

RESEARCH ARTICLE

Life-Style Habits in a High-Risk Area for Upper Gastrointestinal Cancers: a Population-Based Study from Shanxi, China

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Abstract

Background: Cancer is a burden on humanity and ranks as a leading cause of morbidity and mortality in China. Shanxi province has its unique cancer patterns and the burden is increasing. In this study, we aimed to assess the pattern of dietary habits and life-style in Shanxi, a high-risk area for upper gastrointestinal cancers in China and further evaluate the trends in cancer incidence and mortality based on registered data. **Materials and Methods:** Data on lifestyle, diet, physical activity were obtained from the household health survey at Zhongyang from 2013 to 2015. Cancer diagnoses were reported to Shanxi Center for Disease Control and Prevention (SCDCP). Population-based cancer incidence data and mortality data of 2012 were collected from the SCDCP. All incidence and death rates were expressed per 100,000 populations. Univariate analysis was performed using the Chi-squared test or Fisher's exact test. **Results:** Overall, deficiencies in fresh fruits and vegetable food, and intake of hot food, salted food, or pickled food are serious problems in Shanxi, especially in rural areas. Upper gastrointestinal cancers were the most commonly diagnosed cancers, and the incidence in rural areas is higher than those in urban areas. Cervical cancer is the most common cancer for females. Moreover, the age-specific incidence exhibited an increased trend before 40 years old. Consistent with the previous literature, our epidemiological investigation results suggest that lifestyle, nutrition deficient, and infections were major risk factors for upper gastrointestinal cancers or cervical cancer in Shanxi. Facing a serious situation, we further explored defensible recommendations for the general public in order to promote changes in environments that support healthful eating and physical activity habits, to reduce cancer risk. **Conclusions:** Our results present the current cancer trends in Shanxi and its related etiologic risk factors and provide a theoretical basis to guide public health efforts to prevent and control cancers in the province.

Keywords: Cancer trends - risk factors - Shanxi - China

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Introduction

Cancer ranks the second leading cause of death and is becoming a serious health threat in China (Ministry of Health, 2012). It was estimated there were approximately 4.292 million new cases diagnosed as cancer and 2.814 million died from cancer in 2015, and the cancer incidence and mortality keep increasing (Chen et al., 2016). In the whole country, the most commonly diagnosed cancers are lung cancer, stomach cancer, esophageal cancer, liver cancer and colorectum cancer for males. While for females, breast cancer ranks the highest incidence followed by lung cancer, stomach cancer, colorectum cancer and esophageal cancer (Chen et al., 2014). The five leading causes of cancer death among both men and women are cancers of the lung and bronchus, stomach, liver, esophagus, and colorectum in the whole country (Chen et al., 2014).

However, the cancer patterns in Shanxi province were quite different compared to the country's (Chen et al., 2015; Zhang et al. 2015). Shanxi province is located on China's major coal belt and also the Taihang Mountain, north-central area. It has a total population of 33 million and a geographical area of 156,800 km (Chen et al., 2016), and the gross domestic product (GDP) per capita was the last but one in 2015 in China. Due to the specific geographical location, backward economic level and unsound health system, Shanxi was one of the famous cancer areas in China (Shi et al., 2011). Unfortunately, there is limited report on cancer trends and related risk factors in Shanxi province. In this article, we summarized our investigation data from the "Ningyang" epidemiological investigation project and data from Shanxi Center for Disease Control and Prevention (SCDCP) to evaluate the trends in cancer incidence and mortality and the etiologic risk factors contributing to its unique cancer patterns in Shanxi.

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Materials and Methods

Ethics approval and consent to participate

This study was approved by the ethical committee of Shanxi, China. Written informed consent was received from all participants prior to inclusion in the study.

Consent for publication

We have obtained consent to publish from the participant to report individual patient data.

Study population

A total of 7412 households from Zhongyang county, Shanxi province were enrolled in the “Ningyang” epidemiological investigation project. Of this population, 4034 are males and 3378 are females while 3102 were from urban areas and 4310 from rural areas. Data on lifestyle, diet, physical activity were obtained from the household health survey at Zhongyang from 2013 to 2015 (Table 1). The lifestyle part of survey questionnaire consisted on a list of different food groups including hot food, salted food, pickled food, leftovers, contaminant food, fruits, vegetable food, soy, meat. Other factors such as smoke, alcohol, physical activity, healthy status were also included in our survey questionnaire.

