The incidence, mortality, and risk factors of prostate cancer in Asian men

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1. Introduction

Prostate cancer (PCa) is the second most prevalent cancer in men worldwide. However, large variations in incidence rates exist between geographical regions, with a 25-fold difference between countries with the highest and lowest incidence rates. There were 307,000 deaths from PCa in 2012, and it is the leading cause of death in men globally. There is relatively less variation in mortality rates worldwide (10-fold variation from approximately 3 to 30 per 100,000). The mortality rates have been declining in many developed countries in part because of improved treatment.

The incidence of PCa in Asian countries remains significantly lower than in Western countries. The highest estimated age-specific rate of PCa incidence occurs in Australia/New Zealand and Northern America (age-specific rate 111.6 and 97.2 per 100,000, respectively) compared to an estimated rate of 10.5 in Eastern Asia, 11.2 in Southeast Asia, and 4.5 in South Central Asia. However, the incidence and mortality of PCa is rising in several Asian countries. There is a lack of detailed information about the burden of PCa in Asia, which is geographically, ethnically, and economically diverse.

A better understanding of the epidemiology of PCa within Asia, including its modifiable and nonmodifiable risk factors, may facilitate better health-care decision and policymaking.

The objective of this review was to describe the epidemiology and risk factors of prostate cancer (PCa) in Asian populations. English language publications published over the last 10 years covering studies on the incidence, mortality, and risk factors of PCa in Asia were reviewed. The incidence of PCa in Asia is rising but is still significantly lower than that in Western countries. Studies in Asia indicated that the consumption of red meat, fat, dairy, and eggs was associated with a higher risk for PCa. Age and family history were also found to be risk factors. The emergence of genetic data indicates that different genetic backgrounds between Asian and Western populations play a role in the observed differences in PCa incidence. The lower incidence of PCa in Asian men than in Western men may in part be due to a lack of systematic prostate-specific antigen screening, but environmental and genetic factors also play a role.

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types of cancer or to examine surgical treatments for PCa. No
methods were used to assess the risk of bias in individual studies or
across studies, and no meta-analyses were performed.

The methods used for the calculation of incidence and mortality
rates that are reported in the Results section are detailed in the
references associated with the reported data.

3. Results

3.1. PCa epidemiology in Asia

Table 1 summarizes studies that have investigated the incidence
and mortality of PCa in Asia. These studies provide evidence that
the incidence of PCa is increasing in China,1,2 India,3,4 South Korea,5,7
Vietnam,8 Japan,9 and Singapore.10,11 The increase in incidence is
also supported by data from Globocan from 2008 and 2012, shown
in Table 2, which show that PCa incidence has risen in all areas of
Asia in this time.1,2 Table 3 shows the incidence and mortality data
for 2012 for six countries in Asia.12 The incidence and mortality vary
significantly across Asia. Many studies observed that the age-
specific incidence rates increased with increasing age.1,2,10,31

The trends observed in PCa mortality rates in Asian studies were
more variable. Tseng12 observed an increase in mortality in the
Taiwanese population from 1995 to 2006, and increases in mor-
tality have been observed in South Korea from 1983 to 2006.3,16
However, Chen et al10 observed that mortality rates declined
from 1998 to 2006 in Singapore, and Lim et al11 reported that the
mortality rate had remained fairly stable in Singapore from 1998 to
2009. Katanoda et al9 reported that the mortality rate in Japan had
also remained fairly stable from 2004 to 2013. Zhao et al17 observed
that although there appeared to be a general decrease in PCa
mortality from 2000 to 2009 in Shanghai, China, the trend was not
significant. Globocan data showed an increase in mortality rates
across Asia, whereas in North America and Australia, the mortality
rates had remained stable or declined.1,2

The incidence rate in North America was up to 20 times greater
than the incidence rate in Asia. However, the mortality rate was
only around 2.5 times the rate in Asia.1 The mortality rate to inci-
dence rate ratio (MR/IR) can give an indirect index for the evalua-
tion of survival and early diagnosis.10 In 2012, the MR/IR was 0.1 in
America, 0.18 in Europe, and 0.25 worldwide, whereas in Asia, this
ratio ranged from 0.3 to 0.6.1 The high MR/IR ratio may be due to
the diagnosis of PCa at a later stage in Asia than in Western coun-
tries. There is evidence that patients are often diagnosed with late
stage disease in Asia.19–21

