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RESEARCH PAPER

Dietary Patterns and Risk of Gastric Cancer: A Factor Analysis in Uruguay

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Abstract. In the time period 1996-2004 a case-control study on diet and gastric cancer risk was conducted in Montevideo, Uruguay. Two-hundred and seventy-four cases and 548 controls were drawn from the four major public health hospitals located in Montevideo. In order to reduce the numerous foods and nutrients defined in the present database we conducted two factor analyses among controls. The first principal component analysis included food groups and retained four factors labelled as prudent, traditional, drinker, and meat, milk and rice patterns. The second factor analysis was conducted with nutrients and also four patterns were retained. These nutrient patterns were labelled as fats, antioxidants, carotenoids, and carbohydrates. The drinker and meat, milk, rice, and carbohydrates patterns were directly associated with risk of gastric cancer. On the other hand, the prudent and antioxidants patterns were significantly protective. It could be concluded that factor analysis is a powerful tool for establishing the role of diet in the etiology of gastric cancer risk.

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1. Introduction

In the early fifties gastric cancer was the leading cancer site in Uruguay [1]. Since then its incidence and mortality have been declining and reached a plateau in the year 1990 [2, 3]. The role of diet has been considered as of paramount importance in the etiology of gastric cancer [4]. Whereas non-starchy vegetables, allium vegetables, and fruits have been considered as protective, salty foods were associated with increased risk in the recent report from World Cancer Research Fund and the American Insitute for Cancer Research [4].

In fact numerous studies on the role of diet in stomach cancer have been performed all over the World [4]. Most of these studies followed a case-control design and a few were prospective studies. More importantly, they were analyzed using the traditional approach, that is following food groups or nutrients groups.

Since the pioneer studies of Pearson [5] and Spearman [6] factor analysis has been widely employed in psychology, sociology, economic fields, and mathematics. In 1992 Randall et al. performed the first study on cancer using factor analysis [7]. More specifically this study explored the role of diet in colon cancer. Since then numerous studies on factor analysis and cancer were performed. These reports included colon, rectum, breast, lung, larynx, mouth and pharynx, pancreas, bladder, and kidney cancers among other cancer sites. In brief factor analysis has the purpose of reduce numerous food items into a few factors which try to explain the causes of cancer [8-10].

To our knowledge only four studies of dietary patterns and gastric cancer have been published [11-14]. All these studies were exploratory and confirmatory studies have to our knowledge not been conducted up to the present. This is reasonable since the diet is mostly unknown in stomach cancer and this also applies to other cancer sites. Therefore it is urgent to explore diet in detail to confirm its etiologic role.

For all these reasons we decided to perform a factor analysis on diet and gastric cancer. Moreover our hypothesis suggests that factor analysis yield a better result compared with the traditional reductionist approach.

2. Materials and Methods

2.1. Selection of cases

In the time period 1996-2004 all the newly diagnosed and microscopically confirmed cases of gastric adenocarcinoma were considered eligible for this study. From the initial number of cases (290 in total), sixteen patients refused the interview, leaving a final of 274 cases (response rate 94.5%). The cases included 190 males and 84 females.

2.2. Selection of controls

In the same time period and in the same hospitals, all hospitalized patients with conditions not related to tobacco smoking, alcohol drinking and without recent changes in their diet were considered eligible for the study. From an initial number of 795 patients, 49 refused the interview leaving 746 potential controls (response rate 93.8%). From this pool of potential controls, 548 patients were frequency matched to cases on age, sex, and residence. The controls presented the following conditions: eye disorders (119 patients, 21.7%), abdominal hernia (116, 21.2%), diseases of the skin (59, 10.8%), urinary stones (43, 7.8%), varicose veins (43, 7.8%), injuries (39, 7.1%), acute appendicitis (45, 8.2%), hydatid cyst (35, 6.4%), blood disorders (29, 5.3%), and prostate hypertrophy (20, 3.7%).

2.3. Interviews and questionnaire

All the participants (cases and controls) were administered a structured questionnaire. The interviews were performed by two trained social workers shortly after admittance into the hospitals. Proxy interviews were not admitted into the study. The questionnaire included the following sections: sociodemographics (age, sex, residence, urban/rural status, education, monthly income), a complete occupational history which included the last four jobs and its duration, self reported weight and height five years before the date of the interview, family history of

Table 1. Distribution of cases and controls by sociodemographics and selected risk factors.

