

## RESEARCH ARTICLE

# Epidemiology and Prevention of Prostate Cancer in Vietnam

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## Abstract

Prostate cancer is the second most common cancer in men worldwide and a leading cause of mortality. Incidences continues to rise and vary substantially between populations. Although the prevalence of prostate cancer is relatively low in Vietnam, some hospital-based reports have shown an upward trend in recent years. While certain non-modifiable factors such as age, race and genetics are known to be mainly responsible, the literature has also suggested that environmental exposures can delay the onset of this disease. The present study provides a review of the epidemiology of prostate cancer in Vietnam by systematically searching several electronic databases. The results confirm an increasing trend of prostate cancer over the past decade, with age-standardised rate more than doubled from 2.2 per 100,000 men in 2000 to 4.7 per 100,000 men in 2010. However, no study has been found on modifiable risk factors, with the exception of one *in vitro* experiment that showed the inhibitory effect of garlic on the growth of prostate cancer cells. The lack of epidemiological information poses a difficulty to develop public health interventions to prevent this emerging malignant disease in Vietnam.

**Keywords:** Epidemiology - lifestyle - prostate cancer - risk factors - Vietnam

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## Introduction

Globally, prostate cancer (PCa) is recognised as the second most common cancer among men and the fifth most common cancer overall, accounting for 13.8% of total male cancers (Ferlay et al., 2010). The number of incident cases was about 903,500 in 2008, with average age-standardised rate (ASR) being 62 per 100,000 men (Ferlay et al., 2010). The rates were particularly high in Australia (104.2 per 100,000 men) (International Agency for Research on Cancer, 2010) and the USA (154.8 per 100,000 men) (National Cancer Institute, 2012). Worldwide, the variation in PCa incidence was 25 folds between the highest and the lowest countries, while about 75% of the diagnosed cases came from developed countries (Jemal et al., 2011). Among leading cancer deaths in men, PCa ranked sixth and accounted for 6.1% of the total deaths, with the mortality rate ranged from 2.5 per 100,000 (in Eastern Asia) to 26.3 per 100,000 (in Caribbean) across countries. Regardless of treatment, PCa is a significant burden to health care and the society (Crawford et al., 2010). Over the past decade, there has been convincing evidence to show that the incidence rate of PCa continues to rise, particularly in China and other Asian countries (Center et al., 2012). For example, a recent report from India showed that the PCa incidence rate increased by 8.6 percent (Lalitha et al., 2012). Various factors contribute to the increase, including change

in lifestyle, increase in life span, and advancement in detection and diagnosis of PCa (Jemal et al., 2011).

From a public health perspective, the risk factors of PCa can be classified as either modifiable or non-modifiable. Age, race, family history and genetics are established non-modifiable risk factors (Gross, 2013). Under the age of 50, the incidence rate for PCa is very low, but at 55-64 years old, the rate is 72.9 per 100,000 (Baade et al., 2009). In Australia, for example, 85% of PCa cases are over 65 years old, and by the age of 85, about 25% of Australian men are at risk of being diagnosed with PCa (Cancer Council of Australia, 2011). Although both genetics and race belong to the non-modifiable group of factors, their effects can be attenuated by certain environmental exposures (Wang et al., 2011). Modifiable factors, such as sedentary behaviour, cigarette smoking, alcohol consumption, hormonal factors, high blood pressure and obesity, have been found to contribute to the development of PCa (Crawford, 2003; Martin et al., 2010). Dietary habits involving high intake of red meat, dairy products and foods rich in fat, together with low intake of fruits and vegetables, can also increase the cancer risk (Crawford, 2003), even though their epidemiological evidence have not been consistent (Drouin, 2009). A case-control study showed that excessive exposure to sun light can increase the risk of PCa among Asians (Chia et al., 2012). In contrast, traditional diets in most Asian countries, characterised by a high intake of vegetables, fruits,

