EUROPEAN NETWORK OF CANCER REGISTRIES

INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

ENCR CANCER FACT SHEETS

VOL. 1, MARCH 2002

LUNG CANCER IN EUROPE

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The Mission of the ENCR.

The ***European Network of Cancer Registries*** (ENCR) project, established within the framework of the Europe Against Cancer Programme of the European Commission, has been in operation since 1990.

The **main goals** of the Network are:

- to improve the quality, comparability and availability of cancer incidence data,
- to create a basis for monitoring cancer incidence and mortality in the European Union,
- to provide regular information on the burden of cancer in Europe,
- to promote the use of cancer registries in cancer control, health-care planning and research.

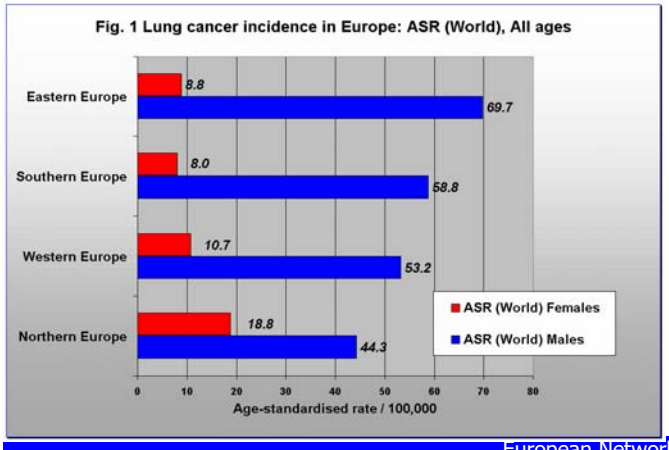
The ENCR promotes collaboration between cancer registries, defines data collection standards, provides training for cancer registry personnel and regularly disseminates information on incidence and mortality from cancer in the European Union and Europe.

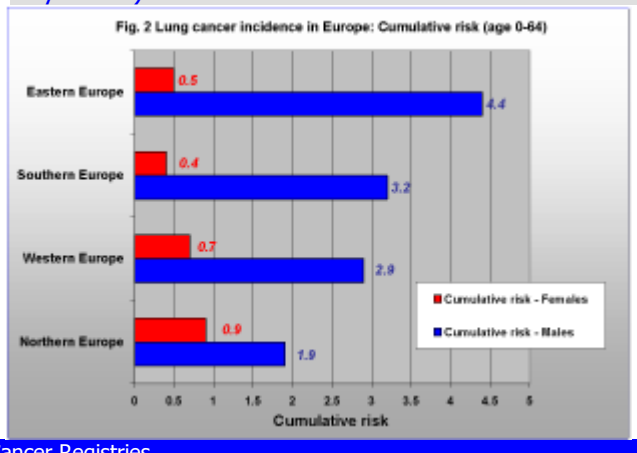
Lung Cancer - Introduction.

Lung cancer is the commonest cancer in the world now – 12.3% of all new cancer cases. In men, the highest incidence rates in the world are observed in Europe (especially Eastern Europe) and in North America. In females, the highest incidence rates are noted in North America and north-west Europe.

Lung cancer is also the most common cancer in Europe. In Europe there are nearly 400,000 new cases each year (Bray et al., 2002). It accounts for nearly one quarter of new cancer cases in European men and 6% of all cancers in women.

The most important risk factor of lung cancer is tobacco smoking. Evidence of the harm done by smoking has been accumulating for 200 years, at first in relation to cancers of the lip and mouth, and then in relation to vascular disease and lung cancer (Doll, 1998). The evidence has been reviewed many times by different scientific groups and institutions (IARC, US Surgeon General, UK Royal College of Physicians).





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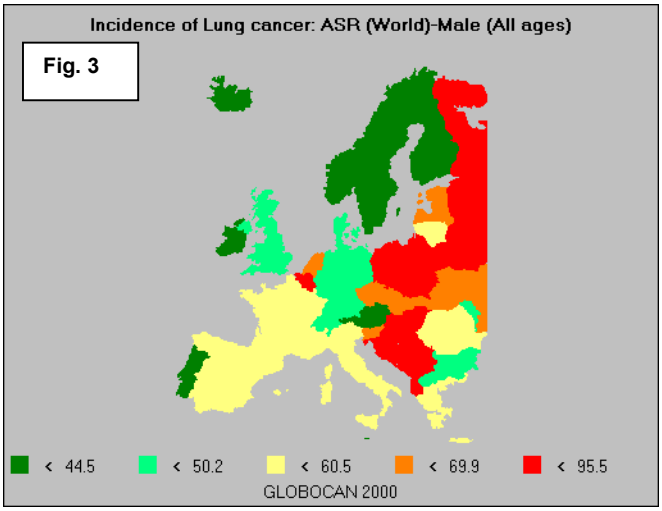
Regional Differences in Lung Cancer.

