Cellular Telephones and Cancer—a Nationwide Cohort Study in Denmark


Background: Use of cellular telephones is increasing exponentially and has become part of everyday life. Concerns about possible carcinogenic effects of radiofrequency signals have been raised, although they are based on limited scientific evidence. Methods: A retrospective cohort study of cancer incidence was conducted in Denmark of all users of cellular telephones during the period from 1982 through 1995. Subscriber lists from the two Danish operating companies identified 420 095 cellular telephone users. Cancer incidence was determined by linkage with the Danish Cancer Registry. All statistical tests are two-sided. Results: Overall, 3391 cancers were observed with 3825 expected, yielding a significantly decreased standardized incidence ratio (SIR) of 0.89 (95% confidence interval [CI] = 0.86 to 0.92). A substantial proportion of this decreased risk was attributed to deficits of lung cancer and other smoking-related cancers. No excesses were observed for cancers of the brain or nervous system (SIR = 0.95; 95% CI = 0.81 to 1.12) or of the salivary gland (SIR = 0.72; 95% CI = 0.29 to 1.49) or for leukemia (SIR = 0.97; 95% CI = 0.78–1.21), cancers of a priori interest. Risk for these cancers also did not vary by duration of cellular telephone use, time since first subscription, age at first subscription, or type of cellular telephone (analogue or digital). Analysis of brain and nervous system tumors showed no statistically significant SIRs for any subtype or anatomic location. Conclusions: The results of this investigation, the first nationwide cancer incidence study of cellular phone users, do not support the hypothesis of an association between use of these telephones and tumors of the brain or salivary gland, leukemia, or other cancers.

The use of cellular telephones has increased rapidly throughout the world. Cellular telephones and their base stations transmit and receive radiofrequency (RF) signals in the range between about 800 MHz and 2000 MHz, which fall in the microwave part of the electromagnetic spectrum. The first cellular systems were based on analogue technologies that are gradually being replaced by digital systems. RF radiation at sufficiently high levels can cause heating by inducing small electric currents and increasing molecular movement (1). A typical cellular phone, however, operates at a power output of 0.25 W, which results in a specific energy absorption rate of about 1.5 W/kg and an associated very low rise in brain temperature (maximum, 0.1 °C) (2). Thus, the possible biologic effects from cellular phone use would not be expected to be thermal in nature. Furthermore, because RF radiation does not possess enough energy to remove electrons from atoms or molecules, it is impossible for ionization to occur. RF radiation is thus termed “nonionizing” and, as such, is very different from ionizing radiations of much higher frequencies such as x-rays and gamma rays, which are genotoxic and known to damage DNA molecules either directly or indirectly through free-radical formation.

Although the potential for RF signals to cause cancer seems unlikely (3,4), scientific interest was raised when Lai and Singh (5,6) reported increased numbers of DNA breaks in rat brain cells after 2-hour exposures to RF radiation of 2450 MHz. Subsequent studies (7–9), however, failed to replicate these findings. The most provocative experimental study to date, also as yet unreplicated, comes from Repacholi et al. (10), who reported an excess of lymphoma in genetically engineered mice exposed to pulsed 900-MHz RF radiation for 1 hour per day for 18 months. The relevance of these findings for human health, however, has been questioned by Repacholi himself as well as by other investigators (4,11). To date, only two epidemiologic studies (12,13) have focused on cancer risk and use of cellular telephones. Overall mortality among more than 250 000 customers of a large cellular phone operator in the United States was not increased after a follow-up of only 1 year (12). The numbers of brain cancers (n = 6) and of leukemias (n = 15) were small, and there were no statistically significant associations with number of minutes of phone use per day or years of phone ownership (14). A recent case–control study from Sweden (13) reported a statistically nonsignificant increased risk for brain tumors on the side of the head on which cellular telephones were used. However, the risk for brain tumors overall was not increased, and there were methodologic concerns related to ascertainment of cases (15). One occupational study (16) has been conducted to date that deals directly with RF exposures from wireless communication technologies. In that study, no association between RF exposure and cancers of the brain and nervous system and leukemia was seen among 195 775 Motorola workers engaged in the manufacturing and testing of cellular telephones.

