

Review

Epidemiology of the major cancers in the Asian Pacific

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Abstract: The descriptive epidemiology of cancer in the Asian Pacific region of the world is now well-established due to the activities of cancer registries. Major differences in the most prevalent cancers continue to be observed, both within and between individual countries, gastric cancer being a prime example with high incidences in Japan, China and Korea but very low burdens in Thailand and Indonesia. Hepatocellular carcinomas are particularly prevalent in Mongolia while cancers of the oral cavity predominate in South Asia and are also relatively common in Taiwan, with a common link to betel chewing. Both ethnicity and specific dietary habits retain importance, for example with nasopharyngeal cancer in southern Chinese and cholangiocarcinoma in the north-east of Thailand. However, there are consistent trends affecting all countries, and cancer of the lung in males and lung and breast in females appear to be on the increase across the region. Of particular concern is the increase in adenocarcinoma of the female lung in non-smokers. Regarding mortality, there is major variation depending on the facilities available, level of awareness and socioeconomic background. For risk and beneficial factor analysis, great advances have recently been made due to the establishment of the Hospital-Based Epidemiologic Research Program at Aichi Cancer Center (HERPACC) and the Korean Multi-center Cancer Cohort Study including a Biological Materials Bank (KMCC-I). These are providing valuable clues as to potential preventive measures, generally in line with the literature for other regions of the globe. Included in HERPACC is a comprehensive approach to analysis of gene-environment interactions and influence of polymorphisms. The future should see greater emphasis on education and practical efforts by epidemiologists across the Asian Pacific to counter the growing threat of cancers due to tobacco smoking and the change to a high fat western diet. In addition to the focus on diet and physical exercise as preventive agents, for example now being tested for efficacy in the colon, further development of primary prevention approaches focusing on vaccines and chemopreventive agents await clinical trials.

Key words: Descriptive epidemiology; country variation; organ specificity; pathophysiology.

Introduction. At the 22nd annual scientific meeting of the International Association of Cancer Registries, held in Khon Kaen, Thailand in November 2000, a special poster session was held to allow descriptive epidemiologists gathered from the cancer registries across the region to present their most recent findings for cancer incidence and mortality.¹⁾ An

overview of incidence data included for the most prevalent cancers is given in Tables I and II for males and females, respectively. Clearly, major inter-country differences continue to exist regarding relative importance of individual cancers. Indeed, this is also the case within countries, for example between Hanoi and Ho Chi Min City in Vietnam,²⁾ and within the various regions of Thailand³⁾ and Indonesia,⁴⁾ and between ethnic groups.⁵⁾ In addition to such specific infectious agent-associated neoplasms as urinary bladders linked to schistosomiasis in the Middle-East⁶⁾ and cholangiocarcinoma development in the liver due to opisthorchiasis,⁷⁾ cultural environmental factors continue to play important roles, like betel nut chewing for buccal cavity cancer in

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Table I. Major cancers in countries of the Asian Pacific - Incidence rates (/100,000) for males^{*)}

Country	Oral cavity	Oesophagus	Stomach	Colo-rectal	Liver	Lungs	Prostate	Urinary bladder
Australia ^{**)}	14.1	5.4	11.7	46.7	3.0	46.0	47.6	18.3
China	1.4	14.8	30.8	11.5	21.0	24.2	2.1	3.4
India	16.2	7.4	6.8	5.4	?	8.5	5.2	3.5
Indonesia	?	?	?	6.8	5.7	14.1	5.6	4.7
Iran	3.9	39.4	17.3	3.8	3.9	8.0	2.0	4.4
Japan	6.0	10.0	67.0	48.0	26.0	37.0	10.0	8.2
Jordan	?	?	6.8	16.1	?	18.8	11.8	14.7
Korea	3.3	10.1	70.0	14.9	48.8	48.4	4.2	9.5
Malaysia (Malay)	?	2.1	9.2	12.0	6.4	7.0	4.7	?
Malaysia (Chinese)	?	2.9	10.9	13.1	7.5	30.7	3.4	3.3
Mongolia	5.8	30.1	47.3	4.7	117.0	39.3	4.5	?
Oman	2.8	2.6	13.7	4.2	8.9	12.1	10.8	5.8
Pakistan	24.7	6.2	4.6	5.9	5.0	20.0	7.6	9.4
Singapore (Malay)	8.7	2.9	8.4	8.4	7.1	9.2	8.3	4.9
Singapore (Chinese)	6.6	7.1	25.6	41.8	21.7	56.8	13.8	7.5
Taiwan	15.1	5.8	15.8	22.1	30.9	25.8	7.9	6.9
Thailand	8.5	3.7	4.9	10.4	37.4	26.5	4.4	5.2
Vietnam	6.2	3.7	23.7	11.4	22.6	29.3	2.2	2.4

