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Per Capita Gross National Product and Summarized Odds Ratio for Epidemiologic Studies on the Relationship between Passive Smoking and Lung Cancer

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The summarized odds ratios of epidemiologic studies on the relationship between exposure to environmental tobacco smoke (ETS) and lung cancer by country were recalculated, using the odds ratio values in a 1992 report entitled, "Respiratory Health Effects of Passive Smoking: Lung Cancer and Other Disorders" by the US Environmental Protection Agency. The relationship between the summarized odds ratio and per capita gross national product (GNP) in 1964 was studied by the country. The graphic relationship between the summarized odds ratio (ordinate) and GNP (abscissa) showed an upward convex curve. The summarized odds ratios of a developing country (China) and developed countries (USA, Western Europe) in 1964 indicated a very weak association, while those of other countries (Greece, Hong Kong, and Japan) were slightly greater than unity (1.0). This means that ETS in the developing and developed countries in 1964 hardly affected lung cancer, whereas that in the other areas affected lung cancer somewhat. Socioeconomic status in developed countries is far better than that in developing countries, and factors related to socioeconomic status may affect the summarized odds ratio. It is recognized that cancer is diagnosed clinically some years after cancer risk factors appear. If the socioeconomic status involves some risk factors which affect lung cancer, the relationship between the summarized odds ratio and the GNP may be significant. Therefore, we can forecast that the summarized odds ratio of Japan will decrease to close to unity and that that of China will increase in the future because of economic growth, making it possible for the Chinese Government to adopt a policy to reduce the influence of ETS on health.

Key Words: Environmental tobacco smoke, Lung cancer, Epidemiologic study, Summarized odds ratio, Per capita gross national product

INTRODUCTION

Meta-analysis in an important method of combining results from different studies in order to review published articles objectively [1]. It is very effective for studies of statistically low power with small sample sizes [1, 2]. The summarized odds ratio is calculated from odds ratios of published studies in meta-analysis for epidemiologic or clinical research.

The US Environmental Protection Agency (EPA) published a report [3] entitled, "Respiratory Health Effects of Passive Smoking: Lung Cancer and Other Disorders." In the EPA Report, summarized odds ratios on the relationship between exposure to environmental tobacco smoke (ETS) and risk of lung cancer were obtained through meta-analysis of epidemiologic studies, and the values obtained indicated a weak association between ETS and lung cancer. The EPA Report has, however, been criticized [4-6] since (i) the 90% confidence interval (CI) for the odds ratio was used instead of the 95% CI, which is usually used; (ii) the heterogeneity of odds ratios was ignored, and (iii) publication bias was not considered.

The summarized odds ratios with 95% CIs

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of the epidemiologic studies on the relationship by country were recalculated [4] using odds ratio values with CIs in the EPA Report taking the above points into consideration. Homogeneity of odds ratios in the studies for meta-analysis [9] was not shown, indicating that the studies are heterogeneous qualitatively or quantitatively. Socioeconomic, occupational, and housing environment of the subjects studied influenced the results in epidemiologic studies concerning the relationship between exposure to ETS and the risk of lung cancer. The variations among the summarized odds ratios and among socioeconomic environments by country were considerable. The relationship between the summarized odds ratios and socioeconomic indices by country was examined in the present study. The objective of the present study was to forecast the summarized odds ratios by country with due consideration given to the relationship between the summarized odds ratio and socioeconomic indices. Forecasting that the odds ratio of a country will increase in the future is discussed in the present study from the viewpoint of health policy.

MATERIALS AND METHODS

Data in Table 5-9 on pages 5-28 to 5-29 in the EPA Report [3] were used for calculations. The summarized odds ratios with 95% CIs for epidemiologic studies on the relationship between ETS and lung cancer were recalculated by Sugita et al. [4] using the odds ratio values with the CIs in the EPA Report. Summarized odds ratios in meta-analysis were calculated by the method described by Fleiss and Gross [9]. When odds ratios for meta-analysis were not homogeneous, *i.e.* the chi-square value for the homogeneity test of odds ratios was greater than the degrees of freedom, DerSimonian's method [9, 10] was used for calculating the summarized odds ratio. The summarized odds ratio for the USA was also calculated with elimination of publication bias indirectly by considering a hypothetical unpublished study [11]. Details of the methods for calculating the summarized odds ratios have been given by Sugita et al. [4].

