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# **Deliverable D17:** Report on health effects of RF with recommendations for non-ionising radiation protection and research needs

## REPORT ON HEALTH EFFECTS OF RADIOFREQUENCY FIELDS

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| **Dissemination Level** | | |
| **PU** | Public | **PU** |
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# CONTENT

# Introduction

The primary natural source of RF fields is the sun. Human-made sources, however, emit the majority of fields in the immediate environment of the community, home or the workplace. Most RF fields found in the environment are due to commercial radio and TV broadcasting and to telecommunications facilities (Table 1). RF sources in the home include microwave ovens, DECT telephones and Wi-Fi routers. In the workplace, there are a number of industrial processes which use RF fields: dielectric heaters used for wood lamination and the sealing of plastics; industrial induction heaters and microwave ovens, medical diathermy equipment to treat pain and inflammation of body tissues and electrosurgical devices for cutting and welding tissues.

**Table 1: RF range: frequencies and type of device or service (adapted from Mathes)**

| Frequency Range | Frequency | Type of Device or Service |
|---|---|---|
| 30 - 300 kHz | LF (low) | LF broadcast and long range radio |
| 300 - 3000 kHz | MF (medium) | AM radio, radio navigation, ship to shore |
| 3 - 30 MHz | HF (high) | CB radio, amateurs, HF radio communications and broadcast |
| 30 - 300 MHz | VHF (very high) | FM radio, VHF TV, emergency services |
| 300 - 3000 MHz | UHF (ultra high) | UHF TV, paging, mobile telephones, amateur radios, DECT |
| 3 -30 GHz | SHF (super high) | Microwaves, satellite communications, radar, point to point microwave communications, Wi-Fi |
| 30 - 300 GHz | EHF (extremely high) | Radar, radio, astronomy, short link microwave communications |

Today the largest source of RF for the general public is the use of mobile telephones. Except when phones are used in a hands-free position or used to send data, mobile telephones are generally held against the head when a call is being made and the antenna receives and sends the signal. The head of the user is in the near field of the source because of the distance of the antenna to the head is typically a few centimetres. Due to this close proximity, most of the RF energy is absorbed in the brain hemisphere on the side where the phone is used, mainly (50ï 60%) in the temporal lobe. The average relative SAR is highest in the temporal lobe (6ï 15%, depending on frequency, of the spatial peak SAR in the most exposed region of the brain) and the cerebellum (2ï 10%) and decreases very rapidly with increasing depth, particularly at higher frequencies(Cardis et al. 2008).

Occupational exposures, on the other hand, can differ from mobile phone exposures in a number of important respects:

- They may occur for more prolonged periods. For example, working next to an industrial heater may expose the subject to radiation for eight hours a day, five days a week, over a number of years.
- They may expose larger areas of the body. Mobile phones tend to expose on a small area of the body adjacent to the ear; whereas some pieces of industrial machinery may expose the entire body to radiation.

This is the third and final report on epidemiological studies of health effects of RF fields. The first two reports focused on new literature published during the project period of EMF-NET, whereas

the final report will make an assessment of the totality of the available epidemiological scientific evidence. Included in the assessment are scientific studies that have been published primarily in peer reviewed scientific journals. The studies have been identified through systematic searches in PubMed, ISI Web of Science, scrutinizing reference lists of published papers and reports, and through participation in scientific conferences focused on biological effects of electromagnetic fields.

# Evaluation

Whereas the original objective of WP3 was to evaluate the epidemiological evidence for health effects of EMF exposure, an evaluation of the effects of RF was not possible within the lifespan of the EMF-Net project because of delays in publication of the results of the international analyses within INTERPHONE, the largest epidemiological study to date. The International Agency for Research on Cancer (IARC) and World Health Organization (WHO) evaluations have likewise not yet taken place because of this delay.

The current report is therefore limited to a critical review of the evidence to date. It is, at present, premature to draw conclusions concerning the presence or absence of health effects from RF at ñathermal levelsò.

Where available studies existed, the following outcomes have been reviewed:

1. Cancer outcomes
    a. Brain and CNS tumours in adults
    b. Other tumours
2. Fertility and pregnancy outcome
3. Cardiovascular effects
4. Other possible health effects

The list is based on the ñKey Issueò list of Main Task 1 (MT1) of EMF-NET, and corresponds to the endpoints evaluated in WP2.1 Laboratory studies, for which evidence from epidemiological studies of RF are available.

# Exposure assessment

As there is at present no known biophysical interaction mechanism for potential health effects of athermal, levels of RF it is not obvious which aspect of exposure is the most relevant.

Where efforts have been made to use an exposure metric, studies have generally focused on estimates of the amount of RF energy absorbed, measured by SAR (the specific energy absorption rate i.e. energy absorption rate per unit mass (measured in W kgī 1)) in mobile phone studies, or on the total RF electromagnetic field exposure.

## *Residential exposure*

As discussed below, most residential studies in relation to RF transmitters are of ecological design. Exposure assessment methods in these studies are generally very crude, based on the measured distance between a house and nearby RF sources. Spot measurements have, however, been used in two recent case-control studies to validate exposure prediction models (Ha et al. 2007;Merzenich et al. 2008), showing a better correlation between measurements and the models than between measurements and distance from the source.

A number of studies have also considered RF exposure from cordless telephones at home (Hardell et al. 2006c;Hardell et al. 2006b;Schuz et al. 2006a;Schuz et al. 2006b). Information on the use of

these telephones has been obtained, together with information on mobile phone use, from questionnaires and include dates of start and stop of use, type of cordless phone and, in the German study, location of the base station in the house or apartment.

Integrated measurements over longer time periods (1-7 days) have also been made in recent RF exposure assessment studies (Thomas et al. 2008;Röösli et al. 2008;Viel et al. 2008) with the use of personal RF meters. These meters allow estimation of exposure in most of the frequency bands of concern for environmental exposure (including TV, radio, mobile phones ï handsets and base stations -, Wifi and DECT routers). These instruments have not, however, yet been used in any of the analytical epidemiological studies published to date.

## *Occupational exposure*

Occupational studies are also characterized by rather crude exposure assessment, sometimes limited to investigations of disease risk associated with individual job titles, or to grouping of occupational titles thought to be exposed to RF. In some of the studies, workers in the groupings considered were also exposed to ELF and it is difficult to separate RF and ELF exposed workers.

Recent studies (Karipidis et al. 2007;Berg et al. 2006) have used detailed occupational history, in conjunction with assessments by occupational hygienists and, in the Karipidis study, linkage with an EMF Job-Exposure Matrix (JEM) to infer exposure levels.

## *Mobile phones*

Most studies to date have been based on historical use of mobile phones rather than any estimate of RF ñexposureò.

Information collected in cohort studies has been limited ï the fact of having a subscription, and, in some instances, the date of start of the subscription and the type of network.

Case-control studies have provided the opportunity of collecting much more detailed information at the individual level. Exposure variables generally collected include: ever having been a regular user (this variable was defined differently in different studies ï within INTERPHONE, it was defined a priori as at least one call per week on average for a period of 6 months or more), time (years) since first regular use, cumulative number of calls, and cumulative duration of calls. For analyses of cancer risk, exposure variables were generally censored some time (often 1 year) before the reference date. Cumulative number and cumulative duration of calls have also been analyzed, generally excluding use with hands-free devices. Use in different time windows has also been analysed in some papers.

Because the absorption of RF energy from phones is localized, if a risk exists it is likely to be greatest for tumours in regions with greatest energy absorption. Most (97ï 99% depending on frequency) appears to be absorbed in the brain hemisphere on the side where the phone is used, mainly in the temporal lobe. The average relative SAR is highest in the temporal lobe and the cerebellum and decreases very rapidly with increasing depth, particularly at higher frequencies. Analyses of risk by location of tumour are therefore essential for the interpretation of results studies of brain tumours in relation to mobile phone use (Cardis et al. 2008).

Major efforts are therefore underway to evaluate the amount of RF energy at the site of the tumour in case-control studies of brain and central nervous system (CNS) tumours.

In the glioma analyses of the Japanese INTERPHONE study (Takebayashi et al. 2008), the maximum amount of RF energy absorbed inside the tumour was estimated. Within INTERPHONE; efforts are underway at the international level to develop an RF ñexposure

gradientò to estimate the amount of RF energy absorbed at the location of the probably origin of the tumour, taking into account the subject´s mobile phone use history as well as historical characteristics of phones (including radiation pattern) and networks in participating countries. This gradient is not yet available, however, in the studies published to date.

An important issue in the interpretation of results of case-control studies that rely on self-reported history of mobile phone use is the potential for errors and biases in recall of amount of phone use. Within INTERPHONE; validation studies have been conducted to evaluate potential error in the recall of phone, indicating that phone use was subject to moderate systematic and substantial random error (Berg et al. 2005;Vrijheid et al. 2006;Vrijheid et al. 2008a;Hours et al. 2007b;Parslow et al. 2003;Hepworth et al. 2006;Samkange-Zeeb et al. 2004;Tokola et al. 2008). Errors appear to be larger for duration of calls than for number of calls, and phone use appears to be under-estimated by light users and over-estimated by heavy users. Comparison of a sample of cases and controls in three countries showed little evidence for differential recall errors overall or in recent time periods, but apparent overestimation by cases in more distant time periods (Vrijheid et al. 2008a).

Laterality of phone use is also subject to recall error and to differential reporting between cases and controls. Hence reported increases in the risk of some tumour types for ipsilateral use in long-term users that are described below, are currently difficult to interpret. These could reflect a real association (since, as indicated above, RF energy absorption is very localised) or an artefact related to laterality recall bias.

# Studies of health effects from environmental sources of RF other than phones

## *Point sources (broadcasting towers and mobile phone base stations)*

Epidemiological studies completed so far have mostly looked at cancer incidence broadcasting towers, using an ecological design. Only two case-control studies have been conducted to date. Ecologic studies are subject to a number of methodological problems, which limit their usefulness for studies of low levels of RF (Cardis and Estève 1991;Goldberg and Cardis 1994). It is difficult to ensure an adequate choice of the geographical areas to be compared: the choice of boundaries of the study regions may exaggerate or diminish the apparent significance of an association. Information on levels of exposure, on confounding factors and population movements is rarely available. In the best of cases, crude estimates of exposure by sub-regions may be available, or sub-regions may be classified as a function of their distance (which may not be a good surrogate for exposure level) from a source of exposure. Because individual exposures are not determined, a causal relationship is not easy to infer and studies are subject to the "ecological fallacy" – the failure of group level data to properly reflect individual level associations – (Greenland and Morgenstern 1989;Piantadosi et al. 1988). In most instances therefore, a "negative" ecological study (i.e. a study in which no increase in risk is observed) cannot be interpreted to mean that no risk exists, and can only provide an upper bound for the risk estimate. A "positive" correlation study, on the other hand, may be difficult to interpret because of potential biases and confounding. Reported clusters (rather than actual epidemiological studies) are even more difficult to interpret as they may suffer a number of methodological limitations (including completeness of case ascertainment and validation of diagnoses) in addition to those of formal ecological studies (Gavin and Catney 2006).

## Case-control studies

In Korea, a case-control study of childhood leukaemia and brain cancer (0-14 years) was conducted (Ha et al. 2007) in order to investigate the possible relation with RF exposure from AM radio broadcasting tower, previously reported in an ecological study (Ha et al. 2003;Park et al. 2004). Controls were individually matched to the cases on age and sex and were chosen among patients with a respiratory illness. The study included 1,928 leukaemia cases and 956 brain cancer cases from 14 South Korean hospitals using the South Korean Medical Insurance Data System, and 3,082 controls. A prediction program incorporating a geographic information system was used to estimate total and peak RF exposure at the subjectsô home address from 31 AM radio transmitters with a power of 20 kW or more. An elevated OR was seen for all types of leukaemia combined (OR 2.15, 95% CI 1.00, 4.67) among children who resided within 2 km of the nearest AM radio transmitter as compared with those resided more than 20 km from it. The corresponding OR for lymphocytic leukaemia was 1.69 (95% CI 0.69, 3.72). In analyses by level of RF exposure, no association was found for brain cancer. A significantly increased risk of lymphocytic leukaemia was found in the highest quartile of peak RF exposure (OR 1.40, 95% CI 1.04, 1.88; peak exposure > 0.6 V/m) for lymphocytic, but not for myelocytic leukaemia (Ha et al. 2008). In this corrected analysis, no association was found, however, with total RF exposure, contrary to the results originally published (Ha et al. 2007).

