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Correlation between Food Expenditure and Breast Cancer in Italy

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Abstract

Background: According to the International Agency of Research on Cancer (IARC), the prevalence of breast cancer in women has been shown to be positively correlated with the consumption of red and processed meats. A number of other studies have suggested that dairy products and alcohol are causative, and that the Mediterranean diet is protective.

Objective: To correlate breast cancer with food expenditure in a sample of 19500 families in 540 Italian municipalities representing the 6.3 % of the total.

Methods: Expenditure on 56 of the most sold food categories were analysed. The ISTAT (Italian National Institute of Statistics) records from 2016 were compared with breast cancer deaths in 2019 to look for correlations. Stochastic analyses (multiple correlation, prediction profiler, and cluster and principal component analyses) and non-stochastic analyses (fourth generation neural networks) were used to determine correlations.

Results: Red and processed meats did not turn out to be causative of breast cancer in any of the analyses. On the contrary, pork was shown to be protective, as was sugar and pasta. Alcohol and, surprisingly, yogurt and fresh vegetables were found to be causative. In particular, the northern regions of Italy were shown to have a significantly higher prevalence of breast cancer deaths than all the other regions.

Conclusion: Our sales analysis of 56 different foods does not confirm

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the correlation between red and processed meats and breast cancer. Besides wine, other types of food, like yogurt and fresh vegetables, seem to be causative. Further studies are needed to confirm these findings.

Key words: Breast cancer, Food, Red meat, Alcohol, Pork, Processed meat, Fresh vegetables, Yogurt.

Introduction

Data on breast cancer show that it is the most common cancer in women.

The WHO Age Standardized Death Rates (ASDRs) for 2019 show that the lowest rate was in São Tomé and Príncipe (0.008) and the highest in China (90.04). In the 48 countries of Europe, the ASDRs range from 0.08 (Malta) to 23.24 (Russia). The value for Italy is 13.72, very close to the figures for France, the United Kingdom and Germany (15.30, 12.63 and 18.63 respectively) and among the 21 countries bordering the Mediterranean Sea, Italy is the highest after France [1].

More recent data for 2020 has been reported by the International Agency of Cancer Research (IARC) [2].

According to PUBMED, as of December 2022, over 11,000 publications had considered the relationship between foods and breast cancer, and around 2,500 either regarded the analysis of single foods, like milk and yogurt, or were meta-analyses of published studies, or were epidemiological studies; most of them were considered in the last report issued by the IARC [3-9].

Many studies paid some attention to the Mediterranean diet (MeD), which is thought to protect against breast cancer.

The MeD is characterised by a relatively high consumption of cereals, fruits, vegetables, legumes, fish, nuts and olive oil, together with a relatively low consumption of dairy food, red meat, wine [10,11].

The high content of micronutrient and phytochemicals may consider protective [12,13].

However, most of the studies were conducted on relatively small numbers of subjects using food intake questionnaires (FIQ). The epidemiological studies also used the same tools but took larger samples to represent the whole population living in the various geographical areas.

This study takes a different approach: it considers the relationship between foods and breast cancer in Italy by studying a sample of 19500 families and analysing their mean expenditure for 56 types of food. All the foodstuffs concerned are available in COOP (Cooperativa sociale di consumatori) supermarkets, the most important and professional food chain in Italy with stores throughout all twenty Italian regions.

Material and Methods

The breast cancer death prevalence (per 10,000 women) in Italy was taken from the ISTAT records for 2019 [14]. The number of women in the twenty regions of Italy was retrieved from official demographic records [15].

The food analysis data were those from published records (ISTAT) obtained using the CAPI (Computer Assisted Personal Interview) system. This system is considered the most reliable, complete, meticulous questionnaire on food expenditure. It is based on 14-day records compiled with technical assistance [16,17].

Expenditure on food purchased from local stores or produced by households in 2016 was calculated for 19500 families in 540 municipalities in the 20 regions of Italy. The sample represents the 6.3 % of the total municipalities, and is considered by ISTAT representative of all the Italy.

The regions were those of Northern Italy (Aosta Valley or VdA, Piedmont, Liguria, Lombardy, Veneto, Friuli-Venezia Giulia or VG and Trentino-Alto Adige or AA), Central Italy (Tuscany, Emilia-Romagna, Lazio, Umbria, Marche and Abruzzo), Southern Italy (Molise, Basilicata, Apulia and Calabria), and the islands (Sicily and Sardinia).

The final data consisted of the expenditure/year (€) on 56 of the most sold food categories (Table 1).

