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Differences in trends of lung carcinoma by histology type in Israeli Jews and Arabs, 1981–1995

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Abstract. Between 1981 and 1995 the national cancer register in Israel received reports on 13,600 new cases of lung cancer. We evaluated the trends in total lung cancer and the histologic subtypes, in Jewish and Arab Israelis. During this period, the age-adjusted incidence of lung cancer increased in the male Arab population, while for male Jews there was a non-significant decrease, for women in both population groups the rates were stable. When analyzed by age group, there was a significant decrease in incidence rates in Jewish males aged 75 years and older. An analysis by histologic subtypes showed two different trends. In the Jewish population, the age adjusted incidence rates of squamous cell carcinoma (SQCC) decreased and the incidence rates of adenocarcinoma (AC) increased, whereas in the Arab population the incidence rates of both subtypes increased, although statistically significantly only for SQCC. The changes found in the Jewish population are similar to those found in other western countries, where the rates of AC are increasing and the rates of SQCC are decreasing. The trends in the Arab population in Israel are different. This may be due to different trends in the prevalence of smoking in the two populations.

Key words: Arabs, Histologic-subtypes, Israel, Jews, Lung-cancer, Trends

Abbreviations: AC = adenocarcinoma; OR = odds ratio; RR = relative risk; SMCC = small cell carcinoma; SQCC = squamous cell carcinoma

Introduction

Lung cancer consists of different histologic subtypes, all associated with cigarette smoking. Squamous cell carcinoma (SQCC) and small cell carcinoma (SMCC) are believed to have a stronger association with smoking compared to adenocarcinoma (AC). In 1984, the relative risk (RR) [1] for men smoking 20–29 cigarettes per day was estimated at 17 for SQCC and only 3.5 for AC. In women the RR was lower (14.8 and 1.1 respectively) [1]. Recently, cigarette smoking was found to be more strongly associated with death from AC [2, 3]. Although SQCC has a higher association with smoking than AC, the difference may not be as large as in the past. The changes in the degree of risk could be associated with the changes made in the composition and design of the cigarettes. In one study, the odds ratio (OR) for SQCC in people who have smoked only filter cigarettes was reduced relative to lifetime non-filter cigarette smokers, no reduction in risk was observed for AC [4].

General changes in the lung cancer epidemic have been taking place over the last decade, but to different degrees around the world. In the past, the most frequent histological type in the United States and Europe was SQCC. However, during the mid-eighties, in the United States, the incidence rate of AC surpassed that of SQCC. In parts of Europe SQCC remains the most frequent subtype [5–7]. In Israel, in 1991 it was reported that SQCC was the most frequent subtype [8]. Consistent upward trends in the incidence of AC were reported in the United States about 20 years ago, making AC the most frequent subtype of lung cancer in North America [5]. The same trend was observed in The Netherlands, Switzerland [9] and in Asia, China [10] and Israel [11].

Differences in morbidity rates between countries can be attributed to many factors including lifestyle (mainly smoking), genetics, environment and others. Israel consists of two sub-populations, comprising about 80% Jews and 20% Arabs, who differ in aspects such as genetics, culture and lifestyle. In the past it was reported that the rates and trends of lung cancer and its subtypes differed in Arabs and Jews [12]. The aim of this study was to analyze the trends of the subtypes of lung cancer in Israel from the national cancer registry, in the different age groups, in Jews and Arabs during 1981–1995.

