RESEARCH ARTICLE

Inpatients' Knowledge about Primary Liver Cancer and Hepatitis

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Abstract

Objective: To assess the level of an inpatient population's awareness about hepatitis and primary liver cancer (PLC), the most common type of which is hepatocellular carcinoma (HCC), and then to initiate education of this group. Methods: A survey was conducted with 1300 participants within the inpatient unit in representative tertiary hospitals in the Chaoshan area of China. Structured questionnaires contained demographic data and statements about different aspects of liver cancer and hepatitis. The questionnaires were completed by trained medical practitioners after they had conducted the interviews. Results: One way ANOVA showed that the sample population lacked adequate knowledge about HCC and hepatitis. Stepwise multiple regression analysis demonstrated that the participant's level of education had the greatest impact on their total knowledge score when other variables remained constant. Conclusions: The study demonstrated: a general lack of awareness amongst the participants about the preventative strategies, and the management options available for people with primary liver cancer and hepatitis; education level was an important factor affecting knowledge levels. The demonstrated deficiencies in people's knowledge about hepatitis and HCC, and their lack of subsequent protective behaviours are likely to play an important role in HCC and hepatitis transmission or prevention.

Keywords: Primary liver cancer (PLC) - hepatocellular cancer (HCC) - hepatitis - knowledge - prevention - education

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Introduction

Primary liver cancer is one of the most common malignancies in the world and is one of the leading causes of cancer-related death (El-Serag et al., 2008; Shariff, et al., 2009; Ferlay et al., 2010; Bruix et al., 2011). Developing countries are disproportionally affected by HCC and over 80% of HCCs occur in such countries (Ferlay et al., 2010), China accounts for approximately 55% of the total world's burden. Despite recent advances in surgical techniques and medical treatment, the 5-year survival rate for liver cancer remains poor. The American Cancer Society (ACS) notes that the overall 5-year survival rate is estimated to be less than 10 per cent, after taking into account patients who have different stages of liver cancer. According to government statistics, HCC is the third most common deadly cancer in China, accounting for about 20% of the total cancer mortality burden. HCC is not the most common cancer in the Chaoshan area, although it is one of the most fatally malignant diseases and the mortality rate is ranked second only to lung cancer in cancer related deaths (Qin et al., 2010). It could be expected that knowledge rates would be substantially greater about a cancer so common in the region where the research was conducted. Approximately, 70% to 80% of HCC cases are attributable to chronic infection with hepatitis B virus (HBV). HBsAg screening was performed in 125,474 primary and secondary school students in Shantou city in 2009 and demonstrated an average total positivity rate for HBsAg of 8.1%, comprised of 7.8% (5108) primary school and 8.5% (5047) secondary school students, totalling 10,147 infected students (Zhang et al., 2011). Hence, there is a relatively high infection rate of HBV amongst the younger generation, but only a percentage of them have chronic active hepatitis and the rest are termed "HBV carriers". According to the Shantou Municipal Centre for Disease Control and Prevention's statistics, hepatitis B accounted for 67.64% of the detected total viral hepatitis burden in the period from 1995 to 2005 (Yao et al., 2007).

Prevention means eliminating or minimizing exposure to the causes of cancer, and also reducing individuals' susceptibility to such causes. The World Health Organization (WHO) announced that, "*at least one-third of the cancer cases that occur annually throughout the world could be prevented. Primary prevention is an important means to improve public health, and it is by far the most cost-effective and sustainable intervention for reducing the burden of cancer globally.*"

There is innumerable research about HCC and

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hepatitis, however studies on the preventative issues of liver cancer are rare. The control of HCC requires the effective implementation of individuals' knowledge. To the best of the researcher's knowledge, there has been no research conducted to ascertain the public's awareness of HCC and hepatitis in China, nor have public education programs been conducted. All of the population, including those people infected with the hepatitis virus should be made aware of: the risk factors, the early signs and symptoms, the transmission routes, and the preventative methods for these diseases, in order to prevent or minimise the development of liver cancer. The results of this study can lead to appropriate priority settings being made by health authorities to direct research and cancer control programs, plus new educational strategies being applied to progress the public's awareness of hepatitis and HCC. Adequate education is expected to lead to improved early diagnosis rates, increased disease assistance seeking behaviours, and preferably the prevention of new cases of HBV and HCC amongst the general population.

