

RESEARCH COMMUNICATION

Lung Cancer in Central Tunisia: Epidemiology and Clinicopathological Features

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Abstract

Lung cancer is the most common cancer worldwide but data from Tunisia are limited. The aim of this research was to describe the epidemiology, pathology and clinical features of lung cancer in Central Tunisia. All lung cancer cases diagnosed during a 15-year period were analyzed based on the data of the Cancer Registry of the Center of Tunisia. Five-year age-specific rates, world age-standardized rates (ASR), and annual percent change were calculated using annual data on population size and the estimated age structure. A total of 1,882 incident cases of lung cancer were registered (1,782 males, 100 females). The median age at diagnosis was 64 years for males and 61 years for females, with ASRs of 35.2 per 100,000 among males and 1.5 among females. Over time, there were significant decreasing trends by -6.5% (95% CI: -12.9%; -0.2%) for females and a stable incidence for males at an annual rate of +0.2% (95% CI: -1.6%; +1.8%). The predominant histological type was squamous cell carcinoma in males (36.9%) and adenocarcinoma in females (52%). During 2003-2007, adenocarcinoma became the most frequent (33.7%) followed by squamous cell carcinoma (30.3%) in males. The majority of tumor cases were diagnosed at advanced stages (79.9%). In conclusion, lung cancer has remained the most common cancer diagnosed at advanced stages among Tunisian men. Our findings justify the need to plan and develop effective programs aiming at the control and prevention of the spread of lung cancer in Tunisia.

Keywords: Lung cancer - incidence - histopathology - advanced stages - Tunisia

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Introduction

Lung cancer has been the most common cancer in the world for several decades, and by 2008, there were an estimated 1.61 million new cases, representing 12.7% of all new cancers (Ferlay et al., 2010). It was also the most common cause of death from cancer, with 1.38 million deaths representing 18.2% of the total (Ferlay et al., 2010). In males, lung cancer is still the most common cancer worldwide with high rates in Central-Eastern and Southern Europe, Northern America and Eastern Asia. Very low rates are still estimated in Middle and Western Africa. Incidence rates are generally lower in women, but, worldwide, lung cancer is now the fourth most frequent cancer of women with 516,000 cases and the second most common cause of death from cancer with 427,000 deaths (Ferlay et al., 2010).

Population-based studies describing the lung cancer incidence were rarely reported from Tunisia (Missaoui et al., 2010). In the Sousse region, Tunisia, lung cancer represented the most common diagnosed cancer among

men with a world age-standardized incidence rate (ASR) of 37.1 per 100,000 during 1998-2002 (Curado et al., 2007). In this paper, we report the burden and characteristics of lung cancer diagnosed in the Center of Tunisia during a 15-year period (1993-2007), based on the database of the population-based Cancer Registry of the Center of Tunisia.

Materials and Methods

We carried out a retrospective study of all cases of lung cancer diagnosed in the Pathology Department of the Farhet Hached University Hospital, Sousse and registered in the Cancer Register of the Center of Tunisia during a 15-year period time (January 1993 – December 2007). The cancer registry has provided important information on cancer patterns over the previous years (Parkin et al., 2003; Curado et al., 2007; Missaoui et al., 2010; Missaoui et al., 2010; Missaoui et al., 2011). The study was approved by the Human Ethics Committee at the Farhet Hached University Hospital of Sousse (Tunisia) and it conformed

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to the provisions of the Declaration of Helsinki.

The International Classification of Diseases, 10th revision (ICD-10) was used for cancer classification (Percy et al., 1992). In the present study, the inclusion criteria were new cases of lung cancer (C33-34) diagnosed between the 1st January 1993 and the 31st December 2007. Medical records were reviewed for data on age, origin, paraclinical data at time of diagnosis, histopathology, and tumor stage and grade. Histological types were categorized into three major types: adenocarcinoma (ICD-O: 8140, 8141, 8200, 8211, 8250, 8251, 8260, 8310, 8323, 8440, 8470, 8480, 8481 and 8490), squamous cell carcinoma (ICD-O: 8050, 8052 and 8070–8076), small cell carcinoma (ICD-O: 8041–8045) and the others.

