Original Article

Attributable Causes of Cancer in China: Fruit and Vegetable

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ABSTRACT

Objective: To provide an evidence-based and consistent assessment of the burden of cancer attributable to inadequate fruit and vegetable intake in China in 2005.

Methods: The proportions of cancers attributable to low consumption of vegetable and fruit were calculated separately to estimate the burden of related cancers for the year 2005 in China. Data on the prevalence of exposure were derived from a Chinese nutrition and health survey. Data on relative risks were mainly derived from meta-analysis. Attributable fractions were calculated based on the counterfactual scenario which was a shift in the exposure distribution.

Results: The total cancer burden attributable to inadequate consumption of fruit was up to 233,000 deaths (13.0% of all cancers) and 300,000 cases (11.6% of all cancers) in 2005. Increasing consumption of vegetable to the highest quintile could avoid total cancer deaths and cases by 3.6% (64,000 persons) and 3.4% (88,000 persons). The contributions to cancer burden were higher in rural areas than in urban areas. They have greater influence on men than on women. The largest proportions of cancer burden attributable to low fruit and vegetable intake were for oral and pharyngeal cancers.

Conclusion: This study showed that inadequate intake of fruit and vegetable makes a significant contribution to the cancer burden. Increasing consumption of fruit and vegetable could prevent many cancer deaths and save many lives. Promoting the consumption of fruit and vegetable is an important component in diet-based strategies for preventing cancer.

Key words: Fruit; Vegetable; Cancer; Population attributable fraction; China

INTRODUCTION

The World Health Report 2002 states that while eating fruits and vegetables can help prevent cardiovascular diseases and some cancers, low fruit and vegetable intake in the diet is responsible for almost three million deaths a year from those diseases[1]. Cancer is the second leading cause of death in China according to the third national death cause survey in 2006. Its mortality was 135.88 per 100,000 and accounted for 22.32% of deaths[2]. Fruits and vegetables contain many nutrients such as vitamins, minerals, and fiber which may individually or in combination be protective against certain cancers. Accumulating evidence suggests that consumption of fruits and vegetables could help prevent certain cancers, particularly those of the digestive system. World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) recognizes that there is possible evidence of decreased risk for cancer of oral cavity, larynx, pharynx, esophagus, lung and stomach with an increased intake of fruits and vegetables[3]. However, their precise contribution had been unclear until the global burden of disease (GBD) was analyzed by using comparative risk assessment (CRA). It has been estimated that globally, 1.8% deaths in 2000 were attributable to low fruit and vegetable intake[4, 5]. The figures were 6% in low-and-middle-income countries, and 3% in high-income countries[6]. It may be considerable that several previous studies in other nations estimated that the low consumption of fruits and vegetables was responsible for 6.0%, 2.7%, 3.6% and 3.2% of the burden of disease in New Zealand[7], Australia[8], the European Union[9] and South Africa[10], respectively. Until now, however, there has been no attempt

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to estimate this contribution in China, which is a developing country with a very large population. This paper reports the research estimating the cancer burden in China that is attributable to low consumption of fruits and vegetables, providing reliable evidence for policy-makers on cancer prevention and control in China.

MATERIALS AND METHODS

The present study is a part of attributable cause of cancer project in China, conducted by the Cancer Institute of Chinese Academy of Medical Sciences (CI-CAMS) and aims to estimate the burden of cancer occurring in China in 2005 and attributable to selected risk factors such as smoking, chronic infection, occupation, hormone, reproduction, and nutrition (including consumption of fruits and vegetables). Population attributable fraction (PAF) was used as an index for the research. It was defined as the proportional reduction in population disease or mortality that would occur if exposure to the risk factor was reduced to an alternative exposure scenario[11] and expressed as a percentage.

The contribution to the cancer burden was estimated separately for fruits and for vegetables, and the estimate was divided by urban and rural regions due to the diverse dietary habit and the difference related cancer incidence and mortality figures between the two populations. In order to be consistent with other parts of the project, we assumed 15 years of latency time for low fruit and vegetable intake to have an effect on the development of cancer.

Definition of Exposure

Fruit and vegetable intakes were treated as continuous variables, and defined as the mean per capita dietary intake of fruit and vegetable measured in grams per day (g/d). The estimates excluded potatoes, preserved vegetables, vegetable juice, fruit juice, and canned fruit based on Chinese studies. "All", "whole", and fresh vegetables were taken into account as well as whole fruits.