Methods

The current analysis is based on the data files of the Israeli national cancer register, which was established in 1960, and is located in the ministry of health. Information on diagnosed cancer cases in Israel is collected from all medical institutions in Israel: hospitals, laboratories, pathology and oncology departments, and death certificates submitted to the Central Bureau of Statistics. Since 1981 all new cases of cancer must be reported by law. The coverage of solid tumors in the register is above 90% nation-wide [13]. The register contains information on sex, age, place of birth, country of origin and other variables such as histologic type and the data are classified according to the International Classification of Diseases, 9th revision. The analysis of the histological types was performed for the period 1981–1995, during which time 13,600 cases of lung cancer were reported. Lung cancers are grouped into histologic types based on the morphologic characteristics of the tumor. The three major types are SQCC, AC and SMCC. In 20% of the cases reported to the register, the subtype of the lung cancer was not available, in about 30% of the cases the subtype was something other than the three subtypes mentioned, this includes about 8% of non-SMCC, 6% of alveolar carcinoma, 4% large cell carcinoma and less than 4% of each of the other types of lung cancer. This pattern was stable during the period 1981–1995.

Age-adjusted incidence rates using the European standard population, were calculated for total lung cancer, for SQCC and AC by population group. Age-specific rates for ages 45–64, 65–74 and 75+ were calculated for total lung cancer and the histologic subtypes SQCC and AC. The data for Arab women is not presented, as the number of cases was low.

The graphs presented are smoothed curves, using moving averages calculated by the mean of 3 years (one year before the specific year and the year after). Trends were estimated using linear regression and the significance of the trend determined by using the Student's *t*-test to test if the regression coefficient differed significantly from zero.

Results

Trends in the incidence of total lung cancer

Since 1970, age-adjusted incidence rates of morbidity from all types of lung cancer in Israeli Jewish men have declined from 40.2 per 100,000 in 1970 to 33.9 in 1995 (not smoothed). The decline is apparent through 1986–1992 where during these 6 years the decline is statistically significant (Figure 1).

There has been a significant rise in morbidity among Israeli Arab men, from 30.6 per 100,000 in 1970 to 41.5 in 1995. Since 1986 the incidence rate of lung cancer in the male Arab population has been higher than in the male Jewish population.

Trends in age-specific rates differ by age (Figure 2). During 1981–1995 the incidence rate at age group 65–74, in Jewish men was constant, but above 75 years old there was a significant decline in the trend of incidence rates ($p < 0.05$). There was a decline of 49% in the incidence rate from 1981 to 1995 (non-smoothed). In the younger age group a small non-significant decline was observed in the last 5 years, but it is too early to indicate an obvious trend.

In the Arab male population a significant rise in the trend of age-specific incidence rates was observed only in the young age group 45–64 ($p < 0.05$) (Figure 2). The increase in age-specific incidence rates is observed

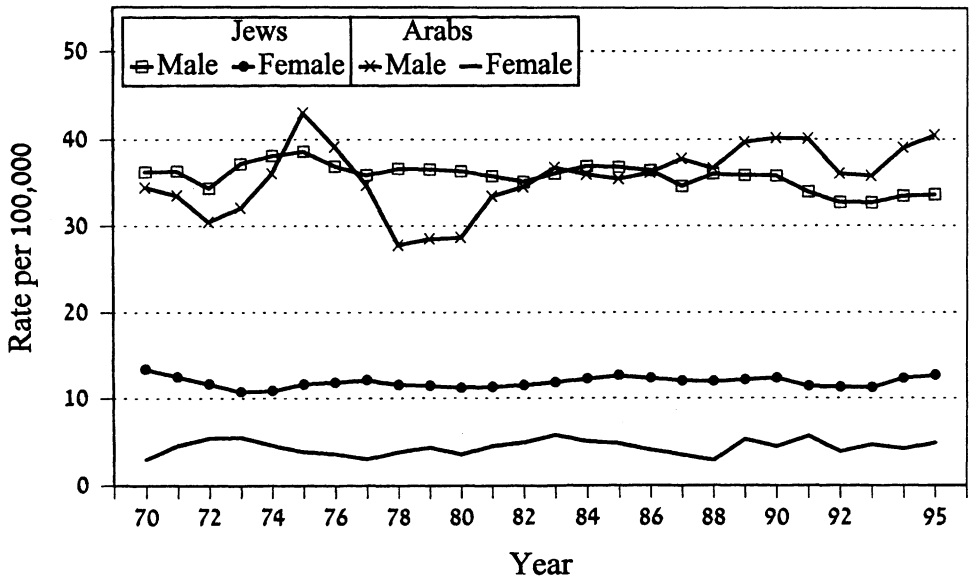

Figure 1. Morbidity from lung cancer by sex and population group, 1970–1995 (smooth age-adjusted rate per 100,000).

