

Time Trends in Brain Tumor Incidence Rates in Denmark, Finland, Norway, and Sweden, 1974–2003

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In Denmark, Finland, Norway, and Sweden, the use of mobile phones increased sharply in the mid-1990s; thus, time trends in brain tumor incidence after 1998 may provide information about possible tumor risks associated with mobile phone use. We investigated time trends in the incidence of glioma and meningioma in Denmark, Finland, Norway, and Sweden from 1974 to 2003, using data from national cancer registries. We used joinpoint regression models to analyze the annual incidence rates of glioma and meningioma. During this period, 59 984 men and women aged 20–79 years were diagnosed with brain tumors in a population of 16 million adults. All statistical tests were two-sided. From 1974 to 2003, the incidence rate of glioma increased by 0.5% per year (95% confidence interval [CI] = 0.2% to 0.8%) among men and by 0.2% per year (95% CI = –0.1% to 0.5%) among women and that of meningioma increased by 0.8% per year (95% CI = 0.4% to 1.3%) among men, and after the early 1990s, by 3.8% per year (95% CI = 3.2% to 4.4%) among women. No change in incidence trends were observed from 1998 to 2003, the time when possible associations between mobile phone use and cancer risk would be informative about an induction period of 5–10 years.

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The etiology of brain tumors is poorly understood; the only well-established risk factors—ionizing radiation and rare hereditary syndromes, such as neurofibromatosis—account for a small proportion of brain tumor cases (1). The introduction of computed tomography in the mid-1970s and magnetic resonance imaging in the mid-1980s improved the detection of brain tumors and possibly resulted in different diagnostic approaches for common symptoms of brain tumors such as headache or dizziness. Improved diagnostic methods and more incidental findings of asymptomatic meningiomas may have led to increased incidence in the absence of an increase in any etiological factor (2). Radio frequency electromagnetic fields emitted from mobile phones have been proposed as a risk factor for brain tumors (3); however, a biological mechanism that could explain the potential effect of radio frequency electromagnetic fields in the risk of brain tumors has not been identified (4). Epidemiological data are sparse for longer term mobile phone users, and open questions about prolonged expo-

sure remain (5). Although mobile phones were first introduced in the Nordic countries in the mid-1980s, their use did not become widespread until the early 1990s, and it increased sharply in the mid-1990s (6) (see also http://www.stat.fi/til/tvie/2008/tvie_2008_2009-06-09_tie_001_en.html).

Previous investigations in Denmark, Finland, Norway, and Sweden found that the incidence of glioma was relatively stable from 1983 to 1998 (7) and that the incidence of meningioma increased from 1968 to 1997, more so for women than for men (8). Time trends in brain tumor incidence after 1998 are likely to be relevant for evaluating possible associations with respect to radio frequency exposure from mobile phones after 5–10 years of exposure. We investigated time trends in brain tumor incidence rates in these four Nordic countries to evaluate whether trends in the incidence of brain tumor changed in Denmark, Finland, Norway, and Sweden from 1998 to 2003.

We obtained the numbers of first primary brain tumors in patients aged 20–79

years at diagnosis in 1974–2003, by calendar year of diagnosis, 5-year age at diagnosis group, and sex, from the national cancer registries of Denmark, Finland, Norway, and Sweden. The cancer registries of Denmark, Finland, and Sweden code diagnose according to the seventh revision of the *International Classification of Diseases, Seventh Revision (ICD-7)* (9), which is modified or supplemented with information on disease morphology (<http://www.ancr.nu/survey.asp>); in Norway, the ICD-7 was previously supplemented with the morphology codes of the *Manual of Tumor Nomenclature and Coding* (10) and beginning in 1993, with the extended morphological codes of the second edition of the *International Classification of Diseases for Oncology* (11). The size of the population at risk by 5-year age groups was acquired from the national population registers for each calendar year. We analyzed glioma and meningioma separately; when the numbers were sufficient, we analyzed the most common glioma subtype, glioblastoma. This study did not involve direct contact with patients nor were personal identifiers obtained. Hence, patient consent and ethical approval was not required.

The annual age-standardized incidence rates of glioma and meningioma per 100 000 person-years were calculated separately for men and women. The age distribution of these four countries in 1985 was used as the reference population for age standardization, as previously described (7). Both the overall age range (20–79 years) and the

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CONTEXT AND CAVEATS

Prior knowledge

Although mobile phone use has frequently been proposed as a risk factor for brain tumors, neither a biological mechanism to explain this association nor the etiology of brain tumors is known. Mobile phone use in Denmark, Finland, Norway, and Sweden increased sharply in the mid-1990s.

Study design

An investigation of time trends in the incidence of glioma and meningioma among adults from 1974 to 2003 in Denmark, Finland, Norway, and Sweden using data from national cancer registries.

Contribution

From 1974 to 2003, brain tumor incidence rates in Denmark, Finland, Norway, and Sweden were stable, decreased, or continued a gradual increase that started before the introduction of mobile phones. No change in incidence trends was observed from 1998 to 2003, the time when possible associations between mobile phone use and cancer risk would be informative about an induction period of 5–10 years.

