 International Journal of Epidemiology 1998;**27**:167–172

Lung cancer among Chinese females in Singapore 1968–1992: time trends, dialect group differences and implications for aetiology

A Seow,[a,b] SW Duffy,[c] TP Ng,[a] MA McGee[c] and HP Lee[a,b]

Background	Chinese females are distinguished internationally as having relatively high lung cancer incidence rates despite a low prevalence of cigarette smoking. In Singapore, this population comprises several dialect groups which have origins in different regions in China, each with its own traditional cultural practices.
Methods	An analysis of 4029 incident cases of the disease notified to the Singapore Cancer Registry for 1968–1992 was undertaken to provide some insight into important aetiologic factors among these women.
Results	The age-standardized incidence rate of lung cancer rose from 17.3 per 100 000 woman-years in 1968–1972 to 23.0 in 1978–1982 before falling off in more recent years. Age-period-cohort analysis indicated significant period and birth cohort effects, with the risk being highest for women born around 1908. Between the major dialect groups, Cantonese women had a significantly high rate compared with Hokkiens (relative risk [RR] = 2.6, 95% CI : 2.4–2.8). Histologically, there appears to be an increase in the proportion of adenocarcinomas diagnosed over this period (25.8% in 1968–1972 to 51.3% in 1988–1992).
Conclusion	Our results suggest that traditional practices which have decreased over the years, and are more prominent among Southern Chinese, may play a part in the aetiology of lung cancer locally.

Keywords	Lung cancer, Chinese women, population-based, incidence, dialect groups, age-period-cohort analysis
Accepted	8 July 1997

Singapore is an island republic with a resident population of 2.7 million,[1] of which 78% are Chinese, 14% Malay and the remainder of Indian or other origin. Lung cancer is currently the third most commonly diagnosed cancer among Singapore females. Among Chinese females, it accounted for 9.8% of all cancers in 1988–1992, and ranked only below breast and colorectal cancer in frequency.[2] From a global perspective, the Chinese population in Singapore has a relatively high incidence rate compared both with other Asian countries as well as those in Europe and America (Table 1).

It is widely recognized that cigarette smoking, a major risk factor among men and in the West, is not responsible for the majority of cases among Chinese women whether living in Asia,[3,4] or in the West.[5,6] Studies among female lung cancer patients have found smoking rates of between 16% and 52% for Chinese in Hawaii, China, San Francisco and Singapore, compared with 77–90% for White women in North America and the UK, and 81–99% among men worldwide.[5–7] A case-control study of three major ethnic groups in Hawaii found that the odds ratio for lung cancer among Chinese smokers was only 1.8 compared with 4.9 for Japanese and 10.5 for Hawaiian women.[5] In a combined analysis of eight case-control studies in China,[4] the odds ratio associated with smoking was 2.3 for females (compared with 3.1 for males), and the attributable risk 25.5% (56.7% for males). In other studies, the attributable risk for lung cancer associated with smoking was reported to be between 25% and 40% in Shanghai, Hong Kong and northern China compared with 78% in the US.[8,9] This suggests that among Chinese females, only a minority of lung cancers can be attributed to smoking, and that other important risk factors are responsible for the high rates of lung cancer among these

[a] Department of Community, Occupational and Family Medicine, National University of Singapore MD3, Lower Kent Ridge Road, Singapore, 119260.

[b] Singapore Cancer Registry, Singapore.

[c] MRC Biostatistics Unit, Cambridge, UK.

Table 1 Incidence of lung cancer among females in selected countries, 1983–1987[34]

Country, City (race or ethnicity)	Age-standardized incidence rate[a]/100 000 females
Hong Kong	32.6
US, Los Angeles (White)	32.1
Singapore (Chinese)	21.9
Canada, Alberta	21.3
England and Wales	20.5
China, Shanghai	18.1
Philippines, Manila	16.3
Australia, New South Wales	13.4
Singapore (Malay)	12.1
Japan, Miyagi	11.0
Colombia, Cali	9.8
Sweden	9.5
Singapore (Indian)	5.2
India, Bombay	3.0

[a] To 'World' population.