mainly between 1982 to 1991. There was an increase of 62% in the incidence rate from 1981 to 1995. In the older age groups there was no significant change.

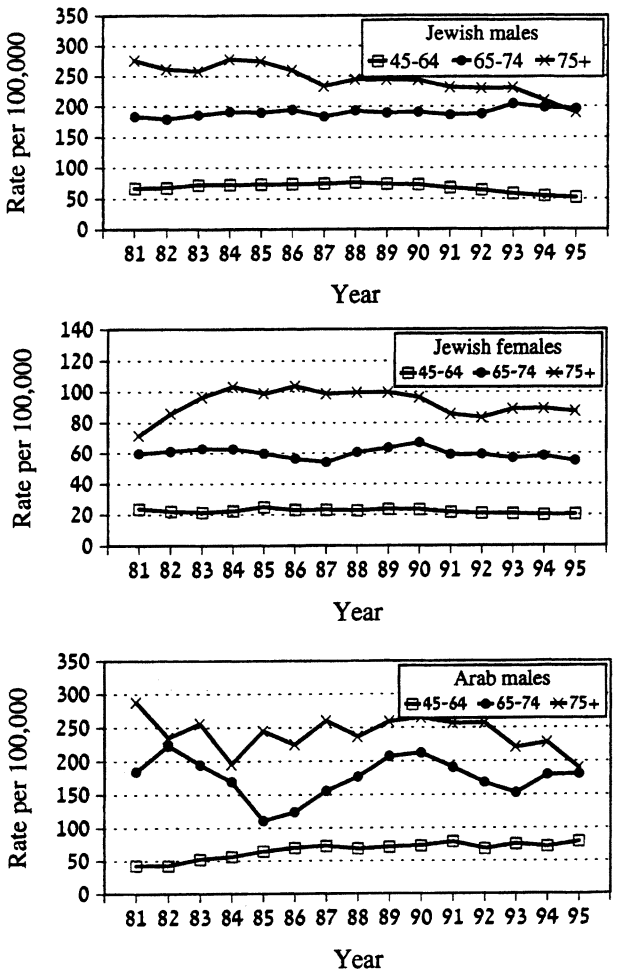

Figure 2. Age-specific incidence rate of lung cancer by age, sex and population group, 1981–1995 (smoothed rates per 100,000).

All in all, the incidence rates of lung cancer in Israel are increasing in the Arab male population and may be decreasing in the Jewish male population.

The female population in Israel is characterized by low lung cancer incidence rates among Jews and Arabs (Figures 1 and 2). The rates have remained constant for 15 years.

Distribution in the histologic subtypes of lung cancer

In 1995, SQCC was the most frequent lung cancer subtype in men, whereas in women AC was the most predominant subtype, as was reported in other countries [2, 5, 6, 8, 9]. From 1981 to 1995, SQCC decreased from 30 to 24% of the total cases of lung cancer in Jewish men and from 17 to 13% in Jewish women ($p < 0.05$) (Figure 3). In Arab men the opposite occurred and the percentage rose from 24 to 29% ($p < 0.05$). The percentage of AC in the Jewish population increased from 12 to 16% in men and from 20 to 23% in women ($p < 0.05$). In the Arab male population, the percentage also rose from 12 to 15%. Changes in the percentage of SMCC since 1981 were not significant due to small numbers of diagnosed patients each year. In 1995, 76 cases in Jews and seven cases in Arabs were diagnosed as SMCC which are about 7% of the total lung cancer cases.