Implications

The lack of a trend change in incidence from 1998 to 2003 suggests that the induction period relating mobile phone use to brain tumors exceeds 5–10 years, the increased risk in this population is too small to be observed, the increased risk is restricted to subgroups of brain tumors or mobile phone users, or there is no increased risk.

Limitations

Possible incompleteness of cancer registration and the increased access to improved diagnostic tools may limit the interpretation of the trends in meningioma incidence over time.

From the Editors

20-year age groups (20–39, 40–59, and 60–79 years) were analyzed. In separate sensitivity analyses, brain tumor cases of uncertain histological type were pooled with either the glioma or meningioma cases to evaluate the robustness of the results. We used a piecewise log-linear model known as joinpoint analysis (12,13) with no constraints on the positions of the joinpoints to detect changes in incidence rate trends and to estimate annual percent changes in incidence rates. Permutation

Table 1. Annual percent changes in glioma and meningioma incidence rates in Denmark, Finland, Norway, and Sweden, with 95% confidence intervals (CIs), estimated with the best-fitting joinpoint model

Age group, y	Men		Women	
	Period*	Annual percent change (95% CI)	Period*	Annual percent change (95% CI)
Glioma				
20–79	1974–2003	0.5 (0.2 to 0.8)	1974–2003	0.2 (–0.1 to 0.5)
20–39	1974–1987.5†	3.8 (2.6 to 4.9)	1974–2003	0.3 (–0.2 to 0.7)
	1987.5†–2003	–1.1 (–1.9 to –0.3)		
40–59	1974–2003	0.1 (–0.2 to 0.3)	1974–2003	–0.1 (–0.4 to 0.2)
60–79	1974–2003	0.7 (0.3 to 1.0)	1974–2003	0.5 (0.1 to 0.9)
Meningioma				
20–79	1974–2003	0.8 (0.4 to 1.3)	1974–1987‡	2.9 (2.2 to 3.7)
			1987‡–1990.5§	–2.1 (–8.1 to 4.2)
			1990.5§–2003	3.8 (3.2 to 4.4)
20–39	1974–2003	0.2 (–0.8 to 1.1)	1974–2003	1.7 (1.0 to 2.4)
40–59	1974–2003	0.9 (0.3 to 1.5)	1974–2003	2.6 (2.3 to 3.0)
60–79	1974–2003	0.9 (0.4 to 1.4)	1974–1988.5	2.8 (1.9 to 3.6)
			1988.5 –1991.5¶	–4.8 (–13.2 to 4.4)
			1991.5¶–2003	4.7 (3.7 to 5.8)

* The model was specified to include a maximum of four joinpoints, which could be placed in the middle of a year (eg, 1987) or between two consecutive years (eg, between 1987 and 1988). We denoted the latter joinpoints by adding 0.5 to the calendar year (eg, 1987.5). The model constrained the joinpoints to be at least 1.5 years from each other and at least 2 years away from the boundaries of the total study period. If the best-fitting model included joinpoints, the timing of the trend changes was estimated along with its precision, reported as table notes.

† 95% CI = 1985 to 1991.5.

‡ 95% CI = 1982 to 1989.

§ 95% CI = 1989 to 1995.5.

|| 95% CI = 1978 to 1991.

¶ 95% CI = 1990 to 1996.5.

tests were used to select the best-fitting model while controlling for an overall two-sided statistical significance level of .05.

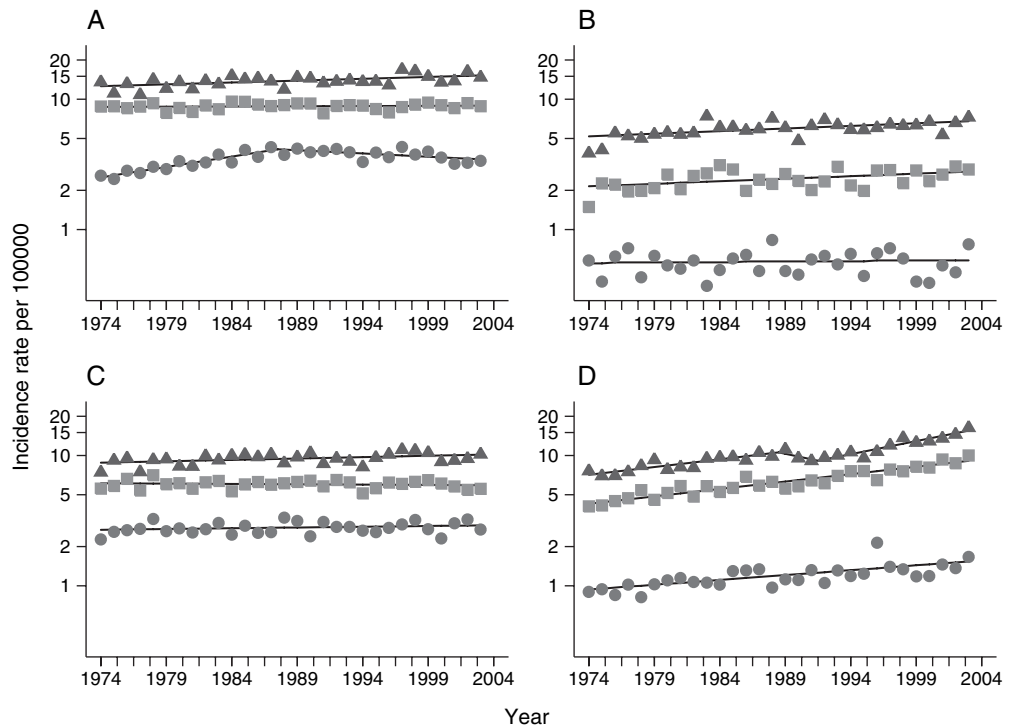
This study was based on 59 984 brain tumor cases that were diagnosed from 1974 to 2003 among 16 million adults aged 20–79 years; the annual average number of glioma and meningioma cases were 1078 and 635, respectively. From 1998 to 2003, Sweden accounted for approximately one-third of the population and approximately one-third of the brain tumor cases, whereas Denmark, Finland, and Norway had populations of similar size and contributed approximately equal numbers of cases.

