The epidemiology of oesophageal cancer in the UK and other European countries

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Introduction

Rates of oesophageal cancer exhibit greater international variation than almost any other cancer. In men, high rates are recorded in France (Calvados 26.5 per 100 000), Brazil (Porto Alegre 25.9 per 100 000) and China (Tianjin 16.6 per 100 000) as well as in several areas of the USA amongst the black population, while low rates of less than 4.0 per 100 000 are reported in Northern Europe (Norway, Sweden, Denmark and Finland) and Eastern Europe [Romania, Hungary (Vas) and the former German Democratic Republic][1]. The average incidence rate among men in the European Community (EC; references to EC do not include Luxembourg due to the very small number of reported cases) in 1980[2] was estimated to be 5.7 per 100 000. In women, the incidence rates are lower but high rates are again noted in China (Tianjin 8.0 per 100 000), Brazil (Porto Alegre 6.9 per 100 000) and black Americans, while the highest rates are from areas of India (Bangalore 8.8 per 100 000 and Bombay 8.4 per 100 000). In Europe, the excess of oesophageal cancer evident among men in France is not present in women, and it is the UK (East Scotland) that reports the highest rate (4.9 per 100 000), more than double the EC average in 1980 of 1.3 per 100 000[1,2].

It is worthy of note, however, that the areas of the world which experience the very highest rates of oesophageal cancer are not represented in *Cancer Incidence in Five Continents*[1]. A so-called 'Asian oesophageal cancer belt' is described stretching from eastern Turkey and east of the Caspian Sea through Northern Iran, Northern Afghanistan and southern areas of the former Soviet Union such as Turkmenistan and Tajikistan to Northern China[3]. In these areas, incidence rates of oesophageal cancer of over 100 per 100 000 are reported with rates often as high among women as men.

In all the countries of the EC estimated incidence rates in men exceed rates in women with on average a sex ratio of 4.4 : 1. There is a sixfold difference between the estimated highest rate (France: 11.5 per 100 000) and lowest reported rate (Greece: 1.9 per 100 000) in men and a sevenfold difference in women between Eire (4.2 per 100 000) and Greece (0.6 per 100 000). Rates in the UK are relatively high in both men (5.7 per 100 000) and women (3.0 per 100 000) ranking as the second highest country in the EC for both sexes. Among women in the British Isles incidence rates are at least double those of other European countries[2]. The variation in mortality rates from oesophageal cancer, and the different distribution among men and women has been clearly exhibited in maps by local area in countries of the EC[4].

Within the UK approximately 4850 new cases of oesophageal cancer are diagnosed per annum[5]. There is no consistent difference in incidence rates between urban and rural areas but rates are currently higher in both sexes in Scotland (males: 8.5 per 100 000; females 4.3 per 100 000) than England/Wales (males: 6.5 per 100 000; females 3.2 per 100 000)[1].

Time trends in oseophageal cancer mortality

For each country in the EC, mortality data on oesophageal cancer is available for approximately 30 years[6]. Over the time period 1960-1964 to 1985-1989 the all-ages age standardized rate (standardized to the world population)[7] in men has increased in all countries with the exception of France (which has the highest rates) and Greece (which has the lowest). Notable increases have occurred in all areas of the UK, Denmark, the Netherlands and Spain. Increases moreover have been greater amongst young and middle aged males (Table 1). In women there has been no clear pattern of change over the past 40 years in oesophageal cancer mortality rates in European countries but rates have increased throughout the UK (Table 2).

Oesophageal cancer mortality rates in the UK when considered by 5 year age group and by median year of birth, appear to have increased successively in male cohorts born after approximately 1900. Since that time, the age-specific rates have increased in all 5 year age groups. Among women, age-specific rates have increased among successive birth cohorts until approximately 1925, after which no further increase has been apparent in rates[6,8,9]. It has already been noted that current rates of oesophageal cancer incidence and mortality are higher in Scotland than England/Wales and mortality rates in both countries from 1911 to 1989 show that the difference has been present throughout this time period for women. Among men a quite different pattern of changing rates is evident. Mortality rates were higher in England/Wales in the early part of this century; rates subsequently declined between 1930 and 1960 in both England/Wales and Scotland with the rate of decline much steeper in England/Wales such that oesophageal cancer rates in the 1940s were lower in these countries in comparison to Scotland. Since 1960 however there have been steady increases in oesophageal cancer mortality rates throughout Great Britain but the rate in Scotland has consistently

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Table 1. All-ages age standardized and truncated (35-64 years) mortality rates for men in the European Community and changes in rates between 1960-1964 and 1985-1989*