Incidence and Mortality Data

Population-based cancer incidence data were collected from SCDCP. Mortality data from 2012 were provided by SCDCP. The cancer incidence rates from 2012 were calculated with reference to the new cancer cases identified in Shanxi province. All incidence and death rates were expressed per 100,000 populations.

Statistics

The statistical analysis was performed using SPSS software, version 13.0 (SPSS Inc., Chicago, IL, USA). The univariate analysis was performed using the Chi-squared test or Fisher’s exact test. $P < 0.05$ was considered

to indicate a statistically significant difference.

Results

Environmental exposures in Zhongyang county, Shanxi province, China

It is proved that genetic or environmental factors account for large geographic differences in human cancer incidences (Wang et al., 2016). Causes of cancers included aging, medication, lifestyle correlation (such as diet and physical activity), tobacco and alcohol use. These factors can be linked to cancers via affecting cellular processes like carcinogen metabolism, DNA repair, proliferation, differentiation, apoptosis, cell cycle, and inflammation and immunity (Hoeijmakers. 2001). In Shanxi province,

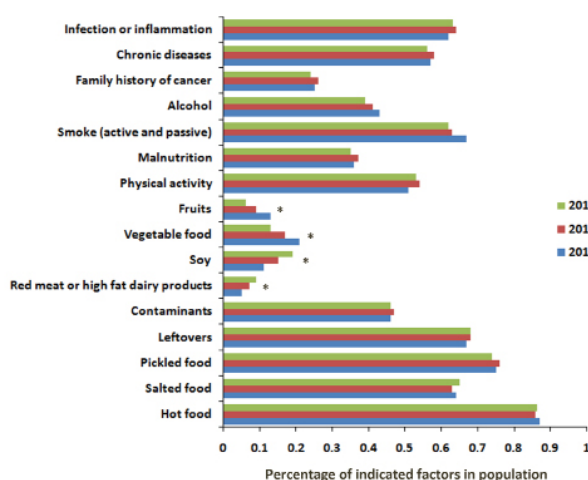


Figure 1. Summarized Results from Epidemiological Investigation Data from Zhongyang Population During 2013 to 2015. The vertical axis denotes reported risk factors related to cancers. Percentage of specific risk factor in the total population was shown on the horizontal axis. * $P < 0.05$

Table 1. Summary of the household health survey at Zhongyang from 2013 to 2015

Lifestyle, diet, physical activity	No. of person with indicated risk factors (n=7412)								
	2013			2014			2015		
	Urban	Rural	Total	Urban	Rural	Total	Urban	Rural	Total
Total	3102	4310	7412	3102	4310	7412	3102	4310	7412
Hot food	2448 (79%)	4000 (93%)	6448 (87%)	2230 (72%)	4144 (96%)	6374 (86%)	2231 (72%)	4180 (97%)	6411 (86%)
Salted food	1974 (64%)	2770 (64%)	4744 (64%)	1690 (54%)	2980 (69%)	4670 (63%)	1803 (58%)	3015 (70%)	4818 (65%)
Pickled food	2340 (75%)	3239 (75%)	5559 (75%)	2113 (68%)	3520 (82%)	5633 (76%)	2375 (77%)	3110 (72%)	5485 (74%)
Leftovers	2053 (66%)	2963 (69%)	4966 (67%)	2030 (65%)	3010 (70%)	5040 (68%)	2030 (65%)	3010 (70%)	5040 (68%)
Contaminants	1040 (34%)	2370 (55%)	3410 (46%)	974 (31%)	2510 (58%)	3484 (47%)	920 (30%)	2490 (58%)	3410 (46%)
Red meat or high fat dairy products	292 (9%)	79 (2%)	371 (5%)	364 (12%)	155 (4%)	519 (7%)	457 (15%)	210 (5%)	667 (9%)
Soy	473 (15%)	342 (8%)	815 (11%)	602 (19%)	510 (12%)	1112 (15%)	738 (24%)	670 (16%)	1408 (19%)
Vegetable food	1311 (42%)	246 (6%)	1557 (21%)	1057 (34%)	203 (5%)	1260 (17%)	774 (25%)	190 (4%)	964 (13%)
Fruits	652 (21%)	312 (7%)	964 (13%)	431 (14%)	236 (6%)	667 (9%)	265 (9%)	180 (4%)	445 (6%)
Physical activity	1689 (54%)	2091 (49%)	3780 (51%)	1702 (55%)	2300 (53%)	4002 (54%)	1813 (58%)	2115 (49%)	3928 (53%)
Malnutrition	890 (29%)	1778 (41%)	2668 (36%)	832 (27%)	1910 (44%)	2742 (37%)	869 (28%)	1725 (40%)	2594 (35%)
Smoke (active and passive)	1940 (63%)	3026 (70%)	4966 (67%)	1750 (56%)	2920 (68%)	4670 (63%)	1705 (55%)	2890 (67%)	4595 (62%)
Alcohol	1996 (64%)	1191 (28%)	3187 (43%)	2003 (65%)	1036 (24%)	3039 (41%)	1901 (61%)	990 (23%)	2891 (39%)
Family history of cancer	703 (23%)	1150 (27%)	1853 (25%)	740 (24%)	1187 (28%)	1927 (26%)	769 (25%)	1010 (23%)	1779 (24%)
Chronic diseases	1365 (44%)	2860 (66%)	4225 (57%)	1371 (44%)	2928 (68%)	4299 (58%)	1151 (37%)	3000 (70%)	4151 (56%)
Infection or inflammation	2030 (65%)	3751 (87%)	5781 (78%)	2095 (68%)	3835 (89%)	5930 (80%)	2255 (73%)	3600 (84%)	5855 (79%)