When necessary (comparison between clusters of regions), the expenditure was transformed into quantities based on the cost/Kg. Since the costs of the foods were not the same throughout Italy, the values in terms of Kg were corrected. For the comparison between the northern regions and all other regions, a correction for a difference of up to 10% was taken into account.

The statistical analysis was conducted in four stages:

[the first was the correlation between mean expenditure/ year for each food category and breast cancer death prevalence (per 10^4); the second was multiple stepwise regression analysis, with the calculation of breast cancer predictor variables; the third was principal component analysis to list the foods with positive or negative effects on breast cancer deaths: the fourth was cluster analysis to determine similarities between regions [18-20]. For some variables, the Mann-Whitney U test was used. The use of expenditure or quantities in Kg does not affect the results of the correlations.

SAS Institute's JMP Pro 14(2019) was used for the analysis.

For the non-stochastic analysis, six different maps depicting minimum spanning trees (MSTs) for the variables were calculated with three metric functions a) values based on the weights produced by an auto-contractive map (Auto-CM) after training; b) values based on linear correlation distance; c) values based on the Euclidean distance. The maps consider the prevalence data as such and also differentiate between "high" and "low" prevalence values, above and below the median respectively [21]. Details of the minimum spanning tree and the three different metrics are provided in the appendix.

Results

Two regions were taken together in the data collected (Piedmont and Aosta Valley). Therefore, the total number of regions that appears in the results is only 19.

Food/breast cancer death correlations

The first finding was that only 15 of the 56 variables were found to be significantly correlated, as shown in Table 1. Six of these were positively correlated since the was an increase in breast cancer death prevalence as the variable increased. Nine other variables were negatively correlated, and could be considered protective against breast cancer deaths. Forty-one variables were totally unrelated (Table 1).

However, the small number of replications (19 regions) suggests that the correlations should be confirmed by multiple regression analysis.

Multiple regression analysis (multiple correlation)

The correlations among the 15 foods that were seen to be related (positively or negatively) with breast cancer deaths are shown in table 2. The foods described are restricted to those with either positive or negative statistically significant r^2 (cut off p <0.01).

There were foods, such as pork meat, pasta, olive oil and dried legumes, which seem to be relatively "independent", while others, such as sugar, yogurt, fresh vegetables and wine, showed some significant correlation (p< 0.01) with other foods.

The presence of correlations among the variables suggests applying multiple regression analysis to determine the contribution of each food to breast cancer deaths and the relative F values that determine the statistical significance. As shown in table 3, none of the single foods (predictors) were statistically significant (F < 0.05) and two values were only < 0.2 (pork and bread & breadsticks). This means that a combination of foods (and not a single food) is necessary to determine the correlation with breast cancer deaths.

The mean total expenditure for the 15 foods in the 19 regions was € 1711 ± 140.5/year. Regarding the foods with positive correlation with breast cancer, the total expenditure was € 1023 ± 149.0, which accounts for about 60% of the correlated foods.

Principal component analysis

This analysis allows us to determine the relative weight of each food (or food group) in determining the correlation with breast cancer deaths. Four components account for almost 76% of the variation in the data. Many possible food combinations were possible, and the only one with a statistically significant forecast profile (p<0.001) is shown in table 4.

Cluster analysis

Cluster analysis was carried out using the factor scores derived from the principal component analysis.

The 19 regions were divided into 3 clusters as shown in table 5. Prevalence of breast cancer for each region is also shown.

Similar regions seem to cluster into Southern Italy (cluster 1), Central Italy (cluster 2), and Northern Italy (cluster 3). The only region that did not follow its geographical location

Food	r^2	Food	r^2
Calf meat	NS	Lard	NS
Beef meat	NS	Margarine	***-0.0061***
Pork meat	***-0.0291***	Milk	NS
Lamb meat	***-0.0021***	Powdered milk	0.0001
Horse meat	NS	Yogurt	0.0430
Poultry	NS	Cheese	NS
Processed meat	NS	Eggs	NS
Game	NS	Citrus fruit	NS
Canned meat	NS	Bananas	NS
Bread & breadsticks	**-0.0040**	Apples	NS
Biscuits	NS	Pears	NS
Pasta	**-0.0175**	Grapes and strawberries	NS
Rice	NS	Nuts	NS
Flour	***-0.0000***	Fruit canned	***-0.0014***
Sugar	***-0.0135***	Fruit frozen	NS
Jams	NS	Legumes fresh/frozen	NS
Ice cream	0.0050	Legumes dry	***-0.0001***
Pastries	NS	Vegetables fresh	0.0076
Coffee	NS	Vegetable dried	NS
Tea	NS	Potatoes	NS
Salt	NS	Tomatoes fresh	NS
Soups	NS	Tomatoes canned	NS
Fish	NS	Mineral water	NS
Fish canned	NS	Fruit Juice	NS
Crustaceans	NS	Non-alcoholic drinks	NS
Olive oil	0.0061	Wine	0.0213
Seed oil	NS	Beer	NS
Butter	NS	Liqueurs	NS
Protective foods are shown in bold italics.			