		Cases	Controls	
Variable	**Category**	**No. / %**	**No. / %**	**Global *p* value**
Age (years)	30 - 39	5 / 1.8	10 / 1.8	
	40 - 49	19 / 6.9	38 / 6.9	
	50 - 59	59 / 21.5	118 / 21.5	
	60 - 69	79 / 28.8	158 / 28.8	
	70 - 79	86 / 31.4	172 / 31.4	
	80 - 89	26 / 9.5	52 / 9.5	1.00
Sex	Males	190 / 69.3	380 / 69.3	
	Females	84 / 30.7	168 / 30.7	1.00
Residence	Montevideo	153 / 55.8	306 / 55.8	
	Other counties	121 / 44.2	242 / 44.2	1.00
Urban/Rural status	Urban	226 / 82.5	465 / 84.8	
	Rural	48 / 17.5	83 / 15.2	0.38
Years of study	0 - 2	78 / 28.5	144 / 26.3	
	3 - 5	102 / 37.2	177 / 32.3	
	6+	94 / 34.3	227 / 41.4	0.13
Monthly income (US)	≤ 141	101 / 36.9	249 / 45.4	
	142+	135 / 43.3	216 / 39.4	
	Unknown	38 / 13.8	83 / 15.2	0.02
Smoking index	Never smokers	94 / 34.3	190 / 34.7	
Former smokers [1]	20+	22 / 8.0	40 / 7.3	
	10 - 19	19 / 6.9	35 / 6.4	
	1 - 9	28 / 10.2	49 / 8.9	
Current smokers [2]	1 - 9	8 / 2.9	32 / 5.8	
	10 - 19	37 / 13.5	91 / 16.6	
	20 - 29	40 / 14.6	61 / 11.1	
	30+	26 / 9.5	50 / 9.1	
Alcohol drinking [3]	Never drinkers	133 / 48.5	279 / 50.9	
	1 - 60	43 / 15.7	110 / 20.1	
	61 - 120	32 / 11.7	77 / 14.0	
	121 - 240	36 / 13.1	56 / 10.2	
	241+	30 / 10.9	26 / 4.7	
Number of patients		274 / 100.0	548 / 100.0	

[1] Years smoked.
[2] Cigarettes/day.
[3] Mililiters of ethanol per day.

cancer among first degree relatives (mother, father, sisters, brothers), a complete history of tobacco smoking (age at start, age of quit, number of cigarettes smoked per day, type of tobacco, type of cigarette, inhalation practices), a complete history of alcohol drinking (age at start, age of quit, number of glasses drunked per day, type of alcoholic beverage), a complete history of consumption of non-alcoholic beverages (mate, coffee, tea), menstrual and reproductive events, and a food frequency questionnaire (FFQ) on 64 foods. This FFQ allowed the estimation of total energy intake and represented the usual Uruguayan diet. Furthermore, the FFQ was tested for reproducibility with good results [15].

2.4. Food and nutrients included in the factor analysis

The following food and food groups were included in the factor analysis: fried red meat, barbecued red meat, boiled red meat, poultry, fish, processed meat, dairy foods, eggs, desserts, rice, bread, other grains, fresh vegetables, cooked vegetables, potato, sweet potato, legumes, total fruits, beer, wine, and hard liquor. Nutrients

Table 2. Factor loadings matrix among controls for food groups [1 2].

Food groups	Factor 1	Factor 2	Factor 3	Factor 4
Fried meat	-0.04	-0.02	0.22	**0.43**
Barbecued meat	0.34	0.15	**0.41**	-0.04
Boiled meat	**0.59**	0.01	0.16	0.11
Poultry	**-0.41**	0.27	-0.25	**0.42**
Fish	**-0.42**	**0.41**	-0.20	0.09
Processed meat	-0.03	0.16	**0.44**	0.28
Dairy foods	0.09	0.07	-0.05	**0.56**
Eggs	0.09	0.05	0.38	0.10
Desserts	0.06	**0.50**	-0.05	0.38
Rice	0.33	-0.09	0.03	**0.40**
Bread	0.28	-0.20	0.31	0.32
Other grains	0.03	0.23	0.12	0.21
Fresh vegetables	-0.13	**0.53**	0.02	0.08
Cooked vegetables	0.38	**0.58**	-0.11	0.04
Potato	**0.65**	0.01	-0.07	0.27
Sweet potato	**0.65**	0.14	-0.11	-0.07
Legumes	0.18	**0.44**	0.29	-0.13
Total fruits	-0.03	**0.64**	0.05	-0.20
Beer	-0.09	-0.05	**0.42**	0.04
Wine	0.07	-0.16	**0.69**	-0.01
Hard liquor	-0.04	0.08	**0.55**	-0.14
Variance (%)	10.0	9.2	9.0	6.7