there are very unique characteristic environmental factors.

Dietary factors With the improvement of living standard in recent years in China, the traditional Chinese dietary pattern has gradually changed to the western dietary pattern, which leads to a rising incidence of many diseases including cancer (Siegel et al., 2015). It was reported that approximately 70% (1.8 out of 2.6 million) of human cancers were caused by harmful dietary habits (Park et al., 2008). Although the higher living standards and urban lifestyle of modern life have resulted in increased attention

to the relationship between tumors and modifiable health behaviors in the country, it has its own characteristics in Shanxi province. According to our investigation data, meat or other high fat dairy products intake per capita among urban residents in Shanxi has increased, however, daily consumption of fruit and vegetables per capita decreased during 2013 to 2015 (Figure 1). Though soy consumption per capita increased, it is still much less than the recommended level. In contrast to this change in dietary patterns in urban areas, the deficiencies in fresh fruits and vegetable food are serious problem in rural areas in Shanxi (Figure 2). Notably, intake of hot food, salted food, or pickled food was popular in both urban and rural areas while contaminant food intake was frequently found in rural areas in Shanxi (Figure 2); great concerns on the consequences caused by this special dietary habit have been raised. Moreover, infection or inflammation was frequently observed in approximately 70-90% of individuals from this population, and more than half of them suffered from chronic diseases.

Physical Activity Physical activity protects against certain cancers, for example, with convincing evidence for colorectal cancer, breast cancer, and probable evidence for lung cancer (Shi et al., 2015). Moreover, equally interpreted as sedentary life may lead to obesity, this is a risk factor for cancer (Singh et al., 2014). According to our investigation data, only approximately half of individuals from this population were physically active as part of everyday life (Figure 1).

Tobacco smoke Tobacco smoke is one of the oldest environmental exposures linked to cancer and contains numerous carcinogenic compounds such as nicotine and its derivatives (Obeidat et al., 2016). Each of them has specific mechanism causing cancer, for example benzo[a]pyrene was metabolized to benzo[a]pyrenediol epoxide resulting in DNA adducts in lung epithelial cells (Linet et al., 2015). Tobacco use (smoking or exposure to tobacco) accounted for 20% of all cancer deaths, with convincing evidence to increase risk for lung cancer (80% in men and 50% women), oral cancer (60% cases, multiple risk with alcohol), esophageal cancer, colorectal cancer and breast cancer (Wang et al., 2013). Our investigation data showed that more than half of people aged over 18 years were smokers in Zhongyang population, and there were more smokers in rural areas than urban areas (Figure 2). Second hand smoke was reported increase the risk for lung cancer incidence and mortality. Based on our investigation data, approximate 80% of women were exposed to second hand smoke from their husband or environment. Among these smokers, approximately 53% suffered smoking-induced diseases and the peak of these diseases is still to come.