As socioeconomic data, per capita gross national product (GNP) values in 1964 [12], 1970 [13], 1980 [14], and 1990 [15] for each country were used. The GNP values of Western Europe were calculated from the GNP values of the U.K. and Sweden using the weighted average method by the inverse square of the standard error for the odds ratio.

RESULTS

The odds ratios with 95% CIs, incident years of lung cancer, and years of publication of epidemiologic studies on the relationship between ETS and lung cancer by researcher are shown in Table 1. The odds ratios are those in Table 5-9 of the EPA Report and the 95% CIs were calculated from the 90% CIs in Table 5-9 [3]. The incident years were not indicated in some articles and only information on collection intervals were given. The differences between the years of observation of lung

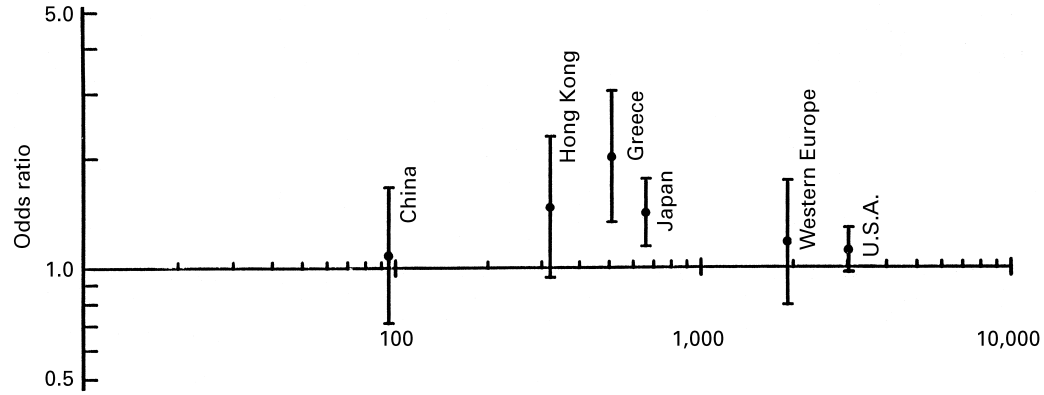

Fig. 1 Summarized odds ratios with 95% confidence intervals of epidemiologic studies on the relationship between environmental tobacco smoke and lung cancer and per capita gross national products in 1964 by country

Table 1 Odds ratios with 95% confidence intervals (CIs), incident years of lung cancer, and years of publication of epidemiologic studies on the relationship between environmental tobacco smoke and lung cancer by researcher

Odds ratio	95% CI Lower limit	95% CI Upper limit	Researcher (country)	Incident year	Published year
1.92	1.02	3.59	Kalandidi (GRC)	1987-89	1990
2.08	1.202	3.600	Trichopoulos (GRC)	1978-80	1981, 1983
0.74	0.430	1.274	Chan (HK)	1979	1982
1.54	0.896	2.645	Koo (HK)	1981-83[int]	1987
1.64	1.145	2.348	Lam T (HK)	1983-86[int]	1987
2.51	1.348	4.674	Lam W (HK)	1981-84	1985
1.50	0.869	2.589	Akiba (JPN)	1971-80	1986
1.37	0.958	1.960	Hirayama (JPN)	1966-81[fol]	1984
2.55	0.739	8.803	Inoue (JPN)	1973-83	1988
1.07	0.637	1.796	Shimizu (JPN)	1982-85	1988
1.57	1.07	2.31	Sobue (JPN)	1986-88	1990
1.50	0.384	5.855	Brownson (USA)	1979-82	1987
0.68	0.281	1.645	Buffler (USA)	1976-80	1984
2.01	0.481	8.403	Bulter (USA)	1977-82	1988
1.89	0.736	4.854	Correa (USA)	?	1883
1.28	0.985	1.664	Fontham (USA)	1985-88	1991
1.27	0.849	1.900	Garfinkel (USA)	1954-72[fol]	1981
1.16	0.843	1.596	Garfinkel (USA)	1971-81	1985
2.00	0.689	5.810	Humble (USA)	1980-84	1987
0.79	0.487	1.281	Janerich (USA)	1982-84	1990
0.73	0.229	2.327	Kabat (USA)	1971-80	1984
1.32	0.508	3.430	Wu (USA)	1981-82	1985
1.97	0.240	16.196	Hole (W-EUR)	1972-85[fol]	1989
1.01	0.408	2.499	Lee (W-EUR)	1982-83[int]	1986
1.17	0.679	2.016	Pershagen (W-EUR)	1961-80[fol]	1987
1.20	0.546	2.636	Svensson (W-EUR)	1983-85	1989
1.19	0.819	1.730	Gao (CHN)	1984-86	1987
2.16	1.085	4.298	Geng (CHN)	?[Gen]	1988
0.77	0.302	1.961	Liu (CHN)	1985-86	1991
0.78	0.607	1.003	Wu-Williams (CHN)	1985-87	1990