Table 1. Questionnaire(originally in Chinese)

Risk factors of liver cancer
Liver cancer occurs mainly in men
Hepatitis B/C infection
Fatty liver disease
Moldy food
Drink pond/ditch water
Pickles
Fish source
Raw fish/seafood
Smoking
Excessive alcohol consumption
Obesity
Diabetes
Family history of liver carcinoma is a risk factor of carcinoma
Micronutrient deficiency (for example, selenium, Vitamin D\E)
Symptoms and signs of liver cancer
Abdomen ache
Abdomen mass
Nausea or loss of appetite
Fatigue
Weight loss
Jaundice
Fevers
Ascites
Prevention methods
If there is a family history of liver cancer, follow up is needed in other members of the family
Smoking cessation helps the prevention of liver cancer
Alcohol cessation helps the prevention of liver cancer
Eating fresh meals
Fresh fruit and vegetables prevent liver cancer
Maintain a good mental state
Exercise
Management
Liver cancer has treatment
Surgery
Ablative treatments Radiofrequency ablation
TACE (transcatheter arterial chemoembolization)
Interventional treatment
Liver transplant
Transmission Routes of Hepatitis
Unsafe injection practices and blood transfusion
Mother to child
Unprotected sexual contact
Sharing shavers, tooth brushes and others with patients
Prevention of hepatitis
HBV vaccination
Condoms can help a safe sexual contact
Not sharing shavers, tooth brushes and others with patients
Do you want to get more knowledge about HCC and Hepatitis?
How did you get the knowledge?
1. TV and radio
2. internet
3.newspapers, magazine
4.medical books
5.medical workers
6.others

Materials and Methods

Study population and design

This study was conducted at two major tertiary hospitals in the Chaoshan area of China from August 2012 to March 2013. These two hospitals provide medical care for residents in that area. Participants were systematically selected from different wards in the inpatient area according to the admission number of each patient. The research proposal was approved by the ethics committee of Shantou University Medical College.

Each of the participants was interviewed by a medical practitioner to assess their level of knowledge regarding liver cancer and hepatitis B, the most common form of hepatitis. The results were recorded in the questionnaire. The total sample size was 1300. A standardized questionnaire was administered by the interviewers to obtain information about: gender, age, income, and other demographic data, risk factors for HCC, symptoms and signs of HCC, prevention and management of HCC, routes of HBV transmission, and practices to prevent transmission. Interviewers used open ended questions to ascertain how participants had gained their knowledge, and how those who were infected with HBV had acquired the infection.

Statistical analysis

This scale used includes 51 items; each item is answered "yes" or "no" or " I do not know". A correct answer is scored 1, a wrong answer scored 0. Total scores range from 0 to 51, with a higher score indicating a greater level of knowledge about HCC and hepatitis. Every participant was scored for all items and their mean knowledge score was recorded. The participants' levels of knowledge, descriptive statistics (frequency and percentage) and the relationship between knowledge and variables such as demographic data, and past history were analysed with SPSS Version 16.0 (SPSS, Inc. Chicago, IL, USA) by descriptive statistics (mean, standard deviation), comparison means (One Way ANOVA Test), and multiple regression analysis.

