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Birth cohort effect on lung cancer incidence in Taiwanese women 1981–1998

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Abstract

Lung cancer has been the main cause of cancer-related mortality in Taiwanese women since 1986. Gradual increases in both awareness of risks and use of extractor fans in kitchens should reduce the incidence of this disease. To investigate the birth cohort effect on lung cancer incidence in Taiwanese women for 1981–1998, an age-period-cohort (APC) model analysis was employed to study the effects of age, time periods, birth cohorts and histological types of lung cancer. A significant increase in lung cancer incidence among women was found for the period 1981–1998 ($r = 0.96$, $P < 0.05$), principally of adenocarcinoma, then squamous cell carcinoma. Age is the strongest predictor according to the APC model. The birth cohort of 1917–1926 has the highest risk of lung cancer. However, in recent cohorts, particularly those born after 1956, the incidence has fallen. The declining incidence in younger cohorts may be due to the increased use of extractor fans in kitchens reducing exposure to carcinogenic fumes from cooking oil.

Keywords: Lung cancer; Incidence; Age-period-cohort analysis

1. Introduction

Lung cancer has been the main cause of cancer-related mortality in Taiwanese women since 1986 [1] and concern about this has been increasing nation-wide since the 1990s [2]. It is widely established that lung cancer has a strong correlation with cigarette smoking and environmental tobacco smoke. However, our previous studies found that the incidence of lung cancer in Taiwanese women who have a history of smoking is less than 10% [3] and development of lung cancer following exposure to environmental tobacco smoke occurs in only a small proportion of women [4].

The major risk predisposing Taiwanese women who are non-smokers to lung cancer seems to be associated with cooking oil fumes. This is especially evident in women aged 20–40 years who cook in kitchens without an extractor fan (odds ratio (OR) = 8.3, attributable risk 76%) [3]. These women, who typically wait until fumes are emitted from the cooking oil before frying their food, have a significantly higher susceptibility to lung cancer (adjusted $OR_s = 2.0–2.6$) [5], primarily of the adenocarcinoma histological type (48%). The attribut-

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able risk of adenocarcinoma (36.1%) and squamous cell carcinoma (28%) in non-users of extractor fans is higher than in users [6].

Potential human carcinogens, such as benzo[a]pyrene, have been found in oil fumes [7,8]. Reducing the distance between the surface of the cooking oil and the extractor fan from 700 to 500 mm results in a 46% reduction in mutagenicity [9]. Overall, after considering factors such as smoking, oil fumes and extractors, more than 50% of attributable risk of lung cancer may be attributable to cooking habit, which relates to being exposed to carcinogenic cooking oil fumes, 30% to cigarette smoking plus environmental smoke, and the remaining 20% to other types of air pollution or unconfirmed factors [6]. Thus, modifying cooking habits and equipping kitchens with suitable extractor fans should reduce, the incidence of lung cancer in Taiwanese women.

In a previous study, the mortality trends of lung cancer in Taiwan were described and a significant cohort effect was displayed [10]. Nonetheless, the major risk factors for lung cancer in Taiwanese women were uncertain at that time. Now, most factors have been identified. In kitchens equipped prior 1960, one study found that extractor fans were present less than 62% of the time, while 82% and 95.2% of kitchens installed in the 1980s and 2000s, respectively, had extractor fans [5].

The wider use of extractor fans, reducing the inhalation of carcinogenic fumes, should be consistent with a reduction in the incidence of lung cancer in Taiwanese women. To verify this hypothesis, this study investigated changes in incidence of lung cancer among Taiwanese women. The incidence pattern in histological types of lung cancer was examined, and the incidence of lung cancer compared with respect to age, time periods and birth cohorts. Each of these factors has different underlying biological interpretations. An age-period-cohort (APC) analysis was used to determine their effects on the incidence of lung cancer, and outlined any interactions between these effects and histological types of lung cancer. The histology ratio of adenocarcinoma to squamous cell carcinoma and small cell carcinoma, permitted us to interpret the effects of histological types on age-specific, period-specific and cohort-specific incidences of lung cancer in Taiwanese women.