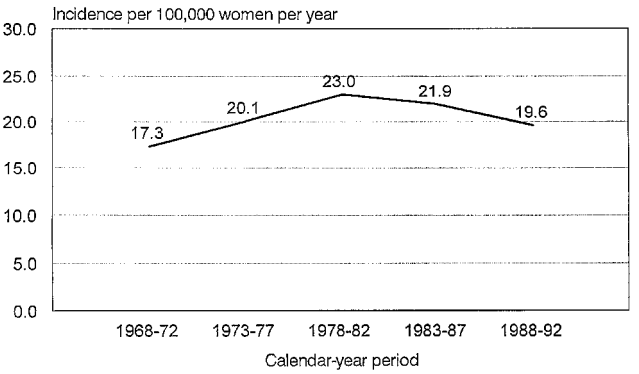

Figure 1 Age-standardized incidence rates for lung cancer in Singapore Chinese females 1968–1992

women. This is further corroborated by case-control studies in China[10] which have pointed to possible associations with cooking and oil vapours[11–13] or to smokey coal.[14]

The overwhelming majority of Chinese women in Singapore are non-smokers. The prevalence of regular smoking among adult females aged 18 and above has ranged consistently between 1.8 and 3.6% in various national surveys conducted between 1984 and 1992.[15] An earlier survey in 1974 reported a rate of 8.2%.[16] Although smoking prevalence rates in the 1950s and 1960s would be of interest, data before the 1970s are not available. A hospital-based case-control study among Chinese females in 1977 concluded that neither smoking nor any of the other exposures examined, such as incense burning or the use of gas or kerosene stoves, could explain the high incidence of lung cancer in this population.[7]

In this study, we sought to examine the effect of age, birth cohort and calendar year period on the incidence of lung cancer among Singapore Chinese females, as well as the overall differences between the major dialect groups. Our objective was to determine if incidence trends do indeed suggest which type of environmental factors may play a role in the aetiology of the disease in this population. The Singapore Chinese population offers a unique opportunity to study these dialect differences because the data collected are standardized across the entire population residing here, and differences cannot be attributed varying degress of accuracy and completeness which may be the case if different registries are compared.

Materials and Methods

Data on incident cases of lung cancer were obtained from the Singapore Cancer Registry, a population-based registry covering the entire resident population of Singapore. Details of registration procedures and coding practices are described elsewhere.[17] All cases registered under the ICD-9 rubric 162 occurring in Chinese females for the period 1968–1992 as of 15 February 1995 were included in the present analysis. Information on histological type was taken from notification forms which were cross-checked with hospital pathology reports.

Population data derived from censuses in 1970, 1980 and 1990,[1,18,19] with interpolation between these years, form the denominators for the present study, both for the total Chinese female population, as well as for the major dialect groups. Where indicated, the rates have also been age-standardized to the 'World' population[20] for international comparison.

Temporal changes were analysed using age-period-cohort models.[21,22] This procedure allowed us to assess which model (a difference in incidence between time periods, birth cohorts or both) provided a better description of the data.

Incidence density ratios and their corresponding confidence intervals were calculated for dialect group comparisons using the DEPID software.[23]

Results

Temporal changes

A total of 4029 cases of lung cancer among Chinese females were registered in the period under review. This constituted 93.8% of cases for all ethnic groups. The trend in the age-standardized rates is shown in Figure 1. The incidence rate appears to have increased from 1968 to 1982 before falling off slightly in more recent years.

Table 2 gives the age-specific rates by 5-year age groups for each 5-year period, and the total number of cases diagnosed in each quinquinneum. The age-incidence pattern shows low rates until after age 45, when the incidence tends to rise almost exponentially with age. Because of small numbers in the younger age groups, only cases above 20 years of age were included in the mathematical modelling.

Table 3 shows the results of the age-period-cohort analysis, which indicate significant period and cohort effects for Chinese women after adjustment for age, and separately for each other. This would suggest both cohort and temporal effects operating simultaneously to influence the rates in this population. The relative risk (RR) estimates by period and by birth cohort are given in Table 4. They indicate low risks for the pre-1905 cohorts, increasing to 1908, remaining stable till 1918 before falling off in cohorts born after the 1920s. It also appears that cohorts born between 1933 and 1953 share very similar risks. The

Table 2 Age-specific lung cancer incidence rates per 100 000 women-years for Singapore Chinese females 1968–1992