Country	All ages ASR† (1985-1989)	% Change (1960-1964 to 1985-1989)	Truncated rate† (1985-1989)	% Change (1960-1964 to 1985-1989)
France	11.95	−11	22.58	1
UK (Scotland)	9.25	75	12.76	98
UK (England-Wales)	7.15	62	9.67	92
Eire	6.60	24	9.32	35
UK (N Ireland)	6.21	83	9.11	107
Portugal	5.75	11	9.65	7
Spain	5.44	49	9.82	79
Germany (FRG)	4.94	28	9.50	145
Belgium	4.61	24	7.73	70
Italy	4.59	5	7.68	37
Denmark	4.50	56	6.75	121
Netherlands	4.47	44	6.33	113
Greece	1.68	−1	2.07	−13

*This does not include Luxembourg due to the very small number of reported cases
†Rates are per 100 000, age standardized to the world population, and are based on years for which data are available between 1985-1989
ASR=Age standardized rate

Table 2. All-ages age standardized and truncated (35-64 years) mortality rates for women in the European Community and changes in rates between 1960-1964 and 1985-1989

Country	All ages ASR* (1985-1989)	% Change (1960-1964 to 1985-1989)	Truncated rate* (1985-1989)	% Change (1960-1964 to 1985-1989)
UK (Scotland)	4.03	27	4.55	14
Eire	3.62	2	4.11	−26
UK (England-Wales)	3.03	28	3.42	17
UK (N Ireland)	2.86	18	3.34	8
Netherlands	1.46	17	1.77	92
Denmark	1.32	3	1.73	166
Portugal	1.24	−30	1.34	−49
Belgium	1.06	0	1.41	41
France	1.02	−9	1.53	49
Germany (FRG)	0.80	−23	1.18	57
Italy	0.75	−14	0.88	−13
Spain	0.68	−37	0.69	−49
Greece	0.48	−31	0.59	−45

See Table 1 for key to Table

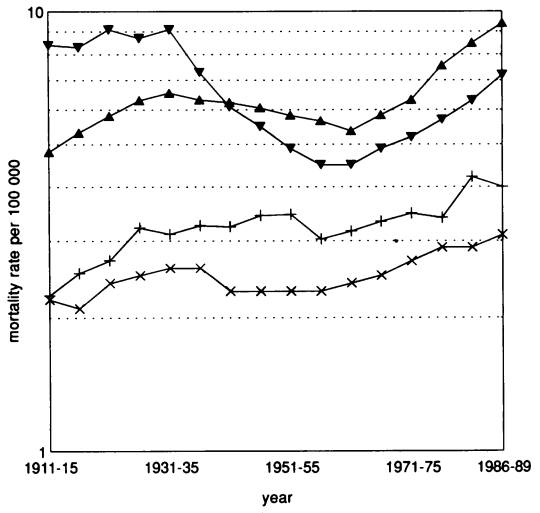

Figure 1. Oesophageal cancer mortality rates in Scotland and England/Wales between 1911 and 1989. △=Males (Scotland); +=females (Scotland); ▽=males (England and Wales); ×=females (England and Wales)

exceeded that in England and Wales by around 2 per 100 000 (Figure 1).

Oesophageal cancer occurrence by histological type

Although rates are increasing of cancer of the oesophagus in the UK, different patterns of change are seen when considered by histological type. In the West Midlands, the rate of squamous cell carcinoma of the oesophagus increased from 1.9 to 2.1 per 100 000 between 1962 and 1981 while adenocarcinoma of the oesophagus showed a sixfold increase over the same time period from 0.1 to 0.6 per 100 000[10]. Similar results have been reported using SEER (Surveillance, Epidemiology and End Results) data from nine areas of the USA. Between 1976 and 1987 in men, there was little change in the incidence of squamous cell carcinoma of the oesophagus, while rates of adenocarcinoma more than doubled[11]. By 1984-1987, adenocarcinoma accounted for 34% of all oesophageal cancers among white men in these areas. In Connecticut squamous cell

carcinoma of the oesophagus has been declining while for adenocarcinoma a fivefold increase has been recorded for men and a threefold increase for women[12].

There is evidence therefore of differing rates of change in incidence when analysed by squamous and adenocarcinoma histological sub-types. There may, however, be difficulty in determining the exact site of origin of tumours occurring around the oesophago-gastric junction. Therefore it is useful to consider the analyses of data relating to oesophageal adenocarcinoma with adenocarcinoma of the gastric cardia. Powell and McConkey[10] found that in the West Midlands while gastric cancer incidence had decreased from 19.2 to 15.3 per 100 000 between 1962 and 1981, the incidence rate of cardia tumours increased from 0.7 to 2.0 per 100 000. This increase could not be accounted for by changes in the number of site unspecified tumours. Using the USA SEER data, increases between 1976 and 1987 in gastric cardia cancers were 4.3% per annum for Caucasian men and 4.1% per annum for Caucasian women. The rate of increase of adenocarcinomas of the oesophagus and gastric cardia, when considered together over this period outpaced increases at all other sites[11].

