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Cancer and Its Relationship with Dietary Patterns in Cordoba, Argentina

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Abstract: Introduction: Diet is an important factor in the occurrence of cancer. Its approach to dietary patterns has attracted increasing attention in nutritional epidemiology, but is rarely used in Latin America. **Objectives:** To determine the dietary patterns of the adult population in Cordoba (Argentina) and assess their impact on the risk of colorectal cancer (CRC), breast cancer (BC), prostate cancer (PC) and urothelial cancer (UC). **Methods:** Case-control studies of CRC, BC, PC and UC were conducted from 2006 to 2012. The food pattern was determined by principal component factor analysis. ORs was estimated by multilevel logistic regression. **Results:** Characteristic patterns were found independently in the general population and in men and women. In the overall population, the Southern Cone and Sugary Drinks Patterns showed a promoter effect for CRC and UC, and the Prudent Pattern showed a protective effect. In women, BC is directly associated with the Female Southern Cone Pattern, Rural and Starchy patterns, as opposed to the Prudent Pattern. In men, the Male Southern Cone pattern, Sugary Drinks and Typical Moderate Patterns showed a promoting effect on PC. **Conclusion:** In order to prevent cancer, it is necessary to promote the normal intake of vegetables, fruits and dairy products (moderate intake for men) and reduce the intake of red meat (mainly fat), processed meat, polysaccharide vegetables, wine and sugary drinks. It is recommended that men eat eggs in moderation and women eat refined grains, pastry products, oil and mayonnaise in moderation.

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1. Introduction

Globally, malignant tumors are the second leading cause of death, and the incidence is rising, especially in low- and middle-income countries[1]. Díaz *et al*.[2] determined that the most common types of cancer in Cordoba, Argentina are breast cancer, cervical cancer, colon cancer and lung cancer in women and prostate cancer, lung cancer, colon cancer and bladder cancer in men. The non-random spatial pattern showing the incidence of these cancers in the province suggests that the geographical distribution of the disease may be partly related to epigenetic factors such as environmental characteristics[3], socioeconomic characteristics[4] and lifestyles[5,6]. Nutrition is also an important environmental factor affecting the development of cancer. It is recognized that 35% of malignant tumors are related to dietary factors and can be prevented through appropriate diet and nutrition[7]. However, given the complexity of the interaction between diet and cancer, its role in promoting or protecting pathology remains to be clarified.

The effect of diet on cancer is variable. Therefore, diets with high-calorie density, processed meat, refined foods, the high proportion of fat and alcohol are associated with an increased risk of breast cancer, prostate cancer and colon cancer, while diets containing large amounts of plants and fruits, micronutrients and fiber are associated with reduced risk[7]. In addition, the presence of natural pollutants in drinking water, such as arsenic, is associated with an increased risk of urothelial tumors[3,6].

In Argentina, the traditional diet pattern is characterized by high consumption of animal protein and fat, mainly from red meat, and low intake of fish, fruits and vegetables[8,9]. In addition, barbecue is very common in this area. There is evidence that this cooking method allows the formation of scabs on the surface of food[8], producing heterocyclic aromatic amines (HAAs), a potential tumor promoter[10]. Several epidemiological studies conducted in Cordoba have shown that it is associated with the risk of certain cancers[8,12]. These findings provide a starting point for further study of the dietary habits of this population and their role in cancer.

In recent years, in the field of nutritional epidemiology, people are more and more interested in the dietary pattern method, because it allows a comprehensive description of diet and can be inferred as dietary recommendations. However, there are few cancer epidemiological studies analyzing food from this perspective, most of which come from developed countries[6,12-15]. According to this method, the dietary pattern is defined by the nature, quality, quantity and proportion of different foods and beverages in an individual's diet and the frequency they usually eat[7]. Analytically, it can be understood as a unique dietary exposure measurement method. It summarizes the information of many food property variables and is characterized by those variables that dominate the individual diet[7,16]. This brings the added benefit of simplifying the analysis and interpretation of complex, multidimensional food intake phenomena.

Another aspect to be considered in the epidemiological study of chronic diseases is that not all health determinants and constraints can be regarded as attributes at the individual level, but it is necessary to consider demographic characteristics, which is a key aspect of modern epidemiology. Recognizing that these hierarchical constraints of the phenomenon under study pose methodological challenges[17].

In view of the above, and in view of the need to further study the relationship between diet and cancer at the regional level, this study aims to determine the dietary patterns of the adult population in Cordoba, Argentina, and analyze their role in the development of colorectal cancer (CRC), breast cancer (BC), prostate cancer (PC) and urothelial cancer (UC), using modeling strategies to include additional family or background interpretation dimensions in the analysis.

