decrease. In the United States, filter cigarette consumption peaked in the late 1970s.

Figure 2 and Table 1 provide the long-term trends in overall lung cancer incidence in Japan and the United States using the joinpoint regression analyses. For males and females combined, while the peak incidence has already occurred in the United States, with a downward trend beginning in 1991, the incidence for Japanese continues to be flat, followed by an upward trend until 1993. While the peak incidence for Japanese males occurred in 1992, the incidence for Japanese females continues to increase. Rates among Japanese males decreased by 0.6% per year from 1992 to 2003, after increasing by 2.2% annually from 1975 to 1992, and rates among Japanese females increased by 3.6% annually from 1975 to 1982 and by 1.1% after 1982. In the United States, peak incidence has already occurred in females in 1988, 7 years later than that in males. Among American males, rates decreased by 0.6% per year from 1981 to 1991 and by 2.2% per year from 1991 to 2005, after increasing by 1.8% annually from 1973 to 1978.

Figure 3 illustrates temporal patterns in ASR for selected histological types of lung cancer in Japan and the United States. For males and females combined (Fig. 3*a*), the peak incidence of SQ in Japanese occurred in 1992, 10 years later than that in the United States. In the United States, the rate of decline in SQ incidence significantly increased after 1992. While the incidence of AD continues to increase in Japan, peak incidence has already occurred in Americans, with a downward trend beginning in 1992. The incidence of AD in Japanese and Americans overtook the incidence of SQ in 1984 and 1976, respectively. For males (Fig. 3*b*), the peak incidence of SQs has already occurred in Japanese, with a downward trend beginning in 1994, 12 years later than that in the United States. While the incidence of AD for Japanese males leveled in 1998 after an upward trend, the peak incidence occurred in the US males, with a downward trend beginning in 1992. For females, the trends of SQ and AD in Japanese are different to those in Americans (Fig. 3*c*). In Japanese, the incidence for SQ continues to decrease and that for AD continues to increase. In contract, the peak incidences of SQ and AD have already occurred in 1982 and 1991 in the United States, respectively.

Table 2 provides the long-term trends in different histological groups of lung cancer incidence using the joinpoint regression analyses. For SQ, rates among Japanese increased by 0.7% annually from 1975 to 1989, were stable from 1989 to 1992, and then decreased by 1.9% from 1992 to 2003. Among Americans, rates increased by 2.1% annually from 1973 to 1982, then decreased by 1.7% from 1982 to 1992 and by 3.6% from 1992 to 2005. For AD, rates among Japanese increased by 2.4% annually from 1975 to 1990, were stable from 1990 to 1993 and then increased by 1.7% from 1993 to 2003. In contrast, rates among Americans increased by 9.4% annually from 1973 to 1978 and by 2.5% from 1978 to 1992 and then decreased by 2.2% from 1992 to 2005. In Japan,

Table 2. Trends of age-standardized rates of lung cancer with joinpoint analyses by sex and histological group in Japan and the United States (Continued)

	Trend 1		Trend 2		Trend 3		Trend 4	
Histology	Years	APC (95% CI)	Years	APC (95% CI)	Years	APC (95% CI)	Years	APC (95% CI)
Small cell carcinoma	1975–1982	8.7† (2.0, 15.7)	1982–2003	−1.6† (−2.3, −0.9)				
USA (1973–2005)								
Suamous cell carcinoma	1973–1984	5.3† (4.2, 6.3)	1984–1995	0.2 (−0.6, 1.1)	1995–2005	−2.5† (−3.3, −1.7)		
Adenocarcinoma	1973–1976	19.1† (9.5, 29.5)	1976–1991	4.2† (3.7, 4.7)	1991–2005	−0.3 (−0.7, 0.1)		
Small cell carcinoma	1973–1982	9.0† (7.2, 10.9)	1982–1991	2.7† (1.3, 4.1)	1991–2005	−1.6† (−2.1, 1.1)		

Source: SEER-9 areas covering about 10% of the US population (States of Connecticut, Hawaii, Iowa, Utah, and New Mexico, and the metropolitan areas of San Fransisco-Oakland, Detroit, Atlanta, and Seattle-Puget Sound), and Japanese nine areas covering about 10% of the Japanese population (Prefectures of Yamagata, Niigata, Fukui, Shiga, Osaka, Okayama, Saga and Nagasaki, Hiroshima City and Nagasaki City).
Joinpoint analyses with up to three joinpoints were based on rates (per 100,000 persons) and were age adjusted to the world population. Joinpoint analysis used the Joinpoint Regression Program, version 3.3.April 1, 2008, National Cancer Institute.
APC is based on rates that were age standardized to the world population.
†APC is statistically significantly different from zero (two-sided $p < 0.05$, calculated using a *t*-test.)
Abbreviations: APC: annual percent change; CI: confidence interval.

Table 3. The relationship between cigarette consumption and lung cancer incidence by histologic type in Japan and the United States

	SQ			AD		
Type of cigarette	**Lag time τ***	$\hat{\beta}_2^{SQ}$ ($\times 10^{-3}$)†	**95% CI ($\times 10^{-3}$)**	**Lag time τ***	$\hat{\beta}_2^{AD}$ ($\times 10^{-3}$)†	**95% CI ($\times 10^{-3}$)**
Japan						
Nonfilter	30	0.464‡	(0.164, 0.764)	24	−1.099‡	(−1.767 to −0.431)
Filter	30	−0.340‡	(−0.518, −0.162)	25	1.946‡	(1.297–2.594)
United States						
Nonfilter	20	0.455‡	(0.319, 0.591)	17	0.353	(−0.020 to 0.757)
Filter	25	−0.268‡	(−0.383–0.152)	15	3.183‡	(1.955–4.411)

*τ is defined as the lag between lung cancer incidence and cigarette consumption; CI, confidence interval. †β_2 is the coefficient for cigarette consumption in the model of $Y(t^+) = \beta_0 + \beta_1 Y(t) + \beta_2 X(t^+ - \tau) + \varepsilon$ ‡Statistically significantly different from zero (two-sided $p < 0.05$, calculated using a *t*-test).

rates for small cell carcinoma increased by 6.7% annually from 1975 to 1984, then leveled off thereafter. In contrast, rates in the United States increased by 6.4% annually from 1973 to 1981 and by 1.8% from 1981 to 1988, and then began to decrease thereafter.

Because sex-specific data on cigarette consumption by cigarette design were not available on public, we examined the relationship between cigarette consumption and lung cancer incidence by histologic type in males and females combined. Table 3 summarizes the statistical relationship between them using multiple regression analyses. The models in Table 3 did not violate assumptions of normality and uncorrelatedness. Among Japanese, the trend in nonfilter consumption was positively associated with the incidence of SQ ($\hat{\beta}_2^{SQ}$, 0.464×10^{-3}, 95% confidence interval (CI), [0.164×10^{-3}, 0.764×10^{-3}], $p = 0.006$) with the appropriate time lag of 30 years, and the trend in filter cigarette consumption was positively associated with AD incidence ($\hat{\beta}_2^{AD}$, 1.946×10^{-3}, 95%CI, [1.297×10^{-3}, 2.594×10^{-3}], $p < 0.001$) with the appropriate time lag of 25 years. Similarly, among Americans, the trend in nonfilter consumption was positively associated with SQ incidence ($\hat{\beta}_2^{SQ}$, 0.364×10^{-3}, 95%CI, [0.109×10^{-3}, 0.619×10^{-3}], $p = 0.008$) with the appropriate time lag of 20 years, while the trend in filter consumption was positively associated with AD incidence ($\hat{\beta}_2^{AD}$, 3.142×10^{-3}, 95%CI, [1.923×10^{-3}, 4.361×10^{-3}], $p < 0.001$) with the appropriate time lag of 15 years. The negative association between trends in nonfilter cigarette consumption and AD and between trends in filter consumption and SQ among Japanese and Americans reflect the shift in market share from nonfilter to filter cigarettes.

Discussion

AD has replaced SQ as the most frequent histologic type of lung cancer in both Japan and the United States. This increase in AD incidence in both the countries is also associated with the introduction of filtered cigarettes and the substantial increase in filter cigarette consumption. The decrease in nonfilter cigarette consumption due to the shift in market share from nonfilter to filter cigarette is associated with the decrease in the incidence of SQ. To our knowledge, these empirical observations, using population-based data from two distinct countries, are the first to support the long-held hypothesis that smoking filtered *vs.* nonfiltered cigarettes leads to separate presentations of lung cancer. These results are consistent with previous epidemiological study obtained using data at the individual level.[32–34]

Another possible explanation for the change in trends for AD of the lung is changes in exposure to air pollution. Long-term exposure to some components of polluted air, particularly NO*x*, might play a role in the development of AD.[12] Given that air pollution can be considered a general phenomenon, this possibility is not contradicted by the similarity in trends in AD incidence in US males and females but is contradicted by the difference in gender-specific trends in Japanese males and females. In addition, compared with current smokers, the lung cancer rate is very low among never smokers.[35] A prospective cohort study in Norway suggested that although air pollution is one of the causes of lung cancer, it may still much less than cigarette smoking that causes lung cancer.[36,37] A second possible explanation for this AD trend might be related to underlying trends in exposure to environmental tobacco smoke (ETS). Recent regulations have strictly reduced ETS exposure in the United States.[38] The consequent decrease in exposure to ETS might explain the recent decrease in incidence of ADs of the lung in the United States, at least, in part. Although this point should be examined in the future with more detailed exposure and outcome evaluation, it is clear that ETS has much less impact on the risk than active smoking.

Reflecting the wide-scale adoption of filter cigarettes beginning in the 1960s, the United States observed a sharp increase in ADs in the early 1970s, with 9.4% increases annually from 1973 to 1979. Interestingly, although filter cigarettes penetrated the Japanese market more rapidly in the 1970s, the increase in ADs in Japan has not been as sharp as in the United States. There are two explanations for this. First, the greater use of charcoal-containing cigarette filters in Japan (70 *vs.* 1% in the United States) may have had a beneficial effect, perhaps by trapping a greater load of fine particulates

than other filters or by removing a greater load of volatile toxic agents, such as hydrogen cyanide, N-nitrosamines and volatile aldehydes known to act as inhibitors of lung clearance.[19] In this regard, Muscat *et al.* found no association between charcoal filters and an attenuated risk of lung cancer in a Japanese population.[39] Second, it is of course also possible that the differences between the Japanese and US experience may have been affected by the assumptions used in allocating specific morphologies to cases of unknown morphology. Additional analyses focused on this issue may clarify the observed differences.

It is considered paradoxical that a proportion of Japanese who smoke is higher than American males but have a lower incidence of lung cancer.[19] Several factors acting either alone or in combination may explain this lower rate in Japan,[19,40] including age at onset of cigarette smoking, specific personal smoking (*i.e.*, manner of smoking, particularly shallow inhalation), and the contents and construction of cigarettes. Despite the higher smoking prevalence in Japan, total cigarette consumption per capita was lower than in the United States until 1987, suggesting that Japanese smokers smoked fewer cigarettes per day than their American counterparts. Other differences may explain the lower lung cancer rates in Japan: *e.g.*, because consumption of filter cigarettes increased rapidly around the same time that smoking became popular in Japan, Japanese smokers were less exposed to unfiltered cigarettes. Additionally, the Japanese diet may have a protective effect against lung cancer, owing to its relatively high consumption of soybeans,[41,42] which contain the strong tumor inhibitor genistein, and fish[41] and relatively low intake of dietary fat.[43] Frequent consumption of green tea[44] may also have a protective effect. Finally, Americans may have a greater genetic susceptibility to tobacco carcinogens than Japanese. In this regard, the lower relative risks by smoking in epidemiological studies conducted in Japan *versus* the United States is well known.[19,45] In this study, we found a shorter lag time of τ in Americans than in Japanese, which represents the shorter sum of induction and latent period in Americans than in Japanese (*e.g.*, lag times for AD after the advent of filter cigarettes were 25 years in Japan *vs.* 15 years in the United States). This might be a reflection of a difference in patterns of smoking behavior, life styles and susceptibility to lung cancer between Japan and the United States.

Our findings suggest that the trends of incidence of lung cancer by histologic type differ in males and females as well as the associations between changes in the incidences and in filter/nonfilter cigarettes differ among males and females, in both Japan and in the United States. That may be due to the differences in patterns of smoking behavior and the susceptibility to lung cancer in cigarette smokers among males and females. Smoking rate is significantly lower for females than for males in both the countries (11.0 and 39.4% in males and females in Japan, respectively, and 17.4 and 23.4% in the United States).[27,46] Females were more likely than men to smoke filter cigarettes (89.0–90.6% *vs.* 75.0–79.3% in the 1970s,[47,48] and 92.9–94.6% *vs.* 87.0–90% in the 1980s). Females with lung cancer are more likely to be never smokers or less intense smoking history, and have AD subtypes.[49] Therefore, the sex-specific analysis for cigarette types and incidence patterns by histology subtype would sharpen the findings. However, unfortunately, the data on filter/nonfilter cigarette consumption are not available both in Japan and the United States so that we could not analyze the sex specific relationships between the trend in lung cancer incidence by histologic type and consumptions of filter or nonfilter cigarettes. Therefore, the analyses in males and females combined may weaken a true relationship between the increased trend in AD and filter cigarette consumption. Nevertheless, we could obtain the statistically significant relationship between them using the data for males and females combined.

