currently available (I-IX), dating back to the first published volume in 1966 up to the most current Volume IX, published in 2007 and reflecting a reporting period from 1998-2002. In contrast, the GLOBOCAN 2008 database includes cancer statistics on 184 countries recognized as independent nations according to the United Nations (UN) World Population Prospects Report.[13] GLOBOCAN 2008 excludes countries with a population of less than 100,000 and does not separate out Hong Kong and Macau from China, as does the UN. While extensive in scope of international coverage, the GLOBOCAN 2008 estimates of cancer incidence and mortality are derived using a variety of methodologies and data sources; whereas CI5 data are derived from 86 cancer registries worldwide, covering 101 populations and 28 cancer sites. In order to directly compare CI5 and GLOBOCAN cancer incidence statistics, one must use the age-standardized incidence rate (ASIR) which accounts for differences in the age structure within each nation or region.[14,15]

According to the most recent reporting periods, CI5 2002 and GLOBOCAN 2008 demonstrate that the nations with the highest PCa ASIRs include Australia, Austria, New Zealand, and the United States. In contrast, the lowest ranking nations with respect to PCa ASIRs include many of the Asian nations, such as India and China, and Japan. Yet, over the past decade, data from a number of independent studies, along with CI5 data from successive reporting periods, reveal a steady increase in PCa ASIRs in several Asian nations. Underscoring the importance of these trends are recent reports using population-based cancer registries that demonstrate steady, incremental rises in PCa ASIRs over time.[16-19] Factors that underlie rising PCa incidence estimates might include the dissemination of PSA screening, routine access to medical care, proximity to medical care, education, income, race/ethnicity, and reported behavior (e.g., diet) and genetic predisposition.[20,21] Ultimately, a complex interplay of these factors may all contribute to PCa development.

A working group on Asian Perspectives on Cancer Control (APCC) was formed to examine patterns in PCa incidence and mortality within Asian nations and to formulate recommendations for cancer screening and treatment[16,22] with recognition for the need to improve cancer incidence and mortality data collection efforts in Asia. Moreover, the APCC recently called for improving early PCa detection by formal recommendation of prostate-specific antigen (PSA) screening for the first time.[19,23]

The purpose of this review is to examine one key component of the descriptive epidemiology of PCa in selected Asian nations, the age-standardized incidence rate (ASIR). The IARC CI5 Volumes I-IX will be used as the primary source of ASIR estimates. The CI5 data will be complemented by GLOBOCAN 2008 international data. A secondary goal is to provide PCa ASIR trends over time based on CI5 Volumes I-IX.

MATERIALS AND METHODS

Selection of countries

The selection criteria for determining which Asian nations would be examined in this review were as follows: using the CI5 Indices of Data Quality for CI5 Volume IX, only nations with a minimum of 80% microscopically verified (%MV) PCa cases were selected, as a metric of data accuracy in cancer case ascertainment.[1] Second, the percent of PCa cases registered from a death certificate, only (%DCO) was considered.[1] Only nations with %DCO of less than 5% were considered. In instances in which multiple registries within a given nation contributed data quality indices, the %MV and %DCO cut points were required of more than 50% of the reporting regions for the nation to be considered for this review. Inadequate data quality based on these cut points led to the exclusion of India, Israel, and the Philippines. Due to concerns of unstable ASIR estimates for nations with low counts of PCa cases, those nations with fewer than 1000 PCa cases for an entire reporting period were excluded. This criterion resulted in the elimination of Kuwait, Malaysia, Oman, Pakistan, and Thailand. Finally, in order to examine change over time, only nations providing ASIR estimates from a minimum of the two most recent CI5 reporting periods (1993-1997 and 1998-2002, respectively) were included.[1,9] This last selection criterion led to the exclusion of Bahrain, Cypress, Turkey and Vietnam.