2. Methods

2.1. Design of Case-control studies

Cordoba province (3,348,000 people) is located in the central part of the Argentine Republic and is divided into 26 departments. Under the project "Environmental Exposures and Cancer in Córdoba: Study of the diet-cancer relationship and construction of a scale of exposure to contaminants" (FONCyTANPCyT, PICT 2008-2014): Four case-control studies (2006–2012) were conducted at the National University of Cordoba in Argentina, one for each tumor site. "Cases" were considered to be subjects with a histopathologically confirmed diagnosis of: (a) primary colorectal cancer (ICD-10 C18–C20), (b) urothelial tumor: transitional cell carcinoma, epidermoid carcinoma or adenocarcinoma (ICD-10 C65–C68), (c) breast adenocarcinoma (ICD-10 C50), (d) prostate adenocarcinoma (ICD-10 C61). "Control group" refers to individuals with the same gender, similar age (± 5 years) and residence similar to their respective cases, no history of pathology or other related history, and special eating habits due to diseases, customs or religious beliefs. Case identification is carried out in cooperation with major public and private health providers in the region. The control group was randomly selected from the reference population according to the inclusion criteria. For each subject case, select at least 2 controls to produce the following sample size (cases/controls): 75/153 (colorectal), 41/82 (urothelial), 100/294 (breast) and 135/282 (prostate).

Obtain the informed consent of each participant. This work was approved by the Committee of Health Research Ethics Institutions (CIEIS) of the National Clinic Hospital (Cordoba, Argentina) and registered in the Provincial Registry of Health Research (REPIS, Registration No.1387, 10/12/2009) of the Ministry of Health of the Cordoba Province.

3. Food survey

Everyone was interviewed at home by centrally trained investigators. A structured questionnaire was used, which consists of two parts: one part involves biological, social and cultural characteristics, anthropometric and lifestyle data, and the other part involves daily dietary consumption. This includes a qualitative-quantitative food frequency questionnaire that has been validated for the epidemiological study of cancer in Cordoba[18], which allows the assessment of food exposure in the past (5 years before diagnosis and at case-control interviews, respectively). In addition, a validated photo food atlas[19] and Nutrio software 1.2[20] were used for nutritional analysis. The food composition database of the software includes data from CENEXA[21] food nutritional composition table and information from other biochemical determinations in Argentina[22].

4. Statistical analysis

4.1. Application of principal component analysis in food pattern recognition

In order to multidimensionally describe the main dietary patterns in the total adult population and by sex in Cordoba, the data of food consumption frequency were analyzed. These data were collected from adult male and female subjects (n = 489), male subjects (n = 381) and female subjects (n = 294) who served as consultants. During 2006–2012, these data were used in the above-mentioned comparative study. A Principal Component Analysis (PCA) with Varimax rotation was used[14]. It examines the correlation matrix between food consumption variables (rotated for interpretation) and simplifies it to a smaller set of dimensions. These factors (patterns) constitute the main characteristics of the diet of the study population.

In this study, the food groups used to construct these patterns were selected based on the representativeness in the regional diet and / or their potential impact on the risk of cancer occurrence.

The correlation matrix was evaluated by Bartlett's sphericity test and Kraiser-Meyer-Olkin (KMO) sample adequacy measure[16]. In the proposed analysis, the number of food patterns (retention factors) was determined based on the following criteria: obtaining eigenvalues greater than 1 and factor interpretability[16].

The name of each factor (pattern) was based on the dominant food group in the analysis, for which the criterion was established as the presence of absolute load of the rotated factor ≥ 0.60.

Then, for everyone (cases and control group), the score or score coefficient of each determined pattern was estimated by regression method. This indicates the extent to which the subject's diet conforms to the above pattern[14]. Then, based on the total path distribution of the studied adult individuals (control group), one third of the above path distribution was used to determine the breakpoint. Therefore, three categories are defined for each model: low, medium and high tercile, indirect indicators of low, medium and high adhesion levels of analytic models.

4.2. Risk assessment: Multilevel modeling

To estimate the risk of cancer (Odds Ratio, OR) associated with the level of compliance with dietary patterns (one-third of scorpions), we estimated a multilevel generalized model[23], adjusted for confounding variables and included different levels of variability (individuals were included in higher-level units, such as family or geographical order). Specifically, the logistic regression model is adopted at two levels, and subjects (Level 1, J) were nested in family or group dimensions (Level 2, I). The common variables were: Family history of CRC, BC and PC, and urban-rural residents of UC. The covariance of linear prediction is the determined dietary pattern, which is controlled by variables selected according to the causal network of each tumor site.

