



Associations of Macronutrients Consumption with Cancer Risks from a Global Prospective

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Abstract

Our objective is to establish global relationships between macronutrients and energy consumption and relative risks of cancers. The consumption and cancer incidence data for 162 countries were obtained from FAO and WHO in 2008. Multiple linear regression models were performed. Incidence rates of most cancers were positively correlated with consumptions of fat, protein and energy. However, liver and cervix/uteri cancers were negatively correlated with protein and energy consumptions, and stomach cancer with fat consumption. Low energy, protein, and fat diets are desirable for prevention of most cancers. However, cancers of the stomach, cervix/uteri and liver are exceptions to this rule.

Keywords: macronutrients; energy; cancer; global; population.

1. Introduction

Tobacco, diet, hormonal factors, chronic infections, physical activity, alcohol and radiation are important leading risk factors for cancer. Cancers are now the second leading cause of death throughout the world right after CVD, with increasing potential of surpassing it. From 2000 to 2020, total cancer cases in the developing and developed countries are projected to rise by 73% and 29%, respectively.

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This difference is caused by the projected dietary changes [1-3]. Cross-cultural studies have found huge variations in dietary macronutrients among populations. This contributed to the different cancers incidences in countries [4]. The relationships between dietary fat, carbohydrate (CHO) and protein and cancer have been hypothesized. Some macronutrients, including fat and protein, may increase the risk of different cancers. For example, Japanese breast cancer mortality increased more than 30% with a gradually increasing in fat consumption from 23 to 52 g/person/day through the 15-year period before 1973 [5,6]. Mohr et al. [7] also found that high animal protein consumption and low ultraviolet B have been associated with increased the incidence rates of kidney cancer. However, other macronutrients, including n-3 fatty acids and dietary fiber, may reduce the risk of certain types of cancers [4]. The Seven Countries Study in Europe found that increasing fiber intake by 10 g/d associated with reducing mortality of colorectal cancer by 33% [8]. Moreover, high intake of n-3 fatty acids was associated with decreasing breast cancer risk [9].

Research to date established certain relationships between macronutrients and cancer risks. However, to our knowledge no global/national approach has been used to explore these relationships. Comprehensive studies including cancer and dietary data from all countries of the world will prove to be important tools in discovering new relationships that will help cancer prevention efforts worldwide. Therefore, the objective of study is to establish relationships between macronutrients and energy consumption and relative risks of different cancers.

2. Methods

2.1. Data Sources

Incidence data. The Cancer Incidences, Mortality and Prevalence Worldwide Database is from the World Health Organization (WHO) that contains cancer cases diagnosed around the world that were collected in 2008 from 184 countries [10]. Age-specific incidence rates of cancer for a specific country per 100,000 people per year for 2008, which were estimated as the annual average for the most recent 5-year, were obtained from GLOBOCAN by WHO and used for the present study. A total of 162 countries were chosen because their nutrition data is available from the Food and Agriculture Organization (FAO). This dataset includes 26 types of cancers. WHO estimated age-specific incidence rates of cancer data depending on the available data for each country [11].

Dietary Data. The Food Balance Sheets Database-Food Consumption Nutrients is from FAO. The macronutrient data of fat and protein was from 2005-2007 and dietary energy data was 2006-2008. Then, CHO was calculated based on the following equation “Total Calories = (9*Fat) + (4*Protein) + (4*CHO)”. A total of 162 countries were chosen from 174 countries because their incidence data is available from WHO. The amount of macronutrients was expressed as g/person/d, and total calories as kcal/person/d. FAO estimated three-year averages of per person available energy and the macronutrients from food for human consumption for each country. However, the actual food consumption may be lower because of the magnitude of waste in the household. The amounts and types of consuming foods are estimated by the Government agencies of each country. Then, FAO calculated nutrient intakes by transforming food consumption data by using food composition databases [12].