2. Methods

2.1. Population and incidence data

The National Cancer Registry of Taiwan was established in 1979. All discharge notes and data pertaining to a patient's primary diagnosis of cancer are reviewed by registry-trained personnel in every hospital. This practice has remained consistent and unaltered up to the present day. Cancer cases from hospitals of at least 50 beds are notified and forwarded to the National Department of Health of Taiwan on a compulsory basis. Almost all such hospitals participate in this scheme (more than 185 hospitals). Cancer is diagnosed on both clinical and histopathological premises. On arrival at the National Department of Health of Taiwan, the data are checked for accuracy and completeness; in the event of inaccuracy, they are returned to the sender for correction, if unclear, they may be tracked and amended. Otherwise, they are logged into a computer and certified again to avoid redundancy. All validated data are kept on computer file in the National Department of Health of Taiwan. In previous studies, we estimated the registry to have a coverage of approximately 95% of patients with cancer [11,12]. Moreover, the accuracy of lung cancer cases confirmed by histopathology is greater than 82% [1].

In this study, the term 'lung cancer' refers to malignant neoplasm of the lung as described in the International Statistical Classification of Diseases and Related Health Problems (ICD 162). Cancer incidence data for 1981–1998 was collected from the National Cancer Registry of Taiwan [2] and coded in accordance to the ninth revision of the ICD. Age groups were as follows: 0, 1–4, 5–9, 10–14, 15–19, up to 80–84 years, then 85+ years. Data were obtained from the *Taiwan–Fukien Demographic Fact Book* published by the Ministry of the Interior, Taiwan [13]. In addition, data on tobacco consumption were obtained from the Tobacco and Alcohol Monopoly [14].

2.2. Descriptive analysis

The incidence of lung cancer, standardised to the world population of 1976 for all ages, was calculated in 3-year aggregates, commencing in 1981 (1981–1983) and ending in 1998 (1996–1998). Correlation coefficients were tested for trends in the annual incidence of lung cancer over this total period. The ratios of lung cancer were also calculated. Traditional cohort analysis was applied to examine a birth cohort effect. Age-specific incidence rates were plotted so that any line parallel to the y-axis joined the values for people belonging to the same birth cohort.

2.3. Age-period-cohort analysis

The statistical APC analysis, adapted from the individual record method [15] was performed to circumvent the problem of identification. The incidence data were grouped into eleven 5-year age groups (30–34, 35–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70–74, 75–79 and 80–84 years) and seven 10- or 12-year birth cohorts (1897–1906, 1907–1916, 1917–1926, 1927–1936, 1937–1946, 1947–1956 and 1957–1968). The incident rate was modelled as a log-linear function of age, period, cohort, histology and the interaction between these factors. For the histology, squamous cell carcinoma was taken as the baseline. Baseline age, period and cohort parameters were 30–34 years, 1981–1983 and 1917–1926, respectively [16]. A statistical analysis program (SAS, Ver 8.2; SAS Institute Inc., Cary, NC, United States of America (USA)) was used for all analyses. For all statistical tests, the significance level was set at $\alpha = 0.05$.

3. Results

The age-standardised incidence rate (ASIR) for all histological types of lung cancer in Taiwanese women has increased from 8.27 per 100,000 in 1981–1983 to 14.59 per 100,000 in 1996–1998 (Table 1) and the ASIR ratio is 1.8. Linear correlation coefficients (r) demonstrated an increasing trend ($r = 0.96$, $P < 0.05$) in incidence rate. All histological types of lung cancer have demonstrated increases in incidence rates, ratios and trends. Adenocarcinoma was the highest proportion of all histological types between 1981–1983 (43.2%) and 1996–1998 (46.9%), with the ASIR ratio equalling 1.9; while squamous cell carcinoma proportion declined from 17.3% (1981–1983) to 12.1% (1996–1998), with the ASIR ratio being 1.2.

The age-specific incidence rate was plotted against median year of birth to assess the cohort effect, and the results are shown in (Figs. 1–3). While age-specific incidence rate of all histological types of lung cancer has risen in older generations of women, in recent cohorts, particularly those women born after 1956, a gradual fall was evident. For example, in the 35–39 year age group, the annual incidence of lung cancer was 0.76 per 100,000 persons (1956 cohort) and 0.39 per 100,000 (1961 cohort). In the 30–34 year age group, it was 0.52 per 100,000 persons (1956 cohort), 0.48 per 100,000 (1961 cohort) and 0.21 per 100,000 (1966 cohort). Markedly declining trends were noticeable in the 30–34 and 35–39 year age groups (Fig. 1). Similar trends were observed for adenocarcinoma (Fig. 2) and squamous cell carcinoma (Fig. 3).