Against this backdrop of public concern and limited scientific evidence, we conducted a nationwide study of all eligible cellular telephone users in Denmark from 1982 through 1995. The incidence of cancers of a priori interest, such as brain and salivary gland cancers, leukemia, and other cancers, was assessed in a cohort of more than 420 000 users of analogue Nordic Mobile Telephone System (NMT) and digital General System for Global Telecommunications, formerly called Group Special Mobile (GSM), cellular telephones.

Subjects and Methods

Study Population

The study was approved by the National Scientific Ethical Board, the National Register Board, and the Danish Ministry of Research. The study population...
tion included all cellular telephone subscribers in Denmark from January 1, 1982—when this service was put into operation—until December 31, 1995. The subscribers were identified from the computerized files of the two Danish operating companies, Sonofon and TeleDanmarkMobil. Both companies furnished records of all cellular telephone numbers issued during the eligibility period. The files also included the name of the subscriber (either a person or a company); the address according to parish, postal code, street, building number, floor, and side of the building; the type of telephone system used (analogue telephones were either NMT 450 or NMT 900, and digital telephones were GSM); and the date of subscription(s). For users of the digital system, the date of termination of subscription(s) or last invoice mailed was also provided and enabled us to compute the duration of subscription in months. One of the operating companies provided the number of minutes billed for outgoing digital calls beginning in 1992; however, because of limitations of these data, further analyses were not pursued.

A total of 723,421 subscribers were initially identified. We excluded 200,507 corporate customers because information on individuals was not available. The names and addresses of the remaining 522,914 noncorporate subscribers were linked to the files of the Central Population Register (CPR) to verify the personal data and to obtain individual personal identification numbers and information on vital status, date of death, or date of emigration, if applicable. The CPR was established in Denmark in 1968, when all citizens were assigned a unique 10-digit personal identification number that incorporates gender and date of birth and permits accurate linkage of information between registers. During the study period, the CPR included both current and past addresses of each inhabitant of the country.

Linkage to the CPR further reduced the size of the cohort because of errors in name (n = 49,352) or address (n = 10,183) of the telephone user or because the address was not residential (n = 11,687). The linkage unambiguously identified 451,679 subscribers (86.4%) by name, address, identification number, and vital status. Additional exclusions included 10,679 duplicates, 17,921 subscriptions after 1995 when the eligibility period ended, 2,550 persons under the age of 18 years at first subscription, and 394 persons permanently residing in Greenland or the Faroe Islands. Our study was based entirely on record linkage, and no one was aware of whether he or she was included. However, once the study had been announced in the media, the two telephone companies published in their quarterly reports a notice that subscribers could contact them if they wished to be excluded. A total of 53 persons contacted the telephone companies in this regard. The final cohort consisted of 420,095 cellular telephone subscribers or 80.3% of the residential subscribers obtained from the phone company lists.

Identification of Cancer Among Subscribers

Cancers were determined from the Danish Cancer Registry on the basis of linkage with the subscribers’ personal identification numbers. The Danish Cancer Registry was initiated in 1942 and has since operated on a nationwide basis. Follow-up began at the date of first subscription and ended at the date of death, emigration, or December 31, 1996, whichever came first. Cancers as well as benign tumors of the brain and papillomas of the urinary tract were classified according to the modified Danish version of the International Classification of Diseases, 7th revision (ICD-7) (17), and since 1978, all tumors have been coded according to the International Classification of Diseases for Oncology (ICD-O) (18). The risk of intracranial tumors was evaluated by morphology and topography groupings, following, in part, a taxonomy suggested by Kleihues et al. (19).

