29. Kaizer L, Boyd NF, Kriukov V, Tritchler D. Fish consumption and breast cancer risk: an ecological study. *Nutr Cancer* 1989, **12**, 61–68.
30. Hirayama T. Epidemiology of breast cancer with special reference to the role of diet. *Prev Med* 1978, 7, 173–195.
31. Jellum E, Andersen Aa, Ørjasæter H, Foss OP, Theodorsen L, Lund-Larsen P. The Janus serum bank and early detection of cancer. *Biochem Clin* 1987, **11**, 191–195.
32. Jellum E, Andersen Aa, Lund-Larsen P, Theodorsen L, Ørjasæter H. The Janus serum bank. The science of the total environment 1991. Accepted for publication.
33. Bjartveit K, Foss OP, Gjervig T, Lund-Larsen PG. The cardiovascular study in Norwegian counties. Background and organization. *Acta Med Scand* 1979, Suppl. No. 634.
34. Bønaa KH, Bjerve KS, Straume B, Gram IT, Thelle D. Effect of eicosapentaenoic and docosahexaenoic acids on blood pressure in hypertension. *N Engl J Med* 1990, **322**, 795–801.
35. Rothman KJ. *Modern Epidemiology*. Boston, Little, Brown & Company, 1986.
36. Dougherty RM, Galli C, Ferro-Luzzi A, Iacono JM. Lipid and phospholipid fatty acid composition of plasma, red blood cells, and platelets and how they are affected by dietary lipids: a study of normal subjects from Italy, Finland, and the USA. *Am J Clin Nutr* 1987, **45**, 443–455.
37. Fønnebø V, Helseth A. Cancer incidence in Norwegian Seventh-Day adventists 1961 to 1986. Is the cancer–life-style association overestimated? *Cancer* 1991, **68**, 666–671.
38. Frankel EN. Lipid oxidation. *Prog Lipid Res* 1980, **19**, 1–22.
39. Quinn D, Shiral K, Jackson RL. Lipoprotein lipase: mechanism of action and the role in lipoprotein metabolism. *Prog Lipid Res* 1982, 22, 35–78.
40. Vogel WC, Bierman EL. Correlation between post-heparin lipase and phospholipase activities in human plasma. *Lipids* 1969, 5, 385–391.
41. Dolecek TA, Grandits G. Dietary polyunsaturated fatty acids and mortality in the Multiple Risk Factor Intervention Trial (MRFIT). In: Simopoulos AP, Kifer RR, Martin RE, Barlow SM, eds. Health effects of omega-3 polyunsaturated fatty acids in seafoods. *World Rev Nutr Diet*, Basel, Karger 1991, **66**, 205–215.

Acknowledgements—This research has been financially supported by the Norwegian Cancer Society, the Norwegian Research Council for Science and the Humanities, the Martin Flatner's Legacy and the Odd Fellow Medical Research Fund.

Eur J Cancer, Vol. 29A, No. 4, pp. 538–544, 1993.
Printed in Great Britain

0964–1947/93 $6.00 + 0.00

Urban–Rural Variation in Cancer Incidence in Denmark 1943–1987

Søren Friis and Hans H. Storm

Urban and rural cancer incidence in Denmark in 1943–1987 was analysed. A consistent urban excess was found for all sites combined for individuals of each sex, irrespective of age at diagnosis. The capital:rural incidence ratio was 1.42 for men and 1.25 for women, and these ratios were not affected to any great extent using another definition of urban areas. Urban:rural ratios were highest for cancers of the respiratory, urinary and upper digestive tracts. The differences cannot be explained by tobacco and alcohol consumption alone. Other risk factors linked to urbanisation may contribute importantly to the "urban factor", and analytical studies of data at an individual level are required to establish their relative importance. Our findings contradict the generally accepted view that there is no urban–rural difference in cancer incidence in the relatively small, homogeneous population of Denmark.
Eur J Cancer, Vol. 29A, No. 4, pp. 538–544, 1993.

INTRODUCTION

IN MOST countries for which data are available, clear differences in cancer incidence exist between urban and rural populations [1]. In general, cancer is more frequent in urban populations, and morbidity and mortality rates for many cancer types increase concurrently with increasing degrees of urbanisation. Only a few cancers (e.g. lip and stomach) have been reported to occur at higher rates in rural areas.

Urban–rural variations in cancer incidence have been studied since the phenomenon was first observed, in the 1930s, as the basis for hypotheses on the aetiology of cancer. These are that environmental changes and different social and cultural behavioural patterns linked to urbanisation are responsible for the excess risk of developing cancer in urban areas. Difficulties still exist, however, in disentangling the specific aetiological factors responsible for variations in cancer occurrence between urban and rural populations.

In Denmark, urban–rural differences in cancer incidence were explored systematically at the Danish Cancer Registry until 1977 [2]. It was discontinued when annual incidence reports emerged, due both to difficulties in achieving comparable data with other countries for reasons outlined by Roginski [3] and to the generally accepted view that Denmark of today is a fairly uniform area in terms of urbanisation. Moreover, the effects of urban life would be expected to be lessened due to higher mobility of the population, including migration of healthy people from rural to urban areas. In order to test whether these assumptions are true, we considered it of interest to analyse the trends in urban–rural differences in cancer incidence in Denmark for the entire period for which incidence data are

Correspondence to H.H. Storm.
The authors are at the Danish Cancer Registry, Institute of Cancer Epidemiology, Danish Cancer Society, Rosenvængets Hovedvej 35, Box 839, DK-2100 København Ø, Denmark.
Revised 30 Sep. 1992; accepted 20 Oct. 1992.

available (1943–1987), using different ways of defining urban areas.