3.2. Modifiable risk factors

An increased incidence of PCa for Asian immigrants in Western
countries compared to their native counterparts22 suggests that
environmental factors may play an important role in the prevention
of PCa. Table 4 outlines the modifiable risk factors that have been
investigated in various Asian studies; Supplementary Table 1 pro-
vides further details including the countries in which the studies
were conducted.

There were often contradictory findings for the various risk
factors which could in part be due to differences in study design.

3.2.1. Dietary factors

The dietary factors in PCa may have an influence on circulating
androgens and estrogens or as a general protective effect against
mitogens.23

3.2.1.1. Meat, fat, eggs, and dairy products. A high intake of red
meat, fat, dairy products, and eggs was found to be associated with
an increased risk of PCa.24–29 Meat is rich in saturated fat and
cholesterol, and dairy products are also rich in saturated fats.
However, this does not necessarily imply that animal fat is a risk
factor for PCa. Other aspects need to be considered. For example,
high levels of red meat consumption may also mean a lower con-
sumption of plant foods. Dairy products also contain calcium and
other substances such as zinc that may have an association with
increased PCa risk.29 The manner in which food is prepared is also
another important consideration.23 The consumption of meat and
dairy products has significantly increased in Asia over recent
years but is still lower than the amount consumed in Western
countries.30,31

3.2.1.2. Fruits and vegetables. The frequent consumption of fruits
and vegetables that contain vitamins, minerals, and other second-
ary plant products has long been thought to decrease cancer inci-
dence and mortality. For PCa, there is some evidence that specific
components or subgroups of fruits and vegetables such as lycopene
or cruciferous vegetables may be associated with a decreased risk of
PCa.12 Several studies found that the consumption of vegetables
and fruits resulted in a decrease in the risk of PCa.24–26,28 However,
two Japanese studies25,33 found that there was no association be-
 tween vegetable and fruit intake and PCa risk. Thakur et al26 found
no association between the consumption of a vegetarian diet and
risk of PCa.

3.2.1.3. Fish. A study in India29 found that the consumption of fish
significantly increased the risk of PCa, whereas a Japanese study35
found that a high intake of fish may be inversely associated with
the risk of PCa death. It is thought that the presence of omega-3
fatty acids in fish may reduce the risk of PCa. However, in these
studies, the type and amount of fish consumed was not assessed
which may help explain the difference in study results.

3.2.1.4. Green tea. Green tea is a popular beverage in Asia and
contains epigallocatechin-3-gallate (EGCG), an antioxidant that
may play an important role in cancer prevention. Kurahashi et al25
found that the consumption of green tea (3 to 4 cups per day to
greater than 5 cups/day) was associated with a decreased risk of
advanced PCa, and Jian et al37 observed that PCa risk was reduced
with increased consumption of green tea. However, several studies
found no association between the consumption of green tea and
the risk of PCa.38,39 The contradictory findings may in part be due to
differences in study design, misclassification of results due to
baseline assessments, or differences in how the tea was brewed.

3.2.1.5. Soy products. Soy products are commonly found in tradi-
tional Chinese and Japanese diets, and there is some evidence that
isoflavones found in soy products, such as genistein and daidzein,
effect oestrogen and testosterone metabolism and exhibit anticar-
cinogenic properties.40–42 Li et al43 found that the consumption of
soy products (either more than twice a week or more than once a
day) resulted in a protective effect against PCa. Nagata et al44 found
that total isoflavones, genistein and daidzein, were significantly
associated with decreased risk of PCa. Kurahashi et al45 found that
although the consumption of genistein, daidzein and other iso-
flavones resulted in a decrease in the risk for localized PCa, they
tended to increase the risk of advanced PCa.