	Calendar year of diagnosis					
Age group	1968–1972	1973–1977	1978–1982	1983–1987	1988–1992	**1968–1992**
20–24	0.3	0.0	0.2	0.2	0.2	0.2
25–29	1.2	0.0	0.9	0.6	1.1	0.8
30–34	2.8	0.9	0.5	1.1	1.6	1.3
35–39	4.9	2.2	3.8	4.7	4.0	4.0
40–44	6.7	8.6	5.6	5.0	6.3	6.3
45–49	15.0	16.9	12.0	15.3	11.4	13.8
50–54	36.1	31.0	37.2	29.6	30.9	32.6
55–59	47.2	49.6	58.6	52.7	35.7	47.9
60–64	93.0	89.8	115.9	90.1	77.5	92.2
65–69	96.7	142.9	146.1	138.7	129.7	132.8
70–74	153.7	165.6	188.0	204.7	169.9	179.2
75–79	114.5	192.3	215.7	245.0	219.4	209.5
80–	92.1	169.3	241.3	234.1	254.0	220.2
No. of cases	462	625	855	993	1094	4029

Table 3 Lung cancer among Chinese women in Singapore, 1968–1992. Deviance χ^2 statistics for age, period and cohort effects (factors adjusted for in parentheses)

Model	**χ^2 tests (d.f.)**
Age	8426 (11) ***
Drift (age)	0.25 (1)
Period (age)	19.86 (4) ***
Period (age and cohort)	10.43 (3) *
Cohort (age and period)	33.94 (14) **
Cohort (age)	43.37 (15) ***

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$

Table 4 Lung cancer among Chinese women in Singapore, 1968–1992. Relative risks by birth cohort and period, adjusted for age

	Relative risk	**95% CI**
Period		
1968–1972	1.00	–
1973–1977	1.11	0.97–1.26
1978–1982	1.23	1.09–1.39
1983–1987	1.19	1.06–1.34
1988–1992	1.05	0.93–1.18
Cohort		
1893	0.54	0.37–0.79
1898	0.91	0.73–1.14
1903	0.94	0.78–1.13
1908	1.13	0.96–1.33
1913	1.11	0.95–1.29
1918	1.12	0.96–1.29
1923	1.06	0.91–1.23
1928	1.00	–
1933	0.83	0.68–1.00
1938	0.89	0.71–1.11
1943	0.72	0.52–0.99
1948	0.78	0.53–1.15
1953	0.79	0.48–1.30
1958	0.96	0.46–2.00
1963	1.40	0.50–3.87

increase in risks subsequent to 1958 should be interpreted with caution until larger numbers of cases become available. Relative risks by period are consistent with the observed incidence rates, with a gradual rise up to 1978–1982 followed by a slight decline.

Trends in histology

In the series of cases included in our analysis, pathological confirmation was present in 66.4%, the remainder being diagnosed clinically or radiologically. Of the 2641 pathologically confirmed cases, 19.4% were reported as squamous cell carcinomas, 38.4% as adenocarcinomas and 7.2% as small/oat cell carcinomas.

Table 5 shows the change in distribution over time by histology of the tumour. Among the major histological types, a threefold increase was observed among the age-standardized incidence rate of adenocarcinomas, and the proportion of this tumour increased correspondingly from 25.8% in 1968–1972 to 51.3% in 1988–1992. There appears to be an increase in small cell carcinomas, although this may be due in part to the instability associated wih small numbers. We note a concurrent decrease in the proportion of 'other' or 'unspecified' cancers from 46.6% to 19.1% over the same period.

Dialect group differences

Of the 4029 cancers analysed, information on dialect group was available for 3753 cases (93.1%). Of these, 88.5% occurred in women of Hokkien, Teochew or Cantonese dialects. Table 6 shows the proportions of cancers in these groups and the respective age-standardized incidence rates. There is a significantly higher rate of lung cancer among Cantonese females compared with the Hokkiens, whose rates are fairly similar to the Teochews. Further analysis shows that the higher risk in Cantonese compared with Hokkiens is more marked for adenocarcinomas (incidence density ratio [IDR] = 2.5, 95% CI : 2.1–2.9) than for squamous cell carcinomas (IDR = 1.9, 95% CI : 1.5–2.4).