MATERIALS AND METHODS

National data on cancer incidence were analysed by administrative area (counties, municipalities), as registered by the Danish Cancer Registry since 1943. The Danish Cancer Registry is a population-based, nationwide cancer registry; although reporting was voluntary until 1987, it is regarded as virtually complete [4]. Cancers are classified according to a modified version of the 7th revision of the International Classification of Diseases (ICD-7) [4], and since 1978 by automatic conversion from the International Classification of Diseases for Oncology (ICD-O) of the WHO. Further details on reported tumours are recorded, which include basis of diagnosis, of which the most valid is histological verification, and the poorest is from death certificate only. Place of residence at the time of diagnosis is obtained by linkage to official registers (1943–1967 Municipality Register, 1968–1987 Central Population Register).

Four major subdivisions of the country, i.e. "capital", "capital suburbs", "provincial towns" and "rural areas", were used until a municipality reform in 1970 redefined and combined several municipalities. The capital area, however, has remained unchanged since 1943 and corresponds to three municipalities, Copenhagen, Frederiksberg and Gentofte, of which Copenhagen is by far the largest. The rural areas in our study were identified by code in the Central Statistical Bureau of Denmark and correspond with municipalities with a population of fewer than 10 000 in built-up areas. The total population in the two areas has remained relatively stable over the given period, at just less than 1 million in the capital and about 2 million in the rural areas. Only the provincial towns and the capital suburbs have changed significantly, due both to population growth and to the municipality reform, and this makes comparisons over time dubious.

In order to validate the concept that "urban areas" could be represented by the capital alone, another category of urban area was formed for the period 1983–1987. This category, "large cities", was defined as municipalities (including Copenhagen) with populations of more than 100 000. The sum total of the population of large cities is around 1.7 million.

Age-standardised incidence rates (World Standard) [1] for 5-year calendar periods in the different geographical subdivisions were used as the basis for the analysis. The ratios of age-standardised incidence rates for grouped sites for the period 1983–1987 were calculated for the capital and rural areas (urban:rural ratio) and for the capital and large cities. Confidence limits for urban:rural ratios were calculated using an approximate variance formula for standardised rate ratios [5]. An international comparison of urban:rural ratios was performed using the latest data from cancer registries that provide information on urban–rural variations in cancer incidence [1].

In order to estimate the effects of age, calendar time and birth cohort, trends in the age-specific incidence of cancers at all sites and of lung cancer with cohort year of birth were plotted for selected age groups in the capital and in rural areas.

RESULTS

The trends in cancer incidence 1943–1987 by geographical area and sex were analysed for each site. Figure 1 shows time trends in the age-standardised incidence of cancers at all sites (except non-melanoma skin cancer) and of lung cancer in the capital and rural areas. Even if the above changes in population made comparison over time difficult to interpret, trends in the capital suburbs and provincial towns (not shown) took up a position intermediate to those of the capital and rural areas.

Throughout the period a clear difference in cancer incidence was observed between the capital and rural areas for cancers at all sites combined, although the urban excess decreased slightly over time. A similar pattern was noticed for cancer of the female breast, and for cancers of the prostate, testis and digestive organs in men (not presented).

The lung cancer incidence in women increased steeply in both the capital and rural areas, resulting in a consistent urban–rural difference throughout the period. Until 1965–1970, a similar pattern was seen for lung cancer among men; thereafter, the incidence rates levelled off and even decreased in the capital, diminishing the urban–rural difference. Cancers of the urinary and upper respiratory tracts exhibited similar trends to that of lung cancer (not presented).

For cancer of the cervix uteri, a large urban–rural difference was observed until 1965–1970. Later a decrease in incidence rates occurred, mainly in urban areas, which removed the urban–rural difference (Fig. 2).

No or only minimal differences in cancer incidence were observed between the capital and rural areas for cancers of lymphatic and haematopoietic tissues, corpus uteri, ovary, eye, thyroid, endocrine glands, bone, connective tissue, brain and nervous tissue, melanoma of skin, and cancers of the lip and digestive organs in women. Cancer of the lip in men is the only site for which consistently higher rates were seen in rural areas (Fig. 2).

The site-specific cancer incidence in urban and rural areas in the period 1983–1987 is shown in Table 1. Interestingly, differences between urbanised and rural areas were apparent and of the same magnitude, using either the capital or large cities as the basis for comparison.

Table 2 summarises the findings by organ groups. Cancer occurred over 40% more frequently in men and 25% more frequently in women in the capital than in rural areas. The capital:rural ratio was highest for cancers of the buccal cavity and pharynx and of the respiratory and urinary tracts. High ratios were also seen for cancer of the digestive organs in men, female breast, male genital organs, and skin in men and women. The confidence intervals for most of the capital:rural ratios contained values above 1.0; only cancer of the lymphatic and haematopoietic tissue exhibited ratios below 1.0.

