International Journal of Epidemiology

Vol. 25, No. 4
Printed in Great Britain

Urban-Rural Differences in Cancer Incidence in The Netherlands, 1989–1991

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Schouten L J (Department of Epidemiology, University of Nijmegen, PO Box 9101, 6500 HB Nijmegen, The Netherlands), Meijer H, Huveneers J A M and Kiemeney L A L M. Urban-rural differences in cancer incidence in the Netherlands, 1989–1991. *International Journal of Epidemiology* 1996; **25:** 729–736.

Background. Differences in cancer incidence have been observed between urban and rural communities for many decades. These differences have been attributed for the most part to lifestyle aspects. In Western populations, however, differences in lifestyle have diminished. This study addressed the question: For which cancer sites can differences in cancer occurrence still be demonstrated between urban and rural communities in the Netherlands?

Methods. Cancer incidence data from 1989 to 1991 inclusive, were obtained from the Netherlands Cancer Registry. Age-adjusted, site-specific incidence rates were calculated for five classes of municipalities classified by address density.

Results. With increasing urbanization, slightly higher incidence rates were observed for all cancer sites combined (rate ratio [RR] = 1.08 in males and 1.12 in females). Statistically significant RR of ≥1.4 were observed for Kaposi's sarcoma (m), mesothelioma (m), cancer of the liver (m), mouth/pharynx (m + f), oesophagus (f), larynx (f), lung (f), other respiratory organs (f), cervix (f) and Hodgkin's disease (m). Significantly lower incidence rates were found in urban areas for non-melanoma skin (m + f) and lip cancer (m).

Conclusions. In males, the urban excess of tobacco-related cancer has largely disappeared. However, urban-rural differences in cancer incidence still exist for other cancer sites and for tobacco-related cancer in females. Apparently, differences in the prevalence of lifestyle factors are still large enough to cause variation in cancer incidence.

Keywords: cancer incidence, urbanization, the Netherlands

Differences in cancer incidence have been observed between urban and rural communities for many decades.[1–7] In general, the risk of cancer is higher in urban populations. However, these differences seem to have diminished over the past few years, especially in industrialized countries.[7]

As in most other populations, urban-rural differences in cancer mortality and incidence were also reported in the Netherlands.[8,9] Hoogendoorn found higher mortality rates for cancer of all sites (males) and cancer of the lung, bladder and uterine cervix in the large cities than in the total Dutch population. In the province of Limburg, higher incidence rates were found for cancer of all sites and cancer of the respiratory tract in urban communities.[9] The power of the latter study was too small to detect any differences in cancer incidence for other sites.

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The Netherlands is a small and densely populated country. Access to health care is excellent, both in urban and rural areas. Lifestyle differences between urban and rural areas are very small.

In view of these aspects, it is doubtful whether there are still any urban-rural differences in cancer incidence in the Netherlands. An exception may be Kaposi's sarcoma, a tumour associated with the epidemic of the Acquired Immuno Deficiency Syndrome (AIDS), because this epidemic is concentrated in the larger cities.[10]

This study was performed to investigate whether there are still any differences in cancer occurrence in the Netherlands between urban and rural areas.

MATERIALS AND METHODS

Cancer incidence data from 1989 to 1991 were obtained from the nationwide population-based Netherlands Cancer Registry by 5-year age group, gender and municipality.[11,12] Malignancies were classified according to the International Classification of Diseases for Oncology, version I (ICD-O).[13] For the years 1988–1990, it

TABLE 1 *Population and average population density on 1 January 1990 and the number of newly registered cancer cases fro 1991, by address density in the Netherlands*

Class	Urbanization of municipalities	No. of inhabitants		Population density	No. of cancer
		Males N	Females N	N/km^2	Males N
1	Non-urban (<500 addresses/km^2)	1 564 549	1 532 604	164	18 607
2	Sparse (500–<1000 addresses/km^2)	1 541 670	1 548 091	349	17 561
3	Moderate (1000–<1500 addresses/km^2)	1 448 743	1 499 048	810	17 243
4	Dense (1500–<2500 addresses/km^2)	1 497 216	1 565 114	1721	18 724
5	Very dense (≥2500 addresses/km^2)	1 305 107	1 388 796	3807	18 788
	Total	7 357 285	7 533 653	439	90 923

was estimated that the cancer registry was only 3.8% incomplete.[14] The Netherlands Cancer Registry does not record basal cell carcinoma of the skin.

Information about population figures by 5-year age group, gender and municipality for 1 January 1989, 1990 and 1991 were obtained from the Dutch Central Bureau of Statistics (CBS).[15] The CBS has classified municipalities by level of urbanization according to an index based on the address density of the surroundings.[16] Address density is defined as the number of addresses within a radius of 1 kilometre of an average address in the area. For each municipality the average address density was calculated for an 'average' address. Using this index, municipalities were classified into five groups: very dense urbanization (class 5), dense urbanization (4), moderate urbanization (3), sparse urbanization (2) and no urbanization (1) (Table 1).