All statistical analyses were performed using Stata software version 12.1[24].

5. Result

Table 1 summarizes the main biological, socio-economic, cultural and other relevant lifestyle characteristics of the subjects participating in the case-control study. The study found that the average ages of male and female subjects were about 67 and 62 years old, respectively. It is worth noting that the average age of the people who participated in the PC study sample was the highest (70.5 years old) compared with other studies. There were statistically significant differences between the case group and the control group in the proportion of subjects with a family history of the disease for CRC (p = 0.02) and PC (p = 0.002), completed secondary education level for PC (p = 0.006), dangerous occupational status for CM (p = 0.04), and smoking status for CRC (p = 0.04) and UC (p = 0.00004).

Table 1. Cases and controls were allocated according to biological, social and cultural variables. A case-control study of colorectal cancer, breast cancer and prostate cancer. Cordoba. Argentina 2006–2011

	CRC		**UC**		**BC**		**PC**	
Age: average (SD)								
Male	67.7 (11.3)		65.1 (10.6)		_		70.5 (8.6)	
Female	59.8 (16.2)		67.8 (18.9)		58.80 (13.4)		_	
Biological, socioeconomic and cultural characteristics†	Case (*n* = 75) N (%)	Control (*n* = 153) N (%)	Case (*n* = 41) N (%)	Control (*n* = 82) N (%)	Case (*n* = 100) N (%)	Control (*n* = 293) N (%)	Case (*n* = 135) N (%)	Control (*n* = 282) N (%)
Socioeconomic level								
Low	45 (60.0)	76 (49.7)	19 (46.34)	41 (50.0)	36 (36.0)	18 (40.3)	32 (23.7)	79 (28.0)
Medium	19 (25.3)	38 (24.8)	16 (39.02)	27 (32.9)	39 (39.0)	84 (28.7)	54 (40.0)	109 (38.6)
High	11 (14.7)	39 (25.5)	6 (14.63)	14 (17.1)	25(25.0)	91 (32.1)	49 (36.3)	94 (33.3)
Education level								
No education or uncompleted primary education	19 (25.3)	30 (19.6)	6 (14.6)	16 (18.3)	6 (6.0)	19 (6.4)	31 (22.9)	48 (17.2)
Primary education	35 (46.7)	71 (46.4)	24 (58.5)	39 (47.6)	61 (61.0)	158 (53.9)	67 (49.6)	133 (47.2)
Secondary education	12 (16.0)	27 (17.6)	3 (7.3)	12 (14.4)	15(15)	57 (19.5)	12 (8.9)*	55 (19.5)*
Higher education/University	9 (12.0)	25 (16.3)	8 (19.5)	16 (19.5)	18 (18.00)	59 (20.1)	25 (18.5)	46 (16.3)
Occupational status								
No risk	62(82.7)	140 (91.5)	35 (85.4)	71 (86.6)	90 (90.0)*	278 (95.9)*	90 d (66.7)	207 (73.7)
At risk	13 (17.3)	13 (8.5)	6 (14.6)	11 (13.4)	10 (10.0)*	12 (4.1)*	45 (33.3)	74 (26.3)
Family history								
No	66 (88.0)*	147 (96.8)*	21 (51.22)	55(67.1)	83 (83.00)	247 (84.0)	117 (86.7)*	269 (95.4)*
Yes	9 (12.0)	6 (3.9)*	20 (48.78)	27 (32.9)	17 (17.00)	47 (16.0)	18 (13.3)*	13 (4.6)*
Lifestyle background†								
Obesity								
No	55 (73.3)	116 (75.8)	33 (80.5)	67 (81.7)	78 (78.0)	235 (80.2)	112 (82.9)	218 (77.3)
Yes	20 (26.7)	37 (24.2)	8 (19.5)	15 (18.3)	22 (22.0)	58 (19.8)	23 (17.0)	64 (22.7)
Physical activity								
Non-sedentary	40 (53.3)	76 (49.7)	10 (24.4)	27 (32.9)	51 (51.00)	136 (46.4)	33 (32.6)	93 (32.9)
Sedentary	35 (46.7)	77 (50.3)	31 (75.6)	55 (67.0)	49 (49.00)	157 (53.6)	91 (67.4)	189 (67.0)
Smoking habit								
Non-smoker	37 (49.3)*	54 (35.3)*	9 (21.9)*	50 (60.9)*	64 (64.00)	176 (60.1)	44 (32.6)	86 (30.5)
Smoker	38 (50.7)*	99 (64.9)*	32 (78.0)*	(39.0)*	36 (36.00)	117 (39.9)	91 (67.4)	196 (69.5)
Alcohol consumption								
Ethanol <30 g/day	58 (77.3)	119 (77.8)	32 (78.0)	69 (84.1)	93(93.00)	282 (96.2)	92 (68.1)	180 (63.8)
Ethanol >30 g/day	17 (22.7)	34 (22.2)	9 (21.9)	13 (15.8)	7 (7.0)	11 (3.5)	43 (31.8)	102 (36.2)