Molecular examinations of lung cancer might give us an insight to interpret different patterns of change in histology-specific incidence by sex and ethnicities discussed above. It has been reported that epidermal growth factor receptor (*EGFR*) mutations commonly present in female, never-smoker and Asian ethnicity.[50] Potential differences in several risk factors including smoking by *EGFR* mutational status have been reported to date.[51,52]

Several limitations of this study warrant mention. First, as an ecological study, it possesses all the limitations inherent to ecological analyses. Aggregate data on exposure and disease—data obtained from population aggregates—cannot be linked to individuals. Although estimated consumption of cigarettes was based on nationally averaged levels for the respective countries, consumption may in fact vary by area (rural *vs.* metropolitan), race/ethnicity, sex, age and education. The increased consumption of filter cigarettes may have played different roles in the increase in AD incidence in males and females, but the present data lacked the sensitivity to detect changes at this level. Second, the data collected from Japanese prefectural population-based cancer registries have major quality issues and fail to meet international data quality standards for the proportion of death-certificate-only cases, incidence-to-mortality ratio and proportion of histologically verified cases.[53] Based on mathematical modeling, true incidence may be underestimated by as much as 20%.[54] Moreover, because one-third of the Japanese cases in this study were of unknown morphology, the data may not adequately reflect the true changes in lung cancer incidence by histologic type. Nevertheless, we do not consider that our allocation methodology biased the results, and reanalysis of the data without the proportional reallocation of cases with unspecified morphology returned virtually identical results. Finally, another limitation may be change over time in the definition of AD[55] or in diagnostic practice,[56] although we consider that these themselves cannot account for the increase in AD incidence. For example, major diagnostic advances such as bronchoscopy, thin-needle aspiration, computed tomography scans

and improved stains for mucin were all introduced in the 1980s,[56] after the increases in the incidence of AD were observed.

While the decreased incidence of SQ among Japanese and Americans is encouraging in terms of cancer prevention and control, it is counterbalanced by the increases in AD, especially among Japanese. As realization of the detrimental health effects of cigarette smoking initially grew, the tobacco industry strove to develop filtered cigarettes as less harmful cigarettes, but subsequent scientific evidence has failed to demonstrate any benefit from changes in cigarette design or manufacturing.[57] Despite the tobacco industry became well aware of the fact that filtered cigarettes were not less harmful, it has been advertised filtered or low-tar cigarettes to intend to reassure smokers and were meant to prevent smokers form quitting since the early 1950s in the United States[58] and later in Japan.[59] The false reassurances provided by marketing strategies of filtered/low-tar cigarettes might be related to the rising incidence of ADs of the lung.

The present results suggest that the shift from nonfilter to filter cigarettes may have had the result of replacing one cancer type with another. These findings emphasize the importance of tobacco control programs, namely programs that prevent the initiation of smoking, hasten the rate of smoking cessation or limit exposure to ETS, have been associated with a decrease in both cigarette consumption and smoking rates, and subsequently with a decrease in lung cancer incidence.[4,60]

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OVERVIEW

Strategies for Cancer Control on an Organ-Site Basis

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Abstract

A great deal of research information has been generated regarding cancer incidence rates and underlying risk factors. Since incidence:mortality ratios are generally less than 2:1 and often approach equivalence there clearly is a need for particular emphasis on preventive measures and early detection. Whether the latter should be through screening or education for improved awareness will depend on the socioeconomic conditions and the organ site. The location within the body, physiological factors and the cell type, whether essentially glandular or squamous, and the particular risk and protective factors operating in the particular social context will all impact on what measures can be recommended. Here the focus is on primary and secondary prevention of cancers in the various regions of Asia, taking into account similarities and differences in etiology for organs/tisssues of the gastrointestinal tract, the respiratory tract, the urinary system, the reproductive system, the nervous system, the thyroid and non-Hogkins lymphomas and leukemias. Globocan 2002 data on incidence and mortality and all of the findings reviewed in the Regional Reviews were taken into account in compiling this overview. The chief recommendations are education in the developing world, to overcome the problem of late presentation at hospital (reflected by high mortality/incidence ratios), betel and tobacco control for the oral cavity and pharynx, reduce salt intake and targeting of *Helicobacter pylori* for the stomach, reduction in food intake, improvement in the diet and more exercise for the colorectum, kidney, prostate, breast, ovary and endometrium, reduction in smoking and exposure to other fumes for the lung, increase in water intake, particularly for the urinary bladder, and avoidance of parasites for the special cases of the urinary bladder and intrahepatic bile ducts. The cancer registry could be a major resource for development of further research capacity, with selection of suitable partners in areas with contrasting cancer rates and lifestyles for detailed comparisons applying the same protocols. This should facilitate future exploration and hopefully elucidation of any anomalies, so that cancer control programs can be optimized in accordance.

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Introduction

The prevailing view is that the majority of cancers are due, very largely, to the environment, with only some 5-10% being primarily related to genetic abnormalities. Naturally, the genetic backgound does play many roles, but this is in the context of interactions with the major environmental factors, whether they be chemical or other types of carcinogenic agents, or causes of inflammation and cell proliferation. This is in line with the initiation-promotion paradigm, whereby neoplasia is 'initiated' at the single cell level (a so-called 'field' effect arising when many cells are hit) by exposure to an agent capable of causing genetic alteration, which can be 'fixed' on cell division, and then 'promoted' by influences which result in growth of initiated populations to form preneoplasias, precancers and eventually malignancies (see Figure 1).

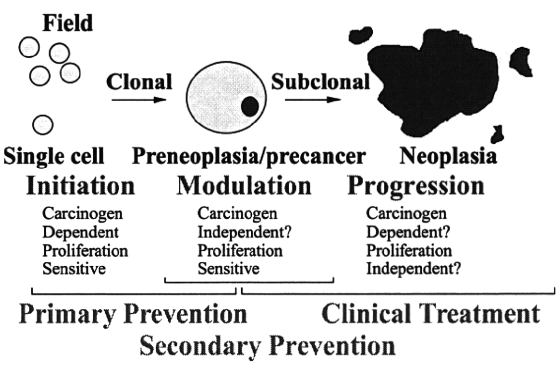

Figure 1. Processes in Neoplasia and Prevention

Primary prevention concerns measures aimed at reducing carcinogen initiation and actions during the phase before focal lesions become apparent, including education for awareness of risk factors, tobacco control and lifestyle changes to reduce inflammatory proliferation pressure. Since both harmful and beneficial factors exist, the term chosen here is 'modulation'. Secondary prevention then covers screening and early detection, along with education to help ensure that patients comply with screening guidelines and present for treatment as soon as symptoms

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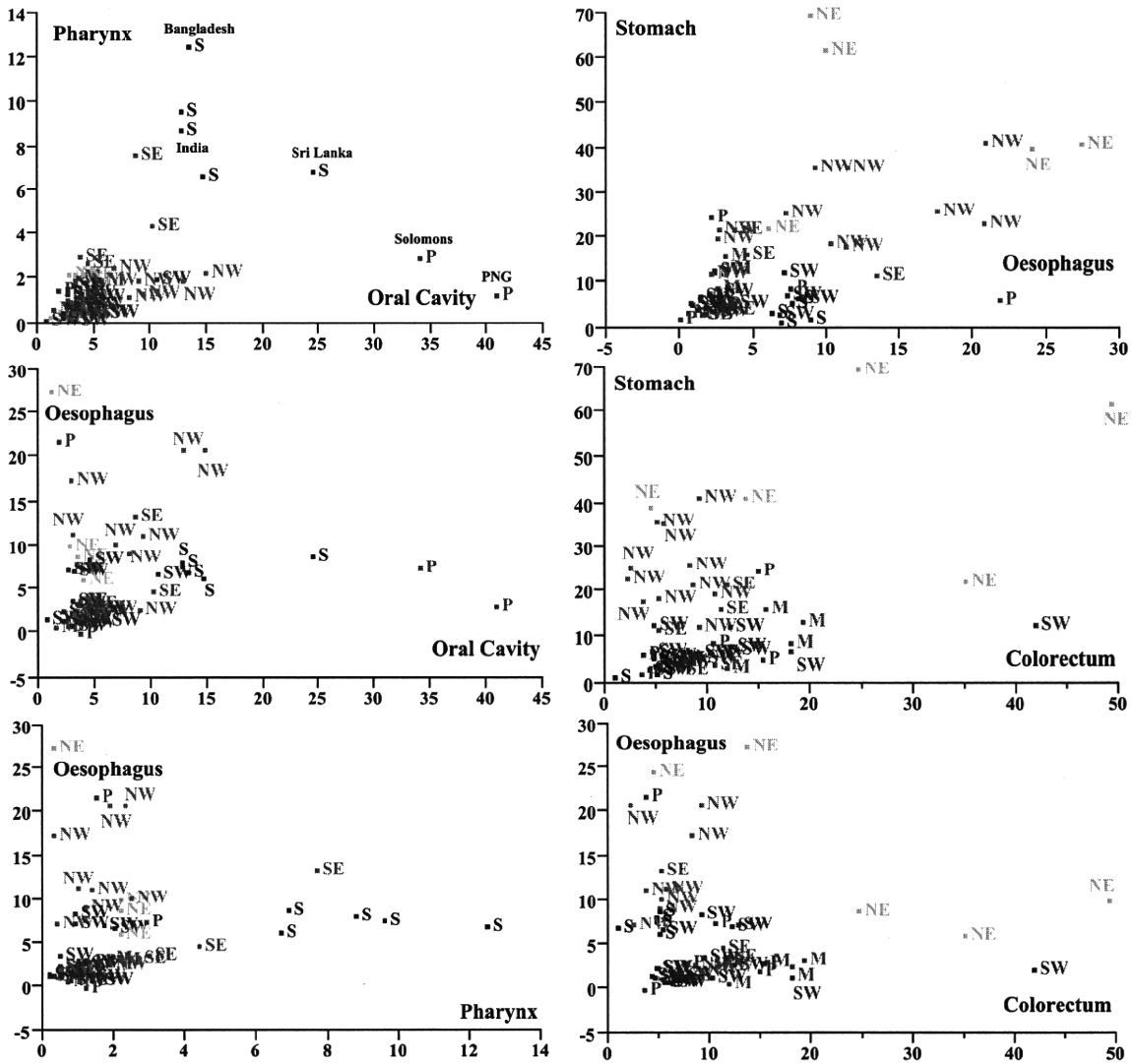

Figure 2. Regional Comparisons Between Globocan Incidence Data for the Various Sites within the Gastrointestinal Tract (M, Southeast, Peninsular and Island; NE, Northeast; NW, Northwest; P, Pacific; SE, Southeast Mainland; SW, Southwest)

develop.

For cancer control there are clearly measures which will impact on all locations in the body, like reduction in tobacco consumption and therefore carcinogen exposure, but this will have differing degrees of influence depending on the organ site. Adjacent or related structures may clearly be affected by the same factors, but at the same time may react differently because of other, sometimes conflicting, influences. In the treatment given below we therefore consider the major organ systems as wholes before going on to the individual tissue sites in discussion.

The Gastrointestinal Tract

Stretching from the lips to the anus, the alimentary tract accounts in total for more than half the cancers in most male populations and about one quarter in females. The lining epithelium is squamous to the junction of the oesophagus and stomach, then presenting as highly differentiated glandular elements through to the anus, where a second transition back to squamous is found. Relationships between estimated incidence rates for pairs of sites in Asian countries are illustrated in Figure 2. For the purpose of these comparisons, division is into regions, Singapore being exceptionally assigned to the North-East region because of the predominately Chinese population.

Despite the shared histology, there are no clear links among oral, pharyngeal and oesophageal cancers overall, although South Asia tends to have relatively high incidences of all three. Some Pacific islands have very prominent oral cancers but neither of the others. North-West and North-East Asia both have high shared oesophageal and stomach cancer incidences. Neither of these latter appear to have any link to colorectal cancer.

Oral Cavity

The Globocan 2002 mortality/incidence data for the oral cavity are plotted in Figure 3. The average ratio is 0.5:1, with very little variation across countries. Males are generally more than twice as likely as females to be effected, although Bangladesh would appear to be exceptional, with similar rates in both sexes, and Sri Lanka

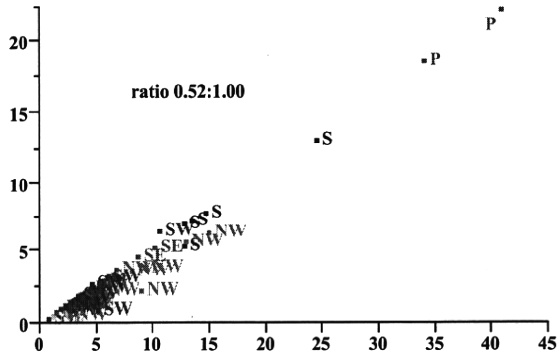

Figure 3. Mortality/Incidence Data for the Oral Cavity (Globocan 2002; Ferlay et al., 2004)

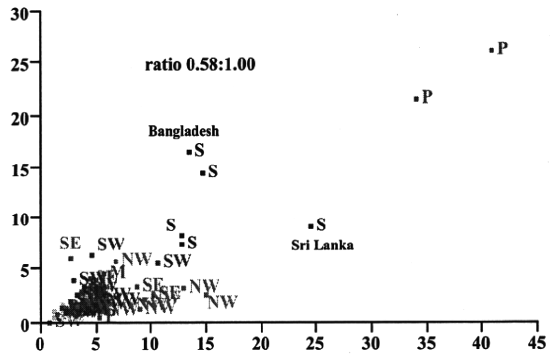

Figure 4. Female/Male Incidence Data for the Oral Cavity (Globocan 2002; Ferlay et al., 2004)

has a particularly strong male predominance (see Figure 4). Underlying causes are unclear and if real this warrants investigation.