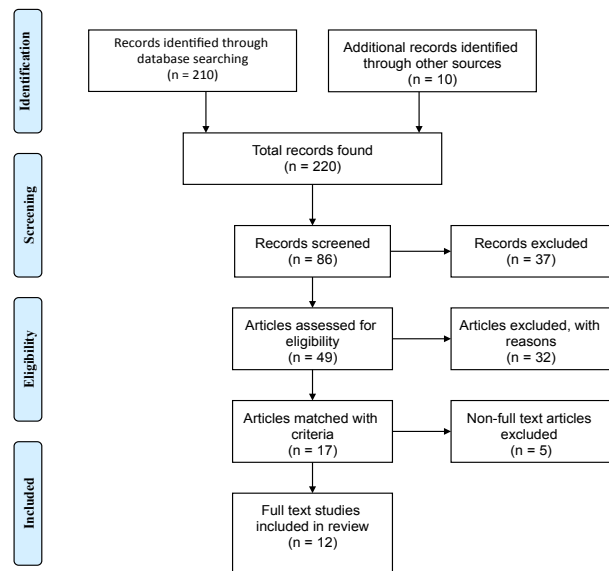
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soybean products and fish, offer protection against the disease (Sonoda et al., 2004; Marshall, 2012). Daidzein, the most abundant isoflavone from soybean products, can be converted by intestinal bacteria into equol that is more bioactive than other isoflavones. Evidence has suggested that men with intestinal equol-producing bacteria are at lower risk of PCa than those without (Sugiyama et al., 2013). In a recent case-control study, Askari et al. (2014) found a significant inverse association between fruit and vegetable consumption and PCa risk among Iranian men. They also reported that western diet, but not healthy diet, was associated with the risk of PCa (Askari et al., 2014). Consumption of two or more cups of tea per day may reduce the PCa risk (Jain et al., 1998), while both dried green tea and green tea leaves appear to be beneficial (Jian et al., 2007; Lee et al., 2009). Moreover, sufficient level of physical activity has been shown to delay the onset of the disease (Young-McCaughan, 2012). Such protective effect is achieved through changes in serum that affect the growth of PCa cells (Tymchuk et al., 2001). Physical activity can further enhance survival after diagnosis of PCa (Walsh, 2011).

In Vietnam, as a consequence of the transition to westernised lifestyle along with economic development and environmental pollution, non-communicable diseases have become a major concern (Vuong, 2005). Prolonged life span is another factor that contributes to the rise in incidence of non-communicable diseases (Do, 2003). Despite recent hospital reports suggesting an upward trend in the incidence of PCa, relatively little attention has been paid to modifiable behavioural factors for the development of appropriate public health interventions. The purpose of this study is to review the epidemiology of PCa in Vietnam, which has important implications on the prevention of this emerging malignant disease. By epidemiology, we focus on risk and protective factors, incidence, prevalence and trend of PCa in Vietnam.

## Materials and Methods

A systematic search strategy was adopted to identify relevant published articles on PCa in Vietnam. The search procedure and literature review was conducted in compliance with the widely used PRISMA guidelines, which is a set of evidence-based items required to be reported in a systematic review or meta-analysis (Moher et al., 2009). Articles in both English and Vietnamese were searched and included in the review if found to be eligible. Databases included in the search for pertinent publications were PubMed, Web of Science, Ovid MEDLINE, National Agency for Science and Technology Information of Vietnam, and Central Health Information and Technology Institute of Vietnam. Initially, potential publications were identified using specific key words, namely, “prostate cancer”, “Vietnam”, “cancer”, “ti ết tuyến (prostate gland)”, and “ung thư (cancer)”, without any restriction on the year, type and language of publication. The search was also extended to published reports from the Vietnam National Cancer Institute and The World Health Organisation (WHO). At the second step, the abstract and/or main text of each identified article was screened



**Figure 1. PRISMA Flow Diagram for Systematic Review of Prostate Cancer in Vietnam**

for eligibility based on following criteria on its content:

- incidence, prevalence or secular trend of PCa in Vietnam

- risk or protective factors of PCa in Vietnam
- prevention of PCa in Vietnam

A guideline from the National Health and Medical Research Council of Australia was used to assess the level of scientific evidence of eligible studies (NHMRC, 1998); those satisfying at least level 4 of evidence were included in the review. Finally, the full text of eligible articles were assessed and summarised.

Figure 1 shows the PRISMA flow diagram of the systematic search. From the total 220 publications identified and retrieved from the databases, 49 articles were found to be related to PCa in Vietnam after initial screening and removal of duplicating records. Of the shortlisted articles, 22 studies actually focused on clinical aspects of PCa, such as histological features, clinical manifestation and the role of prostate-specific antigen in diagnosis and prognosis. Ten other articles reported on screening and some risk factors of PCa, but apparently none of the studies reviewed had been conducted in Vietnam. These references were subsequently removed from further consideration, leaving 17 studies that matched the selection criteria. However, only 12 full text articles were available for downloading from the internet. Table 1 presents a summary of these 12 articles included in the final review.