The APC model was used to examine the effects of age, period and cohort among the different histological types. Three parameters were significant predictors (Table 2). Age (model 1) was the strongest predictor and the best fit was 14199.8 deviance with ten degrees of freedom. The period and cohort were also significant, but less than age. Furthermore, interactions of histological types with age (model 5) and histological types with period (model 6) were significant (both with $P < 0.001$). However, the interaction between histological types with cohort (model 7) did not reach statistical significance ($P = 0.23$).

As age increased, the relative risk of developing lung cancer increased dramatically and progressively ($r = 0.89$, $P = 0.0002$) (Table 3). The relative risk in the oldest age group (80–84 years) was 45 times higher than in the youngest age group (30–34 years). An increasing risk was also apparent in the time period from 1981–1983 to 1987–1989, and declined slightly thereafter ($r = 0.75$, $P = 0.089$) (Table 3).

Table 1
Age-standardised incidence rate (ASIR), average age of onset, and incidence trends for 1981–1998 of all histological types of lung cancer in Taiwanese women

Year	Histological types of lung cancer						
	Incidence (95% CI) proportion						
	Adenocarcinoma	Squamous cell carcinoma	Small cell carcinoma	NOS carcinoma	Bronchiolo-alveolar adenocarcinoma	Others	All
1981–1983	3.57 (2.31–4.83) 43.17%	1.43 (1.21–1.66) 17.29%	0.37 (0.05–0.68) 4.47%	0.60 (0.25–0.95) 7.26%	0.12 (0.10–0.13) 1.45%	2.18 (1.79–2.58) 26.36%	8.27 (5.70–10.83)
1984–1986	3.53 (2.90–4.16) 40.62%	1.59 (1.31–1.88) 18.30%	0.31 (0.25–0.37) 3.57%	0.48 (0.29–0.67) 5.52%	0.20 (0.08–0.32) 2.30%	2.58 (1.90–3.26) 29.69%	8.69 (6.73—10.66)
1987–1989	4.26 (2.51–6.01) 38.98%	1.58 (1.35–1.81) 14.46%	0.45 (0.39–0.51) 4.12%	0.62 (0.39–0.84) 5.67%	0.23 (0.03–0.43) 2.10%	3.79 (3.02–4.55) 34.68%	10.93 (7.70–14.15)
1990–1992	4.78 (3.11–6.45) 40.58%	1.69 (1.61–1.78) 14.35%	0.46 (0.27–0.65) 3.90%	0.75 (0.41–1.09) 6.37%	0.39 (0.24–0.53) 3.31%	3.71 (2.80–4.62) 31.49%	11.78 (8.44–15.12)
1993–1995	5.62 (5.36–5.88) 43.36%	1.66 (1.23–2.10) 12.81%	0.45 (0.28–0.62) 3.47%	0.94 (0.51–1.37) 7.25%	0.52 (0.18–0.86) 4.01%	3.77 (3.06–4.48) 29.09%	12.96 (10.62–15.33)
1996–1998	6.84 (4.89–8.80) 46.88%	1.76 (1.72–1.81) 12.06%	0.47 (0.37–0.57) 3.22%	1.16 (1.14–1.18) 7.95%	0.63 (0.38–0.87) 4.32%	3.73 (2.80–4.67) 25.57%	14.59 (11.29–17.90)
Coefficient	0.88 $P < 0.05$	0.71 $P < 0.05$	0.53 $P < 0.05$	0.80 $P < 0.05$	0.93 $P < 0.05$	0.75 $P < 0.05$	0.96 $P < 0.05$
Mean age (years)	62.04 ± 12.73	61.50 ± 12.43	62.81 ± 11.97	62.74 ± 12.66	60.68 ± 11.96	65.12 ± 13.95	62.91 ± 13.09

Incidence, age-standardised (world) incidence (per 100,000) with 95% confidence intervals (CI) by histological type. Proportion, the proportional rate of the individual histological type of lung cancer to all lung cancer types. Coefficient, linear correlation coefficient of annual incidence. Mean age, average age of onset.
NOS, not otherwise specified.