Statistical Analysis

The incidence rates in Denmark for each cancer, calculated according to sex, 5-year age groups, and 5-year calendar periods, were applied to the person-years of observation in the study cohort to obtain the number of cancers expected (20). Tests of statistical significance and confidence intervals (CIs) for the standardized incidence ratio (SIR), the ratio of the observed to expected number of cancers, were calculated by the Miettinen exact method (21) when the observed number of cancers was small (i.e., fewer than five cancers); otherwise, an accurate asymptotic approximation was used (22). All statistical tests are two-sided and were considered to be statistically significant at P < .05. The relationship between duration of subscription (defined as the aggregated periods of cellular telephone subscriptions available only for digital phone users) or time since first subscription (latency) and the risk for cancer was evaluated. The analysis was conducted for all subscribers combined as well as for subcohorts defined by type of mobile telephone system used (analogue only, digital only, and persons who used both an analogue and later a digital phone).

RESULTS

Table 1 shows the characteristics of the study cohort. The 420,095 cellular telephone subscribers (357,550 men and 62,545 women) accrued 1,128,493 person-years of follow-up (average, 3.1 years; range, 0–15 years). The median age at entry into the cohort (date of first subscription) was 37.4 years for men and 38.4 years for women. On average, persons who subscribed to the analogue system were followed longer (3.5 years) than those who subscribed to the digital system (1.9 years). Just over 69% of the subscriptions began in 1994–1995.

Table 2, gives the total and site-specific SIRs for cancer among male and female subscribers. Overall, there was no evidence of an increased risk for total cancers (SIR = 0.89, 95% CI = 0.86 to 0.92), tumors of the brain or nervous system (SIR = 0.95, 95% CI = 0.81 to 1.12), leukemia (SIR = 0.97; 95% CI = 0.78 to 1.21), or tumors of the salivary glands (SIR = 0.72; 95% CI = 0.29 to 1.49), sites a priori interest. There were 2,876 cases of cancer reported in men, with 3,237.6 expected, yielding an SIR of 0.86 (95% CI = 0.83 to 0.90). The estimate in women was 1.03 (95% CI = 0.95–1.12).

Table 1. Descriptive characteristics of cellular telephone subscribers in Denmark, 1982–95*  

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Men (n = 357,550)</th>
<th>Women (n = 62,545)</th>
<th>Both sexes (n = 420,095)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Year of first subscription</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>1982–1984</td>
<td>3741</td>
<td>78</td>
<td>3819</td>
</tr>
<tr>
<td>1985–1987</td>
<td>7603</td>
<td>263</td>
<td>7866</td>
</tr>
<tr>
<td>1988–1990</td>
<td>20,175</td>
<td>1,117</td>
<td>21,292</td>
</tr>
<tr>
<td>1991–1993</td>
<td>87,773</td>
<td>9,186</td>
<td>96,959</td>
</tr>
<tr>
<td>1994–1995</td>
<td>238,258</td>
<td>51,901</td>
<td>290,159</td>
</tr>
<tr>
<td><strong>Age at first subscription, y</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18–29</td>
<td>118,429</td>
<td>17,920</td>
<td>136,349</td>
</tr>
<tr>
<td>30–39</td>
<td>90,921</td>
<td>16,585</td>
<td>107,506</td>
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<tr>
<td>40–49</td>
<td>79,428</td>
<td>15,706</td>
<td>95,134</td>
</tr>
<tr>
<td>50–59</td>
<td>45,823</td>
<td>8427</td>
<td>54,250</td>
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<tr>
<td>&gt;60</td>
<td>17,948</td>
<td>2821</td>
<td>20,769</td>
</tr>
<tr>
<td><strong>Telephone system at first subscription</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Analogous system (NMT 450)</td>
<td>24,879</td>
<td>1,568</td>
<td>26,447</td>
</tr>
<tr>
<td>Analogous system (NMT 900)</td>
<td>130,670</td>
<td>20,816</td>
<td>151,486</td>
</tr>
<tr>
<td>Digital system (GSM)</td>
<td>202,001</td>
<td>40,161</td>
<td>242,162</td>
</tr>
<tr>
<td><strong>Duration of subscription for digital phone subscribers (GSM), y†</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1</td>
<td>85,828</td>
<td>21,070</td>
<td>106,898</td>
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<tr>
<td>1–2</td>
<td>100,589</td>
<td>17,324</td>
<td>117,913</td>
</tr>
<tr>
<td>&gt;3</td>
<td>15,584</td>
<td>1767</td>
<td>17,351</td>
</tr>
</tbody>
</table>