The proportion of unknown and other subtypes was stable in Jewish men and women, however there was a decrease in the proportion of unknown and other subtypes in Arab men, especially during the period 1991–1995, but the decrease was not significant.

Trends in the histologic subtypes of lung cancer

The trend in age-adjusted incidence rates of SQCC decreased in Jews, in men significantly ($p < 0.05$)

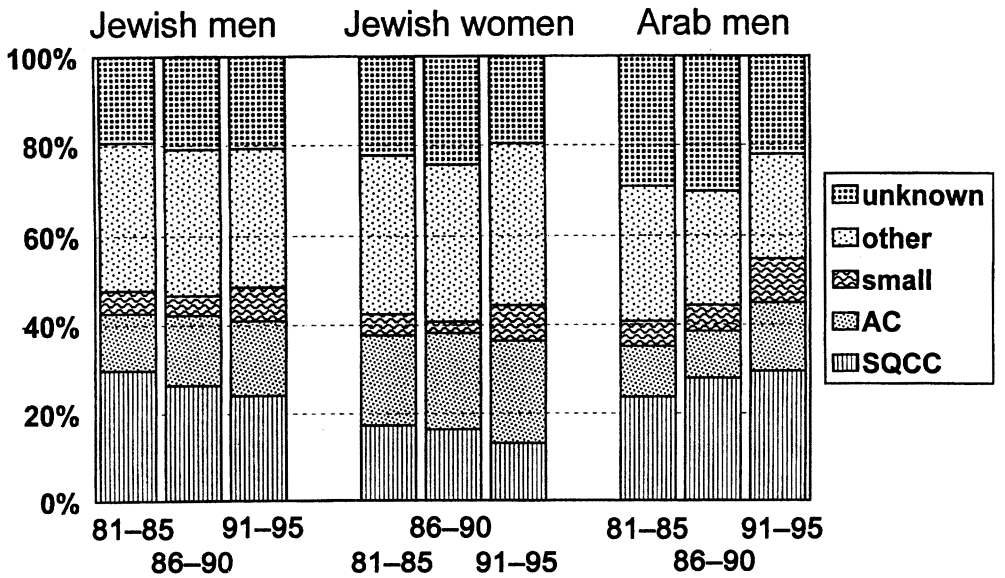

Figure 3. The distribution of histologic subtypes of lung cancer by period and population.

and more apparent between 1988 and 1995 (Figure 4). In women the decrease was not significant. In the Arab population the age-adjusted rate of SQCC increased significantly ($p < 0.05$) mainly after 1984. Age-adjusted rates of AC rose in all population groups. In Jewish men the increase was significant ($p < 0.05$), whereas in Arab men the increase was not significant (Figure 4). In Jewish women a significant increase is apparent especially during 1991–1995. All in all there is a rise in AC, especially in the Jewish population, however SQCC is rising in the Arab population and decreasing in the Jewish population.

The age-specific rate of AC has increased significantly ($p < 0.01$) in Jewish men aged 65–74. In the rest of the population groups and age groups, there was an increase, but it was not significant due to a low number of cases (Figure 5). After dividing the cases of lung cancer into smaller groups, the number of cases in each group decreased and the variability from year to year increased, making it more difficult to show statistically significant trends. The age-specific rates of SQCC in contrast to AC decreased in Jewish men in all three age groups; in age groups 45–64 and 75+ the decrease was significant ($p < 0.02$). In these two age groups there was a decrease in age-specific rates of SQCC in Jewish women too, but only in the younger age group was the decrease significant ($p < 0.05$). In contrast to the trends in Jews, the age-specific rate of SQCC in Arabs increased significantly in the younger and older age groups ($p < 0.05$) (Figure 6). In summary, the morbidity patterns of lung cancer histologic subtypes are different in Arabs and Jews; both in the age-adjusted morbidity and age-specific morbidity.