Incidence rates were analyzed during 1993-2007 period. Crude incidence rates (CR) and five-year age-specific rates were calculated using population denominators derived as described (Bray et al., 2002; Curado et al., 2007). ASR were calculated by the direct method, using the world standard population (Curado et al., 2007). Rates were expressed per 100,000 person-years (Curado et al., 2007).

Trends of incidence rates were analyzed during three periods (1993-1997, 1998-2002 and 2003-2007). The annual percent change (APC) was calculated as previously described (Bray et al., 2005; Chen et al., 2006; Missaoui et al., 2010). In brief, the APC is calculated by fitting log-linear regression line to the natural logarithms of the rates using calendar year as the independent variable (Bray et al., 2005). The APC was obtained from the formula $100 \times [e^{\beta} - 1]$, where β is the parameter estimate obtained on fitting period of event as a continuous variable to the logarithm of the rate (Bray et al., 2005). Statistical significance was determined by calculating 95% confidence intervals (95% CI) for the APC (Szklo and Nieto, 2000). In describing the change, the terms “increase” or “decrease” were used when the rate ratio was statistically significant (two-sided p values < 0.05); otherwise the term “stable” was used.

Results

Epidemiology

During the study period, 1,882 patients with lung cancer were identified accounting for 10.9% of all cancers during the whole 15-year period (1993-2007). The median age at diagnosis was 63 years with a mean age of 62 years (ranging from 17 to 92 years). Among our patients, 82.7% were more than 50 years old (1,557 cases) (Figure 1). In males, lung cancer was accounting for 21.7% of all cancer cases. The median age was 64 years. The CR was 25.4 per 100,000 and the ASR was 35.2 per 100,000. Over time, lung cancer remains the most frequent cancer in men with a stable incidence trend at an annual rate of +0.2% (95% CI: -1.6%; +1.8%) (Figure 2). Figure 3 shows the age-specific incidence rates of the lung cancer during the three periods.

For women, lung cancer account for only 1.4% of all cancer cases. The median age was 61 years. The CR was 1.2 per 100,000 and the ASR was 1.5 per 100,000 ranking the 16th position. Over time, there were significant decreasing trends by -6.5% (95% CI: -12.9%; -0.2%).

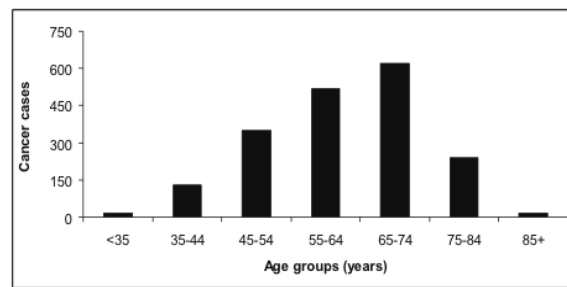


Figure 1. The Distribution of Patients with Cancer of the Lung in Central Tunisia, by Age Groups, 1993-2007

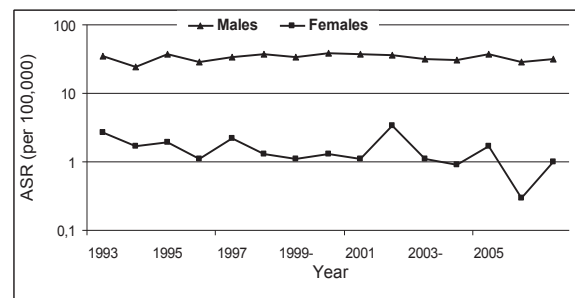


Figure 2. Trends of the Incidence of the Lung Cancer in Central Tunisia, 1993-2007

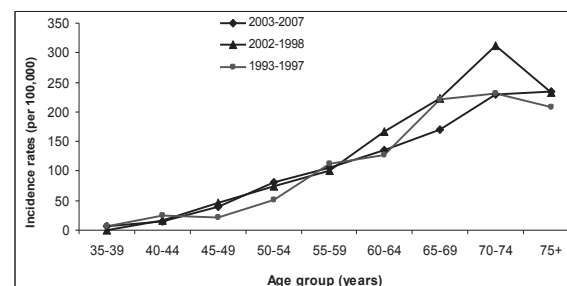


Figure 3. Age-specific Incidence Rates of the Lung Cancer Among Males in Central Tunisia During Three Time-periods

Pathology and clinic features

The tumor was more frequently located in the right lung (60.5% versus 39% in the left lung). The disease was bilateral in only 0.5% of the cases. Upper lobe of the bronchus or lung was the preferential site of the tumor (49.5%) followed by contiguous localizations (19.7%) and the lower lobe of bronchus or lung (17.8%). The tumor size was higher than 2 cm in 93.3% and than to 5 cm in 67.5% of cases. The microscopic verification (histological and cytological method) of diagnosis was 94.6%.