Alcohol consumption Excessive alcohol drinking is another risk factor for cancer. It appeared to increase the risk of colorectal cancer in Japanese and breast cancer in the Korean population (Islami et al., 2011). Alcohol is metabolized as acetaldehyde to affect lipid peroxidation generating free radical species (Wang et al., 2016). In our investigation data, alcohol consumption was found in almost half of individuals in this population (Figure 1). It was implicated that combined use of alcohol and tobacco

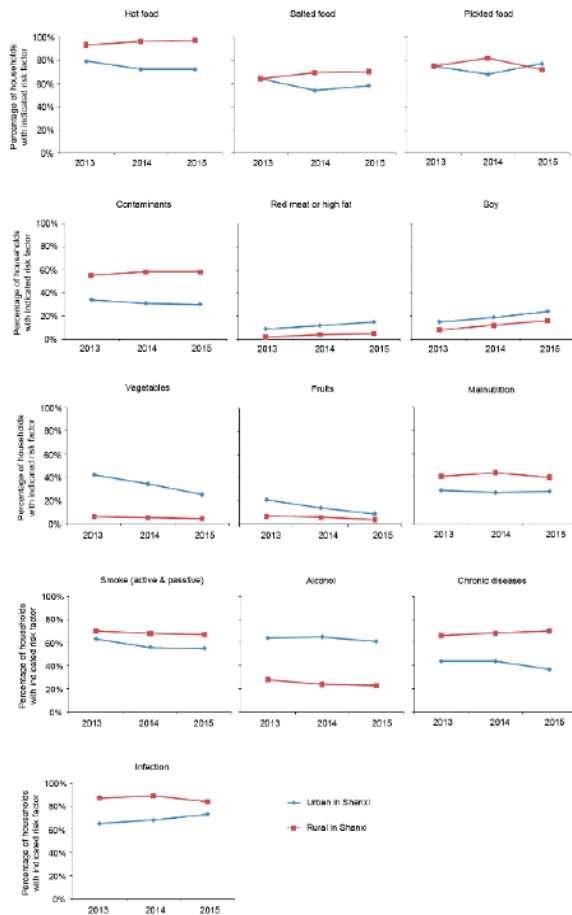


Figure 2. Summary Results from Epidemiological Investigation Data from Urban and Rural Areas of Zhongyang Population during 2013 to 2015

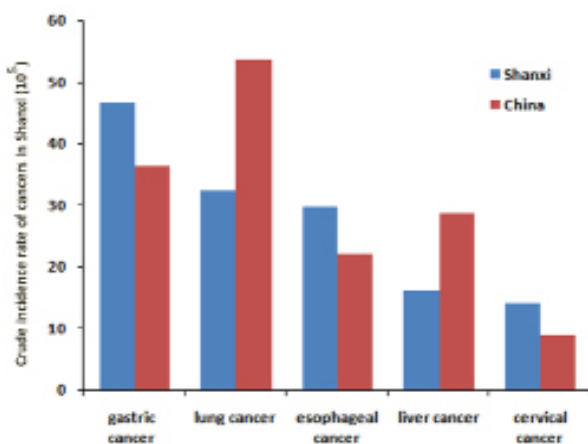


Figure 3. Crude Incidence Rate of Five Leading Cancers in Shanxi. All incidence rates were expressed per 100,000 populations

greatly increases risk compared to drinking or smoking alone (Warren et al., 2016). In Zhongyang population, approximately 70% of smokers have alcohol consumption.

Recent cancer trends in Shanxi

It was estimated there were approximately 50,000 new cases diagnosed as cancer and the crude cancer incidence rate was $202.41/10^5$ in 2012 in Shanxi. Notably, the cancer patterns were quite different between Shanxi and the whole country. Among cancer registration areas in Shanxi, gastric cancer was the most diagnosed cancer ($46.63/10^5$), followed by lung cancer ($32.39/10^5$), and esophageal cancer ($29.78/10^5$), liver cancer ($16.15/10^5$), and cervical cancer ($14.08/10^5$) in 2012. Specially, the crude incidence rate of gastric cancer, esophageal cancer, and cervical cancer in Shanxi were dramatically higher than that of the whole country (Figure 3). In males, the most common sites of cancer were stomach, lung, esophagus, liver, and colon-rectum. While in females, the leading cancer was cervical cancer ($29.08/10^5$) followed by gastric cancer, esophageal cancer, and breast cancer. Furthermore, for all cancers combined, the age-standardized incidence rates per 100,000 populations per year are higher in rural areas than in urban areas. It was relatively lower before 40 years old (27%), then dramatically increased after 40 years old, peaked after 70 years and slightly decreased after 85 years old. However, the incidence of lung cancer, upper gastrointestinal cancer, and cervical cancer were increased before 40 years old recent years in Shanxi.