Table 5 Age-standardized[a] incidence rates for lung cancer and distribution by percentage among Singapore Chinese females by histological type, 1968–1992

	Rate per 100 000 woman-years (Number in parentheses denotes percentage of all cases[b] for the respective calendar period)				
	1968–1972	1973–1977	1978–1982	1983–1987	1988–1992
Squamous cell carcinoma	2.40	2.71	2.53	3.13	3.14
	(23.3)	(22.2)	(15.8)	(19.0)	(19.5)
Adenocarcinoma	2.58	2.46	4.41	7.59	8.31
	(25.8)	(20.4)	(27.7)	(45.9)	(51.3)
Small/oat cell carcinoma	0.43	0.30	0.90	1.41	1.69
	(4.3)	(2.4)	(5.5)	(8.5)	(10.2)
Other or unspecified	4.87	6.67	8.10	4.30	3.12
	(46.6)	(55.0)	(51.0)	(26.6)	(19.1)
Total no. of cases[a]	279	378	582	726	876

[a] To 'World' population.

[b] Includes only pathologically confirmed cases (n = 2841).

Table 6 Lung cancer among Singapore Chinese females, 1968–1992. Age-standardized[a] incidence rates and rate ratios for major dialect groups

Dialect group	Proportion[b] of cases diagnosed among Chinese females in 1968–1992 (no. of cases)	Age-standardized incidence rate (per 100 000 women-years) (95% CI)	Incidence density ratio (95% CI)
Hokkien	33.4% (1254)	18.3 (17.3–19.4)	1.0
Teochew	19.2% (720)	16.7 (15.5–17.9)	1.1 (1.0–1.2)
Cantonese	35.9% (1346)	26.3 (24.9–27.8)	2.6 (2.4–2.8)

[a] To 'World' population.

[b] Of cases with known dialect group only (see text). Percentages do not add up to 100 as women of other dialect groups comprise 11.5% of cases.

Discussion

Our results show that the incidence of lung cancer among Chinese females in Singapore has remained fairly stable over the past 25 years. The age-incidence pattern differs, however, in a manner that can be explained by the inter-related effects of calendar year period and birth cohort. The highest risks are exhibited by women who were born between 1905 and 1920 and these, having passed through the high risk age groups (60–80 years) a decade ago, contributed to the increase in rates observed then. We have also shown that there may be an increase in the proportion of adenocarcinomas, and also that, between dialect groups, Cantonese women have comparatively high rates.

It is unlikely that the trends observed are due to data artefacts or to changes in coding practices or diagnostic accuracy over time. Although notification to the Singapore Cancer Registry is voluntary, a mechanism for checking a wide range of possible sources ensures that coverage is complete. Over the past 25 years, between 63 and 90% of cases have been notified by medical practitioners. Cases based on death certificates only comprised fewer than 6% of all registrations.[2] Compared with other sites, the proportion of cases of lung cancer that are clinically or radiologically diagnosed tends to be relatively high in most registries. Possible errors in diagnosis are minimized by our system of routinely checking all registrations against the death registry, including recorded causes of death. Although improvements in diagnostic accuracy may have occurred, these would have led to a spurious increase in rates, and it is unlikely that a time trend such as the one observed could be attributed to such an error.

Although histological typing of this series was not subject to a separate review, the data from cancer registrations suggest that among cancers with a pathological basis of diagnosis, the frequency of adenocarcinoma has increased over time. It is unlikely that this increase is entirely artefactual. If the change is a result of more exact classification of cancers previously designated 'malignancy/cancer NOS', then the re-distribution should be spread out among all the major histological categories. In contrast, we see that the proportion of squamous cell carcinomas has decreased from 23.3% in 1968–1972 to 19.5% in 1988–1992. A similar preponderance of adenocarcinomas has been observed in other non-smoking populations,[6] and the increase in the proportion of adenocarcinomas is also consistent with other reports.[24,25]

Temporal trends of lung cancer in the West have largely parallelled trends in smoking prevalence, with recent increases in older women and stable or falling rates in the young.[26–28] In Glasgow, the highest rates were observed for women born about 1915–1929, in agreement with other studies of smoking habits of these cohorts.[28] In Shanghai, in a population with female smoking rates of 6–18%, the overall incidence rates have remained fairly constant between 1972 and 1989.[29]

Our results, from a largely non-smoking population, suggest that major sources of exposure which carry an increased risk

of lung cancer for Chinese women locally are becoming less common now. This is evidenced by falling risks in consecutive birth cohorts, as well as in the more recent calendar year periods, when adjusted for the cohort effect. The prevalence of these exposures reached their peak among women born at the beginning of this century, and the highest incidence rates in the past 25 years occurred at the time when these women were in their eighth decade of life. The extent of exposure appears to be highest for Cantonese women. The lower risks experienced by women born between 1890 and 1905 are not easy to explain, bearing in mind that the set of exposures experienced by these cohorts occurred in the distant past and information on these is likely to be obscure.