Table 1: Food expenditure in 540 municipalities in the 19 Italian regions: r^2 between expenditure/year during 2016 and breast cancer death prevalence.

	Pork	Lamb	Bread breadstick	Pasta	Flour	Sugar	Ice cream	Olive oil	Margarine	Powdered milk	Yogurt	Fruit canned	Legumes dry	Vegetable fresh	wine
Pork	1														
Lamb		1					-0.604			-0.611				-0.652	-0.566
Bread breadsticks			1				0.797				0.646			0.591	
Pasta				1											
Flour					1										
Sugar						1			0.633					-0.789	-0.794
Ice cream		-0.604	0.799				1				0.575	0.600			
Olive oil								1							
Margarine					0.689	0.633			1						
Powdered milk		0.614				-0.642				1				0.607	0.639
Yogurt			0.646			-0.653	0.575				1			0.853	0.806
Fruit canned							0.600					1			
Legumes dry													1		
Vegetable Fresh		-0.656	0.591			-0.789				0.656	0.853			1	0.747
Wine						-0.794				0.639	0.806			0.749	1

Table 2: Correlations among 15 foods: r^2 values with $p < 0.01$.

Predictor	Expenditure € Mean ± SD	Probability > F	Breast cancer trend
Bread & breadsticks	427 ± 56.4	0.1727	**positive**
Vegetables fresh	237 ± 51.9	0.7842	**positive**
Pasta	170 ± 19.8	0.4511	negative
Pork	166 ± 32.7	0.1299	negative
Olive oil	149 ± 24.3	0.9931	flat
Wine	147 ± 29.4	0.2889	**positive**
Yogurt	113 ± 21.8	0.2656	**positive**
Ice cream	84 ± 16.6	0.3349	**positive**
Fruit canned	64 ± 1.60	0.9631	flat
Sugar	49 ± 9.40	0.6841	negative
Lamb	31 ± 20.4	0.5717	negative
Flour	29 ± 5.6	0.7379	negative
Legumes dry	25 ± 7.8	0.8429	negative
Powdered milk	16 ± 4.6	0.4818	**positive**
Margarine	5 ± 1.7	0.4498	negative

Table 3: Predictors, expenditure/year, relative probability (> F), and trends (positive, flat, negative).

was Sardinia, which is in the Northern Italy cluster. The higher prevalence of breast cancer deaths in Northern Italy was statistically significant (Mann-Whitney U, $p< 0.01$) compared to clusters 1 and 2 taken separately or together. The food categories in terms of Kg/year are shown in table 6.

The inhabitants of northern Italian regions buy most of the foods considered causative of breast cancer deaths in significantly greater quantities, such as fresh vegetables, yogurt, wine and ice cream, and lower amounts of those seen to be protective (sugar, lamb, flour and dried legumes). Canned fruit, powdered milk, oil and bread and breadsticks (causative), and margarine and pork (protective) were sold in similar quantities.

Minimum spanning tree (MST) maps

Six different maps were considered: three for prevalence data as such, consisting of auto-CM, linear correlation and Euclidean distance; and three concerning the differentiation between "high" prevalence values and "low" prevalence values, above and below the median respectively.

An auto-contractive map is shown in figure 1 as an example.