To study cancer incidence in relation to urbanization, analyses were performed for both sexes. Incidence rates in the five urbanization groups were age adjusted, using direct standardization to the European Standard Population.[17] This standard was chosen because it approximates the age distribution of the population of the Netherlands far better than the World Standard Population. Rate ratios (RR) were calculated by dividing the incidence rates of urbanization groups 2, 3, 4 and 5 by the rate of group 1. Age-specific RR were inspected, because heterogeneity can cause bias in the interpretation of age-standardized RR. Age appeared not to be an effect modifier. The 95% confidence intervals (95% CI) of the RR were calculated using the method described by Miettinen.[18] The slope of linear trends of age-standardized cancer incidence rates according to the level of urbanization were determined using the method described by Rothman.[19]

RESULTS

The RR for densely urbanized versus rural palities for cancer of all sites and for 30 separa sites in males and 31 sites in females are pres Figures 1 and 2. Rate ratios and an estimate o ear trend with 95% CI for all the urbanizatio compared to the rural municipalities are pres the Appendix.

In males and females, slightly higher incide were found for urban versus rural areas for can sites. In males, the RR was 1.08 (95% CI : 1. and in females, the RR was 1.12 (95% CI : 1.(In both males and females a statistically si increasing trend of standardized incidence rat observed with group of urbanization for canc sites.

An extremely large urban excess was obse Kaposi's sarcoma (males: RR = 15.97), meso (m: RR = 3.27), malignancies of the liver a hepatic bile ducts (m: RR = 2.54) and cancer of and bronchus (females: RR = 2.13).

A large urban excess (RR ≥ 1.4) was observe larynx (f: RR = 1.91), the nasal cavity and oth atory organs (f: RR = 1.83), the cervix (f: RR the mouth and pharynx (m: RR = 1.64; f: RR the oesophagus (f: RR = 1.46) and for Hodgk ease (m: RR = 1.43). These observations were s by statistically significant linear trends in i rates, except for cancer of the nasal cavity in f

A smaller but significant urban excess was for seven and six other cancer sites in male males, respectively.

The finding of a higher risk in urban muni was supported by an increasing trend with urb for most of these sites (Appendix).