As for as mortality, approximately 4,5000 died from cancer per year and the cumulative mortality (0-74 years) rate was approximately $185/10^5$, with higher mortality for males than that of females (males/females=1.38:1) in 2012 in Shanxi. The cancer mortality was relatively lower before 50 years old, then was dramatically increased after 50 years old, and reach peak after 80 years old. Rural areas had higher cancer mortality than that of urban areas for both males and females after age standardization. Among various types of cancer, gastric cancer was the leading cancer-killer (23.4%) for both males and females and specifically its mortality in female have been increasing in Shanxi. The other most common cancers of death cause were esophageal cancer, lung cancer, cervical cancer, and breast cancer.

Discussion

Taihang Mountain that includes Shanxi, Hebei, and Henan has been known as high-risk areas for upper gastrointestinal cancers since the 1970s (Chen et al., 2016). Moreover, the results of recent studies from this region showed increasing trends in the incidence of cervical cancer (Wang et al., 2015). Specially, the crude incidence rate of upper gastrointestinal cancers and cervical cancer in Shanxi were dramatically higher than that of the whole country.

In China, overall upper gastrointestinal cancers incidence rates have stabilized during the past few decades, but major increased trends have been observed in Shanxi, the famous high-risk area of upper gastrointestinal cancers worldwide. Due to the limited clinical screening,

surveillance approaches and backward economic level in Shanxi, upper gastrointestinal cancers were rarely detected early and most of them showed distant metastasis at the time of diagnosis, resulting in poor prognosis and an increasing burden (incidence and mortality). Based on the data from Shanxi Cancer Institute & Cancer Hospital during 2009 to 2012, gastric cancer was the leading cause of cancer death, followed by esophageal cancer. The possible reasons for this trend could be genetic and environmental etiologic factors, such as older age, male gender, and lower education level, family history of cancer, smoking cigarettes, and lifestyle. According to statistics, the population of elderly over 60 years old reached 4.77 million in Shanxi at the end of 2013 that is one of main possible reasons why the cancer incidence and mortality rate dramatically increased in Shanxi. Moreover, there was a strong tendency toward familial aggregation of upper gastrointestinal cancers, which suggests that genetic susceptibility in combination with exposure to environmental risk factors contributes to the high rates of upper gastrointestinal cancers in these areas.

Most importantly, epidemiological studies have shown that economic level and dietary habits are associated with the incidence of upper gastrointestinal cancers (Pourhoseingholi et al., 2015). Consistent with previously reports, our investigation showed that consuming salted or hot food, intake of pickled vegetables (nitrosamine-rich), selenium and riboflavin deficiency, low protein and vitamin C diet were associated with upper gastrointestinal cancers in Shanxi. Among these, intake of hot food, salted food, and pickled vegetables were the most important risk factors for Shanxi population. The salted or hot or pickled food can direct damage to stomach lining, increase in endogenous N-nitroso compound formation, enhance the action of carcinogens in stomach, and facilitates *Helicobacter pylori* (*H. pylori*) infection (Chen et al., 2016). *H. pylori* are considered the major risk factor for gastric cancer (Chen et al., 2016). Shanxi typically has a high prevalence of *H. pylori* infection, for instance, in Zhongyang County, 60% of asymptomatic adults were infected by *H. pylori* as shown by our investigation data. Some researchers hypothesize that *H. pylori* and high salt intake may act synergistically to promote gastric cancer.

Cervical cancer morbidity and mortality are heterogeneous across geographic settings in China. Although the average national estimates of cervical cancer burden are low, it is the highest in Shanxi because the backward economic level and the prevalence of the human papillomavirus (HPV) infection. Furthermore, the incidence of cervical cancer has increased among younger women in this area. Compared to older patients, younger cervical cancer patients often exhibit characteristics such as immune deficiency, tobacco smoking, high serum hormone levels, cervical erosions, and HPV16 infection. The HPV prevalence has been found to be similar in rural and urban regions, but cervical cancer mortality is significantly higher among women in rural areas due to the unequal availability and utilization of health services, such as screening and treatment. Therefore, the national government initiated a program to provide free cervical cancer for rural women between ages 35 to 59 years old

Life-Style Habits in a High-risk Area for Upper Gastrointestinal Cancers: a Population-Based Study from Shanxi, China in Shanxi (Li et al., 2015).