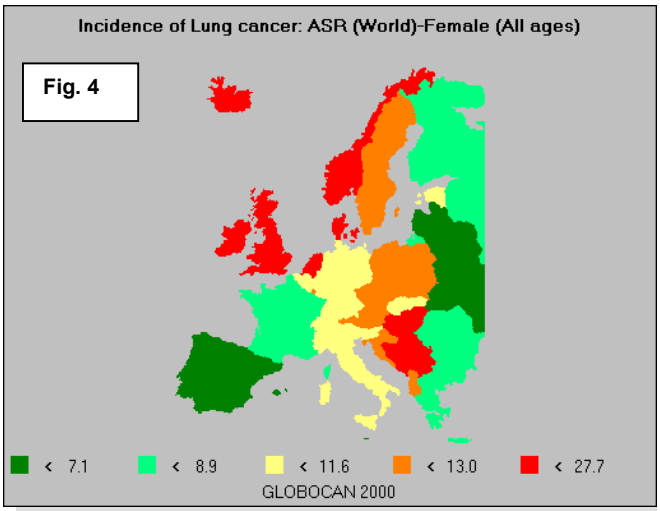
There are differences in the frequency of lung cancer among different regions and populations within Europe. In males, incidence rates and cumulative risk are the highest in Eastern Europe, much higher than in other parts of the continent (see Fig. 1,2,3,4). In females, the highest incidence rates are found in Northern Europe (almost twice as high as in Western Europe, and even more than twice in Eastern and Southern Europe) (see Fig. 1,2,3,4).

The estimates for the individual countries for the year 2000 show that the highest age-standardised incidence rates in male populations are observed in Hungary (95.5/10^5), Croatia (82.5//10^5), Bosnia Herzegovina (82.2/10^5) and Yugoslavia (80.9/10^5). The lowest rates are found in Sweden (21.4/10^5), Iceland (31.5/10^5), Portugal (33.9/10^5) and Norway (35.1/10^5) (Tab. 1). In females the highest rates are observed in Denmark (27.7/10^5), Iceland (23.8/10^5), Hungary (22.6/10^5), and United Kingdom (21.8/10^5). The lowest incidence rates in females in Europe are found in Spain (4.0/10^5), Belarus (5.0/10^5), Malta (5.3/10^5), and Portugal (5.5/10^5) (Tab. 1).

Table 1. Estimates of lung cancer incidence, Europe 2000

Country (region)	Crude rate	ASR (World)	Cumulative risk (age 0-64)	Crude rate	ASR (World)	Cumulative risk (age 0-64)
	Males			Females		
Eastern Europe	***87.2***	***69.7***	***4.4***	***15.1***	***8.8***	***0.5***
Belarus	87.7	71.0	4.7	9.0	5.0	0.3
Bulgaria	74.2	48.9	3.5	14.7	8.0	0.5
Czech Republic	98.4	68.9	3.9	22.5	12.7	0.8
Hungary	136.1	95.5	6.0	40.1	22.6	1.4
Moldova	49.0	47.1	3.5	9.4	7.1	0.5
Poland	94.3	78.2	4.7	19.8	12.8	0.8
Romania	67.1	50.7	3.7	13.3	8.3	0.5
Russian Federation	88.0	74.9	4.6	13.4	7.6	0.4
Slovakia	80.0	68.5	4.1	13.7	9.0	0.5
Ukraine	82.3	61.5	4.1	13.0	7.0	0.4
Northern Europe	***73.5***	***44.3***	***1.9***	***37.5***	***18.8***	***0.9***
Denmark	76.4	46.8	2.2	50.0	27.7	1.8
Estonia	92.3	69.9	4.1	18.7	9.5	0.5
Finland	57.2	36.8	1.5	16.9	8.9	0.5
Iceland	40.5	31.5	1.4	33.0	23.8	1.4
Ireland	50.9	39.5	1.7	28.6	18.7	0.9
Latvia	82.4	61.5	3.7	12.5	6.4	0.3
Lithuania	73.5	57.7	3.2	11.0	5.8	0.2
Norway	55.7	35.1	1.6	28.8	16.6	1.1
Sweden	39.3	21.4	1.0	23.5	12.1	0.8
United Kingdom	82.1	47.6	1.9	44.8	21.8	1.0
Southern Europe	***95.9***	***58.8***	***3.2***	***15.2***	***8.0***	***0.4***
Albania	65.0	79.2	4.7	12.1	13.0	0.8
Bosnia Herzegovina	93.7	81.2	4.9	18.2	13.2	0.8
Croatia	124.1	82.5	4.3	23.0	11.8	0.6
Greece	100.6	55.8	2.9	16.6	8.3	0.4
Italy	107.7	59.4	3.1	19.3	9.0	0.5
Macedonia	55.8	46.9	2.7	10.9	8.1	0.5
Malta	60.1	44.5	1.7	8.3	5.3	0.3
Portugal	52.1	33.9	1.9	10.0	5.5	0.3
Slovenia	90.6	64.4	3.5	19.7	11.1	0.6
Spain	86.8	53.2	2.9	7.7	4.0	0.2
Yugoslavia	110.5	80.9	5.2	21.6	13.8	0.9
Western Europe	***83.9***	***53.2***	***2.9***	***19.4***	***10.7***	***0.7***
Austria	60.5	42.1	2.3	21.4	12.0	0.7
Belgium	125.7	76.4	3.9	20.3	11.1	0.7
France	79.6	53.5	3.3	12.7	7.4	0.5
Germany	83.4	50.2	2.6	22.4	11.4	0.7
Luxembourg	90.4	60.5	3.2	21.2	12.2	0.8
The Netherlands	92.7	62.0	2.7	27.7	17.5	1.2
Switzerland	73.9	48.5	2.5	19.9	11.6	0.8