The consumption of fruits and vegetables is unusual in that there is an inverse relationship between consumption and cancer. Definitive quantification of the protective effects against cancers has yet to be confirmed, and it is not clear whether there is a threshold effect for fruit and vegetable consumption, although many studies have presented a linear dose-response relationship[12]. We categorized the consumption of fruit and vegetable as the quintile, and the counterfactual scenario used in this work was a shift in the exposure distribution, e.g. one quintile shift or shift of all to the lowest quintile for fruit and vegetable intake.

Data Used for Estimating Prevalence of Exposure

Data on exposure prevalence were derived from the Chinese health and nutrition survey (CHNS) in 1991, which covered 8 representative provinces (48 cities and counties) that vary substantially in geography, economic development, public resources, and health indicators and carried out by the Chinese Academy of Preventive Medicine and University of North Carolina Population Center. The data were announced on the website http://www.cpc.unc.edu/china. The quintiles of fruit and vegetable intake divided by regions (urban and rural) and gender were analyzed in SPSS 12.0 (Table 1).

Data Used for Relative Risk (RR) Estimates

For vegetable consumption, the cancer sites selected included oral cavity, pharynx, esophagus, and stomach, while for fruit consumption, included the same sites in addition to the lung. Considering the large variation in study design, study quality, and measurement of fruit and vegetable intake in different studies identified, it was better to use RR of related cancers from the same pooled analysis[12]. The meta-analysis on the dose-response relationship between fruit and vegetable intake and cancer was conducted by Riboli, et al.[12], including case-control and cohort studies and providing RRs for an additional intake of 100 g/d (Table 2). RRs of certain cancers (oral cavity, pharynx, larynx, and lung) were based on international studies, but RRs on esophageal and gastric cancer were from studies in Asia. The RR estimates were first transformed onto a log scale and divided by 100 to give the log (RR/gram per day). They were then multiplied by the lower intake of every quintile. In the end, assuming that RR at quintile 5 (Q_5) was equal to 1, those at other quintiles divided by that at Q_5 gave final estimates for each quintile (Table 3, 4). As the RRs estimated by genders were unavailable, it was assumed RRs between cancers and an increase in fruit and vegetable intake of 100 g/d for males were the same as that for females.

Cancer Mortality and Incidence Data

Cancer mortality data were derived from the third national death cause survey in China. Cancer incidence data were estimated by using mortality to incidence (M/I) ratios from 32 regional cancer registry sites between 2003 and 2004 in China (Table 5). Details were described in another paper[13].

Calculation of PAF

PAF was estimated for a shift of all to the bottom quintile, that is a full shift, by the following formula.

$$PAF = \frac{\sum_{i=1}^{n} P_i(RR_i - 1)}{\sum_{i=1}^{n} P_i(RR_i - 1) + 1}$$

RR_i was RR at quintile i (i=1, 2, 3, 4, 5).

P_i was the prevalence of quintile i in full shift, which was 20%.

RESULTS

Table 6 displays PAFs of selected cancers in China in 2005 estimated according to region and gender. The results in Table 7 show that if everybody had increased consumption of fruit up to the highest quintile of the distribution, the cancer deaths would be avoided by 11.9% and 20.3%, and the cancer cases by 9.8% and 16.3% in

Table 1. Distribution of fruit and vegetable intake (g/d) in 1991 in China

Quintile	Urban				Rural			
	Male		Female		Male		Female	
	Fruit	Vegetable	Fruit	Vegetable	Fruit	Vegetable	Fruit	Vegetable
1	<33.3	<166.7	<33.3	<166.7	<33.3	<158.3	<33.3	<150.0
2	33.3-	166.7-	33.3-	166.7-	33.3-	158.3-	33.3-	150.0-
3	66.7-	250.0-	58.3-	233.3-	50.0-	250.0-	50.0-	233.3-
4	100.0-	333.3-	100.0-	300.0-	66.7-	333.3-	80.0-	316.7-
5	150.0+	441.7+	150.0+	416.7+	133.3+	458.3+	141.0+	433.3+

Table 2. RR of specific cancers due to an increase in fruit and vegetable intake of 100 g/d

Cancer site	RR (95% CI)		Design	Population	Reference
	Fruit	Vegetable			
Oral cavity, pharynx	0.53 (0.37-0.76)	0.84 (0.67-1.07)	Meta-analysis	Worldwide	Riboli 2003
Esophagus	0.68 (0.43-1.06)	0.98 (0.91-1.05)	Meta-analysis	Asian	Riboli 2003
Stomach	0.56 (0.40-0.79)	0.92 (0.86-0.98)	Meta-analysis	Asian	Riboli 2003
Lung	0.85 (0.78-0.92)	-	Meta-analysis	Worldwide	Riboli 2003

95% CI: 95% confidence interval.