^{*)}, ^{**) Data from Parkin and Vatanasapt, 2001¹⁾ and Parkin *et al.*, 1997,¹⁴⁾ respectively. ?, Not given.}

Table II. Major cancers in countries of the Asian Pacific- Incidence rates (/100,000) for females^{*)}

Country	Oral cavity	Oesophagus	Stomach	Colo-rectal	Liver	Lungs	Breast	Uterine		Ovary	Urinary bladder
								Cervix	Corpus		
Australia ^{**)}	4.1	2.4	4.9	33.9	0.7	15.8	66.7	9.4	10.2	9.6	5.0
China	0.7	6.0	14.7	9.0	8.0	10.2	12.7	1.2	1.8	5.3	0.9
India	7.8	5.8	3.5	3.9	?	2.2	22.6	25.3	3.0	5.9	1.0
Indonesia	?	?	?	6.3	?	4.8	14.8	21.8	3.0	5.2	?
Iran	3.0	24.9	5.9	2.9	1.8	1.8	12.3	7.0	1.6	2.5	1.1
Japan	3.7	2.8	54.0	51.0	16.0	23.0	47.0	13.0	6.8	9.6	4.4
Jordan	?	?	4.7	14.4	?	2.6	39.8	?	?	6.7	1.7
Korea	1.0	1.0	25.7	10.3	11.6	12.1	12.5	15.3	1.5	4.0	?
Malaysia (M)	?	?	3.0	3.0	?	1.6	6.4	9.2	1.8	2.3	?
Malaysia (C)	?	?	4.5	9.3	2.3	8.3	23.8	16.2	4.4	5.3	?
Mongolia	4.4	24.2	28.6	3.9	66.7	14.6	7.4	20.7	2.4	4.4	?
Oman	2.1	3.3	7.0	?	4.1	2.3	13.1	5.6	1.6	6.3	3.4
Pakistan	18.7	6.9	3.2	5.0	3.4	2.8	56.6	13.4	?	9.5	3.1
Singapore (M)	7.3	1.8	6.1	14.9	1.6	5.2	36.5	7.5	6.5	9.4	1.4
Singapore (C)	1.8	1.4	12.3	31.7	5.1	19.8	46.5	15.4	8.2	10.7	1.7
Taiwan	?	?	8.6	18.3	10.9	11.9	25.1	21.8	?	4.5	?
Thailand	4.5	1.3	3.0	7.5	15.5	11.1	16.3	20.9	2.9	4.7	1.2
Vietnam	3.4	0.6	10.8	8.3	5.8	6.5	17.4	17.3	2.4	4.4	1.1

^{*)}, ^{**) Data from Parkin and Vatanasapt, 2001¹⁾ and Parkin *et al.*, 1997,¹⁴⁾ respectively. ?, Not given.}

India and Taiwan.^{8),9)} The dietary environment also appears to be a major determinant, for example of levels of gastric and breast cancer.^{10),11)} In addition to the contributions of a large number of individual research groups focusing on particular cancers and risk factors, advances are now being made in comprehensive elucidation of environmental and genetic factors by such programs as the Hospital-Based Epidemiologic Research Program at Aichi Cancer Center (HERPACC)¹⁰⁾ and the

similar Korean Multi-center Cancer Cohort Study including a Biological Materials Bank (KMCC-I).¹²⁾ A major focus within HERPACC is now the elucidation of gene-environment interactions and the influence of gene polymorphisms.¹³⁾ In the present mini-review we concentrate attention on the status of descriptive, analytical and intervention epidemiology regarding major cancer sites in the Asian Pacific countries.