CRC: colorectal cancer; UC: urothelial carcinoma; BC: breast cancer; PC: prostate cancer.

†Comparison of proportions (Normal Approximation) between cases and controls;

*Significant at a level $\alpha = 0.05$

Table 2 shows the average daily energy, macronutrients and food consumption (by food group) of the case and control groups. The results showed that there were significant differences in daily energy value and average macronutrient consumption between CRC patients and the control group ($p < 0.05$). In BC, there are also differences in average energy and fat intake. For consumption in terms of food groups, there were significant differences in the average intake of cereal and vegetable starch, beans, dairy products, meat and eggs, sugar and candy between the case group and the control group, while there were differences in the average intake of milk and alcoholic beverages in UC. Specifically, in BC, most food groups obtained statistically different averages between groups, contrary to what was observed in the PC study, in which only bean consumption decreased significantly in cases.

Table 2. Daily energy intake, macronutrients and food groups (mean, standard deviation) of case and control groups. A case-control study of colorectal cancer, urinary cancer, breast cancer and prostate cancer. Cordoba, Argentina 2006–2012

	CRC		**UC**		**BC**		**PC**	
	Control Average (SD)	**Case Average (SD)**	**Control Average (SD)**	**Case Average (SD)**	**Control Average (SD)**	**Case Average (SD)**	**Control Average (SD)**	**Case Average (SD)**
VET†								
Kcal/day	3112.9* (1266.5)	3661.3* (1322.6)	3090.7 (889.0)	3171.0(861.8)	2844.9*(1114.7)	3389.4* (1283.5)	3526.4 (1212.5)	3630.2 (1139.3)
Macronutrients (g/day)								
Carbohydrates	351.2* (158.8)	418.5* (172.2)	379.1 (126.6)	372.9 (101.2)	355.9 (146.8)	404.6 (169.3)	385.5 (125.0)	399.9 (125.0)
Proteins	112.8* (40.3)	127.5* (2.8)	112.6 (32.1)	111.3 (32.8)	104.5 (39.5)	112.5 (36.0)	127.2 (44.6)	129.7 (45.4)
Lipids	123.4* (61.4)	146.7* (69.6)	115.9 (45.7)	124.1 (43.5)	105.8* (57.1)	137.1* (69.1)	142.7 (70.4)	151.2 (63.9)
Food group (g or CC/day)								
Grains and vegetables								
Starch	339.7* (188.1)	422.9* (196.2)	391.1 (154.6)	384.2 (109.2)	320.4* (182.8)	385.8* (196.1)	410.5 (67.7)	428.6 (203.2)
Non-starchy vegetables and fruit	495.2 (246.9)	472.4 (416.6)	519.6 (242.7)	524.0 (257.9)	512.2* (299.9)	445.7* (241.9)	476.5 (262.2)	474.6 (283.7)
Legumes	5.6* (8.5)	3.4* (9.2)	6.2 (9.2)	4.4 (7.6)	4.1 (10.5)	4.0 (7.5)	5.2* (12.7)	2.9* (5.1)
Dairy	233.8* (210.6)	178.8* (162.8)	274.5* (197.5)	210.2*(215.1)	263.0 (202.4)	250.8 (217.4)	224.1 (222.3)	228.6 (202.0)
Meat and eggs	329.7* (151.5)	392.9* (206.4)	291.1 (133.4)	296.9 (123.7)	270.8* (137.5)	319.3* (150.6)	411.8 (224.4)	423.4 (224.6)
Fat and oil	29.0 (23.7)	33.6 (21.2)	29.0 (20.7)	31.1 (21.7)	24.4* (21.2)	34.7* (31.9)	29.3 (26.0)	33.8 (25.7)
Sugar and jam	85.1* (78.5)	106.2* (90.2)	82.5 (65.9)	72.2 (70.9)	88.5* (82.2)	116.9* (99.1)	82.9 (63.0)	90.3 (635)
Alcoholic beverages	173.5 (275.8)	201.1 (318.9)	112.7* (150.6)	173.0* (269.2)	40.6* (94.5)	67.6* (123.6)	245.7 (272.8)	202.3 (217.1)
Non-alcoholic beverages	297.0 (404.5)	351.1 (401.2)	241.3 (347.6)	255.0 (305.4)	242.2* (323.6)	317.0* (331.1)	247.0 (325.7)	248.7 (283.7)
Herbal teas	666.6 (657.69)	655.4 (565.6)	431.0 (394.4)	529.1 (623.0)	927.0 (691.9)	1044.0 (878.0)	448.8 (356.5)	423.8 (308.2)