Table 3. RR between specific cancers and fruit intake

Fruit	Oral and pharyngeal cancer		Esophageal cancer		Gastric cancer		Lung cancer	
	M*	F*	M*	F*	M*	F*	M*	F*
Urban								
Quintile 5	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Quintile 4	1.37	1.37	1.21	1.21	1.34	1.34	1.08	1.08
Quintile 3	1.70	1.79	1.38	1.42	1.62	1.70	1.14	1.16
Quintile 2	2.10	2.10	1.57	1.57	1.97	1.97	1.21	1.21
Quintile 1	2.59	2.59	1.78	1.78	2.39	2.39	1.28	1.28
Rural								
Quintile 5	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Quintile 4	1.53	1.47	1.29	1.27	1.47	1.42	1.11	1.10
Quintile 3	1.70	1.78	1.38	1.42	1.62	1.69	1.14	1.16
Quintile 2	1.89	1.98	1.47	1.51	1.79	1.87	1.18	1.19
Quintile 1	2.33	2.45	1.67	1.72	2.17	2.26	1.24	1.26

*M: male; F: female.

Table 4. RR between specific cancers and vegetable intake

Vegetable	Urban						Rural					
	Oral and pharyngeal cancer		Esophageal cancer		Gastric cancer		Oral and pharyngeal cancer		Esophageal cancer		Gastric cancer	
	M*	F*	M*	F*	M*	F*	M*	F*	M*	F*	M*	F*
Quintile 5	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Quintile 4	1.21	1.23	1.02	1.02	1.09	1.10	1.24	1.23	1.03	1.02	1.11	1.10
Quintile 3	1.40	1.38	1.04	1.04	1.17	1.17	1.44	1.42	1.04	1.04	1.19	1.18
Quintile 2	1.62	1.55	1.06	1.05	1.26	1.23	1.69	1.64	1.06	1.06	1.28	1.27
Quintile 1	2.16	2.07	1.09	1.09	1.45	1.42	2.22	2.13	1.10	1.09	1.47	1.44

*M: male; F: female.

urban and rural areas, respectively. It was estimated that about 233,000 deaths (13.0% of all cancers) and 300,000 cases (11.6% of all cancers) were attributable to inadequate consumption of fruits throughout China. For vegetables, the estimates of PAFs were 3.0% and 4.2% for cancer deaths, and 2.7% and 4.2% for cancer cases in urban and rural areas, respectively. In all, eating more vegetables can save 64,000 deaths (3.6% of all cancers) and 88,000 cases (3.4% of all cancers) in all regions (Table 7). The contributions of fruit and vegetable consumption were greater in rural areas than in urban areas.

Furthermore, our results showed that if men had more fruits, about 156,000 deaths (13.7% of all cancers) and 203,000 cases (13.3% of all cancers) would be avoided. If they had enough vegetables, the estimate would be 44,000 deaths and 61,000 cases. For women, 11.7% of deaths and 9.2% of cases were attributed to low fruit intake, and 3.1% of deaths and 2.6% of cases attributed to low vegetable intake (Table

8).

It was confirmed that taking more consumption of fruit and vegetable could prevent more deaths and save more lives. However, it seemed that low fruit intake contributed a greater proportion to the cancer burden than low vegetable intake for both men and women, and their effects on cancer for urban residents were more than that for rural. Low fruit and vegetable intake may have a greater influence on cancer burden for men as compared to women. In addition, those results showed that the largest proportions of cancer burden attributable to low fruit and vegetable intake were for oral and pharyngeal cancers (Table 6, 7).