3.2.2. Obesity and physical exercise

Masuda et al46 found a significantly increased risk of PCa and
high-grade disease at biopsy among obese and overweight men in
Japan. A study in Pakistan25 also found an increased risk for PCa for
obese men with a body mass index >25. However, other studies
have found no association with body mass index and risk of
Table 1
Summary of studies investigating prostate cancer incidence and mortality rates in Asia.

| Reference     | Location                      | Key findings                                                                                                                                 |
|---------------|-------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------|
| Zhao et al17, 2014 | Shanghai, China               | Marked increase in PCa incidence between 2000 and 2009. There was an increasing trend in incidence in the 50- to 60-year age group (p = 0.047). |
| Shao et al90, 2012 | Eastern China                 | The overall survival and disease-specific survival rates demonstrated a trend toward improved survival in younger men.                         |
| Yeole5, 2008    | India                         | Higher disease stage correlated with shorter survival (p < 0.05).                                                                                |
| Vu et al8, 2010  | Vietnam                       | Uniformly, the age-specific incidence rates increased with increasing age groups in all Indian population—based cancer registries, especially if aged above 55 years. |
| Lim et al11, 2012 | Singapore, Sweden, and Geneva | Increase in incidence of PCa with AAR at 17.4 per 100,000 person-years in 1998–2002 and 26.7 per 100,000 person-years in 2005–2009. The incidence rates were higher than for Malaysia, China, and India. |
| Ranasinghe et al13, 2011 | Sri Lanka                 | The standardized incidence rate was 5.7 per 100,000 person-years.                                                                             |
| Koo et al6, 2015 | South Korea                   | Incidence of PCa was 18.4 per 100,000; 5-year prevalence as of 2012 was 70.1 per 100,000.                                                   |
| Chi and Chang92, 2010 | South Korea                | The PCa death rate tripled between 1983 and 1988, tripled again by 1996, and more than tripled between 1996 and 2006 to 4.11 per 100,000.        |
| Moon et al95, 2009 | South Korea                  | Low death rates below 60 years of age and dramatically increased rates over 70 years of age, a trend particularly evident since the year 2000. |
| Song et al94, 2008 | South Korea                  | The estimated cancer detection rate adjusted for age (55 years or older) was 3.36%, significantly higher than in most previous East Asian reports. |
| Park et al7, 2006 | South Korea                  | Nationwide incidence was 7.9 per 100,000 man-years.                                                                                            |
| Tseng15, 2011    | Taiwan                       | The trend of PCa mortality in the Taiwanese male general population from 1995 to 2006 has significantly increased (p < 0.0001) for age groups 65–74 and 75 years. |
| Kido et al83, 2015 | Japan                        | PCa was most prevalent among individuals in their 80s (33.3%), followed by those in their 70s (23.6%), 60s (14.3%), and 50s (11.4%). |
| Katanoda et al7, 2015 | Japan                       | Annual percentage change in PCa mortality rate was -1.3% from 2004 to 2013. There was an annual percentage change of 2.4% in PCa incidence from 2003 to 2010. |

AAR, age-adjusted incidence rate; PCa, prostate cancer.
PCa. Studies found no association between smoking and the risk of PCa. The association of PCa with alcohol may be dose dependent. Light alcohol consumption may be antiinflammatory responses or alter sex hormone levels. In the study by Subahir et al., the maximum mean alcohol consumption was two times per day, and this may be one reason why no association was observed.

3.3. Nonmodifiable risk factors

Nonmodifiable risk factors encompass both physiological risk factors, such as age, ethnicity, and family history, and genetic factors, such as gene mutations and chromosomal, gene, or single nucleotide polymorphisms (SNPs). Table 5 outlines the nonmodifiable risk factors that have been investigated in various Asian studies; Supplementary Table 2 provides further details including the countries in which the studies were conducted. Among the physiological risk factors, age and a family history of cancer were significant risk factors for PCa, although a Japanese study found no association between one’s medical or family history and PCa risk.