Analytical epidemiology

In European countries the consumption of alcohol and tobacco is believed to be responsible for the majority of cases of oesophageal cancer. The joint attributable risk in men of the two factors was estimated to be 84% from a case-control study in Northern Italy[13] and 87% in Northern France[14]. In women the attributable risks found for alcohol and tobacco are lower, being 40% in Northern Italy[13].

Alcohol and tobacco

The high risk of oesophageal cancer in occupational groups employed in the liquor trade has been known for many years; Young and Russell in 1926[15] found an excess of such deaths among brewers, inn keepers and publicans, beer bottlers and cellarmen.

Studies of the cause of death amongst male alcoholics have shown a greater than expected number of deaths from cancers of the oesophagus. Such studies, however, while providing evidence of a possible association between alcohol and oesophageal cancer have been unable to take account of potential confounding factors.

One of the first studies to control for confounding factors such as age and tobacco consumption was conducted by Schwartz *et al.* in 1962 in Paris[16]. The excess of alcohol drinkers amongst oesophageal cancer cases remained and subsequent case-control studies consistently demonstrate dose-risk relationships between oesophageal cancer risk and increasing alcohol consumption after controlling for cigarette smoking. Additionally, it has been found that there is an increasing risk with increasing consumption of alcohol even amongst non-smokers[17,18]. The International Agency for Research on Cancer (IARC) working group reviewing evidence on oesophageal cancer and alcohol drinking concluded

> Epidemiological studies clearly indicate that drinking of alcoholic beverages is causally related to cancer of the oesophagus. There is no indication that the effect is dependent on type of beverage[19].

Major cohort (prospective) studies consistently report associations between cigarette smoking and the risk of oesophageal cancer. The risk appears to be around four to fivefold for smokers when compared with non-smokers. Similar results have been obtained from case-control studies with a dose-risk relationship often present after controlling for possible confounding factors such as alcohol. The effects of tobacco smoking have been noted also amongst abstainers and consumers of low amounts of alcohol[17,18], while the effect of black (air-cured) tobacco has been estimated to be around two to three times that of blond (flue-cured) tobacco[20]. The IARC working party on Tobacco Smoking concluded that:

> Tobacco smoking is an important cause of . . . oesophageal cancers. Pipe and/or cigar smoking appears to increase the risk of these cancers to approximately the same extent as cigarette smoking. The risks of these cancers associated with cigarette smoking are substantially increased in conjunction with high-dose exposure to alcohol[21].

The joint effects of alcohol and tobacco have generally been found to be multiplicative. Data from a case-control study conducted in Ille-et-Villaine[14], a high risk area of France, showed risks to increase with increasing alcohol consumption across each tobacco consumption level and similarly for tobacco consumption across each level of alcohol intake. None of the major studies conducted on oesophageal cancer however have provided information on the change in risk with cessation of either tobacco or alcohol habits, taking into account previous consumption levels.

Finally, although tobacco and alcohol have been implicated also in adenocarcinoma occurring around the oesophago-gastric junction[22-24] other studies[25-27] have found no association or an effect which is less than for squamous carcinoma.

Other factors

While tobacco and alcohol are the most important known aetiological factors in European countries for cancers of the oesophagus, dietary factors are also thought to play a role, especially in women among whom tobacco and alcohol apparently are responsible for a lower proportion of cases. Neither alcohol nor tobacco are as important aetiological factors in areas of the world with the highest incidence rates.

The Paterson Brown-Kelly (Plummer-Vinson) syndrome which includes postcricoid dysphagia and hypochromic anaemia was previously common in Northern Europe and almost endemic in rural parts of Sweden[28]. The syndrome was associated with nutritional deficiencies, and Ahlbom in 1936[29] found that many patients presenting with cancers of the upper aerodigestive tract had signs of this syndrome. Wynder *et al.*[30] concluded that previously high incidence rates of upper alimentary tract cancers in Swedish women could at least partly be explained by the high prevalence of the Paterson Brown-Kelly syndrome, and although its prevalence is now thought to be low, modern epidemiological studies find higher risks with deficiencies of vitamins (eg vitamins A and C) or trace metals (eg zinc and copper)[31,32]. Consistent evidence has also arisen from case-control studies that high consumption of fresh fruit and vegetables reduces the risk of oesophageal cancer while some but not all additionally report reduced risks for high intake of fresh meat and/or dairy products.

