Jpn. J. Cancer Res. **89**, 355–360, April 1998

The Relationship between Population Density and Cancer Mortality in Taiwan

Chun-Yuh Yang[1, 3] and Ya-Lun Hsieh[2]

[1]School of Public Health, Kaohsiung Medical College, 100 Shih-Chuan 1st Road, Kaohsiung 80708, Taiwan and [2]Department of Nursing, Mei-Ho College, 23 Ping-Guang Road, Nei-Pu, Ping-Tung County, Taiwan

Many investigators have examined urbanization gradients in cancer rates. The purpose of this report was to identify urban-rural trends in cancer mortality rates (1982–1991) for municipalities in Taiwan. For this purpose, Taiwan's municipalities were classified as rural, suburban, urban, or metropolitan, using population density as an ordinal indicator of the degree of urbanization. Average annual age-adjusted, site-specific cancer mortality rates were calculated for both sexes within each population density group. Significant increasing trends with more urbanization were observed in mortality rates for cancers of the lung, pancreas, and kidney among both males and females, as well as male prostate cancer, and female breast and ovary cancer. In addition, this study revealed a significant rural excess for nonmelanoma skin cancer among both males and females, as well as male non-Hodgkin's lymphoma, and cancers of the female bone, and female connective tissue. Analytic studies for sites with consistent urban-rural trends may be fruitful in identifying the aspect of population density, or other unmeasured factors, that contribute to these trends.

Key words: Population density — Neoplasms — Mortality — Urbanization — Geography

Studies of populations living in urban environments are of considerable interest to epidemiologists since they can suggest the extent to which urban factors are important in the etiology of different cancers. A number of studies have reported variation in cancer incidence and mortality rates across urbanization gradients.[1–14] Almost all these studies have reported higher cancer incidence and mortality rates in urban populations compared to their counterparts who live in rural areas.[1–13] A major drawback has been the lack of a uniform measure used to classify areas as urban or rural.[15] Perhaps the major difficulty lies in defining a rural area. As a result, even when an urban-rural dichotomy has been chosen, definitions have not been consistent.[3, 8, 11, 13, 14] In addition, several studies have used population density as an ordinal indicator in order to examine urban-rural differences in cancer rates.[1, 2, 4–7]

An additional limitation is the limited number of counties in which a subdivision between urban and rural rates is available, due to either deficiencies in the numerator or in the denominator.[15, 16] As a result of this, almost all the studies have been performed in developed countries.[1–14] Furthermore, these reports have generally relied on large areas, such as states or counties, as the basic geographical unit of analysis. This makes it difficult to characterize the true urbanization level due to its heterogeneity within these large areas. As a result of these limitations, the methodology employed in most preceding investigations has been imprecise, and the relationship between population density and cancer mortality has not been adequately examined. Moreover, only six studies[1, 3–7] to date have described trends in cancer mortality patterns associated with increasing levels of urbanization.

Taiwan appears to be appropriate for this type of study. Since it is mandatory to register any birth, marriage, divorce, employment, education, migration, and death in the household registration offices, the vital statistics are accurate and complete. In this paper we used minor civil divisions (administrative units, i.e., cities and towns) as the basic geopolitical unit of analysis. Our report describes sex- and site-specific patterns of cancer mortality within four population density quartiles in Taiwan, between 1982–1991. This methodology allowed an examination of trends in site-specific cancer mortality associated with levels of urbanization as measured by population density.

MATERIALS AND METHODS

Taiwan is divided into 361 administrative districts, which will be referred to herein as municipalities. They are the units that will be subjected to statistical analysis. Excluded from the analysis were 6 municipalities which had changed administrative size during 1982–1991. This left 355 municipalities for the analysis.

Information concerning both number of deaths and midyear population by sex, age, municipality of residence, calendar year during 1982–1991 was obtained from the Bureau of Vital Statistics of the Taiwan Provincial Depart-

[3] To whom correspondence should be addressed.

ment of Health. This bureau is in charge of the death registration system in Taiwan, which has been completely computerized since 1972. The International Classification of Disease, Injury and Causes of Death (9th revision) is used to code the cause of death.

All 355 municipalities were ranked by population density (persons per square kilometer) using the 1989 Taiwan-Fukien Demographic Fact Book,[17] which includes population counts, land area, and population density for all municipalities. This ranking was used to create four population density groups of similar population sizes. The ranges of the population density for each group are summarized in Table I.