## Results and Discussion

### *Incidence and secular trend*

Similar to other Asian countries, Vietnam has sustained a relatively low incidence of PCa. Before 1980s very few PCa cases were diagnosed in Vietnam. An autopsy examination conducted in 1982 showed that 31.5% of the total cancer deaths were attributed to PCa (Dao, 1984). A mass screening program for PCa in South Vietnam indicated that the general prevalence was 2.5%. Most detected cases were at medium grade of lesion (Gleason 7)

(Vu Le et al., 2010). However, the result of this screening might not reflect the actual prevalence for the Vietnamese population. The hospital-based screening program, which recruited participants through mass media, was located in central Ho Chi Minh City. Therefore, participants were most likely men with suspected symptoms and those who lived nearby, while noting the differences in lifestyle between urban and rural residents. Recent statistics from a national project on cancer prevention showed that PCa ranked 9th among 15 most common cancers in 2010, with ASR 4.7 per 100,000 men (Nguyen, 2010), which was much lower than the global rate of 62.0 per 100,000 men (Jemal et al., 2011) and the general incidence of 15.2 per 100,000 among South-East Asian countries, but slightly higher than the lowest reported ASR of 4.3 per 100,000 in Middle Africa (Jemal et al., 2011).

In Vietnam, most of the incident PCa cases were observed in large cities. For example, the 2008 ASR for PCa in Ho Chi Minh City (5.2 per 100,000) and Hanoi (4.3 per 100,000) were higher than those from Hai Phong

(1.5 per 100,000), Thai Nguyen (1.2 per 100,000) and Hue (0.9 per 100,000) (Nguyen, 2010). The differences in PCa incidence between regions might be explained by the accessibility to diagnostic services in large cities, as well as the variations in lifestyle between urban and rural populations.

Despite the overall low incidence of PCa in Vietnam, there has been a significant upward trend in ASR over the last decade (Nguyen, 2010). Indeed, PCa was one of four cancers that exhibited the highest increase in incidence rate between 2000 and 2010, with ASR doubled from 2.2 to 4.7 per 100,000. This upward trend was more rapid in Ho Chi Minh city than Hanoi, from 2.3 in 1996 to 5.2 in 2008 versus 2.5 in 1990 to 4.3 in 2008 (Anh et al., 1993; Quoc et al., 1998; Nguyen et al., 2010). Data from Binh Dan Hospital also showed that the number of annual admitted cases tripled from 117 cases in 1999 to 380 cases in 2009 (Vu Le et al., 2010). The underlying reasons for the rise in PCa incidence among Vietnamese men remain unknown. Increasing awareness and

**Table 1. Summary of Reviewed Studies**

References	Year	Location	Study design	Results
Nguyen (2011)	2011	Hanoi	In vitro experiment	Garlic extract significantly inhibited the growth of PCa cells
Vuong, Velasco-Garrido et al. (2010)	2010	Hanoi, Ho Chi Minh City and Can Tho	Analysis of population-based cancer registry data, 1998-2007	Rapid upward trend in PCa ASR
Vu Le, Dao et al. (2010)	2009	Ho Chi Minh City	Screening for PCa using PSA test; Reviewing medical records of PCa patients, 1999-2009	PCa prevalence of 2.5% in 2009; Upward trend in annual number of diagnosed cases
Tung (2010)	2010	Thua Thien Hue	Analysis of population-based cancer registry data, 2001-2009	PCa accounted for < 3% of all cancers in men; PCa was not a common cancer
Nguyen (2010)	2010	Vietnam	Analysis of population-based cancer registry data, 2000-2010	Rapid upward trend in PCa ASR from 2.2 to 4.7 over 10 year period; PCa was one of four cancers with the most rapid growth rate
Nguyen, Bui et al. (2010)	2010	Hanoi, Ho Chi Minh City, Hai Phong, Thai Nguyen, Thua Thien Hue and Can Tho	Analysis of population-based cancer registry data, 2004- 2008	PCa ASR in Ho Chi Minh City: 5.2 Hanoi: 4.3 Hai Phong: 1.5 Thai Nguyen: 1.2 Thua Thien Hue: 0.9 Can Tho: 4.7 PCa ranked 10th of all cancers in men
Do (2003)	2003	Hanoi	Examine PSA among PCa patients	Mean age: 74.2 ± 6.18 years Mean PSA: 81.24 ± 71.96
Le, Gomez et al. (2002)	2002	Hanoi and California, USA	Analysis of population-based cancer registry data, 1991-1993	PCa ASR in California: 24.1 PCa ASR in Hanoi: 0.7 Changes in diet and culture might explain the difference
Anh and Duc (2002)	2000	Hanoi	Review	PCa incidence in Vietnam lower than other Asian countries PCa incidence in South Vietnam higher than North Vietnam
Quoc, Hung et al. (1998)	1997	Ho Chi Minh City	Analysis of population-based cancer registry data, 1995-1996	PCa ASR: 2.3 PCa ranked 14th among 29 cancer sites investigated
Anh, Parkin et al. (1993)	1993	Hanoi	Analysis of population-based cancer registry data, 1988-1990	ASR of PCa: 2.5 PCa ranked 10th among 28 cancer sites investigated
Dao (1984)	1982	Hanoi	Investigation of autopsies for cancers	PCa accounted for 31.5% of total cancer deaths

