

STRIKING INCREASE IN INCIDENCE OF CANCER OF THE ORAL CAVITY AND PHARYNX IN ESTONIA 1968–92

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Abstract. All incident cases of oral and pharyngeal cancers recorded by the Estonian Cancer Registry from 1968 to 1992 were analysed for time-trend patterns. Standardization (European standard population) was carried out for all ages together and for the age groups 15–44, 45–64, and 65 years and over. To examine possible age, period or cohort effects, age-specific incidence rates were plotted as contour maps and three-dimensional perspective plots. The incidence of cancer of the oral cavity and pharynx increased over this period of time for all ages and for both sexes. The steepest rise was observed for males in younger and middle age groups. The highest rates were for males 60–64 years in 1988–92, who were born around 1928. Cancers of the tongue, mouth, and pharynx show similar patterns of incidence over this time period, possibly indicating exposure to the same risk factors, namely tobacco smoking and alcohol consumption. Rising rates for the younger age groups predict a potential major public health problem associated with cancers of the oral cavity and pharynx.

Key words: cancer, oral cavity and pharynx, incidence, time trend, age–period–cohort, Estonia.

INTRODUCTION

There are wide geographical differences in the incidence of upper digestive and respiratory cancers. For example, oral and pharyngeal cancers are quite common in India and Southeast Asia, and tongue cancer in Brazil. Usually rates for females are much lower everywhere (Blot et al., 1994). In Europe, cancers of the oral cavity, pharynx, larynx, and oesophagus constitute from 2 to 15% of all cancer incidence (Franceschi et al., 1990). The highest rates for oral and pharyngeal cancers have been reported in Bas-Rhin and Calvados in France.

Elsewhere in Europe rates are lower, but time trends in mortality from oral and pharyngeal cancers show rapid increase. A decrease during the period 1950–80 was noted in Finland, Ireland, and the United Kingdom but lately the trend has started to climb (Blot et al., 1994; Coleman et al., 1993). Substantial increases in mortality from oral and pharyngeal cancers were observed in the USSR; its rates for 1990 were among the highest registered in the world (La Vecchia et al., 1994). The incidence of the aforementioned cancers shows rising rates from north to south, with the lowest rates in Scandinavia, and from west to east (Swoboda & Friedl, 1994). A recent report reveals that the increase in incidence of oral and pharyngeal cancer in Slovakia was considerable, with higher rates than elsewhere (Plesko et al., 1994). In Estonia, age-standardized mortality in males from cancers of oral cavity and pharynx increased from 2.2 per 100,000 person-years in 1965–69 to 6.9 in 1985–89 (Leinsalu & Rahu, 1993).

Although the absolute numbers are relatively small, these sites have the highest increase among all cancer sites during this period. New methods of detection and changes in disease classification can also result in spurious disease trends, for example, producing either period effects when all age groups are influenced in the same way, or creating a lifetime effect appearing in different generations (Gardner & Osmond, 1984). Therefore, the effects of age, period, and cohort should be examined separately.

This study aims to report changes in time trends of oral and pharyngeal cancers in Estonia during 1968–92 and to examine changes according to age, period of diagnosis, and birth cohort.

MATERIALS AND METHODS

In Estonia, the registration of cancers has been practiced since 1953 (Rahu, 1992a). By 1968 registration became centralized, and in January 1978 the Estonian Cancer Registry (ECR) was officially founded. The database of the ECR thus initially included prevalence cases as of January 1968, and afterwards incident cases of that and subsequent years. Therefore, 1968 became the first year in this analysis. The ECR serves a population of 1.5 million. By administrative order, every health-care institution is required to send notification of each cancer case to the ECR (Rahu, 1992b; Rahu & Hakulinen, 1994).

Data on all new cancer cases in Estonia are available for the time period from 1968 to 1992. Data of the resident population of Estonia were provided by the Estonian Interuniversity Population Research Centre (Population Age Structure, 1994a, b). The cancer data from 1968 to 1992 were classified according to the International Classification of Diseases, Revision 9, and aggregated as follows: tongue (141); mouth (143–145); pharynx (146, 148); nasopharynx, nose, and sinuses (147, 160); and oral cavity and pharynx (141, 143–146, 148–149) (Manual..., 1977). The sites of lip and salivary glands were excluded because of their different etiology.