Average annual cancer mortality rates per 100,000 population were calculated first for males and females for the period 1982–1991 for each of the 355 municipalities. The age-standardized rates (ASR) were calculated using the direct method, using the world population in 1976 as the standard population.[18] The mean ASR were then calculated within each population density group. To evaluate the relationship between population density and cancer mortality, the results were expressed as standardized relative risk (SRR) of dying from various malignant neoplasms in different population density groups, using the lowest population density group as a reference. This was done separately for males and females. To test the null hypothesis (H_0: SRR=1), 95% confidence intervals for the SRR were calculated using the method of Rothman.[19] Trends in SRR for various malignant neoplasms across different population density groups were tested using the χ^2 test for trend described by Breslow and Day.[20]

Table I. Population Density Ranges Used for Population Density Groups, Taiwan, 1987

Group	Population density range (persons/km^2)	No. of municipalities	1987 total population	Category
I	5–851	211	4,995,093	rural
II	853–2,935	83	4,980,457	suburban
III	2,966–10,557	36	5,054,644	urban
IV	10,781–50,643	25	4,873,717	metropolitan

Table II. Age-standardized Rates (ASR) by Cancer Site and Population Density for Males, Taiwan, 1982–1991

Cancer site (ICD 9 Codes)	Rural	Suburban	Urban	Metropolitan
Oral cavity (141–149, excluding 142,147)	3.96	4.75	3.97	4.44
Salivary gland (142)	0.26	0.17	0.17	0.26
Nasopharynx (147)	6.83	5.71	5.62	6.90
Esophagus (150)	6.06	5.98	6.90	6.35
Stomach (151)	19.16	16.62	17.20	16.84
Small intestine (152)	0.59	0.52	0.43	0.54
Colon (153)	4.98	5.90	5.98	6.62
Rectum (154)	2.86	3.39	3.30	3.58
Liver & intrahepatic bile ducts (155)	31.60	32.43	31.60	34.40
Gall bladder and extrahepatic bile ducts (156)	1.14	1.64	1.54	1.42
Pancreas (157)	2.37	3.01	3.29	3.96
Nasal cavities, middle ear and accessory sinuses (160)	0.96	0.69	0.54	0.67
Larynx (161)	1.49	1.36	1.65	1.50
Trachea, bronchus and lung (162)	21.41	24.33	26.61	28.02
Bone and articular cartilage (170)	1.57	1.66	1.44	1.35
Connective and other soft tissue (171)	0.91	0.76	0.85	0.51
Melanoma of skin (172)	0.26	0.32	0.22	0.14
Non-melanoma skin (173)	0.93	0.76	0.70	0.39
Prostate (185)	1.61	2.01	2.45	2.94
Bladder (188)	2.99	2.90	2.85	3.20
Kidney & urinary organs (189)	1.03	1.32	1.41	1.67
Brain (191)	1.37	1.57	1.42	1.69
Lymphosarcoma (200)	0.38	0.37	0.30	0.44
Non-Hodgkin's lymphoma (200, 202, 203)	3.55	3.45	3.30	3.19
Other lymphoid tissue (202)	2.70	2.46	2.52	2.30
Multiple myeloma (203)	0.48	0.61	0.48	0.45
Leukemia (204–208)	3.88	3.67	3.83	3.96
All sites combined	126.68	129.62	131.39	138.26

RESULTS

The age-standardized death rates classified by site, sex and population density are shown in Tables II and III. The relationship between population density and cancer mortality is presented in Tables IV and V. Among males, a significant positive linear relationship was observed between increasing population density and increasing SRR for deaths due to all cancer sites combined and cancer of the colon, pancreas, lung, prostate, and kidney. A significant inverse relationship, leading to a rural excess, was observed for non-melanoma skin and non-Hodgkin's lymphoma cancers.

Among females, a significant positive linear trend was noted for deaths due to cancer of the pancreas, lung, rectum, breast, ovary, and kidney. Significantly increased rural risks were observed for the following cancer sites: bone, connective tissue, and non-melanoma skin.

DISCUSSION

The higher risks of living in highly urbanized areas have been summarized by a previous study.[16] This review included comparisons among developed countries using data from their cancer registries. Also, most studies on urban risk were similarly conducted in the so-called First World.[1–14] Our report concerning urban risks of cancer in a developing country shows some interesting and divergent results when compared with reports from developed countries.

In an ecological study like this, it should be noted that an association between cancer mortality and population density may not necessarily represent an association at the individual level of causal relationship. Rather, the observed association may serve as a lead for further investigation.