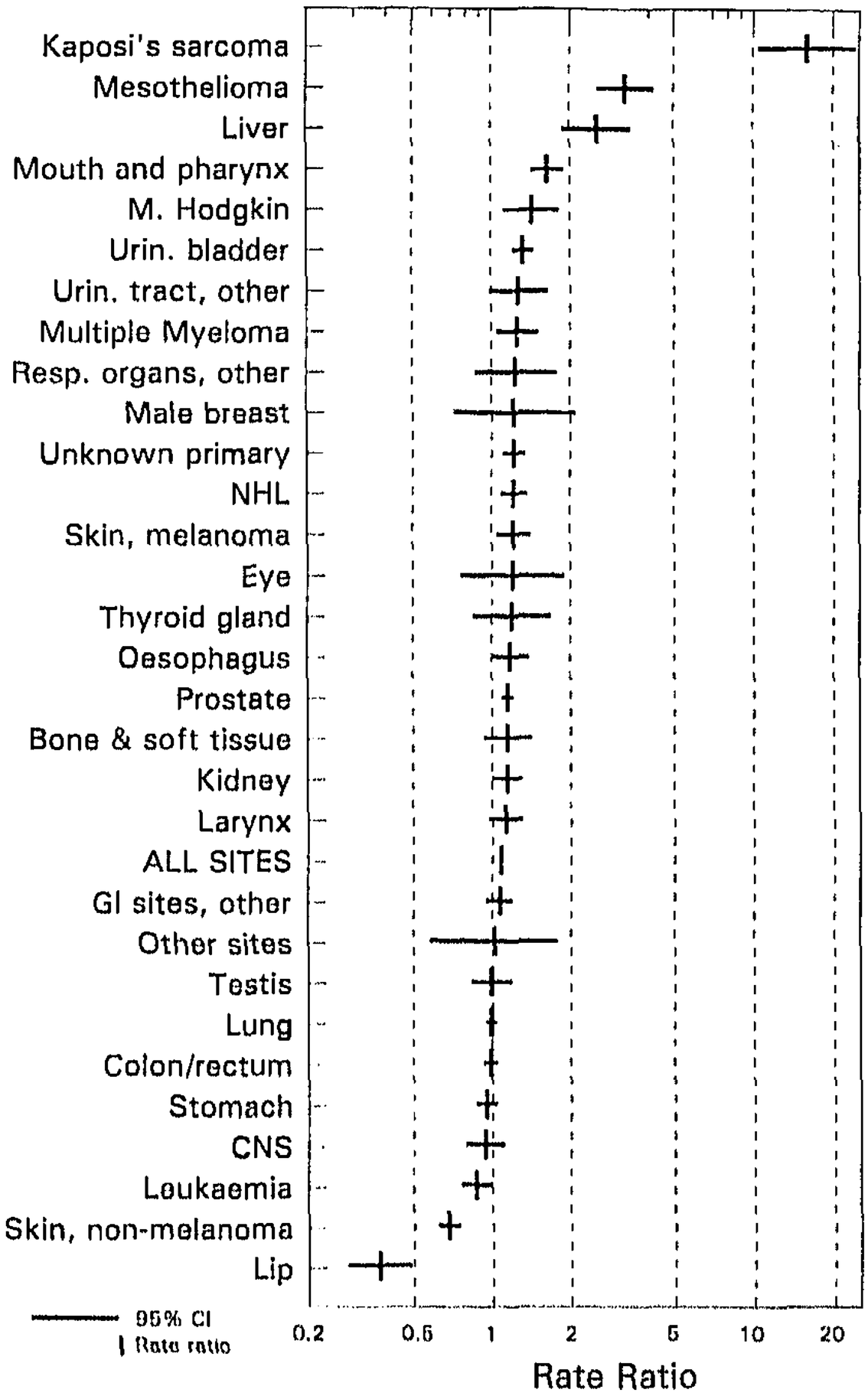

FIGURE 1 *Rate ratios and 95% confidence intervals (95% CI) for cancer occurrence in very densely urbanized areas compared to rural areas in the Netherlands, 1989–1991 for males*

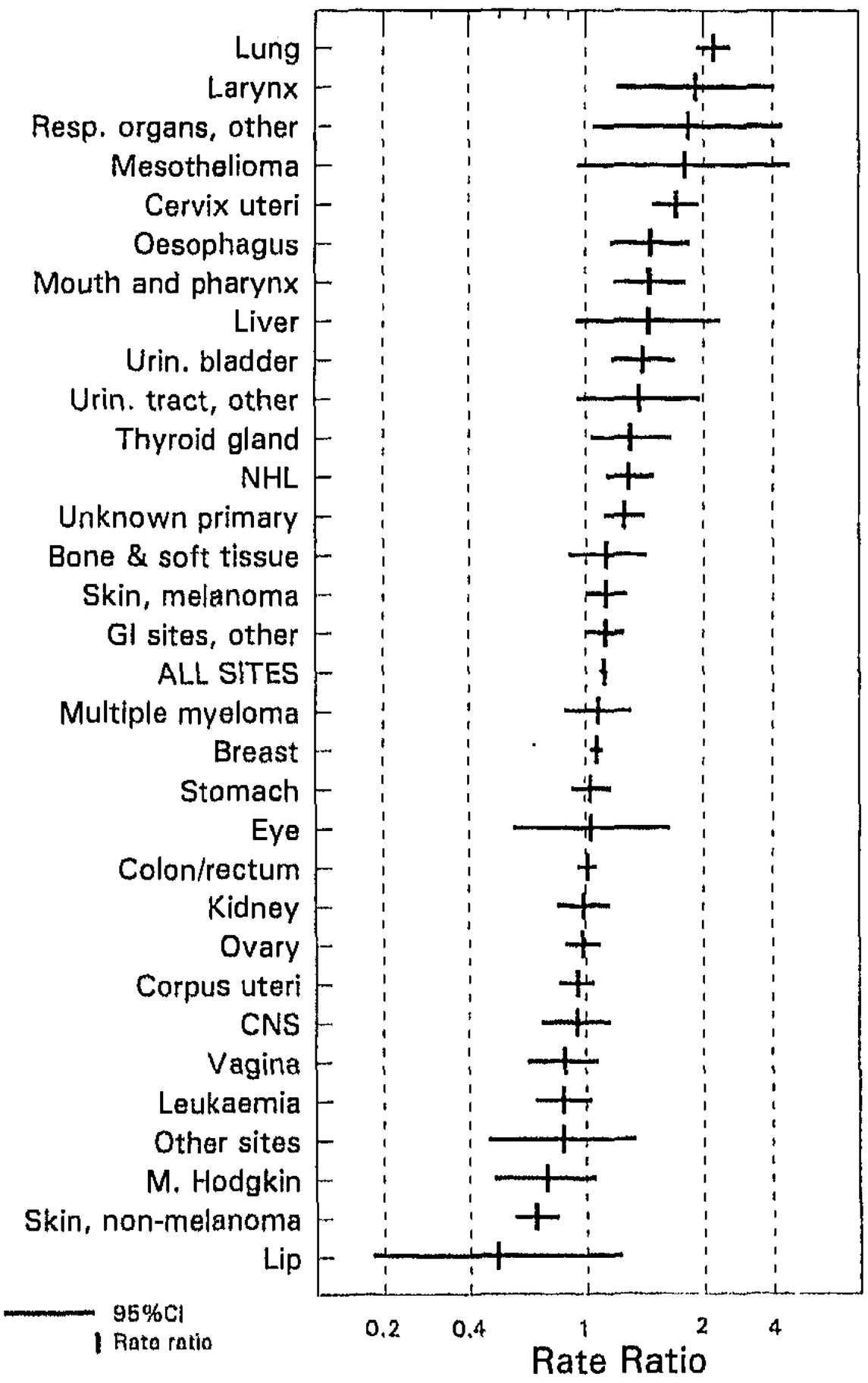

FIGURE 2 *Rate ratios and 95% confidence intervals (95% CI) for cancer occurrence in very densely urbanized areas compared to rural areas in the Netherlands, 1989–1991 for females*

The site-specific results for Kaposi's sarcoma in females are combined with the soft tissue malignancies because of small numbers.