Incidence rates have been age-standardized to the European population. Standardization was carried out for all ages and is presented with truncated age-standardized rates for age groups 15–44, 45–64, and 65 years and over. All rates are presented by 5-year periods from 1968–72 to 1988–92. To show change of standardized rates over time, standardized incidence rate ratios of 1988–92 vs. 1968–72 were calculated with 95% confidence intervals as described by Boyle & Parkin (1991). Cohorts were defined on the basis of their central year of birth, assuming that, for instance, those in the age group 55–59 during period 1973–77 were born in years centered around 1918. Also, rate ratios of males vs. females were calculated as an indicator of the relative importance of cancer of different sites in each sex.

To examine age, period, and cohort effects, a matrix of age specific incidence rates was plotted as a topographic surface, where lines connect points of equal values. Cohorts are represented by diagonal lines, which connect the appropriate calendar year and age. Incidence rates for cohorts can be read as described by Jolley & Giles (1992) from the values and intervals of isolines that the diagonal lines cross. The numbers indicating the value of the isoline are oriented uphill. To aid in the examination of contour maps, the same data are also presented on three-dimensional perspective plots. In fact, this technique is very similar to the traditional method of age, period, and cohort plotting, with the difference that all three features are plotted together on one graph – the contour map. For example, if we slice through the surface along the cohort lines we will get a result similar to Fig. 1. For age–period–cohort analysis we chose only the cancer sites for males because the numbers for females are too low and are subject to a large random variation.

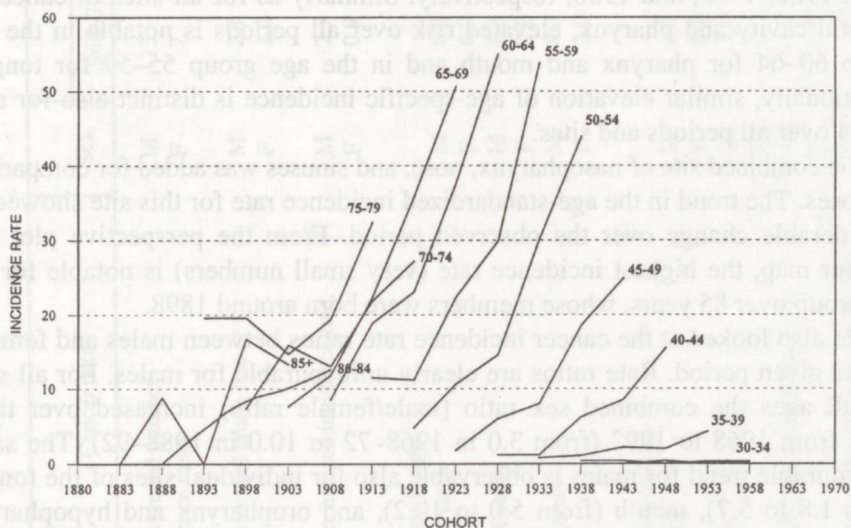


Fig. 1. Age-specific incidence of cancer of oral cavity and pharynx by age and cohort.

RESULTS

The age-standardized incidence rates of cancers of the oral cavity and pharynx in males and females show a constant rise over the period from 1968 to 1992 for all ages, from 2.7 per 100,000 person-years in 1968-72 to 16.0 in 1988-92 for males, and respectively from 0.9 to 1.6 for females. In males the steepest rise occurred for the age group 25-44: from 0.6 to 5.0 per 100,000. The highest incidence rates were in the age group 45-64, with over 40 per 100,000 during 1988-92. These trends are confirmed when we look at the perspective plot of incidence data, where we can observe a steep, peaked mountain of cancer incidence with two distinctive ridges in the middle and on the right side (Fig. 2). Examination of the contour map, which is actually a view of the perspective plot from above, reveals the highest incidence rate (over 40 per 100,000) for males about 60 years old in the cohort 1928. The ridge indicates that rates have always been somewhat higher for this particular age group (60-64). Rates are almost as high also for neighbouring cohorts of 1923 and 1933.

Incidence rates have been rising over time for all observed cancer sites (Table) except nasopharynx, nose, and sinuses. The highest changes in age-standardized rates were for combined sites of oropharynx and hypopharynx, from 1.0 in 1968-72 to 6.9 per 100,000 in 1988-92 for males. Changes were also large for other sites (mouth and tongue) as indicated by rate ratios of the first and last periods.

