in Colombia has not reached that to be considered as a risk factor.¹ Also, some 'snack' food is far from being ultraprocessed and is part of the traditional diet (e.g. sauces, butter and sweets; all homemade). The lack of a snack definition deserves attention and can contribute to the confusion.³¹ Thus it is possible to predict the incidence of breast cancer based on adherence to dietary consumption patterns.

Authors' contributions: OFH designed the study, obtained the databases of the ICBF, prepared the databases, and conducted and led the statistical analyses. DCA and DCQ-L interpreted the results and prepared, reviewed

and wrote the manuscript. All authors reviewed the manuscript and approved the final version.

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