Statistically significant lower RR were found in very densely urbanized versus rural areas for non-melanoma skin cancer (m: RR = 0.68; f: RR = 0.74) and lip (m: RR = 0.37). These findings were supported by a decreasing linear trend in cancer incidence rates with urbanization (Appendix).

DISCUSSION

In general, the cancer risk in the Netherlands is higher in urban areas and the risk increases with the level of urbanization. A statistically significant increasing linear trend of age-standardized incidence rates was demonstrated with increasing address density for 15 out of the 30 sites in males and for 13 out of the 32 sites in females. For cancer of the lip (males) and non-melanoma skin cancer (males and females), a rural excess was found and the incidence rates decreased with increasing urbanization.

The results of this study are in agreement with those of most other reports in the literature.[2–7,9] Extreme urban excesses have been reported for cancer of the lung, liver, larynx, mouth and pharynx, bladder and oesophagus; moderate urban excesses have been reported for cancer of the colon, rectum, cervix uteri, kidney, breast, ovary, brain and pancreas, while slight urban excesses have been reported for Hodgkin's disease, cancer of the testis, stomach, melanoma, other skin, corpus uteri, prostate, leukaemia and non-Hodgkin lymphoma.[7] Two types of cancer have been reported to occur at higher rates in rural areas, i.e. lip cancer and eye melanoma.[7] The most likely explanations for the differences in cancer incidence between urban and rural areas are aetiological factors, such as the inhabitants' personal behaviour, air pollution and occupational hazards. Examples of personal behaviour

are cigarette smoking, alcohol consumption, sexual promiscuity, exposure to ultraviolet radiation, diet and family size.[7]

Cancer of the lip and non-melanoma skin cancer are thought to be caused primarily by exposure to ultraviolet radiation.[20–22] People in rural areas are more likely to be exposed to ultraviolet radiation because of outdoor work. The higher incidence of lip cancer in rural areas is in agreement with other studies,[7] but the excess in the incidence of non-melanoma skin cancer is not. The higher incidence of eye malignancies in rural areas could not be confirmed in this study.

In general, the incidence rates of tobacco-related cancer,[21] such as cancer of the lung, larynx, mouth and pharynx, oesophagus, pancreas, cervix, urinary bladder, renal pelvis and kidney, are higher in urban areas. However, in this study the urban excess was only observed in females. In two earlier studies in the Netherlands, an urban excess was found for cancer of the respiratory tract in females and males.[8,9] In the southeast of the Netherlands, lung cancer incidence rates in males were higher in urban areas until 1975; in females, the lung cancer incidence rates have continued to rise in urban areas.[23] The difference between the sexes in the current study and the findings in the other studies reflect the pattern of smoking habits in the Netherlands.[24]

In 1963, 82% of all Dutch males were smokers. From the 1970s onwards, smoking prevalence in males decreased to 38% in 1993.[25] In 1963, only 32% of all Dutch females smoked. But, in contrast to the trend in males, smoking prevalence in females increased in the1970s, especially in the urban population.[26]

A large urban excess was observed for malignant mesothelioma in males. This malignancy is usually located in the pleura and sometimes in the peritoneum. Asbestos is known to be the main risk factor for pleural mesothelioma.[21] Many shipyards are located in the two largest Dutch cities, Rotterdam and Amsterdam, and shipyard workers have been exposed to asbestos in the past.

It is difficult to interpret the results for cancer of the prostate and breast. In the Netherlands, screening programmes for these types of cancer have been started fairly recently, which makes it difficult to unravel the effects of screening and the degree of urbanization. Besides a screening effect, an explanation for the urban-rural differences in breast cancer incidence can possibly be found in parity. In the past decades the rate of live births in the larger cities has remained lower than that in the rest of the Netherlands.[27]

A large urban excess was observed for cervical cancer. Recently, a screening programme started for this type of cancer. Main causes for cervix cancer are considered to be sexual promiscuity, smoking habits and the human papillomavirus. The incidence of the other malignancies that are related to viruses, Kaposi's sarcoma and malignancies of the liver, are also increased in urban areas. Kaposi's sarcoma is associated with the AIDS epidemic. Because of a deficient immune system, people with AIDS are at increased risk for developing Kaposi's sarcoma. As in other countries, the AIDS epidemic in the Netherlands has settled down in the larger cities, especially in Amsterdam. Liver cancer is very rare in the native Dutch population. However, the incidence rates of liver cancer are higher in sub Saharan Africa, East and Southeast Asia and in Melanesia.[21,28] The Netherlands has a relatively large group of immigrants from the former Dutch colonies (Indonesia, Surinam and the Netherlands Antilles) and from many other countries (especially Morocco and Turkey, but recently also from Ghana, Somalia and Cape Verde). Immigrants tend to concentrate in the larger cities in the Western part of the country.[29] The urban excess of liver cancer in this study may purely reflect the distribution of these peoples.