CRC: colorectal cancer; UC: urothelial carcinoma; BC: breast cancer; PC: prostate cancer; SD: standard deviation; TEV: total energy value;

†Comparison of means between cases and controls by Student's T-hypothesis test;

*Significant at a level α = 0.05

In the multidimensional characterization of food using AFCP (in the total adult population, women and men are respectively), the sample adequacy measures obtained were an overall KMO of 0.75 for both sexes, 0.65 for women and 0.71 for men. This shows that the analysis in the sample range is reasonable.

Table 3 shows the factor (rotation) load matrix of the factors (modes) retained in each study population. The three patterns that appear in the general population are called the Southern Cone Pattern (characterized by high factor load of red meat, polysaccharide vegetables and wine), the Sweet Drink Pattern (soft drinks and juices), and the Prudent Pattern (non-starchy fruits and vegetables and dairy products). Especially in the female population, the first identified dietary pattern includes fatty meat, pastry products, oil and mayonnaise as the main food group, which is called the Female Southern Cone Pattern, and a Prudent Pattern including fruits and non-starchy vegetables. On the other hand, in the male population, the Male Southern Cone Pattern is characterized by the intake of fatty meat, plus eggs, grains and starchy vegetables, while the cautious pattern has the same conformation as the homonymous pattern in the general population. Other identified patterns are known as the Rural Pattern (processed meat) and the Starchy Pattern (high refined grain and low whole grain intake) in women, while the male model is Sugary Drinks Pattern (fruit juice and soda) and the Typical

Measured Pattern (lean meat and black tea).

Table 3. Principal component factor analysis determined the factor load matrix (rotation) of the main food patterns. Cordoba, Argentina 2006–2012

Total population (*n* = 489)[a]				
Food group	**Southern Cone pattern**	**Sugary beverage pattern**		**Prudent pattern**
Dairy	–0.06	–0.03		**0.68**
Red meat	**0.72**	0.10		0.04
Non starch fruits and vegetables	0.05	–0.04		**0.75**
Starchy vegetables	**0.61**	0.15		0.24
Sugary beverage	–0.07	**0.79**		–0.14
Wine	**0.68**	–0.37		–0.21
Explained variability (%)	19.47	13.13		12.43
Cumulative explanatory variability (%)	19.47	32.6		46.03
Female population (*n* = 294)[b]				
Food group	**Southern Cone pattern**	**Rural pattern**	**Prudent pattern**	**Amylaceous pattern**
Fatty meat	**0.7319**	0.15	–0.08	0.18
Processed meat	0.23	**0.71**	–0.05	0.01
Refined grain	0.23	–0.15	0.007	**0.73**
Whole grain	–0.07	–0.08	0.03	**–0.68**
Pastry products	**0.65**	0.35	–0.0006	0.14
Vegetable oil and egg yolk sauce	**0.69**	–0.08	0.23	–0.003
Non-starchy vegetables	0.05	0.03	**0.81**	0.03
Fruits	0.09	–0.13	**0.64**	–0.12
Explained variability (%)	0.13	0.10	0.07	0.06
Cumulative explanatory variability (%)	0.13	0.24	0.31	0.37
Male population (*n* = 381)[c]				
Food group	**Southern Cone pattern**	**Sugary beverage pattern**	**Typical measured pattern**	**Prudent pattern**
Dairy	–0.0014	–0.0114	-0.1221	**0.7915**
Egg	**0.6304**	–0.1821	-0.0458	0.0215
Lean red meat	–0.1128	–0.2575	**0.6282**	0.1412
Fatty red meat	0.7367	–0.1206	0.0810	–0.0046
Non-starchy fruits and vegetables	0.1072	0.1083	0.2804	**0.6779**
Starchy grains and vegetables	**0.6005**	0.2355	0.1219	0.0897
Herbal teas	0.1132	0.1311	**0.7223**	–0.0734
Sugary beverage	0.0422	**0.8006**	0.0415	-0.0591
Explained variability (%)	20.10	13.04	10.48	8.46
Cumulative explanatory variability (%)	20.10	33.14	43.62	52.08