A case-control study was conducted in West Germany to evaluate the possible link between RF from broadcasting towers and the risk of leukaemia in children (0-14 years) (Merzenich et al. 2008). Analyses included 1,959 cases diagnosed between 1984 and 2003, registered in the German Childhood Cancer Registry and living in municipalities near Germanyôs strongest emitting television and radio broadcasting towers. Individual exposure to RF at the subjectsô home address 1 year before diagnosis was estimated with a field strength prediction program. The OR for leukaemia was 1.04 (95% confidence interval: 0.65, 1.67) among children living within 2 km of the nearest broadcast transmitter compared with those living at a distance of 10-<15 km. It was 1.31 (95% CI 0.80, 2.15) when analyses were restricted to lymphoid leukaemia and 1.56 (95% CI 0.77, 3.16) when further restricted to AM transmitters. No association was found, however, between the estimated level of RF exposure and the risk of leukaemia. The OR for leukaemia (all types combined) was 0.86 (95% confidence interval: 0.67, 1.11) when upper (>/=95%/0.701 V/m) and lower (<90%/0.504 V/m) quantiles of the RF distribution were compared. An analysis of AM and FM transmitters separately did not show increased risks of leukaemia. Validation of the field strength prediction programme, show a better correlation of spot measurements with field strength predictions than with distance from the broadcasting towers.

A combined analysis of the lymphocytic leukaemia results from Korea and Germany found no association with total RF exposure (Schuz and Ahlbom 2008). ORs for living within 2 km of broadcasting towers are of similar magnitude in both studies, however.

## Ecological studies

In the USA, spatial clustering of childhood cancer around a large microwave tower was studied in the city of San Francisco, over the period 1973-88. The study included 51 leukaemia, 35 brain cancers and 37 lymphatic cancers and found no association between risk of these diseases and distance from the tower (Selvin et al. 1992).

In the USA, a case-control study was conducted to evaluate the etiology of a cluster of childhood acute leukaemia on the Waianae Coast, Hawaii. The study included 12 cases diagnosed between 1979 and 1990 and 48 controls. Children who lived within 4.2km of the radio towers (median distance) had a non-significantly increased risk of leukaemia (OR 2.0, 95% CI 0.06-8.3) (Maskarinec et al. 1994).

A study of cancer incidence and mortality among residents in the ñinnerò (three municipalities close to the towers) and ñouterò areas (six municipalities which were more distant) around the television towers in Northern Sydney (Australia) was carried out (Hocking et al. 1996). An increased incidence and mortality of childhood leukaemia in the inner area was observed. These data were reanalysed by municipality by (McKenzie et al. 1998) after adding other municipalities close to the towers. The excess of childhood leukaemia was restricted to one of the inner area municipalities. When this municipality was excluded, there was no increased incidence and mortality for childhood leukaemia.

A geographical study of cancer incidence was conducted around the Sutton Coldfield television and FM radio transmitter in the West Midlands, England, following a report of a cluster of leukaemias and lymphomas (Dolk et al. 1997b). The risk of adult leukaemia within 2 km was 1.83 (95% confidence interval 1.22-2.74), and there was a significant decline in risk with distance from the transmitter (p = 0.001). These findings appeared to be consistent over the periods 1974-1980, 1981-1986. A further, more comprehensive study, carried out around 20 television and radio transmission towers in the UK, found no increased risk of adult or childhood leukaemia for persons residing within 2 km (O/E ratio=0.97, 95% CI 0.8-1.2, based on 79 cases) or 10 kms of transmitters. A small significant decline in risk of adult leukaemia with distance from transmitters was seen, however, in the 2-10 km range (Dolk et al. 1997a).

In Italy, a study of childhood leukaemia incidence and adult and adolescent leukaemia mortality was conducted around the powerful Vatican Radio broadcast transmitters in a northern suburb of Rome (Michelozzi et al. 2002). The study covered a 10-km area around the transmitter, with a population of around 50,000. Overall, 40 adult and adolescent leukaemia deaths and 8 childhood leukaemia cases were observed in the study area during the study period (1987-1998 for mortality, 1987-1999 for incidence), compared to 37.4 and 6.5 expected, respectively. For childhood leukaemia, a non-significantly increased risk (SIR 6.1, 95% CI 0.4, 27.5) was seen for residence within 2 km of the transmitter, based on one case, as well as a significant trend of increasing SIR with decreasing distance (p=0.036). Among adolescents and adults, two deaths were reported among men living within 2 km of the transmitter (SMR 2.9, 95% CI 0.5, 9.0) and none in women, and there was a trend of increasing SMR with decreasing distance, which was statistically significant only in men (p=0.03). Results of this study are based on very small numbers of cases.

An ecological study of cancer incidence was conducted in South Korea (Ha et al. 2003) in areas close to 42 AM radio transmitters (11 high-power transmitters ï 100-1500 kW ï and 31 low-power transmitters). Incidence rates were calculated for all cancers, leukaemia, malignant lymphoma, brain and breast cancer in 2km-radius areas around each transmitter, as well as in control areas for the period 1993-1996. Slightly increased rates were seen in high-power transmitter areas compared to low transmitter areas, for all of the outcomes studied; they were significantly increased only for all cancers combined (based on 1,636 cases in high-power areas) and for brain cancer in women (based on about 20 cases). In analyses of individual transmission sites, significant increases of total cancer incidence were observed in 9 out of 11 high-power sites, of leukaemia incidence in 2 and of brain cancer in one; there was no evidence for a relation between the incidence ratio and power level of the transmitter. Numbers of cases for individual cancer types were small, however, particularly when considering individual areas.

An ecological study of cancer mortality was also conducted, in 1994-1995, in South Korea (Park et al. 2004) in 10 RF-exposed areas (defined as regions that included AM radio broadcasting towers of over 100 kW), and in 40 control areas. All cancer mortality was found to be significantly higher in the exposed areas (directly standardised mortality rate ratio (MRR) 1.29, 95%CI = 1.12, 1.49). There was no apparent trend in MRR by electrical power level, however. Mortality from virtually all specific types of cancers considered was also increased (although not statistically significantly

so) in the exposed areas compared to the control areas, in men as well as in women, raising the issue of comparability of the populations in the exposed and control areas. In analyses by age at death, leukaemia mortality was found to be significantly elevated in exposed areas among children (MRR 2.29, 95% CI 1.05, 5.98, based on 11 deaths in the exposed areas) and in adolescents and young adults (MRR 2.44, 95% CI 1.07, 5.24 based on 11 deaths in the exposed areas).

A cross-sectional study of randomly selected inhabitants living in urban and rural areas for near to 10 selected base stations was conducted in Austria to evaluate the possible effect of base stations on subjective symptoms and cognitive performance (Hutter et al. 2006). Cognitive tests were performed on 365 subjects, and their wellbeing and sleep quality were assessed. Field strength of high-frequency electromagnetic fields was measured in bedrooms of 336 households, and the maximum exposure from the base station was computed. Significant relations were found for a number of symptoms, particularly headaches, after adjustment for age, sex, region, mobile phone use and fear of adverse health effects of base stations. No clear difference was found in sleep quality or cognitive performance, although a slightly faster reaction in perceptual speed was associated with higher exposure level.

A cross-sectional health study was conducted in Cyprus in two villages near the Akrotiri salt lake site (part of the UK Sovereign Base Areas Administration, containing a military air base and a large antenna array) and in one control village about 15 km away from the site (Preece et al. 2007). The objective was to compare electromagnetic profile and health status of the population in these villages. The population in the villages totalled about 800 and 350 in Akrotiri and Asomatos (the two villages near the site) and 1,000 in the control village. The prevalence of specific symptoms and diseases was investigated using specifically designed questionnaires, a risk perception survey and collection of health and mortality data from available registry and other sources. The questionnaires were distributed to each household, with response rates of 87%, 77% and 92% respectively in Akrotiri, Asomatos and the control village. Spot RF measurements were also made at a number of places in each village using Delta-T multichannel loggers and portable Narda EMR 20C meter. Overall, during military transmissions, the field strengths were higher in the exposed villages than in the control area (average readings 0.5-0.6 V/m versus <0.01 V/m), though the contribution of the frequencies used by the military antennae (17.6 MHz) was only 10-20% (the dominant sources of RF were cell phone and national broadcast systems). The frequency of reported migraine, headache and dizziness was significantly higher in the exposed villages than in the control village (ORs 2.7, 3.7 and 2.7 respectively ï p<0.001 for each), and higher in Akrotiri than in Asomatos, where, despite similar levels of exposure, the antennae visibility and the aircraft noise are less important. No significant difference was seen in relation to pregnancy, child birth, diabetes, asthma, respiratory problems and most infections. The residents of the exposed village generally had a poorer view of their health status than those of the control village; they also had a higher level of perceived risk, particularly in Akrotiri, from noise and electromagnetic ñpollutionò. These differences could account for the higher reported frequency of migraine, headache and dizziness.

## *Cordless telephones*

Cordless phones have been used extensively in homes since the 1980´s, relying on an analogue system emitting in the 800-900 MHz range, since the late 1990´s however, DECT (Digital Enhanced Cordless Technology) phones, relying on a digital system emitting in the 1900 Mhz range have rapidly taken over the market.

The possible association between the use of cordless telephones and brain tumours has been assessed in studies in Sweden and in Germany

Associations between the use of cordless phones (type unspecified) have been reported in the Swedish studies (Hardell et al. 2006b;Hardell et al. 2006a;Hardell et al. 2005c) for malignant brain tumours, acoustic neurinomas and T-cell lymphomas. Risk appeared to increase with latency and amount of use. The German study did not, however, report an association between the risk of glioma or meningioma and the use of DECT telephones (at home or at work) or with location of the DECT base station close to the bed (Schuz et al. 2006a;Schuz et al. 2006b).

# Studies of health effects from occupational sources of RF

The relation between cancer risk and occupation involving RF or microwave (MW) radiation exposure as been studied both in cohort and case-control studies. They are summarised in the sections below. Results of the most informative studies are given in Table 1: the studies in which no effort was made to separate RF from lower frequency radiation are not reported here.

## *All cancers*

The most widely publicised study of the potential effects of microwave radiation was the study of 1827 embassy employees (and their dependants) who lived and worked in the United States Embassy in Moscow between 1953 and 1976 (Lilienfeld et al. 1978). Workplace measurements between 1963 and 1975 detected microwave radiation of maximum 0.05 $W/m^2$ lasting 9 hours per day at frequencies between 0.5 and 10 Ghz. Cancer mortality was compared to that of 2561 employees from other US embassies in East European countries as well as to that of the US population. Results showed no differences in health status between those who worked or lived in the Moscow embassy and the comparison groups (see Table 1 for comparison with US population). The small number of cancer deaths (17 in total, including two leukaemia), however, makes the study non-informative.

A cohort study of over 40,000 US enlisted naval personnel and aviation workers exposed to microwave radiation during the Korean War (1950-1954) was carried out by (Robinette et al. 1980). Approximately half were chosen among personnel with ñlow exposureò (radiomen, radarmen and aviation electricianôs mates) and half with ñhigh exposureò (electronics technicians, fire-control technicians and aviation electronics technicians). Potential exposure to microwave radiation was assessed in terms of environmental measurements, occupational duties, length of time in occupation and power of equipment at the time of exposure for all deaths from disease, homicide or suicide and for a 5% sample of the cohort. Mortality and morbidity data were obtained from military records. No difference in all cause or cancer mortality or morbidity was seen among the high exposure and low exposure groups or among workers categorised by level of potential exposure after a 20 year follow-up (Robinette et al. 1980) and no difference in mortality rates after 40 years of follow-up (Groves et al. 2002).

A large study of 128,000 Polish military career personnel serving at any time during the period 1971-1985 was followed for cancer morbidity over the same time period using data from military hospital records (Szmigielski 1996). Data on exposure of personnel to RF/MW, obtained from measurements of RF/MW field intensities at and around service posts, served to classify personnel as exposed or non-exposed. A significantly elevated SIR was found for the exposed group compared to non-exposed group for all cancers (Table 1). This result is difficult to interpret, however, as the methods are not clearly described and the authors appear to have invested more effort into finding exposures among the cancer cases than among the personnel that had not been diagnosed with cancer, which could lead to bias.

The bias introduced by this kind of procedure will inevitably lead to findings of increased cancer risks, even if no such associations exist; and no weight can be given these studies in an evaluation of the scientific evidence regarding this question

An investigation of cancer mortality in amateur radio operators in Washington State and California was conducted by linking the US Federal Communications Commission Amateur Radio Station and/or Operator licence file (n=67,829) with the death files in those two states for 1979-1984 (Milham S Jr 1988a). A significantly decreased SMR was found for all cancers, based on a very large number of deaths (2 485) (Table 1). No information about levels of RF exposure was available in this study. When the analyses were carried out by license class (which partly reflect number of years of use), SMRôs were also below 1 (Milham S Jr 1988b).

An investigation of cancer among Norwegian female radio and telegraph operators working at sea was conducted by linking the Norwegian Telecom cohort (2 619) with the Cancer Registry of Norway for 1961-91 (Tynes et al. 1996). No information about individual exposures to RF was provided ï the exposed group was defined as the entire cohort. Workplace RF spot measurements were performed in the radio rooms of the ships; exposure levels varied with location; at the operatorôs desks, however, they were below the detection level. A slight non-significant increase in all cancer incidence was observed compared to the general Norwegian population (Table 1).

A retrospective cohort study of cancer incidence among 22,197 male police officers employed in Ontario (Canada) police departments was conducted by linking the police employee records with the Ontario Cancer Registry for 1964-95 (Finkelstein 1998). No information about individual exposures to radar emissions was provided - the exposed group was defined as the entire cohort. No increased incidence was seen for all cancers compared to the general population of Ontario (Table 1).