In this study address density was used to estimate urbanization. Address density is strongly correlated with population density. The average population density of the very dense urbanized municipalities was in the same range as the highest urbanization classes of the studies conducted in New York and Illinois.[4,6] However, the average population density of the non-urban municipalities was higher than the rural communities in the American studies. The contrast in population density in our study was therefore smaller.

In addition to aetiological factors, bias may also cause the urban-rural variations in risk. Bias can occur due to incompleteness of case ascertainment, errors in case registration and inaccurate residential information. In theory, underdiagnosis or incomplete records of cancer in the rural areas can be a reason for the differences. However, this is unlikely in the Netherlands in view of the good registration systems, both for cancer and place of residence as well as the nearly perfect health care infrastructure.

Cancer latency periods and the migration of patients to other areas is another potential source of bias in ecological studies like this one. It is difficult to determine what the effect is of migration, but it is thought to be small. Annually, 4% of the Dutch population move from one municipality to another,[15] the new municipality may have the same class of urbanization. Moreover, cancer risks are highest in the elderly, whereas most migration takes place in the younger population (less than 2% of the population of 40 years and older move annually).[30]

In males, the urban excess of tobacco-related cancer has largely disappeared, while in females the opposite is true for the occurrence of these types of cancer. Also, differences in cancer incidence have been observed for several other cancer sites. Therefore it is likely that differences in cancer incidence still exist in the Netherlands between urban and rural areas and that these differences can be attributed to a variety of lifestyle factors.

ACKNOWLEDGEMENT

We are grateful to Mrs Judith Abma Hill for checking the English.

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(Revised version received December 1995)

APPENDIX

TABLE A1 *Number of cases, age-standardized rate ratios (ASR), estimate of linear trend and 95% confidence intervals for invasive malignancies according to site and address density for males in the Netherlands 1989–1991*