Questionnaire

The questionnaire developed by the researchers contains two parts; : colon the demographic data, and the data of the participant's awareness regarding liver cancer and hepatitis. The questionnaire was developed by the researchers after reviewing reference books of gastroenterological diseases and related articles and was validated by professors of internal medicine and epidemiology. Demographic data includes: gender, age, occupation, education, income, past medical history and any known family history of cancer. The participants'

Table 2. Descriptive Statistics of Score

Score	N	Range	Minimum	Maximum	Mean	Std. Deviation
Total	1300	49	0	49	28.5	9.46
Risk factors	1300	14	0	14	6.47	3.03
Hepatitis transmission	1300	5	0	5	2.69	1.25
HCC prevention	1300	11	0	11	5.2	3.4
Hepatitis prevention	1300	5	0	5	370	1.41
HCC prevention	1300	11	0	11	8.72	2.15
HCC management	1300	5	0	5	1.74	1.26

awareness regarding liver cancer was categorized into four groups: risk factors (14 statements), symptoms and signs (8 statements), prevention (8 statements), and management strategies (5 statements). Awareness regarding hepatitis was subdivided into two groups: transmission routes (5 statements) and prevention strategies (5 statements).

Before the study, a pilot phase was conducted with 20 persons in order to test the reliability and appropriateness of the questionnaire. The pilot group was re-questioned two weeks later and their answers were found to be primarily the same as on the first occasion, verifying the reliability and appropriateness of the study.

Results

Descriptive statistics

The mean knowledge scores were: 6.47± 3.03 (maximum possible score=14) for risk factors of HCC and HBV, 5.21± 3.38 (maximum possible score= 11) for symptoms and signs of HCC, 5.21± 3.38 (maximum possible score=11) for preventive strategies of HCC, 1.73 ± 1.25 (maximum possible score= 5) for management of liver cancer, 2.68 ± 1.25 (maximum possible score= 5) for transmission mode of hepatitis B, and 3.70 ±1.41 (maximum possible score= 5) for prevention of hepatitis B (Table 1).

One way ANOVA test

The mean knowledge scores were correlated with: education, occupation, income, and any known history of cancer in their family and/or friends (P<0.05). The group with a history of liver disease did not show any significantly higher knowledge score than other groups (P>0.05) (Table 2).

Multiple regression analysis

The researchers investigated the impact of gender, age, education, vocation (job), and family and friend's history of liver diseases on the total knowledge score by performing a multiple regression analysis. Education as the sole predictor (model1), accounted for 15.3% of the variability in the total score (R^2= 0.153. When family history was added as a second predictor (model 2 in Table 4), it accounted for 17.7% of the variability (R^2= 0.177). Friend history accounted for an additional 19.1% of the variability (R^2 = 0.191). When friend history and gender were added (model 3 in Table 4), the 4 predictors accounted for 19.8% of the variability (R^2 = 0.198), which is reasonably higher. However, from model 3 to model 4, adding gender score only increased the variation of the total score by 0.7%.

Table 3. Mean Knowledge Score Regarding to Demographic Variables

Group	Frequency	Knowledge(M±SD)	*P* value
Gender			
Male	475	27.65±9.16	0.004
Female	351	29.78±9.65	
Age group			
< 20	139	24.39±9.30	0
20~39	734	29.45±9.43	
40~59	375	27.37±9.04	
60+	52	30.42±8.75	
Education			
Illiterate	27	23.21±9.83	0
Primary and Junior	527	24.84±9.51	
High school	367	28.94±8.22	
Diploma and higher	379	33.59±7.59	
Income			
No	207	20.18±9.51	0
<2000RMB	194	21.30±7.29	
2000-4000RMB	298	22.80±6.74	
>4000RMB	125	25.02±6.83	
Cancer history in family			
No	614	27.61±9.34	0
Yes	212	31.34±9.12	
Cancer history in friends			
No	538	27.39±9.67	0
Yes	288	30.91±7.98	
History of liver disease			
No	763	28.39±9.47	0.134
Yes	63	31.54±7.96	

For each regression model, SPSS calculated standardized regression coefficients (β) along with and partial regression coefficients (B, often called slop). The β showed to what degree each predictor affected the outcome when the effects of all other predictors are constant. For example, in model 4, the β values of education, family history, friend history and gender were 0.360, -0.131, -0.128 and 0.082, respectively (Table 5). This means that an increase in education of 1 degree (i.e. a difference of 1 SD of education) was associated with 0.360 units (i.e. 3.40, or 0.360 × 9.46) of variation in the total score. This interpretation is valid when all other predictors in the equation (family history, friend history and gender) were constant.