Because PCa is a disease of aging men, the male life expectancy (LE) in these eligible nations was examined to confirm that each had an average male LE of at least 70 years, according to two data sources: the United Nations (UN) Statistical Yearbook for Asia and the Central Intelligence Agency (CIA) World Fact Book.[13,24]

This selection process resulted in the following study sample of Asian nations: China, Japan, Republic of Korea (South), and Singapore.

International data sources

Cancer incidence in five continents (CI5)

The CI5 Volumes I-IX public use data were used as the primary data source for international estimates of PCa ASIR data.[2-4,6-11,13,24] Using the IARC CI5Plus online analysis tool, PCa ASIR estimates were generated per nation for all years in which data were available.[1-3,6-11] Prostate cancer was classified according to the International Classification of Disease

Version 10 (C61). In China, registry data were reported to CI5 2002 from the following regions: Hong Kong; Shanghai; Jiashin; Nangang District, Harbin City; Guangzhou City; and Zhongshan. In Japan, registry data were obtained from CI5 2002 for the following prefectures: Miyagi, Osaka, Nagasaki, Yamagata, Aichi, and Fukui, as well as the city of Hiroshima. For the Republic of Korea, CI5 2002 data were reported from Busan, Daegu, Seoul, Daejeon, Gwangju, Incheon, Jejudo, Ulsan and the Korean Central Cancer Registry. Finally, Singapore data were reported by CI5 2002 at the level of the Chinese, Indian, and Malay populations, as well as for Singapore's National Cancer Registry. The CI5 data were provided at the level of national region or population-based cancer registry. The ASIR estimates are expressed as the number of new prostate cancer cases per 100,000 person-years. A weighted mean of age-specific rates are standardized to an external population known as the 1960 World Standard Population, to account for difference in the population age structure across reporting regions. The details on data sources and computation of age-standardized incidence rates for CI5 2002 data can be found on the IARC website.[1] The CI5 2002 data represent incidence rates for the calendar years 1998-2002.

Time trends for PCa ASIR estimates from CI5 Volumes I-IX were generated on IARC's CI5plus website, using the online analysis graphing tool. Among the four options for line charts, "time trends" was chosen. Selections were then made for type of cancer (prostate), gender (male), registry (Asian nation and its associated registries), time period (first and last available start and end dates), statistic (age-standardized incidence rate), and age (0 to 85+). An aggregated statistic representing the ASIR per national registry was then generated using these selections. Data were not available for the Republic of Korea or the Indian population subset of Singapore when using the online CI5 graphing tool.

GLOBOCAN 2008

The GLOBOCAN 2008 PCa ASIR estimates were extracted from the IARC website.[5] Similar to CI5 estimates, the ASIRs represent a weighted mean of age-specific rates, standardized to the World Standard Population. While GLOBOCAN estimates were also published in 2002, the variation in incidence and mortality estimation methods used previously prevents direct comparison of GLOBOCAN 2008 with GLOBOCAN 2002. Therefore, as recommended by IARC, only the most current estimates are reported in this review.

The detailed methodologies and data sources used by GLOBOCAN to estimate cancer statistics for those nations included in its 2008 database are described in detail on the GLOBOCAN website.[5] Estimates from GLOBOCAN 2008 reflect the most recently available data per nation, varying from two to five years previous to the GLOBOCAN 2008 release. The GLOBOCAN 2008 estimates are provided at the level of the nation.

Similar to the method of obtaining CI5 data, GLOBOCAN 2008 public use data were obtained using an online analysis tool to generate PCa ASIRs after selecting cancer type (prostate, ICD-10-C61), age group (default values of 0 to 75+), gender (male), data type (incidence) and continent (Asia).

RESULTS

Overall findings

In all four Asian nations examined, the PCa ASIRs were observed to increase over time, though not linearly. Table 1 provides a summary of the PCa ASIRs for each nation based on CI5 Volumes I-IX databases. As a criterion for study inclusion, at a minimum all nations were required to have data from the two most recent CI5 reporting periods, 1993-1997 (Volume VIII) and 1998-2002 (Volume IX). However, within a nation, not all reporting regions or registries had data from these two periods.