Because it is mandatory to register death certificates at local household registration offices and the household reg-

Table III. Age-standardized Rates (ASR) by Cancer Site and Population Density for Females, Taiwan, 1982–1991

Cancer site (ICD 9 Codes)	Rural	Suburban	Urban	Metropolitan
Oral cavity (141–149, excluding 142,147)	1.33	0.91	0.56	0.60
Salivary gland (142)	0.11	0.07	0.12	0.11
Nasopharynx (147)	2.80	2.11	2.19	2.01
Esophagus (150)	1.19	1.00	1.16	0.94
Stomach (151)	9.93	8.31	8.31	8.26
Small intestine (152)	0.49	0.37	0.28	0.32
Colon (153)	4.59	5.43	6.13	5.80
Rectum (154)	2.09	2.42	2.76	3.11
Liver & intrahepatic bile ducts (155)	9.33	9.65	9.41	10.35
Gall bladder and extrahepatic bile ducts (156)	1.07	1.27	1.20	1.78
Pancreas (157)	1.62	2.04	2.17	2.43
Nasal cavities, middle ear and accessory sinuses (160)	0.49	0.25	0.25	0.29
Larynx (161)	0.32	0.25	0.14	0.26
Trachea, bronchus and lung (162)	10.23	10.80	12.41	13.36
Bone and articular cartilage (170)	1.46	1.16	1.11	0.89
Connective and other soft tissue (171)	0.70	0.55	0.38	0.36
Melanoma of skin (172)	0.14	0.18	0.13	0.16
Non-melanoma skin (173)	0.71	0.57	0.46	0.39
Breast (174)	4.42	5.78	7.04	8.05
Cervix uteri, uterus(179–180)	12.08	10.89	12.09	11.88
Ovary (183)	1.04	1.67	1.70	2.20
Bladder (188)	1.49	1.36	1.33	1.40
Kidney & urinary organs (189)	0.76	0.94	1.14	1.21
Brain (191)	1.35	1.12	1.26	1.28
Lymphosarcoma (200)	0.30	0.33	0.34	0.20
Non-Hodgkin's lymphoma (200, 202, 203)	2.36	2.13	2.00	2.30
Other lymphoid tissue (202)	1.73	1.51	1.36	1.80
Multiple myeloma (203)	0.28	0.27	0.30	0.30
Leukemia (204–208)	3.09	3.01	2.82	3.14
All sites combined	79.71	78.50	83.09	86.70

Table IV. Standardized Relative Risk (SRR) for Suburban, Urban and Metropolitan Areas in Males,[a] Taiwan, 1982–1991

ICD 9 Codes	Suburban	Urban	Metropolitan
141–149	1.20 (1.02–1.42)	1.00 (0.81–1.25)	1.12 (0.90–1.40)
142	0.66 (0.39–1.11)	0.65 (0.39–1.09)	0.99 (0.56–1.73)
147	0.84 (0.71–0.99)	0.82 (0.69–0.98)	1.01 (0.63–1.61)
150	0.99 (0.84–1.16)	0.82 (0.69–0.98)	1.01 (0.63–1.61)
151	0.87 (0.77–0.98)	0.90 (0.80–1.01)	0.88 (0.76–1.02)
152	0.89 (0.65–1.21)	0.72 (0.51–1.01)	0.92 (0.59–1.43)
153	1.19 (1.05–1.34)	1.20 (1.07–1.35)	1.33 (1.16–1.52)[b]
154	1.19 (1.03–1.37)	1.16 (1.00–1.33)	1.25 (1.08–1.46)
155	1.03 (0.94–1.12)	1.00 (0.92–1.09)	1.09 (1.00–1.19)
156	1.44 (1.16–1.78)	1.35 (1.06–1.73)	1.25 (0.97–1.60)
157	1.27 (1.09–1.49)	1.39 (1.18–1.63)	1.67 (1.40–2.00)[b]
160	0.72 (0.52–1.00)	0.56 (0.41–0.77)	0.70 (0.45–1.10)
161	0.91 (0.75–1.11)	1.11 (0.89–1.38)	1.00 (0.82–1.22)
162	1.14 (1.05–1.23)	1.24 (1.15–1.34)	1.31 (1.21–1.42)[b]
170	1.06 (0.87–1.29)	0.73 (0.57–0.92)	0.86 (0.68–1.08)
171	0.84 (0.63–1.13)	0.93 (0.70–1.24)	0.56 (0.41–0.77)
172	1.22 (0.76–1.96)	0.85 (0.52–1.39)	0.52 (0.31–0.88)
173	0.82 (0.59–1.14)	0.75 (0.50–1.12)	0.41 (0.28–0.62)[c]
185	1.24 (1.04–1.49)	1.52 (1.17–1.98)	1.82 (1.28–2.60)[b]
188	0.97 (0.76–1.23)	0.95 (0.74–1.23)	1.07 (0.82–1.40)
189	1.28 (1.00–1.65)	1.38 (1.07–1.76)	1.62 (1.23–2.15)[b]
191	1.15 (0.93–1.42)	1.04 (0.83–1.31)	1.23 (0.99–1.53)
200	0.98 (0.65–1.47)	0.80 (0.52–1.22)	1.16 (0.79–1.70)
200, 202, 203	0.97 (0.83–1.13)	0.93 (0.80–1.07)	0.90 (0.76–1.06)[c]
202	0.91 (0.77–1.08)	0.93 (0.80–1.09)	0.85 (0.71–1.02)
203	1.26 (0.90–1.76)	1.00 (0.68–1.47)	0.95 (0.67–1.34)
204–208	0.95 (0.83–1.07)	0.99 (0.87–1.12)	1.02 (0.88–1.17)
140–208	1.02 (0.97–1.08)	1.04 (0.98–1.10)	1.09 (1.02–1.16)[b]