The Singapore Chinese population comprises at least nine different groups with origins in the different regions in China, each having its own dialectal language form and cultural practices, including preferences for cooking methods. At around 1980, the mid-point of the period under study, 19.7% of all Chinese residing in Singapore had been born outside. Of these, 51.5% were born in China, Hong Kong or Taiwan. However, among those aged 50 and above, immigrants constituted 63.8%, with 87.8% coming from China, Hong Kong or Taiwan.[17] The older Chinese population in Singapore is thus dominated by people whose early life experiences are related to the traditional practices from their place of origin rather than to the environment in their country of adoption. Between their arrival and the present, many of the distinctive practices would have become more homogeneous between dialect groups. The long latent period associated with a disease such as lung cancer, and its preponderance among the elderly, however, suggests that any differences in incidence between age and dialect groups are likely to be related to distinct exposures earlier in life. Several epidemiological studies have sought to explain the high risk of lung cancer among Chinese females in terms of exposure to cooking oil vapours during high-temperature cooking.[11–13,30] The mutagenicity of condensed vapours from cooking oil such as rapeseed and soybean oils, and of linolenic acid, when heated to temperatures between 240 and 280°C has also been established.[31–33]

Our results, from the experience of Singapore Chinese women, support these findings, and suggest in addition that that the search for a putative aetiologic factor should consider particularly those specific practices and exposures that have decreased in use since the beginning of this century, and appear to be more prevalent among women of Cantonese origin. If indeed an aetiologic factor for lung cancer is to be found in the domestic environment, this would be of important public health significance. A case-control study is currently underway to investigate in detail such exposures among Chinese women in Singapore.

Acknowledgements

The authors wish to thank the staff of the Singapore Cancer Registry for their help in obtaining the data used in this study.

References

[1] Lau KE. Singapore Census of Population 1990. *Statistical Release 1: Demographic Characteristics.* Department of Statistics, Singapore, 1992.

[2] Chia KS, Lee HP, Seow A, Shanmugaratnam K. *Trends in Cancer Incidence in Singapore 1968–1992.* Singapore Cancer Registry Report No. 4, 1996.

[3] Jin F, Devesa SS, Zheng W, Blot WJ, Fraumeni JF, Gao YT. Cancer incidence trends in urban Shanghai, 1972–1989. *Int J Cancer* 1993; **53:**764–70.

[4] Liu ZY. Smoking and lung cancer in China: combined analysis of eight case-control studies. *Int J Epidemiol* 1992;**21:**2–31.

[5] Hinds MW, Stemmermann GN, Yang HY, Kolonel LN, Lee J, Wegner E. Differences in lung cancer risk from smoking among Japanese, Chinese and Hawaiian women in Hawaii. *Int J Cancer* 1981;**27:** 297–302.

[6] Koo LC, Ho JHC. Worldwide epidemiological patterns of lung cancer in nonsmokers. *Int J Epidemiol* 1990;**19:**S14–23.

[7] MacLennan R, Da Costa J, Day NE, Law CH, Ng YK, Shanmugaratnam K. Risk factors for lung cancer in Singapore Chinese, a population with high female incidence rates. *Int J Cancer* 1977;**20:**854–60.

[8] Mason TJ. The descriptive epidemiology of lung cancer. In: Samet JM (ed.). *Epidemiology of Lung Cancer*. New York: Marcel Dekker, Inc., 1994, pp.51–70.

[9] Wu-Williams AH, Samet JM. Lung cancer and cigarette smoking. In: Samet JM (ed.). *Epidemiology of Lung Cancer*. New York: Marcel Dekker, Inc., 1994, pp.71–108.

[10] Gao YT, Blot WJ, Zheng W, Fraumeni JF, Hsu CW. Lung cancer and smoking in Shanghai. *Int J Epidemiol* 1988;**17:**277–80.

[11] Gao YT, Blot WJ, Zheng W *et al*. Lung cancer among Chinese women. *Int J Cancer* 1987;**40:**604–09.