The most represented histological type was squamous cell carcinoma (35.7%), followed by adenocarcinoma (27.9%). Small cell carcinoma represented only 15.9% of tumor cases (Table 1). During the whole 15-year period, the predominant histological type was squamous cell carcinoma in males (36.9%) and adenocarcinoma in females (52%). The proportion of patients with adenocarcinomas increased among men during the study period. The predominant histological type was adenocarcinoma in males (33.7%) followed by squamous cell carcinoma (30.3%) during 2003-2007 (Table 2). Grade III was the most frequent grade (33%) followed by grade II (32.8%) and grade IV (23.6%). According to the lung staging system, advanced stages (stage III and IV) were

Table 1. Morphological Aspects of Lung Cancer in Central Tunisia, 1993-2007

Histological type	Males	Females	Total
Squamous CC	658 (36.9%)	14 (14%)	672 (35.7%)
Adenocarcinomas	474 (26.6%)	52 (52%)	526 (27.9%)
Small CC	292 (16.4%)	8 (8%)	300 (15.9%)
Others	358 (20.1%)	26 (26%)	384 (20.4%)
Total	1782 (100%)	100 (100)	1882 (100%)

CC, cell carcinomas

Table 2. Trends in Histological Types of Lung Cancer in Central Tunisia, 1993-2007

Histological type	1993-1997	1998-2002	2003-2007
Men (n: 1782)	371	681	730
Squamous CC	163 (43.9%)	273 (40%)	221 (30.3%)
Adenocarcinomas	83 (22.4%)	145 (21.3%)	246 (33.7%)
Small CC	66 (17.8%)	113 (16.6%)	114 (15.6%)
Others	59 (15.9%)	150 (22.1%)	149 (20.4%)
Women (n: 100)	26	34	39
Squamous CC	4 (15.4%)	9 (26.5%)	1 (2.6%)
Adenocarcinomas	16 (61.5%)	12 (35.3%)	25 (64.1%)
Small CC	1 (3.8%)	4 (11.4%)	2 (5.1%)
Others	5 (19.2%)	10 (29.4%)	8 (20.5%)

CC, cell carcinomas

the most frequent (79.9%). Early stages (stages 0 and I) represented only 4.9% of lung cancer.

Discussion

The current study investigated epidemiology and clinicopathological patterns of lung cancer in Central Tunisia diagnosed in the Pathology Department of F. Hached University Hospital, Sousse (1993-2007). The cancer of the lung remains the most common cancer among Tunisian men and constitutes a real problem of public health. Cigarette smoking is the major risk factor for the development of this cancer (Wynder and Hoffmann, 1994; Simonato et al., 2001; IARC, 2004). In Tunisia, for instance, smoking is responsible for almost 90% all lung cancer cases (Ministry of Public Health, Tunisia). Nowadays, 1,700,000 smokers aged between 10 and 70 years old amongst whom an annual rate of 7,000 deaths is estimated. A simple equation would show that, in Tunisia, 20 persons die every day because of tobacco (Ministry of Public Health, Tunisia). In addition to tobacco smoke, many other factors could influence individual susceptibility to lung cancer in smokers (Lubin and blot, 1984; Travis et al., 1995; B'chir et al., 2007). Among these are frequently mentioned other carcinogen exposition from the environment such as air pollution, exposure to asbestos, arsenic, etc.

In Central Tunisia, lung cancer remains the most common cancer diagnosed in males. According to Globocan 2008, the incidence of the lung cancer was of 33.5 per 100,000 men in Tunisia which is widely higher than the rates observed in other Arab countries such as Egypt (ASR: 9.6), Saudi Arabia (ASR: 7.2), and Yemen (ASR: 3.2) (Ferlay et al., 2010). While, the incidence rate was weaker than the rates observed in Central-Eastern and Southern Europe, Northern America and Eastern Asia. For instance, the incidence rates were 47.8 per 100,000

in France, 49.5 per 100,000 in the United States, 60.0 per 100,000 in Croatia, 71.2 per 100,000 in Poland, and 80.9 per 100,000 in Hungary (Ferlay et al., 2010). Nevertheless, the incidence rate reported here remains superior to rates reported from Middle and Western Africa such as Zambia (ASR: 2.0), Ethiopia (ASR: 2.4), and Somalia (ASR: 2.9) (Ferlay et al., 2010).