The factors of family and friend history had little effects upon the total score. A family history was associated with

Table 4. Multiple Regression Analysis

Model	Standard regression equation	R	R^2	Adjusted R^2	F	*P*
1	$Y = 4.2\ X_1+16.4$	0.391[a]	0.153	0.151	119.2	0
2	$Y = 4.2\ X_1-3.5\ X_2+22.8$	0.421[b]	0.177	0.175	71.2	0
3	$Y = 4.0\ X_1-2.9\ X_2-2.6\ X_3+26.7$	0.437[c]	0.191	0.188	52	0
4	$Y = 4.0\ X_1-2.9\ X_2-2.6\ X_3+1.6\ X_4+26.7$	0.445[d]	0.198	0.193	40.6	0

[a]Predictors: X_1=education; [b]Predictors: X_1=education, X_2= family history; [c]Predictors: X_1=education, X_2=family history, X_3=friend history; [d]Predictors: X_1=education, X_2=family history, X_3=friend history, X_4=Gender; [e]Dependent Variable: Y= total score

a 0.131 units (1.24, or 0.131×9.46) decrease of the total score, and a friend history was 0.128 units (1.21 min, or 0.128×9.46). Gender had a mild impact upon total score. Every 1 SD change for gender predicted a 0.78 change in the total score.

Discussion

The mortality from liver cancer (HCC) has increased in China in recent decades. It is imperative that solutions are found for the current situation. What reasons lie behind the high incidence and the high mortality rates of primary liver cancer in China? Firstly, China has a high occurrence of HBV infection. A survey of national epidemiology was announced in April 2008 by the Ministry of Health which showed that 93 million confirmed people in China had been infected with HBV, which is approximately 7,000 per 100,000 people. Government statistics illustrate that the incidence of hepatitis had increased from 64.91 to 107.30 per 100,000 people in the period from 2000 to 2009. Chronic infection with HBV in China is considered to be a major risk factor for HCC (Liu et al., 2011). The apparent increase in the incidence of hepatitis could also be due to improved testing programmes to detect the virus. Secondly, there are a lack of regular medical physical examinations conducted amongst chronic virus carriers and many other people are asymptomatic and unaware of their carrier status (Lok et al., 1991). Thirdly, there is a lack of public knowledge about factors such as lifestyle which are important for the prevention of hepatitis and liver cancer (Nobili et al., 2008; Giles et al., 2013). Lastly, liver cancer in adults has a poor prognosis, because it tends to be diagnosed at the advanced stages of the disease, and also, many people with liver cancer also develop co-morbid liver disease such as cirrhosis, which is frequently fatal, leading to low survival rates.

The development of liver cirrhosis has been recognized as a major step in the pathogenesis of most cases of HCC. as it is found in 80-90% of cases of HCC (Llovet et al., 2003). Risk factors that have been associated with the development of HCC additional to cirrhosis and HBV include: diabetes mellitus, alcohol consumption, cigarette smoking, and aflatoxin exposure (Yu et al., 1991; Yu et al., 2004). Chronic infections with hepatitis B and hepatitis C viruses are the most well established environmental risk factors for HCC worldwide. It is generally believed that 15-40% of HBV carriers will die due to end-stage liver disease (Kao et al., 2010). According to the Shantou Municipal Centre for Disease Control and Prevention's statistics, in the period from 1995 to 2005, hepatitis B accounted for 67.64% of the total viral hepatitis burden (Yao et al., 2007). There is still a relatively high infection rate of HBV in the younger generation in China (Zhang et al., 2011). In July 2011, 179 countries vaccinated infants against hepatitis B as a part of their vaccination schedules - a major increase compared with 31 countries in 1992, the year when the World Health Assembly passed a resolution to recommend global vaccination against hepatitis B. HBV vaccination was introduced into China in 1991, and the government commenced free routine infant HBV vaccination in 2002. The high rate of chronic HBV infection in China is mainly the result of perinatal or early childhood transmission. The distribution of HBV vaccination is fewer in some rural areas and amongst people of middle and older age. Most unvaccinated people lack the knowledge to: seek screening for HBsAg, and to become vaccinated. The interview revealed that many people held the wrong opinion, that vaccination was only available for infants, but not for adults. The authors concluded that the important first step to prevent the transmission of hepatitis B was is to educate the population in order to increase HBV vaccination rates.