Discussion

Lung cancer trends are declining in Jewish males and increasing in Arab males. This corresponds with smoking trends in the Israeli population, as smoking is the main risk factor for lung cancer. Smoking rates in Israel have been monitored since 1972, and there has been a decline in tobacco consumption in Israel among both men and women, in the last 25 years

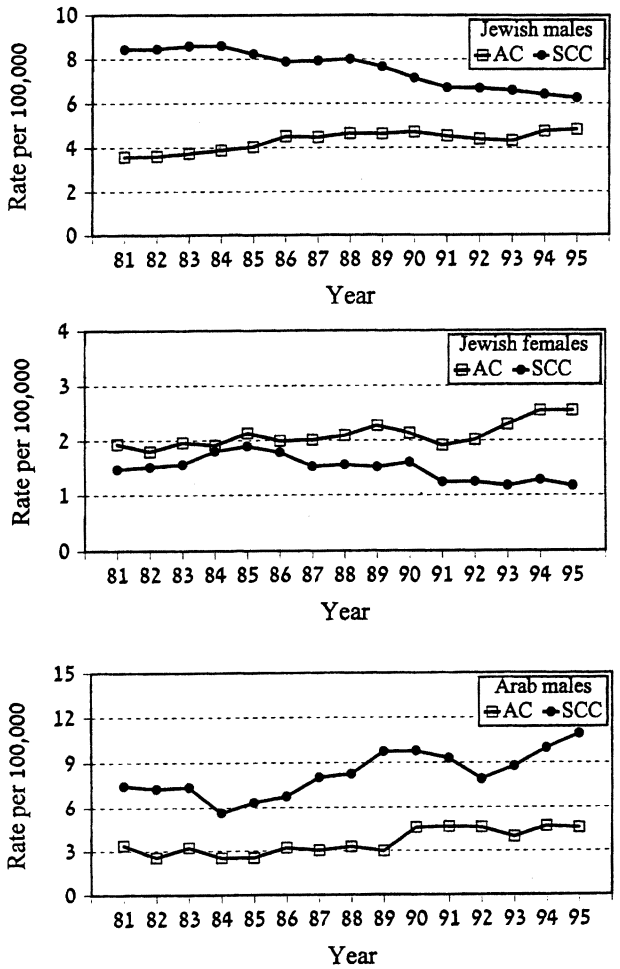

Figure 4. Age-adjusted rate of SQCC and AC, in Jews and Arabs, 1981–1995 (smoothed age-adjusted rates per 100,000).