In females, incidence rates were generally lower than the rates observed among males. Many factors may influence the differences in lung cancer incidence between men and women. They may be connected with cigarette smoking, passive smoking, diet, occupation, indoor exposure and also with host factors that can protect against or facilitate the development of the cancer (Taioli and Wynder, 1994; Zang and Wynder, 1996). In Central Tunisia, the incidence of the lung cancer was only 1.5 per 100,000 women close to that reported in other Arab regions such as Egypt (ASR:2.5) and Morocco (ASR: 2.1) (Ferlay et al., 2010). The highest incidence rate is observed in Northern America where lung cancer is now the second most frequent cancer after breast cancer in women (ASR: 35.8). In the United States, the lung cancer ranked the second with an ASR of 36.2 per 100,000 (Ferlay et al., 2010). The lowest incidence rates in females were found in the same regions of Eastern, Western and middle Africa as in the males. The reason for these lower rates in Africa and the Arab world is still unknown. The problems facing cancer registry and information gathering in these two regions are probably one of the reasons in one side (Salim et al., 2011). Further genetic and environmental studies remain to be estimated.

The epidemic of cigarette smoking is the major determinant of past and future lung cancer trends (Wynder and Hoffmann, 1994; Simonato et al., 2001). During the last few decades, lung cancer incidence has stabilized or even exhibited a slow decline among men in Western countries (Cox and Yesner, 1979; Wu et al., 1986; Simonato et al., 2001). This observation may have resulted from effective cancer prevention programs; especially campaigns against smoking launched in the second half of the 20th century (Simonato et al., 2001; B'Chir et al., 2007). In Tunisia, 2009 was the official year of struggle against smoking as an endorsed campaign has been organized to sensitize people and raise their awareness of the dangers of smoking (Ministry of Public Health, Tunisia).

Carcinoma of the lung is divided into four main types: squamous cell carcinoma, adenocarcinoma, small-cell carcinoma and large cell carcinoma (Chung, 1994). Adenocarcinoma has always been more common in women than in men, in both smokers and non-smokers worldwide (Travis et al., 2004). Adenocarcinomas of lung cancer are more frequent in non-smoking patients, and they are lower in frequency in Europe than in Asia or North America (Dosemeci et al., 1997). In Central Tunisia, squamous cell carcinoma was the most common histological type in males while adenocarcinoma was the predominant among females. Our results were close to that reported from Morocco (Association Lalla Salma de Lutte Contre le Cancer, 2004) where the predominant type of lung cancer was squamous cell carcinoma in men (38%)

and adenocarcinoma (40%) in women. In the Arab Gulf Cooperation Council countries, squamous cell carcinoma was also the most frequent cancer in males accounting for 24.7% followed by adenocarcinoma, whereas adenocarcinoma was the most frequent histological type in females accounted to 29% followed by squamous cell carcinoma (Al-Kawari et al., 2009). While, the study of Benghazi Cancer registry of Eastern Libya (Benghazi Cancer Registry, 2004) showed that the overall ratio for squamous cell carcinomas in both men and women were higher than adenocarcinomas which accounted for 23% of all patients with lung cancer.