Within China, Hong Kong and Shanghai had the most complete data, as well as the highest rates observed [Table 1]. Hong Kong experienced a near tripling in PCa ASIRs, rising from 5.1 to 15.0 new PCa cases per 100,000 person-years between 1974-1977 (Volume IV) and 1998-2002 (Volume IX) whereas Shanghai reported a more than eightfold increase from 0.8 to 6.9 new PCa cases per 100,000 person-years across the same time periods.

In Japan, the Miyagi prefecture had the oldest data and the most significant increase over time, rising from 3.8 to 22.0 new PCa cases per 100,000 person-years [Table 1]. Similarly, all other prefectures and Hiroshima experienced increases in ASIRs over time, with the exception of Aichi and Fukui that only reported data for Volume IX so that change over time could not be examined.

In the Republic of Korea, increases in PCa ASIR estimates were noted [Table 1]. However, only for Busan, Daegu, and Seoul were data available from at least two reporting periods, permitting examination of change over time. In all three of these Korean reporting regions, PCa ASIRs were slightly higher in Volume IX versus Volume VIII. The most significant change was observed in Seoul where rates rose from 8.5 to 12.7 new PCa cases per 100,000 person-years.

In Singapore, the Chinese, Indian and Malay populations

Table 1: Age-standardized incidence rates (ASIR) of prostate cancer by CI5 volume, for registry regions in selected Asian countries

China	**Region**	**Hong Kong**		**Shanghai**		**Jiashin**		**Nangang District, Harbin City**	
	CI5 Volume	**Period**	**ASIR**	**Period**	**ASIR**	**Period**	**ASIR**	**Period**	**ASIR**
	4	1974-1977	5.1	1975-1975	0.8	na	na	na	na
	5	1978-1982	6.2	1978-1982	1.8	na	na	na	na
	6	1983-1987	7.6	1983-1987	1.7	na	na	na	na
	7	1988-1992	7.9	1988-1992	2.3	na	na	na	na
	8	1993-1997	8.6	1993-1997	3	1993-1997	1.9	na	na
	9	1998-2002	15	1998-2002	6.9	1998-2002	1.4	1998-2002	2.1
	Region	**Guangzhou City**		**Zhongshan**					
	CI5 Volume	**Period**	**ASIR**	**Period**	**ASIR**				
	4	na	na	na	na				
	5	na	na	na	na				
	6	na	na	na	na				
	7	na	na	na	na				
	8	na	na	na	na				
	9	2000-2002	6.7	1998-2002	2.2				
Japan	**Region**	**Miyagi Prefecture**		**Osaka Prefecture**		**Nagasaki Prefecture**		**Hiroshima**	
	CI5 Volume	**Period**	**ASIR**	**Period**	**ASIR**	**Period**	**ASIR**	**Period**	**ASIR**
	1	1959-1960	3.8	na	na	na	na	na	na
	2	1962-1964	3.2	na	na	na	na	na	na
	3	1968-1971	2.7	1970-1971	2.7	na	na	na	na
	4	1973-1977	4.9	1973-1977	3.4	1973-1977	10.2	na	na
	5	1978-1981	6.3	1979-1982	5.1	1978-1982	8.8	1978-1980	6.7
	6	1983-1987	7.8	1983-1987	6.6	1983-1987	9.3	1981-1985	10
	7	1988-1992	9	1988-1992	6.8	1988-1992	9.1	1986-1990	10.9
	8	1993-1997	12.7	1993-1997	9	1993-1997	12.6	1991-1995	14.1
	9	1998-2002	22	1998-2002	11.3	1998-2002	20	1996-2000	21.5
	Region	**Yamagata Prefecture**		**Aichi Prefecture**		**Fukui Prefecture**			
	CI5 Volume	**Period**	**ASIR**	**Period**	**ASIR**	**Period**	**ASIR**		
	1	na	na	na	na	na	na		
	2	na	na	na	na	na	na		
	3	na	na	na	na	na	na		
	4	na	na	na	na	na	na		
	5	na	na	na	na	na	na		
	6	1983-1986	6.6	na	na	na	na		
	7	1988-1992	7.9	na	na	na	na		
	8	1993-1997	9.3	na	na	na	na		
	9	1998-2002	13.4	1998-2002	14.2	1998-2002	13.6		
Korea	**Region**	**Busan**		**Daegu**		**Seoul**		**Daejeon**	
	CI5 Volume	**Period**	**ASIR**	**Period**	**ASIR**	**Period**	**ASIR**	**Period**	**ASIR**
	8	1996-1997	7.1	1997-1998	6.6	1993-1997	8.5	na	na
	9	1998-2002	7.3	1998-2002	7.7	1998-2002	12.7	1998-2002	5.8
Gwangju		**Incheon**		**Jejudo**		**Ulsan**		**CCR 3**	
Period	**ASIR**	**Period**	**ASIR**	**Period**	**ASIR**	**Period**	**ASIR**	**Period**	**ASIR**
na	na	na	na	na	na	na	na	na	na
1998-2002	9	1998-2002	7.8	2000-2002	11.8	1999-2002	8.6	1999-2002	8.5