[1] Loadings higher than 0.39 are typed in bold.
[2] Total variance (including error variance): 34.9%.

(and bioactive substances) were included in the second factor analysis: protein, saturated fat, monounsaturated fat, polyunsaturated fat, cholesterol, starch, dietary fiber, glucose, fructose, vitamin C, vitamin E, β-carotene, lutein, other carotenoids, folate, pyridoxine, cobalamine, thiamine, riboflavin, β-sitosterol, campesterol, stigmasterol, quercetin, nitrate, nitrite, iron, and sodium. Food and nutrients was log transformed and energy-adjusted by the residuals method [16].

2.5. Statistical analysis

Factor analysis was performed using the controls and retained four components, both for food groups and nutrients [8-10]. Then the factors were rotated by the quartimax method for food groups and by the oblimin oblique method for nutrients. The reason of using different rotation methods was the fact that nutrients patterns were highly correlated. After that the retained factors were scored employing the regression method of Thomson [17]. Since the scores were continuous, the patterns were categorized in quartiles according to the distribution among the controls.

Multivariate odds ratios of each pattern were estimated using unconditional logistic regression [18]. The models included terms for age, sex, residence, education, tobacco smoking, and total energy intake. Since each pattern was conditional for the others [19], all the scored factors were included in the complete final model. Moreover the nutrient patterns did not included alcoholic variables, a term for alcohol drinking was further included in the final model. All the calculations were performed with the software STATA, version 9.1 [20].

3. Results

The distribution of cases and controls by socio-demographic variables and selected risk factors is shown in Table 1. As a result of the matched design, age, sex, and residence were

Table 3. Odds ratios of gastric cancer for scored food patterns [1].

Dietary pattern	Cases / Controls	OR [2]	95% CI	OR [3]	95% CI
Traditional	51 / 137	1.0	reference	1.0	reference
	67 / 137	1.27	0.82 - 1.99	1.28	0.81 - 2.01
	87 / 137	1.63	0.99 - 2.37	1.47	0.94 - 2.30
	73 / 137	1.37	0.86 - 2.19	1.43	0.89 - 2.30
	p-value for trend	0.08		0.12	
Prudent	81 / 137	1.0	reference	1.0	reference
	70 / 137	0.88	0.58 - 1.33	0.93	0.61 - 1.41
	74 / 137	0.96	0.63 - 1.45	0.99	0.65 - 1.51
	49 / 137	0.58	0.37 - 0.92	0.54	0.34 - 0.85
	p-value for trend	0.04		0.02	
Drinker	54 / 137	1.0	reference	1.0	reference
	63 / 137	1.22	0.78 - 1.90	1.30	0.83 - 2.06
	67 / 137	1.36	0.86 - 2.15	1.48	0.92 - 2.37
	90 / 137	1.95	1.21 - 3.14	2.18	1.33 - 3.58
	p-value for trend	0.006		0.003	
Meat, milk, rice	39 / 137	1.0	reference	1.0	reference
	57 / 137	1.44	0.89 - 2.34	1.42	0.87 - 2.32
	89 / 137	2.49	1.57 - 3.95	2.47	1.56 - 3.93
	89 / 137	2.54	1.61 - 2.02	2.48	1.56 - 3.94
	p-value for trend	<0.0001		<0.0001	

[1] Adjusted for age, sex, residence, education, smoking index, alcohol drinking, and total energy intake.
[2] Without adjustment for the other patterns.
[3] With adjustment for each other.

similar. Cases were less educated than controls but earned higher salaries. Both groups of participants presented a similar pattern of smoking, whereas cases consumed more alcoholic beverages compared with controls (p-value = 0.006).