Only minor differences in cancer incidence were observed between the capital and large cities (Tables 1 and 2); however, the incidence in the large cities was generally slightly lower than that of the capital.

By plotting age-specific incidence rates by year of birth (Fig. 3), the effects of calendar time, birth and age were visualised. A clear excess risk for cancer in urban areas was seen for individuals of each sex and all ages, except for the youngest age group. For lung cancer in men, the urban–rural difference diminished in successive cohorts born after 1890, as incidence rates levelled off and even declined in the capital while they were still increasing in rural areas. For older women, the age-specific incidence rates of lung cancer increased in both the capital and in rural areas, resulting in a relatively stable urban–rural difference.

DISCUSSION

Contrary to the generally accepted view that the urban–rural difference in cancer incidence in Denmark would diminish

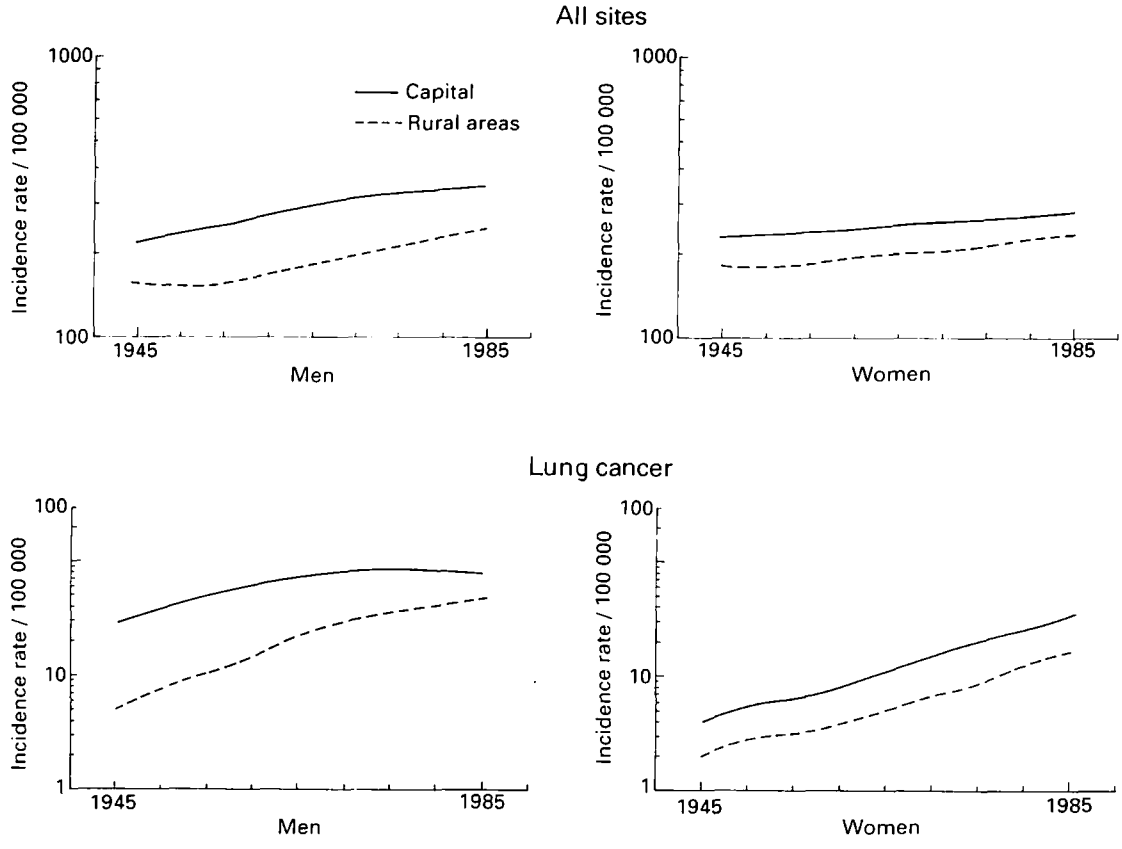

Fig. 1. Trends in age-standardised (World Standard Population) incidence of cancers at all sites (except non-melanoma skin cancer) and lung cancer in the capital and rural areas, 1943–1987.