Table 1 (contd...)

Table 1 (contd...)

Table 1: Age-standardized incidence rates (ASIR) of prostate cancer by CI5 volume, for registry regions in selected Asian countries

Singapore	Region	Chinese		Indian		Malay		National Cancer Registry	
	CI5 Volume	Period	ASIR	Period	ASIR	Period	ASIR	Period	ASIR
	I	1950-1961	0.9	na	na	na	na	na	na
	3	1968-1972	3.6	1968-1972	4	1968-1972	4.8	na	na
	4	1973-1977	4.8	1973-1977	6.7	1973-1977	7.2	na	na
	5	1978-1982	6.6	1978-1982	8.9	1978-1982	7.6	na	na
	6	1983-1987	7.6	1983-1987	11	1983-1987	9	na	na
	7	1988-1992	9.8	1988-1992	6.5	1988-1992	9.1	na	na
	8	1993-1997	14.4	1993-1997	9.9	1993-1997	13.3	na	na
	9	1998-2002	18.6	1998-2002	11.1	1998-2002	16.1	1998-2002	17.3

[1]Cancer Incidence in Five Continents (CI5) Volumes I-IX, [2]ASIR = Age-Standardized Incidence Rate, representing the number of new prostate cancer cases per 105 person-years, [3]CCR = Korean Central Cancer Registry

demonstrated substantial rises in PCa ASIR between 1968-1972 (Volume III) and 1998-2002 (Volume IX). Data from the Singapore National Cancer Registry more closely resembled the estimates from the Chinese and Malay groups, as opposed to the Indian group which skewed lower for all periods examined. An almost five-fold increase from 3.8 to 18.6 new PCa cases per 100,000 person-years was noted in the Chinese population while Malay rose from 4.8 to 16.1 new PCa cases per 100,000 person-years. The Indian rates showed the least consistent pattern, fluctuating in directionality of change over time for the CI5 reporting periods.

In comparing PCa ASIR estimates across CI5 2002 and GLOBOCAN 2008, important differences were noted [Table 2]. The GLOBOCAN ASIR statistics were aggregated per nation as opposed to CI5 data which were reported at the level of the individual registry (i.e., China, Japan, Republic of Korea) or population subgroup (i.e., Singapore). In China, the GLOBOCAN 2008 estimates of 4.3 new PCa cases per 100,000 person-years contrasted from the CI5 registry-level estimates that varied from a low of 2.1 and 2.2 new PCa cases per 100,000 person-years in Nangang District and Zhongshan, respectively, to a high of 15.0 new PCa cases per 100,000 person-years in Hong Kong, China. Similarly, in the Republic of Korea, the summary statistic for PCa ASIR from GLOBOCAN 2008 was 22.4 new PCa cases per 100,000 person-years as compared to a low of 5.8 new PCa cases per 100,000 person-years in Daejeon and a high of 12.7 new PCa cases per 100,000 person-years in Seoul, based on CI5 2002 estimates.