The mortality of a cohort of Italian plastic-ware workers exposed to radiofrequency (RF)-electromagnetic fields generated by dielectric heat sealers was investigated over the period 1962-92 (Lagorio et al. 1997). Workers were classified into 3 groups based on their job title and period of assignment: RF-sealer operators (302 women and 4 men), other labourers and white collar workers. Only the first group was considered to be exposed to RF and findings of a survey in the mid 1980´s showed that in that period, before procedures were adopted to limit exposures, recommended IRPA-ICNIRP limits of 10 $W/m^2$ were frequently exceeded. Analyses were restricted to women workers (481 in total) because of the small number of men RF-sealer operators. The SMR for all malignant neoplasms was 2.0 (95% CI 0.7, 4.3, based on 6 deaths). One leukaemia death was observed among RF-sealers, compared to 0.2 expected. The small number of subjects in this study limits the interpretation of these results.

Cancer mortality was studied in the cohort of all US Motorola workers employed between 1976 and 1996 (Morgan et al. 2000). This cohort was of interest because of the relatively high prevalence of RF exposure of the employees who are involved in designing, manufacturing and testing of wireless devices. A job-exposure matrix allowed the categorisation of workers into four groups on the basis of their likely level of RF exposure (background, low, moderate and high, with average score values of 0, 1, 6 and 100 W respectively). The cohort included 195,775 workers who contributed 2.7 million person-years (PYs) of follow-up during the period 1976-1996. For peak exposure, the moderate and high RF exposure categories included 12,911 and 11,710 workers, respectively, and 7.2% and 6.5% of the total PYs of follow-up. (When usual exposure was considered, the numbers were smaller 8,097 and 8,907 workers, respectively, and 4.3 and 4.9% of the total PYs of follow-up).A substantial healthy worker effect was observed in this cohort, though the SMR for all cancer deaths is not given. Numbers of deaths by specific types of cancer were small among the workers classified as moderately or highly exposed based on their peak exposure: 7 CNS deaths, 21 deaths from neoplasm of the lymphatic and haematopoietic system (Table 1).

## Brain cancer

Results of brain cancer analyses in relation to occupations involving RF/MW field exposures were also reported in all the cohort studies described above. The number of brain cancer cases in all but three studies (Milham S Jr 1988a;Finkelstein 1998;Groves et al. 2002) was very small (<=10). These studies do not therefore provide information on the risk of brain cancer from RF exposure. In the Milham study, a small, non-significant increased risk was seen (Table 1). When analyses were carried out by licence class, elevated SMRôs were found among general and advanced class license holders (SMR 1.8, based on 11 cases in each group ï confidence interval not given), two groups thought by the authors to be long term users (Milham S Jr 1988b). In the Finkelstein study, police officers had a slightly reduced brain cancer incidence than the general population, although this was not statistically significant. In the Groves study, subjects in the high-exposure stratum also had a non-significantly reduced risk of brain tumours.

Brain cancer in relation to occupations involving RF/MW field exposures was also studied in two case-control studies (Grayson 1996;Thomas et al. 1987). (Grayson and Lyons 1996) carried out a case-control study nested within a cohort of male air force workers. The study included 230 cases and 920 controls matched on year of birth and race. A complete lifetime occupational history was obtained by questionnaire. A job title-time exposure matrix utilising potential intensity scores was used to estimate potential exposure to RF/MW fields. Results showed a small excess risk of brain tumours for workers ever exposed to RF/MW fields after adjustment for age, race and military rank based on 94 exposed cases (Table 1); no association was seen between level of exposure and brain cancer risk, however.

A case-control study of brain and CNS tumours was carried out in three states in the US (Thomas et al. 1987). The study included 435 cases and 386 controls, matched on age and year of death and area of residence. Lifetime occupational histories were obtained from interviews and occupations were classified with respect to MW/RF radiation by industrial hygienists. The relative risk for all brain tumours, adjusted for education level, was elevated among men ever exposed to MW/RF radiation, based on 69 exposed cases and was significantly elevated among men exposed for 20 or more years. The excess risk for MW/RF radiation-exposed was restricted to workers with electrical or electronic jobs, however, while no excess was seen for other MW/RF exposed workers. It is noted that an excess was also seen for workers who had electrical or electronic jobs not involving MW/RF exposure. It is thus unlikely that the observed increased risk among MW/RF exposed workers is related to the MW/RF exposure.

The effects of occupational exposure to radiofrequency EMF on brain tumours were assessed in the German Interphone study (Berg et al. 2006). Information from the core INTERPHONE questionnaire (which included information on the subjectôs occupational history and history of working with selected sources of exposure to ELF and RF) was used to classify subjectôs degree and likelihood of occupational exposure to RF, based on a review of the literature and on the opinion of industrial hygienists. The study included 381 meningioma and 366 glioma cases with 1494 controls (Berg et al. 2006). No significant association between occupational exposure to RF and risk of brain tumours was found. For glioma, the OR for highly exposed subjects (22 cases and 37 controls) was 1.22 (95% CI 0.69, 2.15), it was 1.39 (95% CI 0.67, 2.88 ï 13 cases and 20 controls) when restricted to high exposure for 10 years or more. For meningioma, the corresponding ORs were 1.34 (95% CI 0.61, 2.96 ï 11 cases and 17 controls ï for high exposure) and 1.55 (0.52, 4.62 ï 6 cases and 8 controls ï for high exposures for 10 years or more). These results are based on small numbers of subjects and need to be verified in further studies with higher sample size.

The possible relation between RF exposure and glioma was evaluated in the framework of a case-control study in Australia (Karipidis et al. 2007). The study included 416 cases of glioma

diagnosed between 1987 and 1991 in Melbourne and 422 controls matched by age, sex and postcode of residence. A detailed occupational history was obtained for each subject. Exposure to RF was assessed using a Finnish job exposure matrix (FINJEM), self-reports and expert hygienist review. 18 cases and 17 controls were classified as having been exposed to RF. No association was found between RF and risk of glioma (ORs respectively: 0.57 95%CI 0.16, 1.96; 1.80 95% CI 0.53, 6.13; and 0.89 95% CI 0.28, 2.81 in the lowest, middle and highest tertiles of exposures). Numbers of exposed subjects were small however in each of these exposure categories, with only 6 cases and 6 controls in the highest tertile of exposure (>52 $W/m^2$ years).

## Lymphatic and haematopoietic cancers

Lymphatic and haematopoietic cancers (including leukaemia) were also analysed in relation to occupations involving RF/MW field exposures was also studied in the cohort studies described above. The number of cases in the Lilienfield and Tynes studies was very small (n=2) ï these studies do not therefore provide information on the risk of these tumours from RF exposure.

In the Milham study, a small, non-significant increased risk for leukaemia and for all lymphatic and haematopoietic cancers was seen (Table 1); the increase was significant for acute myeloid leukaemia (SMR 1.8, 95% CI 1.0-2.9, based on 15 cases); a non-significant increase was also seen for acute unspecified leukaemia. When analyses were carried out by licence class, elevated SMRôs were found among general (SMR 1.2, based on 26 cases ï confidence interval not given), and technician (SMR 1.6, based on 18 cases) class license holders, two groups thought by the authors to be long term users (Milham S Jr 1988a).

In the Szmigielski study, there was a large significant increased incidence of lymphatic and haematopoietic cancers was seen for military workers who worked in areas with high levels of pulse-modulated RF/MW radiation (Table 1). Among these malignancies, the increase was largest for chronic myelocytic leukaemia (SIR=13.9), acute myeloblastic leukaemia (SIR=8.6) and non-Hodgkin lymphomas (SIR=5.8) (Milham S Jr 1988a). As described above for all cancers, these results are difficult to interpret because of the unclear methodology used in this study.

In the second follow-up of Korean War Navy technicians (Groves et al. 2002), significantly elevated RRs were seen for leukaemia as a whole (Table 1) as well as for non-lymphocytic leukaemia (RR 1.82, 95% CI 1.05, 3.14 based on 20 deaths). Non-significantly increased RRs were also seen for ac. The risk was greatest (though not statistically significant) for acute non-lymphocytic leukaemia (RR 1.87, 95% CI 0.98, 3.58) and non significant increases were also seen for acute and chronic myeloid leukaemia (RR respectively 1.81 and 1.55 based on 11 and 5 cases respectively. In the Finkelstein study a non-significant reduction in risk of leukaemia was observed among police officers.

The study of US Motorola workers included 21 deaths from neoplasms of the lymphatic and haematopoietic system in workers classified on the basis of their peak exposure as moderately or highly exposed (10 in the highly exposed), 11 from leukaemia, 6 from NHL and 3 from HD (Morgan et al. 2000). No increased risk of these neoplasms was seen in comparison with workers with no exposure. The small numbers of cases limits, however, the exposure response analyses that can be done and their interpretation.

## Other tumour types

Increases in risk of other specific tumours types (colorectal, breast, testicular, oesophageal/stomach) were also reported, but only in single studies (Table 1). Considering the number of tumour types examined in these studies, some of the significant results observed may have been due to chance.

## *Fertility and adverse pregnancy outcomes*

Two studies of physiotherapists have been carried out to investigate the relationship between use of specialised equipment during pregnancy and the risk of adverse pregnancy outcomes.

In one study, members of the American Physical Therapy Association (n=42,403) were queried by mail as to pregnancy history and the use of microwave or radio frequency diathermy. (Ouellet-Hellstrom and Stewart 1993). A total of 1,753 reported miscarriages were compared to the same number of ñcontrolò pregnancies (any non-ectopic pregnancy, regardless of outcome). Women who reported use of microwave diathermy in the 6 months prior to conception and the first trimester of pregnancy were at increased risk of miscarriage (RR 1.28, 95% CI: 1.0-1.6). The risk increased with numbers of use of the equipment per month. It is noted that the information about miscarriage and exposure was self-reported, which may introduce a bias in the results.

A cohort study of delivery outcomes of 2,043 infants born to 2,018 physiotherapists in Sweden was conducted by linking the Medical Birth Register with the file of registered physiotherapists (Kallen et al. 1982). All 37 cases of major malformations and perinatal deaths were matched to two controls for maternal age, parity and time of delivery (n=74). Information on occupational exposures (including equipment used during pregnancy) was obtained from mothers by mail questionnaire. None of the mothers of cases used microwave equipment during pregnancy.

A cross-sectional study of employees of the Norwegian Navy (civilians and military, on ships and ashore) was conducted in 2002 through the use of a mail questionnaire (Mageroy et al. 2006). The overall response rate ws 58% (2,265 out of 3,878). Service aboard a missile torpedo boat, with HF, VHF and UHF transmitters in radars was associated with an increased prevalence ratio of congenital malformations (PR 4.0, 95% CI 1.9, 8.6) and still born and perinatal deaths (PR 4.1, 95% CI 1.7, 8.9) in offspring. These results are based on very small numbers ï 8 cases of congenital anomalies and 6 of stillbirths and deaths within 1 week of birth among the offspring of persons who had served on this boat. Further analyses restricted to military men who had completed their compulsory military service showed an increased risk of infertility among telecommunication (OR 1.72, 95% CI 1.04, 4.09) and radar/sonar (OR 1.18, 95%CI 1.27, 4.09) workers(Møllerløkken and Moen 2008).

A record linkage study was conducted in Norway to assess potential associations between paternal occupational exposure to RF and adverse pregnancy outcomes including birth defects (Mjøen et al. 2006). Information on occupation was obtained from census and an expert panel constructed an exposure classification (possible and probable exposure) based on job title. Data on reproductive outcomes was derived from the Medical Birth Registry of Norway. Among the 1.1 million births recorded in the period 1976-1995, information on paternal identity and occupation was available only for about 49%. No increased risks of congenital malformations as a group were observed. In the offspring of fathers most likely to have been exposed, an increased risk was observed for preterm birth (OR 1.08 95% CI 1.03, 1.15) and a decreased risk for cleft lip (OR 0.63 95% CI 0.41, 0.97). In the medium exposed group, an increased risk was observed for a category of ñother defectsò (OR 2.40 95% CI 1.22, 4.70), and a decreased risk for a category of ñother syndromesò (OR 0.75, 95% CI 0.56, 0.99) and upper gastrointestinal defects (OR 0.61, 95% CI 0.40, 0.93).

## *Heart disease*

A cross-sectional survey of 5,187 male physiotherapists was carried out using a mailed questionnaire on personal health history, including use of diathermy (Hamburger et al. 1983). The prevalence of a number of health conditions was compared among groups classified into high and low exposure categories ï based on length of employment and frequency of treatment ï for exposure to various types of diathermy modalities (ultrasound, microwave, short-wave, infrared).

A significant association was seen between heart disease and frequent use of microwave (OR 2.5, 95% CI:1.1-5.8) diathermy. The response rate in the study was low (58%) however and information about health condition and exposure was self-reported, which may introduce a bias in the results.