a) Rural areas were the reference.
b) Significantly increased risk trends were noted.
c) Significantly decreased risk trends were noted.

istration information is verified annually through a door-to-door survey, the death registration in Taiwan is quite complete. Although causes of death may be misdiagnosed and/or misclassified, the problem has been minimized through improvements in the verification and classification of causes of death in Taiwan since 1972. Furthermore, malignant neoplasms have been reported to be one of the most unequivocally classified causes of death in Taiwan,[21] as in other countries.[4] Because of its fatal outcome, it is believed that all patients with malignant neoplasms from rural or urban areas have had access to medical care in recent years, regardless of geographical location in Taiwan.[22] Therefore, variations in the quality of mortality data across the urbanization gradient is unlikely.

If urbanization (population density), *per se*, was responsible for the difference in cancer mortality, then the trends should be similar among both males and females. This was found for three cancer types: cancer of the pancreas, lung, and kidney. Significant trends were also found for male prostate, and female breast and ovary cancers. This observation is consistent with previous reports.[1, 3–7] Urbanization differences in cancers of these sites suggest that further investigation of the relationship between population density and site-specific cancer mortality may be fruitful.

Most studies reported so far have found a clear urban excess for colon and rectum cancers.[1, 4, 6, 8, 10] This was the case for our study also. However, the trends for colon and rectum cancer were sex-linked. A significant trend for colon cancer was identified for males only and that for rectum cancer in females only. Gender differences in occupation or other life-style factors may be important in understanding these trends.[16, 23–25]

The present study revealed excess rural risks for non-melanoma skin cancer and non-Hodgkin's lymphoma among males and for non-melanoma skin cancer, and can-

Table V. Standardized Relative Risk (SRR) for Suburban, Urban and Metropolitan Areas in Females,[a] Taiwan, 1982–1991