*GSM = General System for Global Telecommunications; NMT = Nordic Mobile Telephone System.
†Duration data were available only for the 202,001 subscribers to digital phone systems. The percentage of users in each category of duration of use is calculated as the number of GSM users divided by total number of GSM users.

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to 1.13) based on 515 observed cases. Statistically significantly low SIRs in men were seen for cancers of the lung (SIR = 0.65), pharynx (SIR = 0.62), esophagus (SIR = 0.74), liver (SIR = 0.60), stomach (SIR = 0.78), and other and unspecified sites (SIR = 0.70). The SIR for testicular cancer (i.e., 1.12) was not statistically significantly increased. Among women, we observed no deviations from the expected figures for any of the site-specific cancers, except for cancer of the cervix uteri (SIR = 1.34; 95% CI = 0.95 to 1.85; n = 37).

The SIRs for tumors of the brain and nervous system and for leukemia were not related to time since first subscription (latency), age at first subscription (age at entry), cellular telephone system used, or, for the 202,001 digital system subscribers, duration of subscription (Table 3).

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Tumors of the brain and nervous system were analyzed by morphologic and topographic subtypes (Table 4). Of the 154 reported cancers, 144 were situated intracranially. There were no statistically significant SIRs for any subtype or any anatomic location, including the occipital lobe, which would be closest to the antenna of the cellular phone when in use (SIR = 1.79; 95% CI = 0.58 to 4.17).

The absence of an excess risk was seen not only for the rapidly growing tumors such as gliomas but also for the less aggressive tumors such as meningiomas and acoustic neuromas. A nonsignificant increase was seen for other and unspecified sites (SIR = 1.31), which included tumors of the pituitary gland and pineal gland, i.e., tumors in the periphery of the area typically exposed to the RF radiation from cellular telephones.

**DISCUSSION**

Our nationwide study of more than 420,000 cellular telephone users found that the numbers of tumors of the brain and nervous system, leukemia, and salivary gland tumors, all of which were sites of a priori interest, were remarkably close to those expected on the basis of the incidence rates in the general population. Moreover, there was no evidence for a dose–response relationship for these cancers based on number of years as a subscriber. Analyses by anatomic location of the brain tumors within the head revealed no unusual clusterings that could be related to increased exposure to RF radiation from cellular telephones. The absence of statistically significant increases in cancer risks applied equally to analogue and digital systems.

The decreased risk estimate for total cancers observed among men, who constituted 85% of the cohort, was due in large part to a decreased incidence of lung cancer and several other smoking-related cancer sites, as well as of stomach cancer. This pattern is consistent with a confounding effect of social class—i.e., cellular phone users may differ from the general population by being more well-to-do and less likely to smoke cigarettes. Before 1992, use of cellular telephones in Denmark was expensive and ownership was more common among people of higher socioeconomic status (SES). Moreover, higher SES groups in Denmark tend, on average, to abstain from smoking, to have a lower prevalence of heavy alcohol use, and to have lower rates of stomach cancer (22). Conceivably, heavy users of cellular phones might also find it difficult to smoke while talking on the phone, and it was recently suggested that young persons were choosing to spend their limited resources on cellular phone expenses rather than on purchasing cigarettes (23).

The possible differences in social class or tobacco use between the cellular phone users and the general population, however, should not affect the findings for cancers of the brain and salivary gland and leukemia, which are not strongly associated with smoking. In fact, internal risk comparisons among cellular phone users themselves confirmed the SIR findings, in that there were no statistically significant trends over categories of duration of phone use or latency for these cancers of a priori interest, i.e., brain cancer, salivary gland cancer, and leukemia. Because cost is no longer an important deterrent to cellular phone ownership, we suspect that social class differences between cellular phone users and the general population are less important today than they may have been in the past.