3.3.1. Testosterone levels

The responsiveness of PCa to hormonal therapy supports the view that testosterone might play an important role in the pathogenesis of PCa. However, results from two studies in China and South Korea regarding the association of levels of testosterone and PCa risk were unclear. Dai et al. found that total testosterone levels were lower in patients with high-grade disease. Hong et al. observed no association between testosterone levels and PCa.

3.3.2. Diabetes

Studies have shown an association between diabetes and cancer in Western countries, although the precise underlying biological mechanism remains speculative. Studies in Taiwan and Japan showed that patients with diabetes were reported to have a higher risk for PCa than nondiabetic patients. A study that conducted a pooled analysis from 19 Asian cohorts found that type 2 diabetes was associated with an increased risk of death from PCa. The use of metformin (a biguanide antihyperglycemic agent) was observed to reduce the risk. A study in South Korea found that higher fasting serum glucose levels were positively related to PCa susceptibility risk. The influence of insulin on the risk of PCa was unclear. A study in Nepal reported that high insulin levels were associated with an increased risk for PCa when compared to fasting levels (≥2.75 μU/mL). Separately, a Taiwanese study reported that exposure to human insulin had no effect on the risk of PCa and a South Korean study reported that higher serum insulin levels were inversely related to PCa susceptibility risks. It has been reported in a Japanese study that insulin growth factor (IGF)-1 was not significantly associated with PCa, whereas IGF-2 and IGF-binding protein 3 (IGFBP-3) showed weak, nonstatistically significant associations. A study in South Korea also found no significant

| Table 2 | Incidence and mortality data for prostate cancer from Globocan for regions in Asia. |
|---------|----------------------------------|
| Region  | Incidence | Mortality |
|         | 2008 | 2012 | 2008 | 2012 |
| Eastern Asia | 8.2 | 10.5 | 2.5 | 3.1 |
| South Eastern Asia | 8.3 | 11.2 | 5.1 | 6.7 |
| South Central Asia | 4.1 | 4.5 | 2.8 | 2.9 |

Table 3 | Age-standardized incidence and mortality data from Globocan for 2012 for six countries in Asia.
| Country  | Incidence | Mortality |
|----------|-----------|-----------|
| China    | 46745     | 22603     |
| Japan    | 55970     | 11644     |
| Korea    | 10351     | 1696     |
| Singapore | 1212 | 169     |
| Thailand | 3182     | 1700     |
| India    | 19095     | 12231     |

ASR, age-standardized rate.

3.2.3. Tobacco and alcohol

Smoking may increase the risk of PCa as it is known to affect steroid levels and to contain multiple carcinogens. However, the level of physical activity in the study was poorly defined. The contradictory results may be due to different study designs or a lack of statistical power due to a low frequency of obesity.

| Table 4 | Modifiable risk factors for PCa in Asia. |
|---------|----------------------------------|
| Increased risk | Decreased risk | No effect or unclear association |
| High intake of red meat, fat, dairy, and eggs | Consumption of fish | Consumption of fruits and vegetables, green tea; genistein, daidzein, and isoflavone (in soy foods; localized PCa) |
| Consumption of fish | Consumption of vegetables, fruits, soy bean products, dietary fibre, fluid, green tea, and coffee | Overweight and obesity |
| Genistein, daidzein, and isoflavone (in soy foods); advanced PCa only | Physical exercise | Physical exercise |
| Overweight and obesity | Tobacco smoking; past smokers only | Tobacco smoking |
| Tobacco smoking; past smokers only | Alcohol consumption | Alcohol consumption |
correlation between serum levels of IGF-1 and IGFBP-3 with known prognostic parameters of PCa.

3.3.3. Genetic factors

A study in Sweden found that Asian immigrants had significantly lower PCa risk than native Swedes and that older age at immigration and a recent immigration history were significantly associated with lower PCa risk.60 Lee et al22 found that Korean immigrants living in America had a lower rate of PCa than black and white Americans but that PCa was higher in Korean Americans than in their native counterparts. They also observed that there had been a 71% increase in incidence rate of PCa for Korean Americans from 1988 to 2002. McCracken et al61 found that the incidence and mortality rate of PCa for Korean Americans compared to native Koreans and older immigration history22,60 Family history of cancer70 Testosterone level62 Various P450 polymorphisms62–69 and polymorphisms at the 8q24 region62–79 had a higher incidence and mortality rate than groups with more recent immigration histories.