ICD-O	Primary site of malignancy	No. of cases	ASR[a] non-urban municipalities	Rate ratio according to address density[c]				Estimate of linear trend[d] (95% CI[b])
				2	3	4	5	
T140	Lip	520	4.32	0.72	0.45	0.42	0.37	0.60
				(0.58, 0.91)	(0.34, 0.58)	(0.32, 0.54)	(0.28, 0.49)	(−0.76, −0.44)
T141–149	*Mouth and pharynx*	1956	7.97	1.07	1.18	1.33	1.64	1.15
				(0.92, 1.25)	(1.02, 1.37)	(1.15, 1.54)	(1.42, 1.89)	(0.83, 1.47)
T150	Oesophagus	1508	7.38	0.99	0.90	1.08	1.18	0.41
				(0.84, 1.16)	(0.76, 1.06)	(0.92, 1.27)	(1.01, 1.39)	(0.03, 0.79)
T151–152	*Stomach and small intestine*	5021	25.53	1.03	0.97	0.94	0.95	0.48
				(0.94, 1.12)	(0.89, 1.06)	(0.86, 1.02)	(0.87, 1.04)	(−0.97, 0.01)
T153–154	Colon and rectum	11050	52.58	1.01	1.09	1.10	0.99	0.48
				(0.95, 1.07)	(1.03, 1.16)	(1.04, 1.17)	(0.93, 1.05)	(−0.11, 1.09)
T155	*Liver and intrahepatic bile ducts*	446	1.44	1.06	1.66	1.48	2.54	0.44
				(0.74, 1.52)	(1.20, 2.30)	(1.07, 2.05)	(1.88, 3.44)	(0.39, 0.98)
T156–159	Other gastro-intestinal organs	2904	13.92	1.00	1.07	1.07	1.07	0.28
				(0.89, 1.13)	(0.95, 1.20)	(0.96, 1.20)	(0.95, 1.20)	(−0.09, 0.65)
T161	*Larynx*	1796	8.54	1.07	1.06	1.09	1.13	0.24
				(0.92, 1.24)	(0.91, 1.23)	(0.94, 1.26)	(0.97, 1.31)	(−0.07, 0.54)
T162	Lung and bronchus	22 137	111.29	0.98	0.97	0.99	0.99	0.03
				(0.94, 1.02)	(0.93, 1.01)	(0.95, 1.03)	(0.95, 1.03)	(−0.06, 1.00)
M9050–9053	Mesothelioma	747	1.84	1.59	2.13	2.33	3.27	0.96
				(1.19, 2.12)	(1.62, 2.80)	(1.79, 3.04)	(2.54, 4.21)	(0.77, 1.14)
T160, T164–165	Nasal cavity and other respiratory organs	320	1.35	1.01	1.11	1.49	1.24	0.13
				(0.70, 1.46)	(0.77, 1.61)	(1.06, 2.09)	(0.87, 1.78)	(0.00, 0.25)
T170–171	*Bone and soft tissue*	888	3.90	1.03	0.92	1.20	1.15	0.17
				(0.83, 1.27)	(0.74, 1.15)	(0.98, 1.47)	(0.93, 1.42)	(−0.02, 0.37)
M9140	Kaposi's sarcoma	311	0.31	1.16	1.45	3.45	15.97	0.48
				(0.56, 2.37)	(0.73, 2.88)	(1.97, 6.03)	(10.47, 24.35)	(0.29, 0.67)
T173 and M8720–8780	*Skin, melanoma*	1869	7.85	1.04	1.18	1.18	1.22	0.17
				(0.89, 1.20)	(1.02, 1.37)	(1.02, 1.37)	(1.05, 1.42)	(0.15, 0.76)
T173	Skin, non-melanoma[e]	4773	28.10	0.95	0.88	0.75	0.68	2.34
				(0.87, 1.03)	(0.81, 0.96)	(0.69, 0.82)	(0.62, 0.75)	(−2.81, −1.86)
T175	*Breast*	128	0.63	1.25	0.81	0.79	1.22	0.01
				(0.75, 2.09)	(0.45, 1.46)	(0.44, 1.42)	(0.72, 2.08)	(−0.09, 0.12)
T185	Prostate	12 719	58.26	1.03	1.09	1.11	1.18	2.19
				(0.98, 1.09)	(1.03, 1.15)	(1.05, 1.18)	(1.09, 1.31)	(1.13, 3.25)
T186–187	*Testis and other male genital organs*	1293	5.37	1.12	1.14	0.91	0.99	0.12
				(0.94, 1.32)	(0.96, 1.35)	(0.76, 1.09)	(0.83, 1.19)	(−0.33, 0.56)
T188	Urinary bladder	4687	20.84	0.94	1.11	1.23	1.33	1.93
				(0.85, 1.04)	(1.01, 1.22)	(1.12, 1.35)	(1.22, 1.46)	(1.46, 2.42)
T189.0	*Kidney*	2267	10.35	0.92	1.24	1.21	1.15	0.63
				(0.80, 1.05)	(1.09, 1.41)	(1.06, 1.37)	(1.00, 1.31)	(0.40, 0.86)
T189.1–9	Other urinary organs	595	2.52	1.08	1.02	1.46	1.24	0.24
				(0.82, 1.41)	(0.78, 1.35)	(1.14, 1.87)	(0.98, 1.65)	(0.06, 0.39)
T190	*Eye and orbit*	215	0.90	1.17	1.24	1.14	1.21	0.06
				(0.76, 1.81)	(0.80, 1.92)	(0.87, 2.04)	(0.76, 1.90)	(−0.04, 0.16)
T191–192	Central nervous system	1496	7.09	1.04	1.12	0.98	0.94	0.12
				(0.89, 1.21)	(0.96, 1.31)	(0.83, 1.15)	(0.79, 1.11)	(−0.15, 0.41)
T193–194	*Thyroid and other endocrine glands*	363	1.53	1.08	1.13	1.19	1.20	0.05
				(0.77, 1.51)	(0.81, 1.58)	(0.86, 1.65)	(0.85, 1.69)	(−0.05, 0.31)
M9650–9667	Hodgkin's disease	613	2.49	0.89	0.93	1.04	1.13	0.21
				(0.68, 1.16)	(0.72, 1.21)	(0.80, 1.34)	(0.87, 1.47)	(0.05, 0.36)
M9590–9593, M9670–9723	*Non-Hodgkin lymphoma*	2942	13.32	1.01	1.04	1.15	1.22	0.25
				(0.90, 1.14)	(0.92, 1.17)	(1.02, 1.29)	(1.09, 1.37)	(0.12, 0.37)
M9730-9731	Morbus Kahler	1145	5.24	1.13	1.05	1.00	1.26	0.18
				(0.94, 1.36)	(0.87, 1.27)	(0.83, 1.21)	(1.05, 1.51)	(0.05, 0.32)