2.2. Statistical Analyses

The two databases were merged and used to establish relationships between cancer risks and the consumption of macronutrients, and total calories at the country level. Both simple and multiple linear regression analyses were performed by using SPSS software (IBM SPSS Statistics version 20) to assess the statistical relationship between cancer incidences and the consumption of macronutrients and energy. In a multiple linear regression analysis, incidence rates were used as dependent variables and the corresponding mean macronutrient intakes as independent variables. The *P*-value for statistical significance was $P < 0.05$. Data transformations were needed because the residuals were not normally distributed. In most cases, data transformations will improve normality of variables of interest [13]. Log-transformed variables, which are particularly appropriate for normalizing rates [14] were used for incidence data analyses. The incidence rates data was mathematically modified since the logarithm (log) of zero is undefined. The energy intake variable also was excluded from multiple linear regression analysis since this variable is highly correlated with other independent variables. Collinearity often makes some variables statistically insignificant by inflating the standard error.

3. Results

Figure 1 shows the average consumption of energy, protein, fat, and CHO worldwide from 1990-2008. Energy increased from 2,574.4 to 2,763.1 kcal/capita/d, which is about 7% of increasing during this period. The same trends were also true for protein, fat, and CHO, with increases of 10%, 14%, and 4%, respectively. Overall, CHO was the most dominate macronutrient compared with protein and fat, contributing most calories worldwide. Also, Figure 2A, 2B, 2C and 2D show the global consumption patterns of energy, protein, fat, and CHO from the 2005-2008 FAO dataset. The highest energy, fat and protein consumption occurs mostly in Europe, North America, and Australia, while the highest CHO consumption occurs mostly in Middle East.

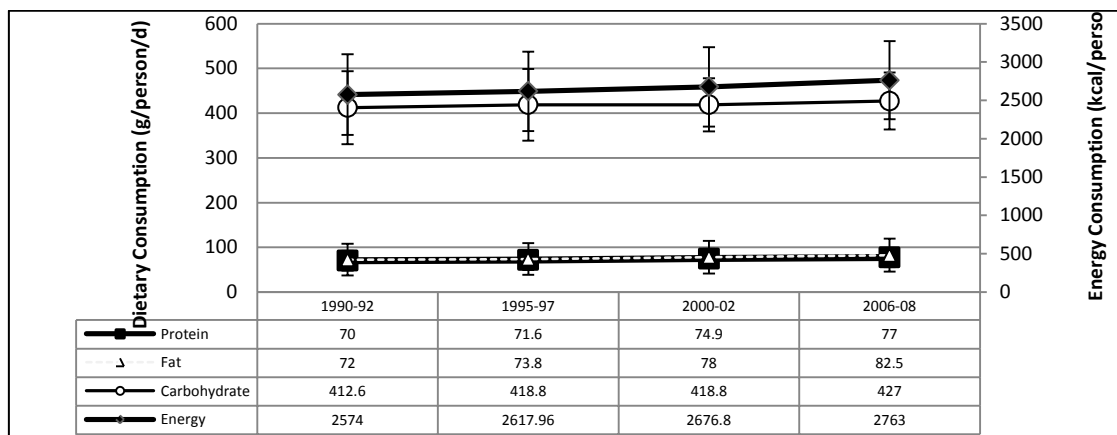


Figure 1: Global trends of macronutrients and energy (1990-2008).

Table 1 shows the estimated multiple linear regression coefficients between the log of different cancer incidence rates and consumption of macronutrients during the period of 2005-2008. Fat consumption was found positively correlated with cancer incidence rates of following cancers: colorectum, gallbladder, pancreas, lung, melanoma of skin, breast, corpus uteri, ovary, prostate, testis, kidney, bladder, thyroid, hodgkin lymphoma, non-hodgkin