ICD 9 Codes	Suburban	Urban	Metropolitan
141–149	0.68 (0.47–0.99)	0.42 (0.28–0.63)	0.46 (0.30–0.69)
142	0.68 (0.35–1.31)	1.12 (0.61–2.04)	0.96 (0.32–2.91)
147	0.75 (0.59–0.96)	0.78 (0.62–0.98)	0.72 (0.55–0.94)
150	0.84 (0.62–1.13)	0.98 (0.72–1.33)	0.79 (0.54–1.16)
151	0.84 (0.72–0.98)	0.84 (0.71–0.98)	0.83 (0.71–0.97)
152	0.75 (0.52–1.08)	0.57 (0.37–0.89)	0.65 (0.43–0.99)
153	1.18 (1.05–1.34)	1.34 (1.19–1.51)	1.26 (1.13–1.41)
154	1.16 (0.98–1.37)	1.32 (1.12–1.55)	1.48 (1.23–1.79)[b]
155	1.03 (0.94–1.14)	1.01 (0.90–1.12)	1.11 (0.97–1.27)
156	1.19 (0.96–1.47)	1.13 (0.87–1.45)	1.67 (1.33–2.10)
157	1.26 (1.05–1.51)	1.34 (1.12–1.60)	1.50 (1.12–2.00)[b]
160	0.50 (0.32–0.77)	0.50 (0.31–0.80)	0.58 (0.37–0.91)
161	0.79 (0.47–1.31)	0.42 (0.24–0.75)	0.76 (0.42–1.37)
162	1.06 (0.95–1.17)	1.21 (1.09–1.35)	1.31 (1.15–1.48)[b]
170	0.80 (0.62–1.02)	0.76 (0.60–0.96)	0.61 (0.45–0.82)[c]
171	0.79 (0.57–1.09)	0.54 (0.38–0.77)	0.52 (0.35–0.76)[c]
172	1.30 (0.67–2.51)	0.94 (0.49–1.79)	1.16 (0.58–2.33)
173	0.80 (0.55–1.17)	0.65 (0.42–1.00)	0.55 (0.35–0.88)[c]
174	1.31 (1.16–1.48)	1.59 (1.40–1.81)	1.82 (1.59–2.09)[b]
179	0.90 (0.82–0.98)	1.00 (0.92–1.08)	0.98 (0.79–1.22)
183	1.61 (1.26–2.05)	1.63 (1.36–1.96)	2.12 (1.63–2.75)[b]
188	0.91 (0.58–1.43)	0.89 (0.57–1.40)	0.94 (0.59–1.51)
189	1.23 (0.85–1.78)	1.50 (1.03–2.17)	1.58 (1.03–2.43)[b]
191	0.83 (0.66–1.05)	0.95 (0.75–1.20)	0.95 (0.73–1.23)
200	0.90 (0.54–1.50)	0.93 (0.58–1.52)	0.55 (0.31–0.99)
200, 202, 203	0.90 (0.75–1.08)	0.85 (0.71–1.01)	0.97 (0.82–1.16)
202	0.87 (0.70–1.08)	0.79 (0.63–0.99)	1.04 (0.85–1.28)
203	0.96 (0.61–1.49)	1.08 (0.68–1.69)	1.07 (0.61–1.88)
204–208	0.97 (0.85–1.11)	0.91 (0.79–1.05)	1.02 (0.87–1.18)
140–208	0.98 (0.93–1.04)	1.04 (0.98–1.11)	1.09 (1.02–1.16)

a) Rural areas were the reference.
b) Significantly increased risk trends were noted.
c) Significantly decreased risk trends were noted.

cer of bone and connective tissue among females. Such findings are not consistent with previously published reports.[1, 3–8, 10, 12, 16] The rural excess in mortality for these cancers is difficult to understand.

These data are most useful for generating hypotheses for further studies to define specific etiological factors operating within population density groupings. Population density, as measured in this investigation, may represent a surrogate measure for other cancer risk factors, such as socioeconomic status, personal health behaviors, and differential exposures to environmental agents, which are related to cancer mortality.[4] Unfortunately, the current data set did not allow us to measure directly the interrelationships between population density, other possible explanatory variables and the risk of developing selected forms of cancer.

In conclusion, evidence for urban-rural differences in site-specific cancer mortality was found to be consistent with previous studies using similar methodology. Analytic studies for sites where trends were consistent across all sex groups may identify the aspect of population density or other unmeasured factor that is contributing to these urban-rural trends.

ACKNOWLEDGMENTS

This study was supported by a grant from the National Science Council, Executive Yuan, Taiwan (NSC-87-2412-H-037-001).

(Received January 6, 1998/Revised February 13, 1998/Accepted February 13, 1998)