From analysis of the map, it can be seen that breast cancer deaths are very close to fresh vegetables, wine, yogurt, bread & breadsticks (all in red circles), and very far away

Predictor	Cosine Squared [a]	Coefficient [b]
Vegetables, fresh	0.78417	0.00681
Yogurt	0.73523	0.01586
Sugar	0.72330	**-0.03560**
Wine	0.71213	0.01144
Ice cream	0.60035	0.01860
Lamb	0.51116	**-0.01397**
Bread & breadsticks	0.45471	0.00477
Powdered milk	0.43721	0.05772
Fruit canned	0.37057	0.02100
Flour	0.36539	**-0.04118**
Margarine	0.17834	**-0.09754**
Pasta	0.14632	**-0.00770**
Pork	0.13034	**-0.00440**
Olive oil	0.07467	0.00449
Legumes dry	0.06332	**-0.00955**

a = the squared cosine indicates the interaction (correlation) with all the other variables.
b = contribution of the variable as a predictor in the principal component analysis.
Key: the foods with a favourable trend towards reducing breast cancer deaths are shown in bold and have negative coefficients. On the contrary, a positive coefficient indicates that a food is causative of breast cancer deaths. Flour, sugar and margarine were seen to be protective and may indicate home-made foods such as bread, pasta and pastries (cakes). Powdered milk is also consistent with the preparation of home-made bakery products.

Table 4: The most probable combination relating foods to breast cancer: squared cosine and coefficients of the first principal component equation.

Cluster 1		Cluster 1		Cluster 1	
Calabria	3.24	Abruzzo	3.62	Piedmont VdA [a]	4.99
Sicily	3.88	Umbria	4.49	Liguria	5.40
Campania	3.51	Basilicata	3.31	Lombardy	4.36
Lazio	3,94	Marche	3.96	Tuscany	4.44
Apulia	4.26	Molise	3.83	Trentino AA [b]	3.73
Mean	**3.77**	Mean	**3.84**	Sardinia	4.44
				Friuli VG [c]	5.29
				Emilia-Romagna	3.99
				Veneto	4.15
				Mean	**4.53**

a = VdA or Aosta Valley; b = AA or South Tyrol; c = VG or Venezia Giulia

Table 5: Italian region clusters according to similar correlation patterns.

Food category	Coefficient	Cluster 1 Mean ± SD	Cluster 3 Mean ± SD	Mann Whitney U up to 10% p value difference
Vegetables, fresh	0.00681	273 ± 26.5	204 ± 47.0	<0.01
Yogurt	0.01586	133 ± 13.3	96 ± 8.9	<0.01
Sugar	**-0.03560**	44 ± 4.1	55 ± 10.2	<0.01
Wine	0.01144	169 ± 15.5	126 ± 22.9	<0.01
Ice cream	0.01860	171 ± 20.9	146 ± 20.1	<0.01
Lamb	**-0.01397**	19 ± 13.0	41 ± 20.6	<0.01
Bread & breadsticks	0.00477	467 ± 45.6	391 ± 38.1	>0.05
Powdered milk	0.05772	18 ± 4.3	14 ± 4.0	>0.05
Fruit canned	0.02100	70 ± 9.9	58 ± 10.5	>0.05
Flour	**-0.04118**	26 ± 5.1	33 ± 4.9	<0.01
Margarine	**-0.09754**	4.3 ± 1.1	5.1 ± 1.97	>0.05
Pasta	**-0.00770**	161 ± 8.4	179 ± 17.5	<0.01
Pork	**-0.00440**	158 ± 35.7	174 ± 29.4	>0.05
Olive oil	0.00449	151 ± 28.2	146 ± 21.3	>0.05
Legumes dry	**-0.00955**	22 ± 2.8	27 ± 9.8	<0.05

Table 6: Food expenditure in the different Italian regional clusters: mean expenditure/year ± SD and p values according to the Mann–Whitney U test.

Maps considering total prevalence of breast cancer deaths		
Auto-contractive	***Linear correlations***	***Euclidean distance***
Foods close to the breast cancer pole		
Wine	Vegetables, fresh	Vegetables, fresh
Yogurt	Beef	Yogurt
Vegetables fresh	Yogurt	Wine
Foods very far away from the breast cancer pole		
Legumes dry	Pears	Legumes dry
Seed Oil	Lamb	Lamb
Pork	Coffee	Pork
Lamb	Non alcoholic drinks	Seed oils
Maps considering low prevalence of breast cancer deaths		
Flour	Flour	Pasta
Pasta	Pork	Flour
Milk	Pork	Pork
Lamb		Lamb
Maps considering high prevalence of breast cancer deaths		
Beef	Wine	Vegetables fresh
Vegetables fresh	Vegetables fresh	Yogurt
Yogurt	Yogurt	Wine
		Beef

Table 7: Neural network map analysis of the relationship between food and breast cancer deaths.