In the United States, United Kingdom and several other developed countries, the frequency of different histological types of lung cancer has changed over the last two decades so that squamous cell carcinoma has become less common and adenocarcinoma more frequent (Devesa et al., 1991; Travis et al., 1995; Janssen-Heijnen and Coebergh, 2003). In Central Tunisia, the frequency of adenocarcinoma increased during the last period (2003–2007) and the squamous cell carcinoma became the second most frequent histological type after adenocarcinoma among men. These results confirmed the study of B'chir et al., (2007). According to the literature, changes in the types of cigarettes smoked as well as modifications in time and geographical trends seem to explain partly the increased incidence of lung adenocarcinoma (Hoffmann et al., 1991; Wynder and Hoffmann, 1994; Van der Boon, 2001; B'chir et al., 2007). Some authors mentioned that changes in diagnostic techniques or classification were responsible for a major part of adenocarcinoma increase (Dodds et al., 1981; Charloux et al., 1997; Thun et al., 1997). The introduction of advances technology such as a fiber optic bronchoscopy allows the access to distal areas to the lung. These changes were not observed in most of the Arab patients with lung cancer except for Qatari patients (Salim et al., 2011). The sex ratio of lung cancer in Qatar was 8:1 representing one of the highest ratios in the world. Adenocarcinomas of the lung in Qatar accounted for about 44% of all lung cancer subtypes while squamous cell carcinomas accounted for only 26% (Salim et al., 2011). Al-Hamdan et al. (2006) showed that only Qatar had the highest percentage of lung cancer adenocarcinoma in males than in females (1998–2001). The same data was confirmed by Ibrahim et al. (2010) who postulated that lung cancer adenocarcinomas predominated in both male Qatari natives and expatriates; although the study showed that a great majority of the patients (82.5%) were current or ex-smokers at the time of diagnosis.

In conclusion, although the relatively low incidence rate compared to that reported from developed countries and the stable incidence trends, lung cancer remains the most common cancer diagnosed at advanced stages among men in the Center of Tunisia. Our findings justify the need to plan and develop effective programs aiming at the control and prevention of the spread of breast cancer in Tunisia.

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References

- Al-Hamdan N, Al-Jarallah M, Al-Jarallah M, et al (2006). The incidence of lung cancer in the Gulf Cooperation Council countries. *Ann Saudi Med*, **26**, 433-8.
- Al-Kawari M, Alsayyad J, Bazarbashi S, et al (2009). Eight-Year Cancer Incidence Among Nationals of the GCC States 1998-2005, 1-151 (www.sgh.org.sa).
- Association Lalla Salma de Lutte Contre le Cancer. Registre des Cancers de la région du grand Casablanca (Année 2004), Edition 2007 at: http://www.emro.who.int/ncd/pdf/cancer_registry_mor.pdf.
- B'chir F, Laouani A, Ksibi S, et al (2007). Cigarette filter and the incidence of lung adenocarcinoma among Tunisian population. *Lung Cancer*, **57**, 26-33.
- Benghazi Cancer Registry. Cancer Incidence and Mortality in Eastern Libya, 2004. (<http://www.cancerlibya.com>)
- Boffetta P, Jarvholm B, Brennan P, Nyren O (2001). Incidence of lung cancer in a large cohort of non-smoking men from Sweden. *Int J Cancer*, **94**, 591-3.
- Bray F, Guilloux A, Sankila R, Parkin DM (2002). Practical implications of imposing a new world standard population. *Cancer Causes Control*, **13**, 175-82.
- Bray F, Loos AH, Tognazzo S, La Vecchia C (2005). Ovarian cancer in Europe: Cross-sectional trends in incidence and mortality in 28 countries, 1953-2000. *Int J Cancer*, **113**, 977-90.
- Charloux A, Quoix E, Wolkove N, et al (1997). The increasing incidence of lung adenocarcinoma: reality or artefact? A review of the epidemiology of lung adenocarcinoma. *Int J Epidemiol*, **26**, 14-23.
- Chen JG, Zhu J, Parkin DM, et al (2006). Trends in the incidence of cancer in Qidong, China, 1978-2002. *Int J Cancer*, **119**, 1447-54.
- Chung A (1994). Lung cancer cell type and occupational exposure. In: J.M. Samet, Editor, *Epidemiology of Lung Cancer*, Marcel Dekker Inc, New York; 413-36.
- Cox JD, Yesner RA (1979). Adenocarcinoma of the lung: recent results from the Veterans Administration Lung Group. *Am Rev Respir Dis*, **120**, 1025-9.
- Curado MP, Edwards B, Shin HR, et al (2007). Cancer incidence in five continents, vol. IX. Lyon: IARC Scientific Publications.
- Devesa SS, Shaw GL, Blot WJ (1991). Changing patterns of lung cancer incidence by histological type. *Cancer Epidemiol BiomarkersPrev*, **1**, 29-34.
- Dodds L, Davis S, Polissar L (1981). A population-based study of lung cancer incidence trends by histologic type. *J Natl Cancer Inst*, **76**, 21-9.
- Dosemeci M, Gokmen I, Unsal M, et al (1997). Tobacco, alcohol use, and risks of laryngeal and lung cancer by subsite and histologic type in Turkey. *Cancer Causes Control*, **8**, 729-37.
- Ferlay J, Bray F, Pisani P, Parkin DM. GLOBOCAN 2002: Cancer Incidence, Mortality and Prevalence Worldwide, Version 2.0. IARC Cancer Base No. 5. IARC Press, Lyon 2004.
- Hoffmann D, Hoffmann I, Wynder EL (1991). Lung cancer and the changing cigarette, vol. 105. Lyon: IARC Scientific Publication, pp. 449-59.
- IARC (2004). Tobacco smoke and involuntary smoking. *IARC Monogr Eval Carcinog Risks Hum*, **83**, 1-1438.
- Ibrahim WH, Rasul KI, Khinji A, et al (2010). Clinical and epidemiological characteristics of lung cancer cases in Qatar. *East Mediterr Hlth J*, **16**, 166-70.