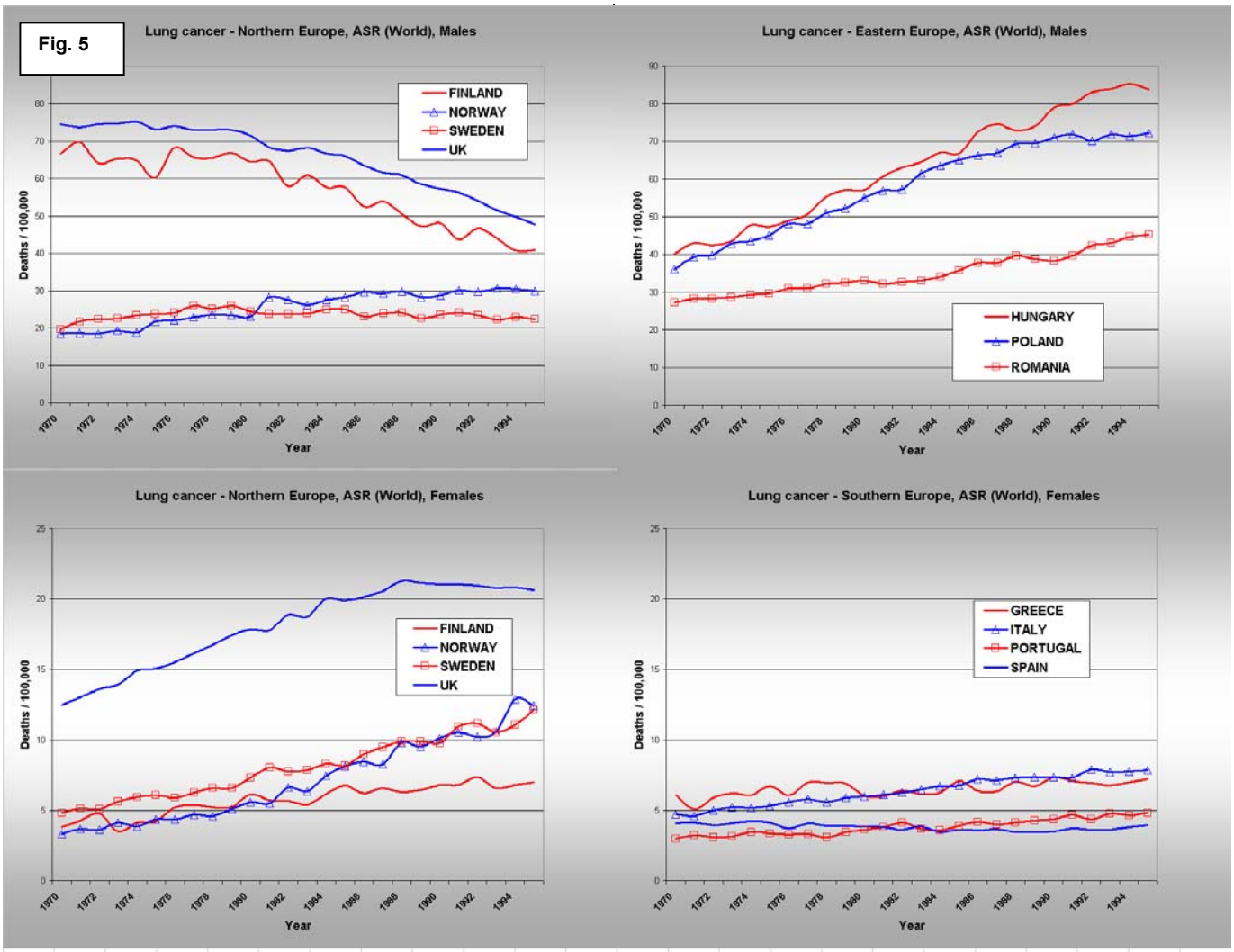


Temporal Changes in Lung Cancer in Europe.

In males, mortality rates are decreasing in countries of Northern and Western Europe (e.g. UK or Finland) or are low but stable (Sweden, Norway) (Fig. 5). At the same time, in many countries of Central and Eastern Europe, an increase in mortality rates has been observed (Hungary, Romania) or the first signs of a levelling off have been noted since the beginning of 1990s (Poland) (Fig. 5).

Until recently, mortality rates in UK females were high and increasing, but signs of a decrease have been present since about 1989. In Sweden and Norway too an increase of rates has been observed during the last 25 years, although the level of rates was much lower than in UK. On the other hand, countries of Southern Europe still have low and stable mortality rates from lung cancer (Greece, Spain) or a relatively small increase is observed (Italy, Portugal).

Fig. 5



Aetiology of Lung Cancer.

Tobacco smoking is well-established as the main cause of lung cancer.

There is a clear dose-response relationship between lung cancer risk and the number of cigarettes smoked per day, the degree of inhalation, and the age at initiation of smoking. A lifetime smoker has a risk some 20-30 times that of a non-smoker.

Smoking increases the risk of all histological types of lung cancer, although the relative risk is greater for squamous cell and small cell carcinomas than for adenocarcinomas (Simonato et al. 2001) (table 2).

Table 2. Relative risk of lung cancer for cigarette smoking by sex and histological type. European multicentre study.

	Males		Females	
	Squamous + small cell carcinoma	Adeno-carcinoma	Squamous + small cell carcinoma	Adeno-carcinoma
Non-smoker	1.0	1.0	1.0	1.0
Ex-smoker	16.2*	3.5*	3.8*	1.1
Current smoker	57.9*	8.0*	18.2*	4.1*

* - p < 0.05

Adenocarcinoma has always been more common in women than in men, in smokers and non-smokers.