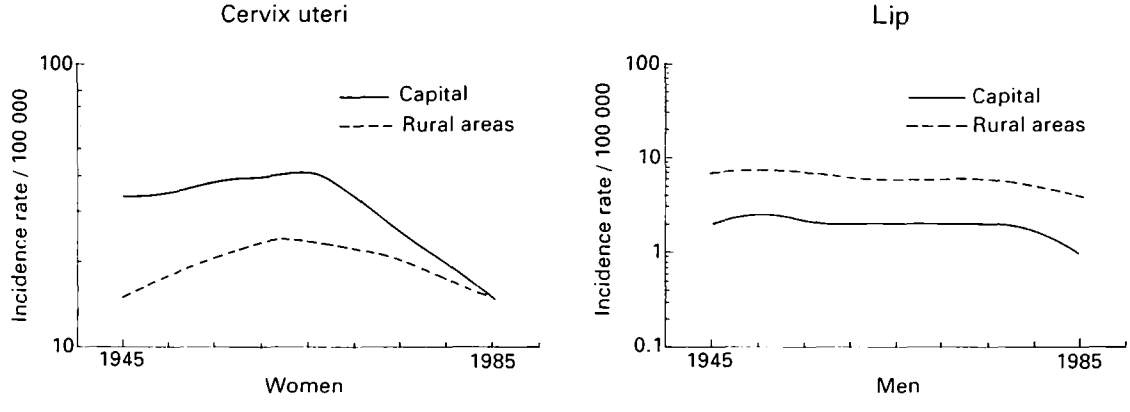

Fig. 2. Trends in age-standardised (World Standard Population) incidence of cancers of the cervix uteri in women and lip in men in the capital and rural areas, 1943–1987.

gradually, we found a consistent range of differences throughout the period 1943–1987, as illustrated in Fig. 1. Moreover, when comparing urban–rural ratios for all sites and for lung cancer in selected registries (Table 3), the urban–rural gradient in Denmark appears to be among the highest internationally; however, comparisons between countries with different medical facilities and cancer registration (completeness, accuracy) must be made with some reservations. Furthermore, interpretation is difficult because of varying definitions between countries of the terms urban and rural [3]; some of the municipalities classified as rural in this study would have been classified as semi-urban using the Finnish definition [6]. Ideally, defined categories representing degrees of urbanisation, identified by features such as population density, industrialisation and range of occupations, should enable more conclusive international comparisons to be made [3]. No clear definition of urban areas exists in Denmark but the excess risk of developing cancer in urban areas is not confined to the capital, as the incidence rates were not affected to any great extent by inclusion of other municipalities in the category "large cities" (see Tables 1 and 2).

In the present study, some of the urban–rural variation in cancer incidence might be due to geographical differences in the

Table 1. Numbers of cases and age-standardised incidence rates by site and geographical area in Denmark, 1983–1987*

ICD 7th Revision	Site	Men					Women				
		Denmark		Capital	Large Cities	Rural Areas	Denmark		Capital	Large Cities	Rural Areas
		Cases	Rate	Rate	Rate	Rate	Cases	Rate	Rate	Rate	Rate
140	Lip	539	2.8	0.9	1.7	3.8	66	0.3	0.1	0.1	0.3
141	Tongue	178	1.1	2.6	1.7	0.6	124	0.5	0.9	0.6	0.4
142	Salivary glands	117	0.6	1.0	0.8	0.5	113	0.5	0.5	0.6	0.6
143–44	Mouth	377	2.1	4.0	3.0	1.4	272	1.1	1.8	1.4	0.8
145–48	Pharynx	459	2.6	5.8	4.0	1.5	187	1.0	2.2	1.5	0.6
150	Oesophagus	742	3.8	7.2	5.3	2.8	346	1.2	1.9	1.6	0.9
151	Stomach	2577	12.3	13.0	13.1	12.2	1704	5.7	7.2	6.2	5.4
152	Small intestine	168	0.8	1.0	1.1	0.5	150	0.6	0.6	0.6	0.5
153	Colon, including rectosigmoid	4568	21.7	25.5	24.3	19.3	5681	20.4	20.4	20.4	19.5
154	Rectum, excluding anus	3173	15.6	16.8	16.5	14.7	2445	9.4	9.3	9.8	9.4
155.0	Liver	711	3.5	7.3	5.4	2.4	469	1.8	2.4	2.1	1.3
155.1	Gallbladder, biliary passages, ampulla of Vater	385	1.8	2.4	2.3	1.5	838	3.0	2.9	2.9	3.1
156	Liver, not specified as primary	467	2.3	1.9	2.1	2.4	468	1.6	1.2	1.5	1.9
157	Pancreas	1861	9.1	11.5	11.0	8.1	1856	6.7	8.5	7.4	6.0
158–59	Peritoneum and other digestive organs	193	1.1	1.1	1.3	1.1	208	0.8	0.9	0.7	0.9
160	Nasal cavities and sinuses	166	0.9	1.0	1.0	0.8	88	0.4	0.3	0.5	0.4
161	Larynx	1006	5.5	8.7	7.3	4.1	226	1.2	1.6	1.7	0.8
162	Lung, primary, trachea	11487	58.3	79.9	73.6	47.3	4937	22.9	33.9	30.0	16.4
162.2	Pleura	274	1.4	2.8	2.5	0.6	113	0.4	0.8	0.6	0.4
163	Lung, not specified as primary	20	0.1	0.1	0.1	0.1	7	0.0	0.0	0.0	0.0
164	Mediastinum	60	0.4	0.7	0.4	0.3	45	0.2	0.2	0.2	0.2
170	Breast	91	0.5	0.6	0.5	0.6	13595	68.4	73.8	75.3	62.5
171	Cervix uteri	0	0.0	0.0	0.0	0.0	2731	15.6	14.7	16.6	14.6
172	Corpus uteri	0	0.0	0.0	0.0	0.0	3198	15.3	15.2	16.1	14.6
173–4	Uterus, other and unspecified parts	0	0.0	0.0	0.0	0.0	155	0.7	0.8	0.6	0.8
175	Ovary, fallopian tube and broad ligament	0	0.0	0.0	0.0	0.0	3061	14.8	15.9	16.0	14.1
176	Other and unspecified female genital organs	0	0.0	0.0	0.0	0.0	562	2.2	2.4	2.3	2.2
177	Prostate	6923	29.8	34.6	33.4	27.0	0	0.0	0.0	0.0	0.0
178	Testis	1189	8.4	8.1	9.1	7.8	0	0.0	0.0	0.0	0.0
179	Other and unspecified male genital organs	220	1.1	1.2	1.2	1.1	0	0.0	0.0	0.0	0.0
180	Kidney	1916	10.2	11.9	13.0	8.0	1553	6.6	7.4	7.3	5.7
181	Urinary bladder, including papilloma	5358	26.5	34.4	33.4	21.5	1734	6.8	8.8	8.8	5.4
190	Melanoma of skin	1238	7.4	8.4	8.9	6.4	1753	9.7	8.9	9.7	9.4
191	Other skin	8675	44.1	52.0	53.2	35.4	7956	33.2	40.9	40.4	25.4
192	Eye and lachrymal glands	146	1.0	1.0	0.9	1.0	137	0.8	1.0	0.9	0.7
193	Brain and nervous system	1663	10.7	11.8	11.8	9.8	1736	10.2	9.4	11.5	9.4
194	Thyroid	171	1.0	1.1	1.1	0.9	382	2.0	1.8	2.2	1.9
195	Endocrine glands	79	0.5	0.9	0.6	0.6	69	0.4	0.4	0.5	0.3
196	Bone	110	0.8	0.8	0.8	0.8	76	0.5	1.0	0.7	0.4
197	Connective tissue	194	1.1	1.5	1.2	1.1	141	0.8	0.6	0.7	0.8
198	Metastases	857	4.4	6.0	4.9	4.0	834	3.4	4.0	3.4	3.3
199	Other and unspecified sites	646	3.1	4.1	3.4	2.8	907	3.0	3.8	3.0	3.0
200, 202	Non-Hodgkin lymphoma	1356	7.6	8.0	8.0	7.7	1266	5.5	4.8	5.7	5.9
201	Hodgkin's disease	365	2.5	2.8	2.7	2.4	234	1.5	1.5	1.7	1.3
203	Multiple myeloma	634	3.0	2.2	2.9	3.4	604	2.3	1.7	2.2	2.4
204	Leukaemia	1828	10.3	9.9	10.5	10.3	1343	6.7	7.0	6.9	6.0
205	Mycosis fungoides	38	0.2	0.1	0.2	0.3	20	0.1	0.2	0.1	0.1
140–205	All sites	63225	322.0	396.6	380.2	278.9	64390	290.2	323.6	323.0	260.0