Cancer sites. As can be gleaned from Tables I and

II, the alimentary canal and liver, as well as the lung in males and the breast and cervix in females, account for the majority of cancers in the Asian countries, squamous cell carcinomas (SCCs) tending to be more important in the developing countries and adenocarcinomas in those that are already industrialized.

Buccal cavity. Cancers of the buccal cavity are very prevalent in Southern Asia and Taiwan, the shared risk factor being betel chewing,^{8),9)} with important roles also for HPV and cigarette smoking.¹⁵⁾ For prevention, although education for cessation of the betel quid chewing habit is important, there are few adequate strategies and policies, and health promotion and education related to oral cancer control is limited, especially in rural areas.¹⁶⁾ Among cancers of the buccal area, a special case is the nasopharyngeal carcinoma, extremely high rates being evident in some Chinese populations. Contributions of Epstein Barr virus (EBV) infection and genetic susceptibility are consistent aetiological factors for this cancer in various ethnic groups, while other factors may depend on distinct dietary practices and the living environment adopted in different geographical regions of the world.¹⁷⁾

Oesophagus. Whereas in the Western world the proportion of adenocarcinomas of the oesophagus has been rapidly increasing over the last decades,¹⁸⁾ so that approximately 40% of the total is of this type in males, this is not the case for example in Taiwan¹⁹⁾ and in most Asian countries the SCC continues to be predominant, accounting for over 90% of esophageal cancers in Japan, between 80 and 90% in India and approximately 70% in Israel.¹³⁾ This points to clear variation in environmental factors, diet and obesity appearing to be especially important for adenocarcinoma, as opposed to tobacco smoke and alcohol for the SCC. In the very high risk belt stretching from Iran to China, other important factors are opium smoking, nutrient deficiency and cereal intake.¹¹⁾

Stomach. Within Asia gastric cancer continues to be most common in Japan and Korea, with intermediate rates in China and Vietnam, and only low levels in Southern Asia and some of the South-East Asian countries. Generally females have only half the rates of males, with the notable exception of Japan. While there is a clear role for salt intake,¹¹⁾ as indirectly evidenced by the close correlation observed between stomach cancer and stroke in country comparisons,²⁰⁾ other factors are important like *Helicobacter pylori* and chronic atrophic gastritis,^{21),22)} different factors impacting at different levels in the cardia and antrum sites within the

Table III. Risk and protective factors for cancer of the gastric cardia and antrum

Factor	Cardia	Antrum
Risk		
Helicobacter	+/-	+++
Epstein-Barr	+	+/-
Gastric ulcers	+/-	++
High fat diet	++	+/-
Obesity	++	+/-
Smoking	++	+
Alcohol	+	++
Protective		
Vegetable intake	--	--

+/-, equivocal influence; +/++/+++ , weak/strong/very strong promotion; --, strong inhibition.
From the Literature.²²⁾⁻²⁴⁾

stomach²²⁾⁻²⁵⁾ (see Table III). A recent prospective study suggests that vegetable and fruit intake, even in low amounts, is associated with a lower risk of gastric cancer.²⁶⁾

Colon and rectum. The total colorectal cancer burden appears clearly related to economic affluence, being high in Australia, Japan, Singapore Chinese, low in South Asia and South-East Asia, with clear effects of the diet and particularly fat intake²⁷⁾ and a role for body mass.²⁸⁾ A recent ecological study showed positive associations with fat and oil intake, of both plant and animal types; and a positive link was noted with animal protein, the association with plant protein consumption being inverse, as is also the case for carbohydrate and cereals.²⁹⁾ At the country level, we can also see a good inverse correlation with consumption of cereals (see Fig. 1) (Tajima *et al.*, 2002).³⁰⁾ While colon and rectal cancer rates generally correlate, there may be a decided influence of additional factors operating in only one site, as shown by a comparison of rates in Eastern and Western Europe.³¹⁾ The relationship between the incidences of rectal and colon cancers is of obvious interest, given the shift in the subsite distribution observed in Japan over time, with a decreasing proportion of rectal cancers.³²⁾