Evidence that the risk of lung cancer may be greater in women than in men, at equivalent levels of exposure to tobacco smoke (Risch et al., 1993; Harris et al., 1993), has been weakened by more recent studies from Europe, that have concluded that risk is similar in the two sexes (Prescott et al., 1998, Kreuzer et al., 2000).

Passive exposure to tobacco smoke (ETS) is also a well known risk factor for lung cancer. It is estimated that exposure to ETS increases risk by 15-20% (Boffetta et al. 1998). It seems that exposure to ETS increases the risk of squamous cell carcinoma more than adenocarcinoma and small-cell carcinoma (Boffetta et al. 1998).

Other factors known to increase risk of lung cancer are occupational exposure to asbestos, some metals (e.g. nickel, arsenic, cadmium), radon, and ionising radiation. However, their contribution to the number of cases occurring in the population is small.

Diets high in vegetables and fruits (especially green vegetables and carrots) may provide some modest protection.

Lung Cancer Prevention and Early Diagnosis (Screening).

Primary prevention

Undoubtedly, **smoking cessation** is the best way to reduce risk of lung cancer. There are many epidemiological studies (both cohort studies and case-control studies) that confirm this.

The risk of developing lung cancer decreases with time since stopping. Table 3 shows the relationship between the length of time since stopping smoking and RR of lung cancer (Simonato et al., 2001).

Table 3. Effect of stopping smoking (by sex).

Time since stopping	Relative Risk	
	Males	Females
Current smokers	1.00	1.00
2-9 years	0.66*	0.41*
10-19 years	0.27*	0.19*
20-29 years	0.17*	0.08*
30+ years	0.08*	0.13*
Never-smokers	0.04*	0.11*

* - $p < 0.05$

It is also easy to demonstrate that, from a public health point of view, a more immediate impact on deaths from lung cancer is achieved by persuading adult smokers to quit, than by attempting to convince adolescents not to start smoking (Doll et al., 1994, Peto, 1994).