### *Other*

A questionnaire survey of subjective symptoms and health status was conducted in Sweden among RF plastic sealer operators (Wilen et al. 2004). The study included 35 sealers and 37 controls. A neurophysiological examination and 24 hour ECG were also conducted. Measurements showed that the RF operators were exposed to rather high electric and magnetic fields. RF sealers appeared to have a lower heard rate and more episodes of bradicardia than controls, to have a higher prevalence of fatigue, headaches and warmth sensation in the hands and a slightly disturbed discrimination ability compared to the control group. Numbers of subjects in this study are small and it is not clear from the methods how the controls were chosen and whether they might differ with respect to age, sex or other variables of importance for the endpoints studied.

## Studies of health effects from mobile phones

### *Descriptive epidemiological studies*

A number of descriptive studies have been conducted to assess the potential impact of mobile phone use on the risk of tumours either through analyses of time trends of brain and other types of tumours - see for example (Cook et al. 2003;Lahkola et al. 2007;Lonn et al. 2004b;Klaeboe et al. 2005;Roosli et al. 2007) or through analyses of distribution of laterality of tumours. While these studies did not identify any increases that could be correlated with increases in mobile phone use in these countries, such ecological analyses are limited in their ability to reveal potentially small increases in risk for diseases with a long latency period.

### *Cohort studies*

Up to now, two cohort studies of mobile telephone studies have been conducted, one in the US and one in Denmark.

In the USA a large cohort study of over 250,000 portable and mobile telephone subscribers was undertaken to investigate all cause mortality for users of the two types of phones. After one year of follow-up, in 1994, no difference in overall mortality among these two groups (RR=0.86 90%C.I: 0.5-1.5 for portable vs. mobile phone users) (Rothman et al. 1996). The cohort was extended to include a second mobile phone operator (resulting cohort size 285,561 subjects) and information was obtained ï for non-corporate users ï concerning start of service date, number of minutes billed and numbers of calls made and received during 2 months in 1993. For legal reasons, the follow-up could not be prolonged and the length of follow-up for this cohort study is restricted to one year, yielding 95 deaths from cancer, including 2 from brain tumours and 4 from leukaemia among mobile phone users. This cohort therefore provides no information on risk of cancers related to RF radiation from mobile telephones.(Dreyer et al. 1999).

A similar study was conducted in Denmark, where a nationwide cohort was set-up including 420,095 persons with a first cellular non-corporate telephone subscription between 1982 and 1995 (Johansen et al. 2001). This cohort was followed-up for cancer morbidity through 2002 (Schuz et al. 2006c). Significant deficits were observed in the incidence of cancer in general (SIR = 0.95; 95% CI 0.93, 0.97, based on a total of 14,249 cancers), of smoking related cancers (SIR 0.88, 95% CI 0.86, 0.91 ï 3,758 cases) and of a number of other cancer types in men, compared to the

general population, suggesting that the population of mobile phone subscribers may have a healthier lifestyle than the general population in Denmark, and hence that the SIRs in this study may be underestimated. For brain tumours, an SIR of 0.97 was observed overall, based on 580 cases; when analyses were restricted to subjects who had subscriptions for 10 years or more, the SIR was significantly reduced (OR 0.66, 95% CI 0.44, 0.95), based on only 28 cases. The SIRs for acoustic neuromas (0.73), salivary gland tumours (0.77) and eye tumours (0.96) were not elevated; they are based on small numbers (32, 26 and 44 cases respectively) and no analyses are presented for long-term subscribers. There was also no increased risk of leukaemia (SIR 1.00, based on 341 cases). The use of information on subscriptions obtained from operators rather than from the study subjects, as is the case in most of the case-control studies described below, has the advantage of not being subject to recall bias. It does, however, carry other problems of its own. In particular, it happens fairly frequently that the subscriber is not the primary user of the phone, in particularly in a family. Further, no information is available on the actual amount of use of the phone and the fact of having had a subscription 10 years in the past does not necessarily mean the subject has used the phone for that long. Also, the cohort does not include persons with corporate subscriptions (who may in fact, particularly in early years, have been heavier users than those with personal subscriptions) or subjects who started their first subscription after 1995. As these subjects are included in the general population (i.e. the comparison population), SIRs in this study are likely underestimated. It is therefore difficult to draw conclusions from this study on the possible association between mobile phone use and the risk of cancer.

## *Case-control studies*

The vast majority of studies of cancer risk in relation to the use of mobile telephones used a case-control rather than a cohort study design, focusing generally on tumours that arise in some of the tissues that absorb most of the RF energy during phone conversations, the CNS (glioma, meningioma and acoustic neurinoma) and the parotid gland.

All of the studies published to date, except the earliest studies (Inskip et al. 2001;Muscat et al. 2000;Muscat et al. 2002;Auvinen et al. 2002), have either been conducted either within the framework of the international collaborative INTERPHONE study (Cardis et al. 2007) or by the group of Hardell and collaborators in Sweden (Hardell et al. 2005b;Hardell et al. 2005a). The study designs are therefore summarised briefly here in order to avoid repetition in the individual subsections below.

### Study design

#### Swedish Hardell studies

The studies by Hardell and collaborators included both men and women aged 20-80 at the time of diagnosis and living (unless otherwise specified in the sections below for specific tumour types) in the medical administrative areas of Stockholm, Uppsala/Örebro, Linköping and Gothenburg in Sweden.

Cases were identified from the regional cancer registries and had to have a histopathology record. An additional eligibility criterion compared to most other studies is that the case had to be still alive at the date of start of the study. One control was extracted from the Swedish Population Registry for each case and was matched for sex, age (in 5-year age groups) and geographical area. Information on mobile and cordless telephone use was collected through a mail questionnaire sent to both cases and controls, at least 6 months after the diagnosis for cases.

Questions were included about the type of phone, years of use and brand name, prefix of phone number (to identify analogue and digital phones) and, for each type of phone, mean number and length of daily calls, use of hands-free devices and side of the head on which the phone was generally used. Calculations of mobile phone variables (number of years of use, cumulative hours of use) did not include phone use in the year preceding the diagnosis for cases (and the same year for matched controls).

## INTERPHONE studies

The national INTERPHONE studies were all based on a common core protocol (Cardis et al. 2007). INTERPHONE was set-up as a multinational caseï control study, to investigate whether mobile phone use increases the risk of cancer and, more specifically, whether the RF fields emitted by mobile phones are carcinogenic. The study focused on tumours arising in the tissues most exposed to RF fields from mobile phones: glioma, meningioma, acoustic neurinoma and parotid gland tumours.

Sixteen study centres in thirteen countries (Australia, Canada ï centres: Montreal, Ottawa, Vancouver ï, Denmark, Finland, France, Germany, Israel, Italy, Japan, New Zealand, Norway, Sweden, and the UKï centres: North and South) participated in INTERPHONE.

### *Study population*

In Australia, Canada, France, Germany, Italy, Japan and New Zealand, the source population was restricted to major metropolitan areas where mobile phones were first introduced. Major treatment centres for the diseases of interest are concentrated in these areas and most of the population is unlikely to go out of the region for diagnosis and treatment. In Denmark, Finland, Israel, Norway and Sweden the study was largely nationwide. The UK-South study was restricted to the South East of England, urban and rural, and the UK-North study encompassed both urban areas and sparsely populated rural areas.

All residents in the study regions (men and women), aged 30 to 59 were eligible for the study; additional eligibility criteria, such as citizenship and proficiency in the local language were imposed in some study centres. The choice of age range aimed to maximise the likelihood of exposure. Mobile phone use is a relatively new phenomenon. Until the late 1990ôs, for economic and social reasons, mobile phone use was mainly restricted to people in the age range most likely to use the phones for business purposes (Cardis and Kilkenny 1999). In some instances, however, individual countries chose to widen the age range for the cases.

### *Case definition and ascertainment*

Eligible cases were all residents of the study region diagnosed during the study period with a confirmed first primary glioma, meningioma, or acoustic neurinoma. Eight centres (Australia; Canada-Montreal, -Ottawa and -Vancouver; Denmark; Israel; Italy; Sweden) also included malignant parotid gland tumours. Because benign parotid gland tumours may be treated in a very large number of institutions, most centres found it logistically difficult to ensure complete ascertainment, and only Canada-Ottawa, Israel and Sweden included them. All diagnoses were either histologically confirmed or based on unequivocal diagnostic imaging.

Each centre established procedures for the rapid ascertainment of cases from participating diagnostic and treatment units, which was particularly important for glioma patients, whose health can deteriorate quickly. Close monitoring of case ascertainment was essential and study centres used secondary sources to improve ascertainment levels. Secondary sources included medical archives, hospital discharge and billing files, and hospital or regional cancer registries. Enrolment

of cases through secondary sources often implied longer delays in case ascertainment and consequently lower participation.

***Control eligibility and selection***

Controls were randomly selected from the source population. The sampling frame depended on the local situation. The study design called for controls to be individual- or frequency-matched to cases, with the number of controls varying according to the tumour type: 1 control per case for brain tumours; 2 for acoustic neurinoma; and 3 for parotid gland tumours. In Germany, two controls were selected for each brain tumour case. In Denmark controls found to have had any previous cancer (excluding non-melanocytic skin cancer) were excluded. Controls were matched at least on year of birth (within 5-year categories), sex and study region. In Israel controls were also matched on country of birth.

Controls were individually matched to cases in seven study centres (Canada-Ottawa, -Vancouver, France, Israel, Japan, New Zealand and UK-North). In the other centres, individual matching was conducted *post hoc*, with cases being assigned one or more controls (depending on the type of tumour), chosen to have been interviewed as close as possible in time to the case, from among those who fit the matching criteria.

***Collection of information on individual study subjects***

Whenever possible, consenting subjects were interviewed face-to-face by trained interviewers using a computer-assisted personal interview (CAPI) questionnaire. Only Finland used a paper version of the questionnaire. In situations where cases were quite ill or confused, a spouse or partner or other family member could assist in the interview. In exceptional cases, telephone interviews were conducted with difficult-to-reach subjects. When the study subject had died or was too ill to participate, a proxy respondent was interviewed where this was possible and permitted by ethics committees.

The study questionnaire covered demographic factors, mobile phone use (detailed below), use of other wireless communication devices including cordless DECT telephones, occupational exposures to EMF and other potential confounders or risk factors for the diseases of interest (including exposure to ionising radiation, smoking and the subjectôs personal and familial medical history). Specific questions on exposure to loud noise and hearing loss were asked of acoustic neurinoma cases and their controls (and of all controls in centres using frequency matching for all tumour types combined).

The questionnaire contained a detailed section on history of mobile phone use. These questions were asked only of regular mobile phone users (defined as those with an average of at least one call per week for a period of 6 months or more). A compendium of show cards of mobile phones, including pictures of hundreds of models, was compiled and updated during the course of the study to assist study subjects in recognising the phones they had used.

For each phone used, detailed questions were asked about the phone model, the operator, the initial pattern of use of the phone (including network operator and average number and duration of calls) and any subsequent changes in use. Questions were also asked about the proportion of time in which the phones were used in urban, suburban or rural settings, while stationary or moving in a vehicle, how often the antenna was extended, and whether headsets or hands-free kits were used. The side of the head on which the phone was usually held (i.e. the laterality of phone use) and the handedness (left or right-handed) of the subject were recorded.

Attained level of education was used as a proxy for SES. As education systems and attained levels do not have a direct correspondence from one country to another, country-specific options for

responses were used. Marital status and, where appropriate, education level of the spouse were also recorded.

Detailed diagnostic information was obtained from medical records for all cases interviewed and for non-interviewed cases in most study centres. This information included anatomical location and side of the tumour, its histopathology, including whether benign, malignant or of uncertain behaviour.

Since intracranial RF-energy deposition from mobile phones is non-uniform, with most of the energy absorbed in the vicinity of the phone, the probable location of the origin of the brain tumours was identified as precisely as possible so that the RF ñexposureò at that location could be evaluated. Neuro-radiologists in each centre reviewed the radiological images (MRI and CT scans) or records and recorded tumour location on a generic 3-dimensional grid map of the human head, made up of cubes 1 $cm^3$ in size, which was developed for the purpose. The cuts used in the grid correspond to the most commonly used acquisition planes in MRI and CT scans (sagittal, coronal and axial). The details of this methodology will be published separately.

***Methodological studies***

A number of methodological papers have been published or are in preparation (Vrijheid, Deltour et al, 2006; Vrijheid, Cardis et al, 2006; Cardis, Richardson et al, 2007; Berg et al, 2005; Hepworth et al, 2006; Parslow et al, 2003; Samkange-Zeeb et al, 2004; Lakhola et al, 2005; Cardis et al, 2008; Vrijheid et al 2008; Tokola et al, 2008; Vrijheid et al, accepted), addressing issues of study design, participation bias, recall error and exposure assessment that are essential in the interpretation of results from the study:

Validation studies were conducted to evaluate potential error in the recall of phone, indicating that of phone use was subject to moderate systematic and substantial random error (Vrijheid et al. 2007;Vrijheid et al. 2008a). Errors appeared to be larger for duration of calls than for number of calls, and phone use was under-estimated by light users and over-estimated by heavy users. Comparison of a sample of cases and controls in three countries showed little evidence for differential recall errors overall or in recent time periods, but apparent overestimation by cases in more distant time (Vrijheid et al. 2008a).