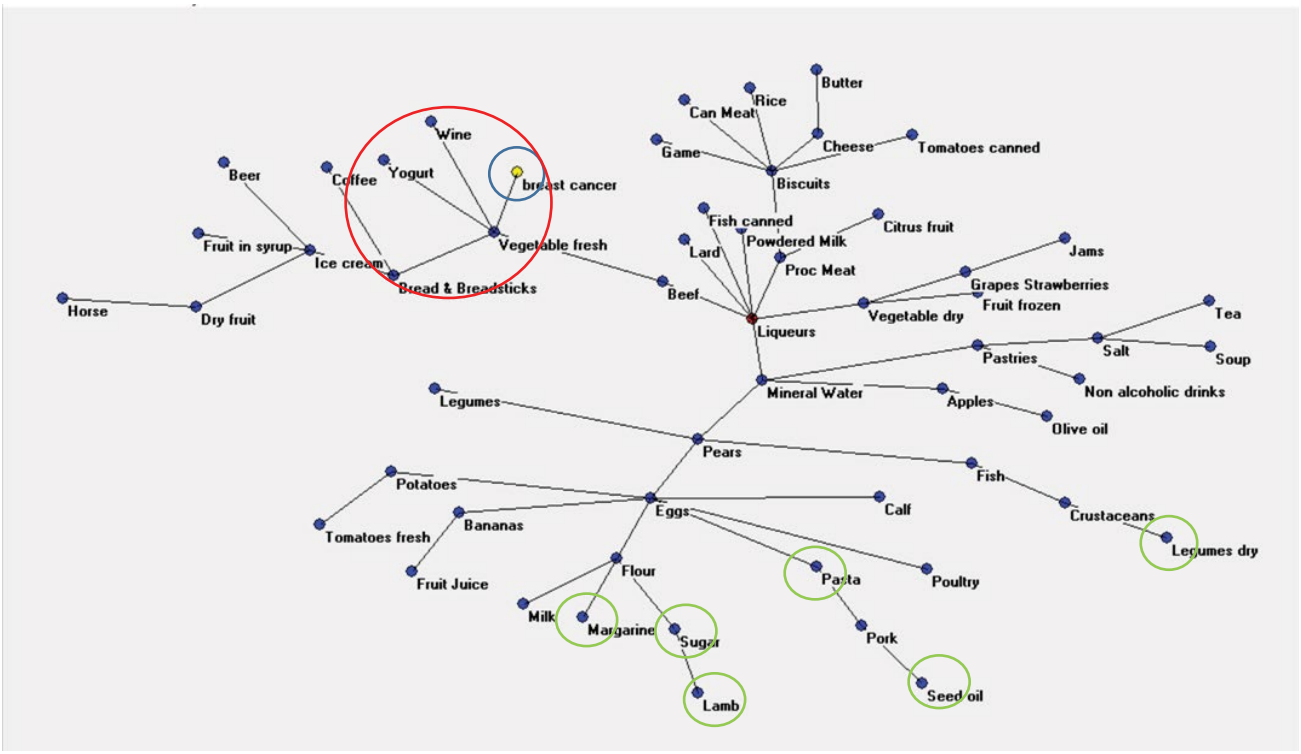

Figure 1: Auto-contractive map of breast cancer deaths in relation to the 56 food variables.

from lamb, seed oil, dried legumes and pasta (all in green circles). The foods which are considered protective are on the opposite side of the map.

A two-pole auto–contractive map (high and low prevalence of breast cancer respectively) is shown in figure 2.

The higher prevalence of cancer (red ellipse) was close to fresh vegetables, wine and yogurt, while the lower prevalence (green ellipse) was close to flour, pork and pasta.

Table 7 summarizes the results of the six maps.

There are foods in common between the six maps. The most frequent with a causative effect were yogurt (6 times), vegetables fresh (6 times), wine (4 times) and beef (3 times). In terms of protection, pork and lamb are the most common (5 times each), followed by flour (3 times), dry legumes and pasta (twice each).

Combination of stochastic and non-stochastic analyses

The foods that appear to be causative in both analyses were: fresh vegetables, wine, yogurt, while lamb, pork, flour and pasta were found to be protective.