REFERENCES

1) Nasca, P. C., Burnett, W. S., Greenwald, P., Brennan, K., Wolfgang, P. E. and Carlton, K. Population density as an indicator of urban-rural differences in cancer incidence, Upstate New York, 1968–1972. *Am. J. Epidemiol.*, **112**, 362–375 (1980).
2) Murata, M., Takayama, K., Fukuma, S., Okamoto N., Kato, I., Hanai, A., Nakayama, H., Fujiwara, K., Ikeda, T. and Fujimoto, I. A comparative epidemiologic study on geographic distributions of cancers of the lung and the large intestine in Japan. *Jpn. J. Cancer Res.*, **79**, 1005–1016 (1988).
3) Miller, M. K., Stokes, C. S. and Clifford, W. B. A comparison of the rural-urban mortality differential for deaths from all causes, cardiovascular disease and cancer. *J. Rural Health*, **3**, 23–34 (1987).
4) Mahoney, M. C., Labrie, D. S., Nasca, P. C., Wolfgang, P. E. and Burnett, W. S. Population density and cancer mortality differentials in New York State, 1978–1982. *Int. J. Epidemiol.*, **19**, 483–490 (1990).
5) Nasca, P. C., Mahone, M. C. and Wolfgang, P. E. Population density and cancer incidence differentials in New York State, 1978–1982. *Cancer Causes Controls*, **3**, 7–15 (1992).
6) Howe, H. L., Keller, J. E. and Lehnherr, M. Relation between population density and cancer incidence, Illinois, 1986–1990. *Am. J. Epidemiol.*, **138**, 29–36 (1993).
7) Vassallo, A., Stefani, E. D., Ronco, A. and Barrios, E. Urbanization gradients and cancer mortality in Uruguay, 1988–1992. *Int. J. Cancer*, **59**, 345–350 (1994).
8) Swoboda, H. and Friedl, H. P. Incidence of cancer of the respiratory and upper digestive tract in urban and rural eastern Austria. *Eur. J. Cancer*, **27**, 83–85 (1991).
9) Blondell, J. M. Urban-rural factors affecting cancer mortality in Kentucky, 1950–1969. *Cancer Detect. Prev.*, **11**, 209–223 (1988).
10) Friis, S. and Storm, H. H. Urban-rural variation in cancer incidence in Denmark 1943–1987. *Eur. J. Cancer*, **29A**, 538–544 (1993).
11) Herity, B. Area of residence and risk of cancer of the cervix uteri in Ireland. *Irel. J. Med. Sci.*, **158**, 107–111 (1989).
12) Greenberg, M. R. "Urbanization and Cancer Mortality: The United States Experience, 1950–1975" (1983). Oxford University Press, New York.
13) Poledank, A. P., Flannery, J. T. and Janerish, D. T. Cervical cancer rates by population size of towns: implications for cancer control programs. *J. Commun. Health*, **16**, 315–323 (1991).
14) Wright, J. S., Champagne, F., Dever, G. E. and Clark, F. C. A comparative analysis of rural and urban mortality in Georgia, 1979. *Am. J. Prev. Med.*, **1**, 22–29 (1985).
15) Roginski, C. Comparison of urban and rural incidence data. *In* "Cancer Incidence in Five Continents," ed. J. Waterhouse, C. Muir, K. Shanmugaratnam and J. Powell, pp. 174–177 (1982). IARC Scientific Publications, Lyon.
16) Doll, S. R. Urban and rural factors in the aetiology of cancer. *Int. J. Cancer*, **47**, 803–810 (1991).
17) Ministry of the Interior, Republic of China. "1989 Taiwan-Fukien Demographic Fact Book," pp. 566–569 (1990). Ministry of the Interior, Taiwan, Taipei.
18) Smith, P. G. Comparison between registries: age-standardized rates. *In* "Cancer Incidence in Five Continents," ed. D. M. Parkin, C. S. Muir, S. L. Whelan, Y. T. Gao, J. Ferlay and J. Powell, pp. 865–870 (1992). IARC Scientific Publications, Lyon.
19) Rothman, K. J. "Modern Epidemiology," pp. 228–233 (1986). Little, Brown and Company, Boston.
20) Breslow, N. E. and Day, N. E. "Statistical Methods in Cancer Research. Vol II. The Design and Analysis of Cohort Studies," pp. 106–115 (1987). IARC Scientific Publications, Lyon.
21) Chen, C. J. and Wang, C. J. Ecological correlation between arsenic level in well water and age-adjusted mortality from malignant neoplasms. *Cancer Res.*, **50**, 5470–5474 (1990).
22) Lee, W. C. and Lin, R. S. Interactions between birth cohort and urbanization on gastric cancer mortality in Taiwan. *Int. J. Epidemiol.*, **23**, 252–260 (1994).
23) Brownson, R. C., Zahm, S. H., Chang, J. C. and Blair, B. Occupational risk of colon cancer: an analysis by anatomic subsite. *Am. J. Epidemiol.*, **130**, 675–687 (1989).
24) Graham, S. and Mettlin, C. Diet and colon cancer. *Am. J. Epidemiol.*, **109**, 1–20 (1979).
25) Spiegelman, D. and Wegman, D. H. Occupation-related risks for colorectal cancer. *J. Natl. Cancer Inst.*, **75**, 813–821 (1985).