lymphoma, multiple myeloma, and leukaemia. However, fat consumption was found negatively correlated with the stomach cancer incidence rates. Protein consumption also was found negatively correlated with the liver and cervix uteri cancer incidence rates. However, protein consumption was found positively correlated with the cancer incidence rates of following cancers: stomach, breast, kidney, and brain with nervous system. CHO consumption was found positively correlated with the cancer incidence rates of following cancers: nasopharynx, gallbladder, larynx, and lung. It clearly demonstrated that consumption of fat is positive correlated with the largest number of cancers, followed by protein and CHO. The most significant negative correlations were between the consumption of protein and cancers of cervix uteri and liver. Incidences of cervix uteri cancer in many European, North American and Middle Eastern nations were relatively low with high protein consumption (Figure 3A). On the other hand, the most significant positive correlation was between prostate cancer and fat consumption. The prostate cancer incidences were high in Europe, North America and Australia where consumptions of fat were high (Figure 3B). Figure 3C shows the positive correlation between CHO consumption and gallbladder cancer incidences, although the magnitude of the correlation was not as strong as the other nutrients.

Energy consumption was not included in the multiple regression model due to its collinearity with other variables. Therefore, simple regression analysis was performed to find its relationships with cancer incidence rates (Figure 4). Energy consumption was found positively correlated with cancer incidence rates of following cancers: lip with oral cavity, other pharynx, stomach, colorectum, gallbladder, pancreas, larynx, lung, melanoma of skin, breast, corpus uteri, ovary, prostate, testis, kidney, bladder, brain with nervous system, thyroid, hodgkin lymphoma, non-hodgkin lymphoma, multiple myeloma, and leukaemia. The strongest positive correlations were with colorectum and lung cancers. For example, Figure 3D is the scattered plot between colorectum cancer incidence rates and energy consumption levels worldwide, which demonstrated a positive association between the two variables. On the contrary, the most significant negative correlations were with cervix uteri and liver cancers. The only cancers did not show significant correlations were nasopharynx and oesophagus (Figure 4).

Figure 5 showed the correlations between total cancer incidence rates and the consumption of macronutrients and energy. Fat and protein intake showed the highest correlation, with an R^2 value of 0.59 and 0.47, respectively. The figure also showed that Europe, North America and Australia peoples are at higher risks.

4. Discussion

In this study, fat consumption was significantly correlated with incidence rates of the following cancers: stomach, colorectum, gallbladder, pancreas, lung, melanoma of skin, breast, corpus uteri, ovary, prostate, testis, kidney, bladder, thyroid, hodgkin lymphoma, non-hodgkin lymphoma, multiple myeloma, and leukaemia. These relationships are in general agreement with the literature. The present study supports the previous findings suggesting that fat consumption has a positive association with the above cancer incidence rates [15-22] However, fat consumption showed a negative correlation with stomach cancer incidence rates and that supports the previous studies [23-25]. In the present study, countries with the highest fat consumption were Belgium, France, Austria, Luxembourg, USA, Italy, Switzerland, Spain, Greece, and Hungary (Figure 2). Total cancer incidence rates vary dramatically among countries and are highest in Europe, Australia, and North America. It

seems that Europeans, North Americans and Australians consume higher fat than the rest of the world and they tend to have higher total cancer incidence rates (Figure 5), with the exception of stomach cancer.

The present study supports the previous findings suggesting that energy consumption was positively correlated with the incidence rates of following cancers: lip with oral cavity, other pharynx, stomach, gallbladder, pancreas, larynx, melanoma of skin, breast, corpus uteri, ovary, prostate, testis, kidney, bladder, brain with nervous system, thyroid, hodgkin lymphoma, non-hodgkin lymphoma, multiple myeloma, leukaemia, lung and colorectum [3, 21, 26-32].

Table 1: Multiple regression coefficients between the log of different cancer incidence rates and consumption of macronutrients, worldwide, 2006-2008.