The majority of people surveyed identified chronic liver diseases, aflatoxin, tobacco and alcohol as risk factors for HCC, but fewer people were aware of other risk factors such as: obesity, diabetes, micronutrient deficiency, raw seafood, pickled vegetables, and fish sauce, and only 40% of participants regarded cancer as a genetic disease. Dietary habits and other family related behaviours associated with HCC may account for some of the observed familial aggregation of the disease. Genetic lesions play a major role in HCC tumorigenesis and progression (Kim et al., 2005; Li et al., 2012). First-degree relatives of patients with HBV-related HCC appear to be at increased risk of HCC and should be considered in the formulation of HCC-screening programs (Yu, et al. 2000). Participants with a history of liver diseases did not show any significantly higher knowledge scores for the risk factors, symptoms and signs, or the preventative strategies against HCC. The majority of participants ate pickled vegetables on a daily basis as side dishes, and yet only 52.51% were aware of the correlation between pickles and cancer. Only 17% of participants regarded eating fish sauce as an unhealthy daily habit, whilst most held the opinion that eating pickles and fish sauce were traditional practices and, even regarded them as healthy foods. It is known that preserved meat and fish sauce are rich in N-nitroso compounds (Deng et al., 1998; Deng et al., 2000; Haorah et al., 2001; Stute et al., 2002). The nitrite from these and other sources, including that purposely added to food, presents a toxic hazard, both because of the direct toxicity of nitrite and by the formation of carcinogenic N-nitroso compounds by reactions with amino compounds (Peter et al., 1975; Wakabayashi et al., 1985). N-nitroso compounds are suspected to be correlated with gastrointestinal tract carcinomas, including liver cancer (Parkin et al., 1991; Mitacek et al., 1999). It is known that dietary exposure to aflatoxins is a risk factor for developing HCC (Montalto et al., 2002). 65.24% of the participants were aware that eating mouldy: peanuts, corn and other foods was harmful.

Tobacco smoking is common amongst Chinese men and is associated with alcohol consumption. Tobacco is responsible for about 50,000 liver cancer related deaths each year in China, chiefly among men with chronic HBV infection and hepatitis (Zhang et al., 1998). The Chaoshan area has high tobacco 'smoking' rates, 70.71% of males and 3.04% of female participants were tobacco smokers, and few people expressed the intention to cease cigarettes. 66.42% of the participants knew the relationship between smoking and liver cancer. Cirrhotic liver damage is chiefly caused by persistent lifelong HBV infection as previously

mentioned. In early adult life, such infection generally remains asymptomatic and is therefore unlikely to deter the initiation of tobacco use. Cigarette smoking, positive HBeAg carrier status and chronic hepatitis all contribute synergistically to the development of liver cirrhosis (Yu et al., 1997). A meta-analysis showed that tobacco was associated with liver cancer development (Lee et al., 2009). There was a dose-response relationship between the consumption of alcohol and the development of HCC, 'heavy drinkers' having an approximately 3-4 fold risk increase, compared with non-drinkers (Zhang et al,1998).