*Age-standardised (World Standard Population) incidence rate per 100 000.

Table 2. Ratio of age-standardised incidence rates of cancers at grouped sites, for urban and rural areas in Denmark, 1983–1987*

ICD 7th Revision	Grouped sites	Capital:rural ratio (95% CI†)		Capital:city‡ ratio	
		Men	Women	Men	Women
140–148	Buccal cavity and pharynx	1.83 (1.53–2.20)	2.03 (1.52–2.71)	1.28	1.31
150–159	Digestive organs and peritoneum	1.35 (1.27–1.43)	1.13 (1.07–1.20)	1.06	1.04
160–164	Respiratory system	1.75 (1.64–1.86)	2.02 (1.81–2.25)	1.09	1.12
170	Breast	1.00 (0.57–2.02)	1.18 (1.11–1.26)	1.20	0.98
171–176	Female genital organs	—	1.06 (0.99–1.14)	—	0.95
177–179	Male genital organs	1.22 (1.14–1.32)	—	1.00	—
180–181	Urinary system	1.57 (1.44–1.70)	1.46 (1.28–1.67)	0.99	1.01
190–191	Skin	1.44 (1.34–1.55)	1.43 (1.32–1.55)	0.99	0.99
192–197	Other specified sites§	1.20 (1.03–1.42)	1.05 (0.90–1.22)	1.04	0.86
198–199	Secondary and unspecified sites¶	1.49 (1.25–1.79)	1.24 (1.01–1.54)	1.22	1.22
200–205	Lymphatic and haematopoietic tissue	0.95 (0.85–1.07)	0.97 (0.85–1.11)	0.95	0.92
140–205	All sites	1.42 (1.38–1.46)	1.25 (1.22–1.29)	1.04	1.01

*World Standard Population.
†Confidence intervals.
‡Large cities (see text).
§Eye and lachrymal glands, brain and nervous system, thyroid, endocrine glands, bone, connective tissue.
¶Metastases, other and unspecified sites.