APPENDIX

TABLE A1 *Continued*

ICD-O	Primary site of malignancy	No. of cases	ASR[a] non-urban municipalities	Rate ratio according to address density[c] 2	3	4	5	Estimate of linear trend[d] (95% CI[b])
M9800–9970	Leukaemia	2098	11.19	0.87 (0.76, 1.00)	1.03 (0.91, 1.18)	0.86 (0.75, 0.98)	0.87 (0.76, 1.00)	–0.29 (–0.61, 0.02)
T195	Other sites	117	0.60	1.40 (0.83, 2.35)	0.80 (0.44, 1.45)	0.67 (0.36, 1.24)	1.02 (0.58, 1.78)	–0.04 (–0.11, 0.04)
T199	Unknown primary site	4000	17.76	1.09 (0.99, 1.21)	1.05 (0.95, 1.17)	1.24 (1.12, 1.36)	1.22 (1.11, 1.35)	1.05 (0.61, 1.48)
T140–199	All sites combined	90 924	434.31	1.00 (0.98, 1.02)	1.04 (1.01, 1.06)	1.06 (1.03, 1.08)	1.08 (1.06, 1.10)	9.00 (6.93, 11.08)

TABLE A2 *Number of cases, age standardized rate ratios, estimate of linear trend and 95% confidence intervals for invasive malignancies according to site and address density for females in the Netherlands 1989–1991*

ICD-O	Primary site of malignancy	No. of cases	ASR[a] non-urban municipalities	Rate ratio according to address density[c] 2	3	4	5	Estimate of linear trend[d] (95% CI[b])
T140	Lip	87	0.39	0.92 (0.48, 1.78)	0.94 (0.49, 1.79)	0.73 (0.37, 1.46)	0.59 (0.28, 1.23)	0.04 (–0.09, 0.01)
T141–149	Mouth and pharynx	1057	3.48	1.22 (0.99, 1.50)	1.11 (0.90, 1.38)	1.44 (1.18, 1.76)	1.45 (1.18, 1.79)	0.39 (0.20, 0.58)
T150	Oesophagus	854	2.44	1.10 (0.86, 1.41)	1.31 (1.03, 1.66)	1.07 (0.84, 1.37)	1.46 (1.16, 1.84)	0.20 (0.05, 0.34)
T151–152	Stomach and small intestine	2937	9.98	1.02 (0.90, 1.15)	0.98 (0.87, 1.11)	1.01 (0.90, 1.14)	1.03 (0.92, 1.17)	0.06 (–0.22, 0.33)
T153–154	Colon and rectum	11 523	40.75	1.03 (0.96, 1.09)	1.01 (0.95, 1.08)	1.03 (0.97, 1.09)	1.01 (0.95, 1.07)	0.08 (–0.48, 0.64)
T155	Liver and intrahepatic bile ducts	237	0.71	0.87 (0.54, 1.40)	1.46 (0.95, 2.23)	1.35 (0.88, 2.07)	1.44 (0.94, 2.21)	0.10 (0.02, 0.18)
T156–159	Other gastro-intestinal organs	3484	11.03	1.07 (0.95, 1.20)	1.19 (1.06, 1.33)	1.04 (0.93, 1.17)	1.13 (1.01, 1.26)	0.25 (–0.05, 0.55)
T161	Larynx	240	0.71	0.97 (0.58, 1.62)	1.57 (0.99, 2.47)	2.31 (1.53, 3.49)	1.91 (1.21, 3.03)	0.22 (0.12, 0.32)
T162	Lung and bronchus	4133	11.95	1.14 (1.01, 1.28)	1.52 (1.36, 1.70)	1.59 (1.43, 1.77)	2.13 (1.92, 2.36)	3.09 (2.70, 3.49)
M9050–9053	Mesothelioma	120	0.36	1.30 (0.69, 2.46)	1.28 (0.66, 2.46)	1.38 (0.74, 2.58)	1.78 (0.95, 3.31)	0.06 (–0.01, 0.12)
T160, T164–165	Nasal cavity and other respiratory organs	143	0.41	1.31 (0.72, 2.37)	1.31 (0.72, 2.38)	1.28 (0.71, 2.33)	1.83 (1.05, 3.18)	0.06 (–0.00, 0.13)
T170 T171	Bone and soft tissue[f]	796	3.07	1.04 (0.83, 1.31)	1.07 (0.85, 1.35)	1.05 (0.84, 1.33)	1.13 (0.90, 1.43)	0.08 (–0.09, 0.25)
T173 and M8720–8780	Skin, melanoma	2848	10.42	1.12 (0.99, 1.27)	1.27 (1.12, 1.43)	1.26 (1.11, 1.42)	1.13 (1.00, 1.28)	0.45 (0.13, 0.76)
T173	Skin, non-melanoma[g]	2648	9.99	0.94 (0.83, 1.06)	0.92 (0.81, 1.04)	0.84 (0.74, 0.95)	0.74 (0.65, 0.84)	–0.64 (–0.89, –0.40)
T174	Breast	25 562	101.61	1.05 (1.01, 1.09)	1.06 (1.02, 1.11)	1.10 (1.05, 1.14)	1.07 (1.03, 1.11)	1.97 (1.00, 2.94)
T180	Cervix uteri	2201	7.05	1.03 (0.89, 1.20)	1.38 (1.20, 1.59)	1.44 (1.25, 1.66)	1.69 (1.47, 1.94)	1.24 (0.96, 1.52)
T182	Corpus uteri	4815	16.45	0.98 (0.85, 1.05)	0.93 (0.83, 1.03)	0.92 (0.83, 1.02)	0.95 (0.85, 1.05)	0.22 (–0.59, 0.15)