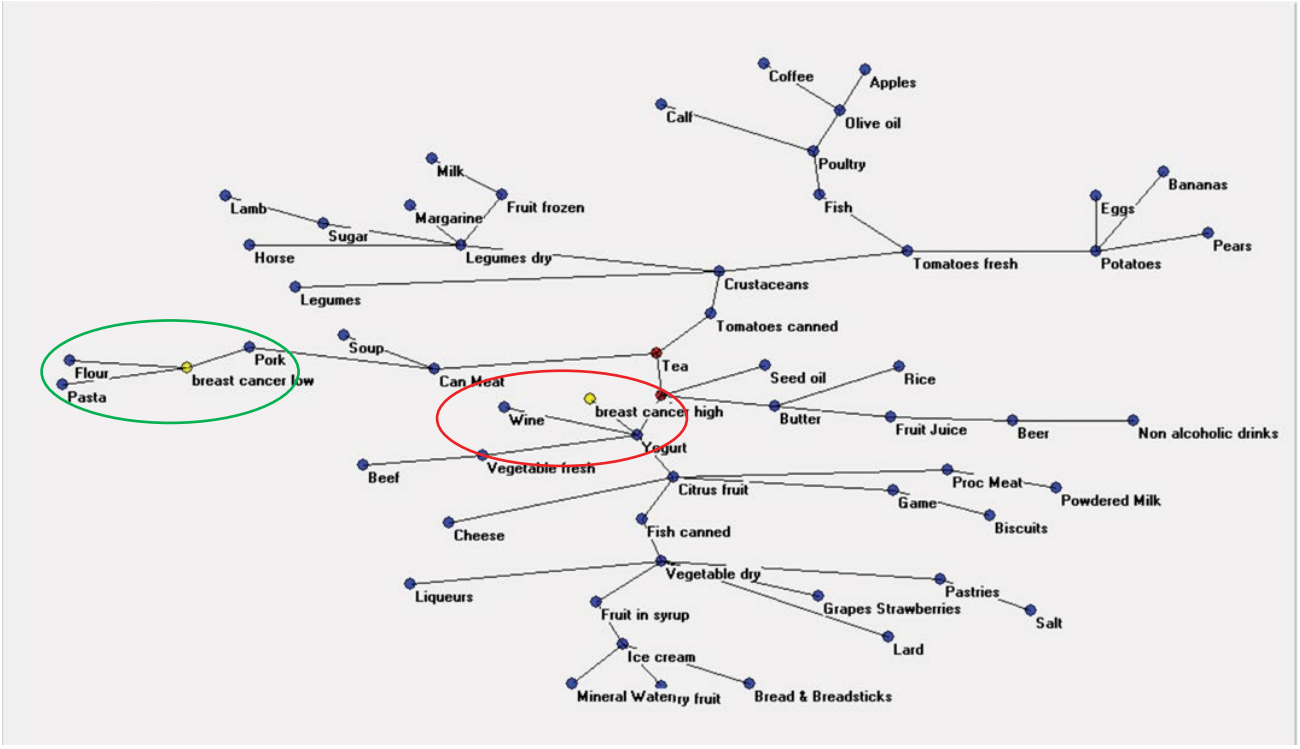

Figure 2: Auto-contractive map of breast cancer deaths in relation to the 56 food variables with regard to high and low prevalence.

Discussion

There are many causes of breast cancer and some of them are well documented, such as genetic traits, family history and lifestyle [22]. The use of some types of medication (e.g., oestrogens, the contraceptive pill, etc.) has been shown to be causative [23]. Environmental factors, including high socio-economic status and pollution (e.g., bisphenol A, parabens, phthalates), have also been well documented as causes of breast cancer [24].

Some foods are also considered causative, such as alcohol and fats.

This study was a preliminary attempt to correlate the foods commonly used in Italy in 2016 with breast cancer deaths.

Our study has several limitations. We will try to identify those that may affect the results.

- The analysis is based on food expenditure, and it may happen that food is bought by one person and eaten by somebody else. Three different cases are possible.

The first is that the subjects do not eat any of the foods that can be considered causative; in this case the data are incorrect, and the correlations have no predictive value.

The second is that the subjects only eat the foods that are considered causative; in this case, the correlations are valid, albeit underestimated.

The third is that the subjects eat both causative and protective foods at random: in this case the correlations can be considered predictive.

Two of the three possibilities lead to valid correlations, and this was considered acceptable by the authors. However, although the results are important, they should be treated with caution.

- The huge number of different foods available were divided into the most common 56 categories using a questionnaire (CAPI) which is a yearly routine system that ISTAT has been using for a long time to determine food categories during only 14 days/year. However, there may be some changes in the food categories during the year.

- Although they belong to the same category, several types of food can be different in different municipalities.

- Each food in a category may have a variable composition in terms of main elements (e.g., fats, proteins, vitamins), which in some cases may vary according to the season (e.g., vegetables). However, this is a common problem in all epidemiological studies, and it is not possible to eliminate this bias.