The possible effects of recall errors were evaluated using Monteï Carlo computer simulations. Results suggest that random recall errors can lead to a large underestimation in the risk of brain cancer associated with mobile phone use. The large random errors seen in the validation study were found to have larger impact than plausible systematic errors. Differential errors in recall had very little additional impact in the presence of large random errors (Vrijheid et al, 2006). However, the apparent overestimation by cases in more distant time periods could cause positive bias in estimates of disease risk associated with mobile phone use (Vrijheid et al, 2008).

Participation rates varied by tumour type and between cases and controls (Table 2). The overall participation was 65% for glioma cases, 78% for meningioma, 82% for acoustic neurinoma and 54% among controls and showed large variation across centres,. Among glioma cases, the major reason for non-participation was death or ill health; in controls it was refusal (65% of non-participants) and inability to contact (27%). The potential for selection bias was therefore evaluated, using information from non-response questionnaires completed by a sub-set of non-participants. This study suggests that refusal to participate is related to less prevalent use of mobile phones. This could result in a downward bias of 10 to 20%, depending on the scenario used, in odds ratios for regular mobile phone use (Vrijheid et al. 2008b).

Because exposure to RF from phones is localized, if a risk exists it is likely to be greatest for tumours in regions with greatest energy absorption. The spatial distribution of RF energy in the

brain was characterised, using results of measurements made on over 100 phones used in different countries. Most (97ï 99% depending on frequency) appears to be absorbed in the brain hemisphere on the side where the phone is used, mainly in the temporal lobe. The average relative SAR is highest in the temporal lobe and the cerebellum and decreases very rapidly with increasing depth, particularly at higher frequencies. Analyses of risk by location of tumour are therefore essential for the interpretation of results studies of brain tumours in relation to mobile phone use (Cardis et al. 2008;Varsier et al. 2008)

***Assessment of exposure from mobile phones***

The study used two main approaches to characterising exposure from use of mobile phones. The first depended only on the mobile phone use history derived from questionnaire responses and the second attempted to evaluate the amount of RF energy absorbed in different areas of the brain.

In both approaches, exposure was calculated up to a given reference date, which was set to one year before the date of the diagnosis of the case in each matched set. Evaluation of RF energy absorption required the localisation of the tumour, which was defined crudely in terms of the side of the head, or lobe of the brain, or more precisely, from the exact location of the tumour ascertained and recorded as described above. Exposure for controls was estimated at the location of the tumour of their matched case.

As described above, the responses to the CAPI questionnaire provided detailed information on historical patterns of mobile phone use for regular users. This information allowed the computation of relevant indices of exposure such as cumulative call time, average call duration and cumulative number of calls, overall and within specific time-windows, with and without use of hands free devices.

The distribution of RF energy absorption in the head varies according to a number of factors, including the type of telephone and network (frequency and type of transmission: digital or analogue, continuous or discontinuous, use of power control), as well as the actual patterns of use of the phone described above. There was no existing algorithm or set of coefficients that could be used to estimate exposure given a specific pattern of mobile phone use. A model was therefore developed and validated for such an algorithm, assessing the relative importance of the different factors and testing the adequacy of the proposed approach. The algorithm combines questionnaire responses with information on tumour location, the distribution of the specific absorption rate (SAR) of RF in the head (Cardis et al. 2008) and factors that modify the amount of RF energy emitted by the phone (Vrijheid et al, submitted).

## *Tumour risk*

### Brain and CNS tumours

#### All brain tumours

Auvinen and collaborators conducted a registry based case-control study of brain tumours and salivary gland cancers among cellular phone users in Finland (Auvinen et al. 2002). The study included all 398 brain tumour cases and 34 salivary gland cancers diagnosed in patients aged 20 to 69 years in Finland in 1996 and registered in the Finnish Cancer Registry. For each case, five age and sex matched controls were selected from the Population Registry. Record linkage allowed the collection of information (type of subscription ï analogue vs. digital ï and start and end date of subscription) from the two network operators that were operating in 1996 for cases and controls who had private mobile phone subscriptions. Use of 450 MHz analogue phones was excluded. The

proportion of mobile phone subscribers was low: 40 (10%) of the 398 brain tumour cases had had an analogue subscription (only 17 for more than 2 years) and 16 (3%) a digital subscription (1 for more than 2 years). The corresponding figures among controls were 134 (7%) and 89 (4%) respectively for analogue and digital subscriptions. The OR for ever having had a mobile phone subscription was 1.3 (95% CI 0.9, 1.8) overall ï 1.6 (95% CI 1.1, 2.3) for analogue only.

A case-control study of brain cancer was conducted in 5 US academic medical centres, in New York, Providence Rhode-Island and Boston, between 1994 and 1998 (Muscat et al. 2000). The study included 469 cases aged 18 to 80 years and 422 matched hospital controls (chosen among inpatients of the same hospital admitted for benign conditions or for cancers excluding leukaemia and lymphoma). An active mechanism was set-up to identify cases rapidly and interview them as soon as possible after their diagnosis. Information was collected using a structure questionnaire that included questions, for each type of mobile phone used (handled, bag, car), about subscriptions, number of years of use, minutes/hours of use per month, year of first use, manufacturer and average monthly bill. Information was also collected about the hand used to hold the telephone. Of 571 eligible cases approached, 469 (82%) were successfully interviewed. Among controls, the response rate was 90%. Use of mobile phones among the study subjects was still at the time of the study a rare phenomenon: 66 cases (14%) and 76 controls (18%) reported using them (OR 0.85, 95% CI 0.6, 1.2). The OR was below one for all histological categories or brain cancer except for neuroepitheliomatous cancers (OR 2.1, 95% CI 0.9, 4.7, based on 35 cases and 14 controls). The mean duration of use was less than 3 years in both cases and controls, and only 17 cases and 22 controls had used phones for 4 years or more.

A case-control study was also conducted in hospitals in Boston, Phoenix (Arizona) and Pittsburgh in the US (Inskip et al. 2001). The study included 782 cases (489 glioma, 197 meningioma and 96 acoustic neurinoma) diagnosed between 1994 and 1998 and 799 matched hospital controls with non-malignant conditions. Participation rate was 92% among cases and 86% among controls. A rapid ascertainment mechanism was set-up to identify the cases rapidly after their diagnosis and most (80%) were enrolled and interviewed within 3 weeks after their diagnosis. Again, in this study, use of mobile phones was a relatively recent phenomenon: 232 cases (29%) reported having used a mobile phone at least 5 times, 139 reported regular use and 22 had used one for 5 years or more. The OR for regular use was 0.8 (95% CI 0.6, 1.1).

## Glioma

Within the above mentioned registry based case-control study in Finland (Auvinen et al. 2002), analyses were also conducted for glioma specifically, based on 198 cases and their matched controls. Again, the proportion of subscribers was small: 26 out of 198 among the cases had analogue subscriptions, only 11 for more than 2 years and only 10 had digital subscriptions, none for more than 2 years. The OR for every having had a mobile phone subscription was 1.5 (95% CI 1.0, 2.4) overall; it was 2.1 (95% CI 1.4, 3.4) for analogue only and 1.0 (95% CI 0.5, 2.0) for digital only. A slight increasing trend was seen with increasing duration of analogue subscription in continuous analyses (OR 1.2 per year ï 95% CI 1.1, 1.5).

Within their case-control study described above, Inskip and collaborators considered specifically the risk of glioma (Table 3) (Inskip et al. 2001). The study included 489 cases of glioma, 85 of which reported regular use of mobile phones (OR 0.8, 95% CI 0.6, 1.2). Only 11 cases had used phones for 5 years or more.

Hardell and collaborators have conducted three case-control studies of malignant brain tumours, mainly glioma, in Sweden (Hardell et al. 1999;Hardell et al. 2002;Hardell et al. 2005b). They have conducted pooled analyses of the results from the later two studies (Hardell et al. 2006a), and only these are shown here as they are the most comprehensive. The combined analyses included

malignant tumours diagnosed between 1997 and 2003 in the regions of Sweden mentioned above (see section on study design above).The analyses included 905 cases and 2,162 controls, respectively 90% and 89% of the cases and controls who were considered eligible for the study. As noted above, unlike most other studies, cases who had died were not considered to be eligible in this study. Results are presented separately for analogue and digital phones and for all malignant tumours, high-grade astrocytoma and low-grade astrocytoma (Table 3). Overall, 178 cases were classified as having used analogue phones and 402 digital phones. The respective ORs were 1.5 (95% CI 1.1, 1.9) and 1.3 (1.1, 1.6) for analogue and digital phones respectively. The ORs appeared to increase with increasing latency ï OR 2.4 (95% CI 1.6, 3.4) and 2.8 (95% CI 1.4, 5.7) for use 10 years or more in the past for analogue and digital phones respectively. The ORs appeared to be higher for high-grade than for low-grade astrocytoma (Table 3). The ORs were also higher for ipsilateral than for contralateral phone use, although an elevated OR was also seen for contralateral use for analogue phones in high-grade astrocytoma patients. For digital phones, the OR for regular use related to having started using mobile phones before the age of 20 appeared to be higher (3.7, 95% CI 1.5, 9.1, based on 16 cases) than for start at later ages. It should be noted that comparisons of results across the three studies show a trend of increasing ORs with time, with statistically significant heterogeneity between studies (Feychting, personal communication 2008). This may in part be related to the fact that the most recent study includes a higher proportion of long term and heavy users than the earlier studies; other methodological differences in the conduct or analysis of the studies may also contribute to this and hence results should be interpreted with caution.

Within INTERPHONE; results have been published of national analyses in Denmark, France, Germany, Japan, Norway, Sweden and the UK, as well as joint analyses of data from Nordic countries and UK-South ((Christensen et al. 2005;Hepworth et al. 2006;Hours et al. 2007a;Klaeboe et al. 2007;Lahkola et al. 2007;Lonn et al. 2005;Schuz et al. 2006a;Takebayashi et al. 2008). Study characteristics and results are summarised in Table 3.

In most studies, the OR related to ever having been a regular mobile phone user was below 1 (Table 3), in some instances statistically significantly so, possibly reflecting participation bias or other methodological limitations.

In analyses by level of use, results by duration of use and time since start of use vary across studies (Table 3). Confidence intervals are wide however, due to the small number of long-term users in individual studies and results are therefore compatible. Pooling of data from Nordic countries and part of the UK yielded the largest number of long term users (143) (Lahkola et al. 2007). Among these, based on 77 cases, a significantly increased risk of glioma was found for reported use of mobile phones for 10 years or more on the side of the head where the tumour developed (OR 1.39, 95% CI 1.01, 1.92). This finding could reflect either a causal association (as the vast majority of the RF energy is absorbed on the side of the head where the phone is held ï see Methodological Issues section above) or an artefact, related to differential recall between cases and controls.

Results of analyses by level of use (total number of calls, total duration of calls) are difficult to compare and to summarise in a tabular form, as most studies have used different cut points. The most comprehensive information comes from the pooling of data from the Nordic and South-UK INTERPHONE studies (Lahkola et al. 2007). Although all of the ORs by level of use, by number of calls and duration of calls are below 1 (Table 4), it is of interest that the magnitude of the ORs appears to increase with increasing amount of use. This increase is in fact statistically significant for number of calls in analyses in which light users are used as the reference group instead of non-users (this type of analysis is conducted to evaluate the possible impact of a selection bias that could be related to use of mobile phones in the study).

In the Japanese INTERPHONE study (Takebayashi et al. 2008), efforts were made to evaluate the maximum amount of RF energy absorbed at the location of the tumour; such analyses, gave an OR of 1.55 (95% CI 0.57, 4.19) related to the highest quartile of cumulative phone time weighted by maxSAR, based on 15 exposed cases; the OR was 5.84 (95% CI 0.96, 35.60) for subjects with cumulative maxSAR-hours of 10 or more W $kg^{-1}$ ï hour; this result, based on few subjects (7 cases and 4 controls) needs to be investigated further.

## Meningioma

Within the above mentioned registry based case-control study in Finland (Auvinen et al. 2002), analyses were also conducted for meningioma specifically, based on 129 cases and their matched controls. The number of subscribers was very small: 8 out of 129 among the cases had analogue subscriptions, only 2 for more than 2 years and only 3 had digital subscriptions, none for more than 2 years. The OR for every having had a mobile phone subscription was 1.1 (95% CI 0.5, 2.4) overall; it was 1.5 (95% CI 0.6, 3.5) for analogue only and 0.7 (95% CI 0.2, 2.6) for digital only (Table 5).

Within their case-control study described above, Inskip and collaborators considered specifically the risk of meningioma (Table 4) (Inskip et al. 2001). The study included 197 cases of glioma, 32 of which reported regular use of mobile phones (OR 0.8, 95% CI 0.4, 1.3). Only 6 cases had used phones for 5 years or more (Table 5).