TABLE A2 *Continued*

ICD-O	Primary site of malignancy	No. of cases	ASR[a] non-urban municipalities	Rate ratio according to address density[c]				Estimate of linear trend[d] (95% CI[b])
				2	3	4	5	
T183.0	Ovary	3622	14.93	0.96 (0.86, 1.07)	1.07 (0.96, 1.19)	1.02 (0.92, 1.14)	0.98 (0.88, 1.09)	0.04 (−0.32, 0.40)
T183.2-184.9	Other female genital organs	963	3.86	0.89 (0.72, 1.09)	0.89 (0.72, 1.09)	0.81 (0.66, 1.00)	0.88 (0.71, 1.08)	0.12 (−0.28, 0.04)
T188	Urinary bladder	1318	3.97	1.07 (0.88, 1.30)	1.17 (0.97, 1.41)	1.20 (0.99, 1.44)	1.40 (1.17, 1.68)	0.36 (0.17, 0.54)
T189.0	Kidney	1564	6.70	0.88 (0.75, 1.03)	0.94 (0.80, 1.10)	0.88 (0.75, 1.04)	0.99 (0.84, 1.16)	0.02 (−0.26, 0.22)
T189.1–9	Other urinary organs	296	1.09	0.78 (0.52, 1.17)	1.12 (0.77, 1.63)	0.87 (0.59, 1.28)	1.37 (0.95, 1.96)	0.07 (−0.03, 0.17)
T190	Eye and orbit	185	0.81	0.86 (0.53, 1.39)	1.04 (0.65, 1.65)	1.08 (0.68, 1.73)	1.03 (0.65, 1.63)	0.02 (−0.06, 0.11)
T191–192	Central nervous system	1081	4.58	1.18 (0.98, 1.42)	1.12 (0.93, 1.36)	0.95 (0.78, 1.15)	0.95 (0.77, 1.16)	0.15 (−0.35, 0.06)
T193–194	Thyroid and other endocrine glands	759	2.91	1.02 (0.81, 1.30)	0.98 (0.77, 1.25)	1.09 (0.86, 1.38)	1.30 (1.03, 1.64)	0.18 (0.01, 0.35)
M9650–9667	Hodgkin's disease	429	2.07	0.80 (0.59, 1.07)	0.83 (0.62, 1.12)	0.72 (0.54, 0.98)	0.79 (0.58, 1.06)	0.10 (−0.22, 0.02)
M9590–9593, M9670–9723	Non-Hodgkin lymphoma	2456	8.21	1.12 (0.98, 1.28)	1.13 (0.99, 1.30)	1.13 (0.98, 1.29)	1.29 (1.13, 1.48)	0.17 (0.30, 0.75)
M9730–9731	Morbus Kahler	997	3.66	0.92 (0.74, 1.13)	0.97 (0.79, 1.19)	0.88 (0.71, 1.08)	1.08 (0.88, 1.31)	0.04 (−0.13, 0.20)
M9800–9970	Leukaemia	1532	6.21	0.88 (0.75, 1.04)	1.01 (0.86, 1.19)	0.97 (0.83, 1.14)	0.87 (0.74, 1.03)	0.10 (−0.32, 0.13)
T195	Other sites	216	0.80	1.24 (0.82, 1.88)	0.89 (0.57, 1.38)	0.74 (0.47, 1.17)	0.87 (0.56, 1.34)	0.06 (−0.13, 0.03)
T199	Unknown primary site	3115	9.95	1.06 (0.94, 1.20)	1.06 (0.94, 1.20)	1.22 (1.09, 1.37)	1.26 (1.13, 1.42)	0.67 (0.48, 0.97)
T140–199	All sites combined	81 087	300.53	1.03 (1.01, 1.05)	1.08 (1.05, 1.10)	1.09 (1.06, 1.11)	1.12 (1.09, 1.14)	8.85 (7.72, 10.19)

[a] Age-standardized incidence rate per 100 000 inhabitants, according to the European Standard Population.
[b] 95% confidence intervals.
[c] Classification address density:
1 = Non-urban municipalities (< 500 addresses/km^2);
2 = Sparsely urbanized municipalities (500–1000 addresses/km^2);
3 = Moderately urbanized municipalities (1000–1500 addresses/km^2);
4 = Densely urbanized municipalities (1500–2500 addresses/km^2);
5 = Very densely urbanized municipalities (> 2500 addresses/km^2).
[d] Linear trend of standardized incidence rates as described by Rothman.[19]
[e] Basal cell carcinomas are not included.
[f] Because of the small number (N = 12) of Kaposi's sarcomas among women, this malignancy has been combined with the category of 'Bone and soft tissue'.