Testicular cancer was slightly increased (12%) in cellular phone users, based on 187 cases. A cluster of testicular cancer among police officers who used hand-held radar guns has been reported
Because RF signals are unlikely to cause gene mutations, the biologic process underlying a possible association between exposure to cellular telephones and the risk of cancer has been proposed to be a thermal or nonthermal mechanism that promotes tumor growth (27). However, experimental data supporting a promotional mechanism are scanty (4). Such a mechanism implies that current use of cellular phones might be of particular importance, although our data show an absence of a brain cancer excess in recent calendar years when phone use dramatically increased. Furthermore, tumors located in the temporal, parietal, or occipital lobes or in the meninges were also not found to be in excess. If it is assumed that tumor promotion occurs close to the site of exposure, this finding provides additional evidence against an association between cellular telephone use and brain cancer.

Our study has several strengths. It is a nationwide cancer incidence study of more than 420,000 cellular telephone users with more than 1 million person-years of follow-up. Nearly all persons in Denmark aged 18 years or older who subscribed to a cellular telephone during the period 1982–1995 were included, making up about 15% of the total adult population of Denmark. Nationwide cancer registry data were available to identify all cancers, and the Danish Cancer Registry is considered to be valid and virtually complete (28,29). Moreover, we were able to subclassify brain tumors with regard to location and morphology. Because the records of the telephone companies were compiled before the cases of cancer occurred among cohort members and because the Danish Cancer Registry information was assembled independently of any company files, the possibility of observational or recall biases is remote.

Follow-up for cancer occurrence was up to 15 years after cellular phone subscription. The average period of follow-up was 3.1 years, reflecting the recent increase in cell phone use in the population; i.e., over two thirds of the subscriptions began in 1994 and 1995. Conceivably, the latency may be too brief to detect an early-stage effect or an effect on the more slowly growing brain tumors. Moreover, our study may currently have too few heavy users to exclude with confidence a carcinogenic effect on brain tissue following intensive, prolonged use of cellular telephones. On the other hand, if RF exposure is assumed to act by promoting the growth of an underlying brain lesion, then the intense recent use, as currently experienced by large numbers in our cohort, might be of more importance than latency or long-term use considerations.
Some misclassification of exposure variables cannot be ruled out because use of the cellular telephone had to be ascribed exclusively to the owner, who is not necessarily the sole user, of the telephone. For example, in a survey of 3949 telephone account holders in the United States (30), only 48% were found to be the sole users of their cellular telephone. This result implies that the duration of phone usage of the subscribers of our study may be overestimated.

Future studies might benefit from refined exposure assessment that would enable risk evaluation over categories of cumulative minutes of cellular telephone use, including both incoming and outgoing calls for individual users. Ideally, an estimate of the energy absorbed in tissue would be a preferred exposure metric, taking into account such factors as the telephone model and system, the distance between the user and the base station, and the duration and intensity of cellular telephone use (31). Several large-scale studies in the United States and in Europe are currently ongoing and should provide additional knowledge on the relation between brain tumors and the use of handheld cellular telephones (32).

In summary, this first nationwide cancer incidence study evaluating cellular telephone use provides no support for an association between use of these telephones and risk of brain cancer, leukemia, salivary gland cancer, or other site-specific cancers.

Note added in proof: Recently, two new carefully conducted case–control studies of brain tumors and cellular phone use have been published (33, 34). Although each suffered from limitations inherent in case–control studies (35), neither provided evidence of a link between cellular telephone use and increased brain cancer risk. These new reports, added to the results of our large-scale nationwide cohort study of cancer incidence among cellular telephone users in Denmark, provide increasing evidence against the hypothesis of a cellular telephone and cancer association.

REFERENCES


Notes

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