The matrix pattern among controls for food groups is shown in Table 2. Factor 1 is characterized by high positive loadings for boiled red meat, potato, sweet potato and high negative loadings for poultry and fish. We labelled this factor as the *traditional* pattern which explained 10% of the total variance. Factor 2 presented high positive loadings for fresh vegetables, cooked vegetables, legumes, total fruits, fish, and desserts. This factor was labelled as the *prudent* pattern and explained 9.2% of the variance. Factor 3 showed high loadings for alcoholic beverages (beer, wine, and hard liquor), barbecued meat, and processed meat and was labelled as the *drinker* pattern. This pattern explained 9% of the variance. Finally factor 4 displayed high positive loadings for fried red meat, poultry, dairy foods, and rice and was labelled as the *meat, milk,* and *rice* pattern. This factor explained 6.7% of the variance.

Odds ratios of gastric cancer for scored food patterns are shown in Table 3. The *prudent* pattern was inversely associated with risk of gastric cancer (OR 0.54, 95% CI 0.34-0.85, *p*-value for trend = 0.02). On the other hand the *drinker* pattern was directly associated with gastric cancer risk (OR 2.18, 95% CI 1.33-3.58, *p*-value for trend = 0.003). Similarly the *meat, milk and rice* pattern increased the risk of stomach carcinoma (OR 2.48, 95% CI 1.56-3.94, *p*-value for trend <0.0001) while the *traditional* pattern displayed a modest non-significant elevation in risk.

The factor loadings matrix for nutrients and bioactive substances is shown in Table 4. Factor 1 presented high loadings for protein, saturated fat, monounsaturated fat, polyunsaturated fat, cholesterol, pyridoxine, cobalamine, and iron. We labelled this factor as the *fats* pattern. Factor 2 showed high loadings for glucose, fructose, vitamin C, β-sitosterol, campesterol, stigmasterol, and quercetin and was labelled as the *antioxidants* pattern, explaining 25.8% of the variance. Factor 3 displayed high loadings for β-carotene,

Table 4. Factor loadings matrix among controls for nutrients [1-4].

Nutrients	Factor 1	Factor 2	Factor 3	Factor 4
Protein	**0.72**	0.04	0.08	0.33
Saturated fat	**0.97**	0.00	-0.04	0.00
MUFA [5]	**0.98**	-0.01	-0.07	0.00
PUFA [6]	**0.85**	0.07	-0.07	0.03
Cholesterol	**0.84**	-0.04	0.11	0.06
Starch	-0.07	-0.08	-0.02	**0.97**
Dietary fiber	-0.12	0.14	-0.01	**0.96**
Glucose	-0.04	**0.90**	-0.02	-0.04
Fructose	-0.11	**0.87**	-0.06	-0.00
Vitamin C	0.03	**0.51**	0.44	-0.01
Vitamin E	0.26	0.44	0.43	0.08
Beta-Carotene	-0.02	-0.07	**0.75**	0.05
Lutein	-0.06	-0.07	**0.90**	-0.03
Other carotenoids	-0.12	0.39	0.39	-0.02
Folate	0.32	0.32	0.49	0.02
Pyridoxine	**0.54**	0.25	0.23	0.15
Cobalamine	**0.97**	-0.06	-0.07	-0.06
Thiamine	0.02	-0.03	-0.04	**0.98**
Riboflavin	0.48	-0.04	0.04	**0.62**
β-Sitosterol	0.03	**0.91**	-0.05	0.03
Campesterol	0.15	**0.87**	-0.14	-0.02
Stigmasterol	0.15	**0.71**	0.09	0.08
Quercetin	-0.16	**0.57**	0.20	0.07
Nitrates	-0.06	0.09	**0.83**	0.08
Nitrites	0.27	0.04	**0.55**	-0.04
Iron	0.59	0.04	0.38	0.24
Sodium	0.34	0.03	0.12	0.48
Variance (%)	25.3	25.8	24.2	22.7

[1] Loadings higher than 0.39 are typed in bold.
[2] Total variance (including error variance): 98.0 %.
[3] Sampling adequacy: 0.83.
[4] Factors are significantly correlated and they were rotated by the oblimin oblique method.
[5] Monounsaturated fat.
[6] Polyunsaturated fat.

lutein, nitrate, and nitrite. It was labelled as the *carotenoids* pattern explaining 24.2% of the variance. Finally factor 4 showed high loadings for starch, fiber, thiamine, and riboflavin and was labelled as the *carbohydrates* pattern. This last pattern explained 22.7% of the variance.