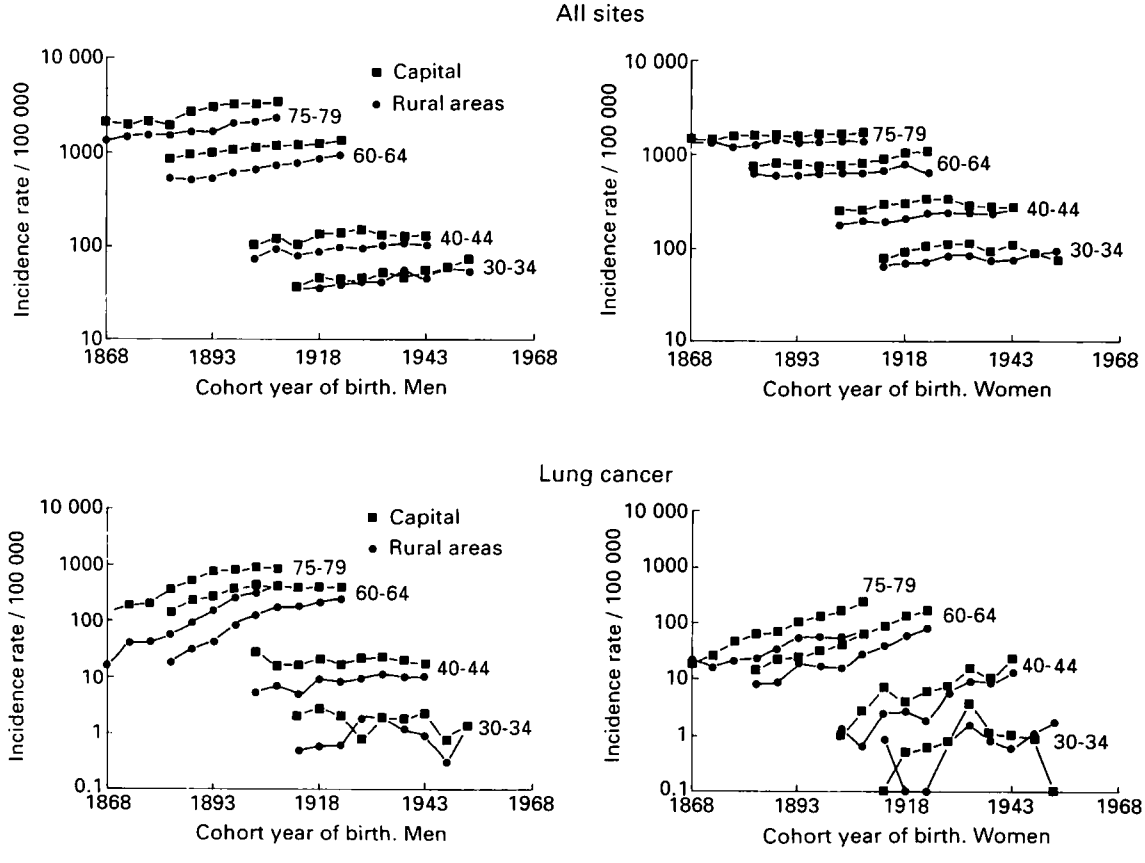

Fig. 3. Trends in age-specific incidence of cancers at all sites (except non-melanoma skin cancer) and lung cancer in selected age groups in Denmark 1943–1987 by cohort year of birth.

Table 3. Urban:rural ratio of age-standardised incidence rates for cancers at all sites (except non-melanoma skin cancer) and lung cancer in selected registries, 1978–1982†*

	Urban:rural ratio			
	All sites		Lung	
Registry	Men	Women	Men	Women
Denmark	1.45	1.21	2.06	1.97
Australia, New South Wales	1.17	1.11	1.19	1.47
Czechoslovakia, Slovakia	1.08	1.34	0.97	1.45
France, Calvados	1.02	1.01	1.16	1.17
France, Doubs	1.11	1.13	1.42	1.65
Germany, Saarland	1.15	1.17	1.23	1.28
Hungary, Szabolcs	1.12	1.39	1.21	1.66
Japan, Miyagi	1.03	1.14	1.09	1.14
Norway	1.21	1.17	1.61	1.85
Switzerland, Vaud	1.12	1.09	1.13	1.55
U.K., England and Wales	1.16	1.05	1.33	1.30

*World Standard Population.
†From reference [1].

availability, quality and use of medical facilities [7]. Although it is difficult to quantify, the "diagnostic intensity" of a given area can be estimated partly on the basis of the percentage of all cases that have been diagnosed by histological examination and from death certificate only [3]. In Denmark, the percentage of all cases with histological verification was markedly higher in urban than in rural areas during the period 1943–1972 (Table 4), whereas the percentage of cases registered only as a result of death certification was highest in rural areas. This implies that the recorded incidence rates in Denmark were probably too low in rural areas during that period. In the period 1973–1987, however, there was only a slight tendency for the percentage of cases with histological confirmation to be higher in urban than in rural areas, and there was practically no difference in the proportion of cases verified from death certificate alone. Neither diagnostic intensity, reporting differences nor misclassification

Table 4. Percentages of cases verified histologically (HV) and from death certificate only (DCO) by geographical area in Denmark, 1943–1987*

	Men				Women			
	Capital		Rural areas		Capital		Rural areas	
Period	HV	DCO	HV	DCO	HV	DCO	HV	DCO
1943–1947	63	9	44	23	68	12	51	26
1948–1952	73	7	53	17	78	7	61	19
1953–1957	81	5	60	14	83	5	66	16
1958–1962	85	3	69	10	86	3	75	11
1963–1967	88	3	75	8	90	2	80	8
1968–1972	91	2	80	6	92	2	84	6
1973–1977	89	4	83	6	89	4	85	6
1978–1982	93	1	90	1	93	1	91	1
1983–1987	92	2	90	2	92	2	92	1

*Percentage of all methods; autopsy without histology, clinical examination alone and unknown methods not shown.

can explain the urban–rural differences in cancer incidence observed in Denmark. Doll [8] concluded that these diagnostic or recording artifacts are generally unlikely to have had a major impact on urban–rural variations in developed countries in the past few decades.