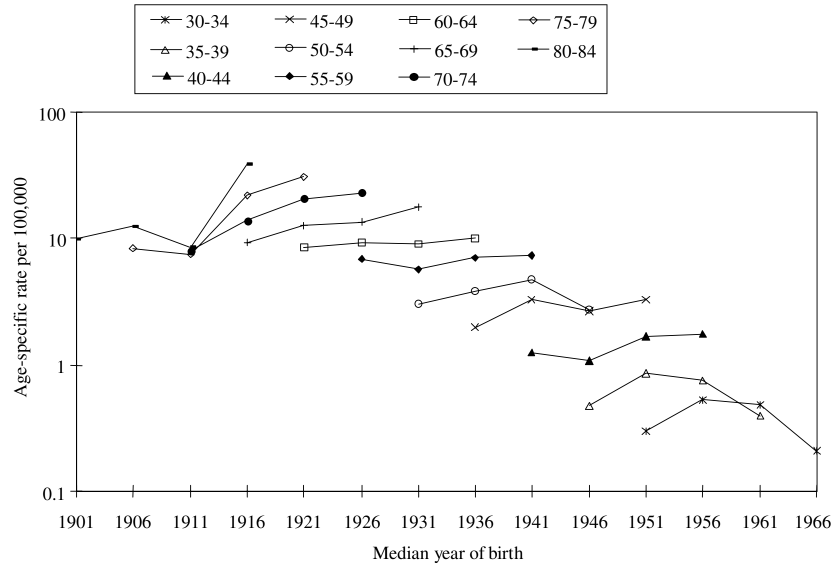

Fig. 1. Age-specific incidence rates of lung cancer by median year of birth in Taiwanese women, 1981–1998.

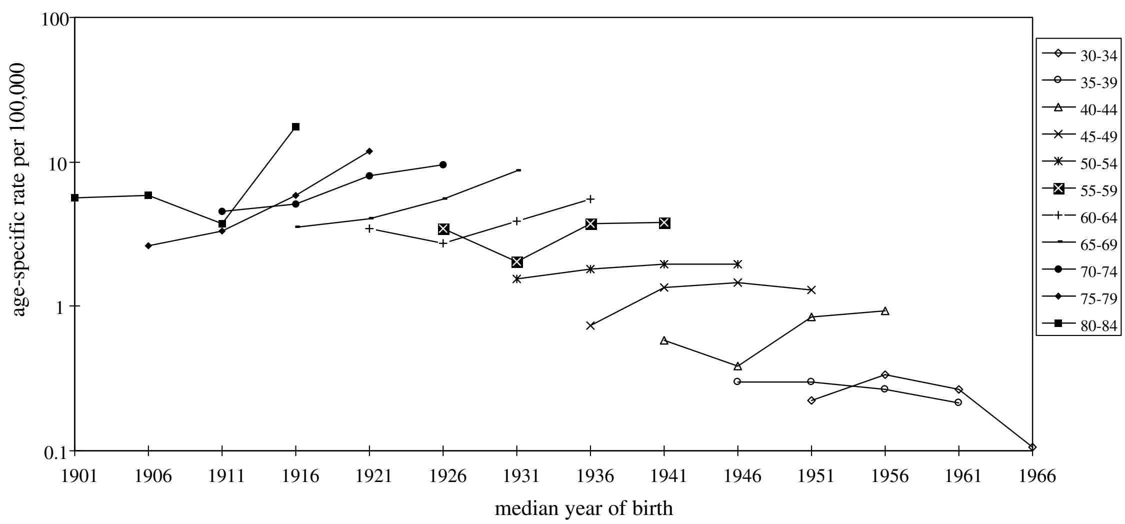

Fig. 2. Age-specific incidence rates of adenocarcinoma of lung cancer by median year of birth in Taiwanese women, 1981–1998.

Regarding the cohort effect, the trend of relative risk graphed a projectile curve (best-fit line: $y = 1.01x–0.12x^2$, coefficient of determination (r^2) = 0.997, $P < 0.05$), increasing in the cohorts from 1897–1906 to 1917–1926, and subsequently decreased (r = –0.92, P = 0.028). Thus, those born in 1917–1926 have the highest risk (a relative risk of 2.02 times higher than the 1897–1906 birth cohort). In later birth cohorts, the risk gradually fell to 0.52 in the1957–1968 birth cohort.

Histology was the second strongest predictor and the best-fit was 6943.1 deviance with five degrees of freedom (Table 2, model 4). The relative risk of adenocarcinoma was 3.5 times higher than of squamous cell carcinoma (Table 3).