Note: Loadings $\geqslant$0.60 (in bold) define the dominant groups for each factor. The Table only presents the food groups that were found to be dominant in some factor. However, after the statistical test of sample adequacy, the intermediate dimensions or variables defined to construct the food model are:

[a]cereals and derived products, starchy vegetables, non-starchy vegetables and fruits, dairy products, processed meats, red meats, white meats, eggs, sugars and jams, sugared beverages, wine, fats and oils.

[b]milk and yogurt, hard cheese, soft cheese, lean meat, fat meat, processed meat, eggs, starchy vegetables, non-starchy vegetables, fruits, whole grains, refined cereals, beans, baking products, candy (ice cream, chocolate, butter, sweet milk), sugar and candy (sugar, jam, honey, sweet milk), butter and cream, vegetable oil and mayonnaise, alcoholic beverages and non-alcoholic beverages.

[c]dairy products, lean red meats, fatty red meats, eggs, non-starchy fruits and vegetables, cereals and starchy vegetables, sugars and jams, fat, vegetable oil, herbal teas, wine, non-alcoholic beverages.

Table 4 shows the estimation results of multi-level logistic model to obtain the correlation degree (ORs) of CRC, UC, BC and PC, and determine different food patterns and their corresponding clustering measures (i.e., based on hierarchical data structure). With regard to the risk of CRC, considering the family history of the disease, the Southern Cone Pattern (OR 2.35, for the upper tercile versus the lower tercile) and the Sugary Drinks Pattern (OR 2.62) showed a promoting effect, while the Prudent Pattern (OR 0.31) showed a protective effect. With regard to the occurrence of UC, an increased risk associated with the Southern Cone Pattern (OR 1.75) and the Sugar Beverage Pattern (OR 2.55, for the middle versus the lower tercile) was also observed, while high adhesion to the latter was negatively associated with disease (OR 0.72, for the upper versus the lower tercile), and significant aggregation associated with residence in urban or rural areas was observed (**Table 4**). In the case-control study of BC, the Female Southern Cone model has a significant priming effect. High scores (upper tercile) for the Rural and Amilaceous Patterns were also positively correlated with the risk of breast cancer (OR 2.02 and OR 1.82, respectively), while the Prudent Pattern of the same category showed a protective effect (OR 0.56). On the other hand, compared with PC, the so-called Male Southern Cone Pattern showed a significant priming effect (OR 1.91, for the upper tercile vs. the lower tercile). Similarly, high consumption (upper tercile) of fruit juice and soda (Sugary Drinks Pattern) and lean meat and infusion (Typical Measured Pattern) were positively correlated with the occurrence of disease (OR 1.66 and 1.09, respectively). It is worth noting that a significant aggregation is also observed here, which is caused by a possible family aggregation dimension of PC family history.

Table 4. Estimation of measures of association (ORs adjusted for selected confounding variables) using Logistic Models. Multilevel for colorectal, urothelial, breast and prostate cancer. Cordoba, Argentina 2006–2012

Case-control study based on tumor location	**Food pattern Reference: Tercile I**	**OR (95% CI)**	**p value**
Colorectal cancer[1]	Southern Cone Pattern, II	1.92 (1.51–2.46)	<0.001
	Southern Cone Pattern, III	2.35 (2.25–2.46)	<0.001
	Sugary Drinks Pattern, II	1.54 (0.86–2.75)	0.144
	Sugary Drinks Pattern, III	2.62 (2.32–2.95)	<0.001
	Prudent Pattern, II	0.84 (0.51–1.41)	0.516
	Prudent Pattern, III	0.31 (0.22–0.43)	<0.001
Urothelial carcinoma[2]	Southern Cone Pattern, II	2.63 (1.99–3.47)	<0.001
	Southern Cone Pattern, III	1.75 (1.10–2.78)	0.017
	Sugary Drinks Pattern, II	2.55 (1.28–5.07)	0.008
	Sugary Drinks Pattern, III	0.72 (0.60–0.85)	<0.001
	Prudent Pattern, II	0.66 (0.25–1.70)	0.386
	Prudent Pattern, III	0.31 (0.08–1.23)	0.097
Breast cancer[1]	Female Southern Cone Pattern, II	1.63 (1.59–1.69)	<0.001
	Female Southern Cone Pattern, III	3.13 (2.58–3.78)	<0.001
	Rural Pattern, II	1.44 (0.64–3.26)	0.370
	Rural Pattern, II	2.02 (1.21–3.37)	<0.001
	Prudent Pattern, II	1.10 (0.88–1.37)	0.370
	Prudent Pattern, III	0.56 (0.41–0.77)	<0.001
	Amylaceous Pattern, II	1.36 (1.04–1.76)	0.020
	Amylaceous Pattern, III	1.82 (1.18–2.79)	<0.001
Prostate cancer[1]	Male Southern Cone Pattern, II	1.39 (0.981–1.99)	0.064
	Male Southern Cone Pattern, III	1.91 (1.734–2.11)	<0.001
	Sugary Drinks Pattern, II	1.17 (0.728–1.89)	0.509
	Sugary Drinks Pattern, III	1.66 (1.094–2.55)	0.017
	Typical Measured Pattern, II	1.30 (0.970–1.74)	0.079