knowledge of both patient and healthcare professionals, and improved diagnostic techniques in recent years could partially explain this upward trend (Vu Le et al., 2010). Another plausible reason is the change in diet and lifestyle together with a high speed of urbanisation during the past decade (Vuong, 2005). Analyses of population-based cancer registry data found that the incidence rate among Vietnamese migrants in the USA was significantly higher than that of Vietnamese living in Hanoi over the period 1988-1992 (Le et al., 2002). In addition, differences in rates were similarly observed for other cancers, such as colon cancer and breast cancer, suggesting the influence of westernised lifestyle on cancer development for the Vietnamese population (Le et al., 2002).

#### Risk factors

Only one publication on protective factors of PCa in Vietnam was found, which concerned an in vitro experiment demonstrating the inhibitory effect of garlic on the growth of PCa cell line PC-3 (Nguyen, 2011). The results appeared to be consistent with other in vitro and epidemiological studies conducted in other countries. A case-control study has shown a reduced risk of PCa among men who consumed garlic at least twice a week when compared to never consumers (Key et al., 1997). Another population-based study also reported similar observations (Hsing et al., 2002), while consumption of aqueous garlic extract lowered both total and free prostate-specific antigen among patients in a clinical trial (Yilmaz et al., 2003). Although garlic is a popular herb in Vietnam, no epidemiological study has been undertaken to ascertain its effect on the PCa risk. Similarly, agent orange has been demonstrated to be a carcinogen associated with increased risk of PCa (Chamie et al., 2008). However, information was lacking on its impact on PCa in Vietnamese men, despite documents of heavy use of agent orange during the Vietnam war (Brodsky et al., 2009). The current evidence for agent orange came from studies on American and Australian veterans of the war (Frumkin, 2003; Ansbaugh et al., 2013). Besides agent orange exposure, pesticides that have been widely and unsafely used in agriculture production, are also major environmental risk factors in Vietnam (Phung et al., 2013; Toan et al., 2013). Current evidence has indicated that pesticides are associated with the risk of PCa (Doolan et al., 2014). However, there is no publication about this issue has been found for Vietnamese men. A meta-analysis of pooled data from Asian countries showed an association between diabetes mellitus and increased risk of PCa (Long et al. 2012), which may be useful in the early detection and prevention of the disease, especially in view of the rapidly increasing prevalence of diabetes in Vietnam (Shaw et al. 2010). Apart from the single reference (Nguyen, 2011), our review did not find any other study that investigated the role of lifestyle modifiable risk factors or dietary habits on the development of PCa in Vietnam.

#### Prevention

Although PCa ranks amongst the top four cancers in terms of fastest increase in incident rate over the past decade, it is not a priority for prevention by the Vietnamese

government according to the action plan of the National Program for Cancer Prevention (Vietnam National Cancer Hospital, 2008). Lack of epidemiological evidence may be an underlying reason. The incidence rate of PCa amongst Vietnamese migrants in the USA was 34.4 times that of Vietnamese living in Hanoi (Le et al., 2002), which could be attributable to changes in lifestyle. Moreover, data from the Vietnam national cancer registry showed that the ASR for PCa in Vietnam was much lower than that in Western countries (Nguyen, 2010). Dietary and environmental factors could play a crucial role towards the large variations in incidence rate. However, there has been no epidemiological study undertaken in Vietnam so that it is difficult to develop appropriate public health interventions to prevent this emerging malignant disease.

#### Limitations

A limitation of this study was that only a small number of articles from the literature were identified to be eligible using a systematic search strategy. Our review found little information on the epidemiology and risk factors for PCa in Vietnam, with existing publications mainly concerned with clinical aspects. Despite the significant upward trend in the incidence rate of PCa, lack of epidemiological evidence on risk and protective factors specifically for the Vietnamese population poses as a major barrier for the formulation of prevention strategies. It is recommended to undertake more research particularly population-based observational studies in order to understand the etiology of PCa in Vietnam.

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