Variable	Protein	Fat	CHO
Lip, oral cavity	0.002	0.001	-0.0004
Nasopharynx	0.0002	0.001	0.001*
Other pharynx	0.001	-0.001	0.0001
Oesophagus	0.001	0.001	-0.0004
Stomach	0.005*	-0.003*	-0.001
Colorectum	0.004	0.004*	0.0003
Liver	-0.007*	0.002	0.001
Gallbladder	-0.001	0.002*	0.001*
Pancreas	0.002	0.003*	0.0004
Larynx	0.0004	0.001	0.001*
Lung	0.004	0.004*	0.001*
Melanoma of skin	0.004	0.004*	-0.001
Breast	0.004*	0.003*	-0.0003
Cervix uteri	-0.008*	-0.001	3.44E-05
Corpus uteri	0.004	0.003*	0.0001
Ovary	0.002	0.002*	0.0001
Prostate	-0.001	0.006*	-0.0003
Testis	0.003	0.004*	-3.94E-06
Kidney	0.004*	0.003*	0.0001
Bladder	0.003	0.003*	0.001
Brain, nervous system	0.005*	0.002	0.0004
Thyroid	0.001	0.003*	0.0003
Hodgkin lymphoma	0.001	0.002*	0.0002
Non-Hodgkin lym.	-0.0002	0.003*	-0.0002
Multiple myeloma	0.002	0.002*	-0.0002
Leukaemia	0.002	0.002*	0.0003

* indicates statistical significance at 0.05 level ($P < 0.05$)