From the contour map we can see that the peak of age-specific incidence for pharyngeal (over 21 per 100,000), mouth (over 19), and tongue (over 13) cancers in males occurred for the age groups 50-69, whose central years of birth are 1923, 1928, 1933, and 1938, respectively. Similarly as for all sites of cancer of the oral cavity and pharynx, elevated risk over all periods is notable in the age group 60-64 for pharynx and mouth and in the age group 55-59 for tongue. Additionally, similar elevation of age-specific incidence is distinct also for ages 75-84 over all periods and sites.

The combined site of nasopharynx, nose, and sinuses was added for comparison purposes. The trend in the age-standardized incidence rate for this site showed no considerable change over the observed period. From the perspective plot and contour map, the highest incidence rate (very small numbers) is notable for the age group over 85 years, whose members were born around 1898.

We also looked at the cancer incidence rate ratios between males and females for the given period. Rate ratios are clearly unfavourable for males. For all sites and all ages the combined sex ratio (male/female ratio) increased over three times from 1968 to 1992 (from 3.0 in 1968-72 to 10.0 in 1988-92). The same unfavourable trend for males is observable also for individual sites of the tongue (from 1.8 to 5.7), mouth (from 5.0 to 10.2), and oropharynx and hypopharynx (from 3.3 to 23.0). The highest sex ratio was observed in the age group 45-64 (from 3.2 to 12.3).

Age-standardized incidence of cancer of the oral cavity and pharynx among males and females in Estonia, 1968-92

Cancer data	Sex	Incidence rate per 100,000 person-years					1988-92/1968-72 rate ratio (95% CI)
		1968-72	1973-77	1978-82	1983-87	1988-92	
Average annual number of incidence cases	M	13	22	35	63	102	
	F	7	7	10	11	15	
Average annual crude rate	M	2.1	3.4	5.1	8.8	13.9	6.62
	F	1.0	0.9	1.2	1.3	1.8	1.80
Age-standardized incidence rate, all ages	M	2.7	4.3	6.4	10.6	16.0	5.93 (4.81-7.29)
	F	0.9	0.8	1.1	1.2	1.6	1.78 (1.21-2.61)
According to age 25-44 years	M	0.6	0.8	2.1	2.7	5.0	8.33 (4.12-16.87)
	F	0.2	0.2	0.5	0.3	0.6	3.00 (0.73-12.30)
45-64 years	M	6.3	11.1	16.3	28.4	43.2	6.86 (5.30-8.86)
	F	2.0	1.2	1.9	3.2	3.5	1.75 (1.01-3.02)
≥ 65 years	M	8.7	12.2	15.9	25.0	34.1	3.92 (2.58-5.95)
	F	3.0	3.7	4.0	2.5	4.9	1.63 (0.91-2.93)
According to site Tongue	M	0.7	1.3	2.0	1.7	3.4	4.86 (3.17-7.45)
	F	0.4	0.3	0.3	0.3	0.5	1.25 (0.70-2.24)
Mouth	M	1.0	1.4	2.1	4.0	5.5	5.50 (3.90-7.76)
	F	0.2	0.2	0.4	0.4	0.7	3.50 (2.01-6.09)
Oropharynx and hypopharynx	M	1.0	1.4	2.1	4.9	6.9	6.90 (4.96-9.60)
	F	0.3	0.2	0.3	0.4	0.3	1.00
Nasopharynx and nose and sinuses	M	1.9	2.0	2.0	1.8	-1.6	0.84 (0.55-1.28)
	F	1.0	0.8	0.8	0.7	-0.9	0.90 (0.59-1.38)