GRC: Greece, HK: Hong Kong, JPN: Japan, W-EUR: Western Europe,
CHN: China, int: years when interviews were carried out,
fol: years when subjects studied were followed up,
Gen: more than 10 years before the year of publication

Table 2 Summarized odds ratios with 95% confidence intervals (CIs) and per capita gross national products in 1964, 1970, 1980, and 1990 by country

Odds ratio	95% CI Lower limit	95% CI Upper limit	Country	Per capita gross national product (US$) 1964	1970	1980	1990
2.01	1.33	3.04	Greece	510	1090	4380	5990
1.46[DS]	0.94	2.29	Hong Kong	320	970	4240	11490
1.41	1.14	1.75	Japan	660	1920	9890	25430
1.11[pb]	0.97	1.28	USA	3020	4760	11360	21790
1.17	0.79	1.73	Western Europe	1919	3643	12264	21964
1.08[DS]	0.71	1.66	China	95	160	290	370
1.28[DS]	1.13	1.46	all				

DS: DerSimonian's method, pb: eliminating publication bias

cancer and years of publication of the epidemiologic articles were considerable.

Table 2 indicates the summarized odds ratios with 95% CIs [4] and GNP (12-15) expressed in US dollars for the years 1964 to 1990 by country. The summarized odds ratios with 95% CIs [4] by country were 2.01 (1.33-3.04) for Greece, 1.46 (0.94- 2.29) for Hong Kong, 1.41 (1.14-1.75) for Japan, 1.11 (0.97-1.28) for the USA, 1.17 (0.79-1.73) for Western Europe, and 1.08 (0.71-1.66) for China. The summarized odds ratios in Table 5-9 of the EPA Report [3] were 2.01 for Greece, 1.48 for Hong Kong, 1.41 for Japan, 1.19 for the USA, 1.17 for Western Europe, and 0.95 for China. The odds ratios for Hong Kong, the USA, and China in the EPA Report [3] were different from those in the recalculation article [4], although the differences were not large. Homogeneity of the odds ratios in all studies was rejected statistically [4] (data not shown). The variations in socioeconomic indices among the countries were very large.

The relationship between per capita GNP (abscissa) and summarized odds ratio (ordinate) is shown in Figure 1 as an upward convex curve. The summarized odds ratios of a developing country (China) and developed countries (USA, Western Europe) in 1964 indicated a very weak association, while those of other countries (Greece, Hong Kong, Japan) were slightly greater than unity (1.0).

DISCUSSION

Homogeneity of the odds ratios in epidemiologic studies on the relationship between ETS and lung cancer was rejected statistically, indicating that the studies were heterogeneous quantitatively. It is not surprising that the subjects studied, their environment, causes, and methods or times of observing outcomes varied qualitatively or quantitatively by study because the epidemiologic studies were conducted in many countries. The socioeconomic environment of the subjects studied influences the results in epidemiologic studies concerning the relationship between exposure to ETS and risk of lung cancer. The differences in the summarized odds ratios of countries calculated by meta-analysis [9] were notable, *i.e.*, they varied from 2.01 for Greece to 1.08 for China. The countries in the present study clearly differ in socioeconomic environment, which includes pure economic status, social infrastructure, occupational and housing environment, and eating habits. Per capita GNP is used as an index of economic status, and the socioeconomic environment is improved by economic growth. Per capita GNP expressed in US dollars has increased remarkably in Japan because of marked economic growth after World War Ⅱ and the rise in the value of the yen from the 1980s. In Japan, economic growth has brought about many changes in daily life, including larger housing space and higher consumption of fat and protein.

Cancer is diagnosed clinically many years after cancer risk factors have appeared. If the socioeconomic environment involves cancer risk factors, the risk factors increase the incidence of cancer in subjects who live or have lived in the socioeconomic environment and acquired such risk factors. Investigators require a rather long period of time to publish articles after they have observed cancer, and major time differences between observation of lung cancer and publication of epidemiologic articles were found. Since economic indices by country are not available prior to 1960, the relationship between the summarized odds ratio and per capita GNP in the 1960s was studied by country, taking into consideration the long period of time between appearance of cancer risk factors and observation of cancer, and the period of time between observation of lung cancer and publication of articles.