Although individuals can be convinced to give up smoking, and adolescents not to start this is very difficult in the absence of reinforcing social pressure to make smoking unattractive, and a legislative framework to make smoking expensive and difficult. There are enormous opposing pressures from many interest groups (such as agricultural and finance ministries, tobacco growers and the tobacco industry).

Early detection (screening)

There are many factors (the huge number of lung cancer cases, the continuing elevated risk in ex-smokers, the poor results of treatment) that make early detection by screening seem an attractive proposition.

Screening means the use of tests or examinations on asymptomatic individuals, to identify disease at early stage (before it becomes clinically apparent). It is essential, if screening is to be of any value, that this results in an improvement in outcome (lowers the risk of death, or complications of treatment). As far as lung cancer is concerned, the main approach to date has been by screening using chest X-ray. Although this can result in the detection of asymptomatic cancers (for which the duration of survival is much greater than usual), there is no demonstrable improvement in terms of reduction in number of deaths from lung cancer. The survival improvement must be the consequence of different types of bias ("lead-time" bias, length bias. and "overdiagnosis" bias) (Parkin & Pisani, 1996).

Recently, there has been renewed interest in screening, because spiral computerised tomography can detect small asymptomatic lesions more effectively than conventional X-ray. Although apparent cure rates for such lesions are very good, the same concerns about effectiveness apply, and this should be demonstrated in well conducted trials before the technique can be proposed for wide scale application.

Conclusions

In the view of current knowledge about lung cancer aetiology, prevention, effectiveness of screening and treatment, it seems that lung cancer mortality can be reduced in future by:

- Deter smoking initiation among minors by implementing school-based tobacco use prevention curricula;
- Increase tobacco prices by appropriate regulation of excise taxes, and use a part of these taxes to finance community interventions and mass-media strategies;
- Widely disseminate proven quitting strategies by involving medical professionals and medical communities;
- Carry out well-designed lung cancer screening trials to find out the extent (if any) of mortality reduction that can be obtained by early diagnosis.

Bibliography

1) Boffetta P, Agudo A, Ahrens W, et al. Multicenter case-control study of exposure to environmental tobacco smoke and lung cancer. J Natl Cancer Inst 1998, 90: 1440-50
2) Bray F, Sankila R, Ferlay J, Parkin DM. Estimates of cancer incidence and mortality in Europe. Eur J Cancer 2002, 38:99-166
3) Doll R, Peto R, et al. Mortality in relation to smoking: 40 years' observations on male British doctors. BMJ 1994, 309: 901-911
4) Doll R. Uncovering the effect of smoking: historical perspective. Stat Methods Med Res 1998; 7:87-117
5) Ferlay J, Bray F, Pisani P, et al. GLOBOCAN 2000: cancer incidence, mortality and prevalence worldwide, version 1.0. IARC Cancer Base No. 5. Lyon, IARC, 2001
6) Fontana RS, Sanderson DR, Taylor WF, et al. Early lung cancer detection: results of the initial (prevalence) radiologic and cytologic screening in the Mayo Clinic study. Am Rev Respir Dis 1984, 130:561-565
7) International Agency for Research on Cancer. Tobacco Smoking. Evaluation of Carcinogenic Risk to Humans, Volume 38, IARC, Lyon 1986
8) Kubik AK, Parkin DM, Zatloukal P. Czech study on lung cancer screening. Post-trial follow-up of lung cancer detahs up to year 15 since enrollment. Cancer 2000, 89: 2363-8
9) Parkin DM, Pisani P. Screening for lung cancer. In: Miller AB. Advances in cancer screening. Kluwer Academic Press, Boston 1996, 121-128
10) Patz EF, Goodman PC, et al. Screening for lung cancer. New Eng. J Med. 2000, 343(22): 1627-1633
11) Peto R. Smoking and deaths: the past 40 years and the next 40. BMJ 1994, 309: 937-939
12) Simonato L, Agudo A, Ahrens W, et al. Lung cancer and cigarette smoking in Europe: an update of risk estimates and an assessment of inter-country heterogeneity. Int J. Cancer 2001, 91: 876-887
13) USDHHS. Reducing the Health Consequences of Smoking. 25 years of progress. A report of the Surgeon General. USDHHS publication 89-8411, 1989