To demonstrate the interactions of histological types with age and period with cohort, the histology ratio (adenocarcinoma as numerator, squamous cell and small cell carcinoma as denominator) of these age-specific, period-specific and cohort-specific incidences were calculated. Their ratios and 95% confidence intervals (CI) are presented in Table 4. Adenocarcinoma rates were consistently higher than squamous cell and small cell carcinoma in all age groups (all ratios >1), but the trend of ratios did not reach statistical significance (r = 0.45, P = 0.17). With respect to time period, the histology ratios depicted a steady rise from 1984–1986 to 1996–1998 (r = 0.89, P = 0.017). Thus, the effect of adenocarcinoma was higher than squamous and small cell carcinoma in the trend of period-specific incidence. As for the histology ratio of the cohort-specific incidence, the trend displayed a projectile curve (best-fit line: $y = 0.87x–0.10x^2$, r^2 = 0.96, $P < 0.05$). The highest ratio

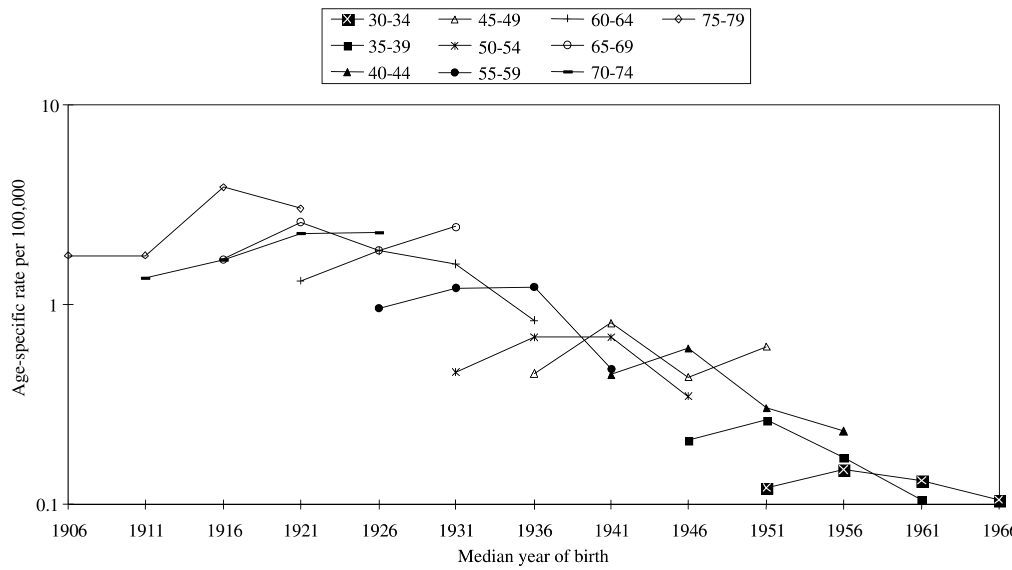

Fig. 3. Age-specific incidence rates of squamous cell carcinoma of lung cancer by median year of birth in Taiwanese women, 1981–1998.

Table 2
Variable selection in age-period-cohort (APC) model of lung cancer incidence in Taiwanese women, 1981–1998

Model	df	Deviance	LRS[a]	(df)	*P* value
1. Age	3862	10,901.31	14,199.80	10	<0.0001
2. Age, period	3857	10,812.92	88.39	5	<0.0001
3. Age, period, cohort	3851	10,725.82	87.10	6	<0.0001
4. Age, period, cohort, histology	3846	3782.72	6943.10	5	<0.0001
5. Age, period, cohort, histology, histology*age	3796	3391.89	390.83	50	<0.0001
6. Age, period, cohort, histology, histology*(age, period)	3771	3197.90	193.99	25	<0.0001
7. Age, period, cohort, histology, histology*(age, period, cohort)	3741	3162.69	35.22	30	0.23

df, degrees of freedom.
[a] LRS, likelihood ratio statistics; each likelihood ratio statistic refers to the last term entered into the model and has an approximate χ^2 distribution with the appropriate (df).

was 1.79, as seen in 1907–1916, after which the ratios have fallen for more recent cohort groups ($r = -0.99$, $P = 0.000$). When we investigated cohort-specific incidence divided by the different histological types, we found that the declining rate of adenocarcinoma was more pronounced than for squamous and small cell carcinomas for birth years 1897–1906 to 1957–1968.