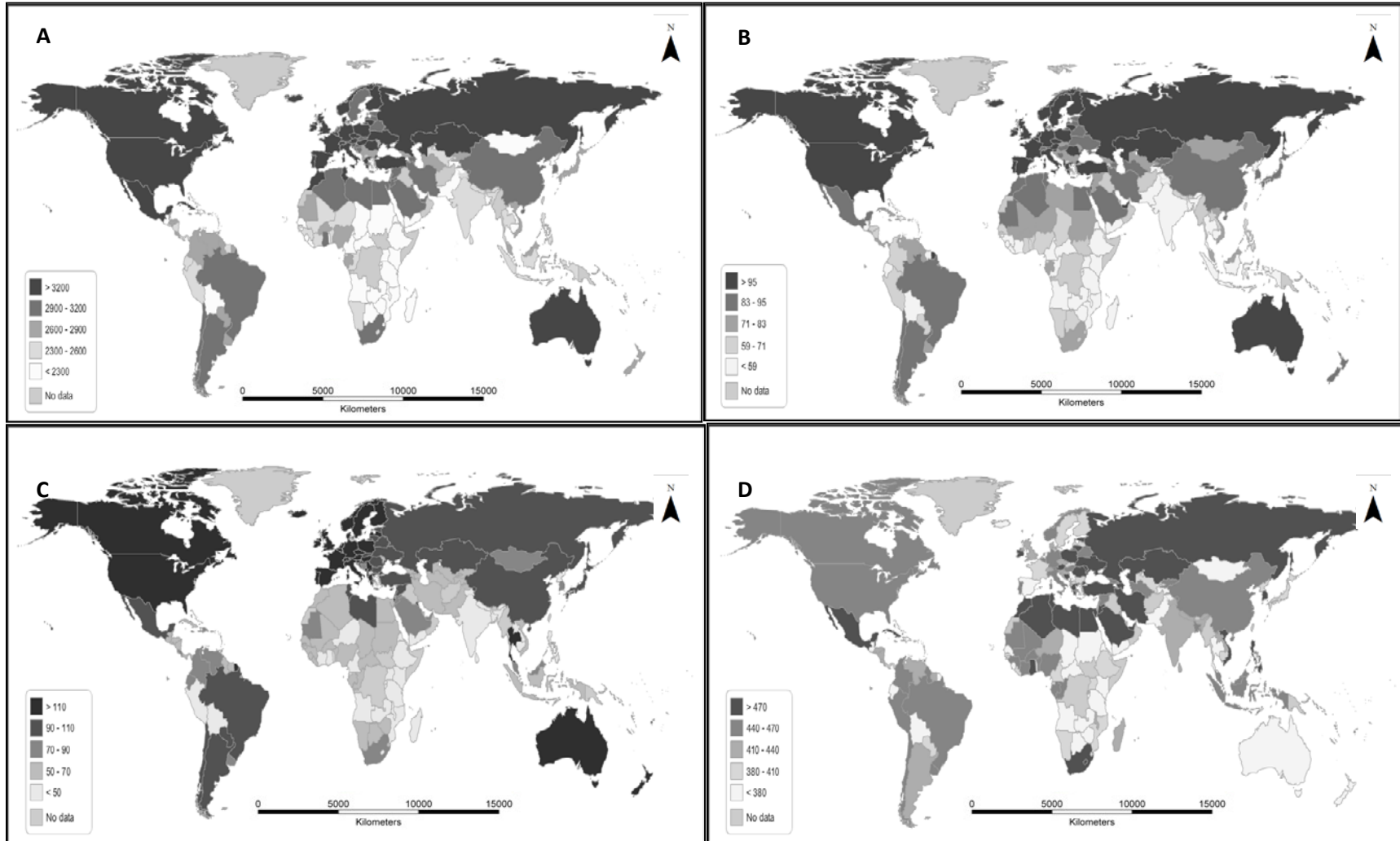


Figure 2: Global consumption patterns of energy and macronutrients. A) energy (kcal/person/d) from 2006-08; B) protein (g/person/d) from 2005-07; C) fat (g/person/d) from 2005-07 and D) carbohydrate (g/person/d) from 2005-07.