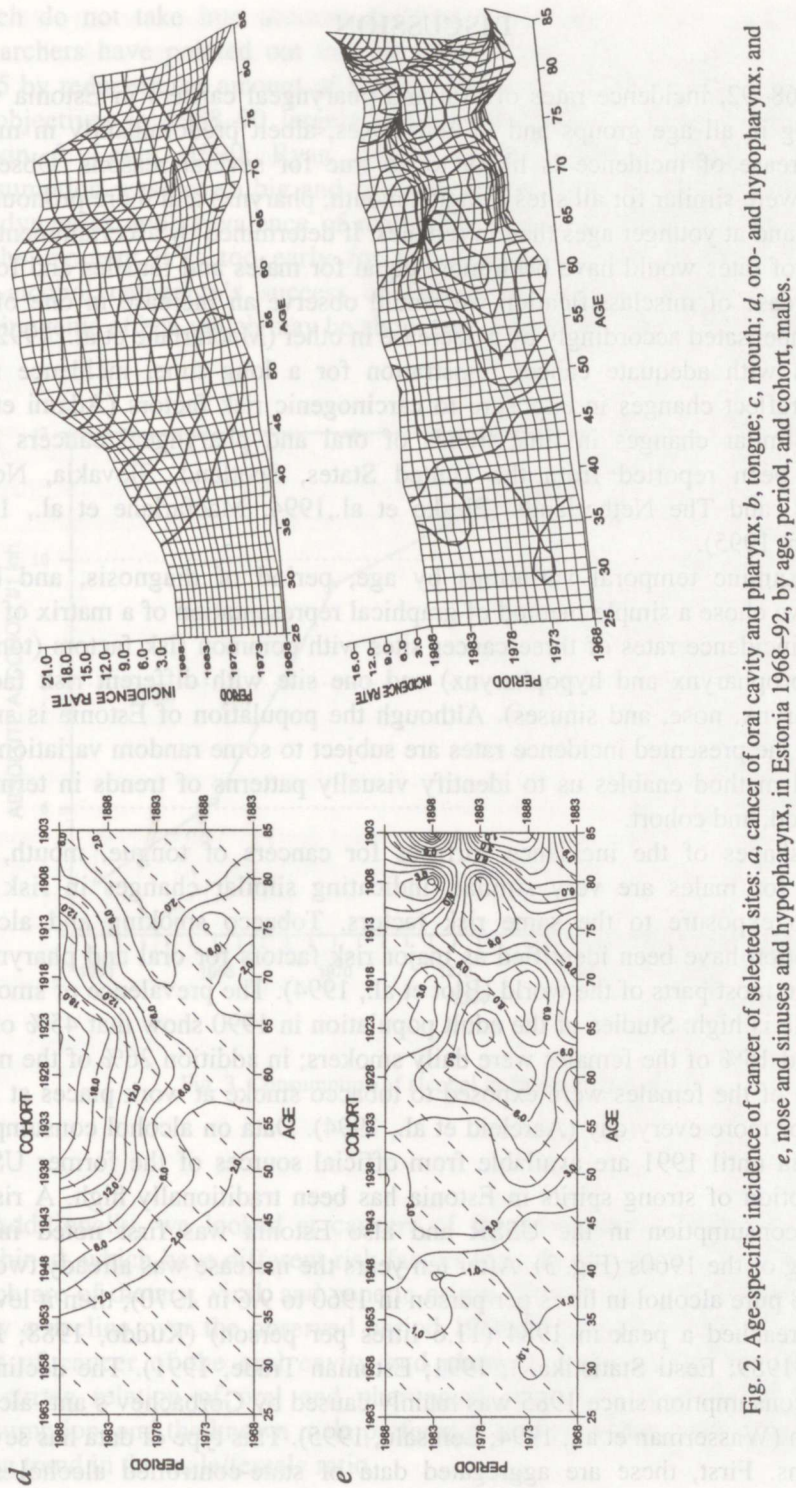


Fig. 2. Age-specific incidence of cancer of selected sites: a, cancer of oral cavity and pharynx; b, tongue; c, mouth; d, oro- and hypopharynx; and e, nose and sinuses and hypopharynx, in Estonia 1968-92, by age, period, and cohort, males.

In 1968–92, incidence rates of oral and pharyngeal cancers in Estonia were increasing in all age groups and in both sexes, albeit predominantly in males. This increase of incidence is likely to be true for several reasons. Observed changes were similar for all sites (tongue, mouth, pharynx) and more pronounced in males and at younger ages than in females. If determined by ascertainment, the increase of rates would have been more equal for males and females and for all ages. In case of misclassification we would observe an increase in one of the sites compensated accordingly by a decrease in other (Macfarlane et al., 1992). In countries with adequate cancer registration for a long time, incidence rates directly reflect changes in exposure to carcinogenic risk factors (Adami et al., 1993). Similar changes in time trends of oral and pharyngeal cancers have recently been reported from the United States, Scotland, Slovakia, Nordic countries, and The Netherlands (Plesko et al., 1994; Macfarlane et al., 1992; Coebergh, 1995).