Table 4. Continued.

Case-control study based on tumor location	Food pattern Reference: Tercile I	OR (95% CI)	p value
	Typical Measured Pattern, III	1.09 (1.052–1.14)	<0.001
	Prudent Pattern, II	0.94 (0.620–1.44)	0.798
	Prudent Pattern, III	1.26 (0.705–2.27)	0.431

OR: odds ratio; CI: confidence interval; II and III, middle and upper tercile of the dietary pattern scales. Clustering variables: [1]family history of the pathology, [2]urban and rural residents.

6. Discussion

This study identified the mode of characteristic food in Cordoba Province. The patterns that appear in the general population are called the Southern Cone Pattern, the Sugary Drinks Pattern and the Prudent Pattern. In the female group, the identified pattern is called Female Southern Cone Pattern, Rural, Prudent and Amilaceous, while in the male group, Southern Cone Male, Sugary Drinks, Typical Moderate and Prudent. Most of these patterns are significantly correlated with the occurrence of CRC, BC, PC and UC in Cordoba Province, Argentina.

It is reported that in Argentina, the incidence of CRC in 2008 was 25.3 in men and 16.7 in women, per 100,000 residents, and 10.7 and 1.7 in men and women respectively for UC[1]. In the same year, at the national level, the ratio of BC was 74.0 and PC was 58.8[1]. In Cordoba, in particular, the ratios between the 26 departments that make up the province varied widely in previous years[2]. Some people believe that this spatial pattern is related to cultural, economic and environmental characteristics (including eating habits) and different urbanization of the population[4,7].

It must be emphasized that the eating habits of Argentines have some particularity, which makes them different from other Latin American countries: high consumption of red meat[9], frequent barbecue[8], frequent drinking of wine[25] and typical "partner" herbal tea[26,40,41], etc. Particularly in Cordoba, in previous studies, certain characteristics of the diet in the capital city were associated with cancer risk[8,11,27]. Even with this in mind, in Cordoba, Argentina, there is no official information about the typical food of the total population, let alone the study on describing the normal food consumption in our population from the approach of food consumption pattern (AFCP). It can only be inferred indirectly from the FAO food balance table that the foods that mainly constitute the national diet are bread, flour and noodles, meat vaccines, sugar, milk, cheese, sunflower seed oil, potatoes, leafy vegetables, rice, oranges, apples, bananas and tomatoes, yellow oil and fat and wine[28]. In general, the food pattern recognition carried out in this work is consistent with this, as several of those described by FAO emerged as dominant food groups (or foods).

Considering the structure of the dietary patterns identified in this study, we found that in the total population, both men and women, the meat group dominated the so-called Southern Cone Pattern, which indicates that these patterns are highly representative in the individual diet. Although these patterns are different from the Western Pattern described in various studies[15], it is consistent with the latter to describe red meat as a characteristic group. It is worth noting that our results in CRC and TU are consistent with those reported in previous studies on the positive association of Western Pattern with these diseases[11,13,15]. Similarly, in most cases, this model is consistent with our results with an increased risk of for BC and PC[16,29-32], although there is also conflicting evidence in this regard[33,34].

The so-called cautious eating pattern in this study has similar characteristics to other patterns published under this study and other names, such as healthy patterns or vegetables and fruits[13,35,36]. Consistent with our findings, the results of most of these studies show that this model has a good effect on reducing the risk of CRC[15] and BC[37-39], although there is evidence that there is no or positive correlation with the latter tumor site[30]. However, although the literature mentioned the antitumor effects of fruits and vegetables[5,7,40], this model had no significant effect on the occurrence of PC and UC in our study.