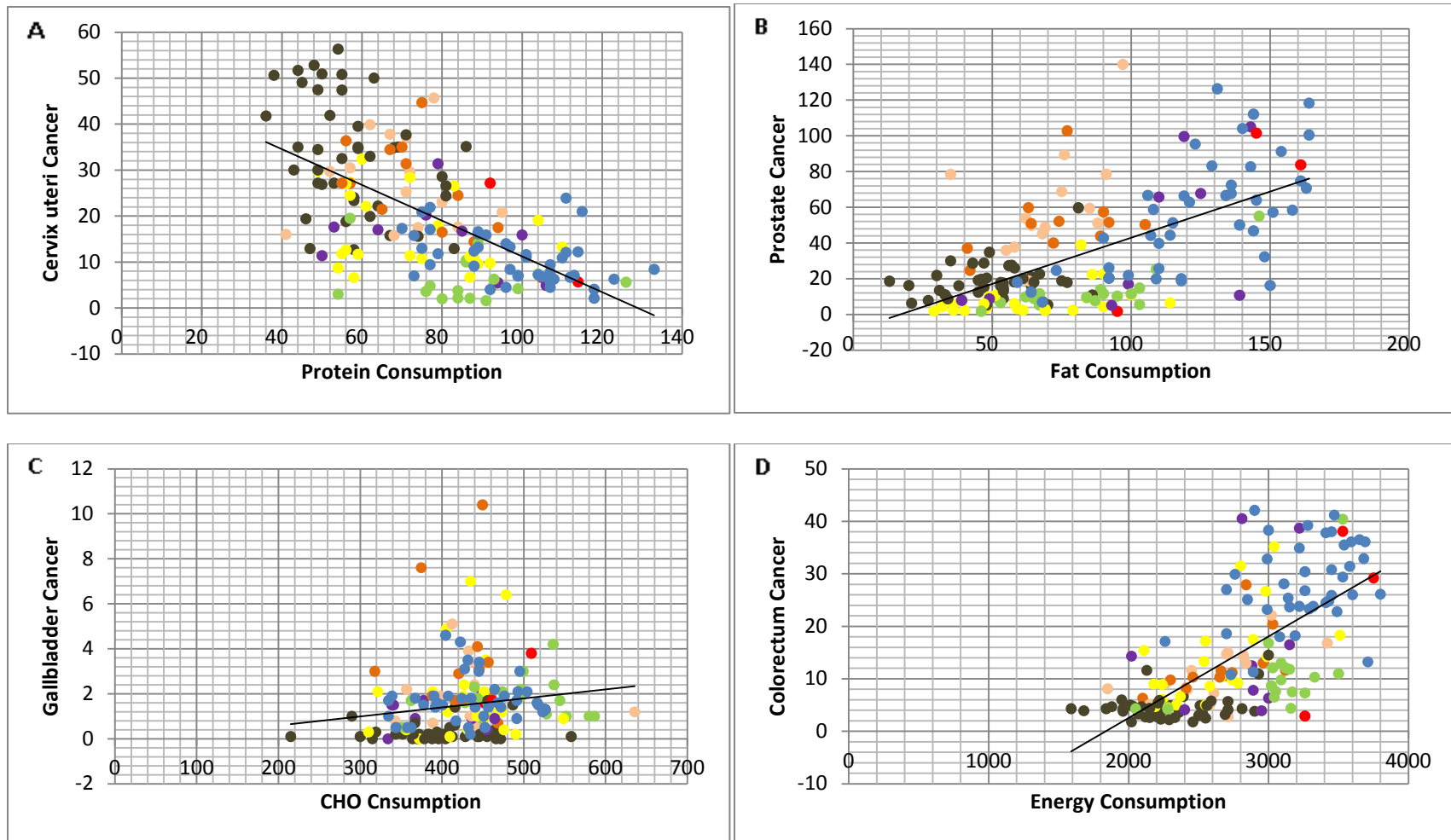


Figure 3: Examples of correlations between cancer incidence rates and consumptions of macronutrients and energy. A) cervix uteri cancer vs. protein consumption; B) prostate cancer vs. fat consumption; C) gallbladder cancer vs. CHO consumption and D) colorectum cancer vs. energy consumption (the color of dots represents the regional of the country “Europe, Middle East, Africa, South America, Australia, Central America, Asia, North America”).

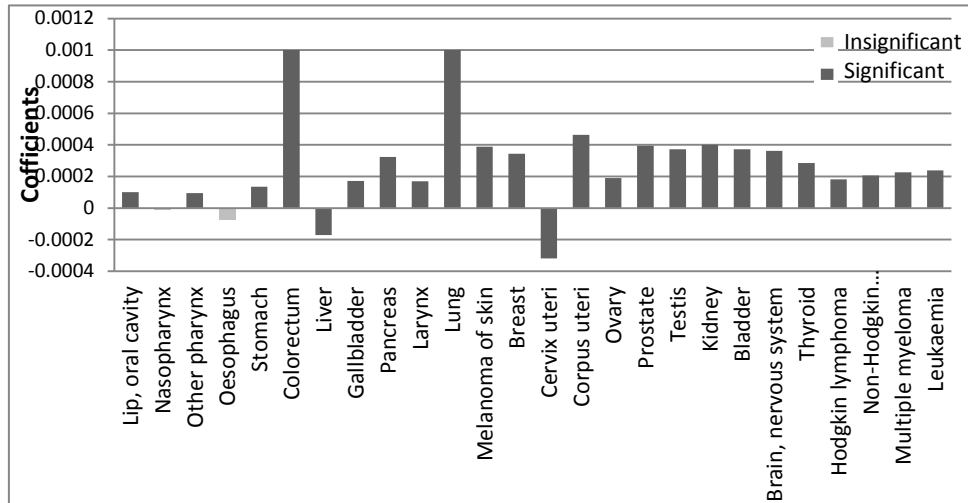


Figure 4: Comparison of simple regression coefficients between energy intakes and cancer rates. The y-axis indicates the coefficients. The p-value for statistical significance is ($P < 0.05$).