Figure 1 provides a graphical depiction of PCa ASIRs over time for three of the four Asian nations examined for which CI5 data were available using the IARC online graphing tool. It is important to note that Korean data were not available in the time trend analysis and are, therefore, not depicted in the figure. Moreover, the plot for China depicts two registries (Shanghai and Hong Kong). Similarly, in Japan, data from three registries are plotted over time, including Miyagi, Osaka, and Yamagata. Finally, for the nation of Singapore, data from Chinese and Malay subgroups are plotted but Indian data were not available using the online graphing tool. The plot reveals evidence of increases over time in PCa ASIR estimates in all regions for which data are available, most notable in China and Singapore Chinese populations.

CONCLUSIONS

In this review, the descriptive epidemiology of PCa, as estimated by ASIRs, was examined within four Asian nations. The primary data source was IARC's CI5 databases, considered to provide the most accurate international cancer statistics on a limited number of countries worldwide. These CI5 data were supplemented with IARC's GLOBOCAN 2008 database. The CI5 2002 data were used as the most recent estimates, while all CI5 volumes were examined for time trends in PCa ASIRs.

An increase in rates was observed in all four Asian nations examined. In China, Japan, and Singapore, meaningful change in the PCa ASIRs was noted. In the Republic of Korea, increases were small. Yet, in 2010, Jung et al., examined the Korea Central Cancer Registry (KCCR) for calendar years 2006 and 2007 and revealed PCa ASIRs of 17.7 and 20.0 new PCa cases per 100,000 person-years, respectively.[25] This is in contrast to the CI5 2002 database estimate of 8.5 new PCa cases per 100,000 person-years from the same registry source (KCCR) for the calendar years 1999-2002.

According to the UN World Population Prospects report,

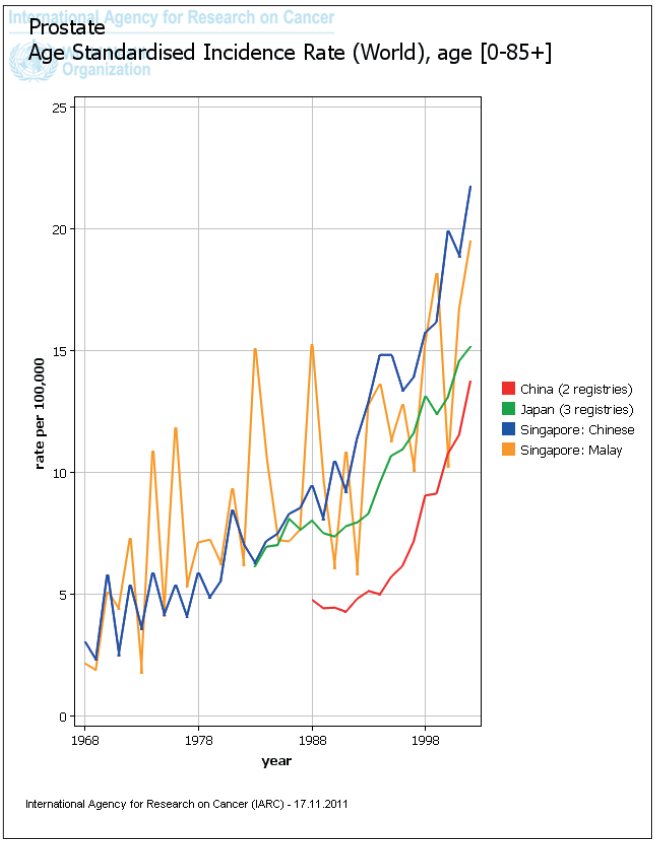

Figure 1: Time trends in Prostate Cancer Age-Standardized Incidence Rates (ASIR)* for Three Asian Nations using "Cancer Incidence in Five, *The ASIRs are measured as data plotted were limited to those available using the online graphing tool on the IARC website.[1-3,6-11], **Data from the Republic of Korea and Indian Singapore populations were not available using this interactive online graphic tool.**