Evidence for risk and protective factors from Asia, detailed in the separate regional sections of this supplement, is summarized in Table 1. Those which obviously need to be avoided as a preventive measure (see Figure 5) are betel chewing and tobacco. Given the role for tobacco, for *a priori* reasons vegetables should be protective, as concluded by the WCRF/AICR (2007), but there is only limited information available in Asia. Alcohol is not a major influence in the very high risk populations of South Asia but could be playing a role elsewhere, like in the Pacific and North. There is limited evidence of protection by coffee drinking. while hot drinks may confer some risk.

Regarding secondary prevention, there has been one randomized clinical trial which provided evidence of efficacy of oral examination, so that use of trained workers for screening of high risk groups can be recommended.

Table 1. Asian Evidence for Modifying Factors for the Oral Cavity

	NW	SW	S	SEM	SEI	Pac	NE	World*
Prevalence	L	L-M	H	L-M	L	L-H	L	NA
Lifestyle								
Tobacco	++	++	+++	+	ND	++	++	NA
Reverse smoking								
	ND	ND	ND	ND	+	ND	ND	NA
Alcohol	+/-	ND	-	-	ND	-	++	+++
Betel	ND	ND	+++	+++	+	++	+	NA
Diet								
Hot Drinks	ND	ND	ND	ND	ND	ND	ND	+
Vegetables	ND	ND	ND	ND	ND	ND	ND	--#
Fruits	ND	ND	ND	ND	ND	ND	ND	--
Coffee	ND	ND	ND	ND	ND	ND	-	+/-

*World Cancer Research Fund,American Institute for Cancer Research 2007; NW, North-West, SW, South-West, S, South; SEM, South-East Mainland; SEI, South-East Island; Pac, Pacific; NE, North-East; L, low; M, medium;, H, high; NA, not applicable; ND, no data; -/--, slight/weak protection, +/-, no effect, +/++/+++, slight, weak, strong risk #Carotenoids

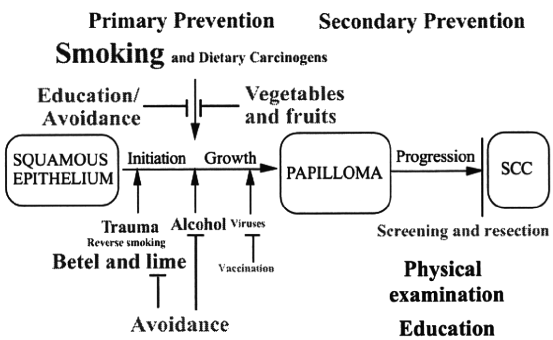

Figure 5. Prevention Measures for the Oral Cavity

Oesphagus

The Globocan 2002 mortality/incidence data for the oral cavity are plotted in Figure 6. The average ratio is 0.8:1, with possible slightly better results for China, Mongolia and Kazakhstan. Whether this is real requires confirmation. Males are generally more than twice as like as females to be effected, although in Japan and China the male predominance is much more marked (see Figure 7). In contrast, Sri Lanka has almost equal values for the

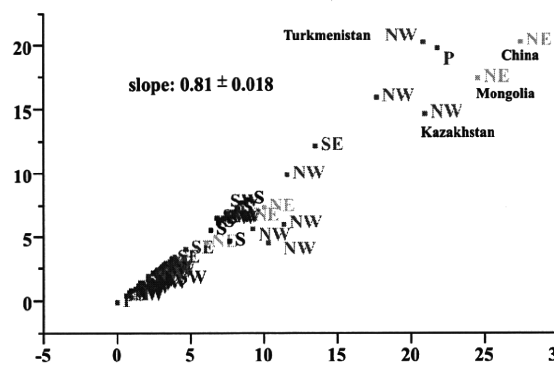

Figure 6. Mortality/Incidence Data for the Oesophagus (Globocan 2002; Ferlay et al., 2004)

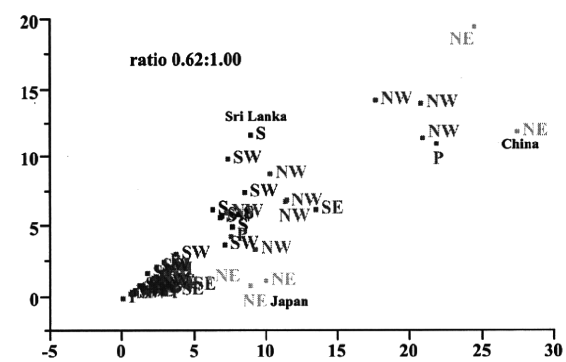

Figure 7. Female/Male Incidence Data for the Oesophagus (Globocan 2002; Ferlay et al., 2004)

Table 2. Asian Evidence for Modifying Factors for the Oesophagus

	NW	SW	S	SEM	SEI	Pac	NE	World*
Prevalence	L-H	L	M	L-M	L	L-H	L	NA
Lifestyle								
Carcinogens	ND	ND	ND	ND	ND	ND	+	NA
Tobacco	++	++	+++	+	ND	ND	++	NA
Alcohol	+/-	ND	-	+	ND	ND	++	+++
Betel	ND	ND	++	+	ND	ND	+	NA
Obesity	ND	ND	ND	ND	ND	ND	+#	+++#
Diet								
Deficiency	++	ND	+	ND	ND	ND	++	+
Hot Drinks	++	ND	ND	ND	ND	ND	+	+
Vegetables	ND	ND	-	ND	ND	ND	--	--
Fruits	ND	ND	-	ND	ND	ND	-	--
Meat	ND	ND	ND	ND	ND	ND	ND	+
Salt	+	ND	ND	ND	ND	ND	+	+/-
Tea	ND	ND	ND	ND	ND	ND	-	+/-

*World Cancer Research Fund,American Institute for Cancer Research 2007; NW, North-West, SW, South-West, S, South; SEM, South-East Mainland; SEI, South-East Island; Pac, Pacific; NE, North-East; L, low; M, medium;, H, high; NA, not applicable; ND, no data; -/--, slight/weak protection, +/-, no effect, +/++/+++, slight, weak, strong risk; # for adenocarcinomas

two genders. In fact, the major variation points to opportunities for collaborative research, taking into account relative rates for adenocarcinomas.

Evidence for risk and protective factors from Asia is summarized in Table 2. The obvious factors which need to be avoided as a preventive measure (see Figure 8) are tobacco, and to a much lesser extent betel chewing. For *a priori* reasons, again vegetables should be protective, as concluded by the WCRF/AICR (2007), but once more data from Asia are limited. However, there are sufficient to allow recommendation of vegetable and fruit intake. Alcohol is not a major influence in the very high risk populations of South Asia but could be playing a role elsewhere, like in the Pacific and North. Very hot drinks may confer some risk, as do other sources of trauma, including salt and grit, and deficiency in zinc or other metals in the diet. These factors all impact on squamous cell carcinoma development. In the adenocarcinoma case, obesity is the main risk determinant.

For secondary prevention there are no specific screening measures which can be advised other than increase in general awareness of symptoms.

Stomach

The Globocan 2002 mortality/incidence data for the stomach are plotted in Figure 9. The average ratio is 0.7:1, with Korea and Japan in the high risk countries exhibiting an appreciably better outcome, than in China for example. How much of this due to screening needs to be clarified. Males are generally more than twice as likely as females to be effected, and in Japan and Korea the predominance is slightly more marked (see Figure 10). Data on the relative prevalences of different sites with their variation

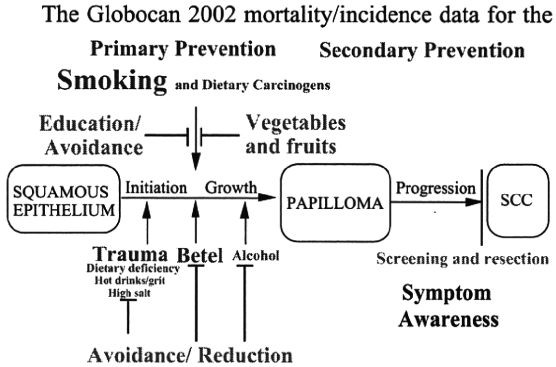

Figure 8. Prevention Measures for the Oesophagus

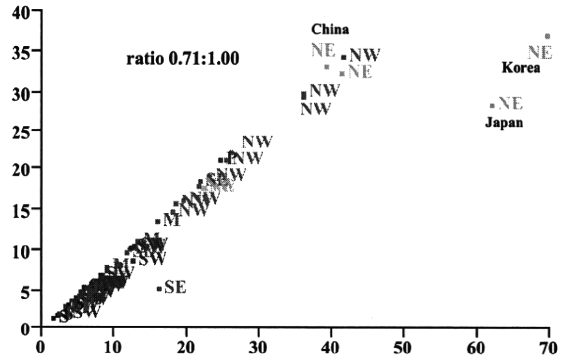

Figure 9. Mortality/Incidence Data for the Stomach (Globocan 2002; Ferlay et al., 2004)

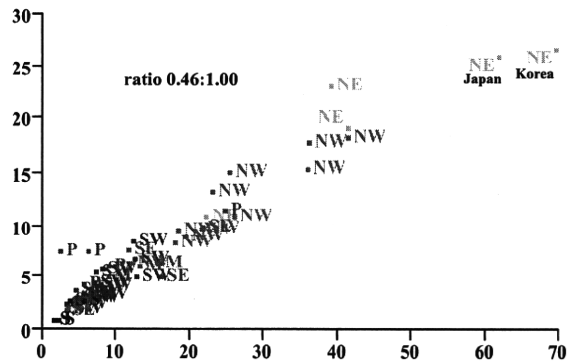

Figure 10. Female/Male Incidence Data for the Stomach (Globocan 2002; Ferlay et al., 2004)

Table 3. Asian Evidence for Modifying Factors for the Stomach

	NW	SW	S	SEM	SEI	Pac	NE	World*
Prevalence	L-H	L	L	L-M	L	L-H	L	NA
Lifestyle								
Helicobacter	++	ND	+	ND	++	ND	++	NA
Tobacco	ND	ND	+/-	ND	+	ND	++	NA
Alcohol	ND	ND	+/-	ND	ND	ND	+	+/-
Obesity	ND	ND	ND	ND	ND	ND	+	+/-
Exercise	ND	ND	ND	ND	ND	ND	-	+/-
Diet								
Vegetables	ND	ND	-	-	--	ND	--	--
Fruits	ND	ND	-	-	-	ND	-	--
Meat	ND	ND	ND	ND	ND	ND	ND	+
Fish	ND	ND	ND	ND	ND	ND	--	+
Smoked food	ND	ND	ND	ND	ND	ND	+	+
Salt	ND	ND	ND	++	++	ND	++	++
Coffee	ND	ND	ND	ND	ND	ND	-	+/-

*World Cancer Research Fund,American Institute for Cancer Research 2007; NW, North-West, SW, South-West, S, South; SEM, South-East Mainland; SEI, South-East Island; Pac, Pacific; NE, North-East; L, low; M, medium;, H, high; NA, not applicable; ND, no data; -/--, slight/weak protection, +/-, no effect, +/++/+++, slight, weak, strong risk

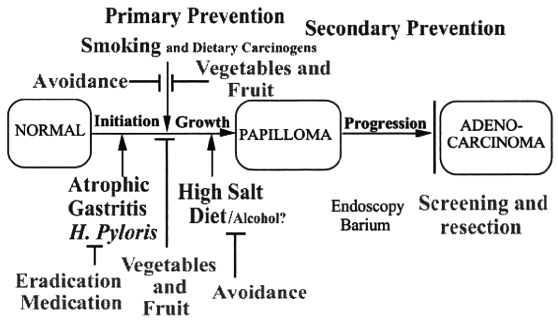

Figure 11. Prevention Measures for the Stomach

in risk factors are lacking, although it is possible that a combination of diet and tobacco might explain the gender effect.

Evidence for risk and protective factors from Asia is summarized in Table 3. The obvious factors which need attention in preventive measures (see Figure 11) are heavy infection with *Helicobacter pylori* and high salt intake. Tobacco should also be avoided, while consumption of vegetables and fruits can be recommended. Alcohol is not a major influence

Regarding secondary prevention, there is ample evidence of efficacy for screening.