In this study, the strongest positive correlations were with colorectum and lung cancers, which seem to be inconsistent with the Albanese³³ findings that energy consumption was negatively associated with lung cancer. However, energy consumption was negatively associated with liver and cervix uteri cancer incidence rates, which seems to be inconsistent with the findings of some previous studies [26, 34]. In the present study, countries with the highest energy consumption were Austria, USA, Greece, Belgium, Luxembourg, Italy, Malta, Ireland, Portugal, and Germany (Figure 2). The total cancer incidence rates vary dramatically among countries and are highest in Europe, Australia, and North America those are also higher in energy consumption than the rest of the world (Figure 5). One possible explanation for these trends is that higher consumption of energy and fat leads to overweight/ obesity, which in turn cause higher risks for a variety of cancers. In addition, higher fat consumption may also cause inflammation which indirectly increases the risks for cancers. Many other factors can also be involved in these relationships.

The present study supports the previous findings suggesting that protein consumption was positively correlated with the incidence rates of following cancers: stomach, breast, kidney, and brain with nervous system [7, 35-38]. However, protein consumption was negatively correlated with the liver and cervix uteri cancer incidence rates. Labani et al. [39] failed to find any relationship between protein consumption and cervix uteri cancer. An Indian study found that rats with higher protein feeding had higher risk for liver cancer [40]. This was very much inconsistent with the present results. In the present study, countries with the highest protein consumption were Iceland, Israel, Luxembourg, Greece, Malta, Lithuania, Portugal, USA, France, and Italy (Figure 3). Those countries also showed higher total cancer incidence rates (Figure 5). It seems, therefore, that higher protein consumption may lead to higher cancer incidence rates. However, higher protein consumption may have protective effects against liver and cervix uteri cancers.