To examine temporal variations by age, period of diagnosis, and birth cohort, we chose a simple method of graphical representation of a matrix of age-specific incidence rates of three cancer sites with common risk factors (tongue, mouth, oropharynx and hypopharynx) and one site with different risk factors (nasopharynx, nose, and sinuses). Although the population of Estonia is small, and thus the presented incidence rates are subject to some random variation, the proposed method enables us to identify visually patterns of trends in terms of age, period, and cohort.

The shapes of the incidence surfaces for cancers of tongue, mouth, and pharynx for males are very similar, indicating similar changes in risk and thus also exposure to the same risk factors. Tobacco smoking and alcohol consumption have been identified as major risk factors for oral and pharyngeal cancers in most parts of the world (Blot et al., 1994). The prevalence of smoking in Estonia is high. Studies of the adult population in 1990 show that 45% of the males and 15% of the females were daily smokers; in addition 26% of the males and 15% of the females were exposed to tobacco smoke at work places at least 5 hours or more every day (Aareleid et al., 1994). Data on alcohol consumption in Estonia until 1991 are available from official sources of the former USSR. Consumption of strong spirits in Estonia has been traditionally high. A rise in alcohol consumption in the USSR and also Estonia was first noted in the beginning of the 1960s (Fig. 3). After ten years the increase was already twofold (from 4.8 pure alcohol in litres per person in 1960 to 9.6 in 1970); then it leveled off and reached a peak in 1984 (11.6 litres per person) (Kuddo, 1988; Eesti NSV..., 1989; Eesti Statistika..., 1991; Estonian Trade, 1991). The decline in alcohol consumption since 1985 was mainly caused by Gorbachev's anti-alcohol campaign (Wasserman et al., 1994; Leinsalu, 1995). This type of data has several limitations. First, these are aggregated data of state-controlled alcohol sales

which do not take into account distribution by age and sex. Second, many researchers have pointed out that the anti-alcohol campaign, which started in 1985 by reducing the amount of alcohol sales and production, failed to achieve its objectives in 1988–90 largely due to unregistered sales, e.g., home brew (Levin & Levin, 1990; Ryan, 1995). So, the actual decrease of alcohol consumption was not so big and stopped earlier. However, these data illustrate the dynamics and prevalence of main risk factors in population under study. At the moment it is too early for any changes to appear which reflect the anti-alcohol campaign's success or failure, due to the latency of alcohol's carcinogenic effect, which may be about two decades (Tuyns & Audigier, 1976).

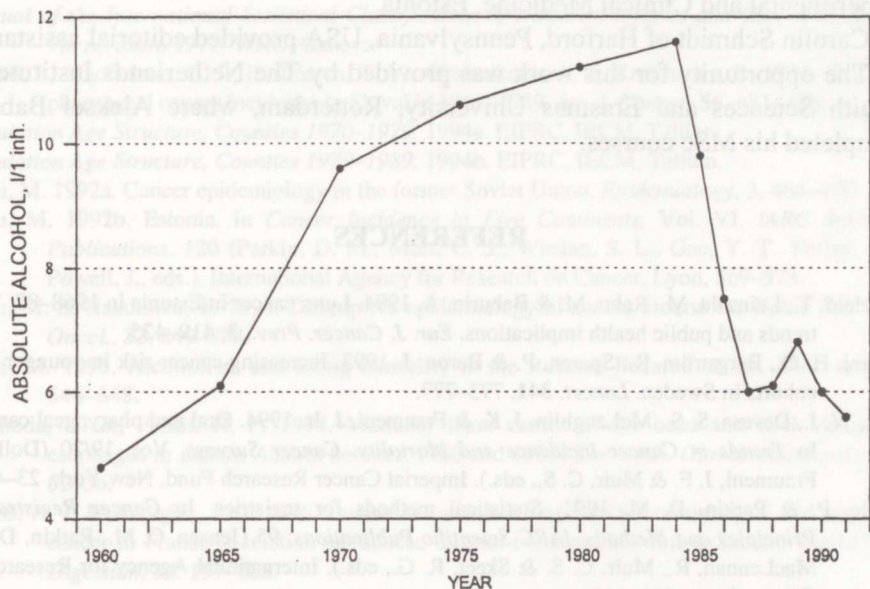


Fig. 3. Consumption of alcohol in Estonia 1960–91.