Colon and Rectum

The Globocan 2002 mortality/incidence data for the colo-rectum are plotted in Figure 12. The average ratio is over 0.5:1, with Japan, Israel and Korea demonstrating appreciably better outcomes, possibly linked to screening. This might be supported by the fact that Singapore has

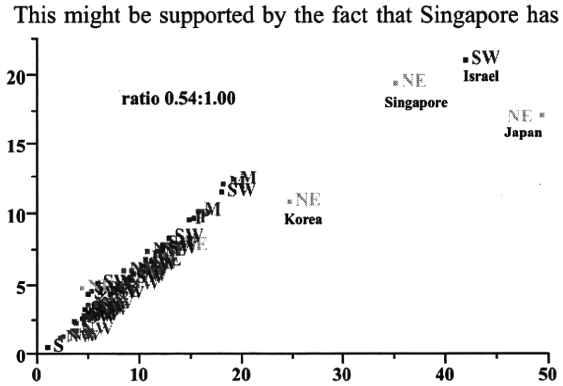

Figure 12. Mortality/Incidence Data for the Colorectum (Globocan 2002; Ferlay et al., 2004)

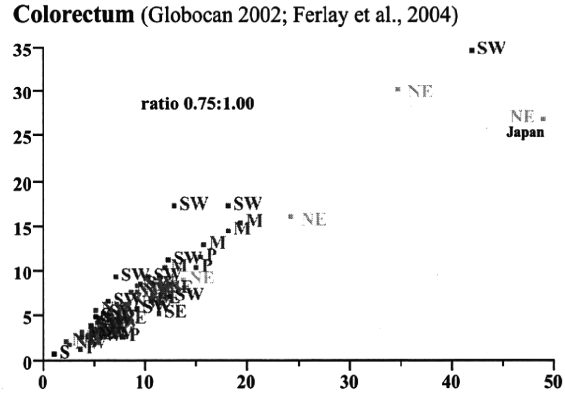

Figure 13. Female/Male Incidence Data for the Colorectum (Globocan 2002; Ferlay et al., 2004)

Table 4. Asian Evidence for Modifying Factors for the Colorectum

	NW	SW	S	SEM	SEI	Pac	NE	World*
Prevalence	L-M	L-H	L	L-M	M	L-H	L	NA
Lifestyle								
Carcinogens	ND	+	ND	ND	+	ND	+	NA
Tobacco	ND	ND	ND	ND	+	ND	+	NA
Alcohol	ND	ND	ND	ND	ND	ND	+	+++
Obesity	ND	ND	ND	ND	ND	ND	+	+++
Exercise	ND	ND	ND	ND	ND	ND	--	---
Diet								
Vegetables	ND	-	ND	-	--	ND	--	--
Fruits	ND	-	ND	-	-	ND	-	-
Fat	ND	ND	ND	ND	ND	ND	++	+
Sugar	ND	ND	ND	ND	ND	ND	ND	+
Meat	ND	ND	ND	+	+	ND	+	+++
Fish	ND	ND	ND	ND	ND	ND	--	-
Milk	ND	ND	ND	ND	ND	ND	ND	--
Tea	ND	ND	ND	ND	ND	ND	-	NA

*World Cancer Research Fund,American Institute for Cancer Research 2007; NW, North-West, SW, South-West, S, South; SEM, South-East Mainland; SEI, South-East Island; Pac, Pacific; NE, North-East; L, low; M, medium;, H, high; NA, not applicable; ND, no data; -/--, slight/weak protection, +/-, no effect, +/++/+++, slight, weak, strong risk

an only slightly better rate. Males are generally 1.25 more likely than females to be effected (see Figure 13), but in Japan the figure is nearer 2.0, pointing to a possible role for alcohol and smoking.

Evidence for risk and protective factors from Asia is summarized in Table 4. The obvious factors which need to be avoided as preventive measures (see Figure 14) are obesity and excessive alcohol consumption. Furthermore a diet high in meat and fat is detrimental, while consumption of vegetables and fish as well as physical exercise are protective. Tobacco and dietary carcinogens may be secondary risk factors.

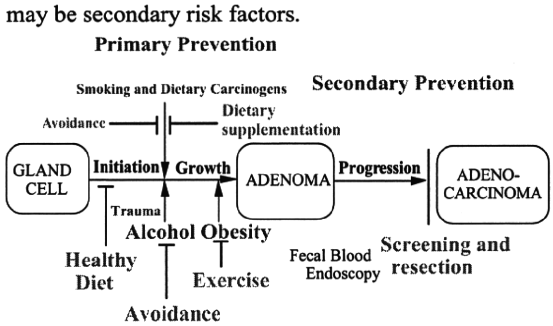

Figure 14. Prevention Measures for the Colorectum

Regarding secondary prevention, there is strong evidence for the efficacy of occult blood based approaches, along with endoscopy and computed tomography in the future.

The Hepatopancreatic Axis

The liver, gallbladder and pancreas form the hepatopancreatic axis, closely juxtaposed and related in many functions. They give rise to hepatocellular carcinomas from hepatocytes and adenocarcinomas from ductal and ductular cell populations (cholangiocarcinomas in the intra- and extra- hepatic bile duct cases). There are conceivable shared risk factors and a comparison of

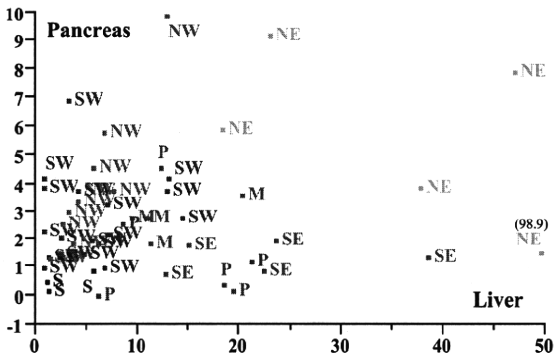

Figure 15. Regional Comparisons Between Globocan Incidence Data for the Liver and Pancreas

Globocan incidence data for the liver and pancreas is shown in Figure 15. While Japan and Korea have relatively high incidences of both, pancreas incidences are generally low, North- and South-West populations tending to have relatively greater values than their South-East and Pacific counterparts.

Liver

The Globocan 2002 mortality/incidence data for the liver are plotted in Figure 16. Survival is very poor, with Korea demonstrating the best M/I ration of 0.76:1. Whether this is a reflection of screening activity needs to be clarified. Males in general are more than twice as likely as females to be effected, and in Korea the predominance is more marked (see Figure 17). Therefore, male factors like alcohol and smoking presumably must interact with the primarily viral etiology. There in fact appears to be

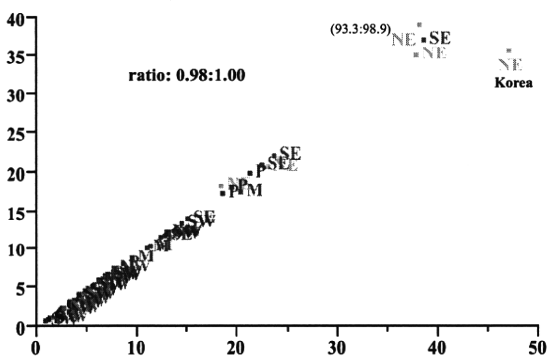

Figure 16. Mortality/Incidence Data for the Liver (Globocan 2002; Ferlay et al., 2004)

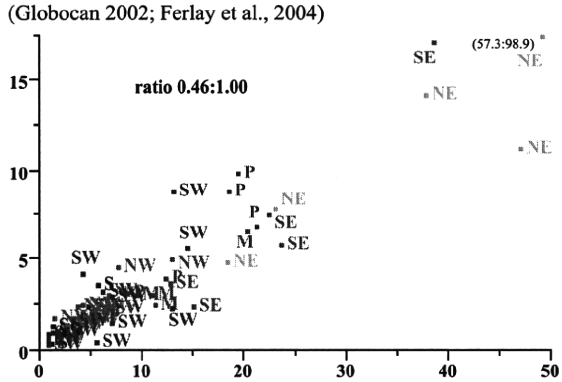

Figure 17. Female/Male Incidence Data for the Liver (Globocan 2002; Ferlay et al., 2004)

Table 5. Asian Evidence for Modifying Factors for the Liver

	NW	SW	S	SEM	SEI	Pac	NE	World*
Prevalence	L-M	L-M	L	M-H	M-H	L-H	H	NA
Lifestyle								
Viruses	++	++	++	++	++	++	+++	NA
Parasites#	ND	ND	ND	+++	ND	ND	+	NA
Carcinogens	ND	+	ND	ND	ND	ND	++	+++
Tobacco	ND	ND	ND	ND	ND	ND	++	NA
Alcohol	+	ND	ND	ND	ND	ND	++	++
Obesity	+	ND	+	ND	ND	ND	+	+/-
Exercise	ND	ND	ND	ND	ND	ND	--	+/-
Diet								
Vegetables	ND	ND	ND	ND	ND	ND	--	+/-
Fruits	ND	ND	ND	ND	ND	ND	-	-
Fat	ND	ND	ND	ND	ND	ND	++	+/-
Fish	ND	ND	ND	ND	ND	ND	-	+/-
Soy	ND	ND	ND	ND	ND	ND	-	+/-
Coffee	ND	ND	ND	ND	ND	ND	-	NA

*World Cancer Research Fund,American Institute for Cancer Research 2007; NW, North-West, SW, South-West, S, South; SEM, South-East Mainland; SEI, South-East Island; Pac, Pacific; NE, North-East; L, low; M, medium;, H, high; NA, not applicable; ND, no data; -/--, slight/weak protection, +/-, no effect, +/++/+++, slight, weak, strong risk; for cholangiocellular liver cancers

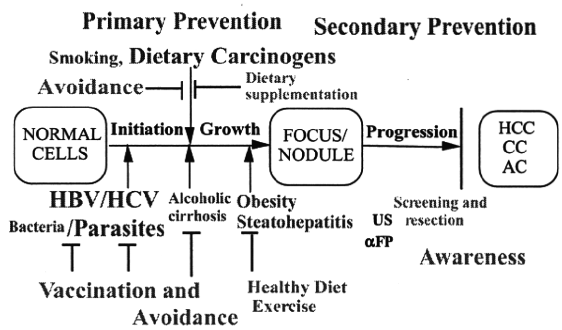

Figure 18. Cancer Prevention and Control for the Liver and Gallbladder Cancer

considerable variation in the sex ratio with the South-West populations, which remains to be explained.

Evidence for risk and protective factors from Asia is summarized in Table 5. The obvious factors which need to be avoided as a preventive measure (see Figure 18) are carcinogen exposure and viral and parasite infection, with lesser roles for alcohol and tobacco. Vegetables and other dietary influences are generally protective. Due to the link with steatohepatitis, avoidance of overweight may also be recommended.

Although ultrasound and serum markers may be useful for high risk individuals, there are no population level screening measures so that secondary prevention is generally limited to awareness of symptoms.

Gallbladder

The gallbladder is not included in Globocan 2002 so that mortality/incidence data are not available. From the available population-based registry data, there is generally a female predominance, which is pronounced in some of the South Asian registries. The main risk factor is obesity, with a possible role for bacterial infection, especially with *Salmonella*, and gallstones.

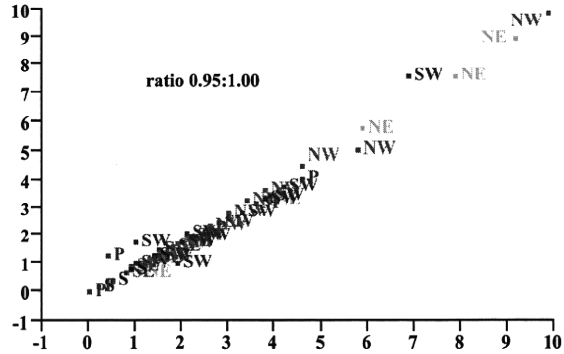

Figure 19. Mortality/Incidence Data for the Pancreas (Globocan 2002; Ferlay et al., 2004)

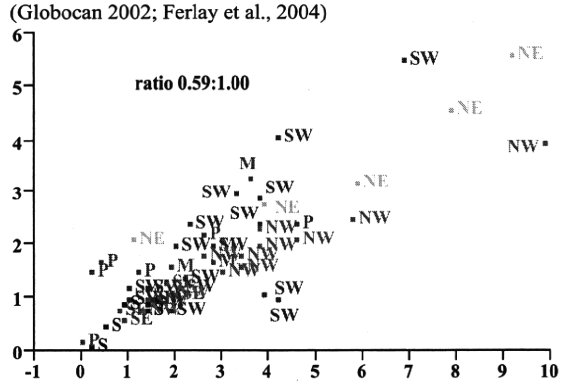

Figure 20. Female/Male Incidence Data for the Pancreas (Globocan 2002; Ferlay et al., 2004)

Table 6. Asian Evidence for Modifying Factors for the Pancreas

	NW	SW	S	SEM	SEI	Pac	NE	World*
Prevalence	L-M	L-M	L	L-M	L-M	M-H	L-H	NA
Lifestyle								
Carcinogens	ND	+	ND	ND	ND	ND	ND	+/-
Tobacco	++	++	ND	ND	ND	ND	++	NA
Alcohol	ND	ND	ND	ND	ND	ND	++	++
Obesity	ND	+	ND	ND	ND	ND	++	+++
Exercise	ND	ND	ND	ND	ND	ND	ND	-
Diet								
Vegetables	ND	ND	ND	ND	ND	ND	--	--
Fruits	ND	ND	ND	ND	ND	ND	-	-
Meat	ND	ND	ND	ND	ND	ND	ND	+
Coffee	ND	ND	ND	ND	ND	ND	-	+/-

*World Cancer Research Fund,American Institute for Cancer Research 2007; NW, North-West, SW, South-West, S, South; SEM, South-East Mainland; SEI, South-East Island; Pac, Pacific; NE, North-East; L, low; M, medium;, H, high; NA, not applicable; ND, no data; -/--, slight/weak protection, +/-, no effect, +/++/+++, slight, weak, strong risk

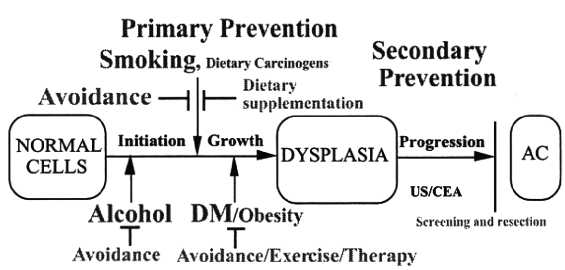

Figure 21. Cancer Prevention and Control for Pancreatic Cancer

Pancreas

The Globocan 2002 mortality/incidence data for the pancreas are plotted in Figure 19. The ratio is almost:1:1, with no exception. Males are generally more than twice as like as females to be effected, but there is considerable variation in the gender ratios (see Figure 7), which might reflect tobacco and alcohol consumption patterns to some extent.