- Another limitation is that some foods belonging to the same category are produced outside the region where they are distributed, and may come from different producers. For example, the foods sold in Campania might be different from those sold in other regions, and foodstuffs can sometimes be imported from countries outside Italy.

It should be noted that in epidemiological studies of the relationship between foods and diseases, food consumption is established using questionnaires that cover a large number of different foods. However, the foods can be of different origins and this bias is hard to eliminate in any study.

- The expenditure/food ratio: prices were not the same

throughout the country and differences of up to 10% for some foodstuffs were found.

- Some food is not used and ends up as waste; this can lead to bias, but it can be expected to have a similar affect in all regions of Italy.

- If a certain food (or a group of foods) was found to be correlated with breast cancer deaths, even only a small consumption was considered a risk, regardless of whether the ratio of that food with all the other foods was high or low. The risk was considered to be proportional to consumption, although this variable is not entirely linear.

- A common major bias in all epidemiological studies based on food categories is the production quality control, which is usually not taken into account.

Although the origin of the foods in this study might be different, the quality control is quite constant.

However, it is possible for some foods to escape control and quality cannot be guaranteed.

In the case of meat, the origin, rearing and slaughterhouse are indicated on the labels. In the case of dairy products, poultry, pasta, rice, bread, oil, and processed meat, the same information is also on the labels. In the case of fruit and vegetables, the origin should be indicated on the shelf, although it is not labelled most of the time.

In other words, this study is of a similar quality as the epidemiological studies based on direct consumption.

- As regards statistical evaluation, the classic epidemiological studies are based on a large number of replications corresponding to the number of subjects studied (usually > 1000), and the power of the analyses used to discriminate the effects (in terms of α and β errors) is very high, so that a 5% higher risk of any disease ends up being statistically significant. In other words, the *true values* of these analyses are the risks.

In this study, there were only 19 replications (the number of Italian regions), and the power of the stochastic analysis is much lower than it would be in more usual epidemiological studies. However, the number of subjects in this study is at least one order of magnitude higher than in the usual studies (at least 19500 women took part in the study), and the *true values* of the analyses are the food quantities, which are more precise than in other studies. From this point of view, the most reliable analyses are the non-stochastic neural networks which are not tied to the concept of α and β errors.

- The food expenditure data refers to 2016 and breast cancer prevalence was recorded for 2019. Both variables are very well correlated between years. Therefore, the gap between food expenditure in 2016 and breast cancer in 2019 was not considered an important bias.

The number of breast cancer deaths in developed countries has declined globally over recent years, but the figures in Italy have only slightly fluctuated between 3.51 per 10^4 to 3.61 per 10^4 in 2019, and the correlation between years is very high: r^2 over the period from 2016 to 2019 is > 0.95 ($p<0.001$) [14,25].

- Death prevalence, rather than disease prevalence, was used as the correlated variable because it is the most robust value for each disease. In the case of breast cancer, it may be important to differentiate by the specific type of hormonal receptor status, and premenopausal or post-menopausal periods. This was not possible in this study, which considered breast cancer as a single entity.

- Diet is also well correlated between years, and we can expect the 2016 data to be close to the 2019 data, particularly in Italy, since the Mediterranean diet is considered UNESCO World Heritage, and the various regions keep as much as possible to the traditional ways of using and preparing foods.

As mentioned above, this study has several limitations, but at the same time, one quite unique strength: 540 municipalities are the most extensive sample ever used in an epidemiological study.

The first finding was that the prevalence of breast cancer deaths was significantly higher in Italian region cluster 3 (all the northern regions plus Sardinia) than in the rest of Italy.

This is due to the higher consumption of foods that are considered to cause the disease and lower consumption of foods that are considered protective.

The two food categories showed an almost identical picture in both stochastic and non-stochastic analyses: fresh vegetables, wine, yogurt, ice cream and bread & breadsticks had a negative effect, and pork, lamb, flour, pasta and dried legumes had a positive effect.

The first observation is that red meat seems to be involved in breast cancer in two different ways: negative for beef in only one analysis (neural maps) and positive for pork and lamb in both stochastic and non-stochastic analyses.

One aspect concerning meat is worth mentioning. Processed meat, which is considered type I carcinogenic (like benzene) in the IARC report (volume 114) was not found to be a causative factor in this study [26]. From this point of view, it is clear that not all processed meats are the same. Prosciutto di Parma (Parma ham), which contains no nitrates, cannot be compared with similar processed meats made by small producers, or from foreign countries with less stringent quality control. The place of origin, product regulations and quality control can make the difference between the same food being beneficial or toxic.