As indicated above, Hardell and collaborators have conducted three case-control studies of benign brain tumours in Sweden (Hardell et al. 1999;Hardell et al. 2002;Hardell et al. 2005a). They have conducted pooled analyses of the results from the later two studies (Hardell et al. 2006b), and only these are shown here as they are the most comprehensive. The combined analyses included 916 meningioma diagnosed between 1997 and 2003 in the regions of Sweden mentioned above (see section on study design above) and 2,162 controls. Results are presented separately for analogue and digital phones (Table 5). Overall, 113 cases were classified as having used analogue phones and 295 digital phones. The respective ORs were 1.3 (95% CI 0.99, 1.7) and 1.1 (0.9, 1.3) for analogue and digital phones respectively. The ORs were slightly higher when use 10 years or more in the past was considered ï OR 1.6 (95% CI 1.02, 2.5) and 1.3 (95% CI 0.5, 3.2) respectively for analogue and digital phones. The ORs were also slightly higher for ipsilateral than for contralateral phone use, although an elevated OR was also seen for contralateral use for analogue phones. .

Within INTERPHONE; results have been published of national analyses in Denmark, France, Germany, Japan, Norway and Sweden, as well as joint analyses of data from Nordic countries and UK-South (Christensen et al. 2005;Hours et al. 2007a;Klaeboe et al. 2007;Lonn et al. 2005;Schuz et al. 2006a;Takebayashi et al. 2008;Lahkola et al. 2008). Study characteristics and results are summarised in Table 5.

The OR related to ever having been a regular mobile phone user was below 1 (Table 5), in all studies, in some instances statistically significantly so, possibly reflecting participation bias or other methodological limitations.

In analyses by level of use, results by time since start of use vary across studies but are generally close to 1 (Table 5). Confidence intervals are wide however, and these results are based on very small numbers of long-term users in individual studies, reflecting the fact that meningioma is more prevalent in women than men and that, in the early years of mobile telephony, most users were ñbusinessmenò. Pooling of data from Nordic countries and part of the UK yielded the largest number of long term users (73) (Lahkola et al. 2008) and an OR of 0.91 (95% CI 0.57, 1.26) related to start of use 10 years or more in the past. As for the glioma results, all of the ORs by number of calls and duration of calls are below 1.

## Acoustic neurinoma

As part of the large case-control study in New York, Providence Rhode-Island and Boston mentioned above, Muscat and collaborators also studied the risk of acoustic neurinoma (Muscat et al. 2002). The study included 90 cases (18 years or older and diagnosed between 1997 and 1999) and 86 hospital controls (chosen among inpatients of the same hospital admitted for benign conditions or for cancers excluding leukaemia and lymphoma). Again, use of mobile phones among the study subjects was infrequent 18 cases and 23 controls reported using them (OR 0.9, CI not given) (Table 6). A non-significant increase was seen in subjects who reported using the phone for 3 years or more (OR 1.7, 95% CI 0.5, 5.1), based on 11 cases.

Within their case-control study described above, Inskip and collaborators considered specifically the risk of glioma (Table 6) (Inskip et al. 2001). The study included 96 cases of glioma, 22 of which reported regular use of mobile phones (OR 1.0, 95% CI 0.5, 1.9). Only 5 cases had used phones for 5 years or more and a non-significantly increased risk was seen among them (OR 1.9, 95% CU 0.6, 5.9),

The combined analyses of the two case-control studies of brain tumours conducted by Hardell and collaborators included 243 acoustic neurinoma diagnosed between 1997 and 2003 in the regions of Sweden mentioned above (see section on study design above) and 2,162 controls (Hardell et al. 2006b). Results are presented separately for analogue and digital phones (Table 6). Overall, 68 cases were classified as having used analogue phones and 105 digital phones. The respective ORs were 2.9 (95% CI 2.0, 4.3) and 1.5 (1.1, 2.1) for analogue and digital phones respectively. The ORs was similar higher for analogue phones when use 10 years or more in the past was considered ï OR 3.1 (95% CI 1.02, 2.5), based on 19 cases ï but lower for digital phones 0.6 (95% CI 0.1, 5.0) based on 1 case only. The ORs were also slightly higher for ipsilateral than for contralateral phone use, although elevated ORs was also seen for contralateral use. .

Within INTERPHONE; results have been published of national analyses in Denmark, France, Germany, Japan, Norway and Sweden, as well as joint analyses of data from Nordic countries and UK-South (Christensen et al. 2004;Lonn et al. 2004a;Takebayashi et al. 2006;Klaeboe et al. 2007;Schlehofer et al. 2007;Hours et al. 2007a;Schoemaker et al. 2005). Study characteristics and results are summarised in Table 3.

Again, in most studies, the OR related to ever having been a regular mobile phone user was below 1 (Table 6), possibly reflecting participation bias or other methodological limitations.

In analyses by level of use, results by time since start of use vary across studies (Table 6). Confidence intervals are wide however, due to the very small number of long-term users in individual studies and results are therefore compatible. Pooling of data from Nordic countries and part of the UK yielded the largest number of long term users (47) (Schoemaker et al. 2005). Among these, based on 31 cases, an increased risk of neurinoma was found for reported use of mobile phones for 10 years or more on the side of the head where the tumour developed (OR 1.30, 95% CI 0.8, 2.0) and a significantly increased risk in relation to duration of use of 10 years or more (OR 1.8, 95% CI 1.1, 3.1, based on 23 cases). As for glioma, this finding could reflect either a causal association (as the vast majority of the RF energy is absorbed on the side of the head where the phone is held ï see Methodological Issues section above) or an artefact, related to differential recall between cases and controls.

## Other adult tumours

### Salivary gland tumours

Within the above mentioned registry based case-control study in Finland (Auvinen et al. 2002), analyses were also conducted for salivary gland tumours specifically, based on 34 cases and their matched controls. The number of subscribers was very small: only 3 cases had analogue subscriptions (1 for more than 2 years) and only 1 had a digital subscription (Table 7)

A case-control study of salivary gland tumours was conducted in Sweden by the group of Hardell and collaborators (Hardell et al. 2004). The study included all cases diagnosed in the whole of Sweden between 1994 and 1999 or 2000, depending on the region. A total of 267 (out of 415 identified) cases and 1,053 (out of 1,152) controls participated in the study. Information about mobile phone use was collected through the same mail questionnaire as used by this group in their brain tumour study described above. The ORs were 0.92 (95% 0.58, 1.44) for use of analogue phones and 1.01 (95% CI 0.68, 1.50) for digital phones, based on 31 and 45 exposed cases respectively. The study included few long term users; only 6 cases had used analogue phones 10 years or more in the past and none had used digital phones for that long. Results for parotid gland tumours specifically were similar (OR for analogue phones 0.73, 95% CI 0.41, 1.29 and for digital phones 0.98, 95% CI 0.62, 1.55, based on 18 and 33 cases respectively) (Table 7).

Within INTERPHONE, results were published of analyses of the parotid gland case-control study in Sweden and Denmark (Lonn et al. 2006) and in Israel (Sadetzki et al. 2007) (Table 7). The analysis of data from Sweden and Denmark (Lonn et al. 2006), included 60 cases of malignant parotid gland tumours, 112 benign (pleomorphic adenoma) and 681 controls. 25 of the malignant cases and 77 of the benign were classified as regular users (ORs 0.7, 95% CI 0.4, 1.3 and 0.9, 95% CI 0.5, 1.5 respectively for malignant and benign tumours). The numbers of long term (2 and 7 respectively among malignant and benign tumour cases) and heavy users was small in this study. For benign tumours, a non-significantly increased OR was observed for reported use of 10 years or more on the side of the head where the phone was held (2.6, 95% CI 0.9, 7.9, based on 6 cases) although a decreased risk was observed when the phone was reported to be held on the other side of the head (OR 0.3, 95% 0, 2.3, based on 1 case). These results are difficult to interpret however as contralateral use is included in the reference group for the ipsilateral analyses and ipsilateral use in the reference group for contralateral analyses, thereby exaggerating any difference between the results of the two analyses.

The Israeli INTERPHONE study (Sadetzki et al. 2007) included 402 benign and 58 malignant cases and 1,266 individually matched controls. For the entire group, the OR related to regular mobile phone use was OR 0.87 (95% CI 0.68, 1.13) (Table 7); this OR, and all of the ORs in relation to level and duration of use were below 1, possibly reflecting selection bias or other methodological limitations. For ipsilateral use, the odds ratios in the highest category of cumulative number of calls and cumulative call time were 1.58 (95% CI 1.11, 2.24) and 1.49 (95% CI 1.05, 2.13), respectively. The risk for contralateral use was reduced, but not significantly so for either of these variables. Analyses restricted to regular users (in which light or recent users were used as the referent category instead of non-users in order to compensate for a possible selection bias related to mobile phone use) and to conditions that may yield higher levels of exposure (e.g., heavy use in rural areas) showed consistently elevated risks, suggesting a possible relation between heavy mobile phone use and risk of parotid gland tumours. Although this study included few long term users (13 cases had used mobile phones for 10 years or more), the Israeli mobile phone users are exceptionally heavy users compared to users in the other INTERPHONE countries. Additional investigations of this association, with longer latency periods and large numbers of heavy users, are needed to confirm these findings.

## Intratemporal facial nerve tumours

A case-control study of tumours of the intratemporal facial nerve (IFN) was conducted in the US (Warren et al. 2003) at an academic, tertiary-care referral centre, using a structured telephone survey. METHODS: Patients with IFN tumours (n = 18) were case-matched with patients treated for acoustic neurinoma (n = 51), rhinosinusitis (n = 72), and dysphonia or gastroesophageal reflux disease (n = 69). The OR for IFN tumour was 0.4 (95% CI, 0.1-2.1) with regular cellular telephone use. Results from this study are difficult to interpret given the small number of cases, the inclusion in the control group of acoustic neurinoma (a tumour possibly related to mobile phone use) and the absence of long term heavy users in the study.

## Uveal melanoma

Two case-control studies of uveal melanoma were conducted in Germany in the mid to late 1990s to assess the effects of occupational exposures on this type of tumour (Stang et al. 2001). Questions were asked about occupational use mobile phones and of radio sets. Together, the studies included 118 cases and 475 controls; 9 cases and 21 controls reported having used radiosets and 6 cases and 15 controls mobile phones at work. Increased ORs were found both for radioset exposures (OR 3. 95% CI 1.4, 6.3) and for probable and certain exposure to mobile phones (OR 4.2, 95% CI 1.2, 14.5). Information about mobile phone use in this study is very limited, and subjectôs answers were uncertain (with some reporting ñpossibleò exposure to mobile phones at work).

A descriptive epidemiological study in Denmark compared trends in the incidence of ocular malignant melanoma and in mobile phone subscriptions (Johansen et al. 2002). There was little evidence of an increase in incidence of this tumour in the period 1943 to 1996 or of a relation with trends in phone subscriptions in the latter part of the period (1982-1996). The number of subscriptions was relatively low, however, until 1992, and this study therefore provides little information about risk of this tumour.

## Lymphoma

A case-control study was conducted in 4 areas of Sweden to evaluate the possible association between mobile phones and risk of non-Hodgkin's lymphoma (NHL) (Hardell et al. 2005c). The study included cases aged 18-74 and diagnosed between 1 December 1999 to 30 April 2002. Controls were frequency matched and selected from the national population registry. Information about mobile telephone use was obtained by questionnaire. A total of 910 (out of 1,129 eligible) cases and 1016 (92%) controls accepted to participate in the study. The vast majority of cases (819) were B-cell lymphomas; there were 53 T-cell lymphoma cases. No association was seen between use of mobile telephones (whether analogue or digital, ever or 10 years or more in the past) and the risk of B-cell lymphoma. Regarding T-cell lymphoma, a non-significantly increased risk was seen for ever use of analogue or digital phones (OR 1.56, 95% CI 0.64, 3.81 and 1.41, 95% CI 0.68, 2.92, based on 14 and 31 exposed cases, respectively). There was no apparent trend with time for analogue phones; for digital phones, the risk appeared to increase with increasing latency but this was based on very small numbers of cases.

## Testicular cancer

A case-control study of testicular cancer was also conducted by the same group in Sweden (Hardell et al. 2007). The study included all cases diagnosed in men aged 20-75 in the whole of Sweden between 1993 and 1997. Overall 981 (out of 1,021 eligible) cases participated (542 seminoma and 346 non-seminoma cases) and 870 (89%) controls participated in the study. The

ORs for seminoma were 1.2 (95% 0.9, 1.6) for use of analogue phones and 1.3 (95% CI 0.9, 1.8) for digital phones, based on 125 and 98 exposed cases respectively. The study included few long term users; only 13 cases had used analogue phones 10 years or more in the past (OR 2.1, 95% CI 0.8, 5.1) and none at that time had used digital phones for that long. For non-seminoma, the ORs were 0.7 (95% CI 0.5, 1.1) and 0.9, CI (95% CI 0.6, 1.4), respectively for analogue and digital phones, based on 50 and 66 exposed cases. There was no evidence of an exposure response relationship and no association was found with place where the mobile phone was kept, such as trousers pocket.