there were 4.1 billion persons residing in Asian nations in 2009; this figure is expected to grow to 6 billion persons by 2050, under the assumption of a constant growth rate.[13] Since increasing age is one of few established risk factors for PCa development, it is noteworthy that the life expectancy of males in several of the largest Asian countries has risen steadily over the past decade, including the nation with the greatest number of persons worldwide, India.[13,20,24] While Asian nations have historically reported among the lowest PCa ASIRs, there are an increasing number of reports of rising PCa incidence in countries such as Japan, Republic of Korea, and China. Autopsy studies in Japan have shown that, while biological aggressiveness of PCa may be lower for Japanese men as indicated by cancer size at autopsy in comparison to men in the US, the detection of latent disease indicates that current incidence estimates among Japanese men may represent an underestimate of the actual disease burden.[26] International autopsy studies have shown that despite varying incidence rates of PCa around the world, prevalence of disease increases with age in many nations around the world.[27]

When PCa is detected in many Asian nations, it is typically due to onset of symptoms and advanced stage.[19,23] Therefore, some have argued for introduction of a PSA screening program, similar to that of the US and other developed nations. This is despite the ongoing controversy over PSA screening in the US, blamed by some as contributing toward over-detection of indolent cancer. PSA introduction in nations without a current, national screening program could have a profound impact on PCa ASIRs in a relatively short period of time. While introduction of PSA screening has been associated with a stage migration toward less advanced cancer and a spike in localized disease, there is debate over the impact of stage migration on reductions in PCa mortality.[28-31]

The relatively high rate of advanced PCa detection in Asian nations has been blamed on lack of a mass screening effort.[32,33] There are serious implications of widespread PCa screening using PSA in a nation as large as China, where the sheer volume of newly detected cases could create a significant demand on the healthcare delivery system. Whether this demand could sustain a rapid shift in PCa incidence as occurred in the US, has been questioned. Currently, the most common treatment strategy in China is castration while radical prostatectomy (RP) is reportedly uncommon.[32,33] In contrast, a Japanese Patterns of Care study recently showed that use of radiation therapy for treatment of PCa – used among Japanese men of older age or with advanced stage disease – may more closely resemble US patterns.[34] In the event of a rapid increase in the volume of newly diagnosed PCa cases, there is some question as to whether adequate medical resources, including trained personnel, would be available. In a 2009 CIA report, 189 nations were ranked according to the percent of the gross domestic product (GDP) spent on health.[24] Among the nations examined in this review, the following rankings were observed: China ranked 148th place at 4.6%, Japan ranked 40th at 9.3%, the Republic of Korea ranked 90th at 6.5%, and Singapore ranked 168 at 3.9% of the national GDP spent on health. Yet despite some concerns of national readiness to address a rapid rise in the volume of PCa patients,[35] the APCC and other independent researchers have begun to propose widespread PSA screening in Asian nations, including the second largest, China.[19] It is well documented that the dramatic shift in newly diagnosed early-stage PCa that occurred in the US in the late 1980s and early 1990s in the United States was driven by dissemination of PSA screening of asymptomatic men.[29,31]

Study considerations

A limitation of examining international estimates and trends in PCa ASIRs is the variation in case recording practices or data coding that may change over time, even among the series of CI5 databases. As indicated in Table 1, the same set

Table 2: Comparison of prostate cancer age-standardized incidence rates from two IARC databases