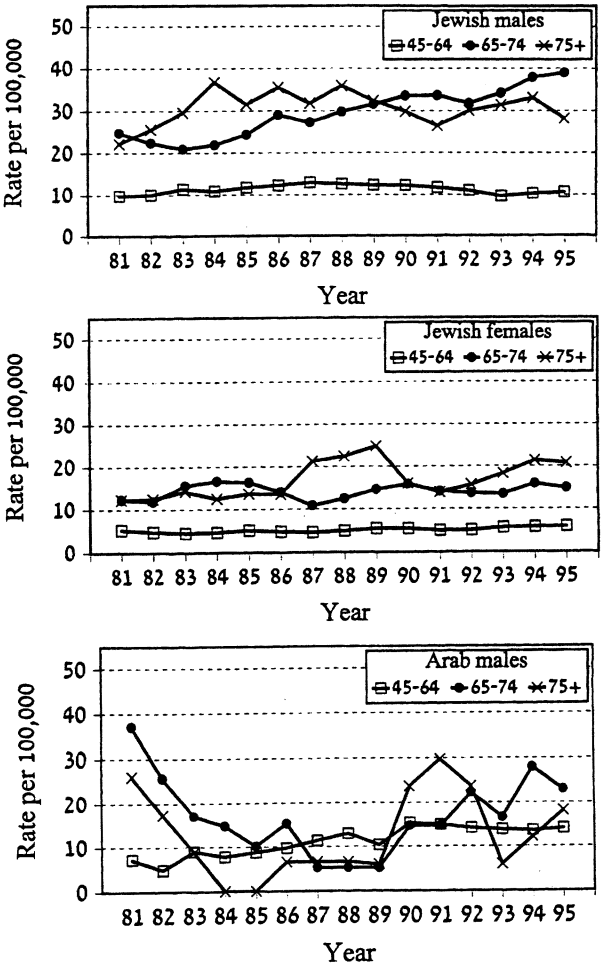

Figure 5. Age-specific incidence rate of AC by age, sex and population group, 1981–1995 (smoothed rates per 100,000).

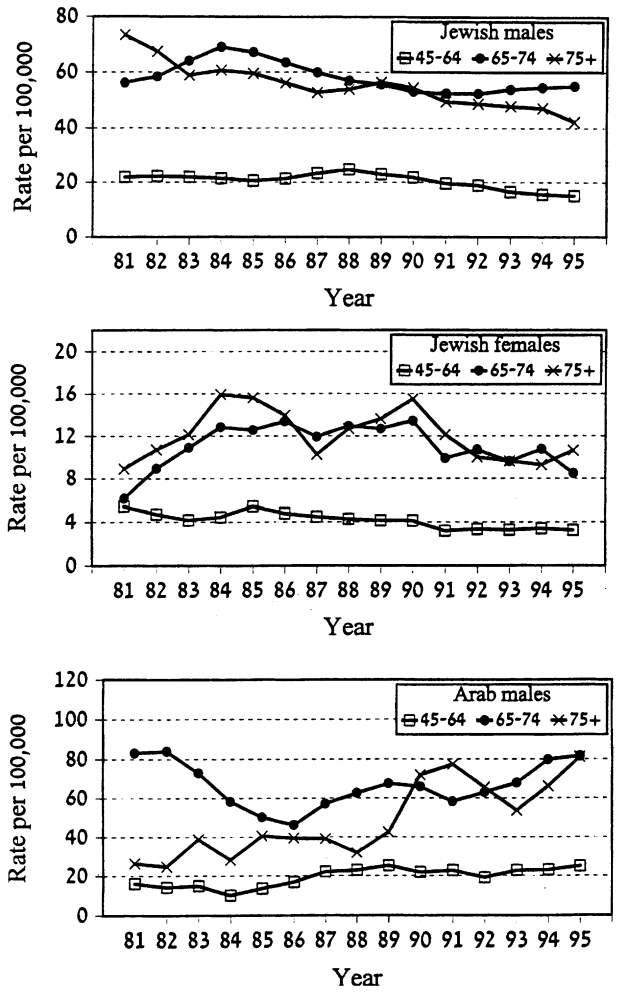

Figure 6. Age-specific incidence rate of SQCC by age, sex and population group, 1981–1995 (smoothed rates per 100,000).

[13]. The effect of the decline in smoking rates can be expected to take up to 20 years or more to express itself via the incidence of lung cancer, thus smoking rates in the seventies and before should correspond to lung cancer incidence rates in the nineties. Cross-sectional surveys of smoking habits in Israel have shown that among men the decline in smoking rates was more obvious in the older age group (55+) compared to the younger group [14]. This may explain the decrease in the rate of lung cancer in the older group (75+) and not in the younger age groups (Figure 2). It may take longer to observe the effects of the decline in smoking rates in the younger group, as 2–3 decades ago the rate of smoking did not decrease in this group. In Switzerland an earlier and larger decline was observed in middle aged men [7].