During the period 1974–2003, the incidence rate of glioma increased gradually by 0.5% per year among men (95% confidence interval [CI] = 0.2% to 0.8%) and by 0.2% per year among women (95% CI = –0.1% to 0.5%) (Table 1). For both sexes, the incidence rate of glioma increased steadily among those aged 60–79 years (annual percent change: 0.7% for men and

0.5% for women), whereas those aged 40–59 years had stable rates (annual percent change: 0.1% for men and –0.1% for women) (Table 1, Figure 1). Among men aged 20–39 years, the incidence rate of glioma decreased slightly beginning in early 1988, whereas no trend changes were observed in women. We observed no change in the glioblastoma incidence rate trend in the overall or age-specific analysis (data not shown).

The overall incidence rate of meningioma increased by 0.8% per year (95% CI = 0.4% to 1.3%) among men and, after the early 1990s, by 3.8% per year (95% CI = 3.2% to 4.4%) among women (Table 1, Figure 1). The rapid changes in trends in the late 1980s and 1990s in women were driven by the 60–79-year age group, which contributed the largest number of cases. Sensitivity analyses in which unclassified tumors were combined with gliomas or with meningiomas yielded results similar to those for the main analysis (data not shown).

Figure 1. Glioma and meningioma incidence rates observed and fitted with the best-fitting joinpoint model, per 100 000 adults in Denmark, Finland, Norway, and Sweden over the period 1974–2003, by sex and 20-year age group, on a logarithmic scale. **Circles** indicate rates for those aged 20–39 years, **squares** indicate rates for those aged 40–59 years, **triangles** indicate rates for those aged 60–79 years, and a **solid line** indicates the regression curve. **A) Men, glioma. B) Men, meningioma. C) Women, glioma. D) Women, meningioma.**



In summary, we did not detect any clear change in the long-term time trends in the incidence of brain tumors from 1998 to 2003 in any subgroup (Table 1, Figure 1). Our finding that brain tumor incidence rates were either stable, decreased, or continued a gradual increase that started before the introduction of mobile phones is consistent with mobile phone use having no observable effect on brain tumor incidence in this period. Our results extend those of previous studies (7,8) of time trends up to 1998 by adding 5 years of follow-up. The observed patterns of brain tumor incidence are consistent with the results of a large Danish cohort study of mobile phone subscribers, which found no increased risk for brain tumors associated with mobile phone use (14,15). Our results are also in line with those of the Nordic and United Kingdom populations (16,17) of the international INTERPHONE case-control study of brain tumors (18), which show no overall increase in glioma or meningioma risk, but leave open the possibility of a small to moderate increased risk for glioma among the heaviest users of mobile phones. Our results are in contrast to those of a Swedish case-control study series (19), which suggested substantially increased risks for glioma among both short- and long-term users of mobile phones.

This study was based on the entire adult populations of Denmark, Finland, Norway, and Sweden—a population base of 16 million people—and is strengthened by the high-quality cancer registration in these countries, which includes benign brain tumors (20–23). The interpretation of the trends in meningioma incidence over time is limited, however, by the possible incompleteness of the registration (24) and the increased access to improved diagnostic tools.

The lack of a detectable trend change in incidence rates up to 2003 in this study suggests that the induction period for brain tumors associated with mobile phone use exceeds 5–10 years, that the increased risk of brain tumors associated with mobile phone use in this population is too small to be observed, that the risk is restricted to subgroups of brain tumors or mobile phone users, or there is no increased risk associated with mobile phone use. Because of the high prevalence of mobile phone exposure in this population and worldwide, longer follow-up of time trends in brain tumor incidence rates are warranted.

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