Liver. In both males and females by far the highest liver cancer incidence rates have been reported in Mongolia, presumably linked to a very high prevalence of hepatitis B and C.³³⁾ A viral component seems prevalent across the region, possibly accompanied by environmental pollutants like dioxin in Vietnam.³⁴⁾ While liver cancer is exceedingly high in the north-east of Thailand, this is due to opisthorchiasis-associated cholangiocellular carcinomas.⁷⁾

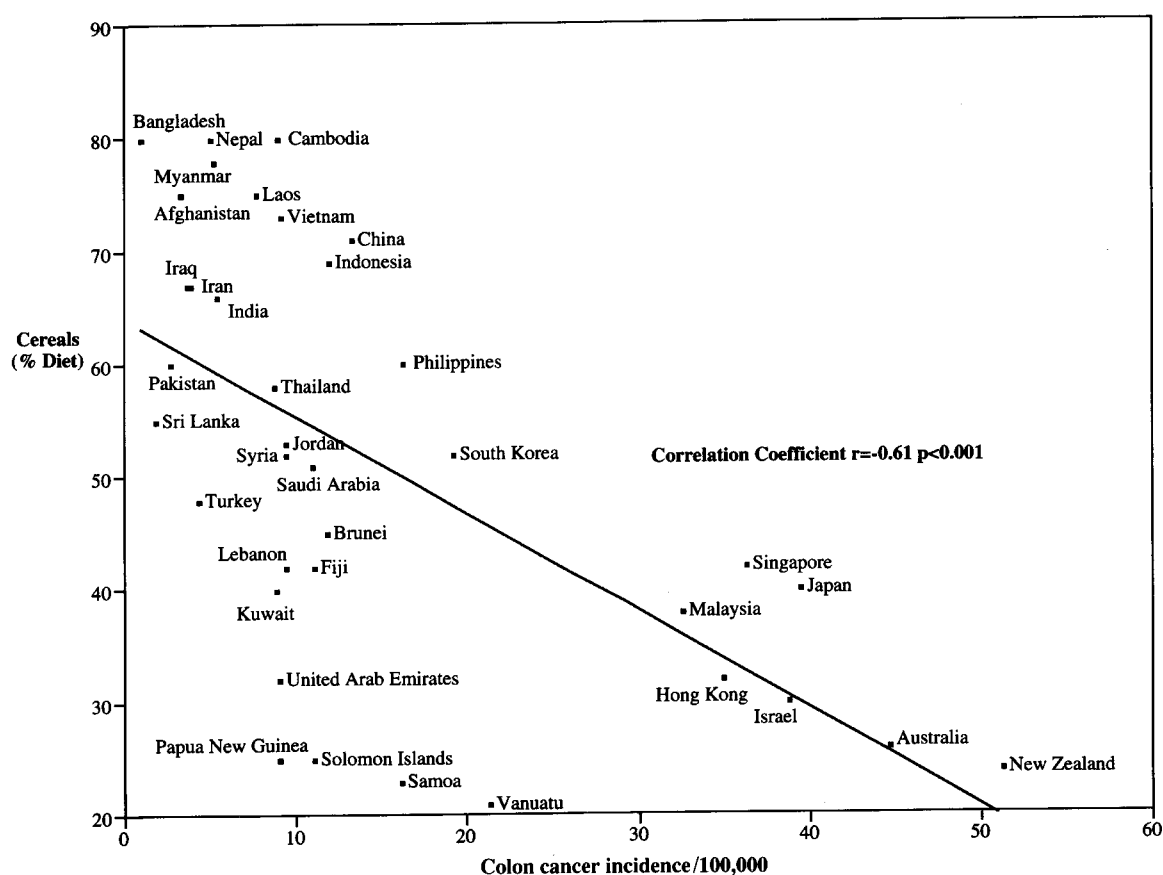


Fig. 1. Correlation between cereal percentage in the diet and colon cancer incidence.