Odds ratios of stomach cancer for scored nutrient patterns are shown in Table 5. The so called *antioxidants* pattern was inversely associated with gastric cancer risk (OR 0.46, 95% CI 0.28-0.74, *p*-value for trend = 0.003) whereas the *carbohydrates* patterns enhanced significantly the risk of this malignancy (OR 1.80, 95% CI 1.13-2.87, *p*-value for trend = 0.004). The *fats* pattern increased the risk of stomach cancer (OR 1.62, 95% CI 1.02-2.56, *p*-value for trend = 0.07). This risk was greatly attenuated when this pattern was controlled for the remaining patterns. Finally the carotenoids pattern was not associated with risk of gastric cancer.

To explore whether specific foods or nutrients accounted for the associations we found for the specific dietary patterns we further adjusted the significant patterns for foods or nutrients that were highly loaded on the specific dietary patterns (Table 6). The results for the *prudent* pattern remained significant after adjustment for fresh and cooked vegetables and fish, but not af-

Table 5. Odds ratios of gastric cancer for scored nutrient patterns [1].

Nutrient pattern	Cases/Controls	OR [2]	95 % CI	OR [3]	95 % CI
Fats	48/137	1.0	reference	1.0	reference
	75/137	1.52	0.97-2.38	1.42	0.89-2.24
	73/137	1.49	0.95-2.34	1.38	0.86-2.21
	78/137	1.62	1.02-2.56	1.45	0.89-2.36
	p-value for trend	0.07		0.20	
Antioxidants	87/137	1.0	reference	1.0	reference
	67/137	0.82	0.54-1.23	0.81	0.53-1.23
	73/137	0.87	0.58-1.30	0.80	0.52-1.23
	47/137	0.52	0.33-0.80	0.46	0.28-0.74
	p-value for trend	0.009		0.003	
Carotenoids	69/137	1.0	reference	1.0	reference
	68/137	0.94	0.61-1.44	0.93	0.60-1.44
	73/137	0.99	0.65-1.53	0.98	0.63-1.54
	64/137	0.93	0.60-1.44	0.98	0.60-1.59
	p-value for trend	0.83		0.98	
Carbohydrates	50/137	1.0	reference	1.0	reference
	54/137	1.03	0.65-1.64	1.01	0.63-1.62
	75/137	1.40	0.89-2.19	1.38	0.87-2.19
	95/137	1.77	1.15-2.74	1.80	1.13-2.87
	p-value for trend	0.003		0.004	

[1] Adjusted for age, sex, residence, education, smoking index, alcohol drinking, and total energy intake.
[2] Without adjustment for the other patterns.
[3] With adjustment for each other.

ter adjustment for total fruit intake. On the other hand the *drinker* and *meat, milk and rice* patterns remained significant after further adjustment for alcohol drinking, fried meat, dairy foods, and rice consumption. Among the nutrient patterns, the *carbohydrates* pattern also was significant after further controlling for starch, fiber, thiamine, and riboflavin. Finally the results for the *antioxidants* pattern remained significant after adjustment for fructose, but not after adjustment for glucose, β-sitosterol, and campesterol.

4. Discussion

Factor analysis for food groups retained the following patterns: traditional, prudent, drinker, and meat, milk and rice scores. On the other hand, factor analysis for nutrients retained four groups: fats, antioxidants, carotenoids, and carbohydrates patterns.

Factor analysis has several difficulties. In fact the drawbacks are related with the use of the technique and not related with the method *per se*. In first place, the use of a questionnaire poorly designed or badly constructed is a major drawback. Secondly, the improper use of the method by a researcher not familiar with factor analysis is another drawback. Therefore, the design of an adequate food frequency questionnaire is essential for obtaining reliable results. Also a proper knowledge of the subject of the study is also highly necessary. Obviously a well defined hypothesis is an important aid in conducting a good factor analysis. The use of principal component analysis (PCA), maximum likelihood analysis, or other variant of factor analysis is mostly irrelevant.