However, in the Arab male population during 1980–1995 there was a rise in age-adjusted lung cancer rates. As of 1986 the incidence rate of lung cancer is higher in Arab men than in Jewish men, making lung cancer the only cancer in which Arabs have a higher incidence rate compared to Jews [13]. The rise in lung cancer incidence in Arab men may be mainly due to a rise in age-specific rates in the younger age groups, 45–64 and 65–74. In the older age group (75+) there does not seem to be a change in rates. A survey of smoking behavior during 1996 found that in the Arab male population the rate was 50% and in Jewish male population it was 32% [13]. It may be that smoking has risen in the younger age groups in the Arab population and not in the older group. There is no available data on tobacco consumption trends in Arabs or on tobacco consumption rates in the different age groups in this population. As such it is difficult to predict if the rates of lung cancer will rise even more or start to decline soon in the future.

There are also no reliable data on smoking rates before 1972 in the Jewish population, but it is assumed that it increased in women in the sixties, as reported in the United States, and since the seventies the reports show that it has declined [13]. The fact that we see no change in morbidity from lung cancer in Jewish women, even though there was a decline in the percentage of Jewish women smokers, may be because the decline is to small to be observed or it is still to early to observe. Other possible explanations could be: a low association between lung cancer and smoking in Jewish women, or an increase in cigarette consumption per day in woman, even though the percentage of smokers is decreasing, which would increase the RR in the fraction of women still smoking. There may be other factors effecting lung cancer in women that we are not aware of yet. Published research show conflicting evidence on the risk of women smokers, some presenting data on the lower risk of women [1, 2] and some on the higher risk of women smokers [15, 16]. There is no data on the relative risk of women smokers in Israel, since studies have only been performed on men [8].

The trends in lung cancer around the world can be divided into two categories, those where lung cancer rates are declining in conjunction with decreasing tobacco consumption, as in the United States [5], and those where lung cancer rates are increasing or are stable as tobacco consumption continues to be high, such as South Korea [17].

Israel consists of both types of populations, which differ in their smoking rates and may also differ in the trends of smoking. Therefore they differ in the incidence trends of lung cancer. These two populations – Arabs and Jews have different lifestyles (such as smoking and diet), culture and ethnicity, enabling research into the aspects effecting health characteristics.

In Jews and Arabs, AC is the most common lung cancer cell type in women but not in men, this sex difference is observed in many countries [2, 5–7, 9, 11, 12, 18].

The trend in incidence rates of the subtypes of lung cancer in Jews are similar to most other countries such as the United States where there is a marked increase in AC and decrease in SQCC [5, 6]. This

trend is unlikely to be due to an artifact such as changes in pathological diagnosis. In Arab men, the incidence rate of both subtypes (AC and SQCC) are increasing as reported for instance in Switzerland in women [9]. It may be that the incidence rates for the subtypes in Arab men are still in an upward trend and have not yet reached a peak. The decrease in unknown and other subtypes of lung cancer may contribute to the increase in this population. In the United States the rate of SQCC in white men started declining after a peak in 1981–1982 but in black men it declined only after a peak in 1986–1987 [5]. In Jews the incidence rate of SQCC peaked in 1981–1984 declining thereafter.

Age-specific incidence rates of AC show an upward trend in the three population groups but significantly only in Jewish men aged 65–74. The non-significant increase may be due also to a small number of cases in each age group other than Jewish men. In the USA, AC is decreasing in recent years in white men younger than 65 and white women younger than 45, so we may start seeing a decline too, in the future [5].

Age-specific incidence rates of SQCC are declining significantly in Jewish men, in the older and younger age group. In Arab men the trend is in the opposite direction in the same age groups. In the USA, SQCC is declining in men younger than 75 and women younger than 64 [5]. Levi et al. [9] presented data for Switzerland on age-specific incidence rates showing a significant decrease of SQCC incidence rate in the younger age group and not the older one. This decrease in Swiss men is mainly since 1988, and in Israeli Jewish men aged 45–64 most of the decline is since 1989. In Jewish women this decline is also mainly since 1989. In Jews we may expect a continuous decline in the future.