The most correctly answered question in the category of 'the symptoms and signs of liver cancer' was for the association of cancer with jaundice (63.17%). The highest percentage of correct answers in the category of 'prevention' was for the association between and the prevention of liver cancer and in the category of management, the most correctly answered question was for the statement that "liver cancer can be cured in the early stage". For the 'transmission of hepatitis', the most correct answer was for the route often being blood transfusion (80.77%). 11.54% of participants held the incorrect opinion that a handshake or hug could transmit the hepatitis virus, which might lead to discrimination in society. Further results showed that even those at high risk of HBV and HCC lacked knowledge about prevention, and the availability of yearly screening for HCC. 20% of those in the healthy group had never been screened for HBsAg and had not received hepatitis B vaccination.

The participants had obtained their knowledge through various media. Television and radio (46.45%) were the most popular media, followed by magazines and newspapers (42.75%).The internet is becoming a popular medium for acquiring knowledge. The least popular way of obtaining information was from medical books. Educational intervention via video material, leaflets, and in verbal format has been proposed as an effective strategy to improve health behaviours and to increase patient's knowledge (Petti et al., 2007; López-Jornet et al., 2012). Education programs can be delivered through multiple channels ways based upon other researchers' results. Flyers and educational pamphlets can be distributed to clinics and can result in improved prevention of liver diseases (Humphris et al., 2003; Elango et al., 2011). Good post test results were shown for group educational programmes regarding breast cancer (Wang et al., 2012). The same would be expected for HBV and HCC. An organized system could initially be developed to improve cancer surveillance and screening and this could ultimately be expanded to other clinical preventive services. Hospital-based programs for example which were focused on vulnerable populations could educate individuals to obtain periodic physical examinations, and adopt healthier behaviours. The researchers concluded that the best media for the delivery of the educational programme would be via television, radio, magazines and newspaper commentaries, as the research demonstrated that around 90% of the respondents' knowledge was obtained from those sources..

Learning can be defined as a relatively permanent change in a behavioral tendency, occurring as a result of reinforced practice (Wedding et al., 2001). Improving a person's knowledge about liver cancer is likely to also change their behavior. According to the American Cancer Society, "if we can effectively promote healthy behaviours, much of the suffering and death from cancer can be prevented or reduced". The authors concluded and highlight the finding that a person's educational level is the most important predictor for their knowledge level. The data obtained from this study highlights the need to better educate the public about health. Cancer prevention and control interventions can be directed at individuals. Regular screening for HCC is of great importance for those at high risk. Encouraging people to obtain regular health checks and to adopt healthy lifestyles can only improve matters. The dissemination of basic knowledge about cancer can lay the basis for better controlling cancer, as it can lead the public towards prevention, early diagnosis and early treatment.

The World Health Organization announced that, despite cancer being a global public health problem, many governments had not included cancer prevention in their agendas. Rates of cancer-related illness and death can be expected to be lowered by education programmes including the media which lead to improved behaviours guided by improved risk perception. The public health system has a responsibility to lead a national approach to cancer control that is comprehensive, strategic, and organized (Plescia et al., 2012). The public awareness campaign will need to be reinforced over time due to the tenacity with which some individuals maintain their habitual behaviours. It would appear most prudent for the authorities to design an education plan appropriate for all of the population with special emphasis upon the highest risk group of people. The government will be rewarded in many ways by adopting a long term commitment to increase the public's knowledge of these liver diseases and to change the behaviour of individuals, in order to decrease the incidence and the mortality of hepatitis and HCC. These diseases cause serious morbidity and mortality and are endemic in the Chinese population. China contains 20% of the world's population and many people travel to and from China annually. Chinese families are spread across the world and the effects of these illnesses are felt globally. HBV, hepatitis and HCC cost the population and the government of China a lot in terms of money and suffering. This study indicates that education is an important avenue to reduce the future burden of these diseases upon the government and the population.