Evidence for risk and protective factors from Asia is summarized in Table 6. The obvious factors which need to be avoided as a preventive measure (see Figure 21) are alcohol, tobacco and obesity/diabetes mellitus. Vegetables are protective, along with coffee drinking, while meat consumption may confer some risk.

Regarding secondary prevention, there are no population based measures to be recommended.

The Respiratory Tract

The respiratory tract comprises the pharynx (including the nasopharynx), the larynx and the lung. In all cases where the epithelium is squamous the SCC is the major cancer. With the lung, adenocarcinomas of the periphery and small and large cell cancers are also found, but no distinction was made in Globocan 2002. Correlations between sites are shown in Figure 22. The South Asian countries, as well as Mynamar, generally feature high rates for both the pharynx and larynx, but elsewhere pharyngeal incidences are low, independent of the laryngeal cancer prevalence. The lung and larynx, in contrast, show a tendency to increase in parallel, although the South and South-West have relatively more laryngeal, the South-East and North-East has more lung and the North-West is intermediate.

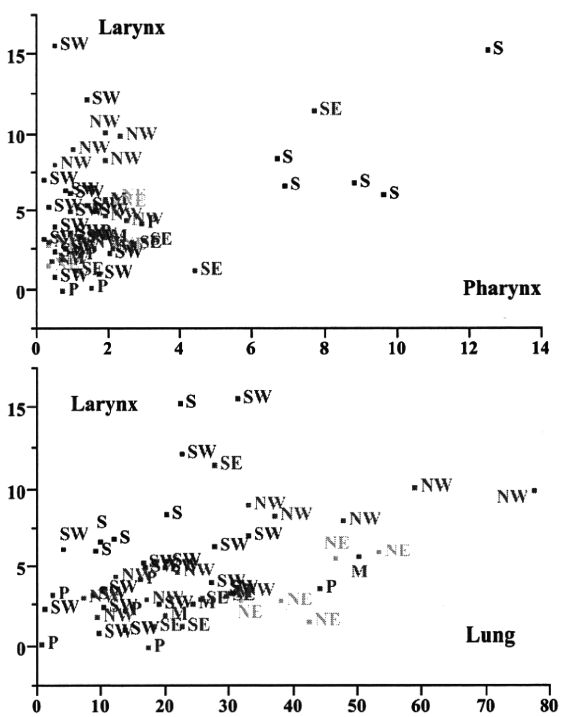

Figure 22. Regional Comparisons Between Globocan Incidence Data for the Pharynx, Larynx and Lung

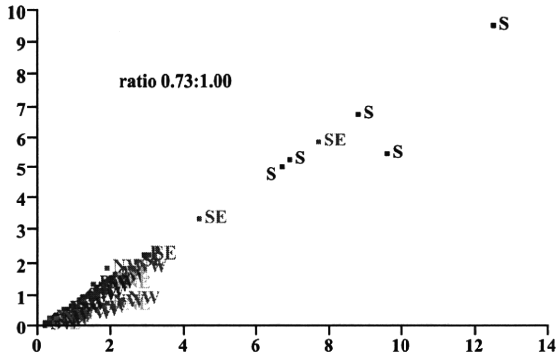

Figure 23. Mortality/Incidence Data for the Pharynx (Globocan 2002; Ferlay et al., 2004)

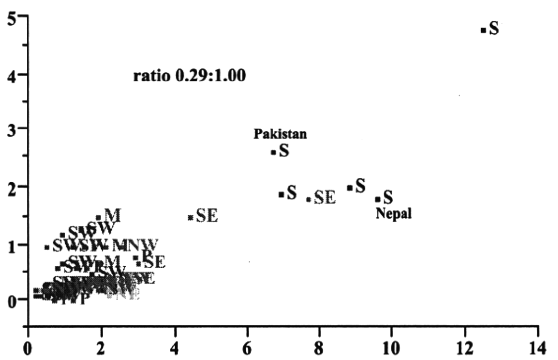

Figure 24. Female/Male Incidence Data for the Pharynx (Globocan 2002; Ferlay et al., 2004)

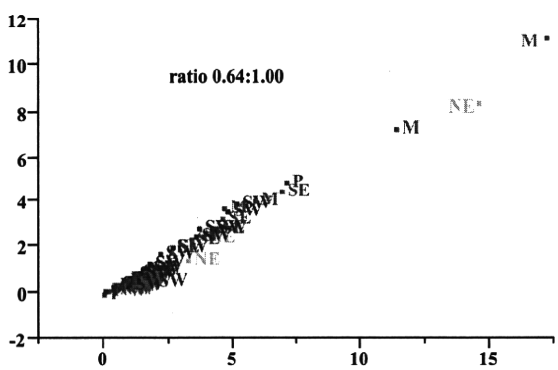

Figure 25. Mortality/Incidence Data for the Nasopharynx (Globocan 2002; Ferlay et al., 2004)

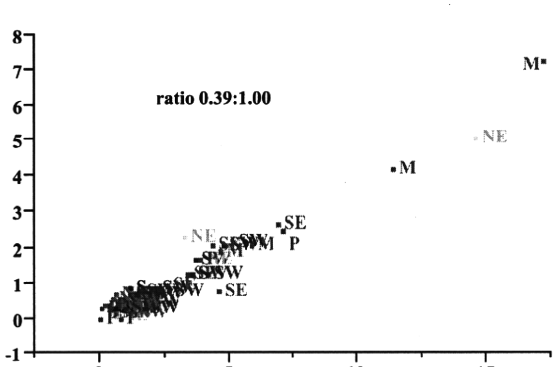

Figure 26. Female/Male Incidence Data for the Nasopharynx (Globocan 2002; Ferlay et al., 2004)

Table 7. Asian Evidence for Modifying Factors for the Pharynx and Larynx

	NW	SW	S	SEM	SEI	Pac	NE	World*
Prevalence	L-H	L-H	M-H	L-M	L-M	M-H	L-M	NA
Lifestyle								
Tobacco	+	ND	++	ND	++	ND	++	NA
Herbs#	ND	ND	ND	ND	+	ND	ND	NA
Alcohol	+	ND	ND	ND	ND	ND	++	+++
Dusts	++	ND	ND	ND	ND	ND	++	NA
Hot drinks	ND	ND	ND	ND	ND	ND	ND	+
Diet								
Vegetables	ND	ND	ND	ND	ND	ND	--	---
Fruits	ND	ND	ND	ND	ND	ND	-	---
Salt#	ND	ND	ND	ND	ND	ND	++	+/-
Coffee	ND	ND	ND	ND	ND	ND	-	+/-

*World Cancer Research Fund,American Institute for Cancer Research 2007; NW, North-West, SW, South-West, S, South; SEM, South-East Mainland; SEI, South-East Island; Pac, Pacific; NE, North-East; L, low; M, medium;, H, high; NA, not applicable; ND, no data; -/--, slight/weak protection, +/-, no effect, +/++/+++, slight, weak, strong risk;# for the nasopharynx

Pharynx, Nasopharynx and Larynx

The Globocan 2002 mortality/incidence data for the pharynx are plotted in Figure 23. The average ratio is 0.7:1, with slightly better outcomes apparently in India. Whether this is real requires confirmation. Males are three times more likely than females to be effected, and this gender bias may be more marked in Nepal (see Figure 24).

The Globocan 2002 mortality/incidence data for the nasopharynx are plotted in Figure 25, with an average

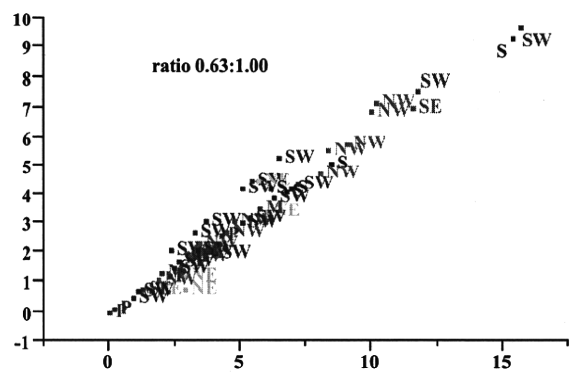

Figure 27. Mortality/Incidence Data for the Larynx (Globocan 2002; Ferlay et al., 2004)

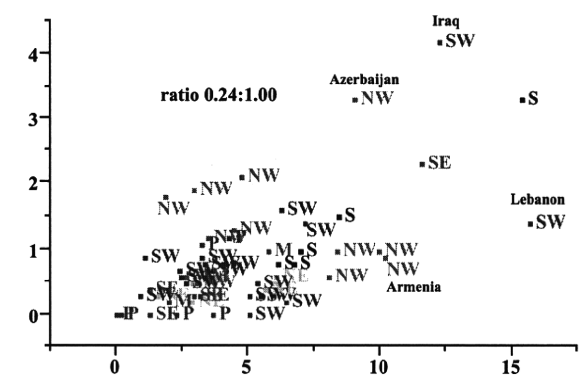

Figure 28. Female/Male Incidence Data for the Larynx (Globocan 2002; Ferlay et al., 2004)

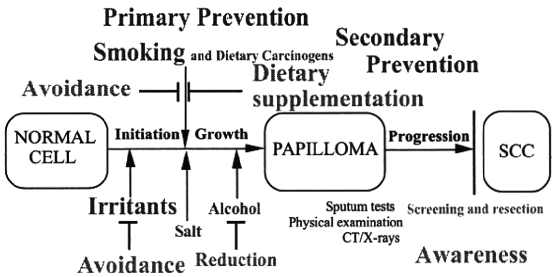

Figure 29. Cancer Prevention and Control Measures for the Pharynx and Larynx

ratio 0.64:1,and the gender distibution is shown in Figure 26) again males having approximately three times the rates of females. In the larynx the situation is similar (Figures 27 and 28), but here there is marked variation in rates for males and females between different countries in the same region, as for example with neighbouring Azerbaijan and Armenia.

Evidence for risk and protective factors for the pharynx and larynx from Asia is summarized in Table 7. The obvious factors which need to be avoided as a preventive measure (see Figure 29) are tobacco dusts (mainly for the larynx) and to a lesser extent alcohol. Both vegetables and fruits are clearly strongly protective, and coffee weakly so. Salty foods are risk factors for the nasopharynx.

There are no secondary prevention measure that can currently be recommended.