4. Discussion

The incidence of lung cancer in Taiwanese women has been increasing steadily in recent years. APC analysis revealed women born in 1917–1926 had the highest risk. These women will shortly be in the highest risk age group (80–84 years), further contributing to the increased risk seen in the older age group. In younger age groups, the risk may well decrease in future years. Indeed, a slight decrease might already be occurring, as evidenced by recent data from the National Cancer Registry of Taiwan [17].

Age is a key predictor of lung cancer according to the APC model. The fact that risk increases with age is consistent with a previous study [10]. Moreover, in all age groups, the rate of adenocarcinoma is higher than squamous and small cell carcinomas. It is apparent that the relative incidence of adenocarcinoma dominates in the risk factors related to age, time period and cohort.

Adenocarcinoma carries an independently higher risk acquired from traditional Chinese methods of cooking, where the oil is brought to a high temperature before being used [3]. Cooking oil fumes have been proven to be both mutagenic and carcinogenic in several *in vitro* short-term test systems [7,8]. A significant cohort effect was revealed between cooking tool and appliance type among age groups [5]. The presence, location and efficiency of extractor fans may be relevant [5,9]. The use of extractor fans prior to 1960 was less than 62%, and in the 1980s and 2000s was 82% and 95.2%, respectively [5]. Their increased usage in more modern kitchens may be a major factor underlying the fall in lung cancer incidence seen in the younger cohorts born after 1956.

Table 3
Relative risk estimates in Taiwanese women, based on APC model of age, period, cohort and histology

Variable trend	Relative risk estimate	95% CI
Age (years) r = 0.89 (P = 0.0002)		
30–34	1.00	
35–39	1.26	1.20–1.32
40–44	1.62	1.49–1.76
45–49	2.87	2.55–3.22
50–54	3.60	3.14–4.13
55–59	6.27	5.32–7.39
60–64	9.18	7.65–11.02
65–69	14.13	11.60–17.22
70–74	22.81	18.47–28.17
75–79	34.48	27.75–42.85
80–84	44.98	34.19–67.34
Period r = 0.75 (P = 0.089)		
1981–1983	1.00	
1984–1986	1.07	1.05–1.09
1987–1989	1.44	1.39–1.49
1990–1992	1.38	1.32–1.45
1993–1995	1.38	1.31–1.45
1996–1998	1.34	1.17–1.54
Cohort [a] r = −0.92 (P = 0.028)		
1897–1906	0.49	0.45–0.54
1907–1916	0.76	0.74–0.78
1917–1926	1.00	–
1927–1936	0.99	0.96–1.01
1937–1946	0.89	0.84–0.94
1947–1956	0.82	0.75–0.89
1957–1968	0.52	0.42–0.67
Histology		
AD	3.50	3.21–3.80
SQ	1.00	–
SC	0.50	0.41–0.61
NOS	0.81	0.77–0.84
b–a AD	0.58	0.47–0.73
Other	3.09	2.45–3.89

AD, adenocarcinoma; b–a AD, bronchiolo-alveolar adenocarcinoma; CI, confidence interval; SC, small cell carcinoma; SQ, squamous cell carcinoma.
[a] Linear correlation coefficient of birth cohort was described for decreasing trend from 1917–1926 to 1957–1968.

Table 4
The histology ratios[a] of age-specific, period-specific and cohort-specific incidences with 95% confidence intervals (CI) in Taiwanese women

Variable trend	Histology ratio[a] AD / SQ + SC	95% CI
Age (years) r = 0.45 (P = 0.17)		
30–34	1.16	0.51–2.66
35–39	1.41	0.67–2.95
40–44	1.49	0.77–2.87
45–49	1.64	0.89–3.00
50–54	1.68	0.96–2.94
55–59	1.64	0.97–2.76
60–64	1.59	0.97–2.61
65–69	1.65	1.03–2.64
70–74	1.54	0.98–2.44
75–79	1.44	0.93–2.24
80–84	1.55	1.01–2.38
Period r = 0.89 (P = 0.017)		
1981–1983	1.16	0.51–2.66
1984–1986	1.02	0.43–2.41
1987–1989	1.24	0.51–3.02
1990–1992	1.24	0.49–3.10
1993–1995	1.45	0.56–3.75
1996–1998	1.66	0.62–4.41
Cohort[b] r = −0.99 (P = 0.000)		
1897–1906	1.16	0.51–2.66
1907–1916	1.79	0.93–3.44
1917–1926	1.65	0.92–2.97
1927–1936	1.55	0.90–2.65
1937–1946	1.46	0.89–2.41
1947–1956	1.37	0.87–2.15
1957–1968	1.27	0.79–2.03