### *Reproductive outcomes*

The association between prenatal and postnatal exposure to cell phones and behavioural problems in young children was investigated within the framework of national birth cohort study in Denmark (Divan et al. 2008). Mothers of 13,159 children completed a follow-up questionnaire when their children reached 7 years of age in 2005 and 2006. The questionnaire included questions concerning the current health and behavioural status of their children, as well as past exposure to cell phone use, specifically use of mobile phone during pregnancy (including numbers of times per day and proportion of time the phone was on, use of hands-free equipment and location of the phone when not in use) and for children, current use of cellular and other wireless phones. After adjustment for potential confounders, the odds ratio for a higher overall behavioural problems score was 1.80 (95% CI 1.45, 2.23) in children with both prenatal and postnatal exposure to cell phones. Similar ORs were seen for different types of behavioural problems and ORs tended to be higher for prenatal than for postnatal exposures. Results of this study are difficult to interpret at present. The fact that the questionnaire was administered post-hoc, at age 7, may have led to differential recall bias. Only 65% of eligible mothers returned the questionnaire and this may represent a selected sample of the cohort. Further, confounding by some factors, including behavioural factors that may correlate with maternal phone use, could affect the results. It will be important to examine this association in other similar cohorts and to collect information about mobile phone use in pregnancy rather than at age 7 when the behavioural problems that are being investigated are already manifest.

## Summary and conclusions - status of knowledge today

This report reviews and evaluates published epidemiological studies on RF and health. Included in the assessment are scientific studies that have been published primarily in peer reviewed scientific journals.

As outlined in the previous sections, many of the epidemiological studies reviewed here suffer from inadequate assessment of radio frequency exposure and, in particular in the case-control studies, from possible recall errors and selection bias. In addition, many studies had inadequate sample size, incomplete follow-up of subjects, lack of information on potential confounding variables and, in some cases, inadequate comparison groups and methods of analyses.

On the basis of the epidemiological studies reviewed, because of the inconsistencies of results and the limitations of these studies, it is not possible to evaluate at this time whether there exists a health risk from exposure to RF radiation, particularly at the levels of concern for mobile communication. A number of recent large studies of glioma, acoustic neurinoma and possibly parotid gland tumours appear to suggest a possible increased risk related to long term or heavy use of phones. It is unclear, however, whether the observed associations are real, reflecting a causal association, or artefactual, reflecting differential reporting between cases and controls.

In the short term, more information on a possible carcinogenic risk will be provided by the results of the international INTERPHONE analyses, based on larger numbers of long-term and heavy users than the individual studies, taking into account the results of the various methodological sub-studies and detailed localisation of tumours. The results of more detailed analyses, also underway, focusing on more precise localization of tumours using 3-dimensional radiological images, and on the analysis of the effect of RF exposure at the location of the tumour, using a gradient of RF emitted by mobile phones, will also be of great importance.

## *Research recommendations*

INTERPHONE will mainly provide information on effects of exposure to RF in adulthood and only on the risk of brain and CNS tumours and of tumours of the parotid gland.

Studies of other outcomes and of exposures in childhood and adolescence are therefore sorely needed, as are surveillance studies of cohorts of mobile phone users in order to assess possible effects on a variety of cancer and non-cancer endpoints ï see for example research recommendations by a number of international bodies (WHO 2006;SCENIHR 2007;EMF-Net 2006). A number of studies are underway or starting that will address these issues (COSMOS, CEFALO, Mobi-Kids) in the medium and longer term future.

Further studies of occupationally exposed populations will also be important.

For these studies to be informative, however, it will be essential that the above described limitations are overcome and, in particular, that reliable and accurate individual estimates of RF exposure be available for all study subjects.

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**Table 1: Rate ratio for cancer: results from epidemiological studies of occupational or recreational RF exposure.** ***(Notes: unless otherwise indicated, the reference group is the ñlowò or ñunexposedò group in the study; numbers in italics were calculated from the data presented in the paper) ï adapted from (Kilkenny and Cardis 1999)***

| Authors | Exposed group definition | Cancer type | Cases | Rate ratio | 95% CI |
|---|---|---|---|---|---|
| *Cohort studies* | | | | | |
| (Lilienfeld et al. 1978) | US embassy personnel | All | 17 | 0.89 | 0.5-1.4 |
| | | Brain | 0 | 0.0 | - |
| | | Leukaemia | 2 | 2.50 | not available |
| | | Lung | 5 | 0.86 | 0.3-2.0 |
| | | Digestive | 3 | 0.65 | 0.1-1.9 |
| | | Breast | 2 | 4.00 | 0.5-14.4 |
| (Robinette et al. 1980;Groves et al. 2002) | ñHigh exposure jobsò among Navy technicians | All | 1,180 | 0.80 | 0.74-0.87 |
| | | Brain | 51 | 0.65 | 0.43-1.01 |
| | | All leukaemia | 44 | 1.48 | 1.01,2.17 |
| (Milham S Jr 1988a) | Amateur radio operator licence holders | All | 2485 | 0.71 | 0.6-0.7 |
| | | Brain | 29 | 1.39 | 0.9-2.0 |
| | | Lymphatic and haematopoietic | 89 | 1.23 | 1.0-1.5 |
| | | - leukaemia | 36 | 1.24 | 0.9-1.7 |
| (Szmigielski 1996) | Workers in areas with high MW/RF field intensities | All | *~67*[1] | 2.07 | 1.1-3.6 |
| | | Brain & CNS | *~2-3* | 1.91 | 1.1-3.5 |
| | | Lymphatic and haematopoietic | *~24* | 6.31 | 3.1-14.3 |
| | | Oesophageal/stomach | *~8-9* | 3.24 | 1.9-5.1 |
| | | Colorectal | *~7* | 3.19 | 1.5-6.2 |
| (Finkelstein 1998) | Police Officers | All | 561 | 0.9 | 0.8-1.0 |
| | | Brain | 16 | 0.8 | 0.5-1.4 |
| | | Leukaemia | 12 | 0.6 | 0.3-1.0 |
| | | Testicular | 23 | 1.3 | 0.9-1.8 |
| (Tynes et al. 1996) | Female Radio & Telegraph operators | All | 140 | 1.2 | 1.0-1.4 |
| | | Brain | 5 | 1.0 | 0.3-2.3 |
| | | Leukaemia | 2 | 1.1 | 0.1-4.1 |
| | | Rectum | 6 | 1.8 | 0.7-3.9 |
| | | Breast | 50 | 1.5 | 1.1-2.0 |
| | | Uterus | 12 | 1.9 | 1.0-3.2 |
| | | Kidney | 3 | 1.6 | 0.3-4.8 |
| (Morgan et al. 2000) | Motorola US employees ***ï*** *moderate and high exposure groups combined* | All | na[2] | na | |
| | | Brain and CNS | 7 | 0.86 | 0.38-1.73 |
| | | Lymphatic and haematopoietic | 21 | 0.61 | 0.39-0.93 |
| | | - leukaemia | 11 | 0.74 | 0.36-1.40 |
| | | - non-Hodgkin lymphoma | 6 | 0.41 | 0.20-0.74 |
| | | - Hodgkin´s disease | 3 | 0.87 | 0.23-2.53 |
| *Case-control studies* | | | | | |
| (Grayson 1996) | Ever exposed to RF ï based on job title ï time exposure matrix | Brain | 94 | 1.39 | 1.0-1.9 |

[1] Although numbers of cancers are not provided in the paper, it was possible to estimate them from the rate data presented.

[2] Not available

| Authors | Exposed group definition | Cancer type | Cases | Rate ratio | 95% CI |
|---|---|---|---|---|---|
| (Thomas et al. 1987) | Ever-exposed to RF/MW - based on occupational history | Brain | 69 | 1.6 | 1.0-2.4 |
| (Berg et al. 2006) | Highly exposed subjects ï based on occupational history and hygienists | Glioma | | | |
| | | - overall | 22 | 1.22 | 0.69-2.15 |
| | | - 10 years or more | 13 | 1.39 | 0.67-2.88 |
| | | Meningioma | | | |
| | | - overall | 11 | 1.34 | 0.61-2.96 |
| | | - 10 years or more | 6 | 1.55 | 0.52-4.62 |
| (Karipidis et al. 2007) | Highest exposed subjects ï based on occupational history, JEM and hygienists | Glioma | 6 | 0.89 | 0.28-2.81 |

**Table 2 Distribution of all cases and controls ascertained and proportion interviewed by study centre (reproduced from (Cardis et al. 2007)**

| Study centre | Glioma | | Meningioma | | Acoustic neurinoma | | Malignant parotid gland tumours | | Controls | |
|---|---|---|---|---|---|---|---|---|---|---|
| | No. ascertained | No. (%) Interviewed | No. ascertained | No. (%) Interviewed | No. ascertained | No. (%) Interviewed | No. ascertained | No. (%) Interviewed | No. from sampling frame | No. (%) Interviewed |
| Australia | 536 | 301 (56) | 413 | 255 (62) | 179 | 127 (71) | 21 | 7 (33) | 1,608 | 669 (42) |
| Canada | | | | | | | | | | |
| Montreal | 101 | 65 (64) | 71 | 48 (68) | 41 | 33 (80) | 13 | 9 (69) | 391 | 234 (60) |
| Ottawa | 38 | 25 (66) | 18 | 15 (83) | 21 | 17 (81) | 6 | 6 (100) | 259 | 180 (70) |
| Vancouver | 134 | 80 (61) | 45 | 31 (69) | 41 | 34 (83) | 19 | 13 (68) | 680 | 239 (35) |
| Denmark | 248 | 181 (73) | 155 | 121 (81) | 73 | 71 (97) | 15 | 15 (100) | 1,277 | 662 (52) |
| Finland | 211 | 178 (84) | 252 | 231 (92) | 87 | 76 (87) | -[3] | - | 1,337 | 559 (42) |
| France | 155 | 94 (61) | 190 | 148 (78) | 140 | 111 (79) | - | - | 639 | 472 (74) |
| Germany | 312 | 256 (82) | 275 | 250 (91) | 76 | 67 (88) | - | - | 1,869 | 1190 (64) |
| Israel | 206 | 180 (87) | 390 | 350 (90) | 78 | 72 (92) | 20 | 19 (95) | 911 | 599 (66) |
| Italy | 128 | 118 (92) | 124 | 110 (89) | 30 | 30 (100) | 11 | 11 (100) | 486 | 340 (70) |
| Japan | 90 | 60 (67) | 102 | 82 (80) | 82 | 69 (84) | - | - | 574 | 287 (50) |
| New Zealand | 132 | 84 (69) | 72 | 54 (75) | 21 | 20 (95) | - | - | 350 | 172 (49) |
| Norway | 236 | 180 (76) | 191 | 148 (77) | 51 | 38 (75) | 21 | 11 (52) | 404 | 278 (69) |
| Sweden | 298 | 227 (76) | 205 | 184 (90) | 107 | 102 (95) | 20 | 18 (90) | 617 | 407 (66) |
| UK | | | | | | | | | | |
| North | 628 | 429 (68) | 222 | 180 (81) | 116 | 102 (88) | - | - | 1,747 | 788 (45) |
| South | 848 | 307 (37) | 390 | 221 (57) | 218 | 152 (70) | - | - | 1,211 | 582 (50) |
| Total | 4,301 | 2,765 (65) | 3,115 | 2,425 (78) | 1,361 | 1,121 (82) | 146 | 109 (75) | 14,360 | 7,658 (53) |

[3] Parotid gland tumours were not included in these centres.