Lung

The Globocan 2002 mortality/incidence data for the

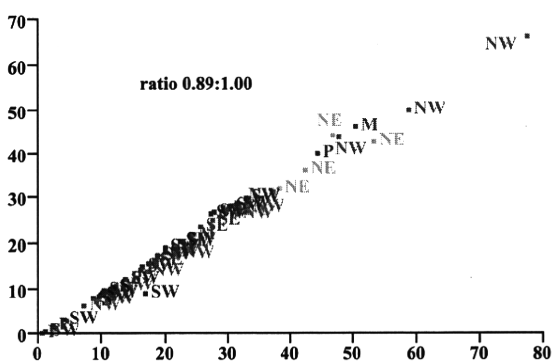

Figure 30. Mortality/Incidence Data for the Lung (Globocan 2002; Ferlay et al., 2004)

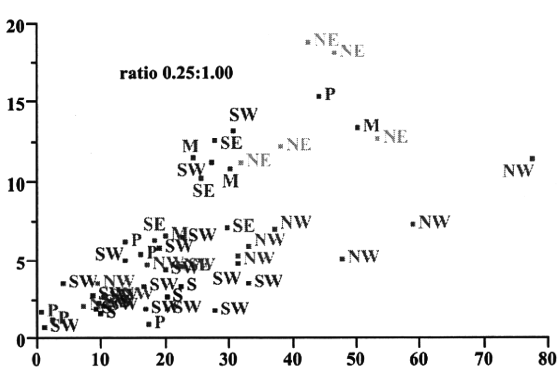

Figure 31. Female/Male Incidence Data for the Lung (Globocan 2002; Ferlay et al., 2004)

Table 8. Asian Evidence for Modifying Factors for the Lung

	NW	SW	S	SEM	SEI	Pac	NE	World*
Prevalence	L-H	L-M	L-M	L-M	L-H	M-H	M-H	NA
Lifestyle								
Tobacco	+	ND	++	++	++	+	++	NA
Carcinogens	++#	ND	ND	ND	+	+#	+	NA
Alcohol	ND	ND	ND	ND	ND	ND	+/-	+/-
Dusts/oils	++	ND	ND	ND	ND	ND	++	NA
Diet								
Vegetables	ND	ND	ND	-	-	ND	--	---
Fruits	ND	ND	ND	-	ND	ND	-	---
Meat	ND	ND	ND	ND	ND	ND	ND	+
Fat	ND	ND	ND	ND	ND	ND	ND	+
Fish	ND	ND	ND	ND	ND	ND	-	+/-

*World Cancer Research Fund,American Institute for Cancer Research 2007; NW, North-West, SW, South-West, S, South; SEM, South-East Mainland; SEI, South-East Island; Pac, Pacific; NE, North-East; L, low; M, medium;, H, high; NA, not applicable; ND, no data; -/--, slight/weak protection, +/-, no effect, +/++/+++, slight, weak, strong risk;# asbestos asnd other fibres for mesotheliomas

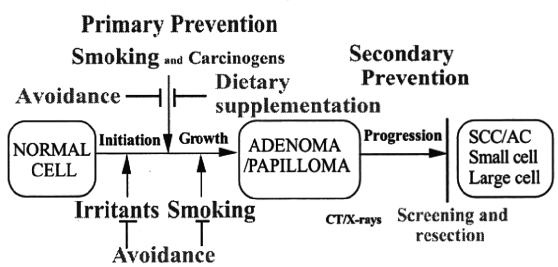

Figure 32. Cancer Prevention and Control Measures for the Lung

the lungs are plotted in Figure 30. The average ratio is almost 0.9:1, with no pronounced exceptions. Males are generally three or four-fold more likely to be affected as females , although there is great variation (see Figure 31). In general, North-East Asian women are more likely to have lung cancer than their North-West counterparts, and South-East more than South-West.

Evidence for risk and protective factors from Asia is summarized in Table 8. The obvious factors which need to be avoided as a preventive measure (see Figure 32) are tobacco and particulate matter that can be breathed in like cooking oils, coal dusts and asbestos, for example. Vegetables and fruits are protective.

Regarding secondary prevention, X-rays for squamous cell carcinoma and spiral computer tomography for adenocarcinoma are in use in some countries, for example in Japan, but these cannot be recommended for general application in Asia.

Urinary Tract

The urinary tract comprises the kidneys, ureter, urinary bladder and associated prostate gland. The cancers in these organs arise from tubular epithelium in the renal case, transitional epithelium where the urine is in contact, and glandular epithelium in the prostate. Since they are linked physically it is conceivable that they might share risk factors to some extent. Comparisons across sites are shown in Figure 33. Generally, incidence rates for kidney cancers

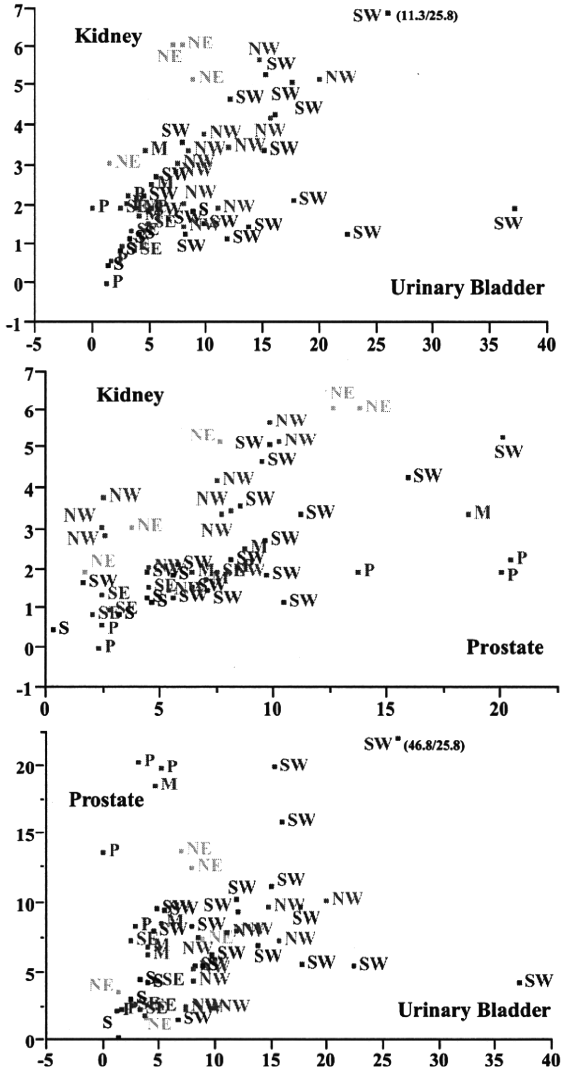

Figure 33. Regional Comparisons Between Globocan Incidence Data for the Sites within the Male Urinary Tract

show a relatively good cross-correlation with data for both urinary bladder and prostate cancers, with notable exceptions of some South-West populations having a bias towards the urinary bladder, and Pacific nations demonstrating high prostate but low kidney rates. North-West Asia tends to have greater incidences of kidney relative to prostate, as compared to neighbouring South-West Asia.

Kidney

The Globocan 2002 mortality/incidence data for the kidney are plotted in Figure 34. The average ratio is 0.65:1, but survival is considerably better in some countries, like Korea and Japan, for example as compared with Kazakhstan in Globocan 2002. Since there is no screening program in place, this presumably reflects clinical treatments. Males are somewhat less than twice as likely as females to be affected, although there is great variation, the ration being apparently almost 1:1 in Bharain but 5:1 in Qatar (see Figure 24).

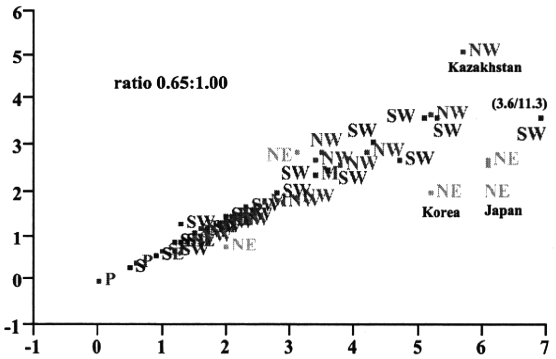

Figure 34. Mortality/Incidence Data for the Kidney (Globocan 2002; Ferlay et al., 2004)

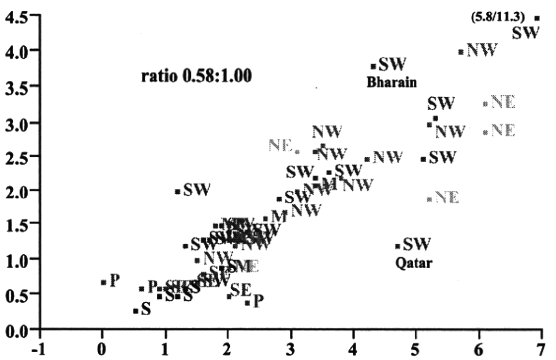

Figure 35. Female/Male Incidence Data for the Kidney (Globocan 2002; Ferlay et al., 2004)

Table 9. Asian Evidence for Modifying Factors for the Kidney

	NW	SW	S	SEM	SEI	Pac	NE	World*
Prevalence	L	L-M	L	L	L	L-M	L-M	NA
Lifestyle								
Obesity	ND	ND	ND	ND	ND	ND	++	+++
Diet								
Vegetables	ND	ND	ND	ND	ND	ND	--	+/-
Fruits	ND	ND	ND	ND	ND	ND	-	+/-

*World Cancer Research Fund,American Institute for Cancer Research 2007; NW, North-West, SW, South-West, S, South; SEM, South-East Mainland; SEI, South-East Island; Pac, Pacific; NE, North-East; L, low; M, medium;, H, high; NA, not applicable; ND, no data; -/--, slight/weak protection, +/-, no effect, +/++/+++, slight, weak, strong risk

Evidence for risk and protective factors from Asia is summarized in Table 9. The only obvious risk factor is obesity, perhas together with excessive food consumption, while vegetables and fruit are protective. There are no screening measures which could be recommended.

Ureter and Urinary Bladder

The Globocan 2002 mortality/incidence data for the urinary bladder are plotted in Figure 36. The average ratio is 0.65:1, with relatively little variation. Males are generally about five fold more likely to be affected than females, although with very contrasting data for different countries, at least in Globocan 2002 (see Figure 37). Looking at other data for South-West Asia, this needs to be confirmed.

Evidence for risk and protective factors from Asia is summarized in Table 10. The obvious factors which need

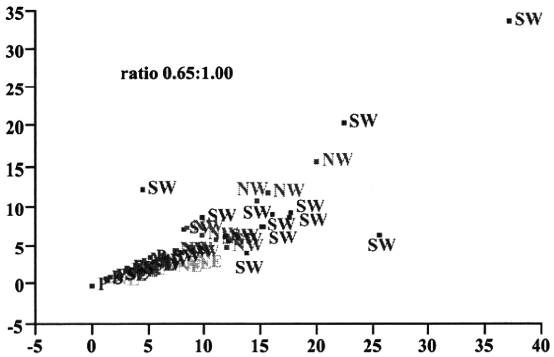

Figure 36. Mortality/Incidence Data for the Urinary Bladder (Globocan 2002; Ferlay et al., 2004)

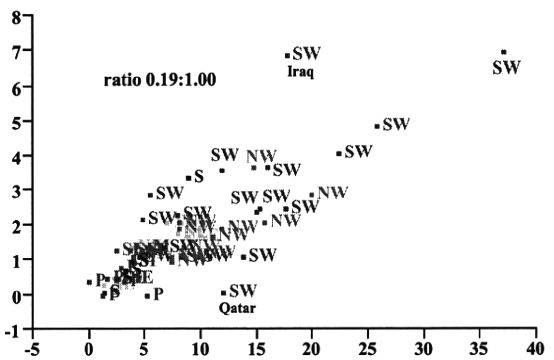

Figure 37. Female/Male Incidence Data for the Urinary Bladder (Globocan 2002; Ferlay et al., 2004)

Table 10. Asian Evidence for Modifying Factors for the Ureter and Urinary Bladder

	NW	SW	S	SEM	SEI	Pac	NE	World*
Prevalence	L-M	L-H	L	L	L	L-M	L	NA
Lifestyle								
Parasites	ND	++	ND	ND	ND	ND	ND	NA
Tobacco	++	++	ND	ND	ND	ND	++	NA
Carcinogens	+	ND	ND	ND	ND	ND	++#	+#
Diet								
Vegetables	ND	ND	ND	ND	ND	ND	--	+/-
Fruits	ND	ND	ND	ND	ND	ND	--	+/-
Meat	ND	ND	ND	ND	ND	ND	+	+/-

*World Cancer Research Fund,American Institute for Cancer Research 2007; NW, North-West, SW, South-West, S, South; SEM, South-East Mainland; SEI, South-East Island; Pac, Pacific; NE, North-East; L, low; M, medium;, H, high; NA, not applicable; ND, no data; -/--, slight/weak protection, +/-, no effect, +/++/+++, slight, weak, strong risk;# arsenic and other environmental carcinogens

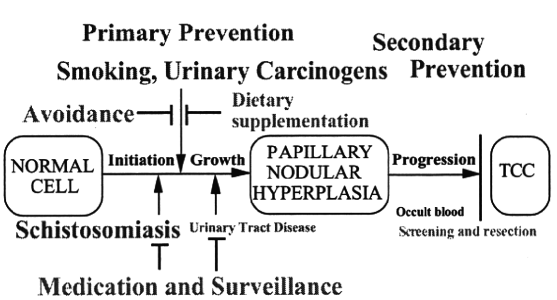

Figure 38. Cancer Prevention and Control Measures for the Urinary Bladder

to be avoided as a preventive measure (see Figure 38) are infestation with Schistosome parasites and tobacco. Other environmetal carcinogens, like arsenic, may also play important roles, while high intake of vegetables and fruits can be recommended, possible because of antioxidant qualities. Meat may be a risk factor.

Regarding secondary prevention, there are no pertinent data, although testing for occult blood is conceivable if a high risk population could be identified.