Other potential sources of bias could be migration of healthy people to rural areas, misclassification of urbanisation, geographical differences in reporting to the registry and genetic differences in susceptibility. Although these sources undoubtedly exist, they are considered to be of minor importance in Denmark, and cannot explain the 25–40% difference in cancer risk.

The majority of human cancers are caused by environmental factors [9], which are likely to differ in urban and rural areas. The term "environment" is used here in its widest sense and includes life-style factors such as tobacco smoking, alcohol consumption, sexual habits, patterns of reproduction, exposure to ultraviolet light, diet, general exposures to air and water pollution, and occupational exposures. It has been argued that geographical variations in tobacco and alcohol consumption are largely responsible for urban–rural differences in cancer morbidity. Indeed, in Denmark, as well as in other countries, the highest per-capita rates of cigarette and alcohol consumption are found in urban areas, and there is a good correspondence between time trends for lung cancer and the pattern of smoking in men and women some 10–20 years earlier [10]. Furthermore, urban–rural differences in Denmark (Tables 1 and 2) were generally most pronounced for cancers accepted by the International Agency for Research on Cancer as being caused by tobacco and alcohol consumption, i.e. cancers of the respiratory, urinary and upper digestive tracts, liver and pancreas [11]. Interestingly, however, and in accordance with findings in other studies [8], an urban excess was also observed for cancer types not linked to tobacco and alcohol consumption, such as cancers of the colon, ovary and prostate. When cancer types related to tobacco and alcohol consumption were excluded, significant urban:rural ratios still existed for both men (1.25) and women (1.16). This finding is in line with those of studies in Sweden, where about 25% of cancers were associated with urbanisation variables other than smoking [7, 12].

The decreasing incidence rates of the cervix uteri mainly in urban areas are somewhat puzzling. They might be due in part to the effects of organised screening programmes for cervical cancer, which started in the capital in the 1960s and have been generally more widespread in urban areas [13].

Many studies investigating urban–rural variations in cancer morbidity have concentrated on lung cancer, with particular emphasis on air pollution as a potential risk factor. Although a vast number of carcinogens have been found in the urban atmosphere [14], and two recent case–control studies showed an association with general air pollution [15, 16], as did a Danish study [17], pollutants from tobacco smoking and perhaps industrial processes are still considered to be much more important in the aetiology of respiratory cancer.

A study by the American Cancer Society of 500 000 men provided no firm evidence to support the hypothesis that general urban air pollution increases the risk of lung cancer [18], and the role of air pollution in the development of cancers other than of the lung is at present impossible to assess [19].

Occupational exposures in the form of industrial emissions, particularly in iron and steel foundries, have been shown to increase the risk for lung cancer [20]. Although industrial districts are situated mainly in urban areas, the contribution of

this risk factor to urban–rural variations in lung cancer is probably minimal [6, 21].

Other studies of cancer morbidity in urban areas have focused on all cancers taken together or on cancers other than lung cancer [6, 21, 22]. As in our study, urban–rural differences in cancer rates were observed for all cancers as well as for cancers at specific sites, although the effects were generally less pronounced than for lung cancer. The urban–rural gradient was estimated to arise primarily from differences in social class—generally considered to be a broad indicator of life-style practices.

The potential contribution of indoor air pollution, including environmental tobacco smoking and radon, to the excess cancer risk in urban areas is the subject of much controversy [23]; in general, however, it is considered to have a minor impact on urban–rural variations.

The influence of diet and sexual habits on urban–rural differences has been examined in studies of the Mormon population in Utah, U.S.A. [24]. Virtually no urban–rural gradient was found in the incidence of cancers at all sites, and the differences for cancers at specific sites were negligible. Furthermore, the absence of any urban–rural gradient for tobacco-related cancers seems to counter the implication that air pollution is a causal factor in lung cancer.

Overall, it is difficult to interpret the epidemiological evidence of urban–rural differences in cancer incidence. Descriptive and correlation studies published in the literature provide only hypotheses about which factors are of possible aetiological importance. In most analytical studies, control for confounding was inadequate, partly because information was unavailable or of insufficient detail.

The findings of our study should be interpreted with caution, like those of any other ecological study. Clear excess risks associated with living in urban areas were found, however, for several types of cancer, even in younger age groups. Consequently, although the population of Denmark is relatively homogeneous, with a high standard of living in both urban and rural areas, differences in aetiological factors of importance for the development of cancer prevail, as the urban–rural gradient can be only partly explained by known risk factors such as tobacco and alcohol consumption.