In this study, another emerging dietary pattern in the Cordoba population associated with increased risk of CRC and PC was the Sugary Drinks Pattern. This model, which is mainly composed of fruit juice and natural gas consumption, has not been determined in other regions of South America or any other research, so it will constitute a special model in the region[5,6]. In other epidemiological studies, high sugar beverage intake was associated with an increased risk of CRC and PC[40,41], although some studies did not confirm this correlation of CRC[42]. The increased risk of CRC and PC is related to the hyperglycemic index of these drinks, that is, their ability to significantly increase blood glucose after intake. Hyperglycemia stimulates the increase of insulin secretion. Insulin itself, as a growth factor, in turn induces the increase of insulin-like growth factor I (IGF-

1), a hormone that promotes mitosis and cell proliferation and inhibits the apoptosis of normal and cancer cells[43]. Other metabolic pathways involving insulin are also associated with an increased risk of PC[44].

It is worth noting that the dietary patterns identified in the male population of Cordoba are more similar to those identified in the total population than in the female population. To some extent, this can be explained by the different proportion of men and women who included the sample in the total population (mostly male controls), but it may also be due to the differences in eating habits between men and women[45]. The main difference between the Female Southern Cone Pattern and the Southern Cone pattern determined in the total population can be proved by gender differences in drinking habits. It is well known that women in Argentina have a higher burden of drinking alcohol than men in the traditional diet. According to the national risk factor survey conducted in Argentina in 2009, men in Cordoba Province have a higher risk of regular drinking and occasional excessive drinking than women[46].

In addition, the identification in the female population of a rural pattern with processed meats as the dominant group coincides with the results of a study carried out in another South American country (Uruguay), in which it was reported that, when stratifying the patterns by gender, the female population presented higher loads for processed meats than the male population[12].

It is necessary to point out some limitations of this work in terms of research design and methods used. The size of the sample may not be sufficient to detect the real impact of food patterns. However, the proposed special statistical method supports small sample size. In addition, the principal component analysis yielded satisfactory KMO measurements, indicating that the sample size for analysis was appropriate.

Case-control studies recognize the possibility of selection bias (due to non-random selection of subjects), information bias (through imperfect measurements), and confusion bias (resulting from non-random exposure assignments). However, in this study, from design to analysis, many strategies were implemented to minimize the possibility of its occurrence. These strategies include the development of a detailed procedure manual, rigorous training of interviewers, standardized data collection procedures, and thorough monitoring of this stage of the study to avoid erroneous exposure classification. In addition, most respondents masked the main assumptions of the study to eliminate an important source of bias, especially when they knew the case or control situation in the study. However, errors in measuring dietary exposure may still exist. However, the equal distribution of these between cases and controls—with the exception of recall bias—suggests that their influence is negligible.

In order to avoid potential significant selection bias and unmeasured confounding factors, this study obtained similar distribution of relevant characteristics in case group and control group. In other words, the control group was selected according to the gender, age and residence of the case to form a group as similar as possible, except for cancer, and interviews were conducted at the same time. In addition, various covariances were incorporated into the model to consider some remaining confusion and obtain a more accurate estimate of the impact of dietary patterns on cancer occurrence.

In view of the above, we can say that, in general, our results are biologically reasonable and consistent with other studies in this field. This work also shows the new methodological development in the field of nutritional epidemiology, which can guide future research.

7. Conclusion

Chronic non-communicable diseases, including cancer, are undoubtedly the current major disease burden in Cordoba, Argentina and around the world. This requires concerted efforts by different social actors, including the scientific and academic communities, to mitigate their impact on the population. In this regard, we believe that this work provides valuable evidence for the role of dietary patterns in the complex etiology of various cancers, and diet is a potentially changeable lifestyle. Therefore, considering the known and published cancer prevention strategies, the results of this study confirm the need to emphasize dietary recommendations to promote the normal intake of vegetables, fruits and dairy products (moderate intake for men) and reduce the consumption of red meat (mainly high-fat), processed meat, starchy vegetables and refined grains, wine and sugary drinks. Especially for men, moderate intake of eggs is recommended, and for women, moderate intake of pastry products, oil and mayonnaise is recommended.

Finally, we highlight the contribution that this study makes to the characterization of population eating habits in a region where there are few antecedents in this regard, especially in relation to a health problem that is of particular importance in modern society and that is strongly linked to environmental determinants, such as cancer.

Conflict of interest

The authors declare no conflict of interest.

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