Prostate

The Globocan 2002 mortality/incidence data for the prostate are plotted in Figure 39. The average ratio is 0.6:1, with the developed countries like Korea and Japan having better survival, for example, than some of the countries

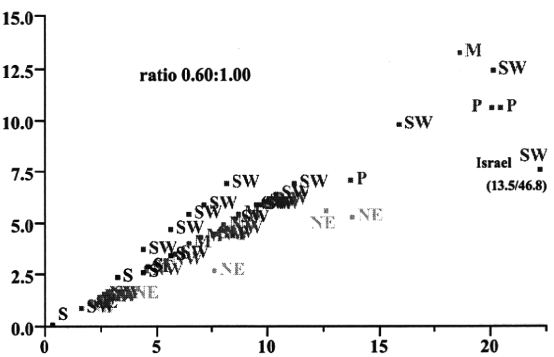

Figure 39. Mortality/Incidence Data for the Prostate (Globocan 2002; Ferlay et al., 2004)

Table 11. Asian Evidence for Modifying Factors for the Prostate

	NW	SW	S	SEM	SEI	Pac	NE	World*
Prevalence	L-M	L-M	L	L	L-M	M-H	L-M	NA
Lifestyle								
Obesity	ND	ND	ND	ND	ND	ND	+	+/-
Exercise	ND	ND	ND	ND	ND	ND	-	+/-
Diet								
Vegetables#	-	ND	ND	ND	ND	ND	--	--
Fruits	ND	ND	ND	ND	ND	ND	-	-
Fat	+	+	ND	ND	ND	ND	+	+/-
Meat	+	+	ND	ND	ND	ND	ND	+/-
Dairy food	ND	+	ND	ND	ND	ND	ND	++
Soy food	ND	ND	ND	ND	ND	ND	---	NA

*World Cancer Research Fund,American Institute for Cancer Research 2007; NW, North-West, SW, South-West, S, South; SEM, South-East Mainland; SEI, South-East Island; Pac, Pacific; NE, North-East; L, low; M, medium;, H, high; NA, not applicable; ND, no data; -/--, slight/weak protection, +/-, no effect, +/++/+++, slight, weak, strong risk; #particular ingredients like lycopene

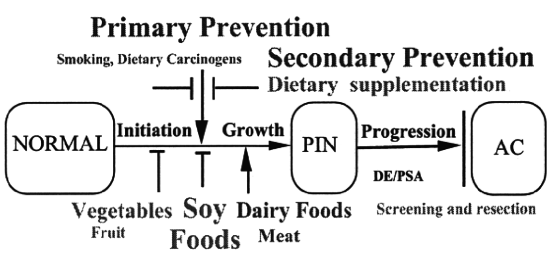

Figure 38. Cancer Prevention and Control Measures for the Prostate

of South-West Asia. The lack of any population-based screening programs in the countries involved would perhaps point to variation in clinical parameters.

Evidence for risk and protective factors from Asia is summarized in Table 11. There are no obvious factors which need to be avoided (see Figure 38), with the possible exception of dairy foods. Regarding prevention, consumption of soy products and vegetables, as well as fruit, would appear to warrant attention.

For secondary prevention, use of prostate specific antigen and digital examination have been examined as possible approaches, but no population-based programs are presently in place anywhere in Asia.

Female Reproductive System

The ovarian, cervical corpus/endometrium and breast constitute the reproductive system, whose cancer development is primarily dependent on hormonal factors. A variety of cancer types arise in the ovary, but in all three sites the adenocarcinoma is prevalent. Cross-site comparisons of incidence data are shown in Figure 39. There is a generally tendency for all three to increase in tandem but there is also interesting regional variation.

For example, North-West Asia clearly demonstrates higher levels of ovarian and particularly endometrial cancer, relative to the breast, than populations in South-West Asia. Within South-East Asia, there are clearly higher levels of all three in the Island and Peninsular countries than in the mainland region.

Ovary, Endometrium and Breast

The Globocan 2002 mortality/incidence data for the three sites are plotted in Figure 40. The average ratios are 0.58:1, 0.58:1 and 0.43:1, respectively, for the ovary, endometrium and breast, in all cases with appreciably better outcomes in the North-East than elsewhere in Asia.

Evidence for risk and protective factors for breast cancer from Asia is summarized in Table 11. The obvious factors which need to be avoided as preventive measure

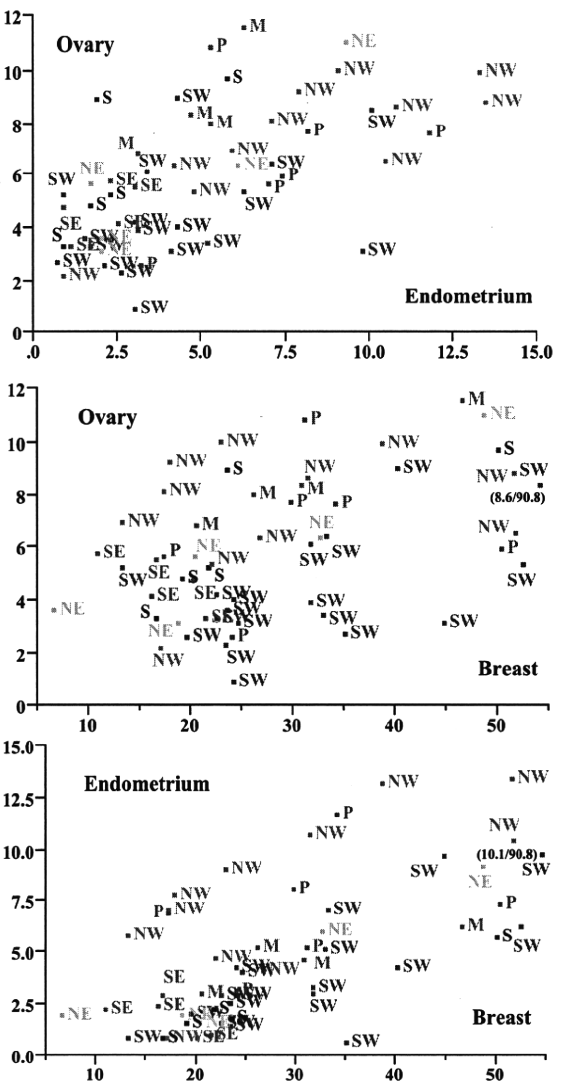

Figure 39. Regional Comparisons Between Globocan Incidence Data for the Various Sites within the Female Reproductive System

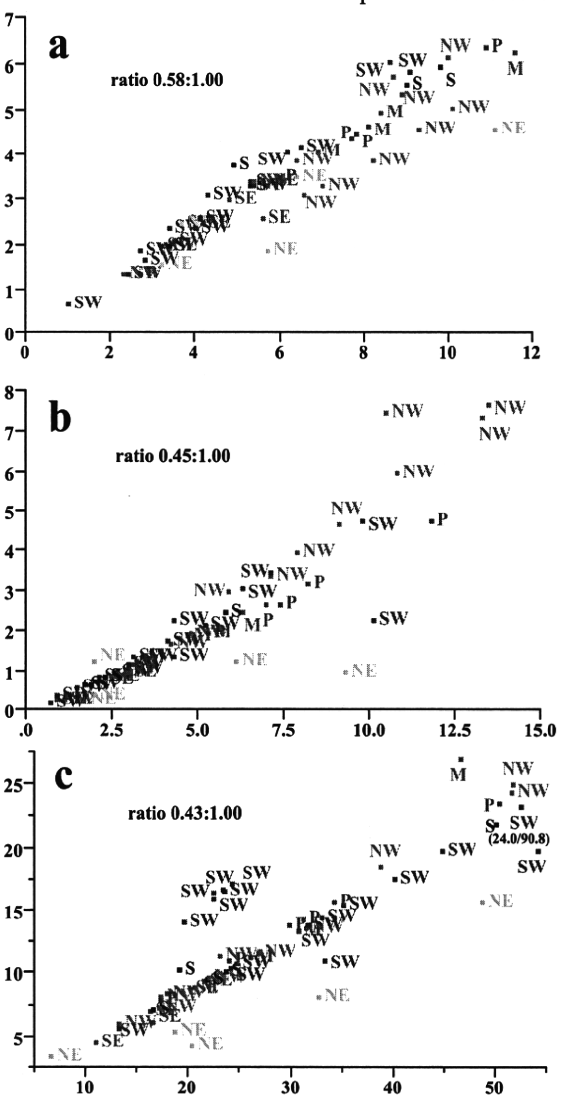

Figure 40. Mortality/Incidence Data for the Ovary (a), Endometrium (b) and Breast (c) (Globocan 2002; Ferlay et al., 2004)

Table 11. Asian Evidence for Modifying Factors for the Breast

	NW	SW	S	SEM	SEI	Pac	NE	World*
Prevalence	L-H	L-M	L-H	L-M	M-H	M-H	L-M	NA
Lifestyle								
Tobacco	+	ND	+	ND	ND	ND	+	NA
Alcohol	ND	ND	ND	+	ND	ND	ND	+++
Obesity	+	++	++	ND	ND	ND	++	++#
Exercise	ND	--	ND	ND	ND	ND	--	--
Reproductive Factors								
Menarche	+	ND	ND	ND	+	ND	++	NA
Menopause	+	ND	ND	ND	+	ND	++	NA
Hormones	ND	+	ND	+/-	+	ND	+	NA
Pregnancy	-	ND	ND	-	ND	ND	--	NA
Lactation	--	--	ND	ND	--	ND	--	---
Diet								
Vegetables#	ND	-	-	ND	-	ND	-	+/-
Fat	ND	+	ND	ND	ND	ND	+	+#
Sugar	ND	+	ND	ND	ND	ND	+	+/-
Fish	ND	ND	ND	ND	ND	ND	--	+/-
Soy food	ND	ND	ND	ND	--	ND	---	NA

*World Cancer Research Fund,American Institute for Cancer Research 2007; NW, North-West, SW, South-West, S, South; SEM, South-East Mainland; SEI, South-East Island; Pac, Pacific; NE, North-East; L, low; M, medium;, H, high; NA, not applicable; ND, no data; -/--, slight/weak protection, +/-, no effect, +/++/+++, slight, weak, strong risk; #postmenopausal

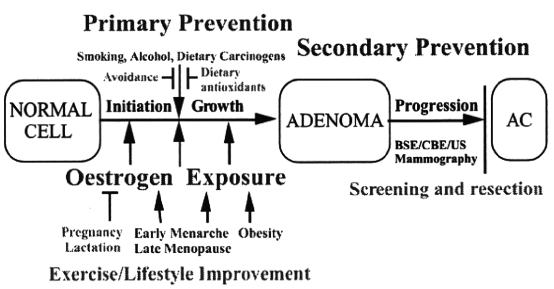

Figure 42. Cancer Prevention and Control Measures for the Breast, Ovary and Endometrium

(see Figure 42) are post-menopausal obesity, early menarche and late menopause, and hormone therapy. Tobacco and alcohol could play minor roles. The strongest protective factors would appear to be exercise, pregnancy, lactation, and consumption of soy products, followed by intake of fish and vegetables.

For the ovary and endometrium, the same factors generally apply, with possibly stronger influence of vegetables, and negative influence of smoking, fat and meat. Lactation may not be important in the endometrium.

Regarding secondary prevention, breast self-examination may be the most effective approach in much of Asia, if only to improve awareness and early presentation at hospital when symptoms are detected. In the developed countries, mammography has proven efficacy. For the ovary and endometrium, no population-based approaches are warranted at present.

Cervix

Since cancer of the uterine cervix has a primarily non-hormonal aetiology, it is here treated separately from the remainder of the female reproductive system. Perhaps the closest site in the body for comparison is the oral cavity, where the human papilloma virus may also be exerting an impact. A comparison of Globocan 2002 incidence data for the two is given in Figure 43. Clearly, some Pacific and South Asian populations do have high rates for both, but there are also a number of exceptions.

The Globocan 2002 mortality/incidence data for the cervix are plotted in Figure 44. The average ratio is 0.53:1, with little variation, except marginally better survival overall in North-West as opposed to South-West Asia.