In summary, this reported study investigated a hospital-based population's awareness of HCC and hepatitis. The results demonstrated a general lack of awareness of: cancer risk factors, symptoms and signs, methods of prevention, hepatitis transmission and prevention, and the importance of early diagnosis and management of hepatitis B virus and hepatocellular cancer. An appropriate and effective cancer education and screening programme needs to be formulated and carried out in China in the future. Appropriate prevention or early treatment of hepatitis B virus infection and hepatocellular cancer will benefit individuals, the community, the nation of China, and the world as a whole.

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References

Bruix J, Sherman M (2011). Management of hepatocellular carcinoma: an update. *Hepatology*, **53**, 1020-2.

Deng DJ, Xin HJ (2000). Formation of N-(Nitrosomethyl)urea in stomachs of experimental pigs and human volunteers given fish sauce in vivo. *J Agric Food Chem*, **48**, 2495-8.

Deng DJ, Ma H, Wang RM, et al (1998). Characterization of N-(Nitrosomethyl)urea in Nitrosated Fermented Fish Products. *J Agric Food Chem*, **46**, 202-5.

El-Serag HB, Marrero JA, Rudolph L, Reddy KR (2008). Diagnosis and treatment of hepatocellular carcinoma. *Gastroenterology*, **134**, 1752-63.

Elango KJ, Anandkrishnan N, Suresh A, et al (2011). Mouth self-examination to improve oral cancer awareness and early detection in a high-risk population. *Oral Oncol*, **47**, 620-4.

Ferlay J, Shin HR, Bray F, et al (2010). Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer*, **127**, 2893-917.

Giles ML, Grace R, Tai A, et al (2013) Prevention of mother-to-child transmission of hepatitis B virus (HBV). during pregnancy and the puerperium: Current standards of care. *Aust N Z J Obstet Gynaecol*, **53**, 231-5.

Haorah J, Wang XJ, Xu GP, et al (2001). Determination of total N-nitroso compounds and their precursors in frankfurters, fresh meat, dried salted fish, sauces, tobacco, and tobacco smoke particulates. *J Agric Food Chem*, **49**,6068-78.

Humphris GM, Field EA (2003). The immediate effect on knowledge, attitudes and intentions in primary care attenders of a patient information leaflet: a randomized control trial replication and extension. *Br Dent J*, **194**, 683-8; discussion 675.

Kao JH, Chen PJ, Chen DS (2010). Recent advances in the research of hepatitis B virus-related hepatocellular carcinoma: epidemiologic and molecular biological aspects. *Adv Cancer Res*, **108**, 21-72.

Kim Y J, Lee HS (2005). Single nucleotide polymorphisms associated with hepatocellular carcinoma in patients with chronic hepatitis B virus infection. *Intervirology*, **48**, 10-5.

Lee YC, Cohet C, Yang YC, et al (2009). Meta-analysis of epidemiologic studies on cigarette smoking and liver cancer. *Int J Epidemiol*, **38**, 1497-511.

Liu.C, Wang YM, Fan K (2011). Epidemiological and clinical features of hepatitis B virus related liver failure in China. *World J Gastroenterol*, **17**, 3054-9.

Llovet JM, Burroughs A, Bruix J (2003). Hepatocellular carcinoma. *Lancet*, **362**, 1907-17.

Li S, Mao M (2012). Next generation sequencing reveals genetic landscape of hepatocellular carcinomas. *Cancer Lett*, pii: S0304-3835(12)00591-5.

Lok AS, Lai CL, Chung HT, et al (1991). Morbidity and mortality from chronic hepatitis B virus infection in family members of patients with malignant and nonmalignant hepatitis B virus-related chronic liver diseases. *Hepatology*, **13**, 834-7.

López-Jornet P, Camacho-Alonso F, Miñano FM, Sanchez-Siles M (2012). Evaluation of the different strategies to oral cancer knowledge: a randomized controlled study. *Psychooncology*, **22**, 1618-23.