AD, adenocarcinoma + bronchiolo-alveolar adenocarcinoma; SQ, squamous cell carcinoma; SC, small cell carcinoma.
Histology ratio: relative ratio estimated by APC model.
[a] Histology ratios were calculated using the SAS procedure 'PROC GENMOD' using the 'log' link function.
[b] Linear correlation coefficient of birth cohort was described for decreasing trend from 1907–1916 to 1957–1968.

Adenocarcinoma is also possibly the main histological type of lung cancer derived from environmental tobacco smoke, as the very nature of the activity delivers the noxious compounds into the peripheral parts of the lung [18,19]. As the prevalence of cigarette smoking in Taiwanese men has declined from 55–62% to 45–50% [14], the risk factor of female lung cancer from environmental smoke has correspondingly diminished in the past decades. The known hazards of passive smoking suggest that the behavioural influence exerted by men on the development of adenocarcinoma in women needs to be closely observed. Reducing passive smoking should be viewed as an important factor in lung cancer prevention in women.

Squamous cell carcinoma, in comparison, seems to be predominant in smokers. The prevalence of cigarette smoking in Taiwanese women for the past 40 years has been steady [14]. If variables such as smoking, environmental tobacco smoke and cooking methods have remained relatively unaltered in past years, the reduction in lung cancer incidence in younger cohorts might be due to the increased use of extractor fans. Furthermore, the fall in the incidences of adenocarcinoma and squamous cell carcinoma indicates that extractor fans, besides eliminating cooking oil fumes that cause adenocarcinoma, have also expelled unknown carcinogens that cause squamous cell carcinoma.

In evaluation of studies from mainland China [20], the age-adjusted incidence of female lung cancer in urban Shanghai for the period 1993–1994 was reported to be 18 per 100,000. This is higher than Taiwan, which was 13 per 100,000 at that time. Shanghai has linked their higher incidence with exposure to smoking and rapeseed oil fumes, which was not used in Taiwan until the 1990s. Nonetheless, while the overall trend for Shanghai has been falling gradually from 1972 to

1994, the opposite trend is seen for Taiwan (except in younger cohorts); and this duality may be due to a gap in knowledge in Taiwan about extractor fan usage between older and younger cohorts. Increased use of extractor fans has resulted in a further decline in incidence of both adenocarcinoma and squamous cell carcinoma in younger cohorts. Shanghai accounted for the reduction in China through improvements in kitchen ventilation and increased use of refined cooking oil, but details as to exact histological type remain unclear. Interestingly, albeit the cooking practice in China is similar to that in Taiwan, the profound effect of more extractor fan usage and cooking oil fumes has yet to be studied.

In addition to the factors discussed above, previous segregation-analysis studies support the profound influence of gene(s) affecting the risk of one or more types of lung cancer [21,22]. Several studies have indicated associations of lung cancer with *Dra I* polymorphism of the *P450IIE1* gene [23], having both the *GSTM1* null and *GYP1A1* Msp1 heterozygous genotypes [24] and a myeloperoxidase polymorphism [25]. The root of these genetic associations could involve the metabolism of carcinogens. The likelihood that multiple genes affect cancer risk raises the possibility that a trigger (such as an environmental parameter) could have several risk-enhancing alleles at different loci [26,27]. Thus, genetic susceptibility and instability are bound to play significant roles in the predilection of women to lung cancer.

In conclusion, this study disclosed the aetiology of lung cancer in Taiwanese women to be significantly associated with age, time periods and older cohorts. Furthermore, adenocarcinoma clearly dominates the pattern of lung cancer in Taiwanese women. Overall, the incidence lung cancer in Taiwanese women is increasing, and this may be due to older cohorts having had less education about the benefit of extractor fan usage, and now sufficient time has elapsed for the disease to manifest itself. Conversely, we also noted in the younger cohorts, particularly those born after 1956, that the incidence of lung cancer has declined, including that of adenocarcinoma and squamous cell carcinoma. This implies that the increased usage of extractor fans has had a 'protective effect' in younger generations.

Conflict of interest statement

None declared.

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