The increase in the incidence rate of AC may be due to a change in the type of cigarette smoked [5]. During the sixties the main type of cigarette smoked was a non-filter cigarette, by the eighties most smokers smoked filter cigarettes, along side this change, smokers started smoking the 'light cigarette'. These two changes may have caused a change in the mechanism of smoking, such as more frequent puffs and deeper inhalation, bringing about a different pattern of damage to the lung tissue and causing the change in the distribution of types of lung cancer. The filters remove the large particles in the cigarette smoke reducing the deposition of those particles in the large airways, where SQCC usually develops [19–21]. Kreuzer et al. [18] found that AC was more prevalently found in young lung cancer patients and suggested it is due to younger patients smoking filter cigarettes more than the older population, the younger patients smoking non-filter cigarettes had a higher rate of SQCC [18]. This change in type of cigarettes may have caused a cohort effect were there is an increase in AC in the Jewish male population aged 65–74, but not in the younger age group that have been smoking filter cigarettes most of their lives.

There is no reason to suspect a different pattern of smoking filter and non-filter cigarettes or light cigarettes in the Jewish and Arab population as the manufacturers and distributors of cigarettes in Israel are the same for both populations. One possibility is that as the Arab population in general has a lower socioeconomic level and the non-filter cigarettes were cheaper it may have taken longer for them to change over to the filter cigarettes, delaying the increase in AC and the decrease in SQCC. Thus the increase in AC is observed in the Jewish male population aged 65–74 and in the Arab male population in the younger age group (45–64).

Lung cancer rates in Israel are low compared to rates in western countries [13, 22]. The national cancer register in Israel has been collecting incident cases for over 35 years and it has been shown that the coverage of cases especially in solid tumors is above 90% [13]. The quality of the data is especially high when dealing with highly fatal cancers such as lung cancer. It does not seem as if underreporting or misdiagnosis can explain the low rates of lung cancer in Israel compared to Europe and America. Lower smoking rates cannot explain this phenomenon either. After adjusting for age, the rate in Israel is about half of the rate in the USA, even though smoking is about 3% higher [13]. In Finland the smoking rates are 8% lower than in Israel but the incidence is nearly twice as high [22].

There may be a few possible explanations of this phenomenon. There are now findings that suggest there is a genetic predisposition to lung cancer [23–26]. It may be possible that the percentage of Jews genetically predisposed to lung cancer is lower than in other population groups. In the USA a few studies showed that Jews had lower rates of lung cancer [27–30]. It was also suggested that there was an association between lung cancer and alcohol consumption [31, 32], and as alcohol consumption in Israel is low [13] this may partly add to the explanation of the low rates of lung cancer. Aspects concerning nutrition were also suggested to be associated with lung cancer [33–35] and as Israeli diet is relatively rich in fruit and vegetables, this might be a possible factor contributing to the low rates of lung cancer. Currently it is not possible to identify which of these variables can add to the explanation of the discrepancies.

Incidence rates in Arab men in Israel are also lower than the incidence rates in the United States and Europe, and the above possible explanations could be equally relevant for this group. However since both Jews and Arabs have lower rates, a genetic factor would be a less likely explanation.

The data were collected on a national basis, and the diagnosis and histological classification did not undergo a standardized pathological review of the

tissue. However, there is no reason to suspect non-differential misclassification of the cancer cases between Jews and Arabs, men or women, as the diagnosis and treatment of lung cancer were obtained from the same health services around the country.

The major limitation in interpreting the data is that we cannot correlate lung cancer incidence directly with data we have on smoking habits. We can only compare national trends in smoking and lung cancer as indicators of trends that can be expected in the future. In addition we do not know the relative risk in these population groups, which may differ from the rates obtained from other population groups.

The changes found in the Jewish population are similar to those found in other western countries, where the rates of AC are increasing and the rates of SQCC are decreasing. The trends in the Arab population in Israel are different. This may be due to different trends in smoking behaviors in the two populations.

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