Data source	GLOBOCAN**		Cancer incidence in five continents (CI5)***		
Asian nations by world region	**ASIR***	**Data source and Method**	**ASIR*****	**Data source**	**Calendar years**
Eastern Asia					
China	4.3	Estimated national mortality was converted to incidence by modeling using sets of age-, sex- and site-specific incidence mortality ratios derived from recorded data in 36 Chinese cancer registries (2003-2005)	na	na	na
Guangzhou City	na	na	6.7	CI5-Volume 9	2000-2002
Hong Kong	na	na	15.0	CI5- Volume 9	1998-2002
Jiashin	na	na	1.4	CI5- Volume 9	1998-2002
Nangang District, Harbin City	na	na	2.1	CI5- Volume 9	1998-2002
Shanghai	na	na	6.9	CI5- Volume 9	1998-2002
Zhongshan	na	na	2.2	CI5- Volume 9	1998-2002
Japan	22.7	National incidence around 2000 was estimated from national mortality (2000) by modeling, using incidence mortality ratios derived from recorded data in 11 Japanese cancer registries: *Aichi, Fukui, Kanagawa, Miyagi, Nagasaki, Niigati, Okayama, Osaka, Saga, Shiga,Yamagata*	na	na	na
Aichi Prefecture	na	na	14.2	CI5- Volume 9	1998-2002
Fukui Prefecture	na	na	13.6	CI5- Volume 9	1998-2002
Hiroshima	na	na	21.5	CI5- Volume 9	1996-2000
Miyagi Prefecture	na	na	22.0	CI5- Volume 9	1998-2002
Nagasaki Prefecture	na	na	20.0	CI5- Volume 9	1998-2002
Osaka Prefecture	na	na	11.3	CI5- Volume 9	1998-2002
Yamagata Prefecture	na	na	13.4	CI5- Volume 9	1998-2002
Korea, Republic of	22.4	National incidence rates (2000-2007) projected to 2008 (Source: Korea Central Cancer Registry)	8.5	CI5- Volume 9	1999-2002
Busan	na	na	7.3	CI5- Volume 9	1998-2002
Daegu	na	na	7.7	CI5- Volume 9	1998-2002
Daejeon	na	na	5.8	CI5- Volume 9	1998-2002
Gwangju	na	na	9.0	CI5- Volume 9	1998-2002
Incheon	na	na	7.8	CI5-Volume 9	1998-2002
Jejudo	na	na	11.8	CI5- Volume 9	2000-2002
Seoul	na	na	12.7	CI5- Volume 9	1998-2002
Ulsan	na	na	8.6	CI5- Volume 9	1999-2002
South-Eastern Asia					
Singapore	20.0	Reported national incidence rates (1968-2002) projected to 2008	17.3	CI5- Volume 9	1998-2002
Chinese	na	na	18.6	CI5- Volume 9	1998-2002
Malay	na	na	16.1	CI5- Volume 9	1998-2002
Indian	na	na	11.1	CI5- Volume 9	1998-2002

*ASIR = Age-Standardized Incidence Rate, representing the number of new prostate cancer cases per 10^5 person-years, **GLOBOCAN 2008 prostate cancer age-standardized incidence rate (ASIR) estimates, ***Cancer Incidence in Five Continents (CI5) 2002 prostate cancer age-standardized incidence rate (ASIR) estimates

of population-based cancer registries were not represented for all time periods examined by CI5. With respect to GLOBOCAN 2008, while extensive in scope of nations represented, this database uses a variety of methodologies and data sources for estimating cancer incidence across countries, depending on data availability within each nation. This varies from use of national registry data, as the most rigorous source, to assignment of neighboring national statistics, as an example of least rigorous.[5] In addition to CI5 and GLOBOCAN data sources, data were sought from cancer registries in these four nations to further capture the PCa ASIR experience. were sought to determine whether PCa ASIRs in the four nations of interest appear to be increasing. Moreover, estimates of PCa ASIRs are collected from a limited number of registry data sources from nations that are geographically and/or ethnically heterogeneous. Such registries offer a limited

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