Additionally, we looked at cancers of the nasopharynx, nose, and sinuses combined, which have different risk factors than do the oral cavity and pharynx, which are of dietary, viral, and genetic origin (Blot et al., 1994). These cancers show a decline over the observed period 1968–92, except at old ages, whereas rates of cancer of the oral cavity and pharynx decline after the age of 70. The strong relation of oral and pharyngeal cancers to smoking and alcohol consumption, and the known male preference in these habits, are reflected in the rising trend in the male/female ratio.

As noted in previous studies (Leinsalu & Rahu, 1993), the mortality situation of oral and pharyngeal cancers among males in Estonia is very alarming. Oral cancers may become a major health problem because, as suggested by Doll (1991), the occurrence of cancer at young ages may predict future trends, since these individuals reflect the latest changes in behaviour and carcinogenic exposures.

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REFERENCES

- Aareleid, T., Leinsalu, M., Rahu, M. & Baburin, A. 1994. Lung cancer in Estonia in 1968–87: Time trends and public health implications. *Eur. J. Cancer. Prev.*, **3**, 419–425.
- Adami, H. O., Bergström, R., Sørensen, P. & Baron, J. 1993. Increasing cancer risk in younger birth cohorts in Sweden. *Lancet*, **341**, 773–777.
- Blot, W. J., Devesa, S. S., McLaughlin, J. K. & Fraumeni, J. Jr. 1994. Oral and pharyngeal cancers. In *Trends in Cancer Incidence and Mortality. Cancer Surveys*, Vol. 19/20 (Doll, R., Fraumeni, J. F. & Muir, C. S., eds.). Imperial Cancer Research Fund, New York, 23–42.
- Boyle, P. & Parkin, D. M. 1991. Statistical methods for registries. In *Cancer Registration: Principles and Methods. IARC Scientific Publications*, 95 (Jensen, O. M., Parkin, D. M., MacLennan, R., Muir, C. S. & Skeet, R. G., eds.). International Agency for Research on Cancer, Lyon, 131–142.
- Coebergh, J. W. W. 1995. Head and neck. In *Cancer Incidence and Survival in the Southeast of the Netherlands 1955–1994* (Coebergh, J. W. W., van der Heijden, L. H. & Janssen-Heijnen, M. L. G., eds.). IKZ, Eindhoven, 20–23.
- Coleman, M. P., Estève, J., Damiacki, P., Arslan, A. & Renard, H. 1993. *Trends in Cancer Incidence and Mortality. IARC Scientific Publications*, 121. International Agency for Research on Cancer, Lyon.
- Doll, R. 1991. Progress against cancer: An epidemiologic assessment. The 1991 John C. Cassel Memorial Lecture. *Am. J. Epidemiol.*, **134**, 675–688.
- Eesti NSV Rahvamajandus 1988 aastal. Statistika aastaraamat*. 1989. ENSV RSK, Tallinn.
- Eesti Statistika Aastaraamat 1990*. 1991. ESA, Tallinn.
- Estonian Trade*. 1991. EVRSA, Tallinn.
- Franceschi, S., Talamini, R., Barra, S., Baron, A. E., Negri, E., Bidoli, E., Serraino, D. & La Vecchia, C. 1990. Smoking and drinking in relation to cancers of the oral cavity, pharynx, larynx, and esophagus in northern Italy. *Cancer Res.*, **20**, 502–507.
- Gardner, M. J. & Osmond, C. 1984. Interpretation of time trends in disease rates in the presence of generation effects. *Stat. Med.*, **3**, 113–130.