Table IV. Ratios for incidences of squamous cell carcinomas and adenocarcinomas of the lung

Country	Male SCC:AC	Female SCC:AC	Male/Female ratio
Kuwait	3.1:1	1.6:1	1.9
Israel	1.3:1	0.5:1	2.6
India	1.8:1	0.6:1	3.0
Singapore	1.2:1	0.4:1	3.0
Thailand	0.6:1	0.3:1	2.0
Vietnam	1.2:1	0.8:1	1.5
Philippines	1.3:1	0.4:1	3.3
Hong Kong	1.0:1	0.3:1	3.3
China-Tianjin	2.0:1	0.7:1	2.9
Korea	5.0:1	0.6:1	8.3
Japan	1.0:1	0.2:1	5.0
Australia	1.5:1	0.7:1	2.1

Data from Parkin *et al.*, 1997.¹⁴⁾

Lung. Cancer of the lungs is a major problem throughout the Asian Pacific. In many countries of the world there has been a shift away from squamous cell carcinoma as smoking rates decline in males towards

adenocarcinomas, particularly in non-smoking females³⁵⁾ and the ratios between the two types are revealing in the context of country and sex variation (see Table IV). Cross country comparison have suggested that blood borne factors, like hormones, may be important as determinants for the increasingly prevalent lung adenocarcinoma³⁶⁾ and recent findings from Singapore point to involvement of estrogen-related pathways in lung cancer among non-smoking females.³⁷⁾ Women exposed to cooking fumes from rapeseed oil appear to be at increased risk of lung cancer³⁸⁾ and tobacco smoking alone may not be able to explain the very high incidence of female lung cancer in Northern Thailand, where chronic benign respiratory disease, possibly caused by infection with fungi, is likely to be involved in the etiology.³⁹⁾

Urinary tract. In the list of countries represented at the Asian cancer registration meeting, the highest incidence of urinary bladder cancers in males was in Jordan, with a possible involvement of schistosomiasis. This was not, however, the case for females. Regarding

Table V. Five rule points for cancer prevention

1st	Stress the strongest weapons for cancer prevention – no smoking and moderation in alcohol consumption
2nd	Focus on green, yellow and red signals for health – consume colored fruits and vegetables
3rd	Reduce risk for all cancer, as well as other chronic diseases – take at least 30 min gentle exercise at least twice a week
4th	Develop a well-balanced health sense – ensure adequate intake of nutrients with variation in food types
5th	Contribute to healthy life in the Asian Pacific in the 21st century – plan a menu of low salt and moderate fat

After Tajima *et al.*, 2001.⁴⁹⁾

prevention efforts, a number of papers have provided evidence that fruit and green-yellow vegetable intake is negatively associated with risk, particularly in men.^{40),41)}

Prostate. The massive inter-country differential in prostate cancer rates, something in the order of 25 fold between China and Australia, clearly reflect the importance of environmental factors. Comparative geographic-pathologic autopsy studies have further suggested that different promoting factors, including both genetic and epigenetic influences, may be responsible for ethnic variation in the postinduction progression of prostate cancer.⁴²⁾

Breast. In most of the countries of the region breast cancer ranks first or second in incidence in women, Mongolia being the only exception. Epidemiologic studies conducted in Korea and Japan have shown that a family history of breast cancer, early menarche, late menopause, late full-term pregnancy, and never having had a breast-fed child are primary risk factors in the development of breast cancer, as in other parts of the world.^{10),43)}

Ovary. Compared to other sites, variation in incidence of ovarian cancer is relatively limited across the Asian Pacific region, with highest rates in Singapore Chinese and lowest in Malaysian Malay. Large numbers of epidemiological studies have pointed to high saturated fat and carbohydrate intake, postmenopausal hormone replacement therapy and use of cosmetic talc as risk factors. Conversely, vegetable consumption, parity, lactation and generally appear to confer protection. Genetic influence also clearly plays a role, women with mutations in the BRCA1 or BRCA2 genes having an elevated risk, for example.^{44),45)}

Uterine cervix and corpus uteri. As shown in Table II, cancer of the cervix has the highest incidence of all neoplasms in females in Thailand, Vietnam, India and Indonesia, with the human papilloma virus as the most important influence. The ratio to endometrial cancers varies widely, the latter only accounting for approximately 10-15% of all uterine cancers in developing countries but about one third in Japan and Singapore, and more than half in Australia, clearly pointing to an importance of the cultural environment.