Table 5. Number of deaths and cases of selected cancer in 2005 in China

Cancer site	ICD 10	Men		Women	
		Deaths	Cases	Deaths	Cases
Urban					
Oral cavity and pharynx	C00-08, C09-10, C12-14	3633	8536	1566	4313
Esophagus	C15	43679	54051	17729	21967
Stomach	C16	86429	118754	42235	56645
Lung	C33-34	154913	174944	74549	83942
All site but non-melanoma skin	C00-96 but C44	526490	753635	312851	572987
Rural					
Oral cavity and pharynx	C00-08, C09-10, C12-14	3721	5321	1630	2601
Esophagus	C15	88006	109310	40819	51261
Stomach	C16	126434	173912	63658	79069
Lung	C33-34	130957	152684	59992	71470
All sites but non-melanoma skin	C00-96 but C44	610387	774112	341885	477427

Table 6. PAFs of selected cancers in China (%)

Cancer site	Urban				Rural			
	Male		Female		Male		Female	
	V*	F*	V*	F*	V*	F*	V*	F*
Oral cavity, pharynx	32.3	42.9	30.7	43.5	34.1	40.8	32.5	42.4
Esophagus	4.1	28.0	3.9	28.5	4.4	26.6	4.1	27.8
Stomach	16.3	39.8	15.5	40.4	17.3	37.8	16.5	39.4
Lung	-	12.5	-	12.7	-	11.9	-	12.5

*V: vegetable; F: fruit

Table 7. Number of cancer deaths and cases attributable to low fruit and vegetable intake by regions in China

Cancer site	Deaths		Cases	
	F*	V*	F*	V*
Urban				
Oral cavity, pharynx	2240	1654	5538	4081
Esophagus	17283	2482	21395	3073
Stomach	51462	20634	70149	28137
Lung	28832	-	32529	-
Total	99816	24771	129610	35291
Percent of all sites (%)**	11.9	3.0	9.8	2.7
Rural				
Oral cavity, pharynx	2208	1800	3273	2662
Esophagus	34776	5523	43350	6883
Stomach	72924	32402	96961	43171
Lung	23117	-	27143	-
Total	133025	39725	170727	52717
Percent of all sites (%)**	20.3	4.2	16.3	4.2
All				
Oral cavity, pharynx	4448	3454	8811	6743
Esophagus	52059	8005	64745	9956
Stomach	124386	53036	167110	71308
Lung	51949	-	59672	-
Total	232841	64496	300337	88008
Percent of all sites (%)**	13.0	3.6	11.6	3.4

*F: fruit; V: vegetable. **All sites but non-melanoma skin

Table 8. Number of cancer deaths and cases attributable to low fruit and vegetable intake by gender in China

Cancer Site	Fruit				Vegetable			
	Male		Female		Male		Female	
	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases
Oral cavity, pharynx	3076	5831	1373	2979	2444	4574	1011	2170
Esophagus	35666	44244	16392	20501	5628	6982	2377	2974
Stomach	82241	113072	42144	54038	36012	49513	17025	21795
Lung	35000	40098	16949	19573	-	-	-	-
Total	155983	203246	76858	97091	44083	61069	20413	26938
Percent of all sites (%)*	13.7	13.3	11.7	9.2	3.9	4.0	3.1	2.6

*All sites but non-melanoma skin

DISCUSSION

Our work suggests that fruit and vegetable intake is an indispensable part of a healthy diet, and that a lack of intake may play an important role in cancer development. It seems that fruit intake has a greater effect on cancer. Fruit and vegetable may have more influence on cancer burden for men. A total of 64,000 deaths (3.6% of all cancer deaths) and 88,000 cases (3.4% of all cancer cases) of cancer may be attributed to the inadequate consumption of vegetables. Among these attributable cases, more than half of cancer deaths and cases happened in rural areas, and about 2/3 involved men. The contribution to cancer cases and deaths of fruit intake was approximately three times greater than that of vegetable intake. However, their contributions to cancer burden in urban areas were both less than those in rural areas.

It was worth mentioning that the estimates of PAFs would be different if another method was used in the study. When the counterfactual scenario used was defined as one quintile shift for fruit and vegetable intake, low fruit intake contributed to about 114,000 cases (4.4% of all cancer) and 88,000 deaths (4.9% of all cancer), and the calculations for vegetable were 84,000 cases (3.2% of all cancer) and 62,000 deaths (3.5% of all cancer). It showed that the PAFs were obviously different by using distinct counterfactual scenario in vegetable and fruit exposure. However, comparing the results of two methods, it may be considerable that the more fruit and vegetable are eaten, the more cancer cases and deaths will be saved.

Most previous estimates of the cancer burden in global and other national projects have covered the synthetic effect of total fruit and vegetable intake[4, 6-8]. We separately estimated the cancer burden attributable to low intake of fruits and vegetables, for the following reasons. Fruits and vegetables contain different nutrients and have different nutritional values. For example, the contents of vitamins, minerals, fiber, and phytochemicals are higher in most vegetables especially in dark vegetables, while carbohydrates and organic acids are higher in fruits. In addition, fruits do not require heating prior to consumption, so their nutritional components are less likely to be affected by cooking. Thus, fruits and vegetables may have different health outcomes. The most powerful evidence available showed that fruits and non-starchy vegetables may help prevent cancers of oral cavity, pharynx, esophagus and stomach. It is also possible for fruit consumption to help prevent lung cancer[3].