- Jolley, D. & Giles, G. G. 1992. Visualizing age-period-cohort trend surfaces: A synoptic approach. *Int. J. Epidemiol.*, **21**, 178–182.
- Kuddo, A. 1988. *Social-economical Causes and Consequences of Distribution of Drunkenness and Alcoholism*. Academy of Sciences of the Estonian SSR, Tallinn (in Russian).
- La Vecchia, C., Levi, F., Lucchini, F., Negri, E. & Boyle, P. 1994. Trends in cancer mortality in the USSR, 1965–1990. *Int. J. Cancer*, **56**, 31–39.
- Leinsalu, M. 1995. Time trends in cause-specific mortality in Estonia from 1965 to 1989. *Int. J. Epidemiol.*, **24**, 106–113.
- Leinsalu, M. & Rahu, M. 1993. Time trends in cancer mortality in Estonia, 1965–1989. *Int. J. Cancer*, **53**, 914–918.
- Levin, B. M. & Levin, M. B. 1990. The anti-alcohol campaign in the USSR – a dubious success. *World Health Forum*, **11**, 253–256.
- Macfarlane, G. J., Boyle, P. & Scully, C. 1992. Oral cancer in Scotland: Changing incidence and mortality. *Br. Med. J.*, **305**, 1121–1123.
- Manual of the International Statistical Classification of Diseases, Injuries and Causes of Death, 9th revision*. 1977. WHO, Geneva.
- Plesko, I., Macfarlane, G. J., Evstifeeva, T. V., Obsitnikova, A. & Kramarova, E. 1994. Oral and pharyngeal cancer incidence in Slovakia 1968–1989. *Int. J. Cancer*, **56**, 481–486.
- Population Age Structure, Counties 1970–1979*. 1994a. EIPRC, IECM, Tallinn.
- Population Age Structure, Counties 1979–1989*. 1994b. EIPRC, IECM, Tallinn.
- Rahu, M. 1992a. Cancer epidemiology in the former Soviet Union. *Epidemiology*, **3**, 464–470.
- Rahu, M. 1992b. Estonia. In *Cancer Incidence in Five Continents*, Vol. VI. IARC Scientific Publications, 120 (Parkin, D. M., Muir, C. S., Whelan, S. L., Gao, Y. T., Ferlay, J. & Powell, J., eds.). International Agency for Research on Cancer, Lyon, 569–573.
- Rahu, M. & Hakulinen, T. 1994. Descriptive epidemiology of cancer around the Baltic Sea. *Acta Oncol.*, **33**, 849–858.
- Ryan, M. 1995. Alcoholism and rising mortality in the Russian Federation. *Br. Med. J.*, **310**, 646–648.
- Swoboda, H. & Friedl, H. P. 1994. Mortality from cancer of the head and neck, lung and esophagus in eastern Austria between 1960 and 1989. *Eur. Arch. Otorhinolaryngol.*, **251**, 52–56.
- Tuyns, A. J. & Audigier, J. C. 1976. Double wave cohort increase for oesophageal and laryngeal cancer in France in relation to reduced alcohol consumption during Second World War. *Digestion*, **14**, 197–208.
- Wasserman, D., Varnik, A. & Eklund, G. 1994. Male suicides and alcohol consumption in the former USSR. *Acta Psychiatr. Scand.*, **89**, 306–313.

SUUÕÕNE- JA NEELUVÄHKI HAIGESTUMUSE JÄRSK TÕUS EESTIS 1968–1992

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On analüüsitud Eesti Vähiregistris aastatel 1968–1992 registreeritud suuõõne- ja neeluvähi esmasjuhte. Standarditud haigestumuskordajad on leitud Euroopa standardrahvastiku alusel kõikide vanuste puhul kokku ning vanuserühmades 15–44, 45–64 ning 65 ja enam aastat. Vanuse, perioodi ja kohordi mõjude leid-

miseks moodustati haigestumuse vanuskordajatest vanuserühmade ja diagnoosi-
perioodi järgi maatriks, mille alusel joonestati haigestumuskordajad nii kontuur-
kaartide kui ka kolmemõõtmeliste pindadena. Kontuurkaartidel on võrdsed
haigestumuskordajad ühendatud samaväärtusjoontega. Et näitlikustada kontuur-
kaarte, on sama maatriks antud ka kolmemõõtmelise pinnana, mis annab kohese
ülevaate suurema haigestumuse piirkondadest. Kohordi efekti väärtusi saab
lugeda kontuurkaartidelt piki diagonaaljooni, mis ühendavad sünniaastaid ja
vanuserühmi.

Suuõõne- ja neeluvähki haigestumus on tõusnud uuritava aja jooksul kõikides
vanuserühmades. Kõige järsem tõus on märgatav meeste nooremas ja keskmises
vanuserühmas. Haigestumuskordajad on kõrgeimad meestel vanuses 60–64 aastat
perioodil 1988–1992. Need inimesed kuuluvad 1928. aasta kohorti. Keele-, suu-
ja neeluvähi esinemissageduse muutumine on vägagi sarnane, viidates sellega
ühesugustele ekspositsiooniteguritele (suitsetamine ja alkoholitarbimine).

Nooremate vanuserühmade haigestumise tendents ennustab tulevikuks suu-
õõne- ja neeluvähiga seotud tervishoiuprobleemide teravamat esilekerkimist.