An important issue for the value of factor analysis is related with its value when it is compared with traditional reductionist analysis. In other words, is the information obtained with factor analysis is similar with the information obtained by traditional analysis or is it better? Factor analysis may capture the effect of the combination of many interacting factors and then provide perhaps stronger or more consistent results

Table 6. Odds ratios for scored foods and nutrients further adjusted for individual food items on a continuous scale.

Patterns and confounders	Food item		Dietary pattern	
Prudent	**OR**	**95% CI**	**OR**	**95% CI**
Fresh vegetables	1.00	0.89-1.13	0.81	0.68-0.97
Cooked vegetables	0.95	0.81-1.11	0.84	0.70-0.99
Total fruits	0.94	0.82-1.08	0.85	0.71-1.02
Fish	1.07	0.90-1.27	0.82	0.70-0.96
Drinker	**OR**	**95% CI**	**OR**	**95% CI**
Alcohol	0.98	0.88-1.08	1.31	1.06-1.62
Meat, milk & rice	**OR**	**95% CI**	**OR**	**95% CI**
Fried red meat	1.01	0.92-1.11	1.34	1.14-1.57
Dairy foods	0.99	0.84-1.17	1.35	1.14-1.61
Rice	0.95	0.85-1.05	1.39	1.18-1.63
Antioxidants	**OR**	**95% CI**	**OR**	**95% CI**
Glucose	0.89	0.61-1.30	0.88	0.65-1.19
Fructose	1.10	0.85-1.42	0.75	0.58-0.97
β-Sitosterol	0.71	0.39-1.27	0.97	0.69-1.37
Campesterol	0.87	0.62-1.24	0.88	0.68-1.14
Carbohydrates	**OR**	**95% CI**	**OR**	**95% CI**
Starch	0.87	0.72-1.05	1.40	1.22-1.77
Dietary fiber	0.62	0.37-1.03	1.36	1.14-1.63
Thiamine	0.95	0.80-1.14	1.30	1.03-1.64
Riboflavin	0.93	0.82-1.05	1.28	1.09-1.49

than studies only assessing one specific food group or nutrient. In fact there are some statistical tools that suggest that factor analysis is superior, as was shown in our Table 6 [21]. This viewpoint is supported by the fact that people do not eat foods or nutrients in isolation but in a complex mixture, as shown in the factors.

The prudent pattern was inversely associated with gastric cancer. This pattern showed high loadings for vegetables, legumes, and fruits. Previous studies [22-26] found the similar results, that is, decreased risk of gastric cancer with high consumption of vegetables and fruits.

The drinker pattern was positively associated with risk of gastric cancer. In fact, when this pattern was further adjusted for total alcohol drinking, the risk was not attenuated. In previous studies, alcoholic beverages were associated with an increased risk of stomach cancer [27-29]. It is possible that alcohol could act in gastric carcinogenesis by inducing chronic superficial gastritis.

The so-called meat, milk and rice pattern was directly associated with gastric cancer risk. Meat intake has been considered as an important risk factor for stomach cancer [30-31]. Concerning rice, Segi et al. [26] reported its direct association with gastric cancer in its pioneer study conducted in Japan.

The antioxidant pattern was inversely associated with the risk of stomach cancer. This is in accordance with previous reports which reported an important role in preventing the early steps of gastric carcinogenesis [32-33]. In particular vitamin C and β-carotene have a strong role against oxidative stress in the gastric mucosa. According to Correa et al. [32] the combination of supplements of ascorbic acid plus β-carotene induces an important regression of intestinal metaplasia and dysplasia of the gastric mucosa.

The carbohydrates pattern was directly associated with risk of stomach cancer. This pattern showed high loadings for starch, fiber, thiamine, riboflavin, and sodium. In fact starchy foods like rice, white bread, and potato are strong determinants of gastric cancer [11, 24-25].

In summary, the drinker, meat, milk and rice, and carbohydrate dietary patterns enhanced the risk of gastric carcinogenesis. On the contrary, both the prudent and antioxidant dietary patterns were inversely associated with risk of stomach cancer. It could be concluded that factor analysis is a powerful tool for exploring the role of diet in relation with gastric cancer.

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