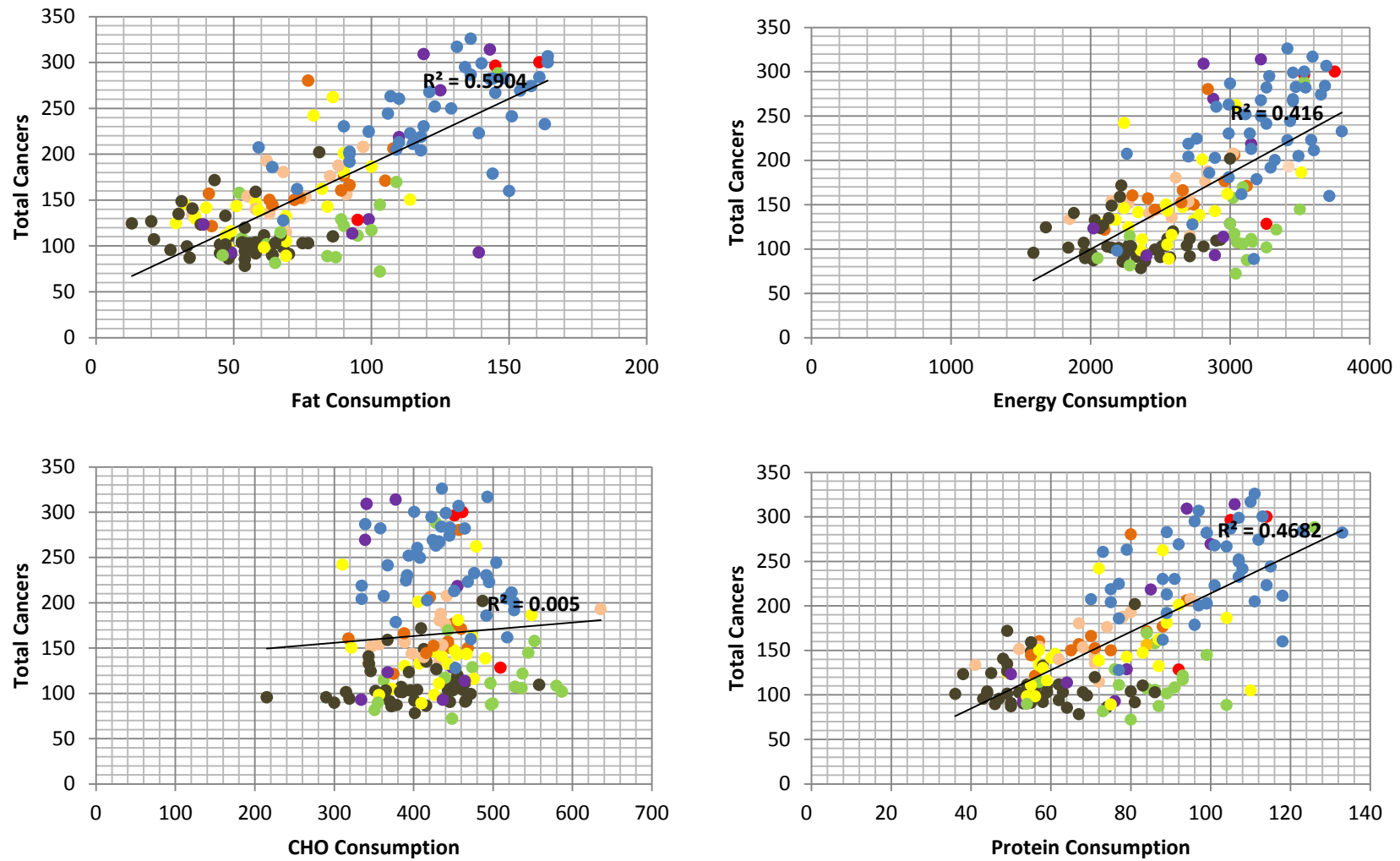


Figure 5: The correlation between total cancer incidence rates and the consumption of macronutrients and energy (the color of dots represents the regional of the country “Europe, Middle East, Africa, South America, Australia, Central America, Asia, North America”)

Our findings confirm the weak association between carbohydrate consumption and cancer risks. The present study found that CHO consumption was positively correlated with cancer incidence rates of following cancers: lung, larynx, gallbladder, and nasopharynx. Zatonski et al. [41] concluded in their study that high CHO consumption is associated with increased risks for lung cancer. However, Nilsson et al. [42] found that low CHO consumption was associated with increasing lung cancer. In the present study, countries with highest CHO consumption were Cuba, Morocco, Egypt, Ghana, Azerbaijan, Kazakhstan, Turkey, Tunisia, Algeria, and Iran (Figure 2). However, much lower total cancer incidence rates in these populations have been observed.

This study had several limitations that may have influenced the associations. First, dietary intake data from FAO rely heavily on gross estimates of the national availability of food rather than the actual consumption. Thus, more accurate global dietary intake data by using different dietary assessment method such as FFQ will be necessary to avoid this error; developing FFQ will be needed for the populations around the world. Second, it is also possible that the 3 years (2005-2008) referent period of dietary intake is insufficient if longer record of diet (eg. 5-10 years) has a stronger influence on cancers risk. Finally, the observed associations in this study do not necessarily indicate the causation relationships between nutrients and cancers since cancer biology is involving many other factors.

5. Conclusions

In conclusion, the global statistics of our study confirm that macronutrients and energy intake is related to cancers risk. Consumptions of macronutrients and energy varied significantly among 162 countries based on data collected by FAO. European, Australian and North American countries tend to have higher consumption of fat, protein, and energy. Middle Eastern countries tend to have higher consumption of CHO. That may also explain some of the geographic variation in cancers incidence rates. Findings of this global study provide further evidence that diets high in energy, fat, and protein may increase the risk, whereas diets high in carbohydrate may not increase the risk of most cancers. However, cancers of the stomach, cervix uteri, and liver are exceptions to this rule because the incidence rates for liver and cervix uteri cancers were negatively associated with consumptions of protein and energy, and stomach cancer with fat consumption. These results recommend that low energy, protein, and fat diets are desirable for prevention of most cancers in many populations. This is consistent with current public health recommendations around the world. Although this study has its limitations, these important relationships established here will help public health policies for global cancer prevention. It also provides a comparison on the relationship between cancer risks and macronutrients between populations. Globally, further investigations are needed to confirm these associations by using another dietary assessment method.

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