Cancer is a kind of disease that cannot be cured completely, but is effectively controlled for many years (Ravegnini et al., 2015). Currently, the increasing of cancer morbidity and mortality in rural areas has surpassed that of urban areas in Shanxi, and the burden of cancers still keep increasing. Seriously, malnutrition and harmful dietary habits were commonly seen in patients with cancer or chronic diseases in Shanxi. Long-term activation of the systemic inflammatory reaction combined with poor nutrition, harmful dietary habit, and physical inactivity were the key reasons leading to cancer in this area. Facing the serious situation, we review the current scientific data on cancer risk factors and explore defensible recommendations for the general public in order to promote changes in environments that support healthful eating and physical activity habits to reduce cancer risk.

Firstly, in addition to specific therapies, patients with cancer and chronic diseases will require integrated health care programs to maintain functional autonomy and quality of life. Unfortunately, the national health-care systems and health insurance cover only a minority of people. There are many rural people in Shanxi having no health insurance or limited medical resources, and many of them are too poor to go for early cancer diagnosis and medical treatments. Therefore, it is urgent for government to know these peoples and help them with more medical assistance such as providing simple and economic screening test, establish and improve the community health service. Moreover, coal smoke or occupational exposures that produced polycyclic aromatic hydrocarbons (PAHs) (Hamidi et al., 2016), may be possible carcinogens for cancer cases from Shanxi. The government should put more efforts to curb environmental pollution.

Secondly, most evidence shows that more than two third of new diagnosed cancer patients attributed to dietary habits and people who have healthy diets have lower risk of many cancers (Lippi et al., 2016). To reduce the risk for upper gastrointestinal cancers, we recommend individuals to eat a variety of foods with an emphasis on plant sources, intake vegetables and fruit each day, choose whole grains in preference to refined grains and sugars, limit consumption of salted and pickled vegetables, avoid hot food, and adopt a physically active lifestyle to maintain a healthful weight throughout life. Additionally, we raised recommendations for community action, for example, public and community organizations should work to create social and physical environments that support the adoption and maintenance of healthful nutrition and physical activity behaviors, increase access to healthful foods in schools, worksites, and communities.

Thirdly, cigarette smoking has already caused significant ill-health to the Chinese including Shanxi population. The respiratory system is harmed most by cigarette smoke and over two-thirds of smoking-induced diseases are attributed to chronic obstructive pulmonary disease, pulmonary tuberculosis, and lung cancer (Lertkhachonsuk et al., 2013). It was shown to be a strong risk factor for lung cancer and moderately associated with an elevated risk for other cancers such as breast cancer, esophagus cancer, stomach cancer, and pancreas cancer

(Lertkhachonsuk et al., 2013). Therefore, it is urgent to strengthen anti-smoking measures.

Fourthly, due to the presence of similar “infection-inflammation-cancer” pathways in the carcinogenesis process, eradicating infective pathogens or attenuating relevant inflammatory factors may reduce digestive cancer incidences (Wu et al., 2010). In light of previous published papers, *H. pylori* eradication led to 33% gastric cancer risk reduction in healthy asymptomatic Asians (Ford et al., 2014). Consequently, the Asian Pacific Consensus on gastric cancer prevention has suggested eradication of *H. pylori* in high-risk populations to prevent gastric cancer (Fock et al., 2008). It is urgently demanded for controlling the prevalence of *H. pylori* infection to prevent gastric cancer in Shanxi.

Finally, the burden of cervical cancer in Shanxi, as well as its unequal impact among women in lower income groups especially in rural areas was very severe. China government has proposed a semi-mandatory HPV vaccination program targeted to low-income, high-risk women living in regions with historically high prevalence of cervical cancer (Wu et al., 2009). Clinical studies have shown HPV vaccination to be highly efficacious and potentially lifesaving if administered to females naive or unexposed to vaccine HPV types (Wu et al., 2009). Therefore, education programs or volunteer projects are needed to translate this clear for the general public.

In conclusion, environmental factors are most important and can be modified. Diet, physical activity, smoking, and infection-inflammation control are primary lifestyle-related, avoidable risk factors for cancer. However, there is lack of health education in counties. Therefore, education for promoting the healthy lifestyle, such as the smoking cessation, physical activity, healthy diet with high consumption of fruits and vegetables, less consumption of salty food, and reduced alcohol consumption, will be essential. It is very important to strengthen various measures so as to have a far-reaching effect on the future health of the Shanxi population.

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