One reason for the large difference in PCa incidence between Asian and Western countries may be due to different genetic backgrounds. Various genome-wide association studies have been carried out in Asia to identify genetic markers associated with PCa risk. Of the genetic risk factors studied, polymorphisms in the various genes of cytochrome P450 appear to be inextricably linked to the risk for PCa,62–69 and a number of polymorphisms at the 8q24 region of chromosome 8 have also been identified as PCa risk factors.69–75 In addition, the predictive potential of a number of PCa risk–associated single nucleotide polymorphisms (SNPs) for PCa in Chinese, Malaysian, and Japanese men has been reported.27–29

Table 5 shows PCa risk–associated SNPs that had been identified in men of European descent which were also identified in Chinese and Japanese men. Yamada et al79 evaluated 23, Liu et al76 evaluated 42 PCa risk–associated SNPs from European populations found in Chinese and Japanese men.

Table 6

PCa risk–associated SNPs from European populations found in Chinese and Japanese men.

| Reference | Study participants’ country | Country of origin of previously identified SNPs | SNPs | P |
|-----------|---------------------------|-----------------------------------------------|------|---|
| Yamada et al79, 2009 | Japan | European | rs2660753 | 0.0005 |
| | | | rsl3254738 | 5.3 × 10^-6 |
| | | | rs9836561 | 4.9 × 10^-8 |
| | | | rs16901979 | 2.3 × 10^-8 |
| | | | rs1447295 | 0.0084 |
| | | | rs1009154 | 0.0038 |
| | | | rs4430796 | 4.9 × 10^-5 |
| Liu et al76, 2011 | China | European | rs1465618 | 0.020 |
| | | | rs21048 | 0.047 |
| | | | rs12621278 | 0.019 |
| | | | rs7676763 | 9.39E-03 |
| | | | rs1512686 | 9.39E-04 |
| | | | rs10086908 | 9.24E-04 |
| | | | rs16901979 | 5.15E-09 |
| | | | rs1447295 | 7.04E-06 |
| | | | rs10993994 | 0.038 |
| | | | rs11649743 | 8.51E-03 |
| | | | rs5759167 | 4.81E-03 |
| Na et al77, 2013 | China | European | rs16901979 | 2.33E-14 |
| | | | rs1447295 | 1.54E-10 |
| | | | rs9836267 | 4.55E-10 |
| | | | rs1512686 | 8.26E-09 |
| | | | rs4430796 | 5.15E-04 |
| | | | rs20861 | 1.63E-03 |
| | | | rs1465618 | 3.54E-03 |
| | | | rs6769391 | 4.38E-03 |
| | | | rs721048 | 1.14E-02 |
| | | | rs12621278 | 1.47E-02 |
| | | | rs11649743 | 3.15E-02 |
| | | | rs5759167 | 3.29E-02 |
| | | | rs10875943 | 3.56E-02 |
| | | | rs887391 | 3.66E-02 |
| | | | rs10463567 | 4.29E-02 |
| | | | rs6465557 | 4.77E-02 |
| | | | rs3964554 | 4.83E-02 |

4. Discussion

Over the last 10 years, PCa incidence rates have steadily increased in a number of Asian countries, although the overall incidence rates for PCa in Asia continue to remain far below that for Western countries. The lack of systematic prostate screening programs in many countries in Asia may partly explain the lower incidence. However, Asian immigrants in the United States and Western Europe, who should have better access to prostate-specific antigen screening, still show a lower incidence of PCa than the native population living in the same regions.