Mitacek EJ, Brunnemann KD, Suttajit M, et al (1999). Exposure to N-nitroso compounds in a population of high liver cancer regions in Thailand: volatile nitrosamine (VNA). levels in Thai food. *Food Chem Toxicol*, **37**, 297-305.

Montalto G, Cervello M, Giannitrapani L, et al (2002). Epidemiology, risk factors, and natural history of hepatocellular carcinoma. *Ann N Y Acad Sci*, **963**, 13-20.

Nobili V, Manco M, Devito R, et al (2008). Lifestyle intervention and antioxidant therapy in children with nonalcoholic fatty liver disease: a randomized, controlled trial. *Hepatology*, **48**, 119-28.

Parkin DM, Srivatanakul P, Khlat M, et al (1991). Liver cancer in Thailand. I. A case-control study of cholangiocarcinoma. *Int J Cancer*, **48**, 323-8.

Petti S, Scully C (2007). Oral cancer knowledge and awareness: primary and secondary effects of an information leaflet. *Oral Oncol*, **43**, 408-15.

Peter FS (1975). The toxicology of nitrate, nitrite and n-nitroso compounds. *J Sci Food Agric*, **26**, 1761-70

Plescia M, Richardson LC, Joseph D (2012). New roles for public health in cancer screening. *CA Cancer J Clin*, **62**, 217-9.

Qin SL, Lin YC, Li CT, Xie XL (2010). Statistical analysis of inpatients with malignancies and death rate in shantou cancer hospital from 2004 to 2008. *IMHGN*, **16**, 889-92.

Shariff MI, Cox IJ, Gomaa AI, et al (2009). Hepatocellular carcinoma: current trends in worldwide epidemiology, risk factors, diagnosis and therapeutics. *Expert Rev Gastroenterol Hepatol*, **3**, 353-67.

Stute R, Petridis K, Steinhart H, Biernoth G (2002). Biogenic amines in fish and soy sauces. *Eur Food Res Technol*, **215**, 101-7.

Wakabayashi K, Nagao M, Chung TH, et al (1985). Appearance of direct-acting mutagenicity of various foodstuffs produced in Japan and Southeast Asia on nitrite treatment. *Mutat Res*, **158**, 119-24.

Wang HH, Chung YC, Sun JL (2012). The effects of education program on knowledge and intention of breast cancer screening in Taiwan. *Asian Pac J Cancer Prev,* **13**, 5545-9.

Wedding D. Behavior and Medicine. 3rd ed. Seattle: Hogrefe & Huber, 2001. Print.

Yao LJ, Huang JY, Huang JH, Huang SS, Liao CH, et al (2007). Analysis on Epidemiological Trend of Class—A and Class—B Infectious Diseases From 1995 to 2005 in Shantou City. *Prac Prev Med*, **14**, 721-3.

Yu MC, Tong MJ, Govindarajan S, Henderson BE (1991). Nonviral risk factors for hepatocellular carcinoma in a low-risk population, the non-Asians of Los Angeles County, California. *J Natl Cancer Inst*, **83**, 1820-6.

Yu MC, Yuan JM (2004). Environmental factors and risk for hepatocellular carcinoma. *Gastroenterology*, **127**, S72-8.

Yu MW, Chang HC, Liaw YF, et al (2000). Familial risk of hepatocellular carcinoma among chronic hepatitis B carriers and their relatives. *J Natl Cancer Inst*, **92**, 1159-64.

Yu MW, Hsu FC, Sheen IS, et al (1997). Prospective study of hepatocellular carcinoma and liver cirrhosis in asymptomatic chronic hepatitis B virus carriers. *Am J Epidemiol*, **145**, 1039-47.

Zhang JY, Wang X, Han SG, Zhuang H (1998). A case-control study of risk factors for hepatocellular carcinoma in Henan, China. *Am J Trop Med Hyg*, **59**, 947-51.

Zhang LL, Lin JX, Zhang JH (2011). The health survey of primary and secondary school students in Shantou. *Chin J School Doctor*, **25**, 557-8.