Evidence for risk and protective factors for uterine cervix cancer from Asia is summarized in Table 12. The

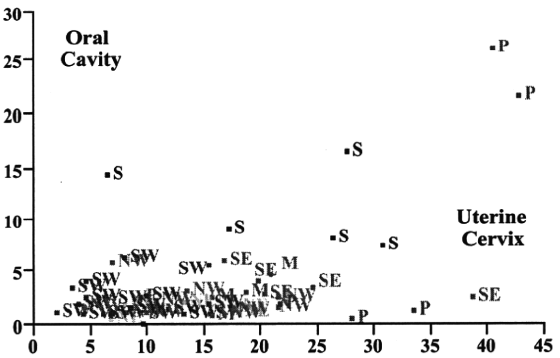

Figure 43. Regional Comparisons Between Globocan Incidence Data for the Cervix and Oral Cavity

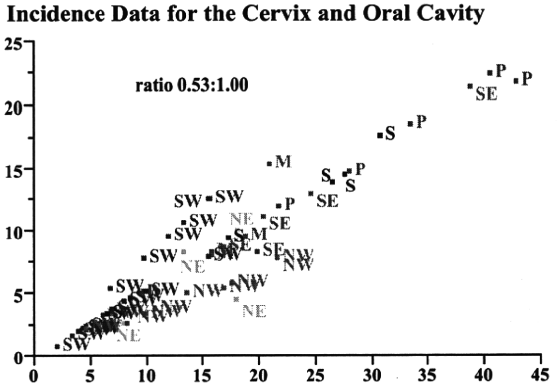

Figure 44. Mortality/Incidence Data for the Uterine Cervix (Globocan 2002; Ferlay et al., 2004)

Table 12. Asian Evidence for Modifying Factors for the Uterine Cervix

	NW	SW	S	SEM	SEI	Pac	NE	World*
Prevalence	L-H	L-M	L-H	M-H	M-H	M-H	L-M	NA
Lifestyle								
HPV	+++	+++	+++	+++	+++	+++	+++	NA
Tobacco	ND	ND	ND	++	++	ND	++	NA
Reproductive Factors								
Pregnancy	ND	ND	ND	+	ND	ND	+	NA
Early Sex	ND	ND	+	ND	ND	ND	+	NA
VD	ND	ND	ND	+	+	ND	++	NA
Diet								
Vegetables	ND	ND	ND	-	ND	ND	ND	-
Fruit	ND	ND	ND	-	ND	ND	-	+/-
Fish	ND	ND	ND	-	ND	ND	-	+/-

*World Cancer Research Fund,American Institute for Cancer Research 2007; NW, North-West, SW, South-West, S, South; SEM, South-East Mainland; SEI, South-East Island; Pac, Pacific; NE, North-East; L, low; M, medium;, H, high; NA, not applicable; ND, no data; -/--, slight/weak protection, +/-, no effect, +/++/+++, slight, weak, strong risk

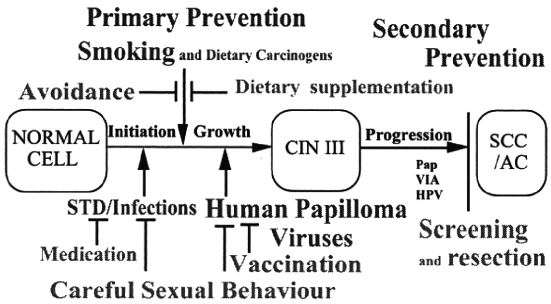

Figure 45. Cancer Prevention and Control Measures for the Uterine Cervix

obvious factors which need to be avoided as preventive measures are infection with high risk human papilloma viruses and smoking, and to a lesser extent sexually transmitted disease (see Figure 45). Dietary factors appear marginal. The main approaches should therefore be vaccination, where this is financially conceivable, and screening and resection using the Pap smear, visual inspection or HPV testing methods. The actual approach adopted will naturally be dependent on physical and financial constraints.

Nervous and Endocrine

Brain and Nervous Tissue

The Globocan 2002 mortality/incidence data for the brain and nervous tissue are plotted in Figure 46. The average ratio is 0.8:1, with little variation except for the slightly better survival evident for North-East Asian populations. Males are somewhat more likely than females to be affected (see Figure 47). Research data for risk factors are limited but certain environmental chemicals, cell phone use, salt and liquor may play roles, while vegetables and fruit are protective.

Thyroid

Since women are generally more susceptible to development of thyroid cancer than males, there may be some sex hormone involvement. In fact there is a very general correlation between thyroid and breast cancer incidences across Asia. As shown in Figure 48, that is also to some extent true for the endometrium, but South-West and North-West populations clearly differ in the relative percentages of cancers in the two sites.

The relevant Globocan 2002 mortality/incidence data are plotted in Figure 49, the average ratio of 0.32:1 having a few exceptions. There is a massive more than three fold

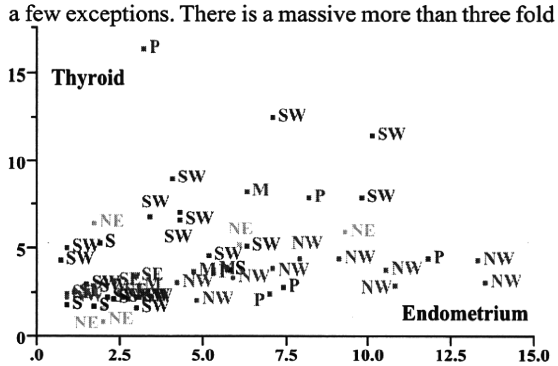

Figure 48. Regional Comparisons Between Globocan Incidence Data for the Throid and Endometrium

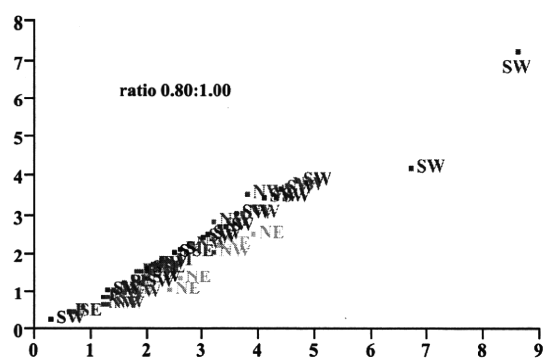

Figure 46. Mortality/Incidence Data for the Brain and Nervous Tissue (Globocan 2002; Ferlay et al., 2004)

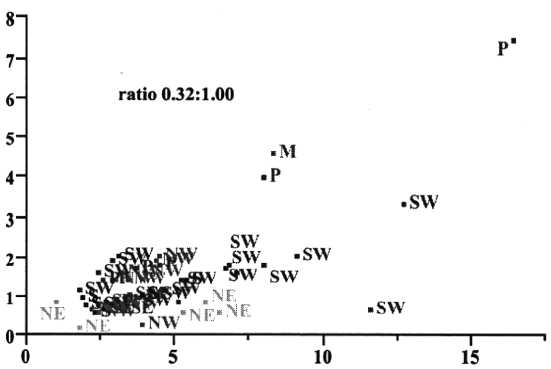

Figure 49. Mortality/Incidence Data for the Thyroid (Globocan 2002; Ferlay et al., 2004)

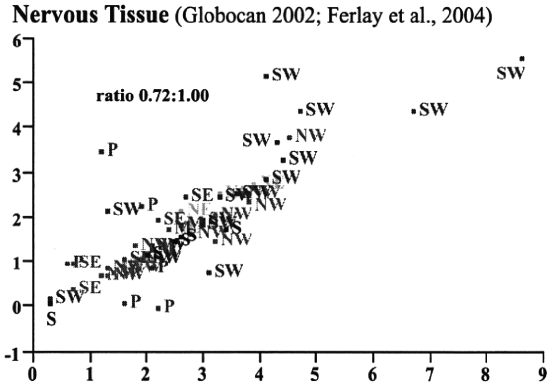

Figure 47. Female/Male Incidence Data for the Brain and Nervous Tissue (Globocan 2002; Ferlay et al., 2004)

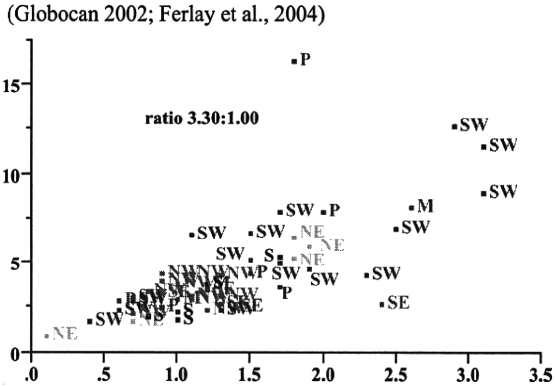

Figure 50. Female/Male Incidence Data for the Thyroid (Globocan 2002; Ferlay et al., 2004)

female predominance (see Figure 50), rising to over seven fold in Vanuatu. Radiation, reproductive parameters, obesity and conditions causing goiter are the best established risk factors but more research needs to be focused on the marked geographical variation.

Hematopoietic System

Globocan incidence data for non-Hodgkins lymphomas and leukemias ares plotted in Fibure 48, a general correlation between the two being apparent. There are marked regional groups, with a cluster of South-West Asian populations demonstrating the highest values.

Non-Hodgkins Lymphoma (NHL)

The Globocan 2002 mortality/incidence data for NHL are plotted in Figure 49. The average ratio is 0.69:1, with very little marked variation except for the better outcome in Israel among the high incidence populations. The gender differential is in the direction of males, but the extent is slight, in line with radiation as the major risk factor. Other etiological agents may be viruses, like HBV, and exogenous environmental carcinogens.

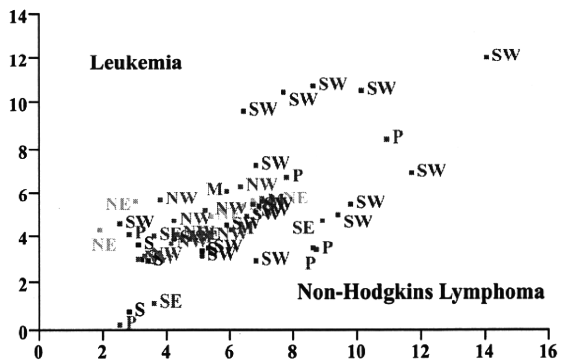

Figure 48. Regional Comparisons Between Globocan Incidence Data for the Throid and Endometrium

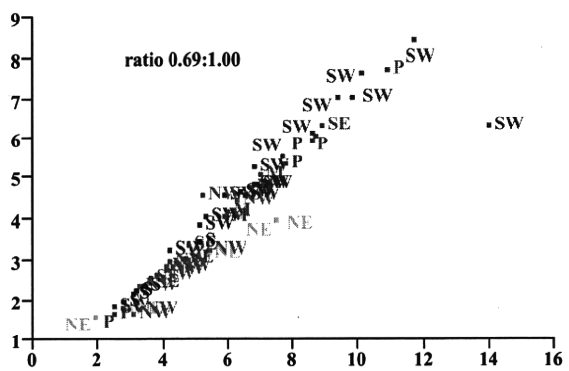

Figure 51. Mortality/Incidence Data for Non-Hodgkins Lymphomas (Globocan 2002; Ferlay et al., 2004)

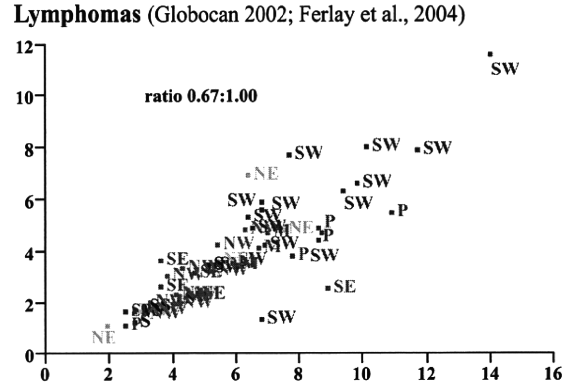

Figure 52. Female/Male Incidence Data for Non-Hodgkins Lymphomas (Globocan 2002; Ferlay et al., 2004)

Leukemia

The Globocan 2002 mortality/incidence data for leukemias are plotted in Figure 53. The average ratio is 0.82:1, again with Israel having a pronouncedly better survival. The slight male predominance is also in line with radiation and environmental pollution as the major risk factors.

Conclusions

From the present survey we can conclude that, for many of the cancers, epidemiological data on risk factors are limited in some regions of the Asian Pacific. This certainly does not mean that no recommendations can be made with regard to preventive measures. Indeed, the findings extracted from the series of seven regional reviews included in this volume (Long et al., 2010; Moore et al., 2010a; 2010b; 2010c; 2010d; 2010e; Salim et al., 2010) are well in agreement with the massive body of results for the entire globe reviewed by the World Cancer Research Fund/American Institute for Cancer Research for its summary document (2007). However, we are just as certainly lacking in a firm understanding of the reasons

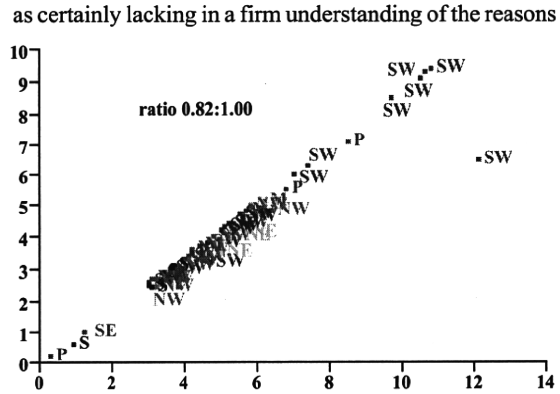

Figure 53. Mortality/Incidence Data for Leukemias (Globocan 2002; Ferlay et al., 2004)

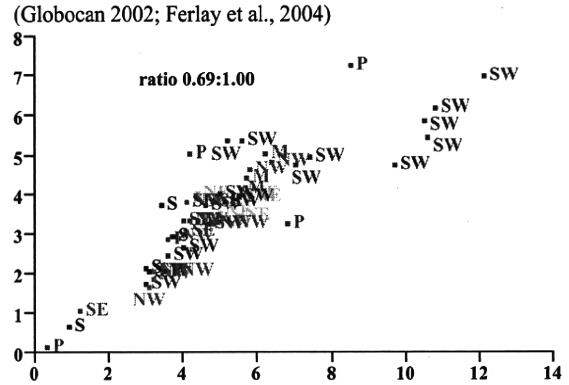

Figure 54. Female/Male Incidence Data for Non-Hodgkins Lymphomas (Globocan 2002; Ferlay et al., 2004)