The small value for MR/IR in North America and Europe may provide evidence that vigorous annual screening with prostate-specific antigen reduces PCa mortality.18 In comparison, survival rates are poor in Asian countries, and the lack of routine screening in Asia has been attributed to the diagnosis of the disease at later stages compared to Western countries.19 Studies of prostate screening programs in Japan found that there was an inverse correlation between the exposure rate to population screening and the proportion of advanced PCa.81 There is resource and economic variation within Asian countries compared to Western countries.
Access to health care and resource availability may be other factors that affect both the incidence and mortality of PCa in Asia.82

The findings obtained for modifiable risk factors for PCa in Asia indicate that environmental exposures probably play a major role, although the only identified factors associated with higher risk of PCa were high consumption of red meat, fat, dairy products, and eggs. These findings are in line with data from studies carried out in Europe and America which found that frequent consumption of dairy products and meat may enhance PCa risk. Similar to the studies carried out in Asia, the data from Western countries for preventative behavioural factors were not entirely consistent.83 A lack of robust data on potentially modifiable factors means that there are no immediate prospects for population-based primary or secondary prevention strategies focused on altering diet or lifestyle.52,82

In line with findings in Western countries, age and family history were nonmodifiable risk factors for PCa.32 There is little doubt that testosterone plays an important role in the development of PCa. However, there have been inconsistent findings on the relationship between testosterone and PCa.84 Various investigators have suggested that racial variations in serum levels of hormones, including testosterone along with its derivatives, exist and that hormonal differences might contribute to differences in PCa risks among different races.85 Han et al63 suggested that it is the age-related declines in testosterone levels that are significant to the genesis of PCa and not just the level at a single point in time, which could explain the inconsistent findings.

The association between diabetes and PCa has also been inconsistently reported. Some findings from studies with Caucasian men indicate that the risk of PCa may have an inverse relationship with diabetes.83,86 Turner et al87 suggest that the stage of diabetes may be important. Higher concentrations of insulin and -IGF-1 are positively associated with PCa and are found in early diabetes, whereas lower insulin and IGF-1 levels occur in long-standing diabetes.83 Studies carried out in Asia indicated that there was a link between diabetes and PCa in Asian men.15,52–54,86 Furthermore, the finding that metformin (which generally works by reducing levels of both circulating glucose and insulin87) reduced PCa risk and that elevated serum glucose levels increased the risk of PCa support an association between diabetes and PCa.

The influence of genetics on incidence of PCa has been well supported by epidemiologic studies of immigrant populations.2,26,60,67 Ewis et al88 found differences in the distribution of Y-chromosome haplotypes between Asian and Western populations. Several studies found that not all SNPs associated with PCa risk identified in men of European descent were replicated in Asian populations.70,71,78 These results also indicate that there may be differences in genetic determinants of PCa between different ethnic populations.76 Mao et al85 identified key differences in the somatic genomic alterations in PCa from Chinese and UK populations. Mao et al suggested that tumors may arise in Western and Chinese populations by alternative pathogenetic mechanisms. Several genetic risk factors for PCa in Asian populations have been reported. The most notable of these are polymorphisms in various cytochrome P450 genes that regulate androgen metabolism and variants at the 8q24 region of chromosome 8.

In summary, we have provided a review of the available data on the epidemiology of PCa in Asia from the last 10 years, and a number of potential risk factors for PCa in Asian populations have been identified.

Conflict of interest declaration

Dr. Chiong reports grants and personal fees from Takeda, Sanofi, and Astellas and personal fees from Astrazeneca and Sanofi-Janssen, outside the submitted work. Dr. Chiong reports nonfinancial support from Takeda Pharmaceutical Company Ltd, during the conduct of the study. Dr. Chung would like to report the following: honoraria and travel expenses from Astellas (Korea), Ipsen (Korea), JW Pharma (Korea), Takeda (Korea) and Janssen (USA); consultation/advisory from Janssen (Korea), Handok (Korea), Astellas (Korea), Ipsen (Korea), Amgen (Korea), Takeda (Korea) and JW Pharma (Korea); researching funding from Janssen (USA), Bayer (Germany), Pfizer (USA), Astra Zeneca (UK), Roche (Switzerland), Myovant Sciences GmbH (Australia).

Acknowledgments

Medical writing services provided by Theresa Wade PhD from WriteSource Medical were funded by Takeda in accordance with Good Publication Practice (GPP3) guidelines.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.prnil.2018.11.001.

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