A correlation between wine consumption and breast cancer was evident in our study, in line with previous publications, and beer and liqueur consumption were found not to be correlated, which means that the *vehicle* of the alcohol should also be considered [27,28].

The slightly negative effect of olive oil was unexpected, although it was not possible to distinguish between extra virgin olive oil (EVOO) and other olive oils. This difference can be important. Common labelling does not include antioxidant content, which is very high in real EVOO, and the degree of acidity can be easily reduced by chemical correction, turning an EVOO into a very poor-quality olive oil.

Calories and other main food components (e.g., fats, proteins and minerals) were not found to be correlated (data not reported). Only some vitamins were found to have both positive and negative effects on breast cancer. These latter data will be part of another ongoing study.

A completely unexpected result was the negative effect of fresh vegetables, although tomatoes and potatoes were not on the list. Fresh vegetables are a very long list of products in any grocery store, and it is currently not possible to consider the individual vegetables separately.

Previous studies have shown that vegetables are not associated with breast cancer or provide some protection [29,30].

In our study, the consumption of fresh vegetables was found to be causative, although it loses some importance in the multivariate analysis (Table 4). In any case, it turned out to be very close to breast cancer on all the maps.

This result must be analysed very carefully because we must not forget that fresh vegetables are very sensitive to environmental pollution, in particular NO_2. This is less important in the case of fruit, since it is protected by its skin, and for legumes, because they are rinsed before boiling.

As regards environmental pollution, the regions in cluster 3 are characterized by a significantly higher presence of NO_2 (nitric oxide) in 2019 compared with the other two clusters. However, there was no significant correlation between breast cancer deaths and NO_2 ($r^2 = 0.0439$) [31].

The presence of aflatoxins in leafy vegetables can also cause harm and this presence has been documented in Italy [32]. Although there are no clinical studies on the relationship between breast cancer deaths and aflatoxin B1, *in vitro* studies have shown that it is possible [34-36].

Unfortunately, fresh vegetables are not routinely checked for aflatoxin.

The negative effect of yogurt was also a surprise.

In a previous meta-analysis study, it was shown that yogurt and milk were not associated with changes in breast cancer prevalence, while yogurt was shown to be protective in another study, unlike milk (and some cheeses) which increased breast cancer prevalence (particularly in the case of ER-negative breast cancer) [37,38].

Aflatoxin M1 could be a possible cause since it may be found in dairy products.

According to the EFSA, milk is checked carefully in Europe for aflatoxin M1 content (limit of 50 ng/L) while, to our knowledge, this is not required for yogurt. Further studies should therefore be carried out [39].

The presence of M1 has been documented in Italy [40,41].

However, despite foods was shown to be important, one may not forget the possible interference of social, ecological, demographic, economical and life style variables.

It was already shown that all the variables connected with the well-being status can be causative of the breast's cancer death, as it is for the presence of concomitant diseases, such as chlamydia and HIV [42].

Conclusion

It is common knowledge that some diseases, including breast cancer, can be caused by foods.

Looking at food expenditure, rather than the methods used in classic epidemiological studies, can be a way of determining those correlations since the number of subjects involved can be much higher than in the classic studies. This method was used to show the difference in breast cancer death prevalence between northern regions of Italy and the others.

The correlations between foods and breast cancer deaths, seen in stochastic and non-stochastic analyses, were similar to those found in classic epidemiological studies. This was the case of alcohol consumption in the form of wine. This study does not however confirm the causative role of red and processed meats. On the contrary, pork and lamb seemed to be protective. Similar protection was seen for pasta and dried legumes, but not for ice cream, canned fruit and bread & breadsticks.

Surprisingly, foods such as yogurt and fresh vegetables (excluding tomatoes and potatoes) were shown to be causative of breast cancer deaths.

Further studies are needed to confirm these correlations, particularly to gain more insight into combinations of foods, as well as routine measurements of possible toxic compounds.

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Conflict of Interest

No conflict of interest.

Authors Contribution

UC and BG conceived the research and wrote the text; MR and EG were responsible respectively for the stochastic and non-stochastic analyses; GSP, BDA, MeR, BC, DFF, TG, AG, PG, RL, MR, GmM, GuM, PR, LC were responsible for food data collection: BL, FF, PL, SN, TS, VL were responsible for prevalence of diabetes 2 deaths data collection; BG, CR, GA, SM, IC, SL were responsible for demographic data collection.

All the authors agreed to the data analysis and to the text preparation.

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