Moreover, the effects on the same cancer are distinct between fruit and vegetable consumption, which are shown by RRs or odds ratios[12]. Therefore, it is better that fruits and vegetables are segregated to estimate their individual contributions to the cancer burden. Furthermore, obtaining the data on separate RR between fruit and vegetable and cancer would have been easier than gathering their data together. No studies in China or Asia have calculated the risks associated with total fruit and vegetable consumption, and few studies have estimated RRs for quantified levels of fruit and vegetable consumption that would allow estimates of a continuous variable. Thus, we use the results of meta-analysis from Riboli and Norat to derive the final RR estimates and calculate the PAFs of fruit and vegetable consumption individually.

From the CHNS, we can find that urban residents eat more fruits and less vegetables than rural residents[14]. This may be due to the distinct availability of fruit and vegetable and economics between two areas. It may be more convenient for urban people to obtain different kinds of fruits, whereas rural people can get more vegetables. There was a little difference between men and women in the consumption of fruits and vegetables. Men eat slightly more vegetables than women, and eat less fruit[14, 15]. The dietary pattern had diverse effects on health in various regions, which was verified by cancer mortality and incidence. Therefore, it was reasonable to divide the estimates of PAFs by regions and gender.

There are several limitations in this study due to the data used and other uncertainties. Firstly, vegetables and fruits both comprise very heterogeneous groups and may be different in studies included in the meta-analysis of vegetable and fruit and cancer. Fruits and vegetables can both be consumed in many different ways that will influence their biochemical content, which in turn may influence their health effects. Secondly, all data on RRs from the dose-response meta-analysis were not from a Chinese study, since the data were not available. Further research is needed on the dose-response relationship between fruit and vegetable and cancer in China. Thirdly, in the present study, only cancers of lung, esophagus, stomach, mouth and pharynx were examined because the evidence in the published literature showed that it was possible for fruit and vegetable to decrease their risk. Cancers for which the WCRF/AICR review reported a limited-suggestive association (cancers of nasopharynx, colorectum, liver, pancreas, etc.) were not included. Fourthly, the gender and age were not considered because many studies did not analyze RRs by sex and age. Due to the limitations of the evidence for men and women separately and different age groups, it was decided to apply the same RR/g estimates to both sexes and all age groups with the age more than 18 years for each outcome, and to only take adults (age ≥18 years) into account when analyzing the distribution of fruit and vegetable intake. However, the consumption of fruits and vegetables between males and females is different in each age group. Generally, men eat a little more vegetables, and women eat more fruits, while the middle-aged eats more fruit and vegetable than the young and the elderly[14, 15]. There is still insufficient information on how age and sex would influence the RRs at varying intakes of fruit and vegetable. To some extent, those limitations have an effect on the accuracy of our estimates.

Although there are some limitations in this study, our estimates of the cancer burden attributable to inadequate consumption of fruit and vegetable can provide evidence applicable to public health policy. An increase in consumption to 150 g/d for fruits and 400 g/d for vegetables could help avoid large numbers of cancer deaths (fruit: 233,000; vegetable: 64,000) and cancer cases (fruit: 300,000; vegetable: 88,000). In the past few years, a large shifts in life style have taken place in China. China is becoming more westernized with greater incorporation of western foods and dietary habits, and the burden of noncommunicable diseases is increasing. Vegetable consumption has decreased and fruit consumption has slightly increased, but both of them do not meet the recommended nutrient intakes (RNIs). CHNS in 2002 reports that the proportions of consumption to RNIs (400-500 g/d for vegetable, 100-200 g/d for fruit in 1997) is only 13% for vegetable and 11% for fruit[14]. It is convincing that low fruit and vegetable intake can promote some noncommunicable diseases including cancers. A number of national and international bodies advocate an increase in consumption of fruits and vegetables to 400-500 g/d. This has been translated into national health promotion campaigns, including the "5-a-day" programs in the USA and the UK and similar initiatives in other countries[5]. Recently, program of Healthy China 2020 has been introduced by Ministry of Health. The promotion of greater fruit and vegetable consumption should be an important component of this initiative.

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