- Janssen-Heijnen ML, Coebergh JW (2003). The changing epidemiology of lung cancer in Europe. *Lung Cancer*, **41**, 245-58.
- Lubin JH, Blot WJ (1984). Assessment of lung cancer risk factors by histologic category. *J Natl Cancer Inst*, **73**, 383-9.
- Ministry of Public Health, Tunisia (<http://www.santetunisie.rns.tn/msp/msp.html>)
- Missaoui N, Jaidaine L, Abdelkader AB, et al (2011). Colorectal cancer in central Tunisia: increasing incidence trends over a 15-year period. *Asian Pac J Cancer Prev*, **12**, 1073-6.
- Missaoui N, Khouzemi M, Landolsi H, et al (2011). Childhood cancer frequency in the center of Tunisia. *Asian Pac J Cancer Prev*, **12**, 537-42.
- Missaoui N, Trabelsi A, Parkin DM, et al (2010). Trends in the incidence of cancer in the Sousse region, Tunisia, 1993–2006. *Int J Cancer*, **127**, 2669-77.
- Muscat JE and Wynder EL (1995). Lung cancer pathology in smokers, ex-smokers and never smokers. *Cancer Lett*, **88**, 1-5.
- Parkin DM, Ferlay J, Hamdi-Chérif M, et al (2003). Cancer in Africa, Epidemiology and Prevention. Lyon: IARC Press.
- Percy C, Van Holten V, Muir C (1992). International classification of diseases for oncology. 2nd ed. Geneva: World Health Organization.
- Salim EI, Jazieh AR, Moore MA (2011). Lung cancer incidence in the arab league countries: risk factors and control. *Asian Pac J Cancer Prev*, **12**, 17-34.
- Simonato L, Agudo A, Ahrens W, et al (2001). Lung cancer and cigarette smoking in Europe: an update of risk estimates and an assessment of inter-country heterogeneity. *Int J Cancer*, **91**, 876-87.
- Szklo M, Nieto FJ (2000). Epidemiology: beyond the basics. Gaithersbury (MD): Aspen Publishers, 438–40.
- Taioli E, Wynder EL (1994). Endocrine factors and adenocarcinoma of the lung in women. *J Natl Cancer Inst*, **86**, 869-70.
- Thun MJ, Lally CA, Flannery JT et al (1997). Cigarette smoking and changes in the hispathology of lung cancer. *J Natl Cancer Inst*, **89**, 1580-6.
- Travis WD, Travis LB, Devesa SS (1995). Lung cancer. *Cancer*, **75**, 191-202.
- Van der Boon J (2001). Low-tar filter cigarettes and an aggressive type of lung cancer. *Lancet Oncol*, **2**, 255.
- Wynder EL, Hoffmann D (1994). Smoking and lung cancer: scientific challenges and opportunities. *Cancer Res*, **54**, 5284-95.
- Wu AH, Henderson BE, Thomas DC, Mack TM (1986). Secular trends in histologic types of lung cancer. *J Natl Cancer Inst*, **77**, 53-6.
- Zang EA, Wynder EL (1996). Differences in lung cancer risk between men and women: Examination of the evidence. *J Natl Cancer Inst*, **88**, 183- 92.