Although occupational factors in the aetiology of oesophageal cancer have traditionally focused on the excess of the disease amongst those employed in the liquor trade; several reports have noted an excess amongst metal workers. Originally Young and Russell in 1926[15] found excesses amongst plumbers; brass and bronze workers; tool, scissors and file makers. The increased risk amongst plumbers has been found also more recently[33] and although it would be necessary to take into account known risk factors before drawing firm conclusions, it may be that exposure to metal dusts and fumes leads to an increased risk of oesophageal cancer.

Finally the condition where the squamous epithelium which normally lines the distal oesophagus is replaced by columnar epithelium (Barrett's oesophagus) is believed to result in an increased risk of oesophageal adenocarcinoma[34]. The true prevalence of this condition is unknown but a recent estimate of 7.4/1000 was based on almost 15 000 consecutive patients presenting for initial evaluation of a variety of upper gastrointestinal conditions[35]. The risk of oesophageal adenocarcinoma with Barrett's oesophagus has not been well documented since many estimates have come from studies where the presence or absence of the change in the mucosa has been made at the time of cancer diagnosis. Currently available data estimate the risk to be around 30 to 40-fold in subject's with this condition[36] although prospective studies will be required to obtain a more accurate assessment of risk.

Conclusions

In global terms, countries of the EC exhibit low rates of oesophageal cancer; the exception to this being males in France. Within the EC among men, the UK exhibits relatively high rates, and among women, the UK and Eire have rates double other EC countries. The rates of oesophageal cancer have been increasing during the previous 40 years in both men and women in the UK, although there may have been a greater increase in adenocarcinoma compared with squamous cell carcinoma. The reasons for such increases in the UK are not clear, especially since the aetiological factors related specifically to adenocarcinoma of the oesophagus and oesophago-gastric junction have been little studied. While tobacco and alcohol are known to be important factors in the aetiology of oesophageal cancer, changes in the consumption of such agents cannot be related well to changes in mortality from the disease[37], and it may be that previously considered less important factors such as nutrition and the interaction of nutrition with tobacco and alcohol should be the focus of future studies of oesophageal cancer in Europe.

References

1 Parkin M, Muir CS, Wheelan SL, Gao Y-T, Ferlay J, Powell J, eds. *Cancer Incidence in Five Continents*, Vol. VI (IARC Scientific Publication No. 120). Lyons: International Agency for Research On Cancer, 1992

2 Jensen OM, Esteve J, Moller H, Renard H. Cancer in the European Community and its Member States. *Eur J Cancer* 1990;**26**:1167-256

3 Day NE, Munoz N. Esophagus. In: Schottenfeld D, Fraumeni JF, eds. *Cancer Epidemiology and Prevention*. Philadelphia, PA: WB Saunders, 1982:596-623

4 Smans M, Muir CS, Boyle P. *Atlas of Cancer Mortality in the European Economic Community* (IARC Scientific Publication No. 107). Lyons: International Agency for Research On Cancer, 1992

5 *Cancer Statistics: Registrations 1985*, Series MB1 No. 18, England and Wales. London: HMSO, 1985

6 World Health Organization. *Mortality Database*. Geneva: WHO, 1992

7 Doll R, Payne P, Waterhouse JAH. *Cancer Incidence in Five Continents*, Vol. 1. Berlin: Springer-Verlag, 1966

8 ICR. *Serial Mortality Tables: Neoplastic Diseases: Scotland 1911-70*. London: Division of Epidemiology, Institute of Cancer Research, 1976

9 ICR. *Serial Mortality Tables: Neoplastic Diseases: England and Wales 1911-70*. London: Division of Epidemiology, Institute of Cancer Research, 1976

10 Powell J, McConkey CC. Increasing incidence of adenocarcinoma of the gastric cardia and adjacent sites. *Br J Cancer* 1990;**62**:440-3

11 Blot WJ, Devesa SS, Kneller RW, Fraumeni JF. Rising incidence of adenocarcinoma of the esophagus and gastric cardia. *JAMA* 1991;**265**:1287-9

12 Zheng T, Mayne S, Holford TR, *et al.* Time trend and age-period-cohort effects on incidence of esophageal cancer in Connecticut 1935-89. *Cancer Causes Control* 1992;**3**:481-92

13 Negri E, La Vecchia C, Franceschi S, DeCarli A, Bruzzi P. Attributable risks for oesophageal cancer in Northern Italy. *Eur J Cancer* 1992;**28A**:1167-71