[12] Wu-Williams AH, Dai XD, Blot ZY *et al*. Lung cancer among women in north-east China. *Br J Cancer* 1990;**62:**982–87.

[13] Xu ZY, Blot WJ, Xiao HP *et al*. Smoking, air pollution and the high rates of lung cancer in Shenyang, China. *J Natl Cancer Inst* 1989;**81:** 1800–06.

[14] Wu AH, Henderson BE, Pike MC, Yu MC. Smoking and other risk factors for lung cancer in women. *J Natl Cancer Inst* 1985;**74:**747–51.

[15] Ministry of Health, Research and Evaluation Department. *National Health Survey 1992: Highlights of Main Survey Findings, and Other Reports*. Singapore, 1993.

[16] Lee HP, Seah CS, Yik TY *et al.* An epidemiological survey of blood pressures in Singapore. *J Chron Dis* 1977;**30:**793–802.

[17] Shanmugaratnam K, Lee HP, Day NE. *Cancer Incidence in Singapore 1968–1977*. IARC Scientific Publications No. 47, 1983.

[18] Khoo C K. *Census of Population 1980, Singapore. Release No. 2: Demographic Characteristics.* Department of Statistics, Singapore, 1981.

[19] Arumainathan P. *Report on the Census of Population 1970, Singapore, Volume 2*. Department of Statistics, Singapore, 1971.

[20] Waterhouse J, Muir C, Shanmugaratnam K, Powell J. *Cancer Incidence in Five Continents. Vol III*. IARC Scientific Publication 15; IARC, Lyon, 1976.

[21] Clayton D, Schifflers E. Models for temporal variation in cancer rates. I: Age-period and age-cohort models. *Statist Med* 1987;**6:**449–67.

[22] Clayton D, Schifflers E. Models for temporal variation in cancer rates. II: The age-period-cohort model. *Statist Med* 1987;**6:**469–81.

[23] Sullivan KM, Foster DA. *DEPID: A Program for Stratified and Standardized Analysis. Version 2.11*. Centers for Disease Control, Atlanta, GA, 1987 (A public domain software)

[24] Dodds L, Davis S, Polissar L. A population-based study of lung cancer incidence trends by histologic type, 1974–81. *J Natl Cancer Inst* 1986; **76:**21–29.

[25] Barsky SH, Cameron R, Osann KE, Tomita D, Carmack Holmes E. Rising incidence of bronchioloalveolar lung carcinoma and its unique clinicopathologic features. *Cancer* 1994;**73:**1163–70.

[26] Ernster VL. The epidemiology of lung cancer in women. *Ann Epidemiol* 1994;**4:**102–10.

[27] Zheng T, Holford TR, Boyle P, Chen Y, Ward BA, Flannery J. Time trend and the age-period-cohort effect on the incidence of histologic types of lung cancer in Connecticut, 1960–1989. *Cancer* 1994;**74:** 1556–67.

[28] Gillis CR, Hole DJ, Lamont DW, Graham AC, Ramage S. The incidences of lung cancer and breast cancer in women in Glasgow. *Br Med J* 1992;**305:**1331.

[29] Jin F, Devesa SS, Zheng W, Blot WJ, Fraumeni JF, Gao YT. Cancer incidence trends in urban Shanghai 1972–1989. *Int J Cancer* 1993; **53:**764–70.

[30] Ko YC, Lee CH, Chen MJ *et al*. Risk factors for primary lung cancer among non-smoking women in Taiwan. *Int J Epidemiol* 1997;**26:** 24–31.

[31] Qu H, Zu GX, Zhou JZ *et al*. Genotoxicity of heated cooking oil vapors. *Mutat Res* 1992;**298:**105–11.

[32] Shields PG, Xu GX, Blot WJ *et al*. Mutagens from heated Chinese and US cooking oils. *J Natl Cancer Inst* 1995;**87:**836–41.

[33] Chen H, Yang M, Ye S. A study on genotoxicity of cooking fume from rapeseed oil. *Biomed Environ Sci* 1992;**5:**229–35.

[34] Parkin DM, Muir CS, Whelan SL, Gao YT, Ferlay J, Powell J. *Cancer Incidence in Five Continents. Vol VI*. IARC Scientific Publication 120; IARC, Lyon, 1992.