Air pollution is the only "urban factor" consistently mentioned in the literature, although its contribution to the urban excess of cancer appears to be of limited importance. Analytical studies are required, e.g. detailed case–control and cohort studies, with data at the individual level on tobacco and alcohol consumption, dietary habits, occupation (including residence), outdoor and indoor air pollution and social class, in order to establish their relative contributions to the "urban factor".

1. Muir CS, Waterhouse JAH, Mack T, Powell J, Whelan S, eds. *Cancer Incidence in Five Continents*, Vol. V. IARC Scientific Publications No. 88. Lyon, International Agency for Research on Cancer, 1987.
2. Clemmesen J. Statistical studies in the aetiology of malignant neoplasms, Vol. V. *Acta Pathol Microbiol Scand* 1977, Suppl. 261.
3. Roginski C. Comparison of urban and rural incidence data. In: Muir C, Waterhouse J, Mack T, Powell J, Whelan S, eds. *Cancer Incidence in Five Continents*, Vol V. IARC Scientific Publications No. 88, Lyon, International Agency for Research on Cancer, 1987.
4. Storm HH. The Danish Cancer Registry, a self-reporting national cancer registration system with elements of active data collection. In: Jensen OM, Parkin DM, MacLennan R, Muir CS, Skeet RG, eds. *Cancer Registration Principles and Methods*. IARC Scientific Publications No. 95, Lyon, International Agency for Research on Cancer, 1991, 220–236.
5. Flanders WD. Approximate variance formulas for standardized rate ratios. *J Chron Dis* 1984, **37**, 449–453.
6. Teppo L, Pukkala E, Hakama E, Hakulinen T, Herva T, Saxén A. Way of life and cancer incidence in Finland. *Scand J Soc Med* 1980, Suppl. 19.
7. Ehrenberg L, von Bahr B, Ekman G. Register analysis of measures of urbanization and cancer incidence in Sweden. *Environ Int* 1985, **11**, 393–399.
8. Doll R. Urban and rural factors in the aetiology of cancer. *Int J Cancer* 1991, **47**, 803–810.
9. Doll R, Peto R. The causes of cancer: quantitative estimates of avoidable risks of cancer in the United States today. *J Natl Cancer Inst* 1981, **66**, 1191–1308.
10. Jensen OM. International and urban-rural variation in cancer. In: Clegg EJ, Garlick JP, eds. *Disease and Urbanization*. London, Symposia of the Society for the Study of Human Biology, 1980, **20**, 107–125.
11. Tomatis L, ed. *Cancer: Causes, Occurrence and Control*. IARC Scientific Publications No. 100, Lyon, International Agency for Research on Cancer, 1990.
12. Ehrenberg L, Ekman G, Svensson Å. Epidemiological studies of geographic variations of cancer incidence in Sweden. *Acta Oncol* 1990, **29**, 961–969.
13. Lynge E, Madsen M, Engholm G. Effect of organized screening on incidence and mortality of cervical cancer in Denmark. *Cancer Res* 1989, **49**, 2157–2160.
14. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Suppl. 7. *Overall Evaluations of Carcinogenicity: An Updating of IARC Monographs Volumes* 1–42. Lyon, International Agency for Research on Cancer, 1987.
15. Jedrychowski W, Becher H, Wahrendorf J, Basa-Cierpialek Z. A case–control study of lung cancer with special reference to the effect of air pollution in Poland. *J Epidemiol Community Health* 1990, **44**, 114–120.
16. Xu ZY, Blot WJ, Xiao HP, *et al.* Smoking, air pollution, and the high rates of lung cancer in Shenyang, China. *J Natl Cancer Inst* 1989, **81**, 1800–1806.
17. Borch-Johnsen K. Urbanization and cancer of the lung. A quantitative and qualitative assessment of the urban factor. *Ugeskr Laeg* 1982, **144**, 1713–1718 (in Danish).
18. Hammond EC, Garfinkel L. General air pollution and cancer in the United States. *Prev Med* 1980, **9**, 206–211.
19. Pershagen G, Simonato L. Epidemiological evidence on air pollution and cancer. In: Tomatis L, ed. *Air Pollution and Human Cancer, European School of Oncology Monographs*. Berlin, Springer, 1990, 63–72.
20. Becher H, Jedrychowski W, Flak E, Gomola K, Wahrendorf J. Lung cancer, smoking, and employment in foundries. *Scand J Work Environ Health* 1989, **15**, 38–42.
21. Adelstein AM. Life-style in occupational cancer. *J Toxicol Environ Health* 1980, **6**, 953–962.
22. Greenberg MR. *Urbanization and Cancer Mortality. The United States Experience*, 1950–1975, *Monographs in Epidemiology and Biostatistics*. New York, Oxford University Press, 1983.
23. Sarraci R, Riboli E. Passive smoking and lung cancer: current evidence and ongoing studies at the International Agency for Research on Cancer. *Mutat Res* 1989, **222**, 117–127.
24. Lyon JL, Gardner JW, West DW. Cancer risk and life style: cancer among Mormons from 1967–1975. In: Cairns J, Lyon JL, Skolnick M, eds. *Cancer Incidence in Defined Populations, Banbury Report* 4. Cold Spring Harbor, New York, CSH Press, 1980, 3–30.