14 Tuyns AJ, Pequignot G, Abbatucci JS. Le cancer de l'oesophage en Ille-et-Vilaine en fonction des niveaux de consummation d'alcool et de tabac. Des risques qui se multiplient. *Bull Cancer* 1977;**64**:45-60

15 Young M, Russell WT. *An Investigation into the Statistics of Cancer in Different Trades and Professions*, Medical Research Council Special Report No. 99. London: HMSO

16 Schwartz D, Lellouch J, Flamant R, Denoix PF. Alcool et Cancer: Resultats d'une Enquête Retrospective. *Rev Franc Etud Clin Biol* 1962;**7**:590-604

17 Tuyns AJ. Oesophageal cancer in non-smoking drinkers and in non-drinking smokers. *Int J Cancer* 1983;**32**:443-4

18 La Vecchia C, Negri E. The role of alcohol in oesophageal cancer in non-smokers, and of tobacco in non-drinkers. *Int J Cancer* 1989;**43**:784-5

19 International Agency for Research On Cancer. Monographs on the evaluation of the carcinogenic risk of chemicals to humans. *Alcohol Drinking*, Vol 44. Lyons: IARC, 1988

20 De Stefani E, Barrios E, Fierro L. Black (air-cured) and blond (flue-cured) tobacco and cancer risk III: oesophageal cancer. *Eur J Cancer* 1993;**29A**:763-6

21 International Agency for Research on Cancer. Monographs on the evaluation of the carcinogenic risk of chemicals to humans. *Tobacco Smoking*, Vol 38. Lyons: IARC, 1986

22 Staszewski J. Cancer of the upper alimentary tract and larynx in Poland and in Polish-born Americans. *Br J Cancer* 1974;**29**:389-99

23 Wang HH, Antonioli DA, Goldman H. Comparative features of esophageal and gastric adenocarcinomas: Recent changes in type and frequency. *Hum Path* 1986;**17**:482-7

24 Wu-Williams AH, Yu MC, Mack TM. Lifestyle, workplace and stomach cancer by subsite in young men of Los Angeles county. *Cancer Res* 1990;**50**:2569-76

25 MacDonald WC, MacDonald JB. Adenocarcinoma of the esophagus and/or gastric cardia. *Cancer* 1987;**60**:1094-8

26 Li J-Y, Ershow AG, Chen Z-J, *et al.* A case-control study of cancer of the esophagus and gastric cardia in Linxian. *Int J Cancer* 1989;**43**:755-61

27 Gray JR, Coldman J, MacDonald WC. Cigarette and alcohol use in patients with adenocarcinoma of the gastric cardia and lower esophagus. *Cancer* 1992;**69**:2227-31

28 Larsson L-G, Sandstrom A, Westling P. Relationship of Plummer-Vinson disease to cancer of the upper alimentary tract in Sweden. *Cancer Res* 1975;**35**:3308-16

29 Ahlbom HE. Simple achlorhydric anaemia, Plummer-Vinson syndrome and carcinoma of the mouth, pharynx and oesophagus in women. *BMJ* 1936;**2**:331-3

30 Wynder EL, Hultberg S, Jacobsen F, Bross JB. Environmental factors in cancer of the upper alimentary tract: a Swedish study with special references to Plummer-Vinson (Paterson-Kelly) syndrome. *Cancer* 1957;**10**:470-82

31 Hormozdiari H, Day NE, Aramesh B, Mahboubi E. Dietary factors and esophageal cancer in the Caspian Littoral in Iran. *Cancer Res* 1975;**35**:3493-8

32 Chen F, Cole P, Mi Z, Xing L. Dietary trace elements and esophageal cancer mortality in Shanxi, China. *Epidemiology* 1992;**3**:402-6

33 Kaminski R, Geissert KS, Dacey E. Mortality analysis of plumbers and pipefitters. *J Occup Med* 1980;**22**:183-9

34 Cameron AJ, Ott BJ, Payne WS. The incidence of adenocarcinoma in columnar-lined (Barrett's) esophagus. *N Engl J Med* 1985;**313**:857-9

35 Gruppo Operativo Per Lo Studio Delle Precancerosi Dell'Esopfago (GOSPE). Barrett's Esophagus: Epidemiological and Clinical Results of a MultiCentric Survey. *Int J Cancer* 1991;**48**:364-8

36 Speckler SJ, Goyal RK. Barrett's esophagus. *N Engl J Med* 1986;**315**:362-71

37 Cheng KK, Day NE, Davies TW. Oesophageal cancer mortality in Europe: paradoxical time trend in relation to smoking and drinking. *Br J Cancer* 1992;**65**:613-17

A full list of references may be obtained from the authors.

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