Intervention strategies for primary cancer prevention. The final goal of epidemiology must be the establishment of prevention measures and the promotion of better human health. Since implementation of cancer control measures requires modification of human behavior based on an awareness of the culture of the people concerned, due regard to ethnic group- or area-specific risk factors for the most common cancers is necessary. Current information obtained from molecular epidemiologic studies on modification of cancer related to lifestyle exposure by gene-environment interactions based on genetic polymorphisms¹³⁾ can only be effectively applied with a knowledge of cultural determinants. Furthermore, to establish effective cancer control programs, basic information on cancer incidence and mortality is clearly essential and efforts to improve cancer registration, especially with reference to pathological diagnoses and organ physiological concerns,⁴⁶⁾ need to be continuously promoted. Similarly, effects of cancer screening programs can only be assessed in terms of reduction in incidence and mortality from twinned cancer registry data. Risk and protective factors may vary with the site and we have to recognize that foods, for example, may exert independent and contrasting risk and protective influence. For example, sufficient intake of grains might be protective for colon cancer in western countries but may become a risk factor for stomach cancer in Northeast Asia. However, in general there are a number of recommendations which can be made.^{10),11),47)} The Union International Contra Cancrum Epidemiology and Prevention Program Nutrition and Cancer has in fact issued guidelines for cancer control in agreement with the five rule points proposed for cancer prevention in the Asian Pacific (Table V).^{48),49)} A holistic approach is essential, with choice of a balanced diet and avoidance of cigarette smoking and other sources of mutagens/carcinogens, for example in cooked food, fungal products, plant and mushroom substances, and nitrite-related materials.⁵⁰⁾

While a great deal of attention is being paid to prac-

tical community intervention in Australia and the US, this area of epidemiological research is only in its infancy in Asia, although a start has been made with the Practical Prevention Program of the Asian Pacific Organization for Cancer Prevention.⁵¹⁾ A model program focusing on a healthy diet and gentle exercise, conducted in Aichi Cancer Center Hospital, should also provide pointers to improvement of lifestyle for prevention of cancer as well as obesity.⁵²⁾ Such modification is also the basis for a major intervention study of colorectal tumor patients in Japan.⁵³⁾ One aspect of major importance to future efforts is appropriate education for nurses and doctors.^{54),55)} The Japanese International Cooperation Agency (JICA) sponsored training course in community-based cancer prevention with the emphasis on epidemiology,⁵⁶⁾ is thus filling a niche which might deserve future expansion, especially if the proposals for an International Agency for Cancer Research in the Asian Pacific can be realised.⁵⁷⁾ Another important type of primary intervention, is to use chemicals with the potential to retard cancer development or cause regression of lesions. Most clinical trials of chemopreventive agents have been conducted in the US, but a number have been performed in Asia,⁵⁸⁾ vitamin E for example being shown to have potential for suppression of intra-epithelial lesions of the cervix.⁵⁹⁾

As stated in the aims of the Asian Pacific Organization for Cancer Prevention (<http://www.apocp.org/>), an awareness of all areas of cancer prevention is necessary for effective reduction in the cancer burden in our societies, with a firm ecological basis.⁶⁰⁾ Great strides have already been made in the descriptive epidemiology of neoplasia in the Asian Pacific area and a firm foundation now exists on which to build practical preventive efforts so that in the future the only cancers we encounter will hopefully be of 'natural-end' character, in line with the 'Tenju-gann' concept.⁶¹⁾

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