An upward convex curve was obtained for the relationship between the summarized odds ratio (ordinate) and the GNP (abscissa) as shown in Figure 1. The summarized odds ratios of a developing country (China) and developed countries (USA, Western Europe) in 1964 indicated a very weak association, while those of other countries (Greece, Hong Kong, Japan) were a little greater than unity. This means that ETS in the developing and developed countries in 1964 hardly affected lung cancer, whereas ETS in Greece, Hong Kong, and Japan affected lung cancer to a certain degree. The reason why a relationship between the odds ratios and per capita GNP by country was detected should be discussed.

The socioeconomic environment in developed countries is better than that in develop-

ing countries, *i.e.*, better housing environment with larger housing space, better occupational environment without exposure to high doses of toxic substances, and good sanitary conditions are available and information on a healthy lifestyle is widespread in developed countries. Some of the effects of good environment in developed countries are supposed to decrease the odds ratio in epidemiologic studies between ETS and lung cancer. In large houses ETS concentrations are lower. Therefore, it is reasonable that the effect of ETS on lung cancer is small in epidemiologic studies in developed countries.

On the other hand, the socioeconomic environment in developing countries is worse than that in developed countries. Small houses in developing countries become filled with smoke from cooking and heating using biofuels and coal. Therefore the smoke from cooking and heating in developing countries is one of the confounding factors in epidemiologic studies on the relationship between ETS and lung cancer [3, 5], and it is reasonable to assume that the effect of ETS on lung cancer is underestimated in developing countries.

The relationship between the odds ratio and GNP in the 1990s by country was not clear-cut, because lung cancer cases in Table 1 were observed before 1990 and the marked economic growth of Japan and the rapid rise in the value of the yen have increased the differences in the GNP of Japan between the 1960s and 1990s. Economic growth has improved the socioeconomic environments in east Asian countries. The amount of information on health from the mass media has increased in Japan. Once the information that ETS may be one of the risk factors for lung cancer became widespread in Japan, many smokers hesitate to smoke in the vicinity of nonsmokers. Housing space in Japan has increased [16] because of the economic growth, and ETS in larger houses is at lower concentrations. Lee [5] reported that the summarized odds ratio between ETS and lung cancer in the USA published before 1989 was greater than that after 1989. Therefore, it is assumed that the effect of ETS on lung cancer will decrease in Japan.

It was pointed out that the use of coal as a fuel may effectively mask detection of the relationship between ETS and lung cancer [3, 5]. In China, the environment in which houses are filled with smoke for cooking and heating using biofuels and coal is improving because of economic growth. Economic growth will cause China to consume more kerosene and less biofuels and coal. Therefore, it is probable that in China the smoke from cooking and heating will not be an important confounding factor in the relationship between ETS and lung cancer, and the effect of ETS on lung cancer will be apparent. When epidemiologic studies between ETS and lung cancer in China are conducted taking confounding factors into sufficient consideration in the future, the effect of ETS will be easily detected. Consequently, we can forecast that the summarized odds ratio of Japan will decrease to close to unity, while that of China will increase in the future.

In the present study, per capita GNP is used as a general indicator of socioeconomic environment, which includes overall economic status, social infrastructure, occupational and housing environments, and eating habits. It may not be adequate to express the multiple factors of socioeconomic environment by a general indicator such as GNP. Many studies on factors subdivided into various parts such as the molecular level, are now being conducted. However, it should be stressed that the whole is not elucidated from the detailed mechanisms revealed by such studies. The degree of influence on health in human society cannot be obtained from detailed mechanisms. Using the GNP as a general indicator of the socioeconomic environment measures macroeconomics, making it possible to look at the main issue. In the present study we were able to obtain the degree of influence on health in human society in the future by an estimation of the summarized odds ratios between ETS and lung cancer in the future.

From the present study we forecast that the summarized odds ratio between ETS and lung cancer for China will increase in the future, making it possible for the Chinese Government to adopt a policy to reduce the influence of ETS on health. Policies are sometimes adopted by governments based on forecasts which do not always rely on sufficient scientific proof.

It is sometimes adequate for the government of a nation to adopt a policy to elimi-

nate the risk factors for some health problems, even if the risk factors lack conclusive scientific proof, before increased incidence of the health problem in the population becomes a recognized social problem. Therefore, in the present study the proposed forecast of the future odds ratio is significant from the viewpoint of government policy related to a nation's health.

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