1 **Table 3 ï Summary of published results from studies of mobile phone use and risk of glioma**

| Country | Age range | Diagnosis years | Number of cases and controls | OR and 95% CI Ever regular use | OR and 95% CI Start of use 10 years or more in the past | OR and 95% CI Ipsilateral use, start of use 10+ years in past | OR and 95% CI Contralateral use, start of use 10+ years in past |
|---|---|---|---|---|---|---|---|
| ***INTERPHONE studies*** | | | | | | | |
| Denmark (Christensen et al, 2005) | 20-69 | 2000-2002 | Low-grade 81 155<br>High-grade 171 330 | Low-grade 1.08 (0.58, 2.00) 47<br>High-grade 0.58 (0.37, 0.90) 59 | Low-grade 1.64 (0.44, 6.12) 6<br>High-grade 0.48 (0.19, 1.26) 8 | NA | NA |
| France (Hours et al, 2007) | 30-59 | 2001-2003 | 96 96 | 1.15 (0.65, 2.05) 59 | *46 months+ 1.96 (0.74, 5.20) 21* | NA | NA |
| Germany (Schuz et al, 2006) | 30-69 | 2000-2003 | 366 1,494 | 0.98 (0.74, 1.29) 138 | 2.20 (0.94, 5.11) 12 | NA | NA |
| Japan (Takebayashi et al, 2008) | 30-69 | 2000-2004 | 83 163 | 1.22 (0.63, 2.37) 56 | *6.5 years + 0.60 (0.20, 1.78) 7* | NA | NA |
| Norway (Klaeboe et al 2007) | 19-69 | 2001-2002 | 289 358 | 0.6 (0.4, 0.9) 161 | *6+ years 0.8 (0.5, 1.2) 70* | *6+ years 1.3 (0.8, 2.1) 39* | *6+ years 0.8 (0.5, 1.4) 32* |
| Sweden (Lonn et al, 2005) | 20-69 | 2000-2002 | 371 674 | 0.8 (0.6, 1.0) 214 | 0.9 (0.5, 1.5) 25 | 1.6 (0.8, 3.4) 15 | 0.7 (0.3, 1.5) 11 |
| UK (Hepworth et al, 2006) | 18-69 | 2000-2004 | 966 1,716 | 0.94 (0.78,1.13) 508 | 0.90 (0.63,1.28) 66 | NA | NA |
| Nordic combined (Lahkola et al, 2007) | | 2000-2004 | 1,522 3,301 | 0.78 (0.68, 0.91) 867 | 0.95 (0.74, 1.23) 143 | 1.39* (1.01, 1.92) 77 | 0.98 (0.71, 1.37) 67 |
| ***Others*** | | | | | | | |
| Sweden (Hardell et al. 2006a) | 20-80 | 1997-2003 | 905 2,162<br>539<br>124 | All malignant tumours<br>Analogue 1.5 (1.1, 1.9) 178<br>Digital 1.3 (1.1, 1.6) 402<br>High grade astrocytoma<br>Analogue 1.7 (1.3, 2.3) 115<br>Digital 1.5 (1.2, 1.9) 244<br>Low grade astrocytoma<br>Analogue 1.2 (0.6, 2.2) 19<br>Digital 1.4 (0.9, 2.3) 56 | Analogue 2.4 (1.6, 3.4) 82<br>Digital 2.8 (1.4, 5.7) 19<br>Analogue 2.7 (1.8, 4.2) 59<br>Digital 3.8 (1.8, 8.1) 15<br>Analogue 1.6 (0.6, 4.1) 19<br>Digital 1.3 (0.2, 11) 1 | NA | NA |

| Country | Age range | Diagnosis years | Number of cases and controls | OR and 95% CI Ever regular use | OR and 95% CI Start of use 10 years or more in the past | OR and 95% CI Ipsilateral use, start of use 10+ years in past | OR and 95% CI Contralateral use, start of use 10+ years in past |
|---|---|---|---|---|---|---|---|
| Finland (Auvinen et al. 2002) | 20-69 | 1996 | 198 989 | Analogue<br>2.1 (1.3, 3.4) 26<br>Digital<br>1.0 (0.5, 2.0) 10 | NA | NA | NA |
| US (Inskip et al, 2001) | 18+ | 1994-1998 | 489 799 | 0.8 (0.6, 1.2) 85 | *5+ years*<br>*0.6 (0.3,1.4) 11* | NA | NA |
| US (Muscat et al, 2000) | 18-80 | 1994-1998 | 469 422 | *All brain cancers*<br>0.85 (0.6, 1.2) 66 | NA | NA | NA |

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**Table 4 ï Results of analyses by cumulative number of calls and cumulative hours of use ï Pooled analyses of glioma data from Nordic and UK-South Interphone studies. Reproduced from (Lahkola et al. 2007)**

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| | Number of cases | OR | 95 % CI |
|---|---|---|---|
| **Cumulative number of calls** | | | |
| Never/nonregular use | 626 | 1.0 | |
| <2,172 | 352 | 0.73 | (0.62, 0.87) |
| 2,172ï 7,792 | 205 | 0.74 | (0.60, 0.91) |
| >7,792 | 265 | 0.91 | (0.74, 1.12) |
| *P for trend* | | *P=0.93* | |
| *P for trend ï users only** | | *P=0.05* | |
| **Cumulative hours of use** | | | |
| Never/nonregular use | 626 | 1.0 | |
| <125 | 368 | 0.75 | (0.64, 0.89) |
| 125ï 503 | 193 | 0.69 | (0.55, 0.85) |
| >503 | 262 | 0.90 | (0.73, 1.10) |
| *P for trend* | | *P=0.98* | |
| *P for trend ï users only* | | *P=0.09* | |

* Results of analyses in which light users are used as the reference category ï such analyses are useful to evaluate the impact of a potential selection bias in studies such as this where the overall OR for regular users is below 1 where it is possible that the proportion of users and non-users is not representative of the population from which the subjects are sampled.

1 **Table 5 ï Summary of published results from studies of mobile phone use and risk of meningioma**

| Country | Age range | Diagnosis years | Number of cases and controls | | OR and 95% CI Ever regular use | | OR and 95% CI Start of use 10 years or more in the past | | OR and 95% CI Ipsilateral use, start of use 10+ years in past | | OR and 95% CI Contralateral use, start of use 10+ years in past | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ***INTERPHONE studies*** | | | | | | | | | | | | |
| Denmark (Christensen et al, 2005) | 20-69 | 2000-2002 | 175 | 316 | 0.83 (0.54, 1.28) | 67 | 1.02 (0.32, 3.24) | 6 | NA | | NA | |
| France (Hours et al, 2007) | 30-59 | 2001-2003 | 145 | 145 | 0.74 (0.43, 1.28) | 71 | 46 months+ *0.73 (0.28, 1.91)* | *15* | NA | | NA | |
| Germany (Schuz et al, 2006) | 30-69 | 2000-2003 | 381 | 762 | 0.84 (0.62, 1.13) | 104 | 1.09 (0.35, 3.37) | 5 | NA | | NA | |
| Japan (Takebayashi et al, 2008) | 30-69 | 2000-2004 | 128 | 229 | 0.70 (0.42, 1.16) | 55 | *5.2 years +* *1.05 (0.52, 2.11)* | *30* | NA | | NA | |
| Norway (Klaeboe et al 2007) | 19-69 | 2001-2002 | 207 | 358 | 0.8 (0.5, 1.1) | 98 | *6+ years* *1.0 (0.6, 1.8)* | *36* | *6+ years* *1.1 (0.6, 2.3)* | *17* | *6+ years* *1.2 (0.6, 2.3)* | *18* |
| Sweden (Lonn et al, 2005) | 20-69 | 2000-2002 | 273 | 674 | 0.7 (0.5, 0.9) | 118 | 0.9 (0.4, 1.9) | 8 | 1.3 (0.5, 3.9) | 5 | 0.5 (0.1, 1.7) | 3 |
| Nordic combined (Lahkola et al, 2008) | | 2000-2004 | 1,209 | 3,299 | 0.76, (0.65, 0.89) | 573 | 0.91 (0.67, 1.25) | 73 | 1.05 (0.67, 1.65) | 33 | 0.62 (0.38, 1.03) | 24 |
| ***Others*** | | | | | | | | | | | | |
| Sweden (Hardell et al. 2006b) | 20-80 | 1997-2003 | 916 | 2,162 | Analogue<br>1.3 (0.99, 1.7)<br>Digital<br>1.1 (0.9, 1.3) | <br>113<br><br>295 | Analogue<br>1.6 (1.02, 2.5)<br>Digital<br>1.3 (0.5, 3.2) | <br>34<br><br>8 | NA | | NA | |
| Finland (Auvinen et al. 2002) | 20-69 | 1996 | 129 | 643 | Analogue<br>1.5 (0.6, 3.5)<br>Digital<br>0.7 (0.2, 2.6) | <br>8<br><br>3 | NA | | NA | | NA | |
| US (Inskip et al, 2001) | 18+ | 1994-1998 | 197 | 799 | 0.8 (0.4, 1.3) | 32 | *5+ years* *0.9 (0.3, 2.7)* | *6* | NA | | NA | |

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**Table 6 ï Summary of published results from studies of mobile phone use and risk of acoustic neurinoma**

| Country | Age range | Diagnosis years | Number of cases and controls | | OR and 95% CI Ever regular use | | OR and 95% CI Start of use 10 years or more in the past | | OR and 95% CI Ipsilateral use, start of use 10+ years in past | | OR and 95% CI Contralateral use, start of use 10+ years in past | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ***INTERPHONE studies*** | | | | | | | | | | | | |
| Denmark (Christensen et al, 2004) | 20-69 | 2000-2002 | 106 | 212 | 0.90 (0.51, 1.57) | 45 | 0.22 (0.04, 1.11) | 2 | NA | | NA | |
| France (Hours et al, 2007) | 30-59 | 2001-2003 | 109 | 214 | 0.92 (0.53, 1.59) | 58 | *46 months+* *0.66 (0.28, 1.57)* | *14* | NA | | NA | |
| Germany (Schlehofer et al, 2007) | 30-69 | 2000-2003 | 97 | 194 | 0.67 (0.38, 1.19) | 29 | NA | 0 | NA | | NA | |
| Japan (Takebayashi et al, 2006) | 30-69 | 2000-2004 | 101 | 339 | 0.73 (0.43, 1.23) | 51 | *8+ years* *0.79 (0.24, 2.65)* | *4* | NA | | NA | |
| Norway (Klaeboe et al 2007) | 19-69 | 2001-2002 | 45 | 358 | 0.5 (0.2, 1.0) | 22 | *6+ years* *0.5 (0.2, 1.4)* | *8* | *6+ years* *0.9 (0.3, 2.8)* | *5* | *6+ years* *0.8 (0.2, 2.5)* | *4* |
| Sweden (Lonn et al, 2004) | 20-69 | 1999-2002 | 148 | 604 | 1.0 (0.6, 1.5) | 89 | 1.9 (0.9, 4.1) | 14 | 3.9 (1.6, 9.5) | 12 | 0.8 (0.2, 2.9) | 4 |
| Nordic combined (Schoemaker et al, 2005) | | 1999-2004 | 678 | 3,553 | 0.9 (0.7, 1.1) | 360 | 1.0 (0.7, 1.5) | 47 | 1.3 (0.8, 2.0)<br>*1.8 (1.1-3.1)** | 31<br>*23* | 1.0 (0.6, 1.7)<br>*0.9 (0.5, 1.8)** | 20<br>*12* |
| ***Others*** | | | | | | | | | | | | |
| Sweden (Hardell et al. 2006b) | 20-80 | 1997-2003 | 243 | 2,162 | Analogue<br>2.9 (2.0, 4.3)<br>Digital<br>1.5 (1.1, 2.1) | <br>68<br><br>105 | Analogue<br>3.1 (1.7, 5.7)<br>Digital<br>0.6 (0.1, 5.0) | <br>19<br><br>1 | NA | | NA | |
| US (Inskip et al, 2001) | 18+ | 1994-1998 | 96 | 799 | 1.0 (0.5, 1.9) | 22 | *5+ years* *1.9 (0.6, 5.9)* | *5* | *NA* | | *NA* | |
| US (Muscat et al, 2002) | 18-80 | 1997-1999 | 90 | 86 | 0.9 | 18 | *3+ years* *1.7 (0.5, 6.1)* | *11* | *NA* | | *NA* | |

* Analysis by duration of use instead of time since start of use.

1 **Table 7 ï Summary of published results from studies of mobile phone use and risk of parotid gland tumours**

| Country | Age range | Diagnosis years | Number of cases and controls | OR and 95% CI Ever regular use | OR and 95% CI Start of use 10 years or more in the past | OR and 95% CI Ipsilateral use, start of use 10+ years in past | OR and 95% CI Contralateral use, start of use 10+ years in past |
|---|---|---|---|---|---|---|---|
| ***INTERPHONE studies*** | | | | | | | |
| Israel<br>(Sadetzki et al, 2007) | 18+ | 2001-2003 | Total<br>460 1,266<br>Benign<br>402 1,072<br>Malignant<br>58 294 | Total<br>0.87 (0.68, 1.13) 285<br>Benign<br>0.85 (0.64, 1.12) 252<br>Malignant<br>1.06 (0.54, 2.10) 33 | Total<br>0.86 (0.42, 1.77) 13<br><br>*Total ï regular users only*<br>*1.45 (0.82, 2.57) 13* | Total<br>1.60 (0.68, 3.72) 10<br>Benign<br>1.97 (0.81, 4.85) 10 | Total<br>0.58 (0.15, 2.32) 3 |
| Sweden and Denmark<br>(Lonn et al, 2006) | 20-69 | 2000-2002 | Benign<br>112 321<br>Malignant<br>60 681 | Benign<br>0.9 (0.5, 1.5) 77<br>Malignant<br>0.7 (0.4, 1.3) 25 | Benign<br>1.4 (0.5, 3.9) 7<br>Malignant<br>0.4 (0.1, 2.6) 2 | Benign<br>2.6 (0.9, 7.9) 6<br>Malignant<br>0.7 (0.1, 5.7) 1 | Benign<br>0.3 (0.0, 2.3) 1<br>Malignant<br>NA 0 |
| ***Others*** | | | | | | | |
| Sweden (Hardell et al. 2004) | 20-80 | 1994-2000 | 199 1,172 | Analogue<br>0.73 (0.41, 1.29) 18<br>Digital<br>0.98 (0.62, 1.55) 33 | NA | NA | NA |
| Finland (Auvinen et al. 2002) | 20-69 | 1996 | 34 170 | Analogue<br>1.0 (0.3, 4.0) 3<br>Digital<br>1